Artemether–Lumefantrine Concentrations in Tablets and Powders from Ghana Measured by a New High-Performance Liquid Chromatography Method

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Abstract. We developed and validated a new analytical method for the simultaneous quantification of artemether and lumefantrine in fixed-dose tablets and powders for reconstitution into pediatric suspensions (PSs). The method showed linearity ($r^2 > 0.9947$), precision (coefficient of variation $< 2\%$), accuracy (deviation of mean from actual concentrations $< 4\%$), and specificity (peak purities $> 99\%$). The validated method was used to analyze 24 batches of fixed-dose tablets and PSs of artemether and lumefantrine. Of the samples, 23 were obtained using convenience sampling of commonly available brands within Accra in Ghana and one was obtained from Aarhus University Hospital. In all, 83.3% (confidence interval: 80–120%) passed for both artemether and lumefantrine contents, 16.7% failed by the U.S. Pharmacopoeia standards, 8.3% failed for one content, and 8.3% failed for both contents. All four products (16.7%) that failed were PSs, and two (8.3%) showed higher levels of artemether than prescribed (222% and 756%).

INTRODUCTION

Malaria is a parasitic disease with huge global public health significance. In 2010, 219 million cases and 660,000 deaths were recorded.^{1,2} Global malaria surveillance systems are believed to detect only 10% of the estimated global number of cases.¹ The spread and increase of parasite resistance to antimalarials poses a great challenge to malaria control,³ and the limited number of antimalarials against *Plasmodium falciparum* has led to increasing difficulties in the development of drug policies and adequate disease management.⁴ The situation is further compounded by counterfeit and substandard drugs, which form 10% of global medicines trade,⁵ and 35% of all antimalarials in southeast Asia and sub-Saharan Africa are substandard.⁶ The World Health Organization's (WHO) recommendation of artemether–lumefantrine as first-line therapy for acute falciparum malaria in endemic areas⁷ has led to widespread use of this fixed-dose combination in tablets, dispersible tablets (DTs), and powders meant for reconstitution into pediatric suspensions (PSs). Some studies have reported methods for the quantification of only artemether,^{8,9} or lumefantrine^{10,11} in pharmaceutical and biological matrices. A few methods have been published for the simultaneous determination of artemether and lumefantrine in biological^{13,12} and drug formulation matrices.^{10,11} In 2011, Cesar and others¹³ improved a method developed by Hodel and others¹² using liquid chromatography tandem mass spectrometry for the simultaneous quantification of artemether and lumefantrine of 14 antimalarials in human plasma, by eliminating a sample drying step and reducing the total chromatogram run time. Cesar and others in 2008 developed a method for the simultaneous quantification of artemether and lumefantrine in fixed-dose combination tablets using high-performance liquid chromatography (HPLC) with ultraviolet (UV) detection. Low sensitivity and selectivity of artemether in biological matrices

made UV detection inadequate necessitating standard addition of artemether in sample preparation. In 2010, Sridhar and others and Sunil and others¹⁰ described methods for simultaneous quantification of artemether and lumefantrine in tablets using reversed-phase HPLC-UV (RP-HPLC-UV), but the excess run times of these methods, 13.8 and 13.9 minutes, respectively, limited their application in routine analysis. One study described an RP-HPLC-UV method for simultaneous artemether and lumefantrine quantification¹⁰ in fixed-dose tablets with a total chromatographic run time of 6 minutes. Sample preparation was based on a 50-mL volume, which may limit its application in large-scale analytical work such as market surveillance carried out by regulatory authorities. In addition, the method was developed for analysis of tablet formulations, and thus a method that facilitates analysis of other dosage forms is necessary.

The aim of this study was therefore to develop and validate an HPLC-UV method that could simultaneously quantify artemether and lumefantrine in tablets, DTs, and PSs. The validated method was used to analyze fixed-dose combinations of artemether and lumefantrine in different formulations and strengths (tablets containing 20 mg artemether + 120 mg lumefantrine, DTs containing 20 mg artemether + 120 mg lumefantrine, tablets containing 40 mg artemether + 240 mg lumefantrine, tablets containing 80 mg artemether + 480 mg lumefantrine, and PSs containing [15 mg artemether + 90 mg lumefantrine]/5 mL and [20 mg artemether + 120 mg lumefantrine]/5 mL when reconstituted). The tablets were further subjected to dissolution studies as a second quality assessment parameter.

