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# Quality Assessment of Artemisinin-Based Drugs Marketed and Used In Maiduguri Metropolitan Council Borno State, Nigeria

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## ABSTRACT

The experiment involves quality analysis of six (6) samples of Antimalarial drug (Artemisinin-based combination) using ultra violet spectrophotometer in the range of (200-400nm) in which the samples were dissolved in methanolic acid and their various absorbance and wavelength determined and compared with that of the standard, wavelength of maximum absorbance was in the range of 240-243nm was used. Percentage content for each sample was determined so as to note if it was within the acceptable range of (95-105%), for those that passed the test or if it was below or above the rage for samples that are substandard or highly concentrated. The amount of Artemisinin base in each sample was determined (actual content) and compared with that of the stated (20mg). The stated drug content in the samples where used alongside the actual drug content to calculate the percentage deviation of each sample from the market standard. It was observed that only one sample Lokmal(97.1%) meet the BPC/Martindale requirement for actual drug content range of (95-105%) while the other five samples , Amatem (72.5%), Artemetrin (70.8%), Lonart (72.1%), Coartem (72.1%), Artin(39.6%), failed the test with values below the acceptable range. The value of Artin was as low as 39.6% and has the lowest actual drug content sample among the six drugs.

**Keywords**: Artemisinin; Antimalarial; Spectrophotometry

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## INTRODUCTION

Over the last few years a great deal of attention has been paid to drugs. The re-eminent position which drugs occupy in health care delivery system seemed to overshadow other activities. No doubt that healthcare delivery without drugs is meaningless. The procurement, storage and distribution of drugs have passed a lot of problems. [1]. the fake drugs phenomenon has further complicated matters to the point that more time is being spent sorting genuine drugs from the fake ones rather than the other way.

In order to counteract the problems of fake and substandard drugs it has become absolutely necessary that all drugs put for sale and use in Nigeria must undergo stringent test to confirm their identity, purity and safety for human consumption. [2]

We should also consider the fact that deterioration and degradation of drugs thus takes place on storage, it has become absolutely necessary to carry out the analysis and assessment to prove that they are of high quality [3].

Artemisinins are potent and fast acting antimalarials with no clinical evidence of resistance. They are particularly well suited for the treatment of severe plasmodium falciparum malaria [4] and now play a key role in the combination therapy of drug-resistant infections. Its endoperoxide moiety is required for antimalarial activity [5].

Chloroquine resistant strains of Plasmodium Falciparum of which artemisinin and its derivatives are used are found in Southeast Asia, parts of the Indian subcontinent, South America, Africa and Oceania. [4] are found in Papua New Guinea and Indonesia. They have been formulated into several routes most especially the semi synthetic artemisinin: Oral route (dihydroartemisinin, artesunate and artemether), Intramuscular route (artesunate, arteether and artemether), Intravenous route :( artesunate) and Rectal route :( artesunate) [4] [6]. Both artesunate and arthemeter are converted to dihydroartemisinin which provide much of their antimalarial activity [6]

They are mostly metabolized through their conversion to the active metabolite dihydroartemisinin. They are also biotransformed to inactive desoxyartemisinin and 9, 10-dihydroxy-hydroartemisinin. It has a plasma half life of 1 to 2 hours; its major urinary metabolite is glucoronide [7] [6], [8], [4]. With repeated dosing, Artemisinin and Artesunate induce their own cytochrome P450 (CYP) mediated metabolism, which may enhance clearance by up to five fold [9]. No clinical pharmacokinetic interactions between the Artemisinin compounds and mefloquine [6]

## EXPERIMENTAL

An accurate weight of 10mg of the sample Artemisinin was weighed using an analytical balance into a 100ml volumetric flask, and 50ml of methanolic hydrochloride was added and

sonicated (shaken) for 15 minutes, it was removed and allowed to cool and then made up to mark with the solvent(methanolic hydrochloride)

To 100ml. 5ml was further pipette into a 50ml volumetric flask and made up to mark with the same solvent (methanolic hydrochloride). The solution was then ran on ultra violet spectrophotometer in the range of 200-400nm.

