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A comparative *in vitro* dissolution of different brands of glibenclamide tablets available in Saudi Arabian market

Mohammad Naushad Alam, Amgad A. Awad El-Gied, Mohamed Rahamathulla*, Mohammed Fathey, Mahmoud Abd El Fattah Shaker.

Department of Pharmaceutics, College of Pharmacy, King Khalid University, PO Box 960, Abha, Kingdom of Saudi Arabia.

SHORT COMMUNICATION

*Author for correspondence
E-mail: rahapharm@gmail.com

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ABSTRACT

The main objective of the present study was to evaluate between four different brands of Glibenclamide which are commercially available in the Saudi Arabian market in comparison with innovator products (Daonil tablets). All the marketed brands were evaluated for quality control test such as thickness, diameter, hardness, weight variation, friability, disintegration and in vitro dissolution test. The results revealed that the thickness and diameter of all marketed brands were within 2.75 mm and 2.76 mm respectively. The friability was less than 1% and passes the content uniformity test. All marketed tablets were disintegrated within 5-12 min. The percentage content of different brands of Glibenclamide tablets showed within the monograph specifications. The in vitro drug release of innovator and all the four generic brands of GLB were carried out in phosphate buffer pH 6.8. All the marketed brands show more than 95 % of drug release for 2 hrs. Among all brands Innovator Daonil and Glibil tablet brand show 99% and 98% drug release respectively. The In vitro drug release result shows insignificant differences in dissolution behavior were observed between the innovator and four different generic brands.

Keywords: Glibenclamide tablets, Dissolution test, Quality Control, in-vitro release.

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INTRODUCTION

Glibenclamide is one of the most widely prescribed drugs for diabetic Mellitus. In this research work, the key rationale was to compare the in vitro dissolution study of glibenclamide generic and marketed products. The generic form of the drug should be generally prescribed to decrease the medication cost and make the treatment economical to the patients. In today's time, the most important quality control test for pharmaceutical dosage form is dissolution. Dissolution test is given so much weight as it is useful for predicting bioavailability. A correct definition of substandard drugs is those drugs which fail the quality specification test, consists of more or less concentration of ingredients, traces of contamination, inadequate quality of ingredients used, poor stability and meager packaging quality (Green et al., 2000; Newton et al., 2001). In practice, despite the presence of According to the legislation for bioequivalence, generic products might differ significantly from the reference drug (Genazzani and Pattarino, 2008). It has been reported worldwide, below the standard medicines are available in the market of various countries (Ehianeta et al., 2012; Ehianeta et al., 2009; Smith et al., 20006; Vial et al., 2008).

In this study, the quality of the oral anti-diabetic drug, glibenclamide of different formulations was assessed through direct purchase from local community pharmacies from Saudi Arabia and subjected them to analysis according to united state pharmacopeia (USP).

Another name for Glibenclamide in the USA is glyburide. It has been in clinical use for a long time as in form of sulfonylurea oral hypoglycemic drug (Luzi and Pozza, 1997). It is used for the treatment of non-independent insulin diabetes. Because of low bioavailability, it is associated with poor dissolution properties. GLB has an action in regulation of sugar level by increasing tissue

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sensitivity towards insulin and also stimulating insulin secretion in the pancreas (Harman et al., 1996). GLB is a class II drug according to the biopharmaceutics classifications system (BCS) as it has low aqueous solubility and high permeability.

In the present study, four different brands of GLB tablets (5 mg) in Saudi Arabia was evaluated and compared with the innovator product (Daonil).

MATERIAL AND METHODS

Materials

Four different brands of glibenclamide 5 mg (Table 1) and innovator were taken from a retail pharmacy in Abha city, Saudi Arabia. The reagents used were potassium dihydrogen orthophosphate (WINLAB chemicals, UK) and sodium hydroxide pellets (Poole BH15, UK). All reagents used were of analytical grade.

Table 1. List of the tested commercial Glibenclamide tablets available in Saudi market.

