IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

"In-Vitro Evaluation Study of Different Brands of Metformin Hydrochloride Tablet (U.S.P.) Available InIndian Market"

Ms. Sakshi M. Nikam, Mr. Mohan Rahul, Dr. Kawade Rajendra M.

Nandkumar Shinde College of Pharmacy, Vaijapur Dist. Chhatrapati Sambhajinagar 423701

Dr. Babasaheb Ambedkar Technological University,Lonere

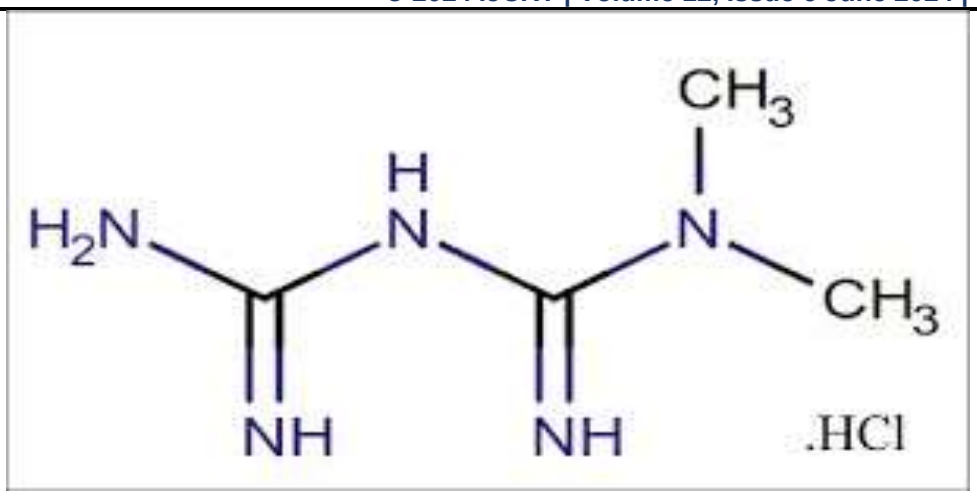
Abstact:

This study aimed to assess the quality and performance of different brands of Metformin Hydrochloride tablets (USP) available in the Indian market. Three commercially available brands were selected for the study and subjected to various tests according to the United States Pharmacopeia (USP) guidelines. Parameters including weight variation, content uniformity, disintegration time, and dissolution profile were evaluated to ensure compliance with established standards. The study revealed significant variations among the tested brands in terms of their quality attributes. While some brands exhibited satisfactory performance within the specified limits, others demonstrated deviations from the pharmacopeial standards. These findings underscore the importance of stringent quality control measures in pharmaceutical manufacturing and highlight the need for regulatory oversight to ensure the consistent quality of medications available to consumers. Further studies incorporating additional quality parameters and clinical evaluations are warranted to provide comprehensive insights into the performance and therapeutic equivalence of different brands of Metformin Hydrochloride tablets in the Indian market.

Keyword : Metformin Hydrochloride, Fribilability, Hardness, Dissolution, Disintegration

Introduction

Chemically speaking, Metformin hydrochloride (also known as 1,1-diamethylbiguanide hydrochloride) is N,N-dimethylimidodicarbionimidic diamide hydrochloride. This oral diabetes medication is mostly used to treat Type II Diabetes Mellitus. They work by lowering intestinal glucose absorption, raising insulin sensitivity, and reducing hepatic glucose synthesis. In the Indian market, Metformin hydrochloride comes in a variety of brands. The purpose of the study was to compare the quality of several brands of Metformin. Therefore, to sustain the therapeutic impact of the drug throughout the day, standard Metformin HCl pills should be taken two to three times daily. The objective of study was to examine, compare, and assess the quality standards of commercially available Metformin hydrochloride tablets that were used to treat Type II Diabetes and were recommended by a doctor.



Pharmacokinetics

- Based on fasting conditions, the bioavailability for Metformin hydrochloride 500 mg pill is 50 to 60%.
- The effect of food is a reduction in the amount of absorption and a delay in absorption (fed vs. fasting, C_{max} 40% lower, AUC 25% lower, T_{max} extended by 35 minutes).
- Plasma protein binding is insignificant.
- Elimination: Excreted unchanged in the urine (no hepatic metabolism or biliary excretion) in a time frame of 24 to 48 hours.
- A 6.2-hour elimination half-life is typical.

