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PHARMACEUTICAL EVALUATION OF SOME COMMERCIAL BRANDS OF NIFEDIPINE (20MG) SUSTAINED RELEASE TABLETS, MARKETED IN COMMERCIAL CITY OF KANO

OYENIYI YJ[1] AND AYORINDE JO[2]

1: Department of Pharmaceutics & pharmaceutical microbiology, Faculty of Pharmaceutics science, Usmanu Danfodiyo University, Sokoto

2: Department of Pharmaceutics & Industrial pharmacy, Faculty of Pharmacy, University of Ibadan

***Corresponding Author: E mail: drdeyinkaoyeniyi@gmail.com**

ABSTRACT

This study was undertaken with the sole objective of evaluating the pharmaceutical equivalence of ten different brands of nifedipine 20mg sustained released tablets available for sales in various pharmaceutical shops (open drug market) in Kano State, North West, Nigeria. The pharmaceutical equivalent testing of these brands was carried out by evaluation of the following physiochemical tablets properties; uniformly of weight, friability test, tablet crushing test disintegration test and dissolution test.

Four brands out of ten complied with all the official specifications, i.e. uniformity of weight, disintegration and dissolution tests etc. Three brands failed both the disintegration and friability tests even though their assessment of weight uniformity and tablet crushing strength were satisfactory. The remaining three brands failed only the content of active ingredient. It was also noticed that only three out of the four brands that passes all the tests were registered in Nigeria by Nafdac. Only four out of ten brands evaluated in this study could be regarded as being pharmaceutical equivalent.

Keyword: Nifedipine, Pharmaceutical Equivalent and Sustained Release Tablets

INTRODUCTION

Most of the third world countries depend heavily on generic brands of pharmaceutical products for their health care; Nigeria is not an exception as most pharmaceutical companies patiently await the expiration of innovative pharmaceutical products before the introduction of their generic pharmaceutical brands to the market.

However there is the need to select (for prescription /dispensing) from among several generic brands. This is a great concern for majority of health care providers that will love to provide quality pharmaceutical products at good price to the patient. Also to be able to monitor the pharmaceutical qualities of all most of the brands in the market, the regulatory authority must regular carry out pharmaceutical equivalent evaluation of these generics.

Nifedipine is a calcium-channel blocking agent that is widely used clinically in the treatment of angina pectoris and systemic hypertension. Nifedipine is a poorly soluble drug; it has a short biological half-life of 4 hrs **[1]**.

Nifedipine act by blocking voltage-gate, calcium channels, in the cardiac muscle and blood vessels. This decreases intracellular calcium leading to a reduction in muscle contraction. And in blood vessels, a decrease in calcium results in less contraction of the vascular smooth muscle and therefore an increase in arterial diameter, (Vasodilatation) [**2]**.

Vasodilatation decrease total peripheral resistance. Nifedipine also slowdown the conduction of electrical activity within the heart, by blocking the calcium channel during the plateau phase of the action potential of the heart, this results in a negative chronotropic effect, or a lowering of heart rate.

Clinical experience gained with oral nifedipine formulations with immediate release (IR) characteristic clearly show that a sudden rise in the plasma concentration of nifedipine leads to increase heart rate and drug-specific side effect [**3,4]**. Sublingual nifedipine has previously been used in hypertensive emergencies. It was however found to be dangerous and the sublingual nifedipine was abandonee [**3, 5]**.

It is therefore generally accepted that sustained-release (SR) formulation of Nifedipine are most efficient for routine hypertension therapy. Chemically nifedipine is dihydropyridine and because

of its short biological half life, nifedipine is mostly formulated as 20 mg sustained-release tablets. Sustained release tablets are design to release active pharmaceutical ingredient at a pre determined rate in order to maintain a constant drug concentration for a specific period of time, this minimized side effects. Nifedipine is a yellow crystalline power with melting point range of 171-175° C. It is light sensitive and it must be protected from light.

