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Quality evaluation and UV spectrophotometric assay of ten brands of amlodipine tablets marketed in Uyo, Nigeria

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Abstract

Amlodipine is a calcium channel blocker that is widely used to treat hypertension, which is a chronic health condition characterized by persistent elevated pressure of blood in the arteries. Hypertension is a predisposing factor to stroke, kidney failure, heart diseases and vision loss. The large demand for amlodipine makes it a good candidate for fakers. Consumption of substandard and/or fake amlodipine tablets will have a negative impact on the management of hypertension. This justifies continuous monitoring of amlodipine preparations in the marketplace and the provision of simple and cost-effective assay method that could be routinely utilised for their assay. Ten different brands of amlodipine tablets were qualitatively assessed for uniformity of weight, friability, hardness, disintegration and dissolution rate using standard physical methods. Quantitative assay was carried out using spectrophotometric method. The spectrophotometric measurement was done at a wavelength of 240 nm. Seven brands met the official requirements for uniformity of weight; eight passed the friability test and the hardness tests. All the brands tested passed the disintegration test and nine brands passed the dissolution test. The spectrophotometric assay showed that all the brands passed the United States Pharmacopoeia (USP) requirement for percentage drug content. The assay method used in this study is reliable, simple and cost-effective and can be routinely used to assay amlodipine tablets.

Keywords: Amlodipine, qualitative, quantitative, assay, ultraviolet spectrophotometry

INTRODUCTION

Amlodipine is a dihydropyridine calcium channel blocker used for the management of hypertension, coronary artery disease and angina [1-3]. It acts by inhibiting the transmembrane influx of calcium ions into vascular smooth muscles and cardiac muscles [1]. This affects their contractile process and in turn results in reduced blood pressure and contraction of the heart. Amlodipine is administered enterally, once a day as it has a half-life of 30-60 hours [4,5]. It reaches peak plasma concentration at 6-12 hours after oral administration, has a bioavailability of 64-90% and protein binding of 93% [6,7]. It is metabolised in the liver into many inactive pyridine metabolites and excreted primarily through the kidney [7,8]. Side effects associated with its use include oedema, headache, tiredness, abdominal pain, nausea, hypotension and heart attack [9,10]. It should be administered with caution in the elderly, people with heart failure and those with hepatic problem. Amlodipine is a white

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crystalline powder with a molecular formula of $C_{20}H_{25}ClN_2O_5$ and molecular weight of 408.9 g/mol [11]. It is freely soluble in methanol, chloroform, sparingly soluble in ethanol and slightly soluble in water [12]. Amlodipine is available as the racemic mixture in 5 mg and 10 mg and as the S-rotatory isomer in 2.5 mg and 5 mg, all of oral dosage forms. Only the S (-) isomer has vasodilating action [13].

Amlodipine is manufactured by various pharmaceutical companies under various brand names. With the presence of various brands in the market, there is the probability of making inappropriate decision on the suitable brand to purchase [14]. There is a need to ascertain that every drug product meets the Pharmacopoeia standards so as to ensure optimal clinical outcomes [15]. Regular monitoring of drugs in circulation is one way of improving surveillance [14]. This necessitated our study of the different brands of amlodipine marketed in Uyo metropolis, Akwa Ibom State, Nigeria.

EXPERIMENTAL

Materials. Ten different brands of amlodipine 10 mg tablets within their shelf-lives were purchased from community pharmacies in Uyo and coded A to J. The reagents used were of analytical grade and used as purchased.

Extraction of pure amlodipine. Five tablets from the innovator brand H (Novasc) were pulverized and extracted using 100 mL methanol, filtered and the solvent evaporated to obtain the amlodipine powder as crystalline solids.

Weight analysis. Twenty tablets of each brand were weighed individually using electronic weighing balance (Shimadzu, Japan). The mean weight, standard deviation and percentage deviation of each brand were calculated.

Friability test. Five tablets of each brand were weighed together to obtain weight, Wo. Each brand was subjected to friability test in a Roche friabilator at 25 revolutions per minute for 4 minutes after which each batch was reweighed to obtain weight W. The weight loss and percentage weight loss were calculated.

Hardness test. Five tablets of each brand were randomly selected and each tablet subjected to crushing force using a Mosanto hardness tester. The average pressure at which each brand crushed was calculated.