Side Effects

Common side effects are weakness, diarrhoea, nausea, vomiting, stomach distress, or a metallic aftertaste. Many users of this medicine report no significant negative effects. Typically, metformin does not result in hypoglycaemia, or low blood sugar. If this medication is administered along with other diabetes medications, low blood sugar may result.

Administration

To lessen GI distress, Metformin in oral form is normally taken with a meal and dosed between 500 and 2550 mg per day. To lessen this side-effect, the daily dose is frequently increased on a weekly basis by 500 mg or 850 mg. It is advised to take Metformin every day at the same time. Extended-release pills should be consumed with a full glass of water and are normally taken once a day with an evening meal.

Materials and methods

Area Of Study :

The study was conducted in the department of pharmacy in the Nandkumar shinde college of Pharmacy . Vaijapur Chhatrapati Sambhajinagr, from March 2024 to April 2024

List of tablets used:

S.No.	Brand name	Manufacturer name	Batch No.	Mfg. Date	Exp. Date
1	Glipizide	Bal pharma	G24640	03/2023	02/2026
2	Glynase	USV	30058098	08/2023	07/2026
3	Dibizide	Micro labs	DMUH0385	11/2023	10/2026

List of instruments used

Evaluation method	Instrument used
Weight variation test	Analytical balance
Friability test	Friabilator
Disintegration test	Disintegration apparatus
Dissolution test	Dissolution apparatus
Content Uniformity test	UV-Visible Spectroscopy(SHIMADZU-1900)

Evaluation methods

1.Thickness

2.Weight variation test.

3.Hardness test.

4.Friability test.

5.Disintegration test.

6.Dissolution test

Thickness

The tablet thickness test is used to determine how thick a tablet is. The vernier calliper is the most often used instrument for measuring tablet thickness.

Weight variation test

Weight variation, which depicts the relative fluctuation of Active Pharmaceutical Ingredients (API) and excipient content, is used to demonstrate drug content homogeneity, particularly in big dose pharmaceuticals such as tablets weighing more than 325mg. To investigate weight variation, 20 pills of each formulation were weighted using an electronic balance and tested, according to the official technique.

Standards uniformity of weight

Avg. Weight of tablet	**% deviation**
Less than 130	10
More than 130mg, equal to 324mg	7.5
More than 324mg	5

Analytical weighing balance

Hardness:

The hardness of tablets determines their resistance to shipment or breakage during storage, transportation, and handling prior to use. The Monsanto hardness tester was used to test the hardness of each batch of tablets. The hardness was measured in kilogrammes per square centimetre. The hardness of 5 pills was determined at random. The average hardness of five determinations was taken. If the crushing strength of the tablet is between 4kg/cm3 and 10kg/cm3, it passes the hardness test.

Pfizer hardness tester

Friability test

Friability is the weight loss of tablets in containers caused by the removal of particles from the tablet surface. Friability is often indicative of poor cohesiveness of tablet components. The starting weight of 20 tablets was recorded and the pills were placed in a Roche friabilator and rotated at a speed of 25 rpm for 100 rotations. The tablets were then withdrawn from the friabilator, fines were brushed off, and the weight was recorded. The formula was used to calculate the percentage friability. The tablets'% friability meets the USP criteria, which statesthat the friability study must not lose more than 1% of their initial weight.

%Friability = Initial weight – Final weight / Initial weight x 100

Friability test apparatus

Disintegration Test

A 1000 ml beaker was filled with about 700 ml of distilled water, and the beaker was then putwithin theapparatus. Each basket rack tube held one azithromycin tablet, a plastic disc covered each tablet, and the basket rack was precisely positioned inside the beaker. The temperature maintained to 37°C +2°C .The time in minutes calculated that the tablets needed todisintegrate and get through the mesh was recorded

Dissolution test

Dissolution is defined in the pharmaceutical industry as the rate of mass transfer from a solid surface into the dissolution medium or solvent under standardised liquid/solid interface, temperature, and solvent content conditions. It is a changing dynamic property that describes the process of obtaining a homogeneous mixing of a solid or a liquid in a solvent. Drug dissolution testing is routinely used in the pharmaceutical industry to provide critical in vitro drug release information for both quality control, assessing batch-to-batch consistency of solid oral dosage forms such as tablets, and drug development, predicting in vivo drug release profiles. In vitro drug dissolving data from dissolution testing procedures can be correlated with in vivo pharmacokinetic data using in vitro-in vivo correlations (IVIVC). According to the Food and Drug Administration, the fundamental goal of creating and evaluating an IVIVC is to establish the dissolving test as a surrogate for human bioequivalence investigations. In many circumstances, analytical data from drug dissolution testing are adequate to show the safety and efficacy of a drug product without in vivo experiments; nevertheless, the dissolve testing performed in dissolution apparatus must be reliable and reproducible.

