OPEN ACCESS

ORIGINAL ARTICLE

Pharmaceutical Analysis of Different Brands of Solifenacin Tablets Available in Pakistani Market

Muhammad Raza[1], Syed Baqir S. Naqvi[1], Muhammad Iqbal Nasiri[2,*], Tariq Ali[3], Kamran Zaheer[1], Ali Saleem[1], Humera Sarwar[1], Muhmmad Azeem[2]

[1]Department of Pharmaceutics, Faculty of Pharmacy, Hamdard University, Karachi, Pakistan
[2]Hamdard Institutes of Pharmaceutical Sciences, Hamdard University, Islamabad Campus, Pakistan
[3]Department of Pharmaceutics, Faculty of Pharmaceutical Sciences, Dow University of Health Sciences, Karachi, Pakistan

Author`s Contribution
All the authors contributed significantly to the research that resulted in the submitted manuscript.

Article info.
Received: April 25, 2018
Accepted: May 21, 2018

Funding Source: *Nil*
Conflict of Interest: *Nil*

Cite this article: *Raza M, S.Naqvi SB, Nasiri MI, Ali T, Zaheer K, Saleem A, Sarwar H, Azeem M Pharmaceutical Analysis of Different Brands of Solifenacin Tablets Available in Pakistani Market. RADS J. Pharm. Pharm. Sci. 2018; 6(2): 152-156.*

****Address of Correspondence Author:***
iqbalnasiri@hotmail.com

ABSTRACT

Objective: The current study was designed to evaluate and compare the quality and physiochemical characteristics of three different most commonly used brands of Solifenacin (10 mg) tablets available in Karachi, Pakistan.

Methods: Both the official and non-official tests were applied for the assessment of physical tests, such as hardness, thickness, weight variation, friability, disintegration and chemical tests like dissolution profile and assay using already reported HPLC method. Model independent approach like similarity factor (f_2) was also applied to compare the dissolution profile of generic drug products with reference (innovator).

Results: The results of physical and chemical test showed that that all brands of Solifenacin were within the specified limits. The amount of Solifenacin in all three brands was within the USP specification of not less than 80% at 45 minutes. Similarly, the value of f_2 indicated that all the brands were found to be similar with reference (innovator).

Conclusion: This study will help physicians and pharmacists for the selection of most appropriate quality brand for the treatment of active urinary bladder and in-continence episodes of urination.

Keywords: Solifenacin, pharmaceutical analysis, quality parameters, HPLC method.

INTRODUCTION

In Pakistan, about 77% of medicines are out of budget for patient; the subjects of access and affordability need to be set on by introducing generic medicines, a major cost suppression tactic used in the world. The cost of drugs, availability and reasonable price is a controversial case in any nation's health care system [1]. Many research articles revealed that physicochemical evaluation of different quality parameters was required to understand the pharmaceutical equivalence of drugs [2-5].

The prevalence of overactive bladder is a main concern in the senior citizen and women of local public, more specifically un-awareness of precaution after multiple pregnancies and life style modification with the passage of age [6]. Over active bladder is capable to serious distraction in quality of life which is difficult to treat with life style modification. The frequency of urination will be increases with the passage of time with same life style, the only few anti-cholinergic agent available in the market, become less effective with the passage of time [7]. The only few new anticholinergic agent are available with effective detection, development and result but are not in compliance with patient in the sense of

pharmacoecnomics [8]. Several brands are available in the market which makes it difficult to select safe, effective and cost effective brand. Product quality is the key issue for the selection between brands of same generic [9].

Comparison of quality control parameters of different brands have been conducted by different researchers [10-12]. However, no comparison of quality control parameters of Solifenacin brands has been conducted in Pakistan.

Therefore, the current study was performed to evaluate and compare the quality control parameters as well as cost analysis of Solifenacin 10 mg tablets of three available brands. The brands were collected from different retail pharmacies of Karachi, Pakistan. The physical and chemical tests such as hardness, friability, weight variation, disintegration time, dissolution, and assay were performed, as per USP specifications and non-compendial limits. This study will be useful in cost effective treatment of active urinary bladder and in-continence episodes of urination by selecting low cost brand having same quality standards.

METHODOLOGY

Solifenacin was purchased from the Naveer Abeer Trading and Supply. Acetonitrile (HPLC grade) and water (HPLC grade) were purchased from Merck (Darmstadt Germany). Triethylamine (AR Grade) and ortho phosphoric acid (AR Grade) were procured from Sigma-Aldrich (St. Louis, MO, USA). All other chemical used were analytical grade.

