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Quality evaluation of locally manufactured amodiaquine tablets in Accra, Ghana

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ABSTRACT

This study was carried out to assess the quality of four brands of locally produced amodiaquine tablets in Accra, Ghana. The assayed samples were characterized for their weight, percentage active ingredients, and percentage active ingredient released during dissolution. All the tablets sampled were within their shelf life period as well as possessing good physical characteristics. Samples from the examined manufacturers were assayed to determine the percentage of active ingredient within the tablets and. Assayed amodiaquine samples from MCI, MC2 and MC4 manufacturers passed the test of percentage active ingredient within the tablets in compliance with British Pharmacopoeia requirement. However, MC3 recorded a higher percentage which could be due to a high amount of active ingredient added. All the samples had good results in the uniformity of weight test, which could be due to free flow of granules during tableting. All the tablets sampled complied with standards with regards to dissolution which could be due to the amount or type of binder used. Therefore based on the findings of this study, amodiaquine tablets manufactured by the local manufacturers are in general of good quality.

Key words: Amodiaquine, Pharmacopoeia, Malaria, Plasmodium parasite

INTRODUCTION

Malaria the most prevalent and most parasitic disease of human is estimated to kill between one and two million people, mainly children, each year [1]. Malaria is a hematoprotozoan parasitic infection transmitted by female *anopheles* mosquitoes. Four species of *Plasmodium* commonly infect humans, namely *Plasmodium malariae***,** *Plasmodium vivax***,** *Plasmodium ovale and Plasmodium falciparium* but *Plasmodium falciparium* accounts for the majority of instances of morbidity and mortality [2].

In recent years, there has been a resurgence of interest in malaria due to the immensity of the burden it imposes on poor countries in the tropics has become apparent. Control has traditionally relied on two arms: control of the *Anopheles* mosquito vector through destruction of breeding sites, use of insecticides and prevention of contacts with human (via the use of screens and bed nets impregnated with insecticides); and effective case management [2]. Case management has relied largely on anti-malaria drugs (mainly the 4 – aminoquinolines and more recently diaminopyrimidines) which are inexpensive, widely available and are eliminated slowly from the body.

The quality of a drug is often used to signify its excellence; that is, the totality of its features and characteristics that bear on its ability to satisfy its implied need. The quality of pharmaceuticals has been a major concern to the World Health Organization. In some cases, drugs sold on the market did people little or no good. However, Article 2 of the World Health Organizations constitution stipulates the setting up of global pharmaceuticals and similar products [3].

Every country has legislation on pharmaceutical preparations that sets standards and obligatory quality indices for medicaments, raw materials and preparations employed in the manufacture of drugs. These regulations are presented in separated articles, general and specific, relating to individual drugs and are published in the form of a book called pharmacopoeia [4]. The British pharmacopoeia, United State pharmacopoeia and European pharmacopoeia are revised periodically to take accounts of the replacement of obsolete drugs by new ones and changes in the methods of analyzing drugs. The quality requirements for drugs set forth in the pharmacopoeia are obligatory for all organization and enterprises that have to do with the manufacture, storage, control and use of drugs. Safety, potency and efficacy are the three aspects of drugs quality [5]. The determination of all these indices forms the basis of pharmaceutical analysis and also as a criteria used by governments to regulate pharmaceuticals [6].

Generally, almost all drugs contain impurities. The contamination of drugs by various admixtures may not only lower therapeutic effect, but can also cause undesirable side effects. Contamination can only be due to poor purification of initial raw material, and the presence of by-products of synthesis, mechanical impurities (remnants of filtering materials such as fabric, filter paper ,etc) and residues of solvents (alcohol, water etc). The materials or the apparatus used for the production of a drug can also contaminate a drug [7]. Consequently, in Ghana, the food and drugs board was formed under the PNDC Law 3055B; food and drugs Amendment Act 1996, and charged with the responsibility for monitory, approving and controlling the quality of drugs manufactured locally and sold on the market [8].

Olaniyi (2000) reported that during distribution of drugs, error may occur, thereby the finished product may not conformed to the required specifications. Such a defect may impair the therapeutic effect of the drug and could even adversely affect the health of the consumers. Manufacturers are supposed to employ good manufacturing practices in the production of drugs.