Phosphate buffer prepration

For Metformin hydrochloride - Complies with the test stated under Tablets.For Glipizide Apparatus. No 1, sind Medium. 900 ml of a buffer solution prepared by dissolving 0.58 g of monobasic potassium phosphate and 8.86 g of anhydrous dibasic sodium phosphate in 1000 ml of water and adjusted to pH 7.8 with orthophosphoric acid or 1M sodium hydroxide, add 10 g of sodium lauryl sulphate and mix. Speed and time.

100 rpm and 90 minutes.

Procedure:

1. Switch the heater of the dissolution device on and manage the temperature to reach 37°C.
2. Wash the vessel (of dissolution apparatus) using water and soap then put 900 ml of medium (phosphate buffer pH 6.8) in each.
3. Elevate the paddle 25±2 mm from the bottom of the vessel.
4. Operate the paddle on a rotation speed equals to 50 rpm.
5. Add one 500 mg tablet in one vessel which you previously cleaned and at once start timing.
6. At specified time intervals (5, 10, 15, 20, 25, 30, 45 and 60 min) Withdraw 1 ml using the volumetric pipette from each filtrated sample (filtrate) and put it in 10 ml volumetric flask (clean and neat), then complete the volume up to 10 ml by the medium (phosphate buffer at pH=6.8).
7. Replace the same volume into dissolution vessel by another volumetric pipette.
8. Read the absorbance of the diluted sample solutions at λ=232 nm using the buffer as a blank.
9. Plot a graph between Time intervals on x-axis vs % of drug release on y-axis.
10. Find out the slope, concentration, amount of drug release, percentage of drug release and report.

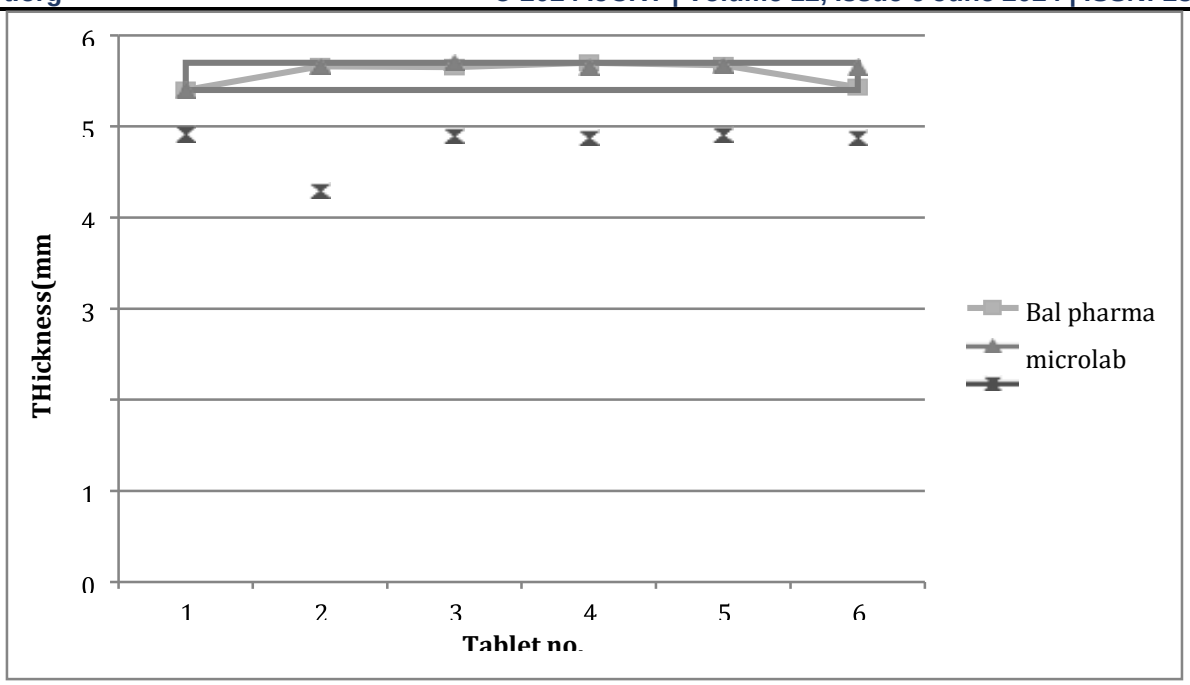
Determination of absorption maxima:

A UV absorption maximum was determined by scanning 10µg/ml solution of metformin hydrochloride in phosphate buffer 6.8, in between 200-400 nm by using UV-visible spectrophotometer. Further a representative spectrum was drawn of Metformin Hydrochlorde in phosphate buffer pH 6.8.

