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RESEARCH ARTICLE

ASSESSMENT OF PHYSICOCHEMICAL PROPERTIES OF EIGHT BRANDS OF ALPHA METHYLDOPA TABLETS MARKETED IN ZARIA, KADUNA STATE,NIGERIA

GIDEON O. OKPANACHI*[1], HASSAN MUSA[2], YUSUF MOHAMMED[2], IFEANYI V. EMENIKE[1] AND MAHMUD S. GWARZO[3]

[1]Lecturer 11 & Senior Lecturer, Department of Pharmaceutics and Pharmaceutical Microbiology, Faculty of Pharmaceutical Sciences, Gombe State University, Gombe State, Nigeria.[2] Professor & Student, Department of Pharmaceutics and Pharmaceutical Microbiology, Faculty of Pharmaceutical Sciences, Ahmadu Bello University, Zaria, Nigeria.[3] Associate Professor, Department of Pharmaceutics and Pharmaceutical Microbiology, Faculty of Pharmaceutical Sciences, Usman Danfodiyo University Sokoto, Sokoto State, Nigeria.**Email:** okpanachigideon@gmail.com

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ABSTRACT

Objective: The aim of this research is to determine the quality and uniformity of brands of α-Methyldopa 250 mg tablets marketed in Zaria, Kaduna State, Nigeria. **Methods**: Eight (8) brands of α-Methyldopa 250 mg tablets labelled as samples A, B, C, D, E, F, G and H were used to ascertain the level of uniformity within each batch and from brand to brand using the quality control tests such as identification test, uniformity of weight test, friability test (FR), crushing strength test (CS), disintegration time test (DT), dissolution test and test uniformity of active content. **Results:** All the brands of the methyldopa tablets used passed the BP standards for identification test, uniformity of weight, thickness, diameter and friability test but failed CS test except sample A and G, which showed CS within the range of 4-8 Kgf. All the brands except sample G complied with the BP, 2009 specification of DT. Also, all the brands except sample G passed the uniformity of active content test (Assay) specified by the BP, 1980 with little significant difference; A=95.96 %, B=97.98 %, C=102.02 %, D=96.40 %, E=100.89 %, F= 102.92 %, G=46.52 %, and H=97.08 %. Similarly, all the brands complied with the dissolution rate test stipulated by the Indian Pharmacopeia 4th Edition except sample G with a significant low dissolution profile after 60 minutes; 95.96 %, 98.01 %, 101.65 %, 95.68 %, 100.69 %, 102.02 %, 42.26 % and 97.16 % for the sample A, B, C, D, E, F, G, and H respectively. **Conclusion**: There is a considerable degree of uniformity among the brands examined except sample G.

Keywords: Physicochemical properties, Brands, Uniformity, α-Methyldopa tablets.

INTRODUCTION

Alpha Methyldopa is a catechol derivative (catecholamine) widely used as antihypertensive agent. It is a centrally acting α-2-adrenoceptor agonist, which reduces sympathetic tone and produces a fall in blood pressure [1]. The spectrum of activity of methyldopa lies between those of the more potent agents, such as guanethidine, and the milder antihypertensive, such as reserpine. Methyldopa is a structural analogue of dihydroxyphenyl alanine (dopa); it differs only in the presence of methyl group on the α-carbon of the side chain [2]. Methyldopa contains a chiral center. It can therefore occur either as S or R-isomer. The activity of methyldopa as antihypertensive is due to the S-isomer of α-methyldopa. There are many brands of methyldopa tablets marketed in Nigeria by different manufacturers; some are locally manufactured while some are of foreign brands. Whatever the case, drugs especially tablets are very important in any healthcare services hence there is need for assessment of their physicochemical properties to ensure that manufacturer complies with the specifications laid down in various monographs. This is to provide assurance to the physicians, pharmacists, patients and other healthcare providers that the products perform its action uniformly in a manner satisfactory for the recommended purpose.

In this regards, this work is directed to assess the physicochemical properties of eight brands of methyldopa tablets 250 mg marketed in Zaria, Kaduna State, Nigeria, using the various quality control tests.

