EVALUATION OF DIFFERENT MARKETED AMLODIPINE BESYLATE TABLETS IN BANGLADESH

By

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A thesis submitted to the School of in partial fulfillment of the requirements for the degree of Bachelor of Pharmcy

School Of Pharmacy

BRAC University

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Declaration

It is hereby declared that

1. The thesis submitted is my own original work while completing degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I have acknowledged all main sources of help.

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Approval

The project titled "Evaluation of Different Marketed Amlodipine Besylate Tablets in Bangladesh" submitted by Mst. Mahfuja Tabassum Miti – ID: 20346057 of Summer, 2020 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy.

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Ethics Statement

Any kind of trial or experiment related to Human or Animal does not involve in this whole study.

Abstract

Amlodipine is a widely used calcium channel blockers as a treatment option for hypertension. In this study some key pharmaceutical parameters such as friability, hardness, disintegration, dissolution and potency of five different brands (A-E) of amlodipine were evaluated following the USP guidelines. UV-VIS spectrophotometer was used to determine the dissolution profile and potency of the drugs. All the brands comply with the USP requirements in friability and disintegration test, however, little variation in hardness and dissolution time was observed. Potency of all the brands meet the specification as per USP except brand D. The evaluation from the analysis highlights the importance of continuous monitoring of quality control parameters in ensuring therapeutic efficacy and patient safety in different brands of amlodipine. The evaluation highlights the importance of monitoring the quality control parameter continuously from the analysis for ensuring the patient safety and therapeutic efficacy in different brands of amlodipine.

Keywords: Amlodipine, Friability Test, Hardness Test, Disintegration Test, Dissolution Test, Potency Test.

Dedication

Dedicated to my beloved Family, Grandfather and my project supervisor Dr. Hasina Yasmin.

Acknowledgement

Firstly, I would like to thank and want to show my heartful gratitude to almighty Allah for his support and assistance. His unlimited blessing and guidance empowered me with enough strength throughout this journey and without his blessing this journey would not have been achieved.

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List of Acronyms

DASH - Dietary Approaches to Stop Hypertension

HBPM - Home Blood Pressure Monitoring

HCl - Hydrochloric Acid

USP - United States Pharmacopeia

ABPM - Ambulatory Blood Pressure Monitoring

ACE - Angiotensin-Converting Enzyme

API - Active Pharmaceutical Ingredient

ARB - Angiotensin II Receptor Blocker

N - Newton (unit of force)

STD - Standard Deviation

Avg - Average

RPM - Revolutions Per Minute

In Vitro - In a controlled environment, outside a living organism

L-type - Referring to a specific type of calcium channel

Abs - Absorbance

Chapter 1

Introduction:

1.1 Hypertension:

Hypertension, known as high blood pressure when the blood vessel raises the pressure above normal ranges. Blood pressure is basically a force that the blood applies averse to the walls of a blood vessel when the heart contracts and relaxes and relies on the ability of the heart and the resistance of the blood vessel (Rodgers et al., 2018). It is an extensive and relevant health issue marked by increased blood pressure within arteries. Premature mortality and cardiovascular disease are happened on a global scale due to the contribution of this situation (Inyang et al.,).

1.2 Classification:

According to the American College of Cardiology and the American Heart Association explain blood pressure ranges as:

Normal blood pressure - (Systolic <120 mm Hg, Diastolic< mm Hg)

Elevated blood pressure - (Systolic 120-129 mm Hg, Diastolic <80 mm Hg)

Grade 1 hypertension - (Systolic 130-139 mm Hg, Diastolic 80-89 mm Hg)

Grade 2 hypertension - (Systolic 140 mm Hg and over, Diastolic 90 mm Hg and over)

When the systolic bp is more than 180 mm Hg and diastolic bp is more than 120 mm Hg then this state is called hypertension crisis. Besides, hypertension can be classified as primary hypertension and secondary hypertension. Most adults are suffering with primary hypertension or essential hypertension. In spite the exact cause of hypertension is

unspecified even with years of research. Amalgamation of genetics, diet, age and lifestyle, smoking, excess alcohol consumption, obesity, too much salt in your diet, lack of exercise, stress are included in the lifestyle factor which may be conferring to primary hypertension. Blood pressure and risk of complication from hypertension can be reduced by modification in diet and lifestyle. Unlike primary hypertension, there is an identifiable and potentially reversible reason for secondary hypertension. But the cases for secondary hypertension is only 5% to 10% which is more widespread in to young people. People of 18 to 40 years old have an estimated 30% of secondary type hypertension. Thyroid malformation, constriction of aorta, obstructive sleep apnea, hormone malformation, adrenal gland disease and side effect of specific medication inclusive of stimulants, antidepressants, birth control pills, diet aids are the fundamental reason for secondary hypertension (Hecht, 2024).

1.3 Epidemiology of Hypertension:

Worldwide hypertension is a prime public health challenge as a consequence of its soaring frequency and accompanying risks of cardiovascular and kidney disease which spotted as the foremost risk factor for mortality and categorized third as a source of disability-adjusted life-years. In 2000 the estimated numbers of hypertension among adults were 972 million (957-987 million), between them 333 million (329-336 million) in economically developed countries and 639 million (625-654 million) in economically developing countries. In 2025 the estimated numbers of hypertension among adults were prognosticated to rise by about 60% to a total of 1.56 billion (1.54-1.58 billion) (Reynolds et al., 2005). Simultaneously in economic development progresses, high socioeconomic status is initially affected by hypertension, however at later level of economic

development, the pervasiveness of hypertension and its repercussion are largest in those with lower socioeconomic status; this circumstance is observed both within and between countries. Additionally, the rate of change in widespread of hypertension from 2000 to 2010 has been significantly expeditious than in earlier epidemiological transition. Universally, around 3.5 billion adults have >110-115 mmHg non-optimal systemic BP levels and 874 million have more than or equal to 140 mmHg BP level (Rodgers et al., 2018). Hypertension works as a primary risk factor for heart disease and stroke bcoming major reason for death in worldwide. As per latest analysis of the year 2000 shown that about 972 million people in worldwide are living with hypertension, in addition it is estimated that the number will increasing rapidly more than 1.56 billion by the year of 2025 (Fodor et al., 2006). As specified by recent studies, among non-communicable diseases hypertension is an issue in developed countries. In low or low-middle-income countries, especially in South Asia, most people are live with hypertension. In Bangladesh the pervasiveness of hypertension was higher in males which was estimated 33.1% than females which was estimated 24.4%. Due to less likely smoking and predispose to use health services and report poor health, the thing that explain women are healthier and less likely to have hypertension. As the age escalating, the risk for developing hypertension is also escalated. People who have more than 60 years old have highest pervasiveness rate as estimated 41% while the lowest was in young people as estimated 22%. There is a positive congruous between the occurrence of hypertension and monthly income, correlating with that people who earn more than 50,000 taka per month have a chance of reaching maximum prevalence at estimated 66.7%. In addition, there was a statistically notable correlation between sedentary work and hypertension (Majumder et al., 2024). Following by a recent study, 20.6% people belong to rural area have high frequency of

hypertension and 15.8% have grade 1 and 4.8% have grade 2 hypertension (Tarafdar et al., 2023).

1.4 Pathophysiology:

Blood pressure is maintained by many physiological mechanisms which play a great role in the development of hypertension. But still some uncertainty remains in the pathophysiology of hypertension. Such as:

Insulin Sensitivity: Some risk factors like obesity, diabetes mellitus, glucose intolerance, included in a single syndrome called metabolic syndrome which can cause vascular damage or increase blood pressure and create hypertension. Besides, high blood pressure and insulin resistance can make the damage higher.

Genetic factors: Hypertension can transfer from one generation to another through genetic components. Multiple genes work together for the elevation of blood pressure. People whose parents have hypertension, the chance of developing hypertension in them is twice more than others. Though the similarities of blood pressure among them can happen due to their same lifestyle or food habits.

Hypercoagulability: Hypertension can increase the abnormalities such as endothelial dysfunction in the vessel wall. Besides, it can damage the blood components and create issues like blood clots. These together can damage several organs.