Result and Discussion

Thickness

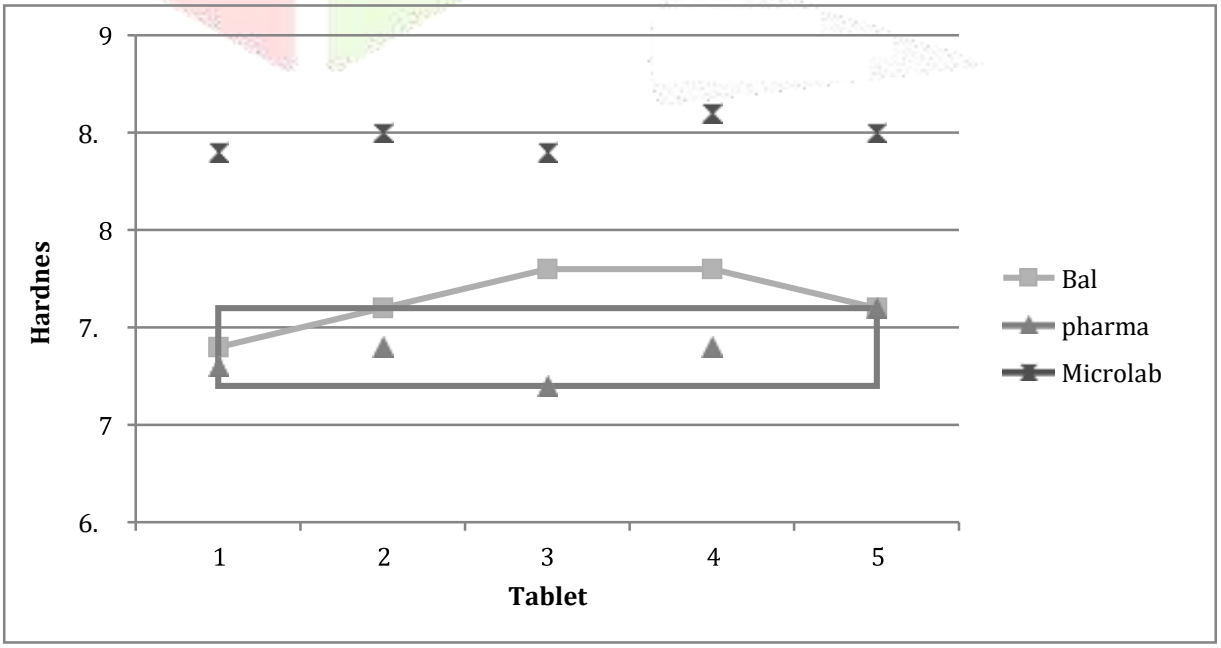
Brand name of tablet	**Thickness**					
	1	2	3	4	5	Average
Bal pharma	5.40	5.66	5.65	5.70	5.67	5.43
Microlab	5.57	5.66	5.70	5.65	5.67	5.65
USV	4.92	4.30	4.90	4.88	4.91	4.88



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. The results are shown in table.

Tablet no.	Bal pharma	Microlab	USV
1	7.4	7.3	8.4
2	7.6	7.4	8.5
3	7.8	7.2	8.4
4	7.8	7.4	8.6
5	7.6	7.6	8.5



