PHYSICOCHEMICAL EVALUATION OF SOME COMMERCIALLY AVAILABLE BRANDS OF ATENOLOL TABLETS OF BANGLADESH

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Abstract: *Atenolol, a cardiovascular drug, is mainly used to reduce blood pressure and available worldwide under various trade names. The purpose of the current study is to ascertain physicochemical equivalence among the five different brands of atenolol 100 mg tablets commercially obtainable in Bangladesh. The sample tablets were examined for their weight variation, hardness, thickness, friability and disintegration time as well as dissolution time were evaluated spectrophotometrically conferring to the official (BP/USP) methods. The results showed that all brands of tablets showed satisfied results when they were tested for weight variation, hardness, thickness, friability, disintegration time and dissolution time. All the five brands were disintegrate within 15 minutes which comply the USP/BP recommendation. The tested brands were identical according to their dissolution evaluation. All brands showed more than 90 % drug release within 45 minutes and ranged from 99.09% to 100.98%. It can be summarized that the physicochemical properties of all five brands of atenolol tablets marketed in Bangladesh meet BP/USP specifications which indicated that they are pharmaceutically equivalent. Therefore, patients can safely choose anyone of the brands.*

Key words: *Atenolol, cardiovascular, disintegration, dissolution, friability.*

Introduction

Atenolol is a β adrenergic antagonist and it's chemical name is 4–[2-(hydroxyl-3-isopropylaminopropoxy) phenyl] acetamide. It is generally used for the controlling of cardiovascular diseases such as hypertension (high blood pressure), angina (chest pain) and coronary heart disease. The drug also minimizes the risk of mortality and non-fatal re-infarction in survivors of acute myocardial infarction. Atenolol is used in combination with cardiac glycosides, diuretics and angiotensin converting enzyme inhibitors (ACE-1) for the treatment of heart failure of ischemic or cardiomyopathic origin, to minimize the risk of progressing the disease (such as death) and improved medical condition of patient [1, 2].

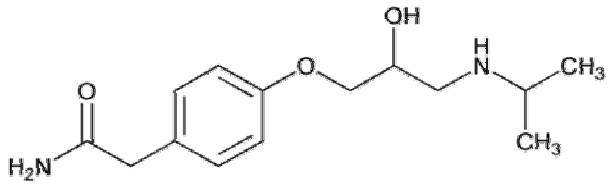

Figure 1: Structure of atenolol

Although many companies manufacture atenolol, not all of them produce high quality products. Some of them are sub-standard. To identify quality drugs as well as substandard drugs Atenolol tablets were assessed regarding their various properties. To observe quality and quantity of the tablet evaluations of chemical, physical and bioavailability properties must be made. Chemical breakdown or interaction between tablet constituents may modify physical properties which significantly change the bioavailability of a tablet system. It is essential for a medicinal product to fulfil some standards to

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declare it to be a quality drug. The chief property for a quality drug product is safety, potency, efficacy, stability and market acceptability [3].

The research work was designed to study the quality evaluation of atenolol and to inform the physicians and patients about the substandard drugs in market. This will make awareness among the general people and physicians so that the manufacturers will produce the quality products and people may not waste their hard earning money by buying low quality substandard drugs. Drug formulationd which are chemically and biopharmaceutically comparable must be similar in strength, quality, purity as well as content uniformity, disintegration and dissolution rates [4]. Dissolution rate of a drug product is an important property for evaluating the quality of a drug and also to observe the batch wise uniformity of release characteristics [5]. Differences in the release characteristics among some drugs specify the deficit in the whole drug formulation and their delivery system. Determination of dissolution time is also used for estimation of *in vivo* bioavailability in most oral preparations [6,7]. The main objective of the current study was to assess the biopharmaceutical equivalency of five brands of atenolol tablets with the use of analytical method, which will be easy to use, simple, and cheap with results, which relate favorably with proven official methods [8].

