Pharmaceutical Evaluation of the Quality Control Parameters of Marketed and Formulated Metformin HCl 500mg Tablet

A Project Report Submitted to the Department of Pharmacy, University of Asia Pacific in Partial Fulfillment of the Requirements for the Degree of Bachelor of Pharmacy (Honors)

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Registration No.: 20103046
Submission Semester: Fall 2023
Submission Date: 16 May 2024

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Abstract

Objective: Metformin hydrochloride, an oral antidiabetic medication belonging to the biguanide category, is primarily employed in managing type 2 diabetes mellitus, also known as non-insulin dependent diabetes. The focal point of this composition is to analyze and evaluate the flowability characteristics of granules formulated for tablet production, subsequently employing these granules in the preparation of metformin HCl tablets and finally the establishment of a comparative analysis between a laboratory-manufactured formulated tablet and commercially available products. **Materials and Methods:** A 10 mg quantity of metformin HCl was used to create a diluted solution with phosphate buffer for establishing a standard curve via UV-spectrophotometry. Granules were prepared meticulously using the wet granulation method, and their bulk density, tapped density, angle of repose, and compressibility index were measured according to US Pharmacopeia standards. These granules were then incorporated into the formulation of metformin hydrochloride tablets through a direct compression process, ensuring precision. Both the commercially available Metformin HCl tablet and the laboratory-manufactured formulated tablet underwent comprehensive assessments for various parameters using specific methodologies and laboratory equipment. **Results and Discussion:** Every sample assessed during the study fulfilled the criteria outlined for the specified quality indicators**.** The standard curve showed a high coefficient of determination (R^2) of 0.9994, indicating strong reliability. Granules exhibited a bulk density of 0.496 gm/ml and a tapped density of 0.714 gm/ml, with an angle of repose of 33.34°, signifying good flowability. However, the compressibility index was 30.53%, suggesting less than ideal flow characteristics. Ten metformin HCl tablets were prepared, each weighing around 203 mg. As per USP standards, all tablets met weight variation requirements, with diameters and thicknesses within specified limits. Marketed tablets had an average hardness of 17.587 kp, while the formulated tablet had 5.81 kp. Marketed tablets showed 0.05% friability and disintegration within 12 minutes 40 seconds. Both formulations released over 80% of the drug within 30 minutes, meeting USP dissolution criteria. Marketed tablets demonstrated 98.08% potency, while formulated tablets exhibited 80.30%. **Conclusion:** The examination of quality parameters in tablet manufacturing followed the guidelines set forth by the USP. The comparative analysis between marketed and formulated tablets adhered fully to USP specifications, suggesting potential enhancements for the formulated tablets and highlighting the necessity for further research on additional brands of marketed tablets to validate the project comprehensively.

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Chapter-1:

Introduction

1. Introduction

Diabetes is one of the leading causes of death and disability worldwide. The World Health Organization or WHO, estimates that 172 million people worldwide had diabetes in 2000. By 2030, it is projected to rise to a minimum of 366 million individuals. Health practitioners are primarily concerned with both illness prevention and treatment (Diabetes UK, 2024). Patients can utilize alternatives, but many think that taking their prescriptions orally can be more convenient (Sandhya, 2013).

There are three forms of diabetes: type-1, type-2, and gestational diabetes.

Diabetes Type 1: The disease's hallmark is a marked absence of insulin as a result of beta cells dying off one at a time in this way. It is thought to be an autoimmune illness of some kind.

Diabetes Type 2: A deficiency in insulin production and tissue that is resistant to the effects of insulin are the causes of type-2 diabetes. Ninety to ninety-five percent of people have type 2 diabetes.

Gestational Diabetes: The term "pediatric diabetes" refers to abnormal blood glucose levels during the first trimester of pregnancy. The embryo's membrane and placental hormones throughout pregnancy produce an insulin resistance that leads to gestational diabetes (Center for Disease Control and Prevention, 2023).

In 1994, the FDA approved metformin for the treatment of type 2 diabetes. It is commonly used in conjunction with other blood sugar-lowering drugs. It is available in formulations for both prolonged and immediate release. It can also be used off-label to treat conditions like pregnancy related diabetes, anti-psychotic-induced obesity, and PCOS. The ADA recommends metformin for those with prediabetes. Current research is looking into its possible benefits for antiaging, cancer prevention, and brain protection. Expert cooperation is required for the effective management of diabetes (Corcoran & Jacobs, 2024).

Metformin is still an essential drug for about 150 million people, having been administered for type 2 diabetes in the later half of the 1950s. Research suggests that there may be benefits in the treatment of a number of diseases, including infections, malignancies, neurological disorders, and COVID-19. However, the effects on glucose reduction and insulin sensitivity seem to be the primary therapeutic benefits; other benefits could manifest later. Further research is necessary to completely comprehend its workings and potential applications in treating a range of ailments. Consequences on human development and ecological concerns are

among the rising subjects (Triggle *et al.,* 2022)

1.1 Metformin Overview

Metformin, a member of the biguanide class of antidiabetic drugs, is used in the treatment of non-insulin-dependent diabetes mellitus. Diabetes, as outlined by the World Health Organization (WHO), is a persistent metabolic condition marked by heightened glucose levels in the bloodstream (Diabetes, 2024). Metformin is known for its unpleasant taste and typically appears as a white or nearly white hygroscopic powder. It has a melting point ranging from 223°C to 226°C (Tilley *et al.,* 2010).

1.1.1 History of Metformin

Metformin has emerged as the preferred medication for the treatment of type 2 diabetes due to its lower toxicity compared to other biguanides. Galega officinalis, a traditional herbal remedy, is used to make metformin. After being created in the 1940s during research on antimalarial medications, its efficacy in lowering glucose levels was observed in the late 1950s. Metformin, which was once less well-known than safer and more successful options, gained notoriety for its ability to treat insulin resistance without contributing to obesity or hypoglycemia. Its status as the most often prescribed glucose-lowering medication globally was solidified in 1998 when the UK Prospective Diabetes Study proved its long-term advantages for cardiovascular health (Bailey, 2017).

1.2 Pharmacology of Metformin Hydrochloride

1.2.1 Drug Profile of Metformin Hydrochloride

Metformin is a first-line treatment for type 2 diabetes due to its potent effects on lowering blood glucose levels, affordability, and dependability. Although its exact method of action is still unknown, most experts concur that it primarily prevents the liver gluconeogenic process. A redox dependent route is suggested by the selective inhibition of glucose synthesis at clinically relevant doses, as per recent research. Despite ongoing debate, the efficacy of metformin in lowering blood glucose levels is undeniable (LaMoia & Shulman, 2021).

1.2.2 Structure of Metformin Hydrochloride

The chemical formula for metformin is 1,1 dimethyl-biguanide hydrochloride. It is a white, crystalline powder that is hygroscopic and has an unpleasant taste. The way it works and the applications it serves are similar to other biguanides. It dissolves in water or 95% alcohol but is almost inert in ether and chloroform. The structural representation was

corrected in 2005. As it decomposes, toxic emissions of nitric oxide (NO) are released. After a two-hour elimination half-life, the kidneys remove metformin, which is mostly processed in the liver. Among the analytical methods are gas-liquid chromatography, mass fragmentation, and high-pressure liquid chromatography. Crystallographic studies reveal the π-conjugation and intermolecular hydrogen bonding of metformin and its analogs. The structure of metformin hydrochloride is shown in Figure 1.1 (Metformin Chemistry, 2024).

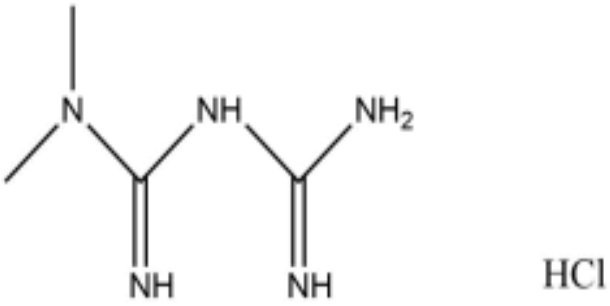

Figure 1.1: Chemical Structure of Metformin Hydrochloride

1.2.3 Synthesis of Metformin Hydrochloride

The medication's salt form, metformin hydrochloride, has a significant nitrogen:carbon ratio. Dimethylamine and cyanoguanidine can be combined to make it via the nucleophilic attack approach. This mechanism forms the distinctive N-C bonding seen in metformin. This synthesis technique uses many patented procedures that include the reaction of dimethylamine hydrochloride and cyanoguanidine. The challenging element is starting those precursors from basic hydrocarbons. The synthesis of metformin hydrochloride is shown in Figure 1.2 (The Science Snail, 2020).

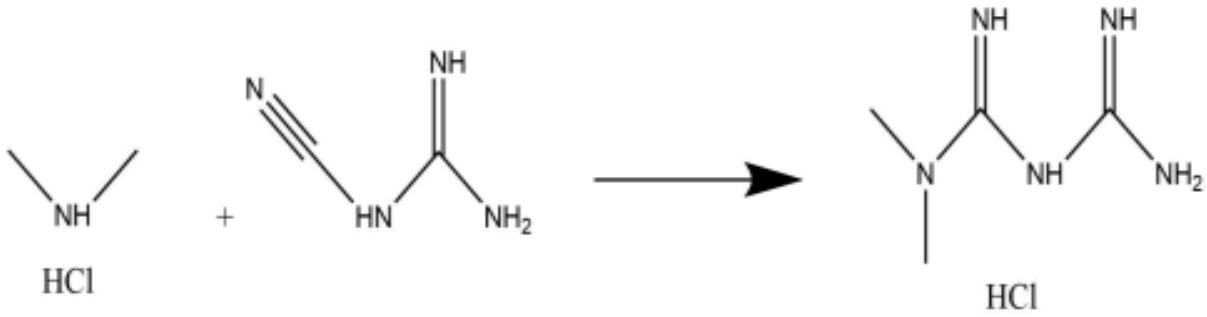

Figure 1.2: Synthesis of Metformin Hydrochloride

1.2.4 Pharmacokinetics

Metformin hydrochloride is an oral medication that lowers the amount of glucose the liver produces while raising insulin sensitivity. Its pharmacokinetics, which mostly involve absorption in the small intestine tract, indicate that maximum plasma concentration is

attained two to three hours after oral administration (Rena *et al.,* 2017). The distribution of metformin, a watery cationic species, is reliant on organic cation exchangers (Gong *et al.*, 2012). Like other biguanides, metformin has a half-life in the plasma of 4.0 to 8.7 hours and is mostly excreted by the kidneys. It is unknown to undergo any metabolic or conjugation processes. Significantly lower clearance rates—which are linked with creatinine clearance rates—are found in individuals with reduced renal function (Scheen, 1996).

1.2.5 Pharmacodynamics

Metformin lowers glucose levels via enhancing oxidation and decreasing fatty acid synthesis while inhibiting hepatic gluconeogenesis. Clinical study supports its efficaciousness in reducing LDL, total, and triglyceride cholesterol levels. In addition, metformin decreases plasma glucagon levels and is primarily eliminated via urine secretion, with an average renal clearance rate of 510 ± 120 ml/min during this process (Sambol *et al.,* 1996).

1.2.6 Physicochemical Properties of Metformin Hydrochloride

Metformin hydrochloride and other anti-diabetic drugs differ from one another based on physicochemical properties. The following Table 1.1 lists the physicochemical properties of metformin hydrochloride (Pharmaceutical Chemistry Journal, 2022).

Table 1.1: Properties of Metformin Hydrochloride

Property Name	**Property Description**
Class	Biguanide
Molecular formula	$C_4H_{12}ClN_5.HCl$
Molecular weight	165.62 g/mol
pH	6.8

Color	White or almost white
Solubility	Freely soluble in water
Form	Powder
Melting Point	223-226°C
λmax	233 nm
Dose	500 mg-2.5 gm
Elimination half-life	6.2 hours

1.2.7 Mechanism of Action

Metformin primarily affects the liver through a variety of processes that prevent glucose from being produced. Through the mouth, it enters the body and is absorbed by hepatocytes via transporters such organic cation transporters 1 (OCT1). Metformin causes the cell's mitochondrial respiratory chain complex 1 to function less efficiently, resulting in a decrease in ATP and an increase in AMP. In addition to other processes that limit glucose production, this results in the activation of Adenosine Monophosphate-Activated Protein Kinase (AMPK), which in turn inhibits gluconeogenic genes and mitochondrial glycerol-3-phosphate dehydrogenase. But because metformin accumulation might increase a patient's risk of lactic acidosis due to conditions like liver cirrhosis, heart disease, sepsis, or renal failure, caution should be used when using this drug in these groups (Pharmwiki, 2022).

