In Vitro Comparative Quality Assessment of Different Brands of Prednisolone Tablets Available in Bangladesh.

A Project Report Submitted to the Department of Pharmacy,

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Registration No.: 45934

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Department of Pharmacy

Faculty of Biological Science

Jahangirnagar University

Savar, Dhaka-1342

Dedicated To:

My Beloved Parents.

CERTIFICATE BY THE SUPERVISOR

This is to certify that the work entitled ***'In Vitro* Comparative Quality Assessment of Different Brands of Prednisolone Tablets 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 Md Rasel Mahamud (Exam Roll No:171813, Reg. No: 45934) in the Department of Pharmacy, Jahangirnagar University under my direct guidance and supervision.

Dr. Mohammad Didare Alam Muhsin
Professor
Department of Pharmacy
Jahangirnagar University
Savar, Dhaka-1342.

DECLARATION

I hereby declare that this work entitled ***'In Vitro* Comparative Quality Assessment of Different Brands of Prednisolone Tablets Available in Bangladesh**', 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 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 for any other degree.

Md Rasel Mahamud
Examination Roll: 171813
Registration No: 45934
Session: 2016-2017

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Md Rasel Mahmud

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ABSTRACT

The aim of the present study was to review different pharmaceutical products marketed in Bangladesh for the healthcare of patients suffering from different respiratory inflammation like asthma, and auto-immune disorders and assess the quality of different brands of Prednisolone tablet products available in Bangladesh. The study was focused on evaluating and comparing the physicochemical equivalence of different brands of Prednisolone 5mg tablet. These tablets were tested through statistical methods, in accordance with the official compendia like BP and USP, for weight variation, thickness, hardness, friability, disintegration, and dissolution. The products were found to have satisfactory levels in terms of weight variation, friability, disintegration, and assay. However, they failed to perform adequately in case of some criteria like diameter and thickness, hardness and dissolution. Further work with samples from more batches including a bioavailability or bioequivalence investigation may be useful to determine their true therapeutic efficacy.

Keywords: Prednisolone, Tablet, Quality, In-Vitro, Comparative, Hardness, Assay, Disintegration, Dissolution.

AIMS AND OBJECTIVES OF THIS STUDY

Aims of the Work:

This work was set out with the following aims ahead:

- To help the manufacturers with quality assurance and control by studying *in vitro* marketed tablet products of Prednisolone to ascertain if they adhere to quality standards and identify potential areas for improvement in their formulations and manufacturing methods.

- To make patients and healthcare professionals aware of the variations in drug release profiles, bioavailability, or other critical characteristics that could affect treatment outcomes by comparing various Prednisolone tablet products available on the market and help them to decide if different brands of the products could be taken interchangeably.

- To help advance science by offering information on the medication's formulation characteristics, release pattern, and other pertinent pharmaceutical qualities.

Objectives of the Work:

With the above aims set forth, attempts were made in this work to achieve following objectives:

- Evaluation of the physical parameters such as organoleptic properties, thickness and diameter. hardness and friability, weight, weight variation, and disintegration time of the immediate release Prednisolone tablet formulations that are being sold in Bangladesh.
- To carry out the product assay in order to ascertain their potencies.
- To conduct dissolution tests in suitable media to ascertain the drug release pattern of the products.

To evaluate if the release profiles of the studied products meet expectations and can be considered equivalent.

CHAPTER 01: INTRODUCTION

Quality is the first priority for every company hoping to prosper and expand. Customer satisfaction is a measure of a product or service's quality based on how well it meets the needs of the customer. A product's quality is determined by its capacity to meet the needs and expectations of the customer. First things first, quality needs to be described in terms of specific traits or standards that vary according to the type of product. Medication, for instance, is assessed based on its chemical and physical characteristics, effectiveness, safety, taste, and shelf life; in contrast, mechanical or electronic devices are assessed based on their functionality, reliability, safety, and aesthetic appeal.

In the pharmaceutical industry, the quality of a product is essential to its long-term survival. It demonstrates a high level of scientific, technological, and managerial expertise. In addition to being mandated by law and regulation, quality is also necessary to earn the trust of the public, particularly when it comes to life-saving drugs. Strict attention to worldwide safety, environmental, and regulatory regulations must be maintained from the product's inception to guarantee quality. Validation is necessary for pharmaceutical quality control.

Throughout history, pharmaceuticals have undergone modifications to ensure their quality; they are often simple substances discovered through experimentation. Each pharmaceutical product needs to be of high quality because, in the absence of it, there could be issues like overdosing or subtherapeutic side effects that would prohibit the products from being marketed.

The WHO has been tracking and documenting the incidences of substandard drugs. The records show that problems of substandard and counterfeit drugs are on increase as 50% of all reported cases occurred in the period 1993 to 1997. Most of these incidences (70%) were reported in developing countries. The report identifies the causes of the poor quality of drugs: in about 50% of all the cases the formulations did not contain any drug, 20% contained the wrong active ingredient and 10% the wrong amount of the active ingredient. Only in 5% of the reported incidences did the drugs contain the right active ingredient in the correct amounts but were judged substandard by failing other quality tests. Nine percent of pharmaceutical sales in Bangladesh have been traced to counterfeit or low-quality drugs, openly sold in pharmacies.

Respiratory disorders are increasing day by day and affecting many people due to increasing air pollution. Glucocorticoids are commonly used to treat a wide range of respiratory inflammatory diseases. They are thought to decrease the chronic inflammation in the 4 bronchiole trees, thereby improving obstructed airflow. The main API (active pharmaceutical ingredient) in this group is prednisolone. Prednisolone is a corticosteroid drug with predominant glucocorticoid and low mineralocorticoid activity, making it useful for the treatment of a wide range of inflammatory and auto-immune conditions including asthma. Prednisolone can also be used as an immunosuppressive drug for organ transplants and in cases of adrenal insufficiency (Addison's disease). It is also used to treat conditions such as arthritis, blood problems, immune system disorders, skin, and eye conditions, breathing problems, cancer, and severe allergies. It decreases the immune system's response to various diseases to reduce symptoms such as pain, swelling and allergic-type reactions.

This project focuses on the evaluation of locally available conventional prednisolone tablet dosage forms. The project evaluated the basic parameters used in the assessment of tablet quality to ascertain whether they meet the compendial requirements as set by regulatory authorities and claimed by the manufacturing companies.

1.1 Important Components of Drug and Drug Product Quality

Regulatory agencies such as the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) set guidelines and standards to oversee quality assurance and control processes throughout the stages of drug research, production, and distribution. This promotes public health, fosters trust in the medical system, and facilitates patients' access to safe and efficient prescription drugs.

Following is brief account of the important quality attributes considered in the assessment of a drug or drug product:

- **Identity:** The drug's identity and form must be clearly stated on the label to prevent misunderstandings or mistakes with other drugs or drug products.
- **Purity:** The medication should not contain any component that may compromise its effectiveness or safety.

- **Safety:** The drug should be safe to use, with little possibility of toxicity or adverse effects, and a balanced risk-benefit ratio.
- **Potency:** For a medication to be effective, the active pharmaceutical ingredient (API) must be present in the specified amount as stated on the label.
- **Efficacy:** The medicine should have the desired therapeutic effect when taken as directed by the prescribed dosage and indications.
- **Uniformity:** Pharmaceutical products must maintain uniformity across the batch and from batch to batch.

1.2 Quality Assessment of Tablets

Following is a brief summary of the various aspects of quality assessment of a tablet dosage form:

- **Appearance:** First of all, the tablet's appearance is to be examined to make sure that it is uniform in size, shape, and color and free of cracks, chips, and discoloration.
- **Packing Integrity:** It has to be checked and confirmed that the manufacturer's information, batch number, and expiration date are correctly labeled and that the package is intact.
- **Physical Characteristics:** The tablet's hardness, thickness, and friability need to be examined to ensure that it can withstand handling and transportation stresses without breaking or degrading excessively.
- **Disintegration Time:** The disintegration time is tested to make sure that the tablet will fragment into smaller pieces within an expected timeframe after exposure to the GI fluid.
- **Chemical composition:** Analytical techniques such as spectroscopy or chromatography are used to confirm the presence of active pharmaceutical ingredients (APIs) and the absence of impurities.
- **Assay:** It is important to make sure that correct amount of the active ingredient is present in the tablet.
- **Uniformity of Dosage:** Weight variation and content uniformity tests are to be conducted to ensure that the dose is the same throughout the batch.
- **Microbiological Purity:** Microbiological limit testing is to be performed to ensure that the tablet meets the parameters for microbiological contamination.

- **Stability Testing:** Quick and real-time stability testing can be used to determine how long a tablet will last in various environmental conditions.
- **Compliance with Regulatory Standards:** It is to be verified that the tablet satisfies the requirements for quality, safety, and efficacy imposed by regulatory bodies like the FDA or EMA.
- **Adherence to Good Production Practices (GMP):** It is to be ascertained that production processes adhere to GMP requirements to guarantee consistent tablet quality and safety.
- **Documentation and Record-Keeping:** It is important to maintain thorough records of all quality assessment processes and results to guarantee regulatory compliance and traceability.

1.3 Profile of Prednisolone – the Drug under Study

Prednisolone was discovered and approved for medical use in 1955. It is on the World Health Organization's List of Essential Medicines. It is available as a generic drug. In 2020, it was the 153rd most prescribed medication in the United States, with more than 3 million prescriptions.

