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# Evaluation of the quality of frequently prescribed antidiabetic medications in Nigeria.

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ABSTRACT

**Background:** Diabetes mellitus is a growing public health concern in Nigeria, and ensuring the quality of antidiabetic medications is crucial for effective management. This study aimed to evaluate the pharmaceutical quality of various marketed brands of metformin and glibenclamide tablets in Nigeria.
**Methods:** The study assessed the physicochemical properties of seven metformin and six glibenclamide brands, including weight variation, hardness, friability, disintegration time, assay, and dissolution profiles. The results were compared to British Pharmacopoeia (BP) and United States Pharmacopoeia (USP) standards.
**Results:** Most brands (~80 %) met the BP/USP specifications for physicochemical parameters. However, dissolution testing revealed variability in release profiles, with only two metformin brands showing similarity to the reference product based on f1 (≤15) and f2 (f2 ≥50) comparison. None of the glibenclamide brands met the similarity criteria.
**Conclusion**: Continuous post-marketing surveillance and stricter regulatory oversight is recommended to ensure consistent product quality and therapeutic reliability.

## 1. Introduction

Diabetes mellitus (DM), particularly Type 2 DM, is a chronic metabolic disorder of growing public health concern worldwide[1]. The International Diabetes Federation (IDF) estimates that about 425 million people globally have diabetes, with nearly half being undiagnosed[2]. Nigeria, the most populous nation in Africa, is experiencing a rising prevalence of Type 2 DM across all regions[3]. Recent studies indicate that the prevalence of diabetes among adults in Nigeria is approximately 7.0%, translating to over 8 million individuals affected nationwide[4]. This escalating burden poses a serious health challenge, as uncontrolled diabetes leads to debilitating complications such as cardiovascular disease, kidney failure, neuropathy, and limb amputations[2]. Effective long-term management of Type 2 DM hinges on consistent access to safe and efficacious medications to

achieve glycemic control and prevent such complications[5].

Ensuring the quality of antidiabetic medications is, therefore, critically important. There are growing concerns that many essential medicines in low- and middle-income countries may be substandard or falsified, undermining treatment outcomes[6]. According to the World Health Organisation (WHO), falsified medicines are those that "deliberately/fraudulently misrepresent their identity, composition or source," while substandard medicines are authorised products that fail to meet quality standards or specifications[7]. Such poor-quality medicines can result in therapeutic failure, disease progression, and increased morbidity and mortality[8]. In the context of diabetes, the use of substandard medications may lead to inadequate blood glucose control with life-threatening complications[9]. According to a systematic review, around 10.8% of sampled antidiabetic drugs in developing countries were found below quality requirements[6]. These findings highlight the public health risks posed by substandard or falsified (SF) medicines in chronic disease management.

Among oral antidiabetic drugs, metformin (a biguanide) and glibenclamide (a sulfonylurea, also known as glyburide) are especially important in Nigeria[10]. Metformin is the first-line oral therapy for Type 2 DM and is the most commonly prescribed antidiabetic medication[11]. Its widespread use has led to the increased importation and local manufacture of numerous metformin brands in Nigeria[12]. Glibenclamide is another frequently used oral hypoglycemic agent, often employed as an add-on or alternative therapy, and it likewise enjoys broad usage. These two medications constitute cornerstone therapies for Type 2 diabetics in Nigeria's healthcare system, accounting for most oral antidiabetic prescriptions[13]. As a result, the Nigerian market is flooded with various brand-name and generic products of metformin and glibenclamide. This proliferation of different brands can complicate clinical practice, where both clinicians and patients struggle with the interchangeability of brands, and regulators must ensure all available products are of reliable quality[9]. The increasing use of glibenclamide and metformin in Nigeria thus necessitates vigilant monitoring of the quality of the various brands available in the drug market[14].

Evidence is emerging that the quality of these frequently prescribed antidiabetic medications can vary considerably between products. A recent evaluation of ten marketed metformin tablet brands in Abuja found that, although all samples were within acceptable limits for weight uniformity, hardness, friability, and disintegration, three brands failed dissolution testing, releasing less than 70% of the labelled drug within 45 minutes[12]. In the same study, one metformin brand was found to contain only 86% of its stated active ingredient by high-performance liquid chromatography (HPLC) assay[12], indicating a sub-potent product. Similarly, quality surveys of glibenclamide have uncovered serious deficiencies in some brands. For example, one multi-state study in Nigeria reported that 9 out of 19 sampled glibenclamide tablet products (47%) did not meet the USP dissolution specifications[15], a result suggestive of poor formulation quality that could impair glucose-lowering efficacy. In a broader review of antidiabetic drug quality, over half of the samples that failed active ingredient content analysis were identified as metformin or glibenclamide products[6]. Some substandard samples had as little as ~82% of the labelled active pharmaceutical ingredient, while others exceeded 110% of the label claim[6]. Such variability in potency and dissolution performance among different brands has clear clinical implications: an underpowered tablet may fail to adequately control blood sugar, whereas an over-potent or erratically releasing tablet could increase the risk of hypoglycemia. These findings underscore the concern that not all marketed brands of metformin and glibenclamide are pharmaceutically equivalent, and they highlight the importance of rigorous quality evaluation for these essential drugs.

