

# **COMPARATIVE EVALUATION OF PREDNISOLONE 5MG TABLETS MARKETED IN BANGLADESH**

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## **Abstract**

The aim of the present study is to determine the quality and to correlate with other different brands of pharmaceutical products marketed in Bangladesh for the healthcare of patients suffering from different respiratory inflammation like asthma, and auto-immune disorders. The experiment is done to evaluate and compare the physicochemical equivalence of different brands of Prednisolone 5mg tablet. These tablets were tested through statistical methods in accordance with the BP and USP like weight variation, thickness, hardness, friability, disintegration, in-vitro dissolution and HPLC assay. The in vitro dissolution studies of Prednisolone 5 mg tablets were carried out in pH 7 distilled water for 30 minutes using USP-II method whose absorbance were taken at 246 nm using UV spectrophotometry. Six samples showed poor in-vitrodissolution which were non-equivalent to the USP monograph specification giving Prednisolone content less than 75%. The percentage content of active ingredient of different brands were tested using HPLC assay. Samples showed values within the specifications (90-110%) except some of the companies. Two samples did not undergo disintegration at all when given in the disintegration tester. However, no major problem was found in others physical parameters like tablet weight variation, thickness, hardness and friability. Finally from the experiment we can conclude that 50% of the companies in the urban area are substandard, whereas 50% companies provide standard drugs.

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**Chapter 1:  
Introduction**

## **1.1 Introduction**

Medicines need to be safe, effective and of good quality in order to produce the desired effect. Ensuring these properties requires the creation of competent national drug regulatory authorities with the necessary human and other resources to control the manufacture, importation, distribution and sale of medicines. The necessity of any drug delivery system is to provide a therapeutic amount of drug to the proper site in the body and then maintain the optimum plasma concentration for a definite period of time. The quality of a drug is an important factor which ensures the health and wellness of a patient. Substandard quality of drugs increases the mortality and morbidity in a country. The objective of this project is to evaluate the quality of drug available in Bangladesh market which is being used for patients suffering from respiratory disorders and various auto-immune disorders.

## **1.2 Conventional Dosage forms:**

Tablets are solid dosage forms usually obtained by single or multiple compressions of powders or granules. In certain cases tablets may be obtained by molding or extrusion techniques. They are uncoated or coated. Tablets contain one or more active ingredients. They may contain excipients such as diluents, binders, disintegrating agents, glidants, lubricants, substances capable of modifying the behavior of the dosage forms and the active ingredient in the gastrointestinal tract, coloring matter authorized by the appropriate national or regional authority and flavoring substances. When such excipients are used it is necessary to ensure that they do not adversely affect the stability, dissolution rate, bioavailability, safety or efficacy of the active ingredient; there must be no incompatibility between any of the components of the dosage form. Tablets are single-dose preparations intended for oral administration. Some are intended to be swallowed whole, some after being chewed and some after being crushed, some are intended to be dissolved or dispersed in water before being taken and some are intended to be retained in the mouth where the active ingredient is liberated. <sup>1</sup>

### **1.3 Advantages of conventional dosage forms:**

- a. They are unit dose form, and they offer the greatest capabilities of all dosage forms for the greatest dose precision and the latest content variability.
- b. their cost is lowest of all dosage forms
- c. They are the lightest and most compact of all oral dosage forms
- d. They are in general the easiest and cheapest to package and ship of all oral dosage forms
- e. Product identification is potentially the simplest and cheapest, requiring no additional processing steps when employing an embossed or monogrammed punch face.
- f. They may provide the greatest ease of swallowing with the least tendency for 'hang-up' above stomach, especially when coated provided that tablet disintegration is not excessively rapid.
- g. they lend themselves to certain special release profile products such as enteric or delayed-release products.
- h. They are better suited to large scale production than other unit oral forms
- i. They have the best combined properties of chemical, mechanical and microbiologic stability of all oral forms.

