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COMPARATIVE ASSESSMENT OF THE QUALITY OF SOME COMMERCIAL BRANDS OF ARTESUNATE AND AMODIAQUINE ANTIMALARIAL COMBINATION DRUGS IN THE NIGERIAN MARKET

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ABSTRACT

In Nigeria, the increase in demand for artemisinin based combination therapy especially the artesunate and amodiaquine combination has lead to the proliferation of different brands for sale of which some are suspected to be counterfeit or substandard. Therefore, this work was undertaken to assess the quality of some artesunate and amodiaquine combination brands sold in Nigeria using HPLC. Three fixed - doses and one co – blistered brands of artesunate were assessed using uniformity of weight, disintegration time, tensile stregnth and friability tests. H.P.L.C. was used to determine the percentage artesunate and amodiaquine content of the tablets. Results showed that crushing strength (N) ranged from 4.49 ± 1.37 to 13.70 ± 4.56 kgf. Friability ranged from 0.001 to 0.800 and disintegration time was from 28.28 ± 4.62 to 92.65 ± 23.37. For weight uniformity test, none deviated by up to 5% which was satisfactory. The retention time for amodiaquine and artesunate were 4.2 min and 6.2 min respectively. The percentage concentration of amodiaquine in batches A, B, C, and D1 were 98, 98, 99 and 98.5% respectively while the percentage artesunate concentration was 97, 98, 98 and 99% for batches A, B, C and D2 respectively. The result showed that the products passed the tests. Having met the pharmacopoeia recommendations, the products were confirmed not to be substandard.

KEYWORDS: Comparative assessment, artesunate/amodiaquine combinations, Nigerian market.

INTRODUCTION

Malaria is a disease of global public health importance. Its social and economic burden is a major obstacle to human development in many of the world's poorest countries. In heavily affected countries, malaria alone accounts for as much as 40% of public health expenditure, 30% to 50% of hospital admissions, and up to 60% of outpatient visits.[1] It has an annual incidence of approximately 250 million episodes and is the cause of more than a million deaths, most of them in infants, young children, and pregnant women.[2]

Malaria is caused by parasites belonging to the genus Plasmodium. Four main species of plasmodia infect humans: Plasmodium vivax, Plasmodium falciparum, Plasmodium ovale and Plasmodium malariae. The insect vector is the female Anopheles mosquito, which breeds in stagnant water, and the disease it spreads is one of the major killers on our planet.

Uncomplicated malaria is the mild form of the disease which presents as a febrile illness with headache, tiredness, muscle pains, abdominal pains, rigors (severe shivering), and nausea and vomiting. If left untreated P. Falciparum malaria can rapidly develop into severe malaria with anaemia (low haemoglobin in the blood), hypoglycaemia (low blood sugar), renal failure (kidney failure), pulmonary oedema (fluid in the lungs), convulsions (fitting), coma, and eventually death.[3] A clinical diagnosis of malaria can be confirmed by detection of the malaria parasite in the patient's blood.

Management of malaria

Management of malaria is executed through non pharmacological and pharmacological approaches.

Non pharmacological approach includes the elimination of mosquitoes by the use of insecticides, draining of stagnant water, clearing of bushes near houses and use of long lasting insecticide treated nets at home, especially at night when the mosquitoes are usually active.

Pharmacological approach involves the use of certain chemical agents called antimalarial drugs. There are many types and they differ in chemical structure, mechanism of action or site of action.

Based on their mechanism of action they are classified as chemo prophylactics, tissue schizonticides, blood schizonticides and gametocides. Based on chemical structure, they include the following:

(i) 4-Aminoquinolines e.g. Chloroquine, amodiaquine, piperaquine
(ii) Amino-alcohols e.g. Quinine, quinidine, mefloquine, halofantrine, lumefantrine
(iii) Sulfonamides and sulfones e.g. Sulfadoxine, sulfalene, dapsone
(iv) Biguanides e.g Proguanil, chlorproguanil
(v) Diaminopyrimidine e.g. Pyrimethamine
(vi) 8-Aminoquinoline e.g. Primaquine
(vii) Sesquiterpene lactones e.g. Artemisinin, arteether, artemether, artesunate, dihydroartemisinin
(viii) Naphthoquinone e.g. Atovaquone
(ix) Antibiotics e.g. Azithromycin, clindamycin, doxycycline, tetracycline.[4]

WHO has recommended artemisinin - based combination therapies (ACTs) as first-line treatment for uncomplicated P. falciparum malaria since 2001, and, during the past decade, most malaria-endemic countries shifted their national treatment policies to ACTs.[5]