Disintegration test. Five tablets of each brand were randomly selected and put in a digital tablet disintegration test apparatus using 900 mL distilled water as the disintegration medium at a bath temperature of 37^{o}C. The time taken for each brand to disintegrate completely was recorded.

Dissolution test. The dissolution profile of each brand of amlodipine was measured according to the method described in the British Pharmacopoeia [16] using a digital tablet dissolution apparatus in 900 mL of 0.1 N HCl at 37^{o}C.

Spectroscopic assay. 50 mg of the extracted amlodipine powder was dissolved in 50 mL of 2 M urea solution and made up to 100 mL using distilled water to obtain a stock solution of 500 µg/mL concentration of amlodipine. The stock solution was further diluted with distilled water to get a concentration of 25 µg/mL, which was scanned, in the UV range of 200-350 nm against reagent blank of 2 M urea to obtain the wavelength of maximum absorption (λ_{max}). Aliquots of the amlodipine stock solutions corresponding to 10µg/mL, 20 µg/mL, 30 µg/mL, 40 mg/mL and 50 µg/mL were prepared and their absorbance measured at the λ_{max} of 240 nm against the reagent blank to obtain the calibration curve of amlodipine. Twenty tablets of each brand of amlodipine were pulverised and portions equivalent to 10 mg of drug extracted with 14

mL of 2 M urea and 5 mL distilled water. The filtrates were diluted with distilled water to 10 µg/mL and 20 µg/mL and the absorbance measured at 240 nm against the reagent blank. These were extrapolated on the standard curve to obtain the respective extrapolated concentrations. The percentage recoveries were obtained by comparing the extrapolated concentrations with the expected concentrations.

RESULTS

Eight brands complied with the British Pharmacopoeia specification for uniformity of weight of uncoated tablets (Table 1). Eight brands passed the friability test as they had a weight loss of less than 1% (Table 2). Nine brands passed the crushing test as shown in Table 3. All the tested brands disintegrated within the prescribed time limit (Table 4).

Nine brands passed the United States Pharmacopoeia specification for dissolution rate (Figure 1). The difference factor (f1) and the similarity factor (f2) values with respect to brand H, the innovator brand, are shown in Table 5. The wavelength of maximum absorption of amlodipine in urea was obtained at 240 nm (Figure 2). Figure 3 shows the calibration curve of amlodipine. The quantitative assay results of the ten brands of amlodipine are in Table 6.

Table 1: Weight uniformity analysis of different brands of amlodipine tablets

Sample	A	B	C	D	E	F	G	H	I	J
Mean weight(mg)	188.80	402.00	159.35	152.80	292.30	191.30	188.75	402.00	183.75	405.45
SD (n=10)	±1.50	±3.20	±2.03	±1.25	±4.33	±11.75	±4.13	±2.99	±10.39	±5.79
% Deviation	0.79	0.79	1.28	0.82	1.48	6.14	2.19	0.74	5.66	1.43

Permissible percentage deviation is 5%

Table 2: Friability analysis of different brands of amlodipine tablets

Sample	A	B	C	D	E	F	G	H	I	J
W_0(g)	1.99	1.23	2.51	1.92	1.46	0.89	2.10	2.09	0.88	3.02
W(g)	1.98	1.22	2.49	1.91	1.44	0.88	2.09	2.07	0.87	3.01
W_0-W	0.01	0.01	0.02	0.01	0.02	0.01	0.01	0.02	0.01	0.01
% Weight loss	0.50	0.81	0.79	0.52	1.37	1.12	0.48	0.95	0.13	0.33

Permissible percentage weight loss is 1%

Table 3: Hardness analysis of different brands of amlodipine tablets

Sample	A	B	C	D	E	F	G	H	I	J
Average crushing strength (Kg/cm^2)	5.90	5.80	9.00	5.40	2.90	5.90	4.30	7.80	4.24	4.00

Permissible crushing strength is 4-10 Kg/cm^2

Table 4: Disintegration analysis of different brands of amlodipine tablets

Sample	A	B	C	D	E	F	G	H	I	J
Mean disintegration time (min)	0.23	0.27	0.27	0.03	0.36	1.54	4.51	0.18	0.02	0.93

Permissible disintegration time is <15 minutes

Table 5: f1 and f2 values of the various brands of amlodipine compared with innovator brand H