MATERIALS AND METHODS

Reagents and materials. Artemether and lumefantrine reference standards were purchased from Sigma-Aldrich (St. Louis, MO). Artemether–lumefantrine tablets, DTs, and PSs were purchased from local pharmacies in Accra, Ghana. Ultrapure water was obtained from a Milli Q system (Millipore, Denmark), and acetonitrile (ACN), dichloromethane, and

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potassium dihydrogen orthophosphate were all obtained from Sigma-Aldrich, Copenhagen, Denmark. Hydrochloric acid, benzalkonium chloride solution, and sodium lauryl sulfate were all analytical grade.

Instrumental and analytical conditions. The HPLC analyses were carried out on an Agilent 1290 HPLC system (Agilent Technologies, Glostrup, Denmark), which consisted of an eluent pump, an autosampler, a diode-array detector (DAD), a column compartment equipped with a 100 × 2.1-mm, 3.5- μ m C18 column (Symmetry; Waters Corporation, Santry, Ireland), and ChemStation software (Agilent Technologies, St. Clara, CA). UV detection was performed at 210 nm, and UV spectra from 190 to 400 nm were recorded online for peak identification. The injection volume was 10 μ L, and chromatography was performed with an isocratic mobile phase containing ACN and 50 mM potassium dihydrogen orthophosphate buffer (pH 3) in a ratio 55:45 with a flow rate of 0.8 mL/minute. Column temperature was maintained at 40°C.

Preparation of standard solution. First, 1.0 mg artemether and 6.0 mg lumefantrine reference standards were accurately weighed and transferred into a 5-mL volumetric flask. Then, a stock solution was prepared by adding dichloromethane (0.5 mL) to ensure complete dissolution followed by addition of ACN to obtain a solution of 0.2 mg/mL artemether and 1.2 mg/mL lumefantrine. Dilutions were made from the stock solution for analyses. All solutions were filtered through 0.2- μ m ultraclean polypropylene filter (Agilent Technologies) under centrifugation at 3,000 rpm for 5 minutes (24°C) before being injected onto the chromatograph.

Validation. *Linearity.* Calibration curves based on triplicate analysis of the standards were prepared, and concentration versus peak area was plotted for artemether and lumefantrine. The obtained data were subjected to regression analysis (Table 1).

Precision. The intra-assay precision was evaluated by performing measurements ($n = 6$) of sample solutions with a concentration of 0.0503 mg/mL of artemether and 0.5028 mg/mL of lumefantrine. Similarly, the inter-assay precision was based on measurements of three consecutive days ($n = 18$). On the basis of these measurements of artemether and lumefantrine concentrations, the relative standard deviations (RSDs) were calculated.

Accuracy. Reference standards of artemether and lumefantrine were accurately weighed and added to formulation excipients at three different concentration levels (0.084, 0.050, and 0.034 mg/mL of artemether and 0.503, 0.402, and 0.302 mg/mL of lumefantrine). At each level, samples were prepared in triplicates, and the recovery percentage was determined.

Specificity. Spectral purities of artemether and lumefantrine chromatographic peaks were evaluated using UV spectra recorded by the DAD. In addition, a solution containing a mixture of the drug excipients was prepared using the sample preparation procedure and injected onto the chromatograph to evaluate possible interfering peaks.

Robustness. Six solutions of drug samples prepared were analyzed under the established conditions and by varying the

following analytical parameters: flow rate of the mobile phase (0.6, 0.8, 1.0, and 1.2 mL/minute), ACN percentage in mobile phase (80%, 60%, 55%, and 50%), and column temperature (30°C, 40°C, and 50°C). The artemether and lumefantrine contents were determined for each condition, and the data were analyzed statistically using SPSS version 20 (analysis of variance test; IBM, Armonk, NY).

Limits of detection and quantification. Combined standard solutions of artemether and lumefantrine were sequentially diluted and injected onto the chromatograph at decreasing concentrations, in the range of 0.00015–0.01 mg/mL of artemether and 0.00045–0.015 mg/mL of lumefantrine. The detection limit was defined as the concentration at which a signal-to-noise ratio of 3 was obtained, and for quantitation limit, a signal-to-noise ratio of 10 was considered.

Analysis of fixed-dose combination tablets, DTs, and PSs.

A total of 24 batches of fixed-dose artemether and lumefantrine dosage forms were analyzed using the validated method. These consisted of 11 tablets, seven DTs, and six PSs. Because of the poor solubility of lumefantrine, dichloromethane was added to ensure the complete solubilization of the samples. For the analysis, six replicates of each batch were assayed.

