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ASSESSMENT OF CHLOROQUINE TABLETS USED IN THE TREATMENT OF MALARIA IN NORTHERN NIGERIA

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Research Article

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Abstract

The present study was undertaken in four States of Northern Nigeria to assess the quality of chloroquine tablets available at registered and unregistered drug outlets of government and private health facilities. Standard methods were employed to assess the following parameters of quality control; friability state of chloroquine tablets, hardness and uniformity of weight. In addition, physical examination of the tablets including colour, odour and whether the tablets are scored or inscribed were determined. A total of 146 samples were collected which gave a breakdown of 35, 37, 52 and 22 for States A, B, C and D respectively. State A seemed to have performed best in respect of friability state, followed by States D, B and C in that order. As for odour, only some samples from states B and C had an irritating smell, the other states had samples that were either odourless or had a faint characteristic smell. On the whole, samples were either white or yellow in colour, except in States B and D where whitish brown and green tablets respectively, were recorded. The packaging in all the states was of acceptable standards except for one sample in state A that bore a photocopied label on the container. Of the four states, only state A had a mean friability value below 1%D. Tablets sampled from all states showed consistency in tablet hardness and weights with an average tablet weight falling within the standard range of 0-10% deviations. The 146 samples contained active chloroquine with only one sample each of states A and D contained the sulphate salt, while the remaining 144 (98.63%) samples contained the phosphate salt. The results of this study showed correlation between the quality of chloroquine tablets in Northern Nigeria and their routes of supply. The poor quality of chloroquine preparations may be considered as a factor which contributed to the emergence of chloroquine resistant *Plasmodium falciparum* in Nigeria.

Keywords: *Malaria, Chloroquine tablet, Friability, Hardness*

Introduction

In developing countries where malaria is endemic, particularly in tropical Africa, the control of malaria has in the past been centered primarily on the use of chemotherapeutic and prophylactic agents [1,2]. This method is limited in its effectiveness. As stipulated by World Health Organization (WHO), other measures are important and all should come into play for a meaningful and effective disease control. In an attempt to provide quality drugs at all facets of the primary health care, the various governments adopt policies that contain regulatory procedures for the importation and local manufacturing of drugs. Observations were made in South-Western Nigeria where *Plasmodium falciparum* has remained sensitive to chloroquine [3] and where only about 20% of chloroquine tablet samples were found to be of low quality [4]. Chloroquine is a synthetic product that was first produced in 1934 by Andersag (Bergqvist, 1983) and accepted for clinical use in 1947 [5]. Chloroquine has antimalarial [6], antiparastitic [7], anti-inflammatory [7], antibacterial [8], antiarrhythmic [9] as well as stabilization of lysosomal membrane. The wide spread use of chloroquine tablets possibly due to the availability and affordability in developing countries like Nigeria has necessitated the assessment of the quality of the chloroquine tablets in northern Nigeria.

Materials and Methods

Selection of study area

The study area comprises of the states of Northern Nigeria and was chosen based on their location. It was selected to statistically represent the regions of North eastern, North western, North central and Federal capital territory (Abuja).

Sample Collection

Determination of types and number of drug outlets

For the purpose of this study, confidential registers and files were obtained from the State Ministry of Health of

each of the 4 states (A, B, C and D) respectively, located in Northern Nigeria. By the aid of these documents, the various outlet types were identified and the total number of each type of drug outlet was determined for the 4 states.

Determination of types and number of drug outlets

In the 4 states, political maps showing the local government area (LGAs), state capital, towns and villages were obtained from each state ministry of land and survey. Three collection sites namely one large, one medium and one small size towns were selected. Each of these collection sites were divided into 10 equal parts of which 2 (one central and one peripheral) were randomly chosen for physical counting of the numbers of registered and unregistered drug outlets. The ratios for central and peripheral sites of large, medium and small towns were determined. Also the average ratio for each state was determined and subsequently adopted for practical use.

