In Vitro Comparative Quality Assessment of Different Brands of Conventional Prazosin Hydrochloride Tablets Available in Bangladesh

A PROJECT REPORT
SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF B. PHARM (PROFESSIONAL)

SUBMITTED BY:
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DEPARTMENT OF PHARMACY
FACULTY OF BIOLOGICAL SCIENCES
JAHANGIRNAGAR UNIVERSITY
SAVAR, DHAKA-1342, BANGLADESH

DEDICATED TO

My Beloved Parents!

CERTIFICATE

This is to certify that the work entitled '*In Vitro* Comparative Quality Assessment of Different Brands of Prazosin Hydrochloride Tablet Available in Bangladesh', a comprehensive laboratory based research project, submitted to the Department of Pharmacy, Jahangirnagar University in partial fulfilment of the requirements for the degree of B. Pharm (Professional) was carried out by Ms. Sal Sabila Zerin (Exam Roll No:171807, Reg. No: 45809) in the Department of Pharmacy, Jahangirnagar University under my direct guidance and supervision.

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DECLARATION

I hereby declare that this work entitled "*In Vitro* Comparative Quality Assessment of different brands of Prazosin Hydrochloride Tablet Available in Bangladesh", a comprehensive laboratory based research project, submitted to the Department of Pharmacy, Jahangirnagar University in partial fulfillment of the requirements for the degree of B. Pharm. (Professional) was carried out by me under the guidance of Dr. Mohammad Didare Alam Muhsin, Professor, Department of Pharmacy, Jahangirnagar University, Savar, Dhaka. I also declare that this work has not been submitted before for any other degree.

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All praises go to the Unbeknownst Almighty, the Most Beneficent and Most Merciful.

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ABSTRACT

Prazosin hydrochloride, a drug belonging to the class of alpha-1 adrenergic blockers, is used to treat high blood pressure (hypertension) and symptoms of benign prostatic hyperplasia (BPH). This study focused on *in vitro* evaluation of 4 (four) brands of conventional prazosin hydrochloride tablet dosage forms of 2 mg strength available in the local market of Bangladesh. There are more licensed brands of the drug according to various public and private publications and records, but only these 4 (four) brands are in active supply in the local market. Among the two strengths available for the conventional tablet products of the drug, *viz.*, 1 mg and 2mg, the second one was chosen for this work because it has been reported by the drug sellers to be the most prescribed strength. The quality control parameters, routinely used for the evaluation of tablet products, *viz.*, organoleptic properties, thickness and diameter, hardness and friability, weight & weight variation, disintegration time, assay and dissolution profile, were studied. In most cases, The United States Pharmacopeia (USP) methods and specifications were followed for conducting the tests and drawing inferences. Out of 4 brands of the drug studied, 3 brands (*viz.*, A-2, B-2 and Q-2) are of white color and round shape. The other one (P-2) was pink in color and rhombus in shape. For all the brands, the thickness and diameter met required specifications with none of them showing any unit with diameter or thickness exceeding ±5% of the average. The hardness of only one product (P-2) was above 4 kg/ cm^2, which is the minimum acceptable crushing strength according to USP recommendation. On the other hand, two brands (*viz.*, A-2 and P-2) showed an acceptable friability of less than 1%, while the other two (B-2 and Q-2) failed to satisfy this requirement. The weight variation of all the brands was within the USP requirement (<±10% for tablets weighing <130 mg, ±7.5% for tablets weighing 130-324 mg). The disintegration time for all the brands in simulated gastric fluid (pH 1.2) was below the limit of 15 minutes as recommended by some pharmacopoeia; however, two brands exceeded this limit when tested in water (17 min for A-2, 15.5 min for P-2). The UV spectrophotometric assay of all the brands gave potencies within the USP limits of 90-110%. The *in vitro* drug release of all the brands, carried out in 0.1N HCl (pH 1.2), was found to be about 65% in 45 min, which is less than the USP specification of not less than 75% in 45 min time point for immediate release dosage forms. The release reached nearly 100% in 90 min. It may be worth noting here, however, that there was complete release within 10 min when 3% sodium lauryl sulfate was

added to the dissolution media (as described in USP for dissolution study of capsule dosage form of the drug). So, the release found in 0.1N HCl without surfactant may be taken to be good enough considering poor solubility of the drug. To conclude, all the brands showed satisfactory performance in terms of most of the parameters used for *in vitro* quality assessment, and their performance was closely similar to each other in most cases. Hardness and friability seem to be the only areas that need attention in the case of some brands. So, the studied tablet products may be regarded to possess satisfactory quality to serve their purpose and may be used interchangeably. The results of this study can also help the pharmaceutical manufacturers of the country and the Drug Control Authority to get an overview of the quality status of the marketed prazosin hydrochloride tablet products in Bangladesh. Further studies with more samples from different areas of the country are warranted to draw more conclusive evidence.

Keywords: Prazosin hydrochloride, hypertension, quality, comparative quality assessment, *in vitro*, UV-vis, hardness, assay, disintegration, dissolution.

Aims & Objectives of the Work

Aims of the Work

This work was set out with the following aims ahead:

- To evaluate the quality parameters of some of the marketed Prazosin Hydrochloride tablet products available in Bangladesh.
- To compare the *in vitro* quality parameters of the studied Prazosin Hydrochloride tablet products.
- To make patients and healthcare professionals aware of the variations in drug release profiles, bioavailability, or other critical characteristics that could affect the treatment outcomes by comparing various Prazosin Hydrochloride tablet products available on the market and help them to decide if different brands of the drug product could be taken interchangeably.

Objectives of the Work

To achieve the aforementioned aims the following objectives were set out for this work:

- To assess the physical parameters like organoleptic properties, thickness and diameter, hardness, friability, weight and weight variation and disintegration time of the Prazosin Hydrochloride tablet products available in the local market of Bangladesh.
- To perform the assay of the products for determining their potencies and compare them.
- To perform dissolution studies to determine the drug release pattern of the products in appropriate dissolution media.
- To compare the release profiles of the studied products and determine if they fulfil expectations and if they could be regarded interchangeable.

Chapter One: Introduction

Pharmaceuticals contribute significantly to safeguarding public health, advancing medical science, and enhancing overall patient's health and well-being. It is necessary to ensure the maintenance of drug quality for preserving pharmacological effectiveness. Pharmaceuticals must fulfill regulatory requirements to meet quality standards.

Quality assessment of drugs is crucial to ensuring the safety, effectiveness, and reliability of pharmaceutical products. Without proper assessment, medications may contain incorrect amounts of active ingredients, be contaminated, or degrade over time. This can lead to ineffectiveness, serious side effects, or even death. That is why the integrity of drugs cannot be compromised. Rigorous quality assessment procedures, encompassing analysis of raw materials, manufacturing processes, and final products, serve as the cornerstone of pharmaceutical regulation. Such assessments mitigate the risks associated with substandard or counterfeit medications, safeguarding public health and bolstering trust in the healthcare system.

Pharmaceutical industries manufacture and market generic drugs under different brand names. The proliferation of generic drug products from numerous manufacturers presents challenges for healthcare providers in selecting seemingly equivalent alternatives. Many prescription medicines are supplied by multiple sources, with potential variability in clinical response; that too if product quality differs. Thus, continuous evaluation of quality is critical to ensure interchangeability. Further complicating matters, in countries like ours, most prescription drugs are available without a prescription. Therefore, thorough assessment of product quality in the marketplace is necessary to avoid mass disaster, particularly for chronic disease therapies requiring daily and long-term use. Rigorous quality control protects patients, fosters consumer trust, and may result in increased sales**.**

Hypertension is a chronic medical condition characterized by elevated blood pressure levels persistently exceeding the normal range. Hypertension often develops silently without noticeable symptoms, earning its reputation as a ‘silent killer’. Treatment may include lifestyle modifications and medications like antihypertensive drugs to control blood pressure levels and reduce associated health risks. Effective management and control of hypertension are crucial for preventing complications and maintaining overall health and well-being. If not controlled and monitored regularly, serious complications may result over time, including cardiovascular diseases like heart attack, stroke, and heart failure.

Prazosin is a medication primarily used to treat hypertension and symptoms of benign prostatic hyperplasia (BPH). It belongs to the class of alpha-adrenergic 1 blockers which works by blocking the action of certain natural substances in the body, such as adrenaline, leading to relaxation of blood vessels and improved blood flow. This effect helps to lower blood pressure and relieve symptoms associated with conditions like hypertension and benign prostatic

hyperplasia (BPH). The drug is available in both conventional and sustained release tablet forms. About 7 pharmaceuticals are manufacturing and marketing the drug in different brand names in the local market of Bangladesh. It is highly imperative to make a regular quality assessment of prazosin, which is prescribed by medical practitioners and importantly for the treatment of chronic hypertension and symptoms of benign prostatic hyperplasia (BPH). A comparative *in vitro* evaluation of several brands of prazosin tablet products of different manufacturers was undertaken in this work in order to assess their quality and interchangeability.

1.1 Quality Assessments of Tablets

1.1.1 Quality

In the pharmaceutical industry, quality refers to the degree to which a drug substance or drug product meets its intended use and fulfills its inherent properties including its essential attributes like identity, strength, and purity.

The quality of a drug product should be strictly controlled to ensure its safety and efficacy. This serves as a basis for formulating quality standards. Generally, the quality standards of drugs contain attributes such as drug definition, identification, assay, and impurities.

1.1.2 Important Components of Drug Quality

Quality of a drug or drug product means its adequacy in terms of a number of different attributes or components. Following is a brief outline of the quality components or attributes of drugs or drug products.

Identity: This refers to confirming the presence of the active pharmaceutical ingredient (API) indicated on the label.

Purity: Apart from the active pharmaceutical ingredient (API), the excipients in the drug products should also be free from potentially harmful contaminants or microorganisms. Cross-contamination from other products should also be avoided.

Potency: It is the amount or quantity of a specific drug in a raw material or drug product. Potency is assessed on an individual drug basis and can be reported as a percent (%) or absolute weight (mg).

Efficacy: It is a measure of a drug's biological activity expressed in terms of the dose required to produce a pharmacological effect of given intensity.

Safety: It is important to consider the frequency of adverse drug effects that may emerge after treatment with the drug/ drug product.

Consistency: It refers to the consistency of the drugs/ drug products in terms of quality and efficacy in a batch or across the batches.

1.1.3 Why is Quality Assessment of Drugs and Drug Products So Important?

Quality assessment of a drug/ drug product involves evaluating its quality attributes like purity, potency, efficacy, safety, reliability, stability, and consistency against to make sure that it meets established standards and specifications. This process typically involves various tests and analyses such as chemical assays, microbiological tests, and physical examinations.

Ensuring the safety, effectiveness, and reliability of pharmaceutical products is vital for public health. Incorrect amounts of active ingredients, contamination with harmful substances, or degradation of the drug/ drug product over time may lead to ineffectiveness or untoward/ toxic effects and, in extreme cases, to event death. Quality assessment safeguards the integrity of the drugs we rely on and plays a critical role in ensuring patients receive safe and efficacious treatments.

Furthermore, quality assessment facilitates adherence to regulatory standards, fostering innovation and continuous improvement in drug development practices. It ensures a brand to deliver what it promises, fostering customer satisfaction and building trust in them. It helps to identify and rectify issues before they can cause harm, assuring the product function as intended. By identifying weaknesses in production, quality assessment allows for continuous improvement. This minimizes errors, reduces waste, and ultimately lowers costs for both the producer and consumer. Ultimately, the meticulous scrutiny of drug quality not only protects consumers but also upholds the fundamental principles of patient care and medical ethics.

In light of the account given above about the quality attributes of a drug/ drug product and the significance of quality assessment, here is a more detailed account of different aspects highlighting the importance of quality assessment:

1. **Safety**: Ensuring the quality of a drug/ drug product is essential to prevent any adverse/ toxic reactions to patients. Quality assessment also helps detect any potential contaminants, impurities, or incorrect ingredients that could pose a risk to a patient's safety.

2. **Efficacy**: Drugs are formulated to deliver specific doses of active pharmaceutical ingredients (APIs) to patients. Quality assessment ensures that drugs/ drug products contain the correct amount of API and that they are formulated in a way that ensures proper dissolution and absorption in the body, thereby ensuring desired therapeutic effectiveness.

3. **Patient Compliance**: Patients rely on drugs to manage their health conditions effectively. Drugs that are of consistent quality are more likely to produce reliable therapeutic outcomes,

which can improve patient compliance with treatment regimens and ultimately lead to better health outcomes.

4. **Regulatory Compliance**: Regulatory agencies require drugs to meet stringent quality standards before they are be marketed and sold to the public. Quality assessment helps ensure compliance with regulatory requirements, reducing the risk of regulatory action, such as product recalls or sanctions.

5. **Manufacturing Consistency**: Drugs are typically produced in large batches through a manufacturing process that involves various steps and parameters. Quality assessment helps monitor and control critical aspects of the manufacturing process to ensure consistency in tablet quality from batch to batch.

6. **Consumer Confidence:** Consistently high-quality tablets contribute to consumer confidence in the pharmaceutical product and the brand. Patients are more likely to trust and continue using tablets from manufacturers known for their quality products.

7. **Cost-Effectiveness:** Detecting quality issues early in the manufacturing process can prevent costly recalls, rejections, or legal disputes later on. Investing in quality assessment upfront can save money in the long run by avoiding potential liabilities and reputation damage.

8. **Global Trade:** Many countries have stringent import regulations for pharmaceutical products, requiring evidence of quality assurance before allowing products to enter their markets. Quality assessment facilitates international trade by demonstrating compliance with regulatory requirements.

9. **Scientific Validity**: Quality assessment ensures trials and research use of drugs with the intended properties.

10. **Combating Counterfeits**: Testing helps identify and remove fake medications from the market.

11. **Dosage Accuracy**: Verifies consistent and correct amounts of active ingredients for predictable effects.

12. **Stability and Shelf Life**: Ensures medications maintain potency and effectiveness throughout their lifespan.

13. **Manufacturing Consistency**: Guarantees drugs produced across batches meet the same quality standards.

14. **Developing New Drugs**: Quality assessment forms the foundation for safe and reliable clinical trials.

15. **Pharmacovigilanc**e: Allows for monitoring and identification of potential drug-related risks after market-launch.

16. **Adverse Effects**: Contaminants or incorrect dosages can cause serious side effects, hospitalization, and even death.
17. **Antimicrobial Resistance**: Improper drug quality can contribute to the rise of antibiotic-resistant bacteria.
18. **Rational Drug Use**: Quality assessment prevents the use of ineffective or contaminated medications.
19. **Ethical Considerations**: Ensures patients are not exposed to potentially harmful or ineffective treatments.
20. **Innovation**: Provides a framework for the development of safe and effective new medications.
21. **Transparency:** Promotes openness and accountability in the pharmaceutical industry.
22. **Sustainable Healthcare**: Reduces waste and promotes efficient use of healthcare resources by ensuring patients receive right medications.