Prednisolone is a corticosteroid --- a steroid hormone used to treat certain types of allergies, inflammatory conditions, autoimmune disorders, and cancers. Some of these conditions include adrenocortical insufficiency, high blood calcium, rheumatoid arthritis, dermatitis, eye inflammation, asthma, and multiple sclerosis. It can be taken by mouth, injected into a vein, used topically as a skin cream, or as eye drops. It differs from the similarly named prednisone in having a hydroxyl at the 11th carbon instead of a ketone.

Side effects of short-term use include nausea, inability to concentrate, insomnia, or feeling tired. More severe side effects include psychiatric problems, which may occur in about 5% of people. Common side effects with long-term use include bone loss, weakness, yeast infections, and easy bruising. While short-term use in the later part of pregnancy is safe, long-term use or use in early pregnancy is occasionally associated with harm to the baby.

1.3.1 Description

Prednisolone is a synthetic glucocorticoid, a derivative of cortisol which is used to treat a variety of inflammatory and auto-immune conditions. It is the active metabolite of the prednisone and is used in patients with hepatic failure as they are unable to metabolize prednisone to prednisolone.

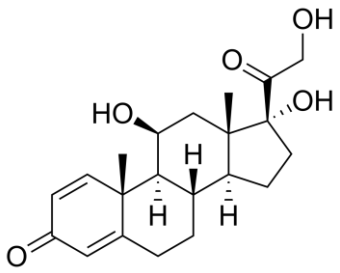
1.3.2 Physicochemical Properties

Systemic (IUPAC) Name: (8S,9S,10R,11S,13S,14S,17R)-11,17-dihydroxy-17-(2-hydroxyacetyl)-10,13-dimethyl-7,8,9,11,12,14,15,16-octahydro-6H-cyclopenta[a]phenanthren-3-one

Molecular formula: $C_{21}H_{28}O_5$

Molecular Mass: 360.44402 g/mol

Structural Formula:



Appearance: White to white crystalline powder

Solubility: In water, 223 mg/L at 25° C

Melting point: 235°C

1.3.3 Pharmacodynamic Properties

Prednisolone acts through replacing adrenal insufficiency as in Addison's disease(a rare disorder where the adrenal glands don't produce enough of the hormones cortisol and aldosterone. These hormones are crucial for maintaining various bodily functions, including blood pressure, blood sugar, and electrolyte balance. Damage to the adrenal cortex, the outer layer of the adrenal glands, is the primary cause.), or after adrenalectomy. It has anti-inflammatory and immuno-suppressant

glucocorticoid properties. It can inhibit leukocyte infiltration at the site of inflammation, interfere with mediators of inflammatory response, and suppress humoral immune responses.

The ant-inflammatory actions of glucocorticoids are thought to involve phospholipase A_2 inhibitory proteins, and lipocortins, which control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes. Prednisolone reduces inflammatory reactions by limiting the capillary dilatation and permeability of the vascular structures. These compounds restrict the accumulation of polymorphonuclear leukocytes and macrophages and reduce the release of vasoactive kinins.

Recent research suggests that corticosteroids may inhibit the release of arachidonic acid from phospholipids, thereby reducing the formation of prostaglandins. Prednisolone is a glucocorticoid receptor agonist. On binding, the corticoreceptor-ligand complex translocates itself into the cell nucleus, where it binds to many glucocorticoid response elements (GRE) in the promoter region of the target genes. The DNA-bound receptor then interacts with basic transcription factors, causing an increase or decrease in the expression of specific target genes, including suppression of IL2 (interleukin 2) expression.

1.3.4 Pharmacokinetic Properties

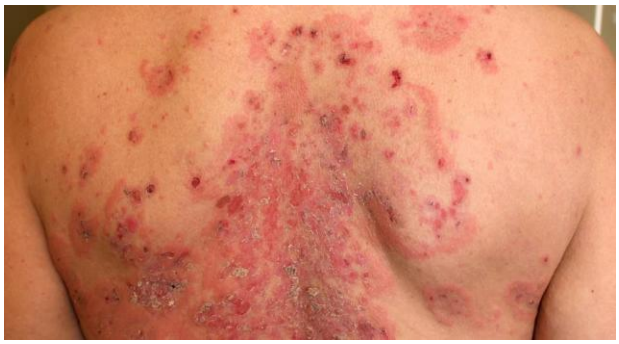
Prednisolone is absorbed from the gastro-intestinal tract and peak plasma concentrations are obtained 1 to 2 hours after administration. The drug has a plasma half-life of 2-3 hours and is extensively bound to plasma protein. Prednisolone is excreted in the urine as free and conjugated metabolites, together with an appreciable amount of unchanged prednisolone. Prednisolone crosses the placenta and small amounts are excreted in breast milk. The biological half-life is in the range of 2.1 to 3.5 hours.

1.3.5 Therapeutic Indications:

Therapeutic Class: Endocrine-metabolic agent, immune suppressant.

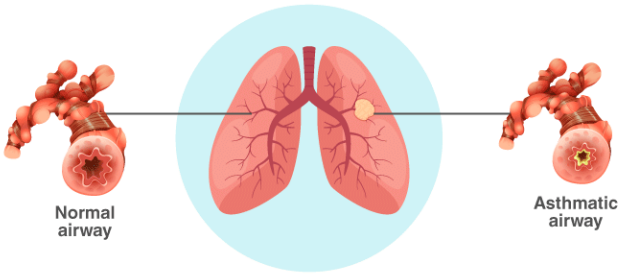
The indications of Prednisolone are summarized below concerning various organ systems of the body:

1. **Skin:**



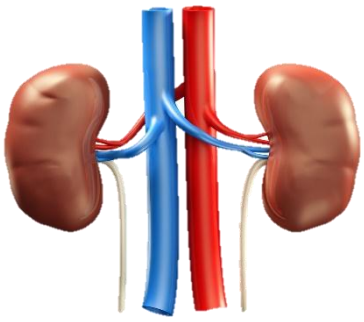
Pemphigus vulgaris, allergic dermatitis, eczema, exfoliative dermatitis, dermatitis herpetic formas, dermatitis medicamentosa, erythema multiforme, disseminated lupus erythematosus, dermatomyositis, polyarteritisnodosa.

2. **Respiratory:**



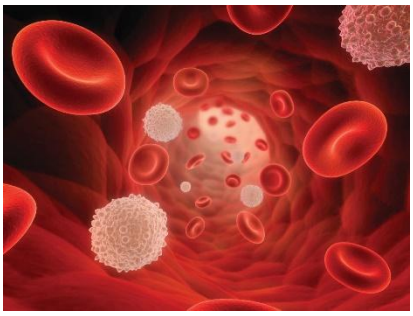
Prednisolone is commonly used for short periods of time during flare-ups of asthma or COPD, when there is a sudden worsening of symptoms. It is also used in severe bronchial asthma and status asthmaticus, emphysema, pulmonary fibrosis.

3. **Adrenal:**



Adrenal hyperplasia (adrenogenital syndrome).

4. **Haematological:**



Idiopathic thrombocytopenic purpura, acquired hemolytic anemia, acute leukemia.

5. **Others:** Nephrotic syndrome, iridochoroiditis, ulcerative colitis, rheumatoid arthritis, ankylosing spondylitis, rheumatic fever, gout, periarthritis of the shoulder.

1.3.6 Dosage and Administration

Route of administration: oral

The lowest dose to produce an acceptable result should be given; when it is possible to reduce the dose this must be in stages. In prolonged treatment, the dose may be increased temporarily during periods of stress or exacerbation of illness.

Adults: Short-term treatment: 20 to 30mg daily for the first few days, reducing by 2.5 to 5mg every 2 to 5 days according to the response.

Rheumatoid arthritis: Initially 7.5 to 10 mg daily, reduced to the lowest effective dose for maintenance.

Most other conditions: 10 to 100 mg daily for 1 to 3 weeks, then reducing to the lowest effective dose.

Elderly: There is no evidence that the dosage should differ; the dose should be the minimum necessary to achieve the desired therapeutic effect.

Children: At 12 years, 75% of the adult dose; at 7 years, 50% of the adult dose; at 1 year 25% of the adult dose dependent on clinical factors. Initial dose: 0.75 to 1.0mg/kg of bodyweight daily, in divided doses.

Usual Adult Dose for Multiple Sclerosis: Tablets and syrup for acute exacerbations - 200 mg daily for one week followed by 80 mg every other day for 1 month.

Usual Adult Dose for Bronchopulmonary Dysplasia: Tablets and syrup for acute exacerbations - 200 mg daily for one week followed by 80 mg every other day for 1 month.

Usual Adult Dose for Anti-inflammatory Effect: Oral - 5 to 60 mg per day in divided doses 1 to 4 times/day. Intravenous or Intramuscular - 4 to 60 mg/day.

For intraarticular, intralesional or soft tissue administration: Large joints: 10 to 20 mg, Small joints: 4 to 5 mg, Bursae: 10 to 15 mg, Tendon sheaths: 2 to 5 mg, Soft tissue infiltration: 10 to 30 mg, Ganglia: 5 to 10 mg.

Injectable suspension (tebutate) for intraarticular, intralesional or soft tissue administration: Large joints: 20 to 30 mg (doses > 40 mg not recommended), Small joints: 8 to 10 mg, Bursae: 20 to 30 mg, Tendon sheaths: 4 to 10 mg, Ganglia: 10 to 20 mg.