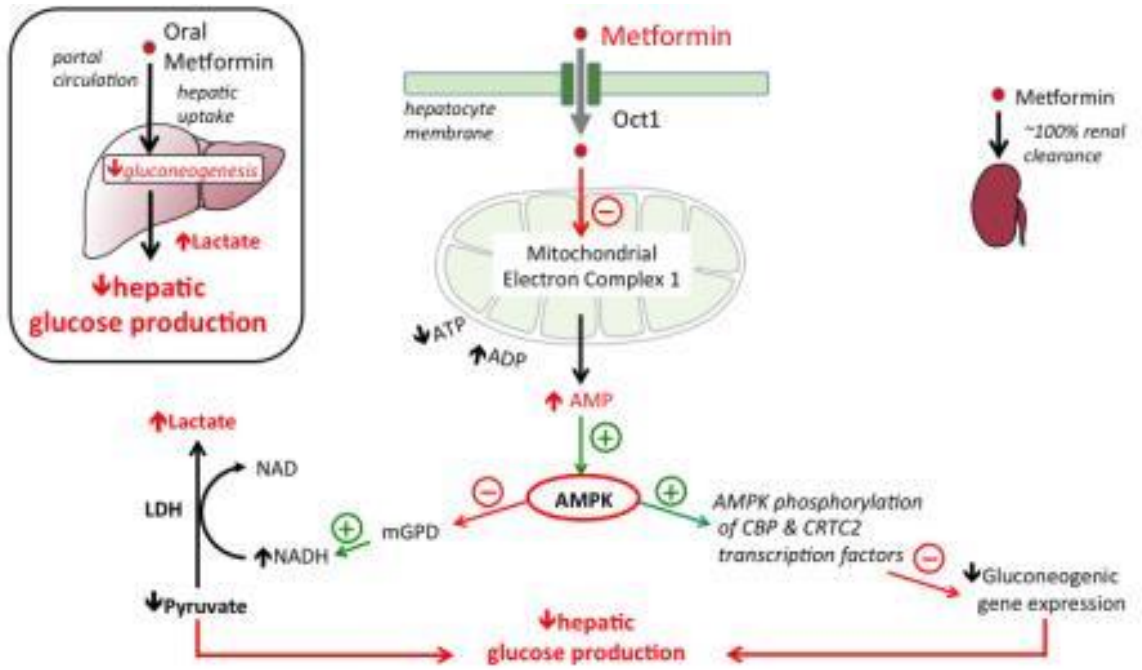

Figure 1.3: The Mechanism of Action of Metformin Hydrochloride

1.2.8 Administration, Metabolism and Elimination Route

Metformin HCl should be taken orally, ideally right after meals. Metformin is mostly excreted from the body by active tubular secretion in the kidney, which primarily leaves the medication unchanged in the urine. Its estimated half-life is five hours. When starting metformin treatment in people 80 years of age and older, renal function tests should be used as a guide to ensure that the patient's creatinine levels are within normal limits (Gong *et al.*, 2012).

1.2.9 Half-life and Clearance

Metformin's half-life for plasma elimination is around 6.2 hours, whereas its half-life for blood elimination is approximately 17.6 hours. This results in a total elimination time of about 96.8 hours. During the first 24 hours after oral administration, the kidneys remove around 90% of the dose of metformin, primarily by tubular secretion, demonstrating the critical role the kidneys play in the drug's clearance (Scheen, 1996).

1.2.10 Side Effects and Adverse Effects

As side effects, metformin HCl tablets usually result in nausea, vomiting, diarrhea, heartburn, and appetite loss. Metformin can also effectively treat obesity and related conditions including metabolic syndrome in non-diabetic individuals. It can also help with weight loss and improve fertility. The rare but potentially fatal adverse effect of metformin is called lactic acidosis,

which presents as extreme exhaustion, dizziness, and trouble breathing. Furthermore, metformin can lower vitamin B12 levels, which can occasionally lead to anemia. Hypoglycemia is generally harmless, although it can occur, particularly in older adults with certain medical conditions or while taking medication that is prescribed under a different name. About 20% of users have gastrointestinal intolerance, which is characterized by constipation, diarrhea, and nausea. Under some conditions, this syndrome may also be associated with reduced absorption of bile acid and osmotic diarrhea (National Health Service, 2022).

1.2.11 Contraindication

Because lactic acidosis is a rare but possibly catastrophic metabolic side effect connected to metformin accumulation, individuals with renal illness, malfunction, or insufficient creatinine clearance should not use metformin hydrochloride tablets. Metformin should be temporarily stopped in patients having radiologic procedures that require an intravenous injection of iodinated contrast elements in order to prevent sudden changes in renal function. It is not advised to take metformin for a number of disorders, including acute trauma, coronary artery disease, major surgical operations, and ongoing illnesses (Tahrani *et al.*, 2007).

1.2.12 Drug-drug Interaction

The list of medications that metformin interacts with is shown below in Table 1.2 (DrugBank Online, 2024).

Table 1.2: Different Types of Drug-drug Interactions with Metformin HCl

Drug name	Drug interactions
Aceclofenac	Reduces rate of excretion of metformin which results an increase in serum level of the drug
Acetazolamide	Increased risk of lactic acidosis
Acebutolol	Increased therapeutic efficacy of metformin
Acetyl Salicylic Acid	Increased risk of hypoglycemia

1.2.13 Food-drug Interaction

When using metformin, refined carbohydrates like white bread and rice should be avoided since they might cause a significant increase in blood glucose levels. Red meat and butter

both include saturated fats, which are bad for you and may make insulin resistance worse. Moderate consumption is also advised while consuming foods rich in salt, such as soda and prepackaged snacks. Green tea consumption should also be avoided since it may interfere with metformin absorption (Xie *et al.*, 2024)

1.2.14 Overdose

In cases where the prescribed dosage of metformin hydrochloride exceeds 50 grams, a particular occurrence may arise. Approximately 32% of instances involving metformin overdose have resulted in the onset of lactic acidosis. Hemodialysis serves as a method to eliminate the buildup of the drug from the body (Wang & Hoyte, 2019).

1.3 Quality Parameters of Pharmaceutical Tablet

1.3.1 Formulation

There is an edge film coating on the metformin hydrochloride 500 mg tablet. The excipients needed for the formulation of the tablet are listed in Table 1.3 (Scheen, 1996).

Table 1.3: Excipients Used in Metformin Hydrochloride Once Daily

Excipients	**Example**
Diluent	Lactose, Spray Dried Lactose, Microcrystalline Cellulose (Avicel 101 and 102), Lactose PVP K30.
Glidant	Cornstarch, Talc, Colloidal Silicon Dioxide (Aerosil)
Lubricant	Insoluble substances include Stearic acid, Mg stearate. Soluble ingredients include Sodium Lauryl Sulphate (SLS), Sodium Benzoate, PEG 400,600,8000 and others.
Super disintegrates	Croscarmellose Sodium (Ac-di-sol), Crospovidone
Anti-adherent	Talc powder
Binders	Methylcellulose, Ethyl Cellulose, Hydroxyl Propyl Methyl Cellulose, Starch

1.3.2 Weight Variation

Weight variation is the divergence from the standard pharmacopoeia's prescribed weight ranges. Every tablet is weighed, and its weight is contrasted with the means to determine the weight variance.

$$\textbf{\%Deviation in Weight Variation} = \frac{\textit{Individual Weight} - \textit{Average Weight}}{\textit{Average Weight}} \; \boldsymbol{X}\; \mathbf{100}\%$$

Table 1.4 below illustrates the maximum weight fluctuation (Wang *et al.,* 2022).

Table 1.4: Limits of Weight Variation

Average weight of tablets (mg)	Maximum % deviation
130 or less	10 % ±
130 to 324	7.5 % ±
More than 324	5 % ±

1.3.3 Diameter

Tablets less than 12.5 mm may deviate from the mean by as much as 5%, whereas larger than 12.5 mm tablets may deviate by no more than 3%. Additionally, the tablet's thickness needs to be within 5% of the normal specification in millimeters for packing processes to go without hiccups.

$$\textbf{\%Deviation in Diameter} = \frac{\textit{Individual Diameter} - \textit{Average Diameter}}{\textit{Average Diameter}} \; \boldsymbol{X}\; \mathbf{100}\%$$

(Arafat *et al.,* 2023).

1.3.4 Thickness

Tablet thickness can be measured with Vernier calipers, thickness gauges, or automated equipment. There are automated testing systems that can evaluate the weight, thickness, hardness, and diameter of tablets. Depending on the tablet's size, tablet thickness must be maintained within a given range, usually within ± 5% of the intended value. Tablet thickness is influenced by a number of variables, including compression force, fill volume, die diameter, and material compaction characteristic.

%Deviation in Thickness = $\frac{Individual\ Thickness - Average\ Thickness}{Average\ Thickness} X\ 100\%$ (Arafat *et al.,* 2023).

1.3.5 Hardness

The acceptable ranges of friability or hardness for tablets may need to be modified for bigger coating pans. A tablet hardness tester can be used to determine a tablet's diametric hardness. In the past, a tablet's hardness—a critical factor in guaranteeing its resistance during handling, packaging, and transit—was used to assess if it was appropriate for coating. It's important to strike the right balance between breaking point and hardness since too-hard tablets may make it more difficult for them to dissolve, and too-soft tablets may break quickly (Lachman *et al.,* 1976).

1.3.6 Disintegration Time

Medication's "disintegration time" is the amount of time it takes for it to decompose, demonstrating its bioavailability. Six different brands of tablets were tested by putting them in a 37°C beaker of water and watching them dissolve as they went through a basket rack. The procedure was watched in order to assess the performance of every tablet. Table 1.5 provides the disintegration times for several tablet kinds (Lachman *et al.,* 1976).

Table 1.5: Disintegration Time for Different Types of Tablets

Type of Tablets	Disintegration Time
Uncoated Tablets	Not more than 15 minutes
Coated Tablets	Not more than 30 minutes
Enteric Coated Tablets	2 hours in gastric fluid (0.1 N HCl) and 1 hour in phosphate buffer (pH 6.8)

1.3.7 *In-Vitro* Dissolution

The dissolving examination analyzes the dissolved particles by running them through a 10-mesh screen and calculates how long it takes for tablets to dissolve in specific conditions. This test assesses the rate at which medications dissolve, which is associated with the pace at which absorption occurs in the gastrointestinal system.

% Drug Release = $\frac{Cumulative\ amount\ of\ drug\ released}{Strength} X100$

Table 1.6 provides the USP specification for the dissolution test (Arafat *et al.,* 2023)

Table 1.6: Specification of Dissolution Test

Stage	Number tested	Acceptance criteria
S1	6	Every value needs to exceed or be equal to Q + 5%.
S2	6	Twelve dose units (S1+S2) have an average value that is equal to or greater than Q; no unit is less than 15% of Q.
S3	12	The 24 dose units (S1+S2+S3) have an average value of Q or above; no more than two units fall below Q 15%, and none below Q-25%.

1.3.8 Friability

Testing for friability involves assessing the physical integrity of tablets, both compressed and uncoated, after they have been subjected to mechanical shock and attrition. Friability can be stated as a percentage and is computed as follows: The formula for friability is (Wi-Wf)/Wi × 100. A revolving device that rotates 100 times at a speed of 25 revolutions per minute and is attached to a plastic drum is used to conduct this evaluation. There is a 1% acceptable friability level and broken tablets are not allowed.

% Friability = $\frac{Initial\ Weight - Final\ weight}{Initial\ Weight}\ X\ 100$ (Lachman *et al.*, 1976).

1.3.9 Potency

The term "drug potency" refers to the amount of an active component in a certain dosage unit needed for a medication to have the intended therapeutic effect. Stronger pharmaceuticals have a more muted impact, whereas weaker drugs respond more pronouncedly at lower dosages. Tablet potency must be between 105 and 115 percent of the prescribed dosage, according to USP regulations. Too much potency can have negative side effects, whereas too little potency may result in less-than-ideal therapeutic outcomes. Consequently, the potency of a medicine or pill determines both its advantageous and disadvantageous effects.

%Potency = $\frac{Drug\ in\ a\ Tablet}{Strength} X100$ (Arafat *et al.*, 2023).

1.4 Granulation

Granulation serves as a crucial procedure within pharmaceutical production, particularly in the production of tablets and capsules, where particles are clustered together to increase their size. This technique, known as agglomeration, is essential for improving the flow properties, compressibility, and uniformity of the final dosage form. Three granulation methods are described below in Table 1.7 (Shanmugam, 2017).

Table 1.7: Granulation Methods

Granulation Technique	Description
Dry granulation	Dry granulation proceeds with the agglomeration of dry powder particles by slugging also known as mechanical compression or by compaction which is roller compaction
Wet granulation	In order to promote agglomeration by the creation of a wet mass through adhesion, wet granulation uses granulation liquid (binder/solvent).
Direct compression	Powders are directly compressed into tablets in direct compression method and it includes three steps: blending, tableting, coating.

