IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

EVALUATING MARKETED METFORMIN HYDROCHLORIDE (500mg) TABLETS: A COMPARATIVE IN-VITRO APPROACH

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ABSTRACT

The research meticulously examined and compared four distinct brands of metformin tablets, each containing 500 mg of the active compound. Employing rigorous evaluation parameters outlined in official compendiums such as the USP and IP, the study scrutinized various aspects including uniformity of weight, friability, hardness, disintegration time, dissolution profile, and drug content. Remarkably, all brands adhered to the stringent standards set forth, showcasing uniform tablet weight, satisfactory resistance to mechanical stress, and consistent disintegration within the prescribed timeframe. Moreover, dissolution rate tests revealed that over 80% of the active ingredient was released within 30 minutes, meeting the official specifications for pharmacological efficacy. Importantly, analysis of drug content confirmed that all brands maintained active ingredient levels within the specified range of 95-105%. While variations were observed among brands, the overarching conclusion underscored their collective compliance with quality control benchmarks, affirming their interchangeability in clinical practice, should one brand be unavailable. These findings carry significant implications for healthcare practitioners and patients, offering assurance regarding the reliability and effectiveness of available metformin formulations in managing type II diabetes mellitus. Furthermore, the study serves as a valuable resource for informed decision-making in selecting the most suitable metformin brand based on factors such as cost and availability without compromising on therapeutic efficacy.

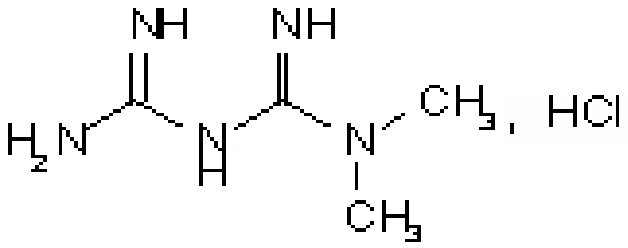
Keywords: Metformin hydrochloride, Comparative evaluation, In-vitro study

INTRODUCTION

Oral drug delivery is not only the most rapid and preferred method of administering medications but also represents the largest and most established segment of the pharmaceutical market. Among these medications, metformin holds significance as it is the prescription medication approved by the USFDA for managing diabetes. Metformin hydrochloride, classified as an oral anti-diabetic drug belonging to the biguanide class of oral hypoglycaemic agents, serves as the primary treatment option for individuals with type II diabetes, particularly those who are overweight or obese and maintain normal kidney function.

Diabetes mellitus encompasses a cluster of metabolic abnormalities characterized by elevated blood sugar levels, disrupting the normal metabolism of carbohydrates, fats, and proteins, thus heightening the risk of vascular complications. Type II diabetes mellitus manifests as a clinical syndrome arising from either

insufficient insulin production or the body's reduced responsiveness to insulin at the cellular level, leading to hyperglycaemia and glycosuria. Notably, type II diabetes is associated with cognitive impairments, affecting learning, memory, and other cognitive functions in affected individuals. Metformin, a medication pivotal in diabetes management, first appeared in scientific literature in 1922 through the work of Emil Werner and James Bell, with French physician Jean Sterne conducting the inaugural clinical trial for its diabetes treatment application. Since its introduction to medical practice, metformin has gained widespread adoption globally, becoming the most prescribed anti-diabetic medication. In the United States alone, the year 2010 saw over 48 million prescriptions filled for its generic formulations, underscoring its pivotal role in managing diabetes mellitus.



MATERIALS AND METHODS

Chemicals and reagent

Metformin hydrochloride, having a label strength of 500mg of four different brands were purchased from registered pharmacy shop of rural area of Panvel and were coded as A,B,C,D. All the study was performed within product expiration dates. 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 four different brands were taken for evaluation.

Code	Brand	Manufacturer
A	Glycomet	USV Ltd.
B	Glyciphase	Franco Indian Pharmaceuticals Ltd.
C	Okamet 500	Cipla Ltd.
D	Glycirite 500	MHS Pharmaceutical Pvt. Ltd.