1.1.4 Evaluation of Quality Parameters

The evaluation of tablet dosage forms involves various quality parameters to ensure their safety, efficacy, and stability. Here are some key tests performed in the evaluation of tablets along with their significance:

1. **Appearance and Physical Characteristics**: This involves visual inspection of the tablets for color, shape, size, surface texture, and presence of any defects like chips or cracks. The appearance gives an initial indication of manufacturing quality and can impact patient compliance and perception.
2. **Content Uniformity**: Content uniformity testing evaluates the uniform distribution of the active pharmaceutical ingredient(s) within individual tablets and across different tablets in a batch. It ensures that each tablet delivers the intended dose of the drug, minimizing the risk of under- or over-dosing.
3. **Thickness, Diameter, and Hardness**: These physical characteristics are important for tablet handling, packaging, and dissolution. Thickness and diameter influence how easily a tablet can be swallowed, while hardness reflects its ability to withstand mechanical stress during handling and packaging.
4. **Friability**: Friability testing evaluates the tendency of tablets to crumble or break under mechanical stress during handling or transportation. It involves subjecting a sample of

tablets to repeated tumbling in a friabilator and measuring the percentage of weight loss. Excessive friability can lead to dose variability and compromise product quality.

5. **Disintegration Time**: Disintegration testing assesses the time it takes for a tablet to break down into smaller particles when exposed to a specified medium. It provides an indication of the tablet's ability to disintegrate in the gastrointestinal tract and release the active pharmaceutical ingredient for absorption. Deviations in disintegration time can affect drug bioavailability.

6. **Dissolution Rate**: Dissolution testing measures the rate and extent of drug release from the tablet formulation into a dissolution medium under standardized conditions. It mimics the process of drug release in the gastrointestinal tract and helps ensure consistent and predictable drug absorption. Deviations in dissolution rate can affect drug efficacy and bioavailability.

7. **Stability Studies**: Stability testing assesses the physical, chemical, and microbiological stability of tablets over time under various storage conditions (e.g., temperature, humidity, light). It provides crucial information on the shelf-life and storage requirements of the product, helping to ensure its quality and efficacy throughout its intended lifespan.

1.2 Hypertension

Hypertension, also known as high blood pressure, is a long-term medical condition in which the blood pressure in the arteries is persistently elevated.

Hypertension is a global public health issue which contributes to the development of heart disease, stroke, kidney failure, premature death and disability (WHO, 2013; James *et al*., 2014; Krakoff *et al*., 2014; Whelton *et al*., 2018). In response to this threat, global and national agencies developed and kept updating health promotion strategies, hypertension management related policies, and guidelines to control hypertension in order to reduce or prevent its potential to cause further disabilities (Whelton *et al*.; 2018, James *et al*., 2014; WHO, 2013; WHO, 2013a). These efforts have resulted in declining levels of hypertension in high income countries, but the condition’s prevalence has been increasing in low and lower-middle income countries (Mills *et al*., 2016).

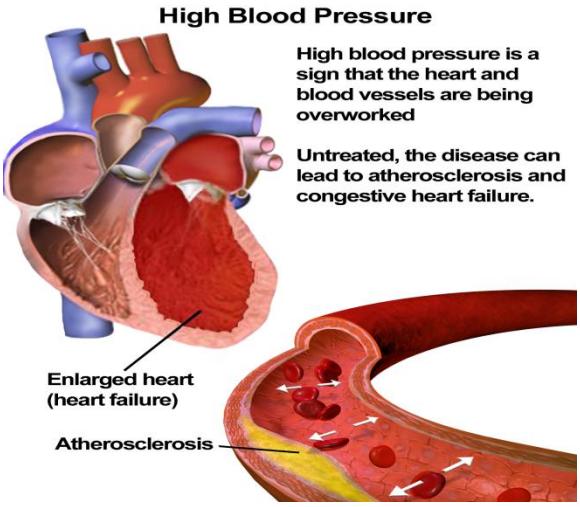


Figure 1.1: Cause of Hypertension

1.2.1 History

- The modern history of hypertension begins with the understanding of the cardiovascular system based on the work of physician William Harvey (1578–1657), who described the circulation of blood in his book *De motu cordis*.
- Ancient civilizations, such as Egypt, Greece, and China, described symptoms consistent with hypertension.
- In the 17th century, physicians began systematic measurements of blood pressure.
- In 1733, Stephen Hales measured blood pressure using tubes inserted into animal arteries.
- In 1896, Scipione Riva-Rocci invented the sphygmomanometer for practical blood pressure measurement.
- The term "hypertension" was coined in the early 20th century.
- The Framingham Heart Study, initiated in 1948, provided insights into hypertension epidemiology and risk factors.
- Mid-20th century saw the development of effective antihypertensive medications like thiazide diuretics and beta-blockers.
- Public health campaigns have raised awareness about hypertension and promoted lifestyle changes.
- Ongoing research aims to improve understanding, prevention, and treatment of hypertension, focusing on personalized medicine and holistic approaches.

1.2.2 Epidemiology

The prevalence of hypertension (HTN) varies significantly worldwide, with rates around 20% in the USA and between 25% to 50% across different regions in Europe. In Bangladesh, however, the exact prevalence of HTN remains unclear due to limited large-scale epidemiological studies.

Initial reports from 1976 indicated a prevalence of 1.10%. Subsequent studies, including a meta-analysis, population-based research, and recent surveys, have reported varying prevalence rates of 11.3%, 18.6%, and 20.1%, respectively.

The Bangladesh Non-communicable Disease (NCD) Risk Factor Survey conducted in 2010 revealed a general prevalence of HTN at 17.9%, with slightly higher rates among men (18.5%) than women (17.3%).

Hypertension appears to be particularly common among the elderly population, with one study reporting rates of 65% overall, 75% in urban areas, and 53% in rural areas. In another study focusing on senior citizens, the prevalence was found to be 44.8%.

Contrary to common belief, HTN is not solely a concern in urban areas; it is also prevalent in rural populations. Studies have shown that the prevalence of diastolic HTN among rural individuals was 6.7% in 1983 and rates of high systolic and diastolic blood pressure were 10.5% and 9% respectively in 1995, with slightly higher rates among females. Among individuals with diabetes, the prevalence of systolic HTN was found to be 23.2% and diastolic HTN 13.6%.

1.2.3 Classification of Hypertension

Hypertension, or high blood pressure, is typically classified based on the level of blood pressure readings. Here is a general classification showing normal blood pressure and different stages of hypertension:

- **Normal Pressure**: Systolic blood pressure less than 120 mm Hg and diastolic blood pressure less than 80 mm Hg.
- **Elevated Pressure (Prehypertension):** Systolic blood pressure between 120-129 mm Hg and diastolic blood pressure less than 80 mm Hg.
- **Hypertension Stage 1:** Systolic blood pressure between 130-139 mm Hg or diastolic blood pressure between 80-89 mm Hg.
- **Hypertension Stage 2:** Systolic blood pressure 140 mm Hg or higher, or diastolic blood pressure 90 mm Hg or higher.
- **Hypertensive Crisis:** Systolic blood pressure over 180 mm Hg and/or diastolic blood pressure over 120 mm Hg. Immediate medical attention is required in a hypertensive crisis.

Blood pressure classification	Systolic BP	Diastolic BP
Normal	less than 120	and less than 80
Prehypertension/Elevated	120-129	and less than 80
Stage 1 Hypertension	130-139	or 80-89
Stage 2 Hypertension	140 or higher	or 90 or higher
Hypertensive Crisis	Higher than 180	and/or higher than 120

Figure 1.2: Classification of Blood Pressure for Adults

1.2.4 Clinical Manifestations

Many people who have hypertension are asymptomatic at first. Physical examination may reveal no abnormalities except for an elevated blood pressure, so one must be prepared to recognize hypertension at its earliest. Here is a brief account of clinical manifestations observed with hypertension:

- **Headache:** The red blood cells carrying oxygen have a hard time reaching the brain because of constricted vessels, causing headache.
- **Dizziness:** Dizziness occurs due to the low concentration of oxygen that reaches the brain.
- **Chest pain:** Chest pain occurs also due to decreased oxygen levels.
- **Blurred vision:** Blurred vision may occur later on because of too much constriction in the blood vessels of the eye so that red blood cells carrying oxygen cannot pass through.
- **Shortness of breath**
- **Nosebleeds**
- **Abnormal heart rhythm**
- **Buzzing in the ear**
- **Anxiety**
- **Nausea**
- **Vomiting**

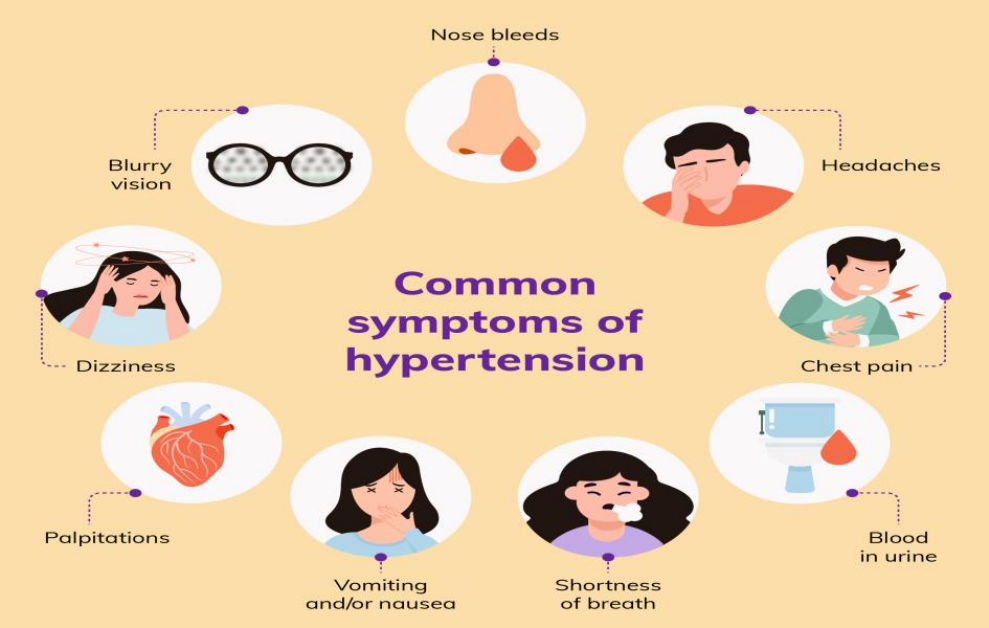


Figure 1.3: Common Symptoms of Hypertension

1.2.5 Complications

If hypertension is left untreated, it could progress to serious complications involving different vital organs of the body. Some of these complications are as follows:

- **Heart failure:** With increased blood pressure, the heart pumps blood faster than normal until the heart muscle goes weak from too much exertion.
- **Myocardial infarction (MI):** Decreased oxygen supply to the heart muscles due to constriction of blood vessels may lead to MI.
- **Impaired vision:** Ineffective peripheral perfusion affects the eye, causing problems in vision because of decreased oxygen.
- **Renal failure**: Blood, carrying oxygen and nutrients, can not reach the renal system because of the constricted blood vessels and this ultimately may lead to renal failure.

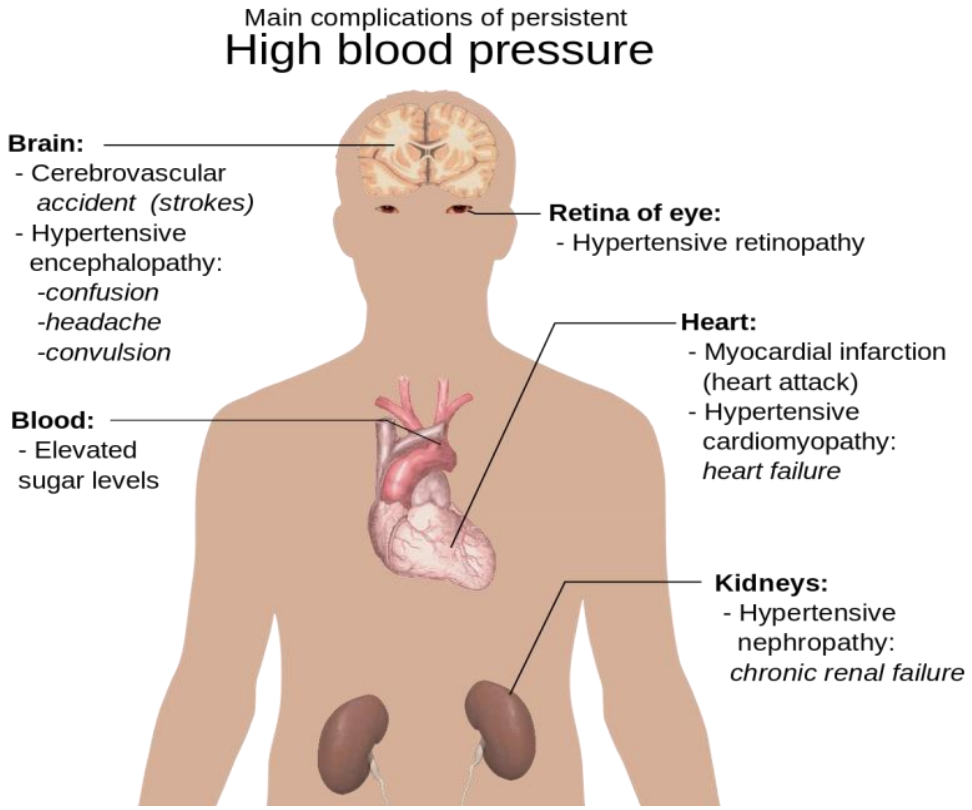


Figure 1.4: Main complications of persistent high blood pressure

1.2.6 Causes of Hypertension

Several factors can contribute to the development of hypertension. Following is a brief account of such factors:

Primary Hypertension

When there is not an obvious cause of high blood pressure, it is called primary (or essential) hypertension. It has been found that in the U.S. 19 out of 20 people with high blood pressure have this type of hypertension. It often takes many years to develop.

Essential hypertension has been linked to certain risk factors in the diet and lifestyle. For example, eating a lot of salt can cause the blood pressure to rise. Many people with this condition are sensitive to salt, so even eating a small amount can trigger a spike in blood pressure.

Other factors that can raise the risk of developing essential hypertension include:

- Not doing enough exercise
- Drinking too much alcohol
- Having a family member with high blood pressure

- Getting older (especially after 65 years of age)
- Obesity
- Diabetes
- Stress
- Insufficient intake of potassium, calcium, and magnesium
- Lack of physical activity
- Chronic alcohol consumption

Secondary Hypertension

When a direct cause for high blood pressure can be identified, the condition is described as secondary hypertension. This type of high blood pressure is caused by a different health condition. It is usually more sudden and severe than essential hypertension. Some causes include:

- **Kidney Disease:** This is the most common cause of secondary hypertension. It has long been thought that renal disease interferes with salt excretion, leading to volume overload and consequent hypertension.
- **Adrenal Disorders:** Hypertension can also be triggered by tumors or other abnormalities of adrenal glands (small structures that sit atop the kidneys). Adrenal tumors or disorders can cause them to release too much of the hormones that elevate blood pressure.
- **Thyroid Disorders:** Too much or too little thyroid hormone can affect your blood pressure.
- **Congenital Heart Defect:** Some people are born with heart or blood vessel problems that may be a cause of hypertension.
- **Obstructive Sleep Apnea:** This condition causes breathing problems and lack of oxygen. This can harm arteries.
- **Narrowing of the Arteries Supplying the Kidneys**
- **Hormonal Problems:** such as an underactive thyroid, an overactive thyroid, Cushing's syndrome, acromegaly, increased levels of the hormone aldosterone (hyperaldosteronism), and phaeochromocytoma.
- **Lupus:** a condition in which the immune system attacks parts of the body, such as the skin, joints and organs.
- **Scleroderma:** a condition that causes thickened skin
- **Medicines:** Some medicines also can increase blood pressure. Medicines that can increase blood pressure include:

- The Contraceptive pill
- Steroids
- Non-steroidal anti-inflammatory drugs (NSAIDs) – such as ibuprofen, aspirin and naproxen
- Some pharmacy cough and cold remedies
- Some herbal remedies – particularly those containing liquorice
- Some recreational drugs – such as cocaine and amphetamines
- Some selective serotonin-noradrenaline reuptake inhibitor (SSNRI) antidepressants – such as venlafaxine

Pregnancy

Sometimes, hypertension suddenly appears or gets worse during pregnancy. When hypertension develops after 20 weeks of pregnancy, it is called preeclampsia. It is important to keep an eye on blood pressure during pregnancy because it can have a big impact both on the mother and the baby. Both high blood pressure and preeclampsia can cause problems such as:

- Slow growth
- Low birth weight
- Prematurity
- Separation of the placenta before delivery
- Organ damage

1.2.7 Assessment and Diagnostic Findings

Assessment of the patient with hypertension must be detailed and thorough. There are also diagnostic tests that can be performed to establish the diagnosis of hypertension.

