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Comparative Evaluation of the Quality Control Parameters and Hypoglycemic Drug Effect of Some Brands of Glibenclamide Tablet

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ABS TRAC T

The medication release profile and bioavailability indices are highly correlated with the quality of pharmaceutical products. The hypoglycemic drug performance test and quality control standards of several brands of glibenclamide tablets were compared. Tests for hardness, friability, and weight uniformity as well as disintegration and dissolution profiles in phosphate buffer (pH 8) were used to evaluate the brands' physicochemical properties. The hypoglycemic medicine performance of the brands was evaluated using fasting blood sugar (FBS) measurements and twice-daily oral administration of a 5 mg glibenclamide tablet under controlled evening meal settings. By comparing the statistical findings on the groups' mean fasting blood sugar (MFBS) with a postulated/expected population MFBS of 5.0 mmol/L, the hypothesis that there was no difference in the population from whom the MFBS was drawn for each group treatment was investigated. The brands satisfied the USP criteria for tablet hardness, weight consistency, and friability and disintegration testing. There was little difference in the chemical composition between the quality of pharmaceutical goods is strongly associated with the medicine release profile and bioavailability indices. A comparison was made between the quality control criteria and hypoglycemic medication performance test of various glibenclamide tablet manufacturers. The brands' physicochemical characteristics were assessed using tests for hardness, friability, and weight uniformity as well as disintegration and dissolution profiles in phosphate buffer (pH 8). Fasting blood sugar (FBS) measurements and twice-daily oral administration of a 5 mg glibenclamide tablet under controlled evening meal conditions were used to assess the hypoglycemic medication performance of the brands. The hypothesis that there was no difference in the population from which the MFBS was obtained for each group treatment was examined by comparing the statistical results on the groups' mean fasting blood sugar (MFBS) with a postulated/expected population MFBS of 5.0 mmol/L. The brands met the USP requirements for weight consistency, friability and disintegration tests, and tablet hardness. There was little variation in the chemical makeup.

Keywords: *Glibenclamide, Hypoglycemia, Diabetes, Performance Evaluation, and Fasting Blood Sugar.*

INTRODUCTION

For non-insulin dependent diabetic mellitus (NIDDM), glibenclamide is an oral hypoglycemic medication belonging to the sulphonyl urea group [1]. The usage of medications according to their generic designations promotes unrestricted brand selection. Therefore, comparable medication performance and clinical effectiveness should be linked with competitive price. Manufacturers may choose active ingredients and receivers that result in fair production costs, which translate to the market cost, in order to effectively reduce costs and allow affordability [2]. The bioavailability profile of the medications used to produce glibenclamide may be characterized by their polymorphic form [3]. Glibenclamide comes in two commercial forms: crystalline and glassy, sometimes known as amorphous [4].

In synthetic chemistry, quench-cooling the melt and cryogenic milling may transform glibenclamide from its crystalline form into its glassy form [4, 5]. The two forms have been distinguished

based on their physiochemical profiles using the solid state characteristics of the amorphous samples, X-ray powder diffraction (XRD), infrared spectroscopy (FTIR), ultra-performance liquid chromatography (UPLC), and broad-band dielectric spectroscopy (BDS) [4-6].

Certain medications pass quality control tests yet exhibit biological inequivalency, according to quality control studies [7]. This has been shown to be mostly caused by problems with polymorphism and the selection of the drug's crystalline form as the raw material. Variations may affect the drug's absorption from the dosage form because distinct lattice energies (and entropies) linked to various polymorphs result in variances in physical characteristics including solubility and dissolution rates [8–10]. Equilibrium solubility, or the concentration of drug dissolved when there is equilibrium between the solid drug material and solution, is the most important problem associated with drug substance polymorphism. For the purpose of evaluating drug products, drug dissolution testing is suitable [11].

The purpose of this research was to evaluate some biopharmaceutical indices of the medication products as well as the quality control criteria of the six glibenclamide brands available on the market.

