Research Article

Comparative *In-Vitro* Analysis of Different Available Brands of Ibuprofen Tablets in India using Statistical Parameters

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ABSTRACT

The purpose of this research work was to check, compare and evaluate the quality standards of different brands of Ibuprofen tablet IP 400mg from local market, Mumbai, India. Ibuprofen tablets are widely used over the counter (OTC) medication. Three batches of four different brands of this drug were tested for physical appearance, dimensions, uniformity of weight, hardness, disintegration, in-vitro dissolution and related substances as per pharmacopeia. Statistical analysis tools like one-way ANOVA and Bonferroni's test were also applied to the results of dissolution in order to find variation between brands and batches. Though all batches were meeting the compendial quality standards, inter brand variation was observed in disintegration time and hardness which was resulted in significant variation in dissolution as per both pharmacopeial methods.

Keywords: Bonferroni's test, Comparative study, Ibuprofen tablets, Indian Pharmacopoeia (IP), one way ANOVA, United States Pharmacopeia (USP).

INTRODUCTION

The Maharashtra food and drugs administration (FDA) have registered a huge increase in the number of sub standard drugs in the routine random inspections being carried out by the agency in the month of October 2011. The FDA has detected 29 not-of-standard drugs during the month of October compared to 15 during the month of September.[1] Thus in order to assure the quality, safety and efficacy of OTC drugs, quality control testing has to be done on continuous basis.

NSAIDS are non steroidal anti inflammatory medications. They are available in market as both OTC and prescription drugs. Some of common NSAIDS available as OTC drugs are aspirin, ibuprofen, paracetamol, naproxen sodium. Ibuprofen tablets are available in more than 100 brands in India, either single or in combination.[2,3] The use of NSAIDS as over the counter drugs has increased immensely in recent years. Due to their increased use, their safety and efficacy parameters have to be monitored continuously.[4]

Therefore this study is planned for comparative *in-vitro* evaluation of different available brands of Ibuprofen tablets in India using statistical parameters.

MATERIALS AND METHODS

Ibuprofen API was obtained from Microlabs, Mumbai, India. Different brands of Ibuprofen tablets (400mg) were purchased from local market. The commercial brands selected were of different manufacturers. The details of the tablets like the brands, batch numbers, manufacturing date and expiry date are given in the Table 1 along with their codes.

Ibuprofen API analyzed for water content and assay by Titrimetry as per IP 2010. This API was used as a standard. Ibuprofen tablets from different manufacturer were tested for physical appearance, dimensions, uniformity of weight, hardness, identification by infrared absorption spectrophotometry, disintegration test and content of active ingredient as per IP 2010. Related substances test was carried out by thin layer chromatography, IP 2007.

As per IP 2010, the dissolution test was executed on the six tablets using Dissolution Test Apparatus (Make: Electro lab, Model: TDT-08L) fitted with paddle rotated at 100 rpm for 30 minutes at 37 ±0.5°C using 900ml of phosphate buffer pH 7.2. Samples withdrawn were filtered and suitably diluted and the absorbance of the resulting solution was measured at about 221nm using UV-VIS spectrophotometry. The % release of ibuprofen was calculated using a calibration curve. As dissolution condition and limits were different in IP and USP, one batch of each Manufacturer was tested using USP dissolution conditions i.e. paddles at 50 rpm and time interval 60 minutes. Percent release was calculated. Statistical analysis of the dissolution results were performed using ANOVA and Bonferrani's comparision test.[7]

RESULTS AND DISCUSSION

Physical Appearance

Negligible variation in description, thickness, length and breadth was observed within the batches as given in Table 2.

Uniformity of Weight

As per IP 2010, for tablets having average weight of 250mg or more, 5% deviation from average weight is allowed. All batches complied with the requirement as shown in Table 2.