Cardiac output and peripheral resistance: Normal blood pressure depends on the cardiac output and peripheral resistance. In case of hypertension, the cardiac output remains normal but due to constriction of small arterioles the peripheral resistance becomes high. Also, the smooth muscle which builds the small arterioles constrict due to high levels of calcium ion that increase the blood pressure, ultimately causing

hypertension. Certain medication helps to relax the arterioles which lower the blood pressure.

Renin-angiotensin system: Renin-Angiotensin system plays a crucial role in the maintenance of blood pressure or hypertension. In this pathway, when Na+ level becomes low then a hormone called renin is released from the kidney which can also be released by the activation of the sympathetic nervous system. Then renin is converted into angiotensin, angiotensin into angiotensin I and angiotensin I into angiotensin II. Angiotensin II works as a vasoconstrictor that raises blood pressure.

Autonomic nervous system: Sympathetic nervous system plays a great role in maintaining blood pressure by constriction or dilation. Here epinephrine and norepinephrine act indirectly to cause hypertension.

Endothelial dysfunction: Endothelial cells in the blood vessel helps to control the blood pressure. It produces nitric oxide which causes vasoconstriction. If the endothelium does not work effectively, it will create hypertension (Breevers et al., 2001).

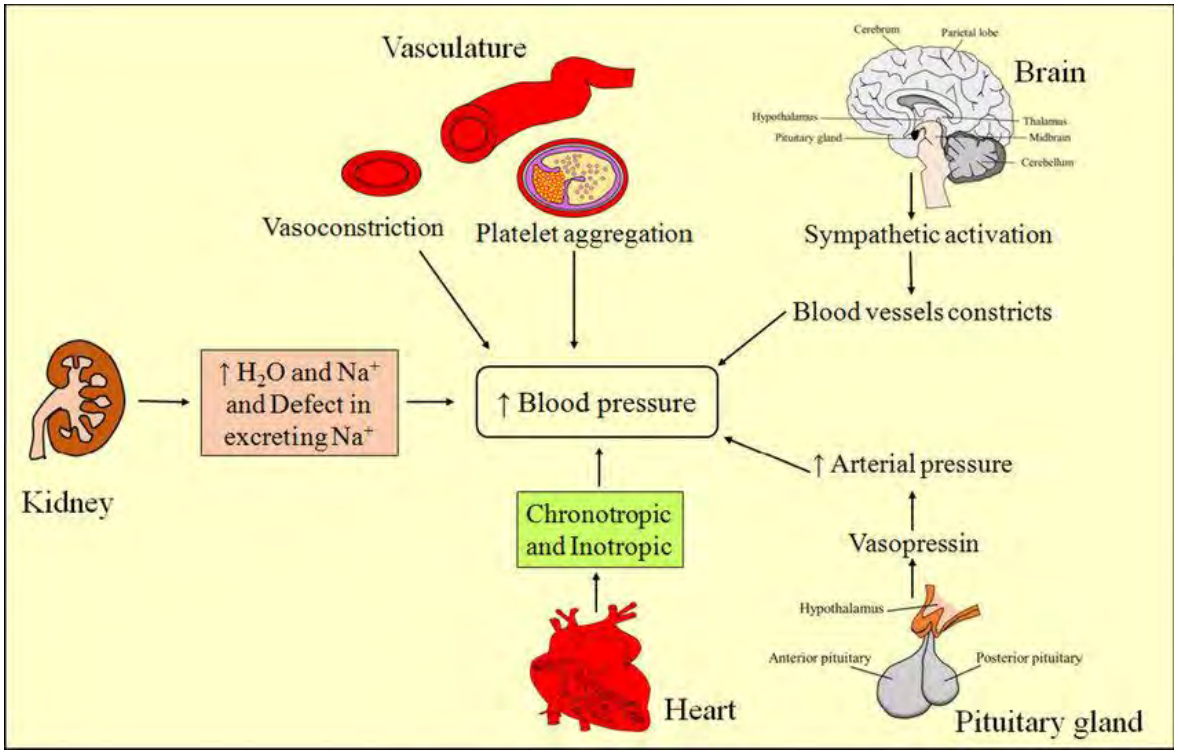

Figure 1: Pathophysiology of Hypertension (Grewal et al., 2023)

1.5 Symptoms:

Progressive exercise dyspnea is the cardinal symptom of hypertension, frequently along with fatigue and exhaustion (Klose et al., 2017). Furthermore, some common symptoms of hypertension are:

- Chest pain
- Headaches
- Dizziness
- Blurred vision or other vision changes
- Buzzing in the ears
- Nausea
- Vomiting
- Difficulty breathing
- Abnormal heart rhythm (WHO, 2023)

As the disease progress, new symptoms can occur like bendopnea (dyspnea on bending down), syncope during or immediately after physical exercise and the existing one become worse. As these symptoms are non-specific, so delay of many months or even years can be happened between the onset of symptoms and diagnosis. People who have hypertension, frequent syncope on slight exertion perspicuously indicate the presence of a life-threatening state associated with high mortality (Klose et al., 2017).

1.6 Diagnosis:

Several national and international guidelines are present for the diagnosis and treatment of hypertension (Tinawi, 2022). To exclude the secondary causes of hypertension and to

determine the target organ damage; history, routine laboratory tests and physical examination are needed. By measurement of blood pressure in home or office, or from the measurement of ambulatory 24-hour blood pressure hypertension can be diagnosed where in all cases recommended measurement technique and equipment are used (Simces et al., 2012). When blood pressure is measured in clinic, the threshold for hypertension is 140/90 mmHg. If the diagnosis of hypertension is based on out-of-office management, there is the possibility or risk of the detection of white-coat hypertension that is determined if the difference of reading is >20/10 mmHg between the ambulatory or average daytime home measurements and clinic readings. Ambulatory BP monitoring (ABMP) is referred as goal standard but is not really recommended because is not suitable for every people where home BP monitoring (HBPM) is offered as an alternative. In case of home BP monitoring, patients at least should have to take two recordings, 1 minute apart, two times a day for 4-7 days. In this case, the readings of the first day should be discounted because of accuracy and the mean of remaining reading is used. If the BP is close to 140/90 mmHg (diagnostic threshold), particularly in younger people (aged <60 years), then ambulatory BP monitoring is suggested to confirm the diagnosis where threshold for ambulatory BP monitoring or home BP monitoring is set 135/85 mmHg. People with type 2 diabetes, aged ≥80 years standing BP measurement should be suggested for them. In case of standing BP measurement, the blood pressure has to measure after the person has been standing for at least 1 minute. If the postural drop in systolic BP is >20 mmHg in comparison with sitting BP, then should have focused on standing BP (Jones et al., 2020). At first, for the investigation of hypertension for all patient, laboratory tests should be performed like blood chemistry (potassium, sodium, creatinine) level, urinalysis, standard 12-lead electrocardiography to evaluate left ventricular hypertrophy or concomitant evidence of previous myocardial infraction. Besides to check all the cardiovascular risk some other

tests are performed. For example: Fasting blood glucose test and fasting lipids test for the identification of total cholesterol level, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol and triglycerides (Simces et al., 2012).

