



## Chemical equivalence study on four brands of $\alpha$ -methyldopa

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### ABSTRACT

Substandard pharmaceutical products have a deleterious effect on health care delivery at all levels. The manufacturers of health products, the medical practitioners and the patients are all affected by substandard medicines but the patient is the worst hit. Methyldopa is an important anti-hypertensive agent used in the management of hypertension. The chemical equivalence of four brands of methyldopa was carried out using the United State Pharmacopoeia (USP) method, which involve non-aqueous titration. Three out of the four brands of methyldopa passed the test that is the percentage content fell within the specified range of 90-110% while one of the samples failed the test with percentage content of 82.07%. This finding points to the need for regular quality checks on pharmaceutical products in circulation.

**Key words:** hypertension, methyldopa, tablet, substandard, non-aqueous titration.

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### INTRODUCTION

The problem of substandard preparations of pharmaceutical products is a global one but it is more prevalent in the developing countries especially Africa. There have been several reports of substandard medicine circulating in the sub-Sahara Africa (SSA) drug market [1-4]. However, the majority of these reports focus on medicines used in infectious diseases [5-8], which are commonly endemic in the region. Medicines used in the management of non-communicable diseases such as hypertension and other cardiovascular diseases (CVD) are rarely reported in the routine quality checks of pharmaceutical products in SSA. Forecast show that, in a few years, CVD will dominate the worldwide fatal illness [9], which implies that more emphasis should be put on both risk factors to prevent the trend [10] and the treatment to reduce mortality. Hypertension is an important risk factor for CVD. The burden of hypertension was estimated at 79.8 million in SSA in 2002 [11]. As for other conditions, in hypertension, the use of substandard quality drugs may result in treatment failure [4], including fatal consequences because of low drug content and toxic degradation products [12]

Methyldopa ( $\alpha$ -methyl-3,4-dihydroxyphenylalanine, MTD) is a catechol derivative (catecholamine) widely used as antihypertensive agent. The MTD is a centrally acting  $\alpha_2$ -adrenoreceptor agonist, which reduces sympathetic tone and produces a fall in blood pressure [13]. To the best of our knowledge, there has been no report on substandard preparation of methyldopa in Nigeria as a whole and the southern Nigeria in particular. This study was undertaken to ascertain the quality of methyldopa tablet formulation circulating in the southern part of Nigeria.

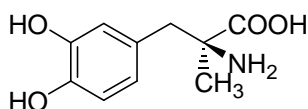


Figure 1. Chemical structure of methyl dopa

## EXPERIMENTAL SECTION

The various brands of methyl dopa tablets used were purchased from pharmaceutical shops in Benin metropolis, Edo state, Nigeria. Reagents used include glacial acetic acid, perchloric acid, acetic anhydride, potassium hydrogen phthalate, and crystal violet powder. They were all of analytical grade.

*Standardization of 0.1N perchloric acid:* Approximately 0.5g of potassium hydrogenphthalate was weighed and placed in a dry conical flask and 25 mL glacial acetic acid was added and warmed until the salt was completely dissolved. The solution was allowed to cool before adding 2 drops of crystal violet solution. It was then titrated with approximately 0.1N acetous perchloric acid solution until a bluish-green end point.

Blank titrations were carried out using 25ml glacial acetic acid. Titre values were adjusted by deducting the blank determination from the standardization. The procedure was carried out in duplicate.

*Assay of drug samples of methyl dopa:* Amount of crushed tablets equivalent to 0.2g of methyl dopa was weighed and dissolved in 25 mL of glacial acetic acid. 0.1 mL of crystal violet was added. The resultant solution was titrated with 0.1 N acetous perchloric acid to a bluish-green endpoint. This was carried out in triplicate and blank determination was carried out. Titre values were adjusted by deducting the blank determination from the assay.

## RESULTS AND DISCUSSION

Table 1. Percentage composition of the sample products

Samples	Percentage content (w/w) $\pm$ SD
A	82.07 $\pm$ 1.24
B	98.85 $\pm$ 0.83
C	94.58 $\pm$ 1.15
D	97.79 $\pm$ 0.34

All the brands used were within their shelf life as at the time of the study. Four brands of  $\alpha$ -methyl dopa purchased from retail pharmacy outlets in Benin metropolis, Edo state were subjected to chemical equivalence assay following the United States pharmacopoeia (USP) method. Non-aqueous titration procedure has been reported for the chemical content determination of various drugs such as chlordiazepoxide, chlorpromazine, pyrimethamine, metronidazole, salbutamol phosphate, promethazine HCl, lignocaine, ofloxacin and norfloxacin [14, 15]. The result of the quantitative determination of the chemical (methyl dopa) content of the sampled products is shown in table 1. The USP states that methyl dopa tablets should contain not less than 90% and not more than 110% of the labeled amount of  $\alpha$ -methyl dopa. From the result of the analysis carried out using the USP method, it was noted that some of the products (B,C,D) complied with this specification while product A with percentage content of 82.07% failed to meet the specification. Different reasons could be proffered for the failure of sample A. One of the reasons that could easily come to mind is deliberate reduction of the active ingredient at the point of formulation. The other possible reason is degradation on storage [16]. However, more investigation ought to be carried out before one can ascertain that the sample has failed the chemical equivalence test.

## CONCLUSION

Chemical equivalence study and other qualitative assay should be a routine exercise for all medicines in circulation in order to be sure of the quality of drug that are used in the treatment of various disease conditions.

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