The calculation of the results of the market standard and one of the six (6) samples Lokmal (as a procedure for all the samples), treated with methanolic hydrochloride and ran on ultra violet spectrophotometer in the range of 200-400nm are obtained as follows:

**SAMPLE 1**

Drug: Lokmal (trade name)
Company: Emzor Pharmaceuticals Ltd.Lagos
Content: 20mg Artemether/120 lumenfantrine
Batch number: 4124N
Production date: 11/2009
Expiry date: 11/2011
NAFDAC registration number: A4-1696
Stated drug content: 20mg of Artemether
Occurrence: Combination drug
Lokmal henceforth represented as or called sample1

**SAMPLE 2**

Trade name: Amatem
Company: Elbe pharma Nig. Ltd.Lagos,
Content: 20mg Artemether/120 lumenfantrine
Batch number: AMMH 0020,
Production date: 09/2009
Expiry date: 08/2012
NAFDAC registration number: A4-1888,
Manufacturer license number: 300
Stated drug content: 20mg of Artemether,
Occurrence: Combination drug
Amatem henceforth represented as or called sample2

**SAMPLE 3**

Trade name: Artemetrin
Company:
Content: 20mg Artemether/120 lumenfantrine
Batch number:

Production date:
Expiry date:
Stated drug content: 20mg of Artemether
Occurrence: Combination drug
Artemetrin henceforth represented as or called sample3

**SAMPLE 4**

Trade name: Lonarte
Company: Manufactured by Bliss GVS Pharma Ltd. Factory 10, Dewan udyog Nagar, Aliyali Palghar, Maharashtra-401 404, India.
Marketed by Greenlife Pharmaceutical Ltd. Number 2 Bank lane, Ilupeju, Lagos, Nigeria
Content: 20mg Artemether/120 lumenfantrine
Batch number: LN-126 Production date: 05/2009
Expiry date: 04/2011
NAFDAC Registration number: 04-8969
Stated drug content: 20mg of Artemether
Occurrence: Combination drug
Lornate henceforth represented as or called sample4

**SAMPLE 5**

Trade name: Coartem
Company: Novartis, manufactured by Novatis Pharmaceutical, Suffern, New York USA
Content: 20mg Artemether/120 lumenfantrine
Batch number: F1411 Production date: 03/2009
Expiry date: 02/2011
NAFDAC registration number:
Stated drug content: 20mg of Artemether
Occurrence: Combination drug
Coartem henceforth represented as or called sample5

**SAMPLE 6**

Trade name: Atrin
Company:
Content: 20mg Artemether/120 lumenfantrine
Batch number: 680391 Production date: 12/08
Expiry date: 12/11
NAFDAC Registration number: A4-1695
Stated drug content: 20mg of Artemether
Occurrence: Combination drug
Artin henceforth represented as or called sample 6

**Market standard.**

This is henceforth represented as or called (MKT STD)
Baseline start wave length (nm) 200nm
Baseline end wavelength ……..400nm
Baseline scan interval……1.0nm
Concentration calculated standard…1.00
Concentration factor……1.00
Concentration offset……0.00
Start wavelength (nm)……200.00nm
End wavelength (nm)……400.00nm
Scan interval……1.00nm
Measure mode……Absorbance
Drug content……Artemisinin 20mg
Absorbance (maximum)……1.429Abs
Wavelength of absorbance……242.00nm

| PEAK | | VALLEY | |
|---|---|---|---|
| nm | Absorbance | nm | Absorbance |
| 201 | 3.000 | 204.0 | 1.133 |
| 205 | 2.199 | 204.0 | 0.518 |
| 341 | 0.779 | | |

**SAMPLE 1**

**Drug: Lokmal** (trade name)

Company: Emzor Pharmaceuticals Ltd.Lagos
Content: 20mg Artemether/120 lumenfantrine
Batch number: 4124N
Production date: 11/2009
Expiry date: 11/2011
NAFDAC registration number: A4-1696
Stated drug content: 20mg of Artemether
Occurrence: Combination drug
Lokmal henceforth represented as or called sample 1

**SAMPLE 1**

Baseline start wave length (nm) …200nm
Baseline end wavelength (nm)……400nm
Baseline scan interval……1.0nm
Concentration calculated standard…1.00
Concentration factor……1.00