1.7 Treatment:

As a treatment plan non-pharmacological and pharmacological treatment options are used to overcome hypertension. As non-pharmacological treatment, healthy life style changes can be used to control hypertension which include:

- DASH diet eating plan
- Avoid or limit alcohol
- Get regular physical exercise
- Quit smoking
- Manage stress
- Aim for a healthy weight
- Get enough good quality sleep (National Heart, Lung and Blood Institute, 2024)
- Loose weight, if obese
- Reduce salt and high fat diets

By changing healthy lifestyle high blood pressure is not able to control, then as a treatment option pharmacological treatment or medicine is used as an option. They are known as antihypertensive drugs which included:

Table 1: Classification of Antihypertensive Drugs (Ademosun et al., 2021)

Class	Medication
Alpha Blockers	Doxazosin, Prazosin, Terazosin
Beta Blockers	Atenolol, Acebutolol, Bisoprolol
Calcium Channel Blockers	Amlodipine, Felodipine, Diltiazem
Angiotensin II Receptor Blockers	Losartan, Olmesartan, Azilsartan
Antiarrhythmics	Flecainide, Propafenone, Amiodarone
Angiotensin Converting Enzyme Inhibitors	Captopril, Fosinopril, Quinapril
Diuretics	Thiazide diuretics – Chlorothiazide Potassium-sparing diuretics – Spironolactone Loop Diuretics – Furosemide

Initially or in step 1 calcium channel blockers (Amlodipine, Felodipine) will be prescribed. In step 2 Angiotensin-converting enzyme inhibitor, Angiotensin II receptor blockers or thiazide like diuretics should have been added. If the patient has type 2 diabetes, < 55 years and not black African or American then angiotensin-converting enzyme inhibitor will be prescribed. In step 2 calcium channel blockers or thiazide like diuretics should have been added. In step 3 combination treatment with ACE/ARB, CCB and thiazide like diuretics are used. In step 4, if the potassium level <4.5 mmol/l, then have to consider adding spironolactone. If potassium >4.5 mmol/l, then have to consider adding an alpha or beta blocker (Constanti et al., 2020).

1.8 Calcium Channel Blocker:

Calcium channel blocker works by inhibiting the flow of extracellular calcium which flow through the ion-specific channels. It spans the cell wall. In human calcium channel blockers

especially inhibit the L-type channels among several types of channels. Currently available calcium channel blockers inhibit the inward calcium influx, resulting in the relaxation of vascular smooth muscle cells which causes vasodilation. Ultimately contraction is reduced in cardiac muscle and atrioventricular conduction velocities and sinus pacemaker are slowed. The examples of Calcium channel blockers include: Amlodipine, Felodipine etc (Elliot and Ram, 2011).

1.9 Amlodipine:

Amlodipine which is an antihypertensive and antianginal drug, belongs to the class of calcium channel blockers. In 2014, it is the sixth most popular commonly prescribed in United States and doctor wrote it in almost 78.3 million prescriptions. It is popular because it is able to treat hypertension and angina without the risk of congestive heart failure which listed as an obstacle for other antihypertensive. Patients with chronic stable angina or vasospastic angina may be able to taking amlodipine without the chance of ejection fraction of greater than 40% or heart failure (Jhonson et al., 2016). Furthermore, amlodipine used to relax blood vessels which lowers blood pressure, helping heart to pump blood without difficulty (Piatnochka and Logoyda, 2020). From randomized studies it is shown that, amlodipine is very active in controlling or reducing Systolic blood pressure and Diastolic blood pressure in case of mild and moderate hypertension. For patients who aged ≥50 years, the efficacy of amlodipine is similar as chlorthalidone in case of reducing mean Blood pressure. Amlodipine titration from 5 to 10 mg per day can able to reduce systolic blood pressure in case of Asian people who have mild to moderate hypertension (Sever et al., 2023).

1.10 Chemical structure of Amlodipine:

Amlodipine is anhydrous and contains not less than 90% and not more than 102% C20H25ClN2O5The chemical name is 3-O-ethyl 5-O-methyl 2-(2-aminoethoxymethyl)-4-(2-chlorophenyl)-6-methyl-1,4- dihydropyridine-3,5-dicarboxylate (Piatnochka and Logoyda, 2020). The exact mass is 408.1451996 g/mol (PubChem, 2023).

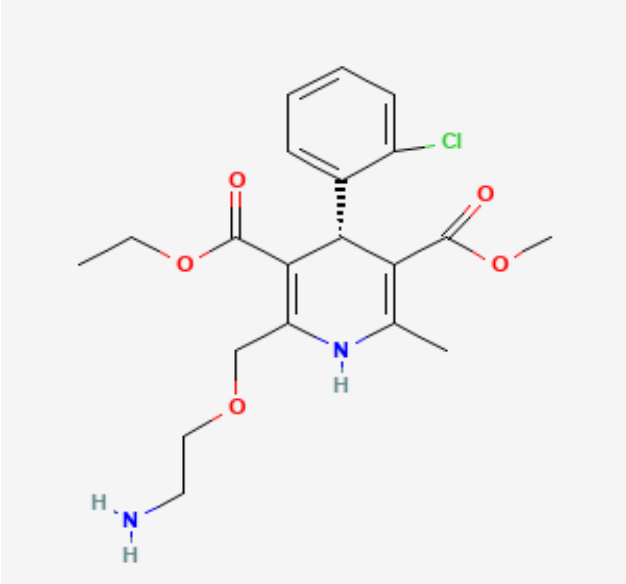

Figure 2: Chemical structure of Amlodipine (PubChem, 2023)

1.11 Solubility:

The solubility of amlodipine Besylate is vary in different solvent based on the properties. The solubility profile:

Table 2: Solubility profile of Amlodipine (Piatnochka & Logoyda, 2020)

Solubility Profile	Name of solvent
Freely soluble	Methanol
Slightly soluble	2-Propanol, Water
Sparingly soluble	Anhydrous ethanol

1.12 Pharmacokinetics and Pharmacodynamics properties:

For oral administration, amlodipine shows 60-65% bioavailability and after the administration the plasma concentration to peak 6-8 hour that comprehensively metabolized by the liver and have terminal elimination half-life of 40-50 hour which is slowly cleared. Furthermore, Amlodipine has a large volume of distribution which is 21 L/kg and create high degree almost 98% protein binding. From several evidence it is found that severe hepatic impairment, age, severe renal impairment affects the pharmacokinetic profile of amlodipine which cause the high plasma concentration and long half-life. Moreover, amlodipine indicates linearity in case of dose-related pharmacokinetics characteristics and in case of steady state, the fluctuation of plasma concentration is small across a dosage interval. Because of the characteristics, amlodipine is more effective for single dosage administration in a day (Meredith & Elliott, 1992).

The pharmacodynamic profile tells how the drug affects the body. In case of hypertensive patients, Amlodipine shows consistent behavior with the disposition of the drug. After the administration of one dose, the blood pressure reduces moderately over 4 to 8 hours and over 24 to 72 hours it returns to the base line slowly. Because of the moderate onset, after the administration of dose, the heart rate remains the same and no changes is observed. Besides, no activation of physiological reflexes is noticed. When amlodipine is taking orally, once a day, it reduced the blood pressure from pretreatment baseline which means it decreases the blood pressure in a certain level compared to the level of before taking the drug. It also shows little fluctuation of blood pressure over the 24 hours dose interval. If any discontinuation of the dose of amlodipine occurs, the blood pressure will slowly return to the baseline within 7 to 10 days and do not find any evidence of rebound effect (Abernethy, 2008).

1.13 Pharmacology:

Amlodipine shows its effect on vascular smooth muscle and cardiac muscle by hindering the influx of extracellular calcium ion through vascular smooth muscles by blocking the L-type calcium channel and myocardial without causing any disturbance on serum calcium concentrations. So, calcium ions cannot enter in the vascular smooth muscle. As a result, dilation occur on the systemic and coronary arteries because of the inhibition of the contraction on cardiac and vascular smooth muscle. (Jhonson and Weinstock, 2016). Muscle relaxation and vasodilation take place, result in decrease in vascular resistance (Rysz et al., 2020). Besides, amlodipine delivers myocardial oxygen in myocardial to the patients who have vasospastic angina (Jhonson and Weinstock, 2016).

