Khwaja Yunus Ali University Journal

Publisher homepage: www.kyau.edu.bd

OPEN ACCESS
ISSN: 2521-3121 (Print)

Journal homepage: www.journal.kyau.edu.bd

Research Article

A comparative Study on Physical Parameters of Different Brands of Metformin Available in Bangladesh

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Abstract:

Metformin hydrochloride is a diabetic medicine that contains 500 mg of metformin. It is biguanide, which is a kind of oral hypoglycemic agent. It is the first-line treatment for type 2 diabetes, especially in overweight or obese individuals. In Bangladesh, many metformin hydrochloride tablets are available through the global drug delivery system. Because numerous brands of metformin tablets are available in the Bangladesh pharmaceutical market nowadays, health practitioners are faced with a generic replacement dilemma. The study's objective was to assess the physicochemical equivalence of five brands of metformin hydrochloride tablets marketed in Bangladesh using in vitro tests. Official and non-official criteria such as weight uniformity, friability, hardness, disintegration, assay, and dissolving rate were used to establish the physicochemical equivalence of different brands of Metformin hydrochloride tablet brands. All the brands adhered to the approved standards.

Keywords: Metformin, Weight Variation, Friability, Disintegration, Hardness.

Introduction:

Hyperglycemia, altered glucose, lipid, and protein metabolism, and an increased risk of vascular consequences are all symptoms of diabetes mellitus (DM). It's caused by issues with insulin secretion, insulin sensitivity, or both (Barbara *et al*., 2009). Due to the growing incidence of diabetes across the world, particularly in developing countries, the growth of diabetic complications as a cause of early morbidity and mortality, and the huge and escalating burden on health care systems, diabetes has become a major public health problem (Khatib, 2006). Long-term effects of diabetes include retinopathy, nephropathy, peripheral neuropathy, amputations, and sexual dysfunction (Bastaki, 2005). Pharmaceuticals are commonly used to prolong life and prevent diabetic problems in the long run. The incidence

of Type 2 diabetes has grown internationally as a result of lifestyle changes such as poor diet, decreased physical activity, and stress (Wild *et al*., 2004). Oral hypoglycemic medicines must be taken when food management and exercise fail to treat this kind of diabetes (Katzung*et al*., 2012). Oral hypoglycemic medications (glitazones) include biguanides (metformin), sulphonylureas (tolbutamide, glibenclamide), and thiazolidinediones (Bastaki, 2005). Metformin is a type 2 diabetes antidiabetic drug that belongs to the biguanide class of oral hypoglycemic medications (Sahra *et al*., 2010).

In the twenty-first century, diabetes mellitus (DM) is increasingly recognized as a worldwide health problem. As a result of rising obesity and physical inactivity rates, as well as population expansion, aging, urbanization, and urbanization, diabetes is becoming more common (Wild *et al*., 2004). Substandard medications are legal drugs that fail to meet the quality standards set out by their manufacturers when evaluated in a laboratory. The introduction of generic pharmaceutical items from a range of sources into many developing countries' health-care delivery systems aims to improve overall health-care delivery. However, the broad availability of counterfeit and substandard medicines has impeded this. Pharmaceuticals in many underdeveloped nations are of poor quality. The use of low-quality medications has resulted in therapeutic failure in a few situations (Petralanda, 1995).Treatment for type 2 diabetes requires a change in eating habits, such as the adoption of a low-sugar, low-carbohydrate, and high-calorie diet, as well as physical activity, which can be coupled with the use of hypoglycemic medicines such biguanides and sulfonylureas (Lerario *et al.*, 2010).

Metformin's hypoglycemic effect is due to its action on hepatic and muscle tissues, which sensitize insulin's effect, resulting in the inhibition of gluconeogenesis and glycogenolysis, as well as the stimulation of glycogenesis in the hepatocyte, particularly in the skeletal muscles, resulting in an increase in glucose production and a decrease in glycemia (Viollet *et al*., 2013).

