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Comparative Evaluation of *In Vitro* Physicochemical Parameters of Some Commercially Available Metformin HCl 500mg Tablets in Bangladesh

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Abstract:- Metformin, a biguanide derivatives, is the first-line drug for the treatment of type-2 diabetes mellitus, particularly in overweight and obese people. Numerous brands of Metformin HCl tablets (500mg) are available in the Bangladeshi market. The objective of this study was to evaluate the physicochemical parameters of seven brands of Metformin HCl tablets available in the market. The tested brands of Metformin HCl tablets were assessed through the evaluation of official standards such as weight variation, hardness, friability, disintegration time, dissolution rate and potency to quantify the quality parameters. All the brands complied with the official specifications for weight variation, hardness and friability tests. Maximum (12 min) and minimum (6 min 23 sec) disintegration time were found for brand M_6 and M_5, respectively. After sixty minutes, an average 92.42%, 86.55%, 85.70%, 94.65%, 89.77%, 95.50% and 87.85% of drug release were found for the samples M_1, M_2, M_3, M_4, M_5, M_6 and M_7, respectively. Potency of the samples M_1, M_2, M_3, M_4, M_5, M_6 and M_7 were 96.55%, 97.82%, 100.54%, 98.21 %, 96.75%, 99.10% and 96.95 %, respectively. All the brands of Metformin HCl successfully met the standard quality parameters.

Keywords:- *Metformin Hcl, Hardness, Friability, Disintegration, Dissolution, Potency.*

I. INTRODUCTION

Diabetes is one of the most common non-communicable diseases globally and currently, this disease is a major public health issue in both developed and developing countries like Bangladesh. It results from defects in insulin secretion, insulin sensitivity or both [1].The higher incidence of diabetes is associated with an increased prevalence of obesity, population ageing, population growth, urbanization and physical inactivity [2]. At present, diabetes related complications such as cardiovascular diseases, kidney damage, eye damage, and nerve damage become life threatening to the people [3].

Though there are several routes of administration but oral route is more convenient for the patients [4]. Metformin HCl belongs to the biguanide class of oral hypoglycemic agents and is widely used for the management of type-2 diabetes mellitus (DM) [5]. It is usually called an anti-hyperglycemic rather than a hypoglycemic drug [6]. Metformin HCl decreases intestinal absorption of glucose, suppresses glucose production, especially hepatic gluconeogenesis and improves peripheral tissue insulin sensitivity by increasing peripheral glucose uptake and utilization [7]. The use of oral anti-diabetic drugs for treatment of type-2 diabetes mellitus increases rapidly. It is widely used with the discovery and approval of several new types of oral anti-diabetic drugs with different mechanism of pharmacological action [8]. This study was performed to compare the physicochemical parameters such as weight variation, hardness, friability, disintegration time, dissolution profile and potency of seven brands of Metformin HCl commercially available in Bangladesh. All the parameters were tested with standard protocol and the values obtained by each test were within the standard limit.

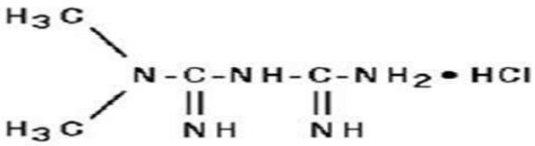

Fig. 1: Chemical structure of Metformin HCl

II. MATERIALS AND METHODS

❖ *Study Design*

Comparative *in vitro* physicochemical parameters among the commercially available seven brands of Metformin HCl were studied through the evaluation of weight variation, hardness, friability, disintegration time, dissolution profile and potency assay. The study was done by performing various test procedures associated to assess the standard of tablets.

❖ *Sample Collection*

To perform this research study selected brands of Metformin HCl 500 mg tablets were purchased from different retail pharmacy located in Rajshahi, Bangladesh and coded as M_1, M_2, M_3, M_4, M_5, M_6 and M_7. The physical appearance, manufacturer name, batch number, manufacturing and expiry date, manufacturing license and DAR (Drug Administration Registration) number of all

samples were properly checked at the time of purchase. All tests were performed within product expiration dates.