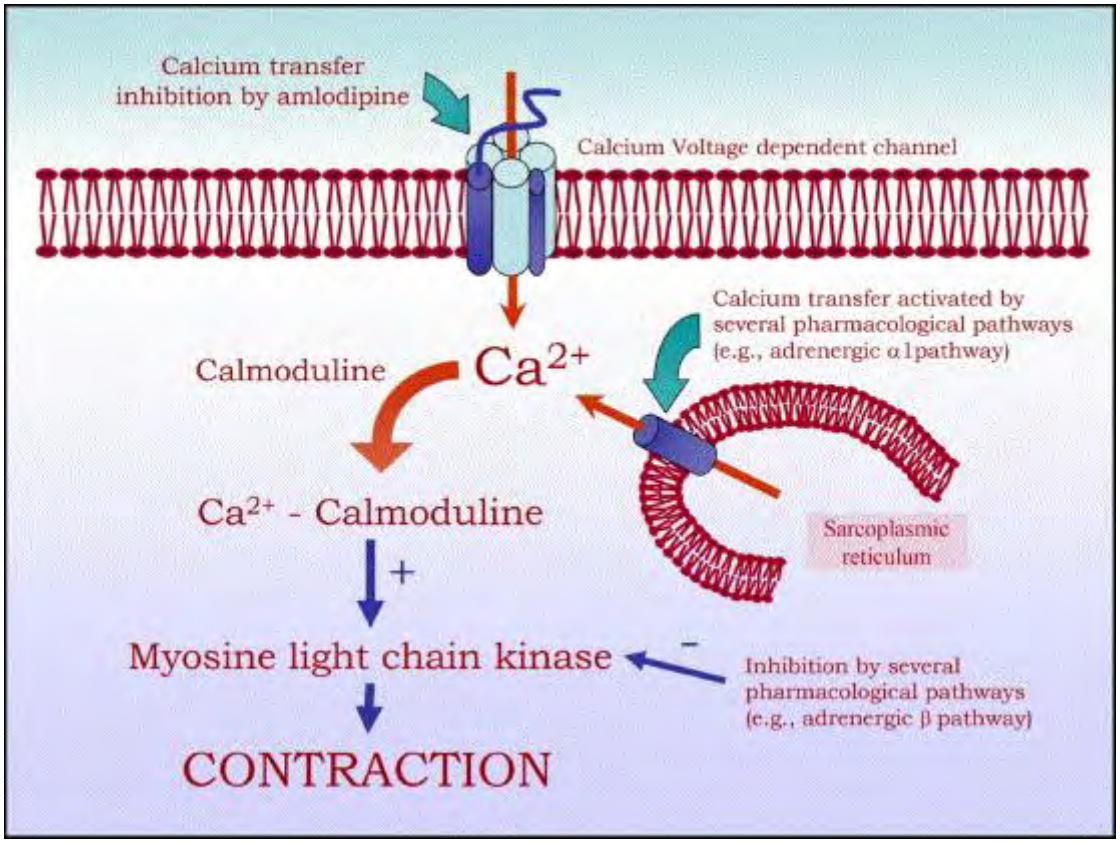

Figure 3: Pharmacology of Amlodipine (Perrot et al., 2005)

1.14 Contraindication:

People cannot take Amlodipine who is allergic to amlodipine any of the excipients used in it (University of Illinois, 2023). Moreover, it is contraindicated in dihydropyridine hypersensitivity due to the chance of causing liver damage. Besides, if a person have severity to narrowing of a certain valve it is contraindicated if someone has aortic stenosis which is a condition when the certain valve in the heart is narrowing extremely or other problems in the heart like clogged arteries; or liver disease (Puckey, 2023).

1.15 Side effects:

Most common side effects of amlodipine are:

- Dizziness
- Swelling of legs or ankles
- Drowsiness
- Pounding of heartbeat or fluttering in your chest
- Irregular heartbeat
- Muscle stiffness
- Feeling tired
- Uncontrolled muscle movements
- Stomach pain
- Nausea
- Flushing such as warmth, redness, or tingly feeling all of a sudden

Emergency medical help is necessary if someone has signs of an allergic reaction to amlodipine like:

- Hives
- Difficulty breathing
- Swelling of face, lips, tongue or throat
- Chest pressure or pain
- Nausea
- Sweating
- Pain spreading to the jaw or shoulder (Puckey, 2023)

1.16 Drug-Drug Interaction

Amlodipine shows interaction with:

- Diltiazem which is used to treat heart problem
- Simvastatin which is used to treat high cholesterol level
- Phosphodiesterase-5 inhibitor which is used for erectile dysfunction
- Cyclosporine which is used to suppress the immune system (Memon, 2024).
- Nefazodone
- Ivacaftor
- Idelalisib
- Dantrolene (Cunha, 2024)
- Antifungal medication
- Antibiotic (University of Illinois, 2023)

1.17 Advantages of Amlodipine:

Amlodipine has distinctive pharmacodynamics and pharmacokinetics properties which make it different from other calcium channel blockers in comparison of safety and efficacy profile, though all CCBs have the same ability to interact with L-type voltage-dependent transmembrane calcium channels. Amlodipine is a dihydropyridine, in comparison with other dihydropyridine, amlodipine has long half-life which is 35 to 50 hours and small renal clearance which is 7 ml/min/mg, though other dihydropyridine have long renal clearance and small half-life. Besides, it has high bioavailability which is 60% to 80% and able to exert its antihypertensive action more than 24 hours after administration of a single oral dose which is helpful for patient compliance. As well, if a single dose is missed, BP level will be controlled. Even after discontinuation of the dose of amlodipine, BP level returns to the baseline within one week without producing any dangerous rebound elevations in the Blood pressure (Wang et al., 2023).

1.18 In vitro Dissolution Testing of Amlodipine:

This article will represent some in vitro testing of amlodipine tablets which are available in the market of Bangladesh. These tests are performed to evaluate the properties and performance of those tablets in a controlled laboratory environment, without the involvement of living organisms which performed to ensure the quality, efficacy and safe administer of tablets in humans. In this article we are going to focus on the dissolution test, disintegration test, potency test, hardness test and friability test.

1.18.1 Friability Test:

Friability test is used to determine how friable tablets are. By doing this test the percentage of weight loss of a tablet is determined (Ahmed, 2023). During packing processes, evaluating the

durability of the tablet is the main purpose of friability test where tablets are placed in a rotating drum over a fixed time. In this research Friability tester was used which was manufactured by Electrolab (EF2 USP) in India. The acceptance range for weight loss is within 1 % (Sabbir et al., 2019). 10 tablets for each brand were used to measure the friability and a total five brands were used in this evaluation.

1.18.2 Hardness Test:

Hardness test is performed for estimating the mechanical strength of the tablets and check the integrity by using a hardness tester. It is basically used to check the breaking point of the tablets or the pressure that requisite to break a tablet. For ensuring the performance and quality of tablets and evaluating the tablet's resistance to stress, hardness test is required (Muller, 2023). For oral tablets, the acceptance range is four to ten kg (Hosen et al., 2018). Tablet Hardness Tester, YD-1 (Wincom, China) was used during the research. 10 tablets for each brand were used to measure the hardness and a total five brands were used in this evaluation.

1.18.3 Disintegration Test:

For allowing the active ingredients to be absorbed in the body tablets are breaking down into smaller particles or granules. This ability is determined by disintegration test. The disintegration test is performed for ensuring the maximum the bioavailability of the API from the majority of solid dosage forms (Zeitler & Markl, 2017). Besides, it is performed to ensure the effectiveness and constant performance of a tablet. In this research, disintegration study was performed by using a disintegration testing device Wincom which was manufactured by china. Four tablets for each brand were used in four baskets to measure the disintegration and a total of five brands were used in this evaluation.

1.18.4 Dissolution Test:

Extent and rate of solution formation from a dosage form is determined by performing dissolution test which is important for tablet's bioavailability, bioequivalence and therapeutic

effectiveness. A dissolving study of the sample tablets was carried out with the assistance of a Tablet dissolution tester Logan instruments Corporation, USA (Model-UDT-804). Six tablets for each brand were used in four baskets to measure the disintegration and a total of five brands were used in this evaluation.

1.18.5 Potency Test:

The quantity of the active pharmaceutical ingredients which present in a tablet is determined by Potency test. This analytical method ensures that each tablet has an appropriate amount of active pharmaceutical ingredients and patients will receive an effective and safe treatment.