Assessment

Assessment should include the following:

- Assessment of the patient's **health history**
- Performing **physical examination** as appropriate
- The retinas should be examined to **assess possible organ damage**
- Laboratory tests to **check target organ damage**.

Diagnostic Tests

- **Urinalysis** is performed though the specific gravity to check the **concentration of sodium** in the urine.

- **Blood chemistry** (e.g. analysis of sodium, potassium, creatinine, fasting glucose, and total and high density lipoprotein cholesterol levels)**:** These tests are done to determine the level of sodium and fat in the body.
- **Twelve-lead ECG:** ECG needs to be performed to rule out the **presence of cardiovascular damage**.
- **Echocardiography:** Echocardiography assesses the presence of **left ventricular hypertrophy**.
- **Creatinine clearance**: Creatinine clearance is performed to check for the level of blood urea nitrogen (BUN) and creatinine that can determine if there is renal damage or not.
- **Renin level**: Renin level should be assessed to determine how the renin–angiotensin–aldosterone system (RAAS) is coping.
- **Hemoglobin/hematocrit:** Not diagnostic but assesses relationship of cells to fluid volume (viscosity) and may indicate risk factors such as hypercoagulability, anemia.
- **Blood urea nitrogen (BUN)/creatinine:** Provides information about renal perfusion/function.
- **Glucose:** Hyperglycemia (diabetes mellitus is a precipitator of hypertension) may result from elevated catecholamine levels (increases hypertension).
- **Serum potassium:** Hypokalemia may indicate the presence of primary aldosteronism (cause) or be a side effect of diuretic therapy.
- **Serum calcium:** Imbalance may contribute to hypertension.
- **Lipid panel (total lipids, high-density lipoprotein [HDL], low-density lipoprotein [LDL], cholesterol, triglycerides, phospholipids):** Elevated level may indicate predisposition for/presence of atheromatous plaques.
- **Thyroid studies:** Hyperthyroidism may lead or contribute to vasoconstriction and hypertension.
- **Serum/urine aldosterone level:** May be done to assess for primary aldosteronism (cause).
- **Urinalysis:** May show blood, protein, or white blood cells; or glucose suggests renal dysfunction and/or presence of diabetes.
- **Creatinine clearance:** May be reduced, reflecting renal damage.
- **Urine vanillylmandelic acid (VMA) (catecholamine metabolite):** Elevation may indicate the presence of pheochromocytoma (cause); 24-hour urine VMA may be done for assessment of pheochromocytoma if hypertension is intermittent.
- **Uric acid:** Hyperuricemia has been implicated as a risk factor for the development of hypertension.
- **Renin:** Elevated in renovascular and malignant hypertension, salt-wasting disorders.
- **Urine steroids:** Elevation may indicate hyperadrenalism, pheochromocytoma, pituitary dysfunction, Cushing's syndrome.
- **Intravenous pyelogram (IVP):** May identify cause of secondary hypertension, e.g., renal parenchymal disease, renal/ureteral calculi.
- **Kidney and renography nuclear scan:** Evaluates renal status (TOD).

- **Excretory urography:** May reveal renal atrophy, indicating chronic renal disease.
- **Chest x-ray:** May demonstrate obstructing calcification in valve areas; deposits in and/or notching of aorta; cardiac enlargement.
- **Computed tomography (CT) scan:** Assesses for cerebral tumor, CVA, or encephalopathy or to rule out pheochromocytoma.
- **Electrocardiogram (ECG):** May demonstrate enlarged heart, strain patterns, conduction disturbances. Broad, notched P wave is one of the earliest signs of hypertensive heart disease.

1.2.8 Treatment

Lifestyle Modification

- **Choose heart-healthy foods such as those in the DASH eating plan:** A research has shown that DASH (Dietary Approaches to Stop Hypertension) combined with a low-salt eating plan can be as effective as medicines in lowering high blood pressure.
- **Avoid or limit alcohol:** The patient may need to limit alcohol or stop drinking. He should talk to his healthcare provider about how much alcohol he can take.
- **Get regular physical activity:** Many health benefits result from getting the recommended amount of physical activity each week. Studies have shown that physical activity can help lower and control high blood pressure levels. Even modest amounts of physical activity may help. Before starting any exercise program, one should ask his healthcare provider what level of activity is right for him.
- **Aim for a healthy weight:** If the individual is an adult with overweight or obesity, losing 5% to 10% of your initial weight over 6 months can improve his health. Even losing just 3% to 5% of weight can improve blood pressure.
- **Quit smoking:** Smokers are more likely to develop high blood pressure and heart disease. In hypertensive patients, quitting smoking can help manage blood pressure better. However, one may see an increase in blood pressure in the short term due to some of the side effects of quitting smoking. But the long-term benefits of quitting are clear.
- Manage stress: Numerous studies have shown that stress can increase blood pressure. Stress reduction has often been regarded as an important component of the lifestyle changes that might be beneficial in reducing an elevated blood pressure in hypertensive patients.
- **Get enough good-quality sleep:** There's a connection between sleep and blood pressure as poor sleep can cause blood pressure to spike. To prevent and better manage hypertension, adults are wise to aim for a consistent 7–8 hours of sleep.

Medications

The type of medicine used to treat hypertension depends on one's overall health and how high one's blood pressure is. Two or more blood pressure drugs often work better than one. It can take some time to find the medicine or combination of medicines that works best for someone. When taking blood pressure medicine, it is important to know the goal blood pressure level. One should

aim for a blood pressure treatment goal of less than 130/80 mm Hg. The ideal blood pressure goal, however, can vary with age and health conditions, particularly for people older than 65.

Following is an account of medicines used to treat high blood pressure:

- **ACE inhibitors:** Angiotensin-converting enzyme (ACE) inhibitors reduce blood pressure by relaxing blood vessels. Commonexamples are enalapril, lisinopril, perindopril and ramipril. The most common side effect is a persistent dry cough. Other possible side effects include headaches, dizziness and a rash.
- **Angiotensin-2 receptor blockers (ARBs):** ARBs work in a way similar to ACE inhibitors. They're often recommended if ACE inhibitors cause troublesome side effects. Common examples are candesartan, losartan, valsartan and olmesartan. Possible side effects include dizziness, headaches, and cold or flu-like symptoms.
- **Calcium channel blockers:** Calcium channel blockers reduce blood pressure by widening blood vessels. Common examples are amlodipine, felodipine and nifedipine. Other medicines, such as diltiazem and verapamil, are also available. Possible side effects include headaches, swollen ankles and constipation.
- **Diuretics:** Diuretics work by flushing excess water and salt from the body through urine. They are often used if calcium channel blockers cause troublesome side effects, or if one has signs of heart failure. Common examples are indapamide and bendroflumethiazide. Possible side effects include dizziness when standing up, increased thirst, needing to go to the toilet frequently, and a rash. One might also get low potassium and low sodium after long-term use.
- **Beta blockers:** Beta blockers can reduce blood pressure by making heart beat more slowly and with less force. They used to be a popular treatment for high blood pressure, but now tend to be used only when other treatments have not worked. This is because beta blockers are considered less effective than other blood pressure medicines. Common examples are atenolol and bisoprolol. Possible side effects include dizziness, headaches, tiredness, and cold hands and feet.
- **Alpha blockers:** Alpha blockers block the action of alpha-adrenergic receptors, leading to relaxation of blood vessels and decreased resistance to blood flow, thereby lowering blood pressure. Common examples are Doxazosin, Prazosin, Terazosin. Possible side effects include dizziness, headache, asthenia, postural hypotension, rhinitis, and sexual dysfunction.

1.2.9 Prevention

Prevention of hypertension mainly relies on a healthy lifestyle and self-discipline. Following are some of the measures that you should take for preventing hypertension:

- **Weight reduction**: Maintenance of normal body weight can help prevent hypertension.
- **Adopt DASH**: DASH or the Dietary Approaches to Stop Hypertension includes consummation of a diet rich in fruits, vegetable, and low-fat dairy.

- **Dietary sodium retention**: Sodium contributes to an elevated blood pressure, so reducing the dietary intake to no more than 2.4 g sodium per day can be really helpful.
- **Physical activity**: One should engage in regular aerobic physical activity for 30 minutes thrice every week.
- **Moderation of alcohol consumption**: One should limit alcohol consumption to no more than 2 drinks per day in men and one drink for women and people who are lighter in weight.

1.3 Antihypertensive Drugs

Antihypertensives are a class of drugs that are used to treat hypertension (high blood pressure). Antihypertensive therapy seeks to prevent the complications of high blood pressure, such as stroke, heart failure, kidney failure and myocardial infarction.

There are many different types of antihypertensive drugs and they work in different ways to lower blood pressure. Some remove extra fluid and salt from the body. Others relax and widen the blood vessels or slow the heartbeat.

1.3.1 Classification of Antihypertensive Drugs

Antihypertensive drugs are mainly classified based on their mechanism of action as follows:

1) ACE Inhibitors (Angiotensin-converting enzyme inhibitors): *e.g.*, Lisinopril, Enalapril
2) ARBs (Angiotensin II receptor blockers): *e.g.*, Losartan, Valsartan
3) Alpha blockers: *e.g.*, Doxazosin, Terazosin
4) Beta blockers: *e.g.*, Metoprolol, Labetalol
5) Ca channel blockers: *e.g.*, Amlodipine, Nicadipine
6) Diuretics: *e.g.*, Furosemide, Hydrochlorithiazide

1.3.2 Mechanism of Action of Antihypertensive Drugs

1. ACE Inhibitors (Angiotensin-converting enzyme inhibitors)

- Decrease angiotensin II & increase bradykinin.
- Vasodilation occurs due to low levels of angiotensin II and increase of bradykinin (Lower BP).
- Decrease secretion of aldosterone, resulting in decreased Na & water retention, (Lower BP).

2. ARBs (Angiotensin II receptor blockers)

- Block AT1 (type-1 angiotensin) receptors.

- The effects are similar to ACE inhibitors.

3. Alpha blockers

- Block alpha-adrenergic receptors.
- This causes relaxation of smooth muscle in blood vessels.
- Smooth muscle relaxation leads to vasodilation. This in turn lowers blood pressure.

4. Beta Blockers

- Beta blockers block beta-adrenergic receptors.
- This reduces the effects of adrenaline (epinephrine) and noradrenaline (norepinephrine).
- It slows down the heart rate It decreases the force of contraction of the heart.

5. Ca Channel Blockers

- Bind to L-type of Ca^{++} channels, which are specific to smooth muscle of blood vessels & heart.
- Block calcium channels and decrease inward flow of calcium into smooth muscle, cardiac muscle & conducting tissue of heart.

6. Diuretics

(i) Thiazide Diuretics

- Inhibit Na^+ & Cl^- Co-transporter in Distal Convoluted Tubules in kidney.
- Decrease Na^+ & Cl^- reabsorption, increase their excretion, along with water.
- Thus decrease Blood Volume & BP.
- Also cause vasodilatation, reduce PR & BP.

(ii) Loop Diuretics

- Inhibit Na^+ , K^+ , Cl^- Co-transporter in thick ascending limb of kidney.
- Decrease reabsorption of Na^+, K^+ & Cl^-, increase their excretion along with water.
- Lower blood volume & BP.

(iii) Potassium Sparing Diuretics

- Increase Na^+ & water excretion.
- Prevent K^+ loss (can cause hyperkalemia).
- Can be used as adjunct with thiazides or loop diuretics (to prevent cardiac arrhythmias).

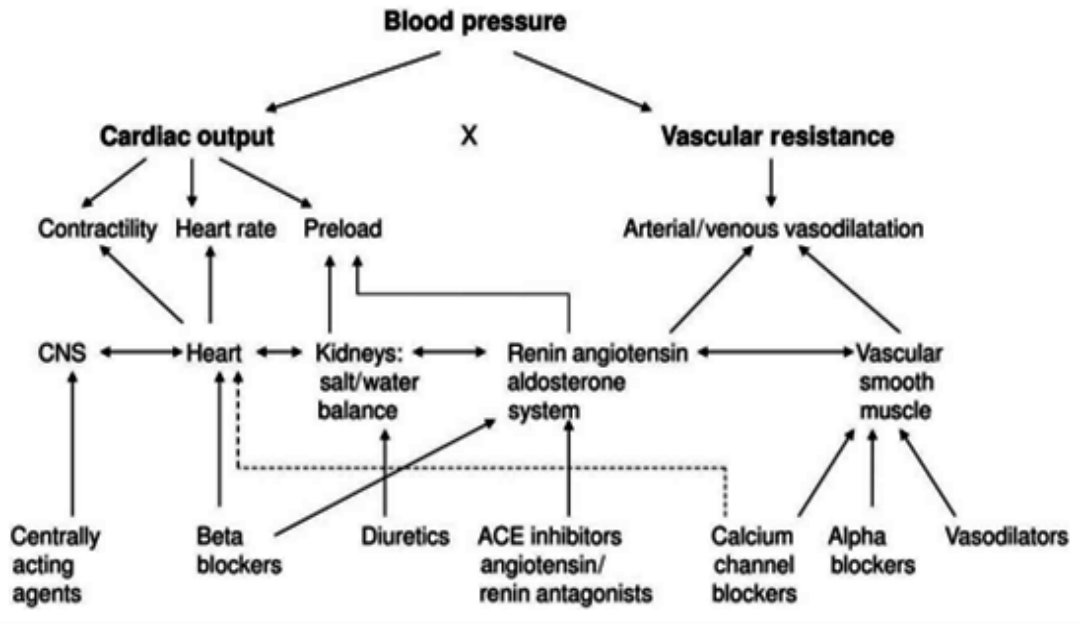


Figure 1.5: Overview of the mechanisms of action of common classes of antihypertensive drugs.

1.4 Profile of Prazosin Hydrochloride – the Drug under Study

Prazosin hydrochloride is the hydrochloride salt form of prazosin, a medication belonging to the class of alpha-adrenergic blockers. It is primarily used to treat high blood pressure (hypertension) and symptoms of benign prostatic hyperplasia (BPH). Thus it belongs to the class of alpha-adrenergic blockers, which works by blocking the action of certain natural substances in the body, such as adrenaline, leading to relaxation of blood vessels and improved blood flow. This effect helps to lower blood pressure and relieve symptoms associated with conditions like hypertension and benign prostatic hyperplasia (BPH).

Prazosin hydrochloride is available in oral tablet and capsule form and is typically prescribed by healthcare professionals to manage high blood pressure, BPH symptoms, and occasionally to alleviate nightmares and symptoms of post-traumatic stress disorder (PTSD). As with any medication, it may have potential side effects and interactions, so it should be used under medical supervision.

