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Research Article

A COMPARATIVE QUALITY CONTROL STUDY ON CONVENTIONAL IBUPROFEN TABLETS AVAILABLE IN BANGLADESHI PHARMA MARKET

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ABSTRACT
The quality of a pharmaceutical product is essential to ensure the safety of the patients. Different parameters of quality control of pharmaceutical products can guarantee the quality and bioavailability and optimal therapeutic activity. Therefore, the present study was undertaken with the aim of assuring the quality and the therapeutic activity of ibuprofen tablets available in the Bangladeshi drug market. Different quality control parameters, i.e., the variation of weight, friability, content uniformity, disintegration time and dissolution profiles were assessed *in vitro*. To demonstrate the differences between the products, the difference (f_1) and similarity (f_2) data were analyzed. The results showed that all products fulfill the given specification selected by Pharmacopeia (USP-NF).
Keywords: Ibuprofen, Dissolution, Disintegration, Friability, USP-NF, Quality control

INTRODUCTION

Quality control is a process that is carried out to ensure a desired level of quality of a product. ISO 8402-1986 standard defines quality in the totality of features and characteristics of a product or service that bears its ability to satisfy stated or implied needs [1]. During the manufacturing of a drug product, quality control is used to check the quality of a product and direct the extent and degree of experience of the process and the products [2]. This process is carried out to verify the quality of the products, to produce drugs superior with respect to efficacy, safety, and quality, and to provide security to doctors, pharmacists and patients, that certain product works satisfactorily and uniform.

When a number of different formulations are available for the same drug, it becomes essential to ensure the equivalence of pharmaceuticals.

Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID) that is widely used in Bangladesh to relieve muscular and skeletal pain; it acts to inhibit the action of the cyclooxygenase enzyme, which catalyzes the conversion of fatty acids to prostaglandins. Thus, the analgesic and anti-inflammatory action is triggered by inhibition of the prostaglandin synthesis. Since ibuprofen is nonsteroidal, it does not alter the hormonal balance in the body. Its anti-inflammatory, analgesic (pain reliever) and antipyretic (fever reducing) actions are comparable to those of aspirin. It is often given as a tablet for the relief of mild to moderate pain, such as headache, toothache, and migraine and fever symptoms. Ibuprofen is available over-the-counter sale [3].

The main objective of this study was to ensure that the products (ibuprofen tablets) that are available in Bangladesh pharmaceutical market, meet specific characteristics, such as being reliable, satisfying, and safe.

MATERIALS AND METHODS

Materials

Ibuprofen (standard) was given by Globe Pharmaceuticals Ltd, Bangladesh. In our study, six conventional commercial brands of Bangladesh (randomly selected) containing 400 mg of ibuprofen were purchased from retail pharmacy store and here represented by IBP 1, IBP 2, IBP 3, IBP 4, IBP 5 and IBP 6. In the study, potassium dihydrogen phosphate (Merck, Germany) was used to prepare a phosphate buffer solution.

Analytical Method

Accurately weighed ibuprofen was dissolved in phosphate buffer solution in a 100 ml volumetric flask. From the stock solution, different dilutions were prepared to generate a calibration curve by measuring absorbance using UV spectrophotometer (UV- 1800, Shimadzu, Japan) at 221 nm. The concentration of ibuprofen was calculated using the linear regression equation of the calibration curve. Mean standard error and RSD (precision) calculated in the study were 0.003% and 0.74% respectively, (n = 6).

Weight Variation

For each brand, ten tablets were randomly selected and weighed individually using an analytical balance (ELB 3000, Shimadzu, Japan). The average weights were determined and the percentage deviations from mean values were calculated [4]. Then the standard deviation, and percentage of related standard deviation (RSD) was determined.

Hardness Test

The hardness of randomly selected ten tablets was determined for all the brands using 'Monsanto' type hardness tester (Intech, Korea). The mean crushing strengths were determined.

Friability Test

Ten tablets from each commercial brand were weighed individually, and each set of tablets was put into the friabilator (EF-2, Electrolab, India). The tablets were rotated at 100 rpm for 1 minute. Then the tablets were removed and weighed again. The friability percentage was calculated for each batch.

Test for Content Uniformity

The quantity of ibuprofen was determined in each product according to USP 30. A standard solution was prepared by dissolving pure ibuprofen in methanol, and sample solutions were prepared by dissolving ibuprofen tablets (n = 20) for each batch in methanol. The absorbance of each solution prepared was determined at 221 nm with the UV spectrophotometer. The amount of ibuprofen in each product was calculated using the equation of the calibration curve.

Disintegration Time Test

USP-30[4] disintegration apparatus (Electrolab, India) containing 6 glass tubes that are 3 inches long, open at the top and are held against a 10-mesh screen in the lower end of the unit basket rack was used in the study. For the test, a tablet

was placed in each tube and the frame of the basket was placed in a beaker containing 1 liter of buffer solution to 37^0C, such that the tablets remain below 2.5 cm the surface of the media in its upward movement and descent no closer than 2.5 cm from the bottom of the beaker. In the apparatus, a standard motor driven device is set for moving the basket containing the tablets upwards and downwards through a distance of 5.3 to 5.7 cm at a frequency of 29 to 32 cycles per minute. The disintegration time of each tablet was determined and the average time was calculated.