S. No.	Batch number	Brands	Manufacture date and expiry date	Manufacturer
1	5CG6A	Danoil (A)	3/2015, 2/2017	Sanofi-Aventis France
2	9062	Glibil (B)	9/2014, 9/2017	Hikma pharmaceuticals, Jordan
3	FT182	Doabetic (C)	2/2015, 3/2018	KSP, Kuwait
4	83043	Diatab (D)	11/2014, 11/2017	SPIMACO, Saudi Arabia
5	0053	Glymide (E)	3/2015, 3/2019	Gulf Pharma, U.A.E.

Experimental Methods

USP was adopted for testing all commercial available glibenclamide products. Visual inspection, hardness, friability, Weight variation, Content uniformity, disintegration and dissolution tests were performed (Lotfipour et al., 2004; Shruthi et al., 2007; Saisivam, 2013). The details of each test are described.

Quality control test for Glibenclamide

Visual inspection

The shape, size, and color of the different brands of tablets were examined visually. The diameter and thicknesses of 5 tablets from each brand were measured and the average was taken and the standard deviation was calculated:

Friability test

Twenty tablets of each brand were weighed and subjected to abrasion using a Roche friabilator at 100 revolutions for 4 min. The tablets were deducted and weighed again then percent of weight loss was recorded. The friability of the tablets was then calculated using the following expression:

$$\% \text{ Friability} = [(\text{Initial weight} - \text{Final weight})/\text{Initial weight}] \times 100$$

Hardness test

The crushing strength of the tablets was determined using ERWEKA (Heusenstamm, Germany) hardness tester. Sample tablets (10) of each brand were taken, a tablet was placed between the spindle of the PHARMA TEST (Germany) hardness tester machine until the tablet breaks and the pressure required to break the tablet was then read off the machine and recorded.

Content uniformity test

Tablets (20) of each brand were weighed individually using a digital analytical balance. The average weight was determined and the percentage (%) deviation of the individual tablets from the mean was determined.

Disintegration test

Tablet disintegration was determined at 37 °C using PHARMA TEST (Germany) disintegration apparatus. The disintegration time of randomly selected six tablets of each brand was determined in distilled water. The disintegration time was taken to be the time no granule of any tablet was left on the mesh.

In-vitro dissolution study

In-vitro drug dissolution was carried by using USP Type II apparatus (Paddle) in 900 mL phosphate buffer 6.8 pH (ERWEKA DT 600). One tablet was put in each of the basket at 37 ± 0.5 °C, at 100 rpm.5 mL of sample was withdrawn from the basket at different time intervals of 30, 60, 90 and 120 minute and replace a fresh 5 ml dissolution medium. The absorbance was measured at 242nm using UV visible spectrophotometer. The concentration was determined against standard solution having a known concentration of glibenclamide tablets in the same medium.

Assay of glibenclamide tablets

The test for assay is done to find out the actual amount of active ingredient present in the tablet and whether it is the same as the labeled amount. 20 tablets from each brand weighed and finely powdered then an accurately weighed

portion of powder equivalent to 100 mg glibenclamide tablets were transferred to a 100 ml volumetric flask, diluted to 100 ml chloroform. Then 10 ml was transferred to another 100 ml volumetric flask and the volume was completed with chloroform to get 10 µg/ml concentrations. The absorbance of the standard preparation and assay preparation were concomitantly determined at λmax 242nm with UV-3300 PC Spectrophotometer using chloroform as a blank.

RESULTS AND DISCUSSION

The results of quality control test for different brands of glibenclamide tablets were shown in Table 2. All the brands used were within their shelf life as at the time of study. The weight uniformity for all brands of glibenclamide tablets gave values that comply with the USP specification with a deviation less than 5% from the mean value. All the brands of glibenclimide tablets passed the weight uniformity test. The hardness tests on different brands of tablets were performed. All brands of tablets were within the limit of USP. Brand Glymide had the maximum hardness 7.5 kg/cm2, and brand Doabetic had the minimum hardness 5.5 kg/cm2. Hardness of the other brands such as Daonil, Glibil and Diatab were 5.8, 6.3, and 7.2 respectively. The friability test is the most 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. All the tested brands passed the test. The friability was less than 0.2% for all the brands. The disintegration test were performed for the different brands and it was observed maximum disintegration time was for Daitab (12 min) whereas minimum is Daonil (6 mints). The Uniformity of weight of glibenclamide was observed that all the brands passed the test, Diatab showed maximum 1.63 and Glymide with minimum 0.325.