Artemesinin and Related Compounds

These sesquiterpene lactones are derived from the herb qing hao, a traditional Chinese remedy for malaria. The scientific name, conferred on the herb by Linnaeus, is Artemisia. Artemisinin, a poorly soluble chemical extract from Artemisia, is a fast-acting blood schizonticide effective in treating the acute attack of malaria (including chloroquine-resistant and cerebral malaria). Artesunate, a water-soluble derivative, and the synthetic analogues artemether and artether, have higher activity and are better absorbed. The compounds are concentrated in parasitised red cells. The mechanism of action is probably by production of free radicals within the plasmodium vacuole, following cleavage of the drug's endoperoxide bridge by heme iron in parasitized erythrocyte. These free radicals will attack the lipids, membranes and the structures of the organism, and inhibit its growth by inhibiting enzyme called sarco. endoplasmic reticulum Ca2+---ATPase (SERCA).

These drugs are without effect on liver hypnozoites. So far, resistance has not been a problem, but recent reports suggest that it is developing in some countries. In randomised trials, the qinghaosu compounds have cured attacks of malaria, including cerebral malaria, more rapidly and with fewer unwanted effects than other antimalarial agents. Artemisinin and

derivatives are effective against multidrug-resistant P. falciparum in sub-Saharan Africa and, combined with mefloquine, against multidrug-resistant P. falciparum in South-east Asia.

When used as monotherapy, the short half life of the artemisinin derivatives (and rapid elimination from the blood) means that patients must take the drug for at least seven days.[6,7] Failure to complete the course, due to the rapid improvement in clinical symptoms, can lead to high levels of treatment failure even in the absence of drug resistance. Artemisinin derivatives are therefore usually given with another longer-acting drug, with a different mode of action, in a combination known as artemisinin-based combination therapy or ACT. These combinations can then be taken for shorter durations than artemisinin alone.[3,8] The artemisinin derivatives also reduce the development of gametocytes (the sexual form of the malaria parasite that is capable of infecting mosquitoes) and consequently the carriage of gametocytes in the peripheral blood.[9,10] This reduction in infectivity has the potential to reduce the post-treatment transmission of malaria (particularly in areas of low or seasonal transmission), which may have significant public health benefits.[3]

Artesunate and amodiaquine combination therapy

Many artesunate and amodiaquine combination therapies were formulated as 200mg of amodiaquine and 50mg of artesunate per tablet, which requires rather many tablets per day. To improve treatment compliance, fixed – dose formulations containing 300 or 600 mg of amodiaquine and 100 or 200 mg of artesunate per tablet were developed for treatment of malaria in children up to 7 years of age and in adults respectively.

Early clinical trials showed that a once-a-day dosage was effective.[11] It was subsequently clinically shown to be equally effective as artemether/lumefantrine[12], although it is likely to be more effective in the field due to its simpler once-a-day dosage compared to artemether/lumefantrine twice-per-day dosage.

Substandard drugs in developing countries

The production of counterfeit drugs is a broad and under reported problem particularly affecting poorer countries. It is an important cause of unnecessary mortality and morbidity, and loss of public confidence in medicines and health structures. Empirical observations show that there may be more counterfeit than genuine drugs in circulation.[13]

Major factors contributing to the prevalence of counterfeit drugs in Nigeria include ineffective enforcement of existing laws, non- professionals in drug business, loose control systems, high cost of genuine drugs, greed, ignorance, corruption, illegal drug importation, chaotic drug distribution network, demand exceeding supply amongst many others.[14,15] Counterfeit drugs pose great threats to the attainment of the millennium development goals 4, 5 and 6 which hopes for a reduction in infant mortality, improved maternal health and combating human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS), malaria and other diseases.[16]

The problem of counterfeit drugs have embarrassed the Nigerian healthcare providers and denied the confidence of the public on the nation's healthcare delivery system. The result of fake drug proliferation has led to treatment failures, organ dysfunction or damage, worsening of chronic disease conditions and death of many Nigerians. Even when patients are treated with genuine drugs, no response is seen due to resistance caused by previous intake of fake drugs.[17]

Common problems associated with substandard medicines include under or over concentration, contamination, poor quality ingredients, poor stability and packaging problems. Contamination of active pharmaceutical ingredient (API) with residues of solvents used in the synthesis or other toxic impurities is another frequent and important concern. The quality of the API is one of the major determinants of quality for all pharmaceuticals. However, it is also here that compromise can lead to the greatest cost saving as APIs can represent over 80% of the price of finished products.

