



**ASSESSMENT OF PHYSICOCHEMICAL PROPERTIES OF GLIBENCLAMIDE TABLETS
MARKETED IN ZARIA, KADUNA STATE, NIGERIA**

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ABSTRACT

This study analyzed six commercially available glibenclamide tablets marketed in Zaria, Nigeria, for quality in terms of content of active ingredients and some physicochemical parameters. The conducted tests were weight variation, thickness, diameter, friability, disintegration time, and assay of active content by UV spectrophotometer. The tests were performed as described by official books. Glibenclamide tablet samples were randomly purchased from pharmacy outlets and patent medicine stores, and they comprised samples manufactured in Nigeria and other countries. The results showed that all the samples passed the weight variation, disintegration time, thickness, and diameter tests. Four out of the six brands passed assay of active content, as they satisfied the BP specifications which required glibenclamide content to be between 95 to 105%, while one of the six tested brands failed the friability test. Overall, only 50% of the tested samples passed the quality control assessment.

KEYWORDS: Quality control assessment, Glibenclamide tablets, Zaria, Diabetes mellitus, Substandard drugs.

INTRODUCTION

Diabetes mellitus is a metabolic disorder in which blood glucose level becomes abnormally and persistently high (chronic hyperglycemia), as a result of insufficient insulin secretion, insulin resistance, or both [1]. The disease is also characterized by disturbance of carbohydrate, fat, and protein metabolisms [1]. There is a tremendous increase in the prevalence of the disease in recent years. According to 2019 data from International Diabetes Federation (IDF), around 463 million adults (20-79 years) are living with diabetes mellitus

worldwide, most of which are type 2, and nearly half of the affected are undiagnosed [2,3]. By the year 2045, this figure will rise to 700 million [3]. The disease accounted for 4.2 million deaths and caused at least 760 billion US dollars in health expenditure in 2019 alone [3]. Moreover, the 2019 IDF data for Nigeria revealed that the prevalence of diabetes mellitus among adult population reached approximately 3% [3], although it was argued that the percentage might be higher since diabetes cases are believed to be under-reported in Nigeria [2]. Researchers in Nigeria have reported the

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disease's prevalence in the country to be up to 7% [2,4].

Glibenclamide (Figure 1), also known as Glyburide (United States adopted name), is a long-acting oral antidiabetic drug used in the treatment of type 2 diabetes mellitus [5,6].

Successful treatment for any disease depends on good quality medicines. Quality of medicines is receiving growing international attention in recent years [5]. The absence or weak quality control measures for pharmaceutical products may lead to the production and prevalence of medicines which do not meet quality specifications [7]. Such medicines may contain no, low or high concentration of active ingredients, wrong ingredients, poor quality ingredients, and may have poor stability [8]. As a result of these, substandard medicines pose a serious threat to public health and safety in Nigeria, ranging from treatment failure, drug poisoning, drug resistance, the masking of clinical symptoms of ailments, and death in worst cases [8]. Besides the health consequences, substandard medicines also constitute a substantial economic problem for the patients, the pharmaceutical companies, and the governments [9]. Studies have shown that substandard and counterfeits medicines are proliferating in Africa, including Nigeria [8–10].

Therefore, quality control is crucial for monitoring the effectiveness of drug products. Quality of glibenclamide tablets has been investigated in various regions of the world. For examples, pharmaceutical evaluation of commercial glibenclamide tablets were investigated in Libya [7]; Addis Ababa, Ethiopia [5]; Jordan [10]; Mexico [11], and Saudi Arabia [12]. Similarly, various researchers have evaluated the quality of marketed glibenclamide tablets in some parts of Nigeria like Jos [13], Maiduguri [14], and Southwest Nigeria [15]. However, despite the variety of brands of glibenclamide tablets in Zaria, Nigeria, there are no reports on the quality evaluations for these brands. Thus, this study was aimed at evaluating the physicochemical parameters of six commercially available brands of glibenclamide tablets in Zaria, Nigeria.