Apparatus used were analytical balance (Sartorius, Germany), Tablet hardness tester (Erweka, Germany), Disintegration test apparatus (ED2-SAPO, Electrolab, India), Dissolution test apparatus USP apparatus II (708-D, Agilent California, US), Friabilator (Co-D2800, Bermen, Germany), Sonicator (Isolab, Germany), 0.45µm Nylon membrane filtersand Magnetic stirrer (Isolab, Germany). The HPLC system (Shimadzu, Tokyo, Japan) consisted of a pump (LC-20AT; Tokyo, Japan), an auto-sampler (SIL-20AHT; Tokyo, Japan), and a UV detector (SPD-20A; Tokyo, Japan).

Sample Collection

Three (3) different national and international brands of Solifenacin 10 mg tablets were collected from retail pharmacies located in Karachi, Pakistan. The collected brands were coded as B1, B2 and B3, presented in Table **1**.

Physicochemical Assessment of Brands

The collected brands were selected for the comparative study of different quality control parameters such as disintegration time, weight variation, hardness, friability, dissolution and assay of Solifenacin content.

Disintegration Time

Six tablets from each brand were randomly selected to determine the disintegration time using disintegration apparatus (ED2-SAPO, Electrolab, India). The purified water maintained at 37±2°C was used as a medium. The time was noted at which the tablet was completely disintegrated. The disintegration time of each brand was compared with the maximum acceptable limit of Pharmacopeia [13].

Weight Variation Test

20 tablets of each brand were selected randomly and weighed using an electronic analytical balance (Sartorius, Germany), and the test was performed according to the official method [13]. The weight of each tablet was recorded in milligrams (mg). The mean and standard deviation was calculated by using Microsoft Excel 2016.

Hardness Test

Hardness test was performed on 20 tablets using Hardness tester (Erweka THB325, Germany) in kilogram per centimeter square (kg/cm^2) and the data was statistically analyzed using control chart.

Friability Test

Friability test on twenty tablets was performed by using friabilator (Erweka GmbH D-63150, Germany), rotated at speed of 25 rpm for 4 minutes. After 4 min, the tablets were reweighed and percentage friability was calculated by the following formula.

$$\text{Friability (\%)} = \frac{\text{(Initial Weight-Final Weight)}}{\text{Initial Weight}} \times 100$$

---------- Eq.1

The Acceptance criteria: % friability less than 1% is considered acceptable.

Assay of Brands

10 tablets of Solifenacin10 mg were crushed into a uniform powder using mortar and pestle to evaluate for their drug content. An amount of 250 mg of the homogenized powder (equivalent to 1 tablet) was accurately weighed and transferred into a 50 mL

volumetric flask. An aliquot of 15 mL of diluent was added, sonicated (Isolab, Germany) for 10 minutes and stirred (Isolab, Germany) for 30 minutes. The volume was made up to the mark with the same diluent and mixed. Then, transferred 5 mL of above solution into a 100mL volumetric flask and was made up volume with diluent, mixed and filtered through membrane filter having 0.45-micron pore size. After filtration and appropriate dilution to 100 µg/mL, the sample was injected into HPLC system (Shimadzu, Tokyo, Japan) consisted of UV detector. The mobile phase consisting of triethylammonium phosphate buffer (adjusted using 30% v/v of ortho-phosphoric acid pH 3.5): acetonitrile in the proportion of 30:70 v/v. The mobile phase was set at a flow rate of 1.0 mL/min and the volume injected was 20µl. The detection wavelength was set at 210 nm and run time was observed about 4.0 minutes. The content of Solifenacin was assessed in comparison with the reference working standard solution having the same concentration of100 µg/mL [14].

Single Point Dissolution Studies

The dissolution test was performed using dissolution USP type II(Paddle) apparatus, using the dissolution method described by US Food and Drug Administration [15]. Six tablets of each brand were selected and put one tablet into each bowl of dissolution apparatus. The bowl was filled with the 900 ml of purified water maintained at 37±0.5 ^{o}C and paddle was agitated at 50 rpm. The samples were collected from each bowl at 45 minutes and filtered using Whatman filter paper. The dissolved amount of Solifenacin was quantified using HPLC system consisted with UV detector using dissolution medium as a blank under the parameters as defined in assay method [14].

Model Independent Approach

The model-independent method i.e. similarity factor (f_2) was also applied to evaluate the release pattern of the drug from each brands as compare to reference, using MS Excel (DD Solver). The brand B1 (innovator) was used as a reference to assess the similarity of different brands in their dissolution pattern.

