African Journal of Pharmacy and Pharmacology Vol. 3(10). pp. 491-495, October, 2009
Available online http://www.academicjournals.org/ajpp
ISSN 1996-0816 © 2009 Academic Journals

Full Length Research Paper

In-vitro evaluation of the pharmaceutical quality of some ibuprofen tablets dispensed in Nigeria

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Accepted 13 August, 2009

The purpose of this study was to determine the pharmaceutical quality of some Ibuprofen tablets dispensed in Nigerian. 19 different brands of Ibuprofen tablets were purchased from pharmacies and open markets in 3 states in Nigeria. The organoleptic and physicochemical properties of these Ibuprofen tablets were assessed according to British Pharmacopoeia (BP), and unofficial standards as recommended by the manufacturers. Of the 19 brands of tablets assessed, 12 brands passed the uniformity of content test while 15 brands passed the disintegration test and only four brands passed the dissolution test. Ibuprofen tablets dispensed in Nigeria varied considerably in their pharmaceutical quality. A strict check of the quality of brands of Ibuprofen by regulatory agencies and distributors before they are dispensed to the public is therefore recommended.

Key words: Ibuprofen tablets, pharmaceutical quality, dissolution, disintegration, dispensed.

INTRODUCTION

Ibuprofen is a non-steroidal anti-inflammatory drug (NSAIDs) with a short half-life (1.8 - 2 h). It is used as an analgesic, antipyretic and an anti-inflammatory agent. The oral dose is 200 - 400 mg (5 - 10 mg/kg in children) every 4 - 6 h to a maximum of 1.2 g per day in adults. Major side effect of NSAIDs is gastrointestinal irritation. Others include nausea and dyspepsia. Ibuprofen, however, have the least of these side effects commonly associated with NSAIDs (Goodman and Gilman, 1997). A very serious adverse drug reaction of ibuprofen can be fatal thrombocytopenia (Jauhari et al., 2009). It is also very cheap and readily available as an over-the-counter (OTC) preparation. Therefore, it ranks as one of the most commonly prescribed NSAIDs in Nigeria.

A counterfeit medicine is defined by the World Health Organisation (WHO) as one, which is deliberately and fraudulently mislabelled with respect to identify and/or source. This can apply to both branded and generic products and may include products; with the correct ingredient or with the wrong ingredients; without active ingredient; with insufficient active ingredient; with fake packaging. In a research by Erhun et al. (2001), the reasons adduced for the availability of counterfeit drugs in Nigeria include: Inadequate laws; ineffective enforcement of existing laws; Non-health professional in drug business; loose control system; high cost of drugs; greed; ignorance and corruption. The African drug market is most affected by the menace of fake drugs. There are reports of 25 - 50% of the drugs sold in Nigeria for example, being fake (Ifudu, 2005; Osibo, 1998). Most commonly counterfeited drugs found in Africa include antibiotics, analgesics and antimalarials, because they are very easy to produce and market (Ohuabunwa, 2002).

This problem of drug faking has made it necessary to routinely assess the pharmaceutical quality of drugs in Nigerian market (Nnamdi et al., 2009). The objective of this work was therefore to evaluate the pharmaceutical quality of some Ibuprofen tablets dispensed in Nigeria.

MATERIALS AND METHODS

Collection of samples

On a cross-sectional basis, Ibuprofen tablets of different strengths and from different generics were purchased in January 2009 from Pharmacies across Anambra, Delta and Edo States, in Nigeria. Approximately half of these samples were purchased from Onitsha

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Table 1. Label information on the ibuprofen tablets evaluated.

