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COMPARATIVE STUDY OF VARIOUS BRANDS OF METFORMIN HCL 500MG WITH INNOVATOR BRAND AVAILABLE IN PAKISTAN

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ABSTRACT

The aim of our research study was to determine and compare the Quality Control of all brands of metformin HCl with the innovator brand available in the market of Pakistan at the city of Quetta Balochistan. Metformin HCl is mostly used in the treatment of type 2 diabetes in the result of debilitated insulin discharge. Metformin, is an oral biguanide, enhances hyperglycemia to improve peripheral sensitivity toward insulin and reduces gastrointestinal glucose breakdown and hepatic glucose formation. Five different brands were selected Glucophage, Neophage, Metphage, Neodipar, and Meteor. The Physiochemical properties of all brands were checked accordingly which includes Weight variation, Hardness, Thickness, Friability, Disintegration, Dissolution and Assay and compared with each other. The results of all these physiochemical properties showed that all the brands were within the acceptable range which followed the specifications of BP and USP. It is recommended that this type of research will be conducted in different formulations to check their physiochemical activities for the Quality of Product.

Keywords: Metformin HCl, Glucophage, Neophage, Metphage, Neodipar, and Meteor

INTRODUCTION

Metformin belongs to the group of drugs called biguanides which is first line medication to treat type 2 diabetes mellitus, which results from reduced secretion of insulin and less sensitivity of peripheral cells towards insulin. Type 2 diabetes can

be controlled by diet, antihyperglycemic agents and insulin. Metformin is an oral anti hyperglycemic agent which improves sensitivity of peripheral receptors towards insulin, reduce absorption of glucose in intestine and formation of glucose in liver. It does not modify the secretion of insulin like sulfonylurea so there will be no hyperinsulinemia, hypoglycemia and weight changes. Metformin also has very adventitious effects on serum lipid profile. In obese and lean diabetic patients whose glucose level is not controlled by diet alone metformin gives have excellent glycemic control compared with placebo.In secondary sulfonylurea failure combination therapy of metformin and other agents significantly improve glycemic control (Davidson., 1997). Biguanides (principally Metformin) are broadly used antihyperglycemic that stifle formation of glucose in liver, augments peripheral glucose uptake, and respectably diminish triglyceride and LDL cholesterol levels. Glucose control with the help of biguanides reduce diabetes linked complexities which is not related to weight gain. Current medicine is reportedly connected with less hypoglycemic episodes than other class of drugs (Sofer et al., 2014). A French researcher Dr. Jean Sterne and his coworker discovered metformin as an antidiabetic drug in 1950 at Paris. Metformin first synthesis (dimethyl biguanide) was credited to Werner and Bell from Trinity College, Dublin, Ireland, in 1922, and was a reason for further exploratory and clinical investigations on the potential remedial use of biguanides. Other two drug of biguanide (phenformin and buformin was stopped soon for use as an antidiabetic due to severe lactic acidosis. It took five decades to convert metformin from minor product to highly effective and safe antidiabetic for type two diabetes mellitus (Andreja, 2010). Metformin is a, hygroscopic crystalline powder with white shading having an unpleasant taste. Synthetically 1, 1 dimethyl-biguanide an instrument the activity of hydrochloride uses parallel in a different biguanides. This little atom remains solvent with the water the percentage in liquor is 95%. On the other hand, it is intents and purposes insoluble in chloroform or ether (Patrick et al., 2013). The method of activity of Metformin is different from other antihyperglycemic agent's metformin brings down glucose level in blood by reducing the formation of glucose in liver and by decreasing the absorption of glucose in the gut. These effects are mediated by first activation by metformin of AMP-activated protein kinase (AMPK). An enzyme of liver that plays an important role in insulin signaling all over body energy stability and fats and glucose metabolism (Alvarez, 2009). The administration of