Injectable suspension (acetate) for intraarticular, intralesional or soft tissue administration: 4 to 100 mg, Bursae: 10 to 15 mg, Tendon sheaths: 2 to 5 mg, Soft tissue infiltration: 10 to 30 mg.

Usual Pediatric Dose for Immunosuppression: Oral: 0.1 to 2 mg/kg/day in divided doses 1 to 4 times a day. Intravenous: 0.1 to 2 mg/kg/day in divided doses 1 to 4 times a day.

Usual Pediatric Dose for Asthma -- Acute: Oral: 1 to 2 mg/kg/day in divided doses 1 to 2 times a day for 3 to 5 days. Intravenous: 2 to 4 mg/kg/day divided 3 or 4 times a day.

Usual Pediatric Dose for Nephrotic Syndrome: First 3 episodes: Initial dose: 2 mg/kg/day (maximum dose 80 mg/day) until urine is free of protein for 3 consecutive days (maximum: 28 days); followed by 1 to 1.5 mg/kg/dose every other day for 4 weeks. Frequent relapses or long-term maintenance dose: 0.5 to 1 mg/kg/dose given every other day for 3 to 6 months.

Usual Pediatric Dose for Bronchopulmonary Dysplasia: 2 mg/kg/day orally divided twice daily for 5 days, followed by 1 mg/kg/day once daily for 3 days, followed by 1 mg/kg/dose every other day for 3 doses.

1.3.7 Adverse Effects

Body as a whole: Leucocytosis, hypersensitivity including anaphylaxis, thromboembolism, fatigue, malaise.

Cardiovascular: Congestive heart failure in susceptible patients, hypertension.

Gastro-intestinal: Dyspepsia, nausea, peptic ulceration with perforation and haemorrhage, abdominal distension, abdominal pain, increased appetite which may result in weight gain, diarrhoea, oesophageal ulceration, oesophageal candidiasis, acute pancreatitis.

Musculoskeletal: Proximal myopathy, osteoporosis, vertebral and long bone fractures, avascular osteonecrosis, tendon rupture, myalgia

Metabolic/Nutritional: Sodium and water retention, hypokalaemic alkalosis, potassium loss, negative nitrogen, and calcium balance.

Skin: Impaired healing, hirsutism, skin atrophy, bruising, striae, telangiectasia, acne, increased sweating, may suppress reactions to skin tests, pruritis, rash, urticaria.

Endocrine: Suppression of the hypothalamo-pituitary adrenal axis particularly in times of stress as in trauma surgery or illness, growth suppression in infancy, childhood and adolescence, menstrual irregularity, and amenorrhoea, Cushingoid facies, weight gain, impaired carbohydrate tolerance with increased requirement for anti-diabetic therapy, manifestation of latent diabetes mellitus, increased appetite.

Nervous system: Euphoria, psychological dependence, depression, insomnia, dizziness, headache, vertigo, raised intracranial pressure with papilledema in children, usually after treatment withdrawal, aggravation of schizophrenia, aggravation of epilepsy, suicidal ideation, mania, delusions, hallucinations, irritability, anxiety, insomnia, and cognitive dysfunction. In adults the frequency of severe psychiatric reactions has been estimated to be 5-6%.

Eye disorders: Increased intra-ocular pressure, glaucoma, papilloedema, posteriorsubcapsular cataracts, exophthalmos, corneal or scleral thinning, exacerbation of ophthalmic viral or fungal disease.

Anti-inflammatory and Immunosuppressive effects: Increased susceptibility to and severity of infections with suppression of clinical symptoms and signs., opportunistic infections, recurrence of dormant tuberculosis.

Withdrawal symptoms: Too rapid a reduction of prednisolone following prolonged treatment can lead to acute adrenal insufficiency, hypotension, and death. A steroid withdrawal syndrome seemingly unrelated to adrenocortical insufficiency may also occur and include symptoms such as anorexia, nausea, vomiting, lethargy, headache, fever, weight loss, and/or hypotension.

1.3.8 Side Effects

Some common side effects of Prednisolone are mentioned below: fluid retention, weight gain, high blood pressure, potassium loss, headache, muscle weakness, puffiness of and hair growth on the face, thinning and easy bruising of the skin, glaucoma, cataracts, peptic ulceration, worsening of diabetes, irregular menses, growth retardation in children, convulsions, and psychic disturbances.

1.3.9 Contraindications

1. Prednisolone is contraindicated in patients with peptic ulcer, osteoporosis, psychoses or severe psychoneuroses.
2. Prednisolone is usually contraindicated in the presence of acute infection.
3. Administration of live virus vaccines.

1.3.10 Drug Interactions

Hepatic microsomal enzyme inducers: Medicines that induce hepatic enzyme cytochrome P450 isozyme 3A4, such as phenobarbital, phenytoin, rifampicin, rifabutin, carbamazepine, primidone and aminoglutethimide, may reduce the therapeutic efficacy of corticosteroids by increasing the rate of metabolism.

Hepatic microsomal enzyme inhibitors: Medicines that inhibit hepatic enzyme cytochrome P450 isozyme 3A4, such as ketoconazole, ciclosporin or ritonavir, may decrease glucocorticoid clearance. A reduction in prednislone dose may be needed to reduce the risk of adverse effects.

Antidiabetic Agents: Prednisolone may increase blood glucose levels. Patients may need dosage adjustment of any concurrent anti-diabetic therapy.

Non-steroidal anti-inflammatory drugs (NSAIDs): Concomitant administration may increase the risk of gastro-intestinal tract ulceration. Aspirin should be used cautiously in conjunction with prednisolone in patients with hypo-thrombinaemia. The renal clearance of salicylates is increased by corticosteroids and steroid withdrawal may result in salicylate intoxication. Patients should be observed closely for adverse effects of either medicine.

Anticoagulants: Response to anticoagulants may be reduced or less often enhanced by corticosteroids.

Antifungals: The risk of hypokalaemia may be increased with amphotericin.

Cardiac glycosides: There is a risk of toxicity if hypokalaemia occurs due to prednisolone treatment.

Cytotoxic agents: There is an increased risk of hematological toxicity when prednisolone is given with methotrexate.

Mifepristone: The effect of corticosteroids may be reduced for 3-4 days after mifepristone.
Vaccines: Live vaccines should not be given to individuals with impaired immune responsiveness. The antibody response to other vaccines may be diminished.

Oestrogens: Oestrogens may potentiate the effects of glucocorticoids. The dose of prednisolone may need to be adjusted if oestrogen therapy is commenced or stopped.

Somatropin: The growth promoting effect may be inhibited.

Sympathomimetics: There is an increased risk of hypokalaemia if high doses of corticosteroids are given with high doses of salbutamol, salmeterol, terbutaline or formoteral.

Diuretics: Excessive potassium loss may be experienced if glucocorticoids and potassium depleting diuretics (such as furosemide and thiazides) or carbonic anhydrase inhibitors (such as acetazolamide) are given together.

Antacids: Concurrent use of antacids with prednisolone may decrease absorption of this glucocorticoid's efficacy. The efficacy may be decreased sufficiently to require dosage adjustments in patients receiving small doses of prednisolone.

1.3.11 Available dosage forms of prednisolone in Bangladesh

Table 1.1: A list of dosage forms of prednisolone available in Bangladesh.

Brand Name	Dosage	Dosage Form	Manufacturer
Cortan	Prednisolone 5mg, 10mg & 20mg	Tablet	Incepta Pharmaceuticals Ltd.
Deltacort Desh	Prednisolone 5mg	Film Coated Tablet	Desh Pahrmaceuticals Ltd.
Deltapred	Prednisolone 5mg	Film Coated Tablet	Ziska Pharmaceuticals Ltd.
Deltasone	Prednisolone 5mg, 10mg & 20mg	Tablet	Renata Ltd.
G-prednisolone	Prednisolone 5mg	Film Coated Tablet	Gonoshasthya Pharmaceuticals Ltd.
Precodil	Prednisolone 5mg & 20mg	Tablet	OpsoninPharma Limited
Prednelan	Prednisolone 20mg	Tablet	Glaxo Smith kline (BD) Ltd
Prednicortil	Prednisolone 5mg	Tablet	GacoPharmceuticals Ltd.
Prednisolone	Prednisolone 5mg	Tablet	Glaxo Smith kline (BD) Ltd

Prexan	Prednisolone 5mg	Film Coated Tablet	Chemist Laboratories Ltd.
Redisone	Prednisolone 5mg	Film Coated Tablet	Rephco Laboratories Ltd.
Zenilon	Prednisolone 5mg	Film Coated Tablet	Zenith Pharmaceuticals Ltd.

Fig-1.2: Some Prednisolone 5mg tablets manufactured and marketed in Bangladesh.

Chapter 2: Materials and Methods

2.1 Materials and Reagents

- **Materials**
  - **Active Pharmaceutical Ingredient (API):** Prednisolone (potency-99.7%; white fine crystalline powder)
  - **Tablet Products:** Five brands of conventional Prednisolone Tablets (400 mg)
- **Reagents and Solvents**

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

Table 2.1: Reagents and Solvents

Name	Source
Distilled water	Pharmaceutics Laboratory, Department of Pharmacy, Jahangirnagar University.
Methanol	Pharmaceutics Laboratory, Department of Pharmacy, Jahangirnagar University.