Brand Code	Brand Name	Batch No	Date of Manufacture	Expiry Date	Labelled strength (mg)	NAFDAC Number	Manufacturer/ Country of Origin
Ibu1	Ibudex 400	901176	Nov-08	Nov-12	400	Yes	Dexel, Isreal
Ibu2	Juilifen -400	G-810	Jul-08	Jun-12	400	Yes	Zim Lab. India
Ibu3	Genafen -400	JA8029	Jul-08	Jun-11	400	Yes	JAY Formulation India
Ibu4	Medprofen - 400	IBS816	Aug-08	Jul-12	400	Yes	
Ibu5	Buprol 400	AJ08536	Sep-08	Aug-11	400	Yes	Hovid Malaysia
Ibu6	Paucofen 200	778	Sept-08	Aug-11	200	Yes	Pauco Nigeria
Ibu7	Ibuflam - 200	P316	Jan-08	Dec-11	200	Yes	Aurochem India
Ibu8	Nkoyo Ibuprofen	IBN8035	July-08	Jun-11	200	Yes	Maxheal India
Ibu9	Espen 400	ERF 08	Jun-08	May-11	400	Yes	Mega India
Ibu10	Ebu – 200	IB14	Oct-08	Sep-11	200	Yes	Mecure Nigeria
Ibu11	Multifen	1BF8019	Aug-08	July-11	400	Yes	
Ibu12	Brustan – N	1911760	Jun-08	May-11	400	Yes	Ranbaxy India
Ibu13	Ibuflamol 200	H819	Aug-08	Jul-12	200	Yes	Zimlab India
Ibu14	Boosten	IBB 603	Nov-06	Oct-09	400	Yes	Maxheal India
Ibu15	B.K.B.	116	Oct-08	Sep-11	200	Yes	Rico Nigeria
Ibu16	Profen 400	28467	Mar-06	Mar-11	400	No	Remedica Cyprus
Ibu17	RGI Ibuprofen	RG789	Sep-07	Aug-10	400	Yes	Richy Gold Nigeria
Ibu18	Ibuprofen U.S.P.	HE17908	Nil	Oct-10	600	No	Interpharm. U.S.A.
Ibu19	Kirkland	7KE0658	Nil	Aug-11	200	No	Perrigo U.S.A.

drug market in Anambra state. The drug market in Onitsha is an open market which has been reported as a centre where faking and counterfeiting occurs mostly in Nigeria. No particular sampling procedure was employed other than one of the researchers posing as a 'normal customer' purchased the drugs from drug shops without prescription. The different brands were obtained from drug stores wherever they could be found until nineteen samples were collected.

Following the purchase, information on manufacturer's address and country of origin of the brands, batch numbers, manufacturing dates, labelled strength, and registration status by the National Agency for Food and Drugs Administration and Control (NAFDAC) were recorded from the product label where available (Table 1). Ibuprofen powder (Analar® grade) which was used as standard was provided by the Department of Pharmaceutics and Pharmaceutical Technology, Faculty of Pharmacy, University of Benin. All other chemicals used for the analysis were of analytical grade and were used as received.

Methods

Assessment of organoleptic properties: The analyses of the tablets were carried out immediately after purchase.

Preliminary examination of the organoleptic properties was carried out for all samples collected. The following properties were evaluated for all the tablets: Colour, taste, inscription on the surface (if any), odour, finishing (dull or glossy) and coating type. For the organoleptic properties evaluated, all the samples and differences in observations were handled objectively. The decision of a majority (at least 2) of the evaluators was taken. The a priori definitions for the evaluation were based on the relativity of our findings to the descriptions of BP 2003 for Ibuprofen tablets.

Analyses of physicochemical properties of tablets: The tablets were further assessed for uniformity of weight, disintegration time and dissolution rate according to B.P. 2003, while content uniformity was carried out according to BP 1993.

Weight uniformity was carried out by determining the weight of twenty randomly selected tablets from each brand using a digital weighing balance (College B154, Mettler Toledo, Switzerland) while the disintegration time of six tablets per brand was determined in distilled water maintained at 37 ± 0.5°C using Manesty Tablet Disintegration Apparatus (Manesty Machines, Liverpool, England). The dissolution rate was carried out according to the procedure of BP 2003, using Manesty Dissolution Test Apparatus (Manesty Machines, Liverpool, England). The samples were analyzed spectrophotometrically at maximum wavelength of 264 nm (T70 UV/Visible Spectrophotometer, PG Instruments Ltd). The test was carried out in triplicate and the mean values were calculated.

