



In-Vitro Evaluation of Different Marketed Brands of Metformin Tablets Using Quality Control Tests

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Article History

Volume 6, Issue Si4, 2024

Received: 01 June 2024

Accepted : 29 June 2024

Doi:

10.48047/AFJBS.6.Si4.2024.1827-1846

Abstracts- Type II diabetes is a prevalent metabolic disorder, particularly affecting obese individuals, where effective management is crucial for mitigating associated health risks. Metformin, a frontline anti-diabetic medication, is widely prescribed due to its efficacy and cost-effectiveness. However, the availability of numerous brands of metformin tablets poses a challenge for healthcare providers and patients in selecting the most suitable option. This study aimed to evaluate the performance of four selected brands of 500 mg metformin tablets, focusing on their physical and chemical parameters using established methods.

The evaluation encompassed several key parameters, including uniformity of weight, friability, hardness, disintegration time, dissolution profile, and drug content, adhering strictly to standards outlined in the United States Pharmacopeia (USP) and Indian Pharmacopoeia (IP). All brands underwent rigorous testing to ensure consistency and adherence to pharmacopoeial specifications.

The results of the evaluation revealed that all four brands of metformin tablets met the specified limits for weight variation and friability, indicating uniformity and stability in their formulations. Furthermore, the disintegration time for each brand fell within the recommended threshold of 15 minutes, as per official guidelines, suggesting efficient breakdown and absorption within the gastrointestinal tract.

Moreover, all brands demonstrated satisfactory performance in the in-vitro dissolution rate test, with over 80% drug release observed within 30 minutes, ensuring adequate bioavailability and pharmacokinetic profiles. UV analysis confirmed that the active ingredient content in all brands remained within the monograph specification range of 95 – 105 %, affirming consistency in drug concentration and potency.

Although variations were observed in the performance metrics among the different brands evaluated, collectively, they met the pharmacopoeial specifications for

quality control. Therefore, based on the findings of this study, any of the evaluated brands can be freely substituted if one brand becomes unavailable or inaccessible.

In conclusion, this study provides valuable insights into the

performance of various brands of 500 mg metformin tablets, facilitating informed decision-making for healthcare providers and patients in the management of type II diabetes, especially in obese individuals. The adherence of all brands to established pharmacopoeial standards underscores their safety, efficacy, and interchangeability, ensuring consistent therapeutic outcomes.

Keywords: Metformin hydrochloride, In-vitro study, Physiocochemical equivalency, Dissolution rate, Comparative evaluation

Introduction: Oral drug delivery stands as the swiftest and most favoured method for administering drugs, constituting the largest and most established sector within the overall drug delivery market. Metformin, endorsed by the US Food and Drug Administration (USFDA) as a prescription medication for managing diabetes, belongs to the biguanide class of oral hypoglycemic agents^[1] It serves as the primary medication for addressing non-insulin dependent diabetes mellitus (type II diabetes), particularly among overweight and obese individuals with normal kidney function.

Diabetes Mellitus:

Diabetes mellitus is a metabolic disorder characterized by elevated blood sugar levels (hyperglycemia) resulting from either inadequate insulin production or the body's inability to respond effectively to insulin. Type II diabetes mellitus specifically involves insulin resistance or insufficient insulin production, leading to hyperglycemia and often glycosuria (sugar in the urine). This condition is associated with an increased risk of vascular complications.

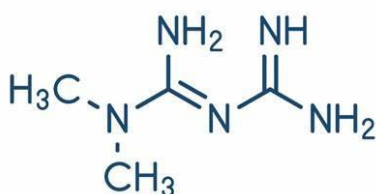
Disturbances in cognitive functions like learning, memory, and cognitive skills have been observed in individuals with diabetes, particularly Type II diabetes mellitus. These cognitive impairments are thought to be linked to the metabolic disturbances and vascular complications associated with the disease.

History and Usage of Metformin:

Metformin, a widely used anti-diabetic medication, has a long history dating back to its first description in scientific literature in 1922 by Emil Werner and James Bell. French physician Jean Sterne conducted the first clinical trial of Metformin for diabetes treatment. Since its introduction to various countries, including the United Kingdom in 1958, Canada in 1972, and the United States in 1995, Metformin hydrochloride has become one of the most commonly prescribed drugs for diabetes management globally. In the United States alone, millions of prescriptions for its generic formulations were filled in 2010, highlighting its widespread use and effectiveness in treating Type II diabetes mellitus.^[2]

Metformin hydrochloride has found expanded use beyond diabetes management, particularly in conditions like polycystic ovary syndrome (PCOS), nonalcoholic fatty liver disease (NAFLD), and premature puberty. In PCOS, Metformin, an insulin sensitizer, has been shown to improve hyperandrogenism (excess male hormone levels), promote ovulation, and increase pregnancy rates.^[3] Its mechanism of action involves improving insulin sensitivity, decreasing intestinal glucose absorption, suppressing hepatic glucose production (especially gluconeogenesis), and enhancing peripheral glucose uptake and utilization.

The chemical name of Metformin hydrochloride is 1,1-Dimethylbiguanide hydrochloride (C₄H₁₁N₅, HCl), with a molecular weight of 165.6 g/mol.



metformin

Pharmacological Action of Metformin:

Metformin hydrochloride primarily works by enhancing the body's sensitivity to insulin, facilitating glucose utilization, and regulating glucose production. It achieves this by reducing glucose absorption from food, inhibiting glucose production by the liver, and increasing peripheral tissue insulin sensitivity, leading to improved glucose uptake and utilization.^[4]

Quality Assurance in Pharmaceutical Products:

Ensuring the quality of pharmaceutical products, including generic versions of Metformin, is crucial for patient safety and treatment efficacy. Drug manufacturers are mandated to conduct rigorous testing of their products during and after manufacturing, as well as throughout the product's shelf life, to guarantee consistency in strength, quality, purity, and the release profile of the active ingredient. This is essential to ensure that generic drugs are pharmaceutically equivalent to their branded counterparts.

Importance of Quality Assurance:

Concerns arise when there are shortages of multinational brand drugs, leading patients to consider alternative local brands of the same generic drug. However, patients may be reluctant to switch due to psychological factors and concerns about efficacy and quality. While multinational brands may be out of reach for some due to high prices, locally available generic alternatives are often more affordable. Nevertheless, ensuring the quality and authenticity of these pharmaceutical products through robust quality assurance mechanisms is imperative for patient well-being and treatment outcomes.

Role of Regulatory Authorities:

Constant screening of marketed drugs by regulatory authorities and consumer organizations using pharmacopoeial methods helps consumers make informed decisions about the quality of drugs available to them, thus contributing to the overall quality of treatment. Therefore, implementing and maintaining quality assurance mechanisms are essential steps to ensure the authenticity and efficacy of pharmaceutical products, including Metformin and its generic formulations.

Quality Assessment of Pharmaceutical Products:

The quality assessment of pharmaceutical products, particularly solid oral dosage forms like tablets, involves various parameters to ensure their effectiveness and consistency. Parameters such as drug content and dissolution tests are critical indicators of quality for solid oral dosage forms like tablets. According to pharmaceutical standards, several parameters including weight variation, hardness, friability, disintegration, dissolution, and content uniformity are evaluated to assure the effectiveness of any drug.