Nifedipine photo reactive by products are nitrosophenyl pridine and nitrophenyl pyridine. Both posses highly diminutized pharmacological activity [**6-9**].

Pharmaceutical equivalent products are expected to contain the same amount of the same active substance (s) in the same dosage form, and must also meet the same comparable physicochemical standards.

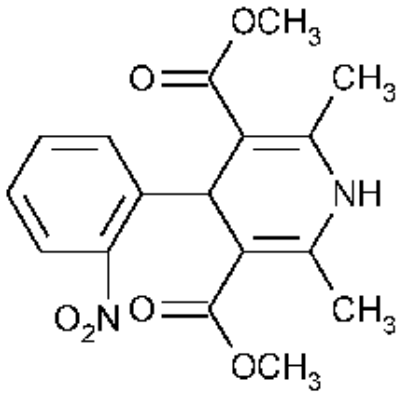

Figure 1: Chemical Structure of Nifedipine

MATERIALS & METHODS

Materials

Nifedipine powder (Sigma-Aldrich GmbH Germany). Nifedipine SR 20mg tablets were purchased from various shops in Kano drug market. All the brands purchased are from different manufacturers, and all are labeled to contain 20mg of Nifedipine as sustained release formulation. The identification & specifications of various samples/brands collected in this study are listed in **Table 1.**

Table 1: Different brands of Nifedipine 20mg S/R tablets

Code Number	Label Country of Origin	Manufactures	Expire Date
LT	Slovenia	11/2010	11/2015
ET	India	09/2009	09/2013
CT	China	08/2008	07/2011
MT	China	01/2010	01/2011
PT	China	07/2009	06/2012
IT	China	04/2010	04/2014
DT	Nigeria	04/2009	03/2012
GM	Nigeria	11/2009	10/2012
LF	China	01/2008	12/2010
XX	Korea	05/2010	04/2015

Disintegration Time Test

Time taken for six tablets, randomly selected from each brands to break up and pass through screen mesh of the disintegrating apparatus to the disintegrating medium was noted. Te statistical mean of the six recording was calculated. This was recorded as disintegration time for the brand. The disintegrator medium was distill water maintained 37^{o}C. This procedure was repeated for all the other nine remaining brands.

The Dissolution Time Test

A) CALIBRATION CURVE OF NIFEDIPINE

Various concentration of nifedipine was prepared using nifedipine powder obtained from sigma & 0.1, 1.5 2.0, 2.5, 5, 10 ug/m). The absorbance's were read at 350nm using a spectrophotometer. The values of absorbance were plotted against concentration.

B) Dissolution Studies

The dissolution rates of the active ingredient from the sustained release tablets were determined using Erweka dissolution apparatus, (GmbH Germany). The dissolution medium was 750 ml 0.1M HCL maintained at 37 ± 0.5^{o}C. The speed of rotation of the basket was 50rpm. 5ml of the dissolution medium was withdrew at regular intervals, filtered & diluted appropriately. The absorbance was read at 350nm against 0.1 M HCL (used as blank) using a un-visible spectrometer (640SGU Jen way).

Fresh 5ml of 0.1M HCL maintained at same temperature was added to the dissolution medium each time, to replenish the withdrawn volume. All measurements were conducted in triplicates. The percentage of Nifedipine release was them calculated using the curve.

Tablet Crushing Strength Test

Twenty tablets randomly selected from each brand were used for this test using a Monsanto hardness tester (Manesty machine ltd). The force require to break the tablet placed in between the month of the machine was noted and recorded. The average crushing force was calculated was statistically determined. This was repeated for all other brands.

Tablet Friability Test

Twenty tablets were weighed and subject to abrasion processing using a Roche friabilator operated at 25 rev/minute. The tablets were re-weighted after 4 minutes and the percentage weight lost noted.

This was repeated to get 3 different readings, from which the average is obtained. The procedure was repeated for all other brands.

Weight Uniformity Test

Twenty tablets from each brand were weighed individually using a mettler 1180 weighing balance. The average weights of the tablets were calculated as well as their percentage deviation from the average weight.