It is important to ensure the quality of a formulation once it has undergone development and stability tests. From this perspective, quality control goals include ensuring the efficacy and safety of increasingly effective and safe drugs with reduced toxicity and better stability (Bernardes *et al*., 2010).To this end, this study was justified by the fact that it is necessary to evaluate the quality of metformin tablets, in different dosage forms, manufactured by different companies.

Materials and Methods:

- Friability test for tablets

Friability testing is a laboratory procedure used by the pharmaceutical industry to determine how long tablets will last while in transportation. Using a revolving wheel with a baffle, a sample of tablets is dropped repeatedly over a set period of time.

Experimental method:

1. A total of ten (metformin) pills were chosen and weighted.
2. All tablets are placed in the friability test drum. The rotation speed is set to 100 rpm, the timer is set for 4 minutes, and the process begins.
3. At the conclusion of the procedure, all pills were removed and dusted or powdered with a brush. After that, all of the pills were weighed once again.
4. The weight decrease percentage was computed.

The friability of the tablets was then calculated using the following method:

$$\% \text{ Friabilit} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \; x \; 100$$

- **Disintegration Test for Tablets**

The disintegration test simply measures the amount of time it takes for a batch of tablets to break into particles under specific circumstances. Disintegration is the process of

breaking down a tablet into smaller bits or grains.

It's a legitimate test. When tablets or capsules are put in a liquid medium under experimental circumstances, the test is used to see if they dissolve within the specified period.
The disintegration test is commonly used to assess the disintegration capabilities of formulations (i.e., different types of tablets) and to ensure the quality of various dosage forms. This test is used to see if tablets or capsules dissolve in the specified amount of time when put in a liquid medium under the circumstances outlined below.

Experimental Method:

1. The apparatus was set up for the disintegration test according to the manufacturer's instructions.
2. A temperature of 37.2°C was maintained in the disintegration medium (water).
3. A 0-minute timer was set. In each tube, one pill was placed.
4. The procedure began once each tube was filled.
5. At the conclusion of the procedure, each tube was verified for the 18 pills.
6. All six pills passed the test since they dissolved after 60 minutes.

- **Uniformity of weight test for tablets:**

It is preferable if the weight of all the pills in a batch is consistent. If there is any weight change, it should be within the permitted limits. If just 10 pills are ingested for the test, the test is regarded as accurate if no more than two tablets fall beyond this range.
In some cases, the weight difference can be used to determine the API in individual dose units. As a result, the WV test may be beneficial in medication quality control.

Official Standard (USP):

Sl.	Average weight of tablet	Range
1	120 or less mg	(+ or -) 10%
2	120-325 mg	(+ or -) 7.5%
3	>324mg	(+ or -) 5%

Experimental Method:

1. 20 tablets previously selected at random were weighed. The average weight was determined.
2. Tablets were weighed individually and the percentage deviation of its weight from the average weight was determined for each tablet.
3. The deviation of an individual's weight from the average weight should not exceed the limits given below.

Average weight of tablets	Deviation (%)	Number of tablets
Less than 80 mg	± 10.0 ± 20.0	Minimum 18 Maximum 2
80 mg to 250 mg	± 7.5 ± 15.0	Minimum 18 Maximum 2
More than 250 mg	± 5.0 ± 10.0	Minimum 18 Maximum 2

- **Hardness Test:**

The weight of the material used, as well as the distance between the upper and lower punches at the moment of compression, determines the hardness of a tablet.

Experimental Method:

1. At first, 10 tablets were taken.
2. Tablets are taken vertically by a hardness tester.
3. Then screw pressure is given until the breakdown of the tablet.
4. Then I took a read by the hardness tester.
5. Finally, the rest of the tablet's hardness was measured individually.

The average hardness of the tablets was then calculated using the following method:

$$\text{Average hardness} = \frac{\text{Total hardness}}{\text{Number of tablets}}$$

Results:

Weight variation Test

$$\text{Deviation (\%)} = \frac{\text{Average weight of tablets} - \text{Weight of each tablet}}{\text{Average weight of tablets}} x\ 100$$

Table-1: Weight variation of different brands of Metformin based on % deviation.