Quality control test in pharmaceuticals

Quality control test (QC) is simply a process by which entities review the quality of all factors involved in production.

In pharmaceutical technology, there are series of quality control tests for various formulations such as tablets, suspensions, syrups, creams, etc. For tablets, there are two stages of quality control test which are; (i) granule quality control test which include the tapped density, Hausner ratio, Carr's index, flow rate, particle size determination and bulk density. (ii) tablet quality control test which include physical tests such as the tablet strength analysis (hardness test and friability test), tablet thickness and diameter, weight uniformity, disintegration test , tests such as content uniformity, dissolution test, and assay[chemical].

The first step in detecting counterfeit drugs is to compare the physical appearance and text on packets, leaflet inserts, and blister packs (when present) of suspected samples with those of known genuine products. However, with increased counterfeiter's sophistication, this careful visual inspection is not sufficient to distinguish between fake and authentic drugs. It must therefore be followed by chemical analysis, such as simple in-field assays (e.g., colorimetric test and thin-layer chromatography (TLC)) or more advanced laboratory techniques (e.g. UV spectroscopy, mass spectrometry (MS), vibration spectroscopy (Raman or IR), high performance liquid chromatography (HPLC) and nuclear magnetic resonance (NMR) spectroscopy). These analytical methods allow one to quantitatively determine the chemical composition of the drug (active pharmaceutical ingredients (APIs)) as well as impurities and excipients and hence to identify poor-quality medicines, which include not only counterfeit drugs but also substandard and degraded drugs.

Over the years HPLC has gained an enviable position in analytical laboratories involving separation and quantification of organic compound mixtures. A chromatogram is not a display of results in concentration units but rather a graphical display in real time of peaks generated as the separated components pass through the detector. The chromatogram is a two-dimensional plot with the ordinate axis giving concentration in terms of detector response and the abscissa represents the time. The detector gives response as a peak whose height should be ideally dependent on concentration of the particular component. However, due to analysis conditions peaks may deviate from ideal shape and peak height can no longer be a true measure of the concentration and instead the area under the peak is considered as a measure of component concentration. Each peak represents a component present in the sample. Retention time is time interval between sample injection and the maximum of the peak. It is characteristic of the identity of the component under the operating conditions. Identity of the component can be confirmed by making injections of reference material under the same operational conditions. The matching of retention time of reference material and the component peak confirms the identity of the unknown sample component.

This work was therefore undertaken to assess the quality of some artesunate and amodiaquine combination brands sold in Nigeria using high performance liquid chromatography (HPLC).

MATERIALS AND METHODS

Materials

Artesunate and amodiaquine reference powders were gifts from Swiss Pharma Nigeria Limited, Lagos. Four brands of artesunate and amodiaquine combi-pack (ASAQ) tablets (Table 1) were purchased from selected pharmacies in Abraka, Nigeria. They were either in combi-packs containing artesunate tablets and amodiaquine tablets packaged as co-blisters or as artesunate and amodiaquine compressed into one tablet. Methanol HPLC grade (BDH Chemicals, Poole England), Concentrated Hydrochloric acid (BDH Chemicals, Poole England), were used.

Table 1: Purchased Artesunate (AS) and Amodiaquine (AQ) combination therapy brands.

CODE NAME	BRAND NAME	GENERIC NAME AND STRENGTH	MANUFACTURER	SHELF-LIFE	PACKAGING
A	IPCA ®	AS 100mg and AQ 270mg	Ipca Laboratories Ltd. Mumbai, India	Two years	Blister pack
B	Artesun - Plus®	AS 100mg and AQ 270mg	Guilin Pharmaceutical Co. Ltd, Guilin, China	Two years	Blister pack
C	Artesunate Amodiaquine Winthrop®	AS 100mg and AQ 270mg	Sanofi – Aventis, Cassablanca, Morocco	Three years	Blister pack
D1	Camosunate®	Amodiaquine 300mg	Adams pharmaceutical (ANHUI) Co., Ltd China	Two years	Blister pack
D2	Camosunate®	Artesunate 100mg	Adams pharmaceutical (ANHUI) Co., Ltd China	Two years	Blister pack

Method

The tablets were analyzed based mainly on Pharmacopoeia standard for disintegration test, weight uniformity test, hardness test and friability test. The packs of the various brands of antimalarials were examined for features of illegal prints. The assay on the tablets was carried out using HPLC according to the method developed by.[18] A Cyberlab HPLC machine with C 18 column and LC100 pump connected to an LC 100 UV detector was used.