EXPERIMENTAL

Materials and Chemicals

HPLC system (Schimadzu LC26A pump, SPD26A UV detector, and column C18x5µm) China, Doublee-Gee glucometer (Doublee-Gee, China); analytical-grade acetonitrile, methanol, monobasic ammonium phosphate, sodium hydroxide, and hydrochloric acid were acquired from Merck (Germany). Glibenclamide 5 mg tablets were obtained from licensed pharmaceutical companies in Nigeria for drug samples GL1, GL2, GL3, GL4, GL5, and GL6 (Table 1). Glibenclamide powder was used as a reference and was provided as a gift sample by Sprem Chemicals and Research Center, China.

Methods

Buffer preparation

Monobasic potassium phosphate buffer of pH 8.0 was prepared according to established protocols [12].

Standard solution

An accurately weighed amount of pure glibenclamide powder equivalent to 50mg was dissolved in 0.2M sodium hydroxide in a 50ml volumetric flask to give a concentration of 1mg/ml. Solutions of glibenclamide of 0.5–20µg/ml were prepared from the stock solution by diluting accurate volumes of the stock solution in phosphate buffer (pH, 8.0). A calibration curve was prepared using the dilutions.

Calibration graph

Linear calibration graphs for the determination of glibenclamide (0.5 – 20µg/ml) was plotted and the linear–regression analysis expressed in Fig. 1.

Linearity

The calibration curve was analyzed for linearity using the least square regression method with triplicate determinations for each concentration.

Sample preparation

An accurately weighed amount of tablet powder of the six samples equivalent to 12.5mg were individually transferred to a 50ml volumetric flask and 20ml of acetonitrile was added and sonicated for 5min. A 5.0ml aliquot of the resulting solution was mixed with the mobile phase to produce a final volume of 1L.

Drug quality control parameters

Disintegration Test

The tablet disintegration was determined at 37°C using a Veego model $VTDH_3$ disintegration testing apparatus (Rutartek, India).

Weight uniformity

Tablets of each brand were weighed individual using a digital analytical balance (Adventure Ohaus) and the mean calculated. The percentage deviation of the individual tablets from the mean was determined.

Tablet hardness test

The crushing strength of the tablets was determined using a Monsanto tablet hardness tester at 25 per/min.

Assay/Chemical content

Twenty tablets of each six of the brands were weighed separately and crushed in a mortar. The powdered drug product of glibenclamide were weighed and an amount equivalent to 5mg was weighed in triplicate into conical flasks and dissolved in methanol to produce 50µg/ml of glibenclamide. The sample was injected into the chromatographic system and analyzed at 229.5nm. The mobile phase for the determination was monobasic ammonium phosphate and acetonitrile (45:55) and flow rate, 1.0ml/min.

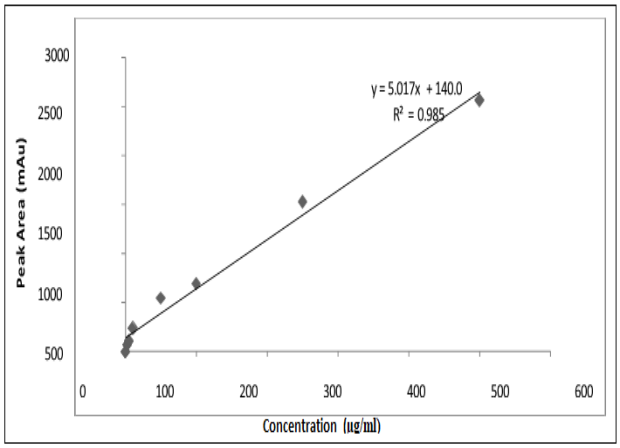

Figure 1: Calibration curve and regression equation of pure glibenclamide powder

Dissolution test

An Erweka DT-6 dissolution tester was used to conduct the dissolution test in accordance with the procedures for dissolution testing. Monobasic potassium phosphate buffer at 37±0.5°C and a rotational speed of 100 rpm made up the 900ml dissolving media. To maintain a consistent volume, 5 ml aliquot samples were taken out at times 5, 15, 30, 45, 60, and 90 minutes and replaced with equal volumes of fresh media. The HPLC apparatus was used to analyse the samples that were removed. C45 (concentration at 45 minutes) and T70 (average time for 70% of the active medication to be released) were calculated.