Content of Active Ingredient

Ten tablets were randomly selected from each brand. They were crushed and powdered, using a mortal & pestle. The amount of this finely powder tablets equivalent to 20mg of Nifedipine was obtained and dissolved in 50ml of methanol using a 100ml volumetric flash. This was shaken vigorously for about 15Min or more until a clear solution is obtained. The flask was then made up to volume with more methanols, and the solution filtered, through what man No. 1 filter paper. 2.5ml of the filtrated was again taken & diluted to 50ml with methanol. The absorbance of this final solution was read at 350nm using methanol as blank. The content of the active drugs was calculated base on absorbance of 10.0ug/ml of Nifedipine.

RESULTS AND DISCUSSION

The result of aesthetic assessment of Nifedipine sustained release tablets **(Table 2)** shows that cell brands had good and impressive physical appearance and all were elegantly color oxblood red to pink. Three of the brands have circular convex shape, the rest are circular convex shape.

It's so obvious from the average weight of tablets that the manufacturers uses different formulation formula and irrespective of this, the standard deviation from the mean of all the brands are within the acceptable limit as none deviate from the mean by up to 2%.

Brands PT, IT & DT failed the friability test and disintegration test **(Table 3)**. Friability values above 1% are generally consider as unsatisfactory, as the tablets may generate lots of powder (in the process of handling & transportation) which may lead to weight variation and variation in dose. In the same manner, plain uncoated tablets are expected to

disintegrate within 15 minutes, disintegration time test above 15 minutes must be rejected and possibly rework.

Table 4 shows that brands label GM, LF & XX all contain active ingredient below the standard which is 90-110% for nifedipine sustain release tablet. (U.S.P/NF 2003).

The in-vitro drug release profile **(Figure 1)** indicate that all the brands released about 50% within 1 h, this is vital in attaining a good blood pressure control level within I hrs.

From the results above it can also be inferred that there is a need for continuous pharmaceutical evaluation of all pharmaceutical products sold in Nigeria drug markets.

Brands like PT, IT & DT that fails to meet friability & disintegration standard should be recall from circulation, and re-work **(Figure 2)**.

Brand Lf is definitely a fake and counterfeit product as it contained only 28% of the labeled amount.

Brands GM & XX are also unfit for consumption as the percentage of nifedipine they contained is less than the pharmacopoeia standard, this could be due to improper storage conditions and exposure to extreme heat, bearing in mind that Nifedipine is photosensitive.

All the stores in Kano drug market have no adequate storage facilities for pharmaceutical products and are mainly manage by un-professional traders will little or no technical knowledge on pharmaceutical products. Brands GM and XX might have been expose to extreme atmospheric temperature that at times is above 40^{o}C as it was observed that none of the shop visited installed air conditioning system.

Table 2: Result of aesthetic Observation

Brand	Color	Shape	Nature of Surface
LT	OX blood red	Circular convex	Smooth
ET	OX blood red	Circular Flat	Smooth
CT	Pink	Circular Flat	„
MT	„	„	„
PT	„	„	„
IT	„	„	„
DT	„	„	„
GM	„	„	„
LF	„	„	„
XX	OX blood red	„	„

Table 3: Result of some Quality Control Tests

Brand	Friability	Crushing Strength (KgF)	Weight
LT	**0.3**	**7.3**	**202 (1.06)**
ET	**0.4**	**7.5**	**202 (1.06)**
CT	**0.3**	**7.5**	**202 (1.06)**
MT	**0.2**	**7.5**	**202 (1.06)**
PT	**1.2%**	**6.2**	**81.51 (1.19)**
IT	**1.1%**	**6.3**	**81.51 (1.19)**
DT	**1.3%**	**6.3**	**81.51 (1.19)**
GM	**0.6**	**7.5**	**83 (0.9)**
LF	**0.6**	**7.5**	**83 (0.9)**
XX	**0.6**	**7.5**	**83 (0.9)**