Anti-malarias are anti-protozoal drugs that are primarily used to treat malaria. Amodiaquine is a popular and effective anti-malaria drug in Ghana and other African countries. Amodiaquine (Figure 1) is a yellow crystalline powder, odourless and has a bitter taste. It is sparingly soluble in ethanol and water [4].

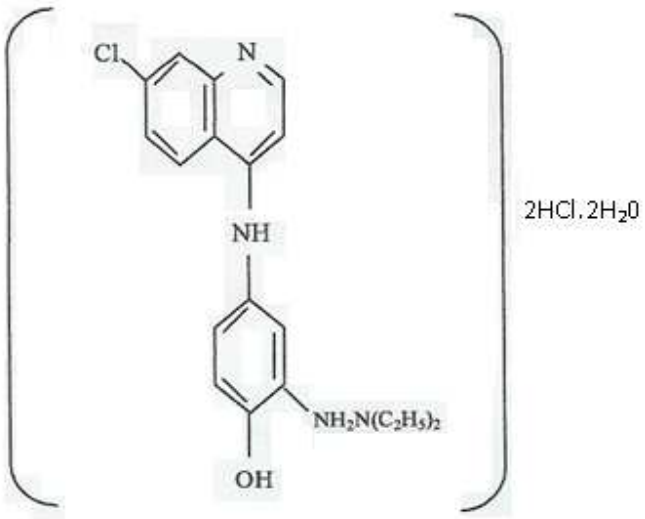

Figure 1: the chemical structure of amodiaquine.

Amodiaquine tablets contain not less than 93% and not more than 107% of the labeled amount of amodiaquine as active ingredients [4]. It is synthesized from 4, 7–dichloroqiunoline and 4 acetamidodiethyl-amino-cresol. Alternatively, it can be synthesized from 2-aminomethyl-4-aminophenol and 4, 7-dichloroquinoline [4]. Formulation containing combination of amodiaquine and other anti-malaria drugs are also available as camoprima infatabs [9].

Amodiaquine is a 4 aminoquinoline anti-malarial drug, which has been interchangeably used with chloroquine for the treatment of acute malaria attacks [9]. Its structure and activity is similar to that of chloroquine. It's an over the counter (OTC) drug and can be bought in any drug shop with or without prescription [9]. Amodiaquine is indicated to have a rapid schizonticidal effect and appears to affect all growth by interfering with DNA. Its activity also seems to depend on preferential accumulation in the infected erythrocyte. Amodiaquine kills the erythrocytic forms of malaria parasites at all stages of developments, but does not affect the malaria parasites in the human liver cells. It will therefore eliminate diseases caused by *Plasmodium falciparium*.

Amodiaquine is used as a first line treatment in cases of resistance to chloroquine. The drug is significantly more effective than chloroqiune in curing uncomplicated *Plasmodium falciparium* malaria. Combinations of amodiaquine with primaquine, and more recently artesunate have

clearly shown to improve treatment efficacy. Amodiaquine-artesunate is a potential combination for inhibiting intensification of a drug resistance and for decreasing malaria transmission levels. It has proved to be effective against the erythrocyte stages of all four species of *Plasmodium* as compared to chloroquine which belongs to the same compounds of chemicals. The anti-malaria properties of amodiaquine often shows adequate clinical parasitological efficacy in chloroquine – resistant infections. It is also useful in patients who cannot tolerate chloroquine because of allergy and gastro-intestinal problems etc. Overdose of amodiaquine may lead to syncope, spasticity, convulsions and involuntary movements [10]. A more severe manifestation of amodiaquine overdose includes cardiac arrhythemias, cardiac arrest, visual disturbances and coma. Acute poising has also resulted in death [9].

For amodiaquine to be said to be of the right quality it should meet the requirements for the following parameters: assay, disintegration, uniformity of weight, hardness test, dissolution test and other test as specified in the respective pharmacopoeia. Research into quality of some locally produced aspirin tablets showed that only 70% of local manufacturers are adhering to good manufacturing practices [11]. Similarly, a study in Ghana by Safo [12] on locally produced paracetamol tablets revealed that 93% of the manufacturers conformed to the British pharmacopoeia standard. In view of the health risk of taking unwholesome drugs it is imperative for relevant bodies and researchers to continuously conduct surveillance on locally manufactured drugs.