Stratified Sample Collection

The sample collection method as described by Harper [10] and Elwood [11] popularly referred to as stratified sample collection, was adopted and modified for the purpose of this study. The application of standard randomized controlled trial sampling was also extended to this study to achieve an optimal level of success in the sample collection procedure. Previous experience showed that samples may not be available at sites chosen by ballot. In such circumstances, the combination of the above two methods will allow for sample collection at certain sites which were initially not included in those obtained by ballot modification made. Samples were collected from registered outlets such as government health facilities, private clinics or hospitals, patent medicine stores, pharmaceutical chemists and industries and from unregistered outlets, usually referred to as open market drug stores. Samples so collected covered a very wide range of various brands and batches of chloroquine (CQ) tablets, resulting in a statistically representative sample pool for analysis. At the collection sites, the following parameters were recorded:- Tablet brand and source, manufacturer's name and address, manufacturing date, expiration date, nature of packaging material, type and address of drug outlet, batch number, national agency for food, drug administration and control (NAFDAC) number, cost of tablets, date of sample collection and the claimed chloroquine content. At each collection site, 100 tablets were sampled and paid for.

Availability of Chloroquine tablets at government and private health facilities

For this purpose, each of the 4 states was divided into approximately three equal zones (Southern, Central and Northern). Twenty of each private and Government health facilities were visited in each of the zones and the availability of chloroquine tablets was assessed.

Quality assurance testing of chloroquine tablets

All the 146 samples collected from different outlets of the 4 states were individually coded such that their identities were not known at the time they were being subjected to quality assurance testing.

Physical examination of tablet samples

Each coded sample was subjected to physical examination. Ten of the 100 tablets of each sample were examined based on the following criteria: colour, odour, friability state i.e. how many of the ten tablets are chipped, abraded, uniform or deformed surfaces, luminosity either dull or shiny or powdery, whether scored and/or inscribed. The taste and packaging were also assessed [1].

Qualitative identification tests

Ten (10%) of the 100 tablets per sample were crushed and of these 20 mg of the CQ salt (phosphate or sulphate) were weighed and dissolved in 2.0 ml of distilled water. Five drops of potassium mercuric iodide were added. The appearance of a white curdy precipitate indicated the presence of CQ moeity. Also 10 mg of the crushed sample were dissolved in 5.0 ml of distilled water, acidified with 1.0 ml of hydrochloric acid (HCl 70g/L) and treated with 1.0 ml of barium chloride (50g/L). The production of a white precipitate differentiated the sulphate from the phosphate [12].

Friability Testing

Ten tablets of each coded sample were initially weighed and there- after placed in the friabilator which operated at 25 revolutions per minute. After a 4 minutes run, the remaining intact tablets were removed and weighed again. The loss in weight was noted and the percentage friability (D%) was determined. Samples were grouped into those with percentage friability (D%) less or greater than 1%.

Hardness Test

Five tablets of each of the coded samples were singly placed in the Monsanto hardness tester. The handle of the machine was screwed until the tablet broke. The force required to break the tablet was recorded in kilogramme force (kgf). The same exercise was carried out for each of the remaining 4 tablets, and the average force was calculated. Generally, tablets weighing about 100 mg, would exhibit force of hardness within 2-3 kgf, while those weighing between 200 mg - 500 mg exhibit such force within 3-8 kgf. The individual samples were therefore placed into any of the following five classes:- Less than 2, between 2-3.90, between 4-5.90, between 6-7.90, and greater than 8.00, kgfs; depending on the average force of hardness of the individual samples.

Uniformity of weight

Twenty (20) tablets of each coded sample were singly weighed by a front loading mettler balance. The average weight was calculated, the percentage, deviations of weight were determined and correlated with expected percentage deviation; for a good manufacturing practice (GMP) not more than 2 of the twenty tablets should deviate from the average weight by more than the deviations given below and none should deviate by more than double the deviation indicated.