RESULTS

The correlation coefficient (r^2) of the standard Ibuprofen curve and assay sensitivity were 0.985 and >95%, respectively as shown in Table 1. Only 4 of the 19 brands of Ibuprofen tablets were manufactured locally. The remaining 15 brands were imported from other countries. They were all within a reasonable shelf life at the time of sampling and analyses (Table 1). Three of the imported samples did not have NAFDAC registration number.

The results of organoleptic properties of tablets presented in Table 2 showed that of the nineteen (19) brands examined, ten were sugar coated; six were film coated while three were un-coated. Furthermore, all the tablets irrespective of their coating type were either smooth or glossy with unbroken inscription on the tablet surface (Table 2). They were all evenly coloured and whitish when the coating was removed. Coatings are included to protect ibuprofen from photode-gradation, as

Table 2. Results of organoleptic and physicochemical properties of ibuprofen tablets.

Code	Brand Name	Colour	Coating type	Taste	Inscription	Finishing/ odour	Mean weight ± SD (mg)	Disintegration time ± SD (min)	Actual Content (%)
Ibu1	Ibudex-400	White	Uncoated	Tastless	None	Smooth/ odourless	530 ± 2.9	2.6 ± 0.4	64
Ibu2	Juilifen–400	Orange	Sugar coated	Sweet	Juli 400	Glossy/ odourless	827 ± 58	8.48 ± 0.8	100
Ibu3	Genafen-400	Orange	Sugar coated	Sweet	Genafen 400	Glossy/ odourless	757 ± 22	10 ± 17	92
Ibu4	Medprofen -400	Orange	Sugar coated	Sweet	Medprofen 400	Glossy/ odourless	774 ± 9.7	13.3 ± 5	101
Ibu5	Buprol 400	Pink	Uncoated	Bitter	HD	Smooth/ odourless	669 ± 10.8	22 ± 2.7	109
Ibu6	Paucofen 200	Pink	Sugar coated	Sweet	Ibu 200	Glossy/ odourless	563 ± 46.4	35 5 ± 5.7	87
Ibu7	Ibuflam 200	Red	Sugar coated	Sweet	Ibuflam 200	Glossy/ odourless	369 ± 6.9	> 60	100.5
Ibu8	Nkoyo Ibupropen	Red	Sugar coated	Sweet	Ibu 200	Glossy/ odourless	366 ± 63.3	33 ± 2	96
Ibu9	Espen 400	Orange	Sugar coated	Sweet	Espen 400	Glossy/ odourless	907 ± 21	1.8 ± 0.6	102
Ibu10	Ebu 200	Red	Sugar coated	Sweet	None	Glossy/ odourless	365 ± 29.5	23.9 ± 5	98.5
Ibu11	Multifen	Orange	Sugar coated	Sweet	Ibu 400	Glossy/ odourless	855 ± 25	1.2 ± 0.5	95
Ibu12	Brustan – N	Orange	Film coated	Bitter	Brustan N	Smooth/ odourless	1000 ± 10	3.7 ± 0.5	104
Ibu13	Ibuflamol 200	Blue	Sugar Coated	Sweet	IBF 200	Glossy/ odourless	719 ± 40	30 ± 6	99
Ibu14	Boosfen	Orange	Film coated	Sweet	Boosfen/400	Glossy/ odourless	875 ± 20	10 ± 8.7	102.5
Ibu15	BKB	Blue	Film coated	Sweet	None	Glossy/ odourless	348 ± 25	6.8 ± 7.6	100.5
Ibu16	Profen 400	Pink	Film coated	Bitter	None	Smooth/ odourless	668 ± 8	0.6 ± 0.3	106.7
Ibu17	RGI Ibuprofen	White	Uncoated	Tasteless	None	Smooth/ odourless	1016 ± 10	0.7 ± 0.4	123
Ibu18	Ibuprofen U.S.P.	White	Film coated	Acidic	600/IB 132	Smooth/ odourless	982 ± 11	28 ± 3	105
Ibu19	Kirkland Ibuprofen	Brown	Film coated	Acidic	1 – 2	Smooth “	320 ± 2.8	1.2 ± 0.1	110.5