To safeguard public health, pharmacopeial standards serve as the benchmark for drug quality. Official compendia like the British Pharmacopoeia (BP) and the United States Pharmacopoeia (USP) define stringent specifications that each pharmaceutical product must meet to be considered of standard quality[9]. These include criteria for identity, assay (acceptable range of active drug content, typically 90–110% of the label claim), dissolution (e.g. a minimum percentage of drug released in a given time for immediate-release tablets), disintegration time, and other physicochemical properties[16]. Each of these in vitro tests is designed to ensure that a drug product will perform as intended in patients; for instance, a tablet must contain the correct dose, not break apart during handling, dissolve at the proper rate, and release the labelled amount of drug. Products that fall outside the compendial specifications in any of these parameters are considered out-of-specification and potentially substandard[17]. By using BP/USP monographs as the gold standard, regulators and researchers can objectively evaluate whether different brands are "pharmaceutically equivalent" to the innovator product and each other[15].

However, in Nigeria, there is a paucity of published data on

the quality and bioequivalence of the many antidiabetic drug brands in circulation[9,14]. Given the vital role of metformin and glibenclamide in diabetes care and the risks posed by substandard medications, there is a clear need for systematic quality assessment of these products. Therefore, the objective of this study is to evaluate the pharmaceutical quality of various marketed brands of metformin and glibenclamide tablets in Nigeria. This investigation focuses on the most frequently prescribed oral antidiabetic agents and employs compendial (BP/USP) standards as benchmarks for quality. Subsequently, the findings will inform healthcare providers, patients, and regulators on the reliability of commonly used antidiabetic drug brands and underscore the importance of continual quality surveillance for chronic disease medications in Nigeria.

## 2. Methodology

### Materials and Sample Collection

This study was an analytical cross-sectional laboratory study that utilised a range of analytical instruments, including a UV/Visible spectrophotometer (Agilent Cary 60), dissolution tester (RC-6, India), disintegration tester (Erweka ZT4-4, Germany), friabilator (Erweka), Monsanto hardness tester, and analytical balance (Ohaus Analytical Plus, AP250D). Additional materials included an ultrasonic bath, Whatman filter papers, micropipettes, standard laboratory glassware, porcelain mortar and pestle, and distilled water. The pharmaceutical samples consisted of seven brands of film-coated metformin tablets (500 mg) and six brands of glibenclamide tablets (5 mg), all purchased from registered pharmacies within the Federal Capital Territory, Abuja, Nigeria. All products were within their shelf life at the time of testing and were verified to carry proper regulatory identification, including NAFDAC registration number, batch number, and manufacturing and expiration dates. The brands were anonymised and coded as M1 through M7 for metformin, and G1 through G6 for glibenclamide (Table 1).

### Weight Variation Test

Uniformity of tablet weight was assessed following official compendial standards. Twenty tablets from each brand were randomly selected and collectively weighed to determine the average tablet weight. Each tablet was subsequently weighed individually, and the percentage deviation from the mean was calculated. Results were evaluated against pharmacopoeial limits to determine compliance with the standard criteria for uniformity of dosage units[18].

### Hardness and Friability Tests

Tablet hardness was evaluated using the Monsanto hardness tester. Ten tablets from each brand were randomly selected and individually tested. The mean crushing strength, expressed in kilogram-force (kgF), was calculated to represent the average mechanical resistance to breakage. For the friability test, ten tablets from each brand were weighed (W1), subjected to 100 revolutions at 25 rpm for 4 minutes in an Erweka friabilator, and then reweighed after removal of surface dust (W2)[18]. The friability percentage was calculated using the formula:

$$f = (w1 - w2)/w1\ x\ 100$$

### Disintegration Time

Disintegration testing was conducted using the Erweka disintegration tester following pharmacopoeial guidelines. Six tablets from each brand were placed individually into the six baskets of the tester. The apparatus was filled with distilled water, maintained at 37 ± 0.5°C. The time required for complete disintegration, defined as the point when no solid residue remained on the mesh, was recorded for each tablet, and the mean disintegration time was calculated[18].

### Assay of Active Ingredient

The assay of metformin hydrochloride content was performed by UV spectrophotometry. Twenty tablets from each brand were weighed, averaged, and finely powdered. A quantity equivalent to 100 mg of metformin was transferred into a 100 mL volumetric flask, dissolved in distilled water using sonication for 15 minutes, diluted to volume, and filtered. After discarding the first 20 mL of the filtrate, successive dilutions were made to yield a final concentration of 10 µg/mL. The absorbance of each sample was measured at 232 nm, and the content was calculated using the specific absorbance value of 798. Each sample was analyzed in triplicate[19].

The assay for glibenclamide tablets followed the British Pharmacopoeia protocol. Four tablets were weighed and crushed, and the average tablet weight was extracted using methanol with 2 mL of water. The solution was sonicated and filtered through a 0.45 µm syringe filter. The mobile phase consisted of potassium dihydrogen phosphate buffer (pH 3) and acetonitrile in a 53:47 ratio. HPLC analysis was performed at a flow rate of 1.5 mL/min and at ambient temperature. Three replicate injections were made for each of three separate sample preparations, and results were compared with those obtained from standard solutions[19].

**Dissolution Studies**

Dissolution testing for metformin tablets was performed using the USP Apparatus 1 (basket method). One tablet from each brand was placed in 900 mL of phosphate buffer (pH 6.8) maintained at 37 ± 0.5°C. The apparatus operated at a rotation speed of 100 rpm. At time intervals of 5, 10, 20, 30, and 45 minutes, 10 mL aliquots were withdrawn and filtered, and an equivalent volume of fresh buffer was added to maintain sink conditions. The absorbance of each sample was measured at 233 nm using a UV-Visible spectrophotometer. The concentration of metformin released was quantified using a specific absorbance value of 806 at λmax 233 nm. Each test was first performed six times to represent the stage S1 criteria for immediate-release solid dosage form[19].