Sample	A	B	C	D	E	F	G	I	J
F1	21.19	11.81	18.82	13.55	23.70	16.97	13.65	18.45	9.23
F2	36.17	54.87	49.25	57.56	35.87	48.36	51.84	46.22	63.55

Table 6: Percentage recovery of amlodipine tablets

Sample	A	B	C	D	E	F	G	H	I	J
%	103.38	100.19	99.53	100.63	99.43	97.26	90.00	98.95	99.27	99.94

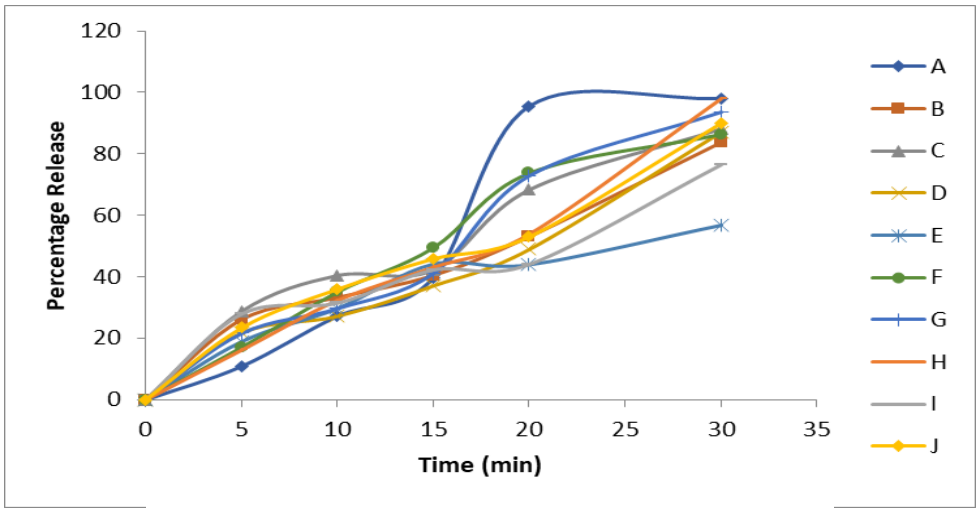

Figure 1: Dissolution analysis of different brands of amlodipine

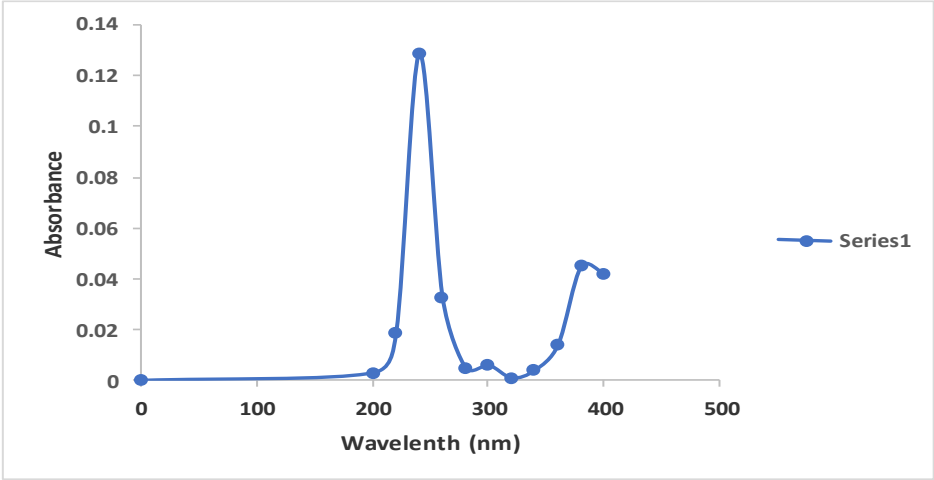

Figure 2: Absorbance spectrum of amlodipine

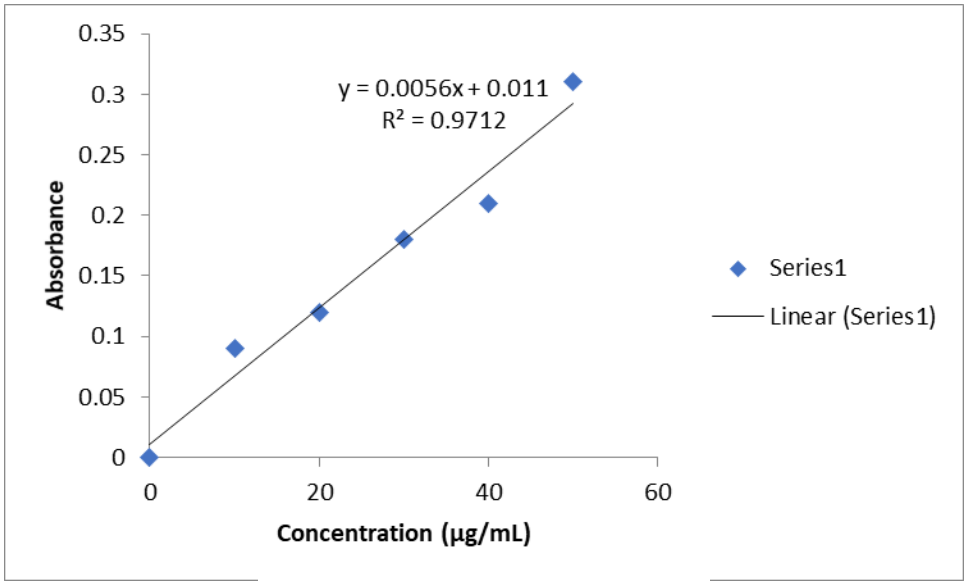

Figure 3: Calibration curve of amlodipine

DISCUSSION

Uniformity of weight is an indication of adherence to Good Manufacturing Practice during the granulation and compression stages. British Pharmacopoeia (2015) specification for uniformity of weight of uncoated tablets is 5% deviation of each tablet from the mean value.

Friability is used to test the resistance of tablets to abrasion during packaging and transit. It is a measure of the tendency of the tablets to break into smaller pieces during contact especially by rubbing. Good friability property ensures tablets do not chip during transportation as a result of abrasion and is an evidence of adherence to good manufacturing practice. It is expected that a batch gives a weight loss of less than 1%.

Crushing/hardness test measures the resistance of the tablets to chipping during handling which can influence friability and disintegration. The harder a tablet is the less friable with longer disintegration time, and vice-versa. A crushing force of between 4-0 Kg/cm^2 is prescribed.

Disintegration test is a quality control test used to determine the ability of solid dosage forms to break down within the prescribed period when placed in a suitable liquid medium. The rate of disintegration affects the dissolution and subsequently absorption of the drug. The presence of suitable disintegrants in adequate proportions ensures the production of tablets that are free from disintegration problems [17]. The British Pharmacopoeia (2015) specifies that uncoated tablets should disintegrate within 15 minutes.