1.5 Ideal Flow Properties of Granules

1.5.1 Tapped Density

Tap density refers to the maximum density achievable by vibrating or tapping a powder under specific conditions (Srinivasan *et al.*, 2023).

$$\text{Tapped density} = \frac{\text{mass of powder}}{\text{compacted volume}}$$

1.5.2 Bulk Density

Bulk density refers to the ratio of a powder sample's mass to its volume without compression, including the void spaces between particles (Srinivasan *et al.*, 2023).

$$\text{Bulk density} = \frac{\text{mass of powder}}{\text{untapped volume}}$$

1.5.3 Angle of Repose

The angle of repose represents the maximum incline at which a heap of granular substance can be stacked without crumbling. This value is determined through the formula $\tan \theta = \frac{h}{r}$, where h denotes the height of the pile and r stands for the radius of the pile (Srinivasan *et al.,* 2023).

1.5.4 Consolidation Index

The Consolidation Index, also known as Carr's index, evaluates the compressibility and flowability of granular powders. The higher the value of Carr's index, poor flowability of granules is observed using below formula (Moghbel & Abbaspour, 2013).

$$\text{Carr's index} = \frac{tapped\ density - bulk\ density}{tapped\ density} X\ 100$$

1.5.5 Standard Curve

A standard curve is a graphical representation used to determine an unknown sample concentration by assimilating it to the standard samples known concentration. The concentration is determined with the help of UV-spectrophotometer (DeMeester & Johnson, 1975).

1.6 Purpose of the Study

This research aims to evaluate the efficacy of Metformin 500 mg tablets, a commonly used treatment for diabetes in Bangladesh. Various manufacturers provide this medication in different oral dosage forms. It is imperative to verify tablet specifications to ensure compliance with quality control regulations. Conducting an analysis post-distribution guarantees sustained quality even after prolonged storage, which is crucial for maintaining high standards of medical care. The study was undertaken for the following purposes:

- To determine adherence to quality control standards, which significantly impact the bioavailability of the medication.
- To evaluate the product quality and therapeutic effectiveness of the Metformin 500 mg sample brand.
- To validate the safety profile of the Metformin 500 mg sample brand.

1.7 Tablet Preparation

Tablets are a type of solid oral medication used to treat various illnesses. Tablets can be categorized as compressed tablets, tablets coated with polymer or sugar, etc. Direct compressor machines are used to make compressed tablets. Active substances, diluents, binders, glidants, etc. are used as excipients in the formulation of tablets (Ubhe & Gedam, 2020).

Chapter-2:

Materials and Methods

2. Materials and Methods

Our study focused on examining a particular brand of metformin hydrochloride tablets through *in vitro* analytical evaluation, requiring a range of pharmaceutical equipment. We conducted a thorough analysis of various aspects of the samples, including their cost, physical attributes, manufacturer details, batch code, expiry date, licensing particulars, and D.A.R. number.

2.1 Materials

For this analysis, a test drug was employed. Throughout the examination, the samples were appropriately stored. The investigation took place in the B Pharm Project Laboratory of the pharmacy school of the University of Asia Pacific.

2.1.1 Sample and Materials Used in the Experiment

Table 2.1 provides a compilation of various substance categories and their corresponding sources.

Table 2.1: Substances Used in the Experiment

Items	Name	Source	Batch No.
API	Metformin Hydrochloride	Project laboratory	
Marketed Samples	Metformin Hydrochloride (500 mg)	Project laboratory	10113030E
Reagents	Potassium dihydrogen phosphate	Project laboratory	
Reagents	Sodium hydroxide	Project laboratory	

2.1.2 Apparatus Used in the Experiment

- Pipette and Pipette filler
- Beaker
- Spatula

- 20 mesh screens
- Funnel
- Holder
- Petri dish
- Glass rod

2.1.3 Instruments Used in the Experiment

In our experimentation, a variety of apparatus was utilized, all readily available within our university's research infrastructure. Each instrument boasted a superior operational capacity, ensuring the generation of results that are pragmatically sound. The names of the experimental apparatus and their countries of origin are delineated in Table 2.2 for reference.

Table 2.2: Auxiliary Tools for this Experiment

Name of Instruments	Manufacturer and Place of Origin
Digital balance (Ay 120)	SHIMADZU, Japan
pH meter (pH 211 Microprocessor pH meter)	HANNA INSTRUMENT, Romania
Automatic Tablet hardness Tester(8M)	DR SCHEUNIGER, Switzerland
Analog Vernier Calipers	Mega Vernier calipers
Tablet Dissolution Tester	ELECTRO LAB, India
Tablet Disintegration tester (VDT0-2)	VEEGO, India
Friability Tester	ELECTRO LAB, India
UV-VIS Spectrophotometer (UV-1700)	SHIMADZU, Japan
Tablet Press Machine	SHAKTI PHARMATECH, India

2.1.4 Ingredients Used in the Experiment

2.1.4.1 Granules Preparation

2.1.4.1.1 Apparatus and Equipment Used in Granulation

1. Beaker
2. Spatula, Pipette and Pipette filler
3. 20 mesh screens
4. Electric balance, Rapid mixer granulator, Tray dryer

2.1.4.1.2 Formulation of the Granules Preparation

Table 2.3 demonstrates the lists the ingredients used in the formulation of the granules preparation.

Table 2.3: Formulation Used in Granulation

Sl. No.	Excipient Name	Justification	Quantity (gm)
1	Maize starch	Diluent	82.5
2	Lactose	Diluent	125
3	Avicel PH 101	Diluent	35
4	Magnesium stearate	Binder	2.5
5	Talc	Binder	8
6	Distilled water	Solvent	Up to 50 mL (Q.S)
		Total	140.5 gm

2.1.4.2 Preparation of Tablets

2.1.4.2.1 Ingredients Used in the Preparation of Tablets

Table 2.4 provides the ingredients used in the preparation of tablets

Table 2.4: Formulation of Metformin HCl Tablet

Ingredients	Quantity for 1 tablet (mg)	Quantity 10 tablets (mg)	Justification
Metformin HCl	10	100	API
Granules	180	1800	Excipient

Talc	4	40	Glidant
Mg Stearate	6	60	Lubricant
SSG	3	30	Super Disintegrate

2.2 Methods

2.2.1 Preparation of Phosphate Buffer Media

A total of 0.896 grams of NaOH and 6.804 grams of KH_2PO_4 were accurately weighed using a precision weighing machine. These were then dissolved in 1000 mL of distilled water with continuous stirring until complete dissolution. The pH of the resulting solution was measured to be 6.8 using a pH meter.

2.2.2 Preparation of Standard Curve

Various tools like test tubes, pipettes, cuvette cells, and UV spectrophotometers are used to construct standard curves. To create the mother solution, 10 mg of metformin HCl was dissolved in 90 ml of phosphate buffer solution (pH 6.8). Then, 12 mL of the mother solution was mixed with 88 mL of buffer solution to make the final diluted solution. The absorbance of the diluted solution was measured with a UV spectrometer, and the standard curve relating concentration to absorbance was generated using Microsoft Office Excel.

2.2.3 Granulation Process

1. A mixture comprising 82.5 grams of maize starch, 150 grams of lactose, and 35.5 grams of Avicel PH 101 was prepared in a beaker. These ingredients were dry mixed in a rapid mixer granulator machine for 10 minutes at a speed of 100 rotations per minute (RPM).

2. To prepare the binder solution, 2.5 grams of maize starch were dissolved in 20 mL of distilled water to produce solution A. Additionally, 10 grams of finely ground Povidone K 30 were dissolved in 30 mL of distilled water to generate solution B. Solution A was then combined with solution B, and the resulting mixture was thoroughly agitated to yield the binder solution. This binder solution was gradually introduced into the granulator through a liquid binder addition nozzle, while initially mixing the contents for 5 minutes at a speed of 300 RPM. Following this, the lid was manually opened, and the mixture was further blended using a spatula for an additional 5 minutes.

3. The granules were gathered from the outlet of the granulator and evenly spread onto trays. These trays were subsequently positioned inside a tray dryer adjusted to a temperature of 40°C for a duration of 45 minutes.

4. After drying, the granules were passed through 20 mesh screens for sieving.

The instrument used in the granulation process is presented in Figure 2.1

Figure 2.1: Rapid Mixture Granulator

2.2.4 Formulation of Metformin Hydrochloride Tablets

Apparatus and machines used for tablet preparation are weighing machine, tablet compressor machine. Ten tablets of metformin HCl were manufactured using a rotary tablet compressor machine equipped with a 3mm die punch. The formulation utilized is detailed in Table 2.4. All the ingredients were measured using a weighing machine, taken in a pouch and mixed manually. From the mixed ingredients 203 mg was weighted for each of the 10 tablets and was subjected to rotatory compressor machine to form tablets.

Figure 2.2 represents the formulated tablets.

Figure 2.2: Formulated Metformin Hydrochloride Tablets

Figure 2.3 represents the Tablet Compressor Machine

Figure 2.3: Tablet Compressor Machine

2.3 Granules Flow Properties

2.3.1 Angle of Repose

Materials and Apparatus used are listed below:

1. Funnel

2. Petri dish

3. Beaker

4. Holder

5. Weighing machine

6. Glass rod

7. Measuring scale

2.3.2 Procedure for the Angle of Repose Determination

1. Granules were moved into a beaker. Next, the petri dish was positioned, and the center of the dish was designated using a measuring scale. A holder was utilized to support a funnel directly above the marked center of the petri dish.

2. The granules were funneled onto the petri dish.

3. Once the granules assumed a conical form, the height of the heap was gauged. The height of the edges was halved, and this value was divided by half of the diameter of the petri dish to ascertain the radius, subsequently used to compute the angle of repose.

2.3.3 Bulk Density, Tapped Density and Compressibility Index

Table 2.5: Determination of Bulk Density, Tapped Density and Carr's Index

Name of Property	Apparatus and Materials	Procedure
Bulk Density	1. Beaker 2. Measuring cylinder 3. Weighing machine	A quantity of 20 grams of the granules was measured and placed into a beaker. Subsequently, the granules were gradually poured into a measuring cylinder at a 45°, and the bulk volume was approximated. This volume was then utilized in conjunction with the formula for bulk density calculation.
Tapped Density	1. Measuring cylinder 2. Tap density test apparatus	A quantity of 20 grams of granules was placed in the apparatus of tapped density and subjected to 300 taps during the initial attempt. The resulting volume was recorded. Subsequently, the same quantity of granules was tapped 200 times in the second attempt, with a condition to repeat the procedure for an additional 200 taps if the volume changed by more than 2 mL. The tapped density was then computed using the formula for tapped density, incorporating the observed tapped volume.

Compressibility Index		Bulk density and tapped density measurements were obtained and subsequently utilized in the compressibility index formula to determine its value.

2.4 Methods for Various QC Parameters

Within the realm of tablet quality assessment, a myriad of tests is conducted to gauge diverse quality parameters. Each test serves as a window into specific characteristics, allowing for a comprehensive evaluation of the tablet's overall quality and performance.

2.4.1 Weight Variation Test

Apparatus: Electronic balance (Originator Company: Shimadzu, Country: Japan)

Process: The weight variation test for pharmaceutical tablets serves to ensure content uniformity and even distribution of the drug within the dosage form. In the examination of metformin HCl 500 mg tablets, both formulated and commercially available variants were subjected to this test. Each tablet was removed from its blister packaging and individually weighed using an electronic balance, as illustrated in Figure 2.4, alongside the total weight of the tablets.

Figure 2.4: Electronic Balance

2.4.2 Diameters and Thickness Test

Apparatus: Analog vernier calipers (Originator Company: Mitutoyo Vernier Calipers, Country: Japan)

Process: Consistency in both diameter and thickness is crucial for both the aesthetic appeal and brand reputation of formulated and commercially available tablets, as it directly impacts content uniformity and the quality of granulation within the tablet mixture. To assess these

parameters, 20 tablets from the market and 6 tablets from the formulation were meticulously measured using Vernier slide calipers. Deviations of up to 5% were deemed acceptable within the varying sizes of the tablets.

Figure 2.5: Analog Vernier Calipers

2.4.3 Friability Test

Apparatus: Roche Friabilator (Originator Company: Electrolab, Country: India), weighing machine

Process: Throughout each cycle of the friability test, the tablets were designed to descend from a six-inch height. Typically, the friabilator rotates at a rate of 25 revolutions per minute (RPM) for a period of 4 minutes. The percentage of friability was determined by reweighing the tablets after 100 revolutions and comparing their initial weights. The difference between the total weight after the friability test and the initial weight before the test was calculated.

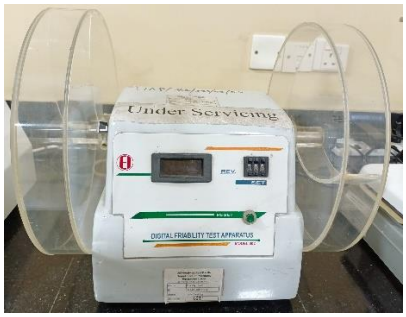

Figure 2.6: Friabilator

2.4.4 Hardness Test

Apparatus: Automated tablet hardness tester (Originator Company: Thermonik, Country: South Korea)

Process: The hardness of three tablets sourced from the market and one tablet prepared in-house was assessed using an automatic tablet hardness tester.

