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Research Article

EVALUATION OF SOME COMMERCIALLY AVAILABLE BRANDS OF PIROXICAM CAPSULES IN THE NIGERIA MARKET

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ABSTRACT

A study of eight brands of piroxicam capsules (20 mg) sold in some parts of Nigeria (Delta and Edo states) was carried out. The purpose was to investigate the quality as well as the physicochemical equivalence of different brands of the product readily available in the Nigerian market. The products were sourced from different retail pharmacy outlets and subjected to various official tests such as weight uniformity, dissolution and chemical assay tests (using HPLC). All the eight brands passed weight uniformity test as specified by the British Pharmacopoeia. Two brands (B and G) were outside the specified melting point range for piroxicam. All the brands passed the dissolution test except brand B in which only 52% of the drug was released in 45 min. The drug chemical assay carried out showed that all the brands were within the USP specified range of drug content (97-103%). This study revealed that brand substitution on assumption of chemical equivalence may not give the desired onset of action and subsequent therapeutic effectiveness It also demonstrated the need for manufacturers to adhere strictly to the principle of GMP. Post marketing surveillance must be intensified by both manufacturers and regulatory bodies to prevent the distribution of substandard drug products.

Keywords: Brands, Comparative study, HPLC, Physicochemical equivalence, Piroxicam.

INTRODUCTION

The pharmacological effect, which includes the toxic and therapeutic effects, of a drug is generally related to its concentration at the site of action. The objective of successful drug therapy is to deliver the drug to its site of action in the right amount and at the right time[1]. Capsule, a solid dosage pharmaceutical form is one of the most common dosage forms, second only to tablets and oral liquids in frequency of dosage form types manufactured in the UK[2]. To be able to deliver the right concentration of drugs at the site of action and at the right time, much has to be done with regard to the quality of the dosage form and the quantity of the Active Pharmaceutical Ingredients (APIs).

The increase in the number of generic drug products from various sources has placed a serious burden on prescribers. Selection has to be made from various seemingly equivalent brands. Due to influx of generic brands, faking has become rampant. It has been posited that: in Nigeria today, there is an influx into the market of fake machine parts, fake motor spare parts, fake chemicals, fake and adulterated food items, amongst many others. It may appear that almost every existing product has a fake counterpart[3].

The period 1983-2000 in Nigeria has witnessed an upsurge of faking and quackery, counterfeit drugs,

quack doctors, illegal chemist shops and hospitals. Drugs are no exception[4]. The problem of fake drugs became common in the last decade and the present situation has become unbearable in Nigeria. Empirical observations have shown that there may be more fake than genuine drugs in Nigeria[5].

Apart from faking, other factors could be attributed to low drugs quality. Research has shown that over 80% of the approximately 10,000 prescription drugs available in 1990 were obtained from more than one source in the United States of America, and variable clinical responses to these dosage forms supplied by two or more drug manufacturers is documented[6]. These variable responses, apart from faking, may be due to the formulation ingredients employed, methods of handling, packaging and storage, and even the rigors of in-process quality control[7]. This emphasizes the need to determine the pharmaceutical and therapeutic equivalence of the numerous brands from time to time in order to ensure interchangeability. It must be pointed out here that effective monitoring is a major problem in Nigeria and other developing countries. The outcome of this is the distribution of substandard and counterfeit drug products. The activities of the National Agency for Food and Drug Administration and Control (NAFDAC) have not significantly ammeliorated matters. This is as a result of the emphasis on NAFDAC registration number rather than emphasis on professionalism in drug related matters. Generic drug products must satisfy the same standards of quality, efficacy and safety as those applicable to the innovator products. Preliminary physicochemical assessment of the products is very necessary and *in vitro* dissolution testing can be a valuable predictor of the *in vivo* bioavailability and bioequivalence of oral solid dosage forms[8].

This study aims at providing base line data towards the establishment of physicochemical equivalence of some commercially available piroxicam capsules using *in vitro* methods. To achieve these objectives the following were carried out:

i. Purchase of several brands of piroxicam capsules from registered pharmacies in Edo and Delta states,

ii. Characterization of the different samples by evaluating uniformity of weight and melting points using flexodene (a brand of piroxicam) as standard,

iii. Determination of uniformity of content using high performance liquid chromatography (HPLC) and

iv. Dissolution testing.

MATERIALS AND METHODS

Materials

Eight (8) different brands of piroxicam 20mg capsules (coded A to H) purchased from different retail pharmacies in Delta and Edo states were used in this study. Brand A is the innovator product. NAFDAC number, country of origin and manufacturing and expiry dates were documented (Table 1).