❖ *Procedure for Evaluation*

➢ *Weight Variation Test*

Weight variation test was performed to determine the uniformity of drug content of each batch of a formulation. To evaluate weight variation, 10 tablets of each brand were randomly selected and weighed individually using an analytical electronic balance (Shimadzu, Japan). The average weights were determined using the subsequent formula:

$X= (X_1+X_2+X_3+\ldots\ldots+X_n)/10$

Then the percentage of weight deviations was determined by using following formulas:
Positive % of deviation (+) = (maximum weight- average weight)/average weight ×100.
Negative % of deviation (-) = (minimum weight- average weight)/average weight ×100 [9].

➢ *Hardness Test*

Hardness, one of the important parameters of a tablet, indicates the amount of force required to break a tablet [10]. If the tablet is too hard, it takes more time for disintegration or not meets the dissolution specification. On the other hand if the tablet is too soft, it will not withstand the pressure during handling and subsequent processing such as coating or packaging and shipping operations [11].

In order to perform this test, 10 tablets of each brand were taken randomly and hardness was measured using automatic hardness tester (Veego, India).The force applied to the edge of the tablets was gradually increased until the tablet was broken. The pressure at which tablet was broken was then recorded [9].

➢ *Friability Test*

For this test, 10 Metformin HCl tablets were taken randomly and the total weight was measured (W_i). Then the tablets were placed into the Roche friabilator and revolved at a speed of 25 rotations per minute (rpm) for 4 minutes. During each revolution the tablets drop from a distance of six inches to undergo shock. After 100 revolutions, the tablets were re-weighed (W_f) and the loss of weight indicates the friability of tablets. The loss should be less than 1% according to United States Pharmacopoeia (USP).
Finally the percent of weight loss was calculated by following formula [12]:

Loss of % of weight = $[(W_i - W_f)/ W_i] \times 100$

➢ *Disintegration Test*

Disintegration test was done using tablet disintegration tester. One Metformin HCl tablet was placed in each tube of basket rack of the disintegration test apparatus. A plastic disk was placed over each tablet and then the basket rack was accurately positioned into the beaker containing 1-L of water, at 37± 2 ºC. The frequency of the movement of basket was 30 cycle per minute. The time at which all the Metformin HCl tablets passed through the sieve was the disintegration time and the average disintegration time were calculated [13].

➢ *Dissolution Test*

In vitro dissolution study of Metformin HCl tablets were performed by USP Type- II (paddle) apparatus. Three tablets of each brand were placed in the test flask and the paddle was rotated at 150 rpm for sixty minutes under the standardized condition in 900 ml phosphate buffer (p^H 6.8) medium; at 37±0.5ºC. During dissolution test, 10 ml of dissolved sample was withdrawn at 0, 5, 15, 30, 45 and 60 minutes and replaced with an equal volume of phosphate buffer solution to maintain an ideal sink condition. The withdrawn samples were filtered and diluted by addition phosphate buffer. The values of absorbance of the diluted samples were determined using UV-VIS spectrophotometer at λ_{max} 233 nm [12].

➢ *Potency Test*

Larger-dose of drugs especially in tablet form, the official potency range that is acceptable is 100±5% of the labeled amount [14]. To perform this test, 10 Metformin HCl tablets were selected randomly and crushed them in the mortar to produce fine powder. The equivalent amount of fine powder containing about 10mg Metformin HCl was taken in the beaker and dissolved in 100 ml of phosphate buffer (pH 6.8) medium and then filtered through filter paper. 10ml of the filtrate was taken in another 100ml volumetric flask and diluted up to 100ml by using the same medium. Samples were assayed by using UV-VIS spectrophotometer at λ_{max} 233 nm. Potency was calculated by using following formula:

Percentage of potency (%) = {Conc. (mg/ml) x dilution factor x total volume (ml) x average weight x 100} / {sample taken (mg) x strength (mg)}

III. RESULT AND DISCUSSION

➢ *Weight Variation Test*

Seven brands of Metformin HCl tablets undergo this test to assure their uniformity of weight and tablet to tablet variability in weight. Since the average weight of all the tablets were more than 500mg so all the tested samples were found within ±5% deviation, according to the USP specification. We found maximum positive % deviation (+) 3.23 and maximum negative % deviation (-) 4.96 for brand M_1.