Therefore, the aim of this paper was to assess the quality of locally manufactured amodiaquine tablets in Ghana, to ascertain whether they comply with standard specifications in relations to their assay, uniformity of weight and dissolution. Using British Pharmacopoiea [4], the following hypotheses were formulated and tested through this study:

1. Locally manufactured amodiaquine tablets of weight 200mg or more have a percentage deviation of ± 5%.
2. Active ingredient in locally produced amodiaquine tablet is in a range of 93.0% to 107.0%.
3. Active ingredient in a locally produced amodiaquine tablet released during dissolution at a time of 30 minutes is not less than 80.0%.

EXPERIMENTAL SECTION

2.1. Sample collection and assay of Amodiaquine Tablets

Forty tablets of amodiaquine hydrochloride from four manufacturing companies (Coded: MC1, MC2, MC3 and MC4) were collected in two different batches (1 and 2) in a month from Accra. Twenty tablets were weighed using the analytical balance (Metler Toledo AG 204) and powdered using mortar and pestle. A quantity of the powder equivalent to 0.1g of amodiaquine was accurately weighed into 100ml volumetric flask. 30ml of 0.1M HCl was added and shaken for 15 minutes using an electronic shaker and sufficient volume of 0.1M HCl added to make up the 100ml mark. This was mixed, filtered and 1ml of the filtrate diluted to 100ml with the same solution. The absorbance of the resulting solution was measured at a wavelength of 342nm with UV spectrophotometer (Shimadzu uv – 1601) using A^{1}_{1}% 1cm = 436.

2.2. Dissolution

Six tablets each of the test samples were collected at random from the sampling points. Each tablet was put into the dissolution vessel (Erweka DT 600) designed to take six tablets containing 900ml of distilled water. The dissolution apparatus was set at a temperature of 37^{o}C for a rotation of 50rpm.The samples were run for 30 minutes using apparatus II (paddle). After dissolution the solutions were filtered. 5ml each of the filtrate were diluted to 100ml with distilled water.

2.3. Uniformity of weight

Twenty tablets each of the test samples collected from the sampling sites were collectively weighed and the average weight per tablet calculated. The tablets were then weighed individual using an analytical balance (metler toledo AG 204) and the percentage deviation from the mean weight per tablet calculated.

2.4. Amodiaquine standard preparation

0.0342g of amodiaquine hydrochloride certified reference standard powder was accurately measured into a 100ml volumetric flask. 50ml of distilled water was added and slackened for 15minutes using electronic shaker and sufficient distilled water added to make up the 100ml mark. The absorbance of both the sample and the certified reference standard were accurately measured at a wavelength of 342nm using water as a blank.

RESULTS AND DISCUSSION

3.1. Assay of amodiaquine tablets

Table 1 presents the percentage of active ingredient in the amodiaquine tablets produced by the studied local manufacturing companies. The pictorial impression of the variation of the % active ingredients of amodiaquine in sampled Tablets (assay) is given by Fig. 2. From the result obtained, it was revealed that the tablets from the manufacturers coded, MC1, MC2, and MC4 had a good level of active ingredient which was within the British Pharmacopoeia range (93.0% - 107.0%), whereas samples from MC3 recorded a high percentage of active ingredient above the range of the standard. The higher percentage in the MC3 tablets could be due to high amount of active ingredient that was added during granulation or could be that the manufacturer did not adhere to the standard operating procedure.