Weighing was performed using an analytical balance (G285 Mettler Toledo); High performance liquid chromatography (HPLC) used is of Cecil England, UK. The stationary phase is Bondapak C18 by Waters. The mobile phase on the other hand, consists of A & B with mixture of methanol 45 and buffer (citric acid and dibasic sodium phosphate) 55, which were degassed in a sonicator for about 10 min. The injection volume was 10 µl and the ultra violet detection was at 240 nm. The conditions of chromatography for optimized performance are shown in Table 2.

USP apparatus one was used for the dissolution test (Erweka, D6, Germany).

Reagents and solutions: Methanol and water used were of HPLC grade. All other chemicals such as phosphoric acid, sodium hydroxide, potassium dihydrogen phosphate used were of analytical grade.

Methods

Uniformity of Weight

From each brand, 20 capsules selected at random were weighed individually, first with content and when empty and their average weight calculated to determine the weight uniformity. The percentage deviation of each capsule from the average weight was determined.

Melting Point

Piroxicam samples were put in capillary tubes which had their open ends sealed by heating. The tubes were inserted into the melting point apparatus (Gallenkamp 29/MF 370, UK). The temperature at which the Piroxicam samples changed colour (charred) was recorded and the average melting point reported.

Dissolution Test

Dissolution medium was 900 ml of simulated gastric fluid, TS, prepared without pepsin. USP

apparatus 1 was used for the test (Erweka D6, Germany). It consisted of a 1000 ml covered cylindrical vessel made of inert glass material, a cylindrical 40 µm mesh stainless steel basket connected to a metallic shaft and a speed regulated motor. The assembly was placed in the dissolution medium maintained at 37 ± 0.5°C during the test. One capsule was inserted into each basket and the six baskets were lowered into the dissolution medium. Samples of 5ml volume were collected at specified time intervals for the determination of drug dissolved. Each sample removed for analysis was replaced by an aliquot at the same temperature.

Standard preparation

The content of one capsule of the standard (sample A) was accurately weighed and transferred into a 100 ml volumetric flask and about 50 ml of diluents (mobile phase) was added. This was sonicated to dissolve and made up to volume with more diluents. A 5 ml aliquot of this solution was transferred into a 50 ml volumetric flask and diluted to volume with mobile phase and mixed well. The solution was filtered through a 0.45 µm filter (nylon membrane). The same procedure was applied to other samples (B to H). These preparations were injected into the HPLC column one at time.

Data analysis

Data for weight uniformity, melting point, content of APP and maximum release of drug from the various capsule brands are presented as mean ± standard deviation (mean ± SD). The data were statistically analyzed using the Students't-test. The level of significance was set at $P<0.05$ (Tables 3 and 4).

RESULTS AND DISCUSSION

This study was carried out to evaluate the quality of some brands of piroxicam capsule (20mg) having the same labeled content and to determine their pharmaceutical equivalence which may be an indication of bioequivalence. At the time of investigation, all the samples used were within their shelf lives and were registered by NAFDAC. The results of the various analyses done are presented in Tables 3 and 4.

Weight Uniformity

All the brands showed acceptable weight uniformity as specified by the British Pharmacopoeia[9], except brands H in which 2 capsules had a relative standard deviation (RSD) greater than 5% and none had an RSD greater than 10%. The coefficient of variation for brands E and H capsules were high (5.12% and 5.88%, respectively), which is an indication of high variation of capsule weight within the batches. This high weight variation could be due to the nature of the powders and granules used in filling the capsules, which may have caused improper delivery from dosator and poor flow characteristics.

Variation in weight could result in variation of API content which may affect therapeutic outcomes. This implies that capsules from such brands will be of unpredictable potency. The importance of the test is therefore to ensure that the capsules in each lot are within an acceptable weight range.

Melting point

All the brands of Piroxicam with the exception of Brands B and G had melting point values within the specified melting point range for Piroxicam, which is 198-200°C[10]. The melting point of brand B was 202 ± 1.5°C, while that of G was 195 ± 3.0°C (Table 3). This slight deviation from the specified melting point range could be due to the presence of impurities in these brands.

Chemical Assay

The results of the assay to determine the amount of piroxicam present in each formulation are presented in Table 4. The assay shows that all the brands of piroxicam 20mg capsules contain between 99 - 103% of the labeled amount of drug. (USP 2004 specifies 97-103%). This implies that all the brands passed the chemical content test. It must be emphasized however that uniformity of content cannot be substituted for dissolution test since the drug can only elicit its desired therapeutic effect if it is released for absorption.