Table 4: Result of Official Quality Control Tests

Brand	Disintegration	Active Center
LT	**06**	**104.3**
ET	**08**	**104.3**
CT	**08**	**104.4**
MT	**08**	**„**
PT	**20 minutes**	**„**
IT	**25 Min**	**„**
DT	**22 Min**	**„**
GM	**06**	**80%**
LF	**08**	**28%**
XX	**08**	**85%**

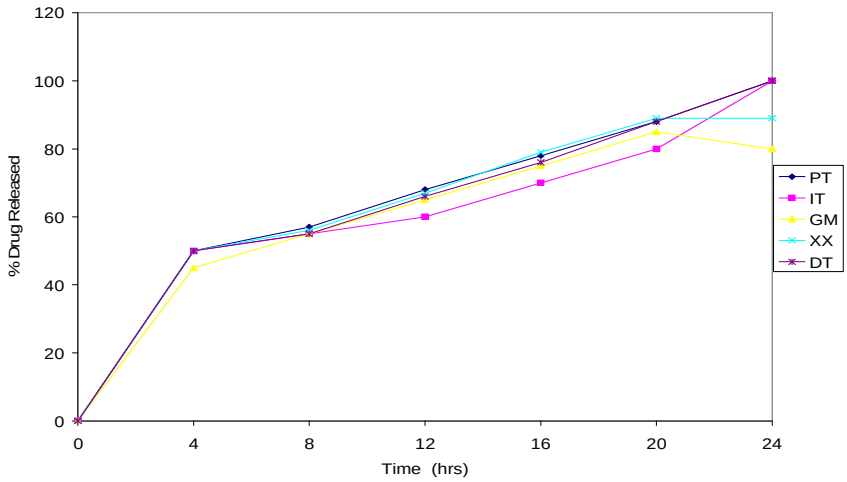

Figure 1: Dissolution Profile of some brands of Nifedipine 20mg SR Tablets

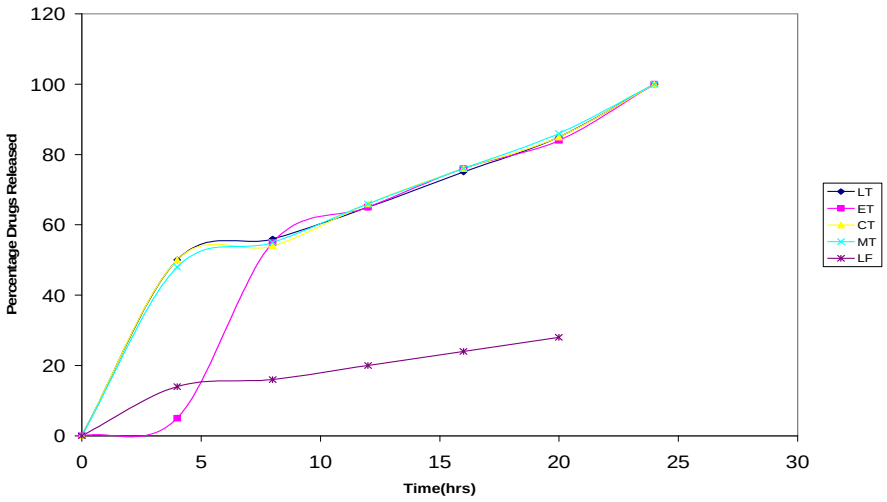

Figure 2: Dissolution Profile of some brands of Nifedipine 20mg SR Tablets

CONLUSION

From the result obtained we came to the following conclusions; that 60 % of Nifedipine 20mg Sustained released sold in Kano drug are sub-standard and are not pharmaceutically equivalent.

That un-necessary exposure of pharmaceutical products to extreme environmental condition could be responsible for lower content of active ingredient observed in some brands.

Thus there is an urgent need by the regulatory agency to constantly and consistently carried out pharmaceutical equivalent testing of most of these generic brands of drugs, and to ensure that drugs sold to the public at the drug market are properly stored to prevent degradation.

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