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Analysis of Brands of Glibenclamide Tablets in Lagos Market

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Abstract: Glibenclamide is an oral antidiabetic drug which belongs to the second generation of sulfonulureas. It is an insulin secretagogue used in the treatment of type 2 diabetes mellitus. Use of substandard products may lead to poor blood glucose control and life threatening complications. The aim of this study was to analyze different brands of glibenclamidetablets for quality in terms of content of active ingredients and some physicochemical parameters. Nine brands of glibenclamide tablets were sourced from various pharmacy retail outlets in Lagos and subjected to chemical assay by HPLC method. Various physical tests including uniformity of weight, hardness, friability and disintegration time were also carried out. The results indicate that 78% of the samples show compliance with the British Pharmacopoeia (BP) standards for content of active ingredients. All the samples passed the tests for uniformity of weight and disintegration time but failure rate of 11% was recorded for both friability and tablet hardness tests. It is recommended that routine quality surveillance systems be established by drug regulatory bodies to monitor drug quality at all levels of the distribution chain to ensure product quality and consumer safety.

Key Words: Glibenclamide, HPLC, Diabetes, Lagos.

INTRODUCTION

Diabetes mellitus is a chronic non-communicable disease. It is a state of elevated blood glucose associated with absence or inadequate pancreatic insulin secretion with or without concurrent impairment of insulin action.

Non-insulin dependent (Type 2) diabetes mellitus is the most common form of the disease and is characterized by tissue resistance to the action of insulin plus a relative deficiency in insulin secretion, that is, inadequate insulin to overcome resistance (Nolte, 2009). Other types of diabetes mellitus include insulin-dependent (type 1) and gestational diabetes mellitus. The high blood glucose level in diabetes mellitus produces the classical symptoms of polyuria, polydipsia, polyphagia, fatigue and exercise intolerance among others. Inadequate management of the condition may lead to complications such as ketoacidosis, diabetic retinopathy and urinary tract infections.

There has been a global increase in the prevalence of Type 2 diabetes mellitus (Wild and Rogli, 2004) due mainly to life style changes such as poor diet, decreased physical activity and stress. This type of diabetes mellitus requires the use of oral hypoglycaemic agents when dietary control and exercise have proved inadequate (Torgerson et al, 2004). A few may also benefit from insulin therapy to supplement endogenous secretion.

There are different classes of oral hypoglycaemic drugs; glibenclamide belongs to the second generation of sulfonulureas. It is an insulin secretagogue used in patients with functional beta cells (Patel et.al, 2008). Like other insulin secretagogues, it acts by increasing insulin release from the pancreas. This it does by inhibiting ATP-sensitive potassium channels in pancreatic beta cells causing cell membrane depolarization and opening voltage-dependent calcium channels. This results in an increase in intracellular calcium in the beta cells and subsequently stimulates release of preformed insulin. Glibenclamide also reduces serum glucagon levels resulting in lowering of blood glucose level (Kunte et al, 2007; Bennett, 2011). Glibenclamide is available in different brands as 1.25 mg, 2.5 mg and 5 mg tablets. Figure 1 shows the chemical structure of glibenclamide.

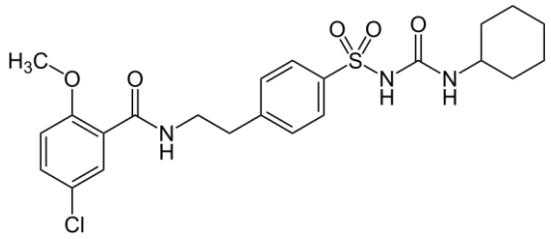

Figure 1: Structure of Glibenclamide

Health care is heavily dependent on drug use and the aim of any drug therapy is to achieve maximum benefit with minimum side effects (Chapman, 2004).For drugs to be efficacious and produce the desired therapeutic effects, they must contain the required amount of active ingredients and meet other official requirements for good quality. Use of poor quality products may lead to therapeutic failure, increased morbidity and mortality (Duckworth et.al, 2009). The need for oral hypoglycaemic drugs to be of high quality cannot be over emphasized considering the consequences of poor blood glucose control, in terms of complications and increased mortality rate.

Tablet is the most widely used oral solid unit dosage form currently available (Winfield, 2004). This is probably due to advantages of compactness, stability, portability, blandness of taste and ease of administration. Thus this dosage form is convenient for both the manufacturer and the patient. Being so popular increases the probability of being faked or counterfeited.