For glibenclamide tablets, dissolution was carried out using USP Apparatus 2 (paddle method). Each tablet was placed in a separate vessel containing 900 mL of 200 mM phosphate buffer (pH 6.8), maintained at 37 ± 0.5°C. The paddle rotation speed was set to 75 rpm. At predetermined intervals (5, 10, 20, 30, and 45 minutes), 10 mL aliquots were withdrawn and replaced with fresh medium. The filtered samples were analysed using high-performance liquid chromatography (HPLC) at a detection wavelength of 250 nm. A calibration curve was established using standard glibenclamide solutions (1.135–5.675 µg/mL), and the percentage of drug released was calculated.

Each test was first performed six times to represent the stage S1 criteria for immediate-release solid dosage form[19].

**Comparative studies and drug release kinetics studies**

To compare the dissolution profiles of different brands, we used two key metrics:

Dissimilarity factor (f1): to calculate the percentage difference between the reference and test products at each time point[18].

$$f1 = \frac{\{\sum_{t=1}^{n} Rt - Tt\}}{\{\sum_{t=1}^{n} Rt\}} \times 100$$

Similarity factor (f2): to measure the similarity between the test and reference dissolution curves[18].

$$f2 = 50 \times \log\left\{1 + \frac{1}{n}\sum_{t-1}^{n}(Rt - Tt)^2\right\}^{-½} \times 100$$

Where Rt is the percentage of dissolved reference or innovative brand at a given time t,

Tt is the percentage of dissolved generic product, while n is the number of times point[2].

We also evaluated:

Dissolution Efficiency (DE): to assess the overall dissolution performance

$$DE = \frac{\int_{t1}^{t2} y.dt}{y100\ x\ (t2 - t1)} x100$$

Where y is the percent of dissolved product, dt is the area under the dissolution curve between time point t1 and t2 expressed as a percentage of the curve at maximum dissolution, y100, over the same time period[18].

Mean Dissolution time (MDT): to determine the average time for drug release

$$MDT = \frac{\sum_{j=1}^{n} tj\Delta Mj}{\sum_{j=1}^{n} \Delta Mj}$$

Where j is the sample number, n is the number of dissolution sampling times, $t_j$ is the time at midpoint between $t_j$ and $t_{j-1}$(expressed as $t_j$+$t_{j-1}$)/2) while ΔMj is the additional amount of drug released between $t_j$ and $t_{j-1}$[18].

To understand the drug release kinetics of 5 mg glibenclamide and 500 mg metformin hydrochloride we applied various mathematical models

Zero order model kinetic:

$$Q\_t = Q\_0 + K\_0\ t\ 6$$

$Q_t$ is the amount of drug dissolved in time t, and $Q_0$ is the initial amount of drug in the solution, while $K_0$ is the zero-order release constant expressed in units of concentration/time[18].

First order model kinetic:

$$\log C = \log C_0 - \frac{K_t}{2.303}$$

$C_0$ is the initial concentration of drug, K is first order rate constant, and t is the time[18].

Higuchi model kinetic:

$$f_t = Q = K_H \times t^{½}$$

Q is amount of drug released in time t per unit area, $K_H$ is Higuchi dissolution constant[18].

Hixson-Crowell kinetic model:

$$W\_0⅓ - W\_t⅓ = Kt$$

$W_0$ is the initial amount of drug in the dosage form, $W_t$ is the remaining amount of drug in the dosage form at time t, and K is a constant incorporating the surface-volume relation[18].

Korsmeyer-Peppas kinetic model:

$$M\_(t\ ÷)\ M\_ω = Kt\^n$$

$M_t ÷ M_ω$ is the fraction of drug released at time t, K is the release rate constant and n is the release exponent[18].

## 3. Results

Table 1. Packaging information for brands of glibenclamide tablets (G1-G6) and those of metformin hydrochloride tablets (M1-M7) used in the study

| S/N | BATCH NO | NAFDAC NO | MAN DATE | EXP DATE | COUNTRY OF ORIGIN |
|---|---|---|---|---|---|
| G1 | 2DN041 | 04-0744 | 10/2022 | 09/2025 | France |
| G2 | 2DN042 | 04-4015 | 03/2023 | 02/2026 | Malaysia |
| G3 | 2DN046 | 04-2450 | 12/2022 | 11/2025 | Nigeria |
| G4 | 2DN047 | A4-4310 | 03/2023 | 02/2026 | Nigeria |
| G5 | 2DN049 | 04-7261 | 07/2023 | 06/2026 | India |
| G6 | 2DN050 | 04-2159 | 02/2023 | 01/2026 | Nigeria |
| M1 | E206414 | 04-6233 | 11/2020 | 10/2025 | France |
| M2 | E206492 | 04-8247 | 12/2020 | 11/2025 | India |
| M3 | E206523 | 04-0810 | 12/2020 | 11/2025 | Malaysia |
| M4 | E207078 | A4-2607 | 03/2021 | 02/2026 | Nigeria |
| M5 | E208654 | A4-6597 | 04/2021 | 03/2026 | Nigeria |
| M6 | E207146 | A4-2278 | 03/2021 | 02/2026 | Nigeria |
| M7 | E209854 | C4-0472 | 03/2021 | 02/2026 | Nigeria |

