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ORIGINAL ARTICLE

Quality Analysis of Various National and International Brands of Glimepirides Available in Pakistan

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ABSTRACT

Objective: The primary focus of this research is to ascertain that these different generic drug products from national and multinational companies competing in the local market are equivalent in quality.

Material and Methods: A comparative quality analysis was executed on national and multinational brands of glimepiride tablets obtained from local pharmacies of Hyderabad. A cumulative of 6 glimepiride brands were selected and internationally accepted in-vitro tests were carried out at Industrial pharmacy laboratory of Department of Pharmaceutics, Faculty of Pharmacy, University of Sindh, Jamshoro, during time period August 2021 to August 2022 to compare with Pharmacopoeia standards.

Results: All the drug products (Glimepiride tablets) obtained from local market were meeting the standards laid by BP for tests of weight uniformity, diameter, thickness, hardness, friability, disintegration, and content uniformity/assay.

Conclusion: Every generic of glimepiride tablets from various local and multinational manufacturers are pharmaceutical equivalents and can be prescribed interchangeably.

Keywords: National, International, Brand, Glimepiride, Quality, Pharmaceutical Equivalents

INTRODUCTION

Diabetes mellitus is a major metabolic disorder in which carbohydrates, fats and protein metabolism is disordered. It is mainly characterized by elevated levels of glucose in the blood circulation. These elevated levels of glucose are because of insufficient insulin production by β-cells of pancreas or inability of the target peripheral receptor to respond to insulin. Diabetes mellitus is majorly classified into two types i.e., T1DM and T2DM.[1] Diabetes mellitus (DM) has a high global burden and high global incidence. In 2007, Pakistan had 7 million people that have been reported with DM and this figure is forecasted to rise to 14.5 million until 2025.[2] International Diabetes Federation has estimated that >537 M people have diabetes mellitus and by year 2030 this figure will reach to 643 million.[3] For the management of Diabetes mellitus type 2 there are 6 classes of oral antidiabetic medications including sulfonylureas, meglitinides (Glinides), thiazolidinediones, biguanides, dipeptidyl peptidase IV (DPP-IIV) inhibitors and α-glucosidase inhibitors.[4,5]

When a pharmaceutical company develops a new drug, it is written on prescription by the brand name and the innovator company are having propriety rights to make and sell that product for a defined period (around 12 years). FDA demands generic drug products to contain the same API, its strength, dosage form and mode of administration as innovator product. The generic product manufacturers should prove experimentally that its drug product is the similar to the innovator brand. Every manufacturer's packing and testing areas must match the same quality levels as of innovator drug. There is 80-85% less average price of a generic formulation versus its innovator and give less expensive drug products to the patients. But this low price should not mean compromised quality.[6] This availability of many generic drug formulations also escalates the probability of quality compromised products. These generics might not be bioequivalent and have different drug release characteristics and may result in sub optimal effectiveness in the patients.[7] Hence, majority of the physicians in Pakistan consider multinational medicines in their prescriptions but cost effectiveness also remain their consideration. Most of the practitioners also agree that their prescription pattern is derived by medical representatives.[8] This study will help to determine the quality of various brands of Glimepiride single active pharmaceutical ingredient tablets available in the local market. This study will help to find sub-standard or counterfeit medicinal products available in the market. This research will collate the quality of oral antidiabetics from different National(N) and Multinational (MN) pharma companies between their own products as well as against the innovator brand.

MATERIALS AND METHODS

To evaluate the physical and chemical tests such as aesthetic test, weight uniformity, thickness of tablet, tablet diameter, test of friability, hardness, test of disintegration, Dissolution and Content uniformity; British and United States Pharmacopoeia standards/limits were used to compare the results. Prime consideration was conferred to every pharmaceutical product that is already present in the local market. Whereas easy availability and more frequently used preparations of foreign origin were given consideration too. Following are the different brands which were randomly collected as a sample from the local market of Hyderabad for this research. Data presented in this work is from the samples tested during the time period between August 2021 to August 2022 at Industrial pharmacy laboratory of Department of Pharmaceutics, Faculty of Pharmacy, University of Sindh, Jamshoro. One of the specimens collected from market was from Multinational company coded as; Sample 01, while other five collected brands were of National origin and given code names as; Sample 02, Sample 03, Sample 04, Sample 05 and Sample 06.

Aesthetic test: The color and shape of the tablet and any contaminants present in the tablet were evaluated visually. In the case of Film Coated Tablets (FCTs), coating quality was also observed.

