QUALITY ASSESSMENT OF SOME COMMERCIALLY AVAILABLE PIROXICAM CAPSULES IN NIGERIA

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ABSTRACT

The quality of some commercial available piroxicam capsules obtained from Bridegehead drug market in Onitsha was determined.

The spectrophotometric absorption spectra of the various brands of the piroxicam capsules were remarkably similar to that of the reference sample with their various λ_{max} falling within the USP specification. A single spot on the TLC plates was detected for all the samples and had the same R_f value with the reference sample.

The organoleptic properties and other physicochemical properties including the capsule content weight variation, disintegration time, and dissolution profile were evaluated. Results showed an indication of poor quality assurance since they all contained amount of active ingredient (piroxicam) far higher than the labeled drug content.

Key Words: Piroxicam Capsules, quality assessment

INTRODUCTION

Faking and adulteration of pharmaceuticals has been widely reported in Nigeria (1,2) and constitutes a major hindrance to the attainment of effective drug based health care delivery in the country. This is mainly because the use of poor-quality medicines can result in treatment failure, drug resistance or toxic side-effects (3). The inability of most Nigerians to afford the relatively more expensive branded products due to the poor economic sutaiton in the country as well as teh slack domestic drug law enforcement has promoted the mass importantion of both generic and unfamiliar branded products. While most of them are counterfeit and of poor quality, others may contain active ingredient in amounts outside the official (labeled claim) range.

Piroxicam is a non-steroidal anti-inflammatory drug (NSAID), which also possesses analgesic and antipyretic properties. It is indicated in the treatment of rheumatoid arthritis, osteoarthrities, ankylosing spondylitis, acute musculo-skeletal disorders, acute gout, post operative and post traumatic pains, dysmenorhoea, upper respiratory tract inflammation and juvenile rheumatoid arthritis (4). Because of its numerous indications it is widely used in Nigeria, thus making it a candidate for faking and adulterations.

Apart from the popular branded piroxicam (Feldene®) capsules marketed by the multinational company Pfizer, many other brands of piroxicam are also available in the open drug markets for example Ontisha bridge head, Idumota in Lagos and Aria-aria in Aba from where they find their way into the various retail outlets (Pharmacy, Patent medicine stores), Clinics and Hospitals across the country. A major attraction of these products is their extreme low cost relative to the branded product. For example the most expensive of the various piroxicam capsules investigated was about 22 times cheaper than Feldene®. The wise spread faking of encapsulated and other drug products has led to evaluation of the physico-chemical properties of some of these products by some workers (2,5-7).

The objective of this study is to determine the various physico-chemical properties and drug content of various brands of piroxicam capsules in circulation in Nigeria with a view to determining their relative quality.

Materials and Methods

Fourteen brands of piroxicam capsules from different manufacturers were bought from Ontisha Bridgehead drug market. All the capsules were evaluated before their expiry dates. Piroxycam crystals was obtained from Neimeth Pharmaceuticals Ltd and used as the reference sample, sodium hydroxide (BDH England), hydrochloric acid (BDH England), methanol (BDH England), chloroform (BDH England), toluene (BDH England), filter paper (Watman England)

Physical Properties - The external packages and capsules of the various brands were carefully visually examined. The content of ten capsules of the various brands

were emptied into a watch glass. The colour, texture, smell and taste of the powders were then determined by a five-member panel.

Capsule Content Weight Variation - Twenty capsules were randomly selected and the content of each capsule was completely emptied into a watch glass and their weights determined with a balace (Metler Toledo). The average weights and percentage deviation for the twenty capsules were then evaluated.

TLC - The USP (1990) method was simulated. The content of twenty capsules were emptied into a watch glass and the weight equivalent to one capsule was dissolved in 20 ml mixture of a solution of chloroform and methanol (1:1) to obtain a 1 mg/ml solution. The mixture was shaken for 10 minutes and filtered. The filtrate was then spotted on activated precoated Whatman TLC plates (10 x 20cm) and allowed to dry. The plates were then developed in a chromatographic tank with a solvent system consisting of toluene and acetic acid (95:5). The TLC plates were removed after the solvent front had moved about three-fourths of the length of the plate and dried. The spots were located by viewing under UV light as 254 nm. The R_f values of the different brands were then calculated.

Disintegration Time - Six capsules from each brand were assed in a disintegration test apparatus (2T 4 Erweka) with distilled water maintained a ta temperature of 37 + 0.50C using the BP (1993) method.

