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Quality assessment of common anti-malarial medicines marketed in Gambella, National Regional State, South Western-Ethiopia

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Abstract

Background Over the past years, there has been a growing concern that a considerable amount of anti-malarial supply in the underdeveloped world particularly in the private sector, is of poor quality. The World Health Organization (WHO) has received about 1500 reports that mentions instances of substandard and falsified products since 2013. The majority of the reports concerned antibiotics and anti-malarials. The majority of reports (42%) originate from the WHO African region.

Objective This study intends to assess the quality of the most widely used anti-malarial medications [artemether-lumefantrine tablets, chloroquine phosphate tablets, primaquine phosphate tablets, artesunate, and artemether injections] in Gambella, South-West, Ethiopia.

Methods A total of 52 samples were collected on June 2022 from Gambella National Regional State, Ethiopia. Half of the districts (six) located in the four zones of the region were chosen using simple random sampling technique. All drug retail outlets available in the selected districts (locally known as woredas) were included. The samples were subjected to visual inspection with a tool adopted from the joint WHO/FIP/ USP checklist. The pharmacopeial tests for identification, uniformity of dosage forms, assay, thickness, diameter, hardness, friability, disintegration test, dissolution, and sterility tests were carried out according to the USP 44-NF 39 and International Pharmacopoeia 11th edition, 2022 monographs.

Results and Discussion Only 25% of the samples were registered on the Ethiopian Food and Drug Authority (EFDA's) electronic regulatory/ registration system (ERIS). Besides, 88.8% of artemether injection products were presented in clear glass ampoules. This might expose the products to photochemical degradation that leads to in loss of anti-plasmodial activity. In addition, 50% of the artemether products assessed were not bioequivalent with the comparator product in the *in vitro* dissolution comparison tests. Overall, the study findings reveal a high prevalence (58.3%) of substandard anti-malarial drugs in the region. The stated percent of the samples had failed in one or more of the quality test parameters assessed in this study.

Conclusion The study findings reveal a high prevalence (58.3%) of substandard anti-malarial drugs in the region. Only a quarter were registered and 38% of the unregistered products failed the quality tests. Hence, the national, regional medicine regulatory bodies and other stake holders should perform the required roles to circumvent presence of Substandard and Falsified (SF) anti-malarial drugs in the study sites.

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Keywords Malaria, Antimalarials, Poor quality, Quality assessment, Substandard and falsified (SF) medicines, Gambella, Ethiopia

Background

Malaria remains a major public health problem worldwide [1]. It is caused by *Plasmodium* parasites, which are transmitted to people through the bites of female *Anopheles* mosquitoes. Although there are multiple *Plasmodium* species, *Plasmodium falciparum* predominates in sub-Saharan Africa [2]. According to the World Health Organization (WHO), malaria is endemic in 84 countries. In some of these nations, the health care systems frequently lack adequate treatments, and also poverty is widespread [3]. The lack of availability of anti-malarial medication and the escalating resistance of mosquitoes to insecticides and of malaria parasites to anti-malarials is a significant concern for malaria control and eradication tasks [4].

Access to safe, effective, high-quality, and affordable medicines is vital for the success of positive and equitable health outcomes [4]. In contrast, drugs that are substandard or falsified have a negative impact by causing treatment failure, resulting in prolonged or severe illness or even death. In addition, the pharmaceutical industry, drug regulatory agencies, and economies are affected by the presence of poor quality anti-malarials worldwide (PQA's) [5]. This will put a further strain on already scarce resources at the provider level and it erodes trust in healthcare system and professionals [6].

Quality control of medicines in the distribution system according to proper specifications is an important prerequisite in ensuring optimal treatment outcomes. Surveys would also act as a preventive strategy against dumping of substandard medicines by manufacturers and importers [7].

The Ethiopian malaria diagnosis and treatment guideline includes quinine, chloroquine, primaquine, artesunate, artemether and lumefantrine as a treatment of choice depending on the parasitological confirmed diagnosis, severity, and additional issues with the patient, such as pregnancy [8].

This study is conducted with the goal of determining whether the artemether-lumefantrine tablets, chloroquine tablets, primaquine tablets, artesunate, and artemether injection currently being sold in Gambella, Southwest Ethiopia comply with pharmacopoeial requirements.

Methods

Study area and study period

The Ethiopian malaria eco-epidemiological stratum map was used to guide the choice of sample collection locations [9]. Accordingly, the Gambella region was selected. Figure 1 shows the map of sampling area. Gambella National Regional State borders South Sudan to the west, Oromia to the north and east, and the Southern Nations, Nationalities and Peoples' Regional State (SNNPRS) to the south. It is situated in the southwest of Ethiopia, 777 kms west of Addis Ababa, the capital. Gambella is mostly flat, and it has a hot, humid climate. The minimum and maximum temperatures are typically 21.1 °C and 35.9 °C, respectively, with an annual rainfall average of 600 mm. The area is primarily lowland with a few midland areas [10]. According to the 2017 Ethiopian population projection, the total population of the region was approximately 436,000 [11]. The region also hosts the largest refugee population in Ethiopia; currently, 337,421 refugees from South Sudan, a population almost equal to its own [12]. While having a relatively small territory, the region has a sizable ethnic diversity, with one-fifth of its residents living in urban areas. There are four administrative zones and 12 districts (woredas) in Gambella Regional State. Agnuak zone (Gambella, Abobo, Gog, Jor, Dimma), Nuwer zone (Lare woreda, Jikawo, Wantawa Woreda, Akobo), Mezhenger-Zone (Godare, Mengesh) and Etang Special Zone (Ethang) [11]. There are 64 private drug retail outlets throughout the region. Among them 2 are rural drug shops, 60 are drug stores and 2 are pharmacies. Samples were collected in June 2022.

Sampling technique and sample size

Half of the (six) woredas located in the four zones of the region were randomly chosen. There are 59 private drug retail outlets in the 6 woredas. In the second stage of sampling, half of (29) the private drug retail outlets were randomly selected using simple random sampling technique. All drug retail outlets available in the selected districts (districts (woredas)) were included in the study. Among these 1 is pharmacy, 27 were drug stores and 1 was rural drug shop. All available artemether-lumefantrine tablets, chloroquine tablets, primaquine tablets, artesunate and artemether injections samples totaling 52 were collected from drug retail outlets.

Mystery shopping method was applied to buy the samples from the drug outlets (drug stores, a pharmacy, and a rural drug shop). The samples were then preserved in the original packages supplied by the manufacturers. The packaging was examined for any features of illegal prints as compared with the original package from the innovators. From each sample, the origin, labelled dose, registration status, and shelf-life

