QUALITY ASSESSMENT OF SOME BRANDS OF PIROXICAM CAPSULES

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Abstract

The quality assessment of eleven brands of piroxicam capsules marketed in Nigeria, which included confirmation of their label claims were carried out. Non-aqueous titrimetric evaluation showed that all but two of the brands contained a chemical equivalent of piroxicam within limits of official compendia specifications. However, one of the brands failed the weight uniformity determination as specified by both the British and United States Pharmacopoeia for enteric coated capsules. The dissolution test results were subjected to statistical analyses using a model independent approach employing difference factor (f1) and similarity factor (f2) to compare the dissolution profiles of the brands. The outcome indicated that five out of the eleven brands tested.

Keywords: Piroxicam; quality assessment; physicochemical; non-aqueous titrimetric evaluation.

Introduction

Piroxicam is a non-steroidal anti-inflammatory drug (NSAID) with antipyretic and analgesic properties (Florey, 1986). It is the prototype drug in the class of Oxicam group of NSAIDs. It is official in the British Pharmacopoeia (B.P. 1988) and United States Pharmacopoeia (USP 1988). One of the popular brands of piroxicam in the Nigerian market is Feldene by Pfizer Inc. New York, U.S.A. manufactured and sold by Neimeth International Pharm. PLC. However, in addition to this brand, there are also Feldene made in Pakistan and Feldene made in China which are also passed off as Feldene made in Nigeria to the unsuspecting customer.

Piroxicam is a weakly acidic and highly lipophilic anti-inflammatory drug available for oral parenteral and topical administration Moghimipour, 2009). The drug inhibits the synthesis of prostaglandins in inflammation (Hardman and Limbrid, 2001; Moffat et al, 2004). The pharmacokinetics of the drug makes a daily dose administration of the drug possible (Katzung, 2001; Sweetman, 2005). The once-daily dosing feature of the drug makes it attractive to patients as it affords easy compliance. Many prescribers recommend it for their patients and quite many consume it as one of the over-the-counter (OTC) drugs. The high demand has made it a regular stock in most pharmacies and drug stores, with various brands being displayed for sales. Some of these brands have comparatively high prices despite having similar label claims with the cheaper brands.

All the samples monitored bore brand names. Unbranded piroxicam preparations are few in the market place. Manufacturers seem to be falling over themselves branding their products. This probably could be to enable them sell their products at higher prices than they would have done if the products were positioned as generics, in line with, perhaps, the erroneous perception by many consumers that the more expensive the drug is, the more effective (Stock, 1997). Some of the brands had very high prices, 2900-3650% higher than the least expensive brands. High prices could not easily be attributed to possession of superior physicochemical properties. The current study aims at comparing some relevant properties of various brands of piroxicam with a view to ascertaining whether they could be used interchangeably.

Experimental

Materials: The reference standard 99.48%w/w piroxicam USP was collected from the Quality Control Unit of Neimeth Pharmaceutical International, Lagos.

Various brands of piroxicam capsules circulating in Nigeria were purchased within their expiry period and coded A-K. Each of the brands had label indicating 20mg piroxicam content per capsule.

Information regarding each brand was recorded (Table 1).

Weight analysis of capsules: Ten (10) capsules of each brand were selected at random and separately weighed on a Mettler UBROR-EB 330H analytical balance. Each capsule was first weighed with the shell and then the shell content (that is the powder alone). The mean weight and the standard deviation of each brand were calculated (Table 2).

Dissolution Test: The B.P. 1988 method (B.P., 1988) was used. The dissolution medium was 0.1N HCl maintained at 37°C±0.5°C. The results are published in table 3.

Non-aqueous tirimetric analysis: The contents of 20 capsules (theoretically containing 400mg piroxicam) of each brand were emptied into a suitable container and thoroughly mixed. This mixture was weighed to determine the total weight of the powder. Out of this weighed mixture, an amount eoretically equivalent to 250mg piroxicam was weighed out and transferred into a conical flask. The piroxicam in the powdered mixture was extracted using chloroform/methanol (1:1) solution and filtered. The filtrate was evaporated to dryness and dried at 110°C using the oven (U.S.P./N.F., 1995). A 60 ml mixture of equal volumes of acetic anhydride and anhydrous acetic acid solution were poured into the conical flask to dissolve the dried powder. The solution was titrated with 0.1M standardized perchloric (Olaniyi and Ogundaini, 1998) using crystal violet as indicator. Average of three determinations was recorded for each sample. The blank titration was carried out. The results obtained were applied to calculate the percentage content of the various brands.