Absorption Spectra/Maxima (max) - An amount of capsule equivalent to 50 mg piroxicam was weighted out from each sample obtained from the twenty emptied capsules) and dissolved in 100 ml of methanol and filtered with a filter paper. A final 6.25×10^{-2} mg/ml was obatained appropriately by diluting with 0.1N HCl. The absorption spectra for the various brands of the piroxicam capsules investigation were then obtained with a Shimoidzu UV 160 spectrophotometer.

Calibration Curve and Drug Content Determination - Various concentrations of reference piroxicam crystals (2×10^{-3}, 7.8×10^{-3}, 1.5×10^{-2}, 3.13×10^{-2}, 6.25×10^{-2} mg/ml) were made by dissolving an appropriate amount of piroxicam powder in 0.01 N methanolic hydrochloric acid solution. The absorbance of these concentrations were determined and used to obtain the calibration curve. The USP method for the assay of piroxicam was used. Twenty capsules were totally emptied into a watch glass and weighted. Sample weight of each brand of piroxicam equivalent to 20 mg piroxicam was accurately weighted into a 100 ml volumetric flask, 70 ml of 0.01 N methanolic hydrochloric acid solution was then added and shaken for 30 minutes and the volume made up to 100 ml and shaken again. A portion of this was centrifuged to obtain a clear solution, 10 ml of which was transferred into a 100 ml volumetric flask to obtain a solution of 2×10^{-2} mg/ml. The absorbance and concentration was determined with the Shimoidzu UV 160 spectrophotometer.

Dissolution Profile - The dissolution profile of the capsules was determined using the USP (1990) method with an Erweka Dissolution apparatus set at a speed of 50 rpm. The dissolution medium was simulated gastric fluid (with out pepsin) maintained at 37 + 0.5°C. 5 ml samples were withdrawn periodically at 5 minutes intervals and replaced with fresh aliquots of the fluid. The content of piroxicam was then determined spectrophotometrically.

All the brands of piroxicam studied were attractively packaged. However, some of the boxes were of a relatively poor quality with respect to their thickness and ability to withstand handling as they readily "gave way" at the joining edges. All of the sample products were presented as bright red hard gelatin capsules. The only exception was sample A whose capsules were dark red in colour. The capsules were all well polished and marked with the logo and/or brand names of the respective manufacturing companies. All batches investigated were within their shelf life. The capsule content for the various piroxicam brands were odourless, however they exhibited different colour, taste and texture (Table 3). The colour of the capsule content of the various brands varied from white, to off white with a tint of yellow. The powder texture varied from very fine to granular but fine. Three out of the fourteen brands investigated had a slight sweet taste while the others had a bland taste (Table 2). It was also

observed that all the brands that had the slight sweet taste also had similar colour (Table 2). The difference/correspondences to taste and colour is probably an indication that the different manufacturers employed different diluents for the formulation fo their respective brands of piroxicam capsule. The formulation that had the slight sweet taste probably contain lactose while those that were bland most probably had starch as diluents.

The R_f values and the max for the various brands of piroxicam capsules are shown on Table 3. The absorption spectra for the different brands of piroxicam all had similar spectral characteristics, by a single peak Fig. 1. The reference sample had a max of 335 nm while those of the various samples varied from 332 to 335 nm (Table 3, Fig 1), all of which conform with the USP (1990) specification which gives the identifying max of piroxicam as "about 333 nm". The various brands of piroxicam capsules also had a single spot on the TLC plate. Their respective Rf values were the same with that of the reference sample (Table 3). It could thus be inferred that the various samples (brands) contain the same compound with the reference sample.

The average weight of the capsule content varied from 176.80 to 299.59 mg (Table 4). Since each capsule is labelled to contain 20 mg pirxicam, this indicates that over 80% of the capsule content weight are diluents. Apart from two brands (Saldin and Vitadene) that gave a comparatively low standard deviation, all the other brands gave large standard deviation which is an indication of poor weight uniformity within the same batch of the same brand. Poor powder flow will result in poor uniformity of ill weight (10). All the brands of piroxicam capsule investigated disintegrated within 5 minutes (Table 4). Since the BP 1993 recommends that all capsules should disintegrate within 30 minutes, all the brands tested passed this test. The capsule drug dissolution profile and drug content for the different brands of piroxicam are shown on Table 4. The various brands released far more drug in 45 minutes than their labeled drug content. The result showed that the brand with the least dissolution rate after 45 minutes released 20 % more piroxicam than the labeled claim while it was 66.30% for the highest.