RESULTS & DISCUSSION

Assessment of Physicochemical Properties

The brands B2 and B3 having variable price ranges were used as test brands, whereas, the innovator brand B1 was considered as reference.

The labeling information of all brands are shown in Table **1**. All the three brands were evaluated for their physical and chemical properties such as, disintegration time, weight variation, hardness, friability and assay. Hardness of all brands was found satisfactory and the values were found to be 12.65 – 25.8 kg/cm^2 as shown in Table **2**. Similar findings were also reported by Hussain et al. [16] and Oishi et al. [17]. Weight variation test of all brands were also determined and the results were found within the described USP specification of ± 7.5 % (Weight more than 130 and less than 324 mg), as mentioned in Table **2** [18]. The friability test results of all brands were less than 1 % and was also found within the limits specified in pharmacopeia [18].

In-Vitro Disintegration Test

The disintegration time was not more than 30 minutes and was found in the range of 10 – 11 minutes (Table **2**), indicating that all brands complying the USP acceptance limits [18]. Results showed that B3 took more time (11 min.), while, B2 took least time (9.5 min.) to disintegrate. This slight variation may be due to differences in their formulation composition.

Table 1. Labeling information of all three brands of Solifenacin 10 mg tablets.

Brand Code	Manufacturing Date	Expiry Date	Retail price per pack (28 tablets)
B1	01-2017	01-2019	Rs 5000 (approx)
B2	01-2017	01-2019	Rs 715 (approx.)
B3	09-2016	09-2018	Rs 1233 (approx)

Assay of Solifenacin Tablets

Assay of Solifenacin10 mg tablets was performed using already reported HPLC method [14]. The assay results of all brands were found in the range of 98.77 to 100.21%, as illustrated in Table **2**. The results were found within the pharmacopoeial limits of 90 – 110 [18].

Table 2. Physicochemical properties of Solifenacin 10 mg tablets.

Brand Code	Hardness**(kg/cm2)	Weight Variation Test**(mg)	Friability** (%)	Disintegration test*** (min.)	Assay*(%)
B1	20.694 ±3.248	247.82± 10.283	0.215 ± 0.16	10.5± 0.29	100.21± 0.65
B2	21.585 ± 2.096	249.25± 5.240	0.326± 0.22	9.5± 0.32	98.88± 0.28
B3	19.655 ±5.113	248.85± 11.138	0.176± 0.20	11.0 ± 0.25	98.77± 1.05

In-Vitro Drug Release Studies

Single point dissolution study was performed for comparison of all the three brands by using the USP dissolution type II apparatus, rotated at 50 rpm. The samples were withdrawn after 45 minutes. The dissolution medium and time points were selected based on the FDA recommendation for Solifenacin tablets [15]. The single point dissolution studies showed satisfactory results of all brands. The results of all three brands were in the range of 98.90 to 99.83% as shown in Table **3**. There was no any study reported yet, regarding the comparative brand study of Solifenacin tablet.

Table 3. Dissolution of Solifenacin 10 mg tablet and similarity factor (f_2).

Brand Code	At 45 Min.	USP Limits	Similarity Factor (f_2) Values (%)
B1	98.95 %	Not less than 80% at 60 min	Reference (innovator)
B2	96.71 %	Not less than 80% at 60 min	B1 &B2= 55
B3	97.90 %	Not less than 80% at 60 min	B1 & B3= 59

Release Profile Comparison

Model independent approach (Similarity factor -f_2) was applied using MS Excel (DD Solver) to evaluate the release pattern of the drug from each brand as compare to the reference. The brand B1 (innovator) was used

All values are expressed as mean ± SD; *n = 10; ** n = 20; *** n = 6

as a reference to assess the similarity of different brands in their dissolution pattern. Similarity factor (f_2) values of B1 and B2 were found to be 55, whereas, f_2 values of B1 and B3 was 59, indicating that all brands are pharmaceutically equivalent (Table **3**). According to the FDA guidelines, if the values of f2 are within the range of 50 – 100%, it indicates equivalence and if the values are less than 50%, then, there is no similarity between two dissolution profiles.

Price Variation

The price list of different brands is presented in Table **1**. Brand B1 (innovator) is very costly as compare to other two brands (B2 and B3), indicating that there is a significant variation in the price of three brands of Solifenacin tablet (PKR 715 to 5000). The above discussion showed that brand B2 and B3 showed similar results as compare to the reference brand (B1), not only in physicochemical studies but also in quality control analysis. Therefore, the brand B2 and B3 can be used despite of brand B1 as it is highly expensive than other two brands.