Hypoglycemic performance evaluation

July 2013 saw the completion of the research. After receiving written informed consent, administrative approval from the community pharmacy management where the study was conducted, and ethics committee approval from the University of Uyo's Faculty of Pharmacy, 36 volunteers (21 males and 15 females) with a mean age of 34.5±2.6 years, a mean body weight of 59.4±5.8 kg, and a body mass index (BMI) of 23.1±1.2 kg/m2. The study entry point (SEP) value was determined by taking the participants' fasting blood sugar (FBS) at 7 a.m. on the first day of the trial. Six groups of six participants each were randomly assigned. For 21 days, each group received a specific brand of glibenclamide twice daily, and daily changes in each volunteer's fasting blood sugar (SEP-FBS) readings were noted.

Statistical Analysis

Using one sample hypothesis and one tailed at α=0.05, statistically significant differences in the daily values for the change in blood sugar levels for group members of each medicine brand with regard to the SEP were evaluated, compared with other members of each brand, and analysed. Two sample hypotheses were used to compare the six brands in order to look for variations in the fasting blood sugar levels that each brand was able to lower. Using SPSS version 17, other factors were statistically examined for significant differences at $P<0.05$ [13].

RESULTS

All of the glibenclamide brands that were chosen at random were within their shelf lives and approved for sale in the nation. The top pharmacies in the research region carried the brands. The results of the evaluation of the physicochemical parameters for the glibenclamide brands were good. The brand with the highest rating had weight uniformity (maximum variation from the mean) of 4.5% and tablet hardness between 3.5 and 4.8 kgF. The highest duration for 70% of active material release was 38 minutes, whereas the lowest C45 value was 78%. The brands' chemical composition ranged from 92.4 -105.5%w/w (Table 2). Neither customers nor prescribers showed a preference for one over the other. The participants had no known metabolic diseases, were 34.5±2.6 years old, and weighed 59.4±5.8 kg.

DISCUSSION

Glibenclamide has been recommended as a medication to effectively manage blood sugar in people with Type 2 diabetes. Some doctors claim that glibenclamide taken twice a day together with a regulated evening meal effectively controls FBS. Our goal was to assess the idea's viability among a small sample of local outpatients. As the number of generic medication products increased, it became necessary to evaluate the quality of the brands that were accessible before assessing the effectiveness of some of the items. All of the brands used were nationally registered goods (Table 1), and they all satisfied the quality control standards examined. Regarding the factors examined, the quality indices of the different brands were adequate. As a result, the goods in circulation are considered medicinal equivalents (Table 2). The results of in-vivo performance will determine if these items may be used interchangeably. Due to the widespread sale of inferior medications, it is expedient to look into the quality control criteria before looking into performance. It has been shown that drug performances are strongly correlated with drug quality metrics [14] (Fig. 2 and Table 2). Glibenclamide is a class 2 medication with limited aqueous solubility according to the Biopharmaceutics Classification System (BCS). It is anticipated that manufacturing procedures from various manufacturers would get around this issue, which might be the cause of any differences in the dissolving properties. However, there were no significant differences in the dissolution result that would indicate a criticism of the different brands' performance. The brand's dissolving qualities were evaluated using a pH 8 buffer, which provides the best solubility capabilities given the drug's acidic nature and the pH of the intestinal environment where maximal absorption is anticipated. The results of the dissolution evaluation