Table 1: Average weight variation of tested tablets

Samples	Average weight (gm)	Positive % deviation	Negative % deviation
M_1	539.77	3.23	-4.96
M_2	682.12	1.32	-1.01
M_3	570.56	2.69	-1.69
M_4	628.65	1.67	-2.36
M_5	594.53	1.46	-1.82
M_6	573.36	1.07	-1.06
M_7	568.43	1.88	-1.81

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➢ *Hardness Test:*

Hardness is one of the most important physical features for assessing tablet quality that indicates the physical strength of the tablets. In this study, it was found that all tested brands of Metformin HCl passed the test of tablet crushing strength or hardness. All these brands fall within the acceptable range of hardness between 4-10 kg/cm^2.

Table 2: Hardness variation profile of tested Metformin HCl tablets

Samples	Average hardness (kg/cm^2)
M_1	8.81
M_2	5.75
M_3	7.80
M_4	8.39
M_5	6.32
M_6	9.01
M_7	7.14

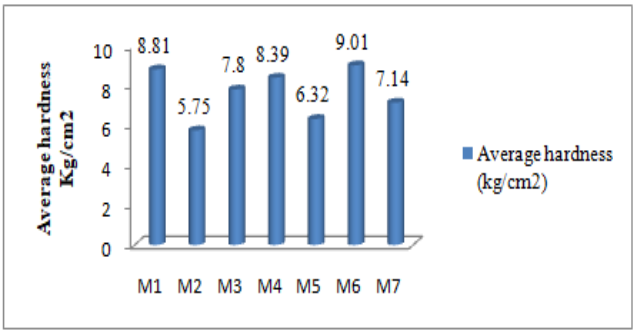

Fig. 2: Hardness of tested brands of Metformin HCl tablets

Friability Test

Friability test was performed to evaluate the ability of Metformin HCl tablets to withstand various shocks and fiction during packaging, handling and transporting. Standard friability value reveals good mechanical strength of tablets. According to the USP specification, friability of tablets should not more than 1%. Under this study finding all of the brands had shown impressive values of friability with brand M_5 and M_7 having maximum (0.330%) and minimum (0.011%) values of % friability, respectively.

Table 3: Friability profile of tested Metformin HCl tablets

Samples	Friability
M_1	0.043%
M_2	0.058%
M_3	0.044%
M_4	0.054%
M_5	0.330%
M_6	0.067%
M_7	0.011%

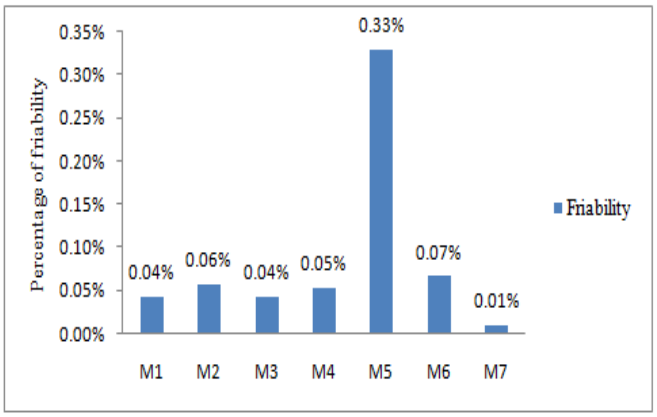

Fig. 3: Percentage (%) of friability of tested brands of Metformin HCl tablets

➢ *Disintegration Test*

The disintegration test is performed to find out the time required for a solid oral dosage form (tablet/capsule) to completely disintegrate in the gastro-intestinal tract. The time of disintegration is a measure of the quality of tablet as it affects the drug release rate. The disintegration time of all tested brands of Metformin HCl was satisfactory as uncoated tablets have disintegration time not more than 30 minutes according to USP specification. Maximum disintegration time was found for brand M_6 (12 min) and minimum disintegration time was found for brand M_5 (6 min 23 sec), respectively.

