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Comparative Study of Branded and Generic Metformin Hydrochloride Tablet

Mr. P. B. More[1], Dr. A. S. Kulkarni[2], Ms. Shivani Chandrakant Kavane[3],
Mr. Bharat Prakash Shinde[4], Mr. Prathmesh Sale[5]Assistant professor, Principal, Student, Student Department of Pharmaceutics
Ashokrao Mane institute of pharmaceutical sciences and research, Save

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ABSTRACT –The use of generic and branded drugs is day by day increased due to various new diseases and most of the people don't know the major differences in between both generic and branded drugs in recent time. A generic drug consist of same active ingredient as its branded counter part & found to be equally elgicient therapeutically. Metformin hydrochloride tablet is non-insulin dependent diabetes mallitus. Here, the study is to compare the differences in dissolution behaviour & asses bioequivalent of same commercially available metformin hydrochloride tablet.

Branded medicine are original product developed in pharmaceutical company & generic medicine is the copy of original branded product when the expiry date of branded drug patent & hence supposed to be of low cast as compared versions. The cost of generic drug are much lesser than the branded drug. As they do not need to go the robust & costly pre-clinical or clinical study as done in the branded one. Which increase the cost. The present study enlightens the effectiveness of generic drug of we perform bioequivalence & bioavailability study & also evaluation of physicochemical properties drug content weight variation. The invitro dissolution apparatus 2 using PH 6.8 phosphate buffer solution for 1 houre. In overall study bioequivalence & bioavailability are same of both drug.

Keywords –Generic medicine, Branded medicine, Healthcare professionals, Pharmaceuticals and Pharmacies.

I. INTRODUCTION –

With the growth in pharmaceutical industries, number of pharmaceutical products (branded as well as generic) are increasing in market so to maintain its quality is the most primary concern for manufacturers. The same generic drug can be manufactured by different pharmaceutical companies, which may look like or different than original and sold under different brand name and different cost. Generally, generic as well as branded product contains the same type and quantity of the active ingredient. So, a generic drug should be identical or bioequivalent to brand drug with respect to dosage form, safety, strength, route of administration, quality, performance characteristics and intended use. But substandard drugs are also finding place in the market due to ignorance, neglectance and personal profit of pharmaceutical companies and these differ from original product in many aspects viz. concentration, quality etc. So, to ensure safety and reliability of any pharmaceutical dosage form in terms of quality, pharmaceutical companies should maintain the pharmacopoeial standards as prescribed by pharmaceutical regulatory authorities during manufacturing of the drugs. Therefore, quality control tests as per the standard official compendia like IP, USP, BPetc. during manufacturing and also on the final product should be performed. The literature reveals that in many countries, people are suffering not because of diseases but their inability to meet cost of medication for their diseases. So, the present study aims to throw away the blind belief of many people that branded drugs show better therapeutic activity than the generic drugs. The generic drugs are also bioequivalent to ethical drugs if all the quality control parameters are being maintained. As per pharmaceutical standards, the parameters like weight variation, hardness, friability, disintegration, dissolution and content uniformity should be checked to assure the effectiveness of any drug.

Metformin (molecular formula C4H11N5, molecular weight, 129.167 gm/mol) is the most widely prescribed anti-diabetic used for treatment of type II (non-insulin dependent diabetes mellitus) which basically acts by decreasing hepatic glucose production, intestinal glucose absorption, and

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improving insulin sensitivity by increasing peripheral glucose uptake and utilization.

Drug Profile

- Drug Name : Gluformin 500 and Metross 500
- Synonyms : Metformin HCL
- Chemical Formula : C4H12CIN5
- IUPAC Name : 1-carbamimibamido-N,N-dimethylmethanimidamide hydrochloride

Difference Between Brand Name and Generic Drugs

When a new drug is discovered, the company that discovered it would apply for patency to prevent other companies from producing and selling the drug. This patency may take up to 20 years and during this period, the company will produce and sell the drug under a brand name to recover its investment and make a profit. With time, this name becomes synonymous with the drug. But after the patency expires, other companies are allowed to produce a similar drug. It is what gave rise to brand and generic name in drugs Examples of brand name and generic drugs can be cited with following diabetes and hypertension drugs. Metformin is a generic drug for diabetes, but its brand name is Glucophage. Similarly, Metoprolol is a generic drug for hypertension but its brand name is Lopressor. These drugs will be known by different names in different countries, but the generic name remains constant.