will forecast the in-vitro performance as medication dissolution influences the bioavailability of the drugs. To the extent of more than 90% response, the volunteers voluntarily took their prescribed drugs and followed the protocol of reporting for FBS tests. This resulted from the volunteers' thorough understanding of the need of achieving a stable FBS. The group's anticipated FBS was 5.0. This FBS number was intended to be the best for efficient medication performance. To determine if there was a difference between the groups' MFBS and the hypothesised FBS, one sample hypothesis and two tail statistical analyses were performed for the observed MFBS in each group with data collecting for 21 days. The MFBS of each group did not significantly vary from the predicted FBS at $P<0.05$ and 0.01 for the brands GL1, GL2, GL3, GL4, and GL5. However, GL6 was enough at $\alpha=0.01$ (Table 3). Therefore, the medications will not result in an FBS value of around 5 mmol/L at the dosage and feeding conditions [15, 16]. However, when the group MSEP and group MFBS values for the six brands were assessed using the paired T-test, there was a significant decrease in MFBS.

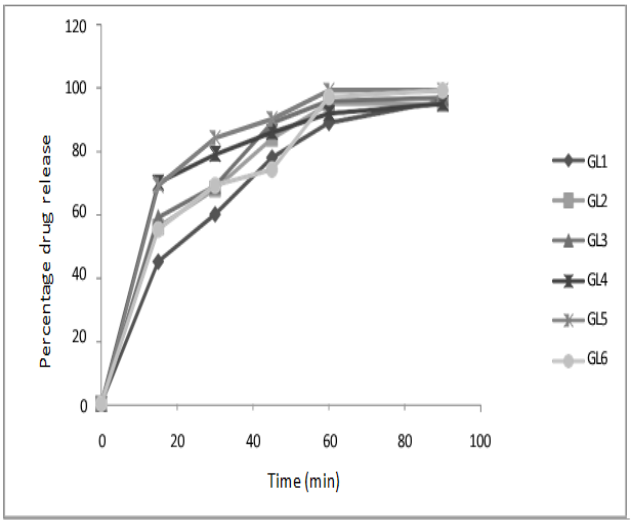

Figure 2: Dissolution profile of the six brands of glibenclamide drug products in dissolution medium (pH 8)

Table 1: The details of the drugs used in the study

Name	Code	Manufact Urer	Manufacturing/ Expiry Date	Nafdac Reg. number	B. No.
Daonil	GL1	May and Baker	08 – 2011/08-2014	04-0744	T028
Glanil	GL2	Nig German chemical	03 – 2011/03-2014	04-2450	W228
Solimide	GL3	Solidum Pharm	03 – 2009/02-2012	04-8751	9C-27
Gliben J	GL4	Juhel	05 – 11/04-2014	04-5735	0019
Clamide	GL5	Hovid	06 – 11/06-2014	04-4015	BB06596
Diabeta	GL6	Greenlife	11 – 10/10-2013	04-3856	DB-02

Table 2: The physicochemical analysis of the brands of glibenclamide in the study

Drugs	Tablet hardness	Weight uniformity MDM%	Chemical content (%w/w)	Disinte-gration time (min)	Friability (%)	Dissolution profile (SIF)	
						C_{45} (%)	T_{70} (min)
GL1	3.5±0.3	3.2	98.5±0.2	4.5±0.2	0.03	80	38
GL2	4.4±0.5	1.5	99.4±0.2	4.0±0.2	0.04	78	36
GL3	3.9±0.2	2.4	101.3±0.5	3.0±0.1	0.03	83	30
GL4	4.8±0.8	4.5	105.5±0.6	5.0±0.2	0.02	85	17
GL5	4.8±0.2	2.8	92.4±0.2	4.0±0.2	0	83	17
GL6	4.0±0.4	3.1	99.6±0.5	4.2±0.1	0.01	82	30

Key: MDM- Maximum deviation from the mean

CONCLUSION

The study found that the different glibenclamide brands that are sold in the nation and imported from various sources have similar quality characteristics. However, none of the brands met the postulated MFBS, which suggests that a supportive therapy may be required to achieve this value. Failure to meet the projected value may not be a drug production factor because the quality parameters of the brands used in this study were satisfactory.

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