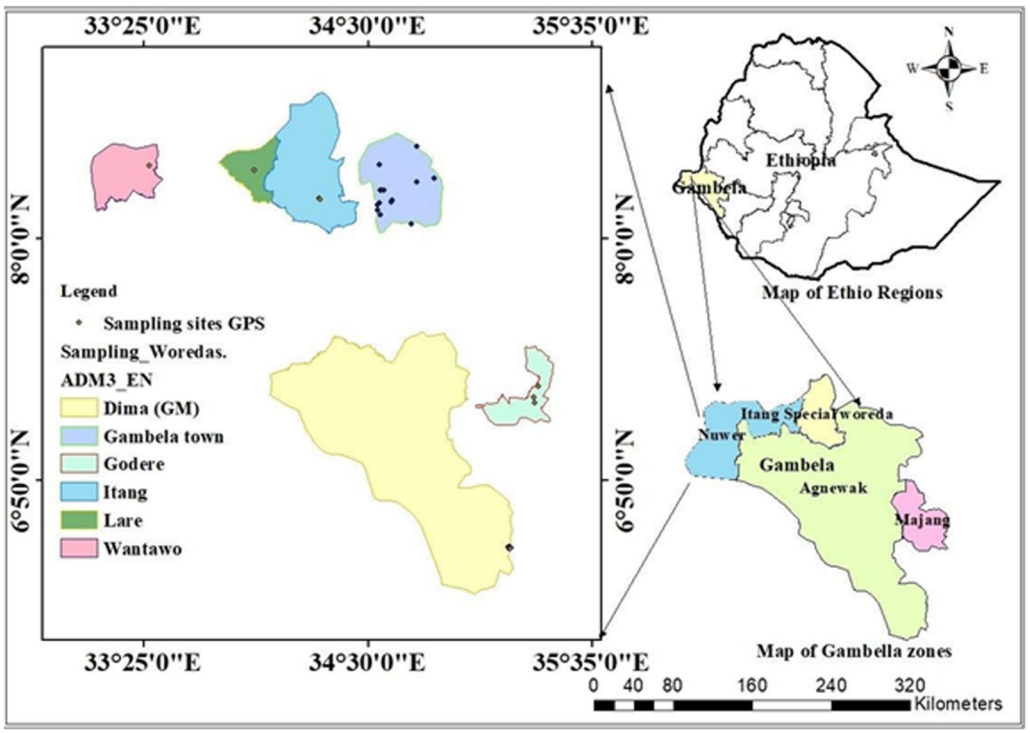


Fig. 1 Map of sampling area

of the active drug were noted. All tests were completed before the product's expiration dates and different batches of a single product were purchased to account for variations. The quality tests including sterility test were conducted at the Ethiopian Food and Drug Authority's drug quality control laboratory (EFDA), an ISO 17025 accredited laboratory located in Addis Ababa, Ethiopia. Calibration curves, standard operating procedures (SOPs), and validated and calibrated instruments were used to provide quality control and guarantee quality assurance mechanisms for the study throughout the testing process. USP primary reference standards were also used. Additionally, the test findings were compared and contrasted with the pharmacopoeias' monographs specified limitations.

The instruments' and chemicals used in this study had been listed as supplementary information (supplementary information 1).

Visual inspection evaluation

Visual inspection of the physical characteristics of dosage form, packaging and labelling information was performed using the joint of WHO/FIP/USP check list. It is attached as supplementary information (Supplementary informtion 2).

Physicochemical analysis

The collected samples were analysed for their identity, uniformity of weight, hardness, friability, disintegration, sterility and dissolution profiles based on United States Pharmcopoeia (USP) and International Pharmcopoeia (Ph.Int.) methods. Additionally, dissolution profile comparison was done. To compare the dissolution profiles of the innovator and the sample brands available were computed, a difference factor (f1) and a similarity factor (f2) were calculated.

Uniformity of weight

It assesses whether each unit doses are manufactured consistently with the same weight. When the API of the drug product is ≥ 25 mg, or when the API from the drug substance ratio is larger than 25%, the USP 44-NF 39 suggests employing weight variation. The international pharmacopoeia on the other hand, uniformity of mass for single-dose preparations to be carried out for uncoated tablets and film-coated tablets formulated to contain 5% or more of the active ingredient should comply with the deviation of individual masses of minimum of 18 and maximum of 2 tablets should not exceed by (± 7.5% and ± 15% from average mass, respectively) [13, 14]. Accordingly, the two techniques were used for the determination of uniformity of mass for the samples.

Identification

It assesses whether the specified active pharmaceutical ingredient is present or absent in the formulation. HPLC was used for identification and assay tests on artemether-lumefantrine tablets, artemether injections, chloroquine, and primaquine tablets. The retention times of the tested products' peaks were compared to standard references. The identification test for artesunate powder for injection was performed according to the described method [13, 14].

Assay

It quantifies the amount of active ingredient in the formulation and compares it with the stated value.

Assay was determined using HPLC and a titrimetric method.

Size

The diameter and thickness measurements of twenty randomly selected tablets were determined using a Mitutoyo® Absolute Micrometer Gauge [14, 19].

Disintegration test

A tablet/capsule had to be disintegrated and dissolved for absorption in the body and subsequent pharmacological effect. It is the first step in the solubility of the drugs to be absorbed from the gastrointestinal tract. It is designed to measure the time required for such step.

Disintegration tests were performed on tablets from each tablet brand, with a disintegration duration of 15 min for uncoated tablets and 30 min for film-coated tablets and hard gelatin capsules. The dissolution time was measured as the time it took for all six dose units to be completely dissolved and pass through the sieve, leaving only a soft mass in the basket [14].

Dissolution test

It determines the solubility of the medicine in the dissolution media and thus simulates subsequent absorption in the gastrointestinal system. It measures the complete solubility of the active pharmaceutical ingredient in the media employed that simulates the body fluids in the gastrointestinal system.

Dissolution tests were performed at a single withdrawal point for every batch of tablet sample according to the specifications set by USP and IP. The dissolution profile was performed for generic brands available on each antimalarial tablet sample, and the dissolution data were analysed using the DDSolver® software (a free Excel add-in software package used to analyse data obtained from dissolution studies) [13, 14].

Results

A total of 52 samples were collected on June 2022 from 29 drug retail outlets comprising of one pharmacy, 27 drug stores and one rural drug shop located in six districts (Fig. 1). Of the 52 collected samples, 46.15% (24/52) were artemisinin-based combinations (artemether + lumefantrine), 19.23% (10/52) artesunate powder for injection, 17.3% (9/52) artemether injection, 9.6% (5/52) chloroquine phosphate tablets and 7.6% (4/52) primaquine phosphate tablets. Figure 2 indicates that the highest percentage of samples were originated from India (65%) and China (25%). Of the samples, 75% are unregistered items, 38% of them failed the quality tests performed.

Visual inspection

Using a checklist developed by the WHO/USP/FIP, all the samples were visually examined for tablet/formulation physical characteristics, packaging, and labelling information. The results of visual inspection did not show any signs of falsified products. However, eight (8) artemether injection products (88.8%) were presented in clear glass ampoules, with only one product (11.1%) in an amber coloured ampoule. Two-third (6/9) of artemether injection samples did not declare the vehicle used to formulate the injectable preparation.

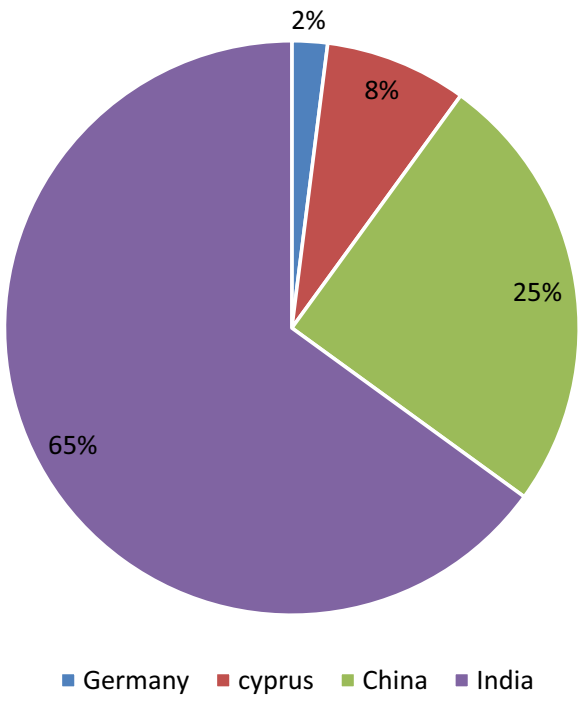


Fig. 2 Country of origin of the samples in terms of percentage

Identification

To ensure that the samples contained the intended active pharmaceutical ingredient (API), they were first put through an identification test in compliance with USP and Ph.Int. monograph descriptions [13, 14]. This test revealed that all samples contain the stated active ingredients per the label.