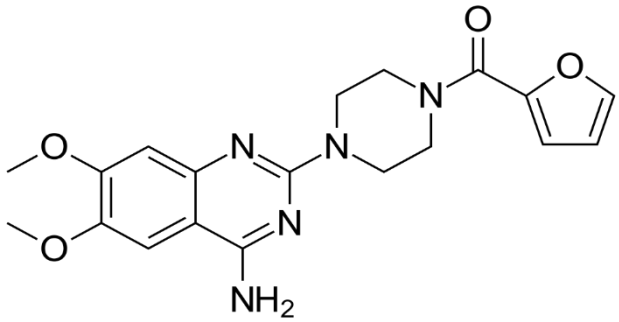


Figure 1.6: Chemical Structure of Prazosin Hydrochloride

1.4.1 Physiochemical Properties

Table 1.1: Physiochemical properties of prazosin hydrochloride tablets

Chemical Name: 2-[4-(furan-2-carbonyl)piperazin-1-yl]-6,7-dimethoxy-3,4-dihydroquinazolin-4-imine hydrochloride
Molecular Formula: $C_{19}H_{22}ClN_5O_4$
Molecular Weight: 419.9 g/mol
Melting Point: 278-280° C
PK_a: Acidic (11.09), Basic (13.32)
Solubility: Soluble in isotonic saline, water, ethanol, methanol, dimethylformamide, dimethylacetamide, chloroform, acetone.
Appearance: A White to tan powder
Stability/ Storage: Stable for at least two years when stored desiccated at room temperature and protected from the light.

1.4.2 Pharmacology

1.4.2.1 Pharmacokinetics

Absorption:

- Prazosin is well absorbed after oral administration.
- Peak plasma concentrations are typically achieved within 1 to 3 hours after ingestion.

Distribution:

- Prazosin has a relatively short half-life of about 2 to 3 hours.
- It is extensively bound to plasma proteins, predominantly albumin.
- The volume of distribution is about 0.6 L/kg

Metabolism:

- Prazosin undergoes extensive first-pass metabolism in the liver.

- In animals, prazosin hydrochloride is heavily metabolized. This occurs through liver demethylation and conjugation. Some studies in humans or human cells in vitro show similar prazosin metabolism.

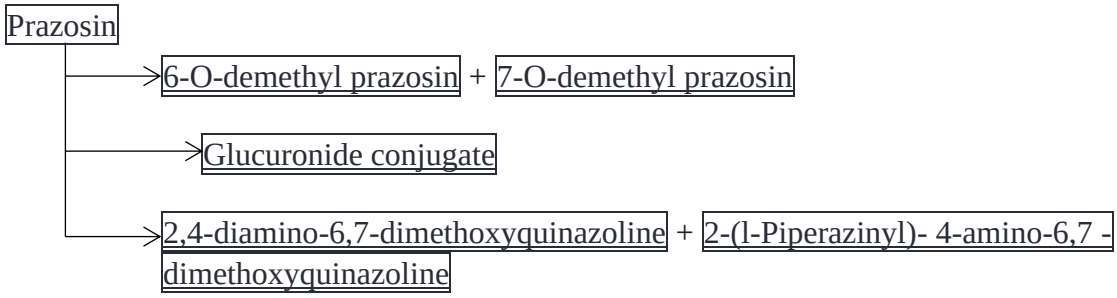


Figure 1.7: An Overview of the Metabolism of Prazosin

Excretion:

- Metabolites of prazosin are mainly excreted in the urine.
- A small portion of metabolites is eliminated through feces.

Protein Binding:

Highly bound to proteins with 97% binding to albumin and alpha 1-acid glycoprotein. About 80-90% is thought to be bound to albumin.

Half-life: The plasma half-life is about 2-3 hours.

Factors Affecting Pharmacokinetics:

- **Liver function:** Hepatic impairment may affect the metabolism of prazosin, requiring dosage adjustments.
- **Age:** Elderly patients may exhibit altered pharmacokinetics due to changes in liver function and clearance.
- **Co-administration with other drugs:** Drugs that affect hepatic enzyme activity or protein binding may influence prazosin's pharmacokinetics.

1.4.2.2 Pharmacodynamics

The pharmacodynamics and therapeutic effect of prazosin includes a decrease in blood pressure as well as clinically significant decreases in cardiac output, heart rate, blood flow to the kidney, and glomerular filtration rate. The decrease in blood pressure may occur in both standing and supine positions.

Many of the above effects are due to vasodilation of blood vessels caused by prazosin, resulting in decreased peripheral resistance. Peripheral resistance refers to the level resistance of the blood vessels to blood that flows through them. As the blood vessels constrict (narrow), the resistance increases and as they dilate (widen), and peripheral resistance decreases, lowering blood pressure.

Some studies suggest that the drug improves sleep in patients suffering from insomnia related to nightmares and post-traumatic stress disorder, caused by hyperarousal. This effect likely occurs through the inhibition of adrenergic stimulation found in states of hyperarousal.

1.4.2.3 Mechanism of Action

Alpha-adrenergic receptors are essential for the regulation of blood pressure in humans. Two types of alpha receptors, alpha 1 and alpha 2, both play a role in regulating blood pressure. Alpha-1 receptors are postsynaptic (located after the nerve junction, or space between a nerve fiber and target tissue). In this case, the target tissue is the vascular smooth muscle. These receptors, when activated, increase blood pressure .

Prazosin inhibits the postsynaptic alpha-1 adrenoceptors. This inhibition blocks the vasoconstricting (narrowing) effect of catecholamine (epinephrine and norepinephrine) on the vessels, leading to peripheral blood vessel dilation. Through blood vessel constriction by adrenergic receptor activation, epinephrine and norepinephrine normally act to increase blood pressure.

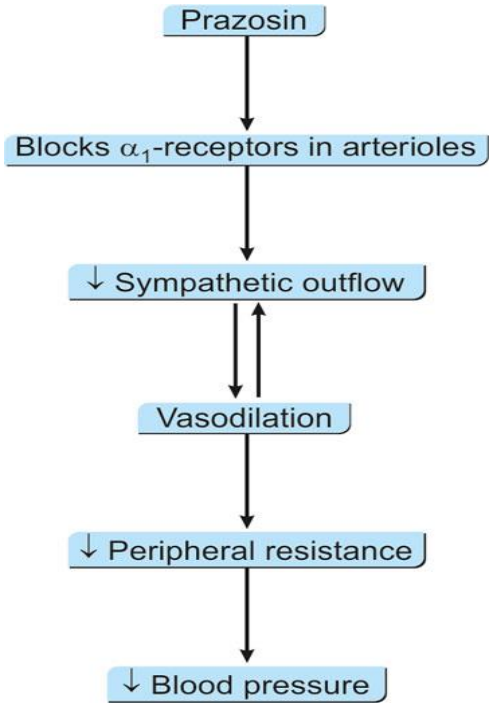


Figure 1.8: Mechanism of action of Prazosin Hydrochloride

1.4.3 Indications and Contraindications

Indications:

- **Hypertension (High Blood Pressure):** Prazosin acts as an alpha-1 adrenergic receptor antagonist, leading to vasodilation and subsequent reduction in blood pressure. It is particularly effective in treating hypertension in patients with sympathetic nervous system over activity.
- **Benign Prostatic Hyperplasia (BPH):** Prazosin can alleviate symptoms associated with BPH, such as urinary hesitancy, urgency, frequency, and nocturia, by relaxing smooth muscle tone in the prostate and bladder neck.
- **Post-Traumatic Stress Disorder (PTSD) Nightmares:** Prazosin has shown efficacy in reducing the frequency and intensity of nightmares associated with PTSD, possibly due to its ability to block the effects of adrenaline on alpha-1 receptors in the brain.

Contraindications:

- **Hypotension:** Prazosin can cause a significant drop in blood pressure, making it unsuitable for individuals with already low blood pressure.
- **Allergy:** People allergic to prazosin or any components of the medication should not take it.
- **Heart Failure:** In some cases, prazosin may exacerbate heart failure symptoms.

- **Hepatic Impairment:** Liver dysfunction can affect the metabolism and clearance of prazosin, so caution is needed in such cases.
- **Pregnancy and Breastfeeding:** Its safety during pregnancy and breastfeeding is not established, so it is generally avoided unless benefits outweigh risks, and a healthcare provider approves its use.

1.4.4 Side Effects

Along with its needed effects, a medicine may cause some unwanted effects. Although not all of these side effects may occur, if they do occur they may need medical attention.

Following are the probable side effects reported with the use of prazosin:

More common:

- Dizziness
- Fast, irregular, pounding, or racing heartbeat or pulse
- Sleepiness

Less common:

- Blurred vision
- Chills
- Cold sweats
- Dizziness, faintness, or lightheadedness when getting up from lying or sitting position
- Swelling
- Trouble breathing

Rare:

- Bloating
- Constipation
- Darkened urine
- Decreased interest in sexual intercourse
- Fever
- Inability to have or keep an erection
- Indigestion
- Loss in sexual ability, desire, drive, or performance
- Loss of appetite
- Nausea
- Painful or prolonged erection of the penis for more than 4 hours
- Pains in the stomach, side, or abdomen, possibly radiating to the back
- Yellow eyes or skin.

1.5 Prazosin Tablet Products Available in the Local Market of Bangladesh

Table 1.2: List of prazosin hydrochloride tablets available in the local market of Bangladesh

Brand Name	Dosage Form	Strength	Manufacturer
Alphalok	Tablet	2 mg	Opsonin Pharma Ltd.
Alphalok	Tablet	1 mg	Opsonin Pharma Ltd.
Alphalok XR	Tablet (Extended Release)	5 mg	Opsonin Pharma Ltd.
Alphalok XR	Tablet (Extended Release)	2.5 mg	Opsonin Pharma Ltd.
Alphapress	Tablet	2 mg	Renata Limited
Alphapress	Tablet	1 mg	Renata Limited
Alphapress XR	Tablet (Extended Release)	5 mg	Renata Limited
Alphapress XR	Tablet (Extended Release)	2.5 mg	Renata Limited
G-Prazosin	Tablet	1 mg	Gonoshasthaya Pharma Ltd.
G-Prazosin	Tablet	2 mg	Gonoshasthaya Pharma Ltd.
G-Prazosin SR	Tablet (Extended Release)	5 mg	Gonoshasthaya Pharma Ltd.
Minipress XL	Tablet (Extended Release)	5 mg	Janata Traders (Mfg. by Pfizer)
Minipress XL	Tablet (Extended Release)	2.5 mg	Janata Traders (Mfg. by Pfizer)

Brand Name	Dosage Form	Strength	Manufacturer
Prazolok	Tablet	2 mg	Square Pharmaceuticals PLC
Prazolok	Tablet	1 mg	Square Pharmaceuticals PLC
Prazolok ER	Tablet (Extended Release)	2.5 mg	Square Pharmaceuticals PLC
Prazolok ER	Tablet (Extended Release)	5 mg	Square Pharmaceuticals PLC
Prazopress	Tablet	2 mg	UniMed UniHealth Pharmaceuticals Ltd.
Prazopress	Tablet	1 mg	UniMed UniHealth Pharmaceuticals Ltd.
Prazopress ER	Tablet (Extended Release)	5 mg	UniMed UniHealth Pharmaceuticals Ltd.
Prazopress ER	Tablet (Extended Release)	2.5 mg	UniMed UniHealth Pharmaceuticals Ltd.
Razosin ER	Tablet (Extended Release)	2.5 mg	Popular Pharmaceuticals Ltd.
Razosin ER	Tablet (Extended Release)	5 mg	Popular Pharmaceuticals Ltd.
Vasofex XR	Tablet (Extended Release)	2.5 mg	Biopharma Limited
Vasofex XR	Tablet (Extended Release)	5 mg	Biopharma Limited

Chapter Two: Materials and Methods

2.1 Materials and Reagents

Materials

- **Active Pharmaceutical Ingredient (API):** Prazosin Hydrochloride (Potency- 98.56%; White a Crystal powder)
- **Tablet Products:** Four brands of conventional Prazosin Hydrochloride Tablets (2 mg)

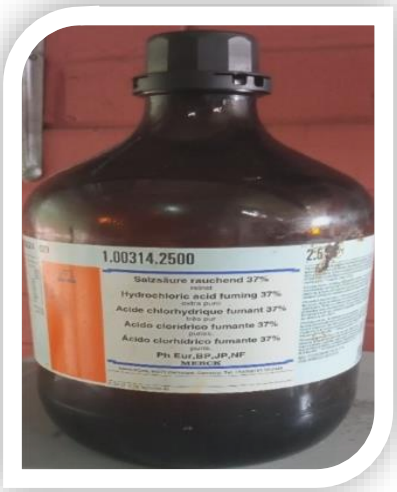
Reagents and Solvents

Table 2.1 lists the reagents and solvents used in the work:

Table 2.1: Reagents and Solvents

Name	Source	Country of origin
Concentrated Hydrochloric Acid (37%)	Merck	Germany
Sodium Lauryl Sulfate	Merck	Germany
Distilled Water	Department of Pharmacy, Jahangirnagar University	

Sodium Lauryl Sulfate



Hydrochloric Acid

Distilled Water

Figure 2.1 : Reagents and Solvents

Apparatus and Glassware

Table 2.2 lists the apparatus and glassware used in the work:

Table 2.2: Apparatus and Glassware

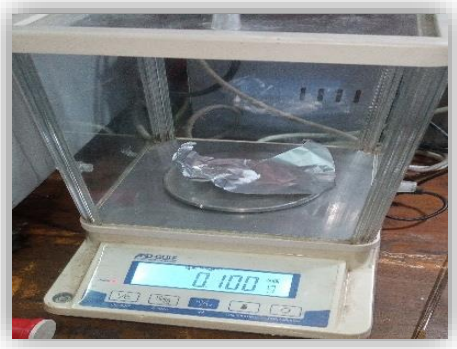
Name	**Specification**
Volumetric Flask	10 ml, 50 ml, 100 ml, 500 ml & 1000 ml
Measuring Cylinder	10 ml & 50 ml
Pipette	10 ml
Funnel	Small & Medium
Test Tubes and Test Tube Racks (steel, plastic & wooden)	Small & Medium
Beaker	25 ml, 50 ml, 100 ml, 250 ml, 500 ml, 800 ml & 1000 ml
Spatula	Small
Stirrer/ Glass Rod	Small
Pipette Filler	Small
Mortar & Pestle	Medium
Aluminum Foil	Standard
Filter Paper	11.0 cm
Kim Wipes	Kimtech (11cm x 21cm)
Falcon Tube	15 ml
Dropper	Small
Conical flask	250 ml, 1000 ml & 2000 ml
Distilled Water Dispenser	250 ml & 500 ml

Fig 2.2: Apparatus and Glassware

Equipment and Instruments

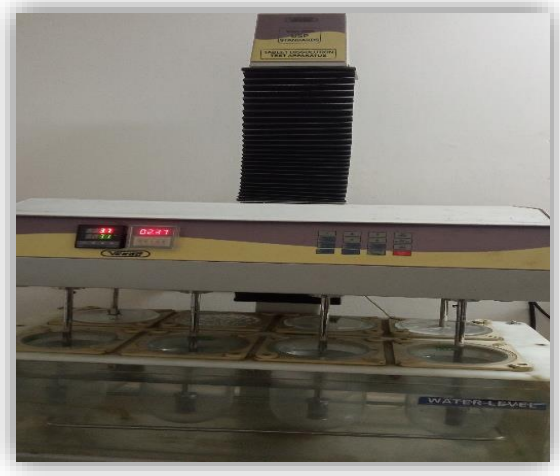
Table 2.3 lists the equipment and instruments used in the study with their models/manufacturer names:

Table 2.3: Equipment and Instruments

Instruments	Model/Manufacturer	Purpose
 **UV-Vis Spectrophotometer**	UV 1601 PC SHIMADZU Japan	To study the release potency and pattern of the tablet
 **UV-Vis Spectrophotometer**	EMC-61PCS-UV Germany	To study the release potency and pattern of the tablet
 **Electronic Balance**	AND-GULF Precision Electronic Balance China	For precise measurement of various ingredients

Instruments	Model/Manufacturer	Purpose
 **Hot Air Oven**	Gallenkamp UK	For drying up the glassware
 **pH Meter**	SI analytics lab 845 Germany	For the measurement of pH of the prepared release media
 **Slide Calipers**	SDK China	To study the thickness & diameter of tablets
 **Hardness Tester**	Campbell Electronics India	To study the hardness of tablets

Instruments	Model/Manufacturer	Purpose
 **Friability Testing Apparatus**	Campbell Electronics Bombay 400025 Thermonik India	To measure the friability of tablets
 **Disintegration Test Machine**	Campbell Electronics Bombay 400025 Thermonik India	To study the disintegration time of tablets
 **Magnetic heating Stirrer**	CJJ78-1 Magnetic Heating Stirrer China	For stirring and mixing materials
 **Centrifuge Machine**	TDL-60B Human Lab Instrument Co Korea	For separation of insoluble solid particles from the solution/sample

Instruments	Model/Manufacturer	Purpose
 **Dissolution Tester**	Veego India	To study the drug release profile of tablets

2.2 Methods

2.2.1 Collection of samples

- **APIs**

  Prazosin Hydrochloride (API) was a kind gift donated by Square Pharmaceuticals Ltd., Bangladesh.

