Verfügbarkeit, Preis und Qualität von Arzneimitteln aus Togo, der Demokratischen Republik Kongo und Kamerun

Dissertation

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der Eberhard Karls Universität Tübingen

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Doktors der Naturwissenschaften

(Dr. rer. nat.)

vorgelegt von

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Tübingen 2020

聞くは一時の恥聞かぬは末代の恥

Fragst du, brauchst du dich nur einen Augenblick zu schämen, fragst du nicht, schämst du dich bis an dein Lebensende

Japanisches Sprichwort

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ABKÜRZUNGSVERZEICHNIS

API	Active pharmaceutical ingredient / Wirkstoff
BNE	Bruttonationaleinkommen pro Kopf
CI	Confidence interval / Konfidenzintervall
DC	Dünnschichtchromatographie
DR Kongo	Demokratische Republik Kongo
EML	Essential Medicines List / Liste der unentbehrlichen Arzneimittel
GPHF	Global Pharma Health Fund e.v.
HAI	Health Action International
HPLC	High-performance liquid chromatography / Hochleistungsflüssigchromatographie
HR-MS	Hochauflösende Massenspektrometrie
ICH	The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
INN	International non-proprietary name / Internationaler Freihandelsname
LC	Liquid chromatography Flüssigchromatographie
MPR	Median Price Ratio
MS	Massenspektrometrie
NAFDAC	Nigerian National Agency for Food and Drug Administration and Control
NCD	Non-communicable disease / Nicht übertragbare Krankheit
NMR	Nuclear magnetic resonance spectroscopy/ Kernspinresonanzspektroskopie
UN	United Nations / Vereinte Nationen
USD	US-Dollar
USP	United States Pharmacopeia / Arzneibuch der Vereinigten Staaten
WHO	World Health Organization / Weltgesundheitsorganisation

ZUSAMMENFASSUNG

Der Zugang zu sicheren, wirksamen, qualitativ hochwertigen und erschwinglichen Arzneimitteln und Impfstoffen für alle ist Teil des Ziels Nr.3.8 der Ziele für nachhaltige Entwicklung der Vereinten Nationen aufgenommen. [1] Trotz erheblicher Anstrengungen ist die Verfügbarkeit von Medikamenten in vielen Ländern noch immer schlecht. [2, 3] Des Weiteren sind laut aktuellen Zahlen der Weltgesundheitsorganisation (WHO) bis zu 10.5% der verfügbaren Arzneimittel in Entwicklungsländern minderwertig oder gefälscht.[4] Allerdings basieren diese Aussagen, trotz des immensen Einflusses auf die Gesundheit der betroffenen Menschen, meist auf nur wenigen Studien und für einige Länder oder Regionen gilt die Thematik als faktisch nicht erforscht. [5, 6] Um vergleichbare und belastbare Daten über Preise, Verfügbarkeiten, Erschwinglichkeit und vor allem die Qualität von 13 ausgewählten Arzneimitteln zu liefern, wurde eine Studie in der Republik Togo, sowie eine Studie in der Republik Kamerun und der Demokratischen Republik Kongo durchgeführt. Die 13 untersuchten Medikamente setzten sich dabei aus sieben Antibiotika und sechs Arzneimittel gegen nicht übertragbare Krankheiten zusammen. Im Süden der Republik Togo wurden 94 Arzneimittelproben (Tabletten und Kapseln) bei sechs Apotheken und von sechs informellen Händlern erworben und deren Preise dokumentiert. Anschließend wurden 92 der gesammelten Arzneimittel mittels Methoden aus dem Arzneibuch der Vereinigten Staaten (USP) auf die korrekte Identität des deklarierten Wirkstoffs, den Gehalt und die Wirkstofffreisetzung untersucht. Eine Analyse der Medikamentenpreise zeigte, dass die Arzneimittel in den Apotheken teurer verkauft werden als bei den informellen Händlern. Bei der Untersuchung nach dem USP konnte kein gefälschtes Arzneimittel identifiziert werden. Sieben der untersuchten Proben (8%) zeigten jedoch moderate Abweichungen von den Qualitätsanforderungen des USP, eine Probe sogar erhebliche Abweichungen. Der Anteil minderwertiger Arzneimittel lag mit 13% bei den informellen Händlern höher als bei den Apotheken (5%). Somit sind die Arzneimittel bei informellen Händlern zwar günstiger aber auch von schlechterer Qualität. In der Republik Kamerun und der Demokratischen Republik Kongo wurden insgesamt 506 Arzneimittel von 60 staatlichen Gesundheitseinrichtungen, kirchlichen Gesundheitseinrichtungen, Apotheken und informellen Händlern erworben. Ebenfalls wurden Verfügbarkeit und Preise

ausgewertet, sowie die Qualität der Proben auf Identität, Wirkstoffgehalt und Wirkstofffreisetzung untersucht. Zusätzlich führten die afrikanischen Kollaborationspartner Analysen auf Identität und Zerfallszeit der Proben mit dem Global Pharma Health Fund e.v.(GPHF) - Minilab durch. Die durchschnittliche Verfügbarkeit der untersuchten Antibiotika lag in beiden Ländern zwischen 62% und 98% in den verschiedenen Arten von Einrichtungen. Die durchschnittliche Verfügbarkeit von Arzneimitteln gegen nicht übertragbare Krankheiten (NCD) zeigte in beiden Ländern eine höhere Schwankungsbreite, die von 11% bis zu 87% reichte. Die Arzneimittelpreise waren in Kamerun deutlich höher als in der DR Kongo, mit einem Median Price Ratio (MPR) zum internationalen Referenzpreis von 5,69 bzw. 2,17 ($p < 0,001$). Bezogen auf die mindestens zu zahlenden Tageslöhne in beiden Ländern konnten Behandlungen mit fünf der sieben untersuchten Antibiotika als erschwinglich angesehen werden, während nur eines der fünf untersuchten Medikamente gegen NCDs als erschwinglich angesehen werden konnte. Bereits bei der Analyse mittels Minilab durch die afrikanischen Partner konnten drei der 506 Proben als gefälschte Arzneimittel identifiziert werden. Weitere chemische Untersuchungen mittels Hochleistungsflüssigchromatographie gekoppelt mit hochauflösender Massenspektrometrie (LC-HR-MS/MS), sowie Kernspinresonanzspektroskopie (NMR) zeigten je einen anderen als den deklarierten Wirkstoff in zwei der drei Fälschungen. Insgesamt entsprachen 15% der gesammelten Proben aus der DR Kongo und 17% der Proben aus der Republik Kamerun nicht den Qualitätsanforderungen des USP. Besonders hervorzuheben ist hierbei, dass bisherige Studien zum Großteil ausschließlich den Gehalt der Medikamente untersuchten und nicht deren Wirkstofffreisetzung (Dissolution). Wenn, wie bisher üblich, nur der Gehalt des deklarierten Wirkstoffs bestimmt wurde, wurden 8.5% der untersuchten Arzneimittel als minderwertig oder gefälscht eingestuft. Nachdem zusätzlich auch die Wirkstofffreisetzung untersucht wurde, zeigte sich, dass noch einmal 7.7% der Proben zusätzlich als minderwertig zu bewerten waren. Durch die vorliegende Arbeit konnte somit gezeigt werden, dass der Anteil minderwertiger und gefälschter Medikamente in Entwicklungsländern unter Einbeziehung der Wirkstofffreisetzung tatsächlich um das Doppelte höher liegen könnte als bisher geschätzt.

SUMMARY

Access to safe, effective, high-quality and affordable medicines and vaccines for all is a component of Goal 3.8 of the United Nations Sustainable Development Goals. [1] Despite considerable efforts, the availability of medicines is still poor in many countries. [2, 3] In addition, according to recent estimates from the World Health Organization (WHO), up to 10.5% of medicines in developing countries are substandard or falsified. [4] However, despite their high relevance for the health of affected people, these statements are usually based on only a few studies, and for some countries or regions the issue is considered to be de facto uninvestigated. [5, 6] In order to provide comparable and reliable data on prices, availability, affordability and, above all, quality of thirteen selected drugs, one study was conducted in the Republic of Togo, and one study in the Republic of Cameroon and the Democratic Republic of Congo (DR Congo). In the south of the Republic of Togo, 94 drug samples (tablets or capsules) were purchased from six pharmacies and from six informal vendors and their prices were documented. Subsequently, 92 of the collected drugs were tested for the correct identity of the declared active ingredient, the content and the dissolution of the active ingredient using methods from the United States Pharmacopoeia (USP). The analysis of the drug prices showed that medicines are more expensive in the pharmacies than in the informal vendors. No counterfeit drug could be identified during the investigation. However, seven of the samples examined (8%) showed moderate deviations from the USP quality requirements, one sample even showed extreme deviations. The proportion of substandard drugs was higher from informal vendors (13%) than from pharmacies (5%). Thus, the drugs are cheaper, but also of inferior quality among informal traders. In the Republic of Cameroon and the DR Congo, a total of 506 drug samples were purchased from 60 government health care facilities, church health care facilities, pharmacies and informal vendors. Availability and prices were also evaluated, and the quality of the samples was examined for identity, active ingredient content and dissolution. In addition, the African partners carried out analysis on the identity of the samples using the minilab of the Global Pharma Health Fund e.v.. The average availability of the antibiotics investigated in both countries ranged between 62% and 98% in the different types of facilities. The average availability of drugs against non-communicable diseases (NCDs) showed a higher variation in both

countries, ranging from 11% to 87%. Drug prices in Cameroon were significantly higher than in the DR Congo, with a median price ratio to an international reference price of 5.69 and 2.17 ($p < 0.001$), respectively. In terms of the minimum daily wages paid in both countries, treatment with five of the seven antibiotics studied could be considered affordable, while only one of the five NCD drugs studied could be considered affordable. Already during the analysis by the African partners using the Minilab, 3 of the 506 samples could be identified as falsified medicines. Further chemical analysis using LC-HR-MS/MS/MS and NMR revealed a different pharmaceutically active substance in two of the 3 falsified medicines. Overall, 15% of the samples collected from DR Congo and 17% of the samples from the Republic of Cameroon did not meet the quality requirements of USP, and it should be emphasized that previous studies have largely investigated only the content of the drugs and not their release of active ingredients (dissolution). In accordance with the focus of previous studies on the content of the declared active ingredient, 8.5% of the drugs investigated were found to contain too little active ingredient. Now that the dissolution of the active ingredient has also been investigated, it was found that additional 7.7% of the samples were assessed as substandard. The studies have shown, that the proportion of substandard and counterfeit drugs in some developing countries, could actually be twice as high as previously estimated, if also dissolution is considered.

PUBLIKATIONSLISTE

AKZEPTIERTE PUBLIKATIONEN

“Quality of medicines in southern Togo: Investigation of antibiotics and of medicines for non-communicable diseases from pharmacies and informal vendors”

Schäfermann, S.; Wemakor, E.; Hauk, C.; Heide, L.;

PLOS ONE 13(11):e0207911, **2018**

“Availability, prices and affordability of selected antibiotics and medicines against non-communicable diseases in western Cameroon and northeast DR Congo”

Schäfermann, S.; Neci, R.; Ngah Ndze, E.; Nyaah, F.; Pondo, V.B.; Heide, L.;

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“Substandard and Falsified Antibiotics and Medicines against Noncommunicable Diseases in Western Cameroon and Northeastern Democratic Republic of Congo”

Schäfermann, S.; Hauk, C.; Wemakor, E.; Neci, R.; Mutombo, G.; Ngah Ndze, E.; Cletus, T.; Nyaah, F.; Pattinora, M.; Wistuba, D.; Helmle, I.; Häfele-Abah, C.; Gross, H.; Heide, L.;

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MÜNDLICHE PRÄSENTATIONEN

“**Antiinfective Medicine in Africa: Detection of Substandard and Falsified Medicines** “

Action Medeor, Tönnisvorst, Deutschland, Oktober 2017

„**Minderwertige und Gefälschte Arzneimittel in Afrika**“

Rotary Club Neckar-Alb, Empfingen, Deutschland, November 2017

„Arzneimittelqualität in Afrika, ein aktueller Studienbericht aus Kamerun“

Kurs “Pharmacy in Global Health”, Tübingen, Deutschland, August 2018

“Quality of medicines in southern Togo: investigation of antibiotics and of medicines for non-communicbale diseases from pharmacies and informal vendors”

MQPH2018 Conference, Oxford, UK, September 2018

“Two case studies of falsified antibiotics in Cameroon: WHO Medical Product Alerts N°4/2017 and N°2/2018”

MQPH2018 Conference, Oxford, UK, September 2018

“Rapid screening of medicine samples with handheld Raman spectroscopy and confirmation with HPLC”

Kanazawa, Japan, März 2019

„Gesundheitssysteme und Arzneimittelmärkte in Afrika und Deutschland, ein Vergleich“

Ludwig-Windhorst Stiftung, Abschluss Workshop, Lingen (Ems), April 2019

POSTERPRÄSENTATIONEN

“Quality of medicines in southern Togo: investigation of antibiotics and of medicines for non-communicable diseases from pharmacies and informal vendors”

“State of the Art Science for Tomorrow’s Medicines”, EDQM, Strasbourg, France, Juni 2019

“Three case studies of falsified antibiotics in Cameroon: WHO Medical Product Alerts N° 4/2017 and N° 2/2018, N° 6/2019”

“State of the Art Science for Tomorrow’s Medicines”, EDQM, Strasbourg, France, Juni 2019

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    - Sammeln der Medikamentenproben in Kamerun

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EINLEITUNG

VERFÜGBARKEIT UND PREISE VON ARZNEIMITTELN IN ENTWICKLUNGSLÄNDERN

Nach Angaben der WHO sterben jedes Jahr Millionen von Menschen unnötigerweise an einer Krankheit oder einem Leiden, für deren Behandlung wirksame Medikamente oder Impfstoffe vorhanden wären. [7] Dies ist unter anderem auch auf die schlechte Verfügbarkeit von lebenswichtigen Medikamenten in guter Qualität zurückzuführen. Der Zugang zu sicheren, wirksamen, qualitativ hochwertigen und erschwinglichen Medikamenten und Impfstoffen für alle ist daher ein Teil des Ziels Nr. 3.8 der Ziele für nachhaltige Entwicklung der Vereinten Nationen. [1] Trotz erheblicher Anstrengungen ist die Verfügbarkeit von Medikamenten in vielen Ländern noch immer schlecht. [2, 3] Im Jahr 2014 berichtete eine Studie aus 25 Ländern mit niedrigem und mittlerem Einkommen eine mittlere Verfügbarkeit von lebenswichtigen Medikamenten von 40,0% im öffentlichen Sektor. [8] Insbesondere für die Behandlung nicht übertragbarer Krankheiten (NCD) ist die Verfügbarkeit essentieller Medikamente gering, wie eine aktuelle Meta-Analyse von 30 Studien durch Ewen et al. [9] und eine Studie von Robertson et al. [10] zeigen. Eine Studie aus dem Jahr 2010 untersuchte die Verfügbarkeit von fünf Herz-Kreislauf-Medikamenten in 36 Ländern und berichtete eine durchschnittliche Verfügbarkeit von 26,3% im öffentlichen Sektor. [11] Bis zum Erreichen des von der WHO für 2025 festgelegten Ziels einer 80%igen Verfügbarkeit von Medikamenten gegen NCDs ist es folglich noch ein langer Weg. [12] Aber selbst wenn lebenswichtige Medikamente verfügbar sind, kann sich nicht jeder Patient in Ländern mit niedrigem und mittlerem Einkommen diese auch leisten. Medikamente zu nicht erschwinglichen Preisen können dazu führen, dass die Patienten ihre Behandlung nicht mehr zu Ende führen und somit die Krankheitslast eines Landes unnötig vermehrt wird [13].

Eine Auswertung von Daten aus 36 Ländern in 2009 zeigte, dass die Behandlung akuter und chronischer Erkrankungen in vielen Ländern für die Bevölkerung nicht bezahlbar war. [14] Die oben bereits genannte Analyse von Herz-Kreislauf-Medikamenten aus dem Jahr 2010 [11] zeigte, dass Therapien für chronische

Erkrankungen besonders teuer sind, wenn dafür Kombinationspräparate erforderlich sind. Die Untersuchungen von Ewen et al. [9] unterstrichen auch, dass in nur wenigen Ländern mit niedrigem und mittlerem Einkommen grundlegende Medikamente gegen NCDs sowohl verfügbar als auch erschwinglich sind.

Nur wenige Studien haben bisher die Verfügbarkeit und Erschwinglichkeit von Medikamenten in Togo, Kamerun oder der Demokratischen Republik Kongo (DR Kongo) untersucht. Ein kurzer Bericht aus dem Jahre 2010 zeigte, dass zahlreiche Krankenhäuser in Togo häufig mit einer unzureichender Versorgung mit Anästhetika zu kämpfen haben. [15] Im Jahr 2005 untersuchten Preux et al. [16] in einer kleinen Studie in der Provinz Mifi in Kamerun die Verfügbarkeit von antiepileptischen Medikamenten und berichteten, dass 32 von 33 Patienten auf eine Behandlung mit einem modernen Antiepileptikum angewiesen ware. Diese waren jedoch in Krankenhausapotheken häufig nicht auf Lager und die Patienten mussten sie in privaten Apotheken oder sogar bei informellen (illegalen) Händlern beziehen. Eine Untersuchung von Jingi et al. [17] ergab, dass im Westen Kameruns im Jahr 2014 eine einmonatige Kombinationsbehandlung für koronare Herzkrankheiten einen Preis von bis zu 41 Tageslöhnen entsprach. Im Jahr 2011 untersuchten O'Connell et al. [18] die Verfügbarkeit von Malariamedikamenten in sechs Ländern, darunter auch in der Demokratische Republik Kongo, mit dem ermutigenden Ergebnis, dass 82% der öffentlichen Gesundheitseinrichtungen in der DR Kongo über Artemisinin-basierte Kombinationsprodukte von gesicherter Qualität verfügten. Im Jahr 2014 veröffentlichte das Gesundheitsministerium der Demokratischen Republik Kongo das sogenannte "Service Availability and Readiness Assessment" (SARA), für das Daten über die Verfügbarkeit von 20 lebenswichtigen Medikamenten erhoben wurden. [19] Insgesamt betrug die Verfügbarkeit der Medikamente lediglich 20% und war für Medikamente gegen nicht übertragbare Krankheiten besonders niedrig. Die beiden Provinzen Nord-Kivu und Süd-Kivu, die im Rahmen dieser Doktorarbeit ebenfalls untersucht wurden, zeigten sich dort als die Provinzen mit der, relativ gesehen, höchsten durchschnittlichen Verfügbarkeit (35% bzw. 30%).

Wie ein Blick in die „Human Development Reports“ der Vereinten Nationen zeigt, weisen Togo, Kamerun und die Demokratische Republik Kongo jedoch sehr unterschiedliche politische und finanzielle Rahmenbedingungen auf:

Bei einem Bruttonationaleinkommen pro Kopf (BNE) von 1,453 US-Dollar (USD) pro Jahr, wird Togo als ein Land mit niedrigem Einkommen klassifiziert. [20] Beinahe die Hälfte der Einwohner Togos (49,2%) leben unterhalb der Armutsgrenze von 1,90 USD Einkommen pro Tag. Die durchschnittliche Lebenserwartung bei Geburt beträgt in Togo 60,5 Jahre. Zum Vergleich sei hier erwähnt, dass die Lebenserwartung bei Geburt in Deutschland mit 81,2 Jahren ganze 20 Lebensjahre höher liegt. [21]

Kamerun ist ein Land mit niedrigem bis mittlerem Einkommen und einem Bruttonationaleinkommen pro Kopf von 3,315 US-Dollar pro Jahr. 23,8% der Gesamtbevölkerung leben unterhalb der Armutseinkommensgrenze von 1,90 USD pro Tag. Die durchschnittliche Lebenserwartung bei Geburt beträgt 58,6 Jahre und liegt damit auf dem gleichen Niveau wie in Togo. [22] Trotz einer relativ stabilen politischen Vergangenheit wurde Kamerun in den letzten Jahren mit Unruhen konfrontiert, die durch Angriffe der Boko Haram im Norden und separatistische Bewegungen in den anglophonen Regionen verursacht wurden. [22]

Die Demokratische Republik Kongo ist ein Land mit niedrigem Einkommen und einem Bruttonationaleinkommen pro Kopf von nur 976 USD pro Jahr, was weniger als 30% des BNE Kameruns entspricht. 77,1% der Gesamtbevölkerung leben unterhalb der Armutsgrenze, ein dreimal höherer Anteil als in Kamerun. Allerdings liegt die Lebenserwartung bei der Geburt bei 60,0 Jahren, was sehr ähnlich ist zu der in Kamerun. [23] Nach einer langen Reihe politischer Konflikte, dem Ausbruch von Ebola in 2018 in der Provinz Nord-Kivu und einem anhaltenden bewaffneten Konflikt ist die Situation für die Bevölkerung im Nordosten der DR Kongo ernst. [24]

Interessanterweise zeigen die Daten aus den „Human Development Reports“, dass alle drei Länder, trotz ihrer deutlich unterschiedlichen wirtschaftlichen Fähigkeiten, eine ähnliche durchschnittliche Lebenserwartung für ihre Einwohner erzielen können.

QUALITÄT VON ARZNEIMITTELN IN ENTWICKLUNGSLÄNDERN

Gute Verfügbarkeit und erschwingliche Preise alleine sind nicht hinreichend für eine adäquate Arzneimittelversorgung in Entwicklungsländern. Die Arzneimittel müssen auch eine gute Qualität aufweisen, um die erwünschte therapeutische Wirkung erzielen zu können. Zwar hat sich in den letzten zehn Jahren der Zugang zu Medikamenten in Entwicklungsländern verbessert, allerdings wurde zeitgleich auch häufiger über das Auftreten von minderwertigen und gefälschten Medikamenten berichtet, deren Vorkommen von einigen Autoren sogar als "Pandemie" bezeichnet wurde. [25] Obwohl minderwertige und gefälschte Medikamente das Risiko auf einen verlängerten Krankheitsverlauf, sowie Therapieversagen erhöhen oder auch Patienten durch toxische, sowie unerwünschte Reaktionen direkt schädigen können, [26, 27] ist über ihre tatsächliche Prävalenz noch wenig bekannt. [4, 28, 29] Während sich die Belastung durch minderwertige und gefälschte Medikamente stark auf Länder mit niedrigem und mittlerem Einkommen konzentriert, [28] schätzte die WHO in 2017, dass minderwertige und gefälschte Medikamente in diesen Ländern eine Prävalenz von bis zu 10,5% aufweisen. [4] Eine aktuelle Meta-Analyse von Ozawa et al. [30] schätzte die Prävalenz von minderwertigen Arzneimitteln in Afrika auf 18,7%. Die genauere Auswertung der bisher berichteten Daten zur Prävalenz von minderwertigen und gefälschten Arzneimitteln zeigt dabei aber auch, dass diese sich stark zwischen den afrikanischen Ländern unterscheiden kann. Beide Schätzungen betonen, dass die Unterschiede in der Methodik der Probenahme und der Labortests, die zur Bestimmung der Qualität der Proben durchgeführt werden, Schlüsselfaktoren sind, die die unterschiedlichen gemessenen Prävalenzen beeinflusst haben und damit zu der beachtlichen Heterogenität der Studien beitragen. [4, 29] Gerade die Länder mit niedrigem und mittlerem Einkommen sind auf kostengünstige, schnelle und tragbare Technologien angewiesen, um minderwertige und gefälschte Medikamente aufzuspüren, [31] da fortgeschrittene Techniken wie die Hochleistungsflüssigchromatographie (HPLC) oder sogar Kopplung von HPLC mit Massenspektroskopie (LC-MS) zu teuer, sowie unter den örtlichen Bedingungen schwer zu warten sind und gut ausgebildetes Personal erfordern. Viele verschiedene Geräte wurden als Schnelltests für minderwertige und gefälschte Medikamente eingesetzt.

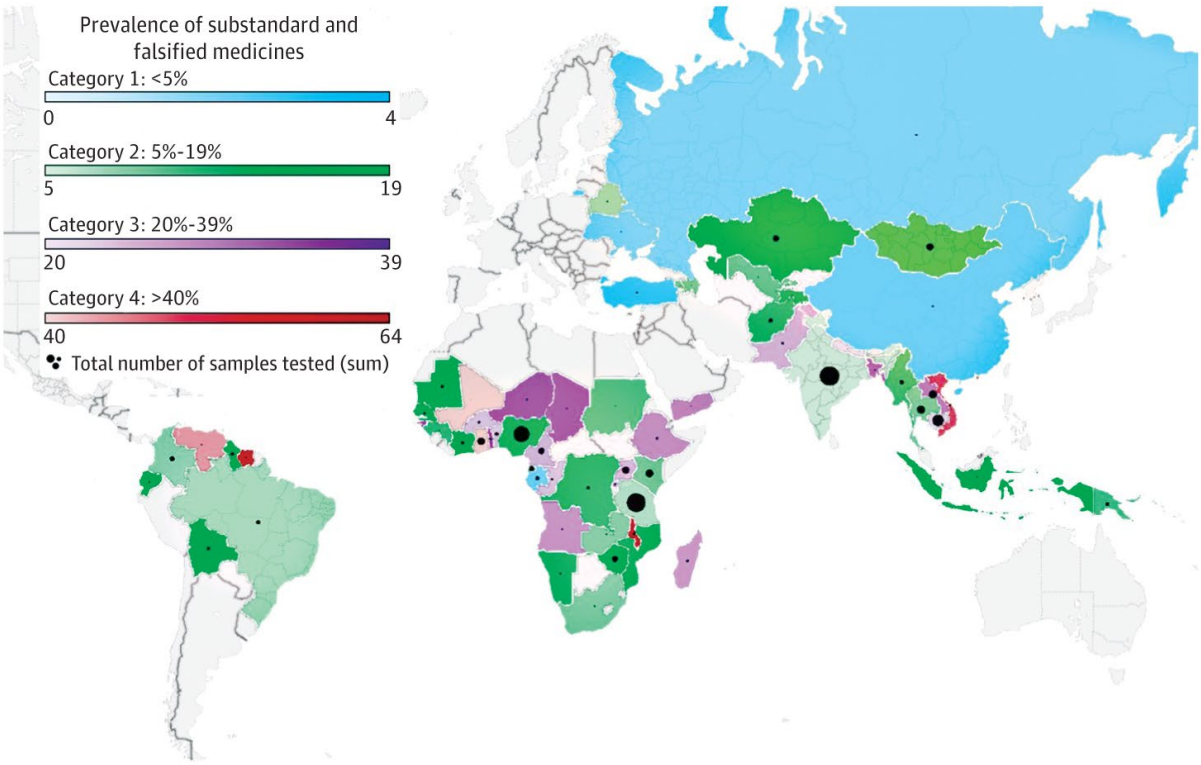

ABBILDUNG 1: BISHER BERICHTETE PRÄVALENZ VON MINDERWERTIGEN UND GEFÄLSCHTEN ARZNEIMITTELN AUS: PREVALENCE AND ESTIMATED ECONOMIC BURDEN OF SUBSTANDARD AND FALSIFIED MEDICINES IN LOW- AND MIDDLE-INCOME COUNTRIES, OZAWA ET AL. [29]

Das prominenteste chromatographische Testgerät ist das GPHF-Minilab (Global Pharma Health Fund e.V.), das zurzeit über 800 Mal in mehr als 96 Ländern im Einsatz vertreten ist und auch von der Arzneibuchkommission der Vereinigten Staaten im Rahmen des „Promoting the Quality of Medicine (PQM) Program“ zum Einsatz kommt. Dabei wird die Dünnschichtchromatographie (DC), sowie die Zerfallszeit zur Identifizierung von gefälschten oder minderwertigen Medikamenten angewendet. [32] Die Dünnschichtchromatographie mit dem GPHF-Minilab hat sich zwar für die Erkennung gefälschter Medikamente als zuverlässig erwiesen, [33-37] hat aber deutliche Schwierigkeiten bei der Erkennung von minderwertigen Produkten. [38] Die Untersuchung der WHO im Jahr 2017 [4] ergab, dass Studien, die das GPHF-Minilab einsetzten, einen deutlich geringeren Prozentsatz an minderwertigen und gefälschten Medikamenten (5,0%) nachweisen konnten als solche Studien, die fortgeschrittene Techniken wie die HPLC (15,6%) anwendeten. Bedenklich im Hinblick auf die aktuellen Schätzungen erscheint außerdem, dass die meisten Studien bisher die Qualität von Arzneimitteln in erster Linie durch die Untersuchung der Identität und des Gehalts des Wirkstoffs beurteilten, [29] wobei mögliche Qualitätsprobleme bei der

Freisetzung des Wirkstoffes vernachlässigt wurden, die möglicherweise zu einer geringeren Bioverfügbarkeit dieser Arzneimittel führen.

Bis sich die WHO im Jahr 2017 auf Definitionen für die Begriffe "minderwertige" und "gefälschte" Medikamente geeinigt hatte, [39] erschwerte zusätzlich das Fehlen einer gemeinsamen Terminologie den Vergleich und die Analyse der verfügbaren Daten über die Prävalenz von Arzneimitteln mit schlechter Qualität. Minderwertige Medikamente werden nun definiert als "zugelassene Arzneimittel, die entweder ihren Qualitätsstandards oder ihren Spezifikationen oder Beiden nicht entsprechen und durch schlechte Herstellungs-, Versand- oder Lagerbedingungen entstehen“. [39] Gefälschte Arzneimittel wiederum sind definiert als "Arzneimittel, die absichtlich oder in betrügerischer Absicht ihre Identität, Zusammensetzung oder Herkunft falsch darstellen“. [39]

Bisherige Studien in Togo, der Demokratischen Republik Kongo und der Republik Kamerun konzentrierten sich hauptsächlich auf Malariamedikamente, antiretrovirale Arzneimittel und Antibiotika. Im Jahr 2014 wurde in Ghana und Togo eine Untersuchung der Qualität von Artemisinin-basierten Antimalariamitteln durchgeführt. [40] 83,7% der Kombinationstherapien auf Artemisinin-Basis und 57,9% der Monotherapien auf Artemisinin-Basis entsprachen hierbei nicht den Anforderungen des Internationalen Arzneibuchs, da der Gehalt an Wirkstoff unzureichend war. Im nördlichen Teil Togos wurde außerdem eine Studie über die Qualität von Tierarzneimitteln durchgeführt. [41] Im Jahr 2017 untersuchten Petersen et al. 869 Medikamente aus sieben Ländern mit dem Minilab, sowie ausgewählte verdächtige Proben mittels HPLC. [34] Von den untersuchten Proben waren 7,1% der in Kamerun und 2,7% der in der DR Kongo gesammelten Medikamente minderwertig oder gefälscht. Schiavetti et al. [42] untersuchten 2018 in Kinshasa (DR Kongo) die Qualität von Arzneimitteln, die bei Kindern angewendet werden und von privaten Großhändlern geliefert wurden. Von den 239 getesteten Proben, die aus Artemeter/Lumefantrin Pulver, Amoxicillin Pulver und Paracetamol-Tabletten bestanden, waren 27% von schlechter Qualität. In einer 2011 veröffentlichten WHO Studie [37] waren 37% der getesteten Antimalariamittel aus Kamerun von minderwertiger Qualität. Im Gegensatz zu diesen Ergebnissen zeigten alle 35 Proben antiretroviraler Medikamente in einer Untersuchung der formellen Lieferkette in Kamerun gute Qualität. [43]

Wie im Globalen Statusbericht der WHO über nicht übertragbare Krankheiten von 2014 [44] betont, ist die Belastung durch nicht übertragbare Krankheiten stark in Länderen mit niedrigem und mittlerem Einkommen konzentriert. Hunter-Adams et al. [45] erwarten außerdem, dass sich die Belastung durch Diabetes in Afrika im nächsten Jahrzehnt mehr als verdoppeln wird. So hat die zunehmende Bedeutung von Medikamenten gegen nicht übertragbare Krankheiten in jüngster Zeit auch dazu geführt, dass sie in Studien über die Arzneimittelqualität in Entwicklungsländern untersucht wurden. Die SEVEN-Studie [46] untersuchte die Qualität von sieben kardiologischen Arzneimitteln aus zehn verschiedenen Ländern, darunter auch Proben aus der Demokratischen Republik Kongo. Da 26,7% der 90 in der DR Kongo gesammelten Proben von schlechter Qualität waren, deutete die Studie auf schwerwiegende Qualitätsprobleme bei Herzkreislauftherapeutika hin. Diese Qualitätsuntersuchung von Herzmedikamenten in zehn afrikanischen Ländern umfasste auch 100 Proben aus Togo. [46] Hiervon waren 9% der Proben minderwertig. Da die bisherigen Studien in Togo, Kamerun und der DR Kongo mit unterschiedlichen Methoden und Medikamenten durchgeführt wurden, ist ein Vergleich dieser Ergebnisse zwischen Ländern oder Indikationsgebieten allerdings kaum möglich.

ZIELSETZUNG

Minderwertige und gefälschte Arzneimittel stellen eine ernsthafte Bedrohung für die Gesundheit und die Patientensicherheit dar. Insbesondere in Ländern mit niedrigem und mittlerem Einkommen ist die Prävalenz von minderwertigen und gefälschten Arzneimitteln Berichten zufolge hoch. [4, 30] Der Zugang zu sicheren, wirksamen und bezahlbaren Arzneimitteln von guter Qualität ist deshalb in den Zielen der Vereinten Nationen für eine nachhaltige Entwicklung enthalten. Darüber hinaus hat die WHO einen Globalen Aktionsplan entwickelt, um den Zugang zu unentbehrlichen Arzneimitteln gegen nichtübertragbare Krankheiten (NCD) auf 80% zu erhöhen und ihre Erschwinglichkeit zu verbessern. [12]

Um einen Beitrag zur Überwachung der Fortschritte bei der Erreichung dieser Ziele zu leisten, wurde im Rahmen dieser Doktorarbeit die Verfügbarkeit und Erschwinglichkeit von sieben Antibiotika und fünf Medikamenten gegen nichtübertragbare Krankheiten im Süden der Republik Togo, sowie von sieben Antibiotika und sechs Medikamenten gegen nichtübertragbare Krankheiten im Nordosten der Demokratischen Republik Kongo und im Westen der Republik Kamerun untersucht.

Ziel dieser Doktorarbeit war es außerdem, die Qualität der in der Republik Togo, der Republik Kamerun und der Demokratischen Republik Kongo gesammelten Medikamente zu bestimmen. Zu diesem Zweck wurde die Identität der deklarierten Wirkstoffe, der Gehalt der Wirkstoffe und die Wirkstofffreisetzung experimentell bestimmt. Um vergleichbare und transparente Untersuchungsmethoden und Qualitätsstandards zu gewährleisten, wurden alle Medikamente unter Verwendung der Methoden und Grenzwerte der Monographien des Arzneibuchs der Vereinigten Staaten für Fertigarzneimittel untersucht. Die gewonnenen Daten über die Qualität der untersuchten Medikamente wurden dann unter anderem auf Zusammenhänge mit der therapeutischen Klasse, der Herkunft der Arzneimittel, Unterschiede zwischen den vier untersuchten Bezugsquellen, sowie den deklarierten Lagerbedingungen statistisch ausgewertet.

Da in vielen Entwicklungsländern eine aufwändige instrumentelle Analytik nicht durchführbar ist, werden häufig so genannte Screening Methoden genutzt, um die Arzneimittelqualität vor Ort zu überprüfen. Ein prominenter Vertreter, der häufig in Entwicklungsländern eingesetzt wird, ist das GPHF Minilab. Um die Grenzen und Möglichkeiten des Minilab zu untersuchen, wurden daher außerdem alle in Kamerun und der DR Kongo gesammelten Proben zusätzlich mit dem Minilab untersucht und die Ergebnisse mit denen der Arzneibuch-Analyse nach USP verglichen.

ERGEBNISSE

DESIGN DER STUDIE IN DER REPUBLIK TOGO

Um die Qualität und Verfügbarkeit von Arzneimitteln in der Republik Togo zu untersuchen, wurden im Februar 2017 insgesamt 94 Arzneimittelproben im Süden Togos gesammelt. Das zugrundeliegende Studienprotokoll basierte auf den von der WHO 2016 veröffentlichten Leitlinien für die Durchführung von Studien über die Qualität von Arzneimitteln [47] und den MEDQUARG-Richtlinien. [48] Für diese Studie wurden sieben Antibiotika und fünf Medikamente gegen nicht übertragbare Krankheiten aufgenommen, die alle in der Liste der unentbehrlichen Arzneimittel der Republik Togo gelistet sind. [49] Diese 12 Medikamente waren feste orale Darreichungsformen von Amoxicillin, Amoxicillin/Clavulansäure, Sulfamethoxazol/Trimethoprim, Ciprofloxacin, Phenoxymethylpenicillin (Penicillin V), Metronidazol, Doxycyclin, Metformin, Atenolol, Hydrochlorothiazid, Furosemid und Salbutamol (Albuterol). Für jedes Medikament wurde eine bevorzugte Stärke und Darreichungsform (Tablette oder Kapsel) definiert, die bei den Händlern explizit angefordert wurde. Wenn diese nicht verfügbar war, wurde eine andere Stärke oder eine andere feste orale Darreichungsform gesammelt, die den gleichen Wirkstoff enthielt.

Die Arzneimittelproben wurden im südlichen Teil Togos, in den Regionen Maritime und Plateaux, gesammelt. In der Hafenstadt Lomé wurden mehrere Bürger nach gut sortierten informellen Arzneimittelhändlern im Süden Togos befragt. Fünf solcher Händler befanden sich in der Region Maritime im Zentrum von Lomé, in den Vororten Agoe-nyvie und Agoe-laogope, sowie in den Städten Tsévié und Tabligbo, 30 km nördlich bzw. 75 km nordöstlich von Lomé. Darüber hinaus wurde ein Händler in der Stadt Kpalimé, 120 km nordwestlich von Lomé und nahe der Grenze zu Ghana, in der Region Plateaux, genannt. Abbildung 2 zeigt die Positionen dieser sechs ausgewählten Händler. Die informellen Händler arbeiteten in kleinen Geschäften abseits der Hauptstraßen. Solche nicht akkreditierten Arzneimittelhändler in Togo und den Nachbarländern wurden bereits in früheren Studien beschrieben. [40, 41]

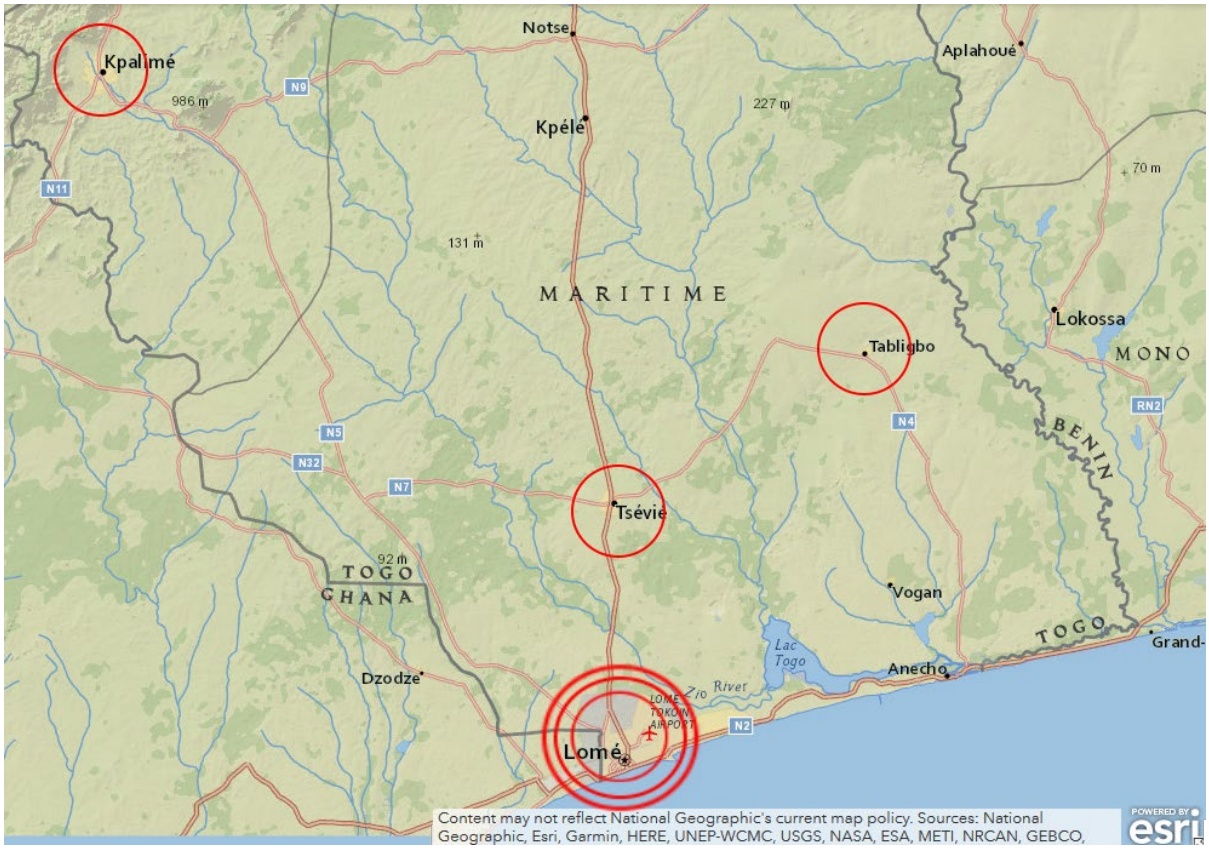

ABBILDUNG 2: KARTE DER PROBENAHMEPUNKTE IN DEN REGIONEN MARITIME UND PLATEAUX DER REPUBLIK TOGO. MODIFIZIERT NACH SCHÄFERMANN ET AL.[50]

Beim Besuch jeder dieser sechs ausgewählten informellen Händlern wurde auch die geografisch nächstgelegene zugelassene Apotheke ermittelt. Eine Liste der lizenzierten Apotheken in Togo ist im Internet verfügbar, [51] und in der Tat sind alle sechs ermittelten Apotheken in dieser Liste zu finden, aber keiner der informellen Händler. In beiden Arten von Arzneimittelbezugsquellen gab sich ein Mitarbeiter als Kunde aus und kaufte je eine Menge von 100 Tabletten oder Kapseln für jedes der 12 Medikamente. Wenn der Verkäufer nach dem Zweck des Kaufes fragte, gab der Mitarbeiter an, dass diese Medikamente für die Verwendung in einer lokalen medizinischen Einrichtung bestimmt seien, die von einem Verwandten betrieben werde. Falls die geforderte Menge von 100 Tabletten oder Kapseln pro Medikament nicht verfügbar war, wurde eine kleinere Menge gekauft, aber mindestens 30 Tabletten oder Kapseln, um eine ausreichende Menge für die chemische Analyse sicherzustellen. Bei jedem der insgesamt zwölf in die Studie eingeschlossenen Händler wurden Preise und Mengen der eingekauften Medikamente erfasst. Jede Probe wurde nach Möglichkeit in der originalen Primär- und Sekundärverpackung gelagert. Wenn keine Primäre- oder Sekundärverpackung vorhanden war, wurden die Proben in lichtgeschützten Schraubverschlussflaschen gelagert. Ein Klebeetikett mit

einer eindeutigen Probennummer wurde auf der Primär- oder Sekundärverpackung jeder Probe angebracht. Die Proben wurden an einem kühlen und trockenen Ort gelagert und innerhalb von drei Wochen nach dem Erwerb an die Universität Tübingen transportiert. Dort wurden alle Medikamente bis zur Analyse bei 21°C in einem klimatisierten Raum gelagert.

VERFÜGBARKEIT UND PREISE VON ARZNEIMITTELN IN DER REPUBLIK TOGO

Wie in Tabelle 1 dargestellt, bestanden die 94 Proben aus 44 verschiedenen Produkten und insgesamt 68 verschiedenen Chargen. Nach den Angaben auf den Etiketten wurden sie von 26 verschiedenen Herstellern in 12 verschiedenen Ländern hergestellt. Die meisten Proben (69 von 94, entsprechend 73%) waren Generika, die unter dem internationalen Freinamen (INN) ihres pharmazeutischen Wirkstoffs verkauft wurden, während 19% sogenannte Markengenerika waren und nur 7 Proben (7%) Originalpräparate waren. Alle sieben Originalpräparate wurden von lizenzierten Apotheken bezogen.

Wirkstoff des Arzneimittels	Apotheke	Informeller Händler	Gesamt	Anzahl verschiedener Produkte	Anzahl verschiedener Chargen
Amoxicillin	6	6	12	6	11
Amoxicillin / Clavulansäure	7	0	7	5	7
Phenoxymethylpenicillin	2	1	3	2	2
Ciprofloxacin	7	6	13	8	11
Doxycyclin	8	3	11	5	7
Sulfamethoxazol / trimethoprim	5	1	6	3	5
Metronidazol	6	6	12	4	6
Atenolol	6	1	7	1	3
Furosemid	6	4	10	5	6
Hydrochlorothiazid	3	1	4	3	4
Metformin	6	1	7	1	5
Salbutamol	2	0	2	1	1
Gesamt	64	30	94	44	68

TABELLE 1: ÜBERBLICK ÜBER DIE IN DER REPUBLIK TOGO GESAMMELTEN MEDIKAMENTE, MODIFIZIERT NACH SCHÄFERMANN ET AL. [50]

In den sechs besuchten Apotheken waren im Durchschnitt zehn der 12 untersuchten Medikamente verfügbar (zwischen acht und 12 Medikamente). Bei den sechs informellen Händlern waren im Durchschnitt nur fünf Medikamente verfügbar (zwischen drei und acht Medikamente). Die beste Verfügbarkeit war für Amoxicillin, Ciprofloxacin und Metronidazol zu beobachten.

Wie in einer gemeinsamen Publikation der WHO und Health Action International (HAI) beschrieben, [52] wurde das Verhältnis des Medians der gezahlten Medikamentenpreise zum Internationalen Referenz Preis [53] berechnet, der so genannte Median-Price-Ratio (MPR). Insgesamt ergab sich ein Median-Price-Ratio von 5,3 in lizenzierten Apotheken, sowie 3,2 bei informellen Anbietern. Somit sind Medikamente in Apotheken erwartungsgemäß teurer als bei informellen Händlern. Ein Bericht der Vereinten Nationen von 2012 stellte fest, [54] dass in Ländern mit niedrigem und mittlerem Einkommen durchschnittlich ein MPR von 5,3 im privaten Sektor zu erwarten ist, was identisch mit dem hier gezeigten Wert für Apotheken in Togo ist. Wie erwartet war die MPR für Generika und Markengenerika (durchschnittliche MPR = 4,1) niedriger als die für Originalpräparate (durchschnittliche MPR = 13,5). Medikamente aus Afrika und Asien (in beiden Fällen durchschnittliche MPR = 3,0) waren günstiger als solche aus Europa (durchschnittliche MPR= 7,2). Insbesondere Medikamente für nichtübertragbare Krankheiten wurden zu wesentlich höheren Preisen (durchschnittliche MPR=10,7) verkauft als Antibiotika (durchschnittliche MPR=3,1). Für die beiden Proben von Salbutamol 2 mg Tabletten, die als Markengenerika in Apotheken verkauft wurden, wurde sogar ein MPR von 49,3 gemessen. Das heißt, diese Medikamente wurden beinahe 50 mal teurer angeboten als der internationale Marktpreis.

QUALITÄT VON ARZNEIMITTELN IN DER REPUBLIK TOGO

Letztlich wurden alle Proben die wie oben beschrieben gesammelt wurden auf ihre Qualität hin untersucht. Die Analysen wurden nach den in den Monographien des USP für die jeweiligen Fertigarzneimittel der 12 Wirkstoffe angegebenen Methoden durchgeführt. Die Qualitätsuntersuchung umfasste die Bestimmung der Identität, des Gehalts an Wirkstoff und der Wirkstofffreisetzung (Anteil des aus der Darreichungsform gelösten Wirkstoffes über die Zeit). Die angewendeten HPLC-Methoden, entsprachen den HPLC-Methoden die in der jeweiligen Monographie des

USP 39 für die Bestimmung des Gehalts vorgeschrieben waren. Auch der Anteil an Wirkstoff der letztlich beim Wirkstofffreisetzungstest in Lösung überging wurde mit diesen HPLC-Methoden gemessen, mit Ausnahme von Metformin, das wie ebenfalls im USP verlangt, mittels UV-Spektroskopie quantifiziert wurde. Da sich im Laufe der Analysen zeigte, dass die Probenaufarbeitung nach USP bei einigen Proben hohe Schwankungen im Messergebnis hervorrief, wurde für zwei Proben von Amoxicillin/Clavulansäure und für eine Probe von Hydrochlorothiazid-Tabletten die Gleichförmigkeit des Gehalts untersucht, indem 10 Tabletten einzeln analysiert wurden. Der für diese drei Proben ausgewiesene Gehaltswert entspricht daher dem Durchschnitt der 10 Einzelmessungen für jede Probe.

Bei der Beurteilung der Konformität der untersuchten Arzneimittel wurden ebenfalls die Kriterien aus den jeweiligen USP Monographien herangezogen. Die vom USP angegebenen Grenzwerte für gute Qualität sind für verschiedene Wirkstoffe unterschiedlich. Proben, die diese Grenzwerte nicht einhalten konnten, wurden als nicht bestanden angesehen. Wie in einer 2011 von der WHO veröffentlichten Studie [37] vorgeschlagen, wurden die als nicht bestanden klassifizierten Proben weiter in diejenigen unterteilt, die nur moderate und solche, die extreme Abweichungen von den USP-Kriterien aufwiesen. Eine extreme Abweichung wurde dabei für Proben festgelegt, deren Gehalt an Wirkstoff mehr als 20% vom deklarierten Gehalt abwich und/oder wenn die durchschnittliche Auflösung der getesteten Proben mehr als 25% unterhalb des Grenzwerts lag (d.h. USP Q-Wert minus 25%).

Die Überprüfung der Primär- und Sekundärverpackung, der Packungsbeilagen sowie der Chargennummern und Verfallsdaten ergab bei den Arzneimitteln aus Togo keine Fehler oder Unstimmigkeiten, wie sie sonst häufig bei gefälschten Arzneimitteln auftreten. [34, 55] Bei einer Probe Doxycyclin Tabletten konnte in einem Blister jedoch eine auffällige Verfärbung der üblicherweise gelben Tabletten beobachtet werden. Tabletten aus diesem Blister wiesen im Gegensatz zu Tabletten aus den anderen Blistern der gleichen Probe einen deutlich zu niedrigen Gehalt an Doxycyclin auf (55% des deklarierten Gehalts). Letztlich fehlte in keiner der 92 Proben der deklarierte Wirkstoff, und in nur einer Probe war der Wirkstoffgehalt niedriger als 80%. Von den insgesamt 92 vollständig analysierten Proben entsprachen 85 (92%, 95%CI= 85 - 97%) den Spezifikationen des USP für den Wirkstoffgehalt und die Wirkstofffreisetzung. Allerdings zeigten sechs Proben (7%, 95%CI = 2 - 14%)

moderate Abweichungen und eine Probe (1%, 95%CI= 0,03 - 6%) extreme Abweichungen von den USP Grenzwerten.

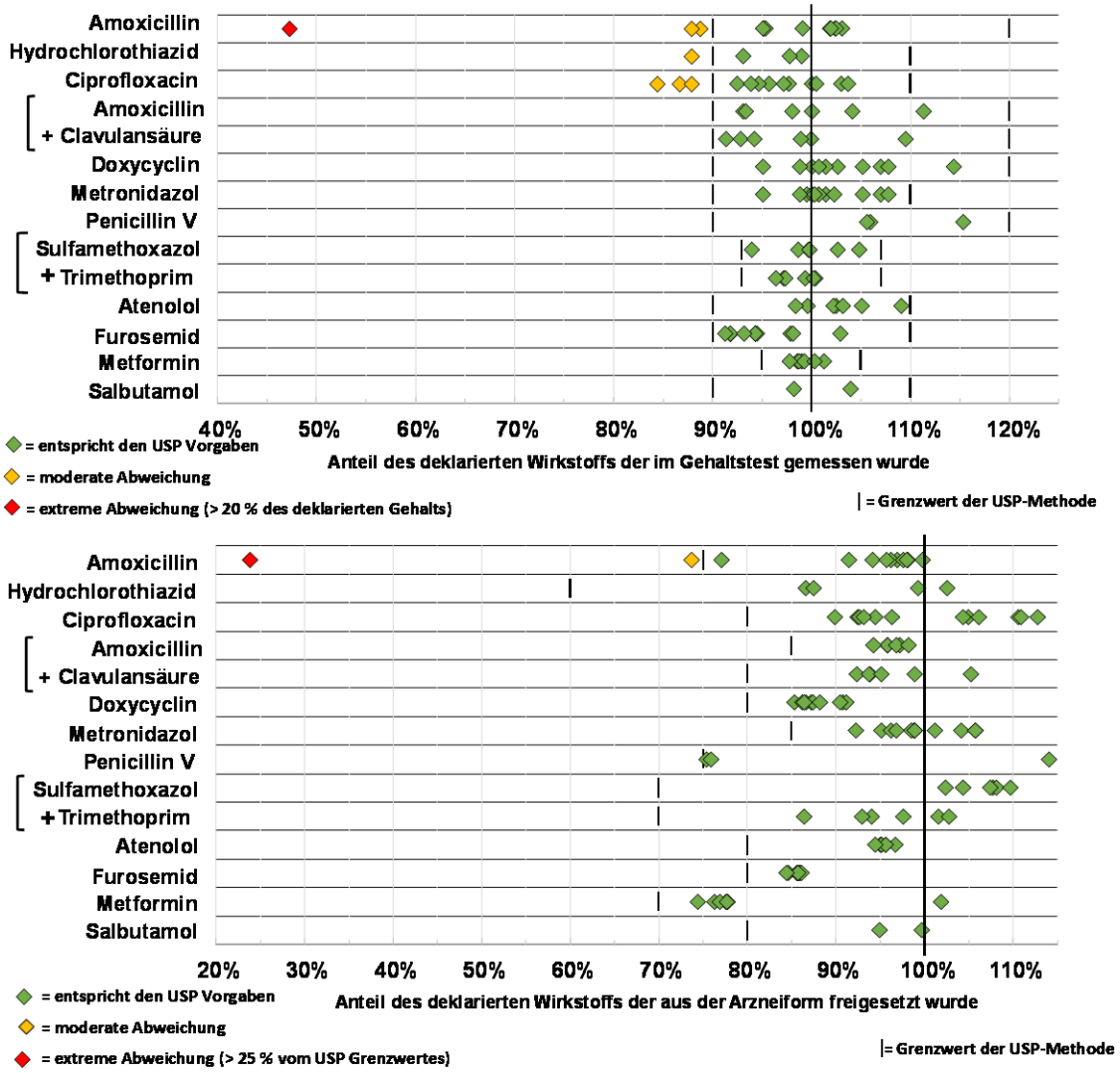

ABBILDUNG 3: ERGEBNISSE DER ANALYSEN AUF GEHALT (OBEN) UND WIRKSTOFFFREISETZUNG (UNTEN) DER GESAMMELTEN ARZNEIMITTELPROBEN. MODIFIZIERT NACH SCHÄFERMANN ET AL. [50]

Minderwertige Arzneimittel wurden für Amoxicillin, Hydrochlorothiazid und Ciprofloxacin beobachtet, aber nicht bei den anderen neun untersuchten Wirkstoffen. Der höchste Anteil an minderwertigen Arzneimitteln wurde insbesondere bei Proben aus Asien beobachtet (24%). Dieser ist damit statistisch signifikant höher als bei den Medikamenten aus anderen Herkunftsländern (durchschnittlich 4%; p=0,007). 18 Arzneimittel wurden in Togo selbst hergestellt, darunter 15 von einem einzigen togolesischen Hersteller. Alle von diesem Unternehmen hergestellten Arzneimittel entsprachen den USP-Spezifikationen. Generika zeigten einen geringeren Anteil an moderaten und extremen Abweichungen als Markengenerika oder Originalpräparate.

Medikamente, die aus lizenzierten Apotheken bezogen wurden, zeigten einen geringeren Anteil an minderwertigen Arzneimitteln als solche von informellen Händlern (5% versus 13%). Der Unterschied in der Durchfallrate zwischen lizenzierten Apotheken und informellen Anbietern erreichte jedoch keine statistische Signifikanz (p= 0,152). Zwar zeigte sich ein Unterschied beim Anteil minderwertiger Arzneimittel zwischen Antibiotika (10%) und den Arzneimitteln gegen nicht übertragbare Krankheiten (3%), jedoch war auch dieser nicht signifikant.

DESIGN DER STUDIE IN DER REPUBLIK KAMERUN UND DER DEMOKRATISCHEN REPUBLIK KONGO

Das Studienprotokoll folgte ebenfalls den von der WHO 2016 veröffentlichten Leitlinien für die Durchführung von Studien zur Arzneimittelqualität [47] und den MEDQUARG-Richtlinien. [48] Da im Rahmen dieser Studie die Arzneimittelqualität, sowohl mit dem GPHF-Minilab als auch mittels USP untersucht wurde, basierte die Arzneimittelauswahl auch auf der Verfügbarkeit einer GPHF-Minilab-Monographie und einer USP-Monographie für die jeweiligen Fertigarzneimittel. Für diese Studie in der Demokratischen Republik Kongo wurden sieben Antibiotika und fünf Medikamente gegen nichtübertragbare Krankheiten ausgewählt. Die ausgewählten Medikamente waren feste orale Darreichungsformen (Kapseln oder Tabletten) von Amoxicillin, Amoxicillin/Clavulansäure, Sulfamethoxazol/Trimethoprim, Ciprofloxacin, Phenoxymethylpenicillin (Penicillin V), Metronidazol, Doxycyclin, Metformin, Atenolol, Hydrochlorothiazid, Furosemid und Salbutamol (Albuterol). Für die Studie in Kamerun wurden die gleichen Medikamente mit Ausnahme von Atenololol ausgewählt, da nach Angaben der lokalen Partner in Kamerun Atenolol von Gesundheitsdienstleistern nicht häufig verwendet wurde. Auf anraten der lokalen Partner in Kamerun wurde anstelle des Blutdrucksenkers Atenolol in diesem Land das Antidiabetikum Glibenclamid (Glyburide) gesammelt. Alle dreizehn Arzneimittel wurden in den Listen der unentbehrlichen Arzneimittel (EML) der Republik Kamerun und der Demokratischen Republik Kongo geführt. [56, 57]

In der Demokratischen Republik Kongo wurde diese Studie in den vier Provinzen Ituri, North-Kivu, South-Kivu und Tanganyika durchgeführt. Aus jeder dieser vier Provinzen wurde eine vollständige Liste der Gesundheitszonen erstellt, die 37, 34, 34, und 11

Gesundheitszonen (insgesamt 116 Gesundheitszonen) umfasst. Davon mussten 70 von dieser Studie ausgeschlossen werden, da das entsenden von Studienpersonal in diese Zonen nach Einschätzung der lokalen Partner in der DR Kongo nicht sicher gewesen wäre. Von den restlichen 46 Gesundheitszonen wurden acht zufällig ausgewählt, zwei aus jeder Provinz. Die ausgewählten Gesundheitszonen waren Nyankunde und Rethy (Ituri), Biena und Goma (Nord-Kivu), Nyangezi und Ruzizi (Süd-Kivu) sowie Kansimba und Nyemba (Tanganyika). Auf Wunsch der lokalen Partner wurde diese Auswahl um die Kadutu Health Zone in Bukavu, Süd-Kivu, erweitert, da der zentrale Markt von Bukavu als der größte nicht lizenzierte Markt für Arzneimittel in dieser Region bekannt ist und die Beurteilung der Arzneimittelqualität dort von großem Interesse war. In jeder der ausgewählten Gesundheitszonen der DR Kongo wurden zunächst Medikamente aus dem Centre Hospital dieser Zone entnommen. Falls das Centre Hospital eine staatliche Gesundheitseinrichtung war, wurde die geografisch nächstgelegene kirchliche Gesundheitseinrichtung, Apotheke und informeller Händler ermittelt und auch von diesen drei Standorten Medikamente entnommen. Dementsprechend wurden, wenn es sich bei dem Centre Hospital um eine kirchliche Gesundheitseinrichtung handelte, die nächstgelegene staatliche Gesundheitseinrichtung, Apotheke und informeller Händler in dieser Zone ermittelt und von dort ebenfalls Medikamente gesammelt.

In Kamerun wurde diese Studie in sechs der 10 Regionen des Landes durchgeführt, Adamawa, Centre, Littoral, Northwest, Southwest und West. Eine Liste aller kirchlichen Gesundheitseinrichtungen in diesen sechs Regionen umfasste 45 Einrichtungen. Für jede Region wurde eine kirchliche Gesundheitseinrichtung nach dem Zufallsprinzip ausgewählt. In jeder Region wurden zuerst Proben von der ausgewählten Einrichtung und anschließend von der geografisch nächstgelegenen staatlichen Gesundheitseinrichtung, der privaten Apotheke und dem informellen Händler von Medikamenten gesammelt. Die Zufallsauswahl der sechs Gesundheitseinrichtungen traf keine der insgesamt zehn Einrichtungen katholischer Kirchenorganisationen in diesen Regionen. Daher wurden zwei der zehn katholischen Gesundheitseinrichtungen nach dem Zufallsprinzip ausgewählt und zusätzlich in den Regionen Northwest und Centre in die Studie mit einbezogen.

So wurden letztlich 60 Einrichtungen in beiden Ländern besucht und Medikamente von dort gesammelt. Die Probenahme erfolgte in der Republik Kamerun von August

2017 bis November 2018 und in der DR Kongo von Juli 2017 bis Mai 2018. In öffentlichen und kirchlichen Gesundheitseinrichtungen wiesen sich die Partner aus und erklärten den Zweck der Studie. Im Gegensatz dazu wurden in privaten Apotheken und illegalen Arzneimittelverkäufern Proben nach dem Mystery-Shopper-Prinzip gesammelt. Für jede Medikamentenprobe, wurde in jeder Einrichtung eine Gesamtzahl von bis zu 100 Tabletten oder Kapseln gekauft, sofern verfügbar, mindestens jedoch 30 Tabletten oder Kapseln. Wenn mehrere verschiedene Produkte desselben Medikaments verfügbar waren, wurde das Günstigste gekauft. Die Proben wurden nach Möglichkeit in deren Originalverpackung oder Behälter gesammelt. In jeder der 60 Einrichtungen wurden Preise und Mengen der eingekauften Medikamente erfasst. Probennummer, Markenname, Chargennummer, Herstellungsdatum, Verfallsdatum, Name des Herstellers, internationale Freinamen (INN) der pharmazeutischen Wirkstoffe, Stärke, Darreichungsform, Verpackungsgröße und Preis wurden ebenfalls, wie auf dem Etikett angegeben, auf einem standardisierten Formular durch das lokale Personal erfasst.

Wie in einer gemeinsamen Publikation der WHO und Health Action International (HAI) beschrieben, [52] wurde das Verhältnis des Medians der gezahlten Medikamentenpreise zum Internationalen Referenz Preis [53] berechnet, der so genannte Median-Price-Ratio (MPR). Außerdem wurde anhand standardisierter Therapiepläne die Erschwinglichkeit einer Therapie mit den gesammelten Medikamenten berechnet, bezogen auf die für das jeweilige Land angegebenen mindestens zu zahlenden Tageslöhne. Als Indikator für die Erschwinglichkeit einer Therapie wurde die Anzahl der Tageslöhne berechnet, die für den Kauf der benötigen Menge an Medikamente für eine komplette Therapie aufgebracht werden müssten. [52] Für chronische Krankheiten wurde die Menge an Medikamenten für eine Behandlung über 30 Tage berechnet. Nach WHO/HAI [52] gilt eine Behandlung als unerschwinglich, wenn sie mehr als einen kompletten Tageslohn kostet.

Alle Proben, die aus mehr als 50 Tabletten oder Kapseln bestanden, wurden aufgeteilt in 25 Tabletten oder Kapseln für die Minilab-Analyse im jeweiligen Land und die Restmenge an Tabletten oder Kapseln (mehr oder gleich 30) für die Arzneibuchanalyse an der Universität Tübingen. Die Ergebnisse der DC-Analysen nach den Minilab-Vorschriften wurden aufgezeichnet, indem ein Bild der entwickelten DC-Platte in einer standardisierten Kammer aufgenommen wurde. Proben, die aus

weniger als 50 Tabletten oder Kapseln bestanden, wurden nicht mit dem Minilab analysiert und direkt an die Universität Tübingen zur Arzneibuchanalyse geschickt.

Die Arzneibuchanalyse aller Proben umfasste die Identifizierung des deklarierten Wirkstoffs (HPLC-Retentionszeit vs. Retentionszeit einer Referenzsubstanz), die Bestimmung des Gehalts (Assay) und die Bestimmung der Wirkstofffreisetzung. Alle HPLC-Analysen wurden mit den in der USP-Monographie aufgeführten HPLC-Methoden für die Gehaltsbestimmung durchgeführt.

Die Wirkstofffreisetzung wurden unter Anwendung der Parameter und Grenzwerte der USP-Monographie des jeweiligen Arzneimittels untersucht, unabhängig davon, ob auf der Probe ein Verweis auf das USP oder auf ein anderes Arzneibuch angegeben war. Proben, die anstelle oder zusätzlich zu dem auf der Verpackung angegebenen Wirkstoffs, unbekannte Substanzen zeigten, wurden mittels LC-HR-MS/MS- und NMR-Analyse analysiert, um die Struktur der unbekannten Substanz aufzuklären.

Ein Test nach Arzneibuch galt als bestanden, wenn die in der jeweiligen USP Monographie angegebenen Grenzwerte eingehalten wurden. Wie bereits in der Studie in der Republik Togo beschrieben, wurden die Proben, die die USP-Grenzwerte nicht einhielten, weiter unterteilt in solche die "moderate Abweichung" und "extreme Abweichung" von den Grenzwerten aufwiesen. Proben, die die Identität ihres Wirkstoffs falsch deklarierten, wurden als gefälscht („falsified“) eingestuft und an das Warnsystem der WHO gemeldet. [55, 58]

VERFÜGBARKEIT, PREISE UND ERSCHWINGLICHKEIT VON ARZNEIMITTELN IN DER REPUBLIK KAMERUN UND DER DEMOKRATISCHEN REPUBLIK KONGO

Die volle Anzahl aller 12 untersuchten Medikamente war nur in sechs der 26 (23%) Einrichtungen in Kamerun und vier der 34 (12%) Einrichtungen in der DR Kongo verfügbar. Die durchschnittliche Verfügbarkeit der jeweils 12 Medikamente betrug 78% in Kamerun und 64% in der DR Kongo. In beiden Ländern wurden keine auffälligen regionalen Unterschiede in der Medikamentenverfügbarkeit beobachtet. Insbesondere sind die staatlichen Gesundheitseinrichtungen im deutlich wohlhabenderen Kamerun nicht besser ausgestattet als in der DR Kongo (50%

durchschnittliche Verfügbarkeit in beiden Ländern). Die insgesamt höhere Verfügbarkeit von Medikamenten in Kamerun ist daher nur auf die besseren Arzneimittelbestände von kirchlichen Gesundheitseinrichtungen, Apotheken und informellen Anbietern in diesem Land zurückzuführen. Wie erwartet, waren die privaten Apotheken in beiden Ländern besser ausgestattet als die anderen Arten von Einrichtungen. Auch die informellen Händler waren in Kamerun sehr gut ausgestattet (93% Verfügbarkeit), ähnlich wie die lizenzierten Apotheken.

Insgesamt lagen die Median Price Ratios (MPRs) für Kamerun und die DR Kongo bei 5,69 und 2,17 ($p<0,0001$), was zeigt, dass Medikamente in Kamerun mehr als doppelt so teuer verkauft werden als in der DR Kongo. Die Arzneimittelpreise in Kamerun sind in allen vier Arten von Einrichtungen höher, am deutlichsten in privaten Apotheken (MPR 9,74 in Kamerun gegenüber 2,70 in der DR Kongo; $p<0,0001$). In der Demokratischen Republik Kongo bieten insbesondere staatliche Gesundheitseinrichtungen einige Arzneimittel zu Preisen an, die weit unterhalb des International Medical Products Price Guide-Referenzpreises liegen. [53] In der DR Kongo verkaufen staatliche und kirchliche Gesundheitseinrichtungen außerdem Medikamente günstiger als informelle Händler. Im Gegensatz dazu sind die Medikamentenpreise in kamerunischen Gesundheitseinrichtungen höher als bei informellen Händlern. Außerdem konnte gezeigt werden, dass Antibiotika in Kamerun deutlich teurer waren als in der DR Kongo (MPR 4,47 gegenüber 1,80; $p<0,0001$). Im Gegensatz dazu waren bei Medikamenten gegen NCDs manchmal Medikamente aus Kamerun teurer, manchmal die aus der DR Kongo, und somit war der MPR für Medikamente gegen NCDs in beiden Ländern nicht signifikant unterschiedlich (MPR 8,81 versus 7,11; $p=0,27$). Insgesamt stellten nur 6% der gesammelten Proben Originalpräparate dar. Wie zu erwarten, waren diese sehr teuer, mit MPRs von 16,92 in Kamerun und 37,79 in der DR Kongo.

Im Gegensatz dazu war der Großteil der Arzneimittel gegen NCDs nicht erschwinglich, insbesondere das wichtige antidiabetische Medikament Metformin. Medikamente, die in Apotheken verkauft wurden, waren weniger erschwinglich als Medikamente, die in anderen Arten von Einrichtungen verkauft wurden. Während Therapien mit Medikamenten aus Afrika und Asien in vielen Fällen bezahlbar waren, galt die für die aus Europa importierten Medikamenten nicht. Ebenso waren Therapien mit Generika erschwinglich, während Therapien mit Originalpräparaten dies nicht waren.