Uniformity of weight and assay

It had showed that the tested products complied with the uniformity of weight requirements. The limits set forth in the international pharmacopoeia for uncoated and film-coated tablets that are formulated to contain 5% or more of the active ingredient should comply with the deviation of individual masses of minimum of 18 and maximum of 2 tablets that should not exceed by (± 7.5% and ± 15% from average mass, respectively) [13]. The uniformity of dosage criteria set by the USP [15] for the chloroquine phosphate tablets had also been complied by the samples.

Table 1 indicates that the uniformity of weight of the artemether lumefantrine combination tablets ranging from 238.73 ± 2.67 to 354.57 ± 3.64 ($\bar{x}$ (gm) ± SD). The uniformity of mass for artesunate powder for injection was conducted according to the Ph. Int. [13]. All the artesunate samples complied with the criteria set for uniformity of mass for single dose preparation with a SD range 1.03 to 14.34. The acceptance value (AV) found for chloroquine phosphate tablet ranges from 2.89 to 8.48 and thus, all the chloroquine phosphate tablet samples met the uniformity of dosage criteria set by the USP [15]. The acceptance value (AV) for the five chloroquine phosphate tablet samples is also shown on Table 1. The SDs for randomly selected twenty tablets weighed per batch for each generic product varied from 2.47% to 10.63%. The uniformity of weight of the primaquine phosphate tablets range from 83.22 ± 1.02 to 84.84 ± 0.90 gm as ($\bar{x}$ (gm) ± SD).

The mean weight of the twenty tablets of fixed dose combination artemether lumefantrine tablets sampled in this study was lowest for sample Artem010 (± 2.67) and highest for Artem020 (± 3.64), while the standard deviation, was lowest for Artem014 (± 1.06) and highest for Artem020 (± 3.64). Artem020 was the least uniform brand as the biggest dispersion/clustering of sample weight around the mean weight was found, whereas Artem014 had the best uniformity of weight variation. Overall, 90% of the evaluated items were more consistently uniform, and the percent deviation of all samples was lower than the upper acceptability limits.

This study indicated that the extractable volumes in five products (55.5%) were significantly less than the expected extracted volume of 3 mL that should be anticipated from 3 ampoules as shown on Table 2.

Assay

All samples, with the exception of a primaquine phosphate tablet sample, satisfied the pharmacopeial acceptance specifications for assay test. The amount of artemether and lumefantrine APIs in the fixed dose combination artemether-lumefantrine tablet samples revealed that all samples complied with the pharmacopeial acceptance specification limit (i.e., 90.0 –110.0%) (% label claim). Table 1 shows that the amount of artemether API in samples analyzed that ranges from 95.4 ± 2.3 to 106.3 ± 0 while for that of lumefantrine, the values obtained ranges from 91.3 ± 0.8 to 103.7 ± 0.9.

Results for the assay of artemether injection indicated that all the artemether injection samples fulfilled the specification set by Ph. Int. [16] which states that artemether injection contains not less than 90.0% and not more than 110.0% of the amount of $C_{16}H_{26}O_5$ stated on the label. The percent mean content ranges from 95.1 to 101.5. A titrimetric method was used to determine artesunate in powder for injection preparations as suggested by the Ph.Int. The artesunate content ranges from 90.59 to 109.04%. All the artesunate samples passed the criteria set by the ph. Int. monograph [16] which states that an artesunate powder for injection should contain not less than 90.0% and not more than 110.0% of the amount of artesunate ($C_{19}H_{28}O_8$) stated on the label.

Chloroquine phosphate tablets should contain not less than (NLT) 93.0% and no more than (NMT) 107.0% of the labeled amount of chloroquine phosphate ($C_{18}H_{26}ClN_3{\cdot}2H_3PO_4$) as stated in the USP. Assay values of all chloroquine phosphate tablet samples indicate that the percent amount of API available in all these drug substances was within their acceptance limit. The API contained in samples coded as Chlor002 and Chlor003 were in the upper limit. The assay results for primaquine phosphate indicated that one batch of primaquine phosphate sample failed to meet the requirements set by the USP as shown in Table 1.

Thickness, diameter, hardness, friability and disintegration

Among the total samples evaluated for thickness, diameter, hardness, friability and disintegration, about 9% of the total samples (2 artemether-lumefantrine and 1 chloroquine phosphate tablet samples) and 18.18% (2 artemether-lumefantrine tablet samples) and all the primaquine phosphate tablets) failed the friability and hardness tests, respectively (Table 3).

It was demonstarted that all the artemether lumefantrine tablet samples examined had passed the specification criteria set by the USP except two samples with a percent friability of 2.615% and 1. 299%. The percent friability values range from 0.008% to 2.615%. In friability test, the maximum weight loss should not be more

Table 1 Uniformity of weight and assay of artemether lumefantrine, chloroquine and primaquine tablets and artesunate powder for injection

Sample ID	Brand name	$\bar{x}$ (gm)	SD	%mean Artem ± RSD	%*mean* Lum ± RSD	Remarks
Artem001	Artemether Lumefantrine	248.22	2.04	103.7 ± 1.4	98.8 ± 0.8	Passed
Artem002	Artemether Lumefantrine	250.46	3.37	105.3 ± 0.4	102.9 ± 3.0	Passed
Artem003	Artemether Lumefantrine	248.45	2.07	98.9 ± 0.5	100.0 ± 1.5	Passed
Artem004	Artemether Lumefantrine	248.17	2.68	105.8 ± 1.1	100.0 ± 0.9	Passed
Artem005	Artemether Lumefantrine	245.04	3.06	101.4 ± 2.9	100.9 ± 1.1	Passed
Artem006	Artemether Lumefantrine	252.89	3.47	95.4 ± 2.3	97.3 ± 1.2	Passed
Artem007	Artemether Lumefantrine	250.68	3.01	97.86 ± 1.0	95.9 ± 0.8	Passed
Artem008	Artemether Lumefantrine	251.51	2.08	100.7 ± 0.2	98.7 ± 1.0	Passed
Artem009	Artemether Lumefantrine	248.9	1.33	98.1 ± 0.9	95.1 ± 0.3	Passed
Artem010	Artefan	238.73	2.67	99.6 ± 0.6	93.6 ± 0.6	Passed
Artem011	Artefan	241.52	2.56	98.8 ± 0.6	98.2 ± 2.2	Passed
Artem012	Artefan	240.63	2.17	98.2 ± 1.0	91.7 ± 1.7	Passed
Artem013	Artefan	240.72	1.22	100.6 ± 0.2	99.2 ± 1.2	Passed
Artem014	Artefan	238.85	1.06	103.3 ± 1.8	98.5 ± 3.0	Passed
Artem015	Artefan	241.44	1.57	95.7 ± 0.8	91.3 ± 0.8	Passed
Artem016	Lumiter	253.97	2.93	105.3 ± 0.3	99.8 ± 2.9	Passed
Artem017	Lumiter	253.33	1.94	99.3 ± 2.7	103.7 ± 0.9	Passed
Artem018	Artefan dispersible	351.18	2.72	101.9 ± 1.1	97.1 ± 0.8	Passed
Artem019	Artefan dispersible	352.87	3.25	98.5 ± 2.9	96.1 ± 2.4	Passed
Artem020	Artefan dispersible	354.57	3.64	97.1 ± 0.3	95.1 ± 0.5	Passed
Artem021	Artefan dispersible	351.74	2.21	103.4 ± 2.8	98.6 ± 1.8	Passed
Artem022	Artefan dispersible	354.31	2.74	100.8 ± 1.2	95.7 ± 1.3	Passed
Artem023	Comether	244.54	1.95	97.8 ± 2.7	96.7 ± 1.6	Passed
Artem024	Lonart	247.19	2.48	106.3 ± 0.0	96.0 ± 0.4	Passed
Artesun001	Artesunate injection	58.99	1.65	93.28 ± 0.3		Passed
Artesun002	Artesun	59.09	3.65	90.59 ± 1.1		Passed
Artesun003	Artesun	59.58	2.39	100.58 ± 5.8		Passed
Artesun004	Artesun	58.91	3.34	92.19 ± 1.6		Passed
Artesun005	Artesun	60.14	2.87	109.04 ± 1.2		Passed
Artesun006	Artesun	60.39	1.59	102.51 ± 0.4		Passed
Artesun007	Artesun	61.15	2.78	92.32 ± 2.8		Passed
Artesun008	SCOSUNATE-60	61.69	1.77	97.45 ± 1.6		Passed
Artesun009	Artemark	61.29	1.03	91.74 ± 1.0		Passed
Artesun010	GSUNATE 60	56.51	14.34	91.17 ± 0.2		Passed
Pri-Gam-001	Primaquine Phosphate	83.82	0.96	94.1 ± 2.5		Passed
Pri-Gam-002	Primaquine Phosphate	83.22	1.02	93.7 ± 1.0		Passed
Pri-Gam-003	Primaquine Phosphate	83.68	0.79	95.9 ± 0.5		Passed
Pri-Gam-04	Primaquine Phosphate	84.84	0.90	80.0 ± 5.4		Fail
Chlor001	Chloroquine	309.76	5.25	99.98 ± 2.14		Passed
Chlor002	Chloroquine	315.47	2.47	102.46 ± 0.55		Passed
Chlor003	Chloroquine	310.8	4.67	102.08 ± 1.30		Passed
Chlor004	Chloroquine	312.13	6.55	100.79 ± 1.02		Passed
Chlor005	Chloroquine	302.57	10.63	100.61 ± 0.98		Passed

