

***In vitro* Quality Analysis of Different Brands of Alprazolam Tablet Available in Bangladesh**

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Abstract

Alprazolam is a benzodiazepine anxiolytic commonly prescribed as a sleeping aid and for the treatment of anxiety disorders. The current study was undertaken with the aim of analyzing quality of commercially available brands of alprazolam tablets available in Bangladesh. To assess the quality, locally available 0.25 mg alprazolam tablet of seven different manufacturers were selected and certain physico-chemical parameters like weight variation, hardness, friability, disintegration time and dissolution profile etc. were evaluated using *in-vitro* analytical methods. All the tablet brands met the requirements of British Pharmacopoeia as they showed acceptable weight variation and friability (below 1%). Brands were slightly different in hardness, disintegration time and dissolution profile from each other. The hardness of all the brands was found to be in the range of 1.50 ± 0.18 to 4.21 ± 0.11 kg-ft. In water medium the disintegration time of all brands were found to be 0.57 ± 0.45 to 2.22 ± 0.23 min. Five out of seven brands showed better dissolution profile as they released more than 90% drug in 30 min. The study revealed that most of the marketed alprazolam tablets met the BP standards for physico-chemical properties which are the indicators of drug quality. It can be concluded that drug products should always comply standard quality parameters that are the prerequisites for getting satisfactory clinical effects.

Key words: Alprazolam, quality analysis, hardness, disintegration time, dissolution profile.

Introduction

Alprazolam is a short-acting drug of benzodiazepine group used for the treatment of moderate to severe anxiety disorders and panic attacks. It is used as an adjunctive treatment for anxiety associated with moderate depression (Ballenger *et al.*, 1988). Alprazolam possesses anxiolytic, sedative, hypnotic, anticonvulsant, and muscle relaxant properties (Marks *et al.*, 1993).

The process of quality control is carried out to confirm an expected level of quality in a product. It includes the necessary actions, a business conceives, essential to provide for the control and verification of certain characteristics of a product or service (Dewan *et al.*, 2013).

There are certain quality parameters like weight variation, hardness, friability, disintegration time, dissolution profile etc. which demonstrate a significant effect on the drug product formulation (Karmakar and

Kibria, 2012). Therefore, the study was aimed to evaluate various *in vitro* quality control parameters of alprazolam tablet brands available in Bangladesh.

Materials and Methods

Study design: The study of *in-vitro* quality analysis of available alprazolam tablet brands in Bangladesh was studied by the evaluation of weight variation, hardness, friability, disintegration time and dissolution profile. The study was conducted using various standard test methods related to estimate the quality of tablets.

Sample collection and identification: Seven (7) brands of alprazolam tablets were purchased from various medicine shops located at Noakhali, Bangladesh. They were randomly marked from ALP01 to ALP07. The samples were properly checked for their manufacturing license numbers, batch numbers, date of manufacture and expiry dates. The entire tablet brands were containing

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labeled shelf life of three years from the date of manufacture and before two years of labeled expiry date it was taken for the evaluation. The labeled active ingredient was 0.25mg of alprazolam and all were packaged in strip or in blister. Reference standard of alprazolam (99.87%) was collected from Incepta Pharmaceuticals Limited, Bangladesh.

Analytical methods: In this study, following quality control tests were performed for the evaluation of all the alprazolam tablet brands.

Weight variation test: The acceptable range of weight variation for tablets should not exceed 10% or more having average weight of 80 mg or less (British Pharmacopoeia, 2005). For each brand, ten tablets were randomly selected and weighed individually using an analytical balance (ELB 3000, Shimadzu, Japan). The average weights were determined using the following formula.

$$\text{Weight variation (\%)} = \frac{\text{Individual weight} - \text{Average weight}}{\text{Average weight}} \times 100$$

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

Friability test: In the study, it was determined by using Electrolab EF-2 Friabilator (USP) and the values of friability were expressed in percentage (%). From each selected brands ten tablets were individually weighed and transferred into friabilator which was operated at 25 rpm and continued up to 4 minutes (100 revolutions). Then the tablets weights were measured again and the percent (%) of friability was calculated using following formula (Kalakuntla et al., 2010).

$$\% \text{ of Friability} = \frac{\text{Weight before test} - \text{Weight after test}}{\text{Weight before test}} \times 100$$

Disintegration time test: The instrument used for this test was Disintegration tester –USP; (Electro lab EF 2L; United Kingdom) with disc in distilled water medium. To test for disintegration time three tablets of each brand were placed in each tube and the basket rack is positioned in a 1 liter beaker of water at $37 \pm 0.5^{\circ}\text{C}$. The time required to break of each tablet into minute particles and pass out

through the mesh was recorded. Then the mean disintegration time was calculated for every brands (Gangwar et al., 2010).

Dissolution test: For all brands of studied tablets, dissolution test was carried out using Dissolution Tester – USP Apparatus-1 (Basket type). Individually 3 tablets of each brand were placed in 3 different beakers in dissolution medium containing 900 ml of 0.1N HCl buffer (pH 7.4). The process was done at a speed of 100 rpm by maintaining temperature at $37 \pm 1^{\circ}\text{C}$ in each test. At regular time intervals of 10 minutes samples were withdrawn as 5 ml which was predetermined and same method was continued up to 30 minutes by replacing equal quantity of fresh dissolution medium. The filtered samples were diluted suitably and analyzed by using UV Spectrophotometer (SHIMADZU UV Spectrophotometer: UV-1800-240V) at 260 nm for alprazolam and percentage (%) of drug release was calculated by measuring the absorbance (Kumar et al., 2011).

Statistics: The data were analyzed by using the above mentioned mathematical formula and MS Excel[®], 2007.

Results and Discussion

Weight variation: The weights of different brands of Alprazolam tablets shown in Table 1 were within the range.