Significance of Dissolution Testing:

In vitro dissolution studies play a crucial role in predicting the in vivo bioavailability of most oral drugs. Dissolution testing is a fundamental quality control tool used to monitor batch-to-batch consistency of drug release from a dosage form. It is essential for evaluating the pharmaceutical quality of different brands of drugs and determining their possible equivalence. With various brands of Metformin available in the market, ensuring the quality of these products is crucial for assessing their quality control and aiding in the selection of the appropriate brand.^[5]

Material Requirement-

Chemical Agent and sample collection- Metformin hydrochloride, having a label strength of 500mg of two different brands were purchased from registered pharmacy shop of rural area of Mandsaur and were coded as A& b. All the study was performed within product expiration dates.

Sample collection point-

(A) Glyciphage – Local Pharmacy shop , Mandsaur

(B) Generic- Govt. Primary Health Centre ,Kyamapur , Mandsaur

All the used reagents like potassium-di-hydrogen phosphate, Sodium hydroxide were of analytical grade. Freshly prepared distilled water was used throughout the work. Finally the following two different brands were taken for evaluation.

Code	Brand	Manufacture	Collection Point	Batch No.	Mfg. Date	Exp. Date
A	Glyciphage	Franco – India Pharmaceutical Pvt Ltd.	Retail Pharmacy	23076	04/2023	03/2026
B	Generic	Nester Pharmaceutical	Govt. PHC	MNTZ-17	09/2022	08/2024

Apparatus and Equipment:**1. Double Beam UV-Visible Spectrophotometer (Simatzu Model no:1900):**

A spectrophotometer analyzes how much light a sample absorbs across UV and visible light wavelengths. It works by passing light through a sample, measuring how much is absorbed at different wavelengths. This helps determine the sample's chemical makeup and concentration. By comparing the intensity of transmitted

light to the incident light, it calculates absorbance. This data forms a spectrum, which scientists interpret to identify substances and quantify their concentration. Spectrophotometers are crucial in fields like biochemistry and environmental science for their precision in analysis.



UV-Visible Spectrophotometer (Simatzu Model no:1900)

2. Analytical Balance (Electric Precision Balance, Model no.: 3003):

An analytical balance functions by comparing the mass of an object with a predetermined standard mass, meticulously calibrated to guarantee accuracy. This comparison enables precise measurements crucial in scientific research, quality control, and industrial applications. Encased within a chamber, the balance is shielded from external factors like air currents and vibrations that could skew measurements, ensuring consistency and reliability in results.

In operation, the balance utilizes a delicate mechanism to detect even the slightest deviations in mass between the object being weighed and the standard mass. This mechanism often involves a beam and pointer system or a digital sensor, both designed to provide highly accurate readings. The balance is typically calibrated regularly to maintain its precision, adjusting for any drift or changes in its performance over time.

The importance of analytical balances in various fields cannot be overstated. In scientific research, they enable the precise measurement of substances and compounds, essential for conducting experiments and analyzing results. Quality control processes in industries such as pharmaceuticals, food production, and manufacturing rely on analytical balances to ensure products meet strict standards of weight and composition. Additionally, analytical balances play a crucial role in settings where accurate measurements are paramount, such as forensic analysis and metrology laboratories.

Overall, analytical balances are indispensable tools for maintaining the highest standards of measurement accuracy, providing confidence in the reliability of data and the quality of products across diverse industries and scientific disciplines.



Electric Precision Balance (Model no.: 3003)

3. Hardness Tester (Monsanto, Mht-20):

The hardness tester, particularly the Monsanto Mht-20 model, serves as an indispensable tool in pharmaceutical manufacturing, specifically for assessing the mechanical strength of tablets. Its primary function revolves around quantifying the resistance of tablets to breakage when subjected to compression forces. This attribute is paramount as it directly influences the tablet's ability to maintain its structural

integrity throughout handling, packaging, and transportation, and ultimately ensures the proper release of the active pharmaceutical ingredient (API) upon ingestion.

The process of tablet hardness testing involves applying controlled compressive forces to individual tablets using specialized equipment, such as the Monsanto Mht-20 model. During testing, tablets are carefully positioned within the instrument, typically between two flat platens or anvils, which exert pressure on the tablet until it fractures or undergoes deformation. The force required to cause this breakage or deformation is then recorded and serves as a measure of the tablet's hardness or resistance to compression.

Pharmaceutical manufacturers utilize hardness testing at various stages of tablet production to monitor and control the quality of their products. In the early stages of formulation development, hardness testing helps researchers optimize tablet compositions and manufacturing processes to achieve desired mechanical properties. By adjusting parameters such as the type and concentration of binding agents, granule size, and compression force, manufacturers can tailor tablet formulations to meet specific hardness targets. During manufacturing, hardness testing is integrated into quality control protocols to ensure consistency and uniformity across batches of tablets



Hardness Tester (Monsanto, Mht-20)

4. Tablet Friability Tester (Dolphione, FTV-2):

The tablet friability tester, exemplified by the Roche FTV-2 model, serves a critical role in pharmaceutical quality control by assessing the susceptibility of tablets to fragmentation or breakage under mechanical stress. Specifically, it simulates the conditions encountered during handling and transportation by subjecting tablets to repeated tumbling within a rotating drum. This test is essential for evaluating the durability and robustness of tablets, ensuring they maintain their structural integrity throughout the manufacturing process, packaging, and distribution.

During friability testing, a sample of tablets is placed inside the drum of the friability tester, which is then rotated at a specified speed for a predetermined duration. As the tablets tumble within the drum, they experience mechanical forces that mimic those encountered during shipping, handling, and patient use. After the test cycle is complete, the tablets are removed from the drum, and any resulting fragmentation or breakage is assessed by comparing the weight loss of the sample to predefined acceptance criteria.

The data obtained from friability testing provides valuable insights into the physical properties of tablets, including their hardness, compactness, and resistance to mechanical stress.



Tablet Friability Tester (Dolphione, FTV-2)

5. *Disintegration Apparatus (Dolphine ED-2L)*:The disintegration apparatus, exemplified by the ED-2L model, serves a pivotal role in pharmaceutical quality control by precisely determining the disintegration time of tablets in a specified liquid medium. This crucial test assesses the ability of tablets to break down into smaller particles under physiological conditions, ensuring they release their active ingredients effectively for absorption in the body.

The disintegration process involves placing individual tablets into separate test tubes filled with a suitable liquid medium, typically water or simulated gastric fluid. These test tubes are then positioned within the disintegration apparatus, which maintains a constant temperature and provides gentle agitation to mimic the conditions encountered in the gastrointestinal tract. As the test proceeds, the apparatus continuously monitors each tablet, recording the time it takes for complete disintegration to occur.

Accurate measurement of disintegration time is essential for ensuring the efficacy and safety of orally administered pharmaceuticals. Tablets that disintegrate too slowly may not release their active ingredients within the desired timeframe, potentially delaying therapeutic effects or compromising bioavailability. Conversely, tablets that disintegrate too quickly may exhibit erratic drug release patterns, leading to suboptimal treatment outcomes or adverse effects.

By utilizing the ED-2L disintegration apparatus, pharmaceutical manufacturers can precisely evaluate the performance of tablet formulations and manufacturing processes, optimizing factors such as excipient composition, tablet hardness, and coating thickness to achieve desired disintegration profiles. Furthermore, regulatory authorities often stipulate disintegration testing as a mandatory requirement for product registration, underscoring its importance in ensuring pharmaceutical quality and compliance with regulatory standards.

In summary, the disintegration apparatus, represented by the ED-2L model, plays a crucial role in pharmaceutical development and quality control by accurately determining the disintegration time of tablets in specified liquid media..