The USP (1990) indicates that piroxicam capsules must contain not less than 92.5% and not more than 107.5% of the labeled claim [9]. This therefore means that all the brands investigated did not comply with this requirement. As the brand with the least amount of piroxicam contained 29.20 mg (46% higher than the labeled claim) while the highest contained 47.60 mg (136% higher than the labeled claim) (Table 4). The high drug content relative to the labeled claim could have resulted from defective formulation operations such as weighing, mixing and capsule filling. Piroxicam being a relatively low dose drug would required extreme care to ensure that the piroxicam content per capsule is within limits especially when high speed automated capsule filling machines are used. The observed result could have resulted from double filling of capsules. Piroxicam is widely prescribed in the treatment of many musculo-skeletal disorders in adults and geriatrics and also in juvenile rheumatoid arthritics. Piroxicam like most of the NSAIDs has several important side effects, which include gastro-intestinal discomfort, nausea, diarrhea, gastric bleeding and ulceration, dyspepsia, hypersensitivity reactions headache, dizziness, vertigo, hearing disturbance, fluid retention, heart failure, hepatic damage, pancreatitis, and toxic epidermal reaction. These side effects and hypersensitivity reactions could be precipitated or triggered off by such large doeses as observed in this study. Moreover most patients on this drug often take it for long duration. From the foregoing results the quality of sample A which is actually Feldene(R) capsules bought from the open market was not better than the other cheaper brands of piroxicam capsules as all of them contained far more piroxicam than the labeled amount. This supports the widely held opinion that expensive and well-established brands are the targets of most faking activities.

Conclusion

The foregoing result is a clear indication of the serious problem of faking and substandard drugs in Nigeria. Hence there is an emergency need for all the drug controlling agencies in Nigeria both at Federal and state levels to step up surveillance activities to track down fake and substandard drugs in circulation and also take adequate steps to prevent their entry into the country.

Results and Discussion

Table 2 : Some Physical Characteristic of the Piroxicam Capsules

S/No.	Piroxicam Brands	Colour of Capsule Content (White)	Taste of Capsule Content	Texture of Capsule Content
1.	A	White 3+	Bland	Fine Powder
2.	B	White 4+	Bland	Granular (fine) powder
3.	C	White 5+	Bland	Fine Powder
4.	D	White 7+	Sweet	Fine powder
5.	E	White 7+	Bland	Fine powder
6.	F	White 6+	Bland	Fine powder
7.	G	White 5+	Bland	Fine powder
8.	H	White 2+	Bland	Coarse granular powder
9.	I	White 4+	Bland	Fine powder
10.	J	White 6+	Sweet	Coarse granular powder
11.	K	White 6+	Sweet	Fine powder
12.	L	White 5+	Bland	Fine powder
13.	M	White 8+	Bland	Fine powder
14.	N	White 5+	Bland	Fine powder

Table 3: R_f and λ-max for the various brands of piroxicam capsules.

S/No.	Drug	Rf	λ mas
1.	Reference Sample	0.39	335
2.	A	0.39	333
3.	B	0.39	333
4	C	0.39	332
5	D	0.39	333
6	E	0.39	335
7	F	0.39	334
8	G	0.39	334
9	H	0.39	334
10	I	0.39	333
11	J	0.39	335
12	K	0.39	333
13	L	0.39	333
14	M	0.39	334
15	N	0.39	335

Table 4: Some Physical Characteristic of the Piroxicam Capsules
*** (Bracketed figures are the percentage deviation)**

S/No	Piroxicam Brands	Average Capsule Weight (mg)	Capsule Content Weight Uniformity (mg)	Disintegration Time (Minutes)	% Dissolution time ($t_{45\,mins}$)	Piroxicam content of capsule (mg)
1.	A	309.34 (55.94)	239.61 (27%)	3.0	130.05	38.00
2.	B	265.98 (31.20)	193.65 (12.07%)	3.0	126.00	31.20
3.	C	3345.39 (88.0)	283.47 (4.67%)	3.0	99.00	30.40
4.	D	371.56 (17.51)	298.83 (2.23%)	3.0	139.50	44.80
5.	E	358.30 (40.60)	290.17 (10.50%)	4.0	99.00	40.80
6.	F	367.63 (19.48)	299.59 (7.01%)	2.0	148.50	40.00
7.	G	368.35 (67.20)	382.48 (6.64%)	5.0	126.90	29.20
8.	H	364.76 (49.99)	294.79 (19.92)	5.0	168.30	44.00
9.	I	329.56 (20.67)	263.42 (6.75%)	4.0	162.90	31.80
10.	J	361.32 (16.40)	292.25 (2.31%)	1.0	141.30	47.60
11.	K	303.89 (67.9)	263.80 (6.71%)	3.0	151.20	30.00.
12.	L	253.38 (46.41)	176.80 (28.55%)	5.0	120.15	33.20
13.	M	261.72 (31.40)	186.75 (17.47%)	3.3	138.15	46.00
14.	N	367.71 (74.43)	294.71 (25.26%)	5.0	142.88	33.60