Brand Name	Informet	Metfo	Metsa-XR	M-Min	Kemin
T_1	-0.14	1.04	-3.57	0	-2.80
T_2	-0.14	-0.69	-3.57	1.36	-0.13
T_3	1.20	-0.69	-3.57	1.36	-1.46
T_4	-0.14	-0.69	-3.57	2.73	1.20
T_5	-0.14	1.04	-3.57	0	-0.13
T_6	-0.14	-0.69	-3.57	1.36	-0.13
T_7	-0.14	1.04	-1.08	2.73	-0.13
T_8	1.29	1.04	-3.57	-1.36	1.20
T_9	-0.14	-0.69	-3.57	-1.36	-0.13
T_{10}	-0.14	-0.69	-3.57	0	-2.80
T_{11}	1.29	1.04	-3.57	0	-0.13
T_{12}	-1.57	-2.43	-3.57	-1.36	2.53
T_{13}	-0.14	1.04	-3.57	0	-0.13
T_{14}	-0.14	1.04	-1.08	1.36	1.20
T_{15}	-0.14	-2.43	0.12	-1.36	-1.46
T_{16}	-0.14	1.04	-3.57	-1.36	-0.13
T_{17}	-0.14	-0.69	-3.57	1.36	0.13
T_{18}	-0.14	1.04	-1.08	-1.36	1.20
T_{19}	-0.14	1.04	-1.08	-1.36	1.20
T_{20}	-0.14	-0.69	0.12	0	1.20

As the average weight of tablets is 700 mg, which is more than 250 mg, the standard deviation should be ±5 in our experiment. So, the tablets are experimented of good quality.

- **Hardness Test**

Table -2: Hardness test of different brands of Metformin based on mechanical strength (N).

Brand Name	Informet	Metfo	Metsa-XR	M-Min	Kemin
T_1	160N	150N	100N	150N	100N
T_2	170N	140N	100N	160N	100N
T_3	150N	140N	90N	150N	90N
T_4	140N	130N	90N	170N	90N
T_5	150N	130N	90N	130N	95N
T_6	150N	125N	95N	130N	100N
T_7	160N	120N	100N	130N	85N
T_8	150N	140N	95N	140N	90N
T_9	140N	130N	110N	175N	100N
T_{10}	160N	140N	110N	145N	110N
T_{11}	160N	150N	95N	160N	90N
T_{12}	150N	140N	90N	135N	95N
T_{13}	150N	130N	100N	160N	85N
T_{14}	140N	125N	100N	145N	100N

T_{15}	170N	120N	95N	130N	105N
T_{16}	150N	150N	95N	175N	90N
T_{17}	140N	130N	110N	150N	95N
T_{18}	170N	140N	100N	130N	85N
T_{19}	160N	150N	95N	130N	100N
T_{20}	160N	140N	100N	130N	95N
Average Hardness	154 N	136 N	98 N	146.25 N	95 N

The mechanical strength should be less than 200 N.
The average hardness of tablets is of good quality. So, all tablets have passed this test.

- **Friability Test**

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

Table-3: Friability Test of different brands of Metformin based on % Friability.

