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Research Article

A COMPARATIVE PHARMACEUTICAL EVALUATION OF AMLODIPINE (5MG)TABLETS REGISTERED IN NIGERIA BY NAFDAC, AND MARKETED BY VARIOUS PHARMACEUTICAL COMPANIES NATIONWIDE.

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ABSTRACT

The current paper is devoted to the evaluation of pharmaceutical equivalency of five different brands of amlodipine 5mg tablets registered and marketed in Nigeria, by five pharmaceutical companies.

The pharmaceutical equivalency of five different brands of amlodipine 5mg tablets were assessed through the evaluation of uniformity of weight, friability test, hardness test, disintegration test, and dissolution test, as well as content of active ingredient.

All the brands evaluated were considered pharmaceutically equivalent, since all the brands under consideration complied with the British Pharmacopoeia 1998 specifications, for uniformity of weight, friability, hardness, disintegration, dissolution and content of active ingredient. All the brands evaluated achieved 85% release of the active ingredient within 30 min, in all the dissolution media with PH 1.2, 4.5 and 6.8 and the dissolution profiles of all the brands were similar at various PH values used. All the brands of amlodipine 5mg registered in Nigeria by NAFDAC and evaluated in this study are deemed pharmaceutical equivalent and all the brands can be inter-changeably prescribe and dispense with confident.

Keywords: Amlodipine 5mg tablets, Pharmaceutical equivalency, Brands and Pharmacopoeia specifications.

INTRODUCTION

Amlodipine is a dighydropyridine calcium antagonist (calcium ion antagonist or slow-channel blocker) that inhibits the trans membrane influx of calcium ions into vascular smooth muscle and cardiac muscle.[1] It is indicated for the treatment of hypertension, chronic stable angina, and confirmed or suspected vasospatic angina. [2]. NAFDAC (National Agency For Food Drug, Administration And Control) is the agency that is charged with the duties of regulating and registering the importation and production of food and drugs in Nigeria.

To ensure access and affordability of most innovative pharmaceutical products, generic pharmaceutical companies are licensed to produce, import and market generic pharmaceutical products similar/pharmaceutical equivalent to the innovative brands, normally at the expiration of drug patents.[3] Problem relating to pharmaceutical in-equivalent had been reported by several authors, among which are tetracycline capsule,[4] Ciprofloxacin, Tablets,[5] ,sulphadoxine-pyrimethamine tablets, [6] and Metronidazole tablets .[7] The need for continuous Pharmaceutical equivalent assessment of multiple brands of clinically useful pharmaceutical products can not be over emphasized, most especially in developing countries where pharmaceutical products faking , counterfeiting and adulterations are prevalent.

The chemical name of amlodipine is 3-ethy 15- methy12- (2 aminoethoxy) methyl)-4- (2-chlorophenyl)-6-methy-1-1,4-dihydropyridine -3,5-dicarboxylate. Its molecular structure is as shown in figure 1.

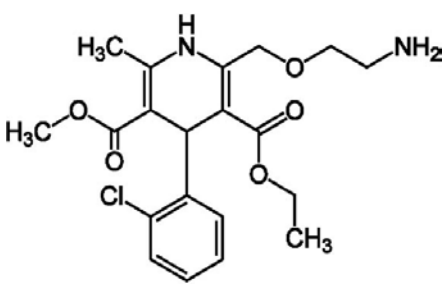

Fig. 1: Molecular Structure of Amlodipine

Five different brands of amlodipine 5mg tablets were pharmaceutically evaluated using pharmaceutical parameters such as , uniformity of active ingredient test, weight uniformity text, disintegration test, hardness test, tablet friability test, and in-vitro dissolution test. These tests are necessary to ascertain the claim of pharmaceutical equivalency by most generic companies.

MATERIALS AND METHODS

Materials

Five different brands of amlodipine 5mg tablets were obtained from five different generic pharmaceutical companies.

Amlodipine powder was obtained from Lifecare Pharmaceutical ltd, Kano, Nigeria.

Chemical

Dissolution media consist of USP buffer solutions

at pH 1.2 (hydrochloric acid solution)
at pH 4.5 (acetate buffer solution)
at pH 6.8 (phosphate buffer solution)

analytical grade Conc. Hydrochloric acid, glacial acetic acid, potassium hydro phosphate dodecanhydrate, methanol, and potassium chloride were used, (BDH chemicals Ltd, Poole England.

Apparatus

The apparatus used in this study include

- Disintegration test apparatus ,Erweka (ZT 71)
- Roche friabilator Erweka (TA3R)
- Erweka hardness Tester (TBH 100)
- Digital electronic Balance Denvar instrument (XP 300)

And Dissolution test apparatus Erweka (DT 600)

Method

Uniformity of Weight Determination

Twenty tablets from each brands were weighted individually using the digital balance. The average weights of the tablets were calculated and their standard deviation from the mean weight calculated.

Friability Test

Twenty tablets were randomly selected from each brand of amlodipine 5mg tablets, the weight of all the twenty tablets per brand were determined using the digital balance, before the commencement of the abrasion process in a Erweka friabilator, operated at 25 revolutions per min(rpm) for 4 min. The tablets were dusted, and reweighed thereafter, the lost in weight due to the abrasion process was determined for each brand.