The difference between brand name and generic drugs is in the circumstances of producing the drugs. While brand name drug refers to the name giving by the producing company, generic drug refers to a drug produced after the active ingredient of the brand name drug. Generic drugs will, however, be sold under different brand names, but will contain the same active ingredients as the brand-name drug. But with regards to the effectiveness of the drugs, generic drugs have the same quality active ingredient as brand name drugs. All drugs must comply with strict directive and supervision of the Food and Drug Administration (FDA) in the US and equivalent institutions in other countries.[4]

II. MATERIALS AND METHODS

Materials: Branded (Gluformin500 Abbott healthcare) and Generic (Metros 500 Maxford healthcare) Metformin hydrochloride tablets having label strength 500 mg were purchased from localmarket. The detailed descriptions for these products are presented in Table 1 All tests were performed within product expiration dates. [5]

Figure No. 1: Gluformin 500, Abbott Healthcare, Mumbai

Fig. No 2: Metross 500, Maxford Healthcare

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Sr. no	Brands selected forstudy	Mfg. Date	Exp. Date	Batch. No	M.R.P/Rs.
1	Gluformin 500	April.2021	March.2022	SSG0061	16.77
2	Metros 500	April.2021	March.2023	35MTA21003	32.90

Table No: 1 Data of Manufacturing & Expiration Date of selected marketed tablets

Instruments and Equipments used

An electronic analytical balance, A double beam UV-visible spectrophotometer (UV-1900 Pfizer Hardness Tester, Friability Tester, Dissolution Apparatus, Disintegration Apparatus were used.

Methods

1) Visual Inspection

The shape, size, and colour of the different formulations of tablets were examined visually. At least 20 tablets were unpacked and inspected. They should be undamaged, smooth, and usually of uniform colour. Evidence of physical instability is demonstrated by:

a. presence of excessive powder and/or pieces of tablets at the bottom of the container (from abraded, crushed, or broken tablets);

b. cracks or capping, chipping in the tablet surfaces or coating, swelling, mottling, discoloration,fusion between tablets; and the appearance of crystals on the container walls or on the tablets.

c. The appearance of crystal on the container walls or on the tablets.[6]

2) Thickness and Diameter

The thickness of the tablet is mostly related to the tablet hardness can be uses as initial control parameter. The thickness and diameter of the tablets were determined by using Vernier calipers. Ten tablets were randomly selected and thickness was determined using a Vernier caliper and the result was expressed in mean and unit in millimeters. [7]

3) Mechanical strength of tablets

Although, the crushing strength test is non-compendial, it is undertaken to determine the ability of the tablets to withstand pressure during handling, packaging and transportation. A Monsanto tablet hardness tester (Copley Scientific Ltd, Nottingham, United Kingdom) was employed to determine the mechanical strength of the tablets. The average force required to crush the tablets from each batch was obtained.

4) Uniformity of weight

The purpose of this test is to verify the uniformity of each batch which ultimately reflect the drug content uniformity in all the formulation batches. The test was performed as per the official procedure, 20 tablets were randomly selected and weighed individually and also average weight, standard deviation and percent deviation was calculated.

5) Friability test

This test is usually performed to check possible wear and tear loss in the tablet during the transportation and this is closely related to tablet hardness. It is usually performed by the Roche Friabilator. Randomly five tablets were selected and their initial weight (W1) was recorded and after that these weighed 05 tablets were placed in the friabilator and the friabilator was operated for 4 minutes at 25 rpm speed and 100 revolutions, the tablets were weighed again (W2) and the percent loss (Friability) was then calculated by using following formula. [8]

% Friability = [(Initial weight – Final weight)/Initial weight] × 100 The official permissiblelimit for friability is 1%.