Uniformity of Weight

20 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 6.3

Bal Pharma			**Microlab**		**USV**	
Tabletno.	**Individual Weight(gm)**	**%weight variation**	**Individual Weight(gm)**	**%weight variation**	**Individual Weight(gm)**	**%weight variation**
1	0.641	0.15	0.663	0.15	0.675	0.29
2	0.640	0.31	0.665	0.45	0.673	0.00
3	0.644	0.31	0.665	0.45	0.671	0.29
4	0.643	0.15	0.664	0.30	0.678	0.74
5	0.644	0.31	0.663	0.15	0.671	0.29
6	0.645	0.46	0.662	0.00	0.675	0.29
7	0.642	0.00	0.662	0.00	0.673	0.00
8	0.641	0.15	0.660	0.15	0.674	0.15
9	0.641	0.15	0.661	0.45	0.675	0.29
10	0.643	0.15	0.665	0.15	0.676	0.44
11	0.642	0.00	0.665	0.45	0.671	0.29
12	0.641	0.15	0.664	0.45	0.670	0.44
13	0.640	0.31	0.662	0.30	0.674	0.15
14	0.643	0.15	0.661	0.00	0.675	0.29
15	0.644	0.31	0.660	0.15	0.674	0.15
16	0.645	0.46	0.663	0.45	0.671	0.29
17	0.643	0.31	0.664	0.30	0.673	0.00
18	0.646	0.62	0.663	0.30	0.675	0.29
19	0.645	0.46	0.661	0.15	0.678	0.74
20	0.646	0.62	0.661	0.15	0.671	0.29
Average	**0.642**		**0.662**		**0.673**	

Friability test

Twenty 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 studymust not lose 1% of their initial weight. The results are shown in Table

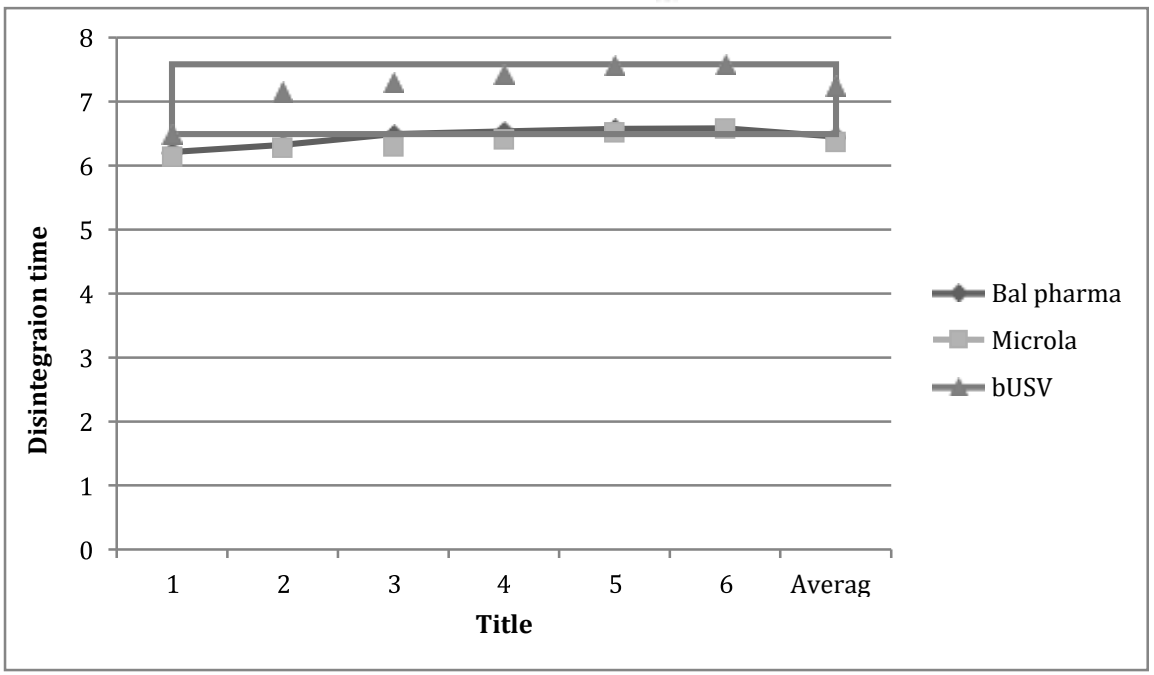
%Friability = Initial weight – Final weight / Initial weight x 100

Brand	Initial weight	Final weight	%Friability
Balpharma	13.192	13.183	0.06%
Microlab	12.604	12.593	0.09%
USV	12.856	12.845	0.08%