QUALITÄT VON ARZNEIMITTELN IN DER REPUBLIK KAMERUN UND DER DEMOKRATISCHEN REPUBLIK KONGO

Von den 506 Arzneimittelproben enthielten drei (0,6%) nicht den deklarierten Wirkstoff, und zwei davon enthielten sogar einen nicht deklarierten anderen Wirkstoff. Alle drei Fälschungen wurden von informellen Händlern verkauft.

Eine der in Kamerun gesammelten Proben war als Augmentin® SmithKline Beecham (Amoxicillin 500 mg/Clavulansäure 125 mg Tabletten) etikettiert und trug eine der Registrierungsnummern, wie sie von der nigerianischen National Agency for Food and Drug Administration and Control (NAFDAC) vergeben wird. Verpackung und Tabletten schienen von ausgezeichneter Qualität zu sein und gaben keinen unmittelbaren Hinweis auf das Vorliegen einer Fälschung. Sowohl die Minilab-DC-Analyse als auch die HPLC-Analyse (nach USP) zeigten das völlige Fehlen der beiden angegebenen Wirkstoffe. Das Schnellwarnsystem der WHO wurde darüber informiert und veröffentlichte daraufhin einen Medical Product Alert. [58]

Eine weitere Probe, die ebenfalls in Kamerun gesammelt wurde, war als Penicillin-V-Tabletten der Firma Oxford Pharma Co. Ltd. Belgien ausgewiesen. Auf dem Etikett wurde der Wirkstoff fälschlicherweise als "Phenoxymetgyl-Penicillin" und nicht als „Phenoxymethyl-Penicillin“ bezeichnet. Der angegebene Hersteller "Oxford Pharma, Belgien" existiert nicht. Während die Tabletten selbst offenbar professionell gepresst und bedruckt wurden, waren die Etiketten und die Verpackung von schlechter Qualität. Die Analysen mittels DC und HPLC zeigten das Fehlen des deklarierten Wirkstoffes, wiesen aber auf das Vorhandensein einer anderen, unbekannten Verbindung hin. Die daraufhin durchgeführte LC-HR-MS/MS-Analyse bewies, dass es sich bei der unbekannten Verbindung um Paracetamol handelte. Sie zeigte die gleiche exakte Masse und das gleiche Fragmentierungsmuster wie der Paracetamol Referenzstandard. Auch hier wurde das Schnellwarnsystem der WHO informiert und diese veröffentlichten einen Medical Product Alert.[55]

ABBILDUNG 4: BILDER DER DREI PROBEN, DIE ALS GEFÄLSCHTE MEDIKAMENTE IDENTIFIZIERT WURDEN. A) GEFÄLSCHTES AUGMENTIN® (QMCA241), ENTHÄLT KEINEN NACHWEISBAREN WIRKSTOFF. B) GEFÄLSCHTE PENICILLIN-V-TABLETTEN (QMCA035) ENTHALTEN TATSÄCHLICH 50 MG PARACETAMOL. C) LINKS: DAS GEFÄLSCHTE METRONYL® (QMC266, HERGESTELLT FEB 2017, CHARGE L3028) MIT 93 MG METRONIDAZOLBENZOAT. RECHTS: EINE WEITERE CHARGE METRONYL® (QMC036, HERGESTELLT MAR 2016, CHARGE K2343), DIE ALLE ARZNEIBUCHTESTS FÜR METRONIDAZOL-TABLETTEN ERFÜLLT. [55, 58] MODIFIZIERT NACH SCHÄFERMANN ET AL. [59]

Eine dritte Probe, die in der DR Kongo gesammelt wurde, war als Metronyl® Metronidazol-Tabletten B.P., Mac's Pharmaceuticals Ltd., Kenia, etikettiert. Sie wurde als Gebinde von 100 Tabletten in einer offenen PVC-Flasche verkauft. Die visuelle Überprüfung ergab keine unmittelbaren Hinweise auf eine Fälschung. Sowohl die Minilab-DC-Analyse als auch die HPLC-Analyse zeigten jedoch erneut das vollständige Fehlen des angegebenen Wirkstoffs und die Präsenz einer anderen, unbekannten Verbindung. Eine Untersuchung mittels LC-HR-MS/MS deutete darauf hin, dass diese Verbindung den Ester Metronidazolbenzoat darstellen könnte. Anschließend wurden 1D- und 2D-NMR-Spektren aufgenommen und eine de-novo-Strukturaufklärung durchgeführt. Dies bestätigte eindeutig, dass es sich bei der unbekannten Verbindung tatsächlich um den Benzoesäureester von Metronidazol handelt. Die ^{1}H- und ^{13}C-NMR-Spektren der unbekannten Verbindung und eines Metronidazol-Benzoat-Standards erwiesen sich als exakt deckungsgleich. Metronidazol hat einen bitteren Geschmack, und der kovalent gebundene

Metronidazolbenzoatester wird manchmal, sowohl in pädiatrischen Formulierungen, als auch in der Veterinärmedizin als sogenanntes Prodrug, mit einem akzeptableren Geschmack verwendet. [60] Der Metronidazolbenzoat-Gehalt der Probe QMC266 wurde mit 93 mg pro Tablette bestimmt, was in deutlichem Gegensatz zur Angabe auf dem Etikett von 200 mg freiem Metronidazol steht. Zusätzlich gibt es kaum verlässliche Daten welcher Anteil des Prodrugs tatsächlich zum freien Metronidazol metabolisiert wird. Daher muss von einer noch geringeren tatsächlichen Bioverfügbarkeit ausgegangen werden.

Insgesamt fielen von den 506 analysierten Proben 20 sowohl bei der Gehaltsprüfung als auch beim Wirkstofffreisetzungstest durch. Weitere 23 scheiterten nur bei der Gehaltsprüfung und weitere 39 nur bei der Wirkstofffreisetzung. Insgesamt entsprachen also 82 Proben (16%) nicht den Spezifikationen der jeweiligen USP-Monographie. Der Anteil minderwertiger und gefälschter Medikamente war in Kamerun (17%) und in der DR Kongo (15%) sehr ähnlich. Abbildung 5 zeigt eine Übersicht der Qualität der untersuchten Arzneimittel in Kamerun und der DR Kongo. Die allgemeine Durchfallrate von Medikamenten gegen nicht übertragbare Krankheiten lag mit 25% signifikant höher als die von Antibiotika mit 12% ($p=0,0004$). Dieser Unterschied war in der DR Kongo besonders ausgeprägt (33% gegenüber 9%; $p < 0,0001$).

Von den 31 Proben, die als Originalpräparate angegeben wurden, lag nur das gefälschte Augmentin® außerhalb der Spezifikationen. Die Durchfallrate der als Originalpräparat ausgewiesenen Proben lag daher bei 3% und damit unterhalb der Durchfallrate für Generika (17%; $p = 0,0431$). Laut Packungsangaben wurden 78 Proben, darunter 30 Originalpräparate und 48 Generika/Markengenerika in Europa hergestellt. Von diesen bestanden nur das gefälschte Augmentin® und das gefälschte Penicillin V, sowohl die Gehaltsprüfung als auch den Wirkstofffreisetzungstest nicht. Die Durchfallrate bei Arzneimitteln, die angeblich in Europa hergestellt wurden, lag insgesamt bei 5% und damit unter der Durchfallrate der in Asien hergestellten Arzneimittel (18%; $p = 0,0050$) und der in Afrika hergestellten Arzneimittel (22%; $p = 0,0042$).

Beim Vergleich der vier verschiedenen Arten von Gesundheitseinrichtungen, wurde die höchste Durchfallrate bei informellen Händlern festgestellt (28%). Die Durchfallrate

ist damit signifikant höher als die durchschnittliche Durchfallrate in den drei anderen Arten von Einrichtungen (12,3%, $p < 0,0001$). Die Durchfallrate der Arzneimittel zeigte jedoch signifikante Unterschiede zwischen den beiden Ländern. In der DR Kongo war die Durchfallrate bei Arzneimittel aus kirchlichen Gesundheitseinrichtungen (5,6%) und aus staatlichen Einrichtungen (7,1%) ähnlich, und beide Werte waren signifikant niedriger als die Durchfallrate bei informellen Anbietern (28,1%; $p=0,0005$ bzw. $p=0,0099$). Kein Einziges, der Medikamente in staatlichen oder kirchlichen Gesundheitseinrichtungen zeigte extreme Abweichungen von den USP Grenzwerten. Im Gegensatz dazu wiesen private Apotheken eine Durchfallrate von insgesamt 18,7% auf, darunter 3,3% mit extremen Abweichungen.

Im Unterschied zu der hohen Durchfallrate bei Arzneimitteln aus privaten Apotheken in der DR Kongo zeigten Medikamente aus Apotheken in Kamerun nur eine Durchfallrate von 5,7% ($p=0,018$). Bemerkenswert ist, dass von den 70 untersuchten Proben aus Apotheken in Kamerun 47 in Europa hergestellt wurden. Wie die Analyse der Verfügbarkeit und der Preise zeigte, waren die Arzneimittelpreise in den Apotheken in Kamerun deutlich höher als in anderen Arten von Gesundheitseinrichtungen und auch viel höher als in den Apotheken in der DR Kongo.

Arzneimittel aus kirchlichen Gesundheitseinrichtungen in Kamerun wiesen eine Durchfallrate von 14,1% auf, die immer noch niedriger war als die von informellen Anbietern (28,4%; $p=0,0589$). Im Gegensatz dazu wiesen die staatlichen Gesundheitseinrichtungen in Kamerun eine besorgniserregende Durchfallrate von 25% auf, was auf einen dringenden Bedarf an Verbesserungen bei der Arzneimittelbeschaffung und der Qualitätssicherung in der Lieferkette hinweist.

Die Durchfallrate der in Europa hergestellten Arzneimittel (laut Packungsangaben) lag bei 5,1% und damit deutlich unter der Durchfallrate der in Asien hergestellten Arzneimittel (17,7%; $p=0,0050$) und der in Afrika hergestellten Arzneimittel (22,2%; $p=0,0042$). Der Unterschied zwischen den Arzneimitteln aus Asien und Afrika war statistisch nicht signifikant ($p=0,385$).

		Kamerun								DR Kongo							
		N gesamt	gesamt minderwertig / gefälscht N	[%]	95% CI	in beiden Tests N	nur Gehalt N	nur Freisetzung N		N gesamt	gesamt minderwertig / gefälscht N	[%]	95% CI	in beiden Tests N	nur Gehalt N	nur Freisetzung N	
Markenbezeichnung	Generika	118	22	19%	[12.6-26.6]	12	6	4		115	12	10%	[6.1-17.4]	1	6	5	
	Markengenerika	108	19	18%	[11.6-25.8]	2	5	12		134	28	21%	[14.9-28.5]	4	6	18	
	Originator Produkte	18	1	6%	[1.0-25.8]	1	0	0		13	0	0%		0	0	0	
Kontinent	Afrika	23	6	26%	[12.5-46.5]	1	0	5		40	8	20%	[11.1-36.3]	4	2	2	
	Die Amerikas	3	0	0%		0	0	0									
	Asien	155	31	20%	[14.8-27.5]	12	8	11		201	32	16%	[11.4-21.4]	1	10	21	
	Europa	57	4	7%	[2.8-16.7]	2	2	0		21	0	0%		0	0	0	
	nicht angegeben	6	1	17%	[2.0-43.5]	0	1	0									
Einrichtung	Staatliche Gesundheitseinrichtungen	36	9	25%	[13.8-41.1]	2	2	5		42	3	7%	[24.6-19.0]	1	1	1	
	Kirliche Gesundheitseinrichtungen	71	10	14%	[7.8-24.0]	3	4	3		72	4	6%	[2.2-13.4]	1	1	2	
	Apotheken	70	4	6%	[2.2-13.8]	1	2	1		91	17	19%	[12.0-27.9]	1	7	9	
	Informelle Verkäufer	67	19	28%	[19.0-40.1]	9	3	7		57	16	28%	[18.1-40.8]	2	3	11	
Indikation	Antibiotika	152	24	16%	[10.9-22.4]	8	6	10		196	18	9%	[5.9-14.0]	2	7	9	
	Medikamente gegen nicht-übertragbare Krankheiten	92	18	20%	[12.8-28.8]	7	5	6		66	22	33%	[23.2-45.3]	3	5	14	
Lager empfehlung	Unter 25 °C	89	8	9%	[4.6-16.7]	4	3	1		50	11	22%	[12.8-35.2]	2	1	8	
	Unter 30 °C	51	5	10%	[4.3-21.0]	1	0	4		140	10	7%	[3.9-12.6]	2	2	6	
	trocken, kühl und lichtgeschützt aufbewahren	62	18	29%	[19.2-41.3]	7	6	5		70	19	27%	[18.1-38.5]	1	9	9	
	nicht angegeben	42	11	26%	[15.3-41.1]	3	2	6		2	0	0%		0	0	0	
Wirkstoff	Amoxicillin und Clavulansäure	19	5	26%	[11.8-48.8]	1	3	1		12	2	17%	[4.7-44.8]	0	0	2	
	Amoxicillin	24	2	8%	[2.3-25.8]	0	0	2		32	2	6%	[1.7-20.1]	0	0	2	
	Ciprofloxacin	25	2	8%	[2.2-25.0]	0	2	0		32	4	13%	[5.0-28.1]	0	3	1	
	Doxycyclin	22	1	5%	[0.8-21.8]	0	0	1		28	1	4%	[0.6-17.7]	0	0	1	
	Metronidazol	25	3	12%	[4.2-30.0]	0	0	3		32	5	16%	[6.9-31.8]	1	2	2	
	Penicillin V	14	7	50%	[26.8-73.2]	6	1	0		27	3	11%	[3.9-28.1]	1	2	0	
	Sulfamethoxazol und Trimethoprim	23	4	17%	[7.0-37.1]	1	0	3		33	1	3%	[0.5-15.3]	0	0	1	
	Atenolol									6	1	17%	[3.0-56.4]	0	0	1	
	Furosemid	17	1	6%	[1.0-27.0]	0	0	1		23	15	65%	[44.9-81.2]	1	1	13	
	Glibenclamid	19	6	32%	[15.4-54.0]	0	2	4									
	Hydrochorothiazid	21	0	0%		0	0	0		6	0	0%		0	0	0	
	Metformin	20	1	5%	[0.9-23.6]	0	0	1		13	1	8%	[1.3-33.3]	1	0	0	
	Salbutamol	15	10	67%	[41.7-84.8]	7	3	0		18	5	28%	[12.5-50.9]	1	4	0	
	Gesamt	**244**	**42**	**17%**	**[13.0-22.4]**	**15**	**11**	**16**		**262**	**40**	**15%**	**[11.4-20.1]**	**5**	**12**	**23**	

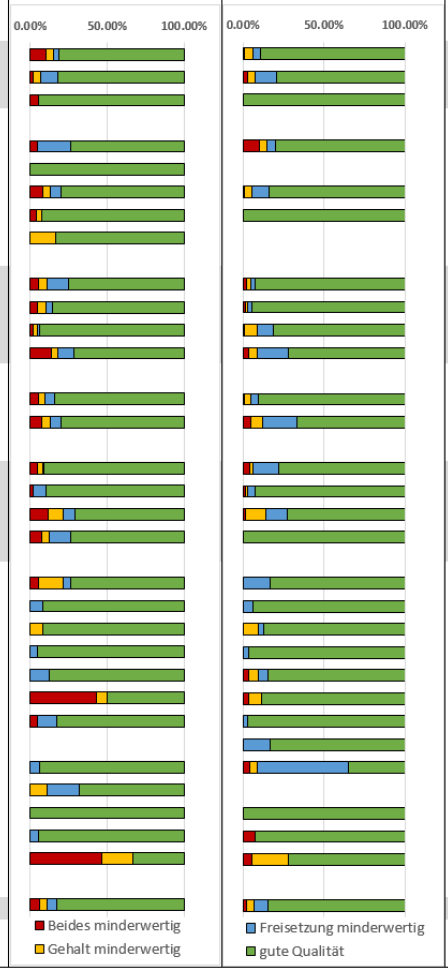

ABBILDUNG 5: ÜBERSICHT ÜBER DIE QUALITÄT DER UNTERSUCHTEN MEDIKAMENTE, ERMITTELT NACH USP. MODIFIZIERT NACH SCHÄFERMANN ET AL.[59]

Verglich man die unterschiedlichen Lagerungsempfehlungen auf den Umverpackungen, so zeigten Medikamente, die mit einer präzisen, von der WHO empfohlenen Lagerempfehlung versehen waren, d.h. entweder "Nicht über 30°C lagern" oder "Nicht über 25°C lagern", eine Durchfallrate von 10%. Diese war niedriger als bei Medikamenten, die eine weniger präzise oder keine Lagerungsempfehlung trugen (27%; $p < 0,0001$). Medikamente mit der Aufschrift "Nicht über 30°C lagern" waren jedoch qualitativ nicht besser als solche mit der Aufschrift "Nicht über 25°C lagern" (8% gegenüber 14% Durchfallrate; $p = 0,0999$).

Beim Vergleich der verschiedenen Wirkstoffe stellte sich heraus, dass bei einem einzigen Wirkstoff alle Proben innerhalb der Spezifikationen lagen, nämlich bei Hydrochlorothiazid. Auffallend dabei ist, dass von den 27 für diesen Wirkstoff untersuchten Proben 14 das Originalpräparat darstellten und zu sehr hohen Preisen verkauft wurden. Bei Penicillin-V-Tabletten war die Durchfallrate in Kamerun mit 50% höher als in der DR Kongo (11%, $p = 0,0175$). Furosemid-Tabletten zeigten in der DR Kongo eine Durchfallrate von 65%, zehnmal höher als in Kamerun (6%, $p = 0,0002$). Hier wurde der Unterschied hauptsächlich durch 11 Proben verursacht, die nach den Packungsangaben von zwei Unternehmen in Indien hergestellt wurden. Salbutamol-Tabletten zeigten in Kamerun eine Durchfallrate von 66%, was hauptsächlich auf 8 Proben zurückzuführen war, die von zwei Unternehmen in Indien hergestellt wurden. Obwohl die Durchfallrate für Salbutamol in der DR Kongo deutlich niedriger war, erreichte sie immer noch 28% ($p = 0,0383$).

UNTERSCHIEDE IN DER GEMESSENEN QUALITÄT VON ARZNEIMITTELN ZWISCHEN DEM MINILAB UND DER BESTIMMUNG NACH USP

Von den 506 gesammelten Proben wurden 451 von den lokalen Projektpartnern in Kamerun und der DR Kongo mit Hilfe der Dünnschichtchromatographie und des Zerfallstests des GPHF-Minilabs analysiert. Bemerkenswert ist, dass alle drei gefälschten Medikamente vom Minilab als gefälscht erkannt wurden, weil die Spots des deklarierten Wirkstoffs fehlten und zusätzlich in zwei Fällen das Vorhandensein von Spots unbekannter Verbindungen erkennbar war. 12 weitere Proben bestanden die DC-Analyse nicht. Drei Proben davon zeigten eine unzureichende Intensität der DC-Flecken, was auf eine unzureichende Menge des Wirkstoffs hinweist. Zwei weitere Proben zeigten zusätzliche Flecken in der DC, und bei sieben Proben wurde nicht

angegeben warum die DC-Analyse als nicht bestanden gewertet wurde. 15 Proben fielen durch den Test auf Zerfallszeit. D.h. sie zersetzten sich nicht innerhalb von 30 Minuten in 37°C warmen Wasser nach dem im GPHF-Minilab-Handbuch beschriebenen Verfahren. [61]

Insgesamt fielen 30 von 451 Proben (6,7%) bei der Minilab-Analyse durch, 15 bei der DC-Analyse und 15 beim Test auf Zerfallszeit. Keine der untersuchten Proben fiel bei beiden Tests durch. Tabelle 2 vergleicht die Ergebnisse der GPHF-Minilab-Tests mit denen der Arzneibuchanalyse nach USP.

Das Minilab ist so konzipiert, dass es keine geringen Abweichungen vom deklarierten Gehalt, d.h. Abweichungen von weniger als 20%, feststellen kann. Wie aus Tabelle 2 B hervorgeht, zeigten von 26 Proben, die eine solche geringe Abweichungen bei der Gehaltsbestimmung zeigten, nur zwei Proben bei der DC- Analyse der Minilabs auffällige Ergebnisse. Umgekehrt wurden von den 14 Proben, die Auffälligkeiten bei der DC-Analyse der Minilabs zeigten, nur für sechs der Proben diese Ergebnisse in der Arzneibuch Analyse auch bestätigt. Die Sensitivität der Minilab DC-Analyse beim Nachweis minderwertiger Medikamente mit geringen Abweichungen von den USP Spezifikationen erreicht daher letztlich nur 43%. Die Gegenüberstellung der Ergebnisse des Tests auf Zerfallszeit des Minilabs und der Untersuchung der Wirkstofffreisetzung nach USP zeigt zunächst deutlich, dass die Zerfallszeit ungeeignet erscheint um daraus die Wirkstofffreisetzung einer Probe abzuschätzen. Da bei der Messung der Zerfallszeit im Gegensatz zur Messung der Wirkstofffreisetzung nicht der Wirkstoff direkt gemessen wird, sondern nur optisch der Zerfall der Arzneiform beurteilt wird, sind die Tests ohnehin nur schwer vergleichbar. Daher war die Sensitivität des Minilabs in diesem Vergleich mit nur 9% sehr gering (Tabelle 2 C). Die Sensitivität stieg auf 36%, wenn nur erhebliche Abweichungen in der Wirkstofffreisetzung nach USP berücksichtigt wurden.

2 A) Identität

		Identität nach USP			
		Nicht bestanden	Bestanden	Gesamt	Sensitivität =100%
Identität nach Minilab	Nicht bestanden	3	0	3	
	Bestanden	0	448	448	Spezifität = 100%
	Gesamt	3	448	451	

2 B) Gehalt

		Gehalt nach USP				Identifizierung von Abweichungen nach USP	Identifizierung von „Erheblichen Abweichungen“ nach USP
		Erhebliche Abweichung	Geringe Abweichung	Bestanden	Gesamt	Sensitivität = 20%	Sensitivität = 43%
Gehalt nach Minilab	Nicht bestanden	6	2	7	15		
	Bestanden	8	24	404	436	Spezifität = 98%	
	Gesamt	14	26	411	451		

2 C) Zerfallszeit nach Minilab versus Wirkstofffreisetzung

		Wirkstofffreisetzung nach USP				Identifizierung von Abweichungen nach USP	Identifizierung von „Erheblichen Abweichungen“ nach USP
		Erhebliche Abweichung	Geringe Abweichung	Bestanden	Gesamt	Sensitivität = 9%	Sensitivität = 36%
Zerfallszeit nach Minilab	Nicht bestanden	5	0	10	15		
	Bestanden	9	40	387	436	Spezifität = 97%	
	Gesamt	14	40	397	451		

TABELLEN 2: SENSITIVITÄT UND SPEZIFITÄT DES GPHF MINILABS BEZOGEN AUF DIE ERGEBNISSE DER QUALITÄTSANALYSE NACH USP. MODIFIZIERT NACH SCHÄFERMANN ET AL.[59]

DISKUSSION

Die durchschnittliche Verfügbarkeit von Medikamenten in Kamerun und der Demokratischen Republik Kongo lag unter der von der WHO angestrebten Quote von 80%. Trotz der hohen Verfügbarkeit von Antibiotika im privaten Sektor sollte die Verfügbarkeit von Medikamenten im öffentlichen Sektor in Kamerun und der DR Kongo verbessert werden. Auch hinsichtlich der Bezahlbarkeit sind zumindest für einige der untersuchten Medikamente weitere Verbesserungen notwendig. Dies gilt insbesondere für die Medikamente gegen nicht übertragbare Krankheiten, um deren Verfügbarkeit und Erschwinglichkeit sicherzustellen. Die Verfügbarkeit von Medikamenten in der Republik Togo war zumindest in den zugelassenen Apotheken zufriedenstellend.

Keine der 94 in der Republik Togo gesammelten Arzneimittelproben war gefälscht. Alle Proben enthielten den/die deklarierten Wirkstoff/e, in einem Fall jedoch weniger als 50% der deklarierten Menge. Eine geringe Prävalenz gefälschter und minderwertiger Arzneimittel stimmt in der Tat mit anderen Ergebnissen der aktuellen wissenschaftlichen Literatur überein. [4, 34, 37, 62] In dieser Studie entsprachen 8% der untersuchten Proben nicht den USP-Spezifikationen, und 1% zeigte sogar eine extreme Abweichung von den Grenzwerten des Arzneibuchs. Diese Prävalenz steht im Einklang mit der von der WHO veröffentlichten Studie, die die Prävalenz von minderwertigen und gefälschten Medikamenten in Ländern mit niedrigem und mittlerem Einkommen auf 10,5% schätzt. [4] Die höchste Rate an gefälschten Arzneimitteln in Entwicklungsländern findet sich in der Regel bei Malariamedikamenten. [34] Im Gegensatz dazu konzentrierte sich die erarbeitete Studie in Togo auf Antibiotika und Medikamente für nicht übertragbare Krankheiten. Daher überrascht es nicht, dass die relativ geringe Anzahl von 94 Proben in der vorliegenden Studie keine gefälschte Probe enthielt. Dieser Befund beweist jedoch nicht, dass gefälschte Medikamente in Togo nicht vorhanden sind.

Die Anteile der in der Republik Kamerun (17%) und der Demokratischen Republik Kongo (15%) entdeckten minderwertigen und gefälschten Arzneimittel lagen höher als in der Republik Togo (8%), damit aber auch nahe an der von Ozawa et al. für afrikanische Länder veröffentlichten Schätzung von 18,7%. [30] Dabei wurde allerdings

deutlich, dass die Ergebnisse vieler der als minderwertig eingestuften Proben in der Qualitätsanalyse noch immer nahe an den von der USP angegebenen Schwellenwerten lagen. Diese Proben lagen damit auch innerhalb des Bereichs, der von der QAMSA-Studie der WHO vorgeschlagen wurde, um zwischen Proben zu unterscheiden, die außerhalb der Spezifikation liegen, aber nur moderate Abweichungen von den Grenzwerten des Arzneibuchs zeigen. [37] Der Anteil der mit dem Minilab nachgewiesenen minderwertigen und gefälschten Medikamente (6,7%) war geringer als der Anteil der minderwertigen und gefälschten Medikamente, die mit Hilfe der HPLC in der Gehaltsbestimmung nachgewiesen wurden (8,5%). Die Prävalenz von minderwertigen und gefälschten Arzneimitteln, die durch die Arzneibuchanalyse ermittelt wurde, verdoppelte sich sogar, wenn die Wirkstofffreisetzung mit einbezogen wurde (16,2%). Die Unterschiede zwischen der Minilab-Analyse und der Gehaltsanalyse nach Arzneibuch stehen im Einklang mit der 2017 veröffentlichten WHO-Studie, die einen durchschnittlichen Anteil an qualitativ minderwertigen Arzneimitteln von 5,0% in Studien mit dem GPHF-Minilab und einen höheren Anteil von 15,6% in Studien mit HPLC zur Bestimmung des Wirkstoffgehalts fand. [4] Die WHO-Studie beinhaltete jedoch keine Studien, die Wirkstofffreisetzung systematisch für alle Proben untersuchten. Die Ergebnisse deuten darauf hin, dass die Prävalenz von qualitativ schlechten Arzneimitteln in einigen Ländern mit niedrigem und mittlerem Einkommen höher sein könnte als die aktuelle, mittels HPLC ermittelte, WHO-Schätzung, wenn man die Wirkstofffreisetzung als Qualitätsparameter mit einbezieht.

Der Einschätzung einer WHO-Publikation [37] folgend, wurden solche Schwellenwerte für extreme Abweichungen in der vorliegenden Arbeit ebenfalls angewendet, um moderate und erheblich Abweichungen besser zu unterscheiden. Innerhalb unserer Studie zeigte eine Probe in der Republik Togo (1%), 19 Proben in der Republik Kamerun (8%) und 5 Proben in der DR Kongo (2%) solche extremen Abweichungen. Auch wenn nicht alle Medikamente extreme Abweichungen aufwiesen, sollten alle als minderwertig erkannten Medikamente als potenziell gefährlich angesehen werden.

Hervorzuheben ist auch, dass alle Antibiotika ohne Rezept in lizenzierten Apotheken und bei informellen Verkäufern gleichermaßen problemlos gekauft werden konnten. Die hohe Verfügbarkeit von Antibiotika von informellen Verkäufern ist besorgniserregend aufgrund des Potenzials der Entwicklung von Resistenzen in

humanpathogenen Organismen, die durch den unsachgemäßen Gebrauch von Antibiotika entsteht. Darüber hinaus wurde auch eine beträchtliche Menge an Penicillin V und Metronidazol-Tabletten in Kamerun und der DR Kongo als gefälscht oder minderwertig eingestuft. Subtherapeutische Dosierungen von Antibiotika hängen mit der Entwicklung von antibiotikaresistenten Bakterien zusammen. [63, 64] Die Ergebnisse legen daher nahe, dass durch die Exposition mit minderwertigen Antibiotika in Kamerun und der DR Kongo das Risiko für die Entwicklung von multiresistenten Bakterien zusätzlich erhöht sein könnte.

Die Prävalenz von minderwertigen und gefälschten Medikamenten in der DR Kongo war bei Medikamenten gegen nichtübertragbare Krankheiten (NCDs) im Vergleich zu Antibiotika um das Dreifache erhöht. Dies ist im Hinblick auf die zunehmende Belastung durch NCDs in Ländern mit niedrigem und mittlerem Einkommen alarmierend. [65, 66] Eine Studie von Antignac et al., analysierte unter anderem eine Untergruppe von Proben aus der DR Kongo, darunter Atenolol, Furosemid und Hydrochlorothiazid. [46] Zusammen mit vier anderen Herzmedikamenten war die dort berichtete Prävalenz von 26,7% minderwertiger Medikamente ähnlich der Prävalenz von 33,3%, die in der hier untersuchten Untergruppe von fünf Medikamenten gegen NCDs ermittelt wurde. Insbesondere die Qualität von Hydrochlorothiazid war in Kamerun und in der DR Kongo in dieser Studie sowie in der Studie von Antignac et al. hervorragend. [46] Wie bereits bei der Bewertung der Verfügbarkeit und Erschwinglichkeit der untersuchten Medikamente gezeigt wurde, waren vier der fünf Medikamente gegen NCDs in beiden Ländern unerschwinglich und in einigen Fällen mehr als doppelt so teuer wie die Antibiotika. Zusammenfassend lässt sich sagen, dass die in dieser Studie untersuchten Medikamente gegen nicht übertragbare Krankheiten teurer waren und eine höhere Prävalenz schlechter Qualität aufwiesen als die Antibiotika. Dies ist ein beunruhigendes Ergebnis, das die Notwendigkeit einer Verbesserung der Versorgung mit erschwinglichen und qualitätsgesicherten Medikamenten gegen NCDs unterstreichen sollte, wie bereits in den Zielen der Vereinten Nationen für nachhaltige Entwicklung und von verschiedenen anderen Autoren gefordert wurde. [9, 17, 67, 68]

Die Ergebnisse von 9% minderwertiger und gefälschter Medikamenten in der Republik Togo, 17,0% in der Republik Kamerun und 15,0% in der Demokratischen Republik Kongo zeigen, dass die Versorgung mit sicheren Antibiotika und Medikamenten gegen nicht übertragbare Krankheiten in diesen Ländern verbessert werden muss. Insbesondere der hohe Anteil an qualitativ minderwertigen Arzneimitteln gegen NCDs ist angesichts der zunehmenden Belastung durch nichtübertragbare Krankheiten in Ländern mit niedrigem und mittlerem Einkommen als alarmierend anzusehen. Darüber hinaus zeigen die Ergebnisse, dass eine schlechte Wirkstofffreisetzung ein häufiges Qualitätsproblem bei einigen Arten von Medikamenten ist, das bei künftigen Studien zur Qualität von Medikamenten nicht mehr vernachlässigt werden sollte.

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ANHANG

PLOS ONE

RESEARCH ARTICLE

Quality of medicines in southern Togo: Investigation of antibiotics and of medicines for non-communicable diseases from pharmacies and informal vendors

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Abstract

Substandard and falsified medicines represent a serious threat for public health and patient safety. Especially in low and middle-income countries, the prevalence of substandard and falsified medicines is reportedly high. However, reliable information on the prevalence of poor-quality medicines is scarce. In this study, 12 essential medicines, including antibiotics, antidiabetics, cardiac drugs and antiasthmatic drugs, were collected from six informal vendors and six licensed pharmacies in the southern part of Togo (regions Maritime and Plateaux). A mystery shopper approach was used in both types of outlets. In total, 64 samples were collected from licensed pharmacies and 30 from informal vendors. Both availability of medicines and prices of medicines were higher in licensed pharmacies than in informal vendors. 92 medicine samples were analyzed by visual examination, followed by chemical analysis for the content and for the dissolution of the active pharmaceutical ingredients according to the respective monographs of the United States Pharmacopoeia. 7 samples (8%) did not comply with the pharmacopoeial specifications, and one sample (1%) showed even extreme deviations. None of the samples was obviously falsified. However, one sample of amoxicillin capsules contained only 47% of the declared content of the active pharmaceutical ingredient, indicating that it may represent amoxicillin capsules 250 mg, rather than 500mg as declared on the label. Medicines stated to originate from Asia (i.e. mainly from India and China) showed a significantly higher proportion (24%) of non-compliant samples than those from Africa and Europe (4%, $p = 0.007$). High failure rates were observed in medicines both from informal vendors (13%) and from licensed pharmacies (5%), but the difference between both groups was not statistically significant ($p = 0.152$). The observed high prevalence of substandard medicines requires action from regulatory authorities and health care providers. Testing of selected samples for related substances indicated that inappropriate transport and storage conditions may have been an important cause for substandard quality.

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Introduction

Access to essential medicines has been included in the Millennium Development Goals (MDG) of the United Nations and is now included in the Sustainable Development Goals as Goal No. 3.8 [1]. It comprises access to medicines for both non-communicable diseases (NCD) and communicable diseases [2, 3]. Access to medicines in developing countries has improved in the past decades [4, 5]. However, at the same time the occurrence of substandard and falsified medicines has been reported frequently and has even been addressed as a "pandemic" by some authors [6]. A recent literature survey by the World Health Organization, estimated that in low and middle-income countries 10.5% of the medicines are substandard or falsified [7]. Several studies and reviews tried to estimate the prevalence for specific countries and regions and for different classes of therapeutics. A systematic review by Almuzaini et al. included eight studies conducted in sub-Saharan Africa which reported prevalence for substandard or counterfeit medicines ranging from 12.2 to 46% [8]. A meta-analysis of 21 surveys in sub-Saharan Africa concluded that 35% of antimalarial medicines had failed chemical analysis, and 20% had been classified as falsified [9]. However, other studies reported a much lower prevalence of falsified medicines. In several studies by the ACT Consortium Drug Quality Program (ACTcDQP), only 98 (0.97%) out of 10,079 antimalarial medicine samples from six developing countries were reported to be falsified [10]. An investigation by the World Health Organization in six countries of sub-Saharan Africa found only 2 (0.2%) out of 935 antimalarial medicine samples in which a stated active ingredient was missing entirely [11]. Several authors emphasize that there is still a severe lack of reliable data on the prevalence of substandard and falsified medicines [8]. The report of the Lancet Commission on Essential Medicines also concluded that so far, the true extent of this problem remains unknown [12]. Also the above-mentioned literature survey by the WHO discusses the problem of the strong heterogeneity of the available studies [7].

Until recently, the lack of internationally agreed definitions of substandard and falsified medicines further complicated the comparison of data on their prevalence. This situation has recently been remedied by the World Health Organization [13]. The misleading term"counterfeit medicines" as well as the provisional term "substandard/spurious/falsely labelled/falsified/counterfeit (SSFFC) medical products" have been replaced by "substandard and falsified medical products" [13, 14]. Notably, "substandard" and "falsified" are now defined as mutually exclusive classifications. Falsified medical products are "deliberately/fraudulently misrepresenting their identity, composition or source", while substandard medical products fail to meet their quality standards or specifications for other reasons than deliberate intent, e.g. due to unintentional shortcomings in the manufacturing process, or due to degradation caused by inappropriate storage conditions. Differentiation between falsified and substandard medicines therefore requires knowledge or clues of the (honest or fraudulent) intentions of the manufacturer, and is not possible on the basis of chemical analysis alone [15].

Most published studies on substandard and falsified medicines have focused on anti-malarials, some on antibiotics and antivirals, but data on medicines for non-communicable-diseases are rare [16, 17]. This is in contrast to the importance of non-communicable diseases also in developing countries. The last report published by the MDGs Gap Task Force in 2015 noted that up to 80% of the deaths from non-communicable-diseases world-wide occur in low-and middle-income countries [18, 19].

The institutional capacity and the resources to monitor the quality of the pharmaceuticals are diverse in between different African countries. Several East-African countries have successfully strengthened their regulatory authorities [20], other African countries still struggle with the implementation of a regulated supply of medicines. For this and for other reasons, the

prevalence of substandard and falsified medicines is very different in between African countries [10, 11]. Tabernero et al. noted that there is a severe lack of knowledge on the prevalence of substandard and falsified medicines in quite a number of African developing countries, including Togo [21].

Only very few studies investigated substandard and falsified medicines in the Republic of Togo so far. In 2014, an evaluation of the quality of artemisinin-based antimalarials was conducted in Ghana and Togo. It reported that 83.7% of artemisinin based combination therapies and 57.9% of the artemisinin-based monotherapies failed to comply with International Pharmacopoeia requirements due to insufficient content of the active pharmaceutical ingredient (API) [22]. The recently published quality evaluation of cardiac medicines in ten countries of Africa [17] also included 100 samples deriving from Togo. It concluded that 9% of the samples deriving from Togo where poor quality drugs. Also a study on the quality of veterinary medicines was carried out in the northern part of Togo [23].

The objective of the present study was to contribute to the knowledge about the prevalence of substandard and falsified medicine in the Republic of Togo, including both anti-infective medicines and medicines for non-communicable diseases. Medicines were sampled from the private sector, i.e. licensed pharmacies, and informal vendors, in several towns in the southern part of Togo.

Methods

Study design

Collection of the samples took place in February 2017. The study protocol was based on the guidelines on the conduct of surveys of the quality of medicines, published by the WHO in 2016 [24] and the MEDQUARG guidelines [25]. Seven antibiotics and five medicines against non-communicable diseases were included in this study, all of them contained in the list of essential medicines of the Republic of Togo [26]. These 12 medicines were solid oral dosage forms of amoxicillin, amoxicillin/ clavulanic acid, sulfamethoxazole/trimethoprim, ciprofloxacin, phenoxymethylpenicillin (penicillin V), metronidazole, doxycycline, metformin, atenolol, hydrochlorothiazide, furosemide and salbutamol (albuterol.) For each medicine, a preferred strength and dosage form (tablet or capsule) was defined which the local investigator asked for at every sampling site. If this was not available, another strength or another solid oral dosage form was collected.

The samples were collected in the southern part of Togo, in the regions Maritime and Plateaux. In Lomé the local investigator asked several citizens for well stocked informal drug vendors in the south of Togo. Five such vendors were named in the region Maritime located in Lomé Centre, in the suburbs Agoe-nyvie and Agoe-laogope, as well as in the towns Tsévié and Tabligbo, 30 km north and 75 km northeast of Lomé, respectively. Furthermore, one vendor was named located in the town of Kpalimé, 120km northwest of Lomé and close to the border to Ghana, in the region Plateaux. S1 Fig (Supporting Information) shows a map of these locations. The informal vendors operated in small shops located away from the main shopping roads. Such non-accredited medicine stores in Togo and neighboring countries have been described already in earlier studies [22, 23]. While visiting each of the six chosen informal drug outlets, the investigator identified the geographically nearest licensed pharmacy. A list of licensed pharmacies in Togo is available in the internet [27], and indeed all six pharmacies named by the local citizens were found in this list, but none of the informal vendors. Licensed pharmacies operated in premises with good professional appearance, located at major shopping roads. In both types of sampling sites the investigator acted as a customer and purchased a quantity of 100 tablets or capsules for each of the 12 medicines, if available. If the vendor

asked for the purpose of the purchase, the investigator stated that these medicines were intended for use in a local medical facility operated by a relative. If the quantity of 100 tablets or capsules per medicine was not available, a smaller quantity was purchased, but not less than 30 tablets or capsules to ensure a sufficient amount for chemical analysis. At each of the twelve sampling sites, prices and quantities of purchased medicines were recorded. Each sample was collected and stored in the original primary and secondary packaging if possible. If no primary or secondary packaging was available, the samples were stored in light protective screw-cap bottles. An adhesive label with a unique sample number was attached to the primary or secondary packaging of each sample. The samples were stored at a cool and dry place and transported to the University of Tuebingen, Germany, within three weeks after collection. There, all medicines were stored at 21˚C in an air-conditioned room until analysis.

Sample size calculation

The sample size calculation was based on the hypothesis that the proportion of out-of-specification medicines would be higher in medicines from informal vendors than in medicines from licensed pharmacies. Estimating the proportions to be 10% in medicines from licensed pharmacies and 40% in medicines from informal vendors, the sample size required to observe a significant difference between these group with 95% confidence and a power of 80% resulted as 29 samples per group, using the following formula:

$$n = (Z_{\alpha/2} + Z_{\beta})^2 * (p_1(1 - p_1) + p_2(1 - p_2))/(p_1 - p_2)^2,$$

where $Z_{\alpha/2}$ is the critical value of the Normal distribution at $\alpha/2$ (e.g. for a confidence level of 95%, α is 0.05 and the critical value is 1.96), Z_{β} is the critical value of the Normal distribution at β (e.g. for a power of 80%, β is 0.2 and the critical value is 0.84) and p_1 and p_2 are the expected sample proportions of the two groups [28].

We decided to attempt the collection of 12 medicines from 6 facilities, i.e. 72 samples, from each group, in order to allow for a contingency since not all medicines were expected to be available in each of the sampling sites.

Medicine quality analysis

Analysis was performed at the Pharmaceutical Institute of Tuebingen University. Prior to chemical analysis, the packaging of each sample was visually examined. Sample number, brand name, type of medicine (originator, branded generic or generic), batch number, manufacturing date, expiry date, name of marketing authorization holder (MAH), name of manufacturer, international non-proprietary names (INN) of the active pharmaceutical ingredients (APIs), dosage form, strength, type of packaging material or container (primary and/or secondary packaging), presence of a leaflet for patients, and price per dosage form were recorded on a standardized form. Digital photos showing the tablets or capsules, the primary packaging, the leaflet, the secondary packaging and the sample number were taken and archived.

Chemical analysis was carried out according to the methods specified in the monographs of the United States Pharmacopoeia 2016 (USP 39) for the respective dosage forms for each of the 12 medicines. The chemical quality assessment included the determination of identity, assay (content of API) and dissolution (proportion of API dissolved from the dosage form over time). Following the respective monographs of the USP 39, the assay (quantification of the content of the API) was carried out by HPLC for all investigated medicines, and dissolution of the API was quantified by HPLC for all investigated medicines except metformin, which was quantified by UV spectroscopy.

Validation of the assay procedures according to USP using medicines purchased in Germany showed good reproducibility of the results. In contrast we initially noticed high variability of the assay results from some of the samples collected in Africa, e.g. of amoxicillin/ clavulanic acid tablets. Further investigation showed that a more thorough mechanical disintegration of these tablets was required in the sample preparation, to yield complete and reproducible detection of the API content. USP specifies these mechanical disintegration procedures only in general terms. ("dissolve not less than 10 tablets in water with the aid of mechanical stirring"). According to our observations, tablets which have been stored under tropical climates require thorough mechanical disintegration in order to achieve correct assay results, and the same observation has recently been reported by Mufusama *et al.* [29].

One sample of amoxicillin (QEW067) was found to contain only 47% of the declared API content; it was tested for content uniformity according to the method for of USP 39, determining the contents of 10 tablets individually. Furthermore, for two samples of amoxicillin/ clavulanic acid and one sample of hydrochlorothiazide tablets, content uniformity was investigated by analyzing 10 tablets individually, after sample preparation with a Branson 250 Sonifier (Emerson Industrial Automation, St. Louis, MO, USA) pulsing at 70% power, in an interval of 10 seconds with 10 seconds intermission for a total duration of three minutes using the same solvent as stated in the USP39 monograph. HPLC analysis according to USP showed a high uniformity of the content (QEW002, amoxicillin SD = 0.70%, clavulanic acid SD = 2.46%; QEW041, amoxicillin SD = 2.63%; clavulanic acid SD = 2.44%; QEW074, hydrochlorothiazide SD = 1.70%, respectively). The assay value reported in this study for these three samples is therefore the average of the 10 individual measurements for each sample.

All methods were validated according to USP instructions for system suitability and the Q2 Guideline of the International Council for Harmonization [30]. HPLC analysis was carried out using an Agilent 1100 HPLC (Agilent Technologies, Santa Clara, CA, USA) and the columns, mobile phases and UV-detection wavelengths specified in the USP 39. UV spectroscopy was carried out using a Perkin-Elmer Lambda 125 UV spectrophotometer (Perkin-Elmer, Waltham, Massachusetts, USA). Dissolution testing was performed using a PTWS 610 Dissolution Testing apparatus (Pharma Test Apparatebau AG, Hainburg, Germany).

Definition of compliance of samples with specifications

The USP 39 criteria of the respective monographs were followed in assessing compliance or non-compliance of the investigated samples. The limits for compliance stated by the USP 39 are different for different APIs and are summarized in Table 1. Samples falling outside of these limits were considered as non-compliant.

As proposed by a study published by the WHO in 2011 [11], the non-compliant samples were further divided into those showing only moderate deviations from the USP 39 criteria, and those showing extreme deviations. As suggested by the mentioned WHO study, extreme deviation was defined as the content of API deviating more than 20% from the declared content and/or the average dissolution of the tested units falling more than 25% below the pharmacopoeial limit (i.e. below the pharmacopoeial Q-value minus 25%).

For the combined results, a sample was rated as "non-compliant" if either assay or dissolution or both tests had failed.

Testing for related substances

Selected samples containing amoxicillin were tested for related substances following the method stated in the USP 39 monograph for amoxicillin trihydrate. HPLC peaks of possible degradation products observed in these samples were compared to peaks appearing in

Table 1. Limits for compliance according to United States Pharmacopoeia 39 [% of declared content].

API	assay	dissolution
Amoxicillin	90–120	75
Amoxicillin / clavulanic acid	90–120	85/80
Penicillin V	90–120	75
Ciprofloxacin	90–110	80
Sulfmethoxazole / trimethoprim	93–107	70/70
Metronidazole	90–110	85
Doxycycline	90–120	80
Metformin	95–105	70
Atenolol	90–110	80
Hydrochlorothiazide	90–110	60
Furosemid	90–110	80
Salbutamol	90–110	80

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reference tablets that had been subjected to forced degradation at 80˚C in a drying oven for 4 days [31]. As explained above, in this study, the classification as compliant or non-compliant was based only on identity, assay and dissolution without considering the absence or presence of related substances, since only few samples were tested for related substances.

Calculation of medicine prices

The prices of all samples were recorded in local currency (CFA francs). The price per dosage form was calculated in US $ with the exchange rate [CFA] to [US $] of 01.02.2017 (1 CFA = 0.00163428 $). As suggested by the WHO/HAI manual on measuring medicines prices [32] a Median Price Ratio (MPR) was calculated, i.e. the ratio of the observed median price of a medicine to an international reference price. As recommended by the WHO/HAI manual, the median supplier price from the MSH 2015 international medical products price guide [33] was chosen as international reference price. If medicines of different strengths were collected, median prices and MPRs were calculated individually for each strength.

Statistical analysis

Statistical analyses were performed using MedCalc (MedCalc Software, Ostend, Belgium) [34, 35].Comparisons of proportions were evaluated by the "N-1" Chi-squared test as recommended by Campbell (2007) and Richardson (2011) [36, 37]. Confidence intervals were calculated as the "exact" Clopper-Pearson confidence interval for the observed proportion [38, 39]. Prices of medicines were compared to an international reference price (see above), and differences of the resulting price ratios were evaluated using the Kruskal-Wallis test.

Results

Overview of collected samples

In this study 12 different medicines were collected from six licensed pharmacies and six informal vendors, resulting in a theoretical total of 144 samples. Because not all sampling sites had all medicines in stock, we were able to purchase a total of 89 samples. Visual examination showed that two samples contained blisters from two different manufacturers and one sample even from three different manufacturers, sold together in one secondary packaging. One further sample contained blisters from the same manufacturer but with two different batch

Table 2. Overview of medicine samples collected and analyzed.

Active pharmaceutical ingredient of the sample	Licensed pharmacies	Informal vendors	Total	No. of commercial preparations (brands)	No. of batches
Amoxicillin	6	6	12	6	11
Amoxicillin / clavulanic acid	7	0	7	5	7
Phenoxymethylpenicillin	2	1	3	2	2
Ciprofloxacin	7	6	13	8	11
Doxycycline	8	3	11	5	7
Sulfamethoxazole / trimethoprim	5	1	6	3	5
Metronidazole	6	6	12	4	6
Atenolol	6	1	7	1	3
Furosemide	6	4	10	5	6
Hydrochlorothiazide	3	1	4	3	4
Metformin	6	1	7	1	5
Salbutamol	2	0	2	1	1
Total	64	30	94	44	68

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numbers. All these four samples had been obtained from licensed pharmacies. The different blisters of these four purchases were separated and analyzed as separate samples. Thereby, the total numbers of samples of this study increased from 89 to 94. For two of these samples the number of tablets was insufficient for analysis according to USP 39. These two samples were analyzed, but their results were excluded from overall data evaluation and statistical analysis.

In one case, hydrochlorothiazide was requested, but actually a combination product containing hydrochlorothiazide 25 mg and captopril 50mg (Ecazide, BristolMyers Squibb) was obtained. This sample was analyzed according to the methods for hydrochlorothiazide tablets (and found to be compliant with the specifications), but it was excluded from the analysis of prices.

As shown in Table 2, the 94 samples represented 44 different commercial preparations (brands) and a total of 68 different batches. According to the information given on the labels, they were produced by 26 different manufacturers in 12 different countries. Table 3 shows that most of the medicines sold in private pharmacies were from European countries, while most of the medicines sold by informal vendors were produced in African countries. Most of the

Table 3. Comparison of medicine samples from licensed pharmacies and informal vendors.

	Licensed pharmacies	Informal vendors
Stated origin of medicines		
- Africa	8 (13%)	19 (63%)
- Asia	11 (17%)	7 (23%)
- Europe	45 (70%)	4 (13%)
Type of medicine		
- generic	44 (69%)	25 (83%)
- branded generic	13 (20%)	5 (17%)
- originator	7 (11%)	0 (0%)
Packaging of purchased sample		
- primary and secondary packaging (blister strips and cardboard boxes)	55 (86%)	11 (37%)
- only primary packaging (blister strips)	9 (14%)	18 (60%)
- no original packaging (sold in plastic bag)	0 (0%)	1 (3%)

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samples (69 out of 94, i.e. 73%) were generic medicines sold under the international nonproprietary name of their active pharmaceutical ingredient, while 19% were so called branded generics, and only 7 samples (7%) were originator products. All seven originator medicines were obtained in licensed pharmacies. A complete list of all 94 samples, including the results of chemical analysis is shown in S1 Table (Supporting Information).

In the six visited pharmacies, on average 10 of the 12 investigated medicines were available (range 8–12 medicines). In the six informal vendors, on average only five medicines were available (range 3–8 medicines). The highest availability was observed for amoxicillin, ciprofloxacin and metronidazole.

S2 Table (Supporting Information) compares the prices of the medicines in licensed pharmacies and informal vendors. Overall, the prices in licensed pharmacies were very similar to those observed previously in the private health care sector in low- and middle- income countries [40]. Prices in informal vendors were cheaper than those in licensed pharmacies by 41%. Further details are given in the legend of S2 Table.

As shown in Table 3, the majority (86%) of samples obtained in private pharmacies were sold with their primary or secondary packaging, i.e. blister stripes and cardboard box. However, the informal vendors sold most of the samples (60%) without secondary packaging. One sample was even dispensed without primary and secondary packaging, i.e. in a plastic bag. Since this sample represented furosemide tablets which are light sensitive, this packaging is in contrast to the requirements specified in the USP 39 monograph. Notably, four further samples of furosemide tablets (two from licensed pharmacies, two from informal vendors) were sold without secondary packaging in clear transparent blisters without light protection, also violating USP39 requirements.

Expiry dates

None of the samples were expired at the time of purchase. The remaining shelf life of the medicines ranged from 1 to 53 months, with a median of 26 months. 11 samples, produced by Denk Pharma (Germany), Aldo Union (Spain) and Roche (France), had remaining shelf lives of more than 36 months, showing that the manufacturers had decided to state quite long shelf lives for these products.

Packaging analysis and visual inspection

Inspection of the primary and secondary packaging, of package leaflets and of batch numbers and expiry dates showed no mistakes or inconsistencies which are frequently found in falsified medicines [15, 41]. Therefore, packaging analysis did not indicate the presence of any obviously falsified medicines. Visual inspection of the dosage forms showed a strong discoloration in one sample of doxycycline tablets, depicted in S2 Fig. This sample had contained blisters with two different batch numbers in one secondary packaging, as mentioned above. While the blisters with uniformly colored tablets (exp. date 05.2019) were found to comply with the USP39 specifications, the blister with ten darkened, spotted tablets (exp. date 12.2017) showed extreme deviations from the USP39 specifications (55% of stated content of doxycycline).

Chemical analysis

As explained above, four samples consisted of blisters of more than one batch and therefore the blisters were analyzed as distinctive samples. For two of the resulting samples (including the ten darkened, spotted doxycycline tablets mentioned above) the number of tablets was too small to perform a complete chemical analysis according to the USP 39. The results of these

Table 4. Compliance of medicine samples with the criteria of the United States Pharmacopoeia 39.

API of sample		Non-compliant in assay (number of samples)		Non-compliant in dissolution (number of samples)		Non-compliant, total	
	Total number	Moderate deviation	Extreme deviation	Moderate deviation	Extreme deviation	Number of samples	%
Amoxicillin	12	2	1	1	1	3	25%
Hydrochlorothiazide	4	1	0	0	0	1	25%
Ciprofloxacin	13	3	0	0	0	3	23%
Amoxicillin/clavulanic acid	6	0	0	0	0	0	0%
Doxycycline	10	0	0	0	0	0	0%
Metronidazole	12	0	0	0	0	0	0%
Phenoxymethylpenicillin	3	0	0	0	0	0	0%
Sulfamethoxazole/ Trimethoprim	6	0	0	0	0	0	0%
Atenolol	7	0	0	0	0	0	0%
Furosemide	10	0	0	0	0	0	0%
Metformin	7	0	0	0	0	0	0%
Salbutamol	2	0	0	0	0	0	0%
Total	**92**	**6**	**1**	**1**	**1**	**7**	**8%**

The limits for compliance of the USP39, and for extreme deviation according to a WHO publication [11], are explained in the methods section.

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two samples were therefore excluded from the evaluation of the results, leaving 92 samples for overall data evaluation.

Notably, in none of the 92 samples the stated API was absent, and in only one sample the content of API was lower than 80% of the declared content. Out of the total of 92 samples, 85 (92%, 95%CI = 85–97%) complied with the specifications of USP 39 for both, assay (= content of API) and dissolution. However, 6 samples (7%, 95%CI = 2–14%) showed moderate deviations and 1 samples (1%, 95%CI = 0.03–6%) showed extreme deviations. Table 4 summarizes the results for the 12 tested medicines. Non-compliant samples were observed for amoxicillin, hydrochlorothiazide and ciprofloxacin, but not for any of the other nine investigated medicines. Of the 7 non-compliant samples, 5 failed only in assay, while 2 failed in both criteria. The data summarized in Table 4 are shown in detail in Figs 1 and 2.

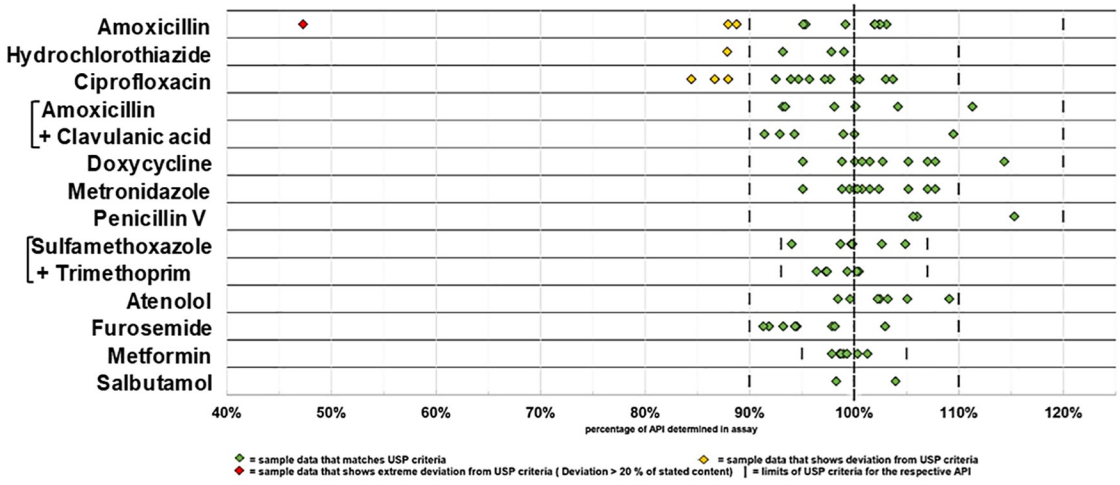

Fig 1. Content of the active pharmaceutical ingredient determined for each sample.

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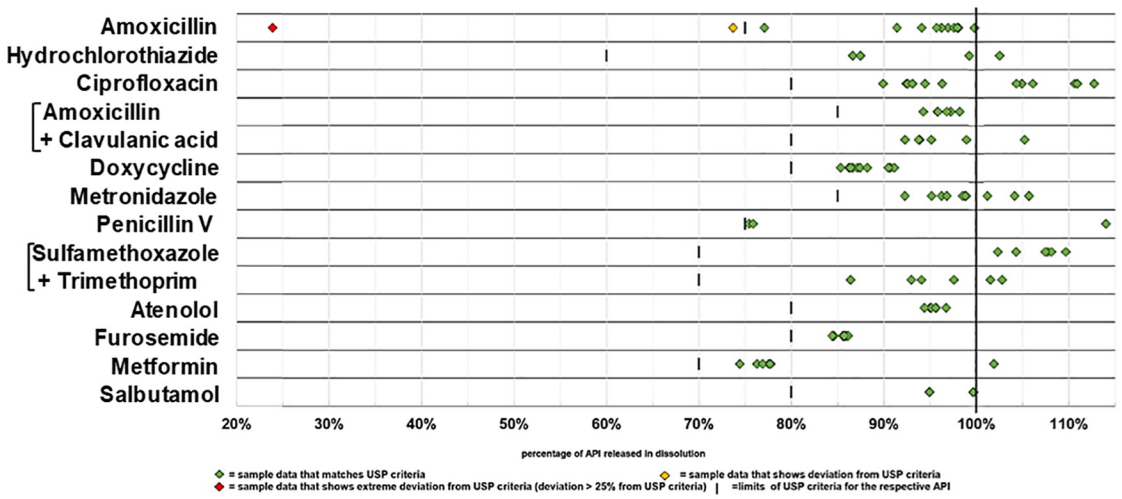

Fig 2. Dissolution of the active pharmaceutical ingredient determined for each sample.

https://doi.org/10.1371/journal.pone.0207911.g002

Table 5 lists the results of the chemical analysis for each of the 26 stated manufacturers located in 12 countries on three continents. Notably, the highest failure rate was observed in samples deriving from Asia (24% non-compliant). This is markedly higher than the failure rate of the other samples of this study (average 4%) and this difference is statistically significant ($p = 0.007$). 18 samples had been produced in Togo itself, including 15 from a single Togolese manufacturer. All of the samples produced by that company complied with the USP specifications. This shows an encouraging achievement of international quality standards by this local manufacturer.

As mentioned above, this study included 7 originator medicines, all of them obtained in licensed pharmacies and (according to the label information) produced by multinational pharmaceutical companies. One of these seven products failed USP 39 specifications (87.9% of the stated API content determined in assay), while another sample of the same brand with the same expiry date passed all pharmacopoeial tests. We speculate that the poor quality may be the result of inappropriate transport and storage conditions of the individual sample. Fig 3 shows the prevalence of non-compliant medicines, grouped according to different criteria. Generic medicines showed a lower percentage of non-compliant and extremely deviant samples than branded generic medicines or originator products. Medicines obtained from licensed pharmacies showed a lower failure rate than those from informal vendors (5% *versus* 13% non-compliant). However, the difference between the failure rates in licensed pharmacies and informal vendors did not reach statistical significance ($p = 0.152$).

Quality problems were found both in antibiotics and in medicines for non-communicable diseases (10% and 3% non-compliant, respectively), but the difference between both groups was not statistically significant ($p = 0.285$).

The frequency of non-compliant samples was not significantly related to the selling price of the medicines (Fig 3). Non-compliant medicines were found in two of the six investigated pharmacies, and in three of the six investigated informal vendors.

Testing for thermal degradation products of amoxicillin

In order to provide some first evidence whether inappropriate storage and/or transport conditions may have contributed to the substandard quality of some of the investigated medicines, we analyzed several amoxicillin samples for the presence of thermal degradation products of

Table 5. Stated origin and manufacturers of medicines, and compliance with USP 39 criteria.

Stated origin	Stated manufacturer	Total samples	Non-compliant samples	% non-compliant	Extreme deviation	% extreme deviation
Togo	Tongmei	15	0		0	
	Sprukfield	3	1		0	
	total	**18**	**1**		**0**	
Benin	Pharmaquick	**5**	**0**		**0**	
Ghana	Letap	**3**	**0**		**0**	
Nigeria	Nuel Pharma	**1**	**1**		**0**	
Africa		**27**	**2**	**7%**	**0**	**0%**
India	Lincoln Pharma	6	1		0	
	Alice	1	0		0	
	Cian	1	1		0	
	CIPLA	1	0		0	
	Fourrts	1	0		0	
	Medopharm	1	0		0	
	total	**11**	**2**		**0**	
China	Greenfield	1	0		0	
	North China Pharmaceutical	3	1		0	
	Yangzhou NO.3	1	1		1	
	total	**5**	**2**		**1**	
Turkey	Billim	**1**	**0**		**0**	
Asia		**17**	**4**	**24%**	**1**	**6%**
France	Baily-Creat	13	0		0	
	GSK-France	3	0		0	
	Roche	1	0		0	
	total	**17**	**0**		**0**	
Germany	Denk Pharma	16	0		0	
	Philco Pharma	1	0		0	
	total	**17**	**0**		**0**	
Austria	Sandoz GmbH	**8**	**0**		**0**	
Spain	Aldo-Union	2	0		0	
	Novartis	2	1		0	
	total	**4**	**1**		**0**	
Italy	Bristol Myers Squibb	1	0		0	
	F.I.R.M.A S.p.A	1	0		0	
	total	**2**	**0**		**0**	
Europe		**48**	**1**	**2%**	**0**	**0%**
Total		**92**	**10**	**11%**	**1**	**1%**

https://doi.org/10.1371/journal.pone.0207911.t005

the API. First, reference tablets of amoxicillin were subjected to a forced degradation (four days in a drying oven at 80˚C). HPLC analysis according to the method for "related substances" of the USP 39 monograph for amoxicillin trihydrate showed that this treatment led to a reduction of the HPLC peak corresponding to amoxicillin (retention time 7.5 min) by 23%, with the concomitant appearance of a new peak at 48 min (peak area a 230 nm: 2.0% of amoxicillin peak).

Three compliant samples of amoxicillin, and one non-compliant sample showing an insufficient amount of the API, were investigated for the presence of this peak at 48 min. The peak was clearly detected in the non-compliant sample, amounting to 2.0% of the peak area of amoxicillin. The amount of this specific impurity in the non-compliant sample indicates that

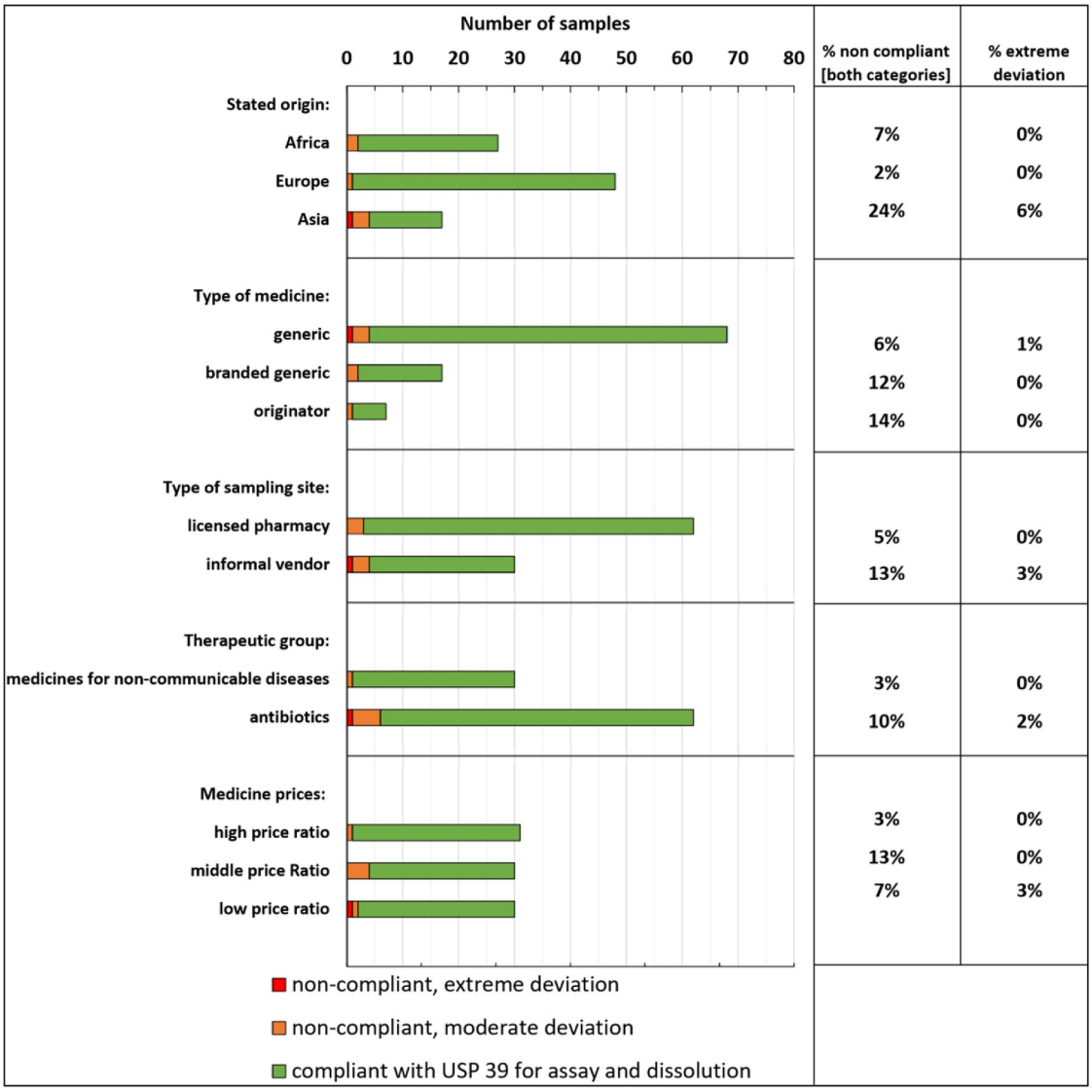

Fig 3. The prevalence of non-compliant medicines grouped according to different criteria.

https://doi.org/10.1371/journal.pone.0207911.g003

amoxicillin had undergone some thermal degradation either before or (more likely) after manufacturing of the tablets.

In contrast two compliant samples showed only traces of this peak (< 0.1% of the peak area of amoxicillin), while the third compliant sample did show the peak of the decomposition product (1.8% of the peak area of amoxicillin).

Discussion

None of the 94 medicine samples collected in this study was obviously falsified, as judged from packaging analysis. All samples contained the declared active pharmaceutical ingredient(s), though in one case less than 50% of the declared amount (Fig 1). A low prevalence of falsified medicines is indeed consistent with results from the current scientific literature [7, 10, 11, 15]. Usually the highest rate of falsified medicines in developing countries is found in antimalarial medicines [15]. In contrast, the present study in Togo focused on antibiotics and medicines

for non-communicable diseases. Therefore, the finding that the relatively small number of 94 samples in the present study did not include an obviously falsified sample is not a surprise. This finding does not, however, prove that falsified medicines are absent in Togo. Higher sample numbers and e.g. the inclusion of antimalarials, would most likely show the presence of such medicines [7, 15].

As mentioned above, one sample of amoxicillin capsules contained only 47% of the decared content of the active pharmaceutical ingredient, and the analysis of 10 individual capsules showed a high uniformity of this individual content (SD = 1.72%). This indicates that this sample may have been manufactured as 250mg amoxicillin trihydrate capsules, rather than 500mg as declared on the label. This may represent a deliberate misrepresentation of its composition, i.e. a falsified medicine.

In this study, 8% of the investigated samples did not comply to USP 39 specifications (in assay, dissolution, or both), and 1% showed even an extreme deviation from the pharmacopoeial limits. This prevalence is consistent with recent review published by the WHO which estimated the prevalence of substandard and falsified medicines in low and middle income countries to be 10.5% [7].

It should be noted that a meaningful comparison of failure rates in between different medicine quality surveys in the literature is very difficult. As correctly stated in the recent literature survey by the WHO [7], different studies use different sampling approaches, different analytical techniques, they include or ignore different pharmacopoeial criteria (e.g. dissolution of API) and they use different thresholds for the percentage of the API in order to classify a sample as "within specification" or "out of specification". In the present study, we investigated the identity, the quantity and dissolution of the API, and followed the analytical methods and the thresholds specified in by the United States Pharmacopoeia 39 (USP 39). The limits for compliance given by the USP 39 are similar to those specified in the International Pharmacopoeia and usually wider than the limits specified by the British Pharmacopoeia.

