

## Comparative Study of Three Different Brands of Metformin Hydrochloride

Imran Bhat, Kanishka Sharma, Satvir Kaur, Nikhil, Umear Malla

(Assistant Professor, Sachdeva College of Pharmacy Mohali)

(Students at Sachdeva College of Pharmacy)

Submitted: 04-04-2024

Accepted: 14-04-2024

### ABSTRACT

Metformin hydrochloride is an oral anti-diabetic drug used mainly to treat type II diabetes mellitus and available as several brands in the market which make it difficult to select the safe, effective and economic one. The aim of this research work was to check, compare and evaluate the quality standards of different brands of Metformin hydrochloride tablets available in local market of Kharar Mohali India. Three brands of Metformin tablets (500mg) were selected and evaluated comparatively for their physical and chemical parameters as per official method. The physiochemical equivalence of all the tablet brands were assessed through evaluation of both official and non-official standards such as uniformity of weight, friability, hardness, disintegration, assay and dissolution rate. Disintegration time for all brands was within 15 minutes prescribed by official compendium. All the brands of Metformin hydrochloride tablets fulfilled the official in-vitro dissolution rate test specification more than 70% of the drug is released within 45 minutes. The present finding suggest that almost all brands of Metformin Hydrochloride that are available in Kharar meet the I.P. specification for quality control analysis and interchangeable.

### I. INTRODUCTION

World health organization has estimated that about 30% of the medicines are counterfeit on sale for the consumption in many countries in Latin America, Africa and parts of Asia. The process of fraudulently manufacturing can apply to both generic and branded products and could include products with the wrong ingredients, without active ingredient, with insufficient active ingredient or fake packaging [1]. While the substandard drugs are genuine drug that do not meet with quality specifications claimed by their manufacturers during laboratory testing. The introduction of generic drug product from multiple sources into the health care delivery system of many developing countries for improving the overall health delivery

system in such countries. Quality of medicinal drugs in many underdeveloped countries is inadequate. In some cases, use of poor quality medicines has resulted in treatment failure [2].

Metformin Hydrochloride is chemically N, N-Dimethylimidodicarbonimidic diamide hydrochloride (1,1-dimethylbiguanide hydrochloride), belongs to the 'biguanide' class (figure 1) [3,4]. It is an oral anti-diabetic drug used mainly to treat type II diabetes mellitus. They act by decreasing intestinal absorbance of glucose, increasing insulin sensitivity and suppressing glucose production by the liver [5, 6, 7]. Many brands are available for Metformin hydrochloride in the Indian market. The study was committed to evaluate the quality of the different brand of Metformin. The biological half life of Metformin HCl is 1.5-4.5hrs. So, conventional Metformin HCl tablets should be administered 2-3 times a day to maintain the therapeutic effect of the drug throughout the day [8].

The aim of this research work was to check, compare and evaluate the quality standards of commercially available Metformin hydrochloride tablets as prescribed by I.P. used for the type II diabetes mellitus. Four brand of Metformin hydrochloride were evaluated comparatively for their physical and chemical parameters. The performed physical and chemical tests like in-vitro dissolution, disintegration, hardness, friability, percentage purity etc. were found to be varying for each tablets, but within the specified limits [9, 10].

In-Vitro bioequivalence studies are commonly used to assess therapeutic equivalence, but these studies involve invasive procedure. The Biopharmaceutics classification system (BCS) can be used to reduce in-vivo bioequivalence requirement. In-vitro dissolution test based on BCS are acceptable for establishing the bioequivalence of generics with the innovator products [11]. Metformin hydrochloride is highly soluble and low permeability, it therefore a BCS class 3 drug and is eligible for bio-waiver based on the WHO criteria.

Dissolution time is the time required for the tablet to go into solution in the suitable medium, dissolution rate is the rate of which a drug goes into solution, both these are determined in simulated gastric fluid at 37°C by the help of dissolution instrument. After oral administration, a tablet undergoes disintegration on and then the drug goes into the solution. The rate of absorption and

bioavailability of the drug are directly related to the dissolution rate of the drug [12, 13].

**Sample** Metformin hydrochloride, having label strength of 500mg of four different brands was purchased from a Kharar India. All the study was performed within product expiration dates. The different brands are listed in table 1:

	Batch No.	Manufacturer	Expiry Date
<b>Melmet</b>	MEAD00099	Micro labs limited	04/2025
<b>Obimet</b>	AMA02321	Acme-Formulation Pvt.Ltd.	09/2026
<b>Glycomet</b>	320010625	FRANCO-INDIAN Remedies Pvt. Ltd.	06/2025

**Table 1: List of brands of Metformin hydrochloride**

### Chemicals and Reagent

Metformin hydrochloride powder (Reference standard) was a gift sample.