Disintegration Apparatus (Dolphine ED-2L)

6. *Ultrasonicator (Toshcon, SW 4)*:The ultrasonicator, exemplified by the Toshcon SW 4 model, serves as a versatile tool in scientific and industrial settings, leveraging ultrasonic vibrations to agitate, disperse, and process samples with precision and efficiency. This powerful instrument finds widespread application across diverse fields, including chemistry, biology, materials science, and pharmaceuticals, where precise sample preparation and manipulation are paramount.

One of the primary functions of an ultrasonicator is sample preparation, where it facilitates the dissolution, homogenization, and dispersion of substances in various solvents or media. By subjecting samples to ultrasonic waves, the ultrasonicator induces cavitation—a phenomenon characterized by the formation and collapse of microscopic bubbles within the sample. These rapid oscillations generate intense shear forces and microstreaming, effectively breaking down particles, disrupting aggregates, and promoting thorough mixing and dissolution.

In addition to sample preparation, ultrasonicators are instrumental in cell disruption techniques, where they assist in the extraction of intracellular components from biological samples. By applying ultrasonic energy, the ultrasonicator ruptures cell membranes, releasing cellular contents for downstream analysis or processing.

Furthermore, ultrasonicators excel in emulsification processes, where they facilitate the creation of stable emulsions by dispersing immiscible liquids or suspending fine particles within a continuous phase. This

capability is particularly valuable in industries such as food, cosmetics, and pharmaceuticals, where emulsions play a vital role in product formulation and stability.

Moreover, ultrasonicators are employed in degassing applications to remove dissolved gases or air bubbles from liquids, ensuring the integrity and quality of samples or products.



Ultrasonicator (Toshcon, SW 4)

7. pH Meter (EI): pH meters are essential tools in various industries and scientific fields, featuring a sensitive electrode that produces a voltage corresponding to the concentration of hydrogen ions in a solution, subsequently converted into pH units. This mechanism facilitates rapid and accurate pH measurements, empowering researchers and technicians to precisely adjust conditions as needed.

These instruments find extensive application across diverse sectors, including food and beverage production, where pH regulation is critical for ensuring product quality, safety, and shelf stability. In pharmaceutical manufacturing, pH meters are indispensable for monitoring and controlling the acidity or alkalinity of formulations, influencing drug solubility, stability, and bioavailability. Moreover, in agricultural practices, pH meters are employed in soil analysis to assess soil fertility and acidity levels, guiding farmers in optimizing crop yields through appropriate soil amendments and fertilization strategies.

In laboratory settings, pH meters play a pivotal role in conducting experiments and analyzing biological, chemical, and environmental samples. Whether determining the pH of biological fluids, monitoring chemical reactions, or assessing water quality in environmental studies, pH meters provide invaluable insights into the acidity or alkalinity of solutions, influencing experimental outcomes and data interpretation.

The versatility of pH meters extends to numerous other applications, including wastewater treatment, brewing and fermentation processes, and industrial manufacturing, where pH control is integral to maintaining process efficiency and product quality. By offering quick, accurate, and reliable pH measurements, these instruments contribute to the optimization of various processes and experiments, ensuring optimal conditions for desired outcomes and enhancing productivity and quality across multiple sectors..^[6]



pH Meter (EI)

Methods:

1. Visual Inspection: During the visual inspection phase, each brand of Metformin tablets undergoes a meticulous examination focused on discerning distinct characteristics such as shape, colour, and texture. This critical step aids in visually identifying any discrepancies, irregularities, or variations among the tablets. The examination begins with an assessment of the tablets' shapes, whether they are round, oval, oblong, or have any unique contours. Variations in shape can indicate differences in manufacturing processes or formulations, and identifying such discrepancies is crucial for maintaining product consistency and quality. Color plays a significant role in tablet identification and differentiation. Tablets are scrutinized under standardized lighting conditions to accurately assess their hues and shades. Any deviations from the expected color, whether subtle or pronounced, are carefully noted. Consistency in colour ensures brand recognition and instills confidence in product quality among consumers and healthcare professionals.

Texture is another important attribute examined during visual inspection. The surface of each tablet is inspected for smoothness, uniformity, and any irregularities such as cracks, chips, or rough patches. Any variations in texture may suggest issues with manufacturing processes, coating quality, or formulation integrity.

By meticulously examining each brand of Metformin tablets for these key characteristics, pharmaceutical manufacturers can detect and address potential quality concerns promptly. Consistency in shape, color, and texture not only enhances product aesthetics but also reflects adherence to stringent quality standards and regulatory requirements.

Overall, visual inspection serves as a fundamental quality control measure in pharmaceutical manufacturing, ensuring that Metformin tablets meet established specifications and deliver consistent performance and efficacy to patients. Through this meticulous examination process, manufacturers can uphold their commitment to product quality, safety, and patient satisfaction..

2. Thickness and Diameter Measurement:

To ascertain the thickness and diameter of the tablets, verniercalipers are employed. This method involves randomly selecting ten tablets, each of which undergoes individual measurement for thickness using the calipers. The measurements obtained are then averaged to derive the mean thickness in millimeters.

During the process, each tablet is carefully placed between the jaws of the verniercalipers, ensuring proper alignment and contact. The calipers are gently closed until they lightly touch the tablet, and the reading is noted from the scale engraved on the caliper's shaft. This step is repeated for each of the ten selected tablets.

Once all measurements are obtained, they are collated and summed before being divided by the total number of tablets measured, yielding the mean thickness value. This average thickness provides valuable insight into the uniformity and consistency of tablet dimensions within the sample batch.

Similarly, the diameter of the tablets can be determined using the same procedure, albeit measuring across the widest portion of the tablet. By employing verniercalipers for both thickness and diameter measurements, pharmaceutical manufacturers can ensure precise and accurate dimensional analysis, crucial for quality control and compliance with regulatory standards.

The data obtained from these measurements contribute to the comprehensive assessment of tablet characteristics, aiding in the identification of variations or irregularities that may impact product performance, packaging compatibility, and patient acceptability. Through meticulous measurement techniques and statistical analysis, manufacturers can uphold the integrity and reliability of their tablet formulations, thereby delivering high-quality pharmaceutical products to consumers..

3. Weight Variation Test:

The weight variation test aims to assess the uniformity of each batch of tablets, reflecting the consistency of drug content across all formulation batches. Twenty tablets are randomly selected from the batch, and each tablet is individually weighed. The average weight, standard deviation, and percent deviation are then calculated to evaluate uniformity.

The percent deviation is calculated using the formula:

$$\% \text{ Deviation} = \frac{[W_{\text{avg}} - W_{\text{ind}}]}{W_{\text{avg}}} \times 100$$

Where:

W_{avg} = Average weight of tablets

W_{ind} = Individual weight of tablet

4. Friability Test:

The friability test assesses the potential wear and tear of tablets during transportation, which correlates with tablet hardness. The test is conducted using a friabilator, such as the Roche Friabilator, with the following steps:

- Selection of Tablets: Five tablets are randomly chosen for the test.
- Initial Weight Recording (W1): The initial weight of the five selected tablets is recorded.
- Friabilator Operation: The tablets are placed inside the friabilator, which is operated for 4 minutes at a speed of 25 rpm and 100 revolutions.
- Final Weight Recording (W2): After operation, the tablets are removed and their final weight is recorded.
- Calculation of Percent Loss (Friability): Percent loss (friability) is calculated using the formula:

$$\text{Friability} = \frac{\{\text{Initial weight} - \text{Final weight}\}}{\{\text{Initial weight}\}} \times 100$$

- Permissible Limit: The official permissible limit for friability is typically 1%.