Table 2. Quality control test for different brands of glibenclamide tablets.

S. No.	Brand Name	Content uniformity (mg)	Hardness (kg/cm²)	Disintegration time (min)	Diameter (mm)	Thickness (mm)	Friability (%)
1	Daonil	0.99	5.8	5	2.75	2.76	0.157%
2	Glibil	1.25	6.3	10	2.69	2.70	0.125%
3	Doabetic	1.30	5.5	11	2.70	2.71	0.152%
4	Diatab	1.633	7.2	12	2.72	2.73	0.742%
5	Glymide	0.325	7.5	9	2.56	2.75	0.183%

In drug product development and manufacturing In vitro drug dissolution studies is a vital part and is also used as a quality control tool, to monitor batch-to-batch consistency of the drug release from a product (Qureshi et al., 1999). In in-vitro dissolution testing, the dissolution process is rate limiting step. As a result, the reliability and discriminatory capabilities of dissolution tests for glibenclamide marketed products have attracted much attention in recent years. USP dissolution apparatus Type-I (basket) most widely used dissolution tests for glibenclamide products at stirring rates of 100 or 50 rpm, respectively (Dumont et al., 2007). The stirring rate is proportional to the dissolution rate, since the higher this rate is, the thinner the surface diffusion layer becomes (Banakar, 1992). According to Graffner 2006, the dissolution profiles were produced and compared at a stirring rate of 50 rpm, using the basket method.

In-vitro dissolution was performed for each brand of glibenclamide according to the USP dissolution apparatus (basket) for immediate release dosage forms. An in-vitro dissolution study was carried out in phosphate buffer pH 6.8. The amount of Glb released from each tablet in the dissolution samples were determined by UV-visible spectrophotometer at 242 nm. Dissolution profiles of each product were compared with the innovator to determine the efficacy of the each generic product.

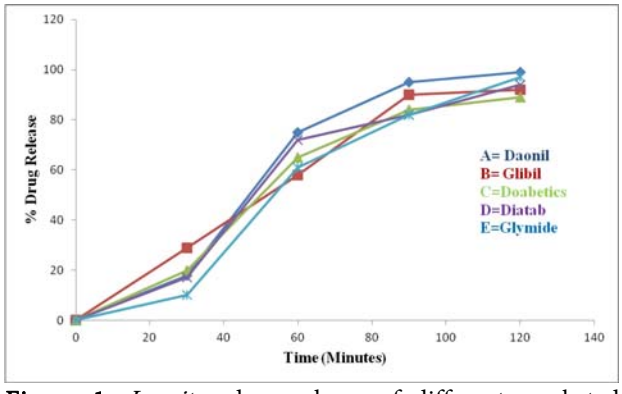

Figure 1. *In vitro* drug release of different marketed brands of Glibenclamide in 6.8 pH phosphate buffer.

Dissolution of drug from an oral solid dosage forms is an important aspect for drug bio-availability. Accordingly, dissolution testing of solid oral drug products has emerged as one of the most important control tests for assuring product uniformity and batch-to-batch equivalence. In order to judge whether these differences in dissolution profiles were significant, all dissolution

profiles were compared to that of the originator (Daonil ®) brand. *In vitro* dissolution methods are developed to assess the potential *in vitro* performance of a solid oral dosage form. In-vitro drug release studies of Daonil brand at 30 mints are less than 20%. At 60 mints 70 %, at 90 mints nearly 80% and at 120 mints more than 99% of drug release was observed. In-vitro drug release studies of Glibil brand at 30 mints is more than 20% ,at 60 mints more than 50% , at 90 mints 80% and at 120 mints 98% of drug release was observed. Invitro release studies of Daobetic brand at 30 mints less than 20%, at 60 mints more than 60%, at 90 mints 70% and at 120 mints 95% drug release was observed. In-vitro release studies of Diatab brand at 30 mints less than 20%, at 60 mints more than 70%, at 90 mints 80% and at 120 mints 97% drug release was observed. In-vitro release studies of Glymide brand at 30 mints more than 10%, at 60 mints more than 60%, at 90 mints more than 80% and at 120 mints 98% drug release was observed. The results obtained from this study exhibit different dissolution profiles shows in Figure 1.