Results and Findings

Samples collected from study States

It can be seen that 50% of the total samples were collected from Pharmaceutical chemists, 32.9% from

patent medicine stores and the rest of outlets types constituted the remaining 17.1%. The main source of tablets sampled from private outlets in State A was from the South-Eastern part of Nigeria. On the other hand, tablets sampled from government establishments had been bought by tender and may therefore have come from any part of the country. For States B, C and D drug supplies linked to South-Eastern Nigeria were 48.65%, 46.15% and 9.09% respectively. Of the four states, only state D recorded a high percentage of locally manufactured tablets. Its other source of supplies was the South-Western region of Nigeria. On the other hand, samples collected from government establishments of states B, C and D and supplied by tender could have come from any part of the country (Table 1 and Figure 1).

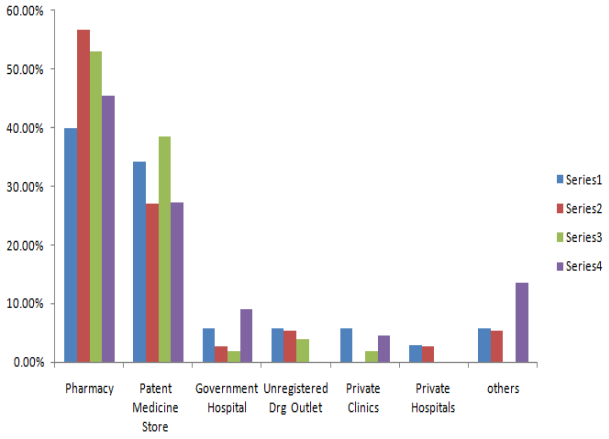

Figure 1: Samples collected from various types of drug outlets in the study states

Table 1: Number of samples collected from various types of drug outlets in the four states

S/no.	*Type of drug outlet*	*Number and percentage of collected samples*				*Total*
		A	*B*	*C*	*D*	
1	Pharmacy	14(40.0%)	21(56.8%)	28(53.9%)	10(45.5%)	73(50.0%)
2	Patent Medicine Stores	12(34.3%)	10(27.0%)	20(38.5%)	6(27.3%)	48(32.9%)
3	Government Hospital	2(5.7%)	1(2.7%)	1(1.9%)	2(9.1%)	6(4.1%)
4	Unregistered Drug Outlet	2(5.7%)	2(5.4%)	2(3.8%)	-	6(4.1%)
5	Private Clinics	2(5.7%)	-	1(1.9%)	1(4.5%)	4(2.7%)
6	Private Hospitals	1(2.9%)	1(2.7%)	-	-	2(1.4%)
7	Others	2(5.7%)	2(5.4%)	-	3(13.6%)	7(4.8%)
Total		**35(100%)**	**37(100%)**	**52(100%)**	**22(100%)**	**146(100%)**

Table 2: Physical examination parameters of collected samples from the four states

No.	*Physical Examination parameter*	*Number and percentage* *A (N=35)*	*B (N=37)*	*C (N=52)*	*D (N=22)*
1.	**Friability**				
	(a) CAD	19(54%)	26(70%)	39(75%)	15(68%)
	(b) NCAD	16(46%)	11(30%)	13(25%)	7(32%)
	(c) SP	22(63%)	29(78%)	49(94%)	18(82%)
	(d) SS	15(43%)	17(46%)	2(4%)	16(73%)
	(e) DU	8(23%)	13(35%)	-	1(5%)
2.	**Odour**				
	(a) Odourless	12(34%)	16(43%)	18(35%)	2(9%)
	(b) FCS	23(66%)	21(57%)	34(65%)	20(91%)
3.	**Colour**				
	(a) White	33(94%)	34(92%)	49(94%)	19(86%)
	(b) Yellow	2(6%)	2(5%)	3(6%)	2(9%)
	(c) Whitish Brown	-	1(3%)	-	1(5%)
4.	**Scored / Inscribed**				
	(a) Scored	20(57%)	19(51%)	36(69%)	6(27%)
	(b) Not scored	15(43%)	18(49%)	16(31%)	16(73%)
	(c) Inscribed	5(14%)	10(27%)	16(31%)	9(41%)
	(d) Not inscribed	30(86%)	27(73%)	36(69%)	13(59%)
Total		**35(100)**	**37(100)**	**52(100)**	**22(100)**