The friability test provides crucial information regarding the ability of tablets to withstand mechanical stress during handling and transportation.^[7]

5. Hardness Test:

Tablet hardness, a critical parameter in pharmaceutical quality control, is assessed using a Monsanto hardness tester. This method involves selecting five tablets at random from each brand and subjecting them to pressure within the hardness tester until they break. The pressure required to cause the tablets to fracture is meticulously recorded for each tablet.

During the testing process, the tablets are carefully positioned between the spindle and anvil of the hardness tester, ensuring uniform alignment and contact. The tester then exerts increasing pressure on the tablets until they reach a point of mechanical failure, typically indicated by audible or visual cues such as cracking or crumbling. The pressure at which this fracture occurs is measured in kilograms per square centimeter (Kg/cm²) and serves as a quantitative measure of tablet hardness.

By testing multiple tablets from each brand and calculating the mean hardness value, pharmaceutical manufacturers can obtain a representative assessment of the tablets' mechanical strength and consistency. Variations in hardness between different brands or batches may indicate differences in formulation, compression force, or manufacturing processes, which can impact tablet integrity, disintegration, and dissolution rates.

The data obtained from hardness testing plays a crucial role in ensuring product quality, regulatory compliance, and patient safety. Tablets with insufficient hardness may be prone to damage during handling, packaging, or transportation, leading to issues such as breakage, capping, or chipping. Conversely, tablets

with excessively high hardness may pose challenges for patients, particularly those with difficulty swallowing or compromised gastrointestinal function.

Overall, hardness testing using a Monsanto hardness tester provides valuable insights into the mechanical properties of tablets, enabling pharmaceutical manufacturers to optimize formulations, manufacturing processes, and quality control measures. By maintaining consistent hardness levels within specified ranges, manufacturers can produce tablets that meet stringent quality standards and deliver reliable therapeutic outcomes for patients.

6 Tablet Disintegration Test:

Tablet disintegration time, a crucial parameter in pharmaceutical quality control, is determined utilizing a disintegration apparatus. This process involves randomly selecting six tablets from each brand and placing them within the apparatus, where they are submerged in distilled water as the test fluid. The temperature is rigorously controlled at 37 ± 0.2 °C to simulate physiological conditions accurately.

Once the tablets are immersed, the disintegration apparatus gently agitates them, mimicking the mechanical forces encountered during ingestion and digestion. Observers closely monitor the process, noting the exact moment when no granules or particles from any tablet remain on the mesh at the bottom of the apparatus. This precise point signifies complete disintegration of the tablets and is recorded as the disintegration time.

The disintegration time serves as a critical indicator of a tablet's ability to break down and release its active ingredients effectively within the gastrointestinal tract. Variations in disintegration time between different brands or batches may indicate differences in formulation, manufacturing processes, or excipient properties, which can impact drug absorption and therapeutic efficacy.

By adhering to standardized testing procedures and strict temperature control, pharmaceutical manufacturers can ensure consistency and reliability in disintegration time measurements. This information enables informed decisions regarding product quality, regulatory compliance, and patient safety, ultimately contributing to the development of effective and reliable pharmaceutical formulations..

7 Assay- These tests collectively provide comprehensive insights into the physical characteristics, uniformity, durability, and performance of metformin tablets from different brands.

The assay test is essential for determining the concentration of the active pharmaceutical ingredient (API) present in the samples, which is responsible for the therapeutic action of the medication. In this case, the UV method was employed to analyze the content of the active ingredient in the Metformin tablets.^[8]

To conduct the assay test, a test solution was prepared by first weighing twenty tablets and then grinding them into a powder. From this powder, an amount containing 0.1 g of Metformin was weighed and dissolved in 70 ml of water. The volume was then adjusted to 100 ml with water. Subsequent dilutions were made to achieve a concentration of approximately 11 parts per million (PPM). The absorbance of the resulting solution was measured. The calculation of the content of Metformin involved using 798 as the specific absorbance at the maximum wavelength of 232 nm, as specified in the Indian Pharmacopoeia (IP). The percent assay was determined using the following formula:

$$\text{Assay} = \frac{\text{Test Abs} \times 1 \times \text{Test dil} \times \text{Avgwt} \times 100 \times 1000}{\text{Specific Abs} \times 100 \times \text{Test wt} \times \text{Claim}}$$

Here,

- Test Abs: Absorbance of the test solution.
- Test dil: Dilution factor of the test solution.
- Avgwt: Average weight of the tablets used for the test.
- Specific Abs: Specific absorbance of Metformin at 232 nm (as per IP).
- Test wt: Weight of Metformin used for preparing the test solution.
- Claim: Claimed content of Metformin in the tablets.

This calculation yields the percentage of the active ingredient present in the Metformin tablets, providing crucial information about their potency and adherence to pharmacopoeial standards.^[9]

Results and Discussion

General Appearance Assessment: In the assessment of Metformin hydrochloride tablets, a meticulous visual examination was conducted to evaluate various attributes including shape, color, and texture. Each tablet

from different brands underwent careful observation, with the findings meticulously recorded. These observations were summarized in a detailed manner in Table 1.

The examination began with an inspection of the overall appearance of each tablet, noting any variations in shape compared to the expected form. Shapes were described, whether round, oval, oblong, or otherwise, along with any irregularities observed. Following this, the color of each tablet was meticulously observed under standardized lighting conditions, with shades noted and compared to the expected color based on the brand's specifications.

Texture played a crucial role in the evaluation process, with the surface of each tablet scrutinized for any anomalies such as cracks, chips, or roughness. The presence of surface coatings or imprints was also noted, as these attributes can influence the tablet's appearance and potentially impact patient adherence and acceptability.

In addition to these primary attributes, other visual characteristics such as size, thickness, and presence of scoring lines were assessed and recorded. Any discrepancies between tablets from different brands were documented, providing valuable insights into potential variations in manufacturing processes or formulation characteristics.

Overall, the visual examination served as an important preliminary step in assessing the quality and consistency of Metformin hydrochloride tablets across different brands. By meticulously documenting observations related to shape, color, texture, and other visual attributes, the examination provided valuable data for further analysis and comparison, informing decisions regarding product selection, quality control measures, and patient satisfaction.

Thickness and Diameter Measurement: To determine the thickness and diameter of the Metformin hydrochloride tablets, a precision measuring instrument known as verniercalipers was employed. Five tablets from each brand were randomly selected for measurement. The thickness of each tablet was measured individually, and similarly, the diameter was measured. These measurements were repeated for all brands, and the average values for thickness and diameter were calculated. The summarized results of these measurements are presented in Table 1 for comparison and analysis.

This detailed assessment provides valuable information regarding the physical characteristics and dimensions of the Metformin hydrochloride tablets from various brands, aiding in quality control and comparison purposes.

Table 1: Data of shape, colour, texture, thickness and diameter of Metformin HCl tablets

	Code	Shape	Colour	Texture	Thikness	Diameter
	A	Cylindrical	white	Smooth	5.0mm	16.66mm
:	B	Rounded	White	Smooth	4.2mm	12.40mm

Weight Variation Test Results:

The weight variation test was conducted on all four brands of metformin hydrochloride tablets to assess their uniformity in weight. This test is essential as it ensures that the tablets within each batch have consistent drug content, meeting the specifications outlined in the United States Pharmacopeia (USP).