Chapter 02

2. Methodology:

2.1. Materials:

Following glassware and others have been used for the study:

Table 3: Lists of Glasswares and others

No	Glasswares
01.	Glass rod
02.	Volumetric flask
03.	Pipette
04.	Pipette filler
05.	Spatula
06.	Morter and pestle
07.	Filter funnel
08.	Filter paper
09.	Beaker

2.2. Reagents and Chemicals:

Following reagents used throughout the study are listed below:

Table 4: Lists of Reagents and Chemicals

No.	Reagents
01.	0.01 N Hydrochloric Acid
02.	100% Methanol
03.	Distilled Water
04.	Standard Amlodipine (API)
05.	50% Methanol and 50% water

2.3. Instruments:

Following instruments used in the whole process are listed below:

Table 5: Lists of Instruments

No.	Name of the equipment	Manufacturer	Model	Origin
01.	Potency Tester	UV-Spectrophotometer	U-2910	Japan
02.	Analytical Balance		XY-6002G	Japan
03.	Hardness tester	Wincom	YD-1	China
04.	Friability tester	Electrolab	(EF2 USP)	India
05.	Disintegration Machine	Wincom	BJ-2	China
06.	Dissolution Machine	Logan instruments Corporation	UDT-804	USA

Figure 4: Friability Tester

Figure 5: Hardness Tester

Figure 6: UV-Vis Spectrophotometer

Figure 7: Disintegration Machine

Figure 8: Dissolution Machine

2.4. Methodology:

Samples of five different reputed brands of 5 mg of amlodipine tablet of Bangladesh were collected which were represented from letter A, B, C, D and E. In vitro testing of these brands was performed in this study to determine their performance and properties without the involvement of living organism rather in a controlled laboratory environment. Following laboratory tests were performed:

2.4.1: Friability Test:

Friability test was performed to determine the percentage of loss of the tablets to ensure the durability of the tablets during packaging, shipping or other mechanical conditions. This measurement helps us to understand cracking, crumbling and breaking properties during handling and storage and withstand enough pressure or not. For this used friability tester EF2 USP, manufactured by Electrolab in India. 10 tablets from each marketed brand were taken, weighed them and note the initial weigh. Placed the tablets in the drum of friability tester in section 1. 25 rpm rotation for 1 minute was placed and the count was set to 100. After succeeding the rotation collected the tablets and reweighed them. Noted down the weigh as final weigh. The percentage of weight loss was calculated by using a formula. As per USP, the percentage of weight loss should be not more than 1%.

Percentage of loss: $\left(\frac{Initial\ Weigh - Final\ Weigh}{Initial\ Weigh}\right)$ x 100

Brand A:

Initial weight: 0.66 gm

After weight: 0.66 gm

% of weight loss: $\left(\frac{0.66-0.66}{0.66}\right)$ x 100

= 0%

Using the same procedure and equation, calculated the percentage of weight loss for remaining brand B, C, D and E respectively.

2.4.2. Hardness Test:

Hardness test is performed to evaluate the breaking point of a tablet to estimate its mechanical strength and integrity for quality and performance of a tablet. If a tablet is too soft, it will disintegrate during shipment. If a tablet is too hard, it will hamper the process of disintegration and dissolution. For this, an acceptable range is decided to provide desire effect which is four to ten kg (Dulla et al., 2018).

In this study 10 tablets from each five brands were taken for testing the hardness. For this Tablet Hardness tester was used, model YD-1, manufactured by Wincom in China. For hardness test placed the tablets in between the two jaws of hardness tester vertically. Then started to rotate the screw thread for applying the force until the tablet gets fractured. Noted down the reading point when tablet gets cracked in kg. The same procedure was repeated one time for each five brands.

2.4.3. Disintegration Test:

Disintegration test is done by measuring the time a tablet needs to disintegrate in liquid medium that represents our body fluid, which estimate the capacity of a tablet to break down into smaller granules so why the active ingredients of a tablet get absorbed in the body.

For this study BJ-2 disintegration machine was used which manufactured by Wincom in China. In this disintegration testing machine, there are six 1000 ml vessel which was filled with 600 ml distilled water. Each vessel contains rotating basket where tablet needs to place. The temperature was set 37°C as same as body temperature. In six baskets placed 4 tablets for each brand and started the machine. Started the stop watch to record the time for each tablet needs

to disintegrate. But there are certain conditions that determine the complete disintegration of a tablet. There should be no residue remain on the basket or screen.

2.4.4. Dissolution Study:

In this study dissolution test was carried out in a tablet dissolution tester, Model-UDT-804, manufactured by Logan instrument Corporation in USA. The purpose of this test was to measure the percentage of drug release from a product under certain test conditions. For this, six tablets from each five brands were used.

2.4.4.1. Preparation of dissolution medium:

Here used 0.01N HCl for the preparation of dissolution medium. For this, in a 1000 ml volumetric flask 0.833 ml pure HCl was taken and make it up to 1000 ml with distilled water.

2.4.4.2. Preparation of Standard solution:

For the preparation of standard solution, from Eskayef pharmaceuticals standard amlodipine was collected. To prepare this, 24 mg standard amlodipine was weighed in a weigh balance and taken in a 50 ml volumetric flask. Made the flask up to 50 ml with 0.01N HCl. Then 3 ml solution was taken from the 50 ml volumetric flask and transferred it into a 100 ml volumetric flask. Made it up to 100 ml with 0.01 N HCl.

2.4.4.3. Preparation of Sample:

As a sample used six tablets from each five brands. Then took 500 ml 0.01N HCl in each six vessels of the dissolution test machine. Waited until the temperature of the machine raised 37+-0.8 C. After that started paddle and dropped six tablets in six vessels. When the tablets were dropped the timer have to start immediately. After 30 minutes collected 10 ml from each vessel and filtered each solution. Followed the same procedure for other brands.

2.4.4.4: Percentage of Release:

The absorbance was measured by using UV Spectrophotometer. After starting the machine, λ_{max} was set 238 nm for dissolution. After that, by using 0.01N HCl in the cubet nullified the absorbance for the solvent. Then took the absorbance for standard solution and the absorbance for the six tablets of each five brands simultaneously.

The equation for the percentage of the labeled amount of amlodipine dissolved:

Result = $\left(\frac{Au}{As}\right)$ x $\left(\frac{Cs}{L}\right)$ x D x $\left(\frac{Mr1}{Mr2}\right)$ x V x 100

Where,

Au = Absorbance of the Sample solution

Au = Absorbance of the Standard solution

Cs = Concentration of the Standard solution (mg/ml)

L = Label claim (mg/Tablet)

D = Dilution factor of the Sample solution

Mr1 = Molecular weight of the amlodipine, 408.88

Mr2 = Molecular weight of the amlodipine besylate, 567.06

V = Volume of the medium, 500 ml

Brand A:

Table 6: Absorbance of Dissolution study

Absorbance
0.376
0.422
0.437
0.445
0.473
0.490

For sample 1,

Au = 0.376

As = 0.551

Cs = 0.0139

L = 5

D = 1

Mr1 = 408.88

Mr2 = 567.06

V = 500

% Of release: ($\frac{0.376}{0.511}$) x ($\frac{0.0139}{5}$) x 1 x ($\frac{408.88}{567.06}$) x 500 x 100 = 73.74%

For sample 2,

% Of release: $= \left(\frac{0.422}{0.511}\right) \times \left(\frac{0.0139}{5}\right) \times 1 \times \left(\frac{408.88}{567.06}\right) \times 500 \times 100 = 82.77\%$

For sample 3,

% Of release: $\left(\frac{0.437}{0.511}\right) \times \left(\frac{0.0139}{5}\right) \times 1 \times \left(\frac{408.88}{567.06}\right) \times 500 \times 100 = 85.71\%$

For sample 4,

% Of release: $\left(\frac{0.445}{0.511}\right) \times \left(\frac{0.0139}{5}\right) \times 1 \times \left(\frac{408.88}{567.06}\right) \times 500 \times 100 = 87.28\%$

For sample 5,

% Of release: $\left(\frac{0.473}{0.511}\right) \times \left(\frac{0.0139}{5}\right) \times 1 \times \left(\frac{408.88}{567.06}\right) \times 500 \times 100 = 92.77\%$

For sample 6,

% Of release: $\left(\frac{0.493}{0.511}\right) \times \left(\frac{0.0139}{5}\right) \times 1 \times \left(\frac{408.88}{567.06}\right) \times 500 \times 100 = 96.01\%$

Avg of percentage of release: 73.74%+82.77%+85.71%+87.28%+92.77%+96.01% = 86.38%

2.4.5 Potency Analysis:

Potency test is performed for the determination of the amounts of active pharmaceuticals ingredients present in a tablet to produce the desired therapeutic effect. For this calibration curve of the standard amlodipine was taken and equation was found from the curve which needed to calculate the amounts of API in the five branded drugs.