MATERIALS AND METHODS

Materials

Standard glibenclamide powder was purchased from Sigma-Aldrich, USA. Glibenclamide tablets, 5mg, were randomly purchased from pharmacy outlets and patent medicine stores in Shika,

Samaru, Kwangila, Sabon Gari, Tudun Wada, and Zaria city center, Zaria, Kaduna State, Nigeria. Six products (brands) from different manufacturers were labelled as sample A, B, C, D, E, and F (Table 1). All the used brands were within their shelf life at the time of this study. All reagents used were of analytical grade.

Experimental Methods

Visual inspection, weight variation, friability, disintegration, diameter, thickness, and assay of active pharmaceutical ingredient (API) were performed as described by official books and various authors [10,12,13,16,17].

Visual inspection

The physical appearance comprising size, shape, colour, and label of each brand sample were inspected visually.

Weight Variation

Ten tablets from each brand were randomly selected and weighed individually using an electronic balance (Mettler Analytical Balance, Phillip Hasrris Ltd., England). The mean weight and standard deviation were calculated for each sample.

Friability

Ten tablets were randomly selected from each brand and then dusted using a sieve. Then the tablets were weighed using an electronic balance. The tablets were subjected to abrasion shock by tumbling in a tablet friabilator (Type TA3R, Erweka, Germany). The machine was operated at 25 revolutions per minute (rpm) for 4 min. The tablets were dusted again and reweighed. The percentage loss in weight was determined for each brand of the tablets using Equation 1.

Friability (%) = $[(\text{Initial weight} - \text{Final weight}) / \text{Initial weight}] \times 100$ Equation 1

Thickness and diameter tests of the tablets

The thickness and diameter of the tablets were measured using an electronic calliper (Fisher Scientific, England). A total of five tablets were used for each sample. Each tablet was placed between the jaws of the instrument, and the micrometer was adjusted to obtain the thickness and diameter of the tablet. The values obtained were recorded in millimeter (mm).

Disintegration Test

Disintegration test was performed using Erweka Disintegration Apparatus (Type WF 31012,

Germany) in a freshly prepared medium made of 0.1N HCl, at a temperature of $37 \pm 0.5^\circ\text{C}$. Six tablets from each brand were randomly selected. The tablets were placed individually in six different tubes of the apparatus. The tablets get disintegrated and passed through mesh, and the time taken for the disintegration was recorded using a stopwatch. The average disintegration time for each of the brand was calculated.

Assay of Active Content

For each brand, three tablets were accurately weighed, crushed, and the equivalent of the average weight of one tablet (5mg) was transferred into a 100 ml volumetric flask. The volume was completed to the mark with 0.1N HCl. The mixture was then sonicated and filtered using filter paper. The drug content was determined using a UV spectrophotometer (Shimadzu, Japan) that was previously calibrated. The samples were analyzed against a blank at a wavelength of 300 nm. The percentage content of glibenclamide for each product was determined from the previously made calibration curve of glibenclamide in the range of 1 to 20 $\mu\text{g/ml}$ concentrations.

Statistical Analysis

Statistical significance of the data sets was assessed by two-way analysis of variance (ANOVA) followed by Tukey's Multiple Comparison Test using version 7.0 Graphpad Prism® statistical software. A 95% confidence interval was considered as to be statistically significant.

RESULTS

Most of the samples had a good physical appearance, and all the samples were white in colour, oblong in shape and bitter in taste (Table 2). The weight variation test for all the tested brands of glibenclamide tablets gave acceptable values, as none of the tablets deviated from the mean by more than 5%, hence conformed to BP standard [16]. The weight variation of the tested samples was found to be in the range of 153 mg to 209 mg (Table 3).

Not all the samples conformed to the BP specifications in percentage content of active ingredient, which required that glibenclamide tablet should contain between 95 to 105% of the labelled amount of glibenclamide [16]. Sample A, C, D, and F satisfied this requirement, while sample B ($94 \pm 1.50\%$) and E ($90 \pm 4.33\%$) failed, as their percentage drug content were below the lower limit (Table 3). The highest percentage drug content was

from sample C ($100 \pm 2.80\%$), while the lowest drug content was from sample E ($90 \pm 4.33\%$).