metformin increases the concentration of AMPK in skeletal muscle. AMPK is known to cause GLUT4 distribution to the membrane of plasma in result uptake of glucose in insulin independent. The infrequent adverse effects cause reduced liver uptake of serum lactate, one of the substrates of the gluconeogenesis in those with strong renal role the slight excess is simply cleared. Other situations that may precipitate lactic acidosis contain severe hepatic disease and acute/decompensate heart failure (Musi, et al., 2002). GMPs are the set of guidelines written by authorities, agencies these guidelines are prerequisite for manufacture of a pharmaceutical's product. A pharmaceutical product must be manufactured in accordance with given guidelines so as desired standard quality of a product or therapeutic device can be attained (Allen et al., 2013). Quality Assurance is wide idea from which all parameters are incorporates that essentially starts overseeing every crude fixing the items and furthermore the officers concern with the creation, and generation, its administration and examination methodology (Wingate et al, 2016).

Quality control is a process employed to ensure the level of quality in product or service. The main purpose of the quality control to ensure that the products, process services meet the standard requirement and depend satisfactory and fiscally sound (Riley, 2010).

MATERIALS AND METHODS:

Chemicals and equipment used

The following materials were used in this research study which were gifted different manufacturer, also following equipment's were used in this research study.

Table 1: Chemicals

Brand name	Manufacturer	Batch no	Manufacturing date	Expiry date	Price
Glucophage	Merck Serono),	Q6479	Dec-17	Nov-20	77.15
(Neophage,	(Abbot labor tries),	75041XV	Mar-17	Mar-20	85.35
Metphage	(Efroze chemical industries),	N19	Jun-18	Jun-20	80.36
Neodipar	(Sanofi Aventis)	WU021	Apr-18	Mar-21	80.36
Meteor	Asian agencies),	LO126	Feb-18	Feb-20	75.00

Hardness tester (Pharma test), Vernier caliper (Absolute Digimatic Caliper), friability Tester (FR 2000), Disintegration tester (Pharma test), Dissolution Tester (ERWEKA), UV-visible spectrophotometer (Shimadzu).

Methodology:

Following steps of physiochemical procedure were done to determine the comparative studies of different brands of metformin HCl available in the market of Quetta.

Physiochemical Assessment

Weight of the tablets: Twenty (20) individual tablets were weighed through the Electronic balance of Mettler Toledo as per standard and the results were tabulated. All

results showed within the range of ±5% that meets the specification of USP.

Hardness: Hardness of all the brands were checked with the help of pharma test byplacing each tablet in the hardness tester of all brands as per the prescribed procedure which were within the standards specified in the USP that is ±5% which meets the specification of USP.

Thickness: Thickness of all brands were checked with the help of Vernier caliper of absolute Digimatic caliper by as limit all these tablets were within the standard specified in USP.

Friability: Friability of the twenty (20) tablets done through the friability test of FR2000 as per standard. The findings of Friability were within the limits mentioned in specifications of USP, i.e. tablets must not loss 0.5% to 1% of their initial weight.

Disintegration: Disintegration of the (06) tablets were checked by pharma test as per process It was found that all the tablets were within the specifications according to the USP.

Dissolution: Dissolution of the (06) tablets were determined through the ERWEKA as per method according to the USP the tolerance is not more than 70% of the labelled amount of the metformin hydrochloride is dissolved in 45 minutes.

Assay: Assay of the all brands was checked through the UV-Spectrophotometer Shimadzu and results were obtained according to the BP which determines the specification % potency for the metformin must be within 90-110%.

RESULTS AND DISCUSSION

Weight of the tablets results (Weight of each tablet in mg)

Weights of tablet are shown in Table 2 and Figure 1 below.

Weight variation

Weight of all brands of tablets were checked and tabulated. The result was found in limit according to the standard. When compared only minute differences were found in the average weight of the tablets from each other. All results showed within the range of ±5% that meets the specification of USP **(Table 2 and Figure 1)**.

Hardness of all brands (in KP)

Hardness result of all brands (in KP) can be seen in **Table 3 and Figure 2** below.