MATERIALS AND METHODS

To achieve the objectives of this study, Methyldopa reference material was obtained from Shinpoong Pharm. Co. Ltd., Seoul, Korea, (through Marley Shree Co. Ltd. Kano state, Nigeria.) labelled to contain 99.65% w/w anhydrous Methyldopa and 8 different brands of tablets containing 250 mg alpha methyldopa were locally purchased from Samaru, Sabon-Gari, Tudun-wada, Kofan-doka and Zaria city, Kaduna State, Nigeria. These tablets were stored at condition specified by the manufacturer prior to assay. The identities of the various samples of methyldopa collected for the study are given in Table 1 below;

Table 1: Various Samples of Methyldopa Collected.

Sample Code	lot/batch no	Date of manufacture	Exp. Date	NAFDAC Reg. no
A	BE02564	FEB. 2014	FEB.2017	04-0682
B	VDT 44	09/10/2013	08/09/2016	A4-1038
C	KPI 409	JAN. 2010	JAN. 2016	B4-0274
D	0901	SEPT. 2013	AUG. 2016	A4-8537
E	130794	JUL. 2013	JUL. 2016	A4-0649
F	S3408	MAR. 2014	SEPT. 2015	04-1344
G	C140	JUN. 2012	JUN. 2015	000311
H	130576	30/05/2013	30/04/2016	04-8648

The following official quality control tests were conducted on the tablets in accordance with BP 2009 specifications.

Weight variation test

Twenty (20) tablets randomly picked from each brand were weighed individually using the analytical balance (Mettler Analytical Balance Philip Harris Ltd., England) and the weight of each tablet was recorded. The mean tablet weight and percentage deviation were calculated using formula below:

Table 2: Mean Tablet Weight and Percentage Deviation.

USP specification weight of tablet (mg)	Average BP specification weight of tablets (mg)	Average percentage (%) weight deviation allowed (±)
130 or less	80 or less	10
130 – 324	81 – 250	7.5
More than 324	251 or more	5

$$\text{Percentage Deviation} = \frac{x - \bar{x}}{x} \times 100$$

Where $x = weight\ of\ the\ tablet\ (mg)$

And $\bar{x} = mean\ weight\ of\ the\ tablets\ (mg)$

The BP states that not more than two of the individual weight must deviate from the weight(x) by more than the Percentage shown in the Table above and none should deviate by more than twice that percentage.

Assay of the uniformity of content (%)

Twenty 20 tablets of α-methyldopa were randomly selected, weighed and powdered. A quantity of the powder containing the equivalent of 0.1 g of anhydrous methyldopa was dissolved as completely as possible in sufficient 0.05 M sulphuric acid to produce 100 mL and filtered. To 5 mL of the filtrate was added 2 mL of iron (II) sulphate citrate-solution (a solution freshly prepared by dissolving 1 g of sodium metabisulphite in 200 mL of water and adding 1 mL of 1Mhydrochloric acid, 1.5 g of ferrous sulphate and 10 g of sodium citrate), 8 mL of glycine buffer solution and sufficient water to produce 100 mL. The absorbance of the resulting solution was measured in a 1 cm cuvette on a spectrophotometer at the maximum at 545 nm using water as a blank.

The percentage active content of methyldopa was calculated using 89 as the value of specific absorbance A (%, 1 cm) and the absorption maxima at 545 nm by the equation below; % Content = Absorbance/ (A %, 1 cm) × Concentration of sample (g/100 mL) × 100.

Friability test

Ten tablets were dusted and weighed on the mettler Analytical balance. The tablet were placed in the rotary friabilator and allowed to rotate at 25 rpm for 4 min (100 rpm).The tablet were dusted and weighed again and the process was conducted for each of the 8 brands.

Hardness (Crushing strength) Test

Using forceps, randomly selected 6 tablets were placed individually between the anvil and the moving jaw of the Monsanto hardness tester (Monsanto Chemical Corp, USA). Force was gradually applied increasingly to the edge of the tablet by turning the screw gradually until the tablet cracks. The instrument gave a visual reading of tablet hardness which was read and recorded for 6 tablets from each brand.

Thickness and diameter measurement

Ten randomly selected tablets were drilled from each brand of methyldopa and using forceps, they were placed individually between the callipers of the three micrometre screw gauge until it is just held between them by adjusting the knob. The instrument gave a visual reading of the tablet thickness and it was recorded. The diameter was also determined.