6) Tablet Disintegration Test

Tablet disintegration time of randomly selected six tablets of each brand was determined using disintegration apparatus employing distilled water as test fluid at 37 ± 0.2 °C. The disintegration time was taken to be the time no granule of any tablet was left on the mesh. The time taken for tablets to disintegrate was noted down. [9]

7) Dissolution TestPrepared reagents:

Simulated intestinal fluid pH 6.8 was

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prepared by dissolving 34 grams of potassium dihydrogen orthophosphate in distilled water in 2-Lvolumetric flask. The pH was adjusted by 1M sodium hydroxide prepared by dissolving accurately weighted 40 grams of sodiumhydroxide pellets in1000 ml distilled water in a volumetric flask. Then the mixture was diluted to volume in a 5-L volumetric flask. [10]

Standard Calibration Curve

0.1gm pure Metformin hydrochloride dissolved in 10ml of buffer solution. The solution concentration of 2,4, 6,8,10 µg/ml were prepared by serial dilution. The results are shown in **Table3.** The dissolution of metformin tablets was done according to the specification of IP 2018 using dissolution apparatus type I (paddle apparatus) with the rate of 50 rpm at 37±0.5∘C on six tablets ofeach brand. 10 ml sample was withdrawn at 10, 20, 30, 45, and 60 min and an equivalent amount of fresh dissolution medium was replaced. Filtered samples were then appropriately diluted and absorbance readings were taken with UV/Visible Spectrophotometer at wavelength of 232nm.The concentration of each sample was determined from calibration curve. The percent of drug releaseat each time was calculated.

8) Assay:

The assay was done to find out the % purity of the given brand of metformin tablet. Initially 20tablets from each brand of metformin hydrochloride were weighed using analytical balanceand average weight was taken. Tablets were then powdered using mortar and pestle. Powder equivalent to 0.1g of Metformin hydrochloride was then stirred with 70 ml of distilled water for 15 minutes using a magnetic stirrer. Weighed quantity of powder equivalent to 0.1 g of metformin hydrochloride was transferred to 100 ml of volumetric flask, to it 70 ml of distilled water was added, stirred for 15 minutes and it was diluted to 100 ml with distilled water and filtered. 10 ml of this filtrate was diluted to 100 ml with distilled water. Further diluted the 10 ml portion to 100 ml with distilled water and the absorbance of the resulting solution was taken at the maximum at about 232nm. [11]

9) INFRARED SPECTROSCOPY: -

Procedure:

Turn on the IR spectrometer and allow it to warm up. Obtain an unknown sample from the instructor and record the letter and appearance of the sample. Collect a background spectrum.Using a metal spatula, place a small amount of sample under the probe. Twist the probe until it locks into place. Record the IR spectrumof the unknown sample. Repeat if necessary to obtain a good quality spectrum. Record the absorption frequencies indicative of the functional groups present. Clean the probe with acetone. Turn off the spectrometer. Analyze the obtained spectrum.[12]

Result and Discussion1)Visual Inspection:

The shape, colour and texture were examined visually and result are shown in **Table 2**

Brand	Color	Shape	Texture
Gluformin 500	White	Round	Smoot
Metros 500	White	Oval	Smooth

Table 2: Data of Visual Inspection

2) Thickness and Diameter

The thickness and diameter of all brands of Metformin hydrochloride tablets was measured by using Vernier caliper. 5 tablets of each brand were used and average values were calculated. The results are shown in **Table 3.**

Brand	**Thickness (cm)**						**Diameter** (cm)					
	1	2	3	4	5	Average	1	2	3	4	5	Average
Gluformin 500	0.7	0.8	0.6	0.7	0.7	0.7	1.4	1.5	1.5	1.3	1.4	1.4

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Metros 500	0.5	0.6	0.4	0.5	0.5	0.5	1.7	1.8	1.7	1.6	1.7	1.7

Table 3: Data of Thickness and Diameter of branded and generic tablets

3) Hardness

Hardness of the tablet was determined using the Monsanto hardness tester. The observed results showed that all the selected brands of metformin have an acceptable crushing strength or hardness. Tablet passes the hardness test if crushing strength between 4kg/cm3 to 10 kg/cm3. The results are shown in **Table no 4**

Tablet no	**Generic Tablet Hardness kg/cm3**	**Branded Tablet Hardness kg/cm3**
1	6.5	6.0
2	7.2	4.4
3	9.9	6.5
4	9.9	7.4
5	8.2	8.3
6	6.0	6.5
7	7.5	8.2
8	6.9	9.2
9	9.1	7.7
10	8.6	6.9

Table 4: Data of Hardness of branded and generic tablet

4) Friability

Six tablets of all selected brand were weighed and placed in Roche friability apparatus. The% friability of the tablets meet the specification of IP which specifies that the friability study must not lose 1% of their initial weight. The results are shown in **Table 5**

%friability = initial weight – final weight / initial weight x 100

Brand	**Initialweight**	**Final Weight**	% **Friability**
Gluformin500	6.50	6.47	0.46%
Metros 500	6.372	6.360	0.18%