Hardness of all formulations were checked accordingly, compared with each other and tabulated. It was found that there was slight difference between these tablets which were within the standards specified in the USP that is ±5% which meets the specification of USP **(Table 3 and Figure 2)**.

Thickness of all brands (in mm)

Thickness of the all tablets were checked and compared with each other which were found that all these tablets were within the

standard specified in USP **(Table 4 and Figure 3)**.

Friability of Twenty coated Tablets (Not more than 1.0%)

The results were compiled as all these brand were checked their Friability and compared with each other. The findings of Friability were within the limits mentioned in specifications of USP, i.e. tablets must not loss 0.5% to 1% of their initial weight **(Table 5 and Figure 4)**.

Disintegration

Disintegration of the all different brands were checked accordingly, compared and tabulated. It was found that all the tablets were within the specifications according to the USP i.e. below than 10 minutes it means pharmaceutical companies are following the standards of USP **(Table 6 and Figure 5)**.

Discussion of Dissolution

Dissolution was performed according to the specified standards all results were found in the limits. As according to the USP the tolerance is not more than 70% of the labeled amount of the metformin hydrochloride is dissolved in 45 minutes **(Table 7 and Figure 6)**.

Discussion of the Assay

According to the BP specification % potency for the metformin must be within 90-110% all have passed the potency specification. Assay test of all brands were performed found all results within the limits **(Table 8 and Figure 7)**.

Table 2: Weight of the tablets results (Weight of each tablet in mg)

No of tablets	Glucophage	Neophage	Metphage	Neodipar	Meteor
1	541	530	577	558	530
2	533	532	596	558	539
3	531	534	587	556	534
4	522	539	576	557	529
5	530	533	593	536	539
6	527	536	593	528	531
7	522	535	584	538	530
8	527	539	592	544	544
9	524	528	590	529	531
10	522	528	590	547	534
11	527	533	585	550	529
12	522	536	581	529	541
13	521	534	589	542	539
14	530	532	570	539	528
15	523	532	577	530	524
16	521	531	562	556	530
17	535	532	581	541	524
18	521	530	590	542	543
19	510	538	579	536	538
20	511	539	577	536	539
Average weight	525mg	533mg	583mg	542mg	533mg
Maximum	541mg	539mg	596mg	558mg	544mg
Minimum	510mg	528mg	562mg	528mg	524mg