Table 1. Results for Assay of Amodiaquine tablets from sampling sites

Sampling site	Batch number	Mean weight/mg	Weight of sample/mg	Volume of Aliquot/ml	absorbance	% of Active ingredient
MC1	1	578.9	1974	1	0.475	106.5
	2	582.3	196.6	1	0.47	106.4
MC2	3	568.4	197.8	1	0.485	106
	4	519.5	201.7	1	0.538	105.9
MC3	5	572.4	198.6	1	0.476	104.9
	6	576.3	198.9	1	0.472	104.6
MC4	7	564.1	193.2	1	0.492	109.2
	8	505.9	197.6	1	0.552	108

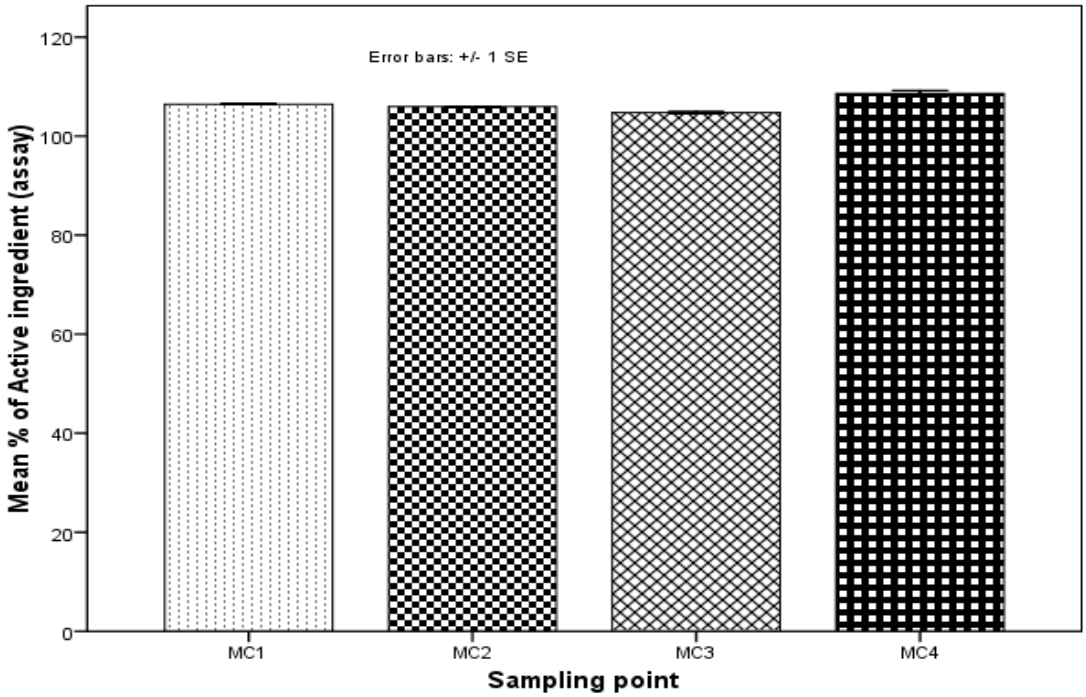

Fig. 2. Variation of the % active ingredients of amodiaquine in Tablet (assay)

3.2. Uniformity of weight

The uniformity of weight test result for amodiaquine tablets from the monitored manufacturers is given by Table 2. The variation of the weights of the tablets is depicted on Fig. 3.

Table 2. Results for Uniformity of weight of amodiaquine from sampling sites

Sampling site	Batch number	Mean weight/mg	Weight range of 20 Tablet/mg	B.P Weight range/mg	Remark
MC1	1	578.9	568.0 – 601.2	549.9 – 607.8	Comply
	2	582.3	573.9 – 604.0	553.2 – 611.4	Comply
MC2	3	568.4	543.4 – 592.4	539.9 – 596.8	Comply
	4	519.5	500.9 – 541.0	493.5 – 545.5	Comply
MC3	5	572.4	544.3 – 598.1	543.8 – 601.0	Comply
	6	576.3	549.7 – 599.1	547.5 – 605.1	Comply
MC4	7	564.3	537.3 – 588.3	535.9 – 592.3	Comply
	8	505.9	496.8 – 530.0	481.0 – 531.0	Comply

From the experiment, it was observed that all the different batches of amodiaquine tablet from the various manufacturers complied with the British Pharmacopoeia range. This result for the uniformity of weight of the tablets could be due to good flow rate of granules in the hopper during tableting. Since granules for tableting consist of a range of particle sizes, segregation and stratification may occur, but from the results obtained it could be seen that there were none or little misdistribution of particles during tableting and resulted in a good uniformity of weight.