The reagents used were of analytical grade. Fresh distilled water was used throughout the work.

### Visual Inspection

The shape and color of the different brands of Metformin tablets were examined visually. The size and thickness of tablets from each brand was examined with the help of Vernier caliper.

### Uniformity of Weights

Sample tablets (20) of each brand were weighed individually on a digital analytical balance. The average weight was determined and the percentage (%) deviation of the individual tablets from mean weight was determined. In order to pass weight variation test, the tablet should be within the limits of the percentage deviation allowed by I.P.

### Hardness Test

The hardness of different brand of tablets was determined by Monsanto hardness tester and measured in terms of Kg/cm<sup>2</sup>. Sample tablets (10) of each brand were taken, a tablet placed between the spindle of the hardness tester machine until the tablet breaks and the pressure required to break the tablet was recorded.

### Friability Test

Ten tablets of each brand were taken and weight, these tablet subjected to abrasion using a Roche Friabilator at 100 revolutions for 4 minutes. The tablets were dedusted carefully and weighed accurately again then percentage of weight loss recorded. The friability of the tablets was calculated using the formula.

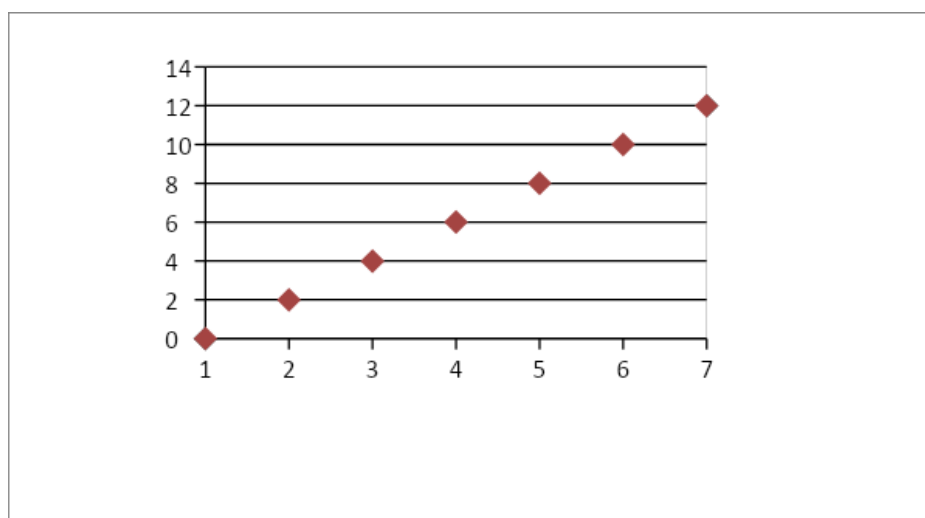
$$\% \text{ Friability} = \frac{[(\text{Initial weight} - \text{Final weight}) / \text{Initial weight}] \times 100}$$

### Disintegration Test

Tablet disintegration time of randomly selected six tablets of each brand was determined at 37°C using disintegration apparatus employing distilled water as test fluid. The disintegration time was taken to be the time no granule of any tablet was left on the mesh.

### Estimation of Metformin Hydrochloride

A U.V. Spectrophotometric method based on the measurement of absorbance at  $\lambda_{\text{max}}$  232nm in phosphate buffer of pH 6.8 was used for estimation of Metformin hydrochloride. Before performing dissolution test, ten serially diluted solutions of reference standard (Metformin Hydrochloride) and a standard solution curve were drawn. The curve was linear between concentration ranges 1-10 µg/ml. Mean peak absorbance was plotted against the concentration t form the calibration curve. The regression equation was established.



#### Dissolution rate determination

Dissolution rate of the each brand of tablets was determined using an 8-compartment dissolution test apparatus using paddle stirrer at 100 rpm and at temperature of  $37 \pm 0.5^\circ\text{C}$ . Phosphate buffer pH 6.8 (900 ml) was used as dissolution fluid. One tablet (500 mg) was used in each test. Sample of dissolution fluid (10ml) was withdrawn at intervals of 5, 10, 15, 30, 45 and 60 minute. A fresh 10 ml dissolution medium was replaced after each sampling to maintain sink condition. Each of the withdrawn samples was filtered and the filtrate diluted. The absorbance was measured at  $\lambda_{\text{max}}$  232nm using U.V. Visible double beam spectrophotometer.