Results and Discussion

Only one of the brands, sample I, failed the British Pharmacopoeia 1988 and United States Pharmacopoeia 1988 specification for capsule uniformity test. The permissible deviation is ±10%. Sample I failed the test with percentage deviation of 20.2% (Table 2).

Table 1. Particulars of brands analyzed.

Sample	Country of origin	Price per sachet of 10 capsules (N)	Price per capsule (N)	Percent times more expensive than cheapest brand.
A	Malaysia	70	7	250
B	India	20	2	-
C	India	40	2	100
D	England	20	2	-
E*	Nigeria*	600	60	2900
F	India	20	2	-
G	Nigeria	750	75	3650
H	India	40	4	100
I	England	20	2	-
J	India	20	2	-
K	Pakistan	100	10	400

This brand will likely have wide variation in the content of active ingredient of various capsules (Aulton, 1999; Aulton, 2002) with some having too much and others having too little. Analysis of variance of the different samples at 5% significance level showed significant variation in weight between brands.This could be as a result of remarkably different quantities of excepients used in bulking the capsules of different brands. For example, the average weight of sample E was 183.6mg and that of sample G 298.0mg, (sample G 60% heavier than Sample E). A similar comparison could be made between samples B or K with sample G. Yet, each brand contained 20mg of piroxicam by the label claim. Four brands (B,E,G,K) met the compendia specification for weight uniformity. Variation of weight between brands may not be as critical as variation of weight within a brand as typified by sample I.

Table 2. Weight uniformity analysis of piroxicam 20mg capsules

Sample	A	B	C	D	E	F	G	H	I	J	K
Mean weight ±SD (n=10)	286.9 ±2.0	199.9 ±14.9	212.0 ±18.3	248.7 ±7.5	183.6 ±6.0	301.7 ±9.3	298.0 ±7.9	283.6 ±5.7	237.5 ±31.7	225.0 ±3.4	194.6 ±8.7
% Deviation	0.8	5.4	6.7	0.9	5.2	1.3	0.6	0.5	20.2	0.2	1.7

- Permissible percentage deviation is ±10

Table 3.f1 and f2 values of the various brands of piroxicam compared with innovator product (Sample G)

Sample	A	B	C	D	E	F	H	I	J	K
f1	9.65	23.13	11.73	10.53	17.36	15.30	22.34	8.14	3.61	28.03
f2	56.46	39.61	55.96	55.18	44.47	47.98	41.82	57.58	76.14	36.64

Table 4. Result of titrimetric analysis

Sample	A	B	C	D	E	F	G	H	I	J	K
Content of piroxicam (% w/w)	95.7	73.8	96.9	101.5	61.1	95.7	99.2	93.5	95.7	95.7	93.5

Significant variation in the weight of capsules within a brand invariably suggests significant variation in the content of active ingredient between capsules. Weight variation should be minimized because a fundamental quality attribute for all pharmaceutical preparations is the requirement for a constant dose of the drug between individual preparations (Aulton, 2002). Though it has been suggested that effectiveness is clinically relevant for only a relatively small number of medicines such as tetracycline, erythromycin, grieseofulvin, digoxin and phenytoin and effectiveness variation among individual patients much larger than the variations among products of different manufacturers (Stock,1997; Dartness, 1998), variations as seen with sample I could be critical when products with low safety margins are involved.

Figure 1 shows a graphical representation of the dissolution profile of the different brands of piroxicam. All the brands passed the dissolution rate test having dissolved more than 80% of their active content within 45minutes. The U.S.P.-prescribed standard is a dissolution of not less than 75% of the label claim within 45 minutes. Difference factor (f1) and similarity factor (f2) were calculated to compare the dissolution profile. Two dissolution profiles are considered similar and bioequivalent if f1 is between 0 and 15 and f2 is between 50 and 100 (FDA, 1997). Table 3 shows f1 and f2 values of different brands with respect to brand G which is the innovator product. Brands A,C,D, and J gave f1 values less than 15 and f2 values more than 50 and therefore could be used interchangeably. Though sample I had f1 and f2 values less than 15 and more than 50 respectively, it failed the capsule uniformity test and, therefore cannot be recommended.

