International Journal of Basic Medical Sciences and Pharmacy (IJBMSP)
Vol. 2, No. 2, December 2012, ISSN: 2049-4963

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In vitro Dissolution Studies of Different Brands of Baclofen Tablets Available in Bangladesh

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Abstract – This study was designed to evaluate the quality of baclofen tablets commercially available in Bangladesh. We studied the in vitro dissolution profile of eleven brands of baclofen tablet of which three were coated and eight uncoated. The study also included the determination of disintegration time and drug content in all these brands. We observed that one of the film-coated brands was suboptimal with respect to average drug content, which was found to be 80.10% and this lies outside the compendial specification. This brand also failed to comply with the compendial in vitro drug release requirement as we observed only 41.30% drug release at the end of 45 min. All other brands tested met the required specifications and complied accordingly in terms of drug release, disintegration time and drug content. In conclusion, our results demonstrate that although most brands of baclofen tablets included in this study showed high dissolution profile and hence good bioavailability, at least one brand failed to meet the quality requirements, suggesting that substandard product is also available in the market that may not provide the expected efficacy.

Keywords – – baclofen tablet, disintegration, dissolution, film coated tablets.

1. Introduction

Baclofen ($C_{10}H_{12}ClNO_2$:213.66), chemically 4-amino-3-(4-chlorophenyl) butanoic acid is a muscle relaxant and antispastic. This is a derivative of gamma-aminobutyric acid (GABA) and acts as an agonist for the $GABA_B$ receptors [1,2]. Baclofen is a white to off-white, odorless or practically odorless crystalline powder, which is slightly soluble in water, very slightly soluble in methanol, and insoluble in chloroform. The poor solubility of the drug in water leads to slow dissolution rate in aqueous medium thus, makes the drug less available for gastrointestinal absorption.

The process of dissolution always plays a vital role in releasing drug from orally taken dosage form for necessary absorption through gastrointestinal tract. In vitro dissolution test is considered to be sensitive, reliable and rational for predicting in vivo drug availability performance [3]. In fact, dissolution analysis of pharmaceutical solid dosage forms has emerged as a 'must do' quality control test to understand the in vivo behavior of the product [4]. In vitro dissolution test can distinguish between formulations of the same therapeutic agent [5]; hence, this test can be used to ascertain batch consistency from the same manufacturer as well as in determining product performance from different manufacturers for comparison. Likewise, disintegration test for compressed tablets, which is included in all pharmacopoeias, is another important quality control tool to indicate not only the time required for the breakdown of a tablet but also to assure batch to batch consistency and performance.

Dissolution of a drug from its dosage form depends on many factors, which include not only the physicochemical properties of the drug, but also the formulation of the dosage form and the process of manufacturing [6]. A change in type and concentration of the excipients because of sudden unavailability or of high price may result in altered behaviour of the product, which may be either beneficial or detrimental. Therefore, regular dissolution analysis of the marketed drug products is essential to ensure availability of quality medicines.

In Bangladesh, currently eleven pharmaceutical companies are manufacturing and marketing baclofen tablets. An extensive literature survey revealed that dissolution studies on baclofen controlled release tablets and orodispersible tablets are reported, however, there is no report on comparative study of commercially available baclofen tablets in Bangladesh. This study deals with various in vitro quality control parameters of eleven available marketed baclofen tablets with special attention to dissolution rate studies in order to assess the quality of the products and to find out if any out of compliance.

2. Materials and Methods

2.1. Materials

Reference standard of Baclofen (99.87%) was a gift from Eskayef Bangladesh Limited.

2.2. Drug samples used in this study

Eleven (11) brands of Baclofen tablets were purchased from various medicine shops located at Dhaka city. They were randomly marked from B1-B11. The samples were properly checked for their manufacturing license numbers, batch numbers, date of manufacture and expiry dates. The labeled active ingredient was 10 mg of Baclofen and all were packaged in strip or in blister. The samples were carefully collected that none of them were older than four months. The strip or blister packs were stored at 25±2°C for four weeks before the dissolution study in order to assess any organoleptic change.