Figure 2.7: Automated Tablet Hardness Tester

2.4.5 Disintegration Time

Apparatus: Disintegration Tester (Originator Company: Electrolab, Country: India)

Process: A tablet disintegration tester was utilized to examine three tablets procured from the market and one tablet prepared in the laboratory. A total of 700 ml of phosphate buffer media was introduced into the vessel of the disintegration tester, with the media temperature maintained at 37 degrees Celsius. Subsequently, the tablets were positioned within the mesh basket and allowed to disintegrate and dissolve completely in the media. The mesh basket was set in motion at a rate of 28-32 cycles per minute. The disintegration time (DT) was determined as the point when no residual particles remained in the system's basket.

Figure 2.8: Disintegration Tester

2.4.6 Potency Test

Equipment's: Pipette, test-tube, test-tube rack, filter paper, volumetric flask

Apparatus: UV-spectrophotometer (originator Company: Shimadzu, Country: Japan)

Process: Samples were selected from both prepared tablets and those already available on the market. These tablets were initially weighed and subsequently crushed using a mortar and pestle. For the prepared tablets, the resulting crushed powder was dissolved in 100 ml of phosphate buffer medium to create a mother solution. Similarly, 20 mg of the active pharmaceutical ingredient (API) was extracted from the crushed powder of commercially available tablets and dissolved in 100 ml of phosphate buffer medium. UV measurements were performed on both solutions, with absorbance readings taken at 232.7 nm. Potency was then determined using a mathematical approach.

Figure 2.9: UV-Spectrophotometer

2.4.7 Dissolution Test

Equipment's: Pipette, test-tube, test-tube rack, filter paper

Apparatus: Dissolution tester (Originator Company: Electrolab, Country: India), UV-spectrophotometer

Process: The dissolution test for the tablets was conducted utilizing the USP Apparatus - II (paddle type) in 900 ml of pH 6.8 phosphate buffer solution as the dissolution media, maintained at a temperature of 37 ± 0.5ºC and a rotation speed of 100 rpm. Three tablets sourced from the market and two prepared tablets were individually placed in separate vessels. At intervals of 5, 15, 30, 45, and 60 minutes, 10 ml of the solution was withdrawn from each vessel, filtered using filter paper, and transferred to separate test tubes. Following the extraction of the solution, 10 ml of phosphate buffer media was promptly added to each vessel to maintain the solution volume. The solutions in the test tubes were diluted using phosphate buffer medium and subsequently subjected to analysis using a UV spectrophotometer, with absorbance values measured at a wavelength of 232.7 nm.

Figure 2.10: Dissolution Test Apparatus

2.4.8 Standard Curve Preparation

Equipment's: Test tubes, pipette, cuvette cell

Apparatus: UV-spectrophotometer

Process: A solution of Metformin HCl was prepared by dissolving 10 mg of the compound in 90 ml of phosphate buffer media with a pH of 6.8, resulting in the formation of a mother solution. This mother solution was further diluted by transferring 12 mL of it into 88 mL of media. The absorbance of the diluted solution was then determined using a UV spectrometer, and a standard curve correlating concentration to absorbance was generated using Microsoft Office Excel software.

Chapter-3:

Results and Discussion

3. Results and Discussion

As part of my project, I conducted a comparative analysis of various tests on both commercially available and developed metformin tablets. These tests encompassed assessments such as weight variation, dimensions (thickness and diameter), potency, hardness, disintegration, and dissolution.

3.1 Flow Properties of Granules

The granule materials underwent testing for tapped density, bulk density, angle of repose, and compressibility index with any deviations from the specified criteria being thoroughly examined and discussed**.**

3.1.1 Test of Bulk Density

Granules Mass = 20 grams

Bulk volume = 40.3 mL

Bulk density = Granules mass / bulk volume

= 20 grams / 40.3 mL

= 0.496 grams/mL

3.1.1.1 Discussion

The observed bulk density of the 20 grams of granule powder is 0.496 grams/mL

3.1.2 Test of Tapped Density

Granules Mass = 20 grams

Tapped volume = 28 mL

Tapped density = Granules mass / tapped volume

= 20 grams / 28 mL

= 0.714 grams/mL

3.1.2.1 Discussion

The increased bulk density obtained after tapping is known as tap density. The resulting tapped density is 0.714 grams/mL, which is higher than the bulk density achieved earlier.

3.1.3 Value of Angle of Repose

Diameter of petri dish = 7.6 cm

Radius of petri dish, r = 3.8 cm (diameter/2)

Height of edges, h = 2.5 cm

Angle of repose, $\theta = \tan^{-1}(h/r)$

$= \tan^{-1}(2.5/3.8)$

$= 33.34°$

3.1.3.1 Discussion

The United States Pharmacopeia (USP) standard for the angle of repose is provided in the table below (Table 3.1) (Beakawi & Baghabra, 2018).

Table 3.1: Angle of Repose Value with Flowability

Degree of angle of repose	Flow property
25 - 30	Excellent
31 - 35	Good
36 - 40	Fair (air is not necessary)
41- 45	Passable (might hung up)
46- 55	Poor (agitation is necessary)
56 - 65	Very poor
>66	Extremely poor

After thorough discussion, it is evident that the angle of repose measured in the test is 33.34°, falling within the acceptable range of 31-35°. Consequently, the flowability of the granules is deemed satisfactory.

3.1.4 Compressibility Index Value

Tapped density value = 0.714 gm/ ml

Bulk density value = 0.496 gm/ ml

% Carr's index = {(tapped density-bulk density)/tapped density}X 100

= {(0.714-0.496)/0.714}X 100

=30.53%

3.1.4.1 Discussion

The United States Pharmacopeia (USP) standard for the %Carr's Index is provided in the table below (Table 3.2) (Moghbel & Abbaspour, 2013).

Table 3.2: The Margin of Flowability Related to Carr's Index

% Carr's Index	Flowability
5-15	Excellent
16-18	Good
19-21	Fair flow
22-35	Poor
>40	Extremely poor

The test yielded a Carr's index value of 30.53%, falling within the range of 22-35%, which signifies suboptimal flowability.

3.2 Weight Variation Test

The weights of 20 commercially available metformin hydrochloride 500 mg tablets were assessed using an electronic balance. The findings, along with the percentage deviation, are outlined in Table 3.3.

Table 3.3: Weight Variation Test of Marketed Metformin Hydrochloride Tablets

SI. No.	Individual Weight of Tablet (mg)	Average weight (mg)	% Deviation
1	570		0.54
2	568		0.19
3	570		0.54

4	567		0.01
5	580	11339/20 = 566.95	2.3
6	577		1.77
7	549		-3.17
8	572		0.89
9	576		1.61
10	568		0.19
11	567		0.01
12	554		-2.28
13	560		-1.23
14	593		4.61
15	557		-1.76
16	565	11339/20 = 566.95	-0.34
17	561		-1.05
18	568		0.19
19	556		-1.93
20	561		-1.05

Now the visual depiction of weight variation of marketed tablets are demonstrated in Figure 3.1.

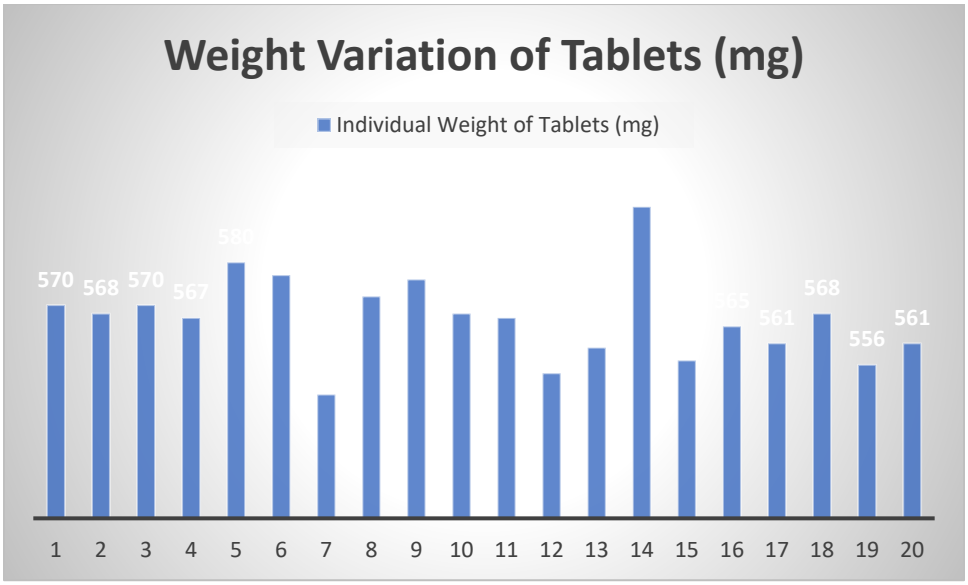

Figure 3.1: Visual Depiction of Weight Variation of Marketed Tablets

Now the graphical illustration of %Deviation of marketed tablets are depicted in Figure 3.2.

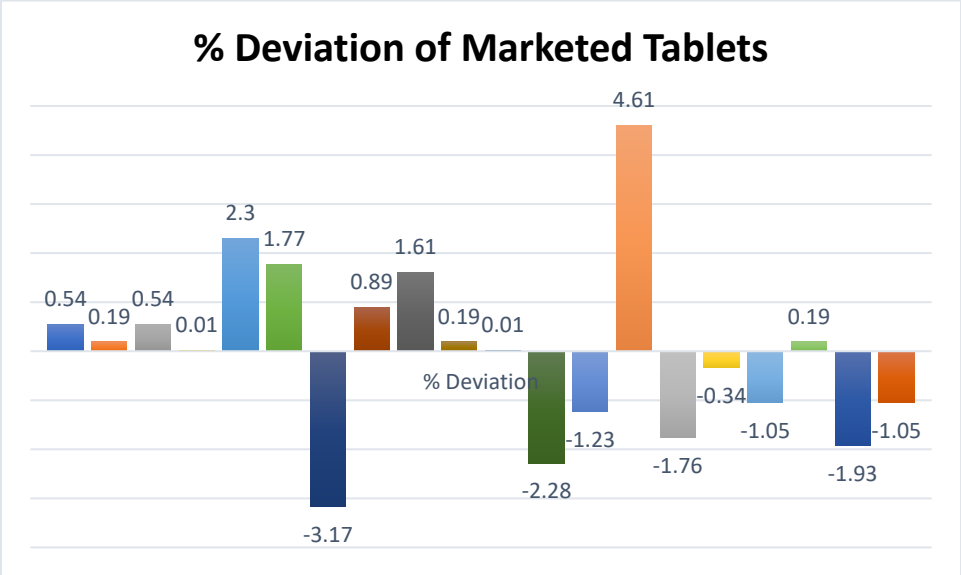

Figure 3.2: Graphical Illustration of %Deviation of Marketed Tablets

Following that the weights of 6 formulated metformin hydrochloride 10 mg tablets were assessed using an electronic balance. The findings, along with the percentage deviation, are outlined in Table 3.4.

Table 3.4: Weight Variation Test of Formulated Metformin Hydrochloride Tablets

SI. No.	Individual Weight of Tablet (mg)	Average weight (mg)	% Deviation
1	203.2		0.2

2	203.2		0.2
3	200	1217/6 = 202.83	-1.38
4	202.6		-0.1
5	204		0.6
6	204		0.6

The visual representation of Weight Variation Test of Formulated Metformin Hydrochloride 10 mg Tablets are demonstrated in Figure 3.3.