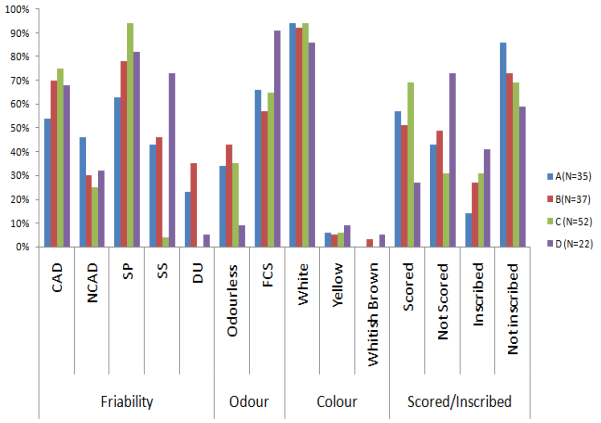

Figure 2: Physical examination parameters of collected samples from the study states

Physical tablet examination

In State A out of the 35 samples examined, 19(54%) had at least one tablet out of every 10 that was either chipped, deformed or abraded and therefore powdery. Twenty three samples (66%) had a faint characteristic smell and 12(34%) were odourless. Only 2(6%) of the samples were yellow in colour, the remaining 33 (94%) were white.

Twenty (57%) and 30 (86%) of the samples were either scored or inscribed with logos of various companies respectively. Two (5.71%) of the 35 samples had a slight bitter taste and the rest (94.29%) were distinctly, bitter. All the samples were neatly packaged and labelled except for one which bore a photocopied label on the container. Twenty three (66%) of the samples were either dull or shiny in luminosity. In State B twenty six (70%) of the 37 samples had at least one of 10 tablets chipped, abraded or deformed and hence were powdery to touch. Twenty (54.3%) had a faint characteristic smell, while 16 (43%) were odourless and 1 (2.7%) had an irritating characteristic smell. Only 2 (5%) samples were yellow in colour, one (3%) had a unique whitish brown colour and the remaining 34 (92%) were white. Nineteen (51%) of the

samples were scored, while 10 (27%) were inscribed with various logos such as "FGN" , "NOROLON", "U" & E", "Melos", "M", "Chemachlor 250", and "CQ". All the samples had a bitter taste and were securely and neatly packaged. Thirty (81.1%) samples were either dull or shiny in luminosity. In State C out of the 52 samples, 39 (75%) had at least 10% of their tablets chipped, abraded or deformed and were powdery to touch. About 18 (35%) were odourless, one (1.90%) had an irritating characteristic smell and the remaining 33 (63.50%) had a faint characteristic smell. More than half (82.7%) of the samples were either scored or inscribed with various company logos. All the samples were bitter in taste and neatly packaged. Luminosity assessment showed that only 2 (3.85%) samples were shiny. In State D Fifteen (68.2%) of the 22 samples had at least one of every 10 tablets, chipped deformed or abraded and such samples were powdery to touch. Two (9.1%) of the samples were odourless and the remaining 20 (90.90%) had a faint characteristic smell. Two (9.1%) of the samples were yellow in colour, one (4.6%) was green and the remaining 19 (86.4%) were white in colour. Half (50.0%) of the samples were either scored or inscribed with various company logos. All samples were bitter in taste except one which was tasteless. The packaging of the various samples was of acceptable standards. Luminosity of samples indicated that 17 (77.3%) of them were either shiny or dull (Table 2 and Figure 2).