The concentration was determined against standard solution of Metformin hydrochloride drug in the same medium. From the concentration, percentage (%) drug release was determined at specified time interval. Each dissolution experiment was run in triplicate (n=3). The percentage of drug released is calculated using formula:

$$\text{Percentage of drug release (\%)} = \left[ \frac{\text{Amount of drug released (mg/ml)}}{\text{drug content in label (mg)}} \right] \times 100$$

#### Assay of Metformin Hydrochloride tablet

The assay was done to find out the % purity of the given brands of Metformin tablet. The test for assay was carried out using U.V. spectrophotometer method at specific absorbance (232nm) as per Indian pharmacopoeia [14].

## II.

### RESULTS

#### Physicochemical properties of Metformin hydrochloride tablets

Uniformity of weight, hardness, friability, disintegration time and drug content as well as size and thickness are shown in Table 2. The in-vitro percentage drug release of Metformin hydrochloride tablets are shown in Table 3. Figure 2 illustrates the dissolution profile of the all tested Metformin hydrochloride tablets of different brands.

The evaluated physicochemical parameters of the different brands of Metformin hydrochloride tablets are shown as:

Brand	Uniformity of weight (gm)±SD	Hardness (kg/cm <sup>2</sup> )	Percent % friability	Percent % purity	Disintegration time (min)
Melmet	12.46 g	7.45±0.21	0.462	96.35	7min 50 sec
Obimet	11.43 g	6.74±0.11	0.8211	97.21	5 min 30 sec
Glycomet	10.46 g	7.98±0.18	0.168	95.71	5 min 15 sec

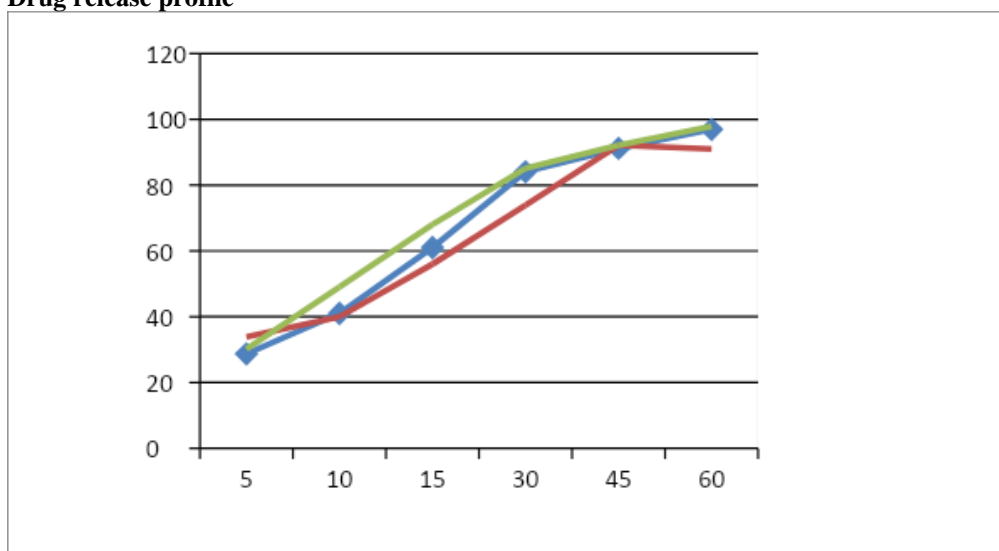
Table 2: Values of different physicochemical parameters

**In vitro percentage drug released of different brands of Metformin hydrochloride tablets**

Brand	Drug released (%) S.D					
	5 mi	10min	15min	30min	45min	60min
Melmet	28.72±0.7	41.02±0.8	61.20±1.2	84.60±0.9	91.16±1.9	96.92±0.4
Obimet	33.84 ± 1.2	39.96 ± 0.4	55.98 ± 0.5	73.94 ± 1.4	84.30± 1.6	91.20 ± 0.8
Glycomet	30.14 ± 0.7	30.14 ± 0.7	68.02 ± 1.1	85.07 ± 1.7	92.12 ± 2.1	92.12 ± 2.1

**S.D Standard Deviation**

**In-Vitro Drug release profile**



**Dissolution profile of different brands of Metformin Hydrochloride**

**III. DISCUSSION**

Metformin hydrochloride is a widely prescribed oral anti-diabetic drug and its official in I.P. 2007. Several brands of Metformin tablets are available in the market leading to a confusion of their quality and prices. The objective of the present study is to make a comparative evaluation of four different brands of Metformin hydrochloride which are commercially available in Kharar Mohali, India. They were subjected to number of quality control tests in order to assess their biopharmaceutical equivalence.