Table 4: Disintegration time of tested Metformin HCl tablets

Samples	Disintegration time
M_1	8 min 30 sec
M_2	9 min 5 sec
M_3	7 min
M_4	11 min
M_5	6 min 23 sec
M_6	12 min
M_7	7 min

➢ *Dissolution Test:*

Dissolution is one of the most important quality control parameters which is directly related to the absorption rate and bioavailability of a drug. The data revealed that at different time intervals drug release rate from the tablets was adequate. All the tablets have given satisfactory percentage of drug release within 60 minutes. Within the specified time, not less than 80% of labeled amount of drug released form Metformin HCl tablets during this assay that meets the USP specification. So, all the tablets comply with the specifications.

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Table 5: Dissolution profile of tested Metformin HCl tablets

Samples	% Drug Content Release (5min)	% Drug Content Release (15 min)	% Drug Content Release (30 min)	% Drug Content Release (45 min)	% Drug Content Release (60 min)
M1	48.32	70.50	85.45	88.79	92.42
M2	15.58	45.35	69.45	78.67	86.55
M3	30.49	50.32	72.64	83.22	85.70
M4	50.43	67.52	83.56	88.31	94.65
M5	18.55	40.72	70.81	87.90	89.77
M6	45.21	75.80	80.23	82.00	95.50
M7	17.54	50.54	70.87	85.54	87.85

➢ *Potency Test*

Potency is a measure of drug activity expressed as the amount of drug required to produce desired therapeutic effect. In our study, all brands of Metformin HCl tablets were within the limit of potency according to the USP specification i.e. they contained not less than 95% and not more than 105% of the labeled amount of drugs. Maximum potency (100.54%) and minimum potency (96.55%) potency were found in brand M_3 and M_1, respectively.

Table 6: Potency of tested Metformin HCl tablets

Samples	Potency (%)
M_1	96.55
M_2	97.82
M_3	100.54
M_4	98.21
M_5	96.75
M_6	99.10
M_7	96.95

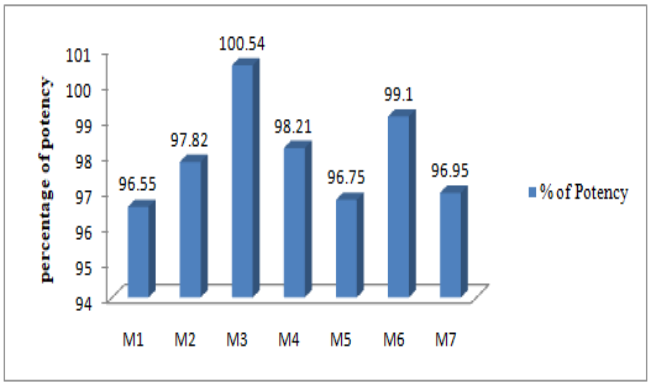

Fig. 4: Percentage (%) of potency of tested brands of Metformin HCl tablets

IV. CONCLUSION

The *in vitro* physicochemical evaluation of tested brands of Metformin HCl 500mg tablets in Bangladesh passed the quality parameters according to USP specifications. Therapeutic response of any formulation significantly depends on its quality control parameters which influence the amount of drugs reaching at the site of action. A quality product meets all the standard quality parameters for giving its desire therapeutic effect. Our study confirmed that all tested brands of Metformin HCl complied with the official specification for weight variation, hardness, friability and disintegration time. *In vitro* dissolution time and potency test results also meet the USP specification despite acceptable variation. It reflects that all brands of Metformin HCl 500mg tablets definitely show proper drug release which ultimately leads to optimum drug absorption and therapeutic effect.

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