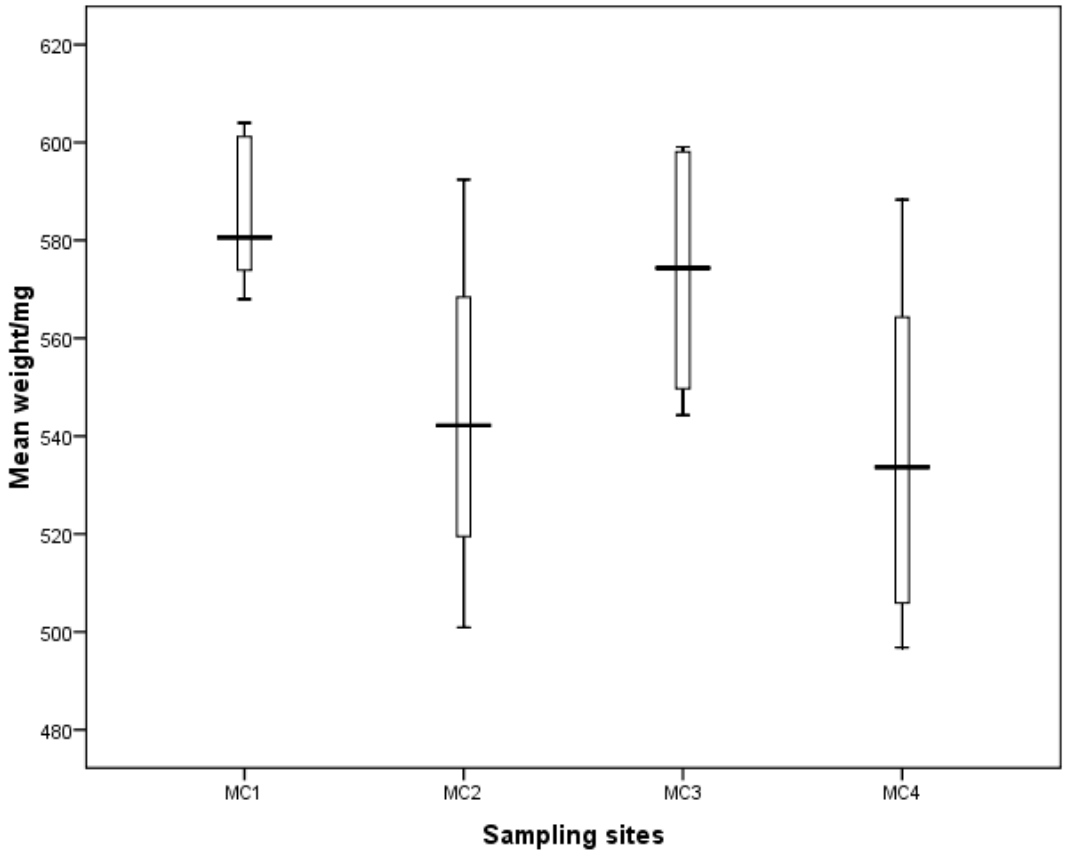

Fig. 3. Box and whisker diagram of the variation of the weights of amodiaquine in Tablet

3.2.Dissolution of amodiaquine tablet

Table 3 shows the dissolution results of amodiaquine tablets from the sampling points. The graphical representation of the variation of the % active ingredients of amodiaquine in sampled Tablets (dissolution) is given by Fig. 4. From the result obtained, it was found that all the amodiaquine from the various manufacturers recorded a percentage of active ingredients above 80.0% indicating that they conformed to the British pharmacopoeia standard. This could be due to stronger effect of the binder used leading to the efficient action of the disintegrating agent resulting in the released of the active ingredient in the tablets. This observation could determine the amount of active ingredient that will be released from the dosage form and subsequently available for absorption.