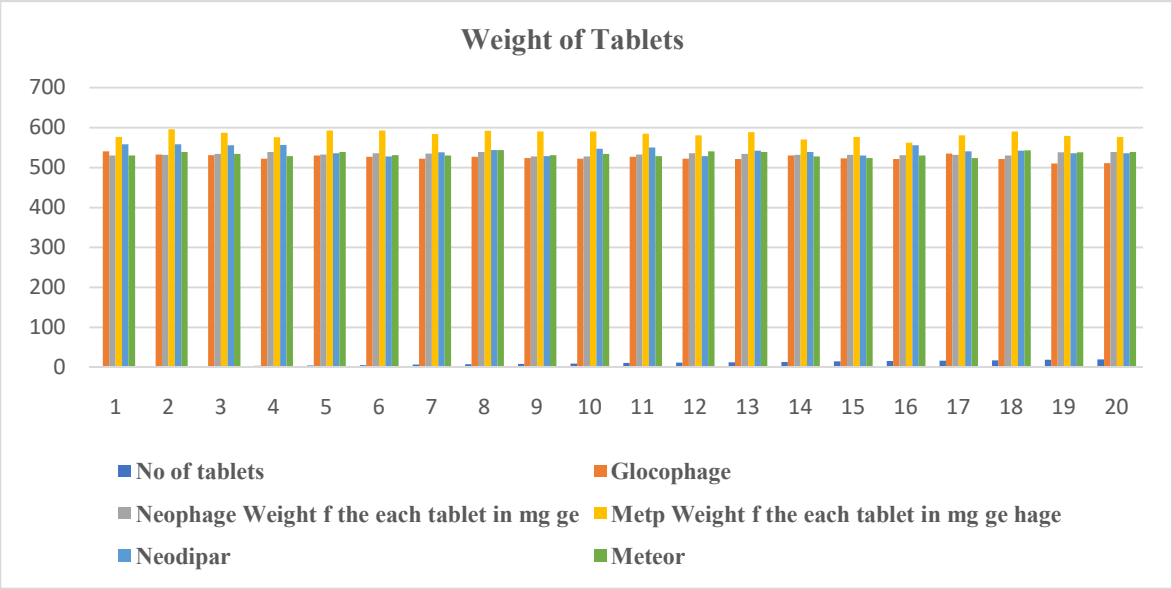

Figure 1: Weight of Tablets

Table 3: Hardness of all brands (in KP)

S.no	Glucophage	Neophage	Metphage	Neodipar	Meteor
1	20.9	30.2	15.3	13.5	30.5
2	20	23.8	11.3	11.9	31.2
3	20.2	29.5	10.8	13	31.2
4	22.3	28.5	13.6	16.3	31.2
5	18	28.5	14.5	15	30.8
6	18.2	27.3	12.4	11	31.1
7	22.4	24.6	15.7	11.6	30
8	18	25.5	12.3	12.6	29.6
9	15	29.7	11.1	13.4	31.2
10	19.1	25.6	11.9	14.4	25.9

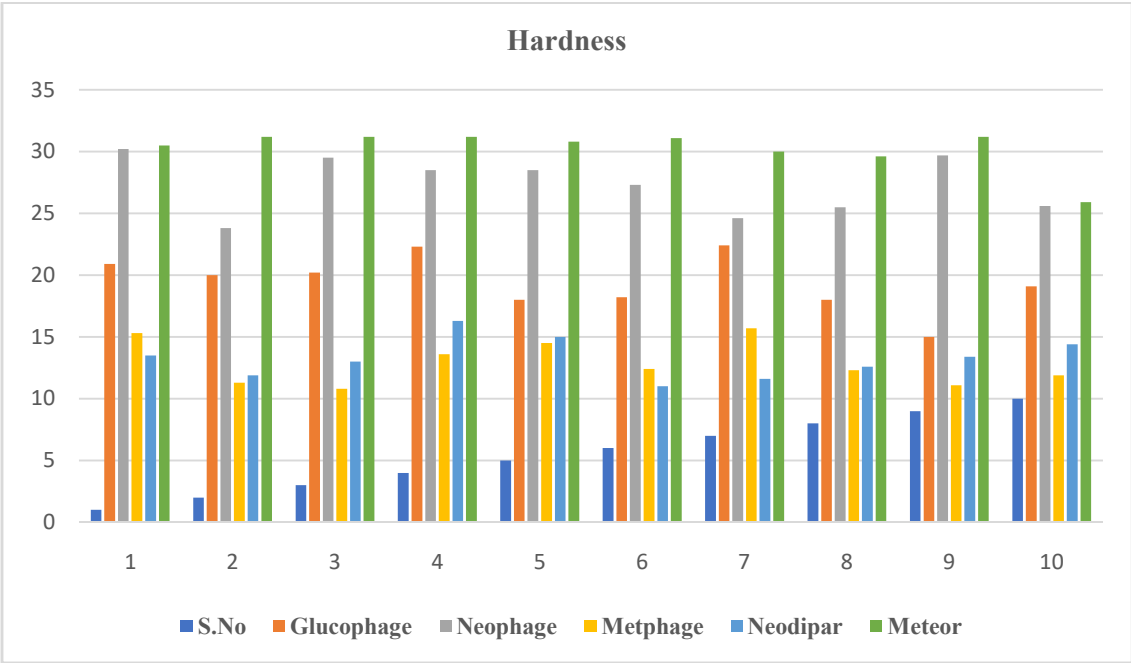

Figure 2: Hardness result of all brands (in KP)

Table 4: Thickness results of all brands (in mm)