CONCLUSION

Four different brands of Glibenclamide tablets with innovator from the Saudi Arabian market were found to be within the USP specification. The results have shown that all the tested brands satisfied the USP requirements in terms of Thickness, diameter, hardness, friability, disintegration and dissolution. Four generic products could be said to be equivalent to the originator (Daonil).The tested different brands of glibenclamide differs mostly in their dissolution behavior when tested in phosphate buffer (pH 6.8). Among all the brands Daonil showed the maximum drug release more than 99%.

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CONFLICT OF INTEREST

None declared

REFERENCES

Banakar UV. Pharmaceutical dissolution testing. New York: Marcel Dekker; 1992. 437

Dumont ML, Berry MR, Nickerson B. Probability of passing dissolution acceptance criteria for an immediate release tablet. Journal Pharmaceutical Biomedical Analysis. 2007; 44(1):79-84.

Ehianeta T, Williams B, Surakat J, Mohammed N, Anyakora. Quality survey of some brands of artesunate-amodiaquine in Lagos drug market. African Journal of Pharmacy and Pharmacology. 2012;6:636-642.

Eichie FE, Arhewoh IM, Ezeobi OC. In-vitro evaluation of the pharmaceutical quality of some ibuprofen tablets dispensed in Nigeria. African Journal of Pharmacy and Pharmacology. 2009;3:491-495.

Genazzani AA, Pattarino F. Difficulties in the production of identical drug products from a pharmaceutical technology viewpoint. Drugs in R&D. 2008;9:65-72.

Graffner C. Regulatory aspects of drug dissolution from a European perspective. European Journal Pharmaceutical Sciences. 2006; 29(3-4):288-93.

Green MD, Mount DL, Wirtz RA, White NJ. A Colorimetric field method to assess the authenticity of drugs sold as antimalarial artesunate. Journal of Pharmaceutical and Biomedical Analysis. 2000;24: 65-70.

Hardman JG, Limbird LE, Molinoff PB, Ruddon RW, Gilman AG. Eds. Goodman & Gilman's The Pharmacological Basis of Therapeutics, 9th ed.; McGrawHill: New York, 1996;1487–1518.

Lotfipour F, Nokhodchi A, Saeedi M, Norouzi SS, Sharbafi J, Siahi SMR, The effect of hydrophilic and lipophilic polymers and fillers on the release rate of atenolol from HPMC matrices. Il Farmaco 2004;59:819-25.

Luzi L, Pozza G. Glibenclamide: an old drug with a novel mechanism of action. Acta Diabetologica. 1997;34:239-244.

Newton P, Proux S, Green M, Smithuis F, Rozendaal J, Prakongpan S, Chotivanich K, Mayxay M, Looareesuwan S, Farrar J, Nosten F, White NJ Fake artesunate in South-east Asia. Lancet. 2001;357:1948-1950.

Qureshi SA, McGilveray IJ. Typical variability in drug dissolution testing: study with USP and FDA calibrators tablets and marketed drug (glibenclamide) product. European Journal Pharmaceutical Sciences 1999;7:249-58.

Saisivam S, M. Rahamath Ulla, Shakeel F. Development of floating matrix tablets of Losartan Potassium: in vitro and in vivo evaluation. Journal of Drug Delivery Science and Technology. 2013;23(6):611-617.

Shruti C, Gayathri VP, sanjay KMV. Release modulating hydrophilic matrix systems of losartan

potassium: optimization of formulation using statistical experimental design. European Journal of Pharmaceutics and Biopharmaceutics. 2007;66:73-82.

Smith JC, Tarocco G, Merazzi F, Salzmann U. Are generic formulations of carvedilol of inferior pharmaceutical quality compared with the branded formulation. Journal of Current Medical Research and Opinion. 2006;22:709-720.

The United States Pharmacopeia and National Formulary USP 34–NF 29; the United States Pharmacopeial Convention, Inc. Rockville, MD, 2011.

Vial J, Cohen M, Sassiat P, Thiébaut D. Pharmaceutical quality of docetaxel generics versus originator drug product: a comparative analysis. Journal of Current Medical Research and Opinion. 2008;24:2019-2033.