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QUALITY ANALYSIS OF DIFFERENT MARKETED BRANDS OF ATENOLOL (50 MG) TABLETS AVAILABLE IN SYRIA AND COMPARING WITH THE REFERENCE DRUG

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ABSTRACT

There are numerous generics of atenolol tablets available in Syria. The purpose of current study is to assess the physicochemical characters of four brands(A, B, C, D) of atenolol(50mg) tablets advertised in Syria and comparing these properties with reference drug(E). The physicochemical equivalence of brands of atenolol tablets were evaluated through performing hardness, friability, weight variation, content uniformity, and dissolution rate tests. The highest values of hardness are founded in tablets brand A while other brands are nearest in hardness to reference drug. All tablets meet the specifications for friability, and weight variation tests. The content values for three brands (B, C, E) are included in the range (90-110%) according to USP specifications, while brands (A, D) failed the test. Brands (B, D, E) released more than 80% of drug in 30 minutes while brands (A, C) release less than 80%, so brands (B, D, E) passed USP specifications, While brands (A, C) failed this test.

KEYWORDS: Atenolol, Hardness, Weight Variation, Content Uniformity, Dissolution Test.

INTRODUCTION

Quality control is an essential part of quality assurance which used to guarantee acertain level of quality in a product. Quality control is the checking process through which manufacturer evaluates real quality performance of their product, comparing it with standards and also finds out the deviation from standard to ensure the quality of product (Chow, 1997; Miller, 1990). Many countries do not own an effective means of monitoring the quality of generic

drug products in the market (Tiola, 1996). As a result, the counterfeit drug products will distribute(Meyer, 1999). Monitoring of drugs in the market is vital. WHO has issued many procedures for global standard and requirements for the assessment, authorization, registration, marketing as well as quality assurance of the drug products (Sweetman, 2002). Monitoring marketed drugs can lessen a country's economic problem as well as health issues due to fraud and substandard drugs usage.

Atenolol is considered asβ-1 heart adrenergic receptor hindering drug. It does not steady on the cell membrane and doesn't have any activity as fractional agonist in other parts of the body.It is used in the treatment of hypertension and ischemic heart disease.

Atenolol chemically has thestructure of benzene acetamide, 4-[2 –hydroxy –3 –[(1- methyl ethyl) amino] propoxy] as shown in figure 1. its solubility in water about 26.5 mg/ml at 37ºC. it has a log partition coefficient (octanol/water=0.23).it is freely soluble in 1N HCL(300mg/ml at 25 ºC).

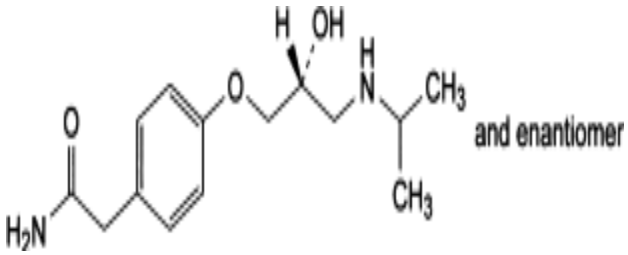

Figure 1: chemical structure of atenolol.

This study aims at evaluating the physicochemical properties of four brands of atenolol tablets marketed in Syria and comparing their properties with the reference drug.

MATERIALS AND METHODS

Four commercial brands (A, B, C, D) of atenolol tablets were randomly selected, reference drug (E). atenolol brands having label strength of 50 mg. The reagents used were hydrochloric acid, sodium acetate, acetic acid.

Hardness test

Hardness test is done to evaluate the prerequisite for pressure adjustment on the tableting machine. 10 tablets were taken from each brand, and the crushing strength that just caused the tablet to break was recorded.

Friability test

The friability test is strongly related to tablet hardness. At first 20 tablets were taken from each brand and the tablets were carefully dusted prior to testing. Then the tablets were weighed which was considered as the initial reading. After that, all the tablets were placed in the device of friability tester and rotated 100 times. After 100 revolutions, then tablets were removed and re-weighed. The percentage was calculated. According to BP the tablets should not lose more than 1% of their total weight (BP, 2009).

Weight Variation

Weight variation test is a very important quality control parameter because it is related with the content uniformity of a drug. It was done by calculating the% of weight variation for 20 tablets of each brand usingthe following formula

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

Not more than two of the individual weights deviated from the official standards BP pharmacopeia (BP, 2009).

Uniformity of content

Uniformity of content is the chemicalcharacteristic of a dosage form. Uniformity of content tests are assay to estimate the quality and quantity of active ingredient in the drug. Quantitative tests such as chemical, physical, pharmacological, biological or microbiological means yield the strength or potency of the drug substance.

10 tablets were taken from each brand. Each tablet was crushed and dissolved separately using a combination of manual agitation and sonication techniques in 50 ml of 0.1N hydrochloric acid. Then the samples were mixed well before filtration through a membrane filter. The samples of each solution were assayed for drug concentration using spectrophotometer at 225 nm.

Several measures were calculated in order to assess the amount and acceptability of variations in drug content. Individual values for eachtablet should be in the range of 90-110% atenolol (proxy USP specification for drug content) (USP, 2013).