Preparation of buffer

A 1.36 g of potassium dihydrogen orthophosphate was dissolved in 900 ml of distilled water. Then the pH was adjusted to 3.0 with ortho phosphoric acid. Then the volume was made up to 1000 ml and was filtered through 0.45µm nylon membrane filter and degassed.

Preparation of mobile phase

A degassed mixture of Buffer and Acetonitrile in the ratio of 30:70 (v/v) was prepared and the mixture was filtered through 0.45 µ membrane filters and it was degassed.

Preparation of Artesunate stock solution

A 10 mg artesunate was weighed and transferred into 100 mL volumetric flask. It was dissolved in methanol and diluted up to the mark with methanol to give a stock solution having strength 100 µg/ml.

Preparation of Amodiaquine HCl stock solution

A 10 mg Amodiaquine HCl was weighed and transferred into 100 mL volumetric flask. It was dissolved in methanol and diluted up to the mark with methanol to give a stock solution having strength 100 µg/ml.

Calibration curve

Calibration curves were prepared by taking 1, 2, 3, 4, 5, 6 ml of stock solution of Artesunate and 1, 2, 3, 4, 5, 6ml stock solution of Amodiaquine HCl in 10 ml volumetric flask and dilute up to the mark by Methanol to give 10-60 µg/ ml of Artesunate and 10-60 µg/ ml of Amodiaquine. The representative chromatogram of the calibration curve for Artesunate and Amodiaquine is shown in Figure 1.

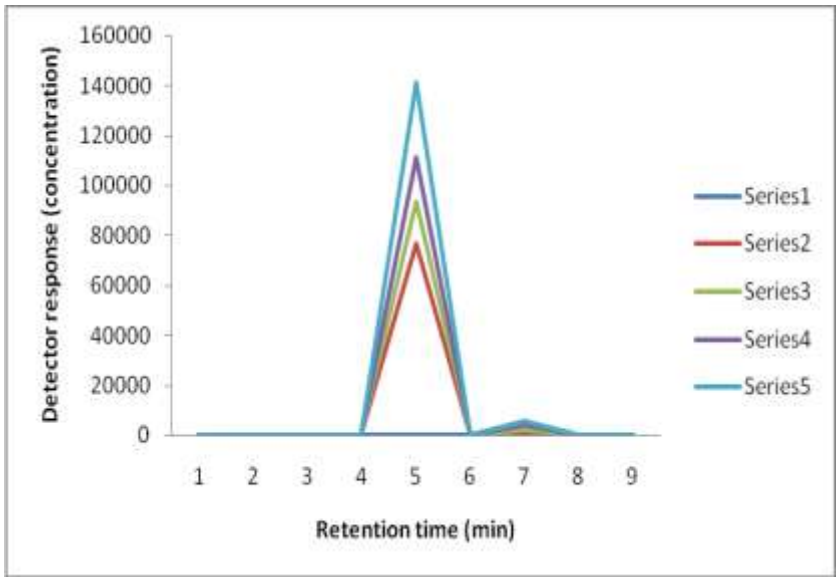

Fig. 1: Representative Chromatogram of the calibration curve for amodiaquine and artesunate.

Procedure for analysis of artesunate/amodiaquine tablets (Assay)

A total of 20 tablets were accurately weighed and triturated with glass mortar and pestle for each batch. The powder equivalent to 50 mg of Artesunate and 150 mg of Amodiaquine HCl were transferred into a 100 ml volumetric flask. Methanol was added and the flask was shaken for 10 min. The volume was made up to mark and the solution was filtered through 0.2 micron nylon membrane filter. The diluted solution was analyzed under optimized chromatographic conditions.

Artesunate + Amodiaquine (ASAQ) tablets disintegration test

Six tablets each were selected randomly from the different brands purchased. They were weighed using the JA5003A analytical balance (Falc Instruments srl, Treviglio, Italy). The tablets were inserted respectively in the six perspex tubes in a basket of the Erweka disintegration tester (Germany) which was used to determine the disintegration time. About 900ml of distilled water maintained at 37±2ºC was used as the disintegration medium. The disintegration time was recorded for each batch. This was performed thrice and the mean time value was calculated.

Weight uniformity test

Twenty tablets each were selected randomly from the different brands and weighed together using the JA5003A analytical balance (Falc Instruments srl, Treviglio, Italy). They were later weighed separately.. This was repeated two more times for each of the batches and their average mass determined. The deviation of each of the individual tablets in each sample from the average mass of the sample was also determined.

Hardness test

Twenty tablets each were selected randomly from the different brands purchased. They were weighed separately and were used for determination of the tablet strength when pressure was exerted on them.