Sample preparation. The tablets were weighed and powdered. An accurately weighed portion of powder, equivalent to about 1.66 mg of artemether and 9.96 mg of lumefantrine was transferred to a 5-mL volumetric flask followed by the addition of 0.5 mL of dichloromethane. The solution was sonicated for 3 minutes and diluted with ACN to a volume of 5 mL. Dilutions were made to obtain final concentrations equivalent to 0.1 mg/mL of artemether and 0.6 mg/mL of lumefantrine.

The total weight of powder for suspension was also determined. Amount of powder equivalent to 1.66 mg artemether and 9.96 mg lumefantrine was weighed into a 5-mL volumetric flask, dissolved with 0.5 mL dichloromethane by sonication for 3 minutes, and made to volume using ACN. Dilutions were made to obtain final concentrations of 0.1 mg/mL artemether and 0.6 mg/mL lumefantrine.

For both analysis of tablets and powder, sample solutions were filtered through 0.2- μ m ultraclean polypropylene filter (Captiva; Agilent Technologies) under centrifugation at 3,000 rpm for 5 minutes (24°C), before analysis on the chromatograph. Sample chromatograms are shown in Figures 1 and 2.

Dissolution studies. *Preparation of dissolution buffer for artemether.* For this, 14.2 g of anhydrous disodium hydrogen phosphate and 100 g of sodium lauryl sulfate were accurately weighed and completely dissolved in about 1 L of Milli Q water. Enough of the Milli Q water was added with continuous mixing to make 10 L of solution, and the pH was adjusted to 7.2 using dilute hydrochloric acid.

Preparation of dissolution buffer for lumefantrine. For this, 10 L of 0.1 M hydrochloric acid solution containing 1% benzalkonium chloride was prepared by adding slowly 98 mL of 10.2 M (32%) concentrated hydrochloric acid to Milli Q water with mixing.

Dissolution of tablets. The dissolution of the tablets was carried out using the paddle apparatus setup as specified in the U.S. Pharmacopeia (USP) Apparatus 2 shown in Figure 3 and following the dissolution testing protocol for immediate-release dosage forms outlined in section 711 of the USP 2011.

In this, one tablet was placed in 1 L of artemether dissolution buffer that had been sonicated to rid it of gases and equilibrated to 37°C, and the setup was operated at a paddle

TABLE 1

Calibration curve data for artemether and lumefantrine

Regression parameters	Artemether	Lumefantrine
Regression coefficient, r^2	0.99472	0.99519
Concentration range, mg/mL	0.01–0.1	0.06–0.6
Number of points	8	8

FIGURE 1. Chromatogram obtained for sample solution with 0.02 mg/mL of artemether and 0.12 mg/mL lumefantrine.

speed of 100 rpm for 1 hour. A sample (30 mL) was taken and filtered through a 0.45- μ m syringe filter (Sartorius Stedim Biotech, Gottingen, Germany) and subsequently analyzed by HPLC. The quantity “Q,” which is the amount of dissolved active ingredient specified in the artemether monograph, expressed as a percentage of the labeled content was determined. This was done for a total of six tablets at the first level S_1 of dissolution testing (refer Figure 3). The value of Q specified for artemether was 70% at the end of 60 minutes.

Similarly for lumefantrine, one tablet was placed in 1 L of the lumefantrine dissolution medium, and the apparatus was operated at 100 rpm for 45 minutes after which the sample (30 mL) was taken, filtered through 0.45- μ m filter, and analyzed. Six determinations were carried out, and the quantity Q for each tablet was calculated. The quantity Q specified for lumefantrine at the end of 45 minutes was 60%.

RESULTS AND DISCUSSION

Evaluation of the chromatographic parameters was initially done using a Symmetry C18 (100 $\times$ 2.1 mm, 3.5 μ) column and a mobile phase composed of ACN and 50 mM potassium

dihydrogen orthophosphate buffer (55:45). Different proportions of mobile phase solvents were evaluated with this column to obtain adequate resolution between artemether and lumefantrine peaks. Under these conditions, the retention time obtained for artemether and lumefantrine was 3.164 and 4.193, respectively, with a short run time (4.8 minutes). This condition promoted adequate separation with resolution 2.94 and was chosen for subsequent analysis (Figures 1 and 2).