2.3. Assay of baclofen by UV spectroscopy

The content of Baclofen per tablet in the samples was determined by a spectrophotometer (Shimadzu, UV - 1800) at 220nm as per procedure described in the USP [7,8].

2.4. Disintegration test

Disintegration time (DT) of the Baclofen tablets were measured using a six station disintegration test apparatus (DST-3, Logan Instruments Ltd, USA) with disc according to the guidelines of British Pharmacopoeia [9]. Distilled water at 37±2º C temperature was used as the disintegration medium. Six tablets of each brand were tested and the average disintegration time was calculated [9].

2.5. Dissolution studies

Dissolution test of baclofen tablets was carried out in a eight station USP type II apparatus (Paddle type, Logan Instruments Ltd, USA) equilibrated at 37±1oC at 50 rpm speed using 500 ml distilled water as a medium. The dissolution study was performed according to Japan Pharmacopeia [10] guidelines except that a multipoint analysis was carried out instead of a single point determination in order to obtain the full drug release pattern. Samples were withdrawn at 10, 20, 30, 40 and 45 min and after suitable dilution, absorbance values were recorded at 220nm using UV-Spectrophotometer. The amount of drug dissolved was expressed as percent release at specified time period [10].

3. Results and Discussion

The amount of drug present in each tablet was determined spectrophotometrically and all the brands, except B2, met the official standard of USP which specifies that the content should not be less than 90% and more than 110% (Table 1). The average amount of the active ingredient per tablet present in the sample B2 (film-coated) was found 80.10% of the claimed potency, which failed to comply with USP specification mentioned before.

Disintegration is a crucial step for immediate release dosage forms since the rate of disintegration affects the dissolution and subsequently the therapeutic efficacy of the medicine in vivo. Generally, a drug will be released rapidly as the tablet disintegrates. British Pharmacopeia specifies that uncoated tablets should disintegrate within 15 min and film coated tablet disintegrate within 30 min. All the brands (coated and uncoated) were complied with the BP specifications for disintegration as the maximum DT found was 10.17 min for the brand B2 (Table 1). Results of disintegration studies and assay are shown in Table 1. Again, all the brands of baclofen tablets were investigated to determine whether they comply with the JP in vitro dissolution specification or not. Our in vitro dissolution studies revealed that all the tested samples, except one (B2), released more than 70% drug within 45 min (Table 2, Figure 1). That brand coded B2 failed to fulfill the JP in vitro dissolution specification. Film-coated samples B1, B3 and uncoated samples B4, B6, B9, B10 and B11 were better than others because of rapid dissolution and drug release. Thus, quick onset of action may be expected from these brands as faster dissolution will ensure rapid absorption from the GI tract.

However, the discrepancy among the brands may not be revealed by single-point dissolution testing as mentioned in official compendium like JP but can be visualized only when full dissolution profiles are constructed by conducting multiple-point analysis. Hence, we performed the drug dissolution study collecting samples at different time points. The percent drug release rate at 10, 20, 30, 40 and 45 min are shown in Table 2. All the test brands except one (B2) passed the JP dissolution specification since drug release was found to be greater than 70% in 30 min. The study revealed that at different time intervals, the brand B3 (film-coated) was the fastest in its drug release rate in comparison to others. The drug release rate after 20 min, however, clarified that the brands like B1 (film-coated), B6, and B9 (uncoated) were faster in their drug release as compared to others. The sample B2 (film-coated) showed the slowest rate of drug release thus slower therapeutic effect may be predicted. Also, this did not comply with the specification as only 39.54% drug release was observed after 40 min, which was even less than the drug release rate of other film-coated brands (B1, B3) and uncoated brands (B4–B11) at 10 min point.

Table 1. Assay* and disintegration time** of commercial brands of baclofen tablets.