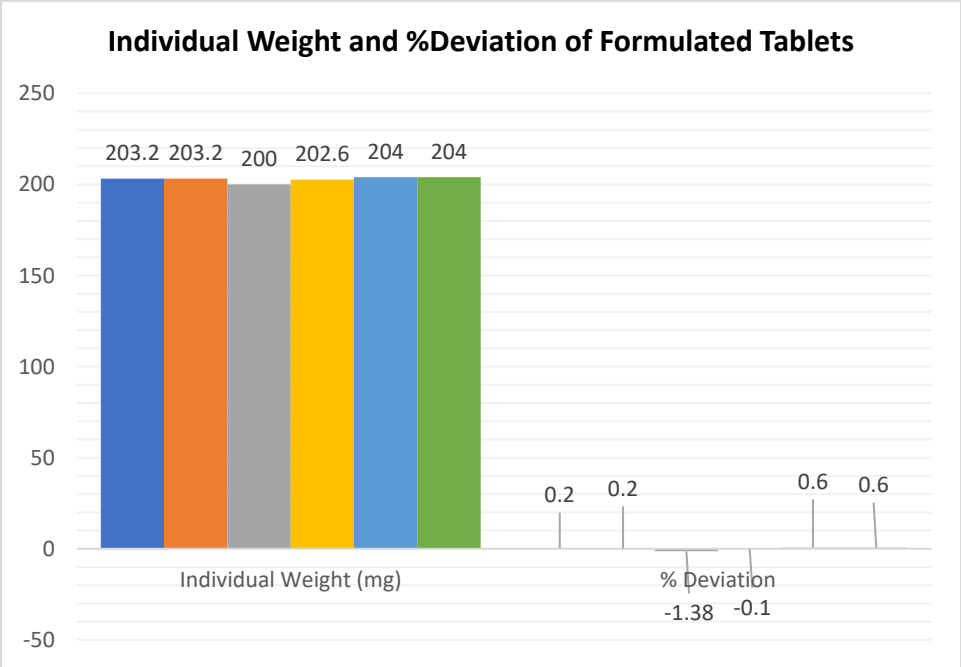

Figure 3.3: Visual Representation of Weight Variation Test of Formulated Tablets

Below is a comparison table illustrating the Study of Marketed and Formulated Metformin Hydrochloride tablets. Table 3.5 delineates the average weight, highest weight, lowest weight, and the maximum and minimum percentage deviations in weight variation observed for both commercially available and laboratory-formulated tablets.

Table 3.5: Comparative Study of Marketed and Formulated Tablets

Type of Tablets	Average Weight	Highest Weight	Lowest Weight	Maximum % Deviation	Minimum % Deviation
Marketed	566.95	593	549	4.61	-3.17
Formulated	202.83	204	200	0.6	-1.38

The graphical depiction of the comparison analysis between the marketed and formulated tablets is presented hereafter in Figure 3.4

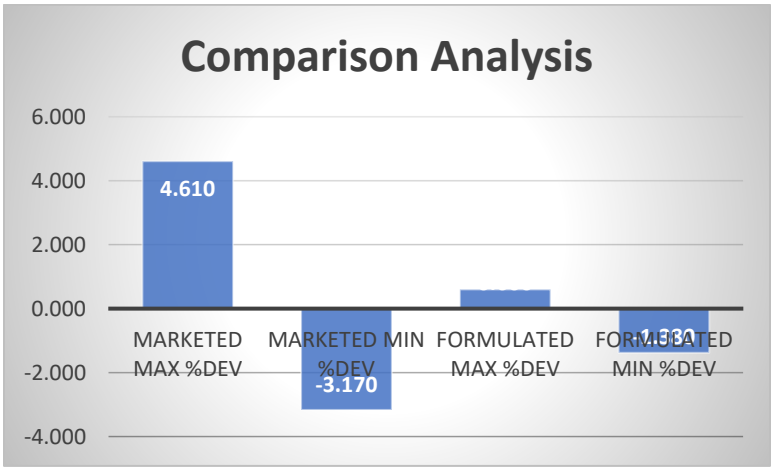

Figure 3.4: Comparison Analysis of Marketed and Formulated Tablets

3.2.1 Discussion

The examination of the tablets aimed to maintain uniform weight distribution among various tablets, in accordance with the allowable fluctuation limits established by the USP, wherein deviations should not surpass ±10% for tablets weighing 130 mg or less, ±7.5% for tablets weighing between 130 mg and 324 mg, and ±5% for tablets weighing over 324 mg (Lachman *et al.*, 1976).

Considering the guidance set forth by the United States Pharmacopeia (USP), it is established that the average weight of commercially available tablets typically exceeds 324 mg. Moreover, adherence to USP standards mandates that the weight variance for metformin hydrochloride tablets should fall within ± 5%. Consequently, tablets meeting these criteria are generally deemed acceptable, signifying compliance with stringent quality benchmarks.

Conversely, upon analysis, laboratory-formulated tablets exhibit an average weight of 202.83

mg, falling below the aforementioned 324 mg threshold yet surpassing the lower limit of 130 mg. In alignment with USP guidelines, this prompts an adjustment in the acceptable range to ± 7.5%. Notably, the maximum deviations observed, both positive and negative, remain within the permissible ±7.5% margin. Thus, it can be concluded that the weight variability in the formulated tablets is within acceptable parameters as stipulated by USP standards.

3.3 Diameter and Thickness

The Diameter and Thickness of 20 commercially available metformin hydrochloride 500 mg tablets were assessed utilizing traditional analog Vernier Calipers. The findings, along with the percentage deviation, are outlined in Table 3.6.

Table 3.6: Diameter and Thickness of Marketed Metformin Hydrochloride Tablets

SI No.	Diameter (mm)	Average Diameter (mm)	%Deviation in Diameter	Thickness (mm)	Average Thickness (mm)	%Deviation in Thickness
1	11.4			5.5		
2	11.4			5.5		
3	11.4			5.5		
4	11.4			5.5		
5	11.4			5.5		
6	11.4	11.4	0	5.5	5.5	0
7	11.4			5.5		
8	11.4			5.5		
9	11.4			5.5		
10	11.4			5.5		
11	11.4			5.5		

12	11.4			5.5		
13	11.4			5.5		
14	11.4			5.5		
15	11.4			5.5		
16	11.4			5.5		
17	11.4	11.4	0	5.5	5.5	0
18	11.4			5.5		
19	11.4			5.5		
20	11.4			5.5		

Now the graphical rendering of diameter and thickness of marketed metformin hydrochloride 500 mg tablets are demonstrated in figure 3.5.

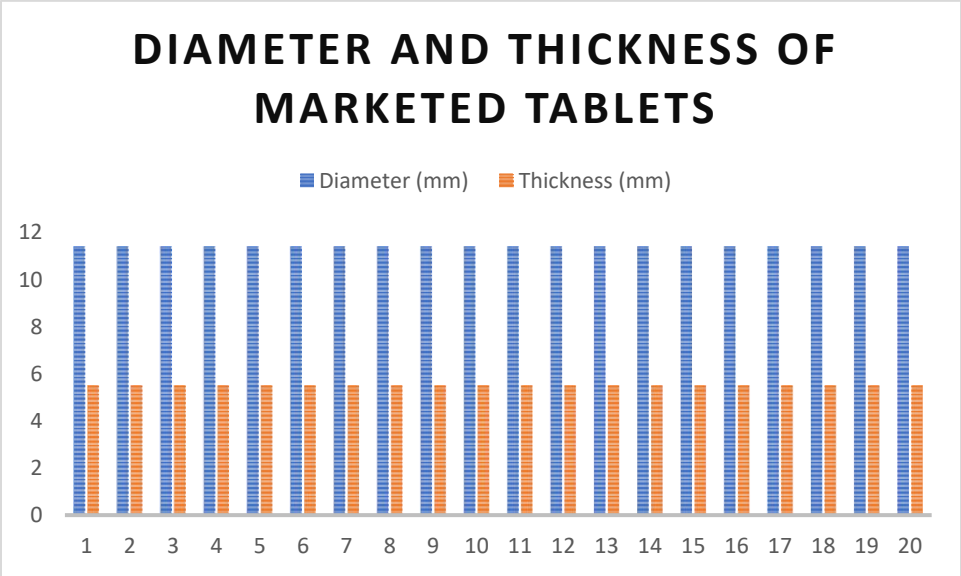

Figure 3.5: Visual Representation of Diameter and Thickness of Marketed Tablets

Following that the diameter and thickness of 6 formulated metformin hydrochloride 10 mg tablets were assessed by utilizing traditional analog Vernier Calipers.

The findings, along with the percentage deviation, are outlined in Table 3.7.

Table 3.7: Diameter and Thickness of Formulated Metformin Hydrochloride Tablets

SI No.	Diameter (mm)	Average Diameter (mm)	%Deviation in Diameter	Thickness (mm)	Average Thickness (mm)	%Deviation in Thickness
1	8			3		
2	8			3		
3	8	8	0	3	3	0
4	8			3		
5	8			3		
6	8			3		

The graphical rendering of diameter and thickness of formulated metformin hydrochloride 10 mg tablets are demonstrated in figure 3.6.

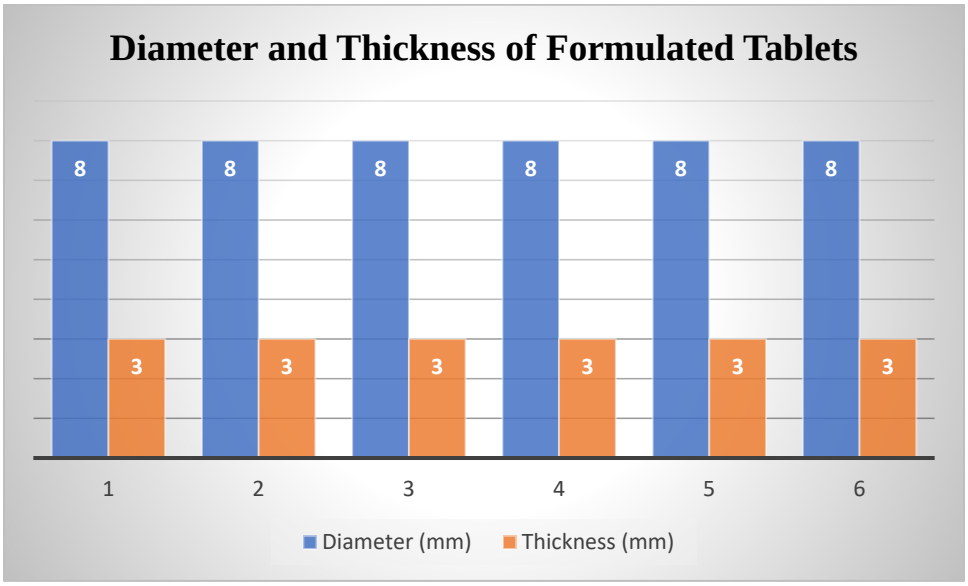

Figure 3.6: Visual Representation of Diameter and Thickness of Formulated Tablets

3.3.1 Discussion

In accordance with USP guidelines, the accepted standards for tablet diameter stipulate a permissible deviation of no more than ± 5% (Lachman *et al.*, 1976). The commercially

available tablets adhere closely to these USP standards. Despite their round shape, the tablets exhibit a slightly greater average weight, as outlined in the USP Monograph. As evidenced here, the formulated tablets meet the prescribed diameter standards outlined in the USP.

Regarding tablet thickness, the USP dictates acceptance criteria with a tolerance level of ± 5% (Lachman *et al.*, 1976). The marketed tablets align seamlessly with these USP regulations. Moreover, the average thickness of the formulated tablets stands at 3, a notable achievement in itself. Consequently, they fall within the specified ranges, demonstrating compliance with regulatory standards.

3.4 Hardness

The hardness of three commercially available metformin hydrochloride tablets was assessed utilizing a digital tablet hardness tester. The hardness values for these three tablets are provided in Table 16.

Table 3.8: Hardness of Marketed Tablets

SI No.	Hardness (kp)	Average Hardness (kp)
Tablet - 1	17.15	
Tablet - 2	13.61	17.587
Tablet - 3	22.00	

The visual representation of hardness of marketed tablets are demonstrated in Figure 3.7

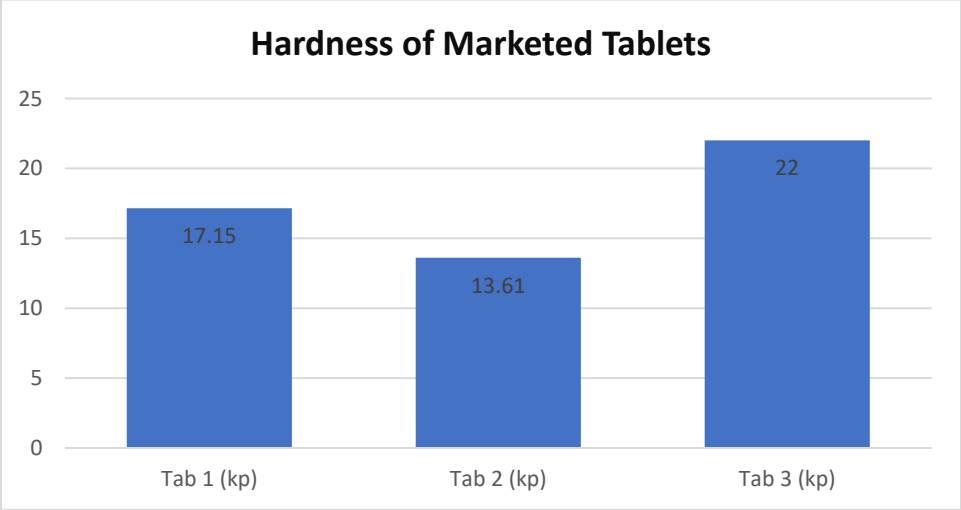

Figure 3.7: Visual Representation of Hardness of Marketed Tablets

Following that utilizing a digital tablet hardness tester, the solidity of a single laboratory-formulated metformin hydrochloride tablet was evaluated, yielding a hardness value of 5.81 kp.