### **1.4 Disadvantages of conventional oral dosage forms:**

- a. Some drugs resist compression into dense compacts, owing to their amorphous nature or flocculent, low-density character.
- b. Drugs with poor wetting, slow dissolution properties, intermediate to large dosages, optimum absorption high in the gastrointestinal tract, or any combination of these features may be difficult or impossible to formulate and manufacture as a tablet that will still provide adequate or full drug bioavailability.
- c. Bitter tasting drugs, drugs with an objectionable odor, or drugs that are sensitive to oxygen or atmospheric moisture may require encapsulation or entrapment prior to compression or the tablets may require coating.<sup>2</sup>

### **1.5 Diseases which are treated with prednisolone:**

Respiratory disorders are an increasing day by day and affecting majority of people due to increasing air pollution. Glucocorticoids are commonly used to treat a wide range of respiratory inflammatory diseases like asthma. They are thought to decrease the chronic inflammation in the

bronchiole tree, thereby improving obstructed airflow. The main API (active pharmaceutical ingredient) of this project 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 such as asthma. Prednisolone can also be used as an immunosuppressive drug for organ transplants and in cases of adrenal insufficiency (Addison's disease).<sup>3</sup> Prednisolone is a man-made form of a natural substance (corticosteroid hormone) made by the adrenal gland. It is used to treat conditions such as arthritis, blood problems, immune system disorders, skin and eye conditions, breathing problems, cancer, and severe allergies. It decreases immune system's response to various diseases to reduce symptoms such as pain, swelling and allergic-type reactions.

Corticosteroids inhibit the inflammatory response to a variety of inciting agents and, it is presumed, delay or slow healing. They inhibit the edema, fibrin deposition, capillary dilation, leukocyte migration, capillary proliferation, fibroblast proliferation, deposition of collagen, and scar formation with inflammation.<sup>4</sup> Corticosteroids are considered to be one of the most effective medicines for asthma by suppressing airway inflammation.<sup>12</sup>

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.<sup>5</sup>

9 percent of pharmaceutical sales in Bangladesh have been traced to counterfeit or low-quality drugs, openly sold in pharmacies.<sup>6</sup>

This project focuses on the evaluation of the prednisolone dosage form and its basic parameters which evaluated the drug quality and shows whether they meet the USP requirements as claimed by the manufacturing companies.

## 1.6 Drug Profile:

**Active Pharmaceutical Ingredient:** Prednisolone

**Therapeutic Class:** Endocrine-metabolic agent, immune suppressant

**Therapeutic Indications:**

- i. Skin: Pemphigus vulgaris, allergic dermatitis, eczema, exfoliative dermatitis, dermatitis herpetica, dermatitis medicamentosa, erythema multiforme, disseminated lupus erythematosus, dermatomyositis, polyarteritis nodosa.
- ii. Respiratory: Severe bronchial asthma and status asthmaticus, emphysema, pulmonary fibrosis.
- iii. Adrenal: Adrenal hyperplasia (adrenogenital syndrome).
- iv. Haematological: Idiopathic thrombocytopenic purpura, acquired haemolytic anaemia, acute leukaemia.
- v. Other: Nephrotic syndrome, iridochoroiditis, ulcerative colitis, rheumatoid arthritis, ankylosing spondylitis, rheumatic fever, gout, peri-arthritis of the shoulder.