Disintegration Time Test

Using Erweka disintegration apparatus (Type ZT3, Erweka – Apparatebau – G.m.b.H Heusenstamm, Germany) six (6) tablet of α-methyldopa were placed in the tube of the basket and a disc was added to each tube. This was suspended in a beaker containing 900 mL distilled water maintained at 37 ^{0}C ± 0.5. The apparatus and the timer were started simultaneously and the time required for the first tablet to disintegrate and the last particle of the tablet to pass through the mesh were recorded. The test was carried out for each brand of the α-methyldopa tablet [3].

Dissolution Rate Test

The rotating basket method of dissolution test was applied [3]. 900 mL of dissolution medium containing 0.1N HCl was introduced in to the vessel of the apparatus and warmed to and maintained at 37 ^{o}C. The dry basket containing one tablet was lowered into the dissolution medium and rotated at 100 rpm for 60 minutes. 10 mL sample was withdrawn from each vessel using a syringe at a point half way between the surface of dissolution medium and the tip of the rotating basket, not less than 10mm from the wall of the vessel after 5, 10, 20, 25, 30, 45, 50 and 60 minute intervals while replacing it with equal volume of the dissolution medium intermittently .The samples were filtered at 37 ^{o}C and 1 mL of the filtrate was diluted to 10 mL with dissolution medium. The absorbance reading of solutions were taken on a spectrophotometer at the absorption maximum specified in the BP (280 nm) and the percentage concentrations of the drug released with respect to time were calculated using the straight line equation (y = mx + c) from the standard curve.

RESULTS

Table 3: Showing the Aesthetic Examination Carried Out on the Tablets.

S/No	Sample Code	Colour	Taste	Odour	Shape
1	A	Yellow	Tasteless	Odourless	Biconvex
2	B	Yellow	Tasteless	Odourless	Biconvex
3	C	Yellow	Tasteless	Odourless	Biconvex
4	D	Yellow	Tasteless	Odourless	Biconvex
5	E	Yellow	Tasteless	Odourless	Biconvex
6	F	Yellow	Tasteless	Odourless	Biconvex
7	G	Yellow	Tasteless	Odourless	Biconvex
8	H	Yellow	Tasteless	Odourless	Biconvex

Table 4: Results of the unofficial quality control tests conducted on samples of methyldopa tablets collected

S/No	Sample	Friability	Crushing strength (kgf)	Thickness (mm) Mean ± SD, n=10	Diameter (mm) Mean±SD, n=10
1	A	0.00	7.40	4.72 ±0.51	10.05 ±0.14
2	B	0.00	3.50	4.70 ±0.49	10.72 ±0.21
3	C	0.00	3.70	4.14 ±0.43	10.33 ±0.35
4	D	0.00	3.40	4.12 ±0.64	10.62 ±0.21
5	E	0.00	4.50	4.27 ±0.46	10.13 ±0.32
6	F	0.00	3.90	4.48 ±0.39	11.12 ±0.36
7	G	0.00	3.20	4.41 ±0.53	10.76 ±0.30
8	H	0.00	3.50	4.38 ±0.50	10.14 ±0.17

Table 5: Results of the official quality control tests conducted on samples of methyldopa tablets collected

Sample	Identification test	Weight variation (mg) Mean±SD, n=20	Active content (% w/w)	Disintegration Time test (min) Mean±SD, n=6	Dissolution rate after 60 min(% w/w)
A	Passed	407.55±4.1	95.96	3:16± 0.80	95.96
B	Passed	411.95±18.3	97.98	2:27±0.30	98.01
C	Passed	339.25±5.58	102.02	2:33±0.40	101.65
D	Passed	329.95±11.4	96.40	9:25±2.80	95.68
E	Passed	359.90±5.6	100.89	16:11±3.11	100.69
F	Passed	378.25±7.9	102.92	14:33±2.37	102.02
G	Passed	402.95±7.4	46.52	66:44±11.8	42.26
H	Passed	340.5±6.3	97.08	10:08±3.10	97.16