Dissolution test is used to determine the rate of release of oral dosage forms. It is a necessary criterion for determination of drug bioavailability. It serves as a useful tool in assessing the probable *in vivo* performance of a drug as well as in identifying unacceptable and substandard drug products [18]. The United States Pharmacopoeia [19] specifies at least 75% dissolution in 30 minutes for amlodipine.

The difference factor (f1) and the similarity factor (f2) were calculated to compare the dissolution profiles of the various brands with the innovator product. Two dissolution profiles are considered similar and bioequivalent if f1 is between 0 and 15 and f2 is between 50 and 100 [20]. Only brands B, C, D, G, and J gave f1 values between 0 and 15 and f2 values between 50 and 100. These brands can be used interchangeably with brand H (Table 5).

The calibration curve for the extracted pure sample of amlodipine is linear over a concentration range of 10 to 50 µg/mL with the regression line equation obtained as $y = 0.0056x + 0.011$ which is in conformity with Beer Lamberts Law (Figure 3). The variation of absorbance with concentration showed correlation with coefficient of correlation (r) of 0.985 and coefficient of determination (r^2) of value 0.971.

From the quantitative assay results, all the ten brands met the United States Pharmacopoeia (2014) specification of 90% to 110% drug content (Table 6).

Conclusion. Only five out of nine brands assayed (55.6%) could be used interchangeably with the innovator product, though all the brands satisfied the USP specification for drug content. Post-market surveillance is very crucial to ensure that dosage forms introduced into the market meet the required standards so as to produce effective clinical outcomes. The quantitative assay method adopted in this study can be routinely used for quick post-market surveillance of amlodipine, as it is simple, cost-effective and reproducible.

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