S.no	Glucophage	Neophage	Metphage	Neodipar	Meteor
1	5.73	5.75	5.15	5.78	5.78
2	5.73	5.76	5.41	5.82	5.82
3	5.56	5.77	5.21	5.80	5.80
4	5.65	5.66	5.18	5.68	5.68
5	5.64	5.73	4.98	5.81	5.81
6	5.74	5.70	5.43	5.80	5.80
7	5.70	5.76	5.40	5.68	5.68
8	5.66	5.71	5.38	5.75	5.75
9	5.68	5.69	5.51	5.82	5.82
10	5.64	5.71	5.27	5.73	5.73

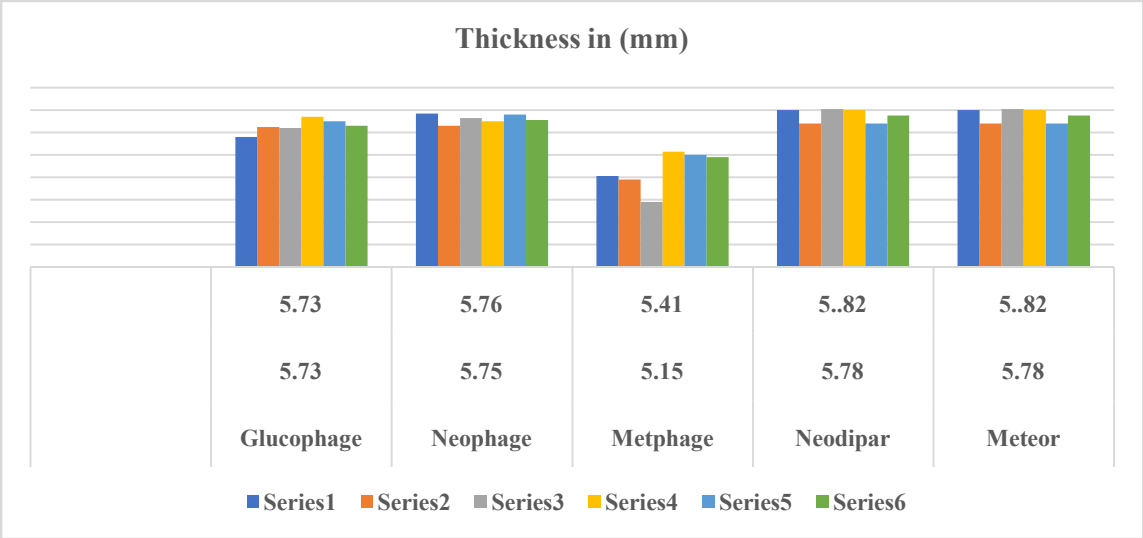

Figure 3: Thickness results of all brands (in mm)

Table 5: Friability of Twenty coated Tablets (Not more than 1.0%)

Weight	Glucophage	Neophage	Metphage	Neodipar	Meteor
Weight before friability	10.427	10.666	10.663	10.751	10.605
Weight after friability	10.416	10.654	10.660	10.748	10.596
Variance	0.011	0.012	0.003	0.003	0.009
%age	0.10	0.11	0.02	0.03	0.08