well as add aesthetic appeal to the product.

The dissolution tests for fifteen brands of tablets are shown in Figures 1 (a and b). Dissolution test for the remaining four brands (ibu6, ibu7, ibu8 and ibu13) were not carried out because they did not pass the disintegration test (Table 2). Out of these fifteen brands, only four (4) brands (ibu2, ibu11, ibu12 and ibu19) released over 70% of their ibuprofen content after 40 min. Twelve (12) of the nineteen brands of tablets complied with the BP Requirement for the uniformity of content, while seven brands did not comply (Table 2).

DISCUSSION

Tablet disintegration time is one of the very important physicochemical properties in solid dosage forms. The BP 2003 stipulates a disintgration time of not less than 15 min for uncoated tablets and 30 min for coated tablets and capsules. The result showed that four of the nineteen brands that is, ibu6, ibu7, ibu8and ibu13 did not conform to the BP requirement, in fact ibu7 did not disintegrate after 60 min. The conformity of the other brands of tablets to the BP specification for disintegration time can be explained to be due to the appropriate use of disintegrant and other excipients like binders and lubricants by the manufacturers. On the other hand, the poor-disintegration of these four brands could have been due to either excessive use of binders or inadequate use of disintegrant hence the tablet core been strongly held together prevented penetration of disintegration fluid into the tablet.

Another possible factor is, poor storage for example storage under high relative humidity or high temperature which interfered with the properties of the disintegrant and binders. It has also been reported that excessive use of lubricants by the manufacturer can prevent the penetration of disintegration fluid, since most lubricants are hydrophobic (Valesco et al., 1995). The type of disintegrant used and the method of incorporation of the disintegrant could also affect the rapid release of the drug into solution.

The weight of the tablets were further observed to be large when compared to the weight of the active ingredient, for example ibu13, a 200 mg formulation had a mean weight of 719 mg. this was as a result of the sugar coating. This coating may also have been partly responsible for the poor disintegration observed in the five brands earlier stated as well as the high variation in weight observed in some brands for example, the