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Concentration offset……0.00
Start wavelength (nm)……200.00nm
End wavelength (nm)…….400.00nm
Scan interval……1.00nm
Measure mode……Absorbance
Drug content……..Artemether 20mg
Absorbance (maximum……1.388Abs
Wavelength of absorbance……241.00nm

| PEAK | | VALLEY | |
|---|---|---|---|
| nm | Absorbance | nm | Absorbance |
| 201 | 3.000 | 204.0 | 1.133 |
| 205 | 2.199 | 204.0 | 0.518 |
| 341 | 0.779 | | |

Determination of drug content mg

$$(\%)\ \text{CONTENT} = \frac{\text{Absorbance of sample}}{\text{Absorbance of standard}} \times 100$$

Range (95-105%) [10] (BPC, 2008)

**STANDARD**

$$\%\ \text{content} = \frac{1.429}{1.429} \times 100\%$$

% content= 1.0 X100%
% content=100%
Amount in mg = 100% will give 20mg
100% will give X mg

$$\text{Amount in mg} = \frac{100\%}{100\%} \times 20\text{mg}$$

Amount in mg=20mg
Actual content 20mg Artemether
Stated content 20mg Artemether

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## RESULTS AND DISCUSSION

| S/no | Sample | Standard | Sample1 | Sample2 | Sample3 | Sample4 | Sample5 | Sample6 |
|---|---|---|---|---|---|---|---|---|
| | Trade name | Market standard | Lokmal | Amatem | Artemetrin | Lonarte | Coartem | Artin |
| 1 | Absorbance | 1.429 | 1.388 | 1.037 | 1.012. | 1.031 | 1.031 | 0.566 |
| 2 | Wavelenth (nm) | 242 | 240 | 243 | 241 | 241 | 241 | 241 |
| 3 | Stated drug content(mg) | 20 | 20 | 20 | 20 | 20 | 20 | 20 |
| 4 | Actual drug content(mg) | 20 | 19.42 | 14.5 | 14.16 | 14.42 | 14.42 | 7.92 |
| 5 | %content | 100 | 97.1 | 72.5 | 70.8 | 72.1 | 72.1 | 39.6 |
| 6 | Accepted %content range | 95-105 | 95-105 | 95-105 | 95-105 | 95-105 | 95-105 | 95-105 |
| 7 | Start wavelength(nm) | 200 | 200 | 2000 | 200 | 200 | 200 | 200 |
| 8 | End wavelength(nm) | 400 | 400 | 400 | 400 | 400 | 400 | 400 |
| 9 | Scan interval(nm) | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 10 | Wavelength range(nm) | 240-243 | 240-243 | 240-243 | 240-243 | 240-243 | 240-243 | 240-243 |
| 11 | %deviation | 0 | 2.9 | 27.5 | 29.2 | 27.9 | 27.9 | 60.4 |
| 12 | Assessment | Standard | Pass | Fail | Fail | Fail | Fail | Fail |

## DISCUSSION

From the result obtained, it could be seen that sample1 has maximum absorbance at 1.388 and a wavelength of 241nm,as compared to the standard that has maximum absorbance 1.429 at a wavelength of 242nm,the percentage content of sample1 was 97.1% which falls within in the acceptable range (95-105%) while the actual drug content was 19.42mg with a percentage deviation of 2.9%, since sample 1 falls within the accepted range of percentage content (95-105%) it is said to pass the test and contains the minimum necessary amount of drug required to elicit it's action pharmacologically

For sample2,with a maximum absorbance of 1.037 and at a wavelength of 240nm when compared with the standard that has a maximum absorbance of 1.429 and at a wavelength of 242nm,the percentage content is said to be 72.5%,which is a sharp contrast from the accepted range (95-105%),the actual drug content was 14.5mg as against 20mg that was stated, the percentage deviation was 27.5%,the drug is said to have failed the test as it does not fall within the accepted percentage content range of(95-105%) and does not contain the required amount of Artemether base(20mg) necessary to elicit it's pharmacological action,

Sample 3, with a maximum absorbance of 1.012 and at a wavelength of 243nm,when compared with the market standard that has a maximum absorbance of 1.429 and at a wavelength of 242nm,the percentage content is said to be 70.8% which is a sharp contrast from the accepted range(95-105%),the actual drug content for sample3 was 14.16mg as against 2omg that was stated, the percentage deviation was 29.2%,sample 3 is said to have failed the test as it does not fall within the accepted percentage content range of (95-105%),therefore

does not contain the required amount of Artemisinin base (20mg) necessary to elicit it's pharmacological action, even as regards it's percentage deviation, it was too high at 29.2%.