Table 5: Data of friability of branded and generic tablets

5) Disintegration Test

Disintegration is essential for better bioavailability which results in better absorption and consequently better therapeutic action. The results of disintegration test shows that the disintegration time of generic and branded metformin tablet is less than 10 minutes which is less than the standard disintegration time proves that all these brands of metformin tablet pass the quality control limits as per the pharmacopoeia. The time taken for disintegration of each tablet are shown in **Table 6**

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Tablet no	Generic Tablet Time in minutes	Branded Tablet Time in minutes
1	9.3	8.3
2	9.1	7.4
3	8.9	9.2
4	7.9	9.7
5	7.5	8.2
6	9.5	8.8
Average	**8.7**	**8.6**

Table 6: Data of disintegration time of branded and generic tablets

6) Uniformity of Weight

Tablets were taken, weighed and their average weight was calculated. The test stated that all the four brands of metformin hydrochloride have passed the weight variation uniformity test which complied with the IP specifications for weight uniformity as none of the brands deviated by up to±5% from the mean value. The results are shown in **Table no.6**

Generic Tablet			Branded Tablets		
Tablet no.	Individiual Weight(g)	%Weight Variation	Tablet no.	Individual weight (g)	%Weight Variation
1	0.605	-4.67	1	0.590	-0.3
2	0.570	1.38	2	0.602	-1.6
3	0.563	2.59	3	0.585	1
4	0.568	1.73	4	0.594	-0.3
5	0.608	-4.67	5	0.579	2
6	0.604	4.49	6	0.582	1
7	0.572	1.03	7	0.596	0.6
8	0.564	2.24	8	0.602	-1
9	0.596	3.11	9	0.589	0.5
10	0.561	2.94	10	0.596	-0.6
11	0.567	1.90	11	0.593	-0.1
12	0.573	1.73	12	0.604	-2
13	0.580	0.86	13	0.607	-2.5
14	0.584	2.42	14	0.600	-1
15	0.564	0.69	15	0.579	-2
16	0.574	-1.21	16	0.589	0.5
17	0.585	-1.55	17	0.592	0
18	0.587	1.73	18	0.592	0
19	0.568	1.74	19	0.590	0.3
20	0.593	-2.59	20	0.590	0.3
Average Weight = 0.578 gm			Average Weight = 0.592 gm		

Table No:-07 Data of Individual Weight of Branded and Generic Tablets

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7) Pharmacopoeial Assay:

The conc. of each sample was determined from a five point of calibration curve (Fig.No.1.5) Which was obtained from standard calibration curve.

Sr. No.	Concentration	Absorbance
1	5	0.025
2	10	0.065
3	15	0.102
4	20	0.136
5	25	0.167

Table 8: Data for calibration curve of assay

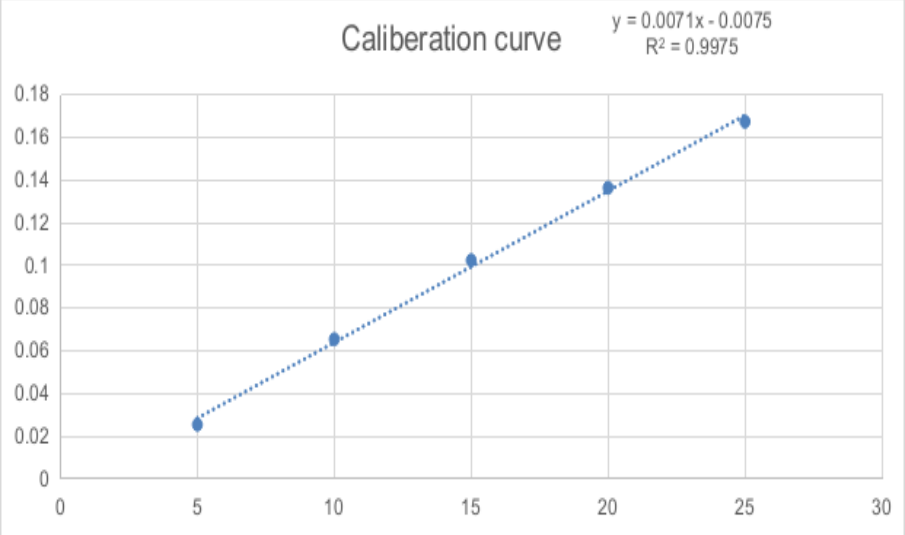

Fig. No.3 Calibration Curve

8) Dissolution Profile:

Dissolution is another studied important quality control parameters directly related to the absorption and bioavailability of drug. Dissolution selected brands of metformin hydrochloride tablets was found to be within the specified limits of not less than 80 % in 30 min (IP). The results are shown in Table No. 9 and Table No 10.