Materials and Methods

The samples of marketed atenolol tablets (100 mg) of different companies were collected at maximum retail prices (MRP) from different regions of Dhaka city for the analytical studies. The samples of tablets were correctly evaluated for their batch number and shelf life, name of manufacturer, manufacturing license number, and DAR number. For ethical consideration samples were then coded for evaluation.

For conducting disintegration and dissolution study hydrochloric acid, Acetic acid and sodium acetate (for preparing acetate buffer) were purchased.

General Appearance

The atenolol tablets were destripped or deblistered carefully. The tablets were evaluated based on the standard limit of British Pharmacopoeia and United States Pharmacopoeia standards. Before proceeding to other evaluations, visual inspections of size, shape & color of the tablets were done.

Hardness of tablet

Hardness of each tablet was measured by using the Monsanto hardness tester. The force needed to break the tablet is determined in kilograms and for a suitable tablet a breaking strength of 4Kg is typically considered to be the minimum[9].

Thickness test of tablet

Thickness of 10 tablets of each sample was measured with a slide calipers. The average thickness of the tablets was determined and then thickness variation was calculated. By this method the thickness variation of all the samples were measured and the perceived result for each brand was recorded.

Weight variation test of tablets

First of all we have taken 10 tablets of each brand, then individual weight of each tablet were measured by using analytical balance. The average weight of each brand was calculated. Finally percent of weight variation was calculated by using the following equation.

$$\% \text{ of weight variation} = \frac{\text{Individual weight} - \text{average weight}}{\text{Average weight}} \times 100$$

Friability

Friability test will impose abrasions and shock in the tablets. A well manufactured tablet must be able to resist any abrasion and shock during its handling, transportation and packing[8]. For friability testing four tablets were taken from each brand and then weighed by weighing balance. Then the tablets were put in a friabilator which was allowed to rotate at 25 rpm for 4 minutes. After that the tablets were dedusted and were weighed again. The percent friability was determined by the following equation:

$$\% \text{ Of friability} = \frac{\text{Initial weight-final weight}}{\text{Initial weight}} \times 100$$

Disintegration

For this study, disintegration machine used as stated by USP 2008 [10]. Six tablets were separately positioned in a basket. The temperature of disintegration medium was retained at 37°C with the ±2°C. The tablets disintegration time was taken as the period when the basket of disintegration apparatus will be free of the particles of tablet. According to Pharmacopeia disintegration machine should be run for 30 minutes for film coated tablet. If the tablet coat remain intact then the test should continue by replacing the media with 0.1M hydrochloric acid. As for uncoated tablet, the test needs to be run for 15 min [11].

Dissolution test of tablet

Drug dissolution testing is usually used to provide critical in vitro drug release information for quality control determinations. The drug dissolution rate in gastric fluid determine the absorption rate and bioavailability of a drug product[12]. In this research work, the dissolution was carried out by rotating paddle technique, taking Acetate buffer pH 4.6 as dissolution media.

Preparation of standard curve

10 mg of standard atenolol BP was taken in a 100ml volumetric flask and the volume was adjusted using acetate buffer pH 4.6. From this stock solution a series of standard solution of atenolol were prepared by proper dilution using acetate buffer. Then absorbance of the prepared solution was taken by UV spectrophotometer at 275nm. The values of measured absorbance of standard solutions were plotted against the corresponding concentration which gives a straight line (Fig-2).