Hardness Test

Tablet crushing strength were determined using a Erweka hardness tester (TBH 100)

Tablet Disintegration

This was conducted using six tablets randomly selected from each brand. The disintegration medium was distilled water maintenance at 37^0C. The time taking from each of the six tablets in the basket to break up into small particles and passes through the orifice at the bottom of the six tubes, unto the disintegrating medium was recorded.

Dissolution Rate Determination

All dissolution studies were performed using USP apparatus (Erweka DT 600 Frankfurt, Germany) at 75rpm. The dissolution media were USP buffer solution at pH 1.2, pH 4.5 and pH 6.8 maintained at 37+ 0.5 ^{0}C. Dissolution media volume was 500ml. 5ml aliquot sample were withdrew at regular time interval of 10, 15, 20, 30 and 45 min using a micropipettes and immediately replacing the withdrew fluid with equal volume of fresh medium solution maintain at the same temperature.

The sample were filtered and diluted appropriately before been analyzed spectophotometrically at 239nm using a uv-visble spectrophotometer (Aigilet)

Content of Active Ingredient

Calibration

100µg /ml standard solution of amlodipine was prepared from pure amlodipine powder and analytical grade methanol. Various dilutions were made from the stock solution to give 2, 4, 5, 7, 9.5, 12, and 17µg/ml, the absorbance was taken. Graph of absorbance against concentration was plotted. The slopes and intercept were calculated.

Assay

Spectrophotometry method was use, twenty tablets randomly selected from each brands were weighed accurately using the digital electronic balance, the mean tablet weight (MTW) was there after determined. These tablets were turned back into powder in a suitable size laboratory mortal. A quantity of the powdered tablets equivalent to 5 mg amlodipine was weighed and dissolved in about 50ml of Methanol in a 100ml volumetric flask. Necessary dilution were carried out to obtained a final concentration of 100 µg/ml, the solution was thereafter filtered through a membrane filter and absorbance determined at 239nm. The same procedure was also repeated for other brands.

RESULT

Uniformity of Weight

All the brands of Amlodipine 5mg tablets investigated in this study complied with the official specification for weight uniformity as none of the brand deviated from the mean by value up to 5%. Weight uniformity of tablets is essential to ensure accurate unit dosing.[8]

Friability

The friability of tablets is an indication of the ability of the tablets to withstand any, stress and abrasion process that may be encounter during transportation and handling. The cut off value is 1%. Batches or brands of tablets with friability value less than 1% are consider satisfactory, batches/brands with higher friability value are totally rejected and a times the batch could be re-work or reprocessed. All the brands of amlodipine 5mg tablets investigated in this study are satisfactory as none had value up to 1% as shown in table 1.

Means Crushing Strength/Tablet Hardness

The crushing strength of a tablet is the force required to break up the tablets when place in between the two edges of tablets hardness tester. Tablets requiring 4KgF and above are consider hard and compact enough to withstand normal handling stress. All brands had values higher than 4KgF and all passed tablet hardness test.

Table 1:

Sample	UW (mg)	CS (KgF)	FR (%)	DT (min)	D45 (pH 1.5)	D45 pH 4.5	D45 pH 6.8	CAI %
LOV	140 + 0.00	7.0	0.10	2.03	97.36	97.36	97.00	101.0
Rb	200 + 0.01	6.00	0.01	0.25	97.71	97.70	97.00	101.1
LK	160 + 0.00	10.00	0.01	0.05	96.97	96.94	96.94	101.0
RD	160 + 0.01	10.0	0.05	0.08	97.76	97.76	97.74	101.0
ME	200 + 0.02	7.2	0.50	0.08	97.76	97.86	97.78	99.9

UW = uniformity of weight
CS = crushing strength
FR = friability
DT = disintegration time test
D45 = % drug released at 45 min(in various pH solutions.)

Disintegration Test

All the brands passed the disintegration test (table 1). The B.P 1988 specified 15 minutes for immediate release uncoated tablets.

The satisfactory disintegration time is a good indication that the tablets will be quickly broken down into smaller fractions presenting increased surface area for dissolution and absorption of the active pharmaceutical ingredient within the gastrointestinal tracks.

Dissolution Studies

For uncoated tablets like amlodipine, the B.P specified that nothing less than 70% of the active pharmaceutical ingredient must go into solution within 45 minutes after administration. The result reveal that all the brands of amlodipine 5mg registered and marketed in Nigeria complied with the B.P requirement as all the brands released about 85% of active ingredient into solution within 45 minutes., dissolution rate has a direct bearing on the bio-availability profile of drugs formulated as tablets as it an be used to predict the drug release pattern in-vivo.[9]

Content of Active Ingredient

According to B.P 2002 amlodipine tablets are expected to contain between 95 -101%w/w of the active ingredient. The content of active ingredient of all the brands fall within the acceptable limits and thus all the brands passed the content of active ingredient test.

CONCLUSION

All the manufacturers of the generic amlodipine 5mg investigated must had observed well documented manufacturing practices

(cGMP) as evident in the data obtained; all brands investigated are satisfactory and are chemically and pharmaceutically equivalent.

And all the brands can therefore be freely interchangeably be prescribe and dispense without fear of pharmaceutical in-equivalent associated with generic pharmaceutical products in developing countries.

The implication of these finding is that patients who are the end users now have a good qualitative alternative, as the cost of procuring the innovative brand of amlodipine is relatively higher.

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