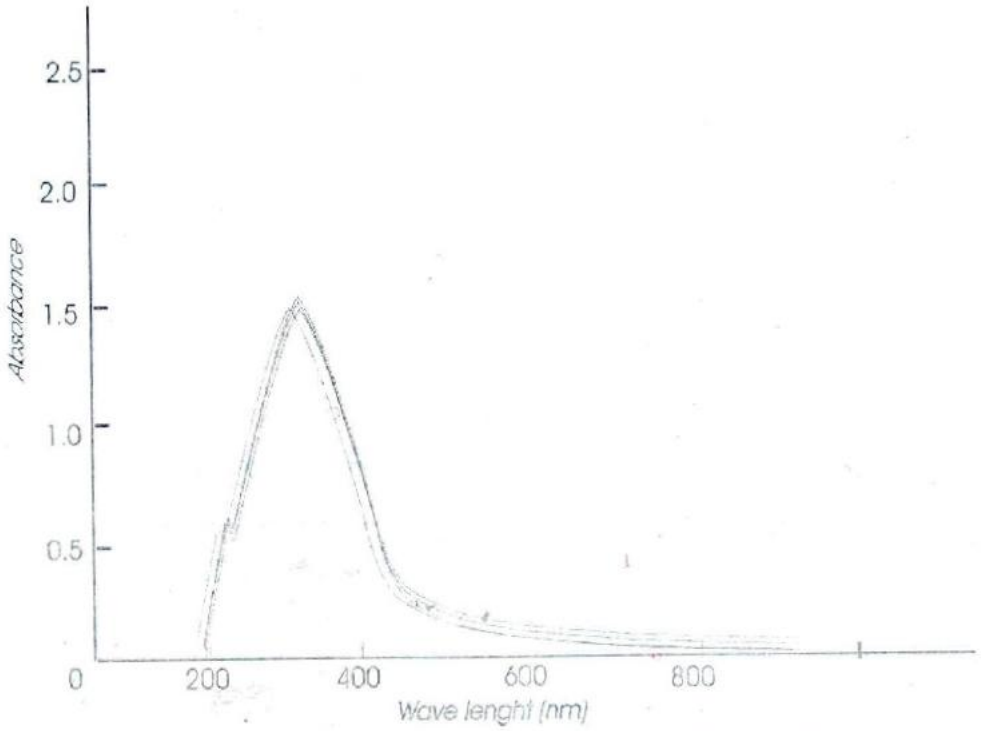

Fig. 1 Absorption Spectrum for the Various Brands of Piroxicam Capsules

REFERENCES

1. Iwuagwu, M. A. (1993) Faking of and Adulteration of Drugs: A Critical Analysis of the Fake and Aldultrated Drugs Legislation Nig. J. Legislation 1, 14-21.
2. Iwuagwu, M. A. and Alalor C. A. (1997) The Problem of Fake and Adultrated Drugs: Physicochemical Study of Diazepam Tablets Marketed in Benin City. West Afr. J. Pharm. 11 : 1 56-59.
3. Robert B. T. (2001) Sub-standard drugs? The quality of medicines in Nigeria. In "id21 health highlights".
4. British National Formulary (March 1999) 435 - 437, 443.
5. Iwuagwu, M. A. Onyekweli, A. O; and Obiora, B. A. (2001) Phytochemical Properties of Paracetamol Tablets Marketed in Benin City Nig. J. Pharm. 032, 49-59.
6. Quereshi, S. A. and McGilveray, I. J. (1998) Assessment of Pharmaceutical Quality of Frusemide Tablets from Multinational Markets. Drug Dev. Ind. Pharm. 24:11 995 1005.5.
7. Iwuagwu M. A. and Onyeonwu, N. (1992). In vitro Assessment of Ampicillin Capsules Marketed in Nigeria. Int. J. Pharm. Pract. 1 : 167-171.
8. Igboechi, A. C. (1988) The Place of Routine Analysis and Quality Control in Checking and Eradicating fake drugs. Pharm. World J. 5:1, 9-11.
9. United States Pharmacopoea (1990) 1091 and 1788 22nd Ed.
10. British Pharmacopoeia 1993 pp 773.
11. Micheal E. A. (1993) Pharmaceutics - The Science of Dosage Form Design Low Priced Edition. Churchil Livingstone. 678 - 685.