The branded products of Metformin tablets evaluated for various physiochemical properties (Table-2). The uniformity of weight for

the brands of Metformin hydrochloride tablet gave values that complied with I.P specification and deviated less than 5% from the mean value. Using hardness tester, the strength of the tablets was tested. Hardness of the tablets was in the range of 5.674±0.11 to 7.98±0.18 /cm<sup>2</sup> with all brands.

The result of tablet friability test showed that all the brands tested had impressive friability values ranging 0.110% to 0.821% w/w in Table-2. According to I.P. no batch should have a friability value greater than 1% w/w.

The observed disintegration times for all the brands of Metformin hydrochloride investigated was less than 15 min limit prescribed by official compendium (Table-2). The fastest disintegration

tablets were of Melmet brand while the slowest one was Obimet brand. The various brands could have employed different disintegrates to improve the penetration of aqueous liquids.

The result obtained from the assessment of the percentage drug content of four brands of Metformin hydrochloride tablets showed within the monograph specification 95% to 105% of stated amount of Metformin HCl as demonstrated in Table 2.

Dissolution of drug from oral solid dosage forms is an important aspect for drug bioavailability. The in-vitro drug release characteristics of the developed marketed tablets were studied. Dissolution data for all the experiments were highly reproducible and hence only the average values were plotted. The dissolution of all four brand tablets indicated the more than 70% of the drug is released within 45 min, which complies with the I.P. (2007) specification (Table 2) [13, 14].

#### IV. CONCLUSION

It can be concluded from above discussion that all the available brands in local market of Kharar Mohali, India are having, within the specified quality range and can be interchange of found any non-compliance due to cost issue. The results have shown that all the tested brands satisfied the I.P requirement in terms of uniformity of weight, friability, disintegration, assay and dissolution.

#### REFERENCES

- [1]. WHO. Counterfeit drugs: guidelines for the development of measures to combat counterfeit drugs, Geneva, WHO, **1999**, 1-60.
- [2]. A.M.Olusola, A.I. Adekoya, O.J. Olanrewaju, J. App. Pharm. Sci., **2012**, Vol. 02(02), 41-44.
- [3]. P. Elango, Ramesh, S. Shanmuganathan, Indian J. Clin. Pract., **2014**, Vol. 24(8), 778-83.
- [4]. S. Baokar, S.V. Mulgund, N.S. Ranpise, Der Pharma Chemica, **2013**, Vol. 5(1), 24-27.
- [5]. L.C. Block, L.O. Schemling, A.G. Couto, S.C. Mourão, T.M.B. Bresolin, J. Basic Appl. Sci., **2008**, Vol. 29(1), 29-35.
- [6]. S.A. Afifi, S. Ahmadeen, Life Sci., **2012**, Vol. 9(4), 4260-66.
- [7]. A.B. Loni, M.R. Ghante, S.D. Sawant, Der Pharma Chemica, **2012**, Vol. 4(3), 854-59.
- [8]. M. Rajesh et al., Int. J. Pharm. Chem. Biol. Sci., **2012**, Vol. 2(3), 318-324.
- [9]. T.W. Hettiarachchi, D.B.M. Wickramaratne, S.H.T. Sudeshika, D. Niyanngoda, M.H.F. Sakeena, H.M.D.R. Herath, Int. J. Pharm. Pharm. Sci., **2015**, Vol. 7(2), 520-24.
- [10]. A.R. Chandrasekaran, C.Y. Jia, C.S. Theng et al., J. App. Pharm. Sci., **2011**, Vol. 01(05), 214-17.
- [11]. P.Z. Milani, S. Ghanbarzadeh, M. Nemati, **2012**, J. App. Pharm. Sci., Vol. 02(08), 194-197.
- [12]. Z. K Labu et al., Asian J. chem. pharm. res., **2013**, Vol. 1(1), 47-52.
- [13]. K.P.R. Chowdary, Ch.P.S.R. MadhuriVikas, World J. Pharm. Res., **2015**, Vol. 4(9), 710-16.
- [14]. Indian pharmacopoeia, Government of India, Ghaziabad. The Indian Pharmacopoeia Commission, **2007**, Vol. 2, 1358-59.
- [15].