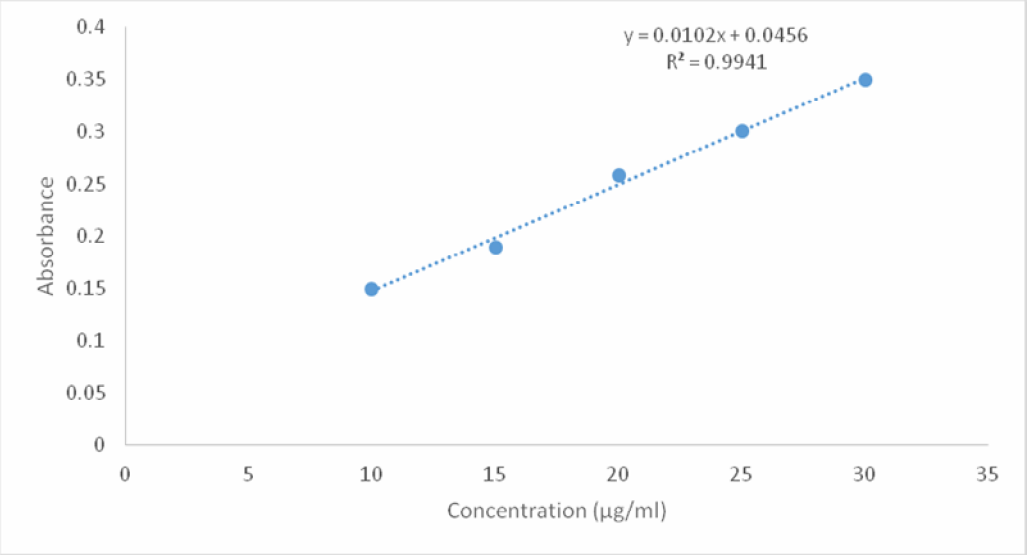

Figure 2: Standard curve for dissolution study of atenolol

Dissolution procedure

To determine the dissolution rate of the samples, tablets were placed at the lowermost part of the dissolution apparatus taking 900ml 0.1N acetate buffer (pH 4.6) as dissolution media. For preparing 0.1N acetate buffer (pH 4.6) 44.9 parts (v/v) of 0.1N sodium acetate was mixed with 55.1 parts (v/v) 0.1N acetic acid solution [13]. The apparatus was set at 37±5°C and 50 rpm using paddle technique. 5ml of samples from the dissolution medium was withdrawn in every 15 minutes interval for 1hour. Later for every removal of sample, 5ml of fresh dissolution medium was added to each basket. Each extracting samples were then clarified by means of filter paper. The absorbance was observed by using UV/Visible Spectrophotometer at wavelength of 275nm & amount of drug dissolved were calculated using following equation[14].

$$\% \text{ Dissolution} = \frac{\text{Absorbance of sample} \times \text{dilution of standard}}{\text{Absorbance of standard} \times \text{dilution of sample}} \times \text{Purity of standard} \times 100\%$$

Results

General appearance

The general appearance of all brands of atenolol tablets has been thoroughly analyzed and the results show that there is not much difference between the brands except color. As there is no specification about the color of tablets in BP/USP, the manufacturers can use any coloring agents in tablet formulation permitted by the concerned authority.

Weight variation test

Weight variation of a tablet serve as a tool of good manufacturing practices (GMP) upheld by the manufacturers as well as the amount of active pharmaceutical ingredient (API) present in the preparation. The weight variation for all the tablets used in this study presented compliance within the official specifications[15].

Table 1: Weight variation of various brands of atenolol tablets

Sample code	No. of tablets	Uniformity of weight (mg)± SD*	Inference
Brand-01	10	165.4±3.58	Satisfied
Brand-02	10	194.8±2.7	Satisfied
Brand-03	10	211.3±1.88	Satisfied
Brand -04	10	219.2±3.65	Satisfied
Brand-05	10	173.2±5.19	Satisfied

* SD = Standard deviation

USP specification of weight variation for tablets of 130 mg or less: ±10

USP specification of weight variation for tablets of 130-324 mg: ±7.5

The result shows that all the samples satisfied the USP standard limits, where maximum weight variation observed only ±5.19%(-3.00 to+2.19) by Brand-05.

Hardness test

The breaking point and structural integrity of a tablet determined by the hardness test and it also find out how it changes under conditions of storage, transportation, packaging and handling before usage. Hardness of all five brands are given below.