The figure below illustrates a comparative analysis of the hardness levels between commercially available and laboratory-formulated tablets.

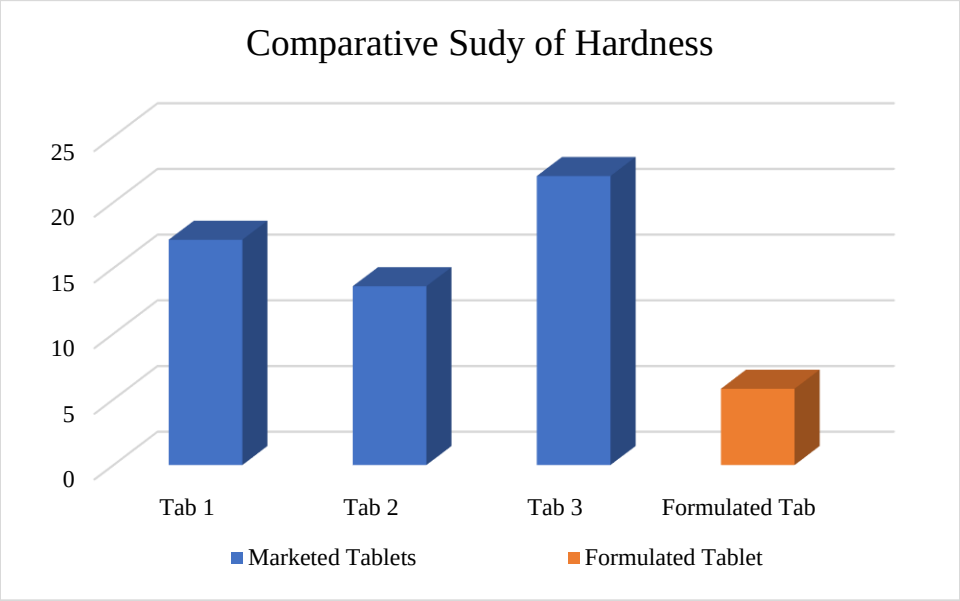

Figure 3.8: Visual Representation of Comparative Study of Hardness

3.4.1 Discussion

The hardness of a tablet plays a crucial role, as it directly influences factors such as disintegration time and dissolution rate. For immediate release tablets, the optimal hardness range is typically between 5-8 kp (Lachman *et al.*, 1976). As per USP guidelines, the formulated tablet aligns with this ideal range, falling within the specified 5-8 kp range. However, the commercially available tablets fail to meet the standards outlined in the USP Monograph, as their hardness exceeds the specified limits. Consequently, it is advisable to consider rejecting this batch following an assessment of its disintegration time.

3.5 Friability Test

A total of seven commercially available metformin hydrochloride 500 mg tablets underwent measurement using a Friabilator. The results of the friability test are provided in Table 3.9

Table 3.9: % Friability of Marketed Tablets

Type of Tablets	Initial Weight (gm)	Final Weight (gm)	% Friability	Comments
Seven Marketed Tablets	3.980	3.978	0.05 %	Acceptable

Now the visual representation of Friability Test is demonstrated in Figure 3.9

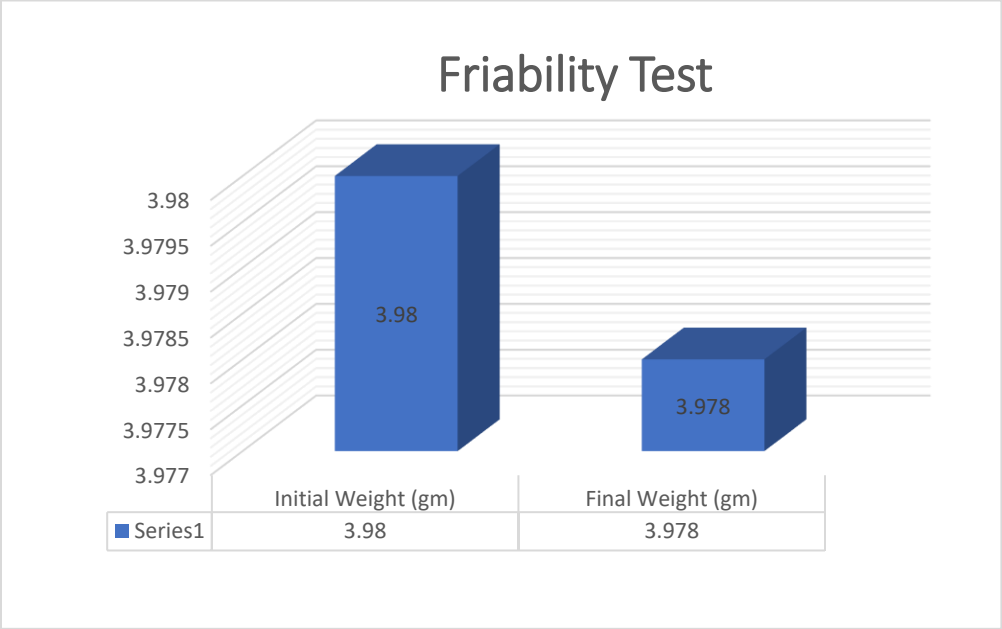

Figure 3.9: Visual Representation of Friability Test of Marketed Tablets

3.5.1 Discussion

According to the specifications outlined by the U.S. Pharmacopeia (USP), the permissible weight variance following the friability test for oral tablets is set at less than 1% (Lachman *et al.,* 1976). The commercially available Metformin hydrochloride tablets conform to these specifications and are deemed acceptable based on this criterion.

3.6 Disintegration Time

Three randomly selected commercially available Metformin Hydrochloride tablets and one laboratory-formulated Metformin Hydrochloride tablet were subjected to a disintegration test. They were placed in a device containing purified water, and the apparatus was activated. Subsequently, the disintegration time was measured, analyzed, and compared against the specified criteria. The table below presents a comparison of the disintegration times for the four different Metformin Hydrochloride tablets.

The Disintegration Time (DT) for both the marketed and formulated tablets are demonstrated below in table 3.10.

Table 3.10: Disintegration Time of Metformin Hydrochloride Tablets

SI No.	Marketed Tablet – 1 (seconds)	Marketed Tablet – 2 (seconds)	Marketed Tablet – 3 (seconds)	Average of Marketed Tablets (seconds)	Formulated Tablet (seconds)
1	628	714	760	700.67	150

The visual representation of disintegration time for both marketed and formulated tablets are displayed in the following figure 3.10.

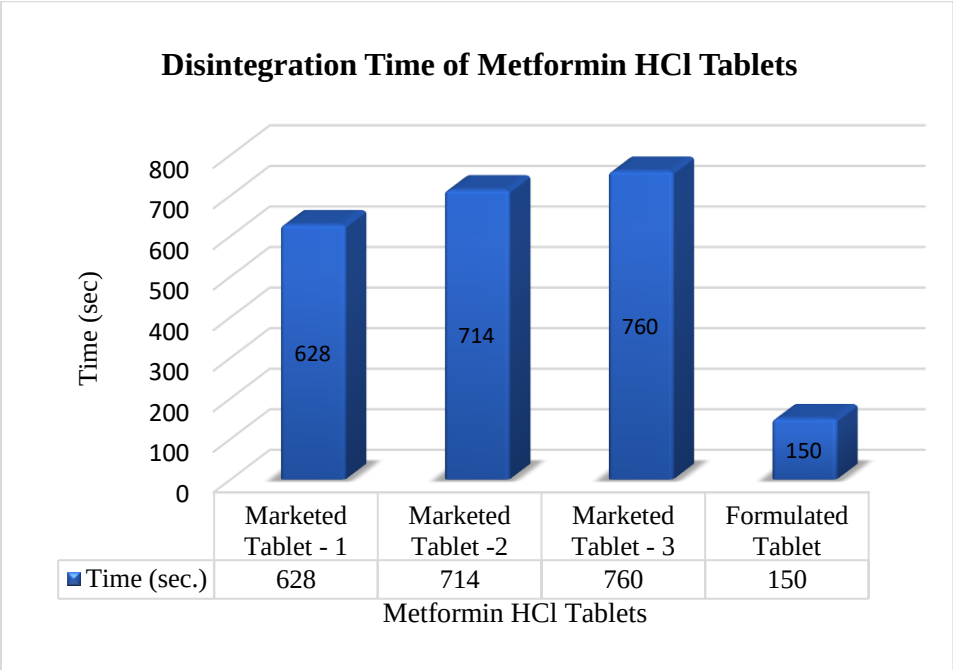

Figure 3.10: Disintegration Time of Metformin Hydrochloride Tablets

3.6.1 Discussion

In accordance with the guidelines outlined by the U.S. Pharmacopeia (USP), the optimal disintegration time for film-coated tablets should ideally fall within a range of 30 minutes (Lachman *et al.*, 1976). The average disintegration time observed for the metformin hydrochloride tablets was recorded as 700.67 seconds, aligning well within the specified range set forth by the USP. Similarly, the laboratory-formulated tablet also conforms to this criterion.

3.7 Potency

Four commercially available metformin hydrochloride 500 mg tablets and two laboratory-prepared metformin tablets were individually crushed using mortar and pestle. Subsequently, a portion of the resulting powder from both the commercial and formulated tablets was extracted and combined with a suitable solvent, with adjustments made for dilution if required. The absorbance of the resulting solutions was then measured using a spectrophotometer. Finally, the potency of the samples was determined based on the absorbance readings.

Table 3.11 represents the potency of marketed metformin hydrochloride tablet.

Table 3.11: Potency of marketed metformin hydrochloride tablet

Absorbance	Conc. (mcg/ml)	Conc. (mg/ml)	Total Volume (ml)	Dilution Factor	Average Tablet Weight (mg)	Sample Taken (mg)	Drug in a Tablet (mg)	Strength (mg)	% Potency
0.928	11.64	0.0116	100	17	566.95	22.8	490.4	500	98.08

Table 3.12 represents the potency of formulated metformin hydrochloride tablet.

Table 3.12: Potency of formulated metformin hydrochloride tablet

Absorbance	Conc. (mcg/ml)	Conc. (mg/ml)	Total Volume (ml)	Dilution Factor	Average Tablet Weight (mg)	Sample Taken (mg)	Drug in a Tablet (mg)	Strength (mg)	% Potency
0.915	11.47	0.0115	100	7	202.83	203.2	8.03	10	80.3

Now the graphical illustration of comparison of potency between marketed and formulated tablets is demonstrated in the following figure 3.11.

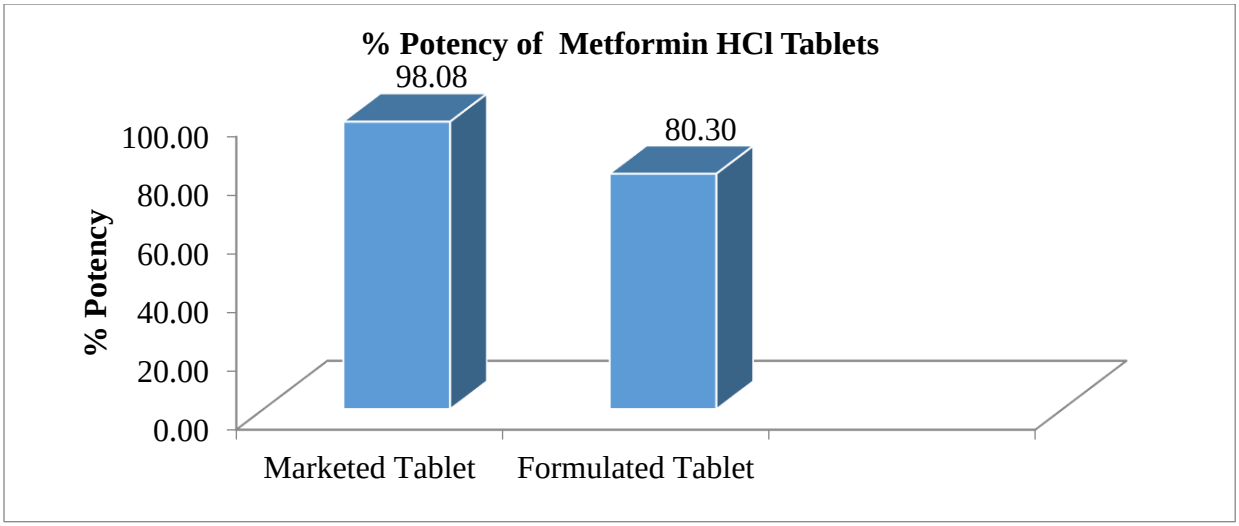

Figure 3.11: %Potency of Metformin HCl Tablets

3.7.1 Discussion

According to the U.S. Pharmacopeia (USP) standard, the potency of metformin hydrochloride tablets should ideally fall within the range of 95%-105% (Lachman *et al.*, 1976). Analysis revealed that the commercially available metformin hydrochloride tablets exhibited a potency of 98.08%, indicating their effectiveness in delivering the desired therapeutic effects. However, the formulated tablet demonstrated a potency of 80.30%, falling short of the ideal range specified by the USP.