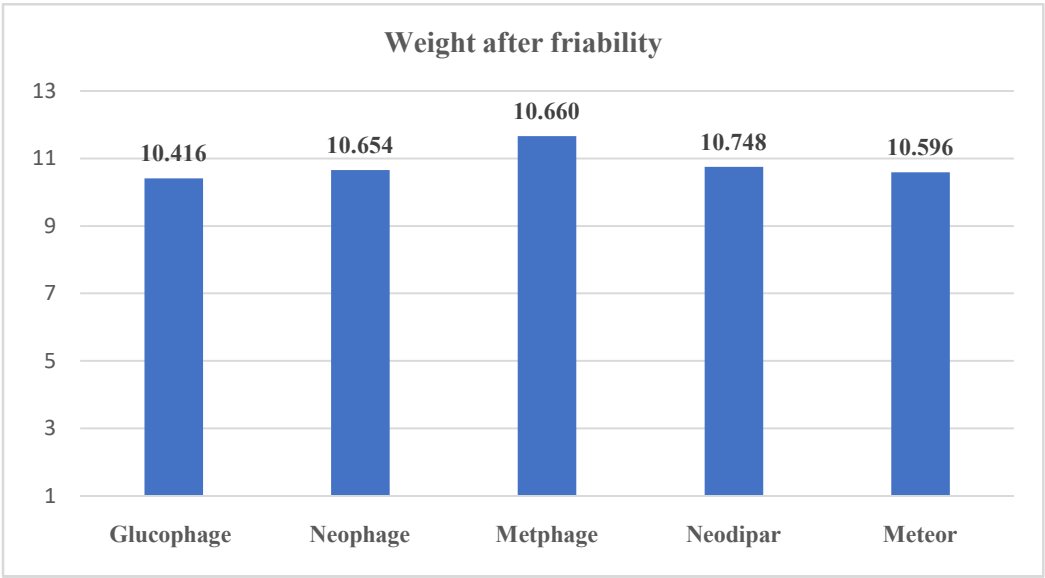

Figure 4: Friability of Twenty coated Tablets (Not more than 1.0%)

Table 6: Disintegration of (06) coated tablets

Product	Time/Minutes
Glucophage	6.00
Neophage	7.00
Metphage	10.00
Neodipar	9.00
Meteor	5.30

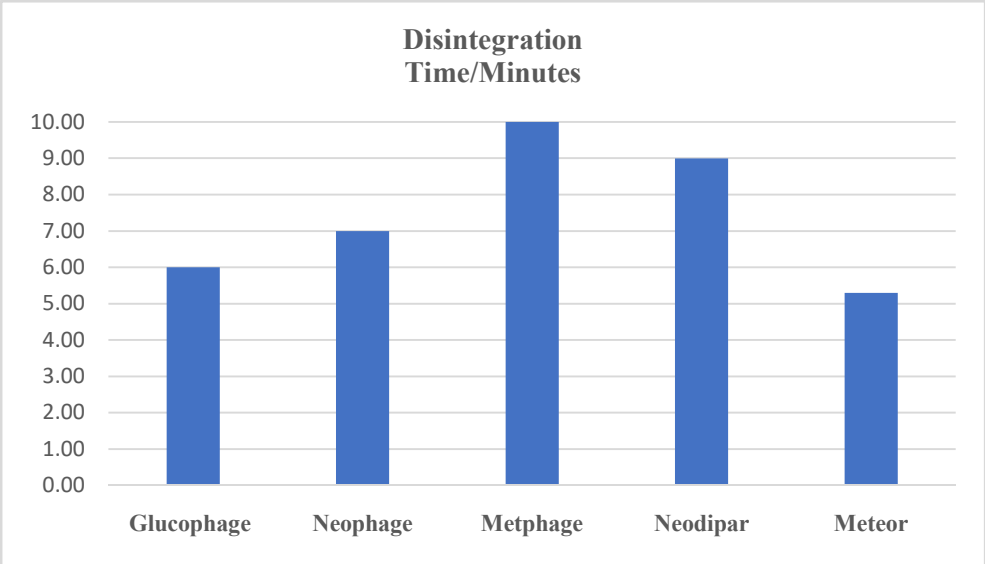

Figure 5: Disintegration of (06) coated tablets

Table 7: Dissolution of (06) tablets

S. no	Brands name	Dissolution %age
01	Glucophage	101.65
02	Neophage	102.00
03	Metphage	101.19
04	Neodipar	102.58
05	Meteor	101.19