As noted in the recent literature survey by the WHO [7], most publications of substandard and falsified medicines only state a pass or fail for a chosen threshold, rather than giving actual percentage of the API determined. For the present study, we depicted the actual percentage of the content of API, and of the percentage of the API dissolved in the dissolution test, for all 92 samples in Figs 1 and 2 as well as in the S1 Table. As strikingly obvious from these figures, the results for assay and dissolution are distributed over a wide range, and the percentage of "substandard medicines" depends on the threshold applied in the respective study. In order to improve the comparability of different studies on the quality of medicines, a general reporting of the percentages of the API detected in the individual samples, e.g. as shown in Figs 1 and 2, may be useful.

As mentioned in a previous publication by the World Health Organization [11], the observed quality failure rates of medicines cannot always be directly related to therapeutic failures of these medicines. Following that WHO publication, however, we used thresholds for extreme deviations which may be associated with health implications. Within our study, one sample (1%) showed such extreme deviations.

In accordance with our expectations, the failure rate observed in medicines from licensed pharmacies was lower than that from informal vendors, but the difference was smaller than expected and did not reach statistical significance. Notably, the sample showing extreme deviations had been obtained from an informal vendor.

Medicines stated to originate from Asia (i.e. mainly from India and China) showed a significantly higher failure rate than those from Africa and Europe. India certainly has excellent pharmaceutical manufacturers and plays an important role in providing quality generic medicines at low prices to developing countries [41, 42]. However, our study indicates that some

manufacturers in India and China supply medicines to Africa which turn out to be substandard. It should be in the interest of regulatory authorities and professional organizations of Asian and African countries to minimize such problems by appropriate regulations and procurement practices, including supplier prequalification schemes.

Several findings reported in the Results section indicate that degradation, possibly due to inappropriate storage and transport conditions, may have contributed to the substandard quality of some of the samples. Notably, the labels of 43 of the 94 samples in this study stated that the products should be stored below 25˚C. Yet, none of the investigated licensed pharmacies and informal vendors used an air condition. According to the ICH Quality Guidelines [43], Togo is assigned to climatic zone IV, and long term stability of medicines for use in Togo should be demonstrated at 30˚C and 65% relative humidity by the manufacturer. Improvements in regulation and in procurement practice should ensure that only medicines which are compliant in such stability tests are imported to Togo. Health care providers need to pay attention to storage requirements stated on the medicine packages, and either improve the storage conditions in their premises or restrict their selection of medicines to those which do not require storage below 25˚C.

Notably, all antibiotics could be purchased without prescription from licensed pharmacies and informal vendors with equal ease. The high availability of antibiotics from informal vendors is worrisome due to the potential of antimicrobial resistance arising from the inappropriate use of antibiotics.

Limitations of this study

The small size (n = 94 samples) presents a principal limitation of this study which was funded exclusively by intramural funds of Tuebingen University. This study was powered to prove an expected difference of 30 percent in the prevalence of poor quality medicines between pharmacies and informal vendors and was insufficiently powered to prove smaller differences in other sub-group analyses. Alternative approaches within the limits of the available budget may have been a concentration on fewer types of medicines (e.g. just two to four rather than 12 types), or the omission of the time-consuming and expensive dissolution testing in the chemical analysis. However, also these alternatives would have had obvious and strong disadvantages. Another principal limitation of this study is the non-random selection of sampling sites which implies that the results cannot be regarded a representative. In any medicine quality study which includes informal vendors, random sampling of these sites is impossible as there is no reliable list of such illegal facilities. We purposefully identified informal vendors which were reported to be well-stocked, in order to ensure that sufficient numbers of samples of the 12 different medicines could be collected. This may introduce a bias since medicine quality may be different between large and small informal vendors. A list of licensed pharmacies in Togo is published on the internet [27] by a private medicine wholesaler; therefore, an alternative approach would have been a random selection of licensed pharmacies from that (unofficial) list, followed by identification of the nearest informal vendor to that pharmacy. On the other hand, this may have introduced other biases, e.g. in favor of more affluent regions where most licensed pharmacies are located. An additional limitation is that this study sampled medicines only from licensed pharmacies and informal vendors, not from other sectors of the pharmaceutical supply system. And while this study included testing for identity, content and dissolution of the APIs, it did not comprehensively include other criteria such as testing for related substances or content uniformity. As emphasized in a recent WHO publication [7], further studies are required which can provide reliable estimates of the prevalence of substandard and falsified medical products, by product type, geographical distribution and severity of

deviation from the pharmacopoeial standards, in Togo as well as in other low- and middle-income countries.

Supporting information

S1 Table. Complete list of all 94 samples.
(XLSX)

S2 Table. Prices of the medicines in licensed pharmacies and informal vendors.
(DOCX)

S1 Fig. Map of the sampling sites in the regions Maritime and Plateaux of the Republic of Togo.
(DOCX)

S2 Fig. Discoloration discovered upon visual inspection of a sample of doxycycline tablets.
(DOCX)

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Author Contributions

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	S1 Table	Overview of all samples														
Sample ID	Name of product	Stated API	Therapeutic class *1*	Stated amount of API [mg]	Dosage Form	Sample site	Site Type	Region of sample site	Obtained quantity [tabs./caps.]	Stated manufacturer	Stated country of origin	Batch number	Manufacturing date	Expiry Date	Shelf life remaining at collection [months]	Stated storage requirements
QEW001	Amoxycillin Sandoz	Amoxicillin	Antibiotic	500	Tablets	Pharmacy Lome 2	formal	Lomè	100	Sandoz GmbH	Austria	GB7776	n.a	February 2020	36	below 25 °
QEW012	Amoxycillin Sandoz	Amoxicillin	Antibiotic	500	Tablets	Pharmacy Kpalime	formal	Lomè	100	Sandoz GmbH	Austria	GB7777	n.a	February 2020	36	below 25 °
QEW020	Amoxycillin Sandoz	Amoxicillin	Antibiotic	500	Tablets	Pharmacy Lome 3	formal	Lomè	60	Sandoz GmbH	Austria	GB7775	n.a	February 2020	36	not stated
QEW032	Amoxycillin Sandoz	Amoxicillin	Antibiotic	500	Tablets	Pharmacie Tsevie	formal	Tsevie	100	Sandoz GmbH	Austria	GB7776	n.a	February 2020	36	below 25 °
QEW040	Amoxycillin Sandoz	Amoxicillin	Antibiotic	500	Tablets	Pharmacy Lome 3	formal	Taligbo	100	Sandoz GmbH	Austria	FW2563	n.a	November 2019	33	below 25 °
QEW049	Amoxicillin Ubithera	Amoxicillin	Antibiotic	500	Capsules	Pharmacy Lome 1	formal	Kpalime	120	Lincoln Pharma	India	163131088	n.a	January 2019	23	not stated
QEW060	Amoxycillin Sandoz	Amoxicillin	Antibiotic	500	Tablets	Informal Vendor Agoe laogope	informal	Lomè	100	Sandoz GmbH	Austria	FW2561	n.a	November 2019	33	below 25 °
QEW067	Derm's Amoxicillin	Amoxicillin	Antibiotic	500	Capsules	Pharmacy Lome 1	formal	Tsevie	100	Yangzhou NO.3	China	160439	April 2016	April 2019	26	cool and dry
QEW070	Amoxicillin	Amoxicillin	Antibiotic	500	Capsules	Informal Vendor Agoe laogope	informal	Lomè	50	Sprukfield	Togo	15061	n.a	July 2018	17	not stated
QEW075 B	Amoxicillin TM	Amoxicillin	Antibiotic	500	Tablets	Pharmacy Lome 1	formal	Taligbo	120	Tongmei	Togo	807	n.a	June 2019	28	not stated
QEW078	Amoxicillin	Amoxicillin	Antibiotic	500	Capsules	Informal Vendor Agoe laogope	informal	Lomè	100	Letap	Ghana	1230196	n.a	July 2018	17	not stated
QEW080 B	Amoxicillin TM	Amoxicillin	Antibiotic	500	Tablets	Informal Vendor Agoe laogope	informal	Kpalime	120	Tongmei	Togo	407	n.a	June 2019	28	not stated
QEW002	Augmentin Adults	Amoxicillin and Clavulanic acid	Antibiotic	500 / 62,5	Tablets	Pharmacy Kpalime	formal	Lomè	32	GSK france	France	2387	n.a	November 2017	9	below 25 °
QEW021 A*	Fleming	Amoxicillin and Clavulanic acid	Antibiotic	500 / 62,5	Tablets	Pharmacy Lome 3	formal	Lomè	16	Medreich	India	160004	n.a	December 2017	10	below 25 °
QEW021 B	Augmentin Adults	Amoxicillin and Clavulanic acid	Antibiotic	500 / 62,5	Tablets	Pharmacy Lome 3	formal	Lomè	16	GSK france	France	2386	n.a	November 2017	9	below 25 °
QEW021 C	AmoxiClav Denk	Amoxicillin and Clavulanic acid	Antibiotic	500 / 62,5	Tablets	Pharmacy Lome 3	formal	Lomè	32	Denk Pharma	Germany	19284	n.a	April 2018	14	below 25 °
QEW033	Clavumoccid	Amoxicillin and Clavulanic acid	Antibiotic	500 / 62,5	Tablets	Pharmacie Tsevie	formal	Tsevie	24	Medopharm	India	16213001	July 2017	April 2018	14	below 25 °
QEW041	Ticasse	Amoxicillin and Clavulanic acid	Antibiotic	500 / 125	Tablets	Pharmacy Lome 3	formal	Taligbo	60	Billim	Turkey	5181058A	n.a	July 2019	29	below 25 °
QEW050	Augmentin Adults	Amoxicillin and Clavulanic acid	Antibiotic	500 / 62,5	Tablets	Pharmacy Lome 1	formal	Kpalime	8	GSK france	France	2388	n.a	November 2017	9	below 25 °
QEW004	Ciprofloxacine Ubigen	Ciprofloxacin	Antibiotic	750	Tablets	Pharmacy Lome 2	formal	Lomè	100	Lincoln Pharma	India	GK6006	n.a	March 2019	25	below 30°
QEW014 A	CI Cian	Ciprofloxacin	Antibiotic	500	Tablets	Pharmacy Kpalime	formal	Lomè	50	Cian	India	CTE6024	n.a	February 2019	24	below 30°
QEW014 B	Ciprofloxacine TM	Ciprofloxacin	Antibiotic	250	Tablets	Pharmacy Kpalime	formal	Lomè	10	Tongmei	Togo	108	June 2016	July 2019	29	below 25 °
QEW023	Ciprofloxacine TM	Ciprofloxacin	Antibiotic	500	Tablets	Pharmacy Lome 3	formal	Lomè	60	Tongmei	Togo	101	November 2015	December 2018	22	not stated
QEW034	Ciprofloxacine TM	Ciprofloxacin	Antibiotic	500	Tablets	Pharmacie Tsevie	formal	Tsevie	80	Tongmei	Togo	205	May 2016	April 2019	26	not stated
QEW043	Ciplox-500	Ciprofloxacin	Antibiotic	500	Tablets	Pharmacy Lome 3	formal	Taligbo	60	CIPLA	India	61512	n.a	March 2019	25	below 30°
QEW052	Ciprofloxacine Ubigen	Ciprofloxacin	Antibiotic	750	Tablets	Pharmacy Lome 1	formal	Kpalime	100	Lincoln Pharma	India	GK6006	n.a	March 2019	25	below 30°
QEW061	Ciprofloxacine	Ciprofloxacin	Antibiotic	500	Tablets	Informal Vendor Agoe laogope	informal	Lomè	100	North China pharmaceu	China	160910	n.a	September 2019	31	not stated
QEW068	CIPRO-500	Ciprofloxacin	Antibiotic	500	Tablets	Pharmacy Lome 1	formal	Tsevie	100	Nuel Pharma	Nigeria	NCP-02	August 2016	July 2019	29	below 30°
QEW071	Cipromax Fort	Ciprofloxacin	Antibiotic	500	Tablets	Informal Vendor Agoe laogope	informal	Lomè	50	Greenfield	China	16090112	n.a	August 2019	30	cool and dry
QEW076	Cipro 500	Ciprofloxacin	Antibiotic	500	Tablets	Pharmacy Lome 1	formal	Taligbo	100	Sprukfield	Togo	AR15003	n.a	January 2018	11	not stated
QEW079	Cipro 500	Ciprofloxacin	Antibiotic	500	Tablets	Informal Vendor Agoe laogope	informal	Lomè	100	Sprukfield	Togo	AR15004	n.a	January 2018	11	not stated
QEW081	Ciprofloxacine	Ciprofloxacin	Antibiotic	500	Tablets	Informal Vendor Agoe laogope	informal	Kpalime	100	North China pharmaceu	China	160910	n.a	September 2019	31	not stated
QEW007 *	Doxycycline	Doxycycline	Antibiotic	100	Tablets	Pharmacy Lome 2	formal	Lomè	10	Bailly-Creat	France	40	n.a	December 2017	10	below 25 °
QEW007X	Doxycycline	Doxycycline	Antibiotic	100	Tablets	Pharmacy Lome 2	formal	Lomè	90	Bailly-Creat	France	45	n.a	May 2019	27	below 25 °
QEW016	Doxynor 100	Doxycycline	Antibiotic	100	Tablets	Pharmacy Kpalime	formal	Lomè	20	F.I.R.M.A S.p.A	Italy	20	n.a	March 2019	25	not stated
QEW016 B	Doxycycline	Doxycycline	Antibiotic	100	Tablets	Pharmacy Kpalime	formal	Lomè	40	Bailly-Creat	France	45	n.a	May 2019	27	below 25 °
QEW026	Doxycycline	Doxycycline	Antibiotic	100	Tablets	Pharmacy Lome 3	formal	Lomè	60	Bailly-Creat	France	45	n.a	May 2019	27	not stated
QEW036	Doxycycline	Doxycycline	Antibiotic	100	Tablets	Pharmacie Tsevie	formal	Tsevie	90	Bailly-Creat	France	45	n.a	May 2019	27	below 25 °
QEW045	Philco-Doxy	Doxycycline	Antibiotic	100	Tablets	Pharmacy Lome 3	formal	Taligbo	60	Philco Pharma	Germany	1404055-2	n.a	March 2017	1	below 25 °
QEW054	Doxycycline	Doxycycline	Antibiotic	100	Tablets	Pharmacy Lome 1	formal	Kpalime	100	Bailly-Creat	France	45	n.a	May 2019	27	below 25 °
QEW063	Doxycycline	Doxycycline	Antibiotic	100	Tablets	Informal Vendor Agoe laogope	informal	Lomè	100	Pharmaquick	Benin	992600	n.a	November 2017	9	not stated
QEW073	Doxefil	Doxycycline	Antibiotic	100	Capsules	Informal Vendor Agoe laogope	informal	Lomè	50	Fourrts	India	B3034A	n.a	January 2018	11	not stated
QEW084	Doxycycline	Doxycycline	Antibiotic	100	Tablets	Informal Vendor Agoe laogope	informal	Kpalime	100	Pharmaquick	Benin	99280	n.a	November 2017	9	not stated
QEW006	Metronidazole Creazol	Metronidazole	Antibiotic	500	Tablets	Pharmacy Lome 2	formal	Lomè	100	Bailly-Creat	France	114	n.a	September 2019	31	below 25 °
QEW015	Metronidazole Creazol	Metronidazole	Antibiotic	500	Tablets	Pharmacy Kpalime	formal	Lomè	100	Bailly-Creat	France	116	n.a	September 2019	31	below 25 °
QEW025	Metronidazole TM	Metronidazole	Antibiotic	500	Tablets	Pharmacy Lome 3	formal	Lomè	60	Tongmei	Togo	604	n.a	March 2019	25	not stated
QEW035	UbiThera Metronidazole	Metronidazole	Antibiotic	250	Tablets	Pharmacie Tsevie	formal	Tsevie	100	Lincoln Pharma	India	GP5001	n.a	April 2018	14	not stated
QEW044	Metronidazole TM	Metronidazole	Antibiotic	500	Tablets	Pharmacy Lome 3	formal	Taligbo	60	Tongmei	Togo	604	n.a	March 2019	25	not stated
QEW053	Metronidazole Creazol	Metronidazole	Antibiotic	500	Tablets	Pharmacy Lome 1	formal	Kpalime	60	Bailly-Creat	France	118	n.a	September 2019	31	below 25 °
QEW062	Metronidazole	Metronidazole	Antibiotic	500	Tablets	Informal Vendor Agoe laogope	informal	Lomè	100	North China pharmaceu	China	160904	n.a	September 2019	31	not stated
QEW069	Metronidazole TM	Metronidazole	Antibiotic	500	Tablets	Pharmacy Lome 1	formal	Tsevie	100	Tongmei	Togo	604	n.a	March 2019	25	not stated
QEW072	Metronidazole TM	Metronidazole	Antibiotic	500	Tablets	Informal Vendor Agoe laogope	informal	Lomè	100	Tongmei	Togo	604	n.a	March 2019	25	not stated
QEW077	Metronidazole TM	Metronidazole	Antibiotic	500	Tablets	Pharmacy Lome 1	formal	Taligbo	100	Tongmei	Togo	604	n.a	March 2019	25	not stated
QEW080 A	Metronidazole TM	Metronidazole	Antibiotic	500	Tablets	Informal Vendor Agoe laogope	informal	Lomè	100	Tongmei	Togo	604	n.a	March 2019	25	not stated
QEW083	Metronidazole TM	Metronidazole	Antibiotic	500	Tablets	Informal Vendor Agoe laogope	informal	Kpalime	100	Tongmei	Togo	604	n.a	March 2019	25	not stated
QEW005	Starpen 1000	Penicillin v	Antibiotic	1000	Tablets	Pharmacy Kpalime	formal	Lomè	60	Sandoz GmbH	Austria	GE6581	n.a	March 2018	13	below 25 °
QEW024	Starpen 1000	Penicillin v	Antibiotic	1000	Tablets	Pharmacy Lome 3	formal	Lomè	60	Sandoz GmbH	Austria	GE6581	March 2016	March 2018	13	below 25 °
QEW082	Penicillin V	Penicillin v	Antibiotic	125	Tablets	Informal Vendor Agoe laogope	informal	Kpalime	100	Letap	Ghana	3909	n.a	August 2017	6	not stated
QEW003	Bactrim Adultes comprime	Sulfamethoxazole and Trimethoprim	Antibiotic	400 / 80	Tablets	Pharmacy Lome 2	formal	Lomè	60	Roche	France	F1067F02	n.a	January 2021	47	below 30°
QEW013	Co-Trimoxazole Ubigen	Sulfamethoxazole and Trimethoprim	Antibiotic	400 / 80	Tablets	Pharmacy Kpalime	formal	Lomè	100	Lincoln Pharma	India	GM6005	June 2015	May 2019	27	not stated
QEW022	Cotrimoxazole TM	Sulfamethoxazole and Trimethoprim	Antibiotic	400 / 80	Tablets	Pharmacy Lome 3	formal	Lomè	60	Tongmei	Togo	206	n.a	May 2019	27	not stated
QEW042	Cotrimoxazole TM	Sulfamethoxazole and Trimethoprim	Antibiotic	400 / 80	Tablets	Pharmacy Lome 3	formal	Taligbo	100	Tongmei	Togo	103	n.a	February 2019	24	not stated
QEW051	Co-Trimoxazole Ubigen	Sulfamethoxazole and Trimethoprim	Antibiotic	400 / 80	Tablets	Pharmacy Lome 1	formal	Kpalime	100	Lincoln Pharma	India	GM6005	June 2015	May 2019	27	below 25 °
QEW085	Cotrimoxazole TM	Sulfamethoxazole and Trimethoprim	Antibiotic	400 / 80	Tablets	Informal Vendor Agoe laogope	informal	Kpalime	90	Tongmei	Togo	211	n.a	January 2019	23	not stated
QEW009	Atenolol Denk	Atenolol	MANCD	50	Tablets	Pharmacy Lome 2	formal	Lomè	100	Denk Pharma	Germany	3089	n.a	May 2019	27	below 25 °
QEW018	Atenolol Denk	Atenolol	MANCD	50	Tablets	Pharmacy Kpalime	formal	Lomè	100	Denk Pharma	Germany	3089	n.a	May 2019	27	below 25 °
QEW028	Atenolol Denk	Atenolol	MANCD	50	Tablets	Pharmacy Lome 3	formal	Lomè	60	Denk Pharma	Germany	3090	n.a	May 2019	27	not stated
QEW038	Atenolol Denk	Atenolol	MANCD	50	Tablets	Pharmacie Tsevie	formal	Tsevie	100	Denk Pharma	Germany	3089	n.a	May 2019	27	below 25 °
QEW047	Atenolol Denk	Atenolol	MANCD	50	Tablets	Pharmacy Lome 3	formal	Taligbo	60	Denk Pharma	Germany	3089	n.a	May 2019	27	below 25 °
QEW056	Atenolol Denk	Atenolol	MANCD	50	Tablets	Pharmacy Lome 1	formal	Kpalime	100	Denk Pharma	Germany	3125	n.a	July 2019	29	below 25 °

Sample ID	Name of product	Stated API	Therapeutic class *1*	Stated amount of API [mg]	Dosage Form	Sample site	Site Type	Region of sample site	Obtained quantity [tabs./caps.]	Stated manufacturer	Stated country of origin	Batch number	Manufacturing date	Expiry Date	Shelf life remaining at collection [months]	Stated storage requirements
QEW065	Atenolol Denk	Atenolol	MANCD	50	Tablets	Informal Vendor Agoe laogope	informal	Lomè	100	Denk Pharma	Germany	3089	n.a	May 2019	27	below 25 °
QEW011	Furo Denk	Furosemide	MANCD	40	Tablets	Pharmacy Lome 2	formal	Lomè	100	Denk Pharma	Germany	92X	n.a	September 2020	43	below 25 °
QEW019	Furosemide	Furosemide	MANCD	40	Tablets	Pharmacy Kpalime	formal	Lomè	60	Bailly-Creat	France	42	n.a	March 2019	25	not stated
QEW030	Furosemide	Furosemide	MANCD	40	Tablets	Pharmacy Lome 3	formal	Lomè	60	Bailly-Creat	France	42	n.a	March 2019	25	not stated
QEW039	Furosemide	Furosemide	MANCD	40	Tablets	Pharmacie Tsevie	formal	Tsevie	100	Bailly-Creat	France	42	n.a	March 2019	25	below 25 °
QEW048	Furosemide	Furosemide	MANCD	40	Tablets	Pharmacy Lome 3	formal	Taligbo	120	Pharmaquick	Benin	9913	n.a	May 2018	15	not stated
QEW058	Furosemide	Furosemide	MANCD	40	Tablets	Pharmacy Lome 1	formal	Kpalime	100	Bailly-Creat	France	42	n.a	March 2019	25	below 25 °
QEW066	Furosemide	Furosemide	MANCD	40	Tablets	Informal Vendor Agoe laogope	informal	Lomè	100	Bailly-Creat	France	42	n.a	March 2019	25	below 25 °
QEW075 A	Furosemide	Furosemide	MANCD	40	Tablets	Informal Vendor Agoe laogope	informal	Lomè	100	Pharmaquick	Benin	9546	n.a	May 2017	3	not stated
QEW086	Furosemide	Furosemide	MANCD	40	Tablets	Informal Vendor Agoe laogope	informal	Kpalime	100	Alice	India	TE6280	n.a	June 2019	28	not stated
QEW087	Furosemide	Furosemide	MANCD	n.n	Tablets	Informal Vendor Agoe laogope	informal	Kpalime	40	Letap	Ghana	n.n	n.a	n.n		not stated
QEW010	Esidrex 25mg	Hydrochlorothiazide	MANCD	25	Tablets	Pharmacy Kpalime	formal	Lomè	100	Novartis	Spain	BC920	n.a	December 2018	22	cool and dry
QEW029	Esidrex 25mg	Hydrochlorothiazide	MANCD	25	Tablets	Pharmacy Lome 3	formal	Lomè	60	Novartis	Spain	BC919	n.a	December 2018	22	cool and dry
QEW074	Hydrochlorothiazide	Hydrochlorothiazide	MANCD	50	Tablets	Informal Vendor Agoe laogope	informal	Lomè	100	Pharmaquick	Benin	9928	n.a	April 2019	26	not stated
QEW057	Ecazide	Hydrochlorothiazide + Captopril	MANCD	25	Tablets	Pharmacy Lome 1	formal	Kpalime	60	Bristol Myers Squibb	Italy	AAK6882	n.a	May 2019	27	below 25 °
QEW008	Metformin Denk	Metformin	MANCD	500	Tablets	Pharmacy Lome 2	formal	Lomè	100	Denk Pharma	Germany	954	n.a	January 2021	47	below 25 °
QEW017	Metformin Denk	Metformin	MANCD	500	Tablets	Pharmacy Kpalime	formal	Lomè	100	Denk Pharma	Germany	959	n.a	March 2021	49	below 25 °
QEW027	Metformin Denk	Metformin	MANCD	500	Tablets	Pharmacy Lome 3	formal	Lomè	60	Denk Pharma	Germany	989	n.a	March 2021	49	below 25 °
QEW037	Metformin Denk	Metformin	MANCD	500	Tablets	Pharmacie Tsevie	formal	Tsevie	100	Denk Pharma	Germany	954	n.a	January 2021	47	below 25 °
QEW046	Metformin Denk	Metformin	MANCD	500	Tablets	Pharmacy Lome 3	formal	Taligbo	60	Denk Pharma	Germany	8ZY	n.a	May 2020	39	below 25 °
QEW055	Metformin Denk	Metformin	MANCD	500	Tablets	Pharmacy Lome 1	formal	Kpalime	100	Denk Pharma	Germany	957	n.a	March 2021	49	below 25 °
QEW064	Metformin Denk	Metformin	MANCD	500	Tablets	Informal Vendor Agoe laogope	informal	Lomè	100	Denk Pharma	Germany	954	n.a	January 2021	47	below 25 °
QEW031	Buto-Asma	Salbutamol	MANCD	2	Tablets	Pharmacy Lome 3	formal	Lomè	80	Aldo-Union	Spain	0619K002	n.a	July 2021	53	below 30°
QEW059	Buto-Asma	Salbutamol	MANCD	2	Tablets	Pharmacy Lome 1	formal	Kpalime	40	Aldo-Union	Spain	0619K002	n.a	July 2021	53	below 30°
	MANCD = medicine against non-communicable disease															
	n.a. = not available															
	* = Results were excluded															

S2 Table: Prices of the medicines in licensed pharmacies and informal vendors

API	Median price per dosage form [$]		median price ratio	
	formal	Informal	formal	Informal
Amoxicillin 500 mg	0.09	0.07	3.36	2.63
Amoxicillin / Clavulanicacid 500/125mg	0.47		4.96	
Phenoxymethylpenicillin 1000mg	0.28	0.02 (125mg)	7.57	1.36
Ciprofloxacin 500mg	0.18	0.06	4.74	1.53
Doxycycline 100mg	0.07	0.04	5.04	3.07
Sulfamethoxazole / Trimethoprim 400/80mg	0.04	0.14	3.30	12.50
Metronidazole 500mg	0.06	0.05	6.63	3.88
Atenolol 50mg	0.13	0.13	11.99	12.22
Furosemide 40mg	0.07	0.04	10.72	6.70
Hydrochlorothiazide 25 / 50mg	0.06	0.03 (50mg)	14.44	6.67
Metformin 500mg	0.08	0.08	5.28	5.25
Salbutamol 2mg	0.12		49.27	
Overall median price ratio			5.28[a]	3.18 [a]

[a] median price ratio of all medicines collected

The table shows the median prices per tablet or capsule. Following a standardized method developed by WHO and Health Action International,[1] those prices were compared to an international reference price, i.e to the median supplier price given in the MSH International Medical Products Price Guide of 2015.[2] Overall, the resulting median price ratio (MPR) was 5.3 in licensed pharmacies, compared to 3.2 in informal vendors. Therefore, as expected, medicines are more expensive in pharmacies. A United Nations report of 2012[3] stated that in low and middle income countries the median price ratio in the (formal) private sector was on average 5.3, identical to the figure found for pharmacies in Togo. As expected, the MPR for generic medicines and branded generics (average MPR = 4.1) was lower than that for originator medicines (average MPR= 13.5). Medicines from Africa and Asia (in both cases average MPR = 3.0) were more affordable than those from Europe (average MPR= 7.2). Notably, medicines for non-communicable diseases were sold at much more unfavorable prices (average MPR=10.7) than antibiotics (average MPR=3.1). For the two samples of salbutamol 2mg tablets, sold as branded generics in private pharmacies, the MPR even reached 49.3.

[1] WHO HAI. Measuring medicines prices, availability, affordability and price components.2008. Available from: http://www.who.int/medicines/areas/access/OMS_Medicine_prices.pdf

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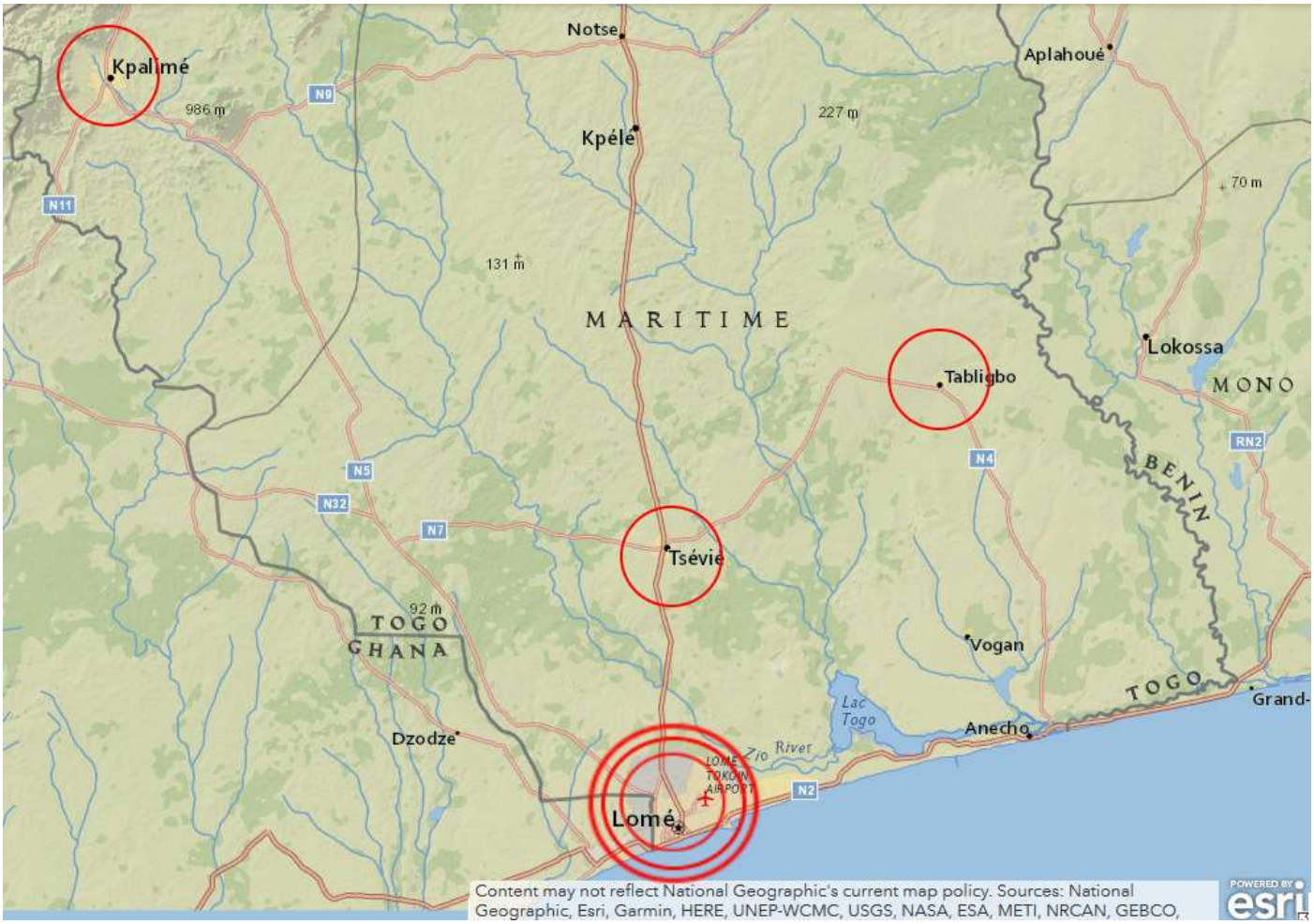

S 1 Figure: **Map of the sampling sites in the regions Maritime and Plateaux of the Republic of Togo** (*https://viewer.nationalmap.gov/advanced-viewer/*)

In Lomé samples were collected in Lomé Centre and in the suburbs Agoe-nyvie and Agoe-laogope. Furthermore, samples were collected in the towns Tsévié and Tabligbo, 30 km north and 75 km northeast of Lomé, respectively, and in the town of Kpalimé, 120km northwest of Lomé and close to the border to Ghana.

S2 Figure: Discoloration discovered upon visual inspection of a sample of doxycycline tablets

This sample of doxycycline 100mg tablets (Bailly-Creat, France) contained blisters with two different batch numbers in one secondary packaging. While the blisters with the uniformly colored tablets (batch no. 45; exp. date 05.2019) depicted on the right side (QEW007X) were found to comply with the USP39 specifications, the blisters with the darkened, spotted tablets (batch no. 40; exp. date 12.2017) depicted on the left side (QEW007) showed extreme deviations from the USP39 specifications both in the assay (58% of stated content of doxycycline) and in dissolution. Since QEW007 consisted of only one blister of 10 tablets, which was lower than the amount required by the USP 39 monographs, the results for this sample were excluded from the overall data analysis.

PLOS ONE

RESEARCH ARTICLE

Availability, prices and affordability of selected antibiotics and medicines against non-communicable diseases in western Cameroon and northeast DR Congo

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Abstract

Access to safe, effective and affordable medicines of good quality is included into the Sustainable Development Goals of the United Nations. Furthermore, WHO has developed a Global Action Plan with the aim to raise access to essential medicines against non-communicable diseases (NCDs) to 80%, and to improve their affordability. In order to contribute to the monitoring of progress towards these goals, the present study investigated the availability and affordability of seven antibiotics and six medicines against non-communicable diseases in the northeast of the Democratic Republic of Congo and the west of the Republic of Cameroon. Data on availability and prices of these medicines were collected in 60 different sites (34 in the DR Congo, 26 in Cameroon), including government health facilities, church health facilities, private pharmacies and informal vendors, as part of a study on medicine quality. The data were analyzed using a standardized procedure developed by WHO and Health Action International (HAI). Average availability of the investigated antibiotics ranged from 62% to 98% in the different types of facilities in both countries, including the informal vendors. Average availability for medicines against NCDs in the different types of facilities showed a higher variation in both countries, ranging from 11% up to 87%. The average availability of medicines against NCDs in government health facilities was only 33% in Cameroon, and as low as 11% in the DR Congo. In contrast, availability of medicines against NCDs in church health facilities in Cameroon was 70%, not far from the 80% availability goal set by WHO. Medicine prices were clearly higher in Cameroon than in the DR Congo, with median price ratios to an international reference price of 5.69 and 2.17, respectively ($p < 0.001$). In relation to the daily minimum wages in both countries, treatment courses with five of the seven investigated antibiotics could be considered as affordable, while in each country only one out of the five investigated medicines against NCDs could be considered as affordable. Especially generic medicines provided by government and church health facilities showed reasonable affordability in most cases, while originator medicines offered

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by private pharmacies were clearly unaffordable to a major part of the population. Despite some encouraging findings on the availability of antibiotics in both countries, the availability and affordability of medicines against NCDs urgently requires further improvements.

Introduction

According to the WHO millions of people each year die unnecessarily from a disease or condition even though effective medicines or vaccines exist for its treatment [1]. This is also attributable to poor availability of essential medicines. Achieving access to safe, effective, quality and affordable medicines and vaccines for all is therefore one component of the target No. 3.8 of the Sustainable Development Goals of the United Nations [2]. Despite considerable efforts, the availability of medicines is still poor in many countries [3, 4]. A survey covering data from 25 low and middle income countries reported a 40% overall median availability of essential medicines in the public sector in 2014. [5]. Especially for the treatment of non-communicable diseases (NCDs) the availability of essential medicines is low, as a recent analysis of 30 surveys published by Ewen et al. [6] and a review by Robertson et al. [7] indicate. In 2010, a study investigated the availability of five cardiovascular medicines in 36 countries, reporting a mean availability of 26.3% in the public sector [8]. There is still a long way to go to reach the goal of 80% availability for medicines against NCDs as set by the WHO for 2025 [9]. But even when essential medicines are available, not every patient in low- and middle-income countries can afford them. Unaffordability of medicines can lead to non-adherence of patients to their treatment and aggravate a country's burden of disease [10]. An evaluation of data from 36 countries showed in 2009 that treatments for acute and chronic diseases were unaffordable in many countries [11]. The above mentioned analysis of cardiovascular medicines in 2010 showed that treatment courses for chronic disease are especially unaffordable when combination therapies are required [8]. The assessment by Ewen et al. [6] also underlined that only in few low—and—middle income countries essential medicines against NCDs are both available and affordable.

Few surveys so far have investigated the availability and affordability of medicines in Cameroon, and even fewer in the Democratic Republic of Congo (DR Congo). In 2005, Preux et al. [12] investigated the availability of antiepileptic medicines in a very small survey in the Mifi Province in Cameroon and reported that 32 out of 33 patients were treated with a modern antiepileptic medicine. But these were frequently out of stock in hospital pharmacies and patients needed to buy them from private pharmacies and even from informal (illegal) vendors. A negative aspect of availability was reported by Becker et al. [13]. Injectable antibiotics in southwest Cameroon were readily available from market stalls and traditional healers at a price lower than in the government clinics. An investigation by Jingi et al. [14] revealed that in the West Region of Cameroon in 2014 a one month combination treatment for coronary heart diseases was as expensive as 41 days wages. In 2011, O'Connell et al. [15] investigated the availability of anti-malarial medicines in six countries including the Democratic Republic of Congo, with the encouraging finding that 82% of the public health facilities in DR Congo had a quality assured artemisinin-based combination therapy available. In 2014, the Ministry of Health of the DR Congo published a "Service Availability and Readiness Assessment" (SARA), including data on the availability of 20 essential medicines [16]. Overall, the availability was only 20%, and was especially low for medicines against non-communicable diseases. Notably,

the two provinces with the highest average availability (35% and 30% respectively) were North-Kivu and South-Kivu, which have also been investigated in the present study.

Cameroon and the DR Congo show different political and financial characteristics: Cameroon is a lower-middle income country with a gross national income per capita (GNI per capita) of 3.315 US–Dollar (USD) per year. 23.8% of the total population live below the income poverty line of 1.90 USD per day. Life expectancy at birth is 58.6 years [17]. Despite a stable political history, in recent years Cameroon faces turmoil caused by attacks of the Boko Haram in the North and separatist movements in the anglophone regions [17]. The DR Congo is a low-income country with a GNI per capita of only 976 USDper year, less than 30% of the GNI of Cameroon. 77.1% of the total population live below the income poverty line, a three times higher proportion than in Cameroon. However the life expectancy at birth (60.0 years) is reported to be similar to that of Cameroon [18]. Following a long series of political conflicts, the outbreak of Ebola starting in 2018 in the province North-Kivu and an ongoing armed conflict, the situation for the population in the northeast part of DR Congo, where the present study was conducted, is grave [19].

The present data on the availability and prices of thirteen selected essential medicines were collected as part of a study on medicine quality in the western regions of Cameroon and the northeastern regions of the DR Congo. While the laboratory investigation of the collected medicine samples is still ongoing, we here present the results on availability, prices and affordability of medicines in government and church health facilities, private pharmacies and informal (illegal) vendors in northeast DR Congo and west Cameroon.

Methods

Selection of medicines

The study protocol followed the guidelines on the conduct of surveys of the quality of medicines, published by the WHO in 2016 [20], and the MEDQUARG guidelines [21]. For the study in the DR Congo seven antibiotics and five medicines against non-communicable diseases (NCDs) were selected. All medicines selected were part of the respective essential medicines list (EML) of both countries and, according to the information by our local partners, frequently used by health care providers. Since this study was carried out as part of a study on medicine quality, using both GPHF Minilab analysis (www.gphf.org) and analysis according to the United States Pharmacopeia (USP), the selection of medicines was also based on the availability of both a GPHF Minilab monograph and a USP monograph. Therefore, the included medicines were solid oral dosage forms of amoxicillin, amoxicillin/clavulanic acid, sulfamethoxazole/trimethoprim, ciprofloxacin, phenoxymethylpenicillin (penicillin V), metronidazole, doxycycline, metformin, atenolol, hydrochlorothiazide, furosemide and salbutamol (albuterol). For the study in Cameroon, the same medicines except atenolol were selected, since according to the local partners in Cameroon atenolol was not frequently used by healthcare providers in the Republic of Cameroon. This is also confirmed by the study of Jingi et.al [14] who reported that out of 11 investigated health facilities in Cameroon, the only one which stocked atenolol was an exceptionally well-stocked private pharmacy shop. Upon request by the local partners in Cameroon, the antidiabetic medicine glibenclamide (glyburide) was collected instead of the antihypertensive medicine atenolol in that country. All of the thirteen medicines were listed in the essential medicines lists (EML) of the Republic of Cameroon and the Democratic Republic of Congo [22, 23]. The preferred strength of the collected medicines is shown in Table 1. If this strength was unavailable, tablets or capsules of an another strength were sampled.

Table 1. Medicines included into this study and calculation of medicine amount of the preferred strength used for one course of treatment.

	Model disease	Strength [mg/tbl. or cps.]	Dosage regimen [tbl. or cps./day]	Treatment duration	Number of tbl./cps. for one course of treatment
Amoxicillin / clavulanic acid tbl.[28]	Adult respiratory infection	500 / 125	3	7 days	21
Amoxicillin tbl./cps. [25]	Adult respiratory infection	500	3	7 days	21
Ciprofloxacin tbl. [25]	Adult respiratory infection	500	2	7 days	14
Metronidazole tbl. [28]	Anaerobic infections	250	6	7 days	42
Penicillin V tbl. [28]	Adult respiratory infection	250	8	7 days	56
Doxycycline tbl./cps. [28]	Malaria	100	2	10 days	20
Sulfamethoxazole and trimethoprime tbl. [25, 28]	Respiratory tract infections	400 / 80	4	7 days	28
Metformin tbl. [28]	Diabetes	500	3	30 days	90
Glibenclamide tbl. [25]	Diabetes	5	2	30 days	60
Atenolol tbl.[25]	Hypertension	50	1	30 days	30
Salbutamol tbl.[28]	Chronic asthma	2	3	30 days	90
Furosemide tbl. [28]	Oedema	40	1	30 days	30
Hydrochlorothiazide tbl. [28]	Hypertension	25	1	30 days	30

tbl. = tablets

cps. = capsules

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In the essential medicines list (EML) of Cameroon, the health care facilities are divided into three main levels, i.e Health Centres, District Hospitals and Central Hospitals [23]. According to the EML, nine of the selected medicines should be available at all three levels of health facilities [23], while doxycycline, furosemide and hydrochlorothiazide are not meant to be stocked at the Health Centre level [23]. In the essential medicines list of the Democratic Republic of Congo the health care facilities are divided in two categories, Centre de Santé (CS) and Hopital General de Reference (HGR), and many of them are run or supplied by non-governmental organisations. The EML of the DR Congo [22] specifies that a HGR should stock all of the 12 medicines included in our study, while a CS should stock 9 of these medicines excluding atenolol, furosemide and hydrochlorothiazide. In practice, these rules are often not followed in either country.

Selection of sampling sites

Medicine samples, and data on availability and prices, were collected from governmental health facilities, church health facilities, private pharmacies and informal (= illegal) vendors.

In the Democratic Republic of Congo, this study was conducted in the four provinces Ituri, North-Kivu, South-Kivu and Tanganyika, since the local partners involved in this study operated in these regions. From each of these four provinces, a complete list of health zones was obtained, comprising 37, 34, 34 and 11 health zones, respectively (total 116 health zones). Of these, 70 had to be excluded from this study since travel of the study personnel to and in these zones was unsafe according to the assessment of the local partners in the DR Congo. From the remaining 46 health zones, eight were randomly selected, two from each province, using the RAND-function of Microsoft Excel. The selected health zones were Nyankunde and Rethy (Ituri), Biena and Goma (North-Kivu), Nyangezi and Ruzizi (South-Kivu) and Kansimba and Nyemba (Tanganyika). Upon request by our local partners the Kadutu Health Zone in Bukavu,

South-Kivu, was added to this selection since the central market of Bukavu is known as the biggest unlicensed market for medicines in this region, and the assessment of medicines quality there was of considerable interest.

In each of the selected health zones of the DR Congo, medicines were sampled from the Centre Hospital of that zone first. When the Centre Hospital was a governmental health facility, the geographically nearest church health facility, private pharmacy and informal vendor of medicines were identified and medicines were sampled also from these three sites. Correspondingly, if that Centre Hospital was a church health facility, the nearest governmental health facility, private pharmacy and informal vendor of medicines in that zone were identified and medicines were sampled from there. In the health zones Nynankunde und Rethy (Ituri Province) the central hospitals were under the authority of the government. However they are run by church-based organisations and obtain most of their medicines from faith-based drug supply organisations. Therefore in the data analysis they were classified as church health facilities. Furthermore in the same two health zones (Nyankunde and Rethy of Ituri province), no informal medicine vendors could be found, since medicine trade is under tight control in that province following a major international scandal involving falsified medicines [24]. Therefore, a total number of 34 medicine outlets, located in 9 health zones in four provinces were included into this study in the DR Congo. These included 10 Centres de Santé (CS) and 8 Hopitals General de Reference (HGR).

In Cameroon this study was conducted in 6 of the 10 regions of this country, i.e. Adamawa, Centre, Littoral, Northwest, Southwest and West, since the local partners involved in this study operated in these regions. A list of all church health facilities in these six regions was obtained, comprising 45 facilities. For each region, one church health facility was selected randomly, using the RAND-Function of Excel. Samples were collected in each region from this facility as well as from the geographically nearest governmental health facility, private pharmacy and informal vendor of medicines.

By chance, the random selection of six out of the 45 church health facilities included none of the ten facilities operated by catholic church organisations in these six regions. Upon request by the local partners, two out of the ten catholic health facilities were randomly chosen and additionally included in the Northwest and Centre regions. Therefore, a total number of 26 medicine outlets located in six regions were included into this study in Cameroon. According to our local partners, all selected medicines were expected to be available at each of the included health facilities.

Collection of data and samples

Samples were collected in the Republic of Cameroon from August 2017 until November 2018 and in the DR Congo from July 2017 until May 2018. In public and church health facilities, the investigators identified themselves and explained the purpose of the study. In contrast in private pharmacies and illegal market vendors of medicines, samples were collected using a mystery shopper approach. For each medicine at each sampling site a quantity of up to 100 tablets or capsules was purchased if available (minimum 30 tablets or capsules). If several brands of the same medicine were available, the cheapest one was purchased. Samples were collected in their original packaging or containers if possible. At each of the 60 sampling sites, prices and quantities of purchased medicines were recorded on a standardized form. Sample number, brand name, batch number, manufacturing date, expiry date, name of manufacturer, international non-proprietary names (INN) of the active pharmaceutical ingredients (APIs), strength, dosage form, package size, and price were recorded as stated on the label, using a standardized form by the local staff.

Calculation of availability, prices and affordability

WHO and Health Action International (HAI) have developed a standardized methodology for the investigation of medicines availability, prices and affordability [25]. The methodology was used in the analysis of the collected data. Availability was calculated as percentage of the sampling sites that had the requested medicine in stock in forms of tablets or capsules, irrespective of the strength [25]. Medicine prices were converted from local currency to US Dollar (USD) based on the exchange rates of January 2018 given by the European Commission [26]: Cameroon, 1000 West African CFA Franc (XOF) = 1.81933 USD; DR Congo, 1000 Congolese franc (CDF) = 0.63244 USD. As suggested by the WHO/HAI Manual [25], the observed individual prices were compared to an international reference price. For different types of medicines, the median of these price ratios was calculated, resulting in the median price ratio (MPR). The 2015 MSH median reference price (Supplier) was used for this purpose [27]. 502 medicine samples were collected in this study, but information on the individual prices of each sample was documented only for 476 of these samples. The remaining 26 collected samples could not be included into the price analysis, since e.g. only a summary price for several medicines bought at the same place had been recorded. For further 15 medicine samples, representing 500 mg amoxicillin / 62.5 mg clavulanic acid tablets, or 750 mg ciprofloxacin tablets, no reference price is given in the MSH price guide [27]. Therefore 461 medicine prices could be included into the analysis of median price ratios. Costs for a course of treatment were calculated using the treatment durations and dosage regimens shown in Table 1.

Statistical analysis

Statistical calculations were performed using JMP version 14.2 (SAS GmbH, Heidelberg, Germany). To test for the statistical significance of median price ratios a Wilcoxon test was used for comparison of two groups.

Ethical approval

This study was approved by the Ministry of Health of the DR Congo (Ref. CAB/Min-Prov/SGFEAHRAP/SK/01/2017), and by the Ministry of Public Health of the Republic of Cameroon, Comité National d' Ethique de la Rechereche pour la Santé Humain (CNERSH), Ref. 243674339.

Results

Availability

Fig 1 shows the approximate locations of the regions of Cameroon and the provinces and health zones of the DR Congo where data and samples for this study had been collected. A complete list of the medicines purchased at the sites, their characteristics and their prices is given in the S1 Table. Although we included only medicines which were comprised in the essential medicines list of these two countries, the full number of the 12 included medicines was only available in 6 of the 26 (23%) facilities in Cameroon and 4 of the 34 (12%) facilities in the DR Congo. The average availability of the 12 medicines was 78% in Cameroon and 64% in the DR Congo (Table 2). As obvious from Fig 1, no striking regional differences in medicine availability were observed within each country. Table 2 shows the detailed availability results of all investigated medicines in all types of facilities. Notably, government health facilities in the decidedly more affluent Cameroon are not better stocked than in the DR Congo (50% average availability in both countries). Therefore, the higher overall availability of medicines in Cameroon is attributable to the better stocks of church health facilities, pharmacies and

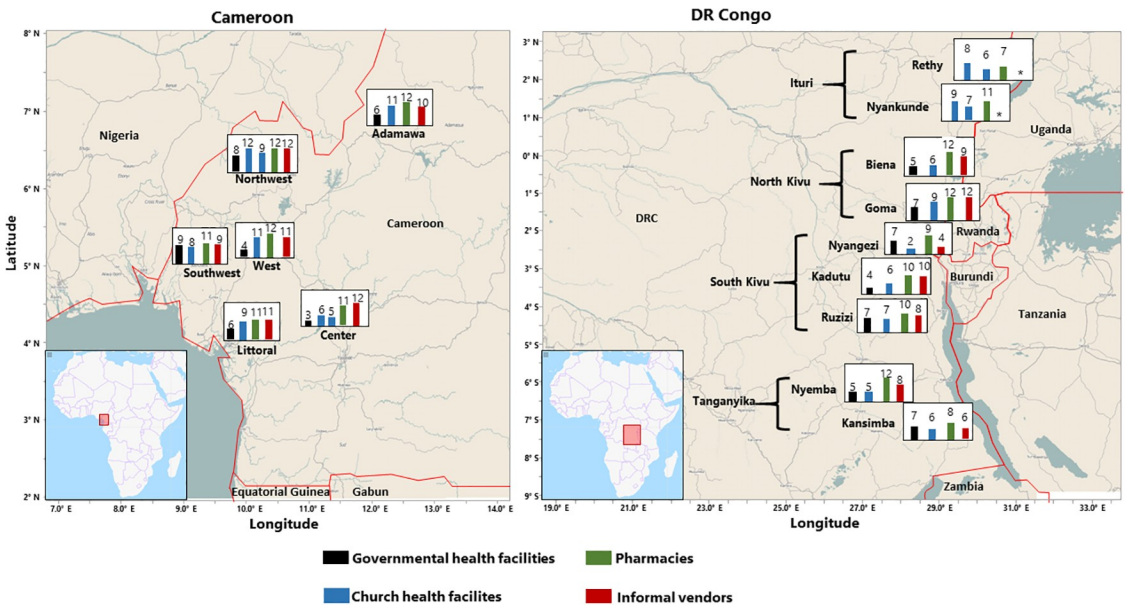

Fig 1. Map of the sampling regions, with numbers of medicines available at different types of facilities. 12 medicines were included into this study in each country. Therefore the maximum number of medicines recorded as available is 12. In the Ituri province in the DR Congo the health facilities under governmental authority were actually run by church organisations, therefore they were classified as church health facilities. * no informal vendor was identified in these health zones.

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informal vendors in this country. As expected, private pharmacy shops were better stocked than other types of facilities in both countries. Somewhat unexpectedly, informal vendors in Cameroon were extremely well stocked (93% availability), equal to licensed pharmacies.

Medicine availability was not very different in Centres de Santé (CS) and Hopitals General de Reference (HGR) (Table 2). Therefore we do not differentiate between these two categories in the following analyses. Fig 2 summarizes the availability of antibiotics and medicines against NCDs in health facilities of Cameroon and the DR Congo. Most striking is the poor availability of medicines against NCDs especially in government health facilities (33% and 11% availability in Cameroon and the DR Congo, respectively). In Cameroon, availability of these medicines in church health facilities reaches 70%.

Prices

As explained in the Methods section, medicine prices recorded during the purchase of the samples were converted from national currency to USD, and medicines prices per unit (tablet or capsule) were calculated for each medicine. The ratio of the median price per unit to the international reference price given in the MSH International Medical Products Price Guide [25, 27] for the same medicine and strength was calculated resulting in the median price ratios (MPRs) shown in Table 3.

Overall, MPRs for Cameroon and the DR Congo resulted as 5.69 and 2.17 ($p<0.0001$), showing that medicines are more than twice as expensive in Cameroon than in the DR Congo. Table 3 and Fig 3 further show that medicine prices are higher in Cameroon in all four types of facilities, most pronouncedly in private pharmacy shops (MPR 9.74 in Cameroon vs. 2.70 in the DR Congo; $p<0.0001$). Fig 3 shows the range of the price ratios to the international reference price in the four different types of facilities. In the DR Congo, especially government

Table 2. Medicine availability in the different types of facilities in Cameroon and the DR Congo.

	Cameroon						Democratic Republic of Congo							
INN	Governmental health facilities (n = 6)	Church health facilities (n = 8)	Pharmacies (n = 6)	Informal vendors (n = 6)	Cameroon, all (n = 26)		Governmental health facilities (n = 7)		Church health facilities (n = 11)		Pharmacies (n = 9)	Informal vendors (n = 7)	DR Congo, all (n = 34)	
							CS (n = 4)	HGR (n = 3)	CS (n = 6)	HGR (n = 5)				
Amoxicillin / clavulanic acid	3/6	4/8	6/6	5/6	18/26	71%	0/4	1/3	1/6	0/5	6/9	4/7	12/34	37%
Amoxicillin	5/6	8/8	5/6	6/6	24/26	92%	4/4	2/3	5/6	5/5	9/9	7/7	32/34	94%
Ciprofloxacin	5/6	8/8	6/6	6/6	25/26	96%	4/4	3/3	5/6	5/5	9/9	6/7	32/34	94%
Doxycycline	4/6	6/8	6/6	6/6	22/26	85%	4/4	2/3	3/6	5/5	9/9	5/7	28/34	82%
Metronidazole	5/6	8/8	6/6	6/6	25/26	96%	4/4	3/3	6/6	5/5	7/9	7/7	32/34	94%
Penicillin V	0/6	2/8	5/6	6/6	14/26	56%	4/4	1/3	4/6	2/5	9/9	7/7	27/34	81%
Sulfamethoxazole / trimethoprim	4/6	7/8	6/6	6/6	23/26	89%	3/4	3/3	6/6	5/5	9/9	7/7	33/34	96%
Atenolol *							0/4	0/3	0/6	1/5	4/9	1/7	6/34	17%
Furosemide *	1/6	5/8	6/6	5/6	17/26	66%	2/4	1/3	1/6	4/5	9/9	6/7	23/34	69%
Glibenclamide	2/6	6/8	6/6	5/6	19/26	73%								
Hydrochlorothiazide *	1/6	6/8	6/6	6/6	19/26	73%	0/4	0/3	0/6	3/5	4/9	1/7	6/34	17%
Metformin	2/6	6/8	6/6	6/6	20/26	77%	0/4	0/3	0/6	3/5	7/9	2/7	12/34	33%
Salbutamol	4/6	5/8	2/6	4/6	15/26	57%	1/4	0/3	1/6	3/5	9/9	4/7	18/34	52%
							2.16/4	1.33/3	2.67/6	3.42/5				
Average	3.00/6	5.92/8	5.58/6	5.58/6	20.28/26		3.50/7		5.94/11		7.56/9	4.76/7	24.14/34	
	50%	74%	93%	93%	78%		50%		54%		84%	68%	64%	

*according to the EML, this medicine is not supplied to the CS-Level in the DR Congo [22]

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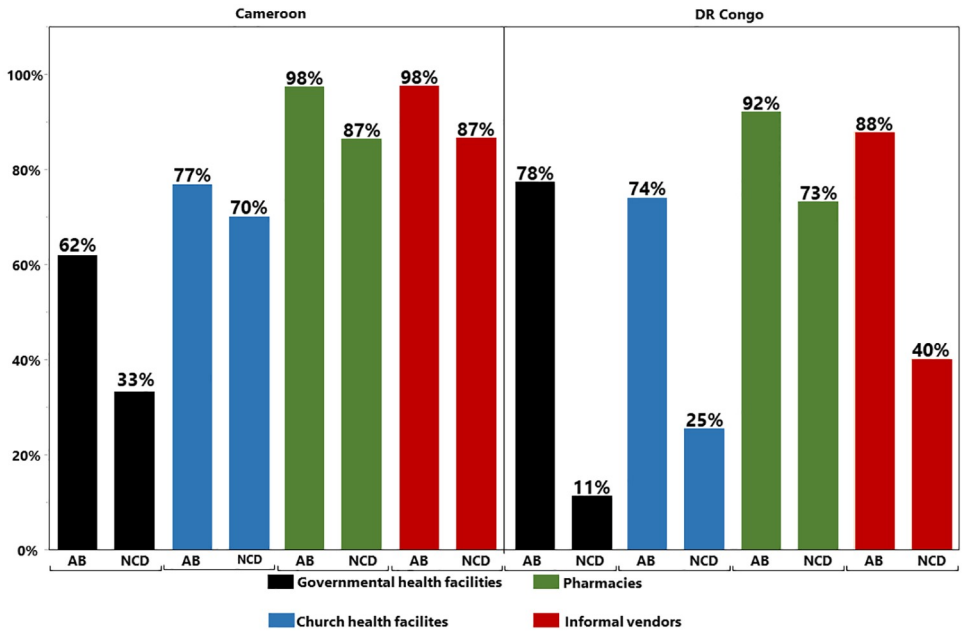

Fig 2. Availability of antibiotics and of medicines against non-communicable diseases in the four different types of health facilities.

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health facilities offer some medicines at prices below the MSH reference price which is a price for international bulk procurement.

Fig 3 and Table 3 also show that in the DR Congo, government and church health facilities sell medicines cheaper than informal vendors. In contrast, in Cameroon medicine prices at church health facilities are higher than those at informal vendors (Fig 3).

Fig 4 shows the ranges of price ratios for different medicines in both countries. Medicines against NCDs show clearly higher MPRs than antibiotics.

Table 3 shows that antibiotics were clearly more expensive in Cameroon than in the DR Congo (MPR 4.47 versus 1.80; $p<0.0001$). In contrast, for medicines against NCDs, sometimes Cameroon was more expensive, sometimes the DR Congo, and altogether the MPR for medicines against NCDs was not significantly different in both countries (MPR 8.81 versus 7.11; $p = 0.27$).

In both countries, most medicines were generics (sold under their international non-proprietary names) or branded generics (off patent, but sold under a trade name given by the marketing authorization holder). Overall, only 6% of the collected samples represented originator medicines. As expected, these were very expensive, with MPRs of 16.92 in Cameroon and 37.79 in the DR Congo. The extremely high MPR observed in the DR Congo is strongly influenced by hydrochlorothiazide, which was solely available in the DR Congo in form of the originator medicine Esidrex® at a very high price (MPR 52.58). As shown in Table 3, out of the 461 medicine samples included in the price analysis, 332 (72%) are manufactured in Asia and this proportion is similar in Cameroon and the DR Congo. However, the prices at which they are sold in both countries are remarkably different (MPR 4.86 versus 2.07, respectively; $p<0.0001$).

Affordability

As an indicator of the local affordability of a therapy regimen, the number of days´ wages needed to purchase a course of treatment was calculated following the WHO/HAI

Table 3. Median price ratios for medicines and days wages' needed for a course of treatment in Cameroon and in the DR Congo. The continent of origin of the medicines is given as stated on the label.

	Median Price Ratio (MPR)				Median Days wages needed for a course of treatment	
	Cameroon		DR Congo		Cameroon	DR Congo
	N	MPR	N	MPR		
Amoxi/Clav	12	3.20	6	4.57	4.34	10.05
Amoxicillin	23	3.03	30	1.61	0.87	1.00
Ciprofloxacin	21	4.88	29	1.70	1.00	0.84
Doxycycline	21	6.16	25	2.18	0.69	0.55
Metronidazole	24	5.37	29	3.11	0.62	0.78
Penicillin V	14	11.70	26	1.63	3.66	1.52
Sulfa/Trimet	22	3.50	30	1.77	0.54	0.56
Atenolol	0		6	10.66		2.68
Furosemide	16	13.42	23	3.89	1.12	0.67
Glibenclamide	18	13.57	0		2.11	
Hydrochlorothiazide	18	13.00	6	52.58	0.62	6.40
Metformin	19	4.25	12	7.35	2.60	8.53
Salbutamol	15	19.90	16	8.89	1.30	1.21
Antibiotics	137	4.47	175	1.80	0.87	0.88
Medicines against NCDs	86	8.81	63	7.11	1.24	1.61
Governmental health facilities	35	2.98	29	1.47	0.49	0.85
Church health facilities	62	6.10	65	1.78	1.16	0.88
Pharmacies	60	9.74	88	2.70	1.90	1.19
Informal vendors	66	4.25	56	2.22	0.61	0.84
Africa	18	6.84	39	2.37	0.64	0.94
Americas	2	8.52	0		0.92	
Asia	150	4.86	182	2.07	0.87	0.88
Europe	44	13.81	17	14.21	2.60	7.82
not stated	9	3.03	0		0.69	
generic	110	5.17	99	1.80	0.83	0.84
branded	97	4.88	129	2.38	0.99	1.00
originator	16	16.92	10	37.79	2.17	6.71
All	**223**	**5.69**	**238**	**2.17**	**0.99**	**0.94**

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methodology [25]. The amount of tablets or capsules required for a course of treatment was calculated as shown in Table 1, Method section. For chronic diseases, the amount of medicine for 30 days of treatment was used [25]. Minimal wages set by the government of Cameroon and the DR Congo are given by the Country Reports on Human Rights Practices of 2018 [29]. The monthly minimal wage for Cameroon was divided by 30 [25], resulting in a daily minimum wage of 2.20 USD. For the DR Congo, we used the minimum daily wage of 1680 Congolese Francs (1.06 USD) which was in effect in January 2018. The Congolese Government has meanwhile started a stepwise increase of the minimum wage [29], but only after data collection for this study was completed. Table 3 shows the median number of days´ wages required for treatment with the different medicines investigated. According to WHO/HAI [25] a treatment course is considered unaffordable when it requires more than one day's minimal wage. As graphically illustrated in Fig 5, several of the basic antibiotic treatment courses were affordable in both countries. In contrast, several of the treatments against NCDs were unaffordable, especially the important antidiabetic medicine metformin.

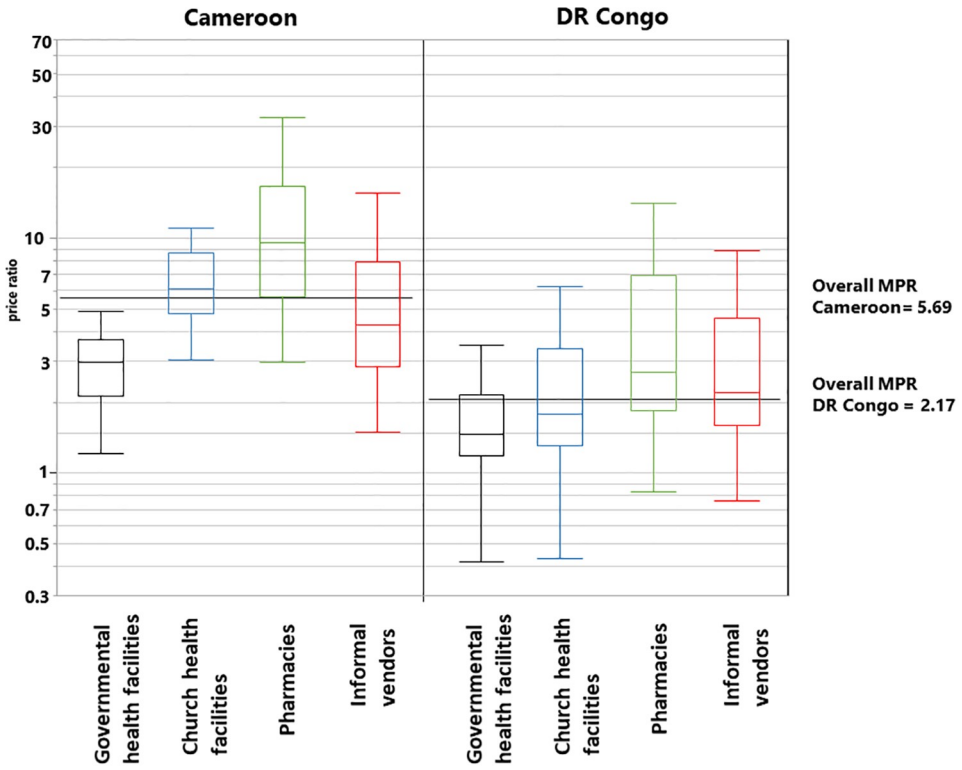

Fig 3. Boxplots of the price ratios in the four different types of facilities.

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As shown in Table 3, medicines sold in pharmacies were less affordable than medicines sold in the other types of facilities. While treatments with medicines produced in Africa and Asia were affordable in many cases, those with medicines imported from Europe were not. Likewise, treatment courses with generic medicines were affordable, while treatment courses with originator medicines were not.

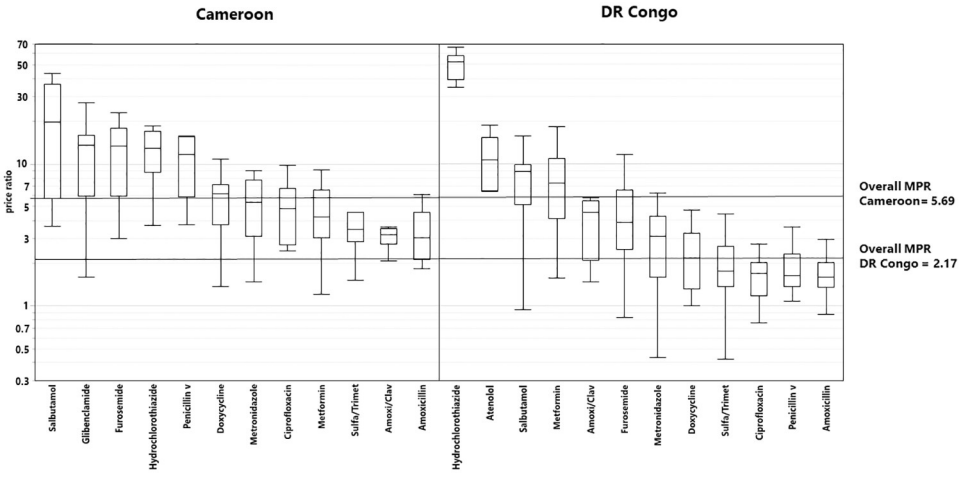

Fig 4. Boxplots of the price ratios of the collected medicines sorted by API and country.

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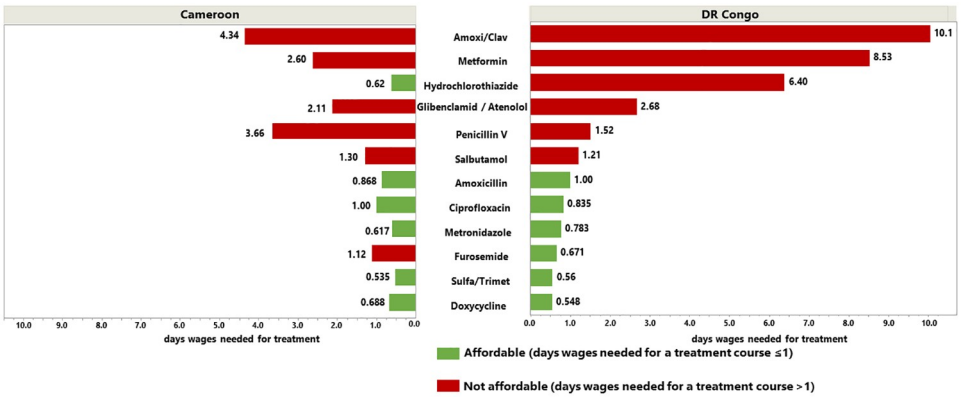

Fig 5. Median prices per treatment and median days' wages needed for treatment.

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Discussion

With price data from a total of 461 medicines purchased at 60 sampling sites this study provides valuable new insight into the availability and affordability of essential medicines in Cameroon and the DR Congo.