- **Tablets**

  Four brands of conventional prazosin hydrochloride tablet products available locally were collected from different retail pharmacies located in Savar area and Dhaka city. The products were coded as **A-2, B-2, P-2, Q-2**. There are some other brands licensed with Directorate General of Drug Administration (DGDA), but they are not in active supply.

2.2.2 Assessment of the physical parameters

The tablet products were assessed for the following physical parameters:

- Organoleptic properties
- Thickness and diameter
- Hardness & Friability
- Weight and weight variation
- Disintegration time

2.2.2.1 Organoleptic properties

The color and odor of the tablet products were observed and recorded.

2.2.2.2 Thickness and diameter

Ten tablets were randomly selected from each group and their thickness and diameters were measured in millimeters using slide calipers (SDK, China).

2.2.2.3 Hardness test

Five tablets from each group were taken randomly and their hardness was measured in kg/cm^2 using the hardness tester (Campbell Electronics, India). The tablet to be tested was placed diametrically between the fixed and the moving jaw and the reading of the indicator was adjusted to zero. Then force was applied until the tablet broke.

2.2.2.4 Friability test

Ten tablets were taken randomly and placed on a sieve. Loose dust was removed with the aid of air pressure or a soft brush. Tablet samples were weighed accurately and placed in the friabilator. After rotating the friabilator for the given number of rotations (100 rotations/4 min), loose dust was removed from the tablets as before. Finally, tablets were re-weighed. The loss in weight indicated the ability of the tablets to withstand this type of wear.

The percent friability was determined by following formula:

$$\textbf{\% friability} = \frac{\textbf{Initial weight} - \textbf{Final weight}}{\textbf{Initial weight}} \textbf{ X 100}$$

2.2.2.5 Weight and weight variation test

- From each group ten tablets were taken at random and weighed. The average weight was calculated.
- Then each tablet was weighed individually, and their weights were compared with the average weight.
- Upper and lower weight variation were calculated using the following formula:

$$\textbf{Upper weight variation} = \frac{\textbf{Highest weight} - \textbf{Average weight}}{\textbf{Average weight}} \textbf{ x 100}$$

$$\textbf{Lower weight variation} = \frac{\textbf{Average weight} - \textbf{Lowest weight}}{\textbf{Average weight}} \textbf{ x 100}$$

2.2.2.6 Disintegration test

As reported before by different investigators, the disintegration test of Prazosin Hydrochloride Tablet products was carried out in two different media, viz., water and simulated gastric fluid.

2.2.2.6.1 Preparation of media for disintegration test

Distilled water: Distilled water was prepared in the Pharmaceutics Laboratory of Pharmacy Department, JU using a Distillation Machine.

Simulated gastric fluid (pH 1.2):

- To prepare simulated gastric fluid (pH 1.2), 8.36 ml of 37% concentrated hydrochloric acid (HCl) was added to approximately 1000 ml of water in a 1000 ml volumetric flask and the final volume was made up to 1000 ml.
- Necessary pH adjustments were done by adding NaOH or HCl as required while monitoring the pH by a pH meter.

2.2.2.6.2 Measurement of Disintegration Time

- The disintegration test was performed using the USP Disintegration Test Apparatus.
- The device uses 6 glass tubes that are 3-inch long, open at the top and held against a 10-mesh screen at the bottom end of the basket rack assembly.

- To test for disintegration time, one tablet was placed in each tube and the basket rack was positioned in a 1-L beaker of water or simulated gastric fluid at 37 ± 2 °C such that the tablet remains 2.5 cm below the surface of liquid on their upward movement and not closer than 2.5 cm from the bottom of the beaker in their downward movement.
- A standard motor driven device was used to move the basket (assembly) containing the tablets up and down through a distance of 5-6 cm at a frequency of 28 to 32 cycles per minute.
- Perforated plastic discs were placed to top of the tablets to impart an abrasive action to the tablets and to retain floating tablets in place.
- Time taken for the tablets to disintegrate (break apart) into small pieces was recorded.

Fig 2.3: Parts of disintegration test machine

2.2.3 Assay

The assay of Prazosin Hydrochloride Tablet products was performed spectrophotometrically by a UV-Vis Spectrophotometer (UV 1601 PC SHIMADZU, Japan). The assay was performed using 0.1 N HCl (pH 1.2) containing 3% sodium lauryl sulfate as the solvent system.

2.2.3.1 Determination of the λ_{max} of Prazosin Hydrochloride in 0.1 N HCl

The λ_{max} of Prazosin Hydrochloride was determined by scanning solutions of the drug prepared in 0.1 N HCl (pH 1.2) containing 3% sodium lauryl sulfate at different concentrations using the UV-Vis spectrophotometer over the wavelength range of 200-400 nm and it was found to be 248 nm.

2.2.3.2 Preparation of standard calibration curve

For analyzing potency of Prazosin Hydrochloride tablet products, a standard calibration curve was created in 0.1 N HCl (pH 1.2) containing 3% sodium lauryl sulfate. Prazosin hydrochloride solutions of 4 different concentrations, *viz*., 1, 2.5, 5 and 7.5 µg/ml, were prepared and their absorbances were determined at the λ_{max} of 248 nm using the fresh media as the blank. The absorbances were plotted against the corresponding concentrations to create the curve, and the straight-line equation of the curve with the coefficient of determination (r^2) was determined using MS Excel program.

2.2.3.3 Preparation of prazosin hydrochloride sample solution

- For each brand of tablet products, 20 randomly selected tablets were weighed and finely powdered.
- Then an accurately weighed portion of the powder, equivalent to about 2 mg of Prazosin hydrochloride, was transferred to a 10 mL volumetric flask containing the media (0.1 N HCl (pH 1.2) containing 3% sodium lauryl sulfate) to give a solution having a concentration of
- Then the mixture was shaken by a Magnetic Stirrer (CJJ78-1, China) for 3 hours, and centrifuged by a centrifuge machine (TDL-60B, Human Lab Instrument Co, Korea) at 5000 rpm for 5 min to separate the undissolved materials.
- The supernatant was diluted sufficiently to give a solution having a concentration of 5 µg/ml (as per the label strength).

2.2.3.4 Determination of the potency of the tablet samples

The absorbance of the prepared sample solution (expected to have a concentration of 5 µg/ml) was determined spectrophotometrically at 248 nm using fresh media as the blank and the actual concentration of was determined from the standard calibration curve equation.

The potency of the tablet sample was determined by comparing the measured concentration of the drug in the test sample with the expected concentration in the same as per the label claim of the drug using the following formula:

$$\textbf{Potency (\%)} = \frac{C1}{C} \textbf{ x 100}$$

where,

Expected concentration of the drug in the sample solution = C

Measured concentration of the drug in the sample solution = C_1

2.2.4 Dissolution study

The dissolution study of the tablet products was performed by a USP Dissolution Testing Apparatus-1 (Basket Apparatus-Veego, India) using 0.1N HCl as the dissolution media.

2.2.4.1 Determination of the λ_{max} of Prazosin Hydrochloride in 0.1N HCl

The λ_{max} of Prazosin Hydrochloride was determined by scanning solutions of the drug prepared at different concentrations in 0.1N HCl by the UV-Vis spectrophotometer over the wavelength range of 200-400 nm and it was found to be 247 nm. Fresh 0.1N HCl solution was used as the blank.

The stock solution was prepared by dissolving 30 mg of Prazosin Hydrochloride in 600 ml of 0.1N HCl giving a concentration of 50 µg/ml. The working solutions were prepared from the stock solution with appropriate dilution.

2.2.4.2 Preparation of standard calibration curve

A standard calibration curve for analyzing Prazosin Hydrochloride in the release media, viz. 0.1N HCl solution (pH 1.2) was created. Prazosin hydrochloride solutions of different concentrations, ranging from 1 to 20 µg/ml, were prepared in 0.1N HCl solution (pH 1.2) and their absorbances were determined at 247 nm using the fresh media as the blank. The absorbances were plotted against the corresponding concentration to create the curve.

2.2.4.3 Dissolution study of tablet products in 0.1N HCl solution (pH 1.2).

- As already mentioned, the dissolution test of the tablet products of Prazosin HCl (2 mg) was performed by a USP Apparatus-1 using 0.1N HCl (pH 1.2) as the release media.
- The apparatus has 7 stations, each of which consists of a motor, a metallic drive shaft, a cylindrical basket, and a covered vessel made of inert transparent material. The basket is fastened to the bottom of the shaft, which is connected to the motor. The vessel is cylindrical with a hemispherical bottom and a nominal capacity of 1000 ml. For the purpose of this study, the vessels were filled with 900 ml of dissolution media and maintained at 37°± 0.5 °C by a constant temperature bath.
- For each of the 4 brands, 6 tablets were placed in 6 baskets, one in each. The 7^{th} vessels was used only for keeping fresh media for subsequent use. The basket was immersed in the dissolution medium (as specified in the monograph) contained in the flask and the motor was adjusted to turn at 100 rpm.
- The experiment was run for 120 min and 5 ml samples were withdrawn for analysis from the vessels at intervals of 0, 5, 10, 20, 30, 45, 60, 90 and 120 min intervals.
- The withdrawn samples were analyzed spectrophotometrically at 247 nm and the amount of drug released (%) at respective time-point was determined using the standard calibration curve constructed for the drug in the media used.
- All of the measurements were done in triplicate.

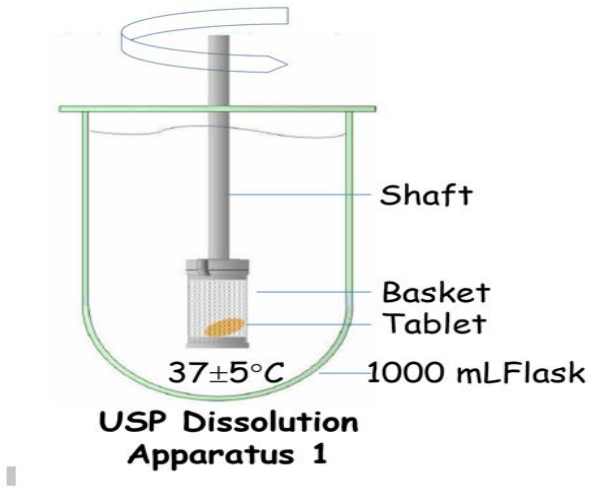


Fig 2.4: USP Apparatus 1 (Basket Apparatus)

Dissolution conditions used in the study at a glance:

Apparatus: USP Apparatus 1 (Basket Apparatus)

Medium: 0.1N HCl solution (pH 1.2)

Volume: 900 ml

Speed: 100 rpm

Temperature: 37°C ± 0.5°C

Time: 120 min

Intervals (min): 0**,** 5, 10, 20, 30, 45, 60, 90, 120 min

Chapter Three: Results

3.1 Physical parameters of tablets

3.1.1 Organoleptic properties

As shown in **Table 3.1**, the tablet products were white and pink in color. None of the tablet products, however, had any odor.

Table 3.1: Organoleptic properties of studied prazosin hydrochloride tablet products

Sample Code	Color	Odor
A-2	White	None
B-2	White	None
P-2	Pink	None
Q-2	White	None

3.1.2 Shape

Shape: As shown in **Table 3.2**, the tablets (A-2, B-2, P-2 and Q-2) were round & rhombus in shape.

Table 3.2: Shapes of the studied tablet products

Sample Code	Shape
A-2	Round
B-2	Round
P-2	Rhombus
Q-2	Round

3.1.3 Diameter and thickness:

Table 3.3 shows the average diameter and thickness of studied tablet products with maximum percentage of deviation from the average. The average diameter and thickness data are graphically illustrated in **Figures 3.1** and **3.2**, respectively. The average diameters of the tablets ranged from 3.7±0.092 mm to 5.30±0.082 mm, while the average thicknesses were in the range of 2.7±0.047 mm to 4.09±0.110 mm.