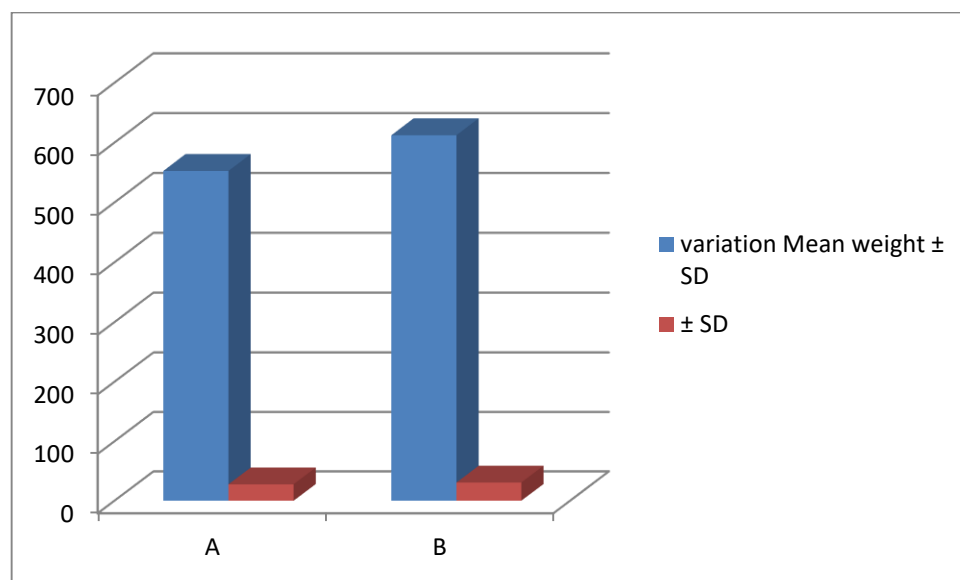
The test involved randomly selecting a sample of tablets from each brand and individually weighing them. The weights of the tablets were compared to the mean weight value for each brand. According to USP guidelines, the acceptable limit for weight deviation is $\pm 5\%$ from the mean weight.

The detailed results of the weight variation test, as shown in Table 2, indicate that all four brands of metformin hydrochloride tablets passed the uniformity test. None of the brands exhibited a weight deviation exceeding the permissible limit of $\pm 5\%$ from the mean weight value. Therefore, all brands complied with the USP specifications for weight uniformity.^[10]

This successful outcome demonstrates the consistency and quality of the manufacturing process for the metformin hydrochloride tablets across all four brands. It ensures that patients receive tablets with accurate and uniform drug content, contributing to their efficacy and safety in clinical use.

Table No.2 Comparative data of variation Mean weight and $\pm$ Standard deviation quality control parameters of two brands of Metformin HCl tablets

Brand Code	variation Mean weight	$\pm$ Standard deviation	Result
A	552.74 mg	$\pm$ 27.63mg	Pass
B	612.37 mg	$\pm$ 30.61mg	Pass



Friability Test Results:

The friability test was conducted on five tablets selected from each of the chosen brands of metformin hydrochloride tablets. This test aims to assess the tablets' resistance to mechanical stress and potential damage during transportation and handling.

The selected tablets were individually weighed to determine their initial weights before undergoing the friability test. Subsequently, they were subjected to the Roche friability apparatus, which simulates mechanical stress by tumbling the tablets in a controlled environment for a specified duration.

After completing the friability test, the tablets were weighed again to measure their final weights. The percentage friability was then calculated using the formula:^[11]

According to the specifications outlined in the United States Pharmacopeia (USP), tablets must not lose more than 1% of their initial weight during the friability study to meet the required standards.

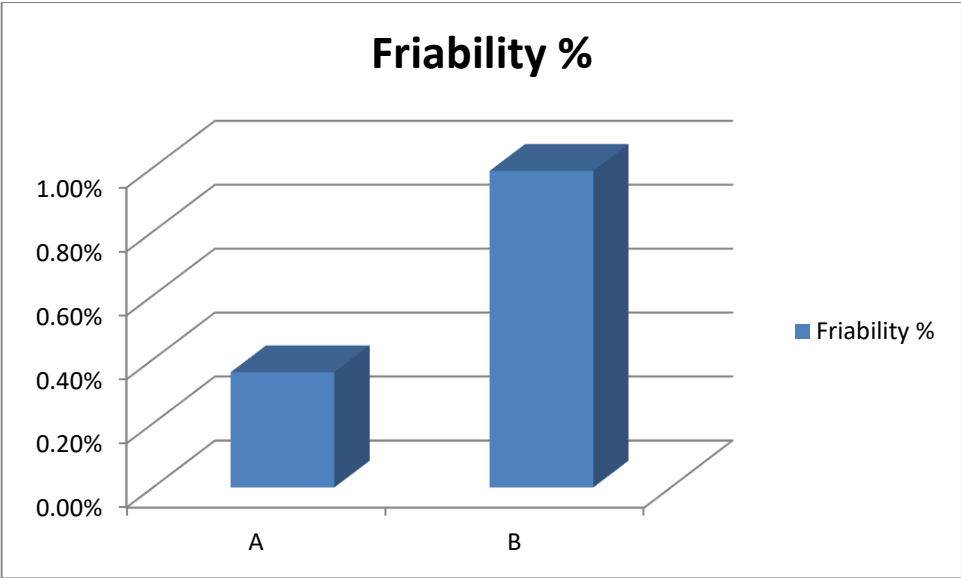
The results of the friability test, as displayed in Table 3, demonstrate that the percentage friability of the tablets from all selected brands met the specifications of the USP. None of the brands exceeded the permissible limit of 1% weight loss during the friability study.

This outcome indicates that the metformin hydrochloride tablets from the chosen brands exhibit satisfactory resistance to mechanical stress, ensuring their integrity and quality throughout handling and transportation. It confirms compliance with regulatory standards and contributes to the tablets' reliability and effectiveness for patient use.

The successful outcome of the friability test underscores the robustness and durability of the metformin hydrochloride tablets from the selected brands. By meeting the stringent requirements outlined in the United States Pharmacopeia (USP), these tablets demonstrate their ability to withstand mechanical stress and maintain structural integrity during handling and transportation. This adherence to regulatory standards not only affirms the tablets' quality but also instills confidence in their reliability and effectiveness for patient use. Additionally, the meticulous testing and adherence to USP specifications reflect the manufacturers' commitment to ensuring product consistency and safety, further enhancing the tablets' reputation in the pharmaceutical market.^[11]

Table No.3 Comparative data of Friability % quality control parameters of two brands of Metformin HCl tablets

Brand Code	Friability %	Result
A	0.36%	Pass
B	0.99%	Pass



Hardness Test Results:

The hardness of the metformin tablets was assessed using the Monsanto hardness tester. This test is crucial as it measures the tablets' resistance to mechanical stress, providing insight into their crushing strength and durability.