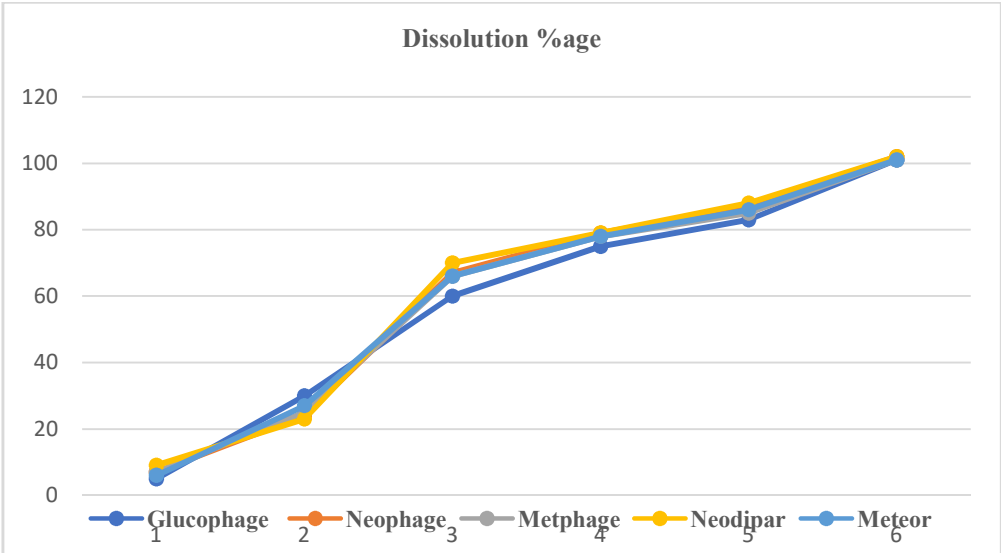

Figure 6: Dissolution of (06) tablets

Table 8: Assay of the tablets

Brands	Assay
Glucophage	99.000
Neophage	100.541
Metphage	99.237
Neodipar	100.602
Meteor	98.988

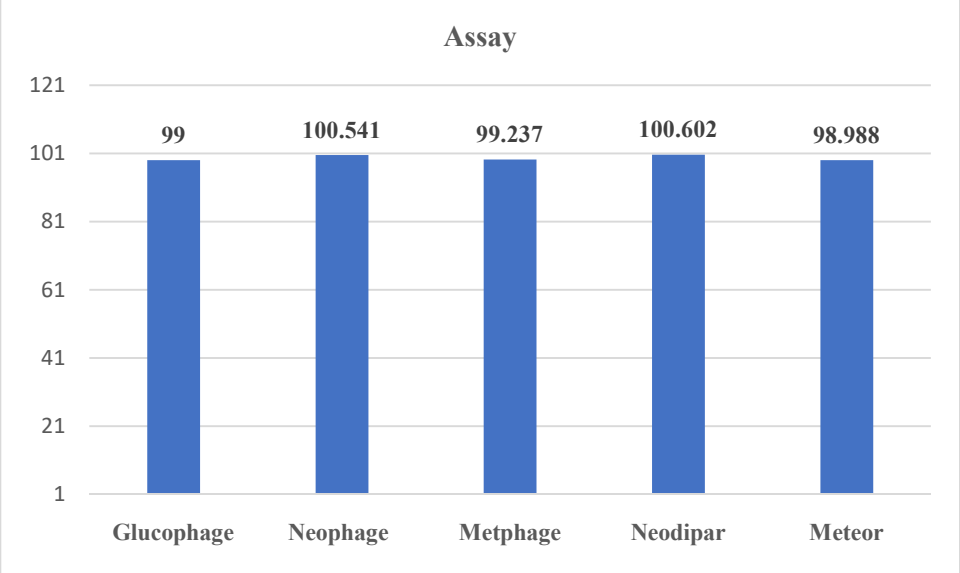

Figure 7: Assay of the tablets

CONCLUSION

The result of this research work concluded as all the physiochemical properties of different innovators of Metformin HCl collected from the Market of Quetta city Pakistan were analyze and it showed that these tablets were within accepted limits. This showed that all five innovators were followed USP standards. It is recommended that this type of research will be conducted in different formulations to check their physiochemical activities.

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