Hardness test: All the brands exhibited satisfactory hardness strength, which is required for safe handling and transportation. The hardness was found to be in the range of 1.50-4.0 kg-ft. (Table 2)

Friability test: All brands showed friability less than 1%. Brand ALP 05 had minimum friability of 0.50% while brand ALP 02 had maximum friability of 0.97% and both were within the limit of specification. (Table 2)

Disintegration time (DT) Test: The disintegration time of all tablet brands of alprazolam ALP 01, ALP 02, ALP 03 ALP 04 ALP 05 ALP 06 and ALP 07 was satisfactory as uncoated USP tablets have disintegration time standards as low as 5 minutes (Banker and Anderson, 2009). However, variations in disintegration time from brand to brand were observed in the study. (Table 2)

Dissolution rate studies: Figure 1 shows the data of dissolution studies

Table 1. Measurement of weight variation of different brands of Alprazolam tablet.

| Alprazolam tablet brands | Minimum weight (g) | Maximum weight (g) | Average weight (g) | Standard deviation (SD) | Relative standard deviation (SD) |
|--------------------------|--------------------|--------------------|--------------------|-------------------------|----------------------------------|
| ALP 01 | 0.1344 | 0.1385 | 0.1364 | 0.0010 | 0.760 |
| ALP 02 | 0.1529 | 0.1563 | 0.1543 | 0.0012 | 0.786 |
| ALP 03 | 0.1328 | 0.1373 | 0.1353 | 0.0017 | 1.266 |
| ALP 04 | 0.1326 | 0.1362 | 0.1347 | 0.0011 | 0.856 |
| ALP 05 | 0.1154 | 0.1211 | 0.1188 | 0.0021 | 1.805 |
| ALP 06 | 0.1317 | 0.1339 | 0.1323 | 0.0007 | 0.540 |
| ALP 07 | 0.1335 | 0.1351 | 0.1343 | 0.0005 | 0.402 |

ALP= Alprazolam, g=gram

Table 2. Results of hardness, friability, disintegration tests of different brands of Alprazolam tablets.

| Alprazolam tablet brands | Hardness (kg-ft) (mean \pm SD) | Friability (%) | Disintegration time (min) |
|--------------------------|-------------------------------------|----------------|------------------------------|
| ALP 01 | 3.26 \pm 0.23 | 0.73 | 0.57 \pm 0.45 |
| ALP 02 | 2.50 \pm 0.16 | 0.97 | 1.26 \pm 0.07 |
| ALP 03 | 4.21 \pm 0.11 | 0.61 | 1.52 \pm 0.31 |
| ALP 04 | 1.50 \pm 0.18 | 0.79 | 1.32 \pm 0.11 |
| ALP 05 | 1.64 \pm 0.15 | 0.50 | 1.15 \pm 0.13 |
| ALP 06 | 2.43 \pm 0.12 | 0.87 | 1.39 \pm 0.12 |
| ALP 07 | 3.53 \pm 0.14 | 0.63 | 2.22 \pm 0.23 |

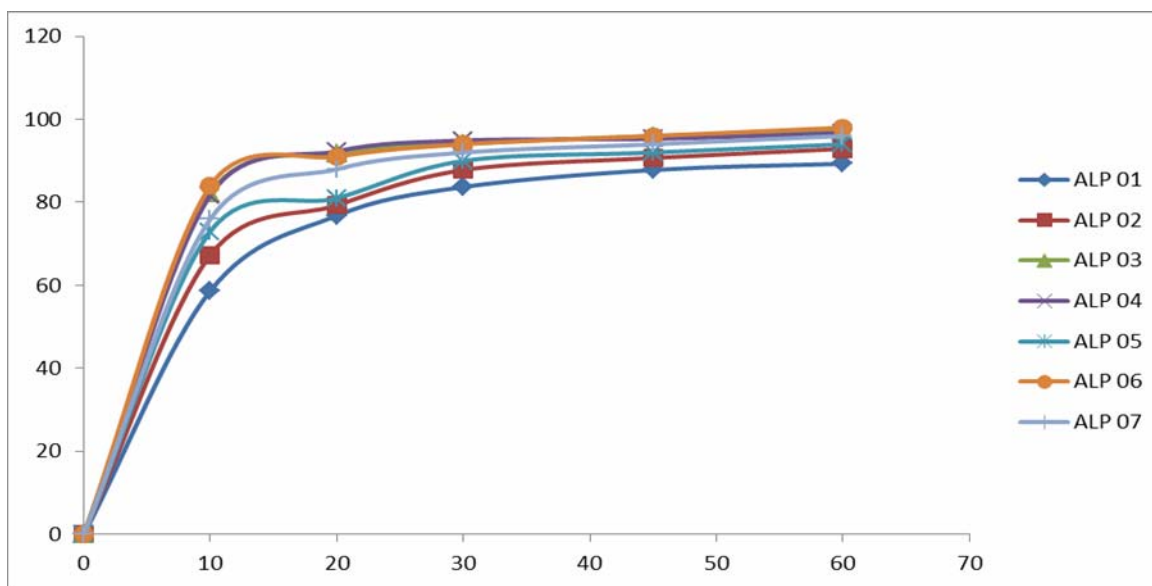


Figure 1. Drug release curve of different brands of Alprazolam tablet ALP= Alprazolam

Conclusion

From the study it was identified that weight variation and friability test of alprazolam tablet brands met the

specification of B.P. Variations were obtained in hardness, disintegration time and dissolution profile. On the other hand almost all alprazolam tablet brands showed better

disintegration time but some were slight different in their dissolution profile which is related to its absorption property. Manufacturers should always maintain highest standard for all quality parameters of any medicine because better quality ensures better medicine to get desired therapeutic effect.

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