Disintegration Test

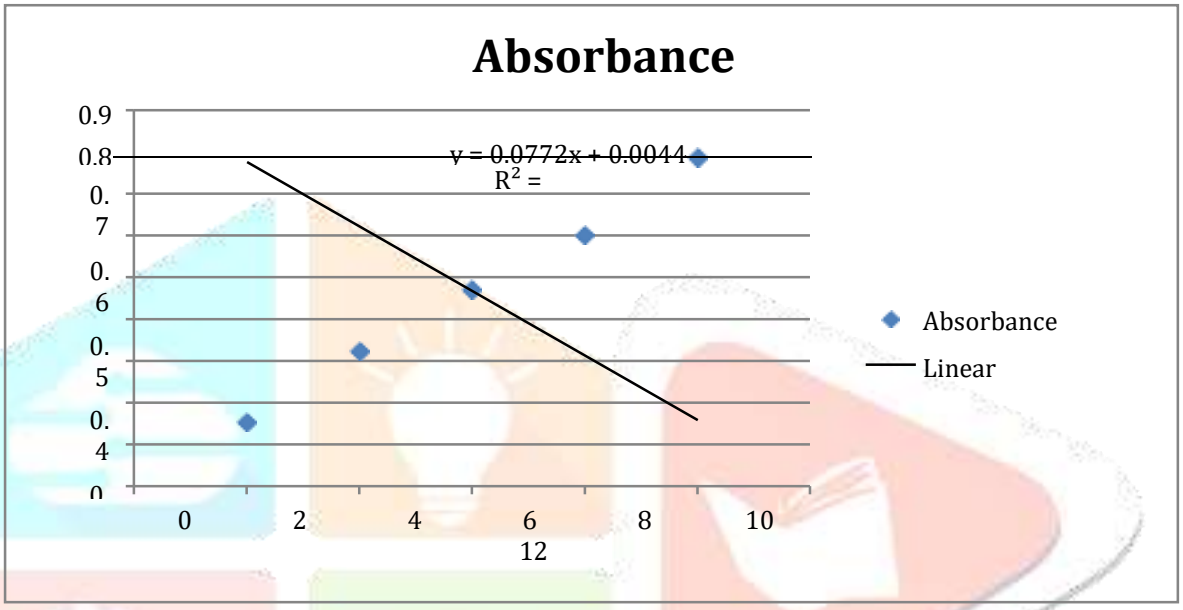
Disintegration time of randomly selected six tablets of each brand was determined at 37˚C using disintegration apparatus employing distilled water as test fluid. The disintegration time was taken to be the time when no granule of any tablet was left on the mesh.

Tablet no	Bal pharma	Microlab	USV
1	6min 21sec	6min 14sec	6min 49sec
2	6min 32sec	6min 28sec	7min 15sec
3	6min 49sec	6min 30sec	7min 29sec
4	6min 53sec	6min 41sec	7min 42sec
5	6min 57sec	6min 52sec	7min 56sec
6	6min 58sec	6min 58sec	7min 58sec
Average	6min 45sec	6min 37sec	7min 24sec



Dissolution testCalibration curve

Concentration [microgram/ml]	Absorbance
2	0.154
4	0.324
6	0.471
8	0.602
10	0.787



Dissolution Profile of Balpharma tablets

S.No	Time interval	Absorbance	Amount of drug release(mg)	Percentage drug released (%)
1	5 min	0.290	33.75	6.75
2	10 min	0.310	69.88	13.97
3	15 min	0.335	147.99	29.40
4	30 min	0.635	296.05	59.20
5	45 min	0.641	445.99	89.00
6	60 min	0.640	498.44	99.60