Hardness Testing

This test was performed on 10 tablets of each batch. Hardness can be correlated to release rate or bioavailability. More the hardness of the tablets more is time taken for disintegration/dissolution and thus lower is the release rate. The results are shown in Table 2. The hardness value is higher in generic tablets (Penta and Scientific) and is lower in branded tablets of Cipla and Abott.

Identification by Infrared absorption spectro photometry

All the batches pass the identification test as shown in Figure 1.

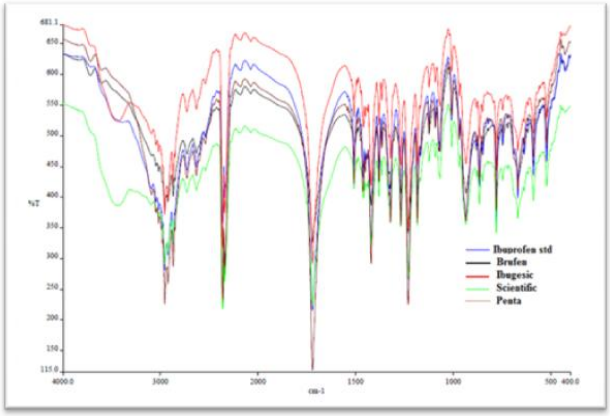

Figure 1: Overlay of IR of Ibuprofen and different brands of Ibuprofen tablets

Table 1: Tablet Information

Brand Names	Manufacturer	Batch no.	Code	Mfg. Dt	Exp. Dt
Brufen 1	Abbott	B-10810D7	B1	Oct-11	Sep-14
Brufen 2	Abbott	B-11802D7	B2	Nov-11	Oct-14
Brufen 3	Abbott	B-14805D7	B3	Feb-12	Jan-15
Ibugesic 1	Cipla Laboratories	B-A01279	I1	May-10	Apr-13
Ibugesic 2	Cipla Laboratories	B-DG1423	I2	Nov-11	Oct-14
Ibugesic 3	Cipla Laboratories	B-A93293	I3	Oct-09	Sep-12
Ibuprofen IP 1	Penta P'ceuticals	B-6996	P1	Nov-11	Oct-13
Ibuprofen IP 2	Penta P'ceuticals	B-7158	P2	Jan-12	Dec-13
Ibuprofen IP 3	Penta P'ceuticals	B-7358	P3	Feb-12	Jan-14
Ibuprofen IP 1	Scientific Remedies	B-306	S1	Apr-11	Mar-13
Ibuprofen IP 2	Scientific Remedies	B-310	S2	Jul-11	Jun-13
Ibuprofen IP 3	Scientific Remedies	B-316	S3	Nov-11	Oct-13

Table 2: Summary of Parameters

Brand code	Physical appearance*	Uniformity of Weight (Average±RSD) (mg)	Hardness testing (min/max) (Kg/cm^2)	Disintegration (average) (min)	Assay Active ingredient (average) (%)
B1	Pink, circular, smooth	567.2 ±1.2	5-6	3.33	102.24
B2		566.6 0.89	5-6	3.83	103.05
B3		564.6±1.3	5-6	4.00	102.24
I1	Pink, circular smooth	556.1±1.1	5-6	3.83	101.96
I2		565.9±0.9	5-6	4.16	103.46
I3		569.7±0.7	5-6	4.00	103.05
P1	Orange, oval, smooth	609.1±1.1	7-10	5.16	100.47
P2		611.1±1.1	7-9	5.00	100.33
P3		610.7±2.3	7-10	5.83	100.33
S1	Orange, cylindrical, smooth	525.2±1.6	7-9	6.16	99.79
S2		524.9±1.3	7-9	6.00	99.11
S3		526.4±1.3	7-10	6.50	99.79

*All tablets are film coated tablets

Disintegration Testing

All batches show disintegration in not more than 30 minutes (as film coated) as reported in Table 2. It was observed that the hardness of Penta and Scientific tablets is higher, so the time taken for disintegration is longer (i.e. 4-7 minutes) as compared to Cipla and Abbott tablets (3-5 minutes).