Table 2: Hardness of various brands of atenolol tablets

Sample code	No. of tablets	Hardness (Kg) ± SD	Inference
Brand-01	10	5.42 ± 0.28	Satisfied
Brand-02	10	4.15 ± 0.50	Satisfied
Brand-03	10	4.07 ± 0.33	Satisfied
Brand -04	10	4.31 ± 0.16	Satisfied
Brand-05	10	7.07 ± 0.35	Satisfied

All the brands satisfied the minimum hardness limit; maximum hardness found with Brand-05.

Thickness test

The thickness of tablets is critical to their therapeutic effectiveness and also by monitoring the thickness at regular intervals, potential problems relating to tablet weight and hence content uniformity can be detected at an early stage.

Table 3: Thickness of various brands of atenolol tablets

Sample code	No. of tablets	Thickness (Kg) ± SD	Inference
Brand-01	10	3.06 ± 0.02	Satisfied
Brand-02	10	3.74 ± 0.06	Satisfied
Brand-03	10	3.95 ± 0.07	Satisfied
Brand -04	10	4.06 ± 0.01	Satisfied
Brand-05	10	4.02 ± 0.05	Satisfied

Friability test

The friability test is mostly important criteria for uncoated tablets (during and after manufacture) to examine that the tablets have a good withstand strength for transportation, packaging, shipping and coating. The friability values of <1% are considered to be highly satisfactory evaluation characteristics and our all brands satisfied this specification.

Table 4: Friability (% loss) of atenolol tablets

Sample Code	No. of tablets	Initial weight (mg)	Final weight (mg)	Friability (%)	Inference
Brand-01	5	829.2	829.1	0.012	Satisfied
Brand-02	5	973.5	973.4	0.01	Satisfied
Brand-03	5	1054	1054	0.00	Satisfied
Brand-04	5	1094.8	1094.6	0.018	Satisfied
Brand-05	5	872	871.9	0.011	Satisfied

According to British Pharmacopoeia 2009 normal compressed tablets that losses less than 1% of weight are considered satisfactory. The result showed that all the five brands conformed to the BP standard limits, where maximum weight lost attained is only 0.018% by brand 04.

Disintegration test

The tablets must to be disintegrated within the acceptable time, otherwise, the prescribed course is affected and also the drug might not exert its effect properly. The disintegration time of our five brands are shown below.

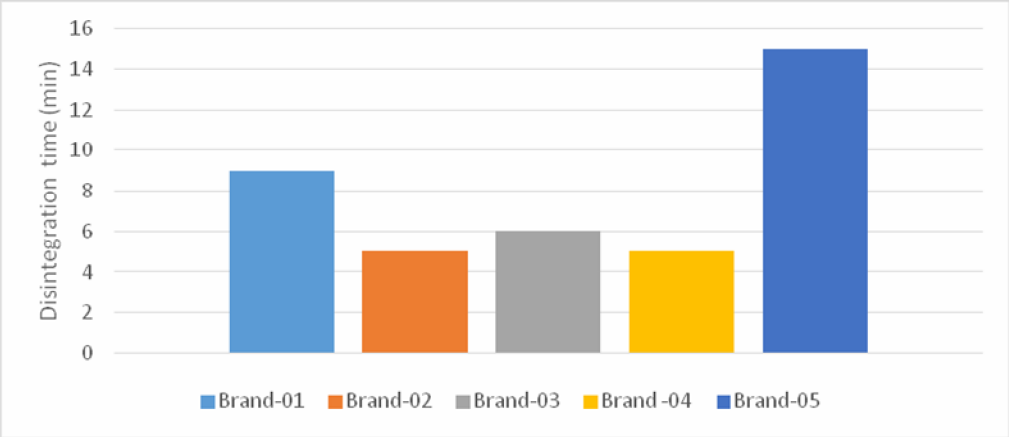

Figure 3: Disintegration time of various brands of atenolol tablet

According to British Pharmacopoeia 2009, uncoated tables should be disintegrated within 15minutes. The graph shows that all five brands conformed to the BP standard limits, where maximum disintegration time attained is 15min by Brand-05.

Dissolution test

The dissolution rate of five brands of atenolol tablets was determined using 0.1N acetate buffer pH 4.6 as dissolution media, which are listed below.