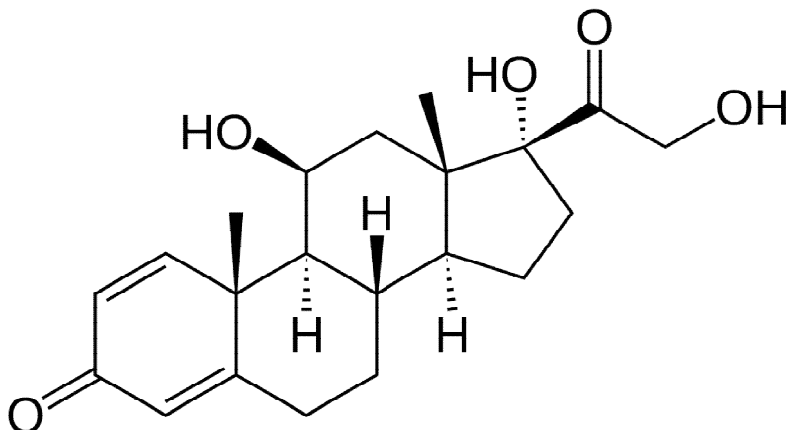
**Description:** Prednisolone is a synthetic glucocorticoid, a derivative of cortisol which is used to treat a variety of inflammatory and auto-immune conditions. It is the active metabolite of drug prednisone and it is used in patients with hepatic failure as they are unable to metabolize prednisone to prednisolone.<sup>7</sup>

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<sub>21</sub>H<sub>28</sub>O<sub>5</sub>

**Molecular Mass:** 360.44402g/mol

**Structural formula:**



**Appearance:** White to white crystalline powder

**Solubility:** in water,  $2.23 \times 10^{-2}$  mg/L at 25° C

**Melting point:** 235°C

**1.7 Mechanism of action:**

Prednisolone can inhibit leukocyte infiltration at the site of inflammation, interfere with mediators of inflammatory response, and suppress humoral immune responses. The anti-inflammatory actions of glucocorticoids are thought to involve phospholipase A<sub>2</sub> inhibitory proteins, lipocortins, which control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes. Prednisolone reduces inflammatory reaction 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 translocate 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 expression of specific target genes, including suppression of IL2 (interleukin 2) expression.<sup>8</sup>

## 1.8 Pharmacodynamic properties:

Prednisolone acts through replacing adrenal insufficiency as in Addison's disease, or after adrenalectomy. Prednisolone has anti-inflammatory and immuno-suppressant glucocorticoid properties.

## 1.9 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 of Prednisolone lasts for several hours.<sup>9</sup>

## 1.10 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 by 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 10mg daily reduced to the lowest effective dose for maintenance.

**Most other conditions:** 10 to 100mg 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.<sup>10</sup>

**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:**

Sodium phosphate:

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.<sup>14</sup>

## 1.11 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, urticarial

**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. Cushingoidfacies, 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 papilloedemain 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 prednisone 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.

## 1.12 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.

### **1.13 Contraindications**

Prednisolone is contraindicated in patients with: peptic ulcer, osteoporosis, psychosis or severe psychoneuroses.

Prednisolone is usually contraindicated in the presence of acute infection

Administration of live virus vaccines

### **1.14 Use during Pregnancy**

The ability of corticosteroids to cross the placenta varies between individual drugs, however, 88% of Prednisolone is inactivated as it crosses the placenta. Administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate, intra-uterine growth retardation and effects on brain growth and development. There is no evidence that corticosteroids result in an increased incidence of congenital abnormalities, such as cleft palate/ lip in man.

However, when administered for prolonged periods or repeatedly during pregnancy, corticosteroids may increase the risk of intra-uterine growth retardation.

Hypoadrenalism may, in theory occur in the neonate following prenatal exposure to corticosteroids but usually resolves spontaneously following birth and is rarely clinically important. As with all drugs, corticosteroids should only be prescribed when the benefits to the mother and child outweigh the risks. When corticosteroids are essential however, patients with normal pregnancies may be treated as though they were in the non-gravid state.<sup>10</sup>

#### **Lactation**

Corticosteroids are excreted in small amounts in breast milk. However doses of up to 40mg daily of prednisolone are unlikely to cause systemic effects in the infant. Infants of mothers taking higher doses than this may have a degree of adrenal suppression but the benefits of breast-feeding are likely to outweigh any theoretical risk.<sup>10</sup>

## 1.15 Drug Interactions:

**Hepatic microsomal enzyme inducers:** Medicines that induce hepatic enzyme cytochrome P-450 isozyme 3A4 such as Phenobarbital, phenytoin, rifampicin, rifabutin, carbamazepine, primidone and amino-gluethimide may reduce the therapeutic efficacy of corticosteroids by increasing the rate of metabolism.