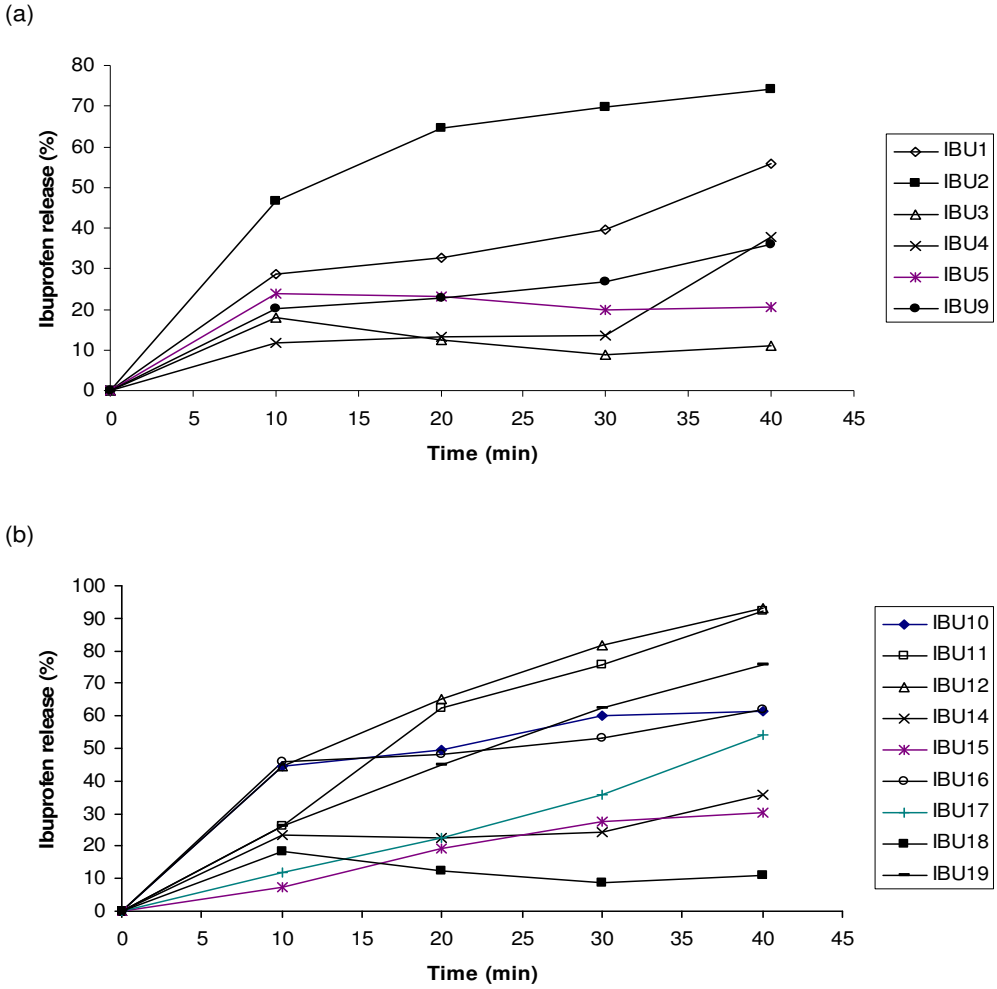

Figure 1 (a and b): Dissolution rate of different brands of Ibuprofen tablets at 0.1M HCl.

standard deviations of ibu2, ibu6 and ibu8, were 58, 46 and 63 respectively.

Seven of the nineteen brands of tablets did not comply with the BP requirement for the uniformity of content. Five of these seven brands (ibu3, ibu5, ibu6, ibu16, and ibu19) varied slightly from the BP requirement for content uniformity of 95 - 105%. The reason for non compliance of these five brands could be due to poor in-process control during manufacture as well as inaccurate weighing and mixing during preparation. For ibu1, the Ibuprofen content was rather low, while that of ibu17 was very high. The reasons for these marginal variations are, however, not clear considering the fact that these products were registered with the regulatory body, NAFDAC.

Dissolution studies give an idea of the amount of drug available for absorption after oral administration. Drugs with poor dissolution profile will not be available in the body system or target organ/tissue to elicit therapeutic effect. The BP 2003 states that, 70% of the tablet drug should dissolve within 40 min. Four of the fifteen brands (ibu2, ibu11, ibu12 and ibu19) passed, while, the remaining eleven brands failed the dissolution test and hence, sufficient amount of the drug would not be available for absorption to elicit the expected therapeutic effect when administered. Dissolution studies were not carried out for four of the nineteen brands (ibu6, ibu7, ibu8, and ibu13 because they did not disintegrate after 30 min.

Conclusion

Ibuprofen tablets in Nigerian market vary remarkably in their pharmaceutical qualities. There is therefore need for proper and stricter measures by regulatory bodies to ensure compliance and consistency. GMP which entails maintenance of the official standard in processing, manufacture and handling of drugs should be strictly observed by stakeholders. While NAFDAC, pharmacies, patients and indeed the civil society should step up the war in form of continuous surveillance, vigilance and

advocacy against fake and counterfeit drugs.

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