Table 3.3: Average diameter and thickness of tablet products with percentage (%) deviation

Sample Code	Average diameter ± S.D. (mm)	Maximum Deviation (%)	Average thickness ±S.D. (mm)	Maximum Deviation (%)
A-2	5.30±0.082	3.774	3.94±0.084	3.553
B-2	4.11±0.010	0.730	2.7±0.047	3.704
P-2	4.04±0.126	4.738	4.09±0.110	4.645
Q-2	3.77±0.092	0.796	3.08±0.092	3.896

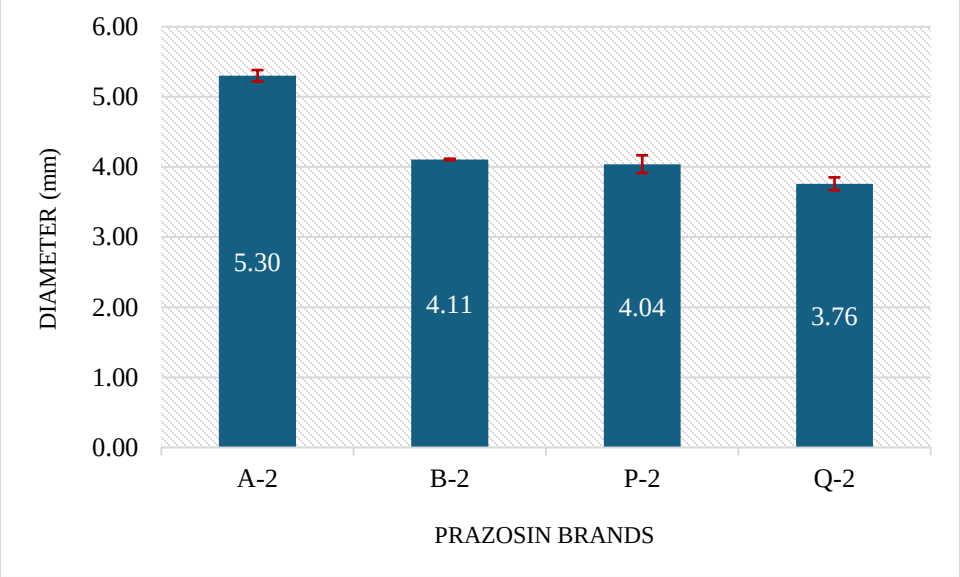


Figure 3.1: Average diameters of studied prazosin hydrochloride tablets

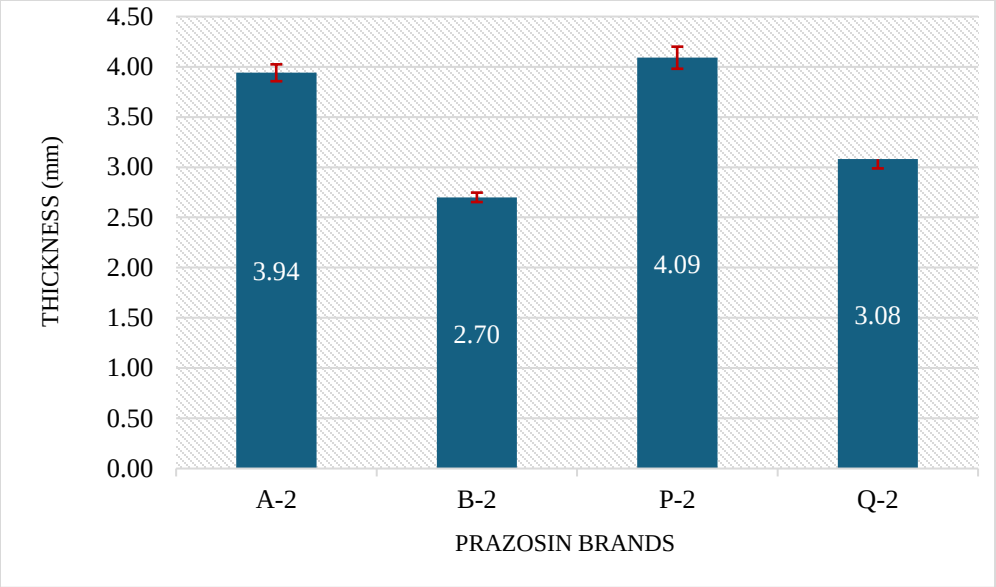


Figure 3.2: Average thickness of studied prazosin hydrochloride tablets

3.2. Hardness test

Table 3.4 shows the hardness of studied Prazosin Hydrochloride tablet products. The hardness of the samples ranged from 2.34±0.152 kg/cm^2 to 4.26±0.089 kg/cm^2.The data are graphically presented in **Figure 3.3**.

Table 3.4: Hardness of studied prazosin hydrochloride tablets

Sample Code	Tab-1	Tab-2	Tab-3	Tab-4	Tab-5	Average Hardness ± S.D. (kg/cm^2)
A-2	2.4	2.5	2.4	2.1	2.3	2.34±0.152
B-2	2.9	3.0	2.8	2.7	2.8	2.84±0.114
P-2	4.2	4.4	4.3	4.2	4.2	4.26±0.089
Q-2	3.1	2.8	3.2	3	3.1	3.04±0.152

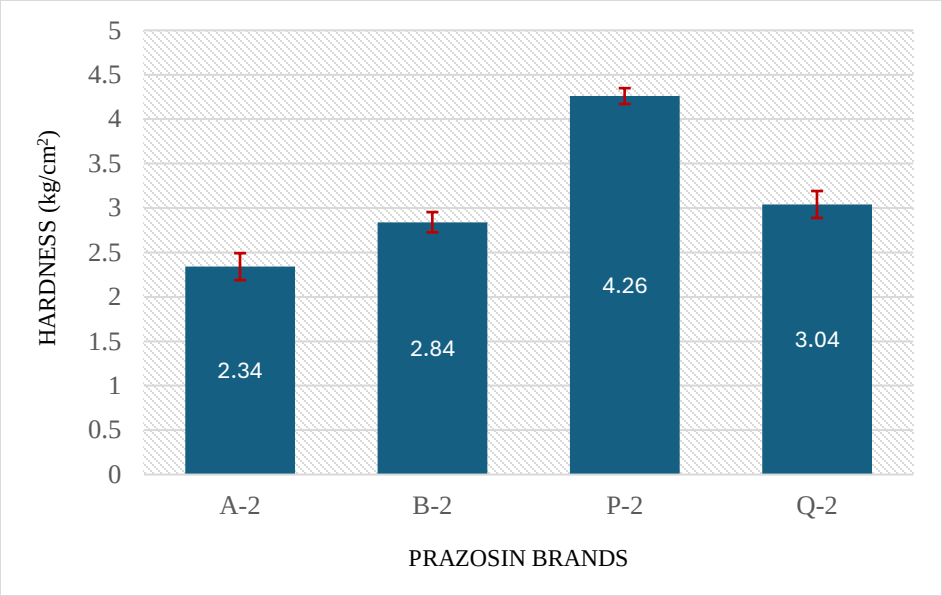


Figure 3.3: Average hardness of studied prazosin hydrochloride tablets

3.3 Friability test

The friability test results of the studied prazosin hydrochloride tablet products ranged from 0.931% to 6.032% (Table 3.5, Figure 3.4).

Table 3.5: Friability of the studied prazosin hydrochloride tablets

Sample code	Number of tablets	Initial weight (mg)	Final weight (mg)	Friability (%)
A-2	10	2040	2021	0.931
B-2	10	630	592	6.032
P-2	10	1930	1911	0.984
Q-2	10	1410	1390	1.418

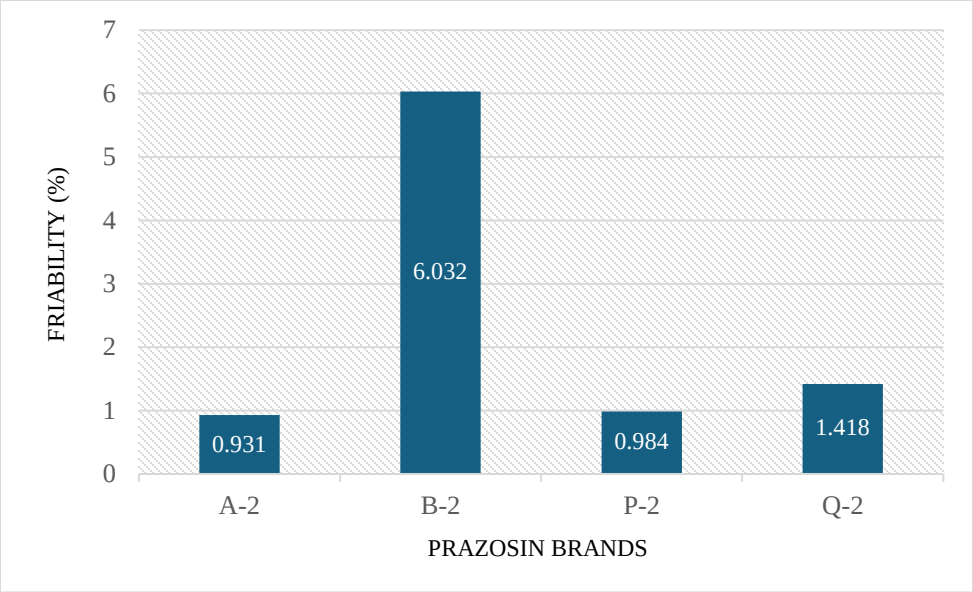


Figure 3.4: Friability of the studied prazosin hydrochloride tablets

3.4 Weight and weight variation test

Table 3.6 presents the average weights and maximum upper & lower weight variations for the tablet samples studied. The weights of the tablet products ranged from 63.1±0.316 mg to 212.4±0.843 mg. The data are represented graphically in **Figures 3.5 (a)** and **(b)**.

Table 3.6: Average weight and weight variation of studied prazosin hydrochloride tablets

Sample code	Average Weight ± S.D. (mg)	Upper weight variation (%)	Lower weight variation (%)
A-2	212.4±0.843	0.753	0.1883
B-2	63.1±0.316	1.426	0.158
P-2	194.5±0.849	0.771	0.257
Q-2	140.9±1.197	1.490	0.639

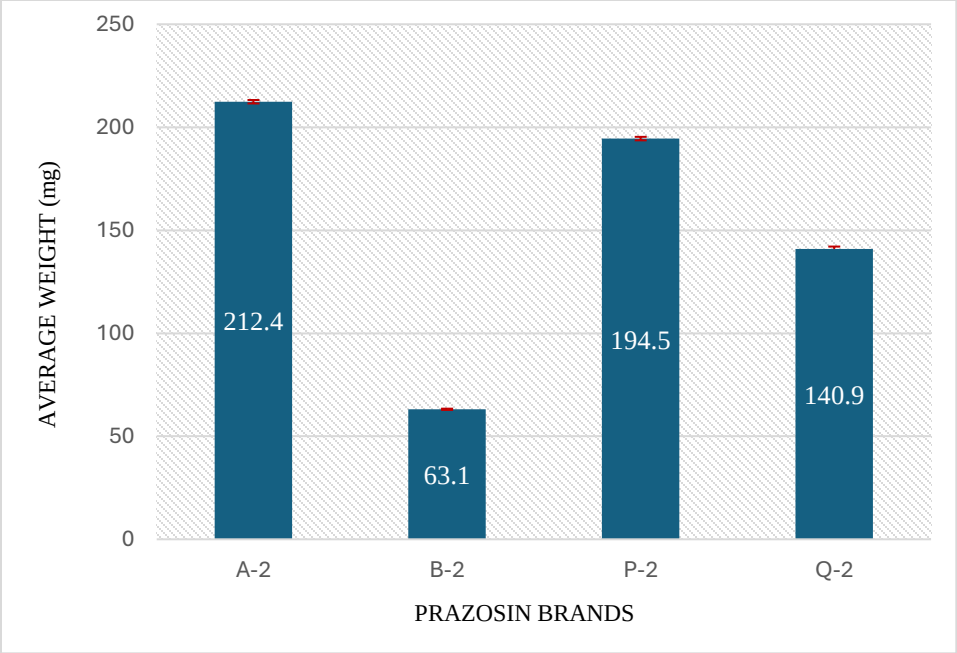


Figure 3.5 (a): Average weights of studied prazosin hydrochloride tablets

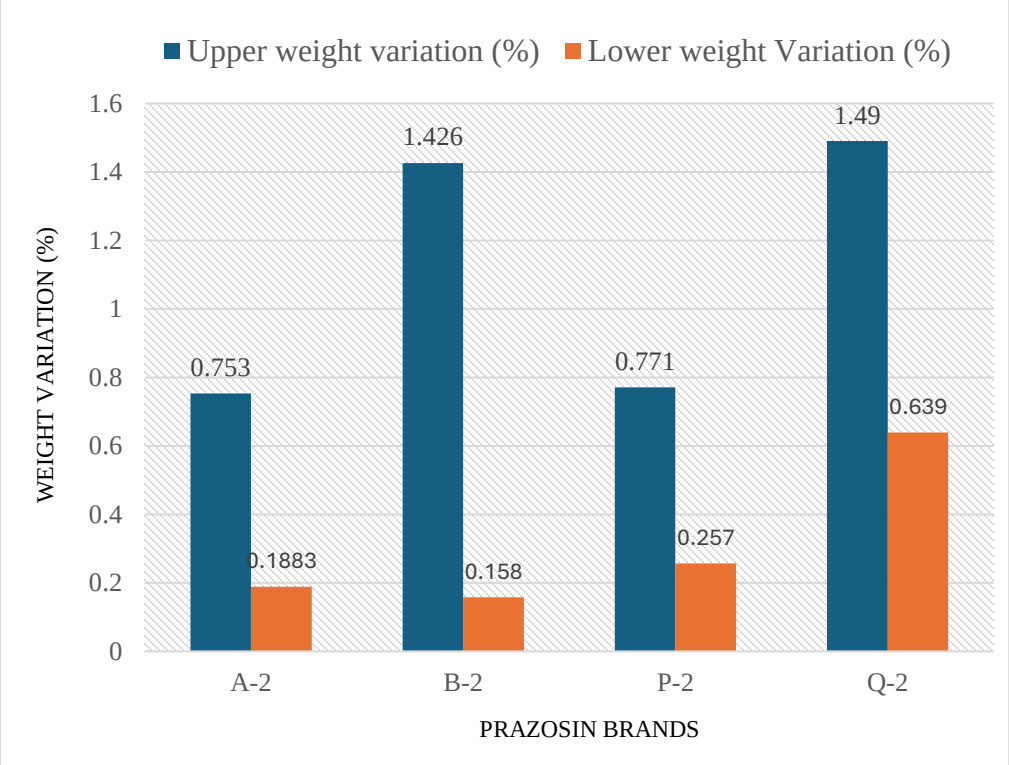


Figure 3.5 (b): Upper and lower weight variation of studied prazosin hydrochloride tablets

3.5 Disintegration test

Table 3.7 presents disintegration times observed for the prazosin hydrochloride tablet products studied using 2 different media, *viz.*, water and simulated gastric fluid (pH 1.2). The data are graphically illustrated in **Figure 3.6.** The disintegration time ranged from 12 min (B-2) to 17 min (A-2) in water and 6.5 min (Q-2) to 11.5 min (A-2) in simulated gastric fluid.

Table 3.7: Disintegration times of studied prazosin hydrochloride tablet products

Sample code	Water (min)	Simulated gastric fluid (min)
A-2	17	11.5
B-2	12	7.5
P-2	15.5	9
Q-2	12.5	6.5

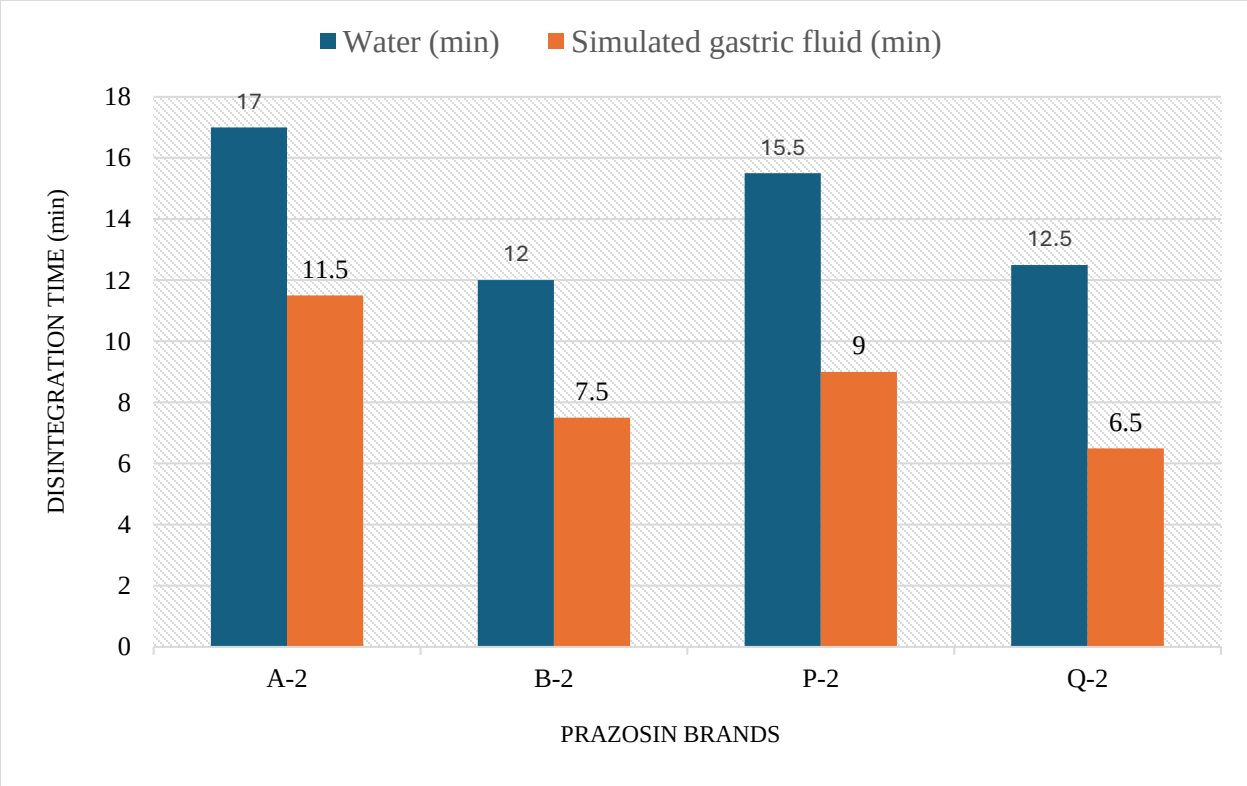


Figure 3.6: Disintegration times of studied prazosin hydrochloride tablets

3.6 Assay

The assay of the prazosin hydrochloride tablets was performed spectrophotometrically using 0.1N HCl solution (pH 1.2) containing 3% sodium lauryl sulfate as the solvent system.