Apparatus and Equipment

Double beam UV-Visible Spectrophotometer , Analytical balance , Hardness Tester , Tablet Friability Tester , Disintegration Apparatus , Dissolution test apparatus and Ultrasonicator and pH meter were used.

Methods

Visual Inspection

The shape, colour and texture of the different Brands of metformin tablets were examined visually.

Thickness and Diameter

The thickness and diameter of tablets were assessed using Vernier callipers, which are crucial parameters for controlling tablet hardness. Ten tablets were randomly selected, and their thickness was measured with precision using Vernier callipers. The individual thickness measurements were averaged to determine the mean thickness, which was reported in millimetres.

Weight variation test

The purpose of this test is to verify the uniformity of each batch of tablets, which is crucial for ensuring consistent drug content across all formulation batches. To conduct the test according to official procedures, 20 tablets were randomly selected from the batch. Each tablet was individually weighed to determine its weight variation. Additionally, the average weight, standard deviation, and percent deviation were calculated from the individual tablet weights to provide a comprehensive assessment of batch uniformity.

$$\% \text{ Deviation} = \frac{W_{avg} - W_{ind}}{W_{avg}}$$

Where,

W_{avg}= Average weight of tablets ,W_{ind} = Individual weight of tablet

Friability test

This test is commonly conducted to assess the potential wear and tear that tablets may experience during transportation, which is closely linked to tablet hardness. It is typically performed using a Roche Friabilator. Five tablets were randomly chosen, and their initial weights (W1) were recorded. These tablets were then placed in the friabilator, which operated for 4 minutes at a speed of 25 rpm, completing 100 revolutions. Afterward, the tablets were reweighed (W2), and the percentage loss (friability) was calculated using the formula provided.

% Friability = [(Initial weight – Final Weight)/Initial weight] × 100

The official permissible limit for friability is 1%.

Hardness Test

The hardness of tablets from different brands was assessed using a Monsanto hardness tester, which measures hardness in terms of kg/cm². For each brand, five sample tablets were individually placed between the spindle of the hardness testing machine until they fractured, and the pressure required to break each tablet was recorded. The average pressure needed to break the tablets was calculated and expressed in units of millimetres.

Tablet Disintegration Test

The disintegration time of six randomly selected tablets from each brand was measured using a disintegration apparatus with distilled water as the test fluid, maintained at 37 ± 0.2 °C. The disintegration time was recorded as the moment when no granules from any tablet remained on the mesh. The duration taken for the tablets to disintegrate completely was noted.

Tablet Dissolution Test

The dissolution test for four brands of metformin hydrochloride tablets was conducted using a single flask dissolution apparatus. A dissolution medium consisting of a 0.68% w/v solution of potassium dihydrogen phosphate, adjusted to pH 6.8 with 1 M sodium hydroxide, was prepared. Each tablet (500 mg) was placed in a rotating basket submerged in 900 mL of the phosphate buffer medium at 37 ± 0.5 °C. The basket rotated at 100

rpm for 45 minutes. At intervals of 5, 10, 15, 20, 30, and 45 minutes, 10 mL samples were withdrawn using a bulb pipette, with 10 mL of fresh dissolution medium added after each sampling to maintain sink conditions. Each withdrawn sample was filtered, diluted, and the absorbance of the resulting solution was measured at a wavelength of 233 nm using a UV-visible double beam spectrophotometer (Systronic 2201). The percentage of drug release from each brand of metformin hydrochloride tablet was calculated using the standard calibration curve method.

Pharmacopoeial Assay

The assay aimed to determine the percentage purity of four brands of metformin tablets. Initially, 20 tablets from each brand were weighed using an analytical balance, and the average weight was calculated. The tablets were then powdered using a mortar and pestle. A portion of the powder equivalent to 0.1 g of metformin hydrochloride was stirred with 70 ml of distilled water for 15 minutes using a magnetic stirrer. This solution was transferred to a 100 ml volumetric flask, and 70 ml of distilled water was added. After stirring for another 15 minutes, the solution was diluted to 100 ml with distilled water and filtered. From this filtrate, 10 ml was taken and diluted to 100 ml with distilled water. This process was repeated once more, resulting in a further diluted solution. The absorbance of the resulting solution was measured at a wavelength of approximately 232 nm, and the drug content was calculated using a value of 798 for A (1%, 1cm) at that wavelength.