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Dissolution Profile of Generic Tablets

Sr. No	Time interval	Absorbance	Amount of Drug released	% Drug Release
1	10 min	0.2086	79.2	15.8
2	20 min	0.3024	199.8	39.96
3	30 min	0.4070	334.26	66.8
4	40 min	0.4610	403.65	80.73
5	50 min	0.5064	461.7	92.34
6	60 min	0.5180	477	95.46

Table No 9: Data for dissolution profile of generic Metformin HCl tablets

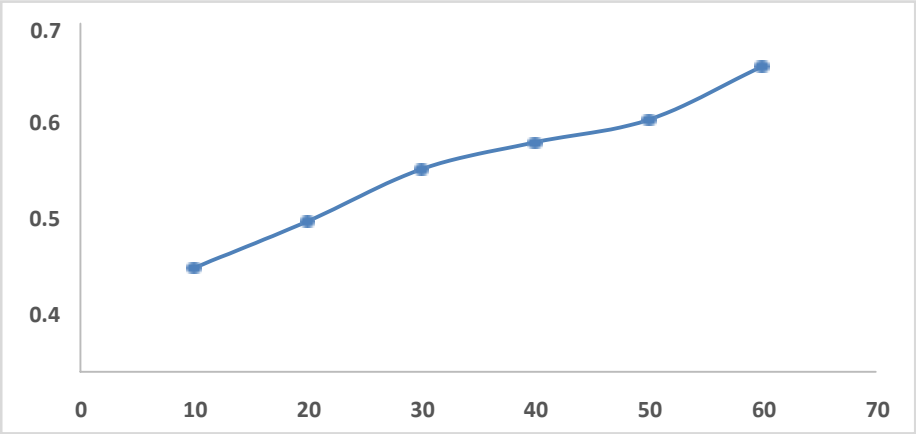

Figure No 4: Dissolution profile of generic Metformin HCl tablet

Dissolution Profile of Branded Tablets

Sr. No	Time interval	Absorbance	Amount of Drug released	% Drug Release
1	10 min	0.267	109.44	21.88
2	20 min	0.289	188.64	37.72
3	30 min	0.310	264.24	52.84
4	40 min	0.321	303.84	60.76
5	50 min	0.350	408.24	81.64
6	60 min	0.365	462.24	92.44

Table No:-10 Data for dissolution profile of branded metformin HCL tablets

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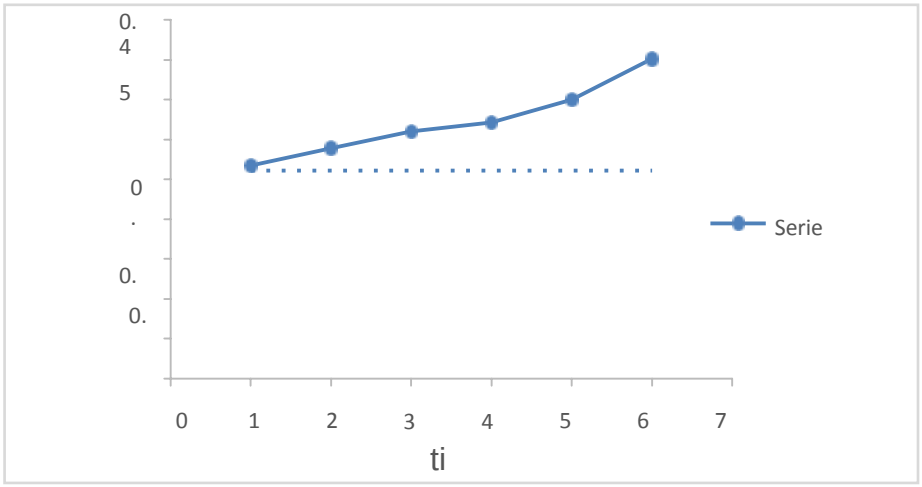