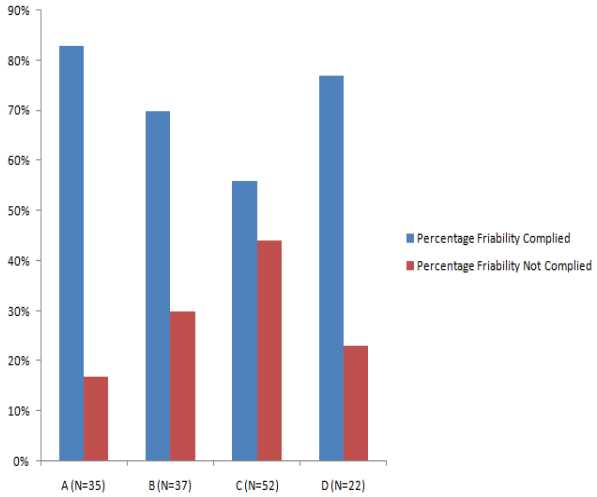

Figure 3: Percentage friability of collected tablets from study states

Table 3: Percentage friability, hardness and weight variation of collected tablets from states

no.	*Parameter*	*Number and percentage*			
		A (N=35)	*B (N=37)*	*C (N=52)*	*D (N=22)*
1.	**Percentage Friability**				
	(a) Complied	0.27±0.001 (83%)	0.47±0.003 (70%)	0.38±0.002 (56%)	0.36±0.001 (77%)
	(b) Not complied	2.47±0.013 (17%)	3.32±0.015 (30%)	5.18±0.019 (44%)	6.93±0.021 (23%)
2.	**Hardness (kgf)**				
	(a) 0-1.9	5(14%)	2(5%)	10(19%)	-
	(b) 2-3.9	17(49%)	23(63%)	19(37%)	6(27%)
	(c) 4-5.9	10(29%)	10(27%)	19(37%)	12(55%)
	(d) 6-7.9	3(8%)	2(5%)	3(5%)	1(4%)
	(e) ≥8	-	-	1(2%)	3(14%)
3.	**Weight Variation**				
	(a) Complied; average % deviation	1.076±0.006 (34%)	1.080±0.005 (54%)	1.109±0.008 (54%)	1.510±0.009 (73%)
	(b) Not Complied; average % deviation	2.468±0.013 (66%)	2.516±0.014 (46%)	2.148±0.012 (46%)	4.290±0.016 (27%)

Qualitative CQ identification tests

All the 'samples in the 4 states gave a white curdy precipitate when their respective solutions were treated with a few drops of potassium mercuric iodide (PMI), indicating that all the samples contained chloroquine moieties. However, when the acidified solutions (HCl) were treated with Barium chloride, only one sample each from states A and D gave a white precipitate, indicating the presence or absence of the sulphate salt. In summary, all the samples contained chloroquine moieties. One sample each from States A and D contained the sulphate salt and the remaining samples in the 4 states were chloroquine phosphates.

Friability testing

In State A 6 (17%) of the samples had percentage friability values above l% and therefore had failed the friability tests (2.470±0.013), while 29 (83%) samples had values less than l% which is the acceptable upper limit (0.270±0.001). The determined mean percentage friability value for this state was 0.65 ± 0.99%. In State B out of the 37 samples, 26 (70%) had percentage friability values less than 1% (0.470±0.003) and the remaining 11 (30%) greater than l% (3.320±0.015). Two of these eleven samples had exceptionally high values of 7.32 and 13.90%, respectively. The mean % friability value for this state was 1.32 ± 2.47%. In State C 29 (56%) of the 52 samples had friability values below l% (0.380±0.002) and 23 (44%) greater than 1% (5.18±0.019). Five of these 23 samples had extraordinarily high % friability values ranging between 6.01 and 37.4%. In State D 16 (77%) of the 22 samples had friability values lower than l% (0.360±0.001) and the remaining 6 (23%), values above the upper limit (6.930±0.021). The mean % friability value for the state was 2.15 ± 5.06%. It can be seen from figure 3 that only state A had a mean % friability value below the standard value of 1%. Next to it in performance was state B, followed by state D and C in that order. State C had an extraordinarily high mean value of about 2.5 times the standard value (Table 3 and Figure 3).

Hardness testing

The hardness of about 80% of all the samples was within

the normal range of 2 and 5.90 kilogramme force. About 10% ranged between 0 and 1.9, 5.5% between 6 and 7.90, and 4.5% had values greater than 8.0 kilogramme force. Samples with forces of hardness of 2.0-7.9 kilogrammes, conformed to the official requirement. The mean individual forces of hardness for states A, B, C and D were 3.80 ± 1.69, 3.68 ± 1.37, 3.56 ± 1.86 and 4.83 ± 2.04 kilogramme forces respectively. The range of values for the 4 states in the same order was 0.9 to 7.60, 1.10 to 7.40, 1.08 to 6.16 and 2.0 to 9.50 kgfs respectively (Table 3 and Figure 4).