3.6.1 Determination of λmax of prazosin hydrochloride in the solvent system used for assay

As shown in **Figure 3.7**, upon scanning prazosin hydrochloride solutions in 0.1N HCl solution (pH 1.2) containing 3% sodium lauryl sulfate over a wavelength range of 200-400 nm the λmax was found to be 248 nm.

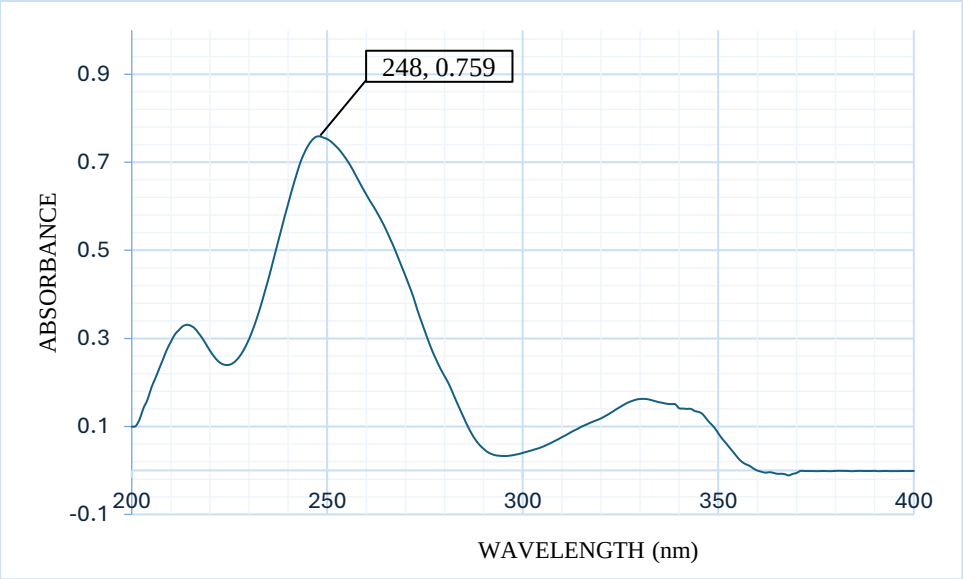


Figure 3.7: UV spectrum of prazosin hydrochloride in 0.1N HCl (pH 1.2) containing 3% sodium lauryl sulfate

3.6.2 Construction of standard calibration curve

Table 3.8 presents the data for the standard calibration curve drawn for prazosin hydrochloride from standard solutions of the drug prepared in solvent systems, *viz*, 0.1N HCl solution (pH 1.2) containing 3% sodium lauryl sulfate over a range of concentrations. The curve drawn based on these data with the straight-line equation and coefficient of determination (r^2) values are shown in **Figure 3.8**. The plot of absorbance against different concentrations shows linearity over the concentration range of 1 to 7.5 µg/ml.

Table 3.8: Data for standard calibration curves of Prazosin Hydrochloride in 0.1N HCl solution (pH 1.2) containing 3% Sodium Lauryl Sulfate at the λmax of 248 nm

Concentration (µg/ml)	1	2.5	5	7.5
Absorbance	0.082	0.198	0.517	0.739

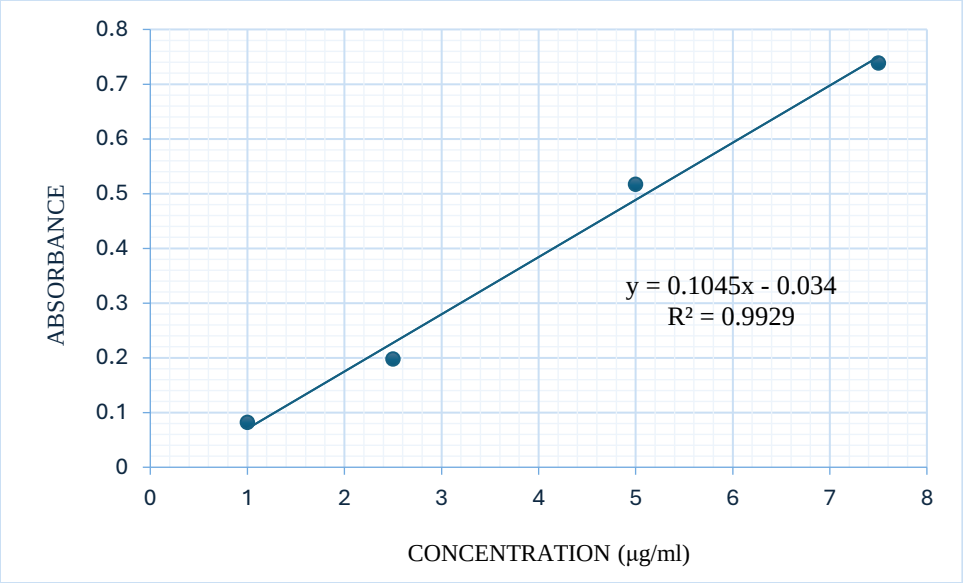


Figure 3.8: Standard calibration curve of Prazosin Hydrochloride in 0.1N HCl solution (pH 1.2) containing 3% Sodium Lauryl Sulfate

3.6.3 Determination of the potency of prazosin hydrochloride tablets

Table 3.9 presents the assay results of prazosin hydrochloride tablet products studied using 0.1N HCl containing 3% Sodium Lauryl Sulfate. The data are graphically presented in **Figure 3.9**. Assay results demonstrate a potency of 101.18% (P-2) to 106.22% (A-2).

Table 3.9: Assay results of studied Prazosin Hydrochloride tablet products

Sample Code	Potency (%)
A-2	106.22
B-2	101.81
P-2	101.18
Q-2	104.816

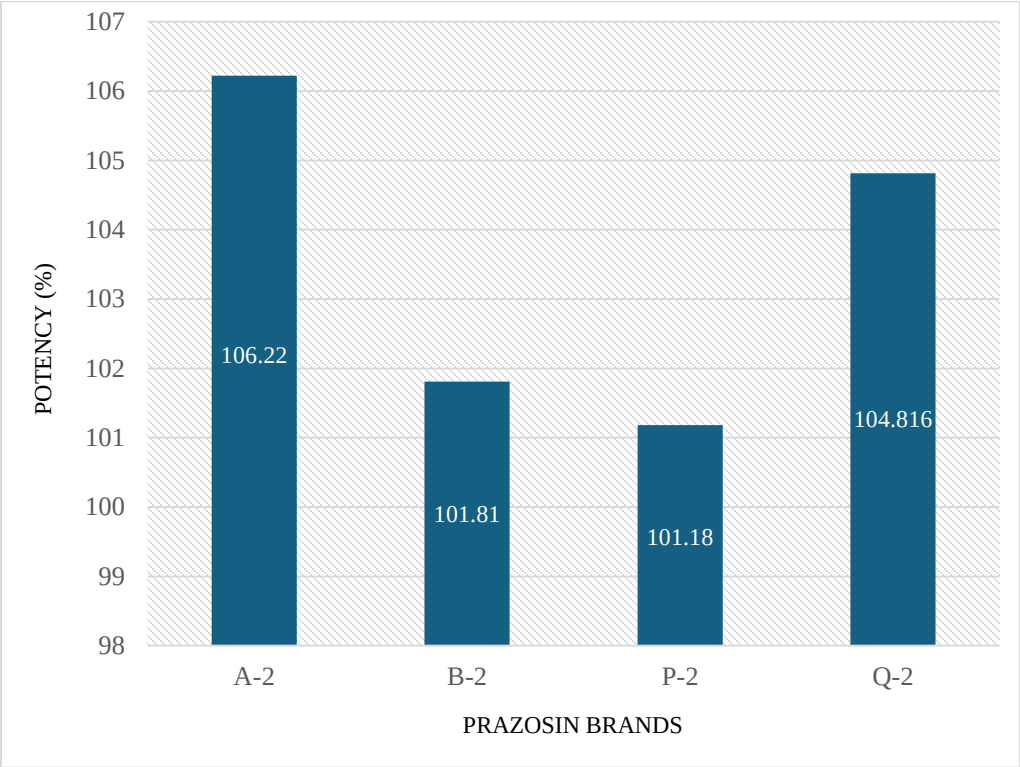


Figure 3.9: Assay results of studied prazosin hydrochloride tablets

3.7 Dissolution study

The dissolution study was conducted in 0.1N HCl solution (pH 1.2) using a USP Dissolution Apparatus-1 (Basket Apparatus).

3.7.1 Determination of λmax of prazosin hydrochloride in 0.1N HCl

As shown in **Figure 3.10**, upon scanning solutions of prazosin hydrochloride in 0.1N HCl by a UV-Vis spectrophotometer over a wavelength range of 200-400 nm the λmax was found to be 247 nm.

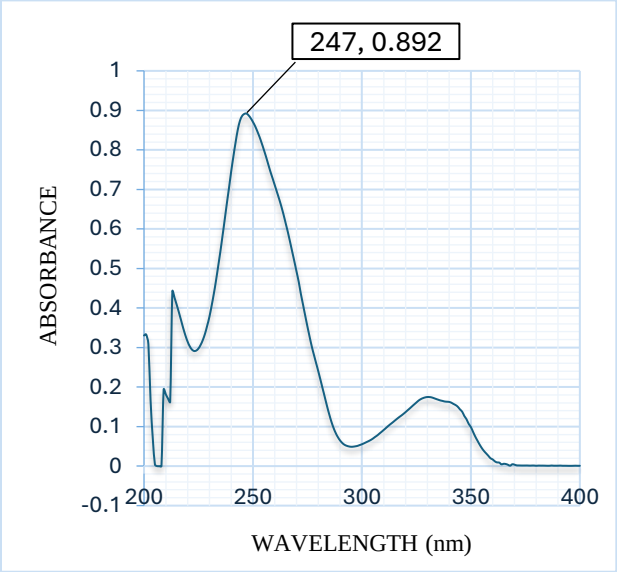


Figure 3.10: UV Spectrum of prazosin hydrochloride in 0.1N HCl

3.7.2 Construction of standard calibration curve of prazosin hydrochloride in 0.1N HCl

Table 3.10 presents the data for standard calibration curve drawn for prazosin hydrochloride from standard solutions of the drug prepared in 0.1N HCl solution (pH 1.2) over a range of concentration. The curve drawn based on these data with the straight-line equation and coefficient of determination (r^2) values is shown in **Figure 3.11**. The plot of absorbances against the concentrations of solutions showed linearity over a concentration range of 1 to 10 µg/ml.

Table 3.10: Data for standard calibration curve of Prazosin Hydrochloride in 0.1N HCl (pH 1.2)

Concentration (µg/ml)	1	2.5	5	7.5	10
Absorbance	0.07	0.265	0.575	0.785	1.008

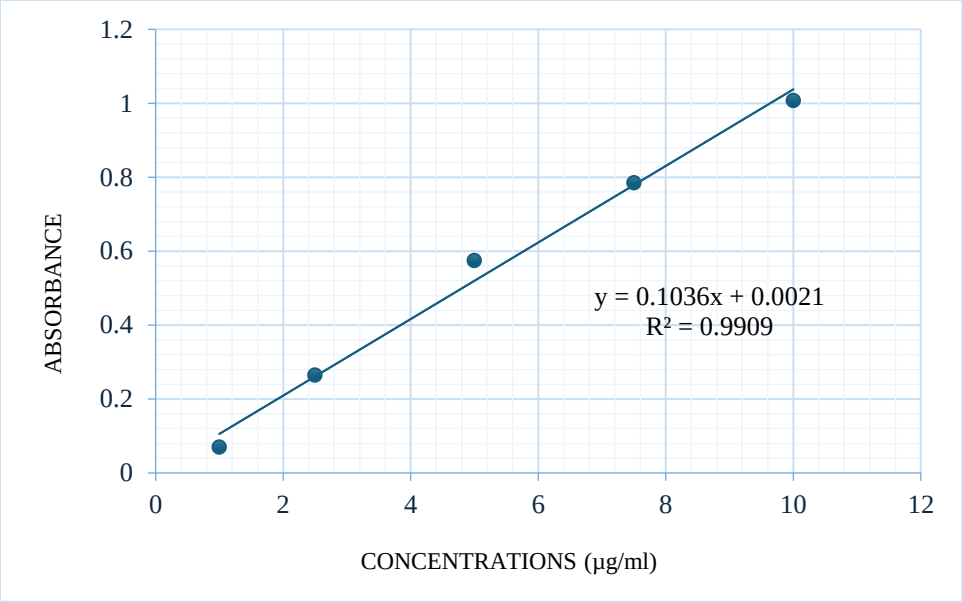


Figure 3.11: Standard calibration curve of prazosin hydrochloride in 0.1N HCl (pH 1.2)

3.7.3 Dissolution study of Prazosin Hydrochloride tablet products

Table 3.11 presents the average cumulative percent release for 6 tablets of each of 4 brands of prazosin hydrochloride tablet products (2 mg) in., 0.1N HCl (pH 1.2). The data are graphically presented in **Figure 3.12**. As is evident from **Table 3.11** and **Figure 3.12**, there was 75-80% and 90-95% release of drug by 60 and 90 min time points for all the brands studied. For most of the brands, after 90 min time point there was not much increase in drug release.