Sample code	Coated/ uncoated	Amount of drug (mg)	Potency (%)	Remarks	DT (mean ±SD) (min)	Compliance of DT
B1	Coated	10.19	101.9	Complied	3.72 ± 0.12	Complied
B2	Coated	8.01	80.1	Not complied	10.17 ± 0.41	Complied
B3	Coated	9.57	95.7	Complied	0.34 ± 0.02	Complied
B4	Uncoated	9.61	96.1	Complied	1.17 ± 0.07	Complied
B5	Uncoated	10.53	105.3	Complied	0.17 ± 0.02	Complied
B6	Uncoated	9.95	99.5	Complied	0.08 ± 0.03	Complied
B7	Uncoated	10.46	104.6	Complied	0.33 ± 0.02	Complied
B8	Uncoated	10.15	101.5	Complied	1.75 ± 0.16	Complied
B9	Uncoated	10.46	104.6	Complied	0.33 ± 0.03	Complied
B10	Uncoated	10.36	103.6	Complied	0.13 ± 0.03	Complied
B11	Uncoated	9.7	97	Complied	0.67 ± 0.05	Complied

*Claimed potency is 10mg per tablet. Accepted range of average drug content per tablet according to BP & USP is from 9 mg to 11 mg. **Six tablets were tested for each brand

Table 2. Baclofen dissolved at specified time intervals from commercial tablets

	Drug Dissolved (%)					
Sample code	**10min**	**20min**	**30min**	**40min**	**45min**	**Compliance**
B1	53.91	82.65	85.35	85.63	85.92	Complied
B2	15.93	27.74	35.99	39.54	41.30	Not complied
B3	85.21	89.62	92.18	89.76	89.12	Complied
B4	70.41	74.68	75.82	76.39	77.11	Complied
B5	60.46	73.83	74.68	72.69	71.56	Complied
B6	62.16	81.51	81.79	81.93	82.24	Complied
B7	46.09	65.58	70.55	73.4	74.68	Complied
B8	56.05	69.56	71.69	73.26	74.20	Complied
B9	58.89	74.11	79.37	78.24	78.10	Complied
B10	52.77	73.26	73.83	78.81	80.36	Complied
B11	68.42	73.83	75.25	75.25	74.94	Complied

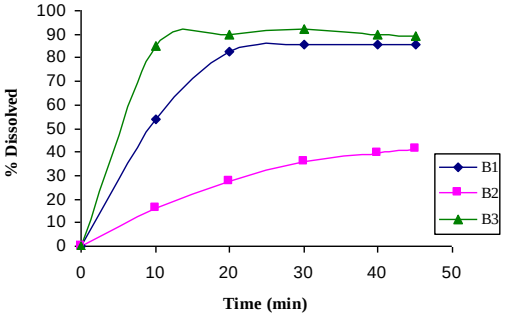

Figure a. Dissolution profile of different brands of baclofen tablets B1-B3 (Coated tablets)

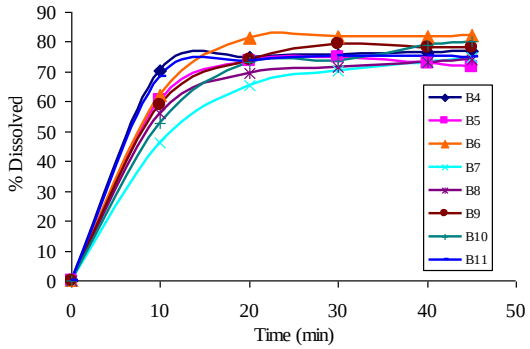

Figure b: Dissolution profile of different brands of baclofen tablets B4-B11 (Uncoated tablets).

4. Conclusion

From this study it has been revealed that one of the eleven commercially available brands of baclofen in Bangladesh failed to fulfill the official specification of dissolution test which might be explained by poor formulation and/or lower content of the active ingredient or excipients. The differences in the drug release patterns of the baclofen tablets also suggest that they cannot be used interchangeably. This is very important in regard to our country's situation where the prevalence of self-medication is high as well as buying and selling of drug products are mostly done without prescription. Therefore, patients may often be victim of consuming low quality products, which not only will increase the expense but also the sufferings tremendously. As, in vitro dissolution test is a sensitive method for differentiating formulations of the same therapeutic agent, this type of study should be performed more frequently and with more samples to build public awareness about the quality of marketed pharmaceutical products.

Acknowledgment

The authors like to thanks Eskayef Bangladesh Limited, for providing standard Baclofen and also wish to acknowledge Ms. Samina Ferdous for providing technical support during the experiment.

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