Weight Variation: Weighing Balance used for this test was of Shimadzu AY220. For weight variation test, 20 samples (tablets) were taken from their final packaging and then weighed separately. Average weight was calculated by dividing the cumulative weight of all tablets by 20 and upper and lower ranges were obtained. As per pharmacopeial standards not greater than 2/20 tablets shall differ by the permitted range and not even one tablet shall differ by double that percentage of permitted limit. The allowed percentage for tablets containing 80mg or less is ±10%, for more than 80mg and less than 250 it is ±7.5% and for more than 250mg it ±5%.

Dimensions: Equipment used for obtaining dimensions was Digital Vernier caliper. To determine the thickness and diameter 10 samples (tablets) were taken from their final packaging material. Every tablet individually was positioned in middle of the jaws of Vernier caliper and screw was made tight. The tablets were observed did not deviate by ±5% of average thickness of 10 tablets

while the stated diameter can deviate by ± 5% for tablets up to 12.5mm diameter and by ± 3% for tablets

Hardness: Monsanto hardness tester was utilized for obtaining the sample tablets' hardness. To observe the hardness, samples (tablets) were drawn out from their packs. Every tablet separately was positioned in middle of the hardness tester jaws along their long axis parallel. Screw of hardness tester was rotated and force in kilograms needed to crush the sample (tablet) was recorded from the scale of tester. The hardness of each tablet uncoated tablet was observed to deviate by 4-10kg/cm^2.

Friability: Roche friabilitor was used for this test. As the tablets were less than 650mg of weight, a sample of wholesome tablets as close as possible to 6.5 g was measured. The sample tablets were dedusted, weighed out, and put in to the friabilitor's drum. The drum was given 100 rotations, and samples were taken out from drum. All tablets were cleaned from their dust, and then these tablets were weighed with care. A highest loss of weight (from single test or by the mean result of 3 tests) not higher than 1% is considered allowed range.

Disintegration test: Disintegration of tablets was ascertained by USP Disintegration Apparatus. Six tablets from each brand were taken for test. If all tablets disintegrated within specified time limit the test was said to be complied with and if 1 tablet did not disintegrate in allowed time, the test should again be done on 12 more tablets and then disintegration time will be checked. The sample passes the test if at least 16/18 units completely disintegrates. In the disintegration, test distilled water 900ml is used as medium while disintegration time for uncoated tablets is 15 minutes and for film coated tablets it is half an hour and for sugar coated tablets it is one hour. During this test, temperature of the medium is controlled up to 37ºC ±2ºC.

Preparation of Standard solution: Standard solution of 100µg/mL was formulated by sonicating weighed amount of Glimepiride (10mg) in 30 mL of 0.1M NaOH in 100mL volumetric flask and quantity sufficient methanol was added. Aliquot of standard solution were taken in 100mL volumetric flask and mixed with enough methanol to produce 10.0µg/ml concentrations. Finally, drug concentration was obtained by noting absorbance at 225nm. Methanol was used as a blank

Dissolution test: Apparatus used was USP Dissolution apparatus type II (Paddle method). A Phosphate buffer solution was prepared having a pH of 7.8. Both vessels of dissolution apparatus were added 900ml of the phosphate buffer and temperature adjusted to 37°c (±0.5°c). A tablet is added to each of the vessel and apparatus was operated at 75rpm for 30 minutes. After 15, 30 and 60 minutes, 20ml sample was taken from both the vessels and then filtered. Meanwhile enough quantity of phosphate buffer equivalent to sample drawn was added in vessels to replace the deficient volume. Concentration of Glimepiride in dissolution medium was finally determined. The Acceptance limit is, 80% of the drug should release in 30 minutes.

Assay: UV Spectrophotometer from Perkin Elmer ƛ25 was used for the assay. To analyze of samples, 20 tablets were carefully weighed and crushed to powder. Weight accurately this powder equivalent to 2mg glimepiride and added to 10mL (volumetric) flask previously been added with 1mL of 0.1M Sodium hydroxide. Then this dispersion was sonicated to homogenize, final volume make-up was done with methyl alcohol and finally filtered through a (0.45µm) syringe/membrane filter. Aliquots of standard were then shifted via A-grade (bulb) pipettes in 100mL volumetric flasks and the solutions were added with quantity sufficient methanol to yield final strength of 10µg/mL. The above-mentioned sample solution was finally assayed for the glimepiride quantity.

RESULTS

All the obtained samples were under their specified shelf life. Appearance test showed that the tablets were intact and neither damaged nor cracked, had smooth surface and no contaminants were visible apparently.