MATERIALS AND METHODS

Nine brands of glibenclamide tablets (5 mg) were bought from different Pharmacy shops in Lagos metropolis and code labeled A to I. The products all had batch numbers, NAFDAC numbers, manufacturers' names and addresses and were within their shelf-lives. The following tests were carried out on each sample.

Uniformity of Weight – Twenty tablets of each sample were weighed individually and the mean weight calculated. The deviation of each tablet from the mean as well as the standard deviation was also calculated for each sample.

Friability – Ten tablets of each sample were weighed and put in a friabilator which was then operated at 25 revolutions per minute for 4 minutes. The tablets were subsequently weighed and the friability calculated as the percent weight loss. Three measurements were made for each sample and the mean calculated.

Hardness (crushing strength) – Tablet hardness was measured by placing each tablet between the anvil of the Monsanto hardness tester. The force required to crush the tablet was recorded as the hardness or crushing strength. Ten tablets were tested per sample and the mean calculated.

Disintegration Time – Disintegration time was measured for six tablets per sample in accordance with the BP specification. Three sets of readings were taken per sample and the mean calculated.

Content of Active Ingredient – This was measured using a HPLC equipped with UV/VIS detector, a C_{18} stainless steel column and rheodyne loop injector. The mobile phase composition was a

mixture of acetonitrile and potassium dihydrogen orthophosphate (previously adjusted to pH 3.0 with 80% orthophosphoric acid) in 43:57 ratio, with flow rate of 1.5 ml/min. The sample injection volume was 20µl and the analytical wavelength set at 300nm.

Standard and sample solutions were prepared as follows:

Preparation of Standard Solutions

Glibenclamide pure standard (50 mg) was weighed and transferred into 50ml volumetric flask, 20ml of methanol was added, and the mixture was sonicated for 20mins, it was later made up to 50ml mark with methanol to obtain a final concentration of 1mg/ml (1000µg/ml) stock solution.

From the 1000µg/ml stock solution, serial dilutions were made to obtain calibration concentrations of 100µg/ml, 150µg/ml, 200µg/ml, 250µg/ml and 300µg/ml.

Preparation of Sample Solutions

Twenty (20) tablets of each sample were weighed and powdered. The quantity equivalent to 5mg of glibenclamide was taken and transferred into 25ml volumetric flask, 2ml distilled water was added and made up to 25ml mark with methanol. The solution was sonicated and this represents 200µg/ml.
Samples were run in triplicates and average values were used to calculate sample concentrations using the standard calibration curve. Percent content of active ingredient was then calculated for each sample.

RESULTS AND DISCUSSION

The uniformity of weight of all the samples was acceptable as none of the tablets deviated from the mean by more than 5%, thereby meeting the BP (2007) standard. Weight variability within each batch was also low as shown by the standard deviation for each sample. The highest variability occurred with Sample F.

Uniformity of weight of tablets is an important parameter because high weight variation indicates variation in amount of active ingredients and/or chemical additives. Variation of active ingredients may lead to toxicity, ineffectiveness or unpredictability of action of the product while variability of additives may affect other physicochemical characteristics of the product and ultimately alter the bioavailability of the drug. Examples of factors affecting uniformity of weight are inconsistency of granule size and uneven filling of dies during the compression of the tablets (Winfield, 2004).

All samples complied with the standard (BP, 2007) of not more than 1% friability except sample F which had a friability of 1.06%. This was only slightly above the standard and the effect minimal as the sample displayed slightly high crushing strength and normal disintegration time. This result shows that the tablets are able to withstand abrasion during packaging and other handling operations without undue loss of tablet material. They would also maintain good appearance without becoming dusty during storage or dispensing.

Crushing strength (Hardness) of tablets should be a minimum of 4kgf and not greater than 8kgf.Crushing strength was below the upper limit for all the samples except Sample F. Samples B and D, however, fell below the lower limit of 4kgf. Excessive hardness of tablets would prolong disintegration time, thereby affecting dissolution and absorption rates, bioavailability and onset of action of the drug. Soft tablets, on the other hand, are unable to withstand conditions of storage, transportation and handling without breaking or chipping. It is, therefore, important that tablets are of optimum hardness. Factors affecting the strength of tablets include the amount of binders used in granulation and the pressure applied during compression of the tablets.

The results of disintegration test show that all the samples complied with the BP standard of not greater than 15 minutes. Sample D had the shortest disintegration time which along with its low value for hardness may be an indication of low amounts of binders or high disintegrants concentrations (Olaniyi, 2000).The value for Sample F was the highest and this is in line with its highest value for hardness test.Tablet disintegration is prerequisite to dissolution and subsequent absorption of the drug from the dosage form. The results of all the physicochemical tests are shown in Table 1.