**Hepatic microsomal enzyme inhibitors:** Medicines that inhibit hepatic enzyme cytochrome P-450 isozyme 3A4 such as ketoconazole, ciclosporin or ritonavir may decrease glucocorticoid clearance. A reduction in prednisone 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 prednisone 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 prednisone treatment.

**Cytotoxic agents:** There is an increased risk of haematological toxicity when prednisone 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 prednisone 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 formoterol.

**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 prednisone may decrease absorption of these glucocorticoids efficacy may be decreased sufficiently to require dosage adjustments in patients receiving small doses of prednisone.

### 1.16 Available dosage forms of prednisolone in Bangladesh:

Brand Name	Dosage	Dosage Form	Manufacturer
Cortan	Prednisolone 5mg, 10mg & 20mg	Tablet	Incepta Pharmaceuticals Ltd.
Deltacort	Prednisolone 5mg	Film Coated Tablet	Desh Pharmaceuticals 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	GacoPharmaceuticals 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.

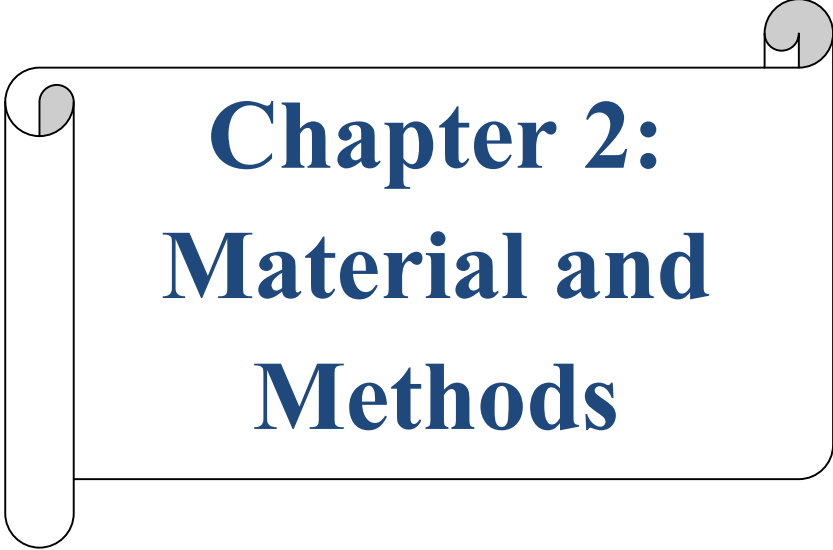
Table 1.1: Table showing the available dosage forms of prednisolone in Bangladesh



Figure 1.1: Picture of Cortan® 5mg& 20mg prednisolone tablets manufactured and marketed by Incepta Pharmaceuticals Ltd.



Figure 1.2: Picture of Inflagic® 5mg tablets manufactured and marketed by Square Pharmaceuticals Ltd.



# **Chapter 2: Material and Methods**



## 2.1 Materials:

<b>Serial number</b>	<b>Instrument</b>	<b>Model/Manufacturer</b>	<b>Country of origin</b>
1.	Slide caliper (0-150X0.05mm)		China
2.	Electronic balance	Shimadzu	Japan
3.	Friabilator (USP)	Electrolab, EF-2	India
4.	Disintegration Tester (USP)	Electrolab, ED-2L	India
5.	Dissolution Tester	Logan Instruments Corp., UDT-804	USA
6.	UV-Visible Spectrophotometer	Hitachi	Japan
7.	High Performance Liquid Chromatography (HPLC)	Shimadzu	Japan
8.	Sonicator	Shimadzu	Bangladesh
9.	pH meter	Shimadzu	Bangladesh
10.	Lab stirrer	Shimadzu	Bangladesh
11.	Water suction filtration	Shimadzu	Bangladesh