Brand Name	Informet	Metfo	Metsa-XR	M-Min	**Kemin**
T_1	0.70gm	0.735gm	0.85gm	0.57gm	0.770gm
T_2	0.70gm	0.720gm	0.85gm	0.58gm	0.758gm
T_3	0.69 gm	0.723gm	0.85gm	0.58gm	0.768gm
T_4	0.70gm	0.714gm	0.85gm	0.58gm	0.740gm
T_5	0.70gm	0.738gm	0.85gm	0.57gm	0.756gm
T_6	0.70gm	0.727gm	0.85gm	0.58gm	0.752gm
T_7	0.70gm	0.714gm	0.84gm	0.57gm	0.756gm
T_8	0.69gm	0.743gm	0.85gm	0.57gm	0.749gm
T_9	0.70gm	0.740gm	0.85gm	0.58gm	0.757gm
T_{10}	0.70gm	0.733gm	0.85gm	0.58gm	0.778gm
T_{11}	0.69gm	0.732gm	0.85gm	0.57gm	0.759gm
T_{12}	0.71gm	0.741gm	0.85gm	0.59gm	0.737gm
T_{13}	0.70gm	0.738gm	0.85gm	0.57gm	0.753gm
T_{14}	0.70gm	0.742gm	0.84gm	0.57gm	0.748gm
T_{15}	0.70gm	0.745gm	0.83gm	0.59gm	0.767gm
T_{16}	0.70gm	0.744gm	0.85gm	0.57gm	0.758gm
T_{17}	0.70gm	0.728gm	0.85gm	0.58gm	0.753gm
T_{18}	0.70gm	0.741gm	0.84gm	0.57gm	0.748gm
T_{19}	0.70gm	0.740gm	0.84gm	0.57gm	0.743gm
T_{20}	0.71gm	0.730gm	0.83gm	0.58gm	0.748gm
Initial	14.08gm	14.67gm	16.99gm	11.61gm	15.10gm
Final	14.05gm	14.66gm	16.87gm	11.59gm	15.08gm
%	0.21%	0.05%	0.70%	0.17%	0.13%.

Friability should be less than 1% for all standard compressed tablets.
The tablets experimented are in the standard range of friability.

- **Disintegration Test**

Table-4: Disintegration test of different brands of Metformin based on time (minutes).

Brand Name	Informet	Metfo	Metsa-XR	M-Min	Kemin
T_1	13m	6m	26m	25m	10m
T_2	11m	7m	24m	25m	7m
T_3	11m	7m	28m	8m	7m
T_4	11m	8m	26m	7m	7m
T_5	10m	9m	27m	27m	9m
T_6	12m	9m	30m	29m	9m
T_7	10m	7m	26m	9m	10m
T_8	11m	5m	24m	6m	9m
T_9	11m	7m	26m	25m	9m
T_{10}	12m	5m	26m	8m	8m
T_{11}	12m	8m	28m	29m	10m
T_{12}	10m	7m	22m	5m	8m
T_{13}	10m	7m	25m	9m	8m
T_{14}	12m	8m	28m	29m	8m
T_{15}	12m	6m	26m	28m	9m
T_{16}	12m	8m	30m	6m	9m
T_{17}	12m	6m	23m	6m	9m
T_{18}	11m	6m	29m	2m	10m

For uncoated compressed tablet, the time of disintegration should be less than 15 minutes. In the case of coated tablets, the time of disintegration should be within 30 minutes. All tablets have passed this test.

Discussion:

- **Weight Variation Test**

This test was performed on five brands of Metformin HCl tablets (Informet, M-Min, Kemim, Metfo, and Metsa-XR) to ensure weight consistency. According to the USP criteria, all the tested samples should be under 5% variation because the average weight of all the tablets was greater than 500 mg. For various brands, I discovered a maximum positive percent deviation of (+) 3.765 and a maximum negative percent deviation of (-) 7.391.

- **Hardness Test:**

Hardness is one of the most significant physical characteristics for evaluating tablet quality since it reflects the tablets' physical robustness. All evaluated brands of Metformin HCl (Informet, M-Min, Kemim, Metfo, Metsa-XR) passed the tablet crushing strength or hardness test in this study. These four brands have a hardness of less than 200 N, which is considered acceptable. Another brand (NVmet) failed the tablet crushing strength and hardness tests. As a result, one brand does not fall

within the permissible hardness range of more than 200 N.

- **Friability Test**

The capacity of five brands of Metformin HCl tablets (Informet, M-Min, Kemim, Metfo, Metsa-XR) to endure different shocks and friction during packing, handling, and shipping was tested. The standard friability rating indicates that tablets have adequate mechanical strength. Tablets should not have more than 1% friable, according to the USP standard. As a result, all the pills are of high quality. According to the findings of this investigation, all the brands exhibited outstanding levels of friability that ranged between the highest (0.21 percent) and least (0.061 percent) friability values, respectively.