Table 1 (continued)

x̄ (gm) = Average weight of 20 tablets SD = Standard deviation Assay = Active pharmaceutical gradient (API) measured content

%mean Artem ± RSD = Percent arthemether content plus or minus relative standard deviation

%mean Lum ± RSD = Percent lumefantrine content plus or minus relative standard deviation

Table 2 Extractable volumes and assay of artemether injections

Sample ID	Volume of extractable injection (mL)			Total volume	Remarks	Assay(%API)	Remarks
	1st	2nd	3rd				
Artem-Inj 001	1	1.1	0.9	3	Passed	98.1 ± 3.0	Passed
Artem-Inj 002	1	1	1	3	Passed	95.1 ± 0.8	Passed
Artem-Inj 003	0.9	0.9	0.9	2.7	Failed	96.1 ± 0.0	Passed
Artem-Inj 004	1.1	0.9	1.0	3	Passed	96.5 ± 2.7	Passed
Artem-Inj 005	0.9	0.9	0.8	2.6	Failed	98.3 ± 2.2	Passed
Artem-Inj 006	0.9	0.8	0.8	2.5	Failed	101.0 ± 2.1	Passed
Artem-Inj 007	1.1	1	1	3.1	Passed	97.3 ± 0.1	Passed
Artem-Inj 008	0.8	0.9	0.9	2.6	Failed	101.5 ± 2.6	Passed
Artem-Inj 009	0.9	1.1	0.7	2.7	Failed	99.6 ± 2.9	Passed

than 1% of the weight of the tablets [17]. All examined artemether-lumefantrine samples, except two, gave a hardness value > 50 N which is the acceptable criteria set by British Pharmacopoeia (BP) [18]. Two of the samples that failed the hardness test had 41.4N and 48.8N values. The average hardness of the products is different from each other, i.e., it is observed that tablet hardness ranged from 52.2N to 84.4 N. Among the five chloroquine phosphate tablets assessed for % friability test, one has failed to meet the criteria set by the USP having a % friability of 2.45%. This was found to be more than 1%.

The disintegration test performed on the chloroquine phosphate samples showed a minimum of 123 s (2.05 min) and a maximum of 198 s (3.3 min).It showed that all the brands passed the disintegration test. The friability test done for the primaquine phosphate tablets showed that all the samples passed the criteria set by the USP [17] as shown on Table 3. The results of disintegration range between 154 to 233 s.

Sterility

Sterility test was also conducted only for artemether and artesunate injections since they should be processed in aseptic environment. Fluid thioglycolate and Soya-bean casein digest culture media were used for sterility test. Fluid thioglycolate medium is primarily intended for the culture of anaerobic bacteria; however, it will also detect aerobic bacteria. Soya-bean casein digest medium is suitable for the culture of both fungi and aerobic bacteria. Preparation of the media was conducted according to the IP for both artemether and artesunate powder for injection samples. Sterility test was conducted for *Candida albicans* and *Escherichia coli* and direct inoculation method was employed. Sterility have been confirmed by incubation portions of the media for 14 days and the detection of no growth of microorganisms [13]. Artemether and artesunate injections did not result in any microbial development, and there was no turbidity or fogginess observed during the 14 day incubation period. It indicates that there is no microbial growth during the 14 day incubation period.

Dissolution

Single point dissolution and dissolution profile was performed for the available brands of the collected tablet samples. Table 4 showed that 10 samples out of 24 (41.6%) failed to meet the percent (%) release criteria of artemether. And three samples out of 24 (12.5%) failed to meet the percent (%) release criteria of lumefantrine. Artem024 did not meet the criteria for both 60 and 180 min. On the other hand, Artem011 had a percent (%) release of 67.65% by the 180 min which is lower than the set standard 70% (Q) while fulfilling the 60 min' release tolerance as it released by52.28%. Table 4 depicts a single point dissolution test, that showed that all of the 5 chloroquine phosphate tablet samples passed the dissolution test. Chloroquine phosphate tablets released from 94.09% to 98.72% of the API within the specified minute set by the pharmacopoeia [19]. On the other hand, for primaquine, two samples passed the single point dissolution test from total of 4 samples investigated,There was a failure in dissolution test for about 42% and 12.5% of the