Prior to this study, only a single comprehensive investigation of medicine availability in the DR Congo had been carried out, as part of the "Service Availability and Readiness Assessment" (SARA) published by the DR Congo Ministry of Public Health in 2014 [16]. This SARA included data on 20 medicines, most of them against NCDs. In contrast to our study, it did not include private pharmacies and informal vendors. For government and church (or private) health facilities, it reported an average medicine availability of 20%, which is in agreement with our findings on the availability of medicines against NCDs in these kind of facilities (Fig 2). The SARA included only four antibiotics, three of them as injectable solutions and one as oral suspension. In contrast, our present study included six first-line ("ACCESS GROUP") and one second-line ("WATCH GROUP") antibiotics in form of capsules or tablets [30]. It is important and encouraging that, with the exception of the expensive amoxicillin/clavulanic acid, these antibiotics showed good availability in the health facilities of the DR Congo. This is in agreement with the finding by O'Connel et al. [15] that first-line antimalarials showed good availability in public health facilities of the DR Congo. In contrast to the SARA [16], our study included pharmacies and informal vendors, showing that they accomplished a higher medicines availability than government and church health facilities. This should be seen as a motivation to further improve availability in government and church facilities. To the best of our knowledge, no comprehensive analysis of medicine prices and affordability has been published from the DR Congo so far. In other low- and middle-income countries, median price ratios have been reported to be, on average 3.1 in the public sector and 5.3 in the private sector [31]. In comparison, median price ratios are remarkably low in the DR Congo (Table 3), indicating either successful cost-effective procurement, or subsidies to medicine prices, or both. Especially government and church health facilities in the DR Congo sell medicines cheaper than informal vendors. This is desirable from a public health perspective, in order to minimize the incentive for patients for to buy from informal vendors where medicine quality problems are expected to occur more frequently.

In Cameroon, prior to our present study one previous comprehensive investigation of medicine availability and prices has been published [14]. It investigated 22 medicines against cardiovascular diseases and diabetes, four of these (furosemide, glibenclamide,

hydrochlorothiazide and metformin) were also included in the present study. The overall availability of each of these four medicines reported by Jingi et al. [14] is similar to the one reported in our study for Cameroon. However, our study showed lower availability in government health facilities. This may indicate a deterioration of medicine availability in the government facilities of Cameroon since 2012. However, informal vendors in Cameroon stocked and readily sold all investigated antibiotics including the expensive amoxicillin / clavulanic acid tablets. In view of the increasing danger of increasing antimicrobial resistance, this is a worrying finding.

Just as we did in our study, Jingi et al. [14] reported median price ratios of the medicines investigated relative to the international reference price published by MSH [27]. The overall MPR from the data published by these authors results as 5.97, similar to the overall value of 5.69 which we show for Cameroon in Table 2. For the individual medicines, the MPRs reported by Jingi et al. [14] range from 0.59 to 70.81. Notably, for the four medicines furosemide, glibenclamide, hydrochlorothiazide and metformin the authors report lower MPRs and consequently better affordability than reported in our present study. Closer investigation showed that the MPRs for these four medicines which we recorded at government health facilities were, in fact, quite similar to those reported by Jingi et al. who mainly focused on government facilities. However, since only few government facilities had these medicines available, in our study most (92%) of the prices of these four medicines derive from pharmacies, church health facilities and informal vendors, where medicines are substantially more expensive than in government facilities. The overall higher MPRs of medicines from private pharmacies may reflect the presence of a more affluent middle class in Cameroon which is able to afford more expensive medicines in private pharmacy shops.

As specific reason for concern resulting from our study is the overall low availability and affordability of medicines against non-communicable diseases. The WHO Global Status Report on NCDs 2014 [32] emphasized that the burden of disease regarding NCDs is heavily concentrated in low and middle-income countries. Hunter-Adams et al. [33] expect that the burden of diabetes in Africa will increase till 2035 by 110%. Also a study from Tsabang et al. [34] revealed that the prevalence of diabetes and hypertension is increasing in Cameroon. Since medicines against NCDs showed only 11% availability in governmental health facilities in the DR Congo and 33% in the governmental health facilities in Cameroon, drastic improvements are needed to ensure that medications against NCDs are available and affordable for the population, and that health care staff is trained in diagnosis, management and the treatment of NCDs. Notably, medicines against NCDs were well available in the private pharmacies in Cameroon and in the DR Congo and in informal vendors in Cameroon.

The affordability of most of the available medicines against NCDs was low. For a 30 days' treatment with metformin, 4.9 days wages in DR Congo and 2.8 days wages in Cameroon would be necessary. In both countries a major share of health care expenditures has to be paid by patients out of pocket [35, 36]. Notably, a 2019 survey indicated that high prices of medicines were a prominent cause for non-adherence among diabetes patients in two hospitals in Cameroon [37]. This underlines the importance of the affordability of essential medicines as a core priority in achieving universal health coverage, as already highlighted by Wirtz et al. [38].

In our study, the most expensive medicines were originator medicines, produced mainly in Europe. Hydrochlorothiazide in the Democratic Republic of Congo was solely available as Esidrex® (Novartis) in private pharmacies at an extraordinary high price 53 times higher than the MSH reference price. This may drive the population to buy hydrochlorothiazide from illicit sources, providing medicines of doubtful quality.

Limitations of this study

This study followed the WHO/HAI methodology [25] in data analysis but not in data collection, since it was part of a medicine quality study. We collected the price of the cheapest brand for each of the 12 requested medicines in each of the sampling sites, and did not ask for both the lowest priced generics and the lowest price originator for every medicine in every sample site, as foreseen by the WHO/HAI methodology [25]. Also most of our sampling sites were located in small or large towns, therefore this survey might not reflect the situation for the rural population in Cameroon and the DR Congo correctly. Since the medicines selected were antibiotics, cardiovascular medicines and antidiabetics, the results are not representative for other therapeutic classes such as antiretrovirals or cytostatics. This survey measured medicine availability and prices only at one time point and does not reflect changes over time. Data analysis has been limited to descriptive statistical methods. The authors are carrying out additional studies on availability, prices and quality of medicines in Africa, and intend to present additional data analyses once these studies have been completed.

Conclusion

The average medicine availability in Cameroon and the Democratic Republic of Congo is lower than the 80% quota targeted by the WHO. Despite the high availability of antibiotics in the private sector, the availability of medicines in the public sector requires improvement in both countries. Also regarding the affordability, further improvements are necessary at least for some of the investigated medicines. This is especially true for the medicines against non-communicable diseases, in order to ensure availability and affordability.

Supporting information

S1 Table.
(XLSX)

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Supervision: Lutz Heide.

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Writing – original draft: Simon Schäfermann.

Writing – review & editing: Lutz Heide.

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S1 Table

Country	Region	Site type	Sample_ID	Product name	INN	Indication	Stated amount of the API	Dosage form	Manufacturer	Labeling	Country of origin	Storage conditions	Price per unit [USD]	Price ratio	Price per Treatment [US dollar]	Days wages needed for treatment
Congo, the Democratic Republic of the	Kadutu	church health facility	QMC001	Amoxy-500	Amoxicillin	antibiotic	500	Capsules	CSPC Zhonguo Pharmaceuticals Co.Ltd	generic	China	dry and cool, protected from light	0.0518601	1.7286693	1.0890617	1.0274167
Congo, the Democratic Republic of the	Kadutu	church health facility	QMC002	Arauclav	Amoxi/Clav	antibiotic	500/ 62.5	Tablets	Medicef Pharma	branded	India	below 25°C	0.4298616		9.0270928	8.5161253
Congo, the Democratic Republic of the	Kadutu	church health facility	QMC003	Eflaron 250	Metronidazole	antibiotic	250	Tablets	DAWA Ltd	branded	Kenya	below 30°C	0.0145461	2.3846098	0.610937	0.5763557
Congo, the Democratic Republic of the	Kadutu	church health facility	QMC004	Ciprofloxacin Tablets	Ciprofloxacin	antibiotic	500	Tablets	Reyoung Pharmaceutical Co. Ltd	generic	China	below 25°C	0.0989769	2.6535351	1.385676	1.3072415
Congo, the Democratic Republic of the	Kadutu	church health facility	QMC005	Doxicilcina	Doxycycline	antibiotic	100	Capsules	Farmasino Pharmaceutical Co.Ltd	generic	China	dry and cool, protected from light	0.0463789	3.4871378	0.9275787	0.8750742
Congo, the Democratic Republic of the	Kadutu	church health facility	QMC006	Co-Trimoxazole USP	Sulfa/Trimet	antibiotic	400 / 80	Tablets	Guillin Pharmaceutical Co.Ltd	generic	China	below 30°C	0.0120164	1.0013633	0.3364581	0.3174133
Congo, the Democratic Republic of the	Kadutu	government health facility	QMC007	Moxyclav	Amoxi/Clav	antibiotic	500/ 62.5	Tablets	Medicef Pharma	branded	India	below 25°C	0.3644752		7.6539786	7.2207345
Congo, the Democratic Republic of the	Kadutu	government health facility	QMC008	Co-trimoxazole BP	Sulfa/Trimet	antibiotic	400 / 80	Tablets	Medopharma	generic	India	below 30°C	0.0193527	1.612722	0.5418746	0.5112024
Congo, the Democratic Republic of the	Kadutu	government health facility	QMC009	Ciprofloxacin	Ciprofloxacin	antibiotic	500	Tablets	Sinoch Jiangsu co. Ltd	generic	China	dry and cool, protected from light	0.0817112	2.1906501	1.1439575	1.0792052
Congo, the Democratic Republic of the	Kadutu	government health facility	QMC010	Metronidazole Tablets	Metronidazole	antibiotic	250	Tablets	Jinzhu Jiuyang Pharmaceutical co. Ltd	generic	China	dry and cool, protected from light	0.0236533	3.877583	0.9934368	0.9372045
Congo, the Democratic Republic of the	Kadutu	pharmacy	QMC012	Ciprofloxacin Tablets USP	Ciprofloxacin	antibiotic	500	Tablets	CSPC Ouyi Pharmaceutical Co.Ltd	generic	China	below 30°C	0.0537574	1.4412172	0.7526036	0.7100034
Congo, the Democratic Republic of the	Kadutu	pharmacy	QMC013	Metformina bluefish	Metformin	medicine against NCD	850	Tablets	Bluefish Pharmaceutical AD	branded	Sweden	dry and cool, protected from light	0.189732	9.4866	10.044635	9.476071
Congo, the Democratic Republic of the	Kadutu	pharmacy	QMC014	Amoxicillin	Amoxicillin	antibiotic	500	Capsules	Yanzhou xierkangata pharmaceutical Co Ltd.	generic	China	dry and cool, protected from light	0.063244	2.1081333	1.328124	1.2529472
Congo, the Democratic Republic of the	Kadutu	pharmacy	QMC015	Atenol	Atenolol	medicine against NCD	100	Tablets	Kerrekappa Eroterapici spa	branded	Italy	dry and cool, protected from light	0.252976	14.212135	3.79464	3.5798491

Country	Region	Site type	Sample_ID	Product name	INN	Indication	Stated amount of the API	Dosage form	Manufacturer	Labeling	Country of origin	Storage conditions	Price per unit [USD]	Price ratio	Price per Treatment [US dollar]	Days wages needed for treatment
Congo, the Democratic Republic of the	Kadutu	pharmacy	QMC016	Doxycycline	Doxycycline	antibiotic	100	Capsules	Yanzhou xierkangata pharmaceutical Co Ltd.	generic	China	dry and cool, protected from light	0.031622	2.377594	0.63244	0.5966415
Congo, the Democratic Republic of the	Kadutu	pharmacy	QMC017	Frusema	Furosemide	medicine against NCD	40	Tablets	Arco Pharma pvt. Ltd	branded	India	below 25°C	0.0237165	3.8879508	0.711495	0.6712217
Congo, the Democratic Republic of the	Kadutu	pharmacy	QMC018	Salbutamol Tablets BP	Salbutamol	medicine against NCD	4	Tablets	Aura pharmaceuticals pvt. ltd	generic	India	dry and cool, protected from light	0.031622	9.881875	1.42299	1.3424434
Congo, the Democratic Republic of the	Kadutu	pharmacy	QMC019	Phenoxymethylpenicillin	Penicillin v	antibiotic	250	Tablets	North China Pharmaceutical Group, PRC	generic	China	below 30°C	0.031622	1.7967045	1.770832	1.6705962
Congo, the Democratic Republic of the	Kadutu	pharmacy	QMC020	Co-Trimoxazole	Sulfa/Trimet	antibiotic	400 / 80	Tablets	Milan laboratories pvt. Ltd	generic	India	not stated	0.0252976	2.1081333	0.7083328	0.6682385
Congo, the Democratic Republic of the	Kadutu	informal vendor	QMC021	Miloxy 250	Amoxicillin	antibiotic	250	Capsules	Milan laboratories pvt. Ltd	branded	India	below 30°C	0.0151786	0.94866	0.6374995	0.6014146
Congo, the Democratic Republic of the	Kadutu	informal vendor	QMC022	Curam 625	Amoxi/Clav	antibiotic	500/ 125	Tablets	Sandoz	originator	Austria	below 25°C	0.242857	1.4799327	5.0999962	4.8113171
Congo, the Democratic Republic of the	Kadutu	pharmacy	QMC024	Moxyclav	Amoxi/Clav	antibiotic	875/ 125	Tablets	Medicef Pharma	branded	India	below 25°C	0.711495	4.5174286	8.53794	8.0546604
Congo, the Democratic Republic of the	Kadutu	informal vendor	QMC025	Sulfatrim	Sulfa/Trimet	antibiotic	400 / 80	Tablets	Shalina Laboratories pvt Ltd	branded	India	below 30°C	0.0189732	1.5811	0.5312496	0.5011789
Congo, the Democratic Republic of the	Kadutu	informal vendor	QMC026	Ciprofloxacin	Ciprofloxacin	antibiotic	500	Tablets	Mepro pharmaceutical pvt- LTd	generic	India	below 30°C	0.0284598	0.7629973	0.3984372	0.3758842
Congo, the Democratic Republic of the	Kadutu	informal vendor	QMC027	Speniv Tablets 250	Penicillin v	antibiotic	250	Tablets	sparsh bio-tech pvt. Ltd	branded	India	below 25°C	0.0252976	1.4373636	1.4166656	1.336477
Congo, the Democratic Republic of the	Kadutu	informal vendor	QMC028	Metrosim-200	Metronidazole	antibiotic	200	Tablets	Strides Shasum Ltd	branded	India	below 30°C	0.0126488	2.0735738	0.664062	0.6264736
Congo, the Democratic Republic of the	Kadutu	informal vendor	QMC029	Agodox	Doxycycline	antibiotic	100	Capsules	Agog pharma pvt.Ltd	branded	India	below 30°C	0.0284598	2.1398346	0.569196	0.5369774
Congo, the Democratic Republic of the	Kadutu	informal vendor	QMC030	Glucophage	Metformin	medicine against NCD	850	Tablets	Merck	originator	Belgium	dry and cool, protected from light	0.0910714	4.553568	4.8214249	4.5485141
Congo, the Democratic Republic of the	Kadutu	informal vendor	QMC031	Frusema	Furosemide	medicine against NCD	40	Tablets	Arco Pharma pvt. Ltd	branded	India	below 25°C	0.0284598	4.665541	0.853794	0.805466
Congo, the Democratic Republic of the	Kadutu	informal vendor	QMC032	Salbutamol Tablets BP	Salbutamol	medicine against NCD	4	Tablets	Aura pharmaceuticals pvt. ltd	generic	India	dry and cool, protected from light	0.031622	9.881875	1.42299	1.3424434

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Congo, the Democratic Republic of the	Ruzizi	government health facility	QMC036	Metronyl	Metronidazole	antibiotic	250	Tablets	MAC'S pharmaceuticals Ltd	branded	Kenya	dry and cool, protected from light	0.0075893	1.2441443	0.3187498	0.3007073
Congo, the Democratic Republic of the	Ruzizi	government health facility	QMC037	Ciproz 500	Ciprofloxacin	antibiotic	500	Tablets	Zenufa Laboratoire	branded	Kongo	dry and cool, protected from light	0.0455357	1.2207957	0.6374995	0.6014146
Congo, the Democratic Republic of the	Ruzizi	government health facility	QMC038	Amoxicilinia USP	Amoxicillin	antibiotic	250	Tablets	Medopharma	generic	India	below 30°C	0.0230714	1.4419632	0.9689993	0.9141503
Congo, the Democratic Republic of the	Ruzizi	government health facility	QMC039	Doxicilcina	Doxycycline	antibiotic	100	Capsules	Farmasino Pharmaceutical Co.Ltd	generic	China	dry and cool, protected from light	0.0222619	1.6738262	0.4452378	0.4200356
Congo, the Democratic Republic of the	Ruzizi	government health facility	QMC040	Phenoxymethylpenicillin Tablets BP	Penicillin v	antibiotic	250	Tablets	North China Pharmaceutical Group, PRC	generic	China	dry and cool, protected from light	0.0252976	1.4373636	1.4166656	1.336477
Congo, the Democratic Republic of the	Ruzizi	pharmacy	QMC042	Zenogyl 250	Metronidazole	antibiotic	250	Tablets	Zenufa Laboratoire	branded	Kongo	dry and cool, protected from light	0.010119	1.658859	0.4249997	0.4009431
Congo, the Democratic Republic of the	Ruzizi	pharmacy	QMC043	Monamox-250 DT	Amoxicillin	antibiotic	250	Tablets	Zee Laboratories	branded	India	dry and cool, protected from light	0.0252976	1.5811	1.0624992	1.0023577
Congo, the Democratic Republic of the	Ruzizi	pharmacy	QMC044	Augmentin Adultes	Amoxi/Clav	antibiotic	500/ 62.5	Tablets	Glaxo Welcome Production	originator	France	below 25°C	0.5270333		11.0677	10.441226
Congo, the Democratic Republic of the	Ruzizi	pharmacy	QMC045	BGMET 850	Metformin	medicine against NCD	850	Tablets	Bliss GVS Pharma Ltd	branded	India	below 30°C	0.0801091	4.0054533	4.2410682	4.0010078
Congo, the Democratic Republic of the	Ruzizi	pharmacy	QMC046	Sulphatrim	Sulfa/Trimet	antibiotic	400 / 80	Tablets	Lincoln Pharmaceuticals Ltd	branded	India	dry and cool, protected from light	0.0202381	1.6865067	0.5666662	0.5345908
Congo, the Democratic Republic of the	Ruzizi	pharmacy	QMC053	Ecoflox-500	Ciprofloxacin	antibiotic	500	Tablets	Medley Pharmaceuticals Ltd	branded	India	below 30°C	0.0404762	1.0851517	0.5666662	0.5345908
Congo, the Democratic Republic of the	Ruzizi	pharmacy	QMC054	Frusemide	Furosemide	medicine against NCD	40	Tablets	Prashi Pharma prvt. Ltd.	branded	India	dry and cool, protected from light	0.0151786	2.4882885	0.4553568	0.4295819
Congo, the Democratic Republic of the	Ruzizi	pharmacy	QMC055	Siphadox 100	Doxycycline	antibiotic	100	Capsules	Societe industrielle Pharmaceutique	branded	Burundi	dry and cool, protected from light	0.0404762	3.0433203	0.8095232	0.7637011
Congo, the Democratic Republic of the	Ruzizi	pharmacy	QMC056	Speniv Tablets 250	Penicillin v	antibiotic	250	Tablets	sparsh bio-tech pvt. Ltd	branded	India	below 25°C	0.0202381	1.1498909	1.1333325	1.0691816

Country	Region	Site type	Sample_ID	Product name	INN	Indication	Stated amount of the API	Dosage form	Manufacturer	Labeling	Country of origin	Storage conditions	Price per unit [USD]	Price ratio	Price per Treatment [US dollar]	Days wages needed for treatment
Congo, the Democratic Republic of the	Ruzizi	pharmacy	QMC057	Salbutamol	Salbutamol	medicine against NCD	4	Tablets	New Cesamex	generic	Kongo	dry and cool, protected from light	0.0252976	7.9055	1.138392	1.0739547
Congo, the Democratic Republic of the	Ruzizi	church health facility	QMC058	Metronidazole Tablets	Metronidazole	antibiotic	250	Tablets	Jinzhu Jiuyang Pharmaceutical co. Ltd	generic	China	dry and cool, protected from light	0.021503	3.5250754	0.9031243	0.8520041
Congo, the Democratic Republic of the	Ruzizi	church health facility	QMC059	Doxycycline Hyclate Tablets USP	Doxycycline	antibiotic	100	Tablets	Nanjing Baijingyu Pahramcuetical Co.Ltd	generic	China	below 30°C	0.029029	2.1826313	0.5805799	0.5477169
Congo, the Democratic Republic of the	Ruzizi	church health facility	QMC060	Co-trimoxazole BP	Sulfa/Trimet	antibiotic	400 / 80	Tablets	Medopharma	generic	India	below 30°C	0.0193527	1.612722	0.5418746	0.5112024
Congo, the Democratic Republic of the	Ruzizi	church health facility	QMC061	Zenamide	Furosemide	medicine against NCD	40	Tablets	Zenufa Laboratoire	branded	Kongo	dry and cool, protected from light	0.0322544	5.2876131	0.9676332	0.9128615
Congo, the Democratic Republic of the	Ruzizi	church health facility	QMC062	Amoxicillin Capsules BP	Amoxicillin	antibiotic	500	Capsules	Sinopharm Weiqida Pharmaceuticals Co.LTd	generic	China	below 25°C	0.0322544	1.075148	0.6773432	0.6390031
Congo, the Democratic Republic of the	Ruzizi	church health facility	QMC063	Ciprofloxacin Tablets USP	Ciprofloxacin	antibiotic	500	Tablets	CSPC Ouyi Pharmaceutical Co.Ltd	generic	China	below 30°C	0.0752604	2.017704	1.053645	0.9940048
Congo, the Democratic Republic of the	Ruzizi	church health facility	QMC065	Shalformin	Metformin	medicine against NCD	500	Tablets	Shalina Laboratories pvt Ltd	branded	India	below 30°C	0.0709598	4.7306512	6.3863791	6.024886
Congo, the Democratic Republic of the	Ruzizi	government health facility	QMC067	Zenamide	Furosemide	medicine against NCD	40	Tablets	Zenufa Laboratoire	branded	Kongo	dry and cool, protected from light	0.0679999	11.147533	2.0399985	1.9245269
Congo, the Democratic Republic of the	Ruzizi	government health facility	QMC068	Co-trimoxazole BP	Sulfa/Trimet	antibiotic	400 / 80	Tablets	Medopharma	generic	India	below 30°C	0.0126488	1.0540667	0.3541664	0.3341192
Congo, the Democratic Republic of the	Ruzizi	informal vendor	QMC069	Moxyclav	Amoxi/Clav	antibiotic	500/ 62.5	Tablets	Medicef Pharma	branded	India	below 25°C	1.517856		31.874976	30.070732
Congo, the Democratic Republic of the	Ruzizi	informal vendor	QMC071	Frusema	Furosemide	medicine against NCD	40	Tablets	Arco Pharma pvt. Ltd	branded	India	below 25°C	0.0151786	2.4882885	0.4553568	0.4295819
Congo, the Democratic Republic of the	Ruzizi	informal vendor	QMC072	Doxicilcina	Doxycycline	antibiotic	100	Capsules	Farmasino Pharmaceutical Co.Ltd	branded	China	dry and cool, protected from light	0.0303571	2.2824902	0.6071424	0.5727758
Congo, the Democratic Republic of the	Ruzizi	informal vendor	QMC073	Amoxy-500	Amoxicillin	antibiotic	500	Capsules	CSPC Zhonguo Pharmaceuticals Co.Ltd	branded	China	dry and cool, protected from light	0.0303571	1.011904	0.6374995	0.6014146
Congo, the Democratic Republic of the	Ruzizi	informal vendor	QMC074	Metrosim-200	Metronidazole	antibiotic	200	Tablets	Strides Shasum Ltd	branded	India	below 30°C	0.015811	2.5919672	0.8300775	0.783092

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Congo, the Democratic Republic of the	Ruzizi	informal vendor	QMC075	Phenoxymethylpenicillin	Penicillin v	antibiotic	250	Tablets	North China Pharmaceutical Group, PRC	generic	China	below 30°C	0.0252976	1.4373636	1.4166656	1.336477
Congo, the Democratic Republic of the	Ruzizi	informal vendor	QMC077	Ciprofloxacin Tablets USP	Ciprofloxacin	antibiotic	500	Tablets	CSPC Ouyi Pharmaceutical Co.Ltd	generic	China	below 30°C	0.0303571	0.8138638	0.4249997	0.4009431
Congo, the Democratic Republic of the	Ruzizi	informal vendor	QMC078	Kam Cotri	Sulfa/Trimet	antibiotic	400 / 80	Tablets	Kampala Pharmaceutical Industries	branded	Uganda	below 30°C	0.0354166	2.9513867	0.9916659	0.9355339
Congo, the Democratic Republic of the	Nyangezi	pharmacy	QMC095	Co-Trimoxazole USP	Sulfa/Trimet	antibiotic	400 / 80	Tablets	Guillin Pharmaceutical Co.Ltd	generic	China	below 30°C	0.0252976	2.1081333	0.7083328	0.6682385
Congo, the Democratic Republic of the	Nyangezi	pharmacy	QMC096	Penicillin VK Tablets	Penicillin v	antibiotic	250	Tablets	Yanzhou xierkangata pharmaceutical Co Ltd.	generic	China	dry and cool, protected from light	0.0252976	1.4373636	1.4166656	1.336477
Congo, the Democratic Republic of the	Nyangezi	pharmacy	QMC097	Mefagyl	Metronidazole	antibiotic	200	Tablets	Farmasino Pharmaceutical Co.Ltd	branded	China	dry and cool, protected from light	0.0126488	2.0735738	0.664062	0.6264736
Congo, the Democratic Republic of the	Nyangezi	pharmacy	QMC098	Doxycycline Hyclate tablets USP	Doxycycline	antibiotic	100	Tablets	CSPC Ouyi Pharmaceutical Co.Ltd	generic	China	below 25°C	0.063244	4.755188	1.26488	1.193283
Congo, the Democratic Republic of the	Nyangezi	pharmacy	QMC099	Amoxin 250	Amoxicillin	antibiotic	250	Capsules	Phatkin B.P	branded	Kongo	dry and cool, protected from light	0.0252976	1.5811	1.0624992	1.0023577
Congo, the Democratic Republic of the	Nyangezi	pharmacy	QMC101	Ciprofloxacine Tablets USP	Ciprofloxacin	antibiotic	500	Tablets	Sinochem Jiangsu co. Ltd	generic	China	dry and cool, protected from light	0.063244	1.6955496	0.885416	0.8352981
Congo, the Democratic Republic of the	Nyangezi	pharmacy	QMC102	Glucophage	Metformin	medicine against NCD	500	Tablets	Merck	originator	Belgium	not stated	0.15811	10.540667	14.2299	13.424434
Congo, the Democratic Republic of the	Nyangezi	pharmacy	QMC103	Frusema	Furosemide	medicine against NCD	40	Tablets	Arco Pharma pvt. Ltd	branded	India	below 25°C	0.0126488	2.0735738	0.379464	0.3579849
Congo, the Democratic Republic of the	Nyangezi	pharmacy	QMC104	Salbesone	Salbutamol	medicine against NCD	4	Tablets	Lord Lifescience Pvt.Ltd	branded	India	dry and cool, protected from light	0.031622	9.881875	1.42299	1.3424434
Congo, the Democratic Republic of the	Nyangezi	informal vendor	QMC105	Amoxicillin Gelules	Amoxicillin	antibiotic	250	Capsules	Medopharma	generic	India	below 25°C	0.0263517	1.6469792	1.10677	1.0441226
Congo, the Democratic Republic of the	Nyangezi	informal vendor	QMC106	Co-Trimoxazole Tablets BP Trimago	Sulfa/Trimet	antibiotic	400 / 80	Tablets	Agog pharma pvt.Ltd	branded	India	below 30°C	0.0221354	1.8446167	0.6197912	0.5847087
Congo, the Democratic Republic of the	Nyangezi	informal vendor	QMC107	Speniv Tablets 250	Penicillin v	antibiotic	250	Tablets	sparsh bio-tech pvt. Ltd	branded	India	below 25°C	0.031622	1.7967045	1.770832	1.6705962
Congo, the Democratic Republic of the	Nyangezi	informal vendor	QMC108	Metrosim-200	Metronidazole	antibiotic	200	Tablets	Strides Shasum Ltd	branded	India	below 30°C	0.0189732	3.1103607	0.996093	0.9397104

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Congo, the Democratic Republic of the	Nyangezi	church health facility	QMC109	Co-trimoxazole BP	Sulfa/Trimet	antibiotic	400 / 80	Tablets	Medopharma	generic	India	below 30°C	0.031622	2.6351667	0.885416	0.8352981
Congo, the Democratic Republic of the	Nyangezi	church health facility	QMC110	Eflaron 250	Metronidazole	antibiotic	250	Tablets	DAWA Ltd	branded	Kenya	below 30°C	0.0379464	6.2207213	1.5937488	1.5035366
Congo, the Democratic Republic of the	Nyangezi	government health facility	QMC111	Amoxicillin Capsules BP	Amoxicillin	antibiotic	500	Capsules	Reyoung Pharmaceutical Co. Ltd	generic	China	below 30°C	0.0645089	2.150296	1.3546865	1.2780061
Congo, the Democratic Republic of the	Nyangezi	government health facility	QMC113	Phenoxymethyl Pencillin	Penicillin v	antibiotic	250	Tablets	NCPC North Best	generic	China	below 30°C	0.0430059	2.4435182	2.4083315	2.2720109
Congo, the Democratic Republic of the	Nyangezi	government health facility	QMC114	Cotrimoxazole Tablets B.P	Sulfa/Trimet	antibiotic	400 / 80	Tablets	CSPC Ouyi Pharmaceutical Co.Ltd	generic	China	below 30°C	0.0322544	2.68787	0.9031243	0.8520041
Congo, the Democratic Republic of the	Nyangezi	government health facility	QMC115	Metronidazole Tablets USP	Metronidazole	antibiotic	250	Tablets	Medopharma	generic	India	below 30°C	0.021503	3.5250754	0.9031243	0.8520041
Congo, the Democratic Republic of the	Nyangezi	government health facility	QMC116	Ciprofloxacine Tablets USP	Ciprofloxacin	antibiotic	500	Tablets	Jiangsu Pengyao Pharmaceutical Ltd	generic	China	below 30°C	0.0752604	2.017704	1.053645	0.9940048
Congo, the Democratic Republic of the	Nyangezi	government health facility	QMC117	Doxycycline Hyclate USP	Doxycycline	antibiotic	100	Tablets	Medopharma	generic	India	below 30°C	0.0139769	1.0508965	0.2795385	0.2637155
Congo, the Democratic Republic of the	Nyangezi	government health facility	QMC118	Furosemid BP	Furosemide	medicine against NCD	40	Tablets	Medopharma	generic	India	below 30°C	0.0150521	2.4675528	0.4515622	0.426002
Congo, the Democratic Republic of the	Nyemba	pharmacy	QMC119	Amoxicillin Capsules B.P	Amoxicillin	antibiotic	500	Capsules	Sinochem Jiangsu co. Ltd	generic	China	dry and cool, protected from light	0.0442708	1.4756933	0.9296868	0.877063
Congo, the Democratic Republic of the	Nyemba	pharmacy	QMC120	Amoxicillin and Clavulanate Potassium Tablets	Amoxi/Clav	antibiotic	500/ 125	Tablets	Intermed	generic	India	below 25°C	0.379464	2.3123949	7.968744	7.517683
Congo, the Democratic Republic of the	Nyemba	pharmacy	QMC121	Cotrimex-480	Sulfa/Trimet	antibiotic	400 / 80	Tablets	Aura pharmaceuticals pvt. ltd	branded	India	dry and cool, protected from light	0.0252976	2.1081333	0.7083328	0.6682385
Congo, the Democratic Republic of the	Nyemba	pharmacy	QMC122	Ecoflox-500	Ciprofloxacin	antibiotic	500	Tablets	Medley Pharmaceuticals Ltd	branded	India	below 30°C	0.0442708	1.1868847	0.6197912	0.5847087
Congo, the Democratic Republic of the	Nyemba	pharmacy	QMC123	Speniv Tablets 250	Penicillin v	antibiotic	250	Tablets	sparsh bio-tech pvt. Ltd	branded	India	below 25°C	0.031622	1.7967045	1.770832	1.6705962
Congo, the Democratic Republic of the	Nyemba	pharmacy	QMC125	Metrosim-200	Metronidazole	antibiotic	200	Tablets	Strides Shasum Ltd	branded	India	below 30°C	0.0126488	2.0735738	0.664062	0.6264736
Congo, the Democratic Republic of the	Nyemba	pharmacy	QMC126	Doxycycline Gelules BP	Doxycycline	antibiotic	100	Capsules	Astra Lifecare	generic	India	below 30°C	0.031622	2.377594	0.63244	0.5966415

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Congo, the Democratic Republic of the	Nyemba	pharmacy	QMC127	Shalformin	Metformin	medicine against NCD	500	Tablets	Ciron Drugs and Pharmaceuticals Ltd	branded	India	below 30°C	0.2740573	18.270489	24.66516	23.269019
Congo, the Democratic Republic of the	Nyemba	pharmacy	QMC128	Catenol 100	Atenolol	medicine against NCD	100	Tablets	Cadila Healthcare Ltd	branded	India	below 30°C	0.252976	14.212135	3.79464	3.5798491
Congo, the Democratic Republic of the	Nyemba	pharmacy	QMC129	Esidrex	Hydrochlorothiazide	medicine against NCD	25	Tablets	Novartis Farmaceutica s.A	originator	Spain	below 25°C	0.2150296	50.006884	6.450888	6.0857434
Congo, the Democratic Republic of the	Nyemba	pharmacy	QMC130	Frusemide	Furosemide	medicine against NCD	40	Tablets	Prashi Pharma prvt. Ltd.	branded	India	dry and cool, protected from light	0.015811	2.5919672	0.47433	0.4474811
Congo, the Democratic Republic of the	Nyemba	pharmacy	QMC131	Salbutamol Tablets BP	Salbutamol	medicine against NCD	4	Tablets	Aura pharmaceuticals pvt. ltd	generic	India	dry and cool, protected from light	0.0189732	5.929125	0.853794	0.805466
Congo, the Democratic Republic of the	Nyemba	informal vendor	QMC132	Amoxyn-500	Amoxicillin	antibiotic	500	Capsules	Farmasino Pharmaceutical Co.Ltd	branded	China	below 25°C	0.0505952	1.6865067	1.0624992	1.0023577
Congo, the Democratic Republic of the	Nyemba	informal vendor	QMC133	Co-Trimoxazole Tablets BP Megatrim	Sulfa/Trimet	antibiotic	400 / 80	Tablets	Fourrts	branded	India	dry and cool, protected from light	0.0252976	2.1081333	0.7083328	0.6682385
Congo, the Democratic Republic of the	Nyemba	informal vendor	QMC134	Ciprofloxacine Tablets USP	Ciprofloxacin	antibiotic	500	Tablets	Sinochem Jiangsu co. Ltd	generic	China	dry and cool, protected from light	0.0505952	1.3564397	0.7083328	0.6682385
Congo, the Democratic Republic of the	Nyemba	informal vendor	QMC135	Peni-V	Penicillin v	antibiotic	250	Tablets	Farmasino Pharmaceutical Co.Ltd	branded	China	dry and cool, protected from light	0.031622	1.7967045	1.770832	1.6705962
Congo, the Democratic Republic of the	Nyemba	informal vendor	QMC137	Metronidazole Tablets	Metronidazole	antibiotic	250	Tablets	Jinzhu Jiuyang Pharmaceutical co. Ltd	generic	China	dry and cool, protected from light	0.0126488	2.0735738	0.5312496	0.5011789
Congo, the Democratic Republic of the	Nyemba	informal vendor	QMC138	Doxycycline Capsules	Doxycycline	antibiotic	100	Capsules	Shanxi Lianbang Pharmaceutical ltd	generic	China	dry and cool, protected from light	0.031622	2.377594	0.63244	0.5966415
Congo, the Democratic Republic of the	Nyemba	informal vendor	QMC139	Frusema	Furosemide	medicine against NCD	40	Tablets	Arco Pharma pvt. Ltd	branded	India	below 25°C	0.0126488	2.0735738	0.379464	0.3579849
Congo, the Democratic Republic of the	Nyemba	informal vendor	QMC140	Kam Vent	Salbutamol	medicine against NCD	4	Tablets	Kampala Pharmaceutical Industries	branded	Uganda	below 30°C	0.015811	4.9409375	0.711495	0.6712217
Congo, the Democratic Republic of the	Nyemba	government health facility	QMC141	Amoxicillin Tablets USP	Amoxicillin	antibiotic	500	Tablets	CSPC Zhonguo Pharmaceuticals Co.Ltd	generic	China	below 30°C				
Congo, the Democratic Republic of the	Nyemba	government health facility	QMC142	Co-trimoxazole BP	Sulfa/Trimet	antibiotic	400 / 80	Tablets	Medopharma	generic	India	below 30°C				

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Congo, the Democratic Republic of the	Nyemba	governmen t health facility	QMC143	Ciprofloxacin USP	Ciprofloxacin	antibiotic	500	Tablets	Medopharma	generic	India	below 30°C				
Congo, the Democratic Republic of the	Nyemba	governmen t health facility	QMC144	Metronidazole BP	Metronidazole	antibiotic	250	Tablets	Medopharma	generic	India	below 30°C				
Congo, the Democratic Republic of the	Nyemba	governmen t health facility	QMC145	Doxycycline Hyclate USP	Doxycycline	antibiotic	100	Tablets	Medopharma	generic	India	below 30°C				
Congo, the Democratic Republic of the	Nyemba	church health facility	QMC146	Co-trimoxazole BP	Sulfa/Trimet	antibiotic	400 / 80	Tablets	Medopharma	generic	India	below 30°C	0.031622	2.6351667	0.885416	0.8352981
Congo, the Democratic Republic of the	Nyemba	church health facility	QMC147	Amoxyn-500	Amoxicillin	antibiotic	500	Capsules	Reyoung Pharmaceutica l Co. Ltd	branded	China	below 30°C	0.0505952	1.6865067	1.0624992	1.0023577
Congo, the Democratic Republic of the	Nyemba	church health facility	QMC149	Ecoflox-500	Ciprofloxacin	antibiotic	500	Tablets	Medley Pharmaceutica ls Ltd	branded	India	below 30°C	0.0442708	1.1868847	0.6197912	0.5847087
Congo, the Democratic Republic of the	Nyemba	church health facility	QMC150	Speniv Tablets 250	Penicillin v	antibiotic	250	Tablets	sparsh bio-tech pvt. Ltd	branded	India	below 25°C	0.0189732	1.0780227	1.0624992	1.0023577
Congo, the Democratic Republic of the	Nyemba	church health facility	QMC151	Megyl	Metronidazole	antibiotic	250	Tablets	Aura pharmaceutica ls pvt. ltd	branded	India	dry and cool, protected from light	0.031622	5.1839344	1.328124	1.2529472
Congo, the Democratic Republic of the	Kansimba	governmen t health facility	QMC152	Amoxicilline Tablets for Oral Suspension	Amoxicillin	antibiotic	250	Tablets	CSPC Zhonguo Pharmaceutica ls Co.Ltd	generic	China	below 30°C				
Congo, the Democratic Republic of the	Kansimba	governmen t health facility	QMC153	Cotrimoxazole Tablets B.P	Sulfa/Trimet	antibiotic	400 / 80	Tablets	CSPC Ouyi Pharmaceutica l Co.Ltd	generic	China	below 30°C				
Congo, the Democratic Republic of the	Kansimba	governmen t health facility	QMC154	Ciprofloxacin Tablets USP	Ciprofloxacin	antibiotic	250	Tablets	Holden Medical Laboratories	generic	India	below 30°C				
Congo, the Democratic Republic of the	Kansimba	governmen t health facility	QMC155	Phenoxymethylpenicil lin Tablets BP	Penicillin v	antibiotic	250	Tablets	North China Pharmaceutica l Group, PRC	generic	China	below 30°C				
Congo, the Democratic Republic of the	Kansimba	governmen t health facility	QMC156	Metronidazole Tablets BP	Metronidazole	antibiotic	250	Tablets	Jiangsu Pengyao Pharmaceutica l Ltd	generic	China	below 30°C				
Congo, the Democratic Republic of the	Kansimba	governmen t health facility	QMC157	Doxycycline Tablets	Doxycycline	antibiotic	100	Tablets	Maneesh Pharmaceutica ls ltd.	generic	India	below 30°C				
Congo, the Democratic Republic of the	Kansimba	governmen t health facility	QMC158	Salbutamol Tablets BP	Salbutamol	medicine against NCD	4	Tablets	Medopharma	generic	India	below 30°C				
Congo, the Democratic Republic of the	Kansimba	church health facility	QMC159	Amoxicillin Capsules BP	Amoxicillin	antibiotic	500	Capsules	Reyoung Pharmaceutica l Co. Ltd	generic	China	below 30°C	0.063244	2.1081333	1.328124	1.2529472

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Congo, the Democratic Republic of the	Kansimba	church health facility	QMC161	Sulfamethoxazole and Trimethoprim Tablets USP	Sulfa/Trimet	antibiotic	400 / 80	Tablets	Nanjing Baijingyu Pahramcuetical Co.Ltd	generic	China	below 30°C				
Congo, the Democratic Republic of the	Kansimba	church health facility	QMC162	Ciprofloxacin Tablets USP	Ciprofloxacin	antibiotic	500	Tablets	CSPC Ouyi Pharmaceutical Co.Ltd	generic	China	below 30°C				
Congo, the Democratic Republic of the	Kansimba	church health facility	QMC163	Doxycycline Hyclate USP	Doxycycline	antibiotic	100	Tablets	Medopharma	generic	India	below 30°C				
Congo, the Democratic Republic of the	Kansimba	church health facility	QMC164	Metronidazole 250 mg tables BP	Metronidazole	antibiotic	250	Tablets	CSPC Ouyi Pharmaceutical Co.Ltd	generic	India	below 30°C				
Congo, the Democratic Republic of the	Kansimba	church health facility	QMC165	Salbutamol Tablets BP	Salbutamol	medicine against NCD	4	Tablets	Medopharma	generic	India	below 30°C				
Congo, the Democratic Republic of the	Kansimba	informal vendor	QMC166	Phenoxymethylpenicillin Tablets BP	Penicillin v	antibiotic	250	Tablets	North China Pharmaceutical Group, PRC	generic	China	below 30°C	0.063244	3.5934091	3.541664	3.3411925
Congo, the Democratic Republic of the	Kansimba	informal vendor	QMC167	Amoxicillin Capsules B.P	Amoxicillin	antibiotic	500	Capsules	Sinochem Jiangsu co. Ltd	generic	China	dry and cool, protected from light	0.063244	2.1081333	1.328124	1.2529472
Congo, the Democratic Republic of the	Kansimba	informal vendor	QMC168	Cotrimoxazole Tablets B.P	Sulfa/Trimet	antibiotic	400 / 80	Tablets	ultra Care International	generic	India	dry and cool, protected from light	0.031622	2.6351667	0.885416	0.8352981
Congo, the Democratic Republic of the	Kansimba	informal vendor	QMC169	Ciprofloxacine Tablets USP	Ciprofloxacin	antibiotic	500	Tablets	Sinochem Jiangsu co. Ltd	generic	China	dry and cool, protected from light	0.063244	1.6955496	0.885416	0.8352981
Congo, the Democratic Republic of the	Kansimba	informal vendor	QMC170	Metro 250	Metronidazole	antibiotic	250	Tablets	Prashi Pharma prvt. Ltd.	branded	India	dry and cool, protected from light	0.031622	5.1839344	1.328124	1.2529472
Congo, the Democratic Republic of the	Kansimba	informal vendor	QMC171	Frusema	Furosemide	medicine against NCD	40	Tablets	Arco Pharma pvt. Ltd	branded	India	dry and cool, protected from light	0.0189732	3.1103607	0.569196	0.5369774
Congo, the Democratic Republic of the	Kansimba	pharmacy	QMC173	HIPEN	Amoxicillin	antibiotic	250	Capsules	sparsh bio-tech pvt. Ltd	branded	India	below 25°C	0.031622	1.976375	1.328124	1.2529472
Congo, the Democratic Republic of the	Kansimba	pharmacy	QMC174	Cotrimoxazole Tablets B.P	Sulfa/Trimet	antibiotic	400 / 80	Tablets	ultra Care International	generic	India	dry and cool, protected from light	0.031622	2.6351667	0.885416	0.8352981
Congo, the Democratic Republic of the	Kansimba	pharmacy	QMC175	Ecoflox-500	Ciprofloxacin	antibiotic	500	Tablets	Medley Pharmaceuticals Ltd	branded	India	below 30°C	0.0505952	1.3564397	0.7083328	0.6682385
Congo, the Democratic Republic of the	Kansimba	pharmacy	QMC176	Peni-V	Penicillin v	antibiotic	250	Tablets	Sinochem Jiangsu co. Ltd	branded	China	dry and cool, protected from light	0.0442708	2.5153864	2.4791648	2.3388347

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Congo, the Democratic Republic of the	Kansimba	pharmacy	QMC177	Megyl	Metronidazole	antibiotic	250	Tablets	Aura pharmaceuticals pvt. ltd	branded	India	dry and cool, protected from light	0.0189732	3.1103607	0.7968744	0.7517683
Congo, the Democratic Republic of the	Kansimba	pharmacy	QMC178	Doxycycline Capsules	Doxycycline	antibiotic	100	Capsules	Shanxi Lianbang Pharmaceutical ltd	generic	China	dry and cool, protected from light	0.031622	2.377594	0.63244	0.5966415
Congo, the Democratic Republic of the	Kansimba	pharmacy	QMC179	Frusemide	Furosemide	medicine against NCD	40	Tablets	Prashi Pharma prvt. Ltd.	branded	India	dry and cool, protected from light	0.0189732	3.1103607	0.569196	0.5369774
Congo, the Democratic Republic of the	Kansimba	pharmacy	QMC180	Salbutamol Tablets BP	Salbutamol	medicine against NCD	4	Tablets	Aura pharmaceuticals pvt. ltd	generic	India	dry and cool, protected from light	0.031622	9.881875	1.42299	1.3424434
Congo, the Democratic Republic of the	Goma	pharmacy	QMC214	Glucophage	Metformin	medicine against NCD	850	Tablets	Merck	originator	Belgium	dry and cool, protected from light	0.1517856	7.58928	8.0357082	7.5808568
Congo, the Democratic Republic of the	Goma	pharmacy	QMC215	Ciprokin-500	Ciprofloxacin	antibiotic	500	Tablets	Phatkin B.P	branded	Kongo	dry and cool, protected from light	0.0758928	2.0346595	1.0624992	1.0023577
Congo, the Democratic Republic of the	Goma	pharmacy	QMC216	Atenolol Tablets BP	Atenolol	medicine against NCD	100	Tablets	Holden Medical Laboratories	generic	India	below 30°C	0.1138392	6.3954607	1.707588	1.6109321
Congo, the Democratic Republic of the	Goma	pharmacy	QMC217	Asix	Furosemide	medicine against NCD	40	Tablets	Astra Lifecare	branded	India	below 30°C	0.0569196	9.331082	1.707588	1.6109321
Congo, the Democratic Republic of the	Goma	pharmacy	QMC218	Moxacil-500	Amoxicillin	antibiotic	500	Capsules	DAWA Ltd	branded	Kenya	below 30°C	0.047433	1.5811	0.996093	0.9397104
Congo, the Democratic Republic of the	Goma	pharmacy	QMC219	Agodox	Doxycycline	antibiotic	100	Capsules	Agog pharma pvt.Ltd	branded	India	below 30°C	0.015811	1.188797	0.31622	0.2983208
Congo, the Democratic Republic of the	Goma	informal vendor	QMC221	Astrogyl	Metronidazole	antibiotic	200	Tablets	Astra Lifecare	branded	India	below 30°C	0.0094866	1.5551803	0.4980465	0.4698552
Congo, the Democratic Republic of the	Goma	informal vendor	QMC222	Ciprofloxacine Comprimes BP	Ciprofloxacin	antibiotic	500	Tablets	Astra Lifecare	generic	India	below 30°C	0.0284598	0.7629973	0.3984372	0.3758842
Congo, the Democratic Republic of the	Goma	informal vendor	QMC223	Unipen 250	Penicillin v	antibiotic	250	Tablets	Regal Pharmaceuticals Ltd.	branded	Kenya	below 30°C	0.0237165	1.3475284	1.328124	1.2529472
Congo, the Democratic Republic of the	Goma	informal vendor	QMC224	Lecotrim	Sulfa/Trimet	antibiotic	400 / 80	Tablets	Laboratory & Allied Ltd.	branded	Kenya	below 30°C	0.0142299	1.185825	0.3984372	0.3758842
Congo, the Democratic Republic of the	Goma	informal vendor	QMC225	Esidrex	Hydrochlorothiazide	medicine against NCD	25	Tablets	Novartis Farmaceutica s.A	originator	Spain	below 25°C	0.237165	55.154651	7.11495	6.712217

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Congo, the Democratic Republic of the	Goma	informal vendor	QMC226	Atenolol Tablets BP	Atenolol	medicine against NCD	100	Tablets	ZIM Laboratories Ltd	generic	India	below 25°C	0.1159473	6.5138951	1.73921	1.6407642
Congo, the Democratic Republic of the	Goma	informal vendor	QMC227	Asur-850	Metformin	medicine against NCD	850	Tablets	Indus Life Sciences	branded	India	below 30°C	0.142299	7.11495	7.5334765	7.1070533
Congo, the Democratic Republic of the	Goma	pharmacy	QMC228	As-V	Penicillin v	antibiotic	250	Tablets	Astra Lifecare	branded	India	below 30°C	0.047433	2.6950568	2.656248	2.5058943
Congo, the Democratic Republic of the	Goma	pharmacy	QMC229	Renetrim	Sulfa/Trimet	antibiotic	400 / 80	Tablets	Rene Industries ltd.	branded	Uganda	below 30°C	0.0189732	1.5811	0.5312496	0.5011789
Congo, the Democratic Republic of the	Goma	pharmacy	QMC230	Unique's Metrogyl 200	Metronidazole	antibiotic	200	Tablets	J.B.Chemicals	branded	India	dry and cool, protected from light	0.0189732	3.1103607	0.996093	0.9397104
Congo, the Democratic Republic of the	Goma	informal vendor	QMC231	Doxyren	Doxycycline	antibiotic	100	Capsules	Rene Industries ltd.	branded	Uganda	dry and cool, protected from light	0.0243941	1.8341439	0.4878823	0.4602663
Congo, the Democratic Republic of the	Goma	informal vendor	QMC233	Acinet	Amoxi/Clav	antibiotic	500/ 125	Tablets	Alkem Laboratories ltd.	branded	India	below 25°C	0.758928	4.6247898	15.937488	15.035366
Congo, the Democratic Republic of the	Goma	pharmacy	QMC234	Esidrex	Hydrochlorothiazide	medicine against NCD	25	Tablets	Novartis Farmaceutica s.A	originator	Spain	below 25°C	0.237165	55.154651	7.11495	6.712217
Congo, the Democratic Republic of the	Goma	pharmacy	QMC235	Sabulin	Salbutamol	medicine against NCD	4	Tablets	DAWA Ltd	branded	Kenya	below 30°C	0.0284598	8.8936875	1.280691	1.2081991
Congo, the Democratic Republic of the	Goma	informal vendor	QMC236	Amoxin 500	Amoxicillin	antibiotic	500	Capsules	Phatkin B.P	branded	Kongo	dry and cool, protected from light	0.0284598	0.94866	0.5976558	0.5638262
Congo, the Democratic Republic of the	Goma	informal vendor	QMC237	Frusema	Furosemide	medicine against NCD	40	Tablets	Arco Pharma pvt. Ltd	branded	India	below 25°C	0.0284598	4.665541	0.853794	0.805466
Congo, the Democratic Republic of the	Goma	pharmacy	QMC238	Moxiclav	Amoxi/Clav	antibiotic	875/ 125	Tablets	Medochemie	branded	Cyprus	below 25°C	0.853794	5.4209143	10.245528	9.6655925
Congo, the Democratic Republic of the	Goma	informal vendor	QMC240	Kam Vent	Salbutamol	medicine against NCD	4	Tablets	Kampala Pharmaceutical Industries	branded	Uganda	below 30°C	0.0189732	5.929125	0.853794	0.805466
Congo, the Democratic Republic of the	Goma	government health facility	QMC241	Amoxicillin Capsules BP	Amoxicillin	antibiotic	500	Capsules	CSPC Zhonguo Pharmaceuticals Co.Ltd	generic	China	below 30°C	0.0445238	1.4841259	0.9349993	0.8820748
Congo, the Democratic Republic of the	Goma	government health facility	QMC242	Metronidazole BP	Metronidazole	antibiotic	250	Tablets	Medopharma	generic	India	below 30°C	0.0091071	1.4929731	0.3824997	0.3608488
Congo, the Democratic Republic of the	Goma	government health facility	QMC243	Ciprofloxacin Tablets USP	Ciprofloxacin	antibiotic	500	Tablets	CSPC Ouyi Pharmaceutical Co.Ltd	generic	China	below 30°C	0.037744	1.011904	0.5284163	0.4985059

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Congo, the Democratic Republic of the	Goma	government health facility	QMC245	Co-trimoxazole BP	Sulfa/Trimet	antibiotic	400 / 80	Tablets	Medopharma	generic	India	below 30°C	0.0050595	0.4216267	0.1416666	0.1336477
Congo, the Democratic Republic of the	Goma	government health facility	QMC246	Doxycycline Hyclate tablets USP	Doxycycline	antibiotic	100	Tablets	Nanjing Baijingyu Pahramcuetical Co.Ltd	generic	China	below 30°C	0.0155833	1.1716783	0.3116664	0.2940249
Congo, the Democratic Republic of the	Goma	government health facility	QMC247	Phenoxymethylpenicillin Tablets BP	Penicillin v	antibiotic	250	Tablets	North China Pharmaceutical Group, PRC	generic	China	below 30°C	0.020744	1.1786382	1.1616658	1.0959111
Congo, the Democratic Republic of the	Goma	government health facility	QMC248	Frusemide	Furosemide	medicine against NCD	40	Tablets	DAWA Ltd	generic	Kenya	below 30°C	0.0050595	0.8294295	0.1517856	0.143194
Congo, the Democratic Republic of the	Goma	church health facility	QMC249	Amoxy-500	Amoxicillin	antibiotic	500	Capsules	Reyoung Pharmaceutical Co. Ltd	branded	China	dry and cool, protected from light	0.0607142	2.023808	1.274999	1.2028293
Congo, the Democratic Republic of the	Goma	church health facility	QMC250	Atenolol Denk	Atenolol	medicine against NCD	50	Tablets	Denk Pharma	branded	Germany	below 25°C	0.2023808	18.914093	6.071424	5.7277585
Congo, the Democratic Republic of the	Goma	church health facility	QMC251	Ciprofloxacine Tablets USP	Ciprofloxacin	antibiotic	500	Tablets	Sinochem Jiangsu co. Ltd	generic	China	dry and cool, protected from light	0.1011904	2.7128794	1.4166656	1.336477
Congo, the Democratic Republic of the	Goma	church health facility	QMC252	Alldox	Doxycycline	antibiotic	100	Capsules	Lincoln Pharmaceuticals Ltd	branded	India	below 30°C	0.1011904	7.6083008	2.023808	1.9092528
Congo, the Democratic Republic of the	Goma	church health facility	QMC253	Metronidazole BP	Metronidazole	antibiotic	250	Tablets	Medopharma	generic	India	below 30°C	0.0202381	3.317718	0.8499994	0.8018862
Congo, the Democratic Republic of the	Goma	church health facility	QMC254	Astalin	Salbutamol	medicine against NCD	4	Tablets	Pharmaceutical Manufacturing Co. Ltd	branded	Kenya	dry and cool, protected from light	0.0809523	25.2976	3.6428544	3.4366551
Congo, the Democratic Republic of the	Biena	church health facility	QMC255	Co-trimoxazole USP	Sulfa/Trimet	antibiotic	400 / 80	Tablets	Medopharma	generic	India	below 30°C	0.0150521	1.2543393	0.421458	0.3976019
Congo, the Democratic Republic of the	Goma	church health facility	QMC257	Co-trimoxazole BP	Sulfa/Trimet	antibiotic	400 / 80	Tablets	Medopharma	generic	India	below 30°C	0.010119	0.8432533	0.2833331	0.2672954
Congo, the Democratic Republic of the	Goma	church health facility	QMC258	Metformin Denk	Metformin	medicine against NCD	1000	Tablets	Denk Pharma	branded	Germany	below 30°C	0.3035712	2.5553131	13.660704	12.887457
Congo, the Democratic Republic of the	Goma	church health facility	QMC259	Asix	Furosemide	medicine against NCD	40	Tablets	Astra Lifecare	branded	India	below 30°C	0.1011904	16.58859	3.035712	2.8638792
Congo, the Democratic Republic of the	Biena	church health facility	QMC260	Metronidazole 250 mg tables BP	Metronidazole	antibiotic	250	Tablets	CSPC Ouyi Pharmaceutical Co.Ltd	generic	China	below 30°C	0.007526	1.2337764	0.3160935	0.2982014
Congo, the Democratic Republic of the	Biena	church health facility	QMC261	Phenoxymethylpenicillin Tablets BP	Penicillin v	antibiotic	250	Tablets	CSPC Zhonguo Pharmaceuticals Co.Ltd	generic	China	below 25°C	0.0258036	1.4661109	1.4449989	1.3632065

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Congo, the Democratic Republic of the	Biena	church health facility	QMC262	Ciprofloxacin Tablets	Ciprofloxacin	antibiotic	500	Tablets	Reyoung Pharmaceutical Co. Ltd	generic	China	below 25°C	0.0664441	1.7813444	0.930218	0.8775642
Congo, the Democratic Republic of the	Biena	church health facility	QMC263	Amoxicillin	Amoxicillin	antibiotic	250	Tablets	CSPC Ouyi Pharmaceutical Co.Ltd	generic	China	below 30°C	0.021503	1.343935	0.9031243	0.8520041
Congo, the Democratic Republic of the	Biena	informal vendor	QMC264	Unidoxy	Doxycycline	antibiotic	100	Capsules	CSPC Ouyi Pharmaceutical Co.Ltd	branded	China	below 25°C	0.063244	4.755188	1.26488	1.193283
Congo, the Democratic Republic of the	Biena	informal vendor	QMC265	Ciprofloxacine comprimes BP	Ciprofloxacin	antibiotic	500	Tablets	Astra Lifecare	generic	India	below 30°C	0.0853794	2.288992	1.1953116	1.1276525
Congo, the Democratic Republic of the	Biena	informal vendor	QMC266	Metronyl	Metronidazole	antibiotic	200	Tablets	MAC'S pharmaceuticals Ltd	branded	Kenya	below 25°C	0.0252976	4.1471475	1.328124	1.2529472
Congo, the Democratic Republic of the	Biena	pharmacy	QMC267	Kemoxyl 250	Amoxicillin	antibiotic	250	Capsules	Laboratory & Allied Ltd.	branded	Kenya	below 30°C	0.047433	2.9645625	1.992186	1.8794208
Congo, the Democratic Republic of the	Biena	informal vendor	QMC269	Unitrim	Sulfa/Trimet	antibiotic	400 / 80	Tablets	Regal Pharmaceuticals Ltd.	branded	Kenya	below 25°C	0.0284598	2.37165	0.7968744	0.7517683
Congo, the Democratic Republic of the	Biena	informal vendor	QMC270	Kam Amoxy Capsules	Amoxicillin	antibiotic	250	Capsules	Kampala Pharmaceutical Industries	branded	Uganda	dry and cool, protected from light	0.0379464	2.37165	1.5937488	1.5035366
Congo, the Democratic Republic of the	Biena	pharmacy	QMC271	Asbutol-P4	Salbutamol	medicine against NCD	4	Tablets	Astra Lifecare	branded	India	below 30°C	0.0379464	11.85825	1.707588	1.6109321
Congo, the Democratic Republic of the	Biena	pharmacy	QMC272	Frusemide BP	Furosemide	medicine against NCD	40	Tablets	Strides Arcolab Limited	generic	India	below 25°C	0.063244	10.367869	1.89732	1.7899245
Congo, the Democratic Republic of the	Biena	pharmacy	QMC273	Cosatrim	Sulfa/Trimet	antibiotic	400 / 80	Tablets	cosmos ltd	branded	Kenya	below 25°C	0.0379464	3.1622	1.0624992	1.0023577
Congo, the Democratic Republic of the	Biena	pharmacy	QMC274	Omacip 500	Ciprofloxacin	antibiotic	500	Tablets	National pharmaceutical industries	branded	sultanat of Oman	below 30°C	0.094866	2.5433244	1.328124	1.2529472
Congo, the Democratic Republic of the	Biena	pharmacy	QMC275	Alldox	Doxycycline	antibiotic	100	Capsules	Lincoln Pharmaceuticals Ltd	branded	India	below 30°C	0.0569196	4.2796692	1.138392	1.0739547
Congo, the Democratic Republic of the	Biena	pharmacy	QMC276	Megyl	Metronidazole	antibiotic	250	Tablets	Aura pharmaceuticals pvt. ltd	branded	India	dry and cool, protected from light	0.031622	5.1839344	1.328124	1.2529472
Congo, the Democratic Republic of the	Biena	pharmacy	QMC277	Glyformin 500	Metformin	medicine against NCD	500	Tablets	Remedica Ltd	branded	Cyprus	below 25°C	0.252976	16.865067	22.76784	21.479094
Congo, the Democratic Republic of the	Biena	pharmacy	QMC278	Hyperlok-100	Atenolol	medicine against NCD	100	Tablets	Astra Lifecare	branded	India	below 30°C	0.126488	7.1060674	1.89732	1.7899245
Congo, the Democratic Republic of the	Biena	government health facility	QMC279	Amoxicillin Tablets USP	Amoxicillin	antibiotic	250	Tablets	CSPC Zhonguo Pharmaceuticals Co.Ltd	generic	China	below 30°C	0.0218255	1.364094	0.9166712	0.8647841

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Congo, the Democratic Republic of the	Biena	governmen t health facility	QMC281	Ciprofloxacin Tablets	Ciprofloxacin	antibiotic	500	Tablets	Reyoung Pharmaceutica l Co. Ltd	generic	China	below 25°C	0.0752604	2.017704	1.053645	0.9940048
Congo, the Democratic Republic of the	Biena	governmen t health facility	QMC282	Phenoxymethylpenicil lin Tablets BP	Penicillin v	antibiotic	250	Tablets	CSPC Zhonguo Pharmaceutica ls Co.Ltd	generic	China	below 25°C	0.0258541	1.4689856	1.4478322	1.3658795
Congo, the Democratic Republic of the	Biena	governmen t health facility	QMC283	Metronidazole Tablets BP	Metronidazole	antibiotic	250	Tablets	Medopharma	generic	India	below 30°C	0.0089237	1.4629063	0.3747966	0.3535817
Congo, the Democratic Republic of the	Biena	governmen t health facility	QMC284	Doxycycline Hyclate USP	Doxycycline	antibiotic	100	Tablets	Medopharma	generic	India	below 30°C	0.0187076	1.4065846	0.3741515	0.3529731
Congo, the Democratic Republic of the	Biena	church health facility	QMC285	Doxycycline Hyclate tablets USP	Doxycycline	antibiotic	100	Tablets	CSPC Ouyi Pharmaceutica l Co.Ltd	generic	China	below 30°C	0.0182775	1.3742493	0.3655503	0.3448588
Congo, the Democratic Republic of the	Biena	pharmacy	QMC286	Augmentin Adultes	Amoxi/Clav	antibiotic	500/ 62.5	Tablets	Glaxo Welcome Production	originator	France	below 25°C	0.94866		19.92186	18.794208
Congo, the Democratic Republic of the	Biena	informal vendor	QMC287	Koact 625	Amoxi/Clav	antibiotic	500/ 125	Tablets	Aurobindo Pharma ltd.	branded	India	below 30°C	0.94866	5.7809872	19.92186	18.794208
Congo, the Democratic Republic of the	Biena	pharmacy	QMC288	Esidrex	Hydrochlorothi azide	medicine against NCD	25	Tablets	Novartis Farmaceutica s.A	originator	Spain	below 25°C	0.284598	66.185581	8.53794	8.0546604
Congo, the Democratic Republic of the	Biena	pharmacy	QMC289	Unipen 250	Penicillin v	antibiotic	250	Tablets	Regal Pharmaceutica ls Ltd.	branded	Kenya	below 30°C	0.047433	2.6950568	2.656248	2.5058943
Congo, the Democratic Republic of the	Biena	informal vendor	QMC290	Sabulin	Salbutamol	medicine against NCD	4	Tablets	DAWA Ltd	branded	Kenya	below 30°C	0.0284598	8.8936875	1.280691	1.2081991
Congo, the Democratic Republic of the	Biena	informal vendor	QMC291	Peni-V	Penicillin v	antibiotic	250	Tablets	Phatkin B.P	branded	Kongo	below 25°C	0.0379464	2.1560455	2.1249984	2.0047155
Congo, the Democratic Republic of the	Biena	informal vendor	QMC293	Frusemide	Furosemide	medicine against NCD	40	Tablets	Prashi Pharma prvt. Ltd.	branded	India	dry and cool, protected from light	0.0711495	11.663852	2.134485	2.0136651
Congo, the Democratic Republic of the	Nyankunde	church health facility	QMC298	Amoxicillin Tablets USP	Amoxicillin	antibiotic	250	Tablets	CSPC Zhonguo Pharmaceutica ls Co.Ltd	generic	China	below 30°C	0.018445	1.1528125	0.77469	0.7308396
Congo, the Democratic Republic of the	Nyankunde	church health facility	QMC299	Phenoxymethylpenicil lin Tablets BP	Penicillin v	antibiotic	250	Tablets	North China Pharmaceutica l Group, PRC	generic	China	below 30°C	0.021654	1.2303409	1.212624	1.1439849
Congo, the Democratic Republic of the	Nyankunde	church health facility	QMC300	Cotrimoxazole Tablets B.P	Sulfa/Trimet	antibiotic	400 / 80	Tablets	CSPC Ouyi Pharmaceutica l Co.Ltd	generic	China	below 30°C	0.018056	1.5046667	0.505568	0.4769509
Congo, the Democratic Republic of the	Nyankunde	church health facility	QMC301	Asflox-500	Ciprofloxacin	antibiotic	500	Tablets	Astra Lifecare	branded	India	below 30°C	0.058737	1.5747185	0.822318	0.7757717
Congo, the Democratic Republic of the	Nyankunde	church health facility	QMC302	Metronidazole 250 mg tables BP	Metronidazole	antibiotic	250	Tablets	CSPC Ouyi Pharmaceutica l Co.Ltd	generic	China	below 30°C	0.002648	0.4340984	0.111216	0.1049208

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Congo, the Democratic Republic of the	Nyankunde	church health facility	QMC303	METFIL	Metformin	medicine against NCD	500	Tablets	Fourrts	branded	India	below 30°C	0.0235	1.5666667	2.115	1.995283
Congo, the Democratic Republic of the	Nyankunde	church health facility	QMC305	Doxycycline Hyclate 100 mg USP	Doxycycline	antibiotic	100	Tablets	Medopharma	branded	India	below 30°C	0.016969	1.2758647	0.33938	0.3201698
Congo, the Democratic Republic of the	Nyankunde	church health facility	QMC306	Frusemide	Furosemide	medicine against NCD	40	Tablets	Elys Chemical Industries	generic	Kenya	below 30°C	0.0061	1	0.183	0.1726415
Congo, the Democratic Republic of the	Nyankunde	church health facility	QMC307	Salbutamol Tablets BP	Salbutamol	medicine against NCD	4	Tablets	Medopharma	generic	India	below 30°C	0.008264	2.5825	0.37188	0.3508302
Congo, the Democratic Republic of the	Nyankunde	church health facility	QMC308	HIPEN	Amoxicillin	antibiotic	250	Capsules	sparsh bio-tech pvt. Ltd	branded	India	below 25°C	0.014	0.875	0.588	0.554717
Congo, the Democratic Republic of the	Nyankunde	church health facility	QMC309	CO-TRI	Sulfa/Trimet	antibiotic	400 / 80	Tablets	Elys Chemical Industries	branded	Kenya	below 30°C	0.017	1.4166667	0.476	0.4490566
Congo, the Democratic Republic of the	Nyankunde	church health facility	QMC310	Ciprofloxacin Tablets USP	Ciprofloxacin	antibiotic	500	Tablets	CSPC Ouyi Pharmaceutical Co.Ltd	generic	China	below 30°C	0.0587	1.5737265	0.8218	0.775283
Congo, the Democratic Republic of the	Nyankunde	church health facility	QMC311	Saarah Pharmacy Penicllin V Potassium 250mg	Penicillin v	antibiotic	250	Tablets	Shendong Ykang Pharmaceutical Co. LTd	branded	China	dry and cool, protected from light	0.0217	1.2329545	1.2152	1.1464151
Congo, the Democratic Republic of the	Nyankunde	church health facility	QMC312	Metronidazole 250 mg tables BP	Metronidazole	antibiotic	250	Tablets	CSPC Ouyi Pharmaceutical Co.Ltd	generic	China	below 30°C	0.0088	1.442623	0.3696	0.3486792
Congo, the Democratic Republic of the	Nyankunde	church health facility	QMC313	Generic Plus Doxycycline Hyclate 100mg USP	Doxycycline	antibiotic	100	Tablets	Medopharma	branded	India	below 30°C	0.014	1.0526316	0.28	0.2641509
Congo, the Democratic Republic of the	Nyankunde	church health facility	QMC314	Salbutamol Tablets BP	Salbutamol	medicine against NCD	4	Tablets	Medopharma	generic	India	below 30°C	0.003	0.9375	0.135	0.1273585
Congo, the Democratic Republic of the	Nyankunde	pharmacy	QMC315	Co-Trimoxazole Tablets BP Trimago	Sulfa/Trimet	antibiotic	400 / 80	Tablets	Agog pharma pvt.Ltd	branded	India	below 30°C	0.04	3.3333333	1.12	1.0566038
Congo, the Democratic Republic of the	Nyankunde	pharmacy	QMC317	Ciprokin-500	Ciprofloxacin	antibiotic	500	Tablets	Phatkin B.P	branded	Kongo	dry and cool, protected from light	0.1	2.6809651	1.4	1.3207547
Congo, the Democratic Republic of the	Nyankunde	pharmacy	QMC318	Saarah Pharmacy Penicllin V Potassium 250mg	Penicillin v	antibiotic	100	Tablets	Shendong Ykang Pharmaceutical Co. LTd	branded	China	dry and cool, protected from light	0.08	4.5454545	11.2	10.566038
Congo, the Democratic Republic of the	Nyankunde	pharmacy	QMC319	Doxycycline Capsules B.P	Doxycycline	antibiotic	100	Capsules	Triveni formulations limited	generic	India	dry and cool, protected from light	0.05	3.7593985	1	0.9433962
Congo, the Democratic Republic of the	Nyankunde	pharmacy	QMC320	Glyformin 500	Metformin	medicine against NCD	500	Tablets	Remedica Ltd	branded	Cyprus	below 25°C	0.1666667	11.111111	15	14.150943