Table 5: Dissolution rate of atenolol tablet

Sample Code	Drug Release (%)			USP Specification
	After 15 Minutes	After 30 Minutes	After 45 Minutes	
Brand-01	78.21	91.08	99.09	Satisfied
Brand-02	77.76	94.77	100.01	Satisfied
Brand-03	78.11	88.11	100.98	Satisfied
Brand-04	81.18	90.09	99.67	Satisfied
Brand-05	85.19	92.21	99.23	Satisfied

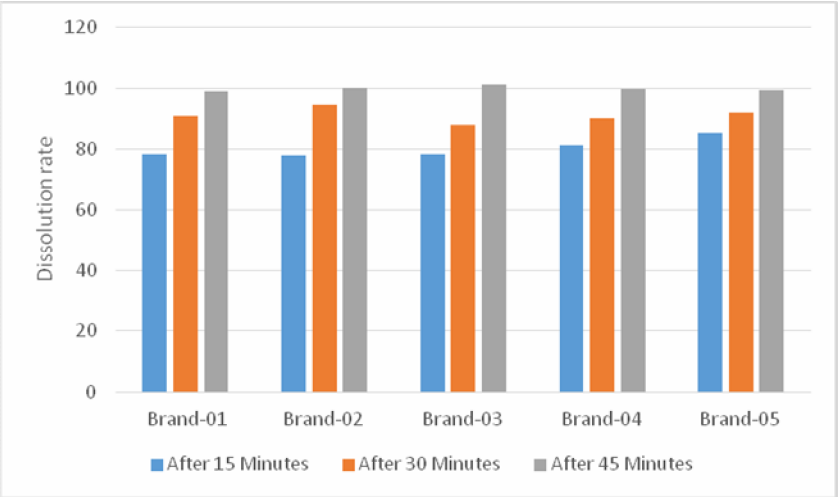

Figure 4: Dissolution rate of various brands of atenolol tablet

USP specification: More than 80% of the labeled quantity of atenolol should be dissolved within 45 minutes. Above table shows that all five brands satisfied the USP specification.

Discussion

The visual organoleptic characteristics of all the selected brands were got in fairly good form where each single tablet were devoid of any cracks, damaged & pinholes. Additionally, the color, texture and surface smoothness were uniform within a batch of each brands. For comparatively study, physicochemical parameter such as weight variation test, thickness, hardness test, friability and disintegration check were executed.

The Table 1 provides information about the average weight of atenolol tablet and % weight variation. According to USP all the five brands of tablets comply with specification, where maximum weight variation observed only ±5.19% by Brand-05.

Hardness and Thickness of various brands also found within the acceptable limit (Table 2 and 3). All the brands pass the minimum hardness limit where the maximum hardness was found with Brand-05 (7.07 Kg). Variation of thickness was also minimum within brands.

From the friability test (Table 4), it appears that all the 5 brands complied with the BP/USP specification of friability, where friability of Brand-04 were maximum which was only 0.018%. Tablet friability may be profoundly affected by the moisture content of the tablet granulation and the finished tablets. Very dry granulation and tablets containing less than 0.5 to 1.0 % of moisture may be much more friable than tablets containing 2 to 4 % of moisture[16].

According to British Pharmacopoeia 2009, the film coated tablet should be disintegrate entirely within 30 minutes and uncoated tablet should be disintegrate entirely within 15 minutes. It is seen from the disintegration test (Table 3) that not any of the tablets exceeded the specification for disintegration time. Thus, we can conclude that all the selected brands fulfilled the BP/USP specification for tablet disintegration time.

According to the USP specification, not less than 80% of the labeled amount of atenolol need to be dissolved in 45 minutes. The dissolution test results (Table 4) shows that every sample meet the USP specification for tablet dissolution rate. The absorption rate of drug is evaluated by the degree of drug dissolution from the dosage form. For this reason, *in vitro* drug dissolution rate is important to achieve high peak blood levels for a drug. Good co-relation exits between in vitro dissolution rate and *in vivo* bioavailability of a tablet product. Tablet has high *in vitro* dissolution rate shows high *in vivo* bioavailability[17].