Table 3 Thickness, diameter, hardness, friability and disintegration tests

Sample ID	Average Thickness ± SD	Average diameter (mm) ± SD	Average Hardness(N) ± SD	% Friability	DT time (Sec)
Artem001	3.1 ± 0.03	9.0 ± 0.02	81.5 ± 4.8	0.075	4
Artem002	3.1 ± 0.04	8.9 ± 0.02	79.8 ± 11.4	0.119	330
Artem003	3.1 ± 0.02	8.9 ± 0.12	84.4 ± 9.3	0.284	260
Artem004	3.1 ± 0.03	8.9 ± 0.05	81.5 ± 9.3	0.404	356
Artem005	3.1 ± 0.02	9.0 ± 0.02	80.5 ± 7.4	2.615*	318
Artem006	3.1 ± 0.04	9.0 ± 0.04	83.6 ± 15.4	1.299*	341
Artem007	3.1 ± 0.03	9.0 ± 0.03	74.8 ± 11.6	0.600	247
Artem008	3.2 ± 0.04	9.0 ± 0.03	71.8 ± 11.8	0.313	280
Artem009	3.1 ± 0.01	9.0 ± 0.01	70.3 ± 11.8	0.074	180
Artem010	3.2 ± 0.03	9.0 ± 0.02	68.5 ± 6.9	0.266	11
Artem011	3.2 ± 0.02	9.0 ± 0.02	67.2 ± 8.9	0.501	10
Artem012	3.1 ± 0.03	9.0 ± 0.01	55.1 ± 7.7	0.021	20
Artem013	3.2 ± 0.04	9.1 ± 0.16	41.4* ± 12.5	0.164	10.3
Artem014	4.3 ± 0.01	9.6 ± 0.01	72.2 ± 6.1	0.269	40
Artem015	3.3 ± 0.02	9.0 ± 0.01	52.2 ± 4.3	0.060	11
Artem016	3.3 ± 0.02	8.8 ± 0.01	48.8* ± 4.3	0.326	361
Artem017	3.2 ± 0.02	8.8 ± 0.01	52.2 ± 5.1	0.144	352
Artem018	4.3 ± 0.01	9.6 ± 0.01	76.4 ± 4.6	0.013	50
Artem019	4.4 ± 0.03	9.6 ± 0.01	67.7 ± 10.1	0.316	43
Artem020	4.4 ± 0.01	9.6 ± 0.02	71.7 ± 6.5	0.250	68
Artem021	4.3 ± 0.05	9.6 ± 0.02	73.7 ± 6.0	0.973	48
Artem022	4.3 ± 0.12	9.6 ± 0.02	75.1 ± 5.4	0.055	49
Artem023	3.8 ± 0.01	9.0 ± 0.01	58.9 ± 6.8	0.008	119
Artem024	3.1 ± 0.01	8.9 ± 0.01	75.0 ± 14.4	0.102	257
Chlor001	4.1 ± 0.0	9.6 ± 0.1	87.9 ± 1.2	0.168	154
Chlor002	4.2 ± 0.1	9.6 ± 0.0	90.9 ± 1.2	0.160	145
Chlor003	4.14 ± 0.0	9.46 ± 0.0	74.9 ± 2.3	0.126	195
Chlor004	2.6 ± 0.0	5.9 ± 0.0	30.7* ± 0.8	2.457*	123
Chlor005	3.14 ± 0.0	8.9 ± 0.0	67.1 ± 3.5	0.829	198
Pri-Gam-001	2.6 ± 0.0	5.9 ± 0.0	27.5* ± 8.0	0.029	185
Pri-Gam-002	2.6 ± 0.0	6.0 ± 0.3	27.4* ± 9.3	0.059	233
Pri-Gam-003	2.6 ± 0.02	5.9 ± 0.0	30.7* ± 7.7	0.011	154
Pri-Gam-004	2.6 ± 0.02	5.6 ± 1.1	31.6* ± 7.2	0	221

SD Standard deviation, *DT* Disintegration time

artemether and lumefantrine samples respectively in the fixed dose artemether-lumefantrine tablets.

Dissolution profiles

Calibration curve was constructed in order to assess the linearity of concentration. The measured peak areas were plotted against the respective concentration of the standard solutions for artemether and primaquine samples. Absorbance was plotted against concentration to construct the calibration curves of lumefantrine and chloroquine tablet samples as shown on the calibration curve on Fig. 3a.

The percentage release values of artemether samples taken at intervals of 15, 30, 45, 60, 90, 120, and 150, 180 and 195 min were computed using the equation derived from the calibration curve. The concentration of the tested substances and the peak area values were correlated on this curve over the concentration of 0.028, 0.024, 0.02, 0.016, 0.012, 0.008, 0.004 mg/mL ($r^2 = 0.974998$). The dissolution profile of these tablet samples is depicted on Fig. 4.

Table 5 indicates that from the six brands of artemether lumefantrine fixed dose combination tablets analyzed, ArtemC01 and ArtemC06 have failed to release their contents in the tolerance limits specified as a dissolution

Table 4 Single point dissolution test of artemether and lumefantrine tablets

Sample ID	Artemether				Lumefantrine	
	60 min	RSD	180 min	RSD	45 min	RSD
	% API release		% API release		% API release	
Artem001	48.63*	9.71	73.33	4.13	117.78	0.38
Artem002	49.60*	6.25	70.10	6.51	96.98	2.33
Artem003	48.48*	4.35	72.41	7.44	89.47	5.28
Artem004	51.89	5.92	89.10	6.76	85.59	0.99
Artem005	48.83*	5.30	83.00	5.84	66.07	10.46
Artem006	45.65*	3.64	74.61	8.00	87.06	5.67
Artem007	43.61*	13.21	75.20	5.46	76.19	7.52
Artem008	47.31*	11.55	76.33	2.35	88.57	18.86
Artem009	49.23*	6.77	76.94	2.50	105.63	2.87
Artem010	56.70	10.79	74.87	4.97	62.05*	8.73
Artem011	52.28	15.16	67.65*	4.46	63.51*	19.50
Artem012	68.13	10.79	111.47	6.87	118.92	2.01
Artem013	65.66	5.35	91.43	10.71	92.96	2.45
Artem014	61.61	5.83	73.67	1.13	66.85	2.34
Artem015	59.86	1.47	77.09	9.05	74.79	4.81
Artem016	51.20	8.01	70.94	9.00	90.82	1.54
Artem017	67.83	15.42	84.64	7.29	40.62*	16.96
Artem018	80.88	11.57	94.03	9.36	90.15	8.28
Artem019	65.03	9.89	91.75	13.11	93.24	3.08
Artem020	55.74	7.15	91.75	77.27	105.05	2.29
Artem021	67.80	22.10	81.03	14.02	72.71	5.23
Artem022	77.97	8.41	90.86	23.10	84.18	6.33
Artem023	55.81	16.02	83.69	16.05	71.57	2.24
Artem024	44.68*	4.80	65.28*	5.80	84.55	6.82

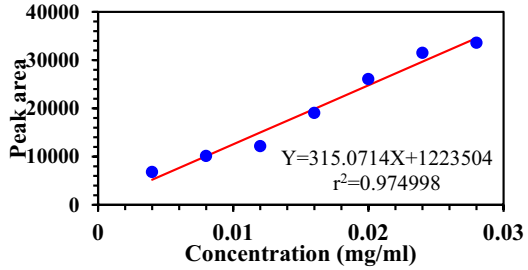
	Chloroquine and primaquine samples at 30 min				
	Mean	RSD		Mean	RSD
	% API release			% API release	
Chlor001	97.13	0.37	Pri-Gam-001	67.33	1.61
Chlor002	97.35	1.18	Pri-Gam-002	66.71	2.21
Chlor003	98.32	2.45	Pri-Gam-003	95.67	2.77
Chlor004	98.72	1.18	Pri-Gam-004	94.59	1.88
Chlor005	94.09	2.03			

NB* Failed

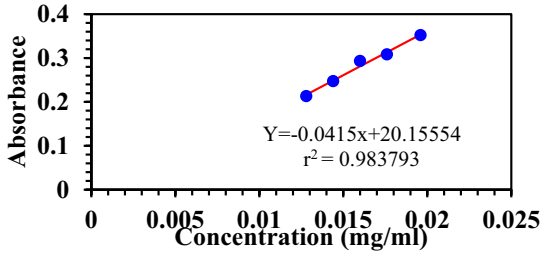
requirement. AretmC01 released 47.95% and 68.21% at 60 and 180 min, respectively. ArtemC06 released 44.68% of its content at the 60th minute and 65.28% at the 180th minute. These results are below the acceptance limits of at both time references (at 1 h and 3 h). ArtemC03 had the highest percentage release than the other brands of artemether-lumefantrine fixed dose combination.

The linear regression equation for lumefantrine was $Y = -0.0415X + 20.1554$ where Y is the absorbance and X is the concentration in mg/mL, as shown on the calibration curve in Fig. 3b. The percentage release values of samples taken at intervals of 5, 15, 30, 45, 60 and 65 min were computed using the calibration curve equation. The concentration of the tested substances and the absorbance values were correlated on this curve over the concentration of 0.0128, 0.0144, 0.016, 0.0176, 0.019 mg/mL. The dissolution profile of lumefantrine tablets is depicted in Fig. 4. All the lumefantrine brands passed the established USP requirement as shown on Table 5.