Sample 4 which has a maximum absorbance of 1.031 and at a wavelength of 241nm,when compared with the market standard that has a maximum absorbance of 1.429 and at a wavelength of 242nm,the percentage content was 72.1%,which represents a sharp contrast from the accepted range of (95-105%),the actual drug content for sample 4 was 14.42mg as against 20mg stated as the Artemisinin base, the percentage deviation was 27.9%,therefore sample 4 is said to have failed the test and is sub-standard since it does not fall within the accepted percentage content range of (95-105%) and has a high percentage deviation. It does not contain the required amount of Artemether base (20mg) necessary to elicit its pharmacological action and hence will not be optimally effective.

Sample 5,with a maximum absorbance of 1.031 and at a wavelength of 241.nm,when compared with the market standard that has a maximum absorbance of 1.429 and at a wavelength of 242nm,the percentage content is said to be 72.1%,which represents a sharp contrast from the accepted range (95-105%), the actual drug content for sample 5 was 14.42mg as against 20mg stated as the Artemether base, the percentage deviation was 27.9%,the drug sample is said to have failed the test and is sub-standard, since it does not fall within the accepted percentage content range of (95-105%) and has a high percentage deviation of 27.9% with the drug content below the stated value, it can be convincingly said to have failed the test and therefore does not contain the required amount of Artemether base (20mg) necessary to elicit pharmacological action, and hence will not be optimally effective.

Sample 6,which has a maximum absorbance of 0.566 and at a wavelength of 241nm,when compared with the market standard that has a maximum absorbance of 1.429 and at a wavelength of 242nm,the percentage content is said to be 39.6% which represents a far sharp contrast from the accepted range of (95-105%),the actual drug content for sample 6 was 7.92mg as against 20mg stated as the Artemether base, the percentage deviation was 60.4%,the drug sample is said to have failed the test and is below standard since it does not fall within the accepted percentage content range of (95-105%) and has a very high percentage deviation even when compared to others, the drug content is below that of the stated, it can be said to have failed the test, therefore does not contain the required amount of Artemisinin base 20mg necessary to elicit it's desired pharmacological action, and hence will not be optimally effective.

From the results obtained it could be seen that sample 6 has the least actual drug content (7.92mg) and sample 1 has the highest actual drug content (19.42mg),there by making the range of percentage deviation for this test to be in the range of 2.9-60.4%.

For sample 1, the percentage was quite much, while that of the other sample continuously increased to give a highest percentage deviation of 60.4% with sample 6. In terms of their potencies, sample 1 will have the highest potency since it contain 19.42mg, with its

difference in drug content with that of the stated (20mg) being 0.58mg and therefore falls within the percentage content range of (95-105%) as its percentage drug content is 97.1%.

With the reduced actual content recorded for sample2 to sample6,this can result in recrudescence of malaria parasite, leading to increased resistance to chemotherapeutic agents by strains of plasmodium most especially falciparum, this coupled with non drug compliance among patients can result in therapeutic failure and increased incidence and persistence of malaria, mostly especially for people in the tropics where the situation is complicated by poor sanitation condition(lack of proper basic hygiene) this is quite evident with increased cases of reoccurrence of malaria in individuals that have taken chemotherapy for curative and prophylactic treatment.

## CONCLUSION

From the qualitative analysis made, it can be concluded that, the six (6) samples subjected to qualitative analysis only one of the sample fell within the acceptable range, the remaining five (5) samples were below the acceptable range of (95-105%). Sample 2 to 6 is said to have failed the test and they are substandard

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