2.4.5.1 Preparation of the Calibration Curve:

For the potency test of the amlodipine standard, amlodipine was taken from the Eskaef Pharmaceuticals. As from solubility profile we know that, amlodipine is slightly soluble in water, but freely soluble in methanol. For potency test 100% and 50% methanol were used as solvent. In starting, 0.1 gm or 100 mg amlodipine standard was weighed by using a weigh

balance and was taken in a 100 ml volumetric flask. 100% methanol was used to dissolved the standard amlodipine and made the volumetric flask up to 100 ml with 100% methanol to prepare the stock solution where the concentration 1mg/ml. 20 µg/ml, 10 µg/ml, 5 µg/ml, 2.5 µg/ml and 1.25 µg/ml solution were prepared simultaneously by serial dilution using 50% methanol. Followed the same procedure 2 times more. For nullifying the solvent concentration, used 50% methanol as a blank and absorbance of five concentration were taken by using UV-Spectrophotometer, where λ_{max} was set 239 nm. Arranged all the absorbance value from three batches and took the average value for the preparation of calibration curve. Put the value in a Microsoft excel and accordingly calibration curve was prepared.

2.4.5.2. Preparation of the Sample Solution:

For the preparation of sample solution 10 tablets from each five brands were taken. Firstly, took 10 tablets and placed them in a weigh balance and noted down the weigh. Then crushed the tablets finely by using mortar and pestal and placed the powder in a 50 ml volumetric flask. Dissolved the powder using 100% methanol and make it up to 50 ml. After that, by using filter paper filtered the solution. This was the stock solution which concentration was 1mg/ml. Then made 20 µg/ml and 10 µg/ml solution respectively by serial dilution using 50% methanol. Did the same procedure 2 times more to exclude any error. Then by using UV-Spectrophotometer measured the absorbance for all three batches where, set the λ_{max} 239 nm. Arranged all the absorbance value from the three batched and took the average one. Then placed it in a Microsoft excel. Repeated the same procedure for all remaining four brands.

2.4.5.3. Determination of Amlodipine:

By using the equation y=mx+c from standard curve, calculated the value of x and by using x calculated the percentage of amount of amlodipine present in a tablet,

The different concentration of standard amlodipine from 1.25 µg/ml to 20 µg/ml were plotted on a Microsoft excel and the calibration curve was found is attached below:

From the calibration curve the equation we found that,

y = 0.0381x + 0.021

Here, m = 0.0381

C = 0.021

For brand A:

Sample 1,

The y value is the absorbance which is in 10 (µg/ml) = 0.383

0.383 = 0.0381x + 0.021

X = 10 µg/ml

Average weight of the tablet is 0.0652 gm or 65.2 mg

Amount of the sample taken from the tablets = 0.652 gm or 652 gm 1

Dilution factor (DF): 50x50x2

Amount of the drug per tablet = $\frac{concentration\ of\ drug\ x\ Dilution\ factor\ x\ Average\ weight\ of\ tablet}{1000\ x\ Amount\ of\ sample\ taken}$

$= \frac{10\ x\ 50\ x\ 50\ x\ 2\ x\ 65.2}{1000\ x\ 652}$

= 5 mg

Potency = $\frac{5}{5}$ x 100

= 100 %

Sample 2,

0.383 = 0.0381x + 0.021

X = 10.05 µg/ml

Average weight of the tablet is 0.0652 gm or 65.2 mg

Amount of the sample taken from the tablets = 0.652 gm or 652 gm 1

Dilution factor (DF): 50x50x2

Amount of the drug per tablet = $\frac{concentration\ of\ drug\ x\ Dilution\ factor\ x\ Average\ weight\ of\ tablet}{1000\ x\ Amount\ of\ sample\ taken}$

$= \frac{10.05\ x\ 50\ x\ 50\ x\ 2\ x\ 65.2}{1000\ x\ 652}$

= 5.02 mg

Potency = $\frac{5.02}{5}$ x 100

= 100.4 %

Sample 3,

0.379 = 0.0381x + 0.021

X = 9.94 µg/ml

Average weight of the tablet is 0.0652 gm or 65.2 mg

Amount of the sample taken from the tablets = 0.652 gm or 652 gm 1

Dilution factor (DF): 50x50x2

Amount of the drug per tablet = $\frac{concentration\ of\ drug\ x\ Dilution\ factor\ x\ Average\ weight\ of\ tablet}{1000\ x\ Amount\ of\ sample\ taken}$

$= \frac{9.94\ x\ 50\ x\ 50\ x\ 2\ x\ 65.2}{1000\ x\ 652}$

= 4.97 mg

Potency = $\frac{4.97}{5}$ x 100

= 99.4 %

Avg potency: 100%+100.4%+99.4% = 99.93%

From the calibration curve of amlodipine calculated the potency of the brand B, C, D and E respectively.

Chapter 3

3 Results and Discussion:

3.1 Results:

3.1.1 Friability Test:

Results found from the Friability Test are given below:

Table 7: Friability Test of Five brands (A-E) of Amlodipine tablet

	Brand A	**Brand B**	**Brand C**	**Brand D**	**Brand E**
Initial Weight	0.66 gm	1.46 gm	1.37 gm	2.49 gm	0.71 gm
After Weight	0.66 gm	1.46 gm	1.37 gm	2.49 gm	0.71 gm
Percentage of weight loss	0%	0%	0%	0%	0%

3.1.2 Hardness Test

Results found from the Hardness Test are given below:

Table 8:Hardness Test of Five brands (A-E) of Amlodipine tablet

Sample no	Brand A	Brand B	Brand C	Brand D	Brand E
01	3.02 kg ≈ 29.59 N	4.54 kg ≈ 44.54 N	6.69 kg ≈ 65.69 N	9.62 kg ≈ 94.31 N	2.94 kg ≈ 28.85 N
02	2.93 kg ≈ 28.75 N	4.65 kg ≈ 45.67 N	6.71 kg ≈ 65.81 N	9.39 kg ≈ 92.02 N	3.79 kg ≈ 37.15 N
03	3.93 kg ≈ 38.56 N	4.12 kg ≈ 40.43 N	5.64 kg ≈ 55.38 N	8.93 kg ≈ 87.55 N	3.07 kg ≈ 30.10 N
04	3.46 kg ≈ 33.96 N	4.97 kg ≈ 48.80 N	5.97 kg ≈ 58.66 N	8.64 kg ≈ 84.73 N	3.97 kg ≈ 38.97 N
05	2.91 kg ≈ 28.54 N	4.01 kg ≈ 39.90 N	6.46 kg ≈ 63.41 N	7.65 kg ≈ 75.03 N	2.52 kg ≈ 24.69 N
06	4.25 kg ≈ 41.69 N	4.06 kg ≈ 39.87 N	6.86 kg ≈ 67.35 N	8.60 kg ≈ 84.38 N	3.94 kg ≈ 38.66 N
07	3.62 kg ≈ 35.48 N	4.12 kg ≈ 40.43 N	6.49 kg ≈ 63.73 N	9.76 kg ≈ 95.92 N	2.81 kg ≈ 27.55 N
08	4.25 kg ≈ 41.69 N	4.07 kg ≈ 39.93 N	5.74 kg ≈ 56.33 N	9.10 kg ≈ 89.25 N	2.18 kg ≈ 21.40 N
09	3.52 kg ≈ 34.55 N	4.34 kg ≈ 42.61 N	5.63 kg ≈ 55.21 N	8.74 kg ≈ 85.77 N	3.08 kg ≈ 30.19 N
10	2.46 kg ≈ 24.16 N	4.72 kg ≈ 46.24 N	6.23 kg ≈ 61.15 N	8.27 kg ≈ 81.20 N	1.85 kg ≈ 18.16 N
Mean±SD	36.427±6.56 N	44.848±3.49 N	61.112±4.13 N	89.409± 6.72 N	36.727±9.69 N