Statistical analysis of the assay data showed no significant difference between the brands and the innovator product, Brand A. However, brand B gave dissolution rate result that showed a significant difference ($P<0.05$) from that of brand A, the innovator product.

Dissolution rate

This is a measure of the amount of drug dissolved in a stated time under standard conditions *in vitro*. Dissolution test is a step towards the evaluation of bioavailability of drug substances. The United State Pharmacopoeia (2004) stipulates that not less than 75% of the labeled amount of piroxicam should be dissolved in 45 min. The amounts dissolved in 45 minutes are shown in Table 4. For

each brand, more than 80% of the labeled content was released after 45 min, except brand B. Only 52% of piroxicam was dissolved after 45 min from brand B. This implies that for all the brands tested, a significant amount of drug would be released for absorption in good time except from brand B. Though brand B passed all the other tests including assay test, it failed the dissolution test, which means that the brand will not be able to give the desired therapeutic response. This poor dissolution profile could be due to poor formulation such as the use of inappropriate or inadequate excipients[11,12]. Even the physical characteristics of the excipients, for example, percentage moisture content, can influence in no small measure the performance of the final product of which it is a component[13].

CONCLUSION

Two brands of Piroxicam capsules (B and G) were not within the specified melting point range. All the brands tested had Piroxicam content within the compendia specification. One of the brands of Piroxicam (B) failed to meet the required specification in the *in vitro* dissolution test and thus should not be substituted with any of the Piroxicam brands be it the innovator brand or generic brands.

This study revealed why some very cheap generics keep having high turnover because they are pharmaceutical equivalents of the innovator product. This has shown a need for sentinel post registration monitory of piroxicam 20 mg by regulatory bodies.

Table 1: Country of origin, manufacture and expiry dates of the different brands of piroxicam (20mg) capsule

BRAND	COUNTRY OF ORIGIN	BATCH NO	DATE OF MANUFACURE	EXPIRY DATE	NAFDAC REGISTRATION
A	NIGERIA		August, 2009	Aug., 2012	YES
B	INDIA	09055	MAY, 2009	MAY, 2012	YES
C	CHINA	090797	JULY, 2009	JULY,2012	YES
D	CHINA	090301	MARCH, 2009	MAR., 2012	YES
E	CHINA	B090401	APRIL 2009	APRIL 2012	YES
F	MALAYSIA	AJ08613	AUG 2008	AUG. 2011	YES
G	CHINA	C-808	MARCH 2008	FEB, 2012	YES
H	INDIA	RA 9002	JAN, 2009	DEC, 2011	YES

Table 2: Chromatographic conditions for optimal performance

Parameter	Conditions
Chromatography	HPLC (Cecil England, UK)
Analytical Column	Bondapak C18, Waters, USA
Mobile phase	Buffer and methanol (55 : 45 v/v)
Flow rate	0.8 ml/min
Column temperature	25^{o} C
Volume injected	10 µl

Table 3: Some physicochemical properties of the different brands of piroxicam (20mg) capsules

PRODUCT CODE	WEIGHT (mg) (MEAN±SD)	COEFFICIENT OF WEIGHT VARIABILITY (%)	MELTING POINT (^{o}C) (MEAN±SD)
A	300 ± 7.07	2.36	200 ±1.0
B	196 ± 5.48	2.79	202 ± 1.5
C	202 ± 4.47	2.21	200 ± 0.9
D	205 ± 4.32	2.11	200 ± 0.5
E	166 ± 8.94	5.39	200 ± 2.0
F	286 ± 5.48	1.92	200 ± 1.0
G	292 ± 8.37	2.87	195 ± 5.0
H	267 ± 8.81	5.88	199 ± 0.5

Table 4: Content of active drug and dissolution profiles of the different brands of piroxicam (20mg) capsules

PRODUCT CODE	DRUG CONTENT PER CAP (mg) (MEAN±SD)	% DRUG RELEASE AFTER 45 MIN (Mean ± SD)
A	19.92 ± 1.20	94.76 ± 2.00
B	20.43 ± 0.20	52.70 ± 10.00
C	20.69 ± 0.25	106.84 ± 0.90
D	20.03 ± 0.05	84.96 ± 7.17
E	20.36 ± 0.35	91.94 ± 0.90
F	19.77 ± 0.50	106.52 ± 1.79
G	20.43 ± 1.11	107.00 ± 0.91
H	19.95 ± 0.28	100.43 ± 2.90

NOTE
i. Range of drug content = (19.4 to 20.6) mg/cap
ii. Dissolution specifications = 75% minimum must be in solution in 45 min

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