Table 2. Physicochemical data for glibenclamide tablets (G1-G6) and metformin hydrochloride tablets (M1-M7) assessed

| S/N | Weight variation (g) (SD) | Hardness (KgF) (SD) | Friability (%) | Disintegration time (min) (SD) | Assay (%) |
|---|---|---|---|---|---|
| G1 | 0.1598±0.22 | 6.10±0.10 | 0.30 | 0.25±0.11 | 98.5 |
| G2 | 0.1600±0.91 | 3.70±0.37 | 0.60 | 0.81±1.11 | 96.3 |
| G3 | 0.1593±1.55 | 5.70±1.50 | 0.28 | 1.20±0.55 | 95.5 |
| G4 | 0.1583±2.00 | 7.00±0.29 | 1.25 | 0.37±0.55 | 98.0 |
| G5 | 0.1595±2.33 | 6.40±0.50 | 1.25 | 2.50±1.01 | 95.0 |
| G6 | 0.1602±2.11 | 6.70±0.99 | 3.79 | 5.11±0.55 | 97.2 |
| M1 | 0.5319±0.51 | 3.30±1.00 | 0.03 | 0.22±0.05 | 95.0 |
| M2 | 0.5299±2.03 | 3.16±0.48 | 0.01 | 0.50±1.02 | 92.0 |
| M3 | 0.5341±1.13 | 0.92±1.02 | 0.02 | 3.19±0.02 | 95.0 |
| M4 | 0.5365±2.58 | 4.70±0.11 | 0.02 | 1.02±0.11 | 95.0 |
| M5 | 0.5309±3.02 | 3.77±0.51 | 0.11 | 2.33±0.22 | 96.0 |
| M6 | 0.5294±2.22 | 0.1±2.01 | 0.00 | 0.75±1.10 | 97.0 |
| M7 | 0.5304±3.21 | 0.50±1.22 | 0.06 | 1.30±0.20 | 96.0 |

The physicochemical tests showed that every brand had acceptable uniformity of weight, indicating consistent dosing per tablet. Tablet hardness varied between products (some metformin brands were markedly harder or softer than others), but all samples remained intact under handling and met the friability criterion (<1% weight loss) (Table 2). Likewise, disintegration times were rapid for both drugs (all metformin and glibenclamide tablets disintegrated well within the 30-minute limit for film-coated tablets). The assay of active ingredient content was within the 90–110% label claim range for most brands, although a few tablets were at the lower end of acceptable potency. Importantly, the in vitro dissolution studies revealed efficient drug release for the majority of brands, meeting the stage S1 criteria in USP monograph, and thereby not requiring further testing: most metformin tablets released ≥80% of the drug within 30 minutes and nearly 90–100% by 45 minutes (Figure 1), while glibenclamide tablets showed more variable yet generally adequate release. Mechanisms for metformin release followed the Hixxson-crowell model, with few obeying the first order and Higuchi models; while those of glibenclamide were mostly the Higuchi model (Table 3). Only M4 and M6 were similar at every dissolution sampling time to M1(Table 4); while all glibenclamide generics differed from the innovator brand (G1)