***In vitro* Dissolution Rate Studies**

The dissolution studies were carried out according to the USP paddle method. The stirring rate was 50 rpm at 37 ± 0.5^0 C. The dissolution medium was 900 ml phosphate buffer solution (pH 7.2 maintained). The samples (n= 12) were at ten minute intervals withdrawn up to 60 minutes and assayed spectrophotometrically at 221 nm. The percentage of cumulative drug release of each tablet was determined using the linear regression equation of the calibration curve.

Comparison of Dissolution Profiles

As a model independent approach, here, two adjustment factors (f_1 and f_2) comparing the dissolution profile of a pair of pharmaceutical products were applied to the dissolution data; f_1 values between 0 and 15, and f_2 values between 50 and 100 were used to define the equivalence of two dissolution profiles [5].

$$f_1 = \{[S_{t=1}^{n}(R_t - T_t)] / [S_{t=1}^{n}. R_t]\}. 100$$

$$f_2 = 50. \log \{[1 + (1/n). S_{t=1}^{n} (R_t - T_t)^2]^{-0.5}. 100\}$$

Where, n is the number of dissolution sample times, and R_t and T_t are the mean percent dissolved at each time point t for the reference and test dissolution profiles respectively.

RESULTS AND DISCUSSION

Weight Variation

According to USP, the range of variation in weight of each tablet (over 324 mg) is ± 5% (w/w), and the weights of different branded ibuprofen products shown in Table 1 are within the acceptance limit.

Hardness Test

Tablet hardness is defined as the force required breaking the tablet in a diametric compression test. If the tablet is too hard, it may not disintegrate in the required period of time to comply with the dissolution specification. Conversely, the hardness must not be so low that the tablets are soft and friable. To get a satisfactory quality tablet hardness should be between 4 and 8 kg [6]. The results of the branded products (Table 2) for the hardness test were satisfactory.

Friability Test

Tablet satisfactory friability value must be less than 0.5 to 1% [7]. Table 2 shows that all brands were within the limits of specification.

Content Uniformity

According to USP-30, contents of ibuprofen tablets must be not lower than 90.0 % and not more than 110.0 % of the labeled amount of active drug. The results (Table 2) show that, all the brand products meet the criteria.

Disintegration time (DT) test

The disintegration is used as a guide to the formulator in the preparation of a satisfactory tablet formula as a control test on the process. Therefore, to ensure batch-to-batch product uniformity, DT test is very important. According to USP, the disintegration time should not be more than (NMT) 30 minutes and the results shown in Table 2 for the branded products meeting the criteria.

Dissolution Rate Studies

The oral bioavailability of a drug depends entirely on the rate of drug dissolution. Therefore, it is very important to evaluate the dissolution data and comparison of dissolution profiles for different products available in the market. Table 2 shows the average percentage of drug release after one hour. Difference (f_1) and similarity (f_2) tests were applied to the release rate, and are shown in Table 3. According to USP, dissolution rate for the tablets of ibuprofen should be at least 80% within 60 minutes, and the branded products meet requirement (Table 2). Table 2 shows that the IBP 2 released maximum amount of drug (102.68%) while IBP 6 released the lowest amount of drug after 60 min. Thus, IBP 2 was considered the benchmark for high drug release. The values f_1 and f_2 indicated that the dissolution profile of IBP 1 and 4 are similar to the reference profile (IBP 2), while IBP profiles 3, 5, and 6 are not similar to those of IBP 2.

Table 1: Weight variation Measurement (n = 10)

Brand products of Ibuprofen	Minimum weight (g)	Maximum weight (g)	Average weight (g)	Standard Deviation (SD)	% Relative Standard deviation (RSD)
IBP 1	0.611	0.657	0.630	0.014	2.26
IBP 2	0.607	0.620	0.613	0.004	0.68
IBP 3	0.611	0.637	0.628	0.009	1.44
IBP 4	0.513	0.526	0.518	0.004	0.80
IBP 5	0.841	0.884	0.864	0.014	1.65
IBP 6	0.568	0.612	0.593	0.015	2.54

Table 2: Results of hardness, friability, content uniformity, disintegration time, and dissolution tests

Brand products of Ibuprofen	Hardness (kg-ft) (mean ± SD)	Friability (%)	Content Uniformity (%)	Average Disintegration time (min)	Average Drug release (%) after 60 minutes
IBP 1	8.17 ± 0.39	0.186	96	5.10	101.42
IBP 2	7.91 ± 1.14	0.214	98	1.55	102.68
IBP 3	5.42 ± 1.32	0.144	101	8.76	93.87
IBP 4	6.02 ± 1.44	0.154	99	5.17	100.16
IBP 5	7.09 ± 1.99	0.112	103	12.60	93.29
IBP 6	6.84 ± 1.35	0.321	95	13.55	86.14

Table 3: f_1 (Difference) and f_2 (similarity) factors for reference (IBP 2) vs. test products (IBP 1, 3, 4, 5, and 6)

Factors	IBP 1	IBP 3	IBP 4	IBP 5	IBP 6
f_1	14.54	35.23	13.14	37.59	42.79
f_2	89.19	48.91	87.94	49.74	47.59

CONCLUSION

Research shows that ibuprofen tablets marketed, manufactured by pharmaceutical companies in Bangladesh are of satisfactory quality and met USP standards with respect to the tested parameter. Although the results suggest the differences in the release profiles, all brand products released 80% of the labeled amount of drug within 1 hour, being compliant with the acceptance limits and therefore of sufficient quality. Further investigation is suggested to establish *in vivo-in vitro* correlation to reveal the accurate pattern of drug release in the *in vivo* environment from marketed ibuprofen formulations.

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