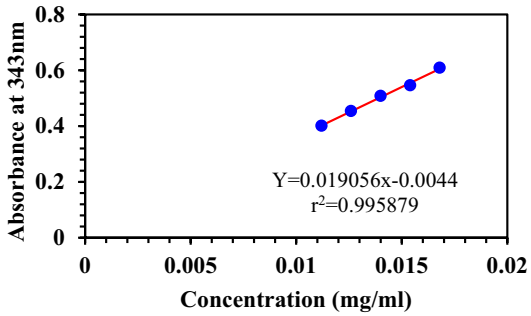
The dissolution profile of chloroquine phosphate was done according to the spectrophotometric method recommended [19]. The measured absorbances were plotted



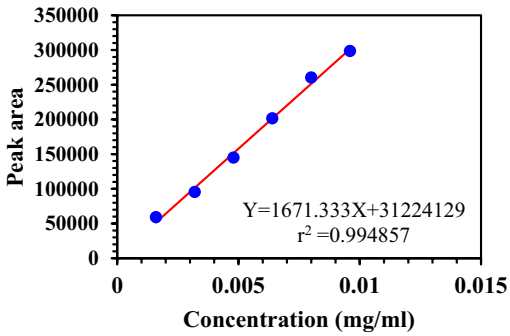
a. Calibration curve of dissolution profile of Artemether Tablets



b. Calibration curve of dissolution profile of Lumefantrine Tablets



c. Calibration curve of dissolution profile of Chloroquine Phosphate



d. Calibration curve of dissolution profile of Primaquine Phosphate

Fig. 3 Calibration Curves for dissolution profiles of tablet samples

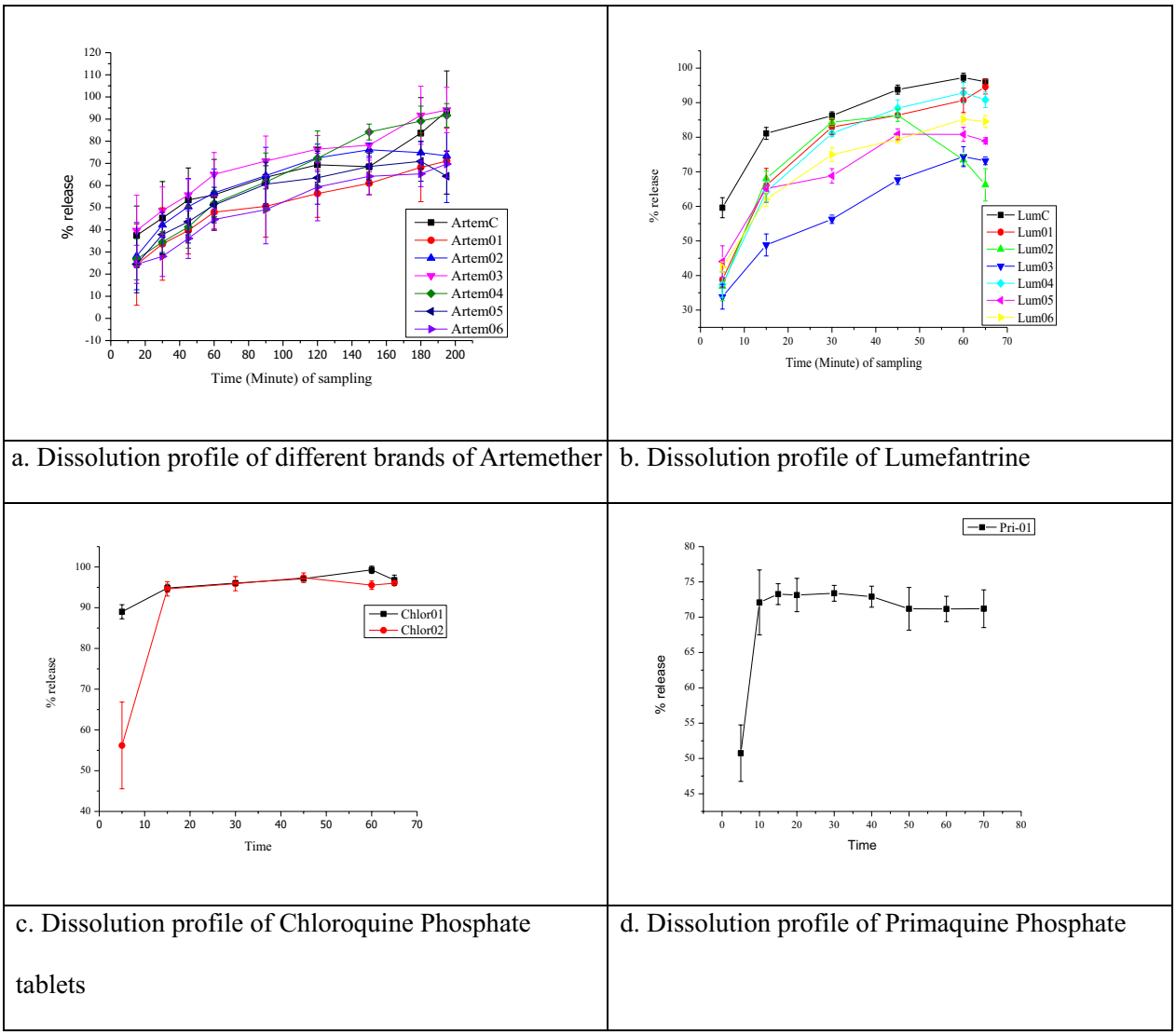
against the respective concentration of the standard solutions which gives a straight line. The linear regression equation was Y = 0.019056 X—0.0044 and a correlation coefficient of 0.995879 as shown on Fig. 3c. The concentration of the tested substances and the absorbance values were correlated on this curve over the concentration of 0.0112, 0.0126, 0.014, 0.0154 and 0.0168 mg/mL. The percentage release values of samples taken at intervals of 5, 15, 30, 45, 60 and 65 min were computed using the equation derived from the calibration curve.

The linear regression equation of primaquine phosphate is Y = 1671.333X + 31,224,129, where Y is the peak area and X is the concentration in mg/mL, as shown on the calibration curve on Fig. 3d. The concentration of the tested substances and the peak area values were correlated on this curve over the concentration of 0.0016, 0.0032, 0.0048, 0.0064, 0.008 and 0.0096 mg/mL ($r^2 = 0.994857$).

Table 5 shows that the generic brand Chlor001which released 97.13 ± 0.37% while Chlor002 released 97.35 ± 1.18%. The release profiles show nearly the same percentage as shown on Fig. 4 at 15,30,45 and 65 min. In the two tested batches, 85% of the active ingredient dissolves within 15 min, therefore the dissolving profiles are assumed to be identical [20]. The percentage release values of primaquine phosphate tablet sample taken at intervals of 5, 10, 15, 20, 30, 40, 50, 60 and 70 min were computed using the equation derived from the calibration curve. Results were computed for primaquine phosphate tablets and there was only one brand of primaquine phosphate which is Primaquine Phosphate 7.5 mg (Remedica, Cyprus). Hence profile was done for the single available brand of primaquine phosphate tablet sample selected randomly from the rest of 4 primaquine samples. And the sample where profile was done for had a low release profile and didn't even meet the dissolution criteria.

Dissolution profile comparison of artemether lumefantrine tablets

Since the value (f1) factor is within the limit (0–15) and the (f2) factor is greater than 50, three of the generic



a. Dissolution profile of different brands of Artemether

b. Dissolution profile of Lumefantrine

c. Dissolution profile of Chloroquine Phosphate tablets

d. Dissolution profile of Primaquine Phosphate

Fig. 4 Dissolution profile

artemether products are measured to be similar and bioequivalent with the innovator product as shown in Table 6. And it was shown that most of the lumefantrine samples were not found similar with the innovator product regarding the dissolution profile. The similarity of the product with respect to dissolution means that the test product has a dissolution performance, that is not different than the reference (comparator) product.