The Monsanto hardness tester (Manesty, Liverpool, England)[19], was used to indicate the strength required to break the tablet. The tablets were placed individually between the spindle and the anvil and pressure was applied by turning the knob just sufficient to hold the tablet in position. The reading of the pointer on the scale was adjusted to zero and pressure increased until tablet cracked and the pointer value was read. Then the mean hardness strength was calculated.

Friability Test

Ten tablets each were selected randomly from the different brands purchased and weighed together. The tablets were placed in the rotating chamber of an Erweka TA – 3R friabilator (Erweka Apparatebau GmbH, Germany) set to rotate at 25 revolutions per minute. The apparatus was allowed to run for 4 minutes. The tablets were removed and reweighed. This experiment was conducted thrice and the mean initial and final weight determined. The loss in weight was recorded and expressed as percentage (%) of the original weight of the tablets.

$$\% \text{ Friability} = \frac{\text{Initial weight} - \text{final weight}}{\text{Final weight}} \text{ X } 100 \text{ ---------- 1}$$

RESULTS AND DISCUSSION

The ability to identify a poor quality formulation is the crucial component of a drug quality assurance system. Quality evaluation studies are important primarily to provide information on the drug content and secondarily, to identify the cause (if any) of poor quality in products. Tablet packaging, country of manufacture (origin), shelf-life and other relevant information on the packaging were recorded. Each of the samples purchased had at least 6 months left on the shelf-life and all analysis were carried out before the expiry dates were up.

Assay (Content of active ingredients)

The retention time for amodiaquine and artesunate obtained using the reference samples were 4.2 min and 6.2 min respectively. In each of of the chromatograms as shown in Figures 2 - 9, two prominent peaks representing amodiaquine and artesunate were noticed. The area under the peaks were used in determining the concentration of amodiaquine and artesunate in each tablet. The percentage concentration of amodiaquine in batches A, B, C, and D1 were 98, 98, 99 and 98.5% respectively while the percentage artesunate concentration was 97, 98, 98 and 99% for batches A, B, C and D2 respectively. International Pharmacopoeia, states that artesunate tablet contains 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. Amodiaquine hydrochloride tablet also contains an amount of amodiaquine hydrochloride ($C_{20}H_{22}ClN_{30}.2H_2O$) equivalent to not less than 93.0% and not more than 107.0% of the labeled amount of amodiaquine.[20]

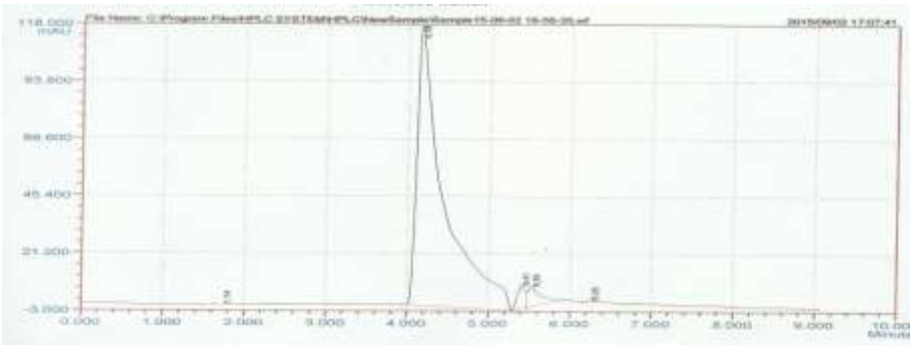

Fig. 2: Chromotogram after injection of 20 µg/ml of artesunate and amodiaquine.

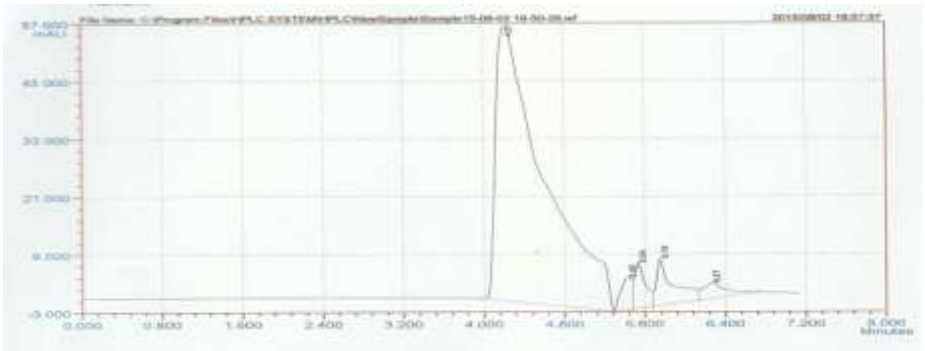

Fig. 3: Chromotogram after injection of 30 µg/ml of artesunate and amodiaquine.