Table 3.11: Release profiles of prazosin hydrochloride tablets in 0.1N HCl (pH 1.2)

Sample code	% of drug released (average of 6 tablets)								
	Time (min)								
	0	5	10	20	30	45	60	90	120
A-2	0	6.51	16.16	35.12	46.68	65.86	75.59	94.72	96.69
B-2	0	6.23	19.28	34.47	47.13	67.91	76.09	89.77	98.25
P-2	0	6.13	21.56	41.99	58.88	65.81	81.71	94.95	103.29
Q-2	0	6.88	16.95	35.22	46.78	66.44	78.84	94.29	99.58

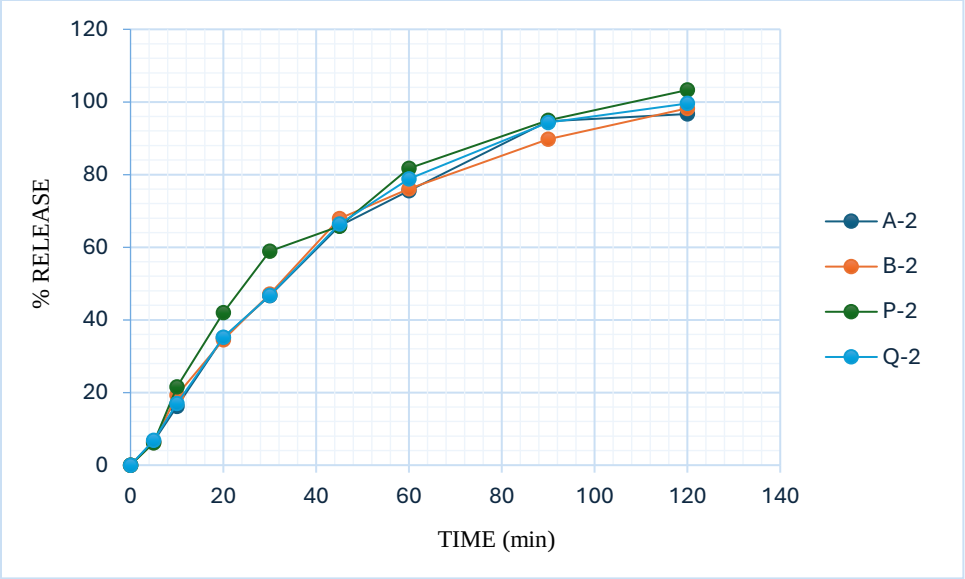


Figure 3.12: Release profiles of prazosin hydrochloride tablets in 0.1N HCl (pH 1.2)

Chapter Four: Discussion

Hypertension is one of the most common chronic diseases worldwide and is a lifelong disease that is generally not curable, but there are medications and lifestyle adjustments that can help keep blood pressure under control. No matter how hypertension begins, it is important to work closely with a doctor and adopt a heart-healthy lifestyle to prevent chronic hypertension from causing severe and potentially life-threatening complications.

It is of particular importance to note that hypertension is a significant risk factor for multiple conditions. For example, the development of coronary heart disease (CHD) and cerebral vascular disease (CVD) is a major problem worldwide because around 54 % of strokes and 47 % of CHD cases are attributable to high blood pressure. Hypertension, especially in mild to moderate stages, is usually considered as an asymptomatic condition. Despite the association between hypertension and health-related quality of life (HRQoL) having been focused on for the last several decades and numerous studies having addressed the impact of hypertension, the influences of high blood pressure and the awareness of having hypertension require further investigation. Previous studies showed a lower quality of life among subjects with hypertension. By contrast, it has been pointed out that impaired HRQoL in hypertensive may be secondary to the awareness of hypertension and comorbidities not due to hypertension *per se*. The inconsistent results on the association between hypertension and HRQoL might be due to differences in several factors, such as participants, study design, measures of HRQoL, and other confounders, but it seems unlikely that there is a simple explanation for it.

The World Health Organization (WHO) supports countries to reduce hypertension as a public health problem. In 2021, WHO released a new guideline for the pharmacological treatment of hypertension in adults. The publication provides evidence-based recommendations for the initiation of treatment of hypertension, and recommended intervals for follow-up. The document also includes target blood pressure to be achieved for control, and information on who, in the health-care system, can initiate treatment.

To support governments in strengthening the prevention and control of cardiovascular disease, WHO and the United States Centers for Disease Control and Prevention (US CDC) launched the

Global Hearts Initiative in September 2016, which includes the HEARTS technical package. The six modules of the HEARTS technical package (Healthy-lifestyle counseling, Evidence-based treatment protocols, Access to essential medicines and technology, Risk-based management, Team-based care, and Systems for monitoring) provide a strategic approach to improve cardiovascular health in countries across the world.

In September 2017, WHO began a partnership with Resolve to Save Lives, an initiative of Vital Strategies, to support national governments to implement the Global Hearts Initiative. Other partners contributing to the Global Hearts Initiative are the CDC Foundation, the Global Health Advocacy Incubator, the Johns Hopkins Bloomberg School of Public Health, the Pan American Health Organization (PAHO) and the U.S. CDC. Since implementation of the program in 2017 in 31 countries low- and middle-income countries, 7.5 million people have been put on protocol-based hypertension treatment through person-centered models of care. These programs demonstrate the feasibility and effectiveness of standardized hypertension control programs.

There is not a cure yet for hypertension, but by adopting effective management strategies to keep good control over blood pressure. One of the key things in the management of the condition is to keep a healthy lifestyle; losing weight, eating healthy food, and being active can really help. Some people may need medications to help manage their blood pressure levels. The effectiveness of hypertension may be compromised by the market circulation of subpar anti-hypertensive pharmaceutical drugs like prazosin, alfuzosin, losartan, valsartan, etc.

Prazosin is a medication used to manage and treat hypertension, benign prostatic hyperplasia, PTSD-associated nightmares, and the Raynaud phenomenon. In research, Prazosin was used as an additional antihypertensive agent for treating 38 patients with hypertension and renal functional impairment. The drug was effective in 29 of these patients at a mean daily dose of 7 mg. The mean blood pressure fall in these 29 patients was 28/22 mm Hg. Most experts consider prazosin to be the safest medicine for chronic hypertension because it has been used for many decades, is effective, affordable, and safe.

This work focused on an *in vitro* comparative assessment of the quality and effectiveness of conventional tablet dosage forms of Prazosin Hydrochloride offered on the local Bangladesh market. Although there are many licensed manufactures of the product Bangladesh according to

various public and private publications and records, only 4 locally manufactured brands are currently in active supply. The tablet products of these 4 brands were collected for the present study. The 2 mg strength of the brands was chosen considering that it is the strength commonly prescribed by doctors. The tests commonly prescribed for *in vitro* evaluation of tablet products were performed, which included those for hardness, thickness and diameter, friability, weight variation, assay, disintegration time, and dissolution study.

Organoleptic assessment has an important place in tablet evaluation. All tablets should have identical size, shape, thickness, color, and surface markings. The general appearance of the tablet is pivotal to consumer acceptance and allows monitoring of lot-to-lot and tablet-to-tablet uniformity. All the tablet products selected and studied in this work were white in color with just one of exception (**P-2**, pink) **(Table 3.1)**. All the tablets were round except the P-2 that was rhombus in shape **(Table 3.2)**. The tablet products had an average diameter of 3.77±0.092 mm to 5.30±0.082 mm **(Table 3.3)**. The thickness of the tablets was in the range of 2.70±0.047 mm to 4.09±0.110 mm. **(Table 3.3)**. As is evident from the data presented in **Table 3.3**, the maximum deviations (%) of diameter and thickness were within ±5% of the average that could be regarded satisfactory as per compendial requirements.

Tablet hardness or crushing strength is important to determine the ability of the tablet to withstand the mechanical shocks encountered during tablet handling, packaging and shipping. Also, it has an important bearing on the disintegration time. That is why tablet hardness determinations are made during tablet compression and are used to determine the need for pressure adjustment on tablet machines. The hardness of a tablet depends on the force of compression and the nature and amount of the binder used. For immediate release tablet products, the tablet hardness should be within 4-10 kg/cm^2 (**USP29–NF24, 2009)**. As is evident from **Table 3.4**, only one brand (**P-2**) satisfied this requirement, which had a crushing strength of 4.26±0.089 kg/cm^2. The crushing strength for other brands was within a rage of 2.34±0.152 kg/cm^2 to 3.04±0.152 kg/cm^2 only.

Friability is considered as a complementary test to the hardness test for tablet products that determines the tendency for a tablet to powder, chip, crumble or break. Friability, determined by regulatory agencies or industry standards, vary based on tablet type, intended use, and manufacturing process. Generally, a friability test result of less than 1% weight loss is considered

acceptable for most tablets. For two brands, *viz.*, A-2 and P-2, among the studied tablet products, the friability result was within the acceptable limit, while for the other two (B-2 and Q-2), it was more than 1% that is not acceptable (**Table 3.5**).

Assessment of the average tablet weight and the variation compared to the average weight is important to ensure the uniformity of dosage units and to make sure that, if any units are excessively overweight or underweight, they do not exceed acceptable limits. The weight variation test may also serve as an indicator of the uniformity of the drug content of tablets when the active ingredient is 90 to 95% of the total tablet weight. The test is performed on 10 tablets and is considered to have met the USP requirements if no more than 2 tablets differ from the average weight by more than the allowed percentage and no tablet differs by more than 2 times that percentage, where the allowed tolerance is 10% for tablets weighing 130 mg or less, 7.5% for those weighing 130-324 mg and 5% for those weighing >324 mg as recommended by the USP. The tablet products studied in this work weighed 63.1±0.316 mg to 212.4±0.843 mg and almost all of them had their weight variation within the acceptable limit **(Table 3.6).**

The disintegration of tablets is a crucial step in drug delivery, as it directly affects how quickly and consistently medications dissolve and are absorbed in the body. Effective disintegration leads to prompt and reliable drug release, enhancing bioavailability and therapeutic effectiveness. The USP disintegration test is performed on 6 tablets using the USP Disintegration Testing Apparatus and to be in compliance with USP requirements all of them must disintegrate within the time specified in the individual monograph. If 1 or 2 tablets fail to disintegrate completely, the test is to be repeated on 12 additional tablets and the requirement is met if not fewer than 16 out of the total 18 tablets are disintegrated. USP does not specify any general time limit for disintegration of uncoated/ coated conventional tablet dosage forms **(USP 40–NF 35, 2017)**. However, some other pharmacopoeia, such as British Pharmacopoeia (2010) and Indian Pharmacopoeia (2007) suggest a timeframe of 15 minute for uncoated tablets, 30 minutes for film coated tablets and 60 minutes for sugar coated tablets. All the tablet products studied in this work were uncoated and as shown in **Table 3.7**, the disintegration time of all of them in simulated gastric fluid (pH 1.2) were within an acceptable limit of 15 min, but 2 of them took more than 15 min to disintegrate in water (**A-2**, 17 min and **P-2**, 15.5 min).

Assay plays an important role in the assessment of the quality of a pharmaceutical product. This procedure determines the potency of a product, which is the amount of a drug present in a dosage form compared to its labeled amount. Unless otherwise specified in the compendial monograph, in general the USP states 90 to 110% as the acceptable potency limits for a dosage form. There is no monograph in USP on Prazosin Hydrochloride tablet, however there is one on Prazosin Hydrochloride capsule. The solvent system described for the assay of Prazosin Hydrochloride capsule (0.1N HCl containing 3% sodium lauryl sulfate) was adopted for use in the assay of the tablet products studied in this work. The UV spectrophotometric analysis of the studied tablet products of Prazosin Hydrochloride, using 0.1N HCl and 3% Sodium Lauryl Sulfate as the solvent system at 248 nm and subsequent calculation using the standard calibration curve, gave potencies in the range of 101.18% (P-2) to 106.22% (A-2), which is well within the compendial limits (**Table 3.9**).

In vivo bioavailability studies are commonly considered as the gold standard to determine a product's ability to perform in delivering the drug to the body to produce its intended action/ effect. These *in vivo* bioavailability studies, however, are typically pricy and necessitate employment of intrusive techniques. As oral solid dosage forms must first disintegrate and dissolve before they may be absorbed, dissolution testing is used to forecast product behavior *in vivo*. Thus, when checking and confirming the bioavailability performance of some products (especially, those already validated by *in vivo* methods), *in vitro* dissolution experiments have been found to be just as beneficial, if not more so, than *in vivo* pharmacokinetic investigations. *In vitro* dissolution studies have additional benefits including lower costs, smoother evaluation of product performance, and less intense ethical concerns. Besides, dissolution testing also serves to determine how manufacturing factors, such as the effect of the binder, the mixing effect, the granulation process, and the kind of excipients, affect the performance of solid dosage form.

The dissolution studies were performed in 0.1N HCl (pH 1.2). Though in the USP monograph for dissolution study of Prazosin Hydrochloride capsule also suggests 0.1N HCl (pH 1.2) containing 3% sodium lauryl sulfate as the dissolution media, addition of 3% sodium lauryl sulfate in this work resulted in too fast dissolution giving complete dissolution of the drug contained in the tablet in less than 10 min time giving the impression that there is no practical need of using the surfactant in the dissolution study of this product. The dissolution of the tablet

products studied in 0.1N HCl without the surfactant gave a similar pattern of release for all the brands with nearly 65% release in 45 min, 75-80% release in 60 min and 90-95% release in 90 min time points. After that the release became slow giving not much further increase in the amount of drug released. According to USP, the acceptable limit for immediate release tablet dosage forms is not less than 75% in 45 min. Obviously, this requirement has not been fulfilled here when the release was studied in 0.1N HCl without a surfactant, but considering that the drug is poorly soluble one requiring a surfactant to enhance its dissolution, a release percentage of 65% in 45 min could be considered satisfactory. What could be added further is that the release reached close to 100% at a time point of 90 min.

Chapter Five: Conclusion

Nowadays, hypertension (HTN) is a chronic medical condition and public health problem worldwide. Globally, the number of adults with hypertension increased from *594 million in 1975 to 1.13 billion in 2015.* In Bangladesh, approximately 20% of adults and 40–65% of elderly people suffer from HTN. The Global Burden of Disease Study for 2019 estimates that about 10 million deaths were attributable that year to high blood pressure, mostly in low- and middle-income countries (LMICs) like Bangladesh.

Elevated blood pressure, if left uncontrolled, poses significant risks to cardiovascular health, including heart disease and stroke. By effectively lowering blood pressure levels, hypertension medications like antihypertensive drug, Prazosin Hydrochloride, reduces the strain on the heart and blood vessels, mitigating the likelihood of life-threatening events such as heart attacks and strokes. Prazosin Hydrochloride also plays a pivotal role in preventing long-term complications associated with untreated hypertension, such as kidney damage, vision loss, and peripheral artery disease.

This study attempted to perform an *in vitro* comparative quality assessment of Prazosin Hydrochloride tablets available in the local market of Bangladesh. Four brands of conventional release Prazosin Hydrochloride tablet products available locally were collected form the market and subjected to *in vitro* studies for the assessment of commonly used quality control parameters including organoleptic properties, thickness and diameter, hardness, weight variation, assay, disintegration and dissolution test. In most cases, USP methods and tolerance limits were followed for performing the tests and drawing inferences.

Almost all the products consistently performed well and met the pharmacopeial requirements in terms of deviation in diameter and thickness (<±5%), weight variation (<±10%), disintegration time (<15 min) and potency (<±10%). The % dissolution was about 65% in 45 min time point in 0.1N HCl without surfactant, which could be considered satisfactory for a slow dissolving drug like Prazosin Hydrochloride. However, there is some concern about the hardness of the tablets, with 3 out of 4 brands showing a hardness of <4 kg/cm^2. However, most of the products showed good friability.

As the products went well and performed consistently in similar pattern, in terms of most parameters, including the critical ones like weight variation, disintegration time, assay and dissolution profile, they may be regarded to possess adequate quality to serve their purpose and may be used interchangeably.

The findings of this research can assist pharmaceutical companies as well as the Drug Control Authority in gaining insight into the quality status of the Prazosin Hydrochloride tablet products available in Bangladesh. Nevertheless, additional investigations with more comprehensive analyses are necessary to formulate a more dependable and insightful conclusion.

Chapter Five: References

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