3.8 Dissolution Profile

When the temperature reached 37 degrees Celsius, three tablets were individually placed into separate containers, and the paddle was set to rotate at a speed of 50 revolutions per minute. Samples of ten milliliters each were collected from each of the three tablets at predefined intervals of 5, 15, 30, 45, and 60 minutes. These samples were subsequently filtered, and the absorbance of each sample was determined using a UV Spectrophotometer. The study investigated the dissolving rates of three distinct tablet compositions. Table 3.13, 3.14, 3.15 as well as figure 3.12, 3.13, 3.14 represent the outcomes derived from forecasting the proportion of drug release from marketed tablets over a period of time.

Table 3.13: Dissolution Profile of Marketed Metformin Hydrochloride Tablet 1

Time (min)	Absorbance	Conc. (mcg/ml)	Conc. (mg/ml)	Dilution Factor	mg/10ml	mg/900ml	Cumulative Amount Released	% Drug Release
0	0	0	0	0	0	0	0	0
5	0.484	6.022	0.006	50	3	270	270	54
15	0.712	8.904	0.0089	50	4.45	400.5	403.5	80.7
30	0.762	9.536	0.0095	50	4.75	427.5	434.95	86.99
45	0.894	11.205	0.0112	50	5.6	504	516.2	103.24
60	0.917	11.496	0.0115	50	5.75	517.5	535.3	107.06

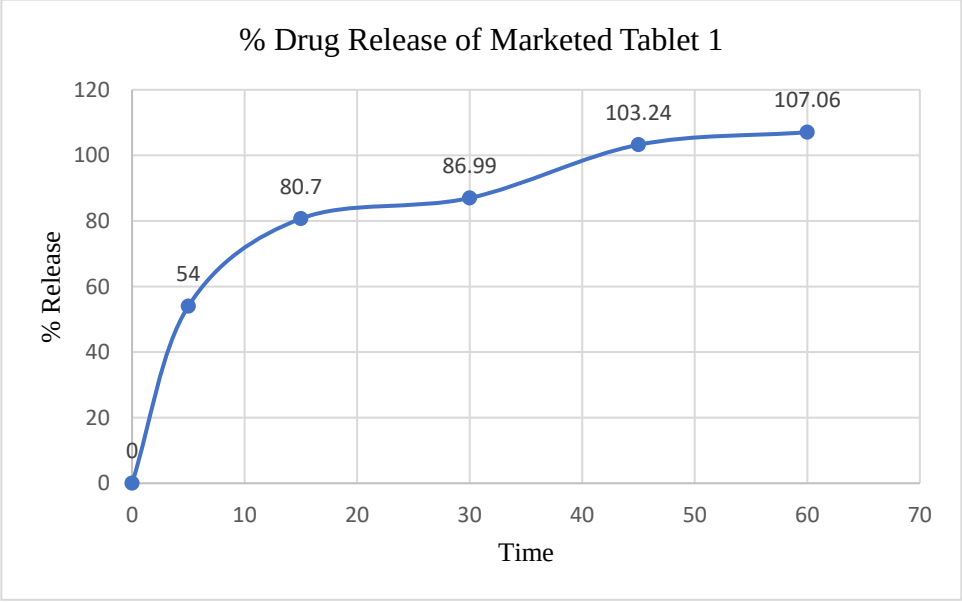

Figure 3.12: %Drug Release of Marketed Metformin Hydrochloride Tablet 1

Table 3.14: Dissolution Profile of Marketed Metformin Hydrochloride Tablet 2

Time (min)	Absorbance	Conc. (mcg/ml)	Conc. (mg/ml)	Dilution Factor	mg/10ml	mg/900ml	Cumulative Amount Released	% Drug Release
0	0	0	0	0	0	0	0	0
5	0.477	5.933	0.0059	50	2.95	265.5	265.5	53.1
15	0.733	9.169	0.0092	50	4.6	414	416.95	83.39
30	0.787	9.852	0.0098	50	4.9	441	448.55	89.71
45	0.897	11.243	0.0112	50	5.6	504	516.45	103.29
60	0.906	11.357	0.0114	50	5.7	513	531.05	106.21

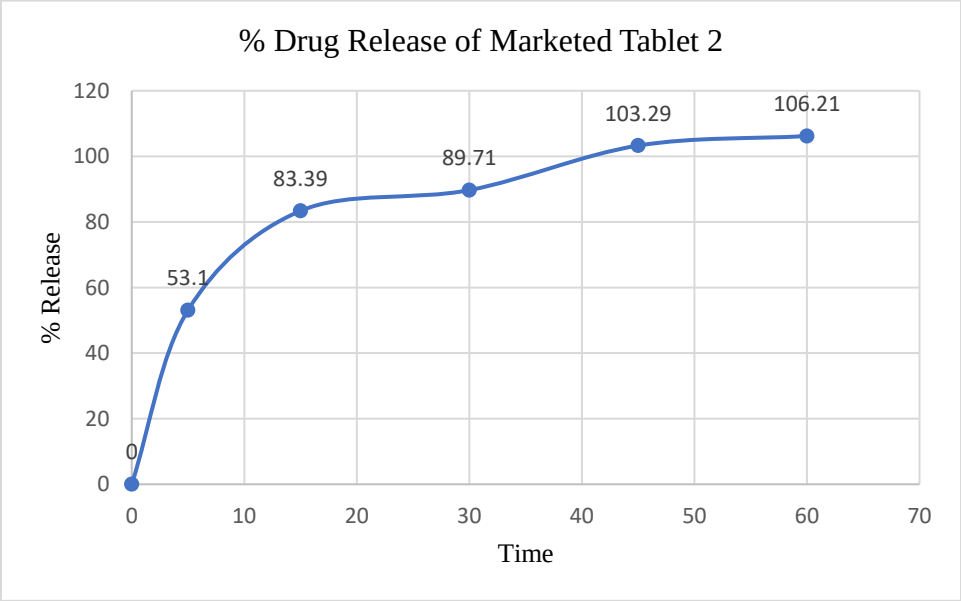

Figure 3.13: %Drug Release of Marketed Metformin Hydrochloride Tablet 2

Table 3.15: Dissolution Profile of Marketed Metformin Hydrochloride Tablet 3

Time (min)	Absorbance	Conc. (mcg/ml)	Conc. (mg/ml)	Dilution Factor	mg/10ml	mg/900ml	Cumulative Amount Released	% Drug Release
0	0	0	0	0	0	0	0	0
5	0.489	6.085	0.0061	50	3.05	274.5	274.5	54.9
15	0.726	9.081	0.0091	50	4.55	409.5	412.55	82.51
30	0.774	9.688	0.0097	50	4.85	436.5	444.1	88.82
45	0.891	11.167	0.0112	50	5.6	504	516.45	103.29
60	0.912	11.432	0.0114	50	5.7	513	531.05	106.21

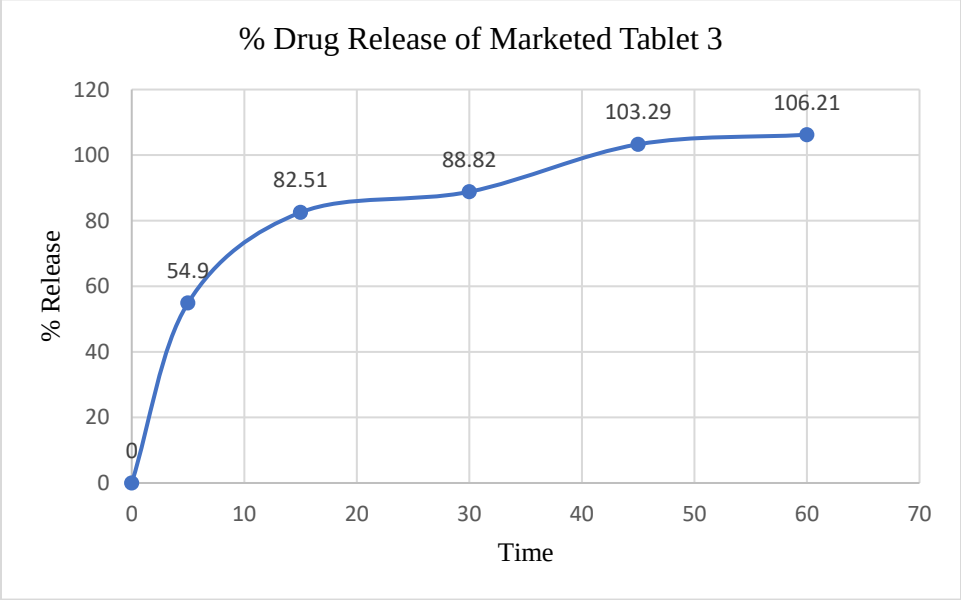

Figure 3.14: %Drug Release of Marketed Metformin Hydrochloride Tablet 3

Now the visual representation of % Drug Release of three different marketed metformin hydrochloride tablets are demonstrated in Figure 3.15

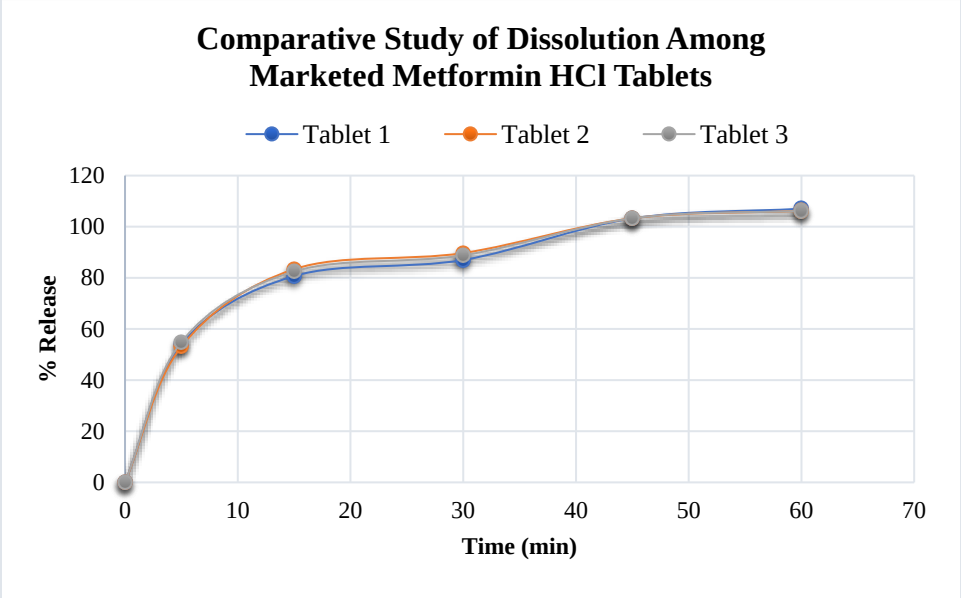

Figure 3.15: Comparative Study of Dissolution among Marketed Metformin HCl Tablets

For determining the potency of the formulated tablet, a total of two tablets were utilized. These tablets were meticulously crushed and combined with the resulting powder. If required, the powder was then appropriately diluted after being mixed with a suitable solvent. Absorbance was measured using a spectrophotometer as part of the process.

Table 3.16, 3.17 as well as figure 3.16, 3.17 represent the outcomes derived from forecasting the proportion of drug release from formulated tablets over a period of time.