Fig No:- 05 Dissolution Profile of Branded Metformin HCL tablet

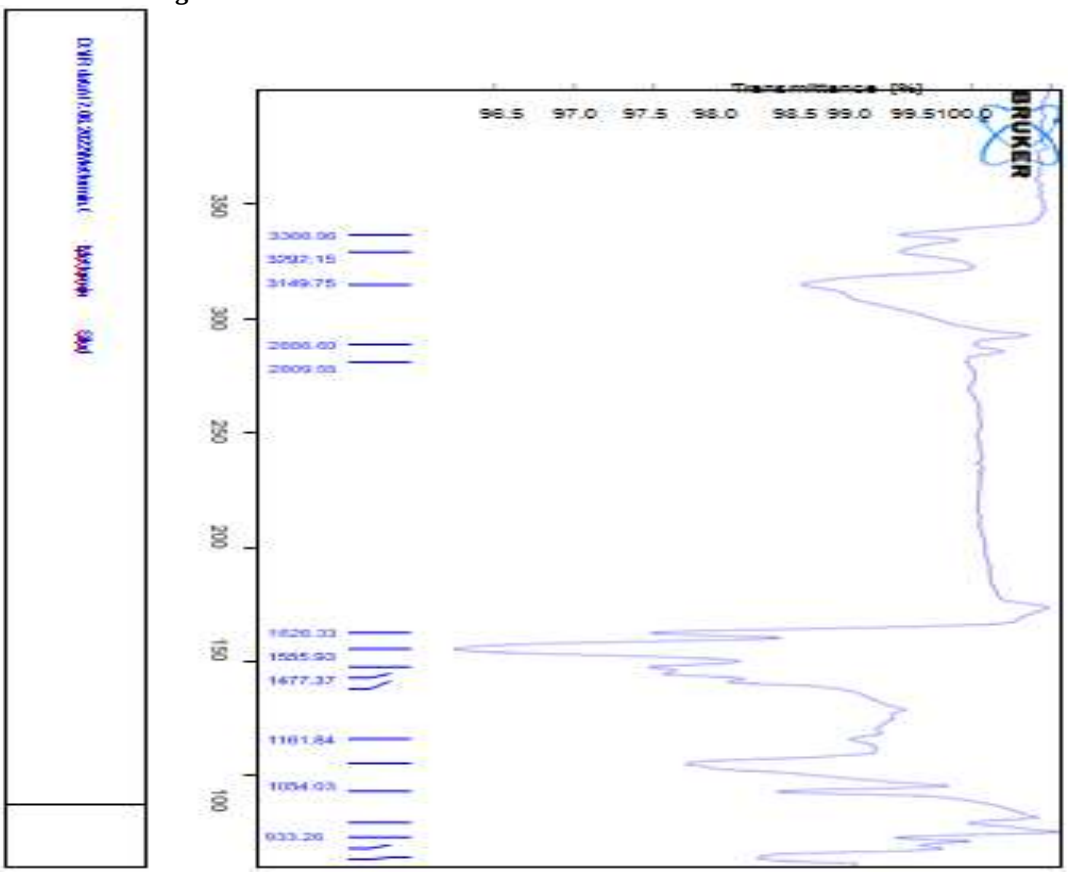

Fig .No.0.6 IR Spectroscopy of Branded Drug

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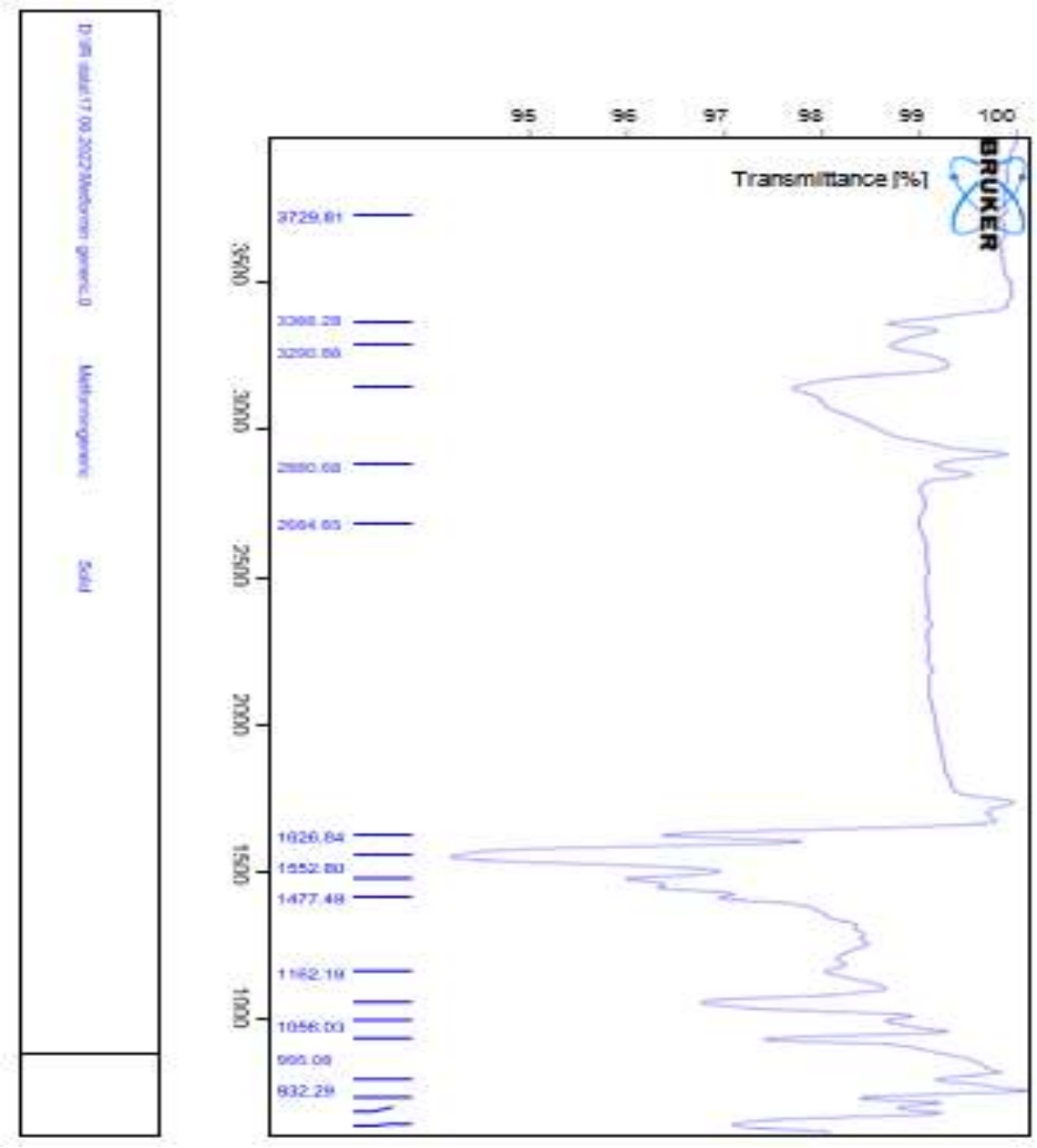

Fig.No.10 IR Spectroscopy of Generic Drug

Interpretation of IR Spectra

Reported Wave Number (cm^{-1})	Observed Wave Number (cm^{-1})		Type of Vibration
	Generic	Branded	
3200-3400 cm^{-1}	3366.96	3366.28	N-H stretch

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3200-3400 cm^{-1}	3292.15	3290.86	O-H stretch
3300 cm^{-1}	3292.15	3290.86	Alkyne C-H stretch
>3000cm^{-1}	3149.75	3146.59	Alkenyl C-H stretch
2850-3100 cm^{-1}	2886.60	2880.68	C─H stretch
<3000cm^{-1}	2809.55	2684.85	Alkyl C─H Stretch

Table. No. 11 Interpretation of IR Spectra.

III. CONCLUSION

This study was aimed to assess quality as well as physicochemical equivalence of Branded and Generic metformin hydrochloride tablet. The study confirmed that the generic and branded metformin hydrochloride tablets complied with the official specification for weight variation, hardness, friability, disintegration, assay and dissolution. All the evaluated metformin tablet showed the released of about 80% of metformin hydrochloride within 30 min as stipulated in the pharmacopoeia, there exist variations in their release profiles. The percent drug content of generic and branded metformin hydrochloride tablets is within the pharmacopoeial limit. From the obtained result we were conclude that the selected metformin hydrochloride tablet taken for comparative evaluation of their quality assessment to assure its efficacy and potency, gives different results from each other but not crosses the limits given in official books. The result indicated that the generic and branded tablets fulfilled the required official specification and thus assures that generic drugs are also bioequivalent to ethical drugs if all the quality control parameters are being maintained.

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