Discussion

Although the visual assessment in our investigation revealed no indications of falsified products, studies conducted elsewhere had shown that damp packages, blue-stained chloroquine and primaquine samples [21] and lack of chloroquine leaflets were observed [22].

Only 25% of the products in this study were registered. This result is in line with a surveillance done by EFDA's MQCL on the quality of antimalarials that had documented 34% unregistered medications [23]. Unregistered/unlicensed medical products, are included in the 2017 WHO definition of poor-quality medicines [24]. Despite advancements in medicine regulation and advice from professional groups, there is evidence suggesting that low levels of implementation of specified standards for unregistered medications. This might raise the possibility of exposing the local population to potentially dangerous medical items of varying efficacy leading to an increased incidence of adverse drug reactions [25]. The prevalence and impact of unregistered medicines are greater in low- and middle-income

Table 5 Cumulative percent release of artemether, lumefantrine, chloroquine and primaquine

Artemether							
%API ± RSD released							
Time (Minute) of sampling	**ArtemC****	**Artem01**	**Artem 02**	**Arpphtem03**	**Artem04**	**Artem05**	**Artem06**
15	37.48 ± 13.28	24.30 ± 18.37	28.12 ± 15.17	39.69 ± 16.01	26.71 ± 9.27	24.50 ± 12.90	24.43 ± 8.60
30	45.32 ± 16.48	33.61 ± 16.37	42.23 ± 5.60	48.71 ± 10.63	34.51 ± 4.67	37.86 ± 8.65	28.01 ± 9.06
45	53.48 ± 14.48	39.71 ± 10.62	50.47 ± 12.72	55.74 ± 7.15	41.26 ± 9.53	43.67 ± 9.64	36.09 ± 9.01
60	55.81 ± 16.02	47.95 ± 7.52*	56.70 ± 10.79	65.03 ± 9.89	51.89 ± 5.92	51.20 ± 8.01	44.68 ± 4.80*
90	63.70 ± 5.25	50.60 ± 13.90	64.48 ± 12.77	71.06 ± 11.30	61.57 ± 13.11	60.59 ± 9.95	49.10 ± 15.41
120	69.36 ± 7.83	56.37 ± 10.72	72.49 ± 6.20	76.42 ± 6.15	72.32 ± 12.33	63.52 ± 11.96	59.32 ± 15.25
150	68.51 ± 5.98	60.99 ± 5.13	76.16 ± 2.92	78.24 ± 6.78	84.17 ± 3.58	68.57 ± 7.66	64.15 ± 8.33
180	83.69 ± 16.05	68.21 ± 15.49*	74.87 ± 4.97	91.75 ± 13.11	89.10 ± 6.76	70.94 ± 9.00	65.28 ± 5.80*
195	93.58 ± 18.17	71.02 ± 14.87	73.40 ± 21.07	94.08 ± 10.26	91.66 ± 5.32	64.20 ± 8.07	69.73 ± 6.00
Lumefantrine							
%API ± RSD released							
Time (Minute) of sampling	**LumC****	**Lum01**	**Lum02**	**Lum03**	**Lum04**	**Lum05**	**Lum06**
5	59.62 ± 2.91	38.82 ± 2.17	36.90 ± 4.19	33.86 ± 3.60	37.41 ± 3.73	44.06 ± 4.53	42.47 ± 1.50
15	81.12 ± 1.72	66.07 ± 4.92	68.02 ± 2.17	48.83 ± 3.19	64.22 ± 2.98	65.16 ± 0.65	62.04 ± 2.04
30	86.22 ± 1.15	82.93 ± 2.14	84.35 ± 1.16	56.27 ± 1.21	81.11 ± 0.90	68.81 ± 2.10	74.97 ± 1.99
45	93.78 ± 1.33	86.39 ± 0.34	86.36 ± 1.78	67.66 ± 1.32	88.39 ± 2.41	80.87 ± 1.56	79.36 ± 0.91
60	97.25 ± 1.29	90.68 ± 3.54	73.43 ± 1.62	74.39 ± 2.88	92.84 ± 2.96	80.84 ± 2.04	85.18 ± 1.51
65	96.06 ± 0.37	94.57 ± 2.06	66.23 ± 4.67	73.17 ± 1.10	90.84 ± 2.25	78.96 ± 0.91	84.55 ± 1.74
Chloroquine							
		% API ± RSD released					
Time		**Chlor001 ± RSD (%)**				**Chlor002 ± RSD (%)**	
5		89.01 ± 1.73				56.20 ± 10.65	
15		94.83 ± 0.92				94.61 ± 1.76	
30		96.04 ± 0.52				95.90 ± 1.75	
45		97.13 ± 0.37				97.35 ± 1.18	
60		99.29 ± 0.90				95.53 ± 1.04	
65		96.78 ± 1.22				96.02 ± 0.36	
Primaquine phosphate tablets							
Time						**% API primaquine ± RSD released**	
5						50.75 ± 4.00	
10						72.09 ± 4.60	
15						73.27 ± 1.48	
20						73.14 ± 2.36	
30						73.39 ± 1.12	
40						72.91 ± 1.49	
50						71.19 ± 3.02	
60						71.17 ± 1.79	
70						71.20 ± 2.67	

NB ** comparator product

Table 6 Dissolution profile comparison

	Arthemether		Lumefntrine	
	f1	f2	f1	f2
ArtemC01	20.7	43.0	10.62	47.21
ArtemC02	10.0	53.2	19.21	35.85
ArtemC03	8.7	59.4	31.10	28.52
ArtemC04	11.5	52.8	11.53	45.76
ArtemC05	15.1	45.0	18.55	39.81
ArtemC06	22.8	40.6	16.63	41.80

countries due to the presence of less developed regulatory mechanisms, financial constraints, and skilled human resource shortages [26].

Similar to our study, a post-marketing surveillance done on artemether injections marketed in Southwest Nigeria indicated that the majority of the samples examined were packaged in plain ampoules, and about 81.8% of the samples lacked information about the formulation's oil base type [27]. In order to protect pharmaceutical items from environmental and transportation stress, which are risk factors for product quality issues, appropriate packaging is crucial [28]. In order for an artemether injection to be accepted as being of high quality, an ampoule that is amber in color or in another container package that provides enough light protection should be used [16]. Additionally, each product's label should include information about the oil base utilized as a vehicle. If Arachis oil is included in the formulation, the recommended HPLC method to screen for the presence of related chemicals may not be appropriate [16].

The findings revealed that all samples contained the required APIs, which is consistent with the study conducted in Jimma, Ethiopia [29] and Nigeria [27] on quality of fixed dose artemether/lumefantrine products and artemether injections, respectively. Similar to our study, Abuye et al. [22] reported that all investigated chloroquine phosphate samples were positive for identification tests. However, a batch of Coartem failed the identification test in a study done in Gabon [30]. A case study also exposed an artesunate with no API which resulted in a treatment failure [31].

Another study at Cape coast metropolis, Ghana also indicated that the percentage weight deviation of the various brands of artemether-lumefantrine tablets from their respective mean weights was less than 10% [32].

A study conducted on the quality of chloroquine phosphate tablet samples in Ethiopia showed a different result than ours indicating a 6.8% of chloroquine phosphate tablet samples failing to meet the USP acceptance criteria for weight uniformity [22]. The RSD for randomly selected twenty tablets weighed per batch for each generic product varied from 1.25% to 4.15%. As per the USP-2015, the weight variation limit for the tablet which is weighing 134 and 300 mg is 7.5% [22].

The USP general chapter on injections recommends that each container of an injectable product should be filled with a volume that slightly exceeds the content indicated in the label. The excess volumes are meant to be sufficient to permit withdrawal and administration of the volumes as labelled. FDA regulations at 21 CFR 201.51(g) provide that for drugs in ampoules or vials that are intended for injection, the declaration of net quantity of contents on the label is considered to express the minimum quantity of contents and further requires that variation above the stated measure must comply with the excess volumes set forth in USP [33].