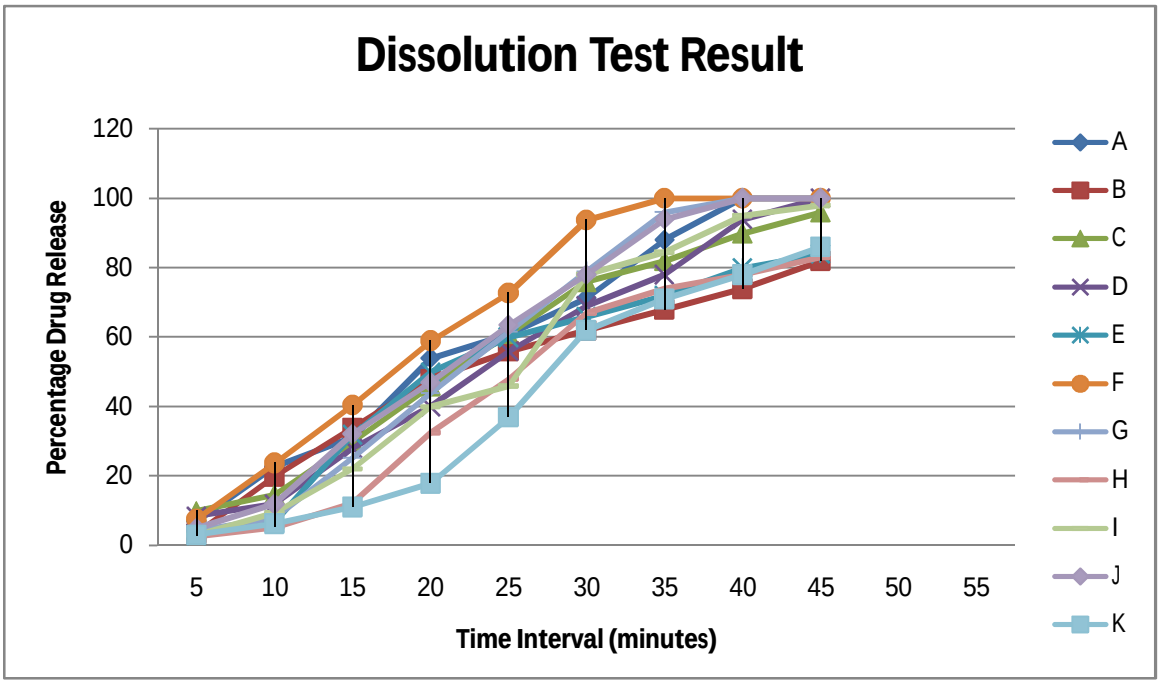

Figure 1. Graph of dissolution test result of different brands of piroxicam 20mg

Table 4, shows that only samples B and E failed the test on percentage purity. Sample E, in spite of its comparatively high price did not meet the standard specification of purity. From the price evaluation data published in Table 2, it could be seen that prices of some brands are comparatively higher than those of others. Indeed sample E was 2900% times higher than the cheapest brand, in spite of its poor quality.

Whilst sample G, another brand with comparatively high price, could be adjudged a good product from all parameters monitored, such cannot be said of sample E. The variation in the weight of capsules between brands requires further attention.

It is advisable for regulatory agencies to regulate capsule weight for a preparation like piroxicam for ease of comparison between products of different manufacturers. Furthermore, NAFDAC registration number is a mark of authenticity and quality and aptly suggests that the preparation is not only fit for use but could be switched with other brands of similar preparation. Thus, insisting that capsule weight meet same standard narrows the range of error in delivering the required level of active ingredient, whether the same brand is used or whether in the course of treatment the patient is constrained to switch to another brand.

The general implication and practical application of this result is that prescribers and patients should be cautious of switching between brands in the course of therapy except it is absolutely necessary. When a patient is stabilized on a brand or a generic product by a particular manufacturer it is advisable to stick to that brand or generic for that treatment.

Conclusion

Five of the eleven brands tested (A, C, D, G and J) were chemically equivalent by titrimetric method of analysis.

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