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Congo, the Democratic Republic of the	Nyankunde	pharmacy	QMC321	Frusemide	Furosemide	medicine against NCD	40	Tablets	Prashi Pharma prvt. Ltd.	generic	India	dry and cool, protected from light	0.04	6.557377	1.2	1.1320755
Congo, the Democratic Republic of the	Nyankunde	pharmacy	QMC322	Kam Vent	Salbutamol	medicine against NCD	4	Tablets	Kampala Pharmaceutical Industries	branded	India	below 30°C	0.05	15.625	2.25	2.1226415
Congo, the Democratic Republic of the	Nyankunde	pharmacy	QMC323	Moxacil-250	Amoxicillin	antibiotic	250	Capsules	DAWA Ltd	branded	Kenya	below 30°C	0.05	3.125	2.1	1.9811321
Congo, the Democratic Republic of the	Nyankunde	pharmacy	QMC324	Augmentin Adultes	Amoxi/Clav	antibiotic	500/ 62.5	Tablets	Glaxo Welcome Production	originator	France	below 25°C	0.9375		19.6875	18.573113
Congo, the Democratic Republic of the	Nyankunde	pharmacy	QMC325	Metazol	Metronidazole	antibiotic	250	Tablets	Chifeng Wanze Pharmaceutical Ltd	branded	China	below 30°C	0.03	4.9180328	1.26	1.1886792
Congo, the Democratic Republic of the	Rethy	church health facility	QMC326	Miloxy 250	Amoxicillin	antibiotic	250	Capsules	Milan laboratories pvt. Ltd	branded	India	below 30°C	0.026667	1.6666875	1.120014	1.056617
Congo, the Democratic Republic of the	Rethy	church health facility	QMC327	Co-trimoxazole BP	Sulfa/Trimet	antibiotic	400 / 80	Tablets	Medopharma	generic	India	below 30°C	0.02	1.6666667	0.56	0.5283019
Congo, the Democratic Republic of the	Rethy	church health facility	QMC329	Ciprofloxacin Tablets USP	Ciprofloxacin	antibiotic	500	Tablets	CSPC Ouyi Pharmaceutical Co.Ltd	generic	China	below 30°C	0.066666	1.7872922	0.933324	0.8804943
Congo, the Democratic Republic of the	Rethy	church health facility	QMC330	Unipen 250	Penicillin v	antibiotic	250	Tablets	Regal Pharmaceuticals Ltd.	branded	Kenya	below 30°C	0.04	2.2727273	2.24	2.1132075
Congo, the Democratic Republic of the	Rethy	church health facility	QMC331	Metronidazole Tablets BP	Metronidazole	antibiotic	250	Tablets	Medopharma	generic	India	below 30°C	0.026667	4.3716393	1.120014	1.056617
Congo, the Democratic Republic of the	Rethy	church health facility	QMC332	Doxyleb	Doxycycline	antibiotic	100	Capsules	Leben Laboratories pvt.ltd.	branded	India	below 25°C	0.023333	1.7543609	0.46666	0.4402453
Congo, the Democratic Republic of the	Rethy	church health facility	QMC333	Frusemide	Furosemide	medicine against NCD	40	Tablets	Elys Chemical Industries	branded	Kenya	below 30°C	0.026667	4.3716393	0.80001	0.7547264
Congo, the Democratic Republic of the	Rethy	church health facility	QMC334	Esidrex	Hydrochlorothiazide	medicine against NCD	25	Tablets	Novartis Farmaceutica s.A	originator	Spain	below 25°C	0.175	40.697674	5.25	4.9528302
Congo, the Democratic Republic of the	Rethy	church health facility	QMC341	Miloxy 250	Amoxicillin	antibiotic	250	Capsules	Milan laboratories pvt. Ltd	branded	India	below 30°C	0.026667	1.6666875	1.120014	1.056617
Congo, the Democratic Republic of the	Rethy	church health facility	QMC342	Cotrimoxazole Tablets B.P	Sulfa/Trimet	antibiotic	400 / 80	Tablets	CSPC Ouyi Pharmaceutical Co.Ltd	generic	China	below 30°C	0.053333	4.4444167	1.493324	1.4087962
Congo, the Democratic Republic of the	Rethy	church health facility	QMC343	CEEPRO-500	Ciprofloxacin	antibiotic	500	Tablets	Lincoln Pharmaceuticals Ltd	branded	India	below 30°C	0.066667	1.787319	0.933338	0.8805075
Congo, the Democratic Republic of the	Rethy	church health facility	QMC344	Unipen 250	Penicillin v	antibiotic	250	Tablets	Regal Pharmaceuticals Ltd.	branded	Kenya	below 30°C	0.04	2.2727273	2.24	2.1132075

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Congo, the Democratic Republic of the	Rethy	church health facility	QMC345	Metronidazole 250 mg tables BP	Metronidazole	antibiotic	250	Tablets	CSPC Ouyi Pharmaceutical Co.Ltd	generic	China	below 30°C	0.026667	4.3716393	1.120014	1.056617
Congo, the Democratic Republic of the	Rethy	church health facility	QMC346	Frusemide	Furosemide	medicine against NCD	40	Tablets	NEM Laboratories Pvt.LTd	generic	India	below 30°C	0.026667	4.3716393	0.80001	0.7547264
Congo, the Democratic Republic of the	Rethy	pharmacy	QMC347	AMYN-250	Amoxicillin	antibiotic	250	Capsules	Kopran limited	branded	India	below 30°C	0.023333	1.4583125	0.979986	0.9245151
Congo, the Democratic Republic of the	Rethy	pharmacy	QMC348	Trim - 480	Sulfa/Trimet	antibiotic	400 / 80	Tablets	Kopran limited	branded	India	below 30°C	0.01	0.8333333	0.28	0.2641509
Congo, the Democratic Republic of the	Rethy	pharmacy	QMC349	As-V	Penicillin v	antibiotic	250	Tablets	Astra Lifecare	branded	India	below 30°C	0.024	1.3636364	1.344	1.2679245
Congo, the Democratic Republic of the	Rethy	pharmacy	QMC350	Ecoflox-500	Ciprofloxacin	antibiotic	500	Tablets	Medley Pharmaceuticals Ltd	branded	India	below 30°C	0.033333	0.8936461	0.466662	0.4402472
Congo, the Democratic Republic of the	Rethy	pharmacy	QMC351	Azudox	Doxycycline	antibiotic	100	Capsules	Kampala Pharmaceutical Industries	branded	Uganda	below 30°C	0.013333	1.0024812	0.26666	0.251566
Congo, the Democratic Republic of the	Rethy	pharmacy	QMC353	Frusemide BP	Furosemide	medicine against NCD	40	Tablets	Strides Arcolab Limited	branded	India	below 25°C	0.015333	2.5136066	0.45999	0.4339528
Congo, the Democratic Republic of the	Rethy	pharmacy	QMC354	Kam Vent	Salbutamol	medicine against NCD	4	Tablets	Kampala Pharmaceutical Industries	branded	India	below 30°C	0.007333	2.2915625	0.329985	0.3113066
Congo, the Democratic Republic of the	Nyankunde	pharmacy	QMC355	Esidrex	Hydrochlorothiazide	medicine against NCD	25	Tablets	Novartis Farmaceutica s.A	originator	Spain	below 25°C	0.15	34.883721	4.5	4.245283
Cameroon	Southwest	church health facility	QMCA001	Salbutamol B.P	Salbutamol	medicine against NCD	2	Tablets	Maxtar Bio-Genics	generic	India	below 25°C	0.0545799	21.83196	4.912191	2.2328141
Cameroon	Southwest	church health facility	QMCA002	Hydrochlorthiazide	Hydrochlorothiazide	medicine against NCD	50	Tablets	Hongkong Prost Medicines and Health Products Co.,Ltd	generic	Hong Kong	not stated	0.0545799	11.138755	0.8186985	0.3721357
Cameroon	Southwest	church health facility	QMCA003	Doxycycline Sprukfield	Doxycycline	antibiotic	100	Tablets	Jiangsu Ruinian Qianjin Pharm. Co.Ltd	branded	China	not stated	0.0909665	6.8395865	1.81933	0.8269682
Cameroon	Southwest	church health facility	QMCA004	Glibenclamide	Glibenclamide	medicine against NCD	5	Tablets	Medicamen biotech Ltd.	generic	India	below 30°C	0.0363866	6.383614	2.183196	0.9923618
Cameroon	Southwest	church health facility	QMCA005	Metformin Tablets BP	Metformin	medicine against NCD	500	Tablets	Strides Arcolab Limited	generic	India	dry and cool, protected from light	0.0545799	3.63866	4.912191	2.2328141

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Cameroon	Southwest	church health facility	QMCA006	Metzole-500	Metronidazole	antibiotic	500	Tablets	Maxtar Bio-Genics	branded	India	dry and cool, protected from light	0.0909665	7.7090254	1.9102965	0.8683166
Cameroon	Southwest	church health facility	QMCA007	Ciprofloxacine	Ciprofloxacin	antibiotic	500	Tablets	Medopharma	generic	India	below 30°C	0.181933	4.8775603	2.547062	1.1577555
Cameroon	Southwest	church health facility	QMCA008	Amoxzem TAB	Amoxicillin	antibiotic	500	Tablets	Ningbo shuangwei	branded	China	below 25°C	0.1455464	4.8515467	3.0564744	1.3893065
Cameroon	Southwest	pharmacy	QMCA009	Metformin Denk	Metformin	medicine against NCD	500	Tablets	Denk Pharma	branded	Germany	below 25°C	0.097698	6.5132014	8.7928219	3.9967372
Cameroon	Southwest	pharmacy	QMCA010	Metronidazole	Metronidazole	antibiotic	500	Tablets	Bailly-Creat	generic	India	below 25°C	0.0982438	8.3257475	2.0631202	0.9377819
Cameroon	Southwest	pharmacy	QMCA011	Lasilix 40 mg	Furosemide	medicine against NCD	40	Tablets	Sanofi-Winthrop	originator	France	below 25°C	0.1391787	22.816188	4.1753624	1.897892
Cameroon	Southwest	pharmacy	QMCA012	Glidiabet	Glibenclamide	medicine against NCD	5	Tablets	Ferrer Internacional	branded	Spain	not stated	0.0821731	14.416328	4.9303843	2.2410838
Cameroon	Southwest	pharmacy	QMCA013	Doxycreat	Doxycycline	antibiotic	100	Tablets	Bailly-Creat	branded	India	below 25°C	0.0756841	5.6905359	1.5136826	0.6880375
Cameroon	Southwest	pharmacy	QMCA014	Amoxiciline Ubigen	Amoxicillin	antibiotic	500	Capsules	Reyoung Pharmaceutical Co. Ltd	branded	China	dry and cool, protected from light	0.1212887	4.0429556	2.547062	1.1577555
Cameroon	Southwest	pharmacy	QMCA015	Cotrimoxazole ubigen	Sulfa/Trimet	antibiotic	400/80	Tablets	Lincoln Pharmaceuticals Ltd	branded	India	dry and cool, protected from light	0.0545799	4.548325	1.5282372	0.6946533
Cameroon	Southwest	pharmacy	QMCA016	Esidrex	Hydrochlorothiazide	medicine against NCD	25	Tablets	Novartis Pharmaceutica	originator	Spain	below 25°C	0.0709539	16.5009	2.1286161	0.9675528
Cameroon	Southwest	government health facility	QMCA017	Amoxicillin	Amoxicillin	antibiotic	500	Tablets	Strides Arcolab Limited	generic	India	below 25°C	0.0636766	2.1225517	1.3372076	0.6078216
Cameroon	Southwest	government health facility	QMCA018	Co-Amoxiclav	Amoxi/Clav	antibiotic	500/125	Tablets	Medopharma	branded	India	below 25°C	0.5094124	3.1042803	10.69766	4.8625729
Cameroon	Southwest	government health facility	QMCA019	Co-Trimoxazole	Sulfa/Trimet	antibiotic	400/80	Tablets	Strides Arcolab Limited	branded	India	below 25°C	0.0181933	1.5161083	0.5094124	0.2315511
Cameroon	Southwest	government health facility	QMCA020	Ciprofloxacine	Ciprofloxacin	antibiotic	500	Tablets	Medopharma	generic	India	below 30°C	0.1455464	3.9020483	2.0376496	0.9262044
Cameroon	Southwest	government health facility	QMCA021	Metronidazole Comprimes BP	Metronidazole	antibiotic	250	Tablets	Strides Arcolab Limited	generic	India	dry and cool, protected from light	0.0181933	2.9825082	0.7641186	0.3473266
Cameroon	Southwest	government health facility	QMCA022	Doxycycline Sprukfield	Doxycycline	antibiotic	100	Tablets	Jiangsu Ruinian Qianjin Pharm. Co.Ltd	branded	China	dry and cool, protected from light	0.0181933	1.3679173	0.363866	0.1653936

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Cameroon	Southwest	government health facility	QMCA023	Glibenclamid Pharmaquick	Glibenclamide	medicine against NCD	5	Tablets	Pharmaquick	branded	Benin	not stated	0.0090967	1.5959035	0.545799	0.2480905
Cameroon	Southwest	government health facility	QMCA024	Maxformin-500	Metformin	medicine against NCD	500	Tablets	Maxtar Bio-Genics	branded	India	dry and cool, protected from light	0.0181933	1.2128867	1.637397	0.7442714
Cameroon	Southwest	government health facility	QMCA025	Salbutamol B.P	Salbutamol	medicine against NCD	2	Tablets	Maxtar Bio-Genics	branded	India	below 25°C	0.0090967	3.63866	0.8186985	0.3721357
Cameroon	Southwest	pharmacy	QMCA026	Clavumoccid	Amoxi/Clav	antibiotic	500/62.5	Tablets	Medopharma	branded	India	below 25°C	0.5571698		11.700566	5.3184391
Cameroon	Southwest	pharmacy	QMCA027	Starpen	Penicillin v	antibiotic	500	Tablets	Sandoz	originator	Austria	below 25°C	0.2956411	12.166301	8.2779515	3.7627052
Cameroon	Southwest	pharmacy	QMCA028	ciprofloxacine Ubigen	Ciprofloxacin	antibiotic	750	Tablets	Lincoln Pharmaceuticals Ltd	branded	India	below 30°C	0.1758382		1.6411569	0.7459804
Cameroon	Southwest	informal vendor	QMCA029	Hydrochlorothiazide Pharmaquick	Hydrochlorothiazide	medicine against NCD	50	Tablets	Pharmaquick	branded	Benin	not stated	0.0454833	9.2822959	0.6822488	0.3101131
Cameroon	Southwest	informal vendor	QMCA030	Ciproin-500	Ciprofloxacin	antibiotic	500	Tablets	JSPY Pharmaceutical	branded	China	below 25°C	0.0909665	2.4387802	1.273531	0.5788777
Cameroon	Southwest	informal vendor	QMCA031	Metrole-500	Metronidazole	antibiotic	500	Tablets	JSPY Pharmaceutical	branded	China	below 25°C	0.0363866	3.0836102	0.7641186	0.3473266
Cameroon	Southwest	informal vendor	QMCA032	Amoxycillin capsules	Amoxicillin	antibiotic	500	Capsules	Jiangxi xierkangtai Pharmaceutical	generic	China	dry and cool, protected from light	0.0636766	2.1225517	1.3372076	0.6078216
Cameroon	Southwest	informal vendor	QMCA033	Metformin	Metformin	medicine against NCD	500	Tablets	Strides Shasum Ltd	generic	India	below 30°C	0.0454833	3.0322167	4.0934925	1.8606784
Cameroon	Southwest	informal vendor	QMCA034	Co-Trimoxazole	Sulfa/Trimet	antibiotic	400/80	Tablets	Strides Arcolab Limited	branded	India	below 25°C	0.0454833	3.7902708	1.273531	0.5788777
Cameroon	Southwest	informal vendor	QMCA035	Penicillin-V Tablets	Penicillin v	antibiotic	500	Tablets	Oxford Pharma	generic	Belgium	dry and cool, protected from light	0.2728995	11.230432	7.641186	3.4732664
Cameroon	Southwest	informal vendor	QMCA036	New Divine Doxycycline	Doxycycline	antibiotic	100	Capsules	New Divine Favour Pharmaceuticals	branded	Nigeria	below 30°C	0.0545799	4.1037519	1.091598	0.4961809
Cameroon	Southwest	informal vendor	QMCA037	Glibenclamid Pharmaquick	Glibenclamide	medicine against NCD	5	Tablets	Pharmaquick	branded	Benin	not stated	0.0454833	7.9795175	2.728995	1.2404523
Cameroon	West	church health facility	QMCA038	Amoxzem TAB	Amoxicillin	antibiotic	500	Tablets	Ningbo shuangwei	branded	China	below 25°C	0.1455464	4.8515467	3.0564744	1.3893065
Cameroon	West	church health facility	QMCA039	Oxynic	Amoxi/Clav	antibiotic	875/125	Tablets	not stated	branded	India	below 25°C	0.8898897	5.6500932	10.678676	4.8539437

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Cameroon	West	church health facility	QMCA040	Cotrimo-480 mg	Sulfa/Trimet	antibiotic	400/80	Tablets	Jiangsu Ruinian Qianjin Pharm. Co.Ltd	branded	China	below 25°C	0.0909665	7.5805417	2.547062	1.1577555
Cameroon	West	church health facility	QMCA041	Zeprox-500	Ciprofloxacin	antibiotic	500	Tablets	Jiangsu Ruinian Qianjin Pharm. Co.Ltd	branded	China	below 25°C	0.2728995	7.3163405	3.820593	1.7366332
Cameroon	West	church health facility	QMCA042	Metrozem 500	Metronidazole	antibiotic	500	Tablets	Ningbo shuangwei	branded	China	below 25°C	0.0909665	7.7090254	1.9102965	0.8683166
Cameroon	West	church health facility	QMCA043	Doxycycline Hyclate Tablets USP	Doxycycline	antibiotic	100	Tablets	Fourrts	generic	India	below 30°C	0.1091598	8.2075038	2.183196	0.9923618
Cameroon	West	church health facility	QMCA044	Maxformin-500	Metformin	medicine against NCD	500	Tablets	Maxtar Bio-Genics	branded	India	dry and cool, protected from light	0.0909665	6.0644333	8.186985	3.7213568
Cameroon	West	church health facility	QMCA045	Transglobe glibenclamide	Glibenclamide	medicine against NCD	5	Tablets	Osaka Pharmaceuticals	generic	India	dry and cool, protected from light	0.0909665	15.959035	5.45799	2.4809045
Cameroon	West	church health facility	QMCA046	Hydrochlorothiazide	Hydrochlorothiazide	medicine against NCD	50	Tablets	Hongkong Prost Medicines and Health Products Co.,Ltd	generic	Hong Kong	below 25°C	0.0909665	18.564592	1.3644975	0.6202261
Cameroon	West	church health facility	QMCA047	Furosemide 40mg BP	Furosemide	medicine against NCD	40	Tablets	Microlabs	generic	India	below 30°C	0.0909665	14.912541	2.728995	1.2404523
Cameroon	West	church health facility	QMCA048	Salbutamol comprimes BP	Salbutamol	medicine against NCD	2	Tablets	Maxtar Bio-Genics	branded	India	dry and cool, protected from light	0.0909665	36.3866	8.186985	3.7213568
Cameroon	West	pharmacy	QMCA050	Amoxycillin Sandoz	Amoxicillin	antibiotic	500	Tablets	Sandoz	branded	Austria	below 25°C	0.1364498	4.548325	2.8654448	1.3024749
Cameroon	West	pharmacy	QMCA051	Metronidazole Comprimes BP	Metronidazole	antibiotic	250	Tablets	Strides Arcolab Limited	generic	India	dry and cool, protected from light	0.0454833	7.4562705	1.9102965	0.8683166
Cameroon	West	pharmacy	QMCA052	Metformin Denk	Metformin	medicine against NCD	850	Tablets	Denk Pharma	generic	Germany	below 25°C	0.1350853	6.7542626	7.1515722	3.2507146
Cameroon	West	pharmacy	QMCA053	Doxycreat	Doxycycline	antibiotic	100	Tablets	Bailly-Creat	branded	India	below 25°C	0.0909665	6.8395865	1.81933	0.8269682
Cameroon	West	pharmacy	QMCA054	Ciprofloxacine	Ciprofloxacin	antibiotic	500	Tablets	Strides Shasum Ltd	generic	India	below 30°C	0.2774478	7.4382795	3.8842696	1.7655771
Cameroon	West	pharmacy	QMCA055 A	Esidrex	Hydrochlorothiazide	medicine against NCD	60	Tablets	Novartis Pharmaceutica	originator	Spain	below 25°C	0.1455464	33.848	4.366392	1.9847236
Cameroon	West	pharmacy	QMCA056	Glidiabet	Glibenclamide	medicine against NCD	5	Tablets	Ferrer Internacional	branded	Spain	not stated	0.0849021	14.895099	5.094124	2.3155109

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Cameroon	West	pharmacy	QMCA057	Furosemide Tabrad	Furosemide	medicine against NCD	40	Tablets	Asence Pharma pvt. Ltd..	branded	India	below 30°C	0.1061276	17.397964	3.1838275	1.4471943
Cameroon	West	pharmacy	QMCA058	Ospen	Penicillin v	antibiotic	500	Tablets	Sandoz	branded	Austria	below 25°C	0.3752368	15.441844	10.506631	4.7757413
Cameroon	West	pharmacy	QMCA059	Cotrim Fort	Sulfa/Trimet	antibiotic	800/160	Tablets	Bailly-Creat	branded	India	below 25°C	0.0836892	3.4725801	1.1716485	0.5325675
Cameroon	West	pharmacy	QMCA060	Klacin BID	Amoxi/Clav	antibiotic	875/125	Tablets	Bilim Pharmaceuticals	branded	Turkey	dry and cool, protected from light	0.9051167	5.7467725	10.8614	4.937
Cameroon	West	informal vendor	QMCA061	Cinclamox	Amoxi/Clav	antibiotic	875/125	Tablets	Cinpharm	branded	not stated	below 25°C	0.4548325	2.8878254	5.45799	2.4809045
Cameroon	West	informal vendor	QMCA062	Lancize	Furosemide	medicine against NCD	40	Tablets	mancare pharmaceutical ltd	branded	India	below 30°C	0.021832	3.5790098	0.6549588	0.2977085
Cameroon	West	informal vendor	QMCA063	Co-Trimoxazole	Sulfa/Trimet	antibiotic	400/80	Tablets	Sprukfield	branded	India	dry and cool, protected from light	0.0363866	3.0322167	1.0188248	0.4631022
Cameroon	West	informal vendor	QMCA064	Doxynol 200	Doxycycline	antibiotic	200	Tablets	Combitic Global Caplet Pvt. Ltd.	branded	India	below 30°C	0.1000632	7.5235451	1.0006315	0.4548325
Cameroon	West	informal vendor	QMCA065	Metronidazole Tablets	Metronidazole	antibiotic	250	Tablets	Anhui chengshi Pharmaceutical Co.	generic	China	dry and cool, protected from light	0.02729	4.4737623	1.1461779	0.52099
Cameroon	West	informal vendor	QMCA066	Maxformin-500	Metformin	medicine against NCD	500	Tablets	Maxtar Bio-Genics	branded	India	dry and cool, protected from light	0.0545799	3.63866	4.912191	2.2328141
Cameroon	West	informal vendor	QMCA067	Penicillin V	Penicillin v	antibiotic	250	Tablets	Shandong Shenglu Pharmaceutical Co	generic	China	dry and cool, protected from light	0.0909665	5.1685511	5.094124	2.3155109
Cameroon	West	informal vendor	QMCA068	Ciproin-750	Ciprofloxacin	antibiotic	750	Tablets	JSPY Pharmaceutical	branded	China	below 25°C	0.1455464		1.3584331	0.6174696
Cameroon	West	informal vendor	QMCA069	Konmoxy Capsules	Amoxicillin	antibiotic	500	Capsules	Shanghai Juchen Import and Exports	branded	China	dry and cool, protected from light	0.0636766	2.1225517	1.3372076	0.6078216
Cameroon	West	informal vendor	QMCA070	Hydrochlorothiazide comprimes BP	Hydrochlorothiazide	medicine against NCD	50	Tablets	global Pharma Healthcare	generic	India	not stated	0.0291093	5.9406694	0.4366392	0.1984724
Cameroon	West	informal vendor	QMCA071	Deominal	Glibenclamide	medicine against NCD	5	Tablets	Jiangxi xierkangtai Pharmaceutical	branded	China	below 30°C	0.02729	4.7877105	1.637397	0.7442714
Cameroon	West	informal vendor	QMCA072	not stated	Salbutamol	medicine against NCD	4	Tablets	not stated	generic	not stated	not stated	0.0181933	5.6854063	0.8186985	0.3721357
Cameroon	Center	church health facility	QMCA073	Amoxiciline Ubigen	Amoxicillin	antibiotic	500	Capsules	Reyoung Pharmaceutical Co. Ltd	generic	China	below 30°C	0.0909665	3.0322167	1.9102965	0.8683166

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Cameroon	Center	church health facility	QMCA074	Co-Trimoxazole	Sulfa/Trimet	antibiotic	400/80	Tablets	Entrance Pharmaceuticals and research Centre	generic	Ghana	not stated	0.0454833	3.7902708	1.273531	0.5788777
Cameroon	Center	church health facility	QMCA075	Coflox-500	Ciprofloxacin	antibiotic	500	Tablets	Macloads Pharmaceuticals LTD	branded	India	below 25°C	0.181933	4.8775603	2.547062	1.1577555
Cameroon	Center	church health facility	QMCA076	Metronidazole	Metronidazole	antibiotic	250	Tablets	Entrance Pharmaceuticals and research Centre	generic	Ghana	not stated	0.0454833	7.4562705	1.9102965	0.8683166
Cameroon	Center	church health facility	QMCA077	Doxycycline Capsules BP	Doxycycline	antibiotic	100	Capsules	Africure Pharmaceuticals Cameroon S.A	generic	Cameroon	below 30°C	0.0909665	6.8395865	1.81933	0.8269682
Cameroon	Center	government health facility	QMCA078	Ciprofloxacine USP 500 mg	Ciprofloxacin	antibiotic	500	Tablets	Medicamen biotech Ltd.	generic	India	below 30°C	0.1455464	3.9020483	2.0376496	0.9262044
Cameroon	Center	government health facility	QMCA079	Amoxdels-500	Amoxicillin	antibiotic	500	Capsules	Prost Pharma (France)	branded	British West Indies	below 30°C	0.0636766	2.1225517	1.3372076	0.6078216
Cameroon	Center	government health facility	QMCA080	Doxycycline Hyclate	Doxycycline	antibiotic	100	Tablets	Medicamen biotech Ltd.	generic	India	below 30°C	0.0545799	4.1037519	0.2183196	0.0992362
Cameroon	West	government health facility	QMCA082	Co-Trimoxazole	Sulfa/Trimet	antibiotic	400/80	Tablets	Entrance Pharmaceuticals and research Centre	generic	Ghana	not stated	0.0363866	3.0322167	1.0188248	0.4631022
Cameroon	West	government health facility	QMCA083	Tafuros 40	Furosemide	medicine against NCD	40	Tablets	Asence Pharma pvt. Ltd..	branded	India	not stated	0.0181933	2.9825082	0.545799	0.2480905
Cameroon	West	government health facility	QMCA083	Metronidazole Tablets	Metronidazole	antibiotic	500	Tablets	not stated	generic	not stated	not stated	0.0545799	4.6254153	1.1461779	0.52099
Cameroon	West	government health facility	QMCA084	Salbutamol comprimes BP	Salbutamol	medicine against NCD	2	Tablets	Maxtar Bio-Genics	generic	India	not stated	0.0090967	3.63866	0.8186985	0.3721357
Cameroon	Center	church health facility	QMCA085	Konmoxy Capsules	Amoxicillin	antibiotic	500	Capsules	not stated	branded	not stated	dry and cool, protected from light	0.0909665	3.0322167	1.9102965	0.8683166
Cameroon	Center	church health facility	QMCA086	Rapiclav-1g	Amoxi/Clav	antibiotic	875/125	Tablets	IPCA Laboratories LTD	branded	India	below 30°C	0.5185091	3.292121	6.2221086	2.8282312
Cameroon	Center	church health facility	QMCA087	Cotrimoxazole Pextran_SS	Sulfa/Trimet	antibiotic	400/80	Tablets	Maxtar Bio-Genics	branded	India	not stated	0.0363866	3.0322167	1.0188248	0.4631022

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Cameroon	Center	church health facility	QMCA088	Metronidazole GP	Metronidazole	antibiotic	500	Tablets	Sinochem Jiangsu co. Ltd	branded	China	dry and cool, protected from light	0.0363866	3.0836102	0.7641186	0.3473266
Cameroon	Center	church health facility	QMCA089	Ciprofloxacine comprimes USP	Ciprofloxacin	antibiotic	500	Tablets	Medopharma	generic	India	below 30°C	0.181933	4.8775603	2.547062	1.1577555
Cameroon	Center	church health facility	QMCA090	Doxycycline Capsules BP	Doxycycline	antibiotic	100	Capsules	Africure Pharmaceuticals Cameroon S.A	generic	Cameroon	below 30°C	0.0909665	6.8395865	1.81933	0.8269682
Cameroon	Center	pharmacy	QMCA091	Cinclamox	Amoxicillin	antibiotic	500	Capsules	Cinpharm	branded	India	not stated	0.1212887	4.0429556	2.547062	1.1577555
Cameroon	Center	pharmacy	QMCA092	AmoxiClav-Denk	Amoxi/Clav	antibiotic	500/62.5	Tablets	Denk Pharma	branded	Germany	below 25°C	0.4491471		9.432089	4.2873132
Cameroon	Center	pharmacy	QMCA093	Cincotrim	Sulfa/Trimet	antibiotic	400/80	Tablets	Cinpharm	branded	India	below 25°C	0.0545799	4.548325	1.5282372	0.6946533
Cameroon	Center	pharmacy	QMCA094	Coflox-500	Ciprofloxacin	antibiotic	500	Tablets	Macloads Pharmaceuticals LTD	branded	India	below 25°C	0.3183828	8.5357306	4.4573585	2.026072
Cameroon	Center	pharmacy	QMCA095	Ospen	Penicillin v	antibiotic	500	Tablets	Sandoz	originator	Austria	below 25°C	0.3790271	15.597822	10.612758	4.8239811
Cameroon	Center	pharmacy	QMCA096	Metronidazole 500	Metronidazole	antibiotic	500	Tablets	Asence Pharma pvt. Ltd..	generic	India	below 30°C	0.0818699	6.9381229	1.7192669	0.7814849
Cameroon	Center	pharmacy	QMCA097	Doxycreat	Doxycycline	antibiotic	100	Tablets	Bailly-Creat	branded	India	below 25°C	0.1455464	10.943338	2.910928	1.3231491
Cameroon	Center	pharmacy	QMCA098	Metformin Denk	Metformin	medicine against NCD	500	Tablets	Denk Pharma	branded	Germany	below 25°C	0.0982438	6.549588	8.8419438	4.0190654
Cameroon	Center	pharmacy	QMCA099	Daonil	Glibenclamide	medicine against NCD	5	Tablets	Sanofi-Winthrop	originator	France	below 25°C	0.1264434	22.183059	7.5866061	3.4484573
Cameroon	Center	pharmacy	QMCA100	Esidrex	Hydrochlorothiazide	medicine against NCD	25	Tablets	Novartis Pharmaceutica	originator	Spain	below 25°C	0.0727732	16.924	2.183196	0.9923618
Cameroon	Center	pharmacy	QMCA101	Furosemide	Furosemide	medicine against NCD	40	Tablets	Asence Pharma pvt. Ltd..	generic	India	below 30°C	0.1091598	17.895049	3.274794	1.4885427
Cameroon	Center	pharmacy	QMCA102	Ventoline	Salbutamol	medicine against NCD	2	Tablets	Aspen Bad Oldesloe GmbH	branded	Germany	below 30°C	0.1091598	43.66392	9.824382	4.4656282
Cameroon	Center	informal vendor	QMCA103	Konmoxy Capsules	Amoxicillin	antibiotic	500	Capsules	not stated	branded	not stated	dry and cool, protected from light	0.0909665	3.0322167	1.9102965	0.8683166
Cameroon	Center	informal vendor	QMCA104	Cinclamox	Amoxi/Clav	antibiotic	875/125	Tablets	not stated	branded	not stated	below 25°C	0.5685406	3.6097817	6.8224875	3.1011307
Cameroon	Center	informal vendor	QMCA105	Co-Trimoxazole Tablets BP	Sulfa/Trimet	antibiotic	400/80	Tablets	Macloads Pharmaceuticals LTD	generic	India	below 25°C	0.0454833	3.7902708	1.273531	0.5788777
Cameroon	Center	informal vendor	QMCA106	Ciprolif-500	Ciprofloxacin	antibiotic	500	Tablets	Sinochem Jiangsu co. Ltd	branded	China	dry and cool, protected from light	0.0909665	2.4387802	1.273531	0.5788777

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Cameroon	Center	informal vendor	QMCA107	Penicillin V	Penicillin v	antibiotic	250	Tablets	Shandong Shenglu Pharmaceutical Co	generic	China	dry and cool, protected from light	0.1061276	6.0299763	5.9431447	2.7014294
Cameroon	Center	informal vendor	QMCA108	Metronidazole GP	Metronidazole	antibiotic	250	Tablets	Sinochem Jiangsu co. Ltd	branded	China	dry and cool, protected from light	0.0545799	8.9475246	2.2923558	1.0419799
Cameroon	Center	informal vendor	QMCA109	Surelife Doxycyline	Doxycycline	antibiotic	100	Capsules	Jiangxi xierkangtai Pharmaceutical	branded	China	below 30°C	0.1091598	8.2075038	2.183196	0.9923618
Cameroon	Center	informal vendor	QMCA110	Metformin Tablets	Metformin	medicine against NCD	500	Tablets	SONMART PHARMA (UK)	generic	United Kingdom	dry and cool, protected from light	0.0636766	4.2451033	5.7308895	2.6049498
Cameroon	Center	informal vendor	QMCA111	Glibenclamide	Glibenclamide	medicine against NCD	5	Tablets	Entrance Pharmaceuticals and research Centre	generic	Ghana	not stated	0.0727732	12.767228	4.366392	1.9847236
Cameroon	Center	informal vendor	QMCA112	Hydrochlorothiazide comprimes BP	Hydrochlorothiazide	medicine against NCD	50	Tablets	global Pharma Healthcare	generic	India	not stated	0.0727732	14.851673	1.091598	0.4961809
Cameroon	Center	informal vendor	QMCA113	Tafuros 40	Furosemide	medicine against NCD	40	Tablets	Asence Pharma pvt. Ltd..	branded	India	not stated	0.0727732	11.930033	2.183196	0.9923618
Cameroon	Northwest	church health facility	QMCA151	Co-Trimoxazole	Sulfa/Trimet	antibiotic	400/80	Tablets	Strides Arcolab Limited	generic	India	below 25°C				
Cameroon	Northwest	church health facility	QMCA152	Metformin Tablets BP	Metformin	medicine against NCD	500	Tablets	Strides Arcolab Limited	generic	India	dry and cool, protected from light				
Cameroon	Northwest	church health facility	QMCA153	Doxycycline	Doxycycline	antibiotic	100	Capsules	Strides Arcolab Limited	generic	India	dry and cool, protected from light				
Cameroon	Northwest	church health facility	QMCA154	Amoxicillin Tablets	Amoxicillin	antibiotic	500	Tablets	Strides Arcolab Limited	generic	India	below 25°C				
Cameroon	Northwest	church health facility	QMCA155	Ciprofloxacine tablets USP	Ciprofloxacin	antibiotic	500	Tablets	Strides Arcolab Limited	generic	India	below 25°C				
Cameroon	Northwest	church health facility	QMCA156	Metronidazole Comprimes BP	Metronidazole	antibiotic	250	Tablets	Strides Arcolab Limited	generic	India	below 25°C				
Cameroon	Northwest	church health facility	QMCA157	Furosemide Pharmaquick	Furosemide	medicine against NCD	40	Tablets	Pharmaquick	branded	Benin	not stated				
Cameroon	Northwest	church health facility	QMCA158	Hydrochlorothiazide Pharmaquick	Hydrochlorothiazide	medicine against NCD	50	Tablets	Pharmaquick	branded	Benin	not stated				

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Cameroon	Northwest	church health facility	QMCA159	Glibenclamide	Glibenclamide	medicine against NCD	5	Tablets	UMEDICA Laboratoires	generic	India	not stated				
Cameroon	Northwest	government health facility	QMCA162	Ciprofloxacine	Ciprofloxacin	antibiotic	500	Tablets	Medopharma	generic	India	below 30°C	0.1091598	2.9265362	1.5282372	0.6946533
Cameroon	Northwest	government health facility	QMCA163	Metformine	Metformin	medicine against NCD	500	Tablets	Medicamen biotech Ltd.	generic	India	below 30°C	0.0181933	1.2128867	1.637397	0.7442714
Cameroon	Northwest	government health facility	QMCA164	Amoxicillin Tablets USP	Amoxicillin	antibiotic	500	Capsules	Medopharma	generic	India	below 25°C	0.0636766	2.1225517	1.3372076	0.6078216
Cameroon	Northwest	government health facility	QMCA165	Co-Trimoxazole	Sulfa/Trimet	antibiotic	400/80	Tablets	Sprukfield	generic	Togo	dry and cool, protected from light	0.0181933	1.5161083	0.5094124	0.2315511
Cameroon	Northwest	government health facility	QMCA166	Metronidazole	Metronidazole	antibiotic	500	Tablets	Medicamen biotech Ltd.	generic	India	below 30°C	0.0363866	3.0836102	0.7641186	0.3473266
Cameroon	Northwest	government health facility	QMCA167	Glibenclamide	Glibenclamide	medicine against NCD	5	Tablets	Medicamen biotech Ltd.	generic	India	not stated	0.0454833	7.9795175	2.728995	1.2404523
Cameroon	Northwest	government health facility	QMCA168	Salbutamol Tablets BP	Salbutamol	medicine against NCD	4	Tablets	Medico remedies	generic	India	not stated	0.0636766	19.898922	2.8654448	1.3024749
Cameroon	Northwest	government health facility	QMCA169	Doxycycline Gelules BP	Doxycycline	antibiotic	100	Capsules	Strides Shasum Ltd	generic	India	dry and cool, protected from light	0.0436639	3.2830015	0.8732784	0.3969447
Cameroon	Northwest	informal vendor	QMCA174	Hydrochlorothiazide Pharmaquick	Hydrochlorothiazide	medicine against NCD	50	Tablets	Pharmaquick	branded	Benin	not stated	0.0545799	11.138755	0.8186985	0.3721357
Cameroon	Northwest	informal vendor	QMCA175	Glibenclamide	Glibenclamide	medicine against NCD	5	Tablets	Medicamen biotech Ltd.	generic	India	not stated	0.0818699	14.363132	4.912191	2.2328141
Cameroon	Northwest	informal vendor	QMCA176	Cotrimoxazole Pextran_SS	Sulfa/Trimet	antibiotic	400/80	Tablets	Maxtar Bio-Genics	branded	India	dry and cool, protected from light	0.0363866	3.0322167	1.0188248	0.4631022
Cameroon	Northwest	informal vendor	QMCA177	Transglobe Pen Tabs	Penicillin v	antibiotic	250	Tablets	Shandong Shenglu Pharmaceutical Co	branded	China	dry and cool, protected from light	0.2728995	15.505653	15.282372	6.9465327
Cameroon	Northwest	informal vendor	QMCA178	Cinclamox	Amoxi/Clav	antibiotic	500/125	Tablets	Cinpharm	branded	Cameroon	below 25°C	0.3411244	2.0787591	7.1636119	3.2561872
Cameroon	Northwest	informal vendor	QMCA179	Salbutamol Tablets BP	Salbutamol	medicine against NCD	4	Tablets	Medico remedies	generic	India	not stated	0.0636766	19.898922	2.8654448	1.3024749
Cameroon	Northwest	informal vendor	QMCA180	Amoxicillin	Amoxicillin	antibiotic	500	Tablets	Nanjing Sino Pharmaceutical Ltd	generic	China	dry and cool, protected from light	0.0636766	2.1225517	1.3372076	0.6078216

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Cameroon	Northwest	informal vendor	QMCA181	Doxycycline	Doxycycline	antibiotic	100	Capsules	Strides Arcolab Limited	generic	India	dry and cool, protected from light	0.0436639	3.2830015	0.8732784	0.3969447
Cameroon	Northwest	informal vendor	QMCA182	Metronidazole Comprimes BP	Metronidazole	antibiotic	250	Tablets	Strides Arcolab Limited	generic	India	dry and cool, protected from light	0.0181933	2.9825082	0.7641186	0.3473266
Cameroon	Northwest	informal vendor	QMCA183	Metformin	Metformin	medicine against NCD	500	Tablets	Strides Shasum Ltd	generic	India	below 30°C	0.0327479	2.183196	2.9473146	1.3396885
Cameroon	Northwest	informal vendor	QMCA184	Wincip-500	Ciprofloxacin	antibiotic	500	Tablets	Maxheal Laboratories	branded	India	below 30°C	0.0909665	2.4387802	1.273531	0.5788777
Cameroon	Northwest	informal vendor	QMCA185	Frunmide	Furosemide	medicine against NCD	40	Tablets	mancare pharmaceutical ltd	branded	India	not stated	0.0636766	10.438779	1.9102965	0.8683166
Cameroon	Northwest	church health facility	QMCA190	Co-Trimoxazole	Sulfa/Trimet	antibiotic	400/80	Tablets	Sprukfield	generic	Togo	not stated	0.0545799	4.548325	1.5282372	0.6946533
Cameroon	Northwest	church health facility	QMCA191	Salbutamol Tablets BP	Salbutamol	medicine against NCD	4	Tablets	Medico remedies	generic	India	dry and cool, protected from light	0.02729	8.5281094	1.2280478	0.5582035
Cameroon	Northwest	church health facility	QMCA192	Furosemide 40mg BP	Furosemide	medicine against NCD	40	Tablets	Microlabs	generic	India	not stated	0.0363866	5.9650164	1.091598	0.4961809
Cameroon	Northwest	church health facility	QMCA193	Moxiclav	Amoxi/Clav	antibiotic	500/125	Tablets	Medochemie	branded	Cyprus	below 25°C	0.545799	3.3260146	11.461779	5.2098995
Cameroon	Northwest	church health facility	QMCA194	Novartis Access Hydrochlorothiazide	Hydrochlorothiazide	medicine against NCD	25	Tablets	Salutas Pharma gmbH	branded	Germany	below 30°C	0.0454833	10.5775	1.3644975	0.6202261
Cameroon	Northwest	church health facility	QMCA195	Doxycycline	Doxycycline	antibiotic	100	Tablets	Mepro pharmaceutical pvt- LTd	generic	India	not stated	0.0909665	6.8395865	1.81933	0.8269682
Cameroon	Northwest	church health facility	QMCA196	Penicillin-Tablets	Penicillin v	antibiotic	250	Tablets	Milan laboratories pvt. Ltd	generic	India	not stated	0.0909665	5.1685511	5.094124	2.3155109
Cameroon	Northwest	church health facility	QMCA197	Ciprofloxacine tablets USP 500 mg	Ciprofloxacin	antibiotic	500	Tablets	CSPC Ouyi Pharmaceutical Co.Ltd	generic	China	below 30°C	0.2274163	6.0969504	3.1838275	1.4471943
Cameroon	Northwest	church health facility	QMCA198	Glibenclamid Tablets B.P	Glibenclamide	medicine against NCD	5	Tablets	Holden Medical Laboratories	generic	India	below 30°C	0.02729	4.7877105	1.637397	0.7442714
Cameroon	Northwest	church health facility	QMCA199	Metronidazole Comprimes BP	Metronidazole	antibiotic	250	Tablets	Strides Arcolab Limited	generic	India	dry and cool, protected from light	0.0545799	8.9475246	2.2923558	1.0419799
Cameroon	Northwest	church health facility	QMCA200	Metformine	Metformin	medicine against NCD	500	Tablets	Medicamen biotech Ltd.	generic	India	below 30°C	0.0454833	3.0322167	4.0934925	1.8606784

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Cameroon	Northwest	church health facility	QMCA201	Amoxzem TAB	Amoxicillin	antibiotic	500	Capsules	Ningbo shuangwei	branded	China	below 25°C	0.181933	6.0644333	3.820593	1.7366332
Cameroon	Northwest	pharmacy	QMCA204	AmoxiClav-Denk	Amoxi/Clav	antibiotic	500/62.5	Tablets	Denk Pharma	branded	Germany	below 25°C	0.5240049		11.004104	5.0018654
Cameroon	Northwest	pharmacy	QMCA205	Esidrex	Hydrochlorothiazide	medicine against NCD	25	Tablets	Novartis Pharmaceutica	originator	Spain	dry and cool, protected from light	0.0727732	16.924	2.183196	0.9923618
Cameroon	Northwest	pharmacy	QMCA206	Metformin Denk	Metformin	medicine against NCD	500	Tablets	Denk Pharma	generic	Germany	below 25°C	0.0982438	6.549588	8.8419438	4.0190654
Cameroon	Northwest	pharmacy	QMCA207	Doxycreat	Doxycycline	antibiotic	100	Tablets	Bailly-Creat	branded	India	below 25°C	0.0755022	5.6768568	1.5100439	0.6863836
Cameroon	Northwest	pharmacy	QMCA208	Proloxcin	Ciprofloxacin	antibiotic	500	Tablets	Cinpharm	branded	India	below 25°C	0.1355401	3.6337824	1.8975612	0.8625278
Cameroon	Northwest	pharmacy	QMCA209	Amoxycillin Sandoz	Amoxicillin	antibiotic	500	Tablets	Sandoz	generic	Austria	below 25°C	0.1037018	3.456727	2.177738	0.9898809
Cameroon	Northwest	pharmacy	QMCA210	Ospen	Penicillin v	antibiotic	500	Tablets	Sandoz	branded	Austria	below 25°C	0.3714465	15.285866	10.400503	4.7275014
Cameroon	Northwest	pharmacy	QMCA211	Daonil	Glibenclamide	medicine against NCD	5	Tablets	Sanofi-Winthrop	branded	France	below 25°C	0.1264434	22.183059	7.5866061	3.4484573
Cameroon	Northwest	pharmacy	QMCA212	Cotrimoxazole ubigen	Sulfa/Trimet	antibiotic	400/80	Tablets	Lincoln Pharmaceuticals Ltd	branded	India	dry and cool, protected from light	0.0422994	3.5249519	1.1843838	0.5383563
Cameroon	Northwest	pharmacy	QMCA213	Metronidazole Comprimes BP	Metronidazole	antibiotic	500	Tablets	Strides Arcolab Limited	generic	India	dry and cool, protected from light	0.0563992	4.7795958	1.1843838	0.5383563
Cameroon	Northwest	pharmacy	QMCA214	Furosemide	Furosemide	medicine against NCD	40	Tablets	Sandoz	generic	USA	below 25°C	0.0909665	14.912541	2.728995	1.2404523
Cameroon	Northwest	pharmacy	QMCA215	Salbutamol B.P	Salbutamol	medicine against NCD	2	Tablets	Maxtar Bio-Genics	generic	India	below 25°C	0.0909665	36.3866	8.186985	3.7213568
Cameroon	Littoral	pharmacy	QMCA218	AmoxiClav-Denk	Amoxi/Clav	antibiotic	500/62.5	Tablets	Denk Pharma	branded	Germany	below 25°C	0.4434617		9.3126954	4.2330434
Cameroon	Littoral	pharmacy	QMCA219	Amoxycillin Sandoz	Amoxicillin	antibiotic	500	Tablets	Sandoz	generic	Austria	below 25°C	0.1273531	4.2451033	2.6744151	1.2156432
Cameroon	Littoral	pharmacy	QMCA220	Ciplox-500	Ciprofloxacin	antibiotic	500	Tablets	Cipla Ltd.	branded	India	below 30°C	0.2910928	7.8040965	4.0752992	1.8524087
Cameroon	Littoral	pharmacy	QMCA221	Flagyl 500	Metronidazole	antibiotic	500	Tablets	Sanofi-Winthrop	originator	Senegal	below 25°C	0.2664019	22.576432	5.5944398	2.5429272
Cameroon	Littoral	government health facility	QMCA222	Co-Trimoxazole Tablets BP	Sulfa/Trimet	antibiotic	400/80	Tablets	Strides Arcolab Limited	generic	India	below 25°C	0.0181933	1.5161083	0.5094124	0.2315511
Cameroon	Littoral	government health facility	QMCA223	Doxycycline Gelules BP	Doxycycline	antibiotic	100	Capsules	Strides Shasum Ltd	generic	India	dry and cool, protected from light	0.0363866	2.7358346	0.727732	0.3307873
Cameroon	Littoral	government health facility	QMCA224	Metronidazole Comprimes BP	Metronidazole	antibiotic	250	Tablets	Strides Arcolab Limited	generic	India	dry and cool, protected from light	0.0181933	2.9825082	0.7641186	0.3473266
Cameroon	Littoral	pharmacy	QMCA225	Tolexine Ge	Doxycycline	antibiotic	100	Tablets	Laboratoires Bailleul	branded	France	not stated	0.4385885	32.976578	8.7717696	3.987168
Cameroon	Littoral	pharmacy	QMCA226	Lasilix 40 mg	Furosemide	medicine against NCD	40	Tablets	Sanofi-Winthrop	branded	France	below 25°C	0.139482	22.865896	4.184459	1.9020268

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Cameroon	Littoral	pharmacy	QMCA227	Ospen	Penicillin v	antibiotic	500	Tablets	Sandoz	branded	Austria	below 25°C	0.3714465	15.285866	10.400503	4.7275014
Cameroon	Littoral	pharmacy	QMCA228	Metformin Denk	Metformin	medicine against NCD	500	Tablets	Denk Pharma	branded	Germany	below 25°C	0.0982438	6.549588	8.8419438	4.0190654
Cameroon	Littoral	pharmacy	QMCA229	Berlocid	Sulfa/Trimet	antibiotic	400/80	Tablets	berlin chemie	branded	Germany	dry and cool, protected from light	0.1591914	13.265948	4.4573585	2.026072
Cameroon	Littoral	pharmacy	QMCA230	Esidrex	Hydrochlorothiazide	medicine against NCD	25	Tablets	Novartis Pharmaceutica	originator	Spain	below 25°C	0.0727732	16.924	2.183196	0.9923618
Cameroon	Littoral	pharmacy	QMCA231	Glidiabet	Glibenclamide	medicine against NCD	5	Tablets	Ferrer Internacional	branded	Spain	not stated	0.0818699	14.363132	4.912191	2.2328141
Cameroon	Littoral	government health facility	QMCA232	Amoxicillin Tablets USP	Amoxicillin	antibiotic	500	Tablets	Medopharma	generic	India	below 30°C	0.0909665	3.0322167	1.9102965	0.8683166
Cameroon	Littoral	government health facility	QMCA233	Tamclav 1 G	Amoxi/Clav	antibiotic	875/125	Tablets	Asence Pharma pvt. Ltd..	branded	India	below 25°C	0.4639292	2.9455819	5.5671498	2.5305226
Cameroon	Littoral	government health facility	QMCA234	Ciprofloxacine tablets USP	Ciprofloxacin	antibiotic	500	Tablets	Strides Arcolab Limited	generic	India	below 25°C	0.181933	4.8775603	2.547062	1.1577555
Cameroon	Littoral	informal vendor	QMCA235	Frunmide	Furosemide	medicine against NCD	40	Tablets	mancare pharmaceutical ltd	branded	India	below 25°C	0.0454833	7.4562705	1.3644975	0.6202261
Cameroon	Littoral	informal vendor	QMCA236	Co-Trimoxazole Tablets BP	Sulfa/Trimet	antibiotic	400/80	Tablets	Strides Arcolab Limited	generic	India	below 25°C	0.02729	2.2741625	0.7641186	0.3473266
Cameroon	Littoral	informal vendor	QMCA237	Metronidazole GP	Metronidazole	antibiotic	250	Tablets	Sinochem Jiangsu co. Ltd	branded	China	dry and cool, protected from light	0.0236513	3.8772607	0.9933542	0.4515246
Cameroon	Littoral	informal vendor	QMCA238	Jeo-Phage Tablets	Metformin	medicine against NCD	500	Tablets	Shandong Xier Kangtai Pharm	branded	China	below 30°C	0.1364498	9.09665	12.280478	5.5820352
Cameroon	Littoral	informal vendor	QMCA239	Salbutamol Tablets BP	Salbutamol	medicine against NCD	4	Tablets	Medico remedies	generic	India	dry and cool, protected from light	0.0909665	28.427031	4.0934925	1.8606784
Cameroon	Littoral	informal vendor	QMCA240	Amoxicillin 500MG	Amoxicillin	antibiotic	500	Capsules	Sinochem Jiangsu co. Ltd	generic	China	dry and cool, protected from light	0.0545799	1.81933	1.1461779	0.52099
Cameroon	Littoral	informal vendor	QMCA241	Augmentin	Amoxi/Clav	antibiotic	500/125	Tablets	SmithKline Beecham Pharmaceuticals	originator	United Kingdom	below 25°C	0.2469091	1.5046257	5.1850905	2.3568593
Cameroon	Littoral	informal vendor	QMCA242	Hydrochlorothiazide comprimes BP	Hydrochlorothiazide	medicine against NCD	50	Tablets	global Pharma Healthcare	generic	India	not stated	0.0309286	6.3119612	0.4639292	0.2108769

Country	Region	Site type	Sample_ID	Product name	INN	Indication	Stated amount of the API	Dosage form	Manufacturer	Labeling	Country of origin	Storage conditions	Price per unit [USD]	Price ratio	Price per Treatment [US dollar]	Days wages needed for treatment
Cameroon	Littoral	informal vendor	QMCA243	Surelife Doxycyline	Doxycycline	antibiotic	100	Capsules	Jiangxi xierkangtai Pharmaceutical	branded	China	below 30°C	0.0454833	3.4197932	0.909665	0.4134841
Cameroon	Littoral	informal vendor	QMCA244	Penicillin V	Penicillin v	antibiotic	250	Tablets	Shandong Shenglu Pharmaceutical Co	generic	China	dry and cool, protected from light	0.1182565	6.7191165	6.6223612	3.0101642
Cameroon	Littoral	informal vendor	QMCA245	cipro 500	Ciprofloxacin	antibiotic	500	Tablets	Anhui medipharm co.	branded	India	dry and cool, protected from light	0.0909665	2.4387802	1.273531	0.5788777
Cameroon	Littoral	church health facility	QMCA246	Amoxzem TAB	Amoxicillin	antibiotic	500	Tablets	Ningbo shuangwei	branded	India	below 25°C	0.1455464	4.8515467	3.0564744	1.3893065
Cameroon	Littoral	church health facility	QMCA247	Metzole-500	Metronidazole	antibiotic	500	Tablets	Maxtar Bio-Genics	branded	India	dry and cool, protected from light	0.0909665	7.7090254	1.9102965	0.8683166
Cameroon	Littoral	church health facility	QMCA248	Metformin Tablets BP	Metformin	medicine against NCD	500	Tablets	Strides Arcolab Limited	generic	India	dry and cool, protected from light	0.0909665	6.0644333	8.186985	3.7213568
Cameroon	Littoral	church health facility	QMCA249	Zeprox-500	Ciprofloxacin	antibiotic	500	Tablets	Jiangsu Ruinian Qianjin Pharm. Co.Ltd	branded	China	below 25°C	0.363866	9.7551206	5.094124	2.3155109
Cameroon	Littoral	church health facility	QMCA250	Transglobe glibenclamide	Glibenclamide	medicine against NCD	5	Tablets	Osaka Pharmaceuticals	generic	India	dry and cool, protected from light	0.0909665	15.959035	5.45799	2.4809045
Cameroon	Littoral	church health facility	QMCA251	Furosemide 40mg BP	Furosemide	medicine against NCD	40	Tablets	Microlabs	generic	India	below 30°C	0.0909665	14.912541	2.728995	1.2404523
Cameroon	Littoral	church health facility	QMCA252	Hydrochlorothiazide	Hydrochlorothiazide	medicine against NCD	50	Tablets	APL "no description"	generic	not stated	below 25°C	0.0909665	18.564592	1.3644975	0.6202261
Cameroon	Adamawa	informal vendor	QMCA253	Penicillin V Potassium - 5000,000	Penicillin v	antibiotic	250	Tablets	Sishui xier kang Pharmaceutical Co.Ltd	generic	China	dry and cool, protected from light	0.139482	7.9251117	7.8109901	3.5504501
Cameroon	Adamawa	informal vendor	QMCA254	Metronidazole Tablets 250mg	Metronidazole	antibiotic	250	Tablets	SONMART PHARMA (UK)	generic	United Kingdom	dry and cool, protected from light	0.02729	4.4737623	1.1461779	0.52099
Cameroon	Adamawa	informal vendor	QMCA255	Sonnmamox Amoxicilline 500mg	Amoxicillin	antibiotic	500	Capsules	SONMART PHARMA (UK)	branded	United Kingdom	dry and cool, protected from light	0.0636766	2.1225517	1.3372076	0.6078216
Cameroon	Adamawa	informal vendor	QMCA256	Co-trimoxazole Tablets BP 480mg	Sulfa/Trimet	antibiotic	400/80	Tablets	not stated	generic	not stated	not stated	0.02729	2.2741625	0.7641186	0.3473266

Country	Region	Site type	Sample_ID	Product name	INN	Indication	Stated amount of the API	Dosage form	Manufacturer	Labeling	Country of origin	Storage conditions	Price per unit [USD]	Price ratio	Price per Treatment [US dollar]	Days wages needed for treatment
Cameroon	Adamawa	informal vendor	QMCA257	Hydrochlorothiazide Pharmaquick	Hydrochlorothiazide	medicine against NCD	50	Tablets	Pharmaquick	generic	Benin	not stated	0.0363866	7.4258367	0.545799	0.2480905
Cameroon	Adamawa	informal vendor	QMCA258	Doxycycline Capsules	Doxycycline	antibiotic	100	Capsules	SONMART PHARMA (UK)	generic	United Kingdom	dry and cool, protected from light	0.0818699	6.1556278	1.637397	0.7442714
Cameroon	Adamawa	informal vendor	QMCA259	Furosemide BP 40mg	Furosemide	medicine against NCD	40	Tablets	mancare pharmaceutical ltd	generic	India	not stated	0.0363866	5.9650164	1.091598	0.4961809
Cameroon	Adamawa	informal vendor	QMCA260	Deominal	Glibenclamide	medicine against NCD	5	Tablets	Jiangxi xierkangtai Pharmaceutical	branded	China	below 30°C	0.0363866	6.383614	2.183196	0.9923618
Cameroon	Adamawa	informal vendor	QMCA261	Metformin Tablets	Metformin	medicine against NCD	500	Tablets	SONMART PHARMA (UK)	generic	United Kingdom	dry and cool, protected from light	0.0636766	4.2451033	5.7308895	2.6049498
Cameroon	Adamawa	informal vendor	QMCA262	Cipromax Fort 500	Ciprofloxacin	antibiotic	500	Tablets	Greenfield Pharmaceutical Jiang Su Co.ltd	branded	China	dry and cool, protected from light	0.0909665	2.4387802	1.273531	0.5788777
Cameroon	Adamawa	informal vendor	QMCA263	Amoxicillin 500mg + Clavulanic acid 125mg BP	Amoxi/Clav	antibiotic	500/125	Tablets	Medopharma	generic	India	below 25°C	0.4447251	2.710086	9.3392273	4.2451033
Cameroon	Adamawa	informal vendor	QMCA264	Salbutamol	Salbutamol	medicine against NCD	4	Tablets	Maxheal Laboratories	generic	India	below 30°C	0.02729	8.5281094	1.2280478	0.5582035
Cameroon	Adamawa	church health facility	QMCA265	Metformin 500 mg BP	Metformin	medicine against NCD	500	Tablets	Medopharma	generic	India	below 30°C	0.0454833	3.0322167	4.0934925	1.8606784
Cameroon	Adamawa	church health facility	QMCA266	Ciprofloxacine tablets USP 500 mg	Ciprofloxacin	antibiotic	500	Tablets	CSPC Ouyi Pharmaceutical Co.Ltd	generic	China	below 30°C	0.2274163	6.0969504	3.1838275	1.4471943
Cameroon	Adamawa	government health facility	QMCA267	Cledomox 562.5	Amoxi/Clav	antibiotic	500/62.5	Tablets	Medopharma	branded	India	below 25°C	0.5185091		10.88869	4.9494046
Cameroon	Adamawa	government health facility	QMCA268	Ciprolif-500	Ciprofloxacin	antibiotic	500	Tablets	Sinochem Jiangsu co. Ltd	branded	China	dry and cool, protected from light	0.1455464	3.9020483	2.0376496	0.9262044
Cameroon	Adamawa	government health facility	QMCA269	Filmox 500	Amoxicillin	antibiotic	500	Capsules	not stated	branded	not stated	below 30°C	0.0727732	2.4257733	1.5282372	0.6946533
Cameroon	Adamawa	government health facility	QMCA270	Metronidazole	Metronidazole	antibiotic	250	Tablets	Entrance Pharmaceuticals and research Centre	generic	Ghana	below 30°C	0.0090967	1.4912541	0.3820593	0.1736633
Cameroon	Adamawa	government health facility	QMCA271	Hydrochlorothiazide comprimes BP	Hydrochlorothiazide	medicine against NCD	50	Tablets	global Pharma Healthcare	generic	India	not stated	0.0181933	3.7129184	0.2728995	0.1240452

Country	Region	Site type	Sample_ID	Product name	INN	Indication	Stated amount of the API	Dosage form	Manufacturer	Labeling	Country of origin	Storage conditions	Price per unit [USD]	Price ratio	Price per Treatment [US dollar]	Days wages needed for treatment
Cameroon	Adamawa	government health facility	QMCA272	Salbutamol comprimes BP	Salbutamol	medicine against NCD	2	Tablets	Maxtar Bio-Genics	generic	India	below 30°C	0.0090967	3.63866	0.8186985	0.3721357
Cameroon	Adamawa	church health facility	QMCA274	Transglobe glibenclamide	Glibenclamide	medicine against NCD	5	Tablets	Osaka Pharmaceuticals	generic	India	dry and cool, protected from light	0.02729	4.7877105	1.637397	0.7442714
Cameroon	Adamawa	church health facility	QMCA275	Fenoximetilpenicilina	Penicillin v	antibiotic	500	Tablets	Medopharma	generic	India	below 25°C	0.0909665	3.7434774	2.547062	1.1577555
Cameroon	Adamawa	church health facility	QMCA276	Salbutamol Tablets BP	Salbutamol	medicine against NCD	4	Tablets	Medico remedies	generic	India	dry and cool, protected from light	0.02729	8.5281094	1.2280478	0.5582035
Cameroon	Adamawa	church health facility	QMCA277	Sulfamethoxazole and trimethoprim	Sulfa/Trimet	antibiotic	400/80	Tablets	Guilin Pharmaceutical Ltd	generic	China	below 25°C	0.0545799	4.548325	1.5282372	0.6946533
Cameroon	Adamawa	church health facility	QMCA278	Co-amoxiclav Tablets BP 625mg	Amoxi/Clav	antibiotic	500/125	Tablets	PIL Pharmaceuticals Pvt. Ltd	generic	India	below 25°C	0.545799	3.3260146	11.461779	5.2098995
Cameroon	Adamawa	church health facility	QMCA279	Metronidazole Tablets BP 250 mg	Metronidazole	antibiotic	250	Tablets	CSPC Ouyi Pharmaceutical Co.Ltd	generic	China	below 30°C	0.0545799	8.9475246	2.2923558	1.0419799
Cameroon	Adamawa	church health facility	QMCA280	Amoxzem TAB	Amoxicillin	antibiotic	500	Capsules	Ningbo shuangwei	branded	China	below 25°C	0.181933	6.0644333	3.820593	1.7366332
Cameroon	Adamawa	church health facility	QMCA281	Furosemide 40mg BP	Furosemide	medicine against NCD	40	Tablets	Microlabs	generic	India	below 30°C	0.0363866	5.9650164	1.091598	0.4961809
Cameroon	Adamawa	church health facility	QMCA282	Novartis Access Hydrochlorothiazide	Hydrochlorothiazide	medicine against NCD	25	Tablets	Salutas Pharma gmbH	branded	Germany	below 30°C	0.0454833	10.5775	1.3644975	0.6202261
Cameroon	Adamawa	pharmacy	QMCA283	AmoxiClav-Denk	Amoxi/Clav	antibiotic	500/62.5	Tablets	Denk Pharma	branded	Germany	below 25°C	0.4605179		9.670876	4.3958527
Cameroon	Adamawa	pharmacy	QMCA284	Doxycycline Capsules	Doxycycline	antibiotic	100	Capsules	SONMART PHARMA (UK)	generic	United Kingdom	dry and cool, protected from light	0.0727732	5.4716692	1.455464	0.6615745
Cameroon	Adamawa	pharmacy	QMCA285	Ciprofloxacine	Ciprofloxacin	antibiotic	750	Tablets	Lincoln Pharmaceuticals Ltd	generic	India	below 30°C	0.2547062		2.3772579	1.0805718
Cameroon	Adamawa	pharmacy	QMCA286	Ospen	Penicillin v	antibiotic	500	Tablets	Sandoz	originator	Austria	below 25°C	0.3843335	15.816192	10.761337	4.8915168
Cameroon	Adamawa	pharmacy	QMCA287	Glucophage 500 mg	Metformin	medicine against NCD	500	Tablets	Famar Lyon (MAH Novartis)	originator	France	below 30°C	0.0636766	4.2451033	5.7308895	2.6049498
Cameroon	Adamawa	pharmacy	QMCA288	Esidrex	Hydrochlorothiazide	medicine against NCD	25	Tablets	Novartis Pharmaceutica	originator	Spain	below 25°C	0.0727732	16.924	2.183196	0.9923618
Cameroon	Adamawa	pharmacy	QMCA289	Lasilix 40 mg	Furosemide	medicine against NCD	40	Tablets	Sanofi-Winthrop	originator	France	below 25°C	0.139482	22.865896	4.184459	1.9020268

Country	Region	Site type	Sample_ID	Product name	INN	Indication	Stated amount of the API	Dosage form	Manufacturer	Labeling	Country of origin	Storage conditions	Price per unit [USD]	Price ratio	Price per Treatment [US dollar]	Days wages needed for treatment
Cameroon	Adamawa	pharmacy	QMCA290	Metronidazole Comprimes BP	Metronidazole	antibiotic	250	Tablets	Strides Arcolab Limited	generic	India	dry and cool, protected from light	0.0363866	5.9650164	1.5282372	0.6946533
Cameroon	Adamawa	pharmacy	QMCA291	Daonil	Glibenclamide	medicine against NCD	5	Tablets	Sanofi-Winthrop	originator	France	below 25°C	0.1546431	27.13036	9.278583	4.2175377
Cameroon	Adamawa	pharmacy	QMCA292	Co-Trimoxazole Tablets BP	Sulfa/Trimet	antibiotic	400/80	Tablets	Strides Arcolab Limited	generic	India	below 25°C	0.0363866	3.0322167	1.0188248	0.4631022
Cameroon	Littoral	church health facility	QMCA295	Co-Trimoxazole	Sulfa/Trimet	antibiotic	400/80	Tablets	Sprukfield	generic	Togo	not stated	0.0909665	7.5805417	2.547062	1.1577555
Cameroon	Littoral	church health facility	QMCA296	Salbutamol comprimes BP	Salbutamol	medicine against NCD	2	Tablets	Maxtar Bio-Genics	generic	India	not stated	0.0909665	36.3866	8.186985	3.7213568

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Substandard and Falsified Antibiotics and Medicines against Noncommunicable Diseases in Western Cameroon and Northeastern Democratic Republic of Congo

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Abstract. Falsified and substandard medicines may undermine the progress toward the Sustainable Development Goals. The present study investigated the quality of 13 essential medicines in Cameroon and the Democratic Republic of Congo (DR Congo). Five hundred six medicine samples were collected from the government and faith-based health facilities, private pharmacies, and informal vendors (total 60 facilities). Collected samples were analyzed according to the U.S. Pharmacopeia (USP) for identity, content, and dissolution of their active pharmaceutical ingredients (APIs) and for uniformity of dosage units. Three samples (0.6%) were identified as falsified. Overall, 8.5% of the samples failed USP specifications for the content of the API and 11.7% failed dissolution testing. Medicines from informal vendors showed a higher out-of-specification rate (28.2%) than other types of drug outlets (12.3%; $P < 0.0001$). All three falsified medicines had been sold by informal vendors. The failure rate of medicines stated to be produced in Europe (5.1%) was lower than that for medicines from Asia (17.7%; $P = 0.0049$) and Africa (22.2%; $P = 0.0042$). Medicines against noncommunicable diseases showed a higher failure rate than antibiotics (25.3% versus 12.1%; $P = 0.0004$). Four hundred fifty-one of the samples were analyzed in Cameroon and the DR Congo with the Global Pharma Health Fund Minilab (thin-layer chromatography and disintegration testing). The three falsified medicines were readily detected in Minilab analysis. However, substandard samples were detected with low sensitivity. A well-enforced ban of medicine sales by informal vendors and increased attention to supplier qualification in the procurement process may reduce the prevalence of substandard and falsified medicines.