This study showed that a higher percentage of failure in the extractable volumes of the artemether injections persisted. It is more than the study carried out in southwest Nigeria which showed a 27.3% of shortfall in the extractable volume of an artemether injection from each ampoule of the goods under investigation. It raises the likelihood that CGMPs weren't followed. When using the assessed artemether injection products, accurate dosage administration may not be possible due to nonconformity with the recommended standards for extractable volume [27]. A reduced extractable volume may cause an inconsistent dose of artemether to be delivered, which may ultimately entail a poor therapeutic outcome. Given the advent of resistance to the artemisinin- based regimen in some areas of the world, particularly in Southeast Asia, where the majority of these products were produced, sub-therapeutic dose is quite concerning [34].

With regard to the results of assay, comparable results were reported in a study done in Jimma, Ethiopia, where only a lumefantrine sample failed [29]. Another study indicated that all of the artesunate and amodiaquine antimalarial combination drugs examined had the necessary amount of active component and complied with the quality specifications [35]. A Cape Coast, Ghana study indicated the percentage of artemether in the samples is with full compliance with the Ph.Int criteria [31]. In contrast a Gabonese study claimed that a questionable Maloxine ® sample contained APIs, however the amount was only roughly half the dose [30]. A study done in the Democratic Republic of Congo discovered that 69% of the tested samples failed the assay test [36].

The results of this study indicated that all the artemether injections passed the assay test. However, a study done on the post-marketing surveillance of quality of artemether injection marketed in Southwest Nigeria' more than half (59.1%) of the examined

samples failed the requirements for the content assay stated in Ph.Int. [27, 37]. In line with this study, in vitro evaluation of the quality of essential drugs on the Tanzanian market showed that the assayed amount of chloroquine phosphate for all the assessed samples was within the acceptance range [38].

Even though the mechanisms underlying resistance are intricate and poorly understood, it is likely to be fueled by a variety of variables, such as sub-therapeutic stated active pharmaceutical ingredient levels in ACT formulations. Hence poor quality medicines may contribute to this worldwide challenge. There are reports that document cases of artemisinin resistance that have been verified in Cambodia, Laos, Thailand, and Myanmar [39].

Tablets' mechanical strength is essential for quality control and product development, and its size and shape affect esophageal transit and administration methods [40, 41]. Simple tablet fracture may result in medication loss, which ultimately results in underdosing. Too hard tablets are also undesirable since they might not dissolve quickly and might leave the body without absorption of the required medication [42]. Hence, tablets must be able to tolerate mechanical shocks during handling, packaging, and shipping [43].

The reason for variability of results concerning thickness, diameter, hardness, friability and disintegration between brands may have been related to pharmaceutical manufacturer's formulation procedures. It might come due to conditions such as alteration in machine speed, granulation methods, and number of lubricants added during manufacturing processes. A study conducted in Cape Coast; Ghana indicated that all the artemether-lumefantrine tablets disintegrated in aqueous medium in less than 15 min (900 s) [31]. Unlike our study, the cape coast study revealed that the percentage friability for all the artemether- lumefantrine tablets tested was lower than 1%.

The disintegration test is a necessary condition for dissolution. It is a rate-determining step in the process of drug absorption [44]. The various manufacturing methods are responsible for the comparatively long disintegration times seen on this study. Excipients like binders and the type of coating materials employed have a significant impact on how quickly a tablet disintegrates into smaller particles and subsequently how the API is released. More time is needed for the API to be released from the formulation for absorption if the binders have an affinity for the API [45].

Dissolution is a crucial quality control test that evaluates a drug's *in-vitro* availability from the formulation and, consequently, its absorption potential, particularly if it includes drugs that aren't very soluble [38, 46].

Chemically identical drug products that are also bio pharmaceutically equivalent must share the same standards for rates of dissolution [47]. Failure of a drug formulation to comply with USP dissolution requirements may be a sign that there is a possible challenging issue in bioavailability [38, 46]. A study done on the effect of different excipients on formulation of immediate release artemether/lumefantrine tablets showed that the dissolution of lumefantrine from virtually all formulations was more than 80%, which is considered to be extremely acceptable, with the exception of two samples with a dissolution value of less than 10% [48].

The chloroquine phosphate dissolution result is found to be comparable with an Indian study [44]. Another study from Tanzania also indicated that a chloroquine tablet drug release pattern had remained well above 80% of labelled potency [38].

Due to the lack of information regarding the formulations' precise composition, it was challenging to determine the reason why some of the samples in this study failed to meet their respective dissolution criteria. Disintegrants like maize starch, which can lose its ability to expand with age or exposure to high humidity or temperature, may have been present in the formulations [38]. It is known that the drug may undergo through polymorphism or crystal modifications changes in high temperature and humidity settings, which could reduce its natural solubility. Additionally, storage conditions of high temperature and humidity that are prevalent in Gambella may cause excipient- excipient and/or excipient-drug interactions, which may slow the dissolution of a formulation containing a chemically stable medication [49].

Conclusion

In this study, the tested products did not show any signs of falsified products as defined by the joint WHO/ FIP/ USP checklist tool for visual inspection. However, only a quarter of the samples were registered on the EFDA electronic regulatory/registration information system (ERIS). This raises the possibility of exposing the local population to unregulated medicines. The findings of the identity test showed that none of the samples had erroneous APIs. The uniformity of mass test for the samples showed that 9.6% of the samples failed. All samples complied with the pharmacopeial acceptance specification for assay test except for one primaquine phosphate tablet sample. About 9% of the samples failed the test for friability while 21.21% failed the hardness test. Regarding, the dissolution test performed on the tablet samples, 54.54% failed to meet the pharmacopeial requirements. Among these, 42% and 12.5% of the artemether and lumefantrine from the fixed dose artemether-lumefantrine tablets failed to meet the dissolution test, respectively.

Generally, the study findings reveal a high prevalence (58.3%) of substandard anti-malarial drugs in the region as the tested samples failed any one of the parameters investigated. Out of the unregistered products, 38% failed the quality tests.

Limitation

Only 52 samples were collected and the brands varieties were also few. The microbiological quality assessment of tablet products was not performed. And also a dissolution profile with comparator products at different p^H medias might generate different perspective of the results.

Recommendations

Regulation and quality control activities should be strengthened to combat low-quality anti-malarials, especially in light of the unregistered drug trade. This includes strict regulatory review of anti-malarial drugs before registration, increased monitoring of illicit drug sales, and necessary regulatory measures on retailers and distributors selling unregistered anti-malarials. Investments should also be made in increment of the capacity of the national quality control laboratories to test and evaluate different anti-malarial medicines for authenticity and quality.

Abbreviations

ART	Artemether
LUM	Lumefantrine
PQAs	Poor quality antimalarials
FDC	Fixed dose combination
ACT	Artemisinin-based combination therapy
WHO	World Health Organization

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12936-024-05091-x.

Supplementary file 1(It should be the Instrunments and chemicals file)

Supplementary file 2 (It should be the check list used for visual inspection)

Supplementary file 3 (it should be the document containing the sample information and other results)

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Author contributions

Ayenew Ashenef and Tadele Eticha contributed to the conception and design of the experiments. Feruza Ahmed performed the experiments. All analyzed the data and wrote the paper. All authors read and approved the final manuscript.

Availability of data and materials

"Data is provided in the manuscript and the supplementary file."

Declarations

Ethics approval and consent to participate

Ethical clearance was obtained from the Ethical Review Board of Addis Ababa University, College of Health Sciences. School of pharmacy as Ref. No (ERB/SOP/471/14/2022).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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