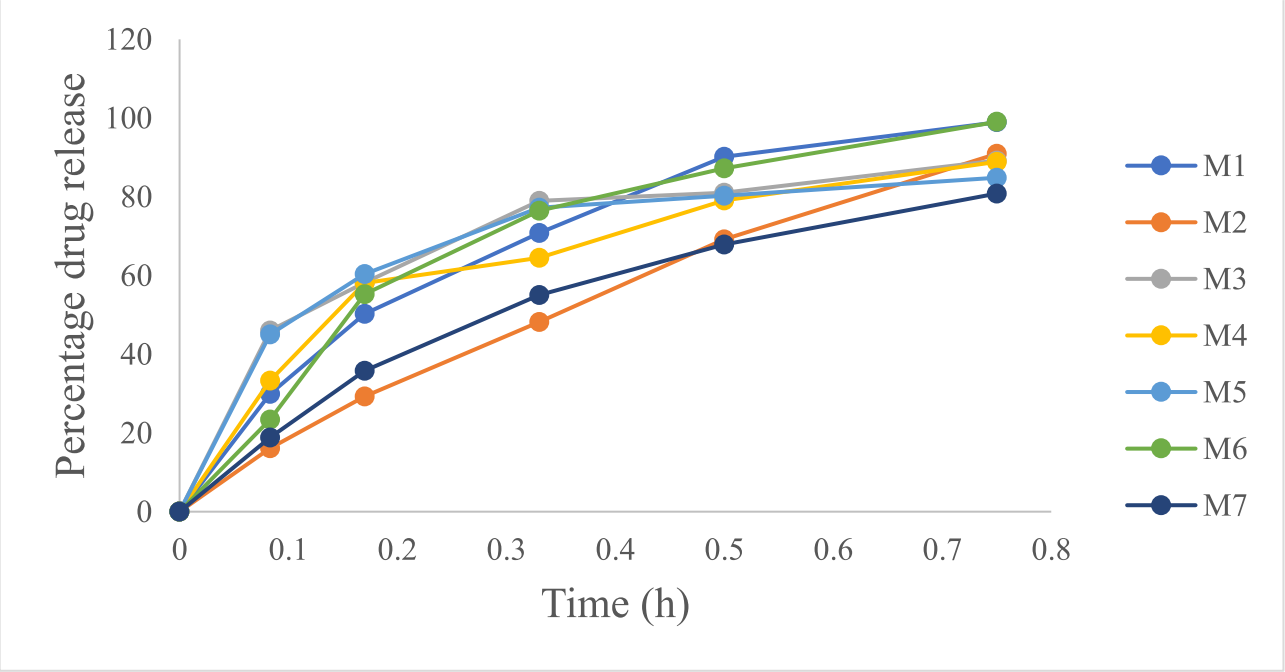


Figure 1: Dissolution profile for metformin hydrochloride tablets

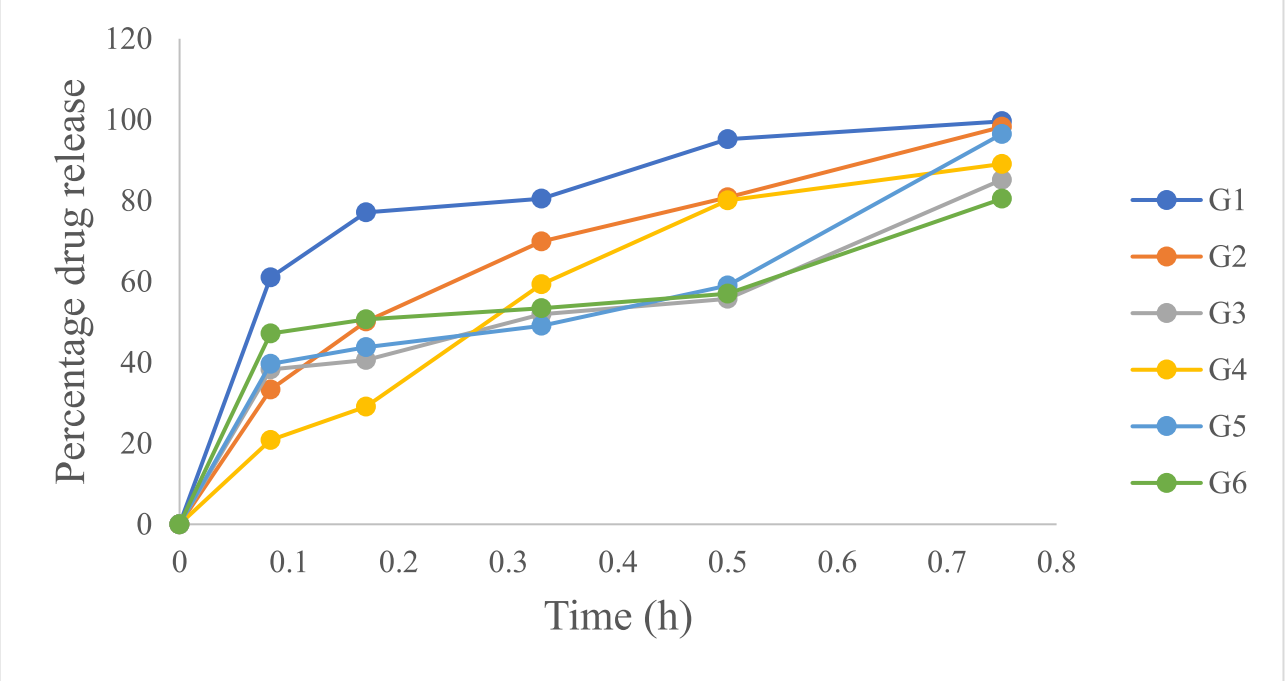


Figure 2: Dissolution profile for glibenclamide tablets

Table 3. Kinetic model data for brands of glibenclamide (G1-G6) and metformin hydrochloride (M1-M7) tablets

| | ZO | FO | HG | HX | KP |
|---|---|---|---|---|---|
| G1 | 0.6274 | 0.9519 | 0.8747 | 0.9267 | 0.0397 |
| G2 | 0.8816 | 0.9242 | 0.9970 | 0.9810 | 0.0128 |
| G3 | 0.8402 | 0.8866 | 0.9369 | 0.8967 | 3E-09 |
| G4 | 0.9331 | 0.9890 | 0.9627 | 0.9825 | 0.0733 |
| G5 | 0.8603 | 0.7893 | 0.9118 | 0.8529 | 0.0015 |
| G6 | 0.6851 | 0.8293 | 0.8653 | 0.7968 | 0.0350 |
| M1 | 0.8816 | 0.9602 | 0.9896 | 0.9971 | 0.0245 |
| M2 | 0.9849 | 0.9557 | 0.9625 | 0.9897 | 0.0956 |
| M3 | 0.7101 | 0.9232 | 0.9304 | 0.8627 | 0.0063 |
| M4 | 0.8032 | 0.9726 | 0.9685 | 0.9341 | 0.0014 |
| M5 | 0.6730 | 0.8657 | 0.9106 | 0.8064 | 0.0112 |
| M6 | 0.8523 | 0.9477 | 0.9695 | 0.9899 | 0.0317 |
| M7 | 0.9200 | 0.9959 | 0.9885 | 0.9802 | 0.0493 |

*ZO=zero order, FO=first order, HG=Higuchi, HX=Hixon-Crowell, KP=Korsmey-Peppas

Table 4. Similarity factor (f2), dissimilarity factor (f1), mean dissolution time (MDT), area between curve (ABC), and percentage dissolution efficiency (% DE) values for brands of glibenclamide (G1-G6) and metformin hydrochloride (M1-M7) tablets

| | F1 | F2 | MDT | ABC | % DE |
|---|---|---|---|---|---|
| G1 | - | - | 0.14 | 14.30 | 110 |
| G2 | 19 | 43 | 0.25 | 24.46 | 96 |
| G3 | 34 | 34 | 0.30 | 30.21 | 86 |
| G4 | 33 | 33 | 0.28 | 27.78 | 95 |
| G5 | 30 | 35 | 0.32 | 32.29 | 82 |
| G6 | 30 | 37 | 0.27 | 26.48 | 93 |
| M1 | - | - | 0.22 | 22.79 | 99 |
| M2 | 25 | 45 | 0.33 | 32.70 | 85 |
| M3 | 15 | 56 | 0.19 | 18.58 | 100 |
| M4 | 11 | 62 | 0.22 | 22.37 | 100 |
| M5 | 16 | 54 | 0.18 | 17.75 | 110 |
| M6 | 6 | 73 | 0.22 | 22.42 | 100 |
| M7 | 24 | 46 | 0.28 | 28.29 | 94 |