Each selected brand of metformin tablets underwent hardness testing, where a sample of tablets was individually placed between the spindle of the Monsanto hardness tester. Pressure was applied gradually until the tablets fractured or broke. The pressure required to break the tablets was recorded, reflecting their hardness or crushing strength.^[12]

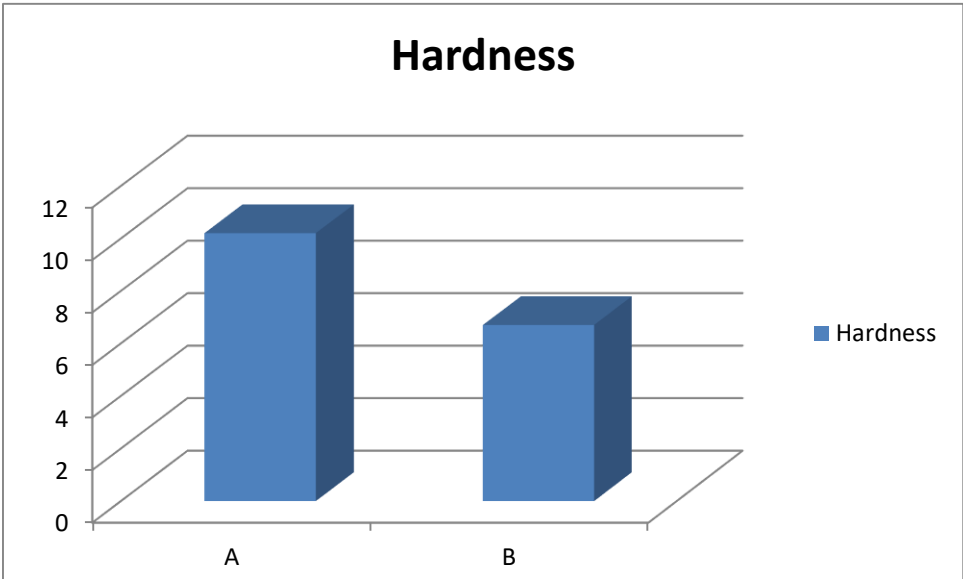
The results of the hardness test revealed that all selected brands of metformin tablets exhibited acceptable crushing strength or hardness. The observed values, representing the pressure required to break the tablets, are detailed in Table 4.

Meeting the acceptable hardness standards is essential as it ensures that the tablets can withstand handling, packaging, and transportation without undergoing excessive damage or breakage. Tablets with adequate hardness are more likely to maintain their structural integrity, ensuring consistent dosing and efficacy for patients.

The successful outcome of the hardness test confirms the quality and reliability of the manufacturing process for the metformin tablets across all selected brands. It indicates compliance with industry standards and regulatory requirements, reinforcing the tablets' suitability for therapeutic use.

Table No.4 Comparative data of Hardness quality control parameters of two brands of Metformin HCl tablets

Brand Code	Hardness Kg/cm2	Result
A	10.2	Pass
B	6.7	Pass



Disintegration Test Results:

Tablet disintegration plays a crucial role in ensuring optimal bioavailability, facilitating improved drug absorption and therapeutic efficacy. Therefore, assessing the disintegration time of tablets is an essential aspect of pharmaceutical quality control.

The disintegration test was conducted on tablets from all four different brands of metformin tablets. This test involved placing a sample of tablets in a disintegration apparatus containing a specified medium, typically distilled water, maintained at a controlled temperature. ^[13] The tablets were observed until complete disintegration occurred, indicated by the absence of any visible tablet residue on the mesh screen.

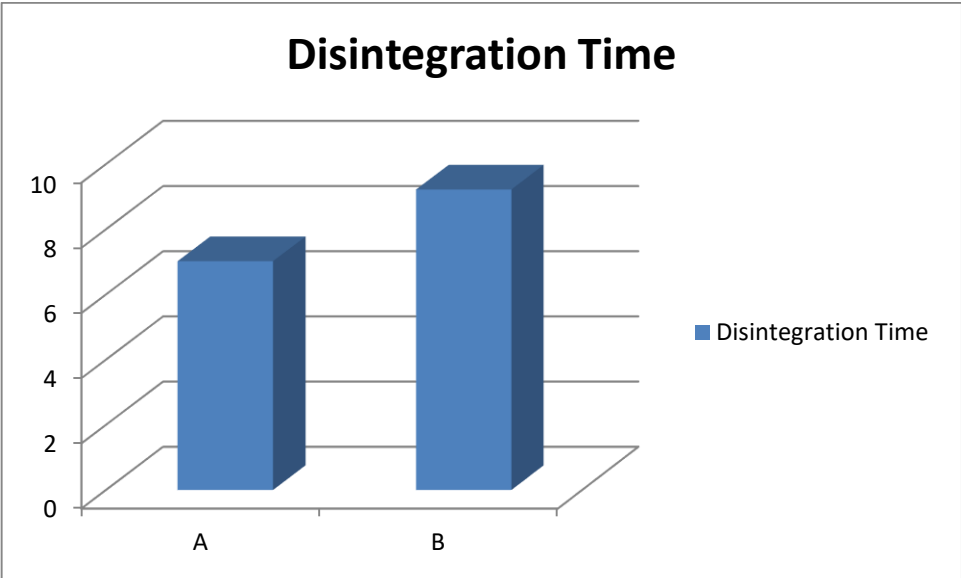
The results of the disintegration test revealed that the disintegration time for all brands of metformin tablets was less than 10 minutes. This finding indicates that all tested brands met the standard disintegration time specified by pharmacopeias, which typically require disintegration within a certain time frame to ensure therapeutic effectiveness.

The disintegration times for each brand of metformin tablet are presented in Table 5. These results demonstrate that all brands passed the quality control limits for disintegration, indicating their suitability for therapeutic use.

Ensuring prompt tablet disintegration is essential for facilitating drug release and absorption in the body, ultimately enhancing the therapeutic action of the medication.

Table No.5 Comparative data of Disintegration Time quality control parameters of two brands of Metformin HCl tablets.

Brand Code	Disintegration Time Min.sec %Drug	Result
A	7min 2 sec	Pass
B	9min 22 sec	Pass



Assay- This test aimed to evaluate the accuracy of the labeled content specified on the label of the Metformin tablets and to determine any variations in the quantity among the samples. Both intraday and interday studies were conducted, including assessments of intra-instrument and inter-instrument variations. The goal was to ensure consistency and reliability in the content of the active pharmaceutical ingredient (API) across different samples.

According to the Indian Pharmacopoeia (IP), the labeled content of the Metformin tablets should fall within the range of 95% to 105% of the specified value. This range ensures that the tablets are within acceptable limits of potency and efficacy.

Results from the analysis revealed that all six brands tested fell within the prescribed range specified in the monograph, demonstrating their efficacy and adherence to pharmacopoeial standards. Among the samples, the government generic sample A exhibited the highest content, measuring at 102.61%, while the branded sample B showed the lowest content at 98.69%. However, despite these variations, Moreover, the comparison between generic versus generic formulations and branded versus branded formulations did not reveal any notable differences in terms of drug content. Additionally, the intraday and interday results met the specified limits outlined in the IP, indicating consistency and reliability in the testing methodology.