Dissolution testing as per IP

All tablets comply with the test as more than 55% (Q+5%) release was seen 30 minutes. Intra brand variation in

mean and variance was calculated using ANOVA and Bonferrani's comparison test was used to differentiate between brands as shown in Table 3. As per table 3, intra brand variation in mean and variance was not found for Brufen and Scientific where as Ibugesic and Penta showed variation in Mean.

Table 3: Summary of results of Dissolution test as per IP

Code	Mean (%)	± 95% Confidence interval	Intra brand variation	
			Mean P(<0.05)	Variance P(<0.05)
B1	100.25	97.67-102.8	No	No
B2	98.12	96.5-99.7		
B3	100.18	98.4-102.0		
I 1	97.40	91.9-102.9	Yes	Yes
I 2	102.64	101.4-103.9		
I 3	100.59	99.5-101.7		
P1	73.77	69.5-75.5	Yes	No
P2	72.63	69.5-72.3		
P3	75.32	73.2-77.3		
S1	72.48	70.2-77.3	No	No
S2	70.91	70.2-77.3		
S3	75.28	71.5-79.1		

Table 4: Bonferroni's Multiple Comparison Test

Bonferroni's Multiple Comparison Test	Mean Diff.	t	Significant (P < 0.05)	Summary	95% CI of diff
Brufen vs Ibugesic	-0.6922	0.6964	No	ns	-3.393 to 2.009
Brufen vs Scientific	25.61	25.76	Yes	****	22.91 to 28.31
Brufen vs Penta	26.63	26.79	Yes	****	23.93 to 29.33
Ibugesic vs Scientific	26.30	26.46	Yes	****	23.60 to 29.00
Ibugesic vs Penta	27.32	27.49	Yes	****	24.62 to 30.02
Scientific vs Penta	1.019	1.026	No	ns	-1.682 to 3.721

As shown in table 4, significant difference in dissolution was seen in branded (Brufen and Ibugesic) and generic (Scientific and Penta) tablets. Brufen and Ibugesic have similar dissolution results.

Dissolution Test as per USP

The % release limit of 50% in IP may be too low for a tablet to be termed as an immediate release tablet so dissolution testing as per USP was also performed. The Q limit mentioned in USP is 80% which is far more than that mentioned in IP. Dissolution results obtained are shown in Table 5. All brands meet the USP dissolution criteria.

Table 5: Summary of results of Dissolution test as per USP

Brand	Average (% ± RSD)
Brufen	101.68±1.58
Ibugesic	103.78±0.80
Penta	89.95±1.22
Scientific	87.85±2.22

Statistical results obtained by USP dissolution method were similar to that of IP showing significant difference in branded and generic drugs as shown in Table 6.

Table 6: Bonferroni's Multiple Comparison Test

Bonferroni's Multiple Comparison Test	Mean Diff.	t	Significant (P < 0.05)	Summary	95% CI of diff
Brufen vs Ibugesic	-2.102	2.515	No	ns	-4.547 to 0.3440
Brufen vs Scientific	13.84	16.56	Yes	****	11.39 to 16.29
Brufen vs Penta	11.74	14.05	Yes	****	9.291 to 14.18
Ibugesic vs Scientific	15.94	19.08	Yes	****	13.50 to 18.39
Ibugesic vs Penta	13.84	16.56	Yes	****	11.39 to 16.28
Scientific vs Penta	-2.103	2.517	No	ns	-4.549 to 0.3423

Related Substances Test

No secondary spots were observed other than that of Ibuprofen when all the batches were tested for the related substances test as per IP 2007.

Content of Active Ingredient/ Assay

Percent content for all batches were obtained between 95-105% as shown in Table 2.

CONCLUSION

Ibuprofen tablets IP from different manufacturers meet all compendial tests. Significant difference was observed in dissolution release of branded and generic tablets when tested as per IP & USP.

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