In the weight variation test 20 of 20 tablets were within the 5% allowed variation of weight complied with the test specification. Similarly, the dimensions of 10 of 10 tablets were within the specified limits of 5% allowed variation. Table 1 shows the detailed observation of weight variation and dimensions of tablets

In hardness test all the tablets (10/10) were within the controlled limit of 4-10kg/cm^2. Table 2 shows the average tablets' hardness of each brand. Moreover, all the brands complied with friability test and percentage loss was less than 1% for each brand. In the disintegration test, all the six-tablet disintegrated within the specified time of 15 minutes. Table 2 shows the average time of disintegrations test percentage loss of in friability tests of each brand. In the assay test of each brand all the samples were within the controlled limits. Table 2 and Figure 1 shows the results of assay.

Table 1: Results of weight variation and dimensions of the tablets

Sample	Average Weight (mg)	SD	UCL	LCL	Allowed limit (±5%)	No. of samples complied
Weight variation						
Sample 01	86.13	±0.907	92.60	79.67	6.46	20/20
Sample 02	79.92	±2.093	85.92	73.93	5.99	20/20
Sample 03	170.18	±0.841	182.94	157.41	12.76	20/20
Sample 04	162.51	±1.955	174.70	150.32	12.19	20/20
Sample 05	119.03	±1.287	127.96	110.10	8.92	20/20
Sample 06	204.41	±4.564	219.74	189.07	15.33	20/20
Thickness						
Sample 01	2.20	±0.027	2.31	2.09	0.11	10/10
Sample 02	8.00	±0.013	8.40	7.60	0.40	10/10
Sample 03	10.21	±0.022	10.72	9.70	0.51	10/10
Sample 04	11.21	±0.019	11.77	10.65	0.56	10/10
Sample 05	10.27	±0.032	10.78	9.76	0.51	10/10
Sample 06	9.81	±0.032	9.64	8.72	0.46	10/10
Diameter						
Sample 01	8.11	±0.022	8.52	7.71	0.41	10/10
Sample 02	2.03	±0.025	2.13	1.92	0.10	10/10
Sample 03	2.71	±0.013	2.84	2.57	0.14	10/10
Sample 04	2.51	±0.012	2.64	2.39	0.12	10/10
Sample 05	2.82	±0.013	2.96	2.67	0.14	10/10
Sample 06	2..73	±0.013	2.87	2.59	0.14	10/10

* SD=Standard Deviation, UCL=Upper Control Limit, LCL-Lower Control Limit

Table 2: Results (hardness, friability, disintegration, dissolution and assay test)

Sample	Average Hardness	Friability	Disintegration Test	Dissolution test (in 30 minutes)	Assay
Sample 01	4.7	0.71%	2 minutes and 22.5 seconds	81%	101.9%
Sample 02	4.95	0.88%	3 minutes and 3.5 seconds	85%	97.14%
Sample 03	4.7	0.67%	2 minutes and 2 seconds	83%	103.4%
Sample 04	6.8	0.58%	4 minutes and 14 seconds	86%	106.6%
Sample 05	5.95	0.82%	3 minutes and 13.5 seconds	88%	108.8%
Sample 06	7.75	0.41%	2 minutes and 3.5 seconds	90%	107.2%

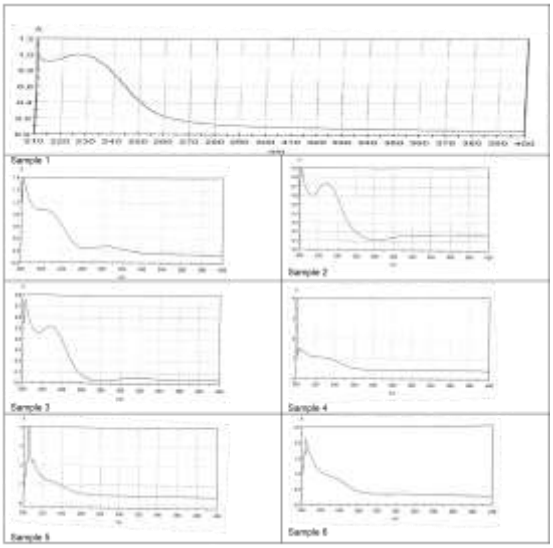

Figure 1: Spectrogram of Assay of 6 brands of Glimepiride along with standard

DISCUSSION

The therapeutic effectiveness of all the medicines depends upon the quality and quantity of active pharmaceutical ingredient claimed to be present in any pharmaceutical dosage form. The conventional scope of quality stems from examination and mensuration approach utilized in quality control when quality is in accordance with pre-set standards. Quality is actually the extent to which a certain material confirms a reference/standard. The meaning of quality, specifically in context of the pharma manufacturing and quality assurance, by far has swift away from narrow approach, and currently the definition accepted is fitness for purpose.[9]