The results for disintegration time test (Table 3) showed that the disintegration time of the six brands ranged from 0.30 to 3.57 min, indicating that all the samples complied with the BP standard of not greater than 15 minutes. Sample B has the shortest disintegration time of 18 seconds, while sample C has the highest disintegration time (3.57 min).

The result of the friability test (Table 4), revealed that sample A, B, D, E, and F satisfied the BP standard, as their respective percentage friability was less than 1%. However, sample C slightly deviated from the standard, as its percentage friability value (1.23% w/w) was significantly ($p < 0.05$) different when compared with sample D and others (Table 4).

The thickness and diameter of the tablets (Table 4) were within the BP specification. There were variations between the samples in both thickness and diameter tests, but the variation was more pronounced in the thickness test.

DISCUSSION

We investigated the physicochemical properties of six brands of glibenclamide tablets being marketed in Zaria metropolis, in order to ascertain their quality. With an increasing number of generic products of the drug, there was the need to assess the quality of the available brands, and this has justified the need for conducting this study. The findings raised concern and suggest the need for the Nigerian drug regulatory agency to act promptly to eradicate the circulation of substandard medicines.

Visual assessment of pharmaceutical products could be regarded as an essential step in quality assurance. It could save time and resources as failure to meet specifications for labelling, uniformity in size, colour and tablet integrity would make further quality control tests unnecessary [13,18]. In the present study, the brands showed no discernable anomalies, and the labelling information was found to be intact.

The result of the weight variation test showed that all the tested brands of glibenclamide tablets passed the test. Based on the compendial requirements, weight variation test is one of the critical quality control parameters for solid dosage forms that is needed to be demonstrated for quality assurance. This is to ensure that all tablets of a particular product contain nearly equal amount of API, hence the uniformity of a unit dosage. The findings of this study for weight variation test were similar to the

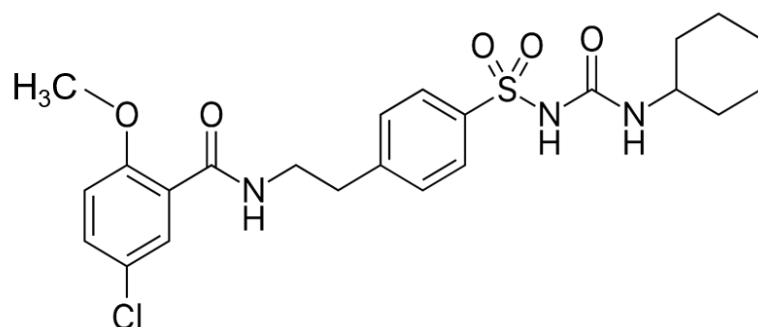


Figure 1: Chemical structure of glibenclamide (5-chloro-N-[2-[4-(cyclohexylcarbamoylsulfamoyl)phenyl]ethyl]-2-methoxybenzamide).

Table 1: Details of the tested brands of glibenclamide tablets available in Zaria market. The brand names are coded.

Brand Sample	Batch Number	NAFDAC Number	Manufacturing Date	Expiry Date	Country of Manufacture	Sources of Medicine
A	160206	-	02/2016	02/2019	Nigeria	Patent medicine store
B	BF12618	04-4015	12/2015	12/2018	Malaysia	Pharmacy outlet
C	T215	04-0744	06/2015	06/2018	Nigeria	Pharmacy outlet
D	5D009	B4-1868	04/2015	03/2018	India	Patent medicine store
E	D9701	04-2450	04/2015	04/2018	Nigeria	Pharmacy outlet
F	DTC001	A4-5856	11/2014	10/2017	India	Pharmacy outlet

NAFDAC, National Agency for Food and Drug Administration and Control.

Table 2: Physical properties of the tested products of glibenclamide tablets.

Brand samples	Colour	Shape	Taste
A	White	Oblong	Bitter
B	White	Oblong	Bitter
C	White	Oblong	Bitter
D	White	Oblong	Bitter
E	White	Oblong	Bitter
F	White	Oblong	Bitter

Table 3: Result of official quality control tests.