- **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	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	50 ml, 100 ml, 250 ml, 500 ml, 800 ml & 1000 ml
Spatula	Small
Stirrer/ Glass rod	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 2.1: Apparatus and Glassware

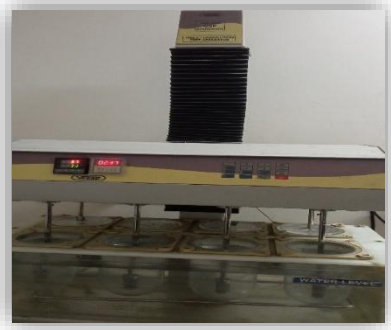
Equipment and Instruments

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 pattern and potency of the tablet
 **Electronic Balance**	AND-GULF Precision Electronic Balance China	For precise measurement of various ingredients
 **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

Instruments	Model/Manufacturer	Purpose
 **Dissolution Tester**	Veego India	To study the release profile of the tablets
 **Slide Calipers**	SDK China	To study the thickness & diameter of the tablet
 **Hardness Tester**	Campbell Electronics India	To study the hardness properties of the tablet

 **Disintegration testing apparatus**	Campbell Electronics Bombay 400025 Thermonik India	To study the disintegration time of the tablet

Instruments	Model/Manufacturer	Purpose
 **Magnetic heating stirrer**	CJJ78-1 Magnetic Heating Stirrer China	For precise stirring
 **Centrifuge Machine**	TDL-60B Human Lab Instrument Co. Korea	For separation of insoluble solid particles from the solution/sample

 **Friability Testing Apparatus**	Campbell Electronics Bombay 400025 Thermonik, India	To measure the friability of tablets.

2.2 Methods

2.2.1 Collection of samples

- **Prednisolone** (API) was a kind of gift donated by ACI Pharmaceuticals Ltd., Bangladesh.

Tablets: Five brands of Prednisolone Immediate Release Tablets were randomly selected and collected from different retail pharmacies located in the Savar area of Dhaka district. The products were coded as Cn-5, Cl-5, Pd-5, Px-5 and S-5. There are more brands of prednisolone from different manufacturers that are officially approved, but they are not in active supply.

2.2.2 Assessment of 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: taste, smell, color, and texture.

2.2.2.2 Thickness and diameter:

Ten tablets were randomly selected from each brand, and their diameter and thickness were measured in millimeters using the slide calipers.

2.2.2.3 Hardness test: Five tablets were randomly chosen from each brand and their hardness was measured using a Monsanto Hardness Tester (Campbell Electronics, India). The test tablet was positioned diametrically between the fixed and moving jaws, and the indicator's reading was set at zero. After that, pressure was applied until the tablet cracked. The unit of measurement was kg/cm^2.

2.2.2.4 Friability test: For friability testing 10 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 a Friabilator. After rotating for 100 times (4 min), loose dust was removed from the tablets as before and the tablets were re-weighed.

The friability (% loss in weight) of the tablet products was determined using the following formula:

$$\% \text{ Friability} = \frac{\textbf{Initial weight} - \textbf{Final weight}}{\textbf{Initial weight}} \textbf{ x 100}$$

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.
- Maximum upper and lower weight variation were calculated using the following formula:

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

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

2.2.2.6 Disintegration test:

A USP disintegration tester (Campbell Electronics Bombay 400025 Thermonik, India) was used to determine the disintegration times of six tablets per brand in distilled water at 37.0 ± 0.5 C. The device consists of 6 tubes that are open at the top and covered with a No. 10 mesh with a diameter of 2 mm at the bottom. The entire tube assembly is then submerged in 900 milliliters of distilled water in a 1-liter beaker. A constant temperature of 37.0 ± 0.5 °C was maintained in the beaker by placing it in a constant temperature water bath. The basket (assembly) holding the tablets was moved up and down a distance of 5–6 cm at a frequency of 28–32 cycles per minute using a typical motor-driven device. A part of the tube containing approximately 2.5 mL was submerged in the medium during the downward stroke when the tube plunged deeply into the medium. The disintegration time was defined as the amount of time needed for each of the six tablets to split up into granules large enough to go past the mesh. The average disintegration time was obtained by repeating the test. Standard deviations were computed.

2.2.3 Assay

The assay of Prednisolone Tablet products was performed spectrophotometrically by a UV-Vis Spectrophotometer (UV 1601 PC SHIMADZU, Japan).

2.2.3.1 Determination of the λ_{max} of prednisolone in distilled water

The λ_{max} of prednisolone was determined by scanning the solutions of the drug in distilled water by the UV-Vis spectrophotometer over the wavelength range of 200-400 nm and it was found to be 247 nm.

2.2.3.2 Preparation of standard calibration curve

A standard calibration curve for analyzing prednisolone in the release media, distilled water was created. Solutions of prednisolone at a series of concentrations, *viz*., 1, 2.5, 5, 7.5, 10 and 12.5, 15, 17.5 and 20 µg/ml, were prepared and their absorbances were determined at 247 nm using the fresh media as the blank. The absorbances were plotted against the corresponding concentrations to create the curve.

Q. How will you make 1, 2.5, 5, 7.5, 10, 12.5, 15, 17.5, 20 microgram/milliliter from 400mg Prednisolone dissolve in 1000ml distill water.

To make solutions with concentrations of **1, 2.5, 5, 7.5, 10, 12.5, 15, 17.5, and 20 µg/mL** (microgram per milliliter) from a **stock solution** of **400 mg Prednisolone dissolved in 1000 mL distilled water**, follow this step-by-step **serial dilution method**.

Step 1: Understand the Stock Solution

- **Stock concentration** = $\frac{400\ mg}{1000\ mL}$ = 0.4 mg/mL = 400µg/mL

So, you have a 400 µg/mL stock solution.

Step 2: Use the dilution formula

Use the formula:

$$C_1V_1 = C_2V_2$$

Where:

- C_1 = concentration of the stock = 400 µg/mL
- V_1= volume of stock solution to use
- C_1 = desired concentration (1, 2.5, 5... µg/mL)
- V_2 = final volume (usually convenient to make 10 mL or 100 mL total)

Let's make **10 mL of each diluted solution**.

Step 3: Calculate required volume of stock (V1) for each concentration

Desired (C_2)	C_1=400µg/mL	V_2=10mL	$V_1=\frac{(C2\times V2)}{C1}$	Take V_1 stock + (10-V_1) mL Water.
1 µg/mL	400	10	$=\frac{1\times10}{400}$=0.025	0.025 mL + 9.975 mL water
2.5 µg/mL	400	10	0.0625 mL	0.0625 mL + 9.9375 mL water.
5 µg/mL	400	10	0.125 mL	0.125 mL + 9.875 mL water.
7.5 µg/mL	400	10	0.1875 mL	0.1875 mL + 9.8125 mL water.
10 µg/mL	400	10	0.25 mL	0.25 mL + 9.75 mL water.
12.5 µg/mL	400	10	0.3125 mL	0.3125 mL + 9.6875 mL water.
15 µg/mL	400	10	0.375 mL	0.375 mL + 9.625 mL water.
17.5 µg/mL	400	10	0.4375 mL	0.4375 mL + 9.5625 mL water.
20 µg/mL	400	10	0.5 mL	0.5 mL + 9.5 mL water.

Notes:

1. Use a **micropipette** for precise volume transfer (as low as 25 µL).
2. Prepare all dilutions in clean, labeled volumetric flasks or tubes.
3. Mix thoroughly after dilution.
4. All solutions should be prepared fresh or stored properly (if stability allows).

2.2.3.3 Preparation of prednisolone 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 5 mg of prednisolone, was transferred to a 50 ml volumetric flask with media.
- Then it was shaken by Magnetic Stirrer (CJJ78-1, China) for 1 hour, and centrifuged to separate the undissolved particles.
- The supernatant was sufficiently diluted to give a concentration of 15 µg/ml as per the label strength.

2.2.3.4 Determination of potency by UV spectrophotometry

The absorbance of the prepared sample solution was measured by the spectrophotometer at 247 nm and the concentration was determined from the standard calibration curve.

The potency of the tablet sample was determined by the following formula:

$$\textbf{Potency (\%)} = \frac{C_1}{C} \textbf{ x 100}$$

where,

Expected concentration of the sample solution = C

Measured concentration of the sample's solution = C_1

It's what **should** be in the solution based on your formulation or label claim.

[Note and Explanation: **Expected concentration of the sample solution = C**

- This is the **theoretical** or **target concentration** you calculated or prepared.

- For example, if you dissolved 100 mg of a drug in 100 mL, the expected concentration (C) is: C= $\frac{100\ mg}{100\ mL}$ = 1mg/mL.

Measured concentration of the sample's solution = C_1

- This is the **actual concentration** you found after performing an assay, spectrophotometric analysis, HPLC, etc.
- For example, using a UV-spectrophotometer, you measured the absorbance and calculated:

C_1 =0.96 mg/mL

Why this matters

- These two are compared to check **accuracy and quality** of a formulation.
- Often, **percentage error** or **% label claim** is calculated:

Percentage of label claim= $\frac{C1}{C} \times 100$

Example:

If expected concentration (C) = 1 mg/mL

and measured concentration (C_1) = 0.96 mg/mL

Then:

Percentage of label claim = $\frac{0.96}{1.00} \times 100$ =96%.