DISCUSSION

In our present study, methyldopa tablet 250 mg from eight (8) different pharmaceutical Companies A, B, C, D, E, F, G and H were used and the basic drug in all the samples was the same with a slight variation in the colour of the coating materials. The post-formulation tests of crushing strength (hardness), Friability, thickness, diameter, weight variation, uniformity of active content, disintegration time and dissolution rate on the tablets have been made using the official method and standard instrument as discussed in the methodology. Using the experimental observation, various results have been obtained. Results for uniformity of weight shows that all the samples passed the weight variation test and there was consistency in weight within a batch and a slight variation in weight among the samples. It recommended that; not more than two of the individual weight deviate by more than the percentage deviation of ±7.5 % and non-deviate by more than twice that percentage [4]. It is imperative that the amount of active ingredient be uniformly distributed in the tablets of the same batch in order to avoid under or over dose that may lead to serious complications. Weight variation occur between tablets during manufacture and this problem may be due to the following reasons; Poor flow of granules to the die, Size separation of granules i.e. small and large size granules, Presence of too much fine in the granules, Separation of the mixed ingredients of granules, Less quantity or poor mixing of lubricants, due to automatic change in the adjustment of punches. In rotary tablet press this effect is due to unequal length of the lower punches.

Table 4 shows the mean crushing strength value of the samples, and only sample A & E had a good crushing strength value that fall within BP recommended range of 4-8 kgF, while sample B, C, D, F, G and H fell below the range which may be a result of binder content, space between the upper and lower punches at the time of compression, pressure applied on the upper punches and the use of excessive proportion of fatty lubricants such as magnesium stearate. The hardness may also increase on a normal storage of tablets therefore, it is important to note that the tablets should not be harder than required, the harder tablet may not disintegrate in the required periods of time and too soft tablet may not withstand the hazard during transporting and dispensing [5].

Table 5, shows that all the brands had a satisfactory percentage active uniformity of content except sample G which fell outside the percentage limit sets [3]; the active content of anhydrous methyldopa should contain 95 -105 % of the stated amount.

However, the failure of sample G may be due to poor mixing time between the drug and the excipients and thus, it is important for a drug to contain the recommended amount for optimum therapeutic activity.

Results for dissolution rate test revealed that after 60 minutes sample A, B, C, D, E, F, G and H had a percentage concentration of drug released of 95.96 %, 98.01 %, 101.65 %, 95.68 %, 100.69 %, 102.02 %, 42.26 %, and 97.16 % respectively. The results on Table 5 shows that sample G had a low concentration of drug released. The reason could be due to high disintegration time of the tablets as the disintegration time was higher than the other batches, which can be explained in terms of the amount of binder or pressure applied during formulation . However the Indian pharmacopoeia 4th Ed. specified that “for each Methyldopa tablet tested, the amount of active ingredient released should not be less than 75 % of the prescribed amount within 60 minutes”.

Table 4; shows that all the samples tested for percentage (%) friability passed the test, this shows that coated tablets are more resistance to the effects of abrasion in packing, handling, transporting and other unavoidable procedures.

Table 5 shows that all the samples had a satisfactory mean disintegration time except sample G. The British Pharmacopoeia recommends 30 minutes for film coated tablets, the disintegration time of a tablet is controlled by inter-dependent variables such as; the type of granulating agent used, the use of water repellents lubricants, the type and the amount of lubricating agent, the force used to compress the tablets [6].

Tablets thickness and diameter test is an important parameter in tablets production; it ensures that each production batch will fit into the selected packaging materials. If some tablets are thicker or larger than specified, there will be problems with packaging. For tablets that are not sugar coated, enteric coated or film coated, a deviation of ±5 % of the stated diameter is allowed except for diameter exceeding 12.5 mm, where the allowed deviation is ±3 % [7]. Table 4 reveals that all the brands passed the thickness and diameter test and factors that affect tablets thickness and diameter are improper filling of the die, fluidity and compressibility of the granules.

CONCLUSION

There is a considerable degree of uniformity among the brands examined as all the brands passed weight variation test, friability test, diameter and thickness test, but only sample A & E passed the crushing strength test. It was also found that all the brands did not differ significantly in the uniformity of active content test, disintegration rate test, and the percentage concentration of drug released in the dissolution rate test except sample G. Hence this sample can be said to be a substandard drug.

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