INTRODUCTION

In the past decades, access to medicines in low- and middle-income countries (LMICs) has improved,[1,2] but the occurrence of substandard and falsified (SF) medicines has been reported frequently and was even described as a "pandemic" by some authors.[3] Substandard and falsified medicines pose a serious risk to global health, and therefore, access to safe, quality, and affordable medicines has been included in the Sustainable Development Goals of the United Nations as Goal No. 3.8.[4] Substandard and falsified medicines may cause prolonged illness and treatment failures and can also directly harm patients through toxic effects or adverse reactions.[5,6] Yet, reliable data about their prevalence are sparse.[7–9] Following the first international conference on Medicine Quality and Public Health in 2018, researchers from all over the world called for investment, policy change, and action to eliminate SF medical products, and they formulated a research agenda stressing the urgent need for epidemiological evidence on the prevalence of SF medical products in different countries, in different sectors of the health system, and for different categories of medicines.[10]

Although medicine quality problems have been reported to occur worldwide, the burden of SF medicines is heavily concentrated in LMICs.[8] A review article by the WHO calculated an average prevalence of 10.5% SF medicines in these countries.[7] A review and meta-analysis by Ozawa et al.[11] estimated their prevalence in Africa to be 18.7%. Both these reviews emphasized the problem of strong heterogeneity of methods and results across different surveys on SF medicines.[7,11] The lack of a common terminology further hampered the comparison of data from different studies, until finally the 2017 World Health Assembly agreed on common definitions for "substandard" and "falsified" medicines.[12] Substandard medicines are now defined as "authorized medical products that fail to meet either their quality standards or specifications or both." They may result from poor manufacturing, or from inappropriate transport or storage conditions. Falsified medicines are defined as "medical products that deliberately or fraudulently misrepresent their identity, composition, or source."[12]

In the Democratic Republic of Congo (DR Congo) and in Cameroon, so far only few medicine quality studies have been conducted, mostly focusing on antimalarials, antiretrovirals, and antibiotics. The QAMSA study conducted by the WHO in six African countries reported that in Cameroon, 37% of the 41 tested antimalarial samples failed quality testing.[13] Petersen et al.[14] investigated 869 medicines from seven African and Asian countries using the Global Pharma Health Fund (GPHF) Minilab.[15] For those samples which failed Minilab testing, confirmatory analysis was carried out using high-performance liquid chromatography (HPLC). In Cameroon and in the DR Congo, 7.1% and 2.7% of the samples collected were found to be falsified or substandard, respectively, although the authors noted that a number of substandard medicines may have escaped detection because of the limited sensitivity of the GPHF Minilab.[14] In 2018, Mufusama et al.[16] reported the quality of artemether/lumefantrine combination products collected in eight cities of the DR Congo. When analyzed using thin-layer chromatography (TLC) with the GPHF Minilab, four of the 150 investigated samples (2.7%) were found not to

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contain the declared active pharmaceutical ingredients (APIs), and this was confirmed by HPLC analysis. The failure rate reportedly increased to 46.7% when also quantitative deviations from the declared amount of the APIs were considered. The authors noted that this failure rate was quite high compared with other medicine quality surveys. Schiavetti et al.[17] investigated the quality of medicines used in children, supplied by private wholesalers in Kinshasa in the DR Congo in 2018. Of the 239 tested samples, representing artemether/lumefantrine and amoxicillin powders for suspension and paracetamol tablets, 27% were of poor quality. By contrast, 35 antiretroviral medicine samples collected in different regions of Cameroon all showed good quality.[18]

As emphasized in the WHO Global Status Report on noncommunicable diseases (NCDs) of 2014,[19] the burden of death and disease resulting from NCDs is heavily concentrated in LMICs. Hunter-Adams et al.[20] expected that the burden of diabetes in Africa will be more than double in the next decade. Nevertheless, so far, the quality of medicines against NCDs has only been evaluated in few studies. The seven studies investigated the quality of seven cardiac medicines from 10 different countries, including the DR Congo,[21] and 26.7% of the 90 samples collected in the DR Congo were reported to be of poor quality.

Following the aforementioned call for research on the prevalence of SF medicines in different countries, in different sectors of the health system, and for different categories of medicines,[10] the present study investigated the prevalence of SF medicines among selected medicines against NCDs and antibiotics in government and faith-based health facilities, private pharmacies, and informal vendors of Cameroon and of the DR Congo. Samples were first tested with the GPHF Minilab. Subsequently, all samples, irrespective of the results obtained in the GPHF Minilab analysis, were also tested with the methods of the U.S. Pharmacopeia (USP) for identity, content, and dissolution of the APIs and for uniformity of the dosage units. The use of both Minilab and compendial analysis in the present study allows an evaluation of the sensitivity and specificity of the screening with the GPHF Minilab. Data on the availability, prices, and affordability of the medicines were collected additionally and have been published elsewhere.[22]

To the best of our knowledge, this is the largest and most comprehensive study on medicine quality conducted in Cameroon and the DR Congo so far, and at the same time, the largest investigation of the dissolution of the APIs of medicines on the African market published until now.

MATERIALS AND METHODS

Study design and included medicines. This study was designed observing the recommendations contained in the WHO guidelines on the conduct of surveys of the quality of medicines[23] and the MEDQUARG guidelines.[24] Thirteen medicines, that is, seven antibiotics and six medicines against NCDs were included, in dosages for adults. They are listed in Table 1. All of them were selected from the essential medicines lists of the Republic of Cameroon[25] and the DR Congo.[26] Medicines were selected for which both a USP-finished pharmaceutical product monograph and a GPHF Minilab method were available for medicine quality analysis. The included medicines were identical in both countries with one exception: in the DR Congo, atenolol tablets were included, but in Cameroon, the local partners and Jingi et al.[27] reported that atenolol was not frequently used. On request by the local partners, glibenclamide (=glyburide) was included instead of atenolol in Cameroon.

Ethical approval. This study was approved by the Ministry of Health of the DR Congo (Ref. CAB/Min-Prov/SGFEAHRAP/SK/01/2017) and by the Ministry of Public Health of the Republic of Cameroon, Comité National d' Ethique de la Recherche pour la Santé Humain (Ref. 243674339).

Sampling sites. This study was conducted in the northeast of the DR Congo in the provinces Ituri, North Kivu, South Kivu, and Tanganyika, and in western Cameroon, in the regions Adamawa, Centre, Littoral, Northwest, Southwest, and West (Figure 1) because these were the provinces/regions where the local partners worked. The selection of the sampling sites has been described in the evaluation of the availability and prices of the included medicines.[22] For the four provinces in

TABLE 1
Limits for compliance/noncompliance, and for moderate and extreme deviations from pharmacopoeial specifications, used in this study.

International nonproprietary names	Dosage form	Content of the API (=assay) (% of declared content)			Dissolution of the API (% of declared content)		
		Complies	Moderate deviation	Extreme deviation	Complies	Moderate deviation	Extreme deviation
Amoxicillin	Tablets	90–120	80 to < 90	< 80 Or > 120	≥ 85	< 85 to 60	< 60
Clavulanic acid		90–120	80 to < 90		≥ 80	< 80 to 55	< 55
Amoxicillin	Tablets	90–120	80 to < 90		≥ 75	< 75 to 50	< 50
Amoxicillin	Capsules	90–120	80 to < 90		≥ 80	< 80 to 55	< 55
Ciprofloxacin	Tablets	90–110	80 to < 90 or > 110 to 120		≥ 80	< 80 to 55	< 55
Doxycycline	Tablets/capsules	90–120	80 to < 90		≥ 85	< 85 to 60	< 60
Doxycycline hyclate	Tablets	90–120	80 to < 90		≥ 85	< 85 to 60	< 60
Doxycycline hyclate	Capsules	90–120	80 to < 90		≥ 80	< 80 to 55	< 55
Penicillin V	Tablets	90–120	80 to < 90		≥ 75	< 75 to 50	< 50
Metronidazole	Tablets	90–110	80 to < 90 or > 110 to 120		≥ 85	< 85 to 60	< 60
Sulfamethoxazole	Tablets	93–107	80 to < 93 or > 107 to 120		≥ 70	< 70 to 45	< 45
Trimethoprim		93–107	80 to < 93 or > 107 to 120		≥ 70	< 70 to 45	< 45
Atenolol	Tablets	90–110	80 to < 90 or >110 to 120		≥ 80	< 80 to 55	< 55
Furosemide	Tablets	90–110	80 to < 90 or > 110 to 120		≥ 80	< 80 to 55	< 55
Glibenclamide (glyburide)	Tablets	90–110	80 to < 90 or > 110 to 120		≥ 70	< 70 to 45	< 45
Hydrochlorothiazide	Tablets	90–110	80 to < 90 or > 110 to 120		≥ 60	< 60 to 35	< 35
Metformin	Tablets	95–105	80 to < 95 or > 105 to 120		≥ 70	< 70 to 45	< 45
Salbutamol (albuterol)	Tablets	90–110	80 to < 90 or > 110 to 120		≥ 80	< 80 to 55	< 55

API = active pharmaceutical ingredients.

the northeast DR Congo, a complete list of the health zones (total 116 zones) was obtained. On consultation with the local partners, 70 of these zones were identified as unsafe for travel by the study personnel and, therefore, had to be excluded from the study. Of the remaining 46 health zones, two from each of the four provinces were randomly selected using the RAND function of Microsoft Excel. In addition, Kadutu Health Zone in Bukavu, South Kivu, was added on request by the local partners because it comprised the biggest unlicensed market for medicines and was considered important in the assessment of medicine quality problems in that region. In the DR Congo, the health zone is a set of health centers linked to a hospital.[28] In each of the selected health zones, the samples were collected first from the main hospital of that zone. When this was a government-operated general referral hospital, medicines were sampled also from the nearest church health center, private pharmacy, and informal vendor of medicines. Correspondingly, if the main hospital was a church-operated centre hospitalier, medicines were sampled also from the nearest governmental health center, private pharmacy, and informal vendor. In Ituri Province, no informal medicine vendors could be found because tight control was enforced by the authorities in that province following a major medicine scandal.[5] Therefore, in the DR Congo, samples for this study were collected from 34 medicine outlets, located in nine health zones in four provinces.

The structure of the health system of Cameroon has been described in two recent documents.[29,30] For the present study, a complete list of the 45 church health facilities in the six included regions was obtained. For each region, one church health facility was randomly selected. Samples were collected from this church health facility and from the geographically nearest governmental health facility, private pharmacy, and informal vendor in that region. By chance, the random selection had not included any church health facility operated by the catholic church, and the local partners requested that of the 10 catholic health facilities existing in the six regions, two were randomly selected and included as well. Therefore, in Cameroon, samples were collected from 26 medicine outlets, located in six of Cameroon's 10 regions.

Sample collection. Samples were collected between August 2017 and November 2018. An overt sampling approach was used in public and church health facilities, that is, the investigators identified themselves and explained the purpose of the study. By contrast, a mystery shopper approach was used in informal vendors and private pharmacies, that is, the local investigators acted as customers, stating that they own a small informal medicine outlet. If the medicine outlets had more than one brand of the included medicines in stock, the cheapest brand was collected. For each sample, an amount of 100 dosage units (capsules or tablets) was purchased if available, otherwise less, but samples were only collected if at least 30 dosage units could be obtained. In government and church health facilities, replacements for the sampled medicines were offered by the sample collectors to avoid that stock-outs would result from this study. Replacement medicines were obtained from the medical stores of the local partner organizations. If the visited facilities preferred, the sampled medicines were paid for.

Samples were purchased in their original containers if possible. Preprinted labels with a unique sample number were attached to each sample on collection. Brand name, batch number, manufacturing date, expiry date, name of manufacturer, international nonproprietary names of the APIs, strength, dosage form, package size, and price were recorded as stated on the labels. All samples were transported from the collection sites to the medical stores of the local partner organizations as fast as possible. Shipment to Tuebingen University, Germany, was done by commercial courier services. At Tuebingen University, the samples were stored in an air-conditioned storage room at 21°C until analysis.

Chemical analysis. Of all samples consisting of more than 50 units (=tablets or capsules), 25 units were retained by the local partners for GPHF Minilab analysis in the respective country and the remaining units were shipped to Tuebingen University, Germany, for compendial analysis. For three samples, less than 50 units had been collected, and in these cases, all units were sent to Germany.

Global Pharma Health Fund Minilab analysis comprised visual inspection, TLC, and disintegration testing according

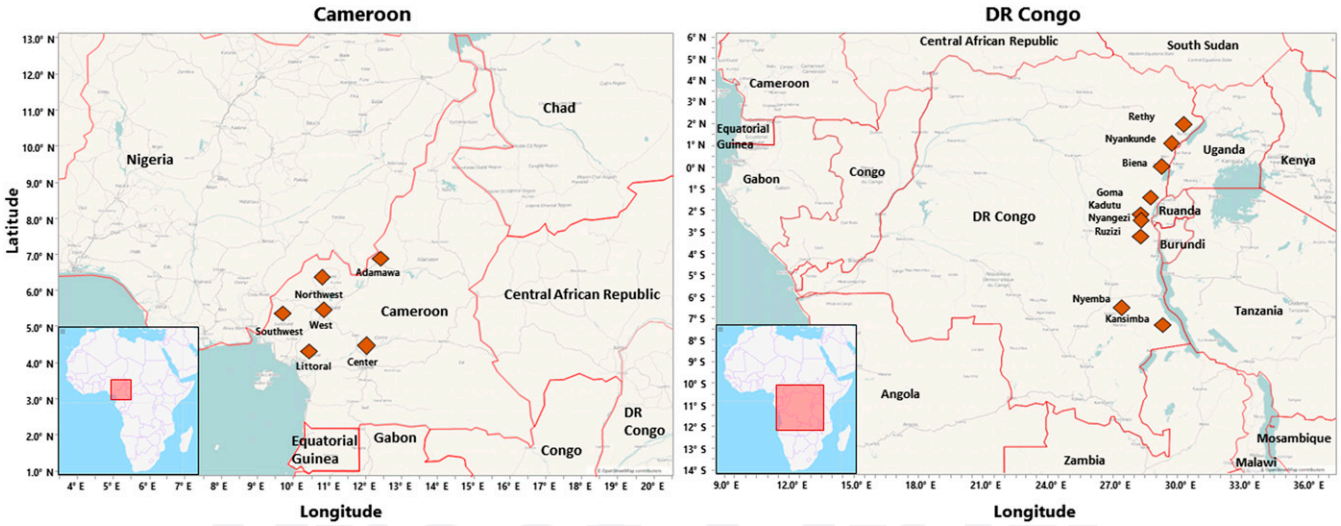

FIGURE 1. Map of the locations from which samples were collected in Cameroon and the Democratic Republic of Congo (DR Congo). This figure appears in color at www.ajtmh.org.

to the Minilab manual[15] and was carried out by the local partners in Cameroon and the DR Congo. Results of TLC analysis were recorded by photographs of the developed TLC plates.

Compendial analysis was carried out at the Pharmaceutical Institute of Tuebingen University according to the monographs of the USP 2018 (USP 41) for the respective finished pharmaceutical products. It comprised identification of the declared API by HPLC in comparison with certified standards, and quantification of the API (=assay), dissolution testing, and testing for uniformity of dosage units. Certified pharmaceutical secondary standards were purchased from Sigma-Aldrich (St. Louis, MO). Using the columns and solvent systems specified by USP 41, HPLC-UV analysis was carried out using an Agilent 1100 HPLC or an Agilent 1260 Infinity II HPLC (Agilent Technologies, Santa Clara, CA). Dissolution tests were performed with a PTWS 610 Dissolution Testing Instrument (Pharma Test Apparatebau AG, Hainburg, Germany) and an Agilent 708-DS Dissolution Apparatus (Agilent Technologies). Uniformity of dosage units was determined using the test for weight variation which, according to USP 41, is applicable if one unit contains at least 25 mg of the API, and the API comprises 25% or more of the whole tablet or the capsule content weight. In this study, this was applicable for the samples containing amoxicillin, ciprofloxacin, doxycycline, penicillin V, metronidazole, sulfamethoxazole, atenolol, furosemide, and metformin, and thereby for 425 of the 506 investigated samples.

Samples that showed unknown substances in LC-UV analysis were further analyzed using LC-HR-MS/MS and, in case of sample QMC266, NMR analysis was performed for identification of these unknown substances. LC-HR-MS/MS analysis was conducted in the Institute of Organic Chemistry, Tuebingen University, on a Thermo Scientific UltiMate 3000 HPLC System coupled with an ESI-TOF Bruker maXis 4G (Bruker Daltonics, Billerica, MA) in the positive mode and using high resolution. For NMR analysis of sample QMC266, the tablets were ground and the API was dissolved in methanol. The resulting solution was filtered and evaporated to dryness, and the residue was redissolved in d_4-MeOH. One-dimensional and 2D NMR spectra were recorded at the Pharmaceutical Institute, Tuebingen University, with a Bruker Avance III HD 400 MHz NMR spectrometer (Bruker BioSpin GmbH, Rheinstetten, Germany). NMR spectra were calibrated to the residual solvent signals (d_4-MeOH resonances at δ_H = 3.31 and δ_C = 49.0 ppm) or the internal offset for[15] N assigned by the instrument manufacturer.

Definitions of medicine quality. For the compendial tests, the limits for compliance described in the respective USP 41 monograph were used. As proposed in the QAMSA study by the WHO[13] and also applied in our previous study in southern Togo,[31] samples deviating from USP 41 specifications for assay and/or dissolution were further divided into those showing only moderate deviations from the pharmacopoeial limits and those showing extreme deviations. Extreme deviation was defined as an API content deviating by more than 20% from the declared amount and/or an average dissolution of the API of the tested units falling more than 25% below the pharmacopoeial limit (i.e., below the pharmacopoeial Q value minus 25%).[13] Table 1 shows the limits for compliance given by USP 41 for all investigated types of medicines and the limits for extreme deviations.

For the definition of falsified medicines, the current WHO definitions were used.[12] Results of GPHF Minilab TLC and disintegration testing were classified as pass/fail following the instructions of the GPHF Minilab manual.[15]

Statistical calculations. Statistical evaluations were performed using JMP 14.2 (SAS GmbH, Heidelberg, Germany). The prevalence of SF medicines and the corresponding CIs were determined by distribution analysis. Significance of differences in the prevalence of SF medicines between different groups was calculated using Fisher's exact test or Pearson's chi-squared test. Comparisons of Minilab testing results to compendial testing results were calculated with contingency analysis.

Information of national authorities and stakeholders. The Laboratoire National de Contrôle de Qualitè de Médicaments de d'Expertise (LANACOME), Cameroon, and the WHO Rapid Alert System were informed immediately about falsified medicines detected in this study. The complete survey results were shared with the national authorities, that is, the Directeur Général de la Santé, Ministère de la Santé Publique, DR Congo; the Direction de la Pharmacie et du Médicament de la Republique du Congo; the Direction de la Pharmacie du Médicament et des Laboratoires, Ministère de la Santé Publique, Cameroon; and the LANACOME, Cameroon; and with the WHO Rapid Alert System. In addition, the findings of this study were presented to representatives of the African national medicine quality control laboratories at the third African Medicines Quality Forum in Abuja, Nigeria, in February 2020.

United States Pharmacopeia 41 specification was used for compliance/noncompliance. Following the suggestion of the QAMSA study by the WHO,[13] extreme deviation was defined as an API content deviating by more than 20% from the declared amount and/or an average dissolution of the API of the tested units falling more than 25% below the pharmacopoeial Q value. In this study, all observed assay failures were due to insufficient API content, and no sample failed because of excessive API content (see the Results section).

RESULTS

Overview of collected medicine samples. A total of 502 medicine samples were purchased from 26 sampling sites in Cameroon and 34 sampling sites in the DR Congo. Visual inspection showed that four samples included packages with two different batch numbers instead of representing a uniform sample. These different batches were subsequently treated as separate samples and analyzed for their quality individually. Therefore, the total sample size was 506.

The total number of samples collected per type of medicine is depicted in Figure 2A. Obviously, not all medicines were available at all of the 60 sampling sites; therefore, the theoretical number of 60 samples was not reached for any of the included medicines, although ciprofloxacin and metronidazole tablets came close with 57 samples each. A detailed analysis of the availability as well as of prices and affordability of the included medicines has been published in a separate article.[22]

As shown in Figure 2B, originator medicines represented only 6% of the collected samples. The vast majority were generic medicines, either sold under their international nonproprietary name ("unbranded generic products") or under a

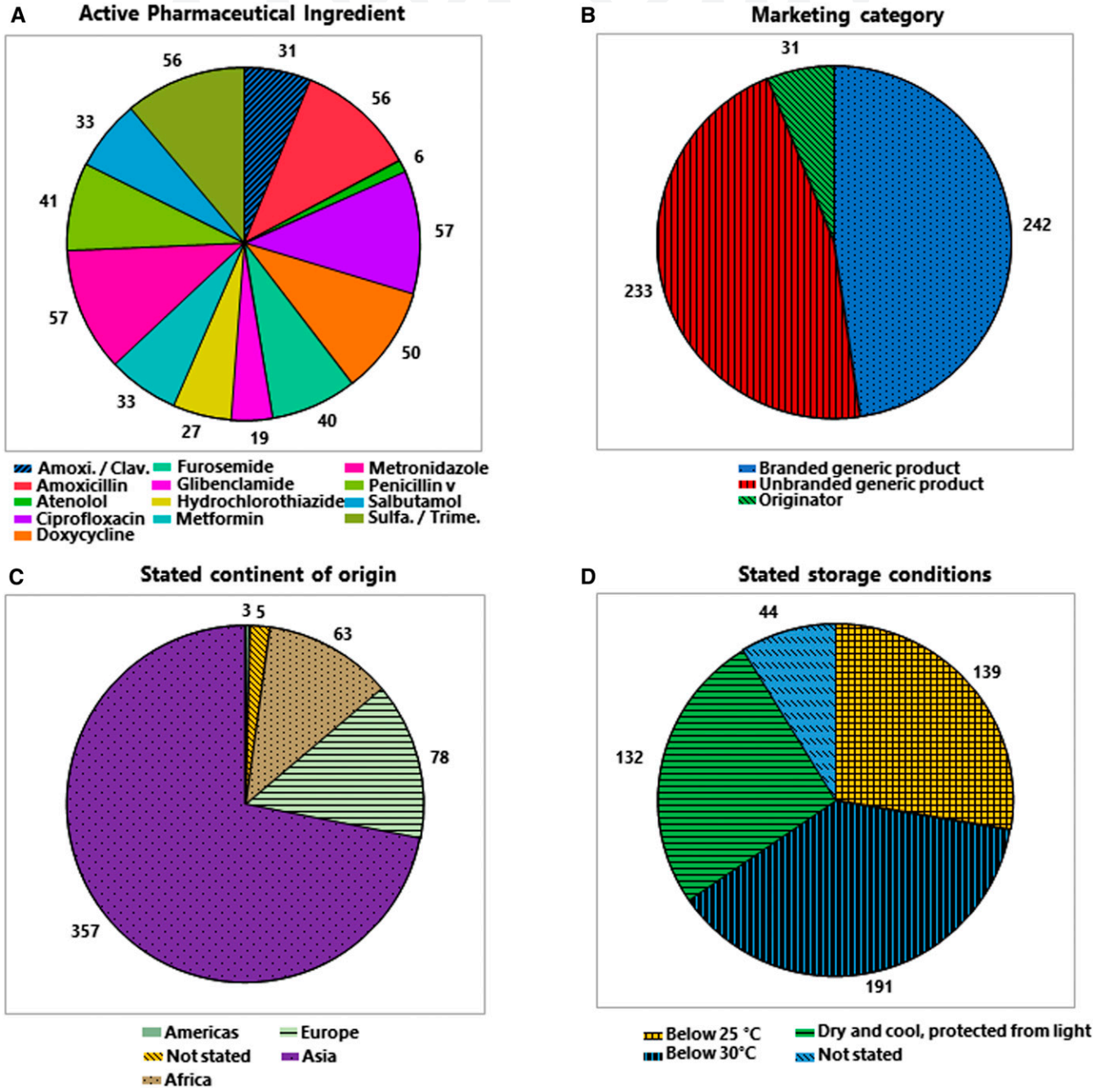

FIGURE 2. Distribution of all collected samples (n = 506) over different categories. In the pie chart in (**A**), the different active pharmaceutical ingredients (APIs) are arranged in clockwise orientation. This figure appears in color at www.ajtmh.org.

brand name decided by the marketing authorization holder ("branded generic products").

Figure 2C shows the dominance of Asian countries as medicine suppliers to Cameroon and the DR Congo. According to the information stated on the packaging, 357 (71%) of the samples collected were manufactured in Asia, of these 231 in India, 121 in China, and five in other Asian countries. Seventy-eight samples (15%) were stated to be manufactured in Europe and 63 samples (12%) in Africa. With only three samples, the Americas played no significant role in the supply of the investigated medicines.

According to the information stated on the packaging, the collected samples represented 260 different brands (414 different batches), produced by 119 different manufacturers in 26 different countries. A complete list of these manufacturers and countries is given in Supplemental Table S1. The most frequently encountered manufacturer was Medopharm, India, representing 42 samples. However, most manufacturers were only represented with very small number of samples (mean = four samples and median = three samples).

According to current stability testing guidelines for pharmaceuticals,[32–34] the DR Congo is regarded as climatic zone IVa (hot and humid) and Cameroon as climatic zone IVb (hot and very humid). Medicines intended to be marketed in these two countries should be tested for long-term stability

at 30°C/65% relative humidity (DR Congo) or at 30°C/75% relative humidity (Cameroon), respectively. Medicines for which stability has been demonstrated under either of these two conditions should carry the WHO-recommended labeling statement "Do not store above 30°C."[32–35] As shown in Figure 2D, however, only 38% of the collected samples indeed showed this statement. Twenty-eight percent of the samples were labeled "Do not store above 25°C," indicating that they may not have been tested for stability under the appropriate conditions for medicines to be marketed in the DR Congo or in Cameroon. Twenty-six percent of the samples carried less precise, with no WHO-recommended labeling statements such as "Store in a cool and dry place, protected from light," and 9% had no storage recommendation at all printed on the packaging or leaflet. However, there was a marked difference between the medicines from the two countries (Figure 3). In the DR Congo, 53% of the medicine samples showed the correct labeling statement "Do not store above 30°C," and only 1% carried no storage recommendation at all. By contrast, in Cameroon, only 21% of the medicine samples showed the correct labeling statement "Do not store above 30°C," and 17% carried no storage recommendation at all.

Figure 3 furthermore shows the distribution of the samples collected across different marketing categories, stated continents of origin, and types of sampling sites, separately for Cameroon and the DR Congo.

In total, 10 of the 506 samples (2%) were already expired at the time of collection. Although these 10 samples were already expired, they were sold at the point of care to be used in patient treatment. Therefore, also these samples were analyzed for their quality, and the results were included into the overall data analysis. Of these 10 expired samples, two (both representing the same product and batch) were found to deviate from USP specifications in the analysis described in the following paragraphs. They are marked in Supplemental Tables S1 and S3.

Visual inspection showed only a single sample which appeared to be falsified based on its incorrect labeling (penicillin V tablets, described in the next paragraph).

Falsified medicines. Among the 506 medicine samples, three (0.6%) were found not to contain their declared API, and two of these even contained a different, non-declared API. These three samples are shown in Figure 4. Notably, all three of them were sold by informal vendors.

One sample (sample no. QMCA241, Figure 4A), collected in Cameroon, was labeled as "Augmentin® SmithKline Beecham (amoxicillin 500 mg/clavulanic acid 125 mg tablets)" and carried a registration number used for Augmentin by the Nigerian National Agency for Food and Drug Administration and Control. Packaging and tablets appeared to be of excellent quality and gave no immediate indication of falsification. However, both Minilab TLC analysis and HPLC analysis according to USP readily showed complete absence of both stated APIs. The WHO Rapid Alert System was informed and thereupon published a Medical Product Alert about this falsification.[36] On request by the WHO, the authors of the present article forwarded this sample to the stated manufacturer, who confirmed that this was a falsified medicine not produced by their company.

Another sample (sample no. QMCA035, Figure 4B), also collected in Cameroon, was labeled as "Penicillin-V Tablets, Oxford Pharma Co. Ltd., Belgium." On the label, the active ingredient was incorrectly spelled as "phenoxymetgyl" rather than phenoxymethylpenicillin (Figure 4). The stated

		Cameroon							DR Congo						
		N total	non-compliant total N	[%]	95% CI	both tests N	only assay N	only dissolution N	N total	non-compliant total N	[%]	95% CI	both tests N	only assay N	only dissolution N
brand	Unbranded generic products	118	22	19%	[12.6-26.6]	12	6	4	115	12	10%	[6.1-17.4]	1	6	5
	Branded generic products	108	19	18%	[11.6-25.8]	2	5	12	134	28	21%	[14.9-28.5]	4	6	18
	Originator	18	1	6%	[1.0-25.8]	1	0	0	13	0	0%		0	0	0
continent of origin	Africa	23	6	26%	[12.5-46.5]	1	0	5	40	8	20%	[11.1-36.3]	4	2	2
	Americas	3	0	0%		0	0	0							
	Asia	156	31	20%	[14.8-27.5]	12	8	11	201	32	16%	[11.4-21.4]	1	10	21
	Europe	57	4	7%	[2.8-16.7]	2	2	0	21	0	0%		0	0	0
	Not stated	5	1	20%	[2.0-43.5]	0	1	0							
site type	Government health facilities	36	9	25%	[13.8-41.1]	2	2	5	42	3	7%	[24.6-19.0]	1	1	1
	Church health facilities	71	10	14%	[7.8-24.0]	3	4	3	72	4	6%	[2.2-13.4]	1	1	2
	Pharmacies	70	4	6%	[2.2-13.8]	1	2	1	91	17	19%	[12.0-27.9]	1	7	9
	Informal Vendors	67	19	28%	[19.0-40.1]	9	3	7	57	16	28%	[18.1-40.8]	2	3	11
indication	Antibiotics	152	24	16%	[10.9-22.4]	8	6	10	196	18	9%	[5.9-14.0]	2	7	9
	Medicines against non-communicable diseases	92	18	20%	[12.8-28.8]	7	5	6	66	22	33%	[23.2-45.3]	3	5	14
store at	Below 25 °C	89	8	9%	[4.6-16.7]	4	3	1	50	11	22%	[12.8-35.2]	2	1	8
	Below 30 °C	51	5	10%	[4.3-21.0]	1	0	4	140	10	7%	[3.9-12.6]	2	2	6
	Dry and cool, protected from light	62	18	29%	[19.2-41.3]	7	6	5	70	19	27%	[18.1-38.5]	1	9	9
	Not stated	42	11	26%	[15.3-41.1]	3	2	6	2	0	0%		0	0	0
active pharmaceutical ingredient	Amoxicillin and Clavulanic acid	19	5	26%	[11.8-48.8]	1	3	1	12	2	17%	[4.7-44.8]	0	0	2
	Amoxicillin	24	2	8%	[2.3-25.8]	0	0	2	32	2	6%	[1.7-20.1]	0	0	2
	Ciprofloxacin	25	2	8%	[2.2-25.0]	0	2	0	32	4	13%	[5.0-28.1]	0	3	1
	Doxycycline	22	1	5%	[0.8-21.8]	0	0	1	28	1	4%	[0.6-17.7]	0	0	1
	Metronidazole	25	3	12%	[4.2-30.0]	0	0	3	32	5	16%	[6.9-31.8]	1	2	2
	Penicillin V	14	7	50%	[26.8-73.2]	6	1	0	27	3	11%	[3.9-28.1]	1	2	0
	Sulfamethoxazole and Trimethoprim	23	4	17%	[7.0-37.1]	1	0	3	33	1	3%	[0.5-15.3]	0	0	1
	Atenolol								6	1	17%	[3.0-56.4]	0	0	1
	Furosemide	17	1	6%	[1.0-27.0]	0	0	1	23	15	65%	[44.9-81.2]	1	1	13
	Glibenclamide	19	6	32%	[15.4-54.0]	0	2	4							
	Hydrochlorothiazide	21	0	0%		0	0	0	6	0	0%		0	0	0
	Metformin	20	1	5%	[0.9-23.6]	0	0	1	13	1	8%	[1.3-33.3]	1	0	0
	Salbutamol	15	10	67%	[41.7-84.8]	7	3	0	18	5	28%	[12.5-50.9]	1	4	0
	Overall	**244**	**42**	**17%**	**[13.0-22.4]**	**15**	**11**	**16**	**262**	**40**	**15%**	**[11.4-20.1]**	**5**	**12**	**23**

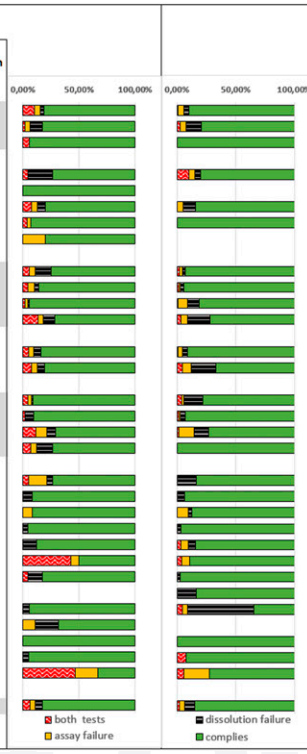

FIGURE 3. Frequency of noncompliance with pharmacopoeial specifications for assay and dissolution in different subgroups of medicines. This figure appears in color at www.ajtmh.org.

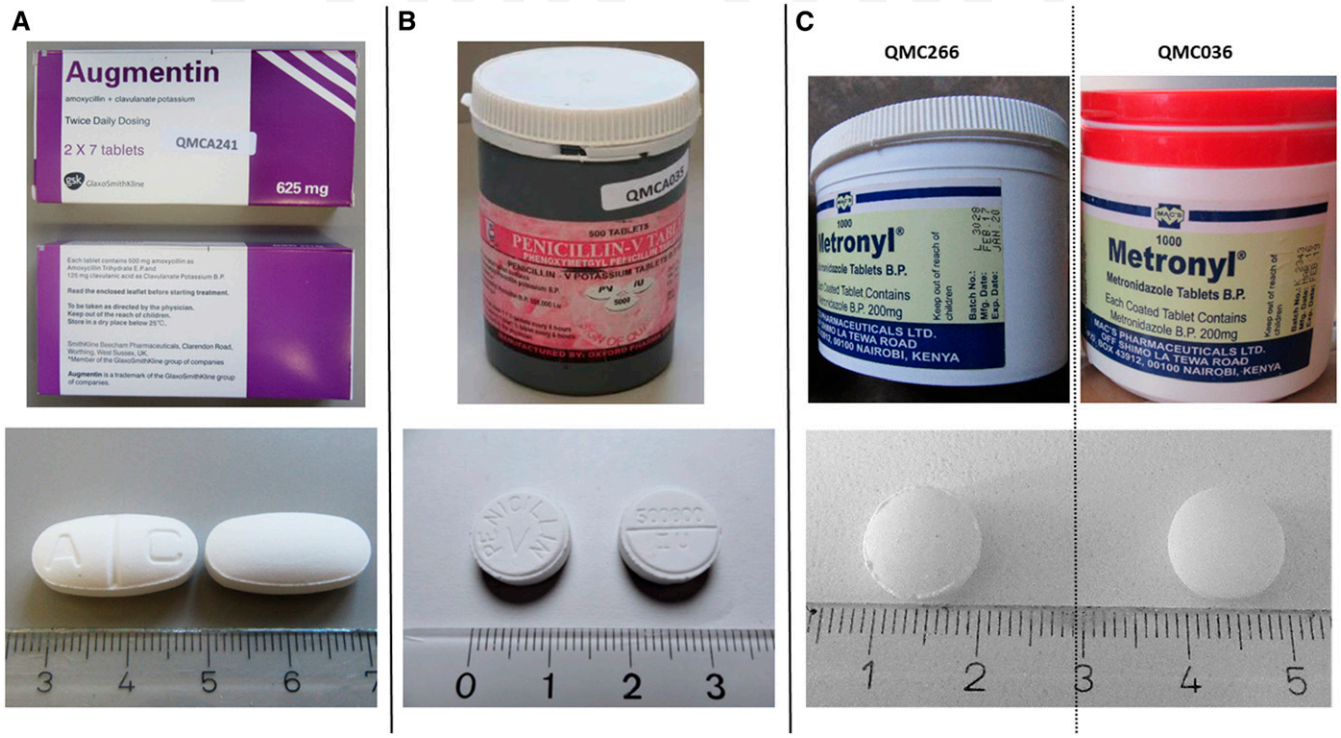

FIGURE 4. Pictures of the three samples identified as falsified medicines. (**A**) Falsified Augmentin (sample no. QMCA241), containing no detectable active pharmaceutical ingredient (API). (**B**) Falsified penicillin V tablets (sample no. QMCA035), containing 50 mg paracetamol. Note that the API is misspelled on the label. (**C**) Left: falsified Metronyl (sample no. QMC266); manufactured date: February 2017, batch no: L3028, containing 93 mg metronidazole benzoate. Right: Metronyl (sample no. QMC036); manufactured date: March 2016, batch no: K2343, complying with U.S. Pharmacopeia 41 specifications for metronidazole tablets. This figure appears in color at www.ajtmh.org.

manufacturer "Oxford Pharma, Belgium" does not exist. Although the tablets appeared to have been professionally pressed and embossed, the labels and packaging were of poor quality. Both Minilab TLC analysis and HPLC analysis readily showed complete absence of the stated API but indicated the presence of another, unknown compound, and LC-HR-MS/MS analysis proved that the unknown compound was paracetamol (Supplemental Figure S1). The paracetamol content was found to be only 50 mg per tablet, clearly lower than the content of paracetamol tablets listed in the current WHO Essential Medicines List (100–500 mg).[37] Again, the WHO Rapid Alert System was informed and published a Medical Product Alert about this falsification.[38]

A third sample (sample no. QMC266; Figure 4C) was labeled as "Metronyl® Metronidazole Tablets B.P., Mac's Pharmaceuticals Ltd., Kenya." It was sold in an already opened plastic container by an informal vendor in the DR Congo. Visual inspection gave no obvious indication of falsification. However, both Minilab TLC analysis and HPLC analysis readily showed complete absence of the stated API and the presence of another, unknown compound, and LC-HR-MS/MS (Supplemental Figure S2) suggested that this compound might represent metronidazole benzoate. Subsequently, 1D and 2D NMR spectra were recorded, and a de novo structure elucidation was carried out (Supplemental Figures S3–S11). This confirmed unambiguously that the unknown compound indeed was the benzoic acid ester of metronidazole. ^{1}H and ^{13}C NMR spectra of the unknown compound and of a metronidazole benzoate standard were perfectly superimposable (Supplemental Figures S9 and S10). Metronidazole has a bitter taste, and the benzoic acid ester of metronidazole is sometimes used as a prodrug with more acceptable taste, both in pediatric formulations and in veterinary medicine.[39] The metronidazole benzoate content of sample QMC266 was determined as 93 mg per tablet, in clear contrast to the labeling claim of 200 mg free metronidazole. Another batch of the same Metronyl brand had been collected in a government health facility of the DR Congo. That sample (QMC036; Figure 4C) showed an exactly identical label as QMC266, except for the different batch number and expiry date, and was found to be fully compliant with USP specifications in identity, assay, dissolution, and uniformity of dosage units. As shown in Figure 4C, the tablets of falsified sample QMC266 had the same diameter and shape (and also the same weight) as the good-quality sample of Metronyl tablets but showed ridges at the edges, indicating poor manufacturing. Possibly, the plastic container in which sample QMC266 was sold may have originally contained authentic, good-quality Metronyl tablets and may have later been filled with the falsified medicine by the informal vendor. However, this cannot be ascertained from the available information. Attempts of the local partners to find further Metronyl packages remained unsuccessful. Both the stated manufacturer and the WHO Rapid Alert System were informed about this falsified medicine. So far, no answer was received from the stated manufacturer.

All remaining 503 samples were found to contain the declared APIs. Several samples of salbutamol and glibenclamide tablets were found to contain an additional substance which was identified by LC-HR-MS/MS as the preservative methyl 4-hydroxybenzoate (methylparaben). This preservative is

considered safe and acceptable, although in most countries, the presence of such a preservative must be stated in the package leaflet.

Analysis of the quantity of the APIs. All collected samples were analyzed for the amount of the API ("assay"). Figure 5 shows the API content determined in each of the 506 samples. Different limits for compliance are specified by USP for different APIs (Table 1), for example, 95–105% of the declared content for metformin tablets or 90–120% of the declared content for penicillin V tablets (Figure 5). Four hundred sixty-three samples (91.5%) complied with the USP specifications for assay and are depicted in Figure 5 as green symbols. Twenty-eight samples (5.5%) showed moderate deviations from the pharmacopoeial limits (i.e., deviations not exceeding 20% of the stated content) and are depicted as yellow symbols. Fifteen samples (3.0%) showed extreme deviations (i.e., deviations of more than 20% of the stated content) and are depicted as red symbols; these include the three falsified medicines described earlier (marked with black circles in Figure 5).

The highest proportions of substandard samples in the assay were observed for salbutamol tablets (24% moderate and 21% extreme deviations) and for penicillin V tablets (10% moderate and 15% extreme deviations). None of the samples with other APIs showed extreme deviations in the assay (except the two falsified products of Metronyl and Augmentin described earlier).

In total, 43 samples (8.5%) were noncompliant in the assay. Figure 3 shows the numbers of noncompliant samples separately for Cameroon and the DR Congo. Supplemental Figure S12 shows the API content determined in each of the 506 samples, analyzed by similar subgroups as used in Figure 3.

Analysis of the dissolution of the APIs. All collected samples were analyzed for the dissolution of the API according to USP 41. Figure 6 shows the dissolution results determined for each of the 506 samples. Again, USP specifies different limits for compliance ("Q values") for different APIs. For example, USP demands for metronidazole tablets that not less than 85% of the declared API content must dissolve under the specified conditions and for hydrochlorothiazide tablets not less than 60%. In total, 447 samples (88.3%) complied with the USP specifications for dissolution and are depicted in Figure 6 as green symbols. Forty-four samples (8.7%) showed moderate deviations from the pharmacopoeial limits (i.e., an amount of dissolved API lower than, but not more than 25% lower than the pharmacopoeial limit) and are depicted as yellow symbols. Fifteen samples (3.0%) showed extreme deviations (i.e., an amount of dissolved API more than 25% lower than the pharmacopoeial limit) and are depicted as red symbols; these included the three falsified medicines described earlier. In total, 59 samples (11.7%) resulted as noncompliant in dissolution by USP 41 criteria. However, it has to be considered that 12 of these samples (including the three falsified medicines)

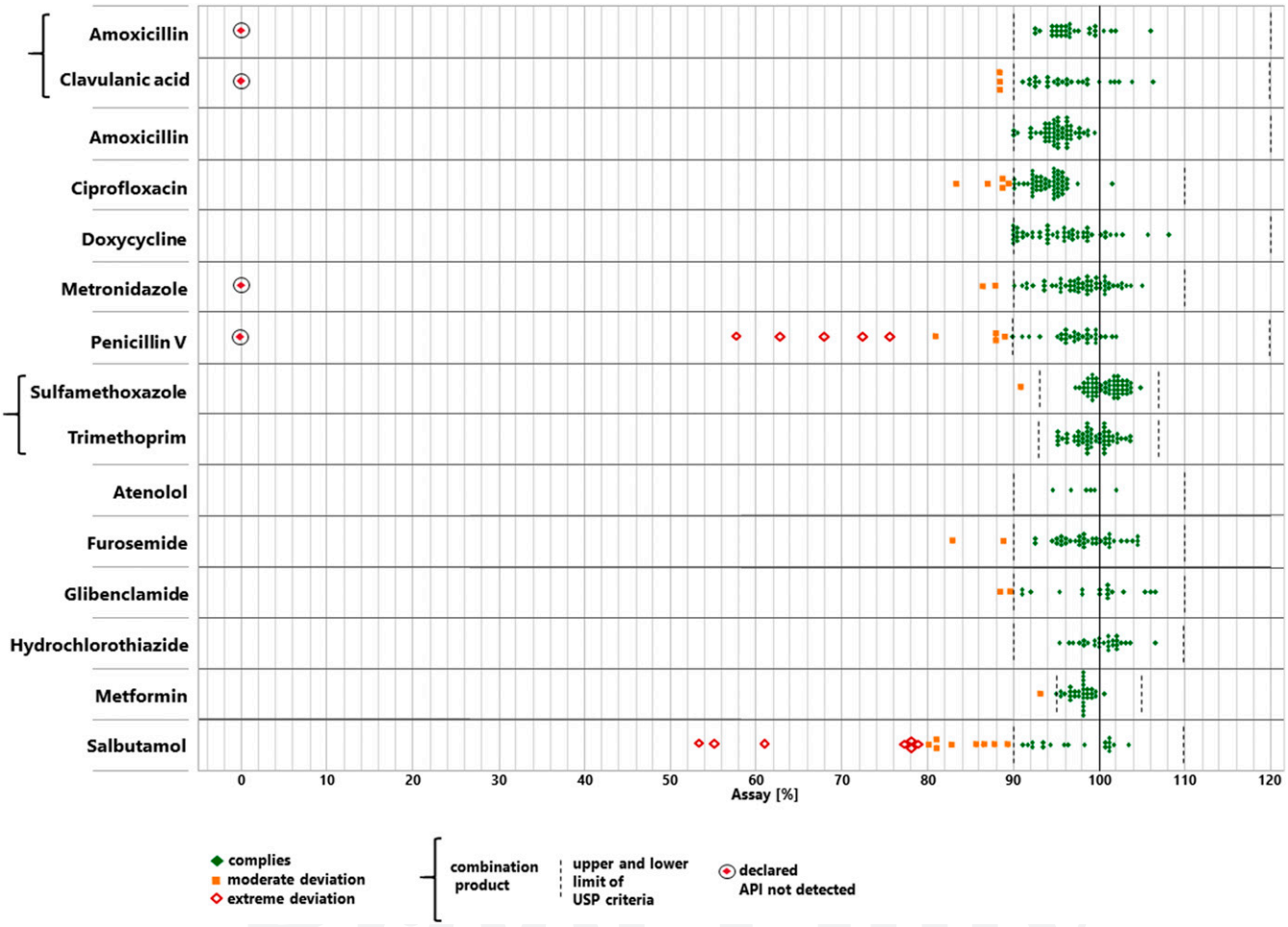

FIGURE 5. Content of the active pharmaceutical ingredient (API) determined for each sample. This figure appears in color at www.ajtmh.org.

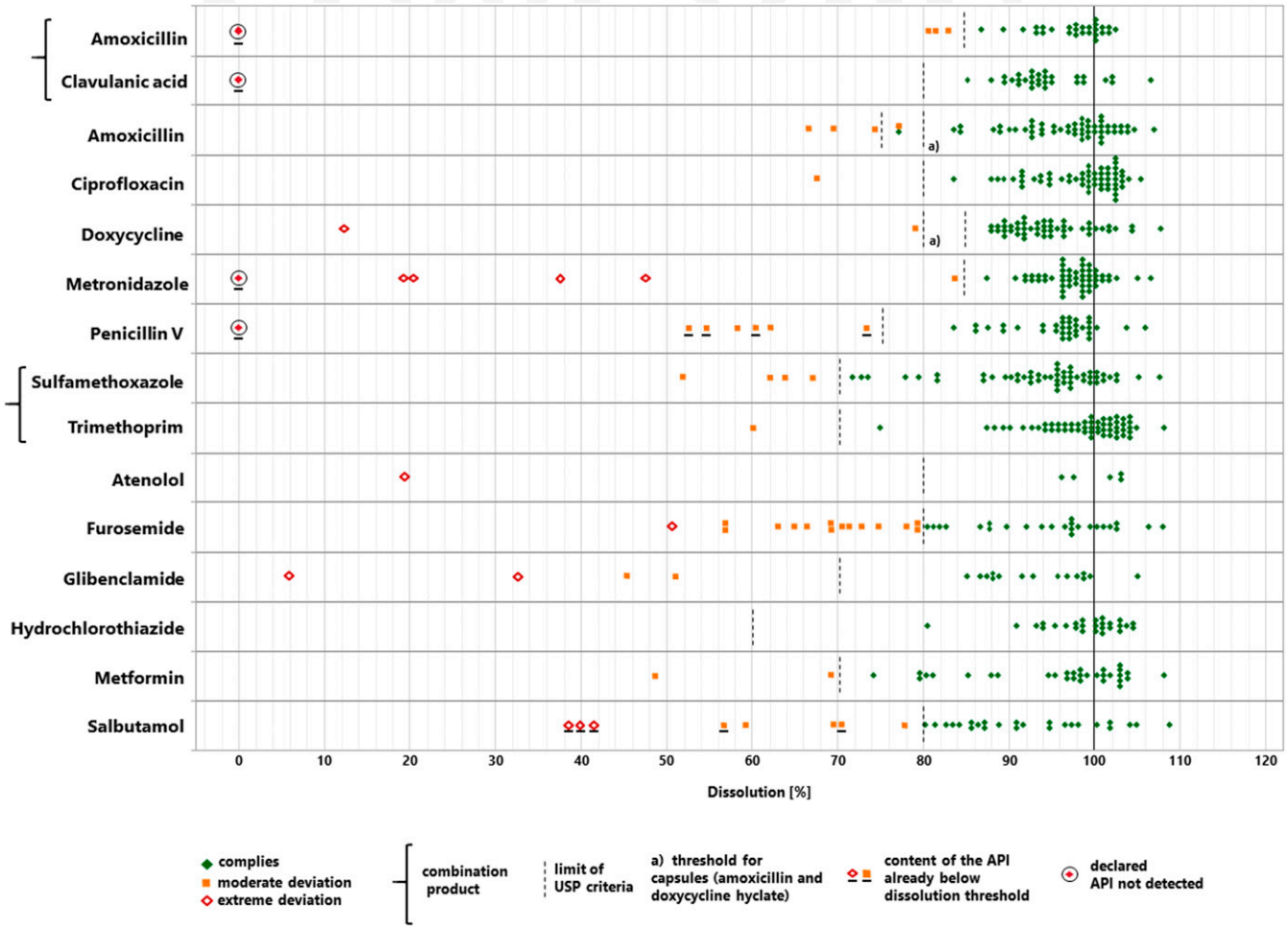

FIGURE 6. Dissolution of the active pharmaceutical ingredient (API) determined for each sample. This figure appears in color at www.ajtmh.org.

had already been shown in assay testing to contain an API amount which was lower than the pharmacopoeial limit for dissolution. These samples are marked in Figure 6.

Dissolution failures were observed most frequently for furosemide tablets (n = 15), salbutamol tablets (n = 8), and glibenclamide tablets (n = 4). However, extreme deviations in dissolution were also found for doxycycline, metronidazole, atenolol, and metformin, and of course for the three falsified products described earlier. Figure 6, therefore, illustrates that noncompliance with dissolution specifications is a frequent and serious problem in many of the investigated types of medicines, even more so than noncompliance with assay specifications shown in Figure 5.

Figure 3 shows the numbers of noncompliant samples in different categories of medicines, separately for Cameroon and the DR Congo. Supplemental Figure S13 shows the dissolution results determined for each of the 506 samples, analyzed by similar subgroups as used in Figure 3.

Uniformity of dosage units. As explained in the Methods section, uniformity of dosage units was investigated using the test for weight variation which, according to USP 41, was applicable for 425 of the 506 samples. Of the 425 tested samples, 26 (6.1%) failed the test for uniformity (including the three falsified samples). Sixteen (3.8%) of these simultaneously failed in assay and/or dissolution, whereas 10 (2.4%) failed in uniformity testing alone.

Combined results of compendial analyses. From the analyzed samples, 8.5% failed in assay testing, 11.7% in dissolution testing, and 6.1% in testing for uniformity of dosage units. Obviously, a number of samples failed in more than one of the mentioned criteria. Therefore, the observed out-of-specification rate calculated from assay testing alone (i.e., 8.5%) increased to 16.2% (i.e., nearly doubled) when also dissolution was considered and to 18.6% when the uniformity of the dosage unit was considered as well.

As correctly stated in an authoritative review by the WHO,[7] if the goal is to assess the health effects of a medicine, API content and dissolution (which affect bioavailability) are the most important quality criteria. Therefore, hereafter, we focus on assay and dissolution results.

The only API for which no sample was found to be out of specification was hydrochlorothiazide (Figure 3). Notably, of the 27 samples investigated for this API, 14 represented the originator medicine and were sold for very high prices.[22]

Especially high failure rates were observed for penicillin V, furosemide, and salbutamol (Figure 3). For penicillin V tablets, the failure rate was 50% in Cameroon. This was especially due to the four penicillin V samples stated to be produced by a certain manufacturer in China (Shandong Shenglu Pharmaceutical Co. Ltd., see Supplemental Tables S1 and S3). All four of these samples showed extreme deviations in the assay. No samples from this manufacturer were found in the DR Congo.

Furosemide tablets showed a failure rate of 65% in the DR Congo. This was mainly caused by samples stated to be manufactured by Arco Pharma Pvt. Ltd. and Prashi Pharma Pvt. Ltd. (see Supplemental Tables S1 and S3). Eleven of the 12 furosemide samples stated to be manufactured by these two companies from India failed dissolution testing. No samples of these two manufacturers were found in Cameroon.

Salbutamol tablets showed a 66% failure rate in Cameroon largely because of the five salbutamol samples stated to be produced by a certain company in India (Medico Remedies Pvt. Ltd., see Supplemental Tables S1 and S3), four of them even failing with extreme deviations. No medicines of this manufacturer were found in the DR Congo.

A complete list of the manufacturers stated on the labels of the investigated medicines and a summary of the analytical results obtained for the individual (stated) manufacturers are given in Supplemental Table S1. Furthermore, a complete list of all batches and brands investigated, with their stated manufacturers and the analytical results, is given in Supplemental Table S3.

Analysis using the GPHF Minilab. Of the 506 collected samples, 451 were analyzed by the local researchers in Cameroon and the DR Congo using the thin-layer chromatographic test and the disintegration test of the GPHF Minilab.[15] No Minilab analysis was performed for the 49 samples from the Ituri Province in the northeast of the DR Congo because the local researcher left for another position during the time of this study, and no trained replacement could be found in time. For three samples, the small number of tablets collected allowed only for compendial analysis but not for an additional Minilab analysis. For three further samples, the required reagents for Minilab analysis had become unavailable at the local laboratory.

Notably, all three falsified medicines shown in Figure 4 were correctly reported as failing Minilab TLC analysis. These three samples were immediately reported by the local researchers and sent to Tuebingen University for confirmatory analysis, allowing a timely publication of the WHO Medical Product Alerts mentioned earlier.[36,38]

Twelve further samples were reported to fail TLC analysis. Three of these were reported to show insufficient intensity of the TLC spots, indicating an insufficient amount of the API. Two were reported to show additional spots in TLC, and for seven samples, it was not stated in which aspects the TLC test had failed.

Fifteen samples were reported to fail disintegration testing, that is, they did not disintegrate within 30 minutes in water of 37°C, following the procedure described in the GPHF Minilab manual.[15]

In total, 30 of 451 samples (6.7%) were reported to fail Minilab analysis, 15 in the TLC test and 15 in disintegration testing. No sample was reported to fail in both tests. Supplemental Figure S14 summarizes the results of the Minilab tests in the same way as Figure 3 summarizes the results of the compendial analysis.

Comparison of the results of GPHF Minilab and compendial analysis. Tables 2–4 compare the results of GPHF Minilab testing with those of compendial analysis according to USP 41. Minilab testing correctly identified all three samples which did not contain the stated API, resulting in 100% sensitivity and specificity for the Minilab in the identification of such falsified medicines in this study.

According to the GPHF Minilab manual,[15] semiquantitative evaluation of TLC analysis is carried out by visual comparison of the spots of the sample with two spots of an authentic reference, representing 100% and 80% of the declared amount of the API, respectively. If the sample spot is considered weaker than the 80% reference spot, the sample is classified as failing and should be forwarded to confirmatory compendial analysis. Minilab testing is, therefore, not designed to detect moderate deviations from the declared API amount, that is, deviations by less than 20%. Indeed, as shown in Table 3, of 26 samples showing moderate deviations in compendial assay testing, only two had been reported to fail Minilab TLC testing. By contrast, of the 14 samples which showed extreme deviations in USP assay testing, six had been reported to fail Minilab TLC testing, resulting in 43% sensitivity of the Minilab in the detection of such medicines. Supplemental Table S2 lists all 15 samples reported to fail Minilab TLC analysis and the eight samples with extreme deviations which still were reported to pass Minilab TLC analysis, with their respective analytical results.

Testing for disintegration is a routine part of compendial medicine quality testing for solid oral dosage forms (e.g., tablets and capsules) and is performed using precisely defined equipment and conditions. The Minilab protocol includes a simplified testing method for disintegration which can be conducted without sophisticated equipment. Notably, disintegration testing measures a different endpoint than dissolution testing according to the USP. Therefore, a comparison of the results of Minilab disintegration testing with those of compendial dissolution testing is not possible in a strict sense. Nevertheless, it may still be of interest how well Minilab disintegration testing can predict the results of compendial dissolution testing. As was to be expected, the sensitivity of the Minilab in this comparison was low, that is, 9% (Table 4). The sensitivity increased to 36% if only extreme dissolution failures were considered.

In Tables 2–4, the values for specificity show the proportion of USP-compliant samples which were correctly predicted by the Minilab test as being compliant. Specificity resulted as 98% for assay and 97% for dissolution because the numbers of good-quality samples which were reported to fail Minilab

TABLE 2

Sensitivity and specificity of Global Pharma Health Fund Minilab testing for the prediction of the outcome of the compendial analysis according to U.S. Pharmacopeia 41: identity

		Compendial result			
		Fail	Complies	Total	
Minilab result	Fail	3	0	3	Sensitivity = $\frac{3}{3+0}$ = 100%
	Pass	0	448	448	
	Total	3	448	451	Specificity = $\frac{448}{448+0}$ = 100%

TABLE 3

Sensitivity and specificity of Global Pharma Health Fund Minilab testing for the prediction of the outcome of the compendial analysis according to U.S. Pharmacopeia 41: assay (= content of active pharmaceutical ingredient)

		Compendial result					
		Extreme deviation	Moderate deviation	Complies	Total	Detection of any deviation (moderate or extreme)	Detection of extreme deviation
Minilab result	Fail	6*	2	7	15*	Sensitivity = $\frac{6+2}{(6+2)+(8+24)}$ = 20%	Sensitivity = $\frac{6}{6+8}$ = 43%
	Pass	8	24	404	436	Specificity = $\frac{404}{404+7}$ = 98%	
	Total	14*	26	411	451*		

See text for definitions of moderate and extreme deviations.
* Includes the three falsified samples mentioned in Tabel 2.

analysis were low (seven samples in TLC testing and 10 samples in disintegration testing).

DISCUSSION

Prevalence of falsified and substandard medicines. Of a total of 506 medicine samples collected in government and church health facilities, pharmacies, and informal vendors in Cameroon and the DR Congo, three samples (0.6%) were falsified, as evidenced by the absence of the stated API and, in two of these cases, by the presence of undeclared APIs (Figure 4). All other samples did contain the stated APIs, and visual inspection gave no indication of falsification. Obviously, a complete absence of falsified medicines must be aimed for. Nevertheless, the percentage of falsified medicines observed in this study is clearly lower than that often portrayed in alarmist media reports about medicine quality in Africa. Our finding is in good accordance with the results of three large medicine quality studies in Africa, conducted by the WHO (QAMSA study),[13] U.S. Pharmacopeial Convention,[40] and ACT Consortium Drug Quality Program,[41] which reported 0.2%, 0.3%, and 1.0% prevalence of falsified medicines, respectively. Two smaller studies conducted in Malawi and Togo by authors of the present article found 0.6%[42] and 0.0%[31] falsified medicines, respectively.

As noted in earlier studies, substandard medicines are much more frequently encountered than falsified medicines. In the present study, the percentage of medicines failing USP specifications for the assay (=content of API), for the dissolution of the API, and for the uniformity of the dosage units was 8.5%, 11.7%, and 6.1%, respectively. This is similar to the result of the WHO QAMSA study,[13] which investigated antimalarial medicines in six African countries and reported failure rates in assay, dissolution, and uniformity of 10.9%, 15.0%, and 6.4%, respectively.

Overall, 18.6% of the medicine samples investigated in the present study did not comply with USP 41 specifications in one or several of the aforementioned three criteria, whereas 16.2% failed in the assay and/or the dissolution. This failure rate is in good agreement with the 18.7% estimate for the prevalence of SF medicines reported by Ozawa et al.[11] from a meta-analysis of more than 40 medicine quality studies conducted in Africa. It is furthermore in reasonable agreement with the results of an authoritative review by the WHO[7] which analyzed the results of 100 medicine quality studies, purposefully selected for their scientific quality. For studies which had used HPLC analysis (as also the present study did), that review reported an aggregated failure rate of 15.6% for medicine samples from LMICs. That review clearly stated that the included studies did not systematically test for dissolution, and our study showed that the failure rate almost doubles when dissolution is considered in addition to assay. Therefore, the reported rate of 15.6%[7] estimated by the WHO must be expected to increase when dissolution is systematically included into the testing procedures.

As clearly visible from Figure 5, many samples which failed assay testing missed the pharmacopoeial limits only by a narrow margin. Although complete compliance of all medicines with the relevant specifications must be demanded, the public health risk posed by small deviations in the assay and/or the dissolution is probably low. Following the classification suggested by the WHO QAMSA study,[13] we, therefore, differentiated between "moderate" and "extreme" deviations in assay and dissolution testing (see the Methods section for definitions). As depicted in Figures 5 and 6, and Supplemental Figures S12 and S13, overall 4.7% of the samples showed extreme deviations from the pharmacopoeial specifications (1.8% only in assay testing, 1.8% only in dissolution testing, and 1.2% simultaneously in assay and dissolution testing).

Figure 5 shows that except for the three falsified medicines, no sample was found to contain less than 50% of the declared content in assay testing. However, 13 of the 506 samples (2.6%) showed less than 50% dissolution of the API (in addition to the three falsified medicines). Also this observation emphasizes the importance of dissolution testing in medicine quality analysis.

Subgroup analysis of the prevalence of SF medicines. As explained in the Results section, we subsequently focus on

TABLE 4

Sensitivity and specificity of Global Pharma Health Fund Minilab testing for the prediction of the outcome of the compendial analysis according to U.S. Pharmacopeia 41: Minilab disintegration testing versus compendial dissolution testing

		Compendial dissolution result					
		Extreme deviation	Moderate deviation	Complies	Total	Detection of any deviation (moderate or extreme)	Detection of extreme deviation
Minilab disintegration result	Fail	5	0	10	15	Sensitivity = $\frac{5+0}{(5+0)+(9+40)}$ = 9%	Sensitivity = $\frac{5}{5+9}$ = 36%
	Pass	9*	40	387	436*	Specificity = $\frac{387}{387+10}$ = 97%	
	Total	14*	40	397	451*		

See text for definitions of moderate and extreme deviations.
* Includes the three falsified samples mentioned in Tabel 2.

the assay and dissolution results, that is, the most important criteria for the health effects of a medicine.[7] Overall, the proportion of medicines which were out-of-specification in assay and/or dissolution was similar in Cameroon (17.2%) and the DR Congo (15.3%; $P = 0.629$) (Figure 3). However, as shown in Supplemental Figures S12 and S13, the number of samples with extreme deviations was clearly higher in Cameroon (7.8%) than in the DR Congo (1.9%; $P = 0.0026$). It is remarkable that in the northeast of the DR Congo, despite extreme poverty, political unrest, and disruptions by the Ebola epidemic, medicine quality is not worse but rather better than in the more affluent Cameroon.

As expected, medicine quality problems were most pronounced in informal vendors, with an out-of-specification rate of 28.2%. This rate was nearly identical in both countries and was significantly higher than in the three other types of outlets combined (12.3%; $P < 0.0001$). Notably, all three falsified medicines encountered in this study were sold by informal vendors, and also the rate of medicines with extreme deviations was significantly higher in informal vendors (11.3%) than in the three other categories of outlets (2.6%; $P = 0.0003$). Therefore, a well-enforced ban of medicine sales by informal vendors, as already implemented successfully in several East African countries, may represent a key intervention to reduce the problem of SF medicines.

In the DR Congo, the rate of out-of-specification medicines was similar in church health facilities (5.6%) and in government facilities (7.1%), and both values were significantly lower than that in informal vendors (28.1%; $P = 0.0005$ and $P = 0.0099$, respectively). None of the medicines in government or church health facilities showed extreme deviations. By contrast, private pharmacies showed an 18.7% failure rate, including 3.3% of medicines with extreme deviations. This indicates a lack of regulatory control of private pharmacies and their supply chains in the DR Congo.

In significant contrast to the high failure rate in medicines from private pharmacies in the DR Congo, Cameroon private pharmacies showed only a 5.7% failure rate ($P = 0.018$). Notably, of the 70 samples investigated from pharmacies in Cameroon, 47 were stated to be manufactured in Europe. As shown in our analysis of availability and prices,[22] medicine prices in pharmacies in Cameroon were considerably higher than in other types of health facilities/outlets, and also much higher than in pharmacies in the DR Congo.

Medicines from church health facilities in Cameroon showed a 14.1% out-of-specification rate. Government health facilities in Cameroon showed an out-of-specification rate of 25.0%, similar to that found in medicines from informal vendors (28.4%). This indicates a need for improvements in medicine procurement and supply chain practices, especially of the government health services.

All authentic originator medicines investigated in this study were found to be within specifications. Of the 31 samples stated to be originator medicines, only the falsified Augmentin depicted in Figure 4 failed specifications. The failure rate of samples stated to be originator medicines was, therefore, 3%, significantly lower than the rate for (unbranded or branded) generic products (17.1%; $p = 0.0431$). Of the 506 samples investigated in this study, 78 were stated to be produced in Europe, including 30 originator medicines and 48 generic products. Of these, the falsified Augmentin and the falsified penicillin V depicted in Figure 4 failed specifications, and two branded generic products of amoxicillin/clavulanic acid which showed 88.6% of the declared amount of clavulanic acid and thereby narrowly missed the pharmacopoeial limit of 90%. The failure rate of medicines stated to be produced in Europe was, therefore, 5.1%, significantly lower than that of medicines stated to be produced in Asia (17.7%; $P = 0.0049$) and for medicines stated to be produced in Africa (22.2%; $P = 0.0042$). The difference between the medicines from Asia and Africa was not statistically significant ($P = 0.385$).

It must be emphasized that for many manufacturers from Asia and Africa, this study found most or all investigated samples to be in specifications (Supplemental Table S1). Notably, there were large manufacturers from India (e.g., Medopharm) or from China (e.g., CSPC Ouyi Pharmaceutical Co. Ltd.), represented by high numbers of samples in this study, whose out-of-specification rates were as low as those of the samples stated to be produced in Europe. On the other hand, there were some manufacturers, mostly represented by smaller numbers of samples in this study, with very high out-of-specification rates (see the Results section and Supplemental Table S1).

As noted in our analysis of the prices of medicines investigated in this study,[22] medicines produced in Europe were much more expensive for the patients than medicines from Asia and Africa (i.e., nearly three times as expensive in Cameroon and nearly seven times as expensive in the DR Congo). Given the financial constraints in LMICs such as Cameroon and the DR Congo, restriction of procurement to medicines from countries with stringent regulatory authorities (i.e., mostly countries from Europe, North America, and Japan)[35] may not be an affordable option. Rather, careful supplier qualification, that is, selection of manufacturers with a proven track record of providing good medicine quality is a key measure for quality assurance in medicine procurement. The WHO has established the Prequalification of Medicines Program to assist procurement agencies in the selection of good-quality products.[43,44] Of the 13 types of medicines investigated in this study, three are included in the WHO Prequalification Program (ciprofloxacin, cotrimoxazole, and doxycycline). However, of 506 samples collected, only a single one (Ciplox-500®, Cipla, India) represented a WHO-prequalified product (and this was found to comply with USP specifications). To achieve a larger impact of the WHO Prequalification of Medicines Program on medicine quality in Cameroon and the DR Congo, a wider range of products may have to be included into the program, and in the procurement processes, more attention may have to be given to the selection of WHO-prequalified products.

Medicines against NCDs showed a 25% failure rate in assay and dissolution testing, significantly higher than that of antibiotics (12%; $P = 0.0004$). This difference was especially pronounced in the DR Congo (33% versus 9%; $P < 0.0001$) (Figure 3). This is alarming in view of the increasing burden of NCDs in LMICs.[45,46] In an evaluation of cardiac drugs in different African countries, Antignac et al.[21] also analyzed samples from the DR Congo, including atenolol, furosemide, hydrochlorothiazide, and four other cardiac medicines. They reported a prevalence of 26.7% poor-quality samples in the DR Congo, similar to the prevalence of 33.3% determined for NCD medicines in that country in the present study. Both the present survey and study by Antignac et al.[21] found

hydrochlorothiazide samples to be of good quality. As mentioned earlier, more than half of the hydrochlorothiazide samples found in the present survey represented the originator medicine Esidrex® (Novartis), which were sold for very high prices in the DR Congo and Cameroon.[22]

Comparing the different storage recommendations on the packaging, medicines that carried a precise, WHO-recommended labeling statement, that is, either "Do not store above 30°C" or "Do not store above 25°C" showed a failure rate of 10%, significantly lower than those carrying a less precise recommendation or none at all (failure rate 27%; $P < 0.0001$). Possibly, suppliers giving attention to precise storage recommendations also give attention to other aspects of good manufacturing practice. However, medicines labeled "Do not store above 30°C" were not found to be better than those labeled "Do not store above 25°C" (8% versus 14% failure rate; $P = 0.0999$; not significant), indicating that this difference in labeling was not correlated with a relevant difference in quality and/or stability in the samples investigated in the present study.