Time (min)	Absorbance	Conc. (mcg/ml)	Conc. (mg/ml)	Dilution Factor	mg/10ml	mg/900ml	Cumulative Amount Released	% Drug Release
0	0	0	0	0	0	0	0	0
5	0.126	1.49	0.0015	6.67	0.099	8.944	8.944	89.44
15	0.159	1.91	0.0019	6.67	0.127	11.466	11.565	115.65
30	0.173	2.09	0.0021	6.67	0.139	12.546	12.674	126.74
45	0.195	2.37	0.0024	6.67	0.158	14.227	14.494	144.94

60	0.264	3.24	0.0032	6.67	0.216	19.450	19.875	198.75

Table 3.16: Dissolution Profile of Formulated Metformin Hydrochloride Tablet 1

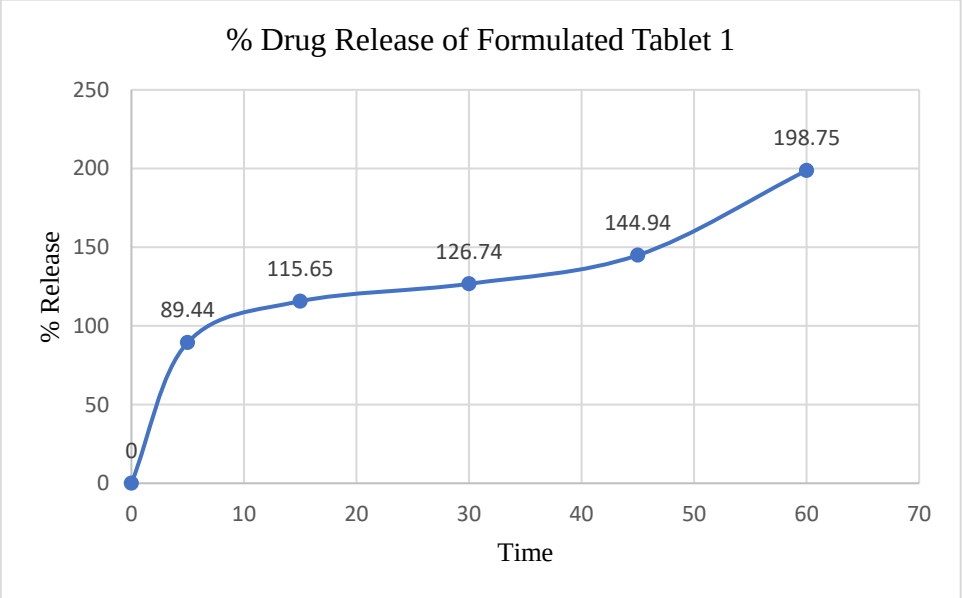

Figure 3.16: %Drug Release of Formulated Metformin Hydrochloride Tablet 1

Table 3.17: Dissolution Profile of Formulated Metformin Hydrochloride Tablet 2

Time (min)	Absorbance	Conc. (mcg/ml)	Conc. (mg/ml)	Dilution Factor	mg/10ml	mg/900ml	Cumulative Amount Released	% Drug Release
0	0	0	0	0	0	0	0	0
5	0.125	1.48	0.0015	6.67	0.099	8.884	8.884	88.84
15	0.154	1.84	0.0018	6.67	0.123	11.046	11.144	111.44
30	0.170	2.05	0.0021	6.67	0.137	12.306	12.429	124.29
45	0.198	2.40	0.0024	6.67	0.160	14.407	14.677	146.77
60	0.26	3.18	0.0032	6.67	0.213	19.170	19.590	195.90

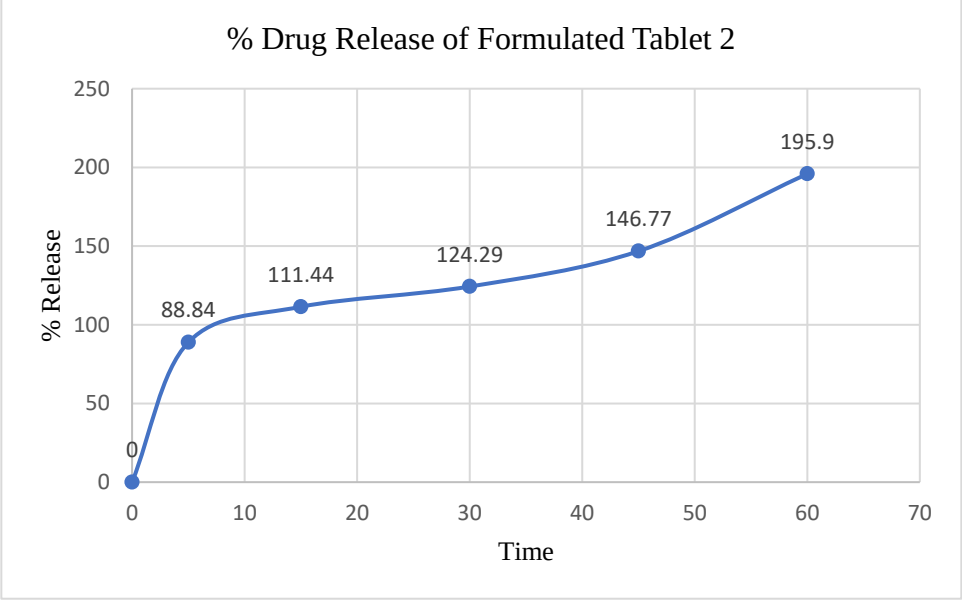

Figure 3.17: %Drug Release of Formulated Metformin Hydrochloride Tablet 2

Now the visual representation of % Drug Release of two different formulated metformin hydrochloride tablets are demonstrated in Figure 3.18.

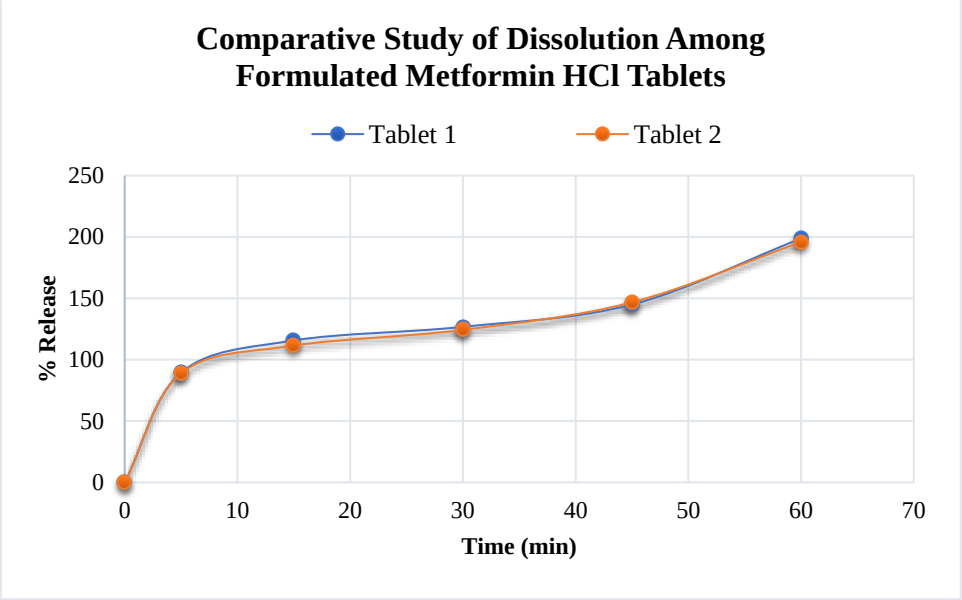

Figure 3.18: Comparative Study of Dissolution among Formulated Metformin HCl Tablets

The visual representation of Comparison for both marketed and formulated Metformin Hydrochloride Tablets' % Drug Release is demonstrated in Figure 3.19

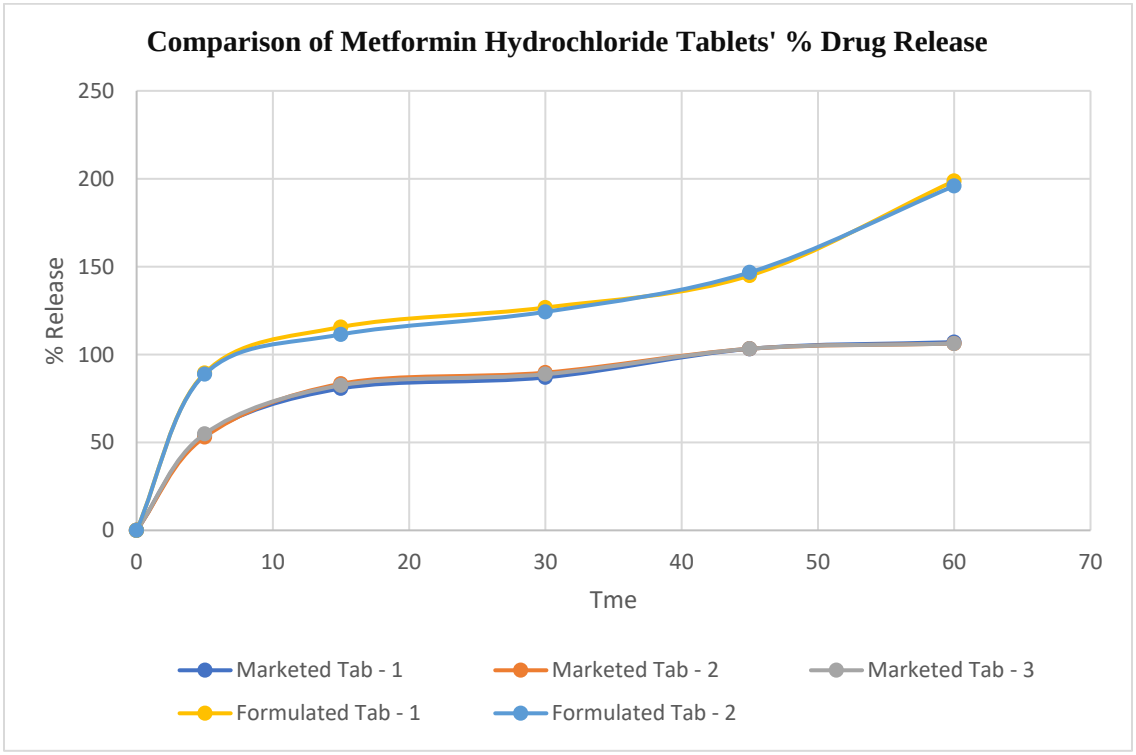

Figure 3.19: Comparative Study of Dissolution among Metformin HCl Tablets

3.8.1 Discussion

As stipulated in the USP Monograph, immediate-release tablets must dissolve by a minimum of 80% within a duration of roughly 30 minutes (Lachman *et al.*, 1976). It is worth mentioning

that both the commercially available tablets and the formulated tablet adhere to this requirement.

3.9 Standard Curve

The correlation between absorbance and concentration, commonly known as the standard curve, is a pivotal aspect of the research, especially when evaluated at different time intervals in comparison to the relevant standard curve. The data illustrating the absorbance-concentration relationship of metformin is provided in Table 3.18.

Table 3.18: Concentration vs Absorbance

Concentration (µg/ml)	Absorbance
1.2	0.096
2.4	0.196
3.6	0.296
4.8	0.39
6	0.491
7.2	0.583
8.4	0.658
9.6	0.766
10.8	0.869
12	0.952

The concentrations of the solutions were depicted on the X-axis, while the corresponding absorbance values were represented on the Y-axis. Subsequently, the standard curve was generated accordingly, as illustrated in Figure 3.20.

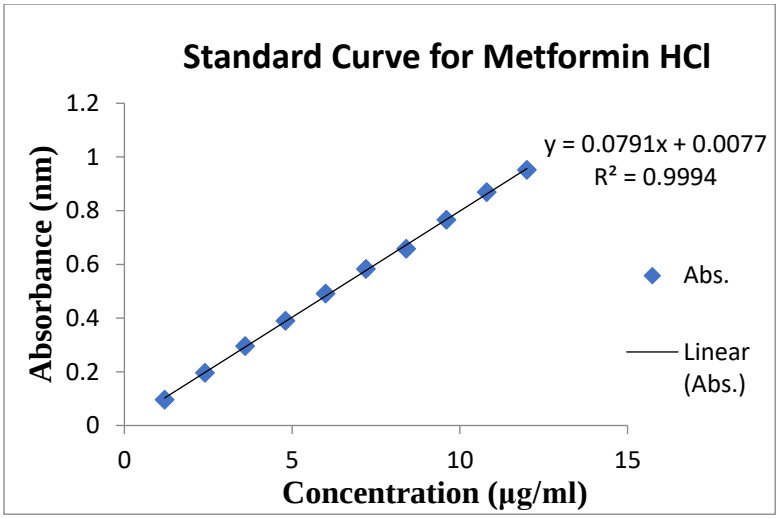

Figure 3.20: Standard Curve for Metformin HCl

3.9.1 Discussion

R^2 is the proportion of variance in a statistical measure. Value of R^2 is observed 0.9994 which indicates a good standard curve as the R^2 value should be as near as possible towards one and should be higher than 0.95 (Chicco *et al.*, 2021).

4. Conclusion

The aim of this investigation was to assess the selected brand using various medical parameters, striving for optimal outcomes within the pharmaceutical market. *In vitro* dissolution tests serve as valuable tools in determining product suitability. Findings reveal chemical uniformity across the products, with all 20 metformin hydrochloride tablets meeting requirements for weight variation, thickness, diameter, dissolution, and potency. While tablet hardness deviated from specifications, the disintegration time was examined to ensure quality, confirming compliance within the specified range. The comparison conducted between the commercially available and laboratory-produced tablets demonstrated strict adherence to the quality standards set forth by the US Pharmacopeia, indicating that both types of tablets met the required criteria. However, the findings also suggested areas for potential improvement in the formulation process of the laboratory-produced tablets. This study serves as a foundation for *in vitro* assessments of brand quality, highlighting the importance of government oversight, manufacturer adherence, and independent drug surveillance. Regular studies of this nature are essential to ensure optimal dosage formulations are consistently employed.

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