Calibration curve of atenolol in 0.1N acetate buffer(PH=4.6)at 240 nm

A standard curve was created for atenolol using pure drug powder diluted to 5 known concentrations (range between 4.8 - 45 µg/ml).

Dissolution Test

Dissolution testing is done to formulate the drug dosage form. Generally dissolution test is performed by using Dissolution Tester-USP 900ml of acetate buffer(pH= 4.6) was used as dissolution medium. The USP Apparatus 2 paddle was used at 50 rpm. 6 tablets from each brand were examined. the percentage (%) of drugrelease was calculated. Atenolol tablets must release 80% of drug within 30 minutes (USP, 2013**).**

RESULTS AND DISCUSSION

Hardness and friability tests

It is essential that the hardness of the tablets are within certain range according to the types of tablets. This results indicates that brand A had the highest crushing strength of all the brands with hardness of 18.35KP and other brands had near values of hardness to reference drug (Table1).

Tablets should have the ability to resist abrasion when they are subjected to stresses from collision and tablet sliding towards one another and other solid substances, which can result in the removal of small fragments and particles from the tablet surface. The results of tablet friability test show that virtually all the tested brands had impressive friability values ranging from 0.01% to 0.22%w/w (Table 1). According to BP no batch should have a friability value greater than 1.0%w/w; therefore, all the brands passed the test.

Table 1: Hardness and friability of atenolol tablets.

Brand	Hardness(kg/cm^2)±SD N=10	Friability(%) N=20
A	18.35±0.92	0.01
B	6.51±1.01	0.19
C	7.23±0.86	0.04
D	5.76±1.21	0.22
Reference drug (E)	6.34±0.91	0.17

Weight Variation

The combined effect of the weight variation test is to ensure that all tablets in a batch are within the reasonable limits, of the same batch. All the individual weights deviated from the official standard less than±5%, so all the brands passed the test for weight variation (Table 2).

Table 2: Weight variation ofatenolol tablets.

Brand	Measured weight mean (mg); N=20	Deviation range (%)	RSD (%)
A	206.17	-4.34 – 3.78	4.55
B	206.31	-2.43 – 2.76	2.32
C	230.11	-3.11 – 2.95	2.67
D	224.51	-3.65 – 4.02	3.09
Reference drug (E)	210.32	-2.56 – 2.11	2.12

Calibration curve of atenolol in hydrochloric acid(0.1N) at 225 nm.

A linear relationship between the absorbance and the concentration of atenolol in hydrochloric acid(0.1N) at 225 nm in the concentration range of 5 - 40µg/ml is observed. The regression equation is Y= 0.019X+0.0901 and the correlation coefficients (r) of the linear regression of the calibration curves is 0.9979 as shown in figure 2.

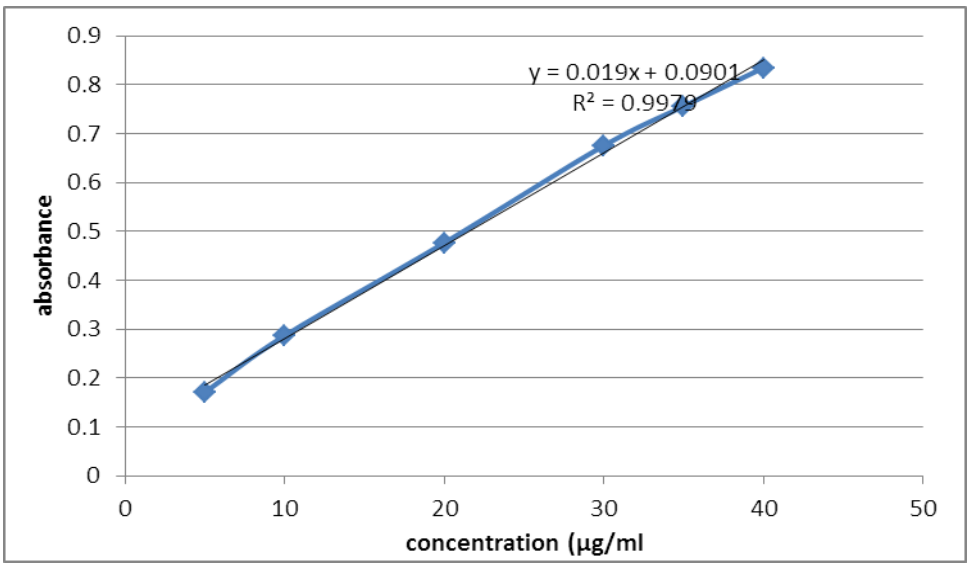

Figure 2: Calibration curve of atenolol in hydrochloric acid.

Uniformity of content

The results obtained from evaluation the percentage content of atenolol in the tablets showed that brands (B, C, E) gave values within the USP monographspecifications (90-110%) while brands (A, D) failed the test with values outside of proxy USP specification in all tablets (table 3). Brand C was the nearest in content to reference drug.

Table 3: Content uniformity of atenolol tablets.