3.1.3 Disintegration Test:

Results found from the Disintegration Test are given below:

Table 9: Disintegration time Test of Five brands (A-E) of Amlodipine tablet

Sample no	Brand A	Brand B	Brand C	Brand D	Brand E
01	2 minutes 3 seconds	14 seconds	23 seconds	28 seconds	1 minute 32 seconds
02	2 minutes 11 seconds	18 seconds	29 seconds	38 seconds	1 minute 44 seconds
03	2 minutes 30 seconds	24 seconds	56 seconds	36 seconds	1 minute 44 seconds
04	2 minutes 39 seconds	24 seconds	36 seconds	38 seconds	1 minute 46 seconds
Average	2 minutes 21 seconds	20 seconds	36 seconds	35 seconds	1 minute 42 seconds

3.1.4 Dissolution Test:

Results found from the Dissolution Test are given below:

Table 10: Percentage of release from dissolution study of Five brands (A-E) of Amlodipine tablet

Sample no	Brand A	Brand B	Brand C	Brand D	Brand E
% Of release for sample 1	73.74%	61.19%	73.15%	71.98%	79.63%
% Of release for sample 2	82.77%	68.25%	82.18%	82.77%	78.25%
% Of release for sample 3	85.71%	76.29%	86.88%	84.53%	79.24%
% Of release for sample 4	87.28%	77.67%	83.36%	83.94%	85.90%
% Of release for sample 5	92.77%	76.10%	83.94%	84.53%	84.53%
% Of release for sample 6	96.01%	76.29%	84.34%	82.38%	85.71%
Avg % of release	86.38%	72.63%	85.64%	83.19%	82.21%
Mean±STD	86.38±7.1%	72.63±6.60%	85.64±5.47%	83.19±4.06%	82.21±3.23%

3.1.5 Potency Test:

Avg Absorbance and Standard Deviation found from the standard Amlodipine are given below:

Table 11: Avg Potency and Standard Deviation of Amlodipine Standard

Conc.	Abs 1	Abs 2	Abs 3	Avg Abs	STD
1.25 µg/ml	0.087	0.059	0.064	0.07	± 0.014933
2.5 µg/ml	0.116	0.108	0.130	0.118	± 0.011136
5 µg/ml	0.204	0.210	0.212	0.208	± 0.004163
10 µg/ml	0.395	0.403	0.410	0.402	± 0.007506
20 µg/ml	0.719	0.820	0.815	0.784	± 0.056924

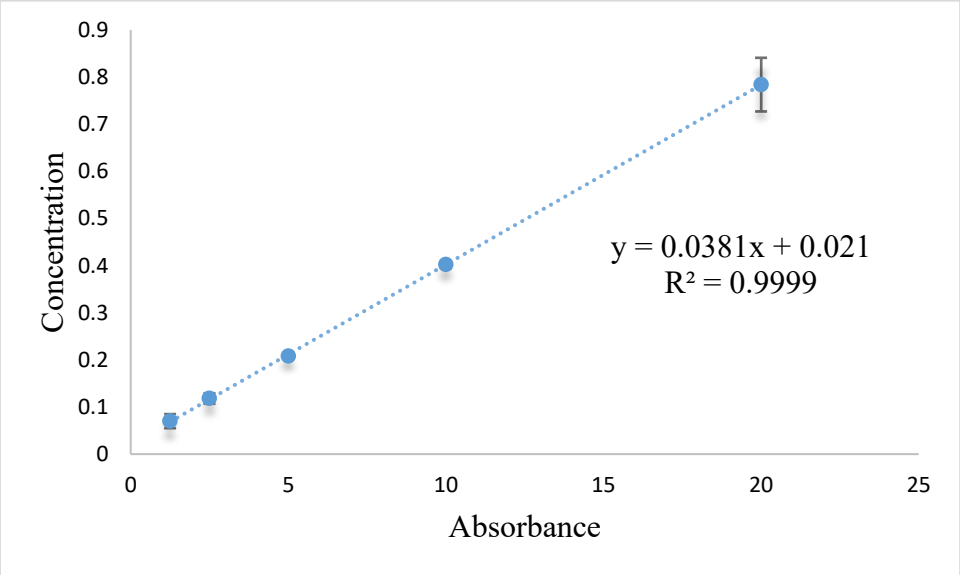

Figure 9: Calibration Curve of Amlodipine

Potency and Standard Deviation value of five brands of Amlodipine are given below:

Table 12: Results of Avg potency and Standard Deviation of five brands (A-E) of Amlodipine

Name	**Brand A**	**Brand B**	**Brand C**	**Brand D**	**Brand E**
Potency of sample 1	100%	105.2%	100.4%	122.2%	96.3%
Potency sample 2	100.4%	104.4%	101.8%	120.8%	100.2%
Potency of sample 3	99.4%	103.8%	103%	123%	87%
Avg potency	99.93%	104.47%	101.73%	122%	94.5%
Mean±STDEV	99.93±0.411 %	104.47±0.573 %	101.73±1.06 %	122±0.91 %	94.5±5.53 %

3.2 Discussion:

According to USP the acceptable range for friability test is, percentage of loss not more than 1%. In this study five brands from reputed pharmaceuticals company were used. All the five brands showed percentage of loss less than 1%. The percentage of loss for all five brands were 0%. That means no loss was happened during the test which indicate that the brands were durable enough to withstand the pressure during shipment. In can be concluded that the tablets are good quality which are able to prevent cracking, crumbling and breaking during handling and storage and showed no variation in the result where the percentage of loss is 0%.

For hardness test the acceptable range is 4-8 kg or 40-80 N for uncoated tablets as per USP guidelines. Here, the tablets of these five brands are uncoated. The results for five brands are between 36.427±6.56 N to 89.409± 6.72 N. In this study brand A showed 36.427±6.56 N which is the lowest value and brand D showed 89.409± 6.72 N which is the highest. Brand A and brand E showed very similar result which are 36.427±6.56 N and 36.727±9.69 N respectively. A is a fast-growing company in Bangladesh. Whereas E is a very popular and leading company in Bangladesh. The ideal range for hardness test is 40-80 N and both brands showed slightly low from that range. These two brands showed very low result which is not satisfactory and can have an impact on the therapeutic effect. Brand B is the most popular and reputed company in Bangladesh which showed 44.848±3.49 N that is under the range, means that the tablets are very good in quality and hard enough to maintain its quality during shipment and handling. Brand C also a reputed company which showed 61.112±4.13 N in hardness test. The result is within the acceptable range, means the tablets are hard enough to withstand the pressure and soft enough to disintegrate in the body. Brand D showed 89.409± 6.72 N on the hardness test which is beyond the acceptable criteria. Brand D is the most popular company in Bangladesh but the hardness value is little high from the range. This can be affects the dissolution and disintegration rate in the body, means it has an markable impact on the desired therapeutic

effect. Lastly, from all the evaluation it can be said that brands A and E showed very low results which is not satisfactory. On the other hand, brand D showed very high result; and brand B and C showed satisfactory results.

The USP guideline for the disintegration time of uncoated tablets are not more than 15 minutes. In this study five marketed drugs of different pharmaceuticals company are used. The results for disintegration time of five branded drugs are between 20 minutes to 3 minutes approximately. Brand B is the most reputed which disintegrate very fast. It disintegrated in 20 seconds, means after entering the body, it quickly breaks into small fragments. On the other hand, brand A took more time to disintegrate which was 2 minutes 21 seconds. Nowadays brand A is the fast-growing company which showed satisfactory result because the rate is under the acceptable range. Brand C and D showed very similar results which were 36 seconds and 35 seconds respectively. Between C and D, D is the most popular and leading company in Bangladesh. D is also a famous company. Though their position in reputation is different, but their results showed similarity which is also satisfactory. Brand E disintegrated in 1 minute 42 seconds which is in the middle range between all the brands results. It is the leading and first rank company in Bangladesh. The result is also satisfactory. All the brands of same class drugs showed different results because of their formulation and excipients like binder, lubricant, filler etc. Lastly from all the evaluation it can be said that all the results are under acceptance criteria, though every brand disintegrated in different rate where brand B and brand A showed lowest and highest results respectively.