RESULTS AND DISCUSSION

General Appearance

The visual characteristics including shape, colour, and texture of the tablets were inspected, and the findings are presented in Table 1.

Thickness and Diameter

The thickness and diameter of all brands of Metformin hydrochloride tablets were measured using a Vernier calliper. Five tablets from each brand were selected, and their thickness and diameter were measured individually. The average values for each brand were then calculated and are presented in Table 1.

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

Brand Code	Shape	Colour	Texture	Thickness (mm)	Diameter (mm)
A	Rounded	White	Smooth	4.1	13.1
B	Cylindrical	White	Smooth	4.2	11.1
C	Cylindrical	White	Smooth	4.1	12.2
D	Cylindrical	White	Smooth	5.2	14.1

Weight Variation

The tablets were weighed individually, and their average weight was determined. The test concluded that all four brands of metformin hydrochloride tablets passed the weight variation uniformity test, meeting the specifications outlined in the US Pharmacopeia (USP). None of the brands exhibited a deviation of more than ±5% from the mean weight. The results are summarized in Table 2.

Friability

Five tablets from each selected brand were weighed and subjected to the Roche Friability apparatus. The percentage friability of the tablets was assessed against the US Pharmacopeia (USP) specification, which states that tablets must not lose more than 1% of their initial weight during the friability study. The results, demonstrating compliance with the USP specification, are presented in Table 2

Hardness

The crushing strength or hardness of the tablets was evaluated using the Monsanto hardness tester. The observed results for all the selected brands of metformin tablets demonstrated satisfactory levels of hardness, indicating their ability to withstand crushing forces. These findings are summarized in Table 2, providing a detailed overview of the hardness measurements for each brand.

Disintegration

Effective disintegration of tablets is crucial for improved bioavailability, leading to better absorption and ultimately enhanced therapeutic effects. The results of the disintegration test indicate that the disintegration time for all four different brands of metformin tablets is less than 10 minutes, which is shorter than the standard disintegration time specified by the pharmacopoeia. This demonstrates that all these brands of metformin tablets meet the quality control criteria outlined in the pharmacopoeia. The disintegration times for each tablet brand are detailed in Table 2.

Pharmacopoeial Assay

The assay test aims to determine the precise quantity of the active ingredient present in the tablet and verify if it matches the labelled amount. The percentage of drug release for all brands of tablets fell within the specified range outlined by the Indian Pharmacopoeia (IP), United States Pharmacopeia (USP), and British Pharmacopoeia (BP) specifications. The percent drug content for each brand is presented in Table 2.

Table 2: Comparative data of different quality control parameters of four brands of Metformin HCl tablets

Brand Code	Weight Variation Mean weight ± SD	Friability %	Hardness kg/cm^2	Disintegration Time Min.sec	%Drug content
A	0.930 ± 0.011	0.085	3.3	6.16	98.49
B	0.871 ± 0.007	0.091	4.1	5.24	99.08
C	0.825±0.005	0.099	3.8	5.42	96.33
D	0.985±0.014	0.048	5.0	4.10	97.08

Dissolution

Another crucial aspect under scrutiny was dissolution, which directly influences the absorption and bioavailability of the drug. The dissolution of all the chosen brands of metformin hydrochloride tablets met the specified criterion of not less than 80% within 30 minutes, as per the US Pharmacopeia standards. See Table 3 for detailed results.

Table 3: Comparative study of dissolution of four brands of Metformin HCl tablets

Sr. No.	Time (min)	% drug release			
		A	B	C	D
1	5	20.78	26.21	21.50	20.06
2	10	34.70	39.97	30.91	33.39
3	15	44.60	50.06	51.06	51.46
4	20	59.25	73.68	64.85	60.07
5	25	86.30	85.79	84.43	90.56
6	30	99.34	98.49	99.98	98.71