## 4. Discussion

Each quality attribute assessed has direct implications for a tablet's performance and therapeutic efficacy. Weight uniformity ensures each tablet delivers a consistent dose; deviations beyond compendial limits (±5% for most tablets) could lead to under- or overdosing[18]. In this study, the tight weight variation observed across all brands signifies good manufacturing control of tablet mass. Tablet hardness and friability reflect the mechanical integrity and handling robustness of the product[19]. The brands tested showed low friability (mostly well below 1% weight loss), meaning they can withstand transport and dispensing without crumbling[20]. Hardness varied among products, but even the softer tablets did not crumble (passing friability), and the harder ones still disintegrated within the required time. The assay results confirm whether each brand contains the labeled amount of drug[21]. The findings revealed that nearly all tablets were within the acceptable range for metformin 500 mg or glibenclamide 5 mg content, which is reassuring for dose accuracy. However, the few instances of slightly low potency (e.g., M2 had ~92% of the label claim) underscore the need for continued quality oversight. Even moderate under-potency could contribute to subtherapeutic dosing, especially in drugs with narrow therapeutic indices. A failed quality assessment of a pharmaceutical product in Nigeria could reflect several issues with the country's regulatory surveillance and importation policies such as inadequate regulatory oversight; weak importation policies; lax enforcement; and supply chain vulnerabilities. To address these issues, Nigeria's regulatory agencies could consider strengthening regulatory frameworks, by reviewing and updating regulations to ensure they aligned with international standards; enhancing surveillance, by increasing monitoring and inspection of pharmaceutical products in the market and manufacturing facilities; improving import controls, by strengthening importation policies and procedures to prevent substandard products from entering the market; build capacity, by providing training and resources for regulatory staff to enhance their capacity to monitor and enforce compliance; and work with international partners and other regulatory agencies to share information and best practices on quality control surveillance.

Analysis of dissolution profiles is a crucial technique for determining how similar generic brands are to their reference product[22]. Despite all brands meeting most quality benchmarks, the data reveal noteworthy inter-brand variability that could impact clinical performance. For example, M7 released only about 68% by 30 minutes and ~80% by 45 minutes, whereas others had exceeded 85% release in the same timeframe (Figure 1). Such slower-release behavior in a few products might be attributed to formulation factors like excipient composition or tablet coating[23]. This single suboptimal dissolution profile among seven metformin brands raises concerns about the interchangeability of all marketed generics regarding in vitro performance.

Similarly, for glibenclamide (Figure 2), two brands (G3 and G6) showed markedly slower initial dissolution (only ~55–60% in 30 minutes, versus >90% for the fastest brand, G1). While all six glibenclamide samples did eventually reach high release levels by 45 minutes, a tablet that dissolves much more slowly than others could lead to a delayed therapeutic effect in patients[24]. Such differences in release kinetics underscore that each manufacturer's formulation and process can yield a distinct in vitro performance profile.

The mechanism of drug release from these oral tablets depends on the tablet matrix and the physicochemical properties of metformin and glibenclamide[25]. Because Metformin HCl is highly water-soluble (BCS Class III), its tablets are expected to disintegrate rapidly as the drug readily dissolves upon fluid exposure[26]. Not surprising, 3 of the brands followed the Hixson-Crowell equation model (Table 4), suggesting that their release is controlled by the dissolution of the drug particles, as the surface area of the particles decreases over time. Hydrophilic excipients such as starch, microcrystalline cellulose, and soluble polymers will swell and wick fluid into the tablet, forming a gel or porous network. The drug then diffuses out of this hydrated structure, and if polymers like hydroxypropyl methylcellulose (HPMC) are present, the tablet surface forms a viscous gel that controls water ingress and drug diffusion[27]. In contrast, glibenclamide is poorly water-soluble (BCS Class II)[28]. Its aqueous solubility is pH-dependent, essentially unionized at stomach pH and dissolving more readily at higher pH (intestinal fluids)[29]. Four of the brands obeyed Higuchi equation model, suggesting that their release is controlled by diffusion through a matrix system. Thus, the drug must dissolve at the solid–liquid interface before it can diffuse away[30]. Formulation factors strongly influence this[23]. Hydrophobic binders or waxy excipients including hydrogenated oil or ethylcellulose can form diffusion barriers that retard release. Conversely, 2 brands followed the first order model suggesting that their release rate is depended to the

concentration of the glibenclamide remaining in the system. Amazingly, the release profiles of these brands followed an initial curve with an initial rapid release preceding a slower release process. Surfactants or solubilizing agents improve wetting and apparent release. Therefore, hydrophilic matrices like sodium CMC or PVP in glibenclamide tablets could swell and create pores, aiding release. In summary, metformin tablets release predominantly by rapid disintegration and dissolution of a soluble drug, whereas glibenclamide tablets rely more on matrix erosion/diffusion of a poorly soluble drug[28].