CONCLUSION

Comparative physicochemical evaluation of three brands of Solifenacin 10 mg tablet was conducted. The quality of brands in terms of weight, hardness, friability disintegration, dissolution and assay were assessed and found comparable. Test brands (B2 and B3) were found similar with reference brand (B1). A major variation in price within the same generic brands of Solifenacin 10 mg tablet was observed from 715 to 5000 Pakistani rupees/28 tablets' pack (US $ 5.77 – 40.34) approximately. Therefore, it was concluded that the cost effective drug/brand can be prescribed and used in place of costly brand.

ACKNOWLEDGEMENT

The authors are especially thankful to Head of Pharmaceutics department, Faculty of Pharmacy,

Hamdard University Karachi and Islamabad Campus, Pakistan for providing the research facilities, equipment, and their valuable guidance, support, and cooperation.

REFERENCES

1. Carstensen JT. Advanced pharmaceutical solids. CRC Press; 2000 Oct 24.
2. Kahsay G, Debella A, Asres K. Comparative in vitro quality evaluation of ciprofloxacin tablets from drug retail outlets in Addis Ababa, Ethiopia. Eth Pharm J. 2007; 25:1-8.
3. Ashour S, Al-Khalil R. Simple extractive colorimetric determination of levofloxacin by acid–dye complexation methods in pharmaceutical preparations. Il Farmaco. 2005;60(9):771-5.
4. Furlanut M, Brollo L, Lugatti E, Di Qual E, Dolcet F, Talmassons G, Pea F. Pharmacokinetic aspects of levofloxacin 500 mg once daily during sequential intravenous/oral therapy in patients with lower respiratory tract infections. Journal of Antimicrobial Chemotherapy. 2003; 51(1):101-6.
5. Lichtenstein SJ, Rinehart M, Levofloxacin Bacterial Conjunctivitis Study Group. Efficacy and safety of 0.5% levofloxacin ophthalmic solution for the treatment of bacterial conjunctivitis in pediatric patients. J AAPOS. 2003;7(5):317-24.
6. Charoo NA, Shamsher AA, Zidan AS, Rahman Z. Quality by design approach for formulation development: a case study of dispersible tablets. Int J Pharm. 2012;423(2):167-78.
7. Kobelt G, Kirchberger I, Malone-Lee J. Quality-of-life aspects of the overactive bladder and the effect of treatment with tolterodine. BJU Int. 1999;83(6):583-90.
8. Brunton S, Kuritzky L. Recent developments in the management of overactive bladder: focus on the efficacy and tolerability of once daily solifenacin succinate 5 mg. Curr Med Res Opin. 2005;21(1):71-80.
9. Bano R, Gauhar S, Naqvi SB, Mahmood S. Pharmaceutical evaluation of different brands of levofloxacin tablets (250 mg) available in local market of Karachi (Pakistan). Int. J. Curr. Pharm. Res. 2011;3(1):15-22.
10. Eichie FE, Arhewoh MI, Isesele JE, Olatunji KT. In vitro assessment of quality control parameters of some commercially available generics of amlodipine besylate in Nigerian drug market. International Journal of Health Research. 2011;4(1):57-61.
11. Garattini L, Tediosi F. A comparative analysis of generics markets in five European countries. Health policy. 2000;51(3):149-62.
12. Shimul FZ. Evaluation of the quality control parameters of different brands of paracetamol available in Bangladesh Pharma market (Doctoral dissertation, East West University).
13. USP32/NF27, General Chapter. 2009.
14. Thota CM, Rathod H, Botumanchi S, Gaddam V, Boddapatti SR, et al. A rapid rp-hplc method development and validation for the quantitative estimation of solifenacin succinate in tablets. Int J Pharm Sci, 2014; 6:201-4.
15. FDA. https://www.accessdata.fda.gov/scripts/cder/dissolution/dsp_getalldata.cfm. 2015.
16. Hussain A, Hanif M, Shoaib MH, Yousuf RI, Ali T, Muhammad IN, Hussain L, Fayyaz M, Shafi N. Comparative Studies of Ciprofloxacin 250 mg Tablets Available in Pakistani Market. Lat Am J Pharm. 2013; 32(4):484-89.
17. Oishi TS, Haque MA, Dewan I, Islam SA. Comparative in vitro dissolution study of some ciprofloxacin generic tablets under biowaiver conditions by RP-HPLC. Int J Pharm Sci Res. 2011;2(12):3129-35.
18. UPS32/NF27, General Chapter. 2009:262.