Brand	Measured drug content mean (mg); N=10	Percent of content mean (%); N=10	RSD (%)
A	42.11	84.22	4.65
B	47.43	94.86	3.54
C	48.98	97.96	2.98
D	43.19	86.38	3.31
Reference drug (E)	49.75	99.5	2.45

Calibration curve of atenolol in 0.1N acetate buffer(PH=4.6)at 240 nm

A linear relationship between the absorbance and the concentration of metformin hydrochloride in acetate buffer(PH=4.6) at 240 nm in the concentration range of 4.5- 45µg/ml is observed. The regression equation is Y= 1.0162X+0.0998 and the correlation coefficients (r) of the linear regression of the calibration curves is 0.0.9991 as shown in figure 3.

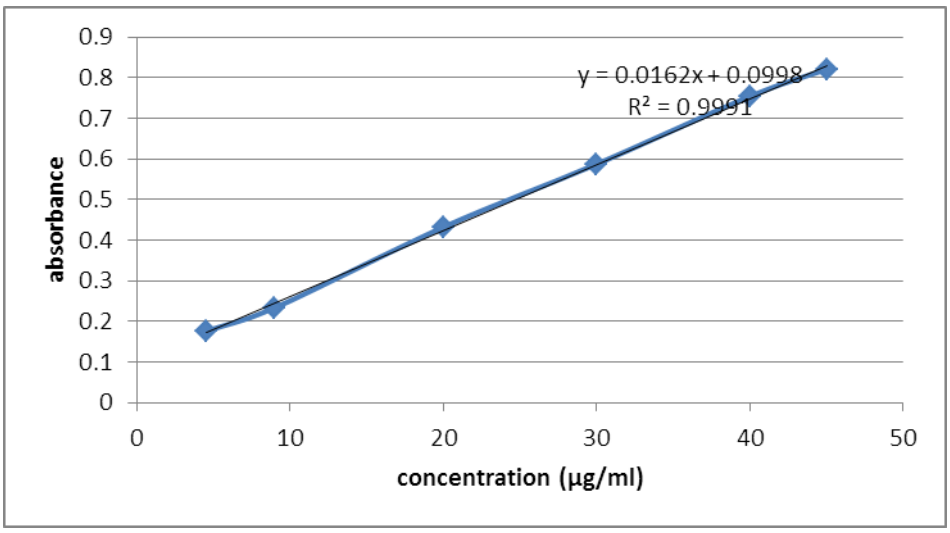

Figure 3: Calibration curve of atenolol in acetate buffer.

Dissolution test

Dissolution test is an important parameter for assessing drug release from pharmaceutical dosage forms. It is used as an indirect method of measuring drug availability. A fast dissolving tablet gets dispersed quickly and release the drug easily. Figure 4 shows the cumulative percentage of atenolol released from the different brands. The brands were found to follow the following dissolution order E> D> B> C> A. The dissolution profiles shows that brands E, D, B release at least 80% within 30 minutes, so these brands passed USP specifications for dissolution test, while brands A, C release less than 80%within 30 minutes,

so these brands failed the test. Brand C was the nearest in dissolution test to reference drug (Kishore, 2011; Kalakuntla, 2010; Aulton, 2001).

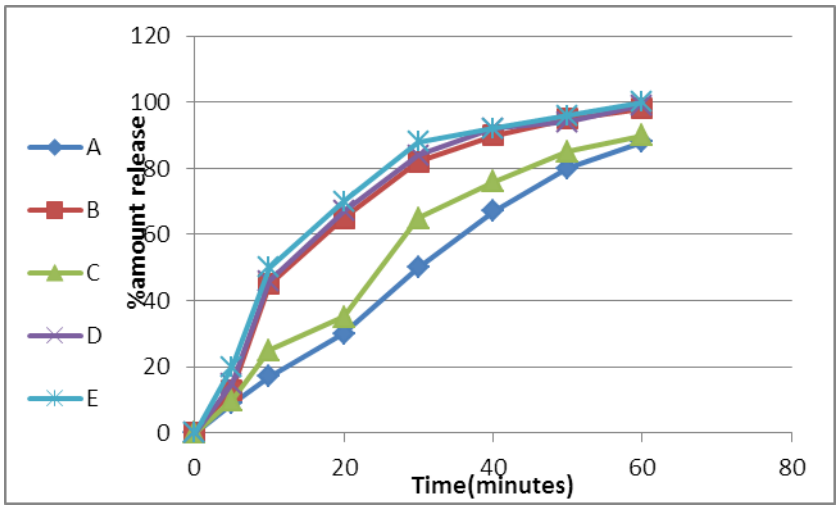

Figure 4: dissolution profiles of atenolol tablets.

CONCLUSION

From the above results, all the studied brands of atenolol passed the test for friability (less than 1%). The values for hardness of all brands are nearest to reference drug except brand A. All brands passed the test for weight variation. Brands (B, C, E) gave values for content within the monograph specifications (90-110%), while brands (A, D) failed the test with values outside of proxy USP specification. In dissolution test brands (B, D, E) release at least 80% of drug within 30 minutes, so these brands passed USP specifications, While brands (A, C) failed this test.

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