Regarding the bioavailability of these drugs, both FDA and WHO guidance state that similar dissolution profiles (f2 ≥50 and f1 ≤15) support pharmaceutical equivalence[7,31]. For immediate-release formulations, this can justify a biowaiver or predict bioequivalence if profiles match. Here, only M4 and M6 met in vitro similarity to M1; all glibenclamide generics differed from G1. Therefore, based on dissolution alone, only those metformin generics might be considered interchangeable with M1 under f1and f2 criteria[7,31]. However, neither M4/M6 nor any glibenclamide brand achieved "very rapid" release (≥85% in 15 min as recommended for BCS III)[26]. In fact, per the metformin biowaiver monograph, a BCS Class III drug requires not only identical API but also very rapid dissolution across media[26]. Our data fall short, suggesting that in vivo absorption (even for metformin) could differ. For glibenclamide (BCS II), any significant dissolution disparity typically mandates full pharmacokinetic BE studies; in vitro failure (f2<50) indicates a low likelihood of interchangeability without further testing. This has implications for drug quality and interchangeability. Healthcare providers and patients cannot automatically assume all brands will work identically, especially if a given generic has a slower release profile or borderline assay content. Close monitoring and regulatory vigilance are warranted to ensure that every brand consistently meets quality standards, lot after lot.

The dissolution behavior suggests limited equivalence: Nigerian regulatory standards (via NAFDAC/WHO) should require manufacturers of dissimilar brands to consider reformulation or conducting in vivo BE studies to ensure therapeutic interchangeability.

Dissolution efficiency (DE) value of a drug can vary depending on the specific drug product, its intended use, and the regulatory requirements. Generally, a higher DE is desirable, as it indicates that the drug is released quickly and efficiently from the dosage form. Drug classification, dosage form, and therapeutic window are factors that could influence the ideal DE value. Typically, values greater than 80 % is considered ideal for immediate-release dosage forms. All brands tested met this specification.

The mean dissolution time (MDT) is a crucial parameter in drug release studies. It helps to understand the rate and extent of drug release from a formulation; and also allows to comparison of different formulations, enabling optimization of drug release characterization; while also enabling the prediction of a drug formulation, including its absorption and bioavailability. It may serve as a useful tool for quality control, ensuring batch-to-batch consistency in drug release characteristics; and may help to predict in vivo performance based on in vitro dissolution data. Although there is no ideal value for MDT as it depends on the specific formulation, drug, and therapeutic goals; a shorter MDT value (usually in minutes) is expected for an immediate release product, for rapid drug absorption. All brands evaluated met the criteria.

This work has a few limitations. First, we restricted our brand sampling to the most prevalent tablet brands. Secondly, no clinical BE study was carried out. As a result, unmodeled aspects like inter-patient variability, dietary effects, and gastrointestinal dynamics were not represented.

## 5. Conclusion

Manufacturers in the pharmaceutical industry are responsible for producing quality health commodities that ensure safety and therapeutic efficacy. However, substandard pharmaceutical products can lead to treatment failures and compromised health outcomes. A high-quality drug product promotes optimal therapeutic effectiveness, patient compliance, and public confidence in the healthcare system.

## Reference


1. Blair M. Diabetes Mellitus Review. Urol Nurs. 2016 Jan-Feb;36(1):27-36.
2. Uloko AE, Musa BM, Ramalan MA, Gezawa ID, Puepet FH, Uloko AT, Borodo MM, Sada KB. Prevalence and Risk Factors for Diabetes Mellitus in Nigeria: A Systematic Review and Meta-Analysis. Diabetes Ther. 2018 Jun;9(3):1307-1316. doi: 10.1007/s13300-018-0441-1
3. Adeloye D, Ige JO, Aderemi AV, Adeleye N, Amoo EO, Auta A, Oni G. Estimating the prevalence, hospitalisation and mortality from