This means the sample contains 96% of the expected drug amount — which might or might not be within the acceptable range, depending on pharmacopeial standards (typically 95%–105%).

2.4 Dissolution study

2.4.1 Determination of the λ_{max} of prednisolone in distilled water

The λ_{max} of prednisolone solutions in distilled water was by the UV-Vis spectrophotometer as described before in the **Section 2.2.3.1**.

2.4.2 Preparation of standard calibration curve

The standard curve for analyzing prednisolone in the samples withdrawn from the dissolution vessels at intervals was drawn following the same procedure as described in the **Section 2.2.3.2.**

2.4.3 Dissolution procedure

A USP Apparatus-2 (Paddle Apparatus, Veego, India) was used to conduct the dissolution study on the collected prednisolone tablet products. Distilled water was used as the release media. The device has 7 stations, each of which comprises of a motor, a covered vessel made of transparent, inert material, and a metallic paddle shaft. The container has a 1000 ml nominal capacity and a cylindrical shape with a hemispherical bottom. One tablet was inserted into each of 6 vessels filled with 900 ml of dissolution media and paddled by the motor-driven shaft. The 7^{th} vessel was used to store fresh media for subsequent used without any added tablet sample for dissolution. The motor was set to rotate at 50 rpm, and 5 ml samples were taken out periodically at intervals of 5, 10, 20, 30, 45, 60, 90, and 120 min intervals to measure the amount of drug dissolved in the media. An equal volume of fresh media was replaced each time a sample was withdrawn. The temperature of the media was maintained at 37±0.5 °C by a constant temperature bath.

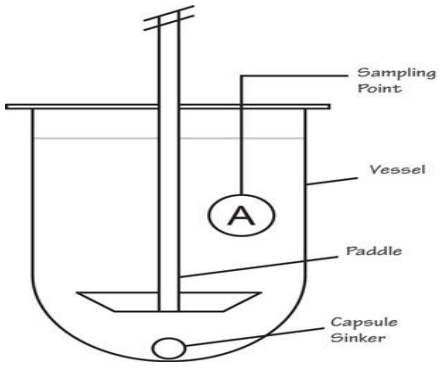


Figure 2.2: Dissolution Apparatus (Paddle)

Dissolution conditions at a glance:

Apparatus	USP dissolution apparatus-II (Paddle)
Dissolution medium	900 ml Distilled water
Temperature	37 ±0.5 °C
Stirring Speed	50 rpm
Time (min)	0, 5, 10, 15, 20, 30, 45, 60, 90, 120

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 **(Cr 5, Px 5 and S 5)**, yellow **(Pd 5)** and pink **(Cl 5)** in color. None of the tablet products, however, had any odor.

Table 3.1: Organoleptic properties of studied Prednisolone tablet products

Sample Code	Color	Odor
Cr 5	White	None
Cl 5	Pink	None
Pd 5	Yellow	None
Px 5	White	None
S 5	White	None

3.1.2 Shape, thickness and diameter

Shape: As shown in **Table 3.2**, the collected tablet products had different shapes including round **(Cl 5** and **S 5)**, oval **(Cr 5)**, rhombus **(Pd 5)** and diamond **(Px 5)**.

Table 3.2: Shapes of the studied tablet products

Sample Code	Shape
Cr 5	Oval
Cl 5	Round
Pd 5	Rhombus
Px 5	Diamond
S 5	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 6.2±0.3672 mm to 8.6±0.256 mm, while the average thicknesses were in the range of 2.7±0.3753 mm to 3.2±0.7601 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 (%)
Cr 5	7.5±0.4013	5.6382	2.7±0.3753	9.5320
Cl 5	6.9±0.3980	7.8239	2.9±0.4839	4.6372
Pd 5	8.6±0.2560	2.7518	2.9±0.3850	5.3240
Px 5	6.5±0.4532	5.1978	3.2±0.7601	7.6824
S 5	6.2±0.3672	4.5925	2.8±0.5722	5.7227

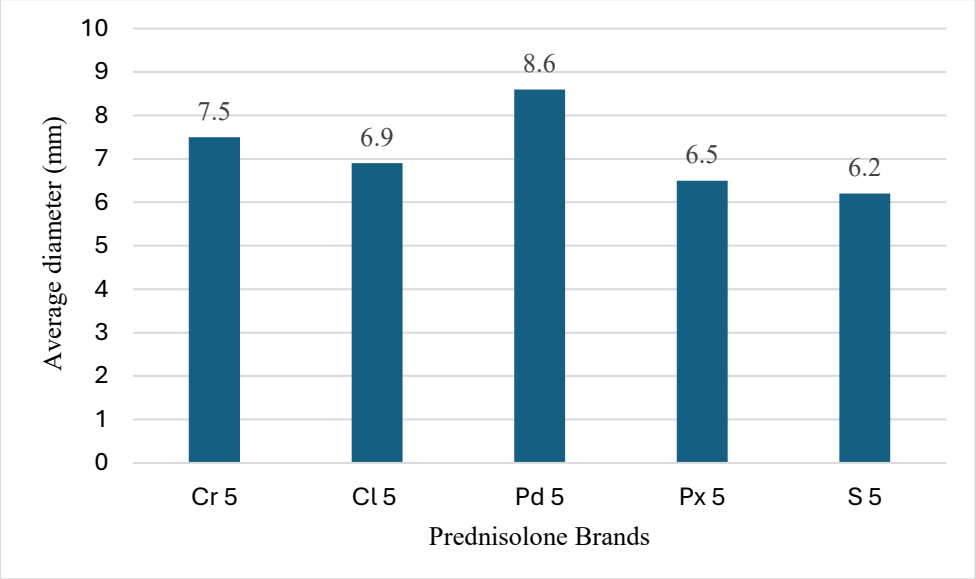


Figure 3.1: Average diameters of studied Prednisolone tablets

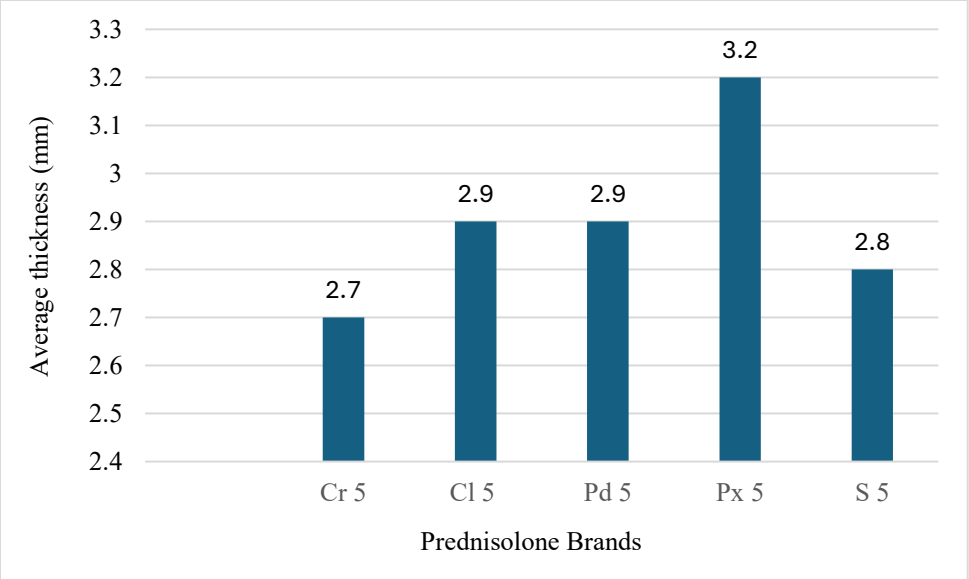


Figure 3.2: Average thickness of studied Prednisolone tablets

3.2. Hardness test

Table 3.4 shows the hardness of studied Prednisolone tablet products. The hardness of the samples ranged from 2.16±0.0329 kg/cm2 to 2.60±0.245 kg/cm^2. The data are graphically presented in **Figure 3.3**.

Table 3.4: Hardness of studied Prednisolone tablets

Sample Code	Tab-1	Tab-2	Tab-3	Tab-4	Tab-5	Average Hardness ± S.D. (kg/cm^2)
Cr 5	2.3	2.1	2.1	2.2	2.1	2.16±0.0329
Cl 5	2.2	2.0	2.2	2.3	2.2	2.18±0.112
Pd 5	2.5	2.5	2.7	2.6	2.7	2.6±0.245
Px 5	2.3	2.3	2.3	2.4	2.3	2.32±0.472
S 5	2.5	2.7	2.6	2.6	2.5	2.58±0.165

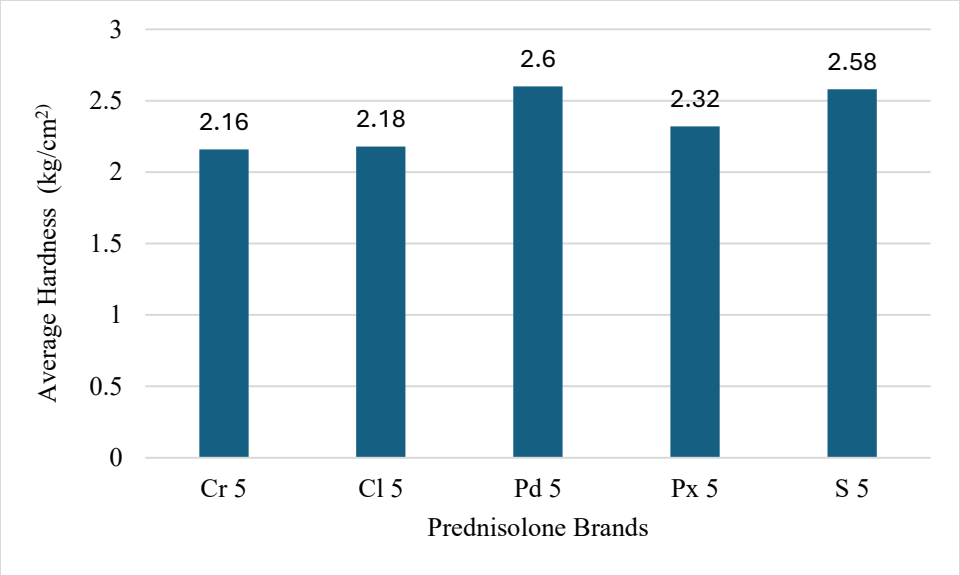


Figure 3.3: Average hardness of studied Prednisolone tablets

3.3 Weight and Weight variation test

Table 3.5 presents the average weights and maximum upper & lower weight variations for the tablet samples studied. The weights of the tablet products ranged from 83.4±2.361 mg to 167.3±1.230 mg. The data are presented graphically in **Figures 3.4 (a)** and **(b)**.