The UV spectrum for artemether and lumefantrine was evaluated in the range of 190–400 nm, and the wavelength of 210 nm was chosen for detection. This is because both artemether and lumefantrine showed good absorbance at this wavelength even though artemether lacks chromophores and shows relatively poor absorption in the other wavelength regions.

Validation. *Linearity.* A linear correlation was found between the peak areas and the concentrations of artemether and lumefantrine in the assayed range. The regression coefficients (r^2) for both artemether and lumefantrine were higher than 0.99.

Precision. Mean concentrations of artemether and lumefantrine in the intra-assay precision analyses ($n = 6$) were 0.0503 mg/mL (RSD = 1.33%) and 0.5031 mg/mL (RSD = 1.5%),

FIGURE 2. Chromatogram in Figure 1 with artemether peak magnified.

A Dissolution Apparatus **B Acceptance Criteria**

Stage	Number Tested	Acceptance Criteria
S_1	6	Each unit $\geq Q + 5$
S_2	6	Average of 12 units ($S_1 + S_2$) $\geq Q$, and no unit is $< Q - 15\%$
S_3	12	Average of 24 units ($S_1 + S_2 + S_3$) $\geq Q$, not more than 2 units are $< Q - 15\%$, and no unit is $< Q - 25\%$

FIGURE 3. Experimental setup of paddle apparatus as per U.S. Pharmacopeia (USP) Apparatus 2 for dissolution of immediate-release tablets (USP 2011) of artemether–lumefantrine brands from Ghana and the acceptance criteria for passing dissolution.

respectively. The mean contents obtained for the inter-assay precision ($n = 18$) were 0.0502 mg/mL (RSD = 1.35%) and 0.503 mg/mL (RSD = 1.26%) for artemether and lumefantrine, respectively. RSD values less than 2% assure the precision of the method.

Accuracy. Accuracy of the method was evaluated by addition of accurately weighed reference standards to tablet and suspension powder granulation excipients. The mean recovery ($n = 9$) for artemether was 99.61 (RSD = 1.78%) and that of lumefantrine was 103.04 (RSD = 0.51%).

Specificity. Artemether and lumefantrine peak purities in the sample solution chromatograms were higher than 99.0% indicating other compounds did not coelute with the main peaks. Chromatograms obtained with solutions containing a mixture of tablet excipients showed no interfering peaks in the same retention time of artemether and lumefantrine.

Robustness. Statistical analyses showed no significant difference between results when analytical conditions established for the method were compared with those in which variations of some parameters were introduced. The method thus showed robustness for variations in mobile phase flow rate from 0.6 to 1.2 mL/minute, ACN to buffer percentage in mobile phase (80:20, 60:40, 55:45, and 50:50), and column temperature (30°C, 40°C, and 50°C).

Limits of detection and quantitation. As per the signal-to-noise ratio determined, the limits of detection were 0.0003 and 0.0018 mg/mL and that of quantitation were 0.005 and 0.03 mg/mL for artemether and lumefantrine, respectively, in the proportions injected onto the chromatogram. Since the method is for simultaneous quantification of artemether and lumefantrine, the values obtained for both compounds should be considered as the limit of method sensitivity.

Analysis of fixed-dose combination tablets, DTs, and PSs. Samples of various brands of fixed-dose combinations of artemether and lumefantrine (ratio 1:6) were analyzed using the validated method. The results are presented in Table 2.

All the 24 batches analyzed contained both artemether and lumefantrine actives as indicated by the manufacturers. Of the 24 batches analyzed, 20 (83%) passed for both contents as per the U.S. Pharmacopeia standards, which require contents of actives to be between 80% and 120% of the indicated values. The artemether content ranged from 80.54% to 107.45%. Four products failed the content analysis. Of

TABLE 2
Content of artemether and lumefantrine in the fixed-dose combination drugs ($n = 6$)