The USP guideline for the dissolution test is not less than 75%±5 amlodipine should be dissolved. Here five brands of amlodipine from different pharmaceuticals company were used for the in vitro dissolution study. It is used to perform to determine the percentage of drug release under certain condition like temperature, rpm. Here brand A showed the highest result and brand B showed the lowest result which are 86.38±7.1% and 72.63±6.60% respectively.

Brand B is the most famous and reputed company in Bangladesh but it's drug release less amount of drug within 30 minutes though it is under the satisfactory range. Though Brand A is the fast-growing company but it showed most satisfactory result. Brand C was released 85.64±5.47% in 30 minutes which is under the acceptance range (75±5%). Besides D was released 83.19±4.06% in this test which was also a good result. Last brand which is E were showed quite similar result like D which was 82.21±3.23%. All the results were noted within 30 minutes and the amounts of drugs are going to the process of solution which is important for the bioavailability and pharmacological action. Both C, D and E are the popular pharmaceutical company in this country. Lastly from all the evaluation, brand A showed the highest result which will show fast onset of action, on the other hand, brand B is showed low result which will show low onset of action and other three brands were showed kind of similar results. Though all the brands showed satisfactory results.

For potency test five brandS of amlodipine was used and potency was calculated by the equation of calibration curve of standard amlodipine. As per USP, 90-110% labeled amount of Amlodipine should be present in a tablet. Brands A, B, C and D showed satisfactory results which are under the range. Brand A showed the perfect result which was 99.93±0.41%. Here the standard deviation is very little which represent good result. Though brand E showed less potency compared to others which was 94.4±5.53%. Brand A is the fast-growing company and becoming popular nowadays, but brand E is the most popular and reputed company in Bangladesh. Brand B, C, D and showed 104.47±0.573%, 107.73±1.06% and 122±0.91% respectively. Brand D showed very high result due to excipients, or due to human error which is not satisfactory.

Chapter 4

4 Conclusion:

Amlodipine is used for different types of Hypertensions. It lowers the blood pressure by blocking the L-type calcium channel for inhibition of the flow of calcium ions through the vascular smooth muscle. Five branded tablets of amlodipine were analyzed following the pharmacopoeial (USP) tests such as friability, hardness, disintegration, dissolution and potency. In the friability, disintegration and dissolution test all the branded drugs showed satisfactory results. In the case of a hardness test, variations from the specifications were observed. In dissolution study, all the brands showed release rates within the specification except brand B. Potency of the tablets were determined by using UV-VIS spectrophotometer and a calibration curve was constructed with standard amlodipine. Except once, all the other brands showed potency within the range. Variability in the results can arise from various factors including sample size, technical errors, human errors etc. In conclusion, it is noticed that the five different brands of amlodipine showed consistent results with little variation. Manufacturers should take appropriate measures to maintain the quality of the drug and to ensure its safety and efficacy to the patients.

Reference:

Abdullah Al Shafi Majumder, Rajib Ghosh, Alimur Reza, & Nayan Ray. (2024). Prevalence and determinants of hypertension among adults: A cross-sectional survey of one tribal area in Bangladesh. *World Journal of Advanced Research and Reviews*, *22*(3), 1629–1637. https://doi.org/10.30574/wjarr.2024.22.3.1824

Acherjya, G. K., Tarafder, K., Dutta, D., Mortuza, Md. G., Sarkar, A. K., Das, N. L., & Ali, M. (2023). Frequency and risk factors stratification of hypertension among the rural population of Bangladesh. *Journal of Family Medicine and Primary Care*, *12*(10), 2488–2495. https://doi.org/10.4103/jfmpc.jfmpc_2481_22

Beevers, G., Lip, G. Y. H., & O'brien, E. (n.d.). *The pathophysiology of hypertension*. www.bmjbooks.com

Clinical Review. (n.d.). www.cfp.ca

Dulla, O., Sultana, S., & Shohag Hosen, M. (2018). In vitro comparative quality evaluation of different brands of esomeprazole tablets available in selected community pharmacies in Dhaka, Bangladesh. *BMC Research Notes*, *11*(1). https://doi.org/10.1186/s13104-018-3285-x

Elliott, W. J., & Ram, C. V. S. (2011). Calcium channel blockers. In *Journal of Clinical Hypertension* (Vol. 13, Issue 9, pp. 687–689). https://doi.org/10.1111/j.1751-7176.2011.00513.x

Gordon, A. C., & Myburgh, J. A. (2014). Vasodilators and antihypertensives. In J. F. Butterworth, D. C. Mackey, & J. D. Wasnick (Eds.), *Oh's intensive care manual* (7th ed.). Elsevier. https://www.sciencedirect.com/topics/medicine-and-dentistry/amlodipine

Hecht, M. (2024, May 17). What are the stages and types of hypertension. *Healthline*. https://www.healthline.com/health/types-and-stages-of-hypertension

Hoeper, M. M., Ghofrani, H. A., Grünig, E., Klose, H., Olschewski, H., & Rosenkranz, S. (2017). Pulmonary hypertension. *Deutsches Arzteblatt International*, *114*(5), 73–84. https://doi.org/10.3238/arztebl.2017.0073

Logoyda, L. S., & Piatnochka, V. I. (2020). Hplc method development and in vitro dissolution kinetics of amlodipine tablets under biowaiver conditions. *Biointerface Research in Applied Chemistry*, *10*(5), 6513–6521. https://doi.org/10.33263/BRIAC105.65136521

Mancia, G., & Oparil, S. (2020). Hypertension: What is old and what is new. *British Journal of General Practice, 70*(691), 90. https://doi.org/10.3399/bjgp20X708029

Markl, D., & Zeitler, J. A. (2017). A Review of Disintegration Mechanisms and Measurement Techniques. In *Pharmaceutical Research* (Vol. 34, Issue 5, pp. 890–917). Springer New York LLC. https://doi.org/10.1007/s11095-017-2129-z

National Heart, Lung, and Blood Institute. (n.d.). *Treatment of high blood pressure*. U.S. Department of Health and Human Services. https://www.nhlbi.nih.gov/health/high-blood-pressure/treatment

Puckey, M. (2023, October 29). *Amlodipine*. Drugs.com. https://www.drugs.com/amlodipine.html

Rysz, J., Franczyk, B., Rysz-Górzyńska, M., & Gluba-Brzózka, A. (2020). Pharmacogenomics of hypertension treatment. In *International Journal of Molecular Sciences* (Vol. 21, Issue 13, pp. 1–26). MDPI AG. https://doi.org/10.3390/ijms21134709

Simces, Z. L., Ross, S. E., & Rabkin, S. W. (2012). Diagnosis of hypertension and lifestyle modifications for its management. *BCMJ, 54*(8), 392-398. https://bcmj.org/articles/diagnosis-hypertension-and-lifestyle-modifications-its-management

Tinawi, M. (2022). New Trends in the Diagnosis and Management of Hypertension. *Cureus*. https://doi.org/10.7759/cureus.22393

Umoh, I., Essien, V., & Inyang, S. (2024). Optimizing Hypertension Risk Classification through Machine Learning. *International Journal of Computer Applications*, *186*(14), 21–29. https://doi.org/10.5120/ijca2024923500

Wang, J. G., Palmer, B. F., Vogel Anderson, K., & Sever, P. (2023). Amlodipine in the current management of hypertension. In *Journal of Clinical Hypertension* (Vol. 25, Issue 9, pp. 801–807). John Wiley and Sons Inc. https://doi.org/10.1111/jch.14709

World Health Organization. (2023). Hypertension. World Health Organization. https://www.who.int/news-room/fact-sheets/detail/hypertension

Zeller, A., & Taegtmeyer, A. B. (2021). Pharmacokinetics and pharmacodynamics of antihypertensive drugs in obesity. *Cardiorenal Medicine, 80*(Suppl. 1), 31-39. https://doi.org/10.1159/000515756