In this research the quality of different brands of glimepiride was determined. In the determination of aesthetics and dimensions the results were within the acceptable limits which is consistent with the researches other researches conducted on glimepiride in Pakistan and Yemen.[10,11] While determining the weight variation among the different brands it was observed that all the brands were within pharmacopeial standards. These results are consistent with the research conducted by Maged Alwan Noman et. al. (2011) on different brands of glimepiride in certain Arab capital markets (Yemen, Saudi Arabia, Syria, and Egypt).[11]

Furthermore, in research conducted by Pilipović et. al. (2014) on four brands of glimepiride tablet form Bosnia and Herzegovina found that weigh, friability, harness, disintegration, and dissolution were within the specified limits. In consonance with these results, the brands in this research also complied with acceptable limits of weight, hardness, friability, and disintegration.[12]

Furthermore, in a study that was conducted by Syeda Arshi Zafar et. al. (2020) to evaluate different commercial brands of glimepiride available in Karachi observed that all the evaluated brands passed the disintegration test by disintegrating with 15 minutes. Similarly in the current study tablets of all the brands disintegrated within the accepted time limit [13].

Sidra Kanwal Ali and associated in a study conducted in 2019 on eight different commercial preparations of glimepiride available in various private hospitals of Karachi. The researchers observed that all the popular brands that were available at the private hospital pharmacies contained the required amount of active pharmaceutical ingredient. While conducting this research it was also observed that all the brands contained the official amount of active pharmaceutical ingredient.[11].

CONCLUSION

All the drug products obtained from the local market were under the standard limits mentioned in British pharmacopoeia at the time when weight uniformity test, thickness and diameter test, test for hardness, friability, test of disintegration, dissolution and content uniformity were executed. During research no any substandard or counterfeit product was found. The drug products from national and international brands are pharmaceutical equivalents and can be utilized interchangeably.

REFRENCES

1 Alberti, K.G.M.M. and P.Z. Zimmet, Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus. Provisional report of a WHO consultation. Diabetic medicine, 1998. 15(7): p. 539-553.

2 Shera, A., F. Jawad, and A. Maqsood, Prevalence of diabetes in Pakistan. Diabetes research and clinical practice, 2007. 76(2): p. 219-222.

3 Federation, I.D., IDF Diabetes Atlas Tenth Edition. IDF Diabetes Atlas, 2021.

4 Ahren, B., DPP-4 inhibitors. Best Practice & Research Clinical Endocrinology & Metabolism, 2007. 21(4): p. 517-533.

5 Nathan, D.M., et al., Management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement from the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes care, 2006. 29(8): p. 1963-1972.

6 Uhl, K. and J.R. Peters, How the FDA ensures high-quality generic drugs. American Family Physician, 2018. 97(11): p. 696-697.

7 Dharmalingam, S.R., et al., Comparative Quality Control Evaluation of Atenolol Tablets Marketed in Kuala Lumpur, Malaysia. 2014.

8 Jamshed, S.Q., et al., Perception and attitude of general practitioners regarding generic medicines in Karachi, Pakistan: a questionnaire based study. Southern med review, 2012. 5(1): p. 22.

9 Lee, D.C. and M. Webb, Pharmaceutical analysis. 2008: John Wiley & Sons.

10 Almaqtari, A.A. and A.A. Thabit, Comparative Study of in vitro Quality Specifications of Yemeni Brand of Glimepiride Tablets Versus Foreign Brands Marketed in Yemen. Al Razi University Journal of Medical Sciences, 2019. 3(1).

11 Ali, S.K., et al., Pharmaceutical quality evaluation of different glimepiride brands marketed in Karachi (Pakistan): In pursuance to global issue of availability and affordability of quality medicines. Pakistan Journal of Pharmaceutical Sciences, 2019. 32(6).

12 Pilipović, S., A. Uzunović, and A. Elezović, Market surveillance of four brands of glimepiride tablets 3 mg collected from bosnia and herzegovina markets. European Journal of Pharmaceutical Sciences, 2014. 50(1): p. E1-E234.

13 Zafar, S.A., et al., Comparative Study of Three Different Brands of Glimperide. Liaquat National Journal of Primary Care, 2020. 2(2): p. 94-96.

14 Madhusudhanareddy Induri, Bhagavan Raju M., Rajendra Prasad Y., Pavankumar Reddy K., Development and Validation of a Spectrophotometric Method for Quantification and Dissolution Studies of Glimepiride in Tablets, Journal of Chemistry, 2012. 9(2), p. 993-998.