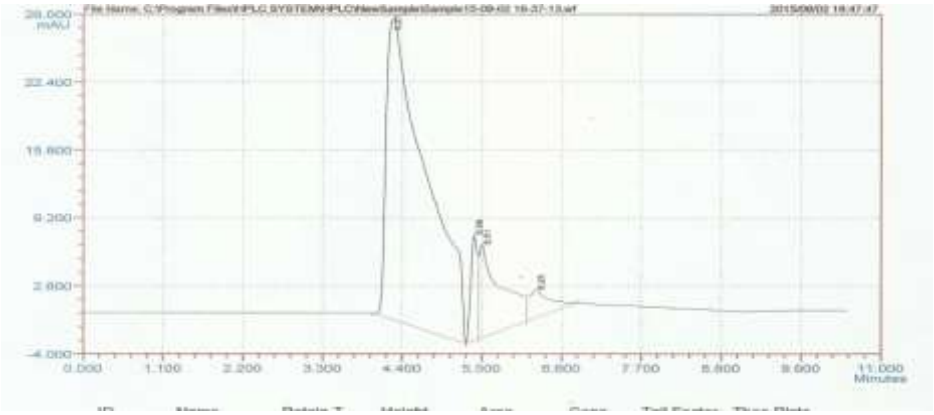

Fig. 4: Chromotogram after injection of 40 µg/ml of artesunate and amodiaquine.

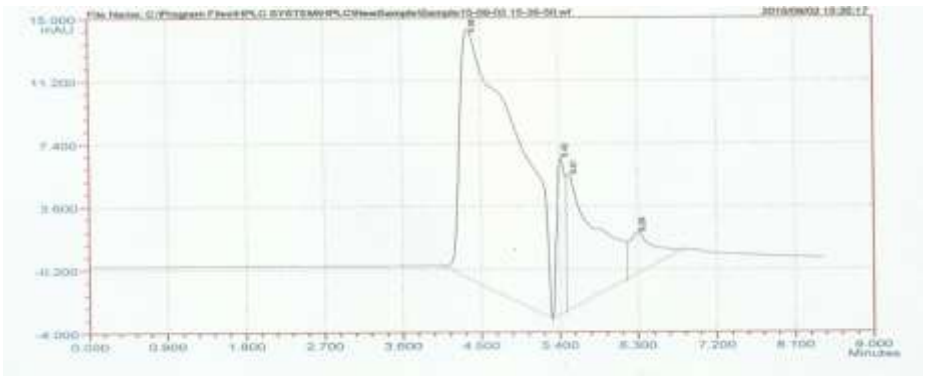

Fig. 5: Chromotogram after injection of 60 µg/ml of artesunate and amodiaquine.

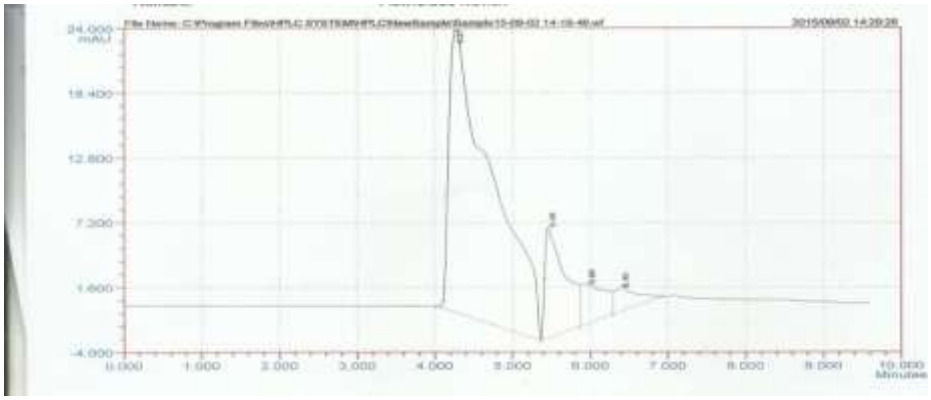

Fig. 6: Chromotogram after injection of batch A.