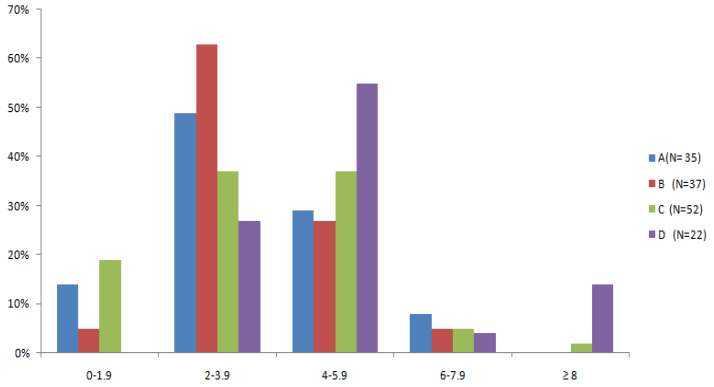

Figure 4: Hardness of collected tablets from study states

Uniformity of weight

The samples collected from states A, B, C and D tablet weight was within normal range in 34%, 54%, 54%, and 73%, respectively. About 66%, 46%, 46% and 27% of the samples from states A, B, C and D respectively did not fall within the normal weight range. The mean average weight of tablets from the 4 states was 0.3437 ± 0.0384gm, 0.3575 ± 0.0414gm, 0.3445 ± 0.0389gm, and 0.375 ± 0.0823 gm respectively. Accordingly, the mean average deviations (%) were 1.076 ± 0.006, 1.080 ± 0.005 and 1.109 ± 0.008 and 1.510±0.009 for states A, B, C and D respectively which are all within accepted values of < 5% (Table 3 and Figure 5).

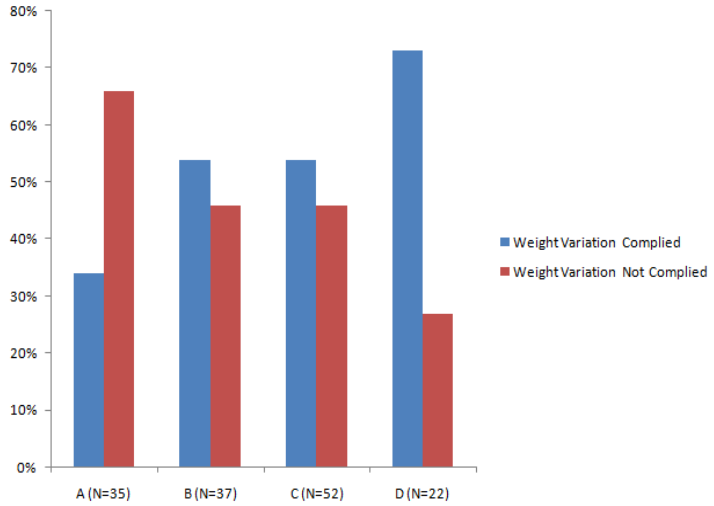

Figure 5: Weight variation among the collected tablets from study state

Discussion

For this study, standard tests [1, 12, 13] were employed to assess the quality of CQ tablets sampled in the study area. Other important methods used in the study were either newly designed or developed by modification of the existing methods to suit the present study. Such important estimations or determinants include the types and number of drug outlets, the relationship between registered and unregistered outlets, sources of drug supplies and the availability of chloroquine tablets at government and private health facilities.