Furthermore, variations in both intra-instrumental and inter-instrumental analyses were not observed, suggesting stability and reproducibility in the measurement process. These findings provide assurance regarding the accuracy and consistency of the drug content across different samples and measurement conditions. ^[14]

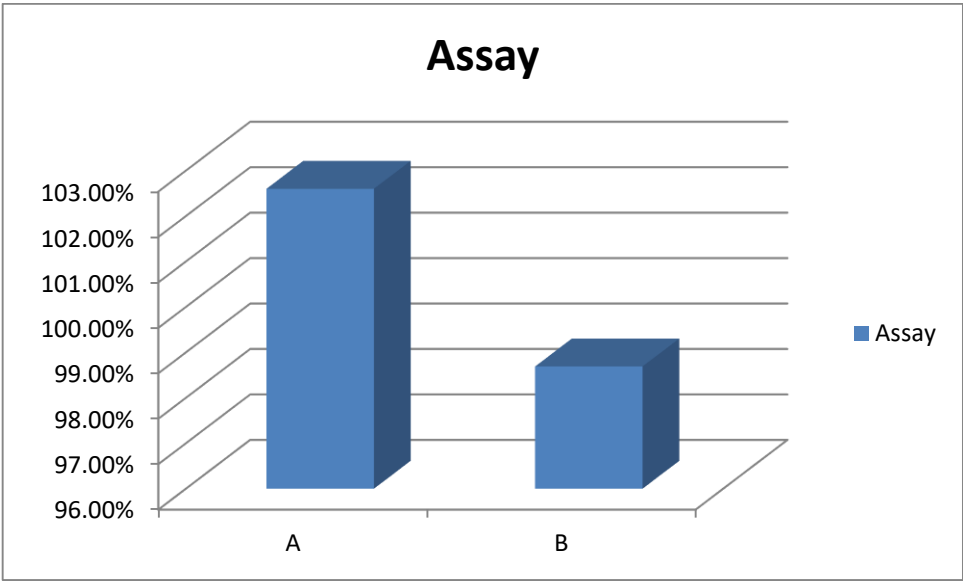
Overall, the percentage of drug content results, as presented in Table 6 confirms the compliance of all tested brands with the specified pharmacopoeial standards, reinforcing their efficacy and suitability for clinical use in the management of type II diabetes. The rigorous evaluation of Metformin tablets according to pharmacopoeial standards underscores their reliability and suitability for treating type II diabetes. Consistency in drug content across various brands, coupled with stable measurement processes, assures clinicians and patients of consistent therapeutic outcomes.

The meticulous assessment of Metformin tablet content, in accordance with Indian Pharmacopoeia standards, affirms the tablets' potency and efficacy for managing type II diabetes. The consistency in drug content across different brands, alongside stable measurement processes, provides reassurance to clinicians and patients regarding consistent therapeutic outcomes. These findings underscore the reliability and suitability of Metformin tablets for treating type II diabetes, reinforcing their importance in clinical practice.

Table No.6 Comparative data of Assay quality control parameters of two brands of Metformin HCl tablets

Brand Code	Assay	Result
A	102.6%	Pass

B	98.69%	Pass
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Standard Calibration Curve:

A standard curve of Metformin is a graphical representation depicting the relationship between the concentration of Metformin, typically measured in milligrams per liter (mg/L) or other relevant units, and the corresponding response, often measured as absorbance or fluorescence intensity, depending on the method of detection used.

To create a standard curve, a series of known concentrations of Metformin are prepared and subjected to the same experimental conditions as the samples of interest. These concentrations typically span a range that covers the expected concentrations in the samples being analyzed.^[15]

Once prepared, each standard solution is analyzed using the chosen analytical method, and the resulting response (e.g., absorbance or fluorescence intensity) is recorded. This process is repeated for each standard solution, generating a set of data points.

The data points are then plotted on a graph, with the concentration of Metformin on the x-axis and the corresponding response on the y-axis. Typically, a linear relationship is observed between concentration and response within a certain range. Therefore, a best-fit line, often determined using linear regression analysis, is drawn through the data points.

The resulting standard curve provides a means to quantitatively determine the concentration of Metformin in unknown samples by measuring their response and comparing it to the standard curve. By interpolating or extrapolating the response of the unknown sample on the standard curve, its concentration can be estimated with reasonable accuracy. This method is commonly used in analytical chemistry and pharmacology for the quantitative analysis of Metformin in various samples, such as pharmaceutical formulations, biological fluids, and environmental samples.

Results:

The standard calibration curve serves as a cornerstone in pharmaceutical analysis, particularly concerning the determination of Metformin concentrations in various formulations or biological samples. This critical component, meticulously constructed and presented in Table 7, outlines the concentrations of precisely prepared Metformin solutions, meticulously aligned with their corresponding analytical responses. These responses, typically measured as absorbance or peak area, offer a tangible representation of the intricate relationship between Metformin concentration and its observable analytical attributes.^[16]

Table 8, in contrast, likely provides a graphical depiction of this calibration curve. Through a series of plotted points, it visually illustrates the complex correlation between the concentration of Metformin and its analytical response. This graphical representation holds immense importance in pharmaceutical research and quality control, as it offers a visual roadmap for accurately quantifying Metformin concentrations in unknown samples based on their observed analytical responses.

In essence, the standard calibration curve acts as the bedrock for quantitative analysis, ensuring the precision and validity of analytical findings within the realm of pharmaceutical sciences. Its significance lies in its ability to furnish researchers and analysts with a reliable framework for assessing Metformin concentrations with confidence and accuracy, thereby bolstering the integrity of pharmaceutical research and product quality assessment. By establishing a robust relationship between Metformin concentration and its corresponding analytical response, this calibration curve empowers researchers to make informed decisions regarding the formulation, quality, and efficacy of pharmaceutical products.

Table 7: Data for standard calibration curve of MetforminHCl tablet (A)

S.No	Concentration (µg/ml)	Absorbance
1	5	0.368
2	10	0.753
3	15	1.115
4	20	1.489
5	25	1.788