The GPHF Minilab as a screening tool for SF medicines. Compendial (=pharmacopoeial) medicine analysis requires sophisticated equipment (usually HPLC) and highly trained personnel and, therefore, is expensive. In LMICs, the overall capacity for such analyses is limited. As a result, there is increasing worldwide interest in simple, inexpensive screening methods that will help in conducting larger post-marketing surveillance studies at an affordable cost.

So far, the most widely applied screening method in LMICs is the GPHF Minilab. The aforementioned review by the WHO,[7] summarizing the result of 100 medicine quality studies, aggregated results for 48,218 samples. Of these, 20,010 had been investigated with the GPHF Minilab, and 5.0% of these had been reported to fail Minilab testing. By contrast, 19,809 samples had been investigated by HPLC, and 15.6% of these had been reported to fail this testing. These percentages are similar to the results of the present study, which found 6.7% of the investigated samples to fail Minilab analysis (which was carried out by local faith-based organizations in Cameroon and the DR Congo), compared with an overall 16.2% which failed the assay and/or dissolution testing according to USP41 (carried out at Tuebingen University, Germany). Whereas the studies reviewed by the WHO[7] mostly used only Minilab or only HPLC for analysis, the present study investigated 451 samples by both Minilab and HPLC, allowing a direct comparison of the results.

Minilab testing readily and reliably identified all three falsified medicines (Tables 2–4). However, as mentioned in the Results section, Minilab is not designed to detect moderate deviations from the declared API amount, and this is clearly visible in the results shown in Tables 2–4. Extreme deviations in API content were detected with a sensitivity of 43%.

As also explained in the Results section, disintegration and dissolution are different endpoints, and therefore, it is no surprise that samples failing USP dissolution testing were detected in the simple Minilab disintegration test with only 9% sensitivity. However, samples showing extreme dissolution failures in USP testing were detected by Minilab disintegration testing with 36% sensitivity.

The sensitivity and specificity values determined in the present study should not be regarded as a final assessment of the analytical capacity of the Minilab because further improvements are certainly possible. For example, among the seven samples which Minilab TLC testing incorrectly reported as "failing" (Supplemental Table S2), three were cotrimoxazole samples reported to show a too weak spot of trimethoprim. Trimethoprim is the minor component of cotrimoxazole, besides the major component sulfamethoxazole. It is difficult to optimize TLC conditions in a way that allows a reliable estimation of the quantity of both components. Our study suggests that, if the trimethoprim spot appears too weak, the analysis should be repeated, applying a larger amount of both sample and reference. This, as well as a routine repetition of all "failed" Minilab analyses by another person or laboratory,[14] is likely to further improve specificity. In addition, both sensitivity and specificity may be improved by quantification of TLC spot intensity with imaging software, for example, using a mobile phone app.[47]

Nevertheless, the results in Tables 2–4 show, besides the power of the Minilab in the detection of falsified medicines which do not contain the declared API, the limitations of the Minilab in the detection of quantitative deviations. This has also been noted in the WHO QAMSA study.[13] The present study confirmed the well-known fact that Minilab testing cannot detect moderate deviations in medicine quality and observed that Minilab testing also missed a considerable number of samples with extreme deviations. As stated by the distributors of the Minilab,[48] Minilab testing, therefore, should not be considered as a replacement for HPLC in the formal evaluation of pharmaceuticals. Rather, when compliance or noncompliance with compendial specifications is to be determined, compendial methods must be used. The value of screening methods, such as the Minilab, is primarily in studies in a low-resource environment, attempting to identify and eliminate as many falsified and grossly substandard medicines as possible with a limited budget. Samples failing Minilab analyses in such studies must subsequently be analyzed with compendial methods for confirmation. The rather high specificity of Minilab testing (Tables 2–4) ensures that the number of expensive compendial analyses to be performed remains limited. The costs of Minilab analyses and of compendial analyses have been estimated in two previous publications.[14,42]

Other simple and (more or less) inexpensive screening methods for medicine quality have recently been reviewed.[49] As stated by the authors of that review, unfortunately, there is a lack of independent evaluations of most of these methods, particularly in field settings. Spectroscopic devices, especially using NIR and Raman spectroscopy, are attractive because of the ease and speed of handling. However, they require a complete library of spectra of all brands to be investigated. In the present study, which investigated only 13 medicines in only two countries, 260 different brands produced by 119 different manufacturers in 26 different countries were found. Creating and maintaining a complete library of reference spectra from such an assortment of brands and manufacturers is a formidable task, and its feasibility has yet to be demonstrated.

Limitations of this study. Although the sample size of our study is quite large in comparison with previous similar studies,[7,11] the selection of medicines was limited to a small number of antibiotics and medicines against NCDs. Therefore, the results are not representative for other types of medicines, and further studies with other types of medicines, especially

against NCDs, are required. In this study, two different sampling approaches had to be used: an overt approach in government and faith-based health facilities because these cannot sell a basket of prescription medicines to persons who are not patients in their facilities and a mystery shopper approach in informal vendors (and in private pharmacies) because informal vendors would not be expected to agree to participate in a medicine quality study. Using an overt approach in government and faith-based health facilities may have potentially created a bias because staff may have preferably offered those medicines for collection which they considered to be of good quality. However, a meta-analysis by Ozawa et al.[11] did not find evidence for a significant bias in studies with overt approaches as compared with studies with mystery shopper approaches. The selection of sampling sites was not strictly random, especially in the northeast of the DR Congo where only health zones could be included which were safe enough for travel by the study personnel. This may have led to an exclusion of health zones with potentially higher rates of SF medicines because political instability may restrict regulatory activities in these health zones.

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Proof Only

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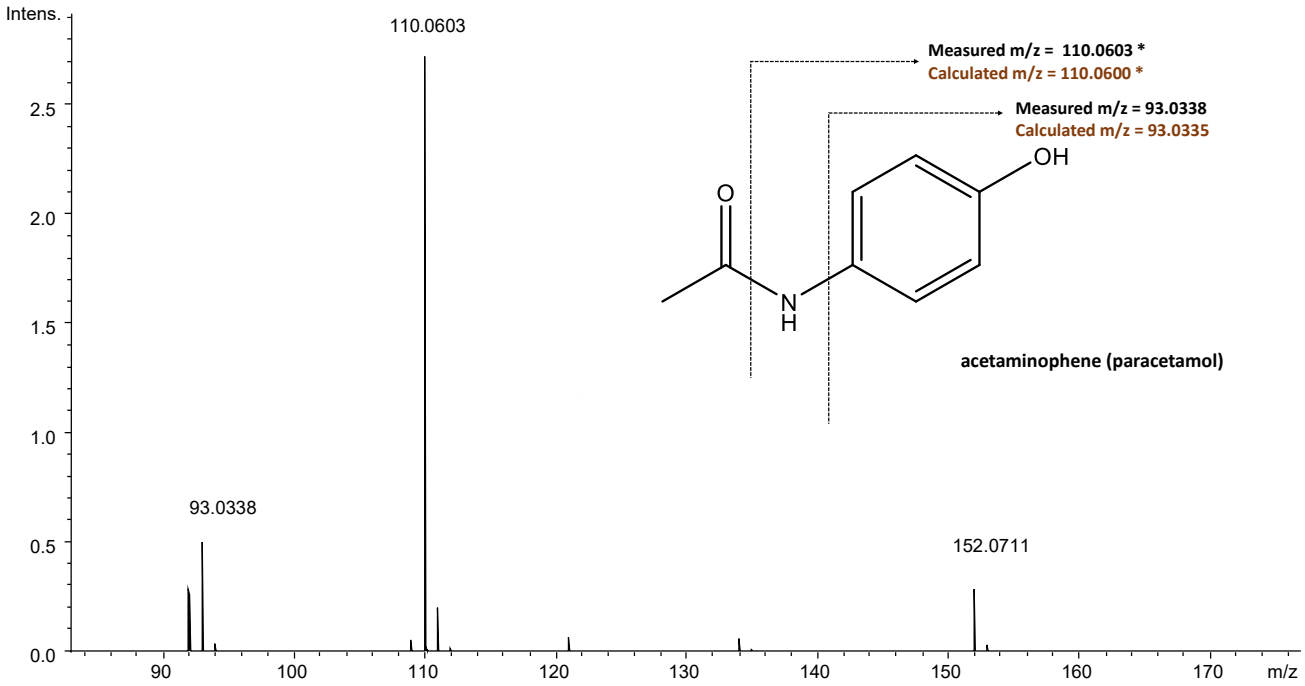
HR - MS/MS Fragmentation pattern measured from the falsified penicillin V samples (QMCA035) collected in the Republic of Cameroon, actually containing acetaminophen (paracetamol) The exact *m/z* of the paracetamol parent ion measured was 152.0711 (calculated 152.0706).



*the fragment ion with a *m/z* of 110, results from the protonated 4-aminophenol ($[H_2N\text{-}C_6H_4OH+H]^+$) formed by loss of ethone ($H_2C{=}C{=}O$).

Figure S2: HR - MS/MS Fragmentation pattern measured for the falsified metronidazole tablets QMC266

HR - MS/MS Fragmentation pattern measured from the falsified metronidazole tablets (QMC266) collected in the DR Congo, actually containing metronidazole benzoate.

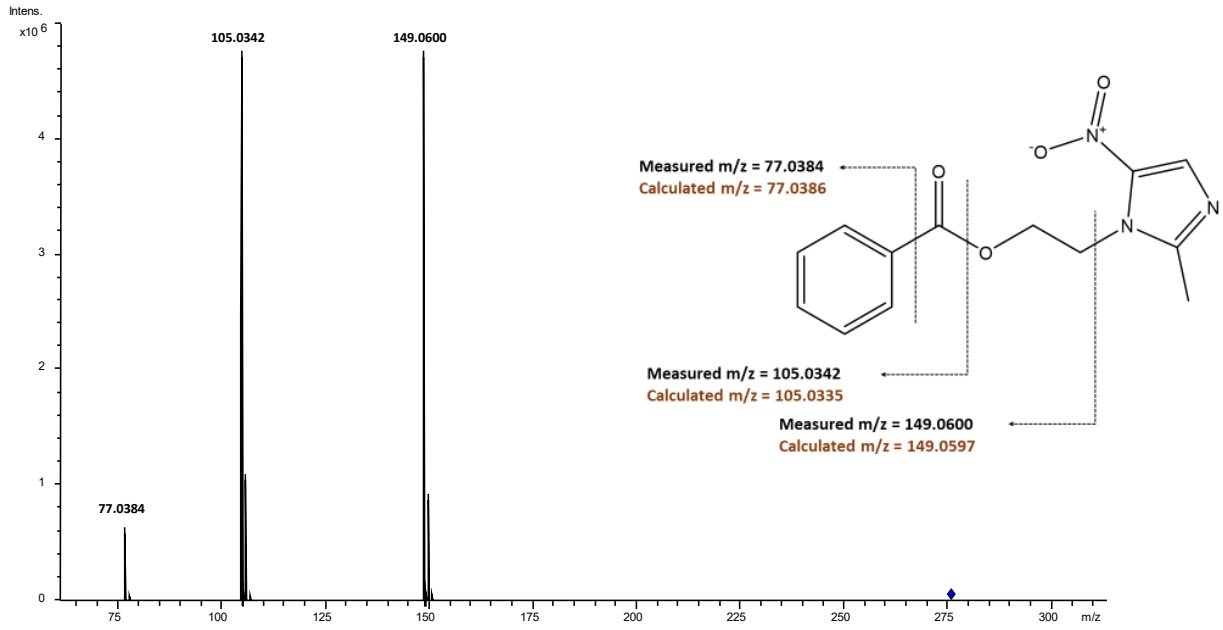


Figure S3: ^{1}H NMR spectrum (400 MHz, d_4-MeOH) of the sample QMC266

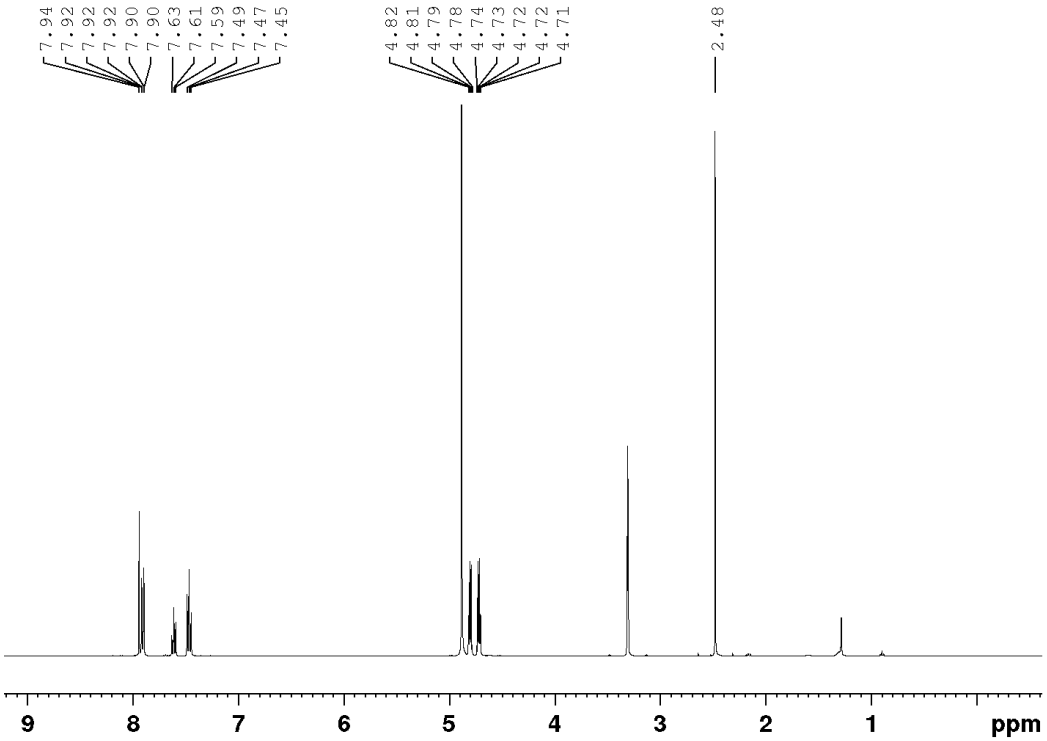


Figure S4: ^{13}C NMR spectrum (101 MHz, d_4-MeOH) of the sample QMC266

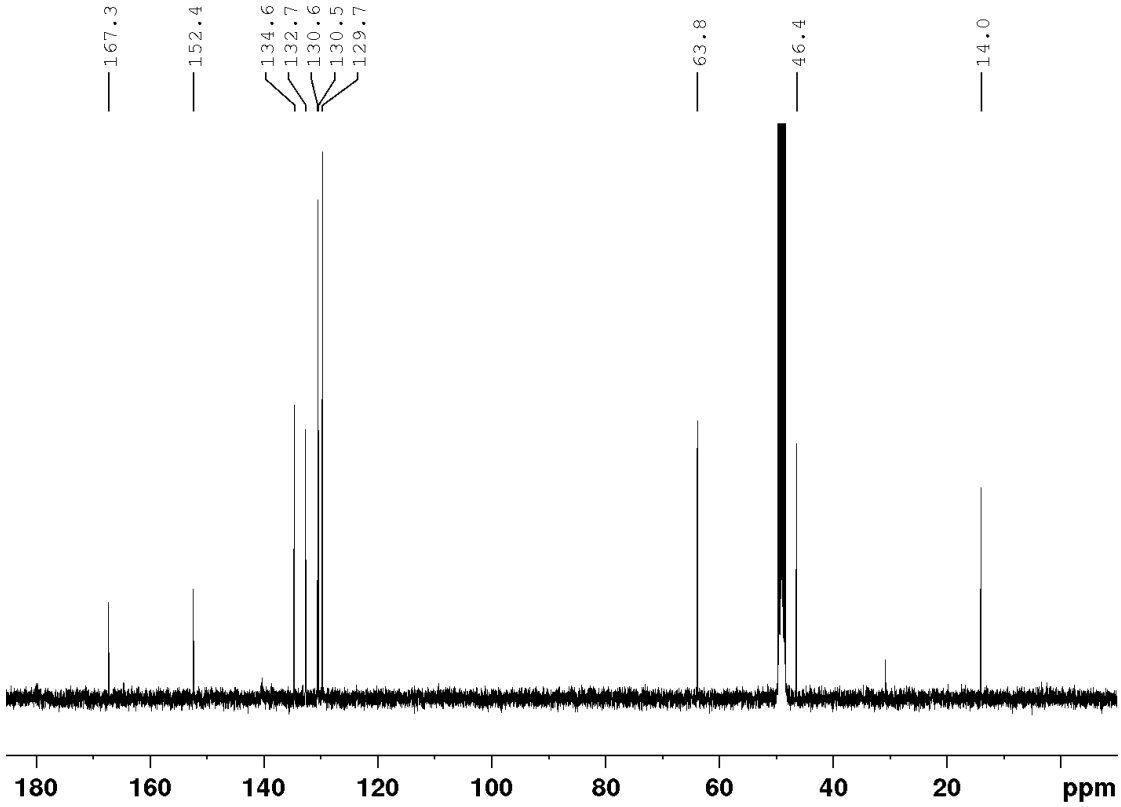


Figure S5: Edited ^{1}H-^{13}C HSQC NMR spectrum (400 MHz, d_4-MeOH) of the sample QMC266

This experiment reveals which proton is directly bond to which carbon. Blue cross peaks indicate CH and CH_3 moieties, while red cross-peaks indicate CH_2-groups.

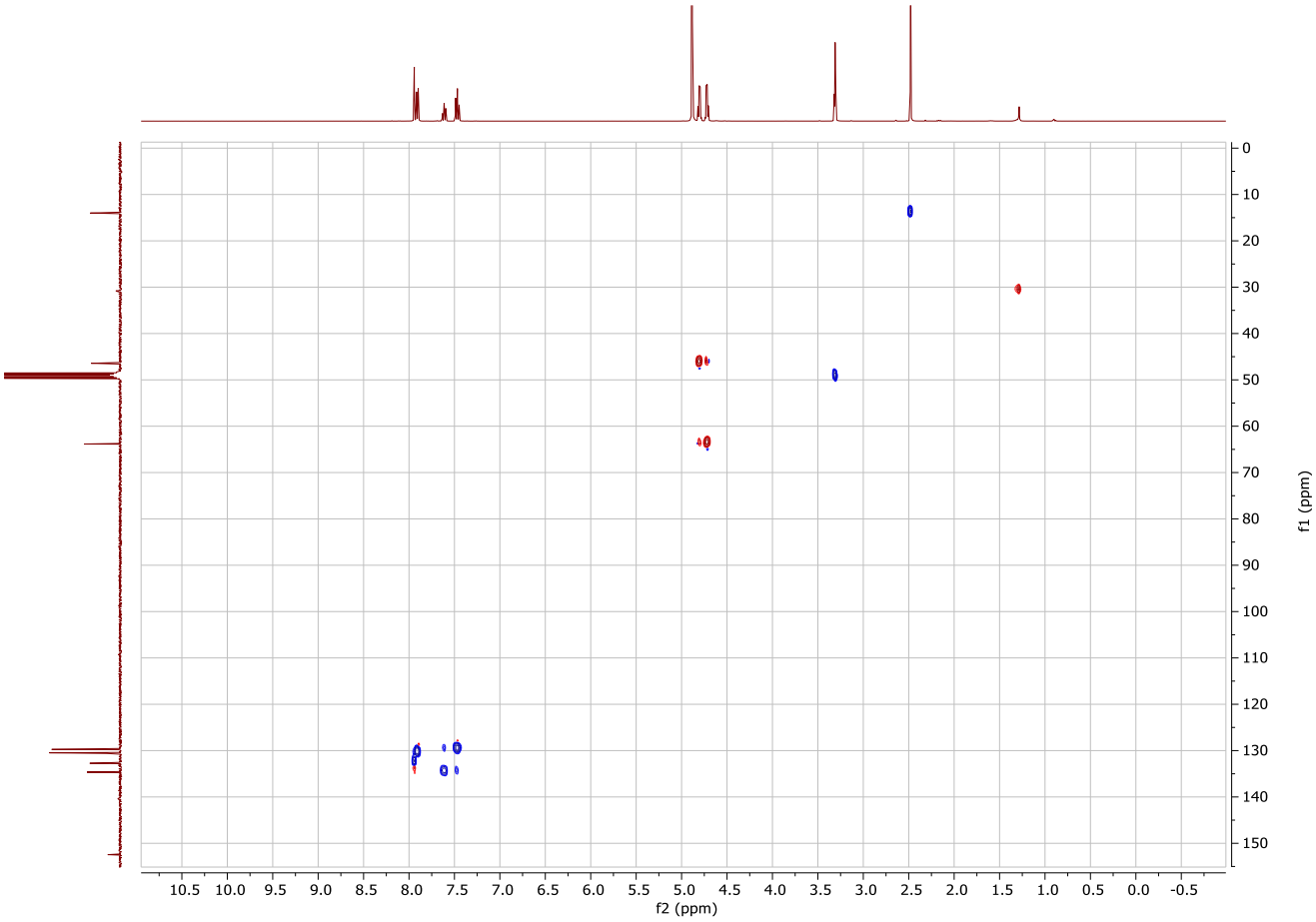


Figure S6: ^{1}H-^{1}H-COSY NMR spectrum (400 MHz, d_4-MeOH) of the sample QMC266

Bold lines in the depicted chemical formula visualize the observed COSY-correlations.

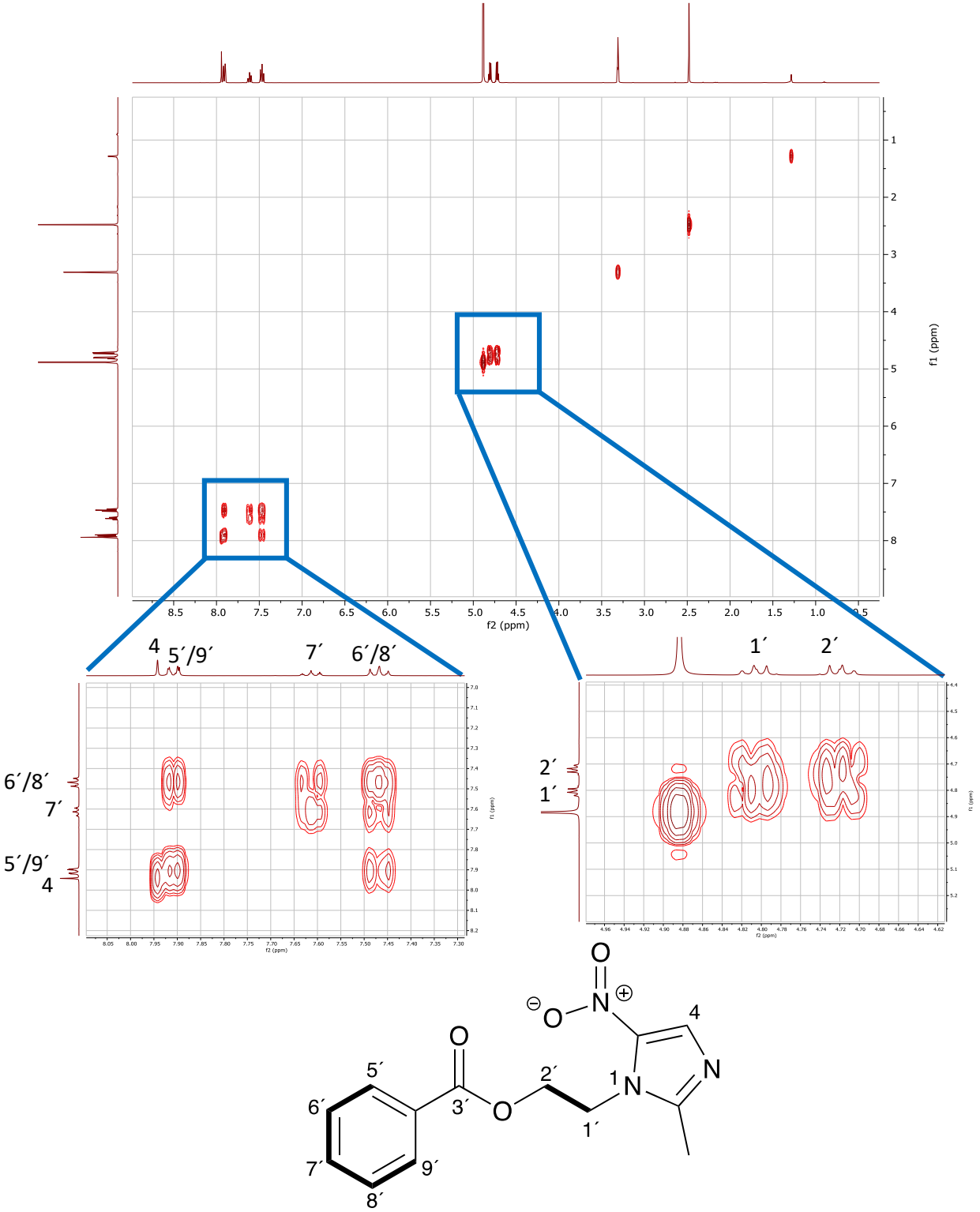
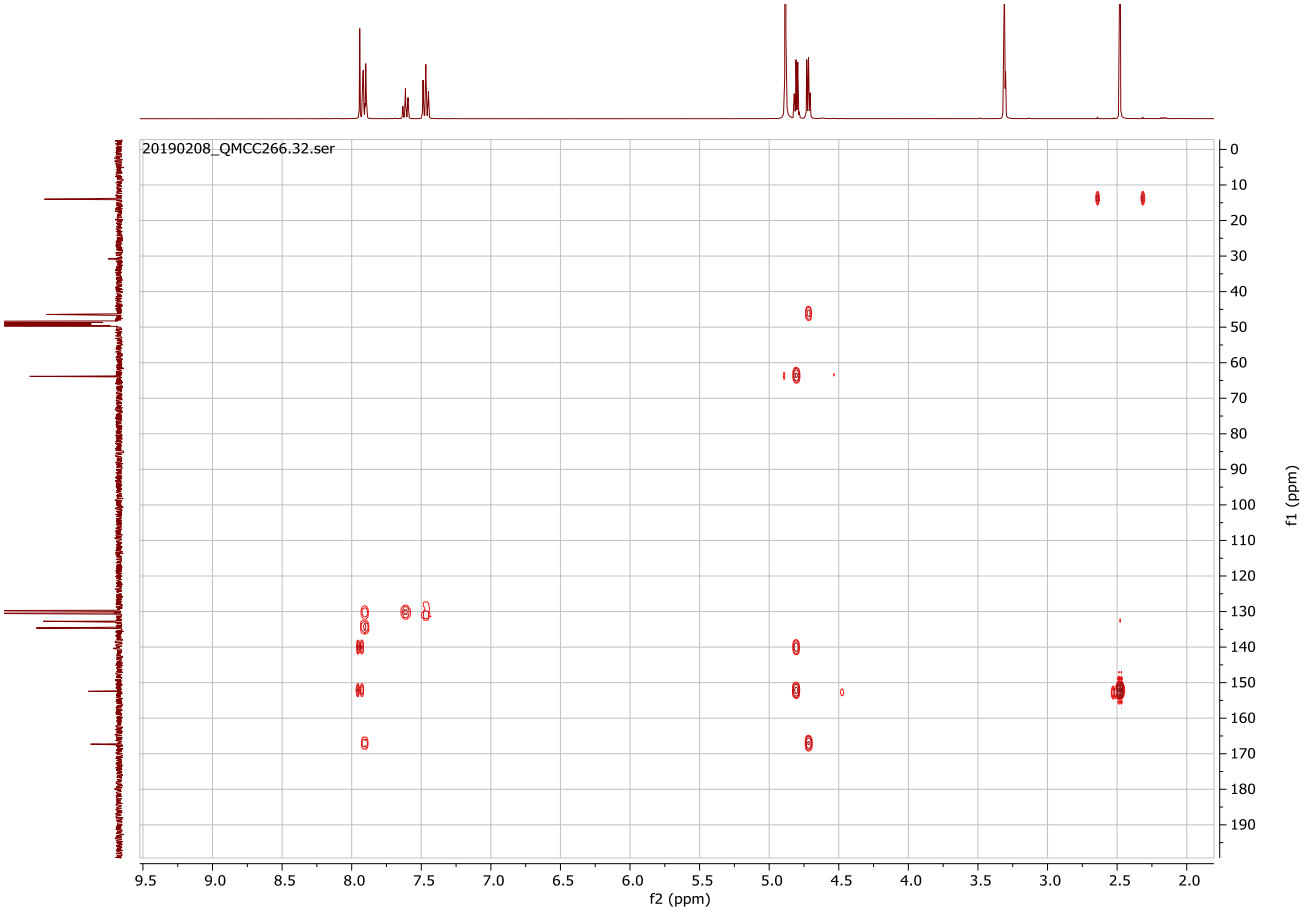


Figure S7: ^{1}H-^{13}C-HMBC NMR spectrum (400 MHz, d_4-MeOH) of the sample QMC266

Red arrows in the depicted chemical structure visualize the observed 2- and 3-bond HMBC long range correlations.



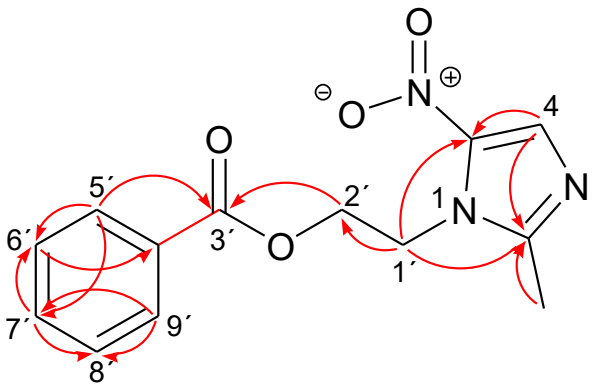
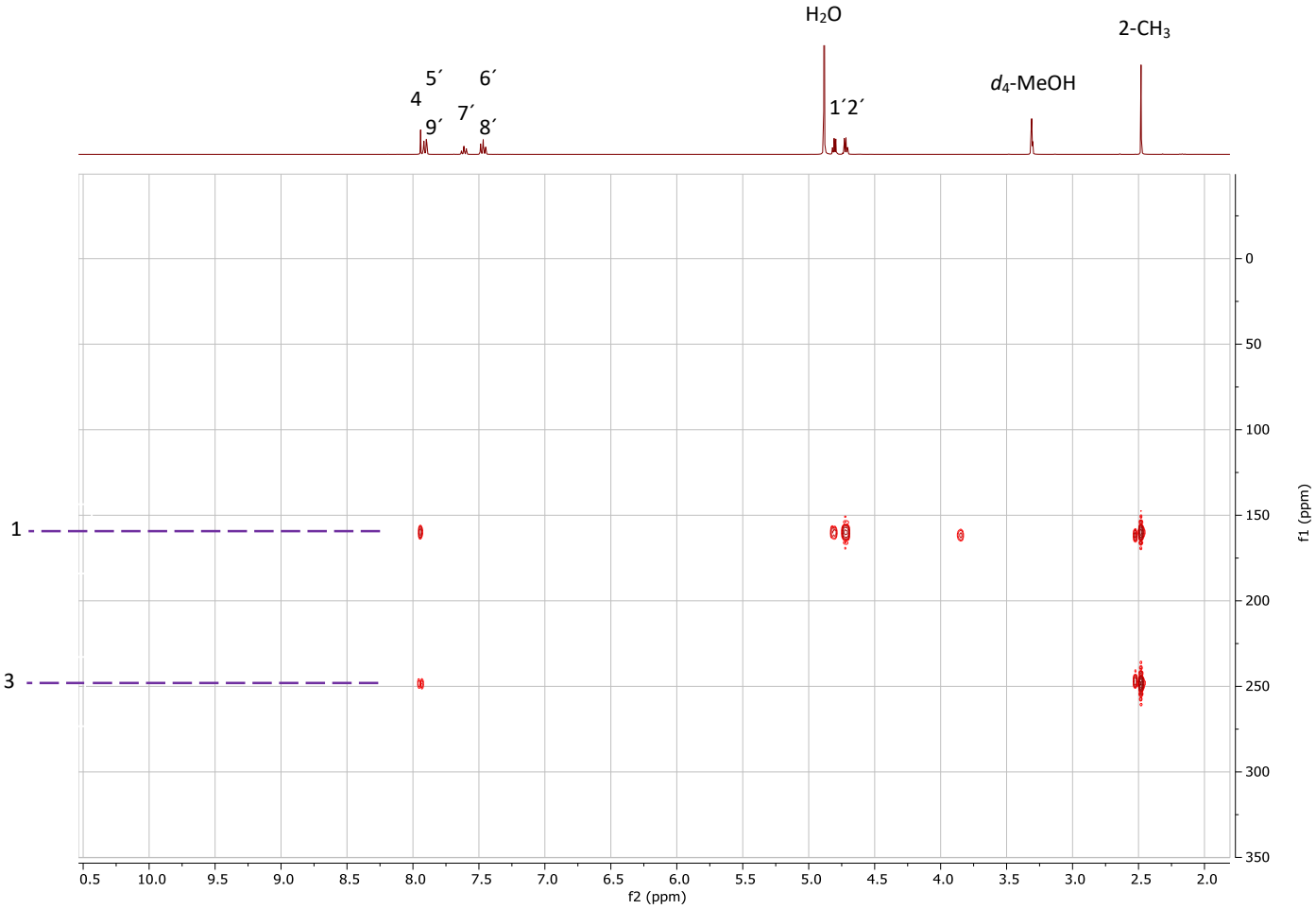


Figure S8: ^{1}H-^{15}N-HMBC NMR spectrum (400 MHz, d_4-MeOH) of the sample QMC266

Red arrows in the depicted chemical structure visualize the observed HMBC long range correlations.



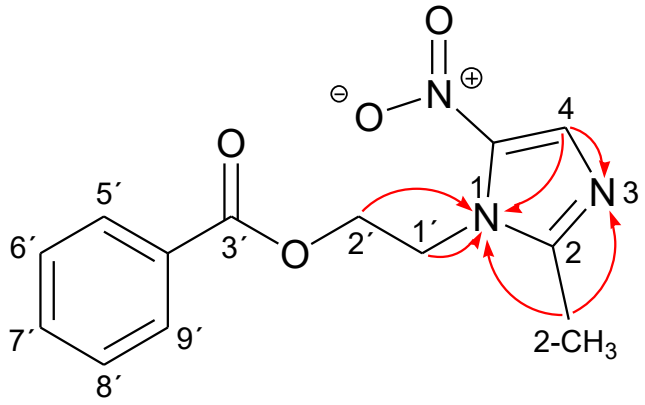


Figure S9: Superimposed ^{1}H NMR spectra (400 MHz, d_4-MeOH) of a metronidazole benzoate standard and the sample QMC266

metronidazole benzoate standard depicted in red (above) and the sample QMC266 depicted in blue (below).

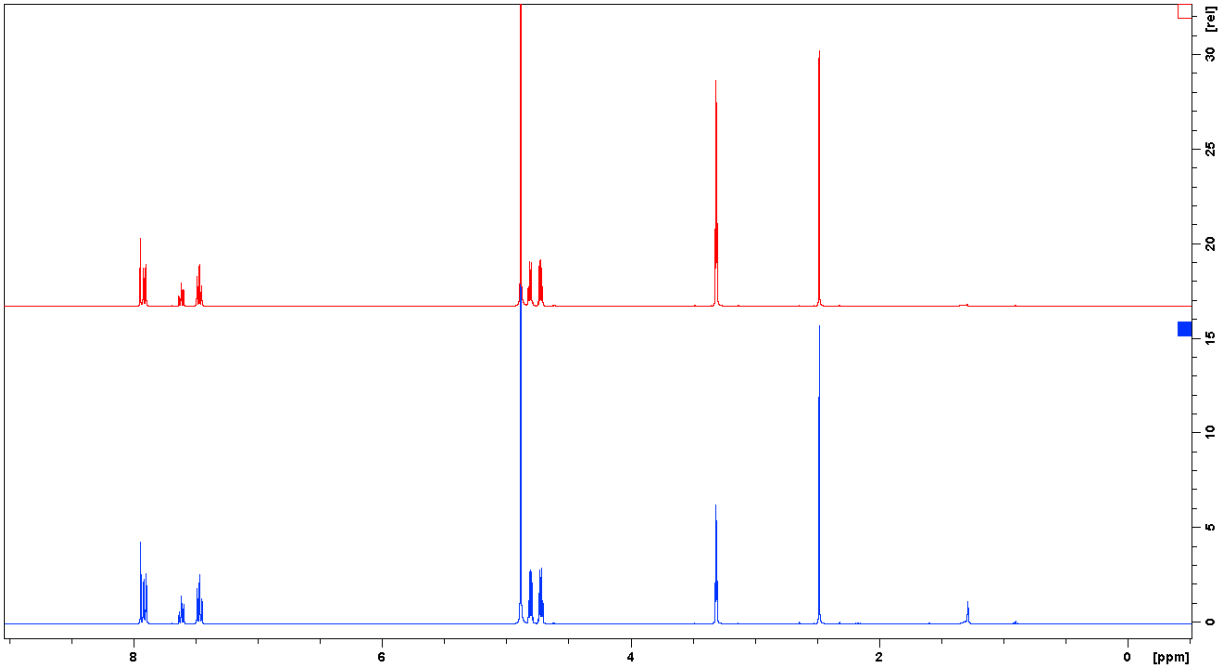


Figure S10: Superimposed ^{13}C NMR spectra (101 MHz, d_4-MeOH) of a metronidazole benzoate standard and the sample QMC266

metronidazole benzoate standard depicted in red (above) and the sample QMC266 depicted in blue (below).

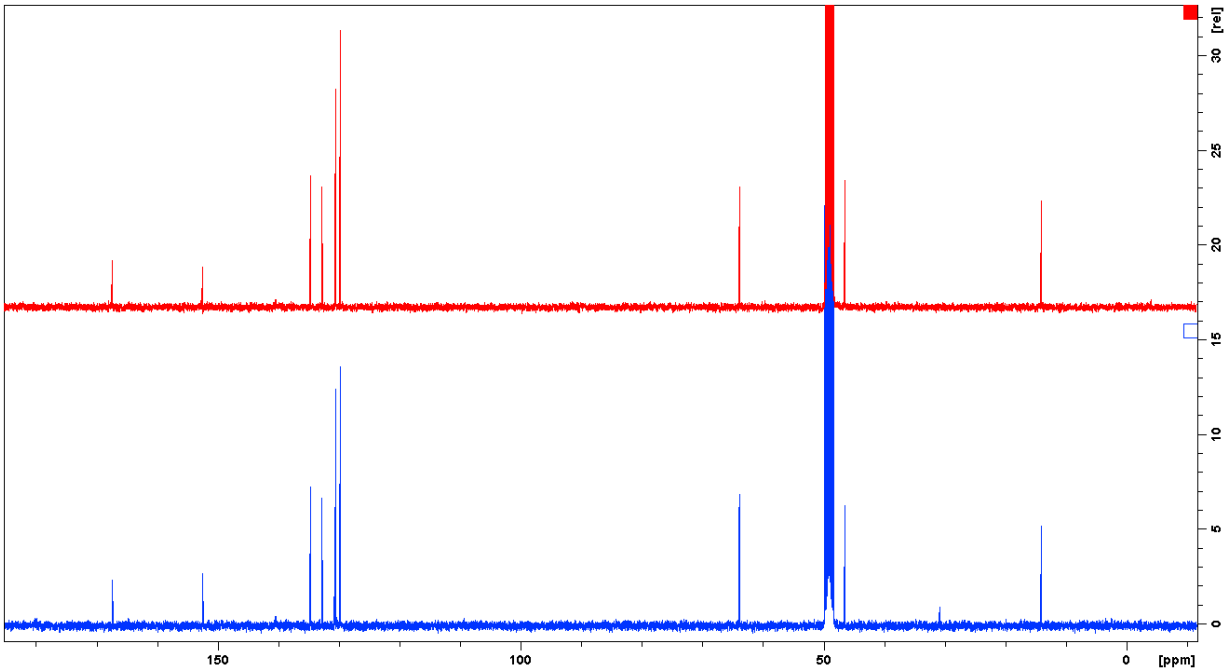
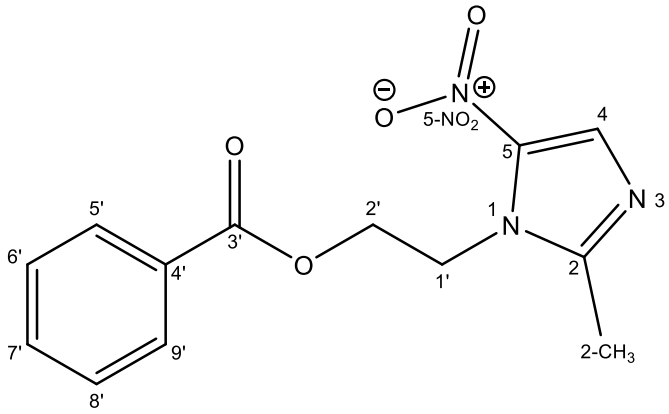


Figure S11: NMR Results for metronidazole benzoate in sample QMC266 collected in the DR Congo

Position	$\delta_{C/N}$[a]	δ_H (integral, multiplicity)[b]	COSY	HMBC[c]
1	160.0 N_t			
2	152.4 C_q			
2-CH_3	14.0 CH_3	2.48 (3H, s)		1, 2, 3
3	248.3 N_t			
4	132.7 CH	7.94 (1H, s)		1, 2, 3, 5
5	140.5 C_q[d]			
5-NO_2	n.o.[e]			
1'	46.4 CH_2	4.81 (2H, m)	2'	1, 2', 2, 5
2'	63.8 CH_2	4.72 (2H, m)	1'	1, 1', 3'
3'	167.3 CO			
4'	130.6 C_q			
5'/9'	130.5 CH	7.90+7.92 (2H, m)	6', 8'	3', 7', 5', 9'
6'/8'	129.7 CH	7.47 (2H, m)	5', 7', 9'	4', 6', 8'
7'	134.6 CH	7.61 (1H, m)	6', 8'	6´, 8'



2'-(2-methyl-5-nitro-1*H*-imidazol-1-yl)ethyl benzoate

[a] Recorded at 101 MHz for ^{13}C. ^{15}N NMR values were extracted from the corresponding ^{1}H-^{15}N HMBC NMR spectrum.

Multiplicity determined by an edited ^{1}H-^{13}C HSQC and a DEPT135 NMR experiment.

[b] Recorded at 400 MHz.

[c] Protons showing long-range correlation with indicated carbon or nitrogen.

[d] ^{13}C NMR value was extracted from a ^{1}H-^{13}C HMBC NMR spectrum.

[e] Not observed.

Figure S12: Content of the active pharmaceutical ingredient determined for each sample, sorted by different categories

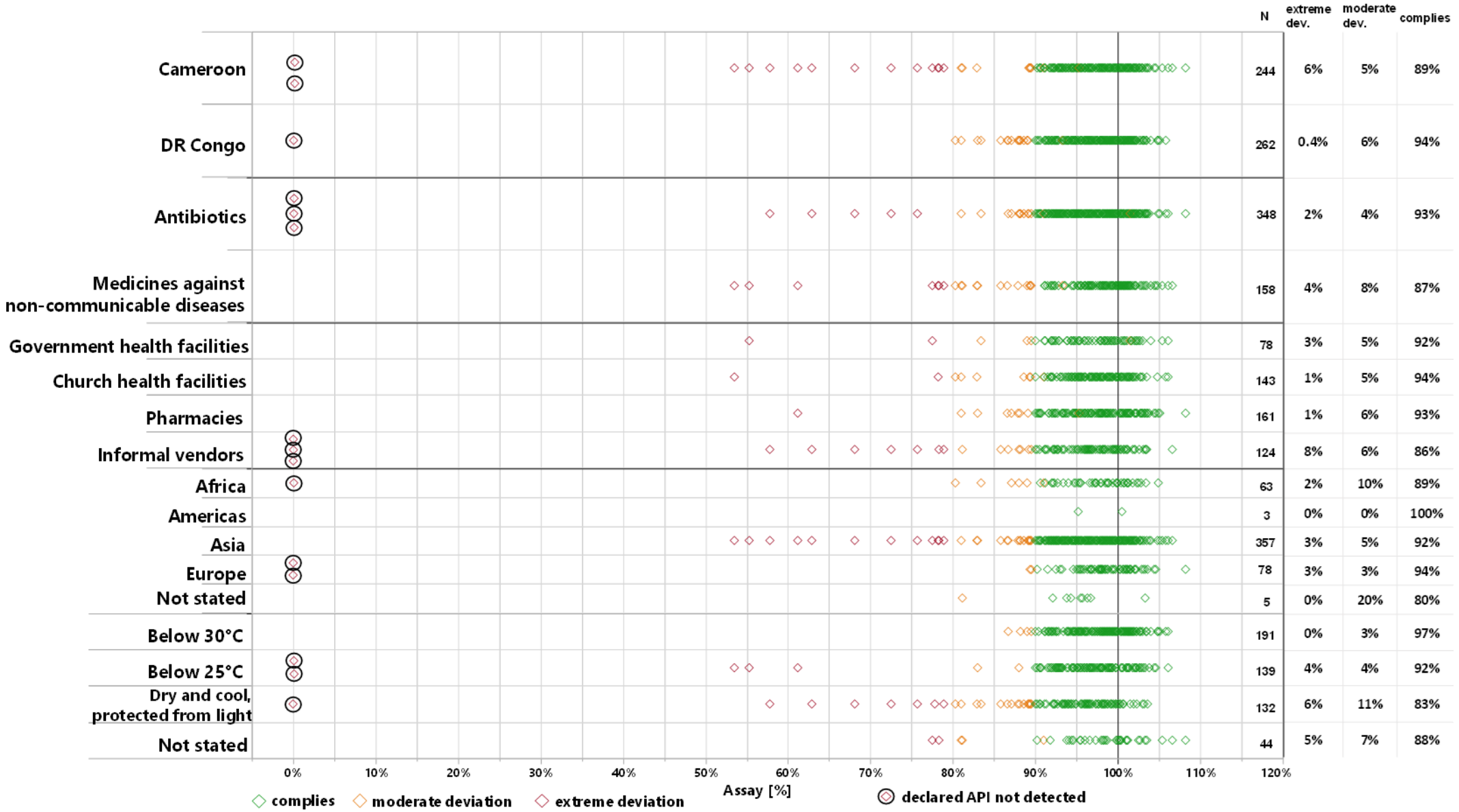


Figure S13: Dissolution of the active pharmaceutical ingredient determined for each sample, sorted by different categories

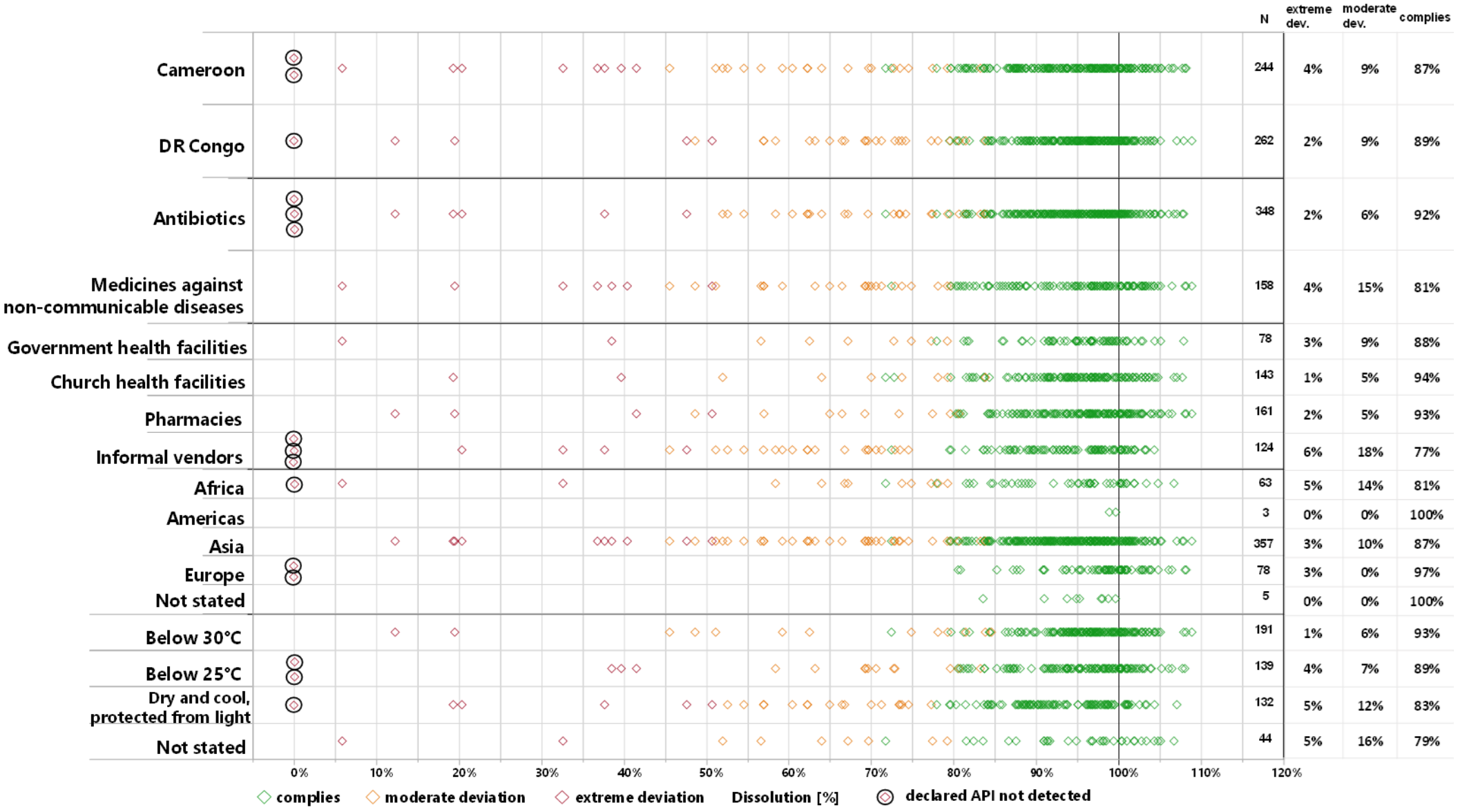
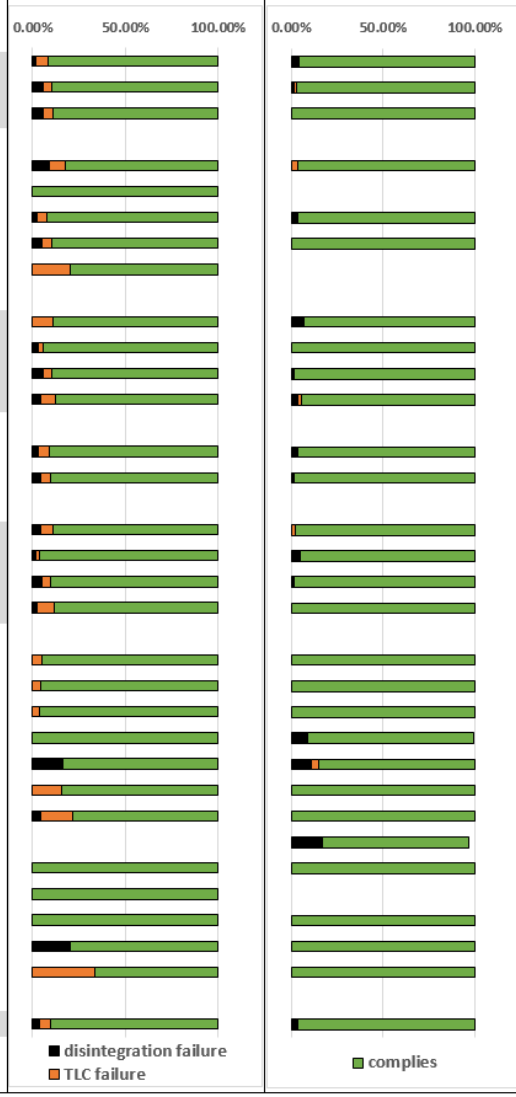


Figure S14: Frequency of non-compliance in Minilab TLC and disintegration testing in different subgroups of medicines

		Cameroon						DR Congo					
			non-compliant total			only disintegration	only TLC		non-compliant total			only disintegration	only TLC
		N total	N	[%]	95% CI	N	N	N total	N	[%]	95% CI	N	N
brand	Generics	117	10	9%	[5-15]	2	8	96	4	4%	[2-10]	4	0
	Branded	108	11	10%	[6-17]	6	5	102	3	3%	[1-8]	2	1
	Originator	18	2	11%	[3-33]	1	1	10	0	0%		0	0
continent of origin	Africa	23	4	17%	[8-42]	2	2	30	1	3%	[1-16]	0	1
	Americas	3	0	0%		0	0						
	Asia	155	12	8%	[4-13]	4	8	162	6	4%	[2-8]	6	0
	Europe	57	6	11%	[6-23]	3	3	16	0	0%		0	0
	Not stated	5	1	20%	[2-44]	0	1						
site type	Government health facilities	36	4	11%	[4-25]	0	4	42	3	7%	[3-19]	3	0
	Church health facilities	71	4	6%	[2-14]	2	2	40	0	0%		0	0
	Pharmacies	70	7	10%	[5-19]	4	3	70	1	1%	[0-8]	1	0
	Informal vendors	66	8	12%	[6-22]	3	5	56	3	5%	[2-15]	2	1
indication	Antibiotics	151	14	9%	[6-15]	5	9	157	6	4%	[2-8]	5	1
	MANCD	92	9	10%	[5-18]	4	5	51	1	2%	[0-10]	1	0
store at	Below 25 °C	89	10	11%	[6-20]	4	6	43	1	2%	[0-12]	0	1
	Below 30°C	51	2	4%	[1-13]	1	1	102	5	5%	[2-11]	5	0
	Dry and cool, protected from light	61	6	10%	[5-20]	3	3	61	1	2%	[0-9]	1	0
	Not stated	42	5	12%	[5-25]	1	4	2	0	0%		0	0
active pharmaceutical ingredient	Amoxicillin and Clavulanic acid	19	1	5%	[1-25]	0	1	11	0	0%		0	0
	Amoxicillin	24	1	4%	[1-20]	0	1	25	0	0%		0	0
	Ciprofloxacin	25	1	4%	[1-20]	0	1	26	0	0%		0	0
	Doxycycline	22	0	0%		0	0	20	2	10%	[2.8-30]	2	0
	Metronidazole	25	4	16%	[6-35]	4	0	27	4	15%	[6-33]	3	1
	Penicillin V	13	2	15%	[4-42]	0	2	21	0	0%		0	0
	Sulfamethoxazole and Trimethoprim	23	5	22%		1	4	27	0	0%		0	0
	Atenolol	0	0	0%		0	0	5	1	20%	[4-62]	1	0
	Furosemide	17	0	0%		0	0	18	0	0%		0	0
	Glibenclamide	19	0	0%		0	0	0	0	0%		0	0
	Hydrochlorothiazide	21	0	0%		0	0	4	0	0%		0	0
	Metformin	20	4	20%	[8-42]	4	0	10	0	0%		0	0
	Salbutamol	15	5	33%	[15-58]	0	5	14	0	0%		0	0
	Overall	**243**	**23**	**9%**	**[6.4-13.8]**	**9**	**14**	**208**	**7**	**3%**	**[1.6-6.8]**	**6**	**1**



TLC= thin-layer chromatography

Table S1: List of stated manufacturers of samples investigated in this study, and results for USP 41 assay and dissolution testing

Stated Continent of Origin	Stated Country of Origin	Stated Manufacturer	N	complies	moderate deviation	extreme deviation
Africa	Benin	Pharmaquick	7	5	0	2
	Burundi	Société industrielle Pharmaceutique (SIPHAR)	1	1	0	0
	Cameroon	Africure Pharmaceuticals Cameroon S.A.	2	1	1	0
		Cinpharm **	3	2	1	0
	DR Congo	Phatkin B.P.	5	2	3	0
		Zenufa Laboratoire	4	3	1	0
	Ghana	Entrance Pharmaceuticals & Research Centre	5	3	2	0
	Kenya	Cosmos Limited	1	1	0	0
		DAWA Limited	7	6	1	0
		Elys Chemical Industries Ltd.	3	2	1	0
		Laboratory & Allied Ltd.	2	2	0	0
		MAC'S Pharmaceuticals Ltd.	2	1	0	1 §
		Pharmaceutical Manufacturing Co. Ltd.	1	0	1	0
		Regal Pharmaceuticals Ltd.	5	5	0	0
	Nigeria	New Divine Favour Pharmaceutical Industries Ltd.	1	1	0	0
	Senegal	Wintrop Pharma Sénégal Group SANOFI	1	1	0	0
	Togo	Sprukfield	4	4	0	0
	Uganda	Kampala Pharmaceutical Industries	7	7	0	0
	Uganda	Rene Industries Ltd.	2	2	0	0
	subtotal		**63**	**49**	**11**	**3**
Americas	British West Indies	Prost Pharma (France)	2	2	0	0
	USA	Sandoz	1	1	0	0
	subtotal		**3**	**3**	**0**	**0**

Stated Continent of Origin	Stated Country of Origin	Stated Manufacturer	N	complies	moderate deviation	extreme deviation
Asia	China	Anhui Chengshi Pharmaceutical Co. Ltd	1	1	0	0
		Anhui Medipharm Co. Ltd.	1	0	1	0
		Chifeng Wanze Pharmaceutical Co. Ltd.	1	1	0	0
		CSPC Ouyi Pharmaceutical Co. Ltd.	22	21	1	0
		CSPC Zhongnuo Pharmaceuticals Co. Ltd.	10	10	0	0
		Farmasino Pharmaceutical Co. Ltd	6	5	1	0
		Greenfield Pharmaceuticals (Jiang Su) Co. Ltd.	1	1	0	0
		Guilin Pharmaceutical Co. Ltd.	4	4	0	0
		Jiangsu Pengyao Pharmaceutical Co. Ltd.	2	2	0	0
		Jiangsu Ruinian Qianjin Pharm. Co.Ltd	4	4	0	0
		Jiangxi Xier Kangtai Pharmaceutical Co. Ltd.	5	3	2	0
		Jinzhou Jiuyang Pharmaceutical Co. Ltd	3	2	0	1
		JSPY Pharmaceutical Co. Ltd.	3	3	0	0
		Nanjing Baijingyu Pharmaceutical Co. Ltd.	3	3	0	0
		Nanjing Sino Pharmaceutical Ltd.	1	1	0	0
		Ningbo Shuangwei Pharmaceutical Co. Ltd	6	6	0	0
		North China Pharmaceutical Co. Ltd. ***	8	8	0	0
		Reyoung Pharmaceutical Co. Ltd.	9	9	0	0
		Shandong Shenglu Pharmaceutical Co. Ltd	4	0	0	4
		Shandong Xier Kangtai Pharm Co. Ltd	1	1	0	0
		Shandong Yikang Pharmaceutical Co. Ltd.	2	1	1	0
		Shanghai Juchen Import and Exports Co. Ltd.	4	4	0	0
		Shanxi Lianbang Pharmaceutical Co. Ltd.	2	2	0	0

Stated Continent of Origin	Stated Country of Origin	Stated Manufacturer	N	complies	moderate deviation	extreme deviation
		Sinochem Jiangsu Co. Ltd	14	8	3	3
		Sishui xier Kang Pharmaceutical Co. Ltd	1	0	0	1
		Yanzhou Xierkangtai pharmaceutical Co. Ltd.	3	2	1	0
	Hong Kong	Hongkong Prost Medicines and Health Products Co. Ltd	3	3	0	0
	India	Agog Pharma Ltd.	4	4	0	0
		Alkem Laboratories Ltd.	1	0	1	0
		Arco Pharma Pvt. Ltd	7	1	6	0
		Asence Pharma Pvt. Ltd.	6	4	2	0
		Astra Lifecare Pvt. Ltd.	11	9	0	2
		Aura pharmaceuticals Pvt. Ltd	9	5	4	0
		Aurobindo Pharma Ltd.	1	0	1	0
		Axon Drugs Pvt. Ltd.	1	1	0	0
		Bliss GVS Pharma Ltd.	1	0	1	0
		Cadila Healthcare Ltd.	1	1	0	0
		Cipla Ltd.	1	1	0	0
		Ciron Drugs and Pharmaceuticals Ltd.	2	2	0	0
		Combitic Global Caplet Pvt. Ltd.	1	1	0	0
		Fourrts	3	3	0	0
		Global Pharma Healthcare Pvt. Ltd.	4	4	0	0
		Holden Medical Laboratories Pvt. Ltd.	3	3	0	0
		Intermed	1	1	0	0
		Ipca Laboratories Ltd.	1	1	0	0
		J. B. Chemicals and Pharmaceuticals Ltd.	1	1	0	0
		Kopran Limited	2	2	0	0
		Leben Laboratories Pvt. Ltd	1	1	0	0
		Lincoln Pharmaceuticals Ltd.	8	8	0	0
		Lord Lifescience Pvt. Ltd.	1	0	1	0
		Macleods Pharmaceuticals Ltd.	4	4	0	0
		Mancare pharmaceutical Ltd	4	4	0	0

Stated Continent of Origin	Stated Country of Origin	Stated Manufacturer	N	complies	moderate deviation	extreme deviation
		Maneesh Pharmaceuticals Ltd	1	1	0	0
		Maxheal Laboratories Pvt. Ltd.	2	1	1	0
		Maxtar Bio-Genics	14	9	2	3 *
		Medicamen Biotech Ltd.	8	7	1	0
		Medicef Pharma	4	4	0	0
		Medico Remedies Pvt. Ltd.	5	0	1	4
		Medley Pharmaceuticals Ltd.	5	5	0	0
		Medopharm Pvt. Ltd.	41	39	2	0
		Mepro Pharmaceuticals Pvt. Ltd.	2	2	0	0
		Micro Labs Ltd.	4	4	0	0
		Milan Laboratories (India) Pvt. Ltd	6	5	1	0
		Nem Laboratories Pvt. Ltd.	1	1	0	0
		not stated	1	1	0	0
		Osaka Pharmaceuticals Pvt. Ltd.	3	1	2	0
		PIL Pharmaceuticals Pvt. Ltd.	1	1	0	0
		Prashi Pharma Pvt. Ltd	6	1	4	1
		Shalina Laboratories Pvt. Ltd.	1	1	0	0
		Sparsh Bio-Tech Pvt. Ltd.	7	7	0	0
		Strides Arcolab Limited	23	21	2	0
		Strides Shasun Limited	11	9	2	0
		Triveni Formulations Limited	1	1	0	0
		Ultra Care International	2	2	0	0
		UMEDICA Laboratories	1	1	0	0
		Zee Laboratories	1	1	0	0
		ZIM Laboratories Ltd.	1	1	0	0
	Sultanat of Oman	National pharmaceutical industries	1	1	0	0
	Turkey	Bilim Pharmaceuticals	1	1	0	0
	subtotal		**357**	**294**	**44**	**19**
Europe	Austria	Sandoz	10	10	0	0
	Belgium	Merck	3	3	0	0
		Oxford Pharma	1	0	0	1 §
	Cyprus	Medochemie Ltd.	2	2	0	0

Stated Continent of Origin	Stated Country of Origin	Stated Manufacturer	N	complies	moderate deviation	extreme deviation
		Remedica Ltd	2	2	0	0
	France	Famar Lyon	1	1	0	0
		Glaxo Welcome Production	3	3	0	0
		Laboratoires Bailleul	1	1	0	0
		Laboratoire Bailly-Creat	6	6	0	0
		Sanofi-Winthrop Industrie	6	6	0	0
	Germany	Aspen Bad Oldesloe GmbH	1	1	0	0
		Berlin Chemie	1	1	0	0
		Denk Pharma GmbH & Co. KG	12	10	2	0
		Salutas Pharma GmbH	2	2	0	0
	Italy	Errekappa Euroterapici S.p.A	1	1	0	0
		Laboratori Guidotti S.p.A	1	1	0	0
	Spain	Ferrer Internacional S.A.	3	3	0	0
		Novartis Farmacéutica S.A.	14	14	0	0
	Sweden	Bluefish Pharmaceuticals AD	1	1	0	0
	United Kingdom	SmithKline Beecham Pharmaceuticals	1	0	0	1 §
		Sonmart Pharma (UK)	6	6	0	0
	subtotal		**78**	**74**	**2**	**2**
not stated	not stated	Cinpharm **	3	3	0	0
		not stated	2	1	1	0
	subtotal		**6**	**5**	**1**	**0**
total			**506**	**424**	**58**	**24**

* Two of these three samples had been expired at the date of collection.

** Cinpharm recently became a Cameroonian company. However, three samples did not state the country of manufacture, therefore these three samples were listed in the category “not stated”.

*** The name of this manufacturer was given on different samples as "North China Pharmaceutical Co. Ltd.", or as "NCPC, PRC", or as "NCPC North Best". Since all of them appear to have the same contact address, they were considered in this study as a single manufacturer.

§ Falsified medicine; poor quality can not be attributed to the stated manufacturer.

Table S2: List of samples reported to fail GPHF Minilab TLC analysis, and of samples reported to pass GPHF Minilab TLC analysis but showing extreme deviations in USP assay testing, with their respective USP assay results

Sample ID	API	USP assay classification	USP assay result [%]
1) Samples reported to <u>fail</u> GPHF Minilab TLC analysis:			
QMCA241	Amoxicillin / clavulanic acid	extreme deviation	0% / 0%
QMC266	Metronidazole	extreme deviation	0%
QMCA035	Penicillin V	extreme deviation	0%
QMCA001	Salbutamol	extreme deviation	54%
QMCA025	Salbutamol	extreme deviation	55%
QMCA215	Salbutamol	extreme deviation	61%
QMCA072	Salbutamol	deviation	81%
QMCA074	Sulfamethoxazole / Trimethoprim	deviation	91% / 95%
QMCA019	Sulfamethoxazole / Trimethoprim	complies	99% / 98%
QMCA212	Sulfamethoxazole / Trimethoprim	complies	102% / 100%
QMCA082	Sulfamethoxazole / Trimethoprim	complies	103% / 100%
QMCA032	Amoxicillin	complies	92%
QMCA210	Penicillin V	complies	93%
QMCA084	Salbutamol	complies	94%
QMCA184	Ciprofloxacin	complies	95%
2) Samples reported to <u>pass</u> GPHF Minilab TLC analysis but showing extreme deviations in USP assay testing:			
QMCA253	Penicillin V	extreme deviation	58%
QMCA107	Penicillin V	extreme deviation	68%
QMCA244	Penicillin V	extreme deviation	73%
QMCA177	Penicillin V	extreme deviation	76%
QMCA168	Salbutamol	extreme deviation	78%
QMCA179	Salbutamol	extreme deviation	78%
QMCA191	Salbutamol	extreme deviation	78%
QMCA239	Salbutamol	extreme deviation	79%

The following are supplemental materials and will be published online only

Table S3: List of all batches and brands investigated in this study, with their stated manufacturers and analytical results for assay and dissolution

Note: Medicines were collected in health facilities, i.e. at the point of care, and it is unknown whether the manufacturers' storage recommendation have been complied with from the time of manufacture until the time of sample collection. Changes in medicines quality may have occurred due to inappropriate transport and storage conditions, and non-compliance with USP specifications is therefore not necessarily due to substandard manufacturing or packaging. However, the quality results listed below reflect what patients receive in the investigated health facilities.

* Two of these three samples had been expired at the date of collection.

** Cinpharm recently became a Cameroonian company. However, three samples did not state the country of manufacture, therefore these three samples were listed in the category "not stated".

*** The name of this manufacturer was given on different samples as "North China Pharmaceutical Co. Ltd.", or as "NCPC, PRC", or as "NCPC North Best". Since all of them appear to have the same contact address, they were considered in this study as a single manufacturer.

§ Falsified medicine; poor quality can not be attributed to the stated manufacturer.