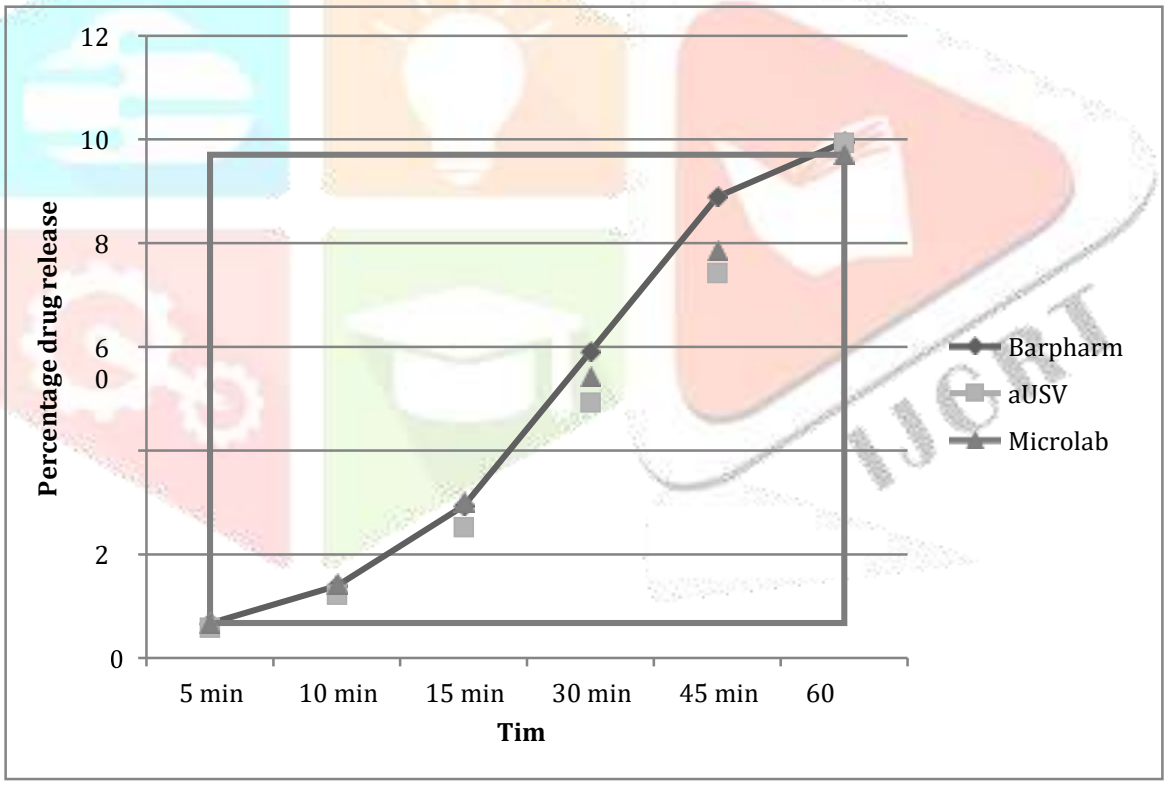
Dissolution Profile of USV tablets

S.No	Time interval	Absorbance	mount of drug release (mg)	Percentage drug released (%)
1	5 min	0.252	29.37	5.87
2	10 min	0.274	61.32	12.26
3	15 min	0.284	126.53	25.30

4	30 min	0.515	246.63	49.32
5	45 min	0.536	371.58	74.31
6	60 min	0.539	497.02	99.40

Dissolution Profile of Micro labs tablets

S.No.	Time interval	absorbance	mount of drug release (mg)	Percentage drug released (%)
1	5 min	0.292	34.04	06.80
2	10 min	0.324	71.81	14.36
3	15 min	0.339	150.85	30.17
4	30 min	0.517	271.39	54.27
5	45 min	0.521	392.93	78.58
6	60 min	0.519	485.90	97.18



Discussion

In present work, we have done the evaluation of Metformin hydrochloride tablet by various methods mentioned in United States Pharmacopoeia and literature. We collected 100 tablets of each brands (Bal Pharma, USV Pharma, Microlab) from local market. Firstly we did the weight variation test by using analytical balance and calculations were performed as per United States Pharmacopoeia. After that we performed the friability test of 20 tablet from each brand by using Roche friabilator in phase wise manner. Tablets were kept outside and dedusted followed by weighing and the results were obtained within 1% variation as per USP standard .Then disintegration test was performed by using disintegrator where water was used as a medium and 6 tablets of each brand were taken and the disintegration time were recorded. In USP the disintegration time for Metformin Hydrochloride should be within 15 minute which matched our test results.. After that hardness test was performed by using Pfizer hardness tester.Five tablets were taken from each brand and tested. Strength was recorded and results matched to the USP standard values. Pharmacopeial Assay was done by using a suitable method. Initially 20 tablets from each brand of Metformin hydrochloride were weighed using analytical balance and average weight was taken. Tablets were then powdered using mortar and pestle. Powder equivalent to 0.1g of Metformin hydrochloride was then taken and 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 and then further dilutions were made and the absorbance of the resulting solution was taken at the maximum at about 232nm. All brands of tablets showed appropriate percentage purity as per the specification. Dissolution test was performed by using dissolution apparatus. Phosphate buffer (pH 6.8) was used as a medium. Calibration curve (Absorbance vs Concentration) of pure Metformin hydrochloride was prepared. Absorbance was measured by UV-visible spectroscopy (SHIMADZU-1900) at an interval of interval of 5,10,15,30,45,60 minute and the concentration of drug release were noted. From the dissolution study it was observed that the formulation of Microlab showed good release rate while the other formulations showed the appropriate release as per the USP specification.