The results on numbers and types of drug outlets provided a document which was used in determining the stratified number of samples which statistically resulted in optimal sample collection. The sample collection procedure involved the application and modification of Harper's [10] and Elwood's [11] stratified and randomized controlled trial sampling procedures. However, in all the states studied, numbers and types of drug outlets obtained from records of Ministries of Health did not correspond exactly with what the state was found on ground. For example, states B and C, the ministerial inspection networks of which are not well coordinated had up to a 10% difference between data found and corresponding available findings on ground. On the other hand, states A and D had percentages of only 7% and 2% respectively. The low value for State D may be associated with an adequate inspection network checking any excesses that might have been spearheaded by unscrupulous individuals. State A also reportedly has a good inspection network, but because of the topography of the state, a few areas may have been inaccessible to effective inspection activities. This could therefore be attributed to the relatively high percentages compared to state D. Thus there was a limitation to the establishment of exact numbers and types of drug outlets in each of the states and consequently 100% accurate information for sampling could not be provided. It is to be appreciated that the establishment of the ratio between registered and unregistered drug outlets carried out in this study was a deliberate attempt meant to increase the level and scope of statistical coverage and it did provide a statistically representative sample pool for the study area. For states with a low ratio, provision was made for inclusion of samples from unregistered outlets. Health policies of the Nigerian government have primarily been focused on providing basic health facilities at the grassroots level popularly referred to as primary health care system. In this study, the availability of CQ tablets at various health care levels, particularly at government health facilities did not correlate with the government policy on bringing basic health services to the communities. Thus, it has been found that only 54.6% of government health facilities could provide CQ tablets at the various levels of primary health care, as opposed to 98.8% obtained for private health facilities. Of all the facilities studied, pharmaceutical chemists constituted the single outlet that made at least 3 different brands of CQ tablets in large quantities. The other facilities such as patent medicine stores (PMS) and private clinics could only make available one brand and in most cases a restricted total number was available at a time. Thus the

availability of CQ tablets at the various levels of health facilities largely depended on the presence of pharmaceutical chemists. This study also revealed that pharmaceutical chemists alone provided more than 50% of all the CQ tablets. Furthermore, estimation revealed that 90% of the various drug outlet types were located in large or medium size towns and big villages. Wherever such facilities were located in small / remote towns, other neighboring villages and hamlets crowdedly converged in such towns for their medical requirements.

Usually, government health establishments could not provide adequate quantities of CQ tablets when malarial transmission was at its peak. Most of the government clinics, although they were located at the grassroot level, could also not provide simple analgesics such as acetylsalicylic acid or paracetamol. At times, the workers did not avail themselves at the clinics. These deficiencies may tend to increase malarial morbidity and mortality, since anti-malarial agents are not available for the effective treatment of acutely ill patients who will then serve as parasite reservoirs. However, state D, performed creditably in this regard, because CQ tablets were available in 83.3% of various government health facilities. Workers were always found in the clinics, even in remote towns, and appeared alert when interacting with visitors. State D may therefore be taken as a model. Though 98.8% of private facilities made CQ tablets available, these facilities did not adequately reach communities in remote areas because they were inappropriately distributed, leaving malarial cases unchecked and thus allowing malarial morbidity and mortality uncontrolled.

The results of quality assessment testing which comprised several parameters were compared and rated. Results on the physical friability of tablets indicated that 65.1% of all the samples in the study area were chipped, abraded or deformed. This proportion seems to be high, since more than 50% of the samples could not withstand handling processes. At state level, state A performed best followed by state D. This means that samples from states A and D did withstand transportation and handling stresses and they reached the point of use intact. In states B and D, friability states were high and tablets could therefore not withstand distribution and handling processes. In such a situation the bioavailability of CQ tablets is likely to be impaired when used for malaria treatment [14]. The assessment of tablet scoring showed an average of 67.9% scored samples. State C had the highest value (82.7%) followed by states B, A and D with 73.0%, 65.7% and 50% respectively. In good manufacturing practice (GMP), the active ingredients of a tablet are consistent throughout the entire tablet, thus there is uniformity in the amounts of all the constituents. For such tablet formulations, breaking along the scoring lines means that the tablet has been approximately halved in all respects including the active ingredients.