type 2 diabetes mellitus in Nigeria: a systematic review and meta-analysis. BMJ Open. 2017 May 11;7(5):e015424. doi: 10.1136/bmjopen-2016-015424.
4. Olamoyegun MA, Alare K, Afolabi SA, Aderinto N, Adeyemi T. A systematic review and meta-analysis of the prevalence and risk factors of type 2 diabetes mellitus in Nigeria. Clin Diabetes Endocrinol. 2024 Dec 6;10(1):43. doi: 10.1186/s40842-024-00209-1.
5. Khunti K, Zaccardi F, Amod A, Aroda VR, Aschner P, Colagiuri S, Mohan V, Chan JCN. Glycaemic control is still central in the hierarchy of priorities in type 2 diabetes management. Diabetologia. 2025 Jan;68(1):17-28. doi: 10.1007/s00125-024-06254-w.
6. Saraswati K, Sichanh C, Newton PN, Caillet C. Quality of medical products for diabetes management: a systematic review. BMJ Glob Health. 2019 Sep 24;4(5):e001636. doi: 10.1136/bmjgh-2019-001636.
7. World Health Organisation. A Study on the Public Health and Socioeconomic Impact of Substandard and Falsified Medical Products. 2017 Available at: https://www.who.int/publications/i/item/9789241513432 (Accessed May 6, 2025).
8. Ozawa S, Higgins CR, Yemeke TT, Nwokike JI, Evans L, Hajjou M, Pribluda VS. Importance of medicine quality in achieving universal health coverage. PLoS One. 2020 Jul 9;15(7):e0232966. doi: 10.1371/journal.pone.0232966.
9. Musa GA. Evaluation of The Pharmaceutical Quality of Different Brands of Glibenclamide Tablets Marketed in Kaduna, Nigeria. Nigerian Journal of Pharmaceutical and Biomedical Research, 2019;4(2):192-197.
10. Offu OF. A Systematic Review of the Prevalence and Treatment of Type 2 Diabetes in Nigeria. IDOSR Journal of Biology, Chemistry and Pharmacy, 2019;3(1):124-146.
11. Baker C, Retzik-Stahr C, Singh V, Plomondon R, Anderson V, Rasouli N. Should metformin remain the first-line therapy for treatment of type 2 diabetes? Ther Adv Endocrinol Metab. 2021 Jan 13;12:2042018820980225. doi: 10.1177/2042018820980225.
12. Eraga SO, Arhewoh MI, Oruh EP, Iwuagwu MA. A comparative evaluation of the pharmaceutical quality of different brands of metformin hydrochloride tablets available in Abuja, Nigeria. West African Journal of Pharmacy, 2017;28(1):61-71.
13. Fadare J, Olamoyegun M, Gbadegesin BA. Medication adherence and direct treatment cost among diabetes patients attending a tertiary healthcare facility in Ogbomosho, Nigeria. Malawi Med J. 2015 Jun;27(2):65-70. doi: 10.4314/mmj.v27i2.7.
14. Osuafor NG, Ukwe CV, Okonta M. Evaluation of availability, price, and affordability of cardiovascular, diabetes, and global medicines in Abuja, Nigeria. PLoS One. 2021 Aug 12;16(8):e0255567. doi: 10.1371/journal.pone.0255567.
15. Gabel J, Lächele M, Sander K, Gnegel G, Sunny-Abarikwu N, Ohazulike RE, Ngene J, Chioke JF, Häfele-Abah C, Heide L. Quality of Essential Medicines from Different Sources in Enugu and Anambra, Nigeria. Am J Trop Med Hyg. 2024 May 14;111(1):179-195. doi: 10.4269/ajtmh.23-0837.
16. Pharmapproach Quality Control Tests for Chewable Tablets, Pharmapproach.com. Pharmapproach Limited. Available at: https://www.pharmapproach.com/quality-control-and-evaluation-parameters-for-chewable-tablets/ (Accessed: May 6, 2025).
17. Chavan H, Chhabra G, Gujarathi N, Jadhav A.Comparative study of In-process and finished products quality control test for tablet and capsules according to pharmacopoeias. Asian Journal of Pharmaceutical Research and Development, 2018;6(3):60-68.
18. Ibekwe NN, Isaac JA, Ajiboye A, Adigwe OP. Interchangeability for brands of promethazine teoclate (25 mg) tablets available in Abuja metropolis of Nigeria. West African Journal of Pharmacy, 2022;33: 47–52.
19. Osei-Yeboah F, Sun CC. Validation and applications of an expedited tablet friability method. Int J Pharm. 2015 Apr 30;484(1-2):146-55. doi: 10.1016/j.ijpharm.2015.02.061.
20. Isaac JA, Hayatu GI, John JE, Ekere KE, Daburi A, Omachoko SO. Quality assessment of brands of prednisolone (5 Mg) tablets marketed in abuja metropolis of Nigeria. Dissolution Technol, 2021;28(1):24-31.
21. Rahman MM, Jahan FI, Fahim NF, Paul N, Jahan

N, Harun-Or-Rashid M. *In vitro* comparative quality evaluation of leading brands of metronidazole tablets available in Bangladesh. Pharmacology Online,2020;2:63-72.

22. Al-Kubati SS, Ahmed OS, Saif RM. The evaluation of some brands of levocetrizine dihydrochloride film-coated tablets for quality and equivalence sold in Aden, Yemen. Electronic Journal of University of Aden for Basic and Applied Sciences, 2022;3(4):313-321.
23. Alam MN. Pulsatile release drug delivery system based on compression-coated tablets (Doctoral dissertation). http://dx.doi.org/10.17169/refubium-40005
24. Masih A, Kumar A, Singh S, Tiwari AK. Fast dissolving tablets: a review. International Journal of Current Pharmaceutical Research, 2017;9(2):8-18.
25. Quodbach J, Kleinebudde P. A critical review on tablet disintegration. Pharm Dev Technol. 2016 Sep;21(6):763-74. doi: 10.3109/10837450.2015.1045618.
26. Metry M, Shu Y, Abrahamsson B, Cristofoletti R, Dressman JB, Groot DW, Parr A, Langguth P, Shah VP, Tajiri T, Mehta MU, Polli JE. Biowaiver Monographs for Immediate Release Solid Oral Dosage Forms: Metformin Hydrochloride. J Pharm Sci. 2021 Apr;110(4):1513-1526. doi: 10.1016/j.xphs.2021.01.011.
27. Ghori MU, Conway BR. Hydrophilic matrices for oral control drug delivery. American Journal of Pharmacological Sciences, 2015;3(5):103-109.
28. Mardiyanto M, Fithri NA, Amriani A, Herlina H, Sari DP. Formulation and Characterization of Glibenclamide Solid Lipid Submicroparticles Formated by Virgin Coconut Oil and Solid Matrix Surfactant. Science and Technology Indonesia, 2021;6(2):58-66.
29. Leão AD, Oliveira VV, Marinho FA, Wanderley AG, Aguiar JS, Silva TG. Hybrid systems of glibenclamide and layered double hydroxides for solubility enhancement for the treatment of diabetes mellitus II. Applied Clay Science, 2019; 181:105218.
30. Sandri G, Bonferoni MC, Rossi S, Caramella CM, Ferrari F (2018) Effects of particle size, surface nature and crystal type on dissolution rate. Particles and Nanoparticles in Pharmaceutical Products: Design, Manufacturing, Behavior and Performance, 2018:303-328.
31. Center for Drug Evaluation and Research. Bioavailability Studies Submitted in NDAs or INDs – General Considerations. FDA. 2024. Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/bioavailability-studies-submitted-ndas-or-inds-general-considerations (Accessed: 23 May 2025)