Conclusion

The purpose of this study was to evaluate the quality and physicochemical equivalence of several brands of Metformin hydrochloride tablet. According to the findings, all of the tablets met the regulatory specifications for Weight variation, Hardness, Friability, Disintegration, Assay and Dissolution. Although all the tablets released approximately 80% of the metformin hydrochloride within 30 minutes as required by the pharmacopoeia, there were some differences in their release characteristics. The drug concentration of Metformin hydrochloride tablets of all brands was within the Pharmacopeial limit. We concluded from the data that the selected Metformin hydrochloride tablets used for comparative evaluation of their quality assessment to ensure efficacy and potency yielded diverse results but did not exceed the limitations specified in official books. The results showed that all brand tablets satisfied the required official specifications, ensuring that all pharmaceuticals are also bioequivalent to ethical drugs if all quality control requirements are met. It may be concluded that all the accessible brands in the local market of India have similiar quality

range and can be interchanged if any non-compliance is discovered owing to a cost issue. According to the current study, patients can safely transition from one brand to another if they are informed of the chance of small GIT complications that may emerge after therapy with the new alternativemedicine.

Reference:

1. The United States Pharmacopoeia national formulary USP 41 NF 36 volume, 2018Page no. 2781 – 2788
2. Madan Mohan Gupta et al/ Journal of pharmaceutical research and science vol.8(4),2016, 238 – 243
3. Anupam Kr. Et al Sachan Vineet Kumar and Ankita Gupta Scholars Research LibraryDer Pharmacia Lettre, 2016, 8(5):419-424
4. Olubukola A etal Rukaiyatu A. Journal of Pharmacy And Bioresources Vol.18 no.3PP. 215 – 222(September 2021)
5. Tesfay etal, Kahsay and Dinda Austin Journal of Analytical and PharmaceuticalChemistry Volume 6 Issue 2 – 2019
6. Roop K Khar etal sp vyas, Farhan j Ahmad lachman's theory and practice of industrial pharmacy CBS publication 4th edition 2018 page no. 449-489
7. Arora A, Parle A, Dahiya M, Rani R. Comparative evaluation of Metformin tablets available under government supply and brands available in open market in Delhi, India. IOSR J Pharm. 2021;11(5):8–20.
8. Indian Pharmacopeia, Government of India, Ministry Of Health and Family Welfare Ghaziabad 8th edition volume 2 page no. 2172 – 2182
9. Prithi IJ, Chowdhury SF, Chowdhury S. Comparative in vitro dissolution test and other physicochemical parameters of some commercially available metformin HCl brands in Bangladesh. Pharma Innov. 2018;7(6):5–8.
10. Tesfay K, Kahsay G, Dinda S. In Vitro Quality Evaluation of Metformin Hydrochloride Tablets Marketed in Western and North Western Tigray, Ethiopia. Austin J Anal Pharm Chem. 2019;6(2):1119.
11. Prithi IJ, Chowdhury SF, Chowdhury S. Comparative in vitro dissolution test and other physicochemical parameters of some commercially available metformin HCl brands in Bangladesh. Pharma Innov. 2018;7(6):5–8.
12. Newton PN, Lee SJ, Goodman C, et al. Guidelines for field surveys of the quality of medicines: a proposal. PLoS Med. 2009;6(3):e1000052. doi:10.1371/journal.pmed.1000052
13. Stationery Office. British Pharmacopoeia 2013: Published on the Recommendation of the Commission on Human Medicines Pursuant to the Medicines Act 1968 and Notified in Draft to the European Commission in Accordance with Directive 98/34/EEC. London: Stationery Office; 2012.
14. Peck GE, Baley GJ, McCurdy VE, Banker GS. Tablet formulation and design. Pharm Dos Forms Marcel Dekker N Y. 1989;75–130.
15. Aulton ME. Pharmaceutics: the science of dosage form design. Royal Soc Chem. 2002.
16. Allen L, Ansel HC. Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems. Lippincott Williams &

Wilkins; 2013.

17. Hamdan II, Jaber AKB. Pharmaceutical evaluation of metformin HCl products available in the Jordanian market. Jordan J Pharm Sci. 2010;3(22):1–7.
18. Hani U, Alhamhoom Y, Alqahtani A, et al. In-vitro Comparative Study of Different Brands of Metoclopramide Hydrochloride Tablets Marketed in Saudi Arabia. Curr Drug Ther. 2020;15(5):512–517. doi:10.2174/1574885515666200305101840