Code assigned to brand	Assay content (%) $\pm$ SD		Dosage form
	Artemether	Lumefantrine	
1	105.43 $\pm$ 0.016	105.28 $\pm$ 0.109	T
2	107.45 $\pm$ 0.011	102.31 $\pm$ 0.070	T
3	91.13 $\pm$ 0.011	88.75 $\pm$ 0.038	T
4	80.54 $\pm$ 0.004	83.65 $\pm$ 0.035	T
5	83.83 $\pm$ 0.001	87.53 $\pm$ 0.009	T
6	93.48 $\pm$ 0.003	92.92 $\pm$ 0.010	T
7	95.98 $\pm$ 0.001	90.55 $\pm$ 0.008	T
8	81.18 $\pm$ 0.001	90.39 $\pm$ 0.010	T
10	89.60 $\pm$ 0.003	89.85 $\pm$ 0.031	T
11	84.55 $\pm$ 0.001	87.54 $\pm$ 0.010	T
13	54.76 $\pm$ 0.002	28.45 $\pm$ 0.006	PS
14	83.73 $\pm$ 0.003	87.54 $\pm$ 0.015	DT
15	87.69 $\pm$ 0.002	90.93 $\pm$ 0.016	DT
16	87.71 $\pm$ 0.003	90.24 $\pm$ 0.014	T
17	96.62 $\pm$ 0.003	97.56 $\pm$ 0.026	T
18	85.93 $\pm$ 0.003	93.71 $\pm$ 0.017	T
19	90.80 $\pm$ 0.003	90.21 $\pm$ 0.017	T
20	86.63 $\pm$ 0.003	90.72 $\pm$ 0.017	T
21	72.86 $\pm$ 0.001	94.60 $\pm$ 0.013	PS
22	85.64 $\pm$ 0.001	95.21 $\pm$ 0.005	T
23	105.24 $\pm$ 0.002	110.01 $\pm$ 0.024	PS
24	222.14 $\pm$ 0.002	104.07 $\pm$ 0.011	PS
25	101.98 $\pm$ 0.003	100.28 $\pm$ 0.010	PS
26	756.85 $\pm$ 0.015	73.62 $\pm$ 0.023	PS

DT = dispersible tablet; PS = powder for reconstitution into suspension; SD = standard deviation; T = tablet.

these, two products (8.3%) failed for only the artemether content and the other two products (8.3%) failed for both the artemether and lumefantrine contents (refer Table 2).

WHO survey of counterfeit medicine reports from 20 countries between January 1999 and October 2000 showed that 60% of all counterfeit medicine finds occurred in poor developing countries because of weak drug regulation control and enforcement, inconsistent supply, and scarcity of basic medicines.¹⁴ Also, 77% of 771 cases of substandard medicines entered into the WHO database in April 1999 were from developing countries,¹⁴ and poor quality artemisinin-based combination therapy (ACT) medicines are widespread.^{15–17} A study of artesunate content in tablets sampled from pharmacies in Kumasi, Ghana, in 2008, showed varied contents ranging from 47.9% to 99.9% with only 17.6% passing for content of active ingredients by the European Pharmacopoeia standards.¹⁸

In this study, 20 of 24 (83.3%) samples from the market passed the assay for content; they contained the active ingredients indicated by the manufacturers and in the requisite amounts as indicated by the USP. Also, all the samples contained the active ingredients specified. These observations are suggestive of improving antimalarial quality with respect to content. A possible reason may be due to the Global Fund's affordable medicines facility for malaria (AMFm) policy, which aimed at reducing the price of ACTs to prices comparable to other antimalarials such as chloroquine and sulfadoxine–pyrimethamine, increasing the availability of ACTs in public and private outlets and increase in the use of ACTs among poor rural communities.¹⁹ Easily available cheap ACTs provided by this program through the Government of Ghana, both in the private and public sector, will make it unprofitable for trading of counterfeit products.

All the four products (16.7%) that failed for content were PSs for pediatric use. Two of the products (8.3%) showed particularly high levels of artemether of about 222% and 756%. Given that producers of fake drugs are profit motivated, these high levels of artemether may be suggestive of poor manufacturing practices, particularly of the granulation processes that are aimed at ensuring uniform distribution of the active pharmaceutical ingredients (API), and if not properly managed may result in some products with more and others with less API. These findings are suggestive of poorer quality pediatric formulations, particularly PSs. Since all the AMFm green leaf-bearing products provided by the Global Fund are tablets and the pediatric formulations are DTs

meant to be dispersed in a small volume of water just before administration, it could be argued that a niche still exists for other pediatric formulations such as the PSs. These PSs are usually nicely flavored and better tasting than the DTs making them acceptable by patients. Also, about 85% of all malaria cases are children under 5 years²⁰ of age; hence, a large market exists for PSs. Poor quality pediatric formulations have the potential of causing treatment failure when the API content is below the prescribed dose. Since children are more prone to malaria than adults²¹ and disease progression of falciparum malaria from uncomplicated to severe or cerebral malaria is rapid, disease fatality is likely to be higher with these under-dosed pediatric powders. Pediatric powders containing higher than prescribed doses, on the other hand, will result in toxicity. It is therefore important that drug formulations, such as powders for pediatric use, are within prescribed pharmacopeial standards to guarantee efficacy and prevent adverse drug reactions with their use. Policies such as the AMFm should also consider acceptable dosage forms for children, since this will ensure quality pediatric formulations in acceptable dosage forms are available cheaply, to crowd out fake and substandard ones. Good regulatory and monitoring measures through product registration and market surveillance will be useful to ensure good quality products.