Table 1: Results of Physicochemical Tests on the Various Brands of Glibenclamide.

Sample Code	Name	Mean Weight (mg) ± Standard Deviation	Friability (% Loss)	Hardness (KgF)	Disintegration Time (min.)
A	Gluben-5®	153.4±1.5	0.22	4.33	1.28min.
B	Glidanil®	203.3±1.4	0.04	2.37	2.69min.
C	Deominal®	141.9±3.9	0.27	4.0	1.47min.
D	Sanclamide®	152.6±1.6	0.08	3.0	20.04sec.
E	Glibenclamide®	158.4±1.8	0.25	6.5	2.5min.
F	Glanil®	157.5±5.4	1.06	8.67	3.29min.
G	Diatab®	181.1±3.3	0.12	4.33	2.68min.
H	Solimde®	189.4±3.5	0.02	5.17	2.1min.
I	Daonil®	161.9±1.7	0.20	6.33	24.57sec.

Assay for the content of active ingredients is a critical test of quality, as all the physical properties tested are meant to optimize release of the drug from the product. So, no matter how perfect a product may be in terms of physical parameters, failure to meet the standard for content of active ingredients will result in poor quality with adverse consequences. The content of active ingredient for glibenclamide tablets should be 95 – 105% of stated amount per tablet (BP, 2007). Most of the samples used in this study had content within this range. However, two samples (C and F) failed this test with % content below the lower limit (that is, low content failure). The results are presented in Table 2 while Figure 2 shows the standard calibration curve for glibenclamide.

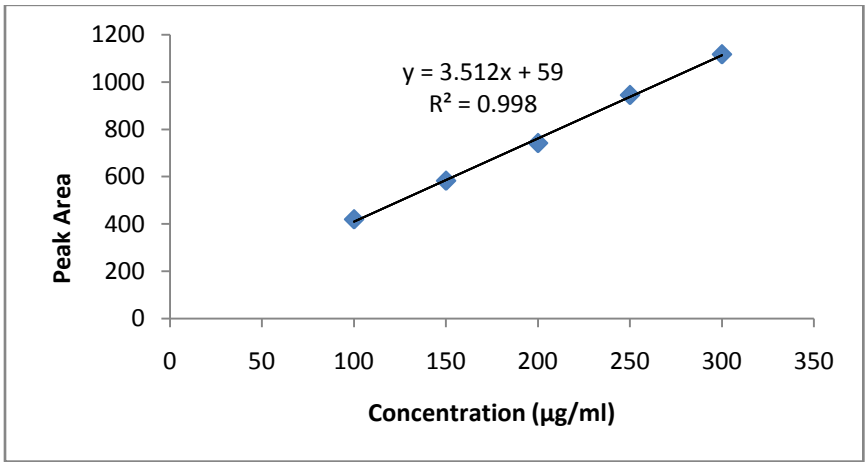

Figure 2: Standard Calibration Curve for Glibenclamide

Table 2: Content of Active Ingredients of the Various Brands of Glibenclamide

Brand Code	Peak Areas	Concentration (µg/ml)	Amount Per Tablet (mg)	% Purity
A	740	193.9	4.85	97
B	777	204.4	5.11	102
C	719	187.9	4.70	94
D	733	191.9	4.80	96
E	741	194.2	4.85	97
F	686	178.5	4.46	89
G	737	193.1	4.83	97
H	728	190.5	4.76	95
I	725	189.6	4.74	95

Low content products may lead to treatment failure and development of complications of diabetes mellitus.Inaccurate weighing, poor mixing techniques (leading to non-uniformity of active ingredients) and general non-compliance with the principles of Good Manufacturing Practice (GMP) are factors that could affect the content quality of the product. Other factors include deliberate attempts to cut costs and activities of counterfeiters.

In all, the samples recorded a pass rate of 78% for content of active ingredient. The innovator brand (Sample I) was within limits in all the parameters tested.

The need to maintain high quality of pharmaceutical products cannot be over-emphasized as the main aim of any drug policy is to ensure that only safe and effective drugs get into the distribution system (Nigeria National Drug Policy, 2005). A quality surveillance system should therefore be set up by the regulatory authorities for regular testing in the market place. This will greatly improve the quality of drugs and ensure consumer safety.

CONCLUSION

It can be concluded from this study and based on the parameters measured that glibenclamide tablets in Lagos, Nigeria are of acceptable standards. Pass rates of samples were 100% for uniformity of weight and disintegration time tests, 89% for friability and hardness tests and 78% for content of active ingredient. However, a wider study may be required to establish these findings.

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