- **Disintegration Test**

The disintegration test is used to determine how long it takes for a pill to fully dissolve in the gastrointestinal system. The time it takes for a tablet to disintegrate is a measure of its quality, since it influences the pace at which the medication is released. All the Metformin HCl brands examined had a suitable disintegration time, since uncoated tablets should disintegrate in less than 30 minutes according to USP specifications. Brand had the longest disintegration time (21 minutes) and the shortest disintegration time (5 minutes), respectively. As a result, all the pills are of high quality.

Conclusion:

Metformin hydrochloride tablets are available in Bangladesh under several brand names and may be obtained through a pharmaceutical delivery system. The increasing use of metformin hydrochloride tablets in clinical practice demands quality control and generic replacement by monitoring and assessing the quality of the numerous brands available on the pharmaceutical market. In terms of weight uniformity, hardness test, friability test, thickness, disintegration, all the brands showed satisfactory findings. Every test was performed according to the guidelines of BP and the results were found satisfactorily. Metformin HCL 500 mg tablets BP have well-defined and regulated key quality features. There are no significant quality concerns that would negatively affect the benefit balance. The effectiveness of these pills has been proven, indicating that diabetic patients receive the desired therapeutic results with minimal adverse effects. The items were of decent quality. As a result of this research, it was discovered that the metformin 500 mg tablet samples gathered comply with the standard monograph.

Authors' Contributions:

Mukul MEH and Abedin MZ designed the experiments, Rabiya MAK and Munia MFY collected the samples and analyzed, Mukul MEH and Sharil MI carried out the study and participated in design to draft, Mukul MEH and Abedin MZ supervised and reviewed the manuscript; all the authors read and approved the final manuscript.

Acknowledgement:

We thank laboratory personnel of Pharmacy and Microbiology department of Khwaja Yunus Ali University (KYAU) for their assistance in the laboratory analysis. We also acknowledge the administrative personnel of KYAU who provided the equipment needed to conduct the experiment.

Conflict of Interest: All authors declare that there is no conflict of interest.

References:

1. Barbara G, Joseph T, Terry L and Cecily V. (2009). Pharmacotherapy Handbook, 7th Ed. McGraw Hill, New York, USA, pp 210-2011.
2. Bastaki S. (2005), Diabetes mellitus and its treatment. *International Journal of Diabetes and Metabolism*. 13:111-134.
3. Bernardes MLP, Mueller A and Gebara KS. (2010). Development and quality control of capsules containing captopril 25 mg. *Interbio.*, 4(1):15-21.
4. Katzung BG, Masters SB and Trevor AJ. (2012). Basic and clinical pharmacology, 12th Ed., McGraw-Hill, USA, pp 737-747
5. Khatib O. (2006). Guidelines for the prevention, management and care of diabetes mellitus, World Health Organization Regional office for Eastern Mediterranean, EMRO Technical Publications Series 32, Cairo.
6. Lerario AC, Chacra AR, and PimazoniNetto A, et al. (2010). Algorithm for the treatment of type 2 diabetes: a position statement of Brazilian Diabetes Society. DiabetolMetabSyndr., 2(1):35.

7. Petralanda I. (1995). Quality of antimalarial drugs and resistance to Plasmodium vivax in Amazonian region. *Lancet.* 345(8962):1433.
8. Sahra IB, Marchand-Brustel YL, Tanti JF and Bost F. (2010). Metformin in Cancer Therapy: A New Perspective for an old Antidiabetic Drug, *Molecular Cancer Therapeutics.* **9**: 1092-1099.
9. Viollet B andForetz M (2013), Revisiting the mechanisms of metformin action in the liver. *Ann Endocrinol.*, 74(2):123-9.
10. Wild S, Roglic G, Green A and Sicree R. (2004). Global prevalence diabetes: Estimates for the year 2000 and projection 2030, *Diabetes Care.* **27**: 1047-1053

Citation: Mukul MEH, Sharil MI, Rabiya MAK, Munia MFY, and Abedin MZ. (2021). A comparative study on physical parameters of different brands of Metformin available in Bangladesh. *KYAU Journal*. 4(1),33-40