A simple and reliable analytical method that uses small-volume sample preparation is a useful addition to the few methods for identification and quantification of artemether–lumefantrine. The relatively short run time of 4.8 minutes together with small volumes of solvent used in sample preparation have cost-sparing implications and potential for real-time monitoring and is likely to find application in market surveillance and quality control, particularly in developing countries. Such real-time monitoring will facilitate market surveillance to help rid the market of poor quality antimalarials and assure effective treatment with antimalarial use.

Dissolution of tablets. The recommended specifications for the dissolution per the monographs of artemether and lumefantrine are Q equals 70% at the end of 60 minutes for artemether and 60% at the end of 45 minutes for lumefantrine.

Apart from three of the tablet samples, 11, 19, and 20, which were not subjected to the dissolution studies due to inadequate samples, all the other tablets investigated passed dissolution at S₁. This reflects a high level of tablet quality since the tablets contain two active ingredients and have to pass dissolution for both (Table 3).

TABLE 3
Dissolution results for sampled tablets at 60 and 45 minutes for artemether and lumefantrine, respectively

Sample code	% Dissolved 6 units at S ₁		Comments
	Artemether	Lumefantrine	
1	94.6, 90.0, 85.1, 94.5, 92.2, 87.7	98.6, 99.8, 99.6, 99.1, 97.7, 97.9	Passed at S ₁
2	86.7, 83.5, 83.8, 86.6, 83.5, 83.9	101.3, 100.8, 100.1, 97.3, 98.0, 96.8	Passed at S ₁
3	104.5, 102.1, 96.1, 99.0, 106.2, 107.7	88.2, 87.2, 93.2, 88.2, 87.5, 86.7	Passed at S ₁
4	100.7, 90.6, 104.6, 106.7, 101.5, 95.1	81.2, 82.1, 83.0, 81.5, 81.9, 80.3	Passed at S ₁
5	96.7, 105.1, 103.9, 105.9, 98.5, 96.6	93.2, 92.4, 92.2, 95.5, 87.9, 92.8	Passed at S ₁
6	83.1, 86.3, 84.7, 85.2, 88.3, 82.9	99.0, 92.9, 85.7, 97.6, 98.3, 90.1	Passed at S ₁
7	92.8, 102.0, 99.2, 103.2, 102.3, 100.8	99.0, 92.9, 85.7, 97.6, 98.3, 90.1	Passed at S ₁
8	93.5, 94.8, 94.9, 96.7, 93.1, 95.1	92.1, 97.0, 101.1, 95.3, 94.8, 97.8	Passed at S ₁
16	93.7, 85.2, 85.8, 86.8, 75.4, 95.4	74.3, 66.9, 73.6, 72.9, 75.8, 68.1	Passed at S ₁
17	91.9, 108.8, 103.6, 102.7, 99.2, 90.5	81.6, 81.1, 78.7, 80.2, 83.4, 83.2	Passed at S ₁
18	95.4, 94.7, 94.0, 93.1, 100.2, 89.2	82.5, 81.0, 81.1, 80.8, 84.2, 81.3	Passed at S ₁
22	90.9, 100.8, 82.9, 89.7, 91.7, 90.1	78.8, 78.7, 79.3, 79.4, 76.4, 78.3	Passed at S ₁

S₁ = first level of dissolution testing.

Dissolution studies as a product quality assessment tool is very important and gives an indication of the bioavailability of the product. It helps to identify and prove the availability of active drug materials in their delivered form and helps simulate the complete release of the drug from the dosage form. This provides a pointer for the in vitro–in vivo correlation.

CONCLUSIONS

A simple, small-volume sample preparation RP-HPLC method for simultaneous identification and quantification of artemether and lumefantrine in tablets, DTs, and PSs has been developed. This method has short run time (4.8 minutes) and will facilitate quantification of large numbers of samples in routine and quality control analyses of this fixed-dose combination dosage forms.

A high percentage of artemether–lumefantrine products in Ghana currently are of very high quality.

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