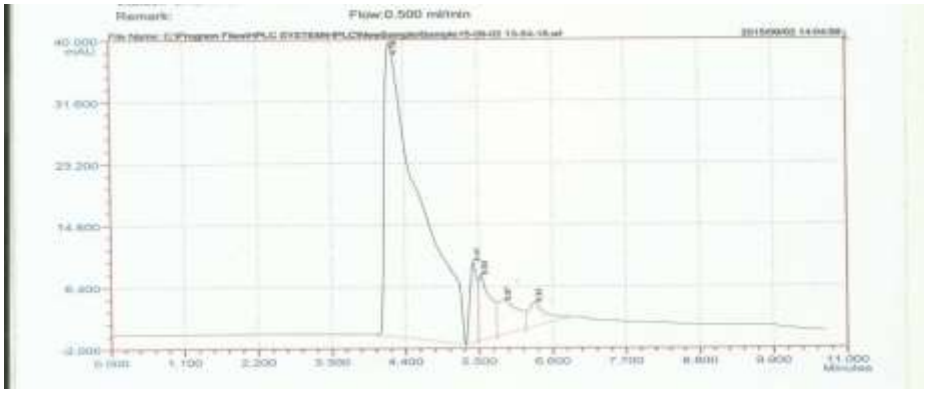

Fig. 7: Chromotogram after injection of batch B.

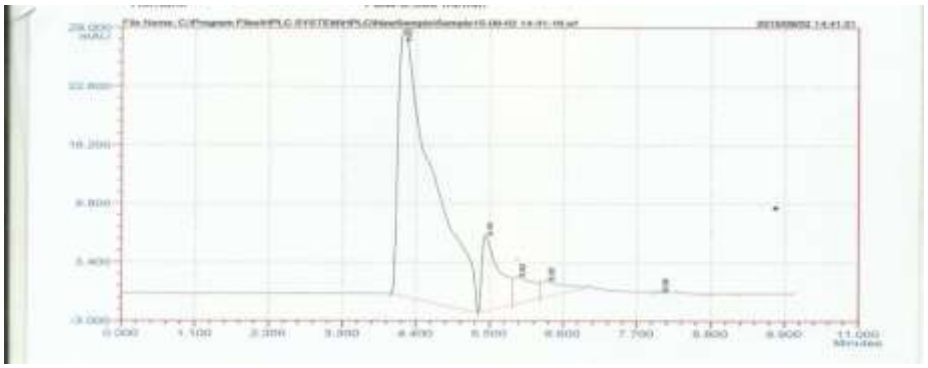

Fig. 8: Chromotogram after injection of batch C.

Fig. 9: Chromotogram after injection of batch D1 and D2 combined.

Friability test

The friability for brands A to C were 0.610%, 0.800%, 0.355% respectively and D1 and D2 were 0.001% and 0.001%. All the samples passed the test with a result of < 1% as specified by the British pharmacopoeia.[20] These samples (tablets) were strong and can withstand pressure of handling and transportation thereby preventing loss of drug particles which could lead to under dosage.

Table 2: Friability, Hardness and Disintegration Test for diferrent brands of Artesunate/Amodiaquine Tablets.

	TABLET WEIGHT (g)	% FRIABILITY	DIAMETER (mm)	THICKNESS (mm)	HARDNESS (Kgf)	DISINTEGRATION TIME (min)
IPCA	0.698 ± 0.004	0.610	13.042 ± 0.038	4.502 ± 0.085	8.438 ± 0.829	47.2 0 ± 4.43
ARTESUN – PLUS	0.728± 0.015	0.800	12.755 ± 0.096	4.742 ± 0.159	13.695 ± 4.563	92.65 ± 23.37
WINTHROP ARTESUNATE/ AMODIAQUINE	0.707 ± 0.009	0.355	12.967 ± 0.051	4.25 ± 0.050	12.302 ± 2.237	38.14 ± 4.83
CAMOSUNATE (AMODIAQUINE)	0.510 ± 0.007	0.001	12.565 ± 0.041	4.587 ± 0.132	9.816 ± 2.864	42.69 ± 10.42
CAMOSUNATE (ARTESUNATE)	0.296 ± 0.000	0.001	9.146 ± 0.062	4.283 ± 0.264	4.487 ± 1.368	28.28 ± 4.62

Hardness test

The samples had mean crushing strength of 8.44 ± 0.83, 13.70 ± 4.56, 12.30 ± 2.24, 9.82 ± 2.84, and 4.49 ± 1.37 kgf for sample A, B, C, D1 and D2 respectively which were higher than the minimum required value, 4kg (40 N). The resistance of tablet to capping, abrasion or breakage under conditions of storage, transportation and handling before usage depends on its hardness. Easy breakage of tablet may also lead to loss of medicament which eventually leads to under dosing. Tablets that are too hard are also undesirable because they may not disintegrate easily and may be passed out of the body without releasing the needed drug. Therefore, a balance is usually struck.