These types of formulation are useful in situations where a quarter or half a tablet is required for exact dosing in individuals with different body weights. Scored tablets are commonly employed in children and individuals who require strict drug monitoring. Also in illiterate communities, scored tablets are useful, since the only instruction that goes with such dispensations is breaking of the tablet into two or four equal parts. States C and B registered high values of scored tablets and this may suggest that these states have comparatively more children? or illiterate adults than in states A and D where values are lower. The literacy level of the population in these states seems to agree with this speculation. That is, states A and D have indeed less illiterates and children than states C and B. Results of the qualitative CQ identification tests proved that all the samples from the 4 states contained CQ moieties, 1.4% are the sulphate and 98.6% the phosphate salt. The two different salts have no special significance since both have been implicated in inducing itching, which is related to the, ratio of unchanged CQ to desethylchloroquine in the skin; thus the higher the parent drug/metabolite ratio, the likelier the pruritus [15]. This finding also tends to weaken the claim that of the 60% fake, adulterated or expired drugs circulating in Nigeria, a high % contain inert substances [16].

Friability testing is a quantitative measure of the friability state of tablets. On the whole, the percentage friability value of samples that failed the tests was found to be 1.56 ± 3.56%, indicating a wide deviation from the mean values range between 0-5.22% while for those samples that passed the tests, it was 0.594%-0.814% with a mean of 0.704 ± 0.11%. The friability values correlated well with those for friability states (r = 0.85). State A had the lowest deviation, followed by states B, D and C. This means that in terms of friability, state A performed creditably and stood all the handling and transportation stresses and similarly in this order by states B, D and C. Thus samples from state C could not withstand the stresses associated with handling and transportation.

When the amounts of excipients in various tablet formulations remain unaltered, the determinant factor for the hardness of such tablet formulations is the weight. This means tablets with small weight are expected to have low force of tablet hardness, whereas heavy ones would exhibit higher force of tablet hardness [14]. The samples from the 4 states had weights varying between 0.2977-0.4573g. The average force of tablet hardness, based on weight variations, ranged between 4-6 kgf as compared to the theoretical values of 4-8 kgfs. It follows that the average values for the force of hardness of samples from the 4 states fell within the standard range of 4-8 kgfs. Tablets with very high values of force of hardness are likely to form a hard cake within the alimentary canal and therefore are unlikely to be bioavailable when employed for treatment [14]. Since none of the samples in the study area had very high values, all samples are expected to be bioavailable when used.

Weight variation of tablets is a measure which tells how consistent weights of tablets of the same batch number are. During tablet formulation, the proportions of tablet constituents are thoroughly mixed to present a homogeneous mixture of powder which, when compressed in standard punches produce tablets the weights of which do not vary by more than 10%. The performance of the states in descending order for uniformity of weight may be summarized as C, D, B and A (see Fig. 5). As long as GMP has been applied, the consistency in tablet weights within individual samples depicts the consistency in the amounts of active ingredients or other constituents in the tablet samples. The mean average weight of samples from the study area

was found to be "0.3552 ± 0.05025g, while the mean deviations from the average weight were 1.9 ± 1.12%. This means that samples from the study area exhibited a high level of weight consistency, such that the active ingredients are expected to be consistent in a similar manner. Thus in terms of uniformity of weight and therefore consistency in constituents state C performed well, followed by states D, B and A, in that order. Thus when tablets from state A were to be employed for treatment, there would be variations in the CQ blood levels because of variations in the tablet weights which conversely affect the constituents.

Conclusion

In conclusion and for the first time, a comprehensive study has been carried out on the quality of CQ tablets available at various levels of the health care system in a large area of Northern Nigeria. Also, this study has provided data on the types and number of drug outlets and has given an insight into the availability of CQ tablets within the health care system of Northern Nigeria. The study has also shown a correlation between the quality of CQ tablets and their supply routes. As chloroquine resistant *Plasmodium falciparum* (CRPF) in Nigeria was first recorded in the South-Eastern parts of the country, it would appear that the use of low quality CQ preparations was an important factor for the emergence of CRPF in Nigeria.

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AUTHORS' CONTRIBUTIONS

Authors contributed equally to all aspects of the study.

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.