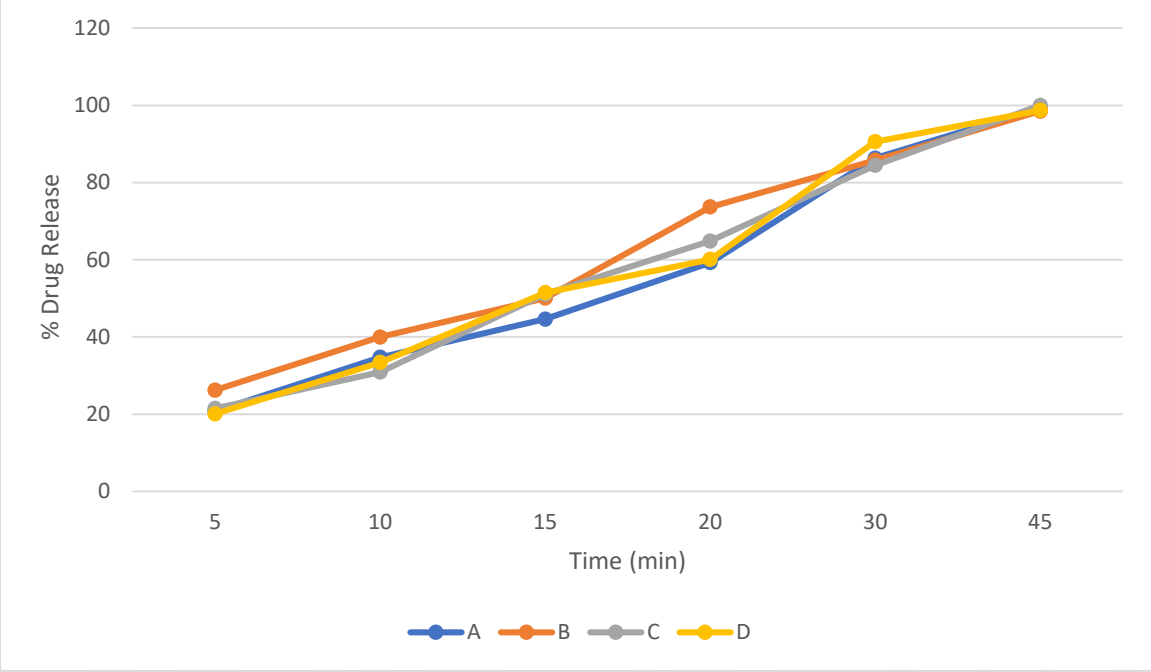


Fig 2. Comparative dissolution profile of four different brands of Metformin HCl

CONCLUSION

The objective of this research was to meticulously assess the quality and physicochemical equivalence of four distinct brands of metformin hydrochloride tablets available in the market. The study methodically examined various parameters including weight variation, hardness, friability, disintegration, assay, and dissolution to ensure compliance with official specifications.

Remarkably, all evaluated brands of metformin hydrochloride tablets met the stipulated official standards for the aforementioned parameters. Specifically, the tablets exhibited uniformity in weight, adequate hardness, minimal friability, timely disintegration, accurate drug content, and appropriate dissolution rates. Notably, each brand demonstrated the release of approximately 80% of the metformin hydrochloride within the specified 30-minute timeframe, aligning with Pharmacopoeial requirements.

However, despite meeting these regulatory criteria, variations were observed in the release profiles among the different brands. This suggests that while all brands perform satisfactorily in terms of meeting official specifications, subtle differences exist in their release kinetics.

Despite these variations, the drug content of all brands remained within the Pharmacopoeial limits, underscoring their overall quality and efficacy. Consequently, the study concludes that all selected brands of metformin hydrochloride tablets can be considered equivalent in terms of their quality and performance.

Importantly, the findings suggest that even though these brands are manufactured by different pharmaceutical companies, they can be used interchangeably. This implies that if one brand is unavailable in the market, any of the other three brands can serve as a suitable substitute without compromising efficacy or safety. Thus, healthcare providers and patients can confidently rely on the interchangeability of these metformin hydrochloride tablet brands for consistent therapeutic outcomes.

ACKNOWLEDGEMENTS

We would like to thanks our Principal, Teaching Staff, and Non-Teaching Staff of CSMU School of Pharmacy for their guidance, support, and valuable insights throughout the duration of the project.

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