Table2.1: List of instruments and Equipment used in the analysis

<b>Serial Number</b>	<b>Name</b>	<b>Specification</b>
1.	Volumetric flask	10ml, 20ml, 50ml, 1000ml
2.	Pipette(graduated & volumetric)	1ml, 2ml, 4ml, 5ml, 10ml
3.	Beakers	10ml, 25ml, 50ml, 100ml, 500ml, 1000ml
4.	Funnel	Small, medium
5.	Measuring cylinder	500ml, 1000ml
6.	Pipette filler	Bangladesh
7.	Filter paper	Whitman
8.	Injection syringe with 0.45 $\mu$ disk filter	Bangladesh
9.	Mortar & Pestle	Small, medium

Table2.2: List of apparatus and glass wares used in the experiment

<b>Sample Number</b>	<b>Batch No.</b>	<b>Expiry date</b>
Sample 1	602-28-50	APR 16
Sample 2	602-28-50	MAY 16
Sample 3	13059 E0816	AUG
Sample 4	13059 E0816	AUG 16
Sample 5	B166	AUG 16
Sample 6	B167	AUG 16
Sample 7	336E0916	SEP 16
Sample 8	346E0916	SEP 16
Sample 9	408002	JULY 16
Sample 10	408004	SEP 16
Sample 11	B06E02 2017	FEB 17
Sample 12	B10E02 2017	FEB 17

Table 2.3: List of tablets from different samples and their batch number and expiry date