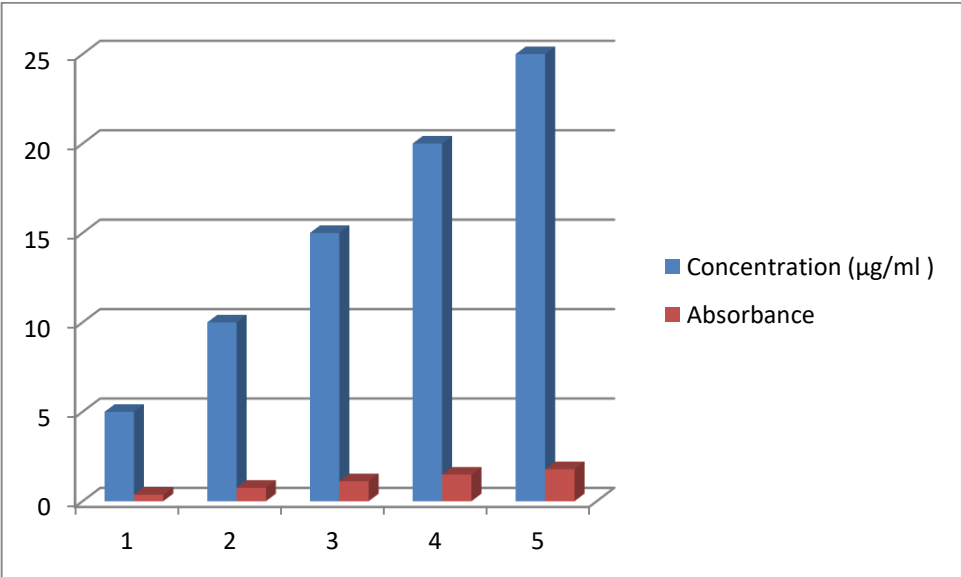
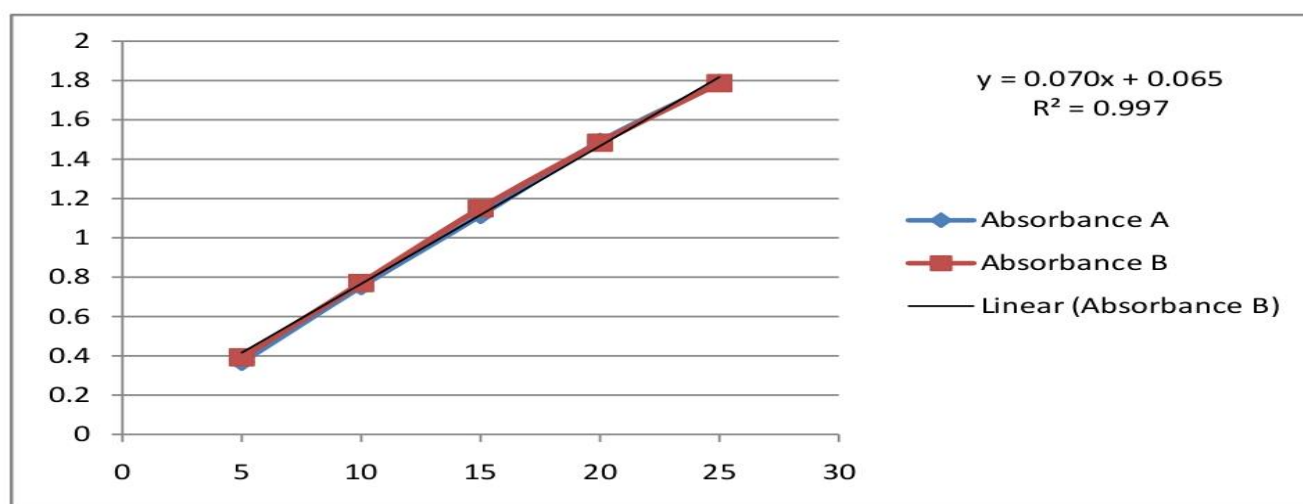
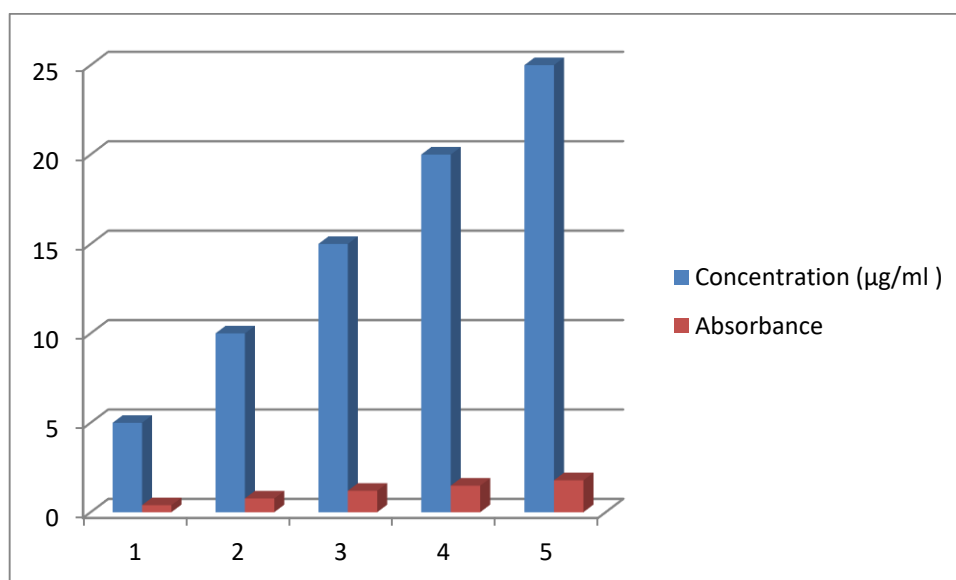


Table 8: Data for standard calibration curve of Metformin HCl tablet (B)

S.No.	Concentration (µg/ml)	Absorbance
1	5	0.392
2	10	0.770
3	15	1.200
4	20	1.484
5	25	1.787



Comparative Standard curve of Metformin HCL tablet 500mg Glyciphase (A) and Generic (B)

Conclusion:

This study aimed to evaluate the quality and physicochemical equivalence of two different marketed brands of metformin hydrochloride tablets. The findings confirm that all both of metformin hydrochloride tablets met the official specifications for weight variation, hardness, friability, disintegration, assay, and dissolution

- Compliance with Official Specifications:

All evaluated brands of metformin tablets complied with the official specifications for various quality parameters, ensuring their adherence to pharmacopeial standards.

- Drug Content within Limits:

The percent drug content of all brands of metformin hydrochloride tablets fell within pharmacopeial limits, indicating consistent potency across brands.

- Interchangeability of Brands:

Despite differences in their quality assessment results, none of the brands exceeded the limits specified in official standards. Therefore, the selected brands of metformin hydrochloride tablets can be considered interchangeable. If one brand is unavailable in the market, any of the other three brands can be used as a substitute without compromising efficacy or potency.

Overall, the study's findings assure healthcare providers and patients that these brands of metformin hydrochloride tablets, despite being manufactured by different pharmaceutical companies, maintain

consistent quality and can be used interchangeably, ensuring continuous availability and effectiveness of treatment options.

Based on the comprehensive evaluation of various quality control parameters for four different brands of 500 mg metformin tablets, it can be concluded that all brands met the specified pharmacopoeial standards for weight variation, friability, hardness, and disintegration time. Additionally, the in-vitro dissolution rate test showed that all brands achieved over 80% drug release within 30 minutes, indicating their effectiveness in delivering the active ingredient.^[17]

Moreover, UV analysis confirmed that the active ingredient content in all brands fell within the monograph specification (95 – 105 %), further ensuring their pharmacological equivalency. While there were variations in the results among brands, they collectively demonstrated compliance with quality control specifications, highlighting their suitability for substitution if one brand is unavailable.

This study provides valuable insights for healthcare professionals and patients in selecting an appropriate and economical brand of metformin tablets for the management of type II diabetes, particularly in obese patients. The findings support the interchangeability of these brands based on their comparable performance in terms of physical and chemical parameters, thereby promoting accessibility and affordability of essential medication.^[18]

The study conducted a thorough evaluation of the quality and physicochemical equivalence of two different marketed brands of metformin hydrochloride tablets. The findings revealed that both brands of metformin hydrochloride tablets met the official specifications for various critical parameters including weight variation, hardness, friability, disintegration, assay, and dissolution. This compliance with official specifications underscores their adherence to pharmacopoeial standards, ensuring their quality and effectiveness.

One of the key observations from the study was that the drug content of all brands of metformin hydrochloride tablets fell within pharmacopoeial limits, indicating consistent potency across the brands. This consistency in potency is crucial for ensuring predictable therapeutic outcomes for patients.

Despite differences in their quality assessment results, none of the evaluated brands exceeded the limits specified in official standards. This suggests that the selected brands of metformin hydrochloride tablets can be considered interchangeable. In practical terms, this means that if one brand is unavailable in the market, patients can safely use any of the other brands as a substitute without compromising efficacy or potency. This interchangeability enhances the accessibility of the medication and ensures continuity of treatment for patients.

The study also highlighted the in-vitro dissolution rate of the tablets, demonstrating that all brands achieved over 80% drug release within 30 minutes. This indicates their effectiveness in delivering the active ingredient, which is essential for achieving therapeutic effects in patients.

Furthermore, UV analysis confirmed that the active ingredient content in all brands fell within the monograph specification (95 – 105 %), further ensuring their pharmacological equivalency. While there were variations in the results among brands, they collectively demonstrated compliance with quality control specifications, highlighting their suitability for substitution if one brand is unavailable.

Overall, the study provides valuable insights for healthcare professionals and patients in selecting an appropriate and economical brand of metformin tablets for the management of type II diabetes, particularly in obese patients. The findings support the interchangeability of these brands based on their comparable performance in terms of physical and chemical parameters, thereby promoting accessibility and affordability of essential medication. This reassures both healthcare providers and patients about the consistent quality and effectiveness of these metformin hydrochloride tablets, irrespective of the brand chosen.

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