Brand samples	Mean tablet weight (mg) \pm SD	Average disintegration time (min) \pm SD	Percentage drug content (%) \pm SD
A	163 \pm 2.45	3.10 \pm 0.52	96 \pm 3.00
B	158 \pm 4.49	0.30 \pm 0.10	94 \pm 1.50
C	153 \pm 6.53	3.57 \pm 0.45	100 \pm 2.80
D	177 \pm 3.27	0.68 \pm 0.08	95 \pm 4.56
E	154 \pm 6.12	1.83 \pm 0.20	90 \pm 4.33
F	209 \pm 6.33	2.21 \pm 0.91	95 \pm 3.90

SD, Standard deviation.

Table 4: Result of unofficial quality control tests.

Brand samples	Mean Tablet Friability (%) \pm SD	Mean Tablet Thickness (mm) \pm SD	Mean Tablet Diameter (mm) \pm SD
A	0.00 \pm 0.00	2.43 \pm 0.07	4.90 \pm 0.14
B	0.00 \pm 0.00	2.67 \pm 0.06*	5.00 \pm 0.04
C	1.23 \pm 0.16*	2.16 \pm 0.02*	5.00 \pm 0.01
D	0.56 \pm 0.04	3.49 \pm 0.07*	4.92 \pm 0.03
E	0.00 \pm 0.00	2.43 \pm 0.10	5.04 \pm 0.02
F	0.00 \pm 0.00	3.83 \pm 0.04*	5.89 \pm 0.09*

* $p < 0.05$

findings reported in a similar investigation in Southwest of Nigeria [15] and Saudi Arabia [12].

The percentage drug content of oral solid dosage forms is a critical quality attribute that has a direct impact on the safety and efficacy for the patient [19]. Therefore, the concentration of the active ingredient is a requirement that must be fulfilled by every proper tablet product. According to BP, the percentage content of active ingredient for glibenclamide tablets should be between 95 to 105% of the claimed amount [16]. The present study showed that 2 out of the 6 tested brands did not fulfil this requirement, as their percentage drug content was below the standard lower limit. This indicates that substandard glibenclamide tablets products may be in circulation in Zaria metropolis.

Disintegration of tablets involves their break down into smaller pieces or granules within a prescribed time and in a liquid medium, such as gastric juice or intestinal fluid [15]. The disintegration of tablets is prerequisite to tablets' dissolution and subsequent absorption of the drug into the body. All the evaluated six brands of glibenclamide tablets passed the disintegration time test, by disintegrating within 15 min as required by the BP. Other researchers elsewhere have also found the disintegration time of glibenclamide tablets to be less than 15 min [5,12,13,15]. The rapid disintegration time exhibited by all the brands might be as a result of nature and amount of disintegrant used in the production of the tablets.

Friability test is another vital quality control parameter that is required to be demonstrated for tablet dosage forms. It determines the loss in weight of compressed uncoated tablets which may occur as a result of the loss of fine particles from tablet surfaces [15]. The test gives an indication of how compressed uncoated tablets like glibenclamide tablets can withstand chipping, breaking into smaller pieces or crumbling, when

they are subjected to mechanical shock and attrition that can occur during their production, packaging, and transportation. The friability test result revealed that all samples met the BP standard of less than 1%, except sample C. This deviation could be attributed to the amount and quality of binders used in its production. This study is in contrast with reported findings for friability test in some parts of Nigeria [13, 15, 20] which reported that their tested brands of glibenclamide tablets conformed to specification. However, all the tested brands in the present study passed the specifications for thickness and diameter tests.

CONCLUSION

This study confirmed that all the tested glibenclamide brands satisfied the compendial specification for weight variation, disintegration time, thickness, and diameter tests. However, some samples were unable to meet the requirements for assay of active content and friability test. Therefore, it is concluded that not all the marketed glibenclamide tablets in Zaria, Nigeria are of acceptable standards.

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