Table 3. Results for dissolution of amodiaquine Tablets from sampling sites

Sampling site	Batch number	Absorbance	% of Active ingredient	REMARKS
MC1	1	0.681	100.7	Comply
	2	0.679	100.4	Comply
MC2	3	0.667	98.67	Comply
	4	0.665	98.37	Comply
MC3	5	0.658	97.34	Comply
	6	0.622	92.01	Comply
MC4	7	0.713	105.47	Comply
	8	0.722	106.81	Comply

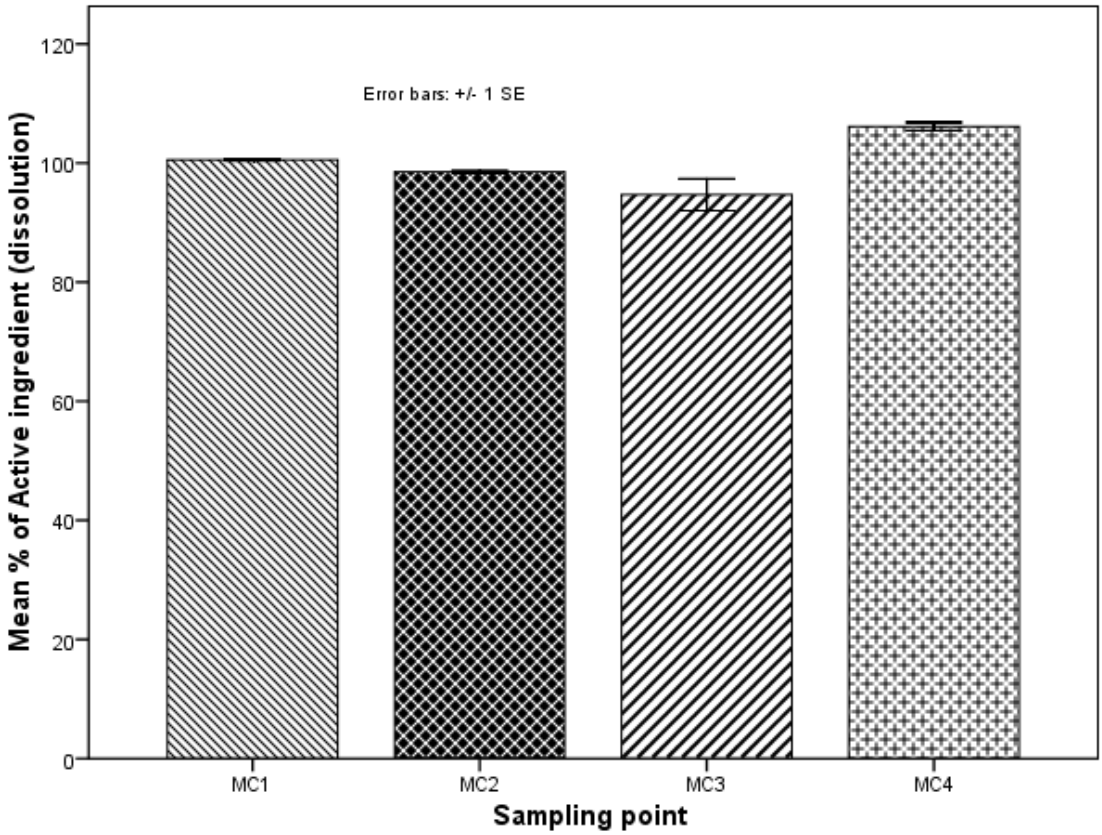

Fig. 4. Variation of the % active ingredients of amodiaquine in Tablet (dissolution)

CONCLUSION

The basic essence of manufacturing and administering a drug is to achieve a desired therapeutic effect. The production of a good quality tablet is therefore imperative for any manufacturer. It is therefore important that locally manufactured drugs are regularly examined to determine their compliance with specific and accepted standards.

It is evident from this study that almost all the locally manufactured amodiaquine tablets sampled from the four manufacturers complied with the required standards with regards to the uniformity

of weight and dissolution. However, with regards to the assay, all the percentage of active ingredients of the various sampling sites conformed to the standard with the exception of MC3 which recorded values above the British pharmacopoeia standard range which could be attributed to high amount of active ingredient that was added during granulation. It is recommended that further studies should be carried out to determine the disintegration and hardness of locally manufactured amodiaquine tablets. It is envisaged that the result of this study will enrich the discussion on the quality of locally manufactured drugs especially amodiaquine.

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