## Pictures & Images of the Instruments:

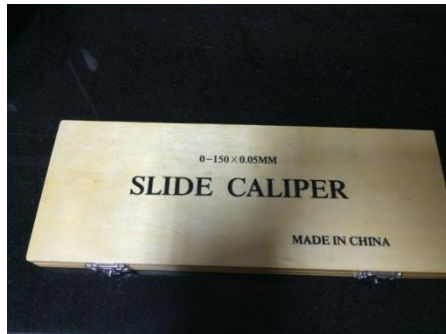


Figure 2.1: Picture showing slide caliper



Figure 2.2: Picture showing an electronic balance

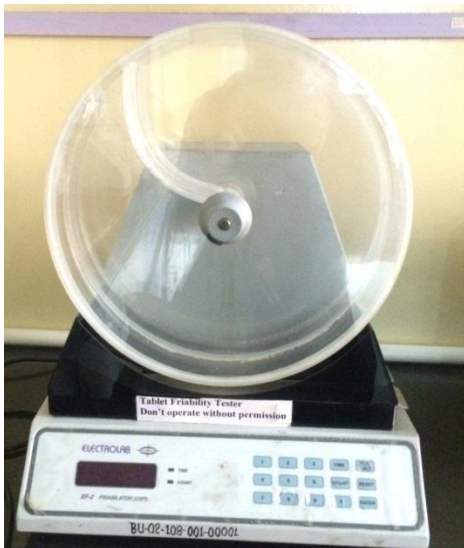


Figure 2.3: Tablet friability tester



Figure 2.4: Picture showing disintegration tester



Figure 2.5: Picture showing UV-Visible spectrophotometer



Figure 2.6: Picture showing dissolution tester

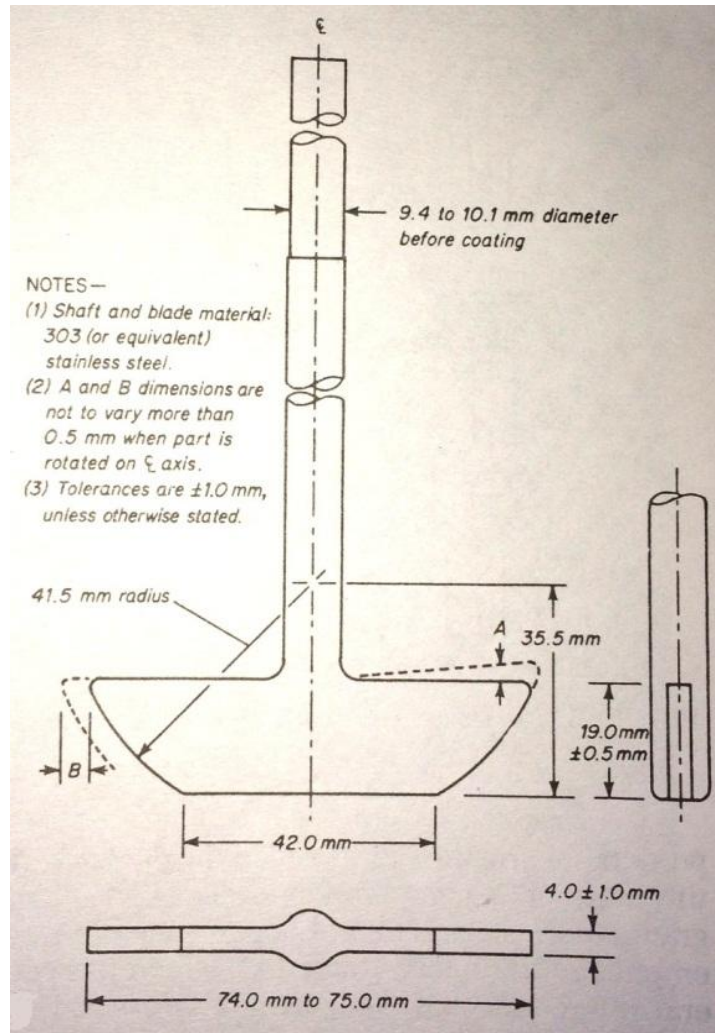


Figure 2.7: Picture showing the paddle of dissolution tester



Figure 2.8: Picture showing the HPLC machine

## 2.2 Assay of Prednisolone by High Performance Liquid Chromatography (HPLC)

### Principle:

A prepared standard and sample solution are injected consequently into suitable column of High Performance Liquid Chromatography (HPLC). The content of Prednisolone present in each sample is calculated by comparing both the peak areas of active Prednisolone present in the standard preparation and prepared sample.

### Procedure:

### Chromatographic Conditions:

Apparatus	Specifications
HPLC machine	Shimadzu HPLC-prominence integrated with spectrophotometric UV detector
Column	4.6mmX 30cm, C18
Mobile phase, Mixture of Solution	Water saturated butyl chloride, Tetrahydrofuran, Methanol and Glacial acetic acid (95:14:7:6).
Flow rate	1.0 $\mu$ l
Wavelength	254nm
Load	10 $\mu$ l
Temperature	40°C



**Standard preparation:**

5mg of working standard of prednisolone was weighed and transferred into a clean and dry 25ml volumetric flask. Solution was made by adding diluting solution and was put in the sonicator for 5 minutes to make homogenous solution. 5ml of the above solution was transferred into a clean and dry 50ml volumetric flask and diluted with diluting solution. The solution was mixed well in the sonicator to make a homogenous solution of 20µg/ml. the solution was injected to two vials through 0.45µ disk filter. These were called as standard solutions.

**Sample preparation:**

Approximately 5mg Prednisolone tablets were weighed and made fine powder by crushing with mortar and pestle. Then the fine powdered sample was transferred into a clean and dry 25ml volumetric flask. The 10ml of diluting solution was added and shaken well. The solution was then put in the sonicator for 5 minutes and the volume was adjusted to the mark with the diluting solution and mixed well. 5ml of the above solution was then transferred into a 50ml clean and dry volumetric flask. 20ml of diluting solution was added and shaken well. The solution was put in the sonicator for 5minutes and made up to the mark with diluting solution. The concentration of the sample is the 20µg/ml. the solution was mixed well and injected into four vials through 0.45µ disk filter. These were called as sample solution. The above procedure was followed