							USP assay			USP dissolution			USP assay and dissolution combined		
Stated continent of origin	**Stated country of origin**	**Stated manufacturer**	**INN**	**Stated product name**	**Batchnumber**	**N**	**complies**	**deviation**	**extreme deviation**	**complies 2**	**deviation2**	**extreme deviation 2**	**complies 3**	**deviation 3**	**extreme deviation 3**
Africa	Benin	Pharmaquick	Furosemide	Furosemide Pharmaquick	991300	1	1	0	0	1	0	0	1	0	0
Africa	Benin	Pharmaquick	Glibenclamide	Glibenclamid Pharmaquick	965500	2	2	0	0	0	0	2	0	0	2
Africa	Benin	Pharmaquick	Hydrochlorothiazide	Hydrochlorothiazide Pharmaquick	992701	2	2	0	0	2	0	0	2	0	0
Africa	Benin	Pharmaquick	Hydrochlorothiazide	Hydrochlorothiazide Pharmaquick	992801	2	2	0	0	2	0	0	2	0	0
Africa	Burundi	Société industrielle Pharmaceutique (SIPHAR)	Doxycycline	Siphadox 100	SDC-001	1	1	0	0	1	0	0	1	0	0
Africa	Cameroon	Africure Pharmaceuticals Cameroon S.A.	Doxycycline	Doxycycline Capsules BP	4517001	2	2	0	0	1	1	0	1	1	0
Africa	Cameroon	Cinpharm **	Amoxicillin	Cinamox	18026	1	1	0	0	0	1	0	0	1	0
Africa	Cameroon	Cinpharm **	Sulfa/Trimet	Cincotrim	16001	1	1	0	0	1	0	0	1	0	0
Africa	Cameroon	Cinpharm **	Ciprofloxacin	Proloxcin	16001	1	1	0	0	1	0	0	1	0	0
Africa	DRC	Phatkin B.P.	Amoxicillin	Amoxin 250	02-16	1	1	0	0	1	0	0	1	0	0
Africa	DRC	Phatkin B.P.	Amoxicillin	Amoxin 500	09-16	1	1	0	0	0	1	0	0	1	0
Africa	DRC	Phatkin B.P.	Ciprofloxacin	Ciprokin-500	03-17	1	1	0	0	1	0	0	1	0	0
Africa	DRC	Phatkin B.P.	Ciprofloxacin	Ciprokin-500	17-17	1	0	1	0	1	0	0	0	1	0
Africa	DRC	Phatkin B.P.	Penicillin V	Peni-V	04-17	1	0	1	0	0	1	0	0	1	0
Africa	DRC	Zenufa Laboratoire	Ciprofloxacin	Ciproz 500	16T-141	1	0	1	0	1	0	0	0	1	0
Africa	DRC	Zenufa Laboratoire	Furosemide	Zenamide	14T-35	1	1	0	0	1	0	0	1	0	0
Africa	DRC	Zenufa Laboratoire	Furosemide	Zenamide	15T-75	1	1	0	0	1	0	0	1	0	0
Africa	DRC	Zenufa Laboratoire	Metronidazole	Zenogyl 250	16T-98	1	1	0	0	1	0	0	1	0	0
Africa	Ghana	Entrance Pharmaceuticals & Research Centre	Sulfa/Trimet	Co-Trimoxazole	NT17127	1	0	1	0	0	1	0	0	1	0
Africa	Ghana	Entrance Pharmaceuticals & Research Centre	Sulfa/Trimet	Co-Trimoxazole	NT17208	1	1	0	0	0	1	0	0	1	0
Africa	Ghana	Entrance Pharmaceuticals & Research Centre	Glibenclamide	Glibenclamide	NT17149	1	1	0	0	1	0	0	1	0	0
Africa	Ghana	Entrance Pharmaceuticals & Research Centre	Metronidazole	Metronidazole	NT17122	1	1	0	0	1	0	0	1	0	0
Africa	Ghana	Entrance Pharmaceuticals & Research Centre	Metronidazole	Metronidazole	NT17145	1	1	0	0	1	0	0	1	0	0
Africa	Kenya	Cosmos Limited	Sulfa/Trimet	Cosatrim	60446	1	1	0	0	1	0	0	1	0	0
Africa	Kenya	DAWA Limited	Metronidazole	Eflaron 250	1607130	2	2	0	0	2	0	0	2	0	0
Africa	Kenya	DAWA Limited	Furosemide	Frusemide	1605057	1	0	1	0	0	1	0	0	1	0
Africa	Kenya	DAWA Limited	Amoxicillin	Moxacil-250	1707321	1	1	0	0	1	0	0	1	0	0
Africa	Kenya	DAWA Limited	Amoxicillin	Moxacil-500	1706107	1	1	0	0	1	0	0	1	0	0

							USP assay			USP dissolution			USP assay and dissolution combined		
Stated continent of origin	**Stated country of origin**	**Stated manufacturer**	**INN**	**Stated product name**	**Batchnumber**	**N**	**complies**	**deviation**	**extreme deviation**	**complies 2**	**deviation2**	**extreme deviation 2**	**complies 3**	**deviation 3**	**extreme deviation 3**
Africa	Kenya	DAWA Limited	Salbutamol	Sabulin	1504062	1	1	0	0	1	0	0	1	0	0
Africa	Kenya	DAWA Limited	Salbutamol	Sabulin	1608101	1	1	0	0	1	0	0	1	0	0
Africa	Kenya	Elys Chemical Industries Ltd.	Sulfa/Trimet	CO-TRI	4E46	1	1	0	0	1	0	0	1	0	0
Africa	Kenya	Elys Chemical Industries Ltd.	Furosemide	Frusemide	4G68	1	1	0	0	1	0	0	1	0	0
Africa	Kenya	Elys Chemical Industries Ltd.	Furosemide	Frusemide	5H102	1	1	0	0	0	1	0	0	1	0
Africa	Kenya	Laboratory & Allied Ltd.	Amoxicillin	Kemoxyl 250	66735	1	1	0	0	1	0	0	1	0	0
Africa	Kenya	Laboratory & Allied Ltd.	Sulfa/Trimet	Lecotrim	67056	1	1	0	0	1	0	0	1	0	0
Africa	Kenya	MAC'S Pharmaceuticals Ltd.	Metronidazole	Metronyl	K2343	1	1	0	0	1	0	0	1	0	0
Africa	Kenya	MAC'S Pharmaceuticals Ltd.	Metronidazole	Metronyl	L3028	1	0	0	1 [§]	0	0	1 [§]	0	0	1 [§]
Africa	Kenya	Pharmaceutical Manufacturing Co. Ltd.	Salbutamol	Astalin	15-02040	1	0	1	0	0	1	0	0	1	0
Africa	Kenya	Regal Pharmaceuticals Ltd.	Penicillin V	Unipen	151876	1	1	0	0	1	0	0	1	0	0
Africa	Kenya	Regal Pharmaceuticals Ltd.	Penicillin V	Unipen 250	170093	1	1	0	0	1	0	0	1	0	0
Africa	Kenya	Regal Pharmaceuticals Ltd.	Penicillin V	Unipen 250	170888	1	1	0	0	1	0	0	1	0	0
Africa	Kenya	Regal Pharmaceuticals Ltd.	Penicillin V	Unipen 250	170890	1	1	0	0	1	0	0	1	0	0
Africa	Kenya	Regal Pharmaceuticals Ltd.	Sulfa/Trimet	Unitrim	160732	1	1	0	0	1	0	0	1	0	0
Africa	Nigeria	New Divine Favour Pharmaceutical Industries Ltd.	Doxycycline	New Divine Doxycycline Capsules	17	1	1	0	0	1	0	0	1	0	0
Africa	Senegal	Wintrop Pharma Sénégal Group SANOFI	Metronidazole	Flagyl 500	9705	1	1	0	0	1	0	0	1	0	0
Africa	Togo	Sprukfield	Sulfa/Trimet	Co-Trimoxazole	AT15001	2	2	0	0	2	0	0	2	0	0
Africa	Togo	Sprukfield	Sulfa/Trimet	Co-Trimoxazole	AT15007	1	1	0	0	1	0	0	1	0	0
Africa	Togo	Sprukfield	Sulfa/Trimet	Co-Trimoxazole	I3617	1	1	0	0	1	0	0	1	0	0
Africa	Uganda	Kampala Pharmaceutical Industries	Doxycycline	Azudox	2517	1	1	0	0	1	0	0	1	0	0
Africa	Uganda	Kampala Pharmaceutical Industries	Amoxicillin	Kam Amoxy Capsules	2417	1	1	0	0	1	0	0	1	0	0
Africa	Uganda	Kampala Pharmaceutical Industries	Sulfa/Trimet	Kam Cotri	1816	1	1	0	0	1	0	0	1	0	0
Africa	Uganda	Kampala Pharmaceutical Industries	Salbutamol	Kam Vent	0217	1	1	0	0	1	0	0	1	0	0
Africa	Uganda	Kampala Pharmaceutical Industries	Salbutamol	Kam Vent	0417	1	1	0	0	1	0	0	1	0	0
Africa	Uganda	Kampala Pharmaceutical Industries	Salbutamol	Kam Vent	0617	1	1	0	0	1	0	0	1	0	0
Africa	Uganda	Kampala Pharmaceutical Industries	Salbutamol	Kam Vent	0716	1	1	0	0	1	0	0	1	0	0
Africa	Uganda	Rene Industries Ltd.	Doxycycline	Doxyren	00217	1	1	0	0	1	0	0	1	0	0
Africa	Uganda	Rene Industries Ltd.	Sulfa/Trimet	Renetrim	04617	1	1	0	0	1	0	0	1	0	0
Americas	British West Indies	Prost Pharma (France)	Amoxicillin	Amoxdels-500	160952	1	1	0	0	1	0	0	1	0	0
Americas	British West Indies	Prost Pharma (France)	Sulfa/Trimet	Cotrimo-480mg	170610	1	1	0	0	1	0	0	1	0	0
Americas	USA	Sandoz	Furosemide	Furosemide	FT4986	1	1	0	0	1	0	0	1	0	0

							USP assay			USP dissolution			USP assay and dissolution combined		
Stated continent of origin	Stated country of origin	Stated manufacturer	INN	Stated product name	Batchnumber	N	complies	deviation	extreme deviation	complies 2	deviation2	extreme deviation 2	complies 3	deviation 3	extreme deviation 3
Asia	China	Anhui Chengshi Pharmaceutical Co. Ltd	Metronidazole	Metronidazole Tablets	170627	1	1	0	0	1	0	0	1	0	0
Asia	China	Anhui Medipharm Co. Ltd.	Ciprofloxacin	Cipro 500	1704581	1	0	1	0	1	0	0	0	1	0
Asia	China	Chifeng Wanze Pharmaceutical Co. Ltd.	Metronidazole	Metazol	X6021	1	1	0	0	1	0	0	1	0	0
Asia	China	CSPC Ouyi Pharmaceutical Co. Ltd.	Ciprofloxacin	Ciprofloxacine Tablets USP 500 mg	527160901	1	1	0	0	1	0	0	1	0	0
Asia	China	CSPC Ouyi Pharmaceutical Co. Ltd.	Ciprofloxacin	Ciprofloxacine Tablets USP 500 mg	527170206	1	1	0	0	0	1	0	0	1	0
Asia	China	CSPC Ouyi Pharmaceutical Co. Ltd.	Ciprofloxacin	Ciprofloxacine Tablets USP 500 mg	527170207	1	1	0	0	1	0	0	1	0	0
Asia	China	CSPC Ouyi Pharmaceutical Co. Ltd.	Ciprofloxacin	Ciprofloxacine Tablets USP 500 mg	784150901	1	1	0	0	1	0	0	1	0	0
Asia	China	CSPC Ouyi Pharmaceutical Co. Ltd.	Ciprofloxacin	Ciprofloxacine Tablets USP 500 mg	784150902	1	1	0	0	1	0	0	1	0	0
Asia	China	CSPC Ouyi Pharmaceutical Co. Ltd.	Ciprofloxacin	Ciprofloxacine Tablets USP 500 mg	784150904	1	1	0	0	1	0	0	1	0	0
Asia	China	CSPC Ouyi Pharmaceutical Co. Ltd.	Ciprofloxacin	Ciprofloxacine Tablets USP 500 mg	784160201	1	1	0	0	1	0	0	1	0	0
Asia	China	CSPC Ouyi Pharmaceutical Co. Ltd.	Ciprofloxacin	Ciprofloxacine Tablets USP 500 mg	784160501	1	1	0	0	1	0	0	1	0	0
Asia	China	CSPC Ouyi Pharmaceutical Co. Ltd.	Ciprofloxacin	Ciprofloxacine Tablets USP 500 mg	784161002	1	1	0	0	1	0	0	1	0	0
Asia	China	CSPC Ouyi Pharmaceutical Co. Ltd.	Sulfa/Trimet	Cotrimoxazole Tablets B.P	541141102	1	1	0	0	1	0	0	1	0	0
Asia	China	CSPC Ouyi Pharmaceutical Co. Ltd.	Sulfa/Trimet	Cotrimoxazole Tablets B.P	541150603	1	1	0	0	1	0	0	1	0	0
Asia	China	CSPC Ouyi Pharmaceutical Co. Ltd.	Sulfa/Trimet	Cotrimoxazole Tablets B.P	541161201	2	2	0	0	2	0	0	2	0	0
Asia	China	CSPC Ouyi Pharmaceutical Co. Ltd.	Doxycycline	Doxycycline Hyclate tablets USP	503150911	1	1	0	0	1	0	0	1	0	0
Asia	China	CSPC Ouyi Pharmaceutical Co. Ltd.	Doxycycline	Doxycycline Hyclate tablets USP	6140911	1	1	0	0	1	0	0	1	0	0
Asia	China	CSPC Ouyi Pharmaceutical Co. Ltd.	Metronidazole	Metronidazole 250 mg tables BP	825151102	1	1	0	0	1	0	0	1	0	0
Asia	China	CSPC Ouyi Pharmaceutical Co. Ltd.	Metronidazole	Metronidazole 250 mg tables BP	825160701	1	1	0	0	1	0	0	1	0	0
Asia	China	CSPC Ouyi Pharmaceutical Co. Ltd.	Metronidazole	Metronidazole 250 mg tables BP	825160702	1	1	0	0	1	0	0	1	0	0
Asia	China	CSPC Ouyi Pharmaceutical Co. Ltd.	Metronidazole	Metronidazole 250 mg tables BP	82516202	1	1	0	0	1	0	0	1	0	0
Asia	China	CSPC Ouyi Pharmaceutical Co. Ltd.	Metronidazole	Metronidazole 250 mg tables BP	825170302	1	1	0	0	1	0	0	1	0	0
Asia	China	CSPC Ouyi Pharmaceutical Co. Ltd.	Metronidazole	Metronidazole 250 mg tables BP	825170306	1	1	0	0	1	0	0	1	0	0

							USP assay			USP dissolution			USP assay and dissolution combined		
Stated continent of origin	Stated country of origin	Stated manufacturer	INN	Stated product name	Batchnumber	N	complies	deviation	extreme deviation	complies 2	deviation2	extreme deviation 2	complies 3	deviation 3	extreme deviation 3
Asia	China	CSPC Ouyi Pharmaceutical Co. Ltd.	Doxycycline	Unidoxy	160820	1	1	0	0	1	0	0	1	0	0
Asia	China	CSPC Zhongnuo Pharmaceuticals Co. Ltd.	Amoxicillin	Amoxicillin Capsules BP	706170381	1	1	0	0	1	0	0	1	0	0
Asia	China	CSPC Zhongnuo Pharmaceuticals Co. Ltd.	Amoxicillin	Amoxicillin Tablets USP	677150802	1	1	0	0	1	0	0	1	0	0
Asia	China	CSPC Zhongnuo Pharmaceuticals Co. Ltd.	Amoxicillin	Amoxicillin Tablets USP	678150103	1	1	0	0	1	0	0	1	0	0
Asia	China	CSPC Zhongnuo Pharmaceuticals Co. Ltd.	Amoxicillin	Amoxicillin Tablets for Oral Suspension	797160904	1	1	0	0	1	0	0	1	0	0
Asia	China	CSPC Zhongnuo Pharmaceuticals Co. Ltd.	Amoxicillin	Amoxicillin Tablets for Oral Suspension	797160908	2	2	0	0	2	0	0	2	0	0
Asia	China	CSPC Zhongnuo Pharmaceuticals Co. Ltd.	Amoxicillin	Amoxy-500	B6011	1	1	0	0	1	0	0	1	0	0
Asia	China	CSPC Zhongnuo Pharmaceuticals Co. Ltd.	Amoxicillin	Amoxy-500	B6012	1	1	0	0	1	0	0	1	0	0
Asia	China	CSPC Zhongnuo Pharmaceuticals Co. Ltd.	Penicillin V	Phenoxymethylpenicillin Tablets BP	688151109	2	2	0	0	2	0	0	2	0	0
Asia	China	Farmasino Pharmaceutical Co. Ltd	Amoxicillin	Amoxyn-500	160777	1	1	0	0	0	1	0	0	1	0
Asia	China	Farmasino Pharmaceutical Co. Ltd	Doxycycline	Doxiciclina	W160507	3	3	0	0	3	0	0	3	0	0
Asia	China	Farmasino Pharmaceutical Co. Ltd	Metronidazole	Mefagyl	SU20110076	1	1	0	0	1	0	0	1	0	0
Asia	China	Farmasino Pharmaceutical Co. Ltd	Penicillin V	Peni-V	W160939	1	1	0	0	1	0	0	1	0	0
Asia	China	Greenfield Pharmaceuticals (Jiang Su) Co. Ltd.	Ciprofloxacin	Cipromax Fort 500	173121091	1	1	0	0	1	0	0	1	0	0
Asia	China	Guilin Pharmaceutical Co. Ltd.	Sulfa/Trimet	Co-Trimoxazole USP	XN150764	1	1	0	0	1	0	0	1	0	0
Asia	China	Guilin Pharmaceutical Co. Ltd.	Sulfa/Trimet	Co-Trimoxazole USP	XN150766	1	1	0	0	1	0	0	1	0	0
Asia	China	Guilin Pharmaceutical Co. Ltd.	Sulfa/Trimet	Sulfamethoxazole and trimethoprim	XN150932	1	1	0	0	1	0	0	1	0	0
Asia	China	Jiangsu Pengyao Pharmaceutical Co. Ltd.	Ciprofloxacin	Ciprofloxacine Tablets USP	1510241	1	1	0	0	1	0	0	1	0	0
Asia	China	Jiangsu Pengyao Pharmaceutical Co. Ltd.	Metronidazole	Metronidazole Tablets BP	1608262	1	1	0	0	1	0	0	1	0	0
Asia	China	Jiangsu Ruinian Qianjin Pharm. Co.Ltd	Doxycycline	Doxycycline Sprukfield	141110	2	2	0	0	2	0	0	2	0	0
Asia	China	Jiangsu Ruinian Qianjin Pharm. Co.Ltd	Ciprofloxacin	Zeprox-500	170116	2	2	0	0	2	0	0	2	0	0
Asia	China	Jiangxi Xier Kangtai Pharmaceutical Co. Ltd.	Amoxicillin	Amoxycillin Capsules	150866	1	1	0	0	1	0	0	1	0	0
Asia	China	Jiangxi Xier Kangtai Pharmaceutical Co. Ltd.	Glibenclamide	Deominal	170303	2	2	0	0	0	2	0	0	2	0

							USP assay			USP dissolution			USP assay and dissolution combined		
Stated continent of origin	Stated country of origin	Stated manufacturer	INN	Stated product name	Batchnumber	N	complies	deviation	extreme deviation	complies 2	deviation2	extreme deviation 2	complies 3	deviation 3	extreme deviation 3
Asia	China	Jiangxi Xier Kangtai Pharmaceutical Co. Ltd.	Doxycycline	Surelife Doxycyline	161109	2	2	0	0	2	0	0	2	0	0
Asia	China	Jinzhou Jiuyang Pharmaceutical Co. Ltd	Metronidazole	Metronidazole Tablets	T20160801	2	2	0	0	2	0	0	2	0	0
Asia	China	Jinzhou Jiuyang Pharmaceutical Co. Ltd	Metronidazole	Metronidazole Tablets B.P. 250mg	T21	1	1	0	0	0	0	1	0	0	1
Asia	China	JSPY Pharmaceutical Co. Ltd.	Ciprofloxacin	Ciproin - 750	160422	1	1	0	0	1	0	0	1	0	0
Asia	China	JSPY Pharmaceutical Co. Ltd.	Ciprofloxacin	Ciproinh - 500	160713	1	1	0	0	1	0	0	1	0	0
Asia	China	JSPY Pharmaceutical Co. Ltd.	Metronidazole	Metrole-500	150205	1	1	0	0	1	0	0	1	0	0
Asia	China	Nanjing Baijingyu Pharmaceutical Co. Ltd.	Doxycycline	Doxycycline Hyclate Tablets USP	DHA15007	1	1	0	0	1	0	0	1	0	0
Asia	China	Nanjing Baijingyu Pharmaceutical Co. Ltd.	Doxycycline	Doxycycline Hyclate Tablets USP	DHA17001	1	1	0	0	1	0	0	1	0	0
Asia	China	Nanjing Baijingyu Pharmaceutical Co. Ltd.	Sulfa/Trimet	Sulfamethoxazole and Trimethoprim Tablets USP	TSH15051	1	1	0	0	1	0	0	1	0	0
Asia	China	Nanjing Sino Pharmaceutical Ltd.	Amoxicillin	Amoxicillin	160103	1	1	0	0	1	0	0	1	0	0
Asia	China	Ningbo Shuangwei Pharmaceutical Co. Ltd	Amoxicillin	Amoxzem	161025	1	1	0	0	1	0	0	1	0	0
Asia	China	Ningbo Shuangwei Pharmaceutical Co. Ltd	Amoxicillin	Amoxzem	161212	1	1	0	0	1	0	0	1	0	0
Asia	China	Ningbo Shuangwei Pharmaceutical Co. Ltd	Amoxicillin	Amoxzem Tab.	151121	2	2	0	0	2	0	0	2	0	0
Asia	China	Ningbo Shuangwei Pharmaceutical Co. Ltd	Amoxicillin	Amoxzem Tab.	170617	1	1	0	0	1	0	0	1	0	0
Asia	China	Ningbo Shuangwei Pharmaceutical Co. Ltd	Metronidazole	Metrozem-500	171034	1	1	0	0	1	0	0	1	0	0
Asia	China	North China Pharmaceutical Co. Ltd.***	Penicillin V	Phenoxymethylpencillin 250mg BP	150923	1	1	0	0	1	0	0	1	0	0
Asia	China	North China Pharmaceutical Co. Ltd.***	Penicillin V	Phenoxymethylpenicillin Tablets 250mg	160334	2	2	0	0	2	0	0	2	0	0
Asia	China	North China Pharmaceutical Co. Ltd.***	Penicillin V	Phenoxymethylpenicillin Tablets BP	160405	1	1	0	0	1	0	0	1	0	0
Asia	China	North China Pharmaceutical Co. Ltd.***	Penicillin V	Phenoxymethylpenicillin Tablets BP	160906	1	1	0	0	1	0	0	1	0	0
Asia	China	North China Pharmaceutical Co. Ltd.***	Penicillin V	Phenoxymethylpenicillin Tablets BP	160907	2	2	0	0	2	0	0	2	0	0
Asia	China	North China Pharmaceutical Co. Ltd.***	Penicillin V	Phenoxymethylpenicilline	C6007	1	1	0	0	1	0	0	1	0	0
Asia	China	Reyoung Pharmaceutical Co. Ltd.	Amoxicillin	Amoxiciline Ubigen	163131260	1	1	0	0	1	0	0	1	0	0
Asia	China	Reyoung Pharmaceutical Co. Ltd.	Amoxicillin	Amoxiciline Ubigen	173132202	1	1	0	0	1	0	0	1	0	0
Asia	China	Reyoung Pharmaceutical Co. Ltd.	Amoxicillin	Amoxicillin Capsules BP	153132033	1	1	0	0	1	0	0	1	0	0

							USP assay			USP dissolution			USP assay and dissolution combined		
Stated continent of origin	Stated country of origin	Stated manufacturer	INN	Stated product name	Batchnumber	N	complies	deviation	extreme deviation	complies 2	deviation2	extreme deviation 2	complies 3	deviation 3	extreme deviation 3
Asia	China	Reyoung Pharmaceutical Co. Ltd.	Amoxicillin	Amoxicillin Capsules BP	163132143	1	1	0	0	1	0	0	1	0	0
Asia	China	Reyoung Pharmaceutical Co. Ltd.	Amoxicillin	Amoxyn-500	160863	1	1	0	0	1	0	0	1	0	0
Asia	China	Reyoung Pharmaceutical Co. Ltd.	Amoxicillin	Amoxyn-500	P6064	1	1	0	0	1	0	0	1	0	0
Asia	China	Reyoung Pharmaceutical Co. Ltd.	Ciprofloxacin	Ciprofloxacin Tablets	163121042	1	1	0	0	1	0	0	1	0	0
Asia	China	Reyoung Pharmaceutical Co. Ltd.	Ciprofloxacin	Ciprofloxacin Tablets	163121044	2	2	0	0	2	0	0	2	0	0
Asia	China	Shandong Shenglu Pharmaceutical Co. Ltd	Penicillin V	Penicillin V	20160919	3	0	0	3	0	3	0	0	0	3
Asia	China	Shandong Shenglu Pharmaceutical Co. Ltd	Penicillin V	Transglobe Pen Tabs	170310	1	0	0	1	0	1	0	0	0	1
Asia	China	Shandong Xier Kangtai Pharm Co. Ltd	Metformin	Jeo-Phage Tablets	1610110	1	1	0	0	1	0	0	1	0	0
Asia	China	Shandong Yikang Pharmaceutical Co. Ltd.	Penicillin V	Penicillin V Potassium 250mg	170322	2	1	1	0	2	0	0	1	1	0
Asia	China	Shanghai Juchen Import and Exports Co. Ltd.	Amoxicillin	Konmoxy Capsules	173131530	1	1	0	0	1	0	0	1	0	0
Asia	China	Shanghai Juchen Import and Exports Co. Ltd.	Amoxicillin	Konmoxy Capsules	173131532	1	1	0	0	1	0	0	1	0	0
Asia	China	Shanghai Juchen Import and Exports Co. Ltd.	Amoxicillin	Konmoxy Capsules	173131533	1	1	0	0	1	0	0	1	0	0
Asia	China	Shanghai Juchen Import and Exports Co. Ltd.	Metronidazole	Metronidazole Tablets	171287	1	1	0	0	1	0	0	1	0	0
Asia	China	Shanxi Lianbang Pharmaceutical Co. Ltd.	Doxycycline	Doxycycline Capsules	160565	2	2	0	0	2	0	0	2	0	0
Asia	China	Sinochem Jiangsu Co. Ltd	Amoxicillin	Amoxicillin 500mg	170710	1	1	0	0	0	1	0	0	1	0
Asia	China	Sinochem Jiangsu Co. Ltd	Amoxicillin	Amoxicillin Capsules B.P	161011	2	2	0	0	2	0	0	2	0	0
Asia	China	Sinochem Jiangsu Co. Ltd	Ciprofloxacin	Ciprofloxacine Tablets USP	160283	1	1	0	0	1	0	0	1	0	0
Asia	China	Sinochem Jiangsu Co. Ltd	Ciprofloxacin	Ciprofloxacine Tablets USP	1605603	4	3	1	0	4	0	0	3	1	0
Asia	China	Sinochem Jiangsu Co. Ltd	Ciprofloxacin	Ciprolif-500	170751	2	1	1	0	2	0	0	1	1	0
Asia	China	Sinochem Jiangsu Co. Ltd	Metronidazole	Metronidazole GP	170717	1	1	0	0	0	0	1	0	0	1
Asia	China	Sinochem Jiangsu Co. Ltd	Metronidazole	Metronidazole GP	171201	2	2	0	0	0	0	2	0	0	2
Asia	China	Sinochem Jiangsu Co. Ltd	Penicillin V	Peni-V	170504	1	1	0	0	1	0	0	1	0	0
Asia	China	Sishui xier Kang Pharmaceutical Co.Ltd	Penicillin V	Penicillin V Potassium - 5000,000	160718	1	0	0	1	0	1	0	0	0	1
Asia	China	Yanzhou Xierkangtai pharmaceutical Co. Ltd.	Amoxicillin	Amoxicillin	S37	1	1	0	0	1	0	0	1	0	0
Asia	China	Yanzhou Xierkangtai pharmaceutical Co. Ltd.	Doxycycline	Doxycycline	S06	1	1	0	0	1	0	0	1	0	0
Asia	China	Yanzhou Xierkangtai pharmaceutical Co. Ltd.	Penicillin V	Penicillin VK Tablets	S20170329	1	0	1	0	1	0	0	0	1	0
Asia	Hong Kong	Hongkong Prost Medicines And Health Products Co. Ltd.	Hydrochlorothiazide	Hydrochlorothiazide	160815	3	3	0	0	3	0	0	3	0	0

							USP assay			USP dissolution			USP assay and dissolution combined		
Stated continent of origin	**Stated country of origin**	**Stated manufacturer**	**INN**	**Stated product name**	**Batchnumber**	**N**	**complies**	**deviation**	**extreme deviation**	**complies 2**	**deviation2**	**extreme deviation 2**	**complies 3**	**deviation 3**	**extreme deviation 3**
Asia	India	Agog Pharma Ltd.	Doxycycline	Agodox	C55016	1	1	0	0	1	0	0	1	0	0
Asia	India	Agog Pharma Ltd.	Doxycycline	Agodox	C73018	1	1	0	0	1	0	0	1	0	0
Asia	India	Agog Pharma Ltd.	Sulfa/Trimet	Co-Trimoxazole Tablets BP Trimago	T64108	1	1	0	0	1	0	0	1	0	0
Asia	India	Agog Pharma Ltd.	Sulfa/Trimet	Co-Trimoxazole Tablets BP Trimago	T71155	1	1	0	0	1	0	0	1	0	0
Asia	India	Alkem Laboratories Ltd.	Amoxi/Clav	Acinet	6150096	1	1	0	0	0	1	0	0	1	0
Asia	India	Arco Pharma Pvt. Ltd	Furosemide	Frusema	562E	1	1	0	0	0	1	0	0	1	0
Asia	India	Arco Pharma Pvt. Ltd	Furosemide	Frusema	618E	3	3	0	0	1	2	0	1	2	0
Asia	India	Arco Pharma Pvt. Ltd	Furosemide	Frusema	619E	3	3	0	0	0	3	0	0	3	0
Asia	India	Asence Pharma Pvt. Ltd.	Furosemide	Furosemide Tabrad	T-799002	2	2	0	0	2	0	0	2	0	0
Asia	India	Asence Pharma Pvt. Ltd.	Metronidazole	Metronidazole 500	T-800003	1	1	0	0	1	0	0	1	0	0
Asia	India	Asence Pharma Pvt. Ltd.	Furosemide	Tafuros 40	AC25701	2	2	0	0	1	1	0	1	1	0
Asia	India	Asence Pharma Pvt. Ltd.	Amoxi/Clav	Tamclav 1G	PT7088	1	1	0	0	0	1	0	0	1	0
Asia	India	Astra Lifecare Pvt. Ltd.	Salbutamol	Asbutol-P4	023	1	1	0	0	1	0	0	1	0	0
Asia	India	Astra Lifecare Pvt. Ltd.	Doxycycline	Asdoxin	617	1	1	0	0	0	0	1	0	0	1
Asia	India	Astra Lifecare Pvt. Ltd.	Ciprofloxacin	Asflox-500	463	3	3	0	0	3	0	0	3	0	0
Asia	India	Astra Lifecare Pvt. Ltd.	Furosemide	Asix	028	1	1	0	0	1	0	0	1	0	0
Asia	India	Astra Lifecare Pvt. Ltd.	Furosemide	Asix	031	1	1	0	0	1	0	0	1	0	0
Asia	India	Astra Lifecare Pvt. Ltd.	Metronidazole	Astrogyl	497	1	1	0	0	1	0	0	1	0	0
Asia	India	Astra Lifecare Pvt. Ltd.	Penicillin V	As-V	185	1	1	0	0	1	0	0	1	0	0
Asia	India	Astra Lifecare Pvt. Ltd.	Penicillin V	As-V	187	1	1	0	0	1	0	0	1	0	0
Asia	India	Astra Lifecare Pvt. Ltd.	Atenolol	Hyperlok-100	025	1	1	0	0	0	0	1	0	0	1
Asia	India	Aura pharmaceuticals Pvt. Ltd	Sulfa/Trimet	Cotrimex-480	01	1	1	0	0	0	1	0	0	1	0
Asia	India	Aura pharmaceuticals Pvt. Ltd	Metronidazole	Megyl	006	2	2	0	0	2	0	0	2	0	0
Asia	India	Aura pharmaceuticals Pvt. Ltd	Metronidazole	Megyl	009	1	1	0	0	1	0	0	1	0	0
Asia	India	Aura pharmaceuticals Pvt. Ltd	Salbutamol	Salbutamol Tablets BP	001	5	2	3	0	5	0	0	2	3	0
Asia	India	Aurobindo Pharma Ltd.	Amoxi/Clav	Koact 625	EL5016026-D	1	1	0	0	0	1	0	0	1	0
Asia	India	Axon Drugs Pvt. Ltd.	Metformin	Asur-850	16ASU01	1	1	0	0	1	0	0	1	0	0
Asia	India	Bliss GVS Pharma Ltd.	Metformin	BGMET 850	BMT004	1	0	1	0	0	1	0	0	1	0
Asia	India	Cadila Healthcare Ltd.	Atenolol	Catenol 100	GR2742	1	1	0	0	1	0	0	1	0	0
Asia	India	Cipla Ltd.	Ciprofloxacin	Ciplox-500	ID55812	1	1	0	0	1	0	0	1	0	0
Asia	India	Ciron Drugs and Pharmaceuticals Ltd.	Metformin	Shalformin	5E01015	2	2	0	0	2	0	0	2	0	0
Asia	India	Combitic Global Caplet Pvt. Ltd.	Doxycycline	Doxynol 200	CDY-13	1	1	0	0	1	0	0	1	0	0
Asia	India	Fourrts	Sulfa/Trimet	Co-Trimoxazole Tablets BP Megatrim	C1796	1	1	0	0	1	0	0	1	0	0
Asia	India	Fourrts	Doxycycline	Doxycycline Hyclate Tablets USP	E1193	1	1	0	0	1	0	0	1	0	0
Asia	India	Fourrts	Metformin	METFIL	C0335	1	1	0	0	1	0	0	1	0	0

							USP assay			USP dissolution			USP assay and dissolution combined		
Stated continent of origin	Stated country of origin	Stated manufacturer	INN	Stated product name	Batchnumber	N	complies	deviation	extreme deviation	complies 2	deviation2	extreme deviation 2	complies 3	deviation 3	extreme deviation 3
Asia	India	Global Pharma Healthcare Pvt. Ltd.	Hydrochlorothiazide	Hydrochlorothiazide comprimes BP	TE399	4	4	0	0	4	0	0	4	0	0
Asia	India	Holden Medical Laboratories Pvt. Ltd.	Atenolol	Atenolol Tablets BP	HE15C28	1	1	0	0	1	0	0	1	0	0
Asia	India	Holden Medical Laboratories Pvt. Ltd.	Ciprofloxacin	Ciprofloxacin Tablets USP	HE16D39	1	1	0	0	1	0	0	1	0	0
Asia	India	Holden Medical Laboratories Pvt. Ltd.	Glibenclamide	Glibenclamide Tablets B.P	HE15L66	1	1	0	0	1	0	0	1	0	0
Asia	India	Intermed	Amoxi/Clav	Amoxicillin and Clavulanate Potassium Tablets	QTN02	1	1	0	0	1	0	0	1	0	0
Asia	India	Ipca Laboratories Ltd.	Amoxi/Clav	Rapiclav-1g	CIJ177040	1	1	0	0	1	0	0	1	0	0
Asia	India	J. B. Chemicals and Pharmaceuticals Ltd.	Metronidazole	Unique's Metrogyl 200	AM56004	1	1	0	0	1	0	0	1	0	0
Asia	India	Kopran Limited	Amoxicillin	AMYN-250	S3646054	1	1	0	0	1	0	0	1	0	0
Asia	India	Kopran Limited	Sulfa/Trimet	Trim - 480	K3806011	1	1	0	0	1	0	0	1	0	0
Asia	India	Leben Laboratories Pvt. Ltd	Doxycycline	Doxyleb	C137	1	1	0	0	1	0	0	1	0	0
Asia	India	Lincoln Pharmaceuticals Ltd.	Doxycycline	Alldox	AA5006	1	1	0	0	1	0	0	1	0	0
Asia	India	Lincoln Pharmaceuticals Ltd.	Doxycycline	Alldox	AA7001	1	1	0	0	1	0	0	1	0	0
Asia	India	Lincoln Pharmaceuticals Ltd.	Ciprofloxacin	CEEPRO-500	DY6028	1	1	0	0	1	0	0	1	0	0
Asia	India	Lincoln Pharmaceuticals Ltd.	Ciprofloxacin	Ciprofloxacine Ubigen	GK6007	1	1	0	0	1	0	0	1	0	0
Asia	India	Lincoln Pharmaceuticals Ltd.	Ciprofloxacin	Ciprofloxacine Ubigen	GK7010	1	1	0	0	1	0	0	1	0	0
Asia	India	Lincoln Pharmaceuticals Ltd.	Sulfa/Trimet	Cotrimoxazole Ubigen	GM6006	2	2	0	0	2	0	0	2	0	0
Asia	India	Lincoln Pharmaceuticals Ltd.	Sulfa/Trimet	Sulphatrim	NE6004	1	1	0	0	1	0	0	1	0	0
Asia	India	Lord Lifescience Pvt. Ltd.	Salbutamol	Salbesone	HONO	1	0	1	0	1	0	0	0	1	0
Asia	India	Macleods Pharmaceuticals Ltd.	Ciprofloxacin	Coflox-500	FCF657A	1	1	0	0	1	0	0	1	0	0
Asia	India	Macleods Pharmaceuticals Ltd.	Ciprofloxacin	Coflox-500	FCF659A	1	1	0	0	1	0	0	1	0	0
Asia	India	Macleods Pharmaceuticals Ltd.	Sulfa/Trimet	Co-trimoxazole Tablets BP 480mg	1708	1	1	0	0	1	0	0	1	0	0
Asia	India	Macleods Pharmaceuticals Ltd.	Sulfa/Trimet	Co-trimoxazole Tablets BP 480mg	HTF713A	1	1	0	0	1	0	0	1	0	0
Asia	India	Mancare pharmaceutical Ltd	Furosemide	Frunmide	TPF03	1	1	0	0	1	0	0	1	0	0
Asia	India	Mancare pharmaceutical Ltd	Furosemide	Frunmide	TRI18	1	1	0	0	1	0	0	1	0	0
Asia	India	Mancare pharmaceutical Ltd	Furosemide	Lancize	TRF28	1	1	0	0	1	0	0	1	0	0
Asia	India	Mancare pharmaceutical Ltd	Furosemide	Lancize	TRF32	1	1	0	0	1	0	0	1	0	0
Asia	India	Maneesh Pharmaceuticals Ltd	Doxycycline	Doxycycline Tablets	S01	1	1	0	0	1	0	0	1	0	0
Asia	India	Maxheal Laboratories Pvt. Ltd.	Salbutamol	Salbutamol	SW7003	1	0	1	0	0	1	0	0	1	0
Asia	India	Maxheal Laboratories Pvt. Ltd.	Ciprofloxacin	Wincip-500	WC6001	1	1	0	0	1	0	0	1	0	0
Asia	India	Maxtar Bio-Genics	Sulfa/Trimet	Cotrimoxazole Pextran_SS	MT4T-1601	2	2	0	0	0	2	0	0	2	0
Asia	India	Maxtar Bio-Genics	Metformin	Maxformin-500	MT3M-1602	1	1	0	0	1	0	0	1	0	0
Asia	India	Maxtar Bio-Genics	Metformin	Maxformin-500	MT3M-1607	1	1	0	0	1	0	0	1	0	0
Asia	India	Maxtar Bio-Genics	Metformin	Maxformin-500	MXTEJ1701	1	1	0	0	1	0	0	1	0	0

							USP assay			USP dissolution			USP assay and dissolution combined		
Stated continent of origin	Stated country of origin	Stated manufacturer	INN	Stated product name	Batchnumber	N	complies	deviation	extreme deviation	complies 2	deviation2	extreme deviation 2	complies 3	deviation 3	extreme deviation 3
Asia	India	Maxtar Bio-Genics	Metronidazole	Metzole-500	MT7T-1601	2	2	0	0	2	0	0	2	0	0
Asia	India	Maxtar Bio-Genics	Salbutamol	Salbutamol Comprimes BP	MTSA-1402	3*	0	0	3*	0	0	3*	0	0	3*
Asia	India	Maxtar Bio-Genics	Salbutamol	Salbutamol Comprimes BP	MTSA-1602	4	4	0	0	4	0	0	4	0	0
Asia	India	Medicamen Biotech Ltd.	Ciprofloxacin	Ciprofloxacine USP 500 mg	NT6698	1	1	0	0	1	0	0	1	0	0
Asia	India	Medicamen Biotech Ltd.	Doxycycline	Doxycycline Hyclate	NT7540	1	1	0	0	1	0	0	1	0	0
Asia	India	Medicamen Biotech Ltd.	Glibenclamide	Glibenclamide	NT5047	1	1	0	0	1	0	0	1	0	0
Asia	India	Medicamen Biotech Ltd.	Glibenclamide	Glibenclamide	NT5048	2	2	0	0	2	0	0	2	0	0
Asia	India	Medicamen Biotech Ltd.	Metformin	Metformin	NT5524	1	1	0	0	1	0	0	1	0	0
Asia	India	Medicamen Biotech Ltd.	Metformin	Metformin	NT5525	1	1	0	0	0	1	0	0	1	0
Asia	India	Medicamen Biotech Ltd.	Metronidazole	Metronidazole	NT5371	1	1	0	0	1	0	0	1	0	0
Asia	India	Medicef Pharma	Amoxi/Clav	Arauclav	ET16G014	1	1	0	0	1	0	0	1	0	0
Asia	India	Medicef Pharma	Amoxi/Clav	Moxyclav	ET16E008	1	1	0	0	1	0	0	1	0	0
Asia	India	Medicef Pharma	Amoxi/Clav	Moxyclav	ET16G010	1	1	0	0	1	0	0	1	0	0
Asia	India	Medicef Pharma	Amoxi/Clav	Moxyclav	ET16G020	1	1	0	0	1	0	0	1	0	0
Asia	India	Medico Remedies Pvt. Ltd.	Salbutamol	Salbutamol Tablets BP	SAU513	2	0	0	2	0	2	0	0	0	2
Asia	India	Medico Remedies Pvt. Ltd.	Salbutamol	Salbutamol Tablets BP	SAU537	1	0	0	1	1	0	0	0	0	1
Asia	India	Medico Remedies Pvt. Ltd.	Salbutamol	Salbutamol Tablets BP	SAU602	1	0	1	0	0	1	0	0	1	0
Asia	India	Medico Remedies Pvt. Ltd.	Salbutamol	Salbutamol Tablets BP	SAU630	1	0	0	1	1	0	0	0	0	1
Asia	India	Medley Pharmaceuticals Ltd.	Ciprofloxacin	Ecoflox-500	D60130	1	1	0	0	1	0	0	1	0	0
Asia	India	Medley Pharmaceuticals Ltd.	Ciprofloxacin	Ecoflox-500	D60184	1	1	0	0	1	0	0	1	0	0
Asia	India	Medley Pharmaceuticals Ltd.	Ciprofloxacin	Ecoflox-500	D60246	1	1	0	0	1	0	0	1	0	0
Asia	India	Medley Pharmaceuticals Ltd.	Ciprofloxacin	Ecoflox-500	D60263	1	1	0	0	1	0	0	1	0	0
Asia	India	Medley Pharmaceuticals Ltd.	Ciprofloxacin	Ecoflox-500	D60445	1	1	0	0	1	0	0	1	0	0
Asia	India	Medopharm Pvt. Ltd.	Amoxi/Clav	Amoxicillin 500mg + Clavulanic acid 125mg BP	F456733	1	1	0	0	1	0	0	1	0	0
Asia	India	Medopharm Pvt. Ltd.	Amoxicillin	Amoxicillin Gelules	1475017	1	1	0	0	1	0	0	1	0	0
Asia	India	Medopharm Pvt. Ltd.	Amoxicillin	Amoxicillin Tablets USP 250	15329002	1	1	0	0	1	0	0	1	0	0
Asia	India	Medopharm Pvt. Ltd.	Amoxicillin	Amoxicillin Tablets USP 500	16144002	1	1	0	0	1	0	0	1	0	0
Asia	India	Medopharm Pvt. Ltd.	Amoxicillin	Amoxicillin Tablets USP 500	16363002	1	1	0	0	1	0	0	1	0	0
Asia	India	Medopharm Pvt. Ltd.	Ciprofloxacin	Ciprofloxacine 500 mg USP	5E 101	1	1	0	0	1	0	0	1	0	0
Asia	India	Medopharm Pvt. Ltd.	Ciprofloxacin	Ciprofloxacine Comprimes USP	217090001	1	1	0	0	1	0	0	1	0	0
Asia	India	Medopharm Pvt. Ltd.	Ciprofloxacin	Ciprofloxacine Comprimes USP	6C66	1	1	0	0	1	0	0	1	0	0
Asia	India	Medopharm Pvt. Ltd.	Ciprofloxacin	Ciprofloxacine Comprimes USP	6C67	2	2	0	0	2	0	0	2	0	0
Asia	India	Medopharm Pvt. Ltd.	Amoxi/Clav	Clavumoccid	16213003	1	1	0	0	1	0	0	1	0	0
Asia	India	Medopharm Pvt. Ltd.	Amoxi/Clav	Cledomox 562.5	17361003	1	0	1	0	1	0	0	0	1	0
Asia	India	Medopharm Pvt. Ltd.	Amoxi/Clav	Co-amoxiclav	1680002	1	1	0	0	1	0	0	1	0	0
Asia	India	Medopharm Pvt. Ltd.	Sulfa/Trimet	Co-trimoxazole BP	4J32	1	1	0	0	1	0	0	1	0	0
Asia	India	Medopharm Pvt. Ltd.	Sulfa/Trimet	Co-trimoxazole BP	4J34	1	1	0	0	1	0	0	1	0	0
Asia	India	Medopharm Pvt. Ltd.	Sulfa/Trimet	Co-trimoxazole BP	4MB107	1	1	0	0	1	0	0	1	0	0
Asia	India	Medopharm Pvt. Ltd.	Sulfa/Trimet	Co-trimoxazole BP	6MD354	1	1	0	0	1	0	0	1	0	0
Asia	India	Medopharm Pvt. Ltd.	Sulfa/Trimet	Co-trimoxazole BP	6MD360	1	1	0	0	1	0	0	1	0	0
Asia	India	Medopharm Pvt. Ltd.	Sulfa/Trimet	Co-trimoxazole BP	6MD364	2	2	0	0	2	0	0	2	0	0
Asia	India	Medopharm Pvt. Ltd.	Sulfa/Trimet	Co-trimoxazole BP	6MG195	1	1	0	0	1	0	0	1	0	0

							USP assay			USP dissolution			USP assay and dissolution combined		
Stated continent of origin	Stated country of origin	Stated manufacturer	INN	Stated product name	Batchnumber	N	complies	deviation	extreme deviation	complies 2	deviation2	extreme deviation 2	complies 3	deviation 3	extreme deviation 3
Asia	India	Medopharm Pvt. Ltd.	Sulfa/Trimet	Co-trimoxazole BP	6MG198	1	1	0	0	1	0	0	1	0	0
Asia	India	Medopharm Pvt. Ltd.	Sulfa/Trimet	Co-trimoxazole USP	XN150772	1	1	0	0	1	0	0	1	0	0
Asia	India	Medopharm Pvt. Ltd.	Doxycycline	Doxycycline Hyclate USP	4MJ124	1	1	0	0	1	0	0	1	0	0
Asia	India	Medopharm Pvt. Ltd.	Doxycycline	Doxycycline Hyclate USP	5MH47	1	1	0	0	1	0	0	1	0	0
Asia	India	Medopharm Pvt. Ltd.	Doxycycline	Doxycycline Hyclate USP	5MJ146	2	2	0	0	2	0	0	2	0	0
Asia	India	Medopharm Pvt. Ltd.	Penicillin V	Fenoximetilpenicilina	1208524	1	1	0	0	1	0	0	1	0	0
Asia	India	Medopharm Pvt. Ltd.	Furosemide	Furosemid BP	4MJ129	1	1	0	0	1	0	0	1	0	0
Asia	India	Medopharm Pvt. Ltd.	Doxycycline	Generic Plus Doxycycline Hyclate 100mg USP	6MF123	2	2	0	0	2	0	0	2	0	0
Asia	India	Medopharm Pvt. Ltd.	Metformin	Metformin Tablets 500 mg BP	7MA42	1	1	0	0	1	0	0	1	0	0
Asia	India	Medopharm Pvt. Ltd.	Metronidazole	Metronidazole	4MJ164	1	1	0	0	1	0	0	1	0	0
Asia	India	Medopharm Pvt. Ltd.	Metronidazole	Metronidazole 250 mg BP	5B07	1	1	0	0	1	0	0	1	0	0
Asia	India	Medopharm Pvt. Ltd.	Metronidazole	Metronidazole 250 mg BP	5F42	1	1	0	0	0	1	0	0	1	0
Asia	India	Medopharm Pvt. Ltd.	Metronidazole	Metronidazole 250 mg BP	5MA91	2	2	0	0	2	0	0	2	0	0
Asia	India	Medopharm Pvt. Ltd.	Metronidazole	Metronidazole 250 mg BP	5ME187	1	1	0	0	1	0	0	1	0	0
Asia	India	Medopharm Pvt. Ltd.	Salbutamol	Salbutamol Tablets BP	6MF93	2	2	0	0	2	0	0	2	0	0
Asia	India	Medopharm Pvt. Ltd.	Salbutamol	Salbutamol Tablets BP	6MF94	2	2	0	0	2	0	0	2	0	0
Asia	India	Mepro Pharmaceuticals Pvt. Ltd.	Ciprofloxacin	Ciprofloxacin	UCP224	1	1	0	0	1	0	0	1	0	0
Asia	India	Mepro Pharmaceuticals Pvt. Ltd.	Doxycycline	Doxycycline	UDH220	1	1	0	0	1	0	0	1	0	0
Asia	India	Micro Labs Ltd.	Furosemide	Furosemide 40mg BP	FRIH0077	4	4	0	0	4	0	0	4	0	0
Asia	India	Milan Laboratories (India) Pvt. Ltd	Sulfa/Trimet	Co-Trimoxazole	MG16041	1	1	0	0	1	0	0	1	0	0
Asia	India	Milan Laboratories (India) Pvt. Ltd	Amoxicillin	Miloxy 250	MP17005	1	1	0	0	1	0	0	1	0	0
Asia	India	Milan Laboratories (India) Pvt. Ltd	Amoxicillin	Miloxy 250	MP17069	1	1	0	0	1	0	0	1	0	0
Asia	India	Milan Laboratories (India) Pvt. Ltd	Amoxicillin	Miloxy 250	MP17210	1	1	0	0	1	0	0	1	0	0
Asia	India	Milan Laboratories (India) Pvt. Ltd	Amoxicillin	Miloxy 250	MP17258	1	1	0	0	1	0	0	1	0	0
Asia	India	Milan Laboratories (India) Pvt. Ltd	Penicillin V	Penicillin-Tablets	MP0268	1	0	1	0	1	0	0	0	1	0
Asia	India	Nem Laboratories Pvt. Ltd.	Furosemide	Frusemide	FRS615	1	1	0	0	1	0	0	1	0	0
Asia	India	not stated	Amoxi/Clav	Oxynic	B1730	1	1	0	0	1	0	0	1	0	0
Asia	India	Osaka Pharmaceuticals Pvt. Ltd.	Glibenclamide	Transglobe glibenclamide	6A038	3	1	2	0	3	0	0	1	2	0
Asia	India	PIL Pharmaceuticals Pvt. Ltd.	Amoxi/Clav	Co-amoxiclav Tablets BP 625mg	AAGB6027	1	1	0	0	1	0	0	1	0	0
Asia	India	Prashi Pharma Pvt. Ltd	Furosemide	Frusemide	FR-01	2	2	0	0	0	1	1	0	1	1
Asia	India	Prashi Pharma Pvt. Ltd	Furosemide	Frusemide	FR-02	2	2	0	0	0	2	0	0	2	0
Asia	India	Prashi Pharma Pvt. Ltd	Furosemide	Frusemide	FR-03	1	1	0	0	0	1	0	0	1	0
Asia	India	Prashi Pharma Pvt. Ltd	Metronidazole	Metro 250	MT-133	1	1	0	0	1	0	0	1	0	0
Asia	India	Shalina Laboratories Pvt. Ltd.	Sulfa/Trimet	Sulfatrim	J7007	1	1	0	0	1	0	0	1	0	0
Asia	India	Sparsh Bio-Tech Pvt. Ltd.	Amoxicillin	HIPEN	HC225	1	1	0	0	1	0	0	1	0	0

							USP assay			USP dissolution			USP assay and dissolution combined		
Stated continent of origin	Stated country of origin	Stated manufacturer	INN	Stated product name	Batchnumber	N	complies	deviation	extreme deviation	complies 2	deviation2	extreme deviation 2	complies 3	deviation 3	extreme deviation 3
Asia	India	Sparsh Bio-Tech Pvt. Ltd.	Amoxicillin	HIPEN	HC232	1	1	0	0	1	0	0	1	0	0
Asia	India	Sparsh Bio-Tech Pvt. Ltd.	Penicillin V	Speniv Tablets 250	PT448	1	1	0	0	1	0	0	1	0	0
Asia	India	Sparsh Bio-Tech Pvt. Ltd.	Penicillin V	Speniv Tablets 250	PT457	1	1	0	0	1	0	0	1	0	0
Asia	India	Sparsh Bio-Tech Pvt. Ltd.	Penicillin V	Speniv Tablets 250	PT460	1	1	0	0	1	0	0	1	0	0
Asia	India	Sparsh Bio-Tech Pvt. Ltd.	Penicillin V	Speniv Tablets 250	PT467	2	2	0	0	2	0	0	2	0	0
Asia	India	Strides Arcolab Limited	Amoxicillin	Amoxicillin Tablets	AG-044	1	1	0	0	1	0	0	1	0	0
Asia	India	Strides Arcolab Limited	Amoxicillin	Amoxicillin Tablets	AG-064	1	1	0	0	1	0	0	1	0	0
Asia	India	Strides Arcolab Limited	Ciprofloxacin	Ciprofloxacine Tablets USP	7750797	1	1	0	0	1	0	0	1	0	0
Asia	India	Strides Arcolab Limited	Ciprofloxacin	Ciprofloxacine Tablets USP	7750816	1	1	0	0	1	0	0	1	0	0
Asia	India	Strides Arcolab Limited	Sulfa/Trimet	Co-trimoxazole Tablets BP	7750175	1	1	0	0	1	0	0	1	0	0
Asia	India	Strides Arcolab Limited	Sulfa/Trimet	Co-trimoxazole Tablets BP	7750676	1	1	0	0	1	0	0	1	0	0
Asia	India	Strides Arcolab Limited	Sulfa/Trimet	Co-trimoxazole Tablets BP	7750677	1	1	0	0	1	0	0	1	0	0
Asia	India	Strides Arcolab Limited	Sulfa/Trimet	Co-trimoxazole Tablets BP	7750714	1	1	0	0	1	0	0	1	0	0
Asia	India	Strides Arcolab Limited	Sulfa/Trimet	Co-trimoxazole Tablets BP	7750718	1	1	0	0	1	0	0	1	0	0
Asia	India	Strides Arcolab Limited	Sulfa/Trimet	Co-trimoxazole Tablets BP	7750719	1	1	0	0	1	0	0	1	0	0
Asia	India	Strides Arcolab Limited	Furosemide	Frusemide BP	7351588	2	1	1	0	1	1	0	0	2	0
Asia	India	Strides Arcolab Limited	Metformin	Metformin Tablets BP	7351219	1	1	0	0	1	0	0	1	0	0
Asia	India	Strides Arcolab Limited	Metformin	Metformin Tablets BP	7351823	1	1	0	0	1	0	0	1	0	0
Asia	India	Strides Arcolab Limited	Metformin	Metformin Tablets BP	7351824	1	1	0	0	1	0	0	1	0	0
Asia	India	Strides Arcolab Limited	Metronidazole	Metronidazole Comprimes BP	7750163	1	1	0	0	1	0	0	1	0	0
Asia	India	Strides Arcolab Limited	Metronidazole	Metronidazole Comprimes BP	7750581	2	2	0	0	2	0	0	2	0	0
Asia	India	Strides Arcolab Limited	Metronidazole	Metronidazole Comprimes BP	7750973	1	1	0	0	1	0	0	1	0	0
Asia	India	Strides Arcolab Limited	Metronidazole	Metronidazole Comprimes BP	7751013	1	1	0	0	1	0	0	1	0	0
Asia	India	Strides Arcolab Limited	Metronidazole	Metronidazole Comprimes BP	7751017	1	1	0	0	1	0	0	1	0	0
Asia	India	Strides Arcolab Limited	Metronidazole	Metronidazole Comprimes BP	7751018	1	1	0	0	1	0	0	1	0	0
Asia	India	Strides Arcolab Limited	Metronidazole	Metronidazole Comprimes BP	7751038	1	1	0	0	1	0	0	1	0	0
Asia	India	Strides Shasun Limited	Ciprofloxacin	Ciprofloxacine	7352249	1	1	0	0	1	0	0	1	0	0
Asia	India	Strides Shasun Limited	Doxycycline	Doxycycline Gelules BP	7750636	4	4	0	0	4	0	0	4	0	0
Asia	India	Strides Shasun Limited	Metformin	Metformin	7352132	2	2	0	0	2	0	0	2	0	0
Asia	India	Strides Shasun Limited	Metronidazole	Metrosim-200	7351898	1	0	1	0	1	0	0	0	1	0
Asia	India	Strides Shasun Limited	Metronidazole	Metrosim-200	7352023	1	1	0	0	1	0	0	1	0	0
Asia	India	Strides Shasun Limited	Metronidazole	Metrosim-200	7352053	1	1	0	0	1	0	0	1	0	0
Asia	India	Strides Shasun Limited	Metronidazole	Metrosim-200	7352173	1	0	1	0	1	0	0	0	1	0
Asia	India	Triveni Formulations Limited	Doxycycline	Doxycycline Capsules B.P	WF607	1	1	0	0	1	0	0	1	0	0
Asia	India	Ultra Care International	Sulfa/Trimet	Cotrimoxazole Tablets B.P	UT035	2	2	0	0	2	0	0	2	0	0
Asia	India	UMEDICA Laboratories	Glibenclamide	Glibenclamide	NB502	1	1	0	0	1	0	0	1	0	0
Asia	India	Zee Laboratories	Amoxicillin	Monamox-250 DT	416-170	1	1	0	0	1	0	0	1	0	0
Asia	India	ZIM Laboratories Ltd.	Atenolol	Atenolol Tablets BP	FO38J601	1	1	0	0	1	0	0	1	0	0
Asia	Sultanat of Oman	National Pharmaceutical Industries Co. (SAOG)	Ciprofloxacin	Omacip 500	2016312	1	1	0	0	1	0	0	1	0	0
Asia	Turkey	Bilim Pharmaceuticals	Amoxi/Clav	Klacin BID	16256320A	1	1	0	0	1	0	0	1	0	0
Europe	Austria	Sandoz	Amoxicillin	Amoxycillin Sandoz	GM3744	1	1	0	0	1	0	0	1	0	0
Europe	Austria	Sandoz	Amoxicillin	Amoxycillin Sandoz	HD4437	1	1	0	0	1	0	0	1	0	0
Europe	Austria	Sandoz	Amoxicillin	Amoxycillin Sandoz	HD4445	1	1	0	0	1	0	0	1	0	0
Europe	Austria	Sandoz	Amoxi/Clav	Curam 625	FL5158	1	1	0	0	1	0	0	1	0	0
Europe	Austria	Sandoz	Penicillin V	Ospen	GM5718	1	1	0	0	1	0	0	1	0	0

							USP assay			USP dissolution			USP assay and dissolution combined		
Stated continent of origin	**Stated country of origin**	**Stated manufacturer**	**INN**	**Stated product name**	**Batchnumber**	**N**	**complies**	**deviation**	**extreme deviation**	**complies 2**	**deviation2**	**extreme deviation 2**	**complies 3**	**deviation 3**	**extreme deviation 3**
Europe	Austria	Sandoz	Penicillin V	Ospen	GY5549	2	2	0	0	2	0	0	2	0	0
Europe	Austria	Sandoz	Penicillin V	Ospen	HC8534	1	1	0	0	1	0	0	1	0	0
Europe	Austria	Sandoz	Penicillin V	Ospen	HK8732	1	1	0	0	1	0	0	1	0	0
Europe	Austria	Sandoz	Penicillin V	Starpen	GH3937	1	1	0	0	1	0	0	1	0	0
Europe	Belgium	Merck	Metformin	Glucophage	18664	1	1	0	0	1	0	0	1	0	0
Europe	Belgium	Merck	Metformin	Glucophage	18670	1	1	0	0	1	0	0	1	0	0
Europe	Belgium	Merck	Metformin	Glucophage	F0471	1	1	0	0	1	0	0	1	0	0
Europe	Belgium	Oxford Pharma	Penicillin V	Penicillin-V Tablets	190	1	0	0	1 [§]	0	0	1 [§]	0	0	1 [§]
Europe	Cyprus	Medochemie Ltd.	Amoxi/Clav	Moxiclav 1g	PE042	1	1	0	0	1	0	0	1	0	0
Europe	Cyprus	Medochemie Ltd.	Amoxi/Clav	Moxiclav 625mg	P9H020	1	1	0	0	1	0	0	1	0	0
Europe	Cyprus	Remedica Ltd	Metformin	Glyformin 500	67721	1	1	0	0	1	0	0	1	0	0
Europe	Cyprus	Remedica Ltd	Metformin	Glyformin 500	68397	1	1	0	0	1	0	0	1	0	0
Europe	France	Famar Lyon	Metformin	Glucophage 500 mg	F0554	1	1	0	0	1	0	0	1	0	0
Europe	France	Glaxo Welcome Production	Amoxi/Clav	Augmentin Adultes	2478	1	1	0	0	1	0	0	1	0	0
Europe	France	Glaxo Welcome Production	Amoxi/Clav	Augmentin Adultes	HN8F	2	2	0	0	2	0	0	2	0	0
Europe	France	Laboratoire Bailly-Creat	Sulfa/Trimet	Cotrim Fort	CR479	1	1	0	0	1	0	0	1	0	0
Europe	France	Laboratoire Bailly-Creat	Metronidazole	Creazol	124	1	1	0	0	1	0	0	1	0	0
Europe	France	Laboratoire Bailly-Creat	Doxycycline	Doxycreat	45	1	1	0	0	1	0	0	1	0	0
Europe	France	Laboratoire Bailly-Creat	Doxycycline	Doxycreat	47	1	1	0	0	1	0	0	1	0	0
Europe	France	Laboratoire Bailly-Creat	Doxycycline	Doxycreat	50	1	1	0	0	1	0	0	1	0	0
Europe	France	Laboratoire Bailly-Creat	Doxycycline	Doxycreat	51	1	1	0	0	1	0	0	1	0	0
Europe	France	Laboratoires Bailleul	Doxycycline	Tolexine Ge	T1701500	1	1	0	0	1	0	0	1	0	0
Europe	France	Sanofi-Winthrop Industrie	Glibenclamide	Daonil	6LP5A	1	1	0	0	1	0	0	1	0	0
Europe	France	Sanofi-Winthrop Industrie	Glibenclamide	Daonil	7M74A	1	1	0	0	1	0	0	1	0	0
Europe	France	Sanofi-Winthrop Industrie	Glibenclamide	Daonil	7M74E	1	1	0	0	1	0	0	1	0	0
Europe	France	Sanofi-Winthrop Industrie	Furosemide	Lasilix 40 mg	6NV5A	1	1	0	0	1	0	0	1	0	0
Europe	France	Sanofi-Winthrop Industrie	Furosemide	Lasilix 40 mg	7KF7A	1	1	0	0	1	0	0	1	0	0
Europe	France	Sanofi-Winthrop Industrie	Furosemide	Lasilix 40 mg	7M33F	1	1	0	0	1	0	0	1	0	0
Europe	Germany	Aspen Bad Oldesloe GmbH	Salbutamol	Ventoline	G3415	1	1	0	0	1	0	0	1	0	0
Europe	Germany	Berlin Chemie	Sulfa/Trimet	Berlocid	61001	1	1	0	0	1	0	0	1	0	0
Europe	Germany	Denk Pharma GmbH & Co. KG	Amoxi/Clav	AmoxiClav-Denk	19694	1	1	0	0	1	0	0	1	0	0
Europe	Germany	Denk Pharma GmbH & Co. KG	Amoxi/Clav	AmoxiClav-Denk	20014	1	1	0	0	1	0	0	1	0	0
Europe	Germany	Denk Pharma GmbH & Co. KG	Amoxi/Clav	AmoxiClav-Denk	20517	1	0	1	0	1	0	0	0	1	0
Europe	Germany	Denk Pharma GmbH & Co. KG	Amoxi/Clav	AmoxiClav-Denk	20518	2	1	1	0	2	0	0	1	1	0
Europe	Germany	Denk Pharma GmbH & Co. KG	Atenolol	Atenolol Denk	3231	1	1	0	0	1	0	0	1	0	0
Europe	Germany	Denk Pharma GmbH & Co. KG	Metformin	Metformin Denk	19965	1	1	0	0	1	0	0	1	0	0
Europe	Germany	Denk Pharma GmbH & Co. KG	Metformin	Metformin Denk	20384	1	1	0	0	1	0	0	1	0	0
Europe	Germany	Denk Pharma GmbH & Co. KG	Metformin	Metformin Denk	95H	1	1	0	0	1	0	0	1	0	0

							USP assay			USP dissolution			USP assay and dissolution combined		
Stated continent of origin	**Stated country of origin**	**Stated manufacturer**	**INN**	**Stated product name**	**Batchnumber**	**N**	**complies**	**deviation**	**extreme deviation**	**complies 2**	**deviation2**	**extreme deviation 2**	**complies 3**	**deviation 3**	**extreme deviation 3**
Europe	Germany	Denk Pharma GmbH & Co. KG	Metformin	Metformin Denk	9C7	2	2	0	0	2	0	0	2	0	0
Europe	Germany	Denk Pharma GmbH & Co. KG	Metformin	Metformin Denk	9DE	1	1	0	0	1	0	0	1	0	0
Europe	Germany	Salutas Pharma GmbH	Hydrochlorothiazide	Novartis Access Hydrochlorothiazide	GN5244	2	2	0	0	2	0	0	2	0	0
Europe	Italy	Errekappa Euroterapici S.p.A	Atenolol	Atenol	0008639	1	1	0	0	1	0	0	1	0	0
Europe	Italy	Laboratori Guidotti S.p.A	Metformin	Metforal	58042	1	1	0	0	1	0	0	1	0	0
Europe	Spain	Ferrer Internacional S.A.	Glibenclamide	Glidiabet	J010	1	1	0	0	1	0	0	1	0	0
Europe	Spain	Ferrer Internacional S.A.	Glibenclamide	Glidiabet	J011	1	1	0	0	1	0	0	1	0	0
Europe	Spain	Ferrer Internacional S.A.	Glibenclamide	Glidiabet	J012	1	1	0	0	1	0	0	1	0	0
Europe	Spain	Novartis Farmacéutica S.A.	Hydrochlorothiazide	Esidrex	B1789	1	1	0	0	1	0	0	1	0	0
Europe	Spain	Novartis Farmacéutica S.A.	Hydrochlorothiazide	Esidrex	BA453	1	1	0	0	1	0	0	1	0	0
Europe	Spain	Novartis Farmacéutica S.A.	Hydrochlorothiazide	Esidrex	BJ475	2	2	0	0	2	0	0	2	0	0
Europe	Spain	Novartis Farmacéutica S.A.	Hydrochlorothiazide	Esidrex	BL800	1	1	0	0	1	0	0	1	0	0
Europe	Spain	Novartis Farmacéutica S.A.	Hydrochlorothiazide	Esidrex	BL801	2	2	0	0	2	0	0	2	0	0
Europe	Spain	Novartis Farmacéutica S.A.	Hydrochlorothiazide	Esidrex	BR630	1	1	0	0	1	0	0	1	0	0
Europe	Spain	Novartis Farmacéutica S.A.	Hydrochlorothiazide	Esidrex	BR631	1	1	0	0	1	0	0	1	0	0
Europe	Spain	Novartis Farmacéutica S.A.	Hydrochlorothiazide	Esidrex	BT359	1	1	0	0	1	0	0	1	0	0
Europe	Spain	Novartis Farmacéutica S.A.	Hydrochlorothiazide	Esidrex	BT900	1	1	0	0	1	0	0	1	0	0
Europe	Spain	Novartis Farmacéutica S.A.	Hydrochlorothiazide	Esidrex	BV229	1	1	0	0	1	0	0	1	0	0
Europe	Spain	Novartis Farmacéutica S.A.	Hydrochlorothiazide	Esidrex	BV384	1	1	0	0	1	0	0	1	0	0
Europe	Spain	Novartis Farmacéutica S.A.	Hydrochlorothiazide	Esidrex	BV831	1	1	0	0	1	0	0	1	0	0
Europe	Sweden	Bluefish Pharmaceuticals AD	Metformin	Metformina Bluefish	5150657	1	1	0	0	1	0	0	1	0	0
Europe	United Kingdom	SmithKline Beecham Pharmaceuticals	Amoxi/Clav	Augmentin	562626	1	0	0	1 [§]	0	0	1 [§]	0	0	1 [§]
Europe	United Kingdom	Sonmart Pharma (UK)	Doxycycline	Doxycycline Capsules	170821	2	2	0	0	2	0	0	2	0	0
Europe	United Kingdom	Sonmart Pharma (UK)	Metformin	Metformin Tablets	170820	2	2	0	0	2	0	0	2	0	0
Europe	United Kingdom	Sonmart Pharma (UK)	Metronidazole	Metronidazole Tablets 250mg	170832	1	1	0	0	1	0	0	1	0	0
Europe	United Kingdom	Sonmart Pharma (UK)	Amoxicillin	Sonmamox Amoxicilline 500mg	170801	1	1	0	0	1	0	0	1	0	0

							USP assay			USP dissolution			USP assay and dissolution combined		
Stated continent of origin	**Stated country of origin**	**Stated manufacturer**	**INN**	**Stated product name**	**Batchnumber**	**N**	**complies**	**deviation**	**extreme deviation**	**complies 2**	**deviation2**	**extreme deviation 2**	**complies 3**	**deviation 3**	**extreme deviation 3**
not stated	not stated	Cinpharm **	Amoxi/Clav	Cinclamox	DW3311	2	2	0	0	2	0	0	2	0	0
not stated	not stated	Cinpharm **	Amoxi/Clav	Cinclamox	DW3312	1	1	0	0	1	0	0	1	0	0
not stated	not stated	not stated	Amoxicillin	Filmox 500	SAECB002	1	1	0	0	1	0	0	1	0	0
not stated	not stated	not stated	Salbutamol	not stated	not stated	1	0	1	0	1	0	0	0	1	0