Weight uniformity test

The samples had a percentage weight variation of 0.31, 1.52, 1.03, 1.20 and 1.22% for sample A, B,C,D1and D2 respectively. They were all below 5% and therefore passed the test. The uniformity of weight test is one way of determining whether proper mixing of ingredients occurred during production. Also, even distribution of active ingredient is

necessary in order to avoid overdosing or under dosing, both of which have negative impact on the patient. The results shown in Tables 3 and 4, indicated that the four brands of artesunate/ amodiaquine hydrochloride tablets had weights with deviation of less than 5% and hence conformed to the British Pharmacopoeia specification of not more than 5% deviation for more than two of the individual masses and no deviation by more than 10% of the average mass of the tablets.[20]

Table 3: Uniformity of tablet test for IPCA, Artesun –plus and Winthrop brands of Artesunate/Amodiaquine tablets.

IPCA		ARTESUN – PLUS		ARTESUNATE/AMODIAQUINE WINTHROP	
WEIGHT (g)	% DEVIATION	WEIGHT (g)	% DEVIATION	WEIGHT (g)	% DEVIATION
0.696	0.349	0.718	1.381	0.707	0.034
0.697	0.248	0.760	4.462	0.710	0.402
0.696	0.277	0.744	2.276	0.714	0.925
0.697	0.148	0.748	2.812	0.697	1.366
0.695	0.406	0.716	1.628	0.693	1.989
0.711	1.872	0.718	1.312	0.723	2.212
0.699	0.052	0.761	4.599	0.717	1.392
0.699	0.037	0.712	2.150	0.704	0.447
0.697	0.177	0.723	0.625	0.706	0.178
0.699	0.152	0.718	1.339	0.694	1.805
0.694	0.635	0.711	2.247	0.702	0.716
0.698	0.077	0.728	0.089	0.717	1.462
0.700	0.195	0.721	0.968	0.708	0.175
0.698	0.019	0.725	0.405	0.716	1.194
0.700	0.209	0.731	0.531	0.701	0.928
0.695	0.521	0.724	0.501	0.700	0.970
0.699	0.066	0.731	0.462	0.714	1.010
0.697	0.248	0.725	0.377	0.718	1.505
0.700	0.195	0.713	2.068	0.701	0.871
0.701	0.324	0.726	0.226	0.700	1.041

Table 4: Uniformity of tablet test for Camosunate brand of Artesunate/Amodiaquine tablets.

CAMOSUNATE (AMO DIAQINE)		CAMOSUNATE (ARTESUNATE)	
WEIGHT (g)	% DEVIATION	WEIGHT (g)	% DEVIATION
0.496	2.836	0.291	1.404
0.519	1.792	0.297	0.592

0.520	1.949	0.292	1.370
0.498	2.307	0.296	0.152
0.514	0.849	0.298	0.694
0.520	1.849	0.287	2.758
0.515	0.969	0.296	-0.017
0.513	0.633	0.311	5.160
0.518	1.537	0.297	0.457
0.509	0.228	0.300	1.607
0.510	0.072	0.303	2.521
0.506	0.875	0.294	0.389
0.502	1.503	0.296	0.051
0.516	1.084	0.295	0.355
0.502	1.601	0.289	2.216
0.510	0.032	0.289	2.318
0.506	0.817	0.292	1.066
0.509	0.287	0.296	0.254
0.503	1.483	0.298	0.761
0.517	1.380	0.294	0.389

Disintegration test

The disintegration time for samples A , B, C, D, D2 were, 47.20 ± 4.43, 92.65 ± 23.37, 38.14 ± 4.83, 42.69 ± 10.42 and 28.28 ± 4.62 min respectively. For a drug to be absorbed from a solid dosage form after oral administration, it must first be in solution, and the first important step toward this condition is usually disintegration. The British Pharmacopoeia states that, for uncoated tablets, disintegration should occur within 15 minutes and for coated tablets within 30 minutes.[20] All samples were uncoated tablets. None disintegrated in less than 15mins.

CONCLUSION

From this study, it can be concluded that all the samples analyzed contained the appropriate active ingredients and met the quality specification requirements (reference standard) especially content of active ingredients (asssay). Also that the brands of Artesunate and Amodiaquine combination analyzed were confirmed not to be counterfeit and substandard as they met the pharmacopoeia recommendation.

It is recommended that further work should be carried out on new brands of ACTs emerging into the market. There is therefore, the need for a continuous evaluation of the quality of artesunate and amodiaquine in the Nigerian market to safeguard the health of the populace especially children.

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