Conclusion

It is concluded that the results of all the tests (weight variation test, hardness, thickness, friability, disintegration test and dissolution test) of selected brands of atenolol exhibits some differences but these variations are in specified limits. All the five brands evaluated could be considered pharmaceutically equivalent and hence patients can simply choose anyone of the above brands. Additionally in future bioavailability and bioequivalence studies could be done for better understanding on the potency and safety of the marketed products of atenolol.

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References

1. *Alfred GG, Joel GH, Lee EI, The Pharmacological basis of therapeutics, (Eds 10), McGraw-Hill Companies Inc. USA; 2001, pp 249 –256.*
2. *Martindale. The Extra Pharmacopeia, (Eds 35), Vol. I, Pharmaceutical Press, London, 2007 pp 1093.*
3. *Lachman L, Libermann AH, Kanig JL, The Theory And Practice Of Industrial Pharmacy, Lea and Febiger, Philadelphia; 2nd Edition 1976, pp 293-345.*
4. *Shah HK, Generic captures new prescription markets. Perspectives in Pharmacy Economics vol **4:** 3, pp 199.*
5. *Awofisayo OS, Oladoja AA, Nse E, Imo EU. Comparative Assessment of the quality control measurements of multisource ofloxacin tablets marketed in Nigeria. Dissolution Technologies 2010. Vol 6, pp20-25.*
6. *Esiomone CO, Okoye FBC, Onah BU, Nworu CS, Omeje EO. In-vitro bioequivalence study of nine brands of artesunate tablets marketed in Nigeria. J.Vector Borne Dis. 45:60-65 (2008).*
7. *Pamula RB, Surender G, Reddy KVS, Ujwala P, Jyosthna G, Kumar RM. Comparative in vitro evaluation of commercial metformin HCL tablets. JITPS 1:152-157 (2010).*
8. *Adegbolagm OA, Olalade OA, Osumah SE, Comparative evaluation of biopharmaceutical and chemical equivalence of some commercially available brands of ciprofloxacin hydrochloride tablets, Tropical Journal of Pharmaceutical Research; Sep 2007, Vol.6(3), pp737-745*
9. *Anonymous. Hardness or Crushing strength, Pharmainfo.net, 1, 2008, 1-4.*
10. *The United States Pharmacopeia, Revision Bulletin <701> Disintegration issued June 6, 2008, and official August 1, 2008.*
11. *British Pharmacopoeia 2000; Version 4.0; May 2000; The Stationary office (general notices section, CD-ROM ver.).*
12. *Brahmankar DM, Sunil BJ, Bioavailability and bioequivalence Biopharmaceutics and pharmacokinetics – A Treatise, 1st Edition, Vallabh Prakashan, New Delhi, India; 1995, pp296-302.*
13. *The United States Pharmacopeia 30- National Formulary 25, May 1, 2007.*
14. *Aziz MABA, Comparative evaluation of physicochemical properties of some commercially available five leading brands of Atenolol tablets marketed in Kualalumpur, B.Pharm dissertation, International Medical University, Malaysia, November 2013, pp12.*
15. *Murtha JL, Julian TN, Radebaugh GW. Simultaneous determination of pseudoephedrine hydrochloride, chlorpheniramine maleate, and dextromethorphan hydrobromide by second-derivative photodiode array spectroscopy. Journal of pharmaceutical sciences. 1988 Aug 1;77(8):715-8.*
16. *Gilbert S. Banker, Tablet and Tablet product design. In Sprowls' American Pharmacy (Lews W. Dettert), J. B. Lippincott Company, Philadelphia, USA 7th Edition, 1971.*
17. *Tripathi KD Histamine, 5-Hydroxytryptamine and their Antagonists. In: Essentials of Medical Pharmacology, Jaypee Brothers, New Delhi, 4th Edition, 19*