Table 3.5: Average weight and weight variation of studied Prednisolone tablets

Sample Code	Average Weight ± S.D. (mg)	Upper weight variation (%)	Lower weight Variation (%)
Cr 5	167.3±1.230	0.839	0.791
Cl 5	125.7±1.835	0.946	0.856
Pd 5	83.4±2.361	0.799	0.597
Px 5	140.6±926	1.354	1.112
S 5	110.5±712	0.977	0.937

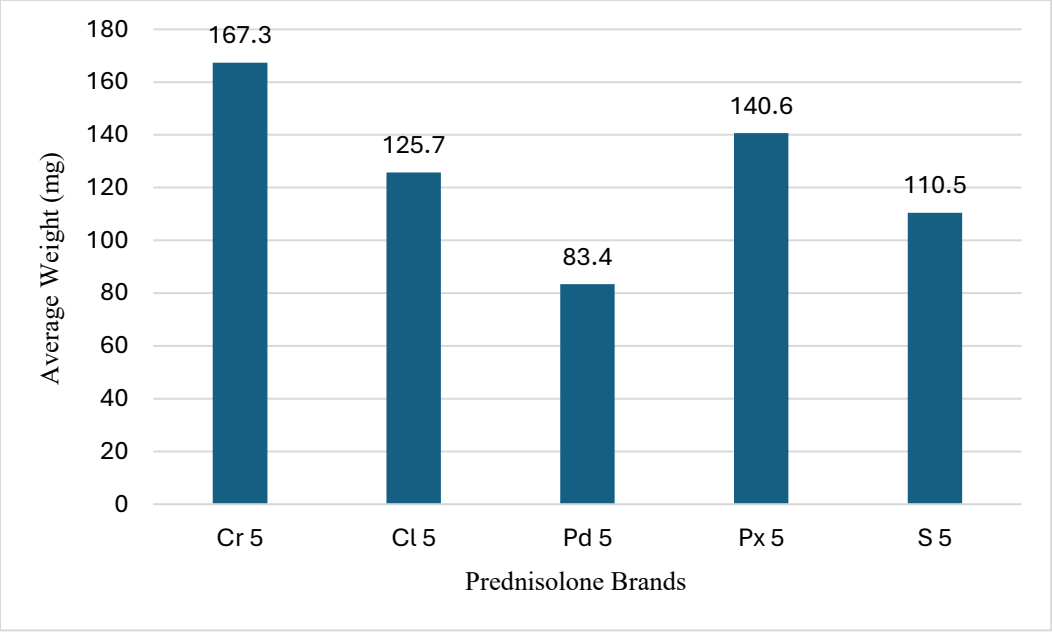


Figure 3.4 (a) Average weight of studied Prednisolone tablets

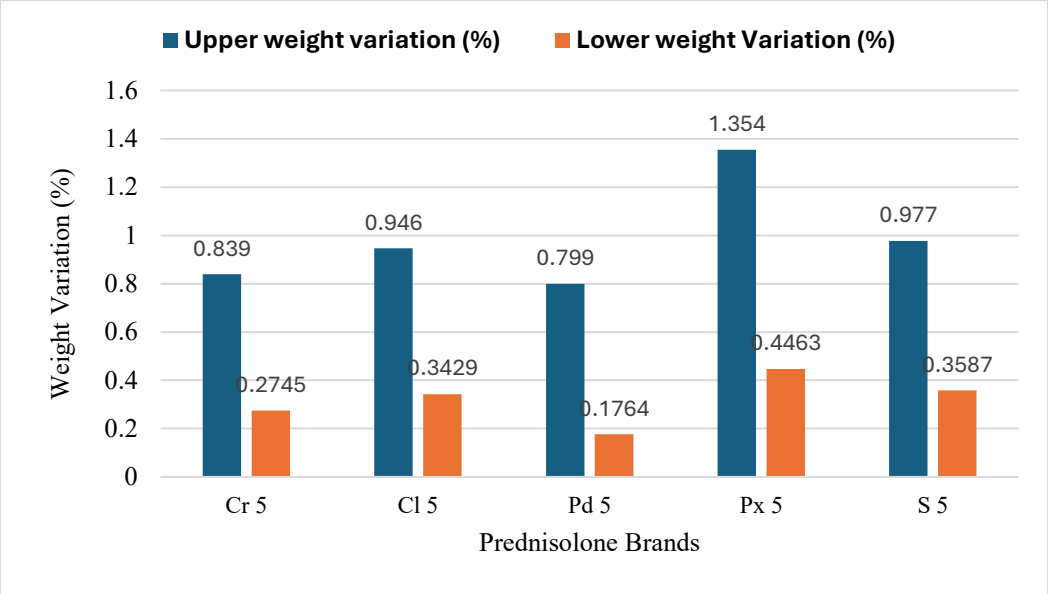


Figure 3.4 (b): Maximum upper and lower weight variation of studied Prednisolone tablets

3.4 Friability test

The friability result of Prednisolone tablets products ranged from 0.417% to 0.904% **(Table 3.6, Figure 3.5)**.

Table 3.6: Friability of the studied Prednisolone tablets

Sample Code	Number of Tablets	Initial weight (mg)	Finish weight. (mg)	Friability (%)
Cr 5	10	1675	1668	0.417
Cl 5	10	1260	1252	0.634
Pd 5	10	836	829	0.837
Px 5	10	1406	1398	0.568
S 5	10	1105	1095	0.904

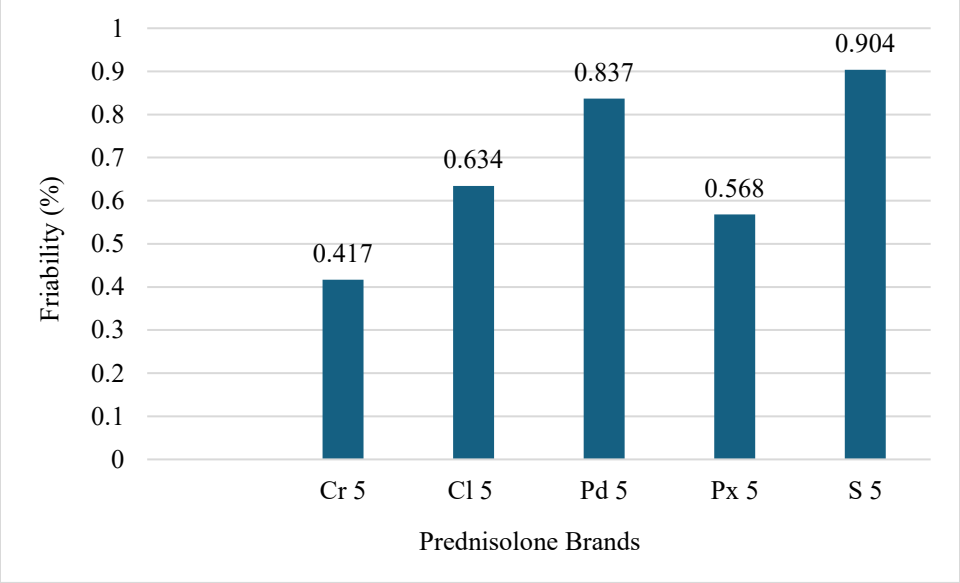


Figure 3.5: Friability of the studied Prednisolone tablets

3.5 Disintegration test

Table 3.7 presents disintegration times observed for the Prednisolone 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 6 min (Cl 5) to 8 min (Px 5) in water and 3.9 min (S 5) to 5.5 min (Px 5) in simulated gastric fluid.

Table 3.7: Disintegration times of studied Prednisolone tablet products

Sample code	Water (min)	Simulated gastric fluid (min)
Cr 5	7.5	5
Cl 5	6	4.3
Pd 5	6.6	5.1
Px 5	8	5.5
S 5	6.5	3.9

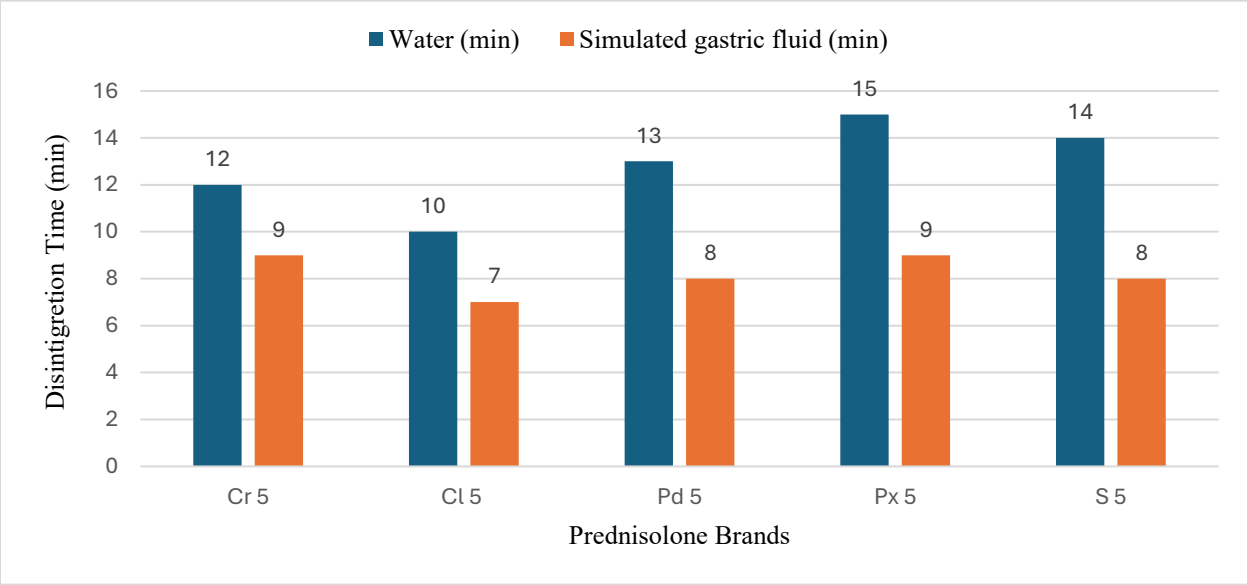


Figure 3.6: Disintegration times of studied conventional Prednisolone tablets

3.6 Assay

UV spectrophotometric canning of a solution of prednisolone over a concentration range of 200-400 nm gave the maximum absorption (λmax) at 247 nm (**Figure 3.7).**

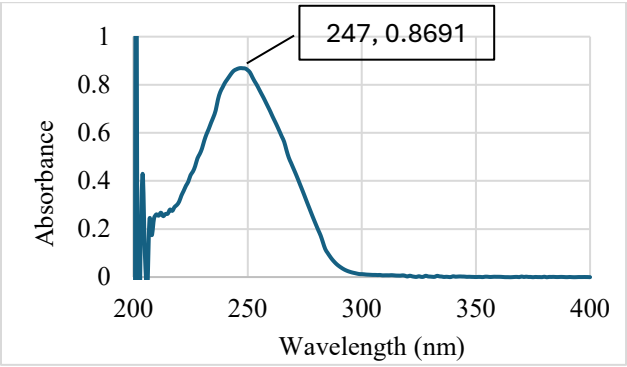


Figure 3.7: UV spectrum of prednisolone in distilled water

As demonstrated in **Table 3.8** and graphically presented in **Figure 3.8**, plot of absorbances of prednisolone solutions at different concentrations against corresponding concentrations shows a linear relationship over a concentration range of 5-30 µg/ml giving a straight line with a coefficient of determination (r^2) of 0.9718.

Table 3.8: Data for standard calibration curve of prednisolone in water

Concentration (µg/ml)	Absorbance
5	0.053
10	0.197
15	0.309
20	0.623
25	0.654
30	0.892

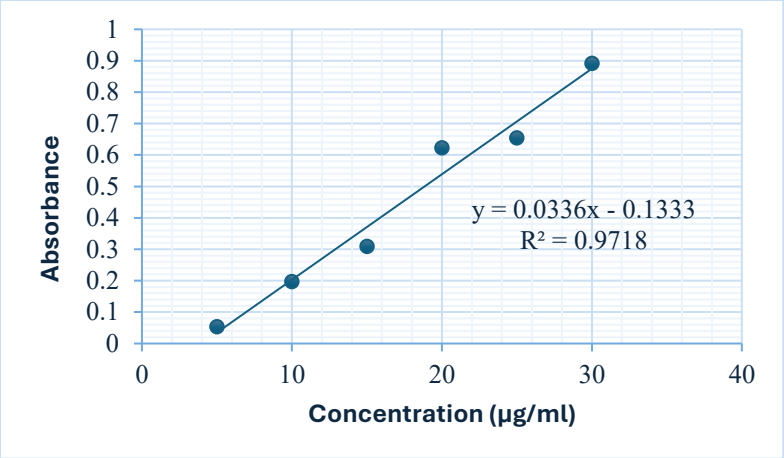


Figure 3.8: Standard calibration curve of prednisolone in water

Table 3.9 presents the assay results of studied Prednisolone tablet products found using distilled water as the solvent system. The data are graphically presented in **Figure 3.9**. Assay results demonstrate that the potency of the products studied fall in the of 95.45% **(Px 5)** to 105.12% (**Pd 5**).

Table 3.9: Assay results of studied Prednisolone tablet products

Sample Code	Potency (%)
Cr 5	100.28
Cl 5	95.45
Pd 5	105.12
Px 5	95.53
S 5	102.29

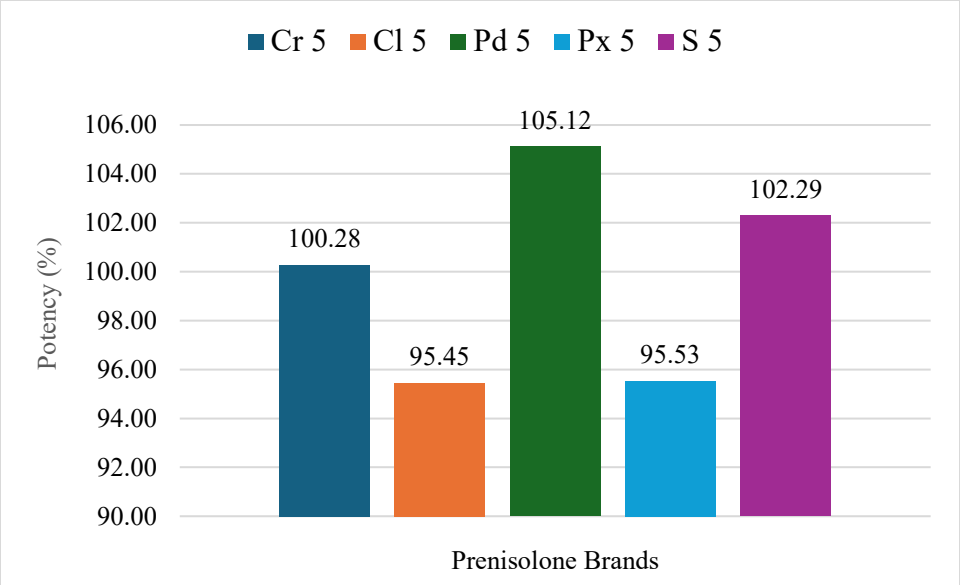


Figure 3.9: Assay results of studied Prednisolone tablets.

[Summary: How to calculate potency using UV-spectroscopy?

To **calculate potency using UV-spectroscopy**, you essentially compare the **absorbance** of your **sample solution** to that of a **standard solution** with a known concentration.

Potency Calculation — Step-by-Step

1. Prepare a standard solution

- Use a **pure reference standard** of known concentration.
- Example: 10 µg/mL of pure drug.

2. Measure absorbance of the standard (A_s)

- At the drug's **λmax** (maximum absorbance wavelength).

3. Prepare your sample solution

- Weigh and dissolve your **formulated drug product** (e.g., tablet or capsule) in suitable solvent.
- Dilute to a comparable concentration as the standard.

4. Measure absorbance of the sample (A_x)

5. Use the formula to calculate concentration (C_x) of the sample:

If **Beer–Lambert's Law** applies and both are measured under the same conditions:

$$\frac{Cx}{Cs} = \frac{Ax}{As}$$

$$Cx = \frac{Ax \times Cs}{As}$$

Where:

- Cx = concentration of sample
- Cs= concentration of standard
- Ax= absorbance of sample
- As = absorbance of standard

6. Calculate potency (%)

Once you've determined CxC_x, compare it to the **expected (label claim)** concentration:

Potency = $\frac{Cx}{Cs} \times 100\%$

Example

Parameter	Value
Standard Conc. (C_s)	10 µg/mL
Abs. of standard (As)	0.500
Abs. of sample (Ax)	0.470
Label Claim	10 µg/mL

Step 1: Calculate C_x

$C_x = \frac{Ax \times Cs}{As} = \frac{0.470 \times 10}{0.500} = 9.4$ µg/mL.

Step 2: Potency

Potency= $\frac{9.4}{10}$ =90%]

3.7 Dissolution study

Table 3.10 presents the average % release of prednisolone in distilled water from 6 tablets for each of the 5 brands of Prednisolone tablet at different time points over a period of 120 min. The data are graphically presented in **Figure 3.10**.

Table 3.10: Release profiles of studied Prednisolone tablet samples in distilled water

Sample Code	% of drug released (average of 6 tablets)								
	Time (min)								
	0	**5**	**10**	**20**	**30**	**45**	**60**	**90**	**120**
Cr 5	0	12.78	17.25	25.2	41.75	48.86	53.21	70.77	76.92
Cl 5	0	7.11	12.69	17.43	25.42	41.4	49.04	51.45	72.95
Pd 5	0	12.42	17.08	25.2	41.14	48.64	50.49	67.26	69.89
Px 5	0	12.6	17.17	25.2	41.22	48.56	52.33	68.14	71.65
S 5	0	12.69	17.43	25.51	42.15	50.88	63.75	69.01	78.23

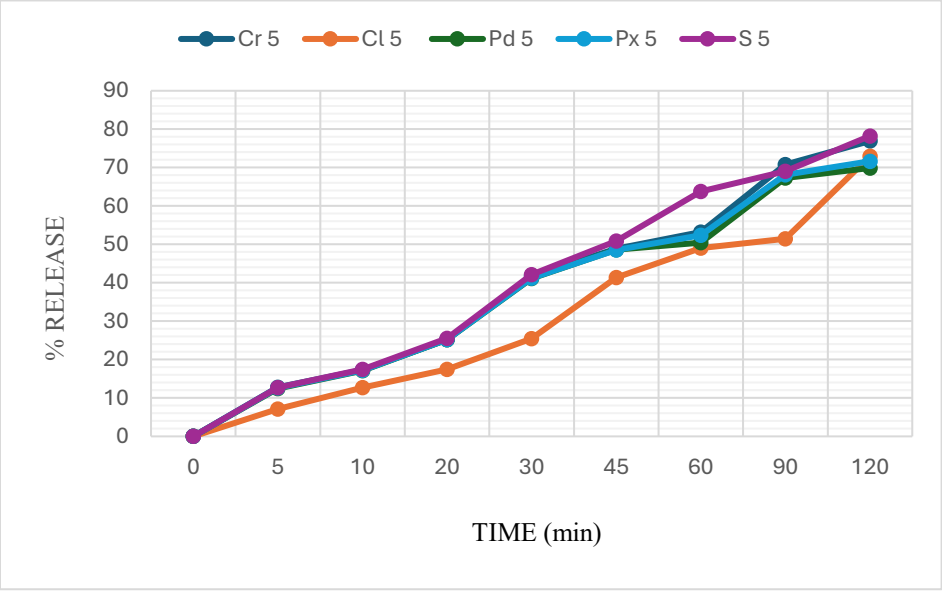


Figure 3.10: Release profiles of Prednisolone in distilled water.

Chapter-4: Discussion

In this study, five different brands of conventional Prednisolone tablets (5 mg), collected from different retail pharmacies located in the Savar area of Dhaka district, were subjected to several tests. Different quality assessment parameters (*e.g.*, thickness and diameter, hardness and friability, weight and weight variation, assay of content, disintegration time and dissolution profile) were tested to assess the quality of various conventional prednisolone tablets available in Bangladesh drug market and determine the differences among them.

The pharmacopeial compliance as regards the weight uniformity of tablet products is crucial since assessment of weight variation is the primary step to prove the uniformity dosage units. It measures the quantity of drug material in the tablet indirectly. Five different brands of Prednisolone tablets produced consistent weight determination results with values that are within acceptable bounds **(Table 3.5)**. There was, however, a difference in their mean weights. This difference in mean weights was due to the varied excipients utilized and, so, should not be taken as an indicator of inconsistent efficacy of the tablets. However, the variations in tablet weight, which reflect their sizes, between brands may have a negative psychological impact on clinicians and their patients even though each brand passed the weight uniformity test. This is because it may cast doubt on the general equivalency of the various brands, all of which are of 5 mg strength.

The World Health Organization model formulary suggests that a patient be started on a certain brand for likely pharmacokinetic and psychological reasons. The amount of drug material in each tablet unit should match the amount stated on the label. To assess the content, an assay should be carried out. **Table 3.9** shows the findings of the chemical content assay, which used UV spectrometric analysis to ascertain the quantity of Prednisolone contained in every brand. The range of the samples' Prednisolone active component content was 95.45% to 105.12%. According

to USP guidelines, the drug concentration in an assay should not exceed 110% and should be less than 90%. Assay values of all the studied Prednisolone tablets were within the limits recommended by the USP. The variations in the figures might be the result of various manufacturing processes and additives employed in various plants.

One of the most important factors in determining whether or not the tablets will be able to withstand breaking, chipping, or abrasion during handling, shipping, and storage is their hardness. To provide resistance to damage during handling, packing, and transportation, tablets must have sufficient hardness. Tablet hardness of 4 kg/ cm^2 is considered to be the minimum limit for a satisfactory tablet. An excessively hard tablet, however, would drastically reduce the breakdown period and, consequently, the dissolution rate, but a minimum hardness of 4 kg is required, and tablets with a high compact nature may be produced at a hardness of 6.0 kg or more. This has to do with the influence of one or more factors on hardness. Tablet density and porosity variations are reflected in variations in tablet hardness by altering the pace at which dissolving fluid penetrates the tablet's surface. **Table 3.4** on tablet hardness demonstrated that the tablet hardness of the studied brands was in the range of 2.16±0.0329 kg/cm2 to 2.60±0.245 kg/cm^2, which means that they failed to meet the minimum allowance of 4 kg/ cm^2.

As one of the most important tablet properties, tablet hardness is typically evaluated as an in-process-control parameter during tablet manufacture. It characterizes the compatibility of tableting materials and the mechanical strength of the tablet to withstand potential stresses during tableting, packaging, shipping, and dispensing. However, tablet hardness cannot be taken not be as the absolute indicator of strength since certain tablets have a tendency to cap on attrition, losing their crown sections when squeezed into extremely hard tablets. Friability is another criterion of tablet strength that is frequently tested to complement tablet hardness. According to some pharmacopoeia, tablets should have a friability value of less than 1%. The studied Prednisolone brands met this requirement with their friability being in the range of 0.417% to 0.904% **(Table 3.6, Figure 3.5)**.

The factor that primarily determines how quickly a medicine is absorbed is its disintegration time. Drug breakdown and, in turn, its bioavailability might be impacted by the kind and quantity of

excipients utilized by various manufacturers. Thus, although there is a positive relationship between the crushing strengths of the tablets and their disintegration time, tablet crushing strength ratings alone could not be used to forecast the disintegration times. Studied Prednisolone tablets' disintegration times ranged from 6.0 min (Cl 5) to 8.0 min (Px 5) in distilled water and 3.9 min (S 5) to 5.5 min (Px 5) in simulated gastric fluid (**Table 3.7**), which were within the acceptable limit of 15 min as recommended by some pharmacopoeia for uncoated tablets. The five brands' adequate disintegration times may be predictive of their good bioavailability since the tablets will disintegrate quickly in the gastrointestinal system, increasing the surface area available for medication dissolution and absorption.

The dissolution of the medication in the aqueous environment of the gastrointestinal system is a prerequisite for drug bioavailability. Assuring product homogeneity is another ground that has led to the development of dissolution testing for solid oral medicinal formulations. A drug's pharmacological action is greatly influenced by its dissolving behavior. *In vitro-in vivo* correlation, so named because it is commonly accepted, refers to the established direct link between the *in vitro* dissolution rate of many medicines and their bioavailability. Depending on how they were made, solid dosage forms might or might not dissolve adequately when they come into contact with gastrointestinal fluid after being taken orally. The USP guidelines require a dissolution rate of not less than 75% in 45 min. The five brands of Prednisolone studied here were found to be short of expectations as per the specifications provided by the USP **(Table 3.10)**.

The physicochemical characteristics of the active components and excipients as well as the manufacturing process may have an impact on the product's formulation, which can have a major impact on the rate of disintegration and dissolution. The parameters of disintegration and dissolution are known to be influenced by the kind and quantity of excipients utilized in tablet formulation as well as the manufacturing method. Disintegration time, hardness, friability, weight variation, dissolution profile, and other quality criteria can all be significantly impacted by the way a pharmacological product is formulated. Together with the methods employed in the production process, this also covers the physiochemical characteristics of the excipients and active components.

Altogether, the Prednisolone tablet products studied here performed well in terms of weight variation, friability, disintegration and assay. There are, however, some concerns with diameter and thickness, hardness and dissolution.

Chapter-5: Conclusion

Pharmaceutical items are becoming more and more important due to the expanding human population. For the best possible safety and efficacy, meeting and maintaining quality requirements are crucial for pharmaceutical products. Quality assessment is required to avoid any fake or subpar medication. The regulatory organizations are primarily concerned with regular monitoring of the quality attributes. However, institutional research can also make important contributions to making surveillance on the quality of this kind of product. Such quality assessment may be particularly crucial in underdeveloped nations where the provision of healthcare services has been severely hampered by the prevalence of fake and inferior medications.

With this viewpoint, an *in vitro* assessment of adequacy and uniformity of thickness, diameter, weight, hardness, friability, disintegration time, and dissolution profile of five brands of conventional Prednisolone tablets were performed. The products were found to have satisfactory levels in terms of weight variation, friability, disintegration and assay. However, they failed to perform adequately in case of some criteria like diameter and thickness, hardness and dissolution.

Further work with samples from more batches including a bioavailability or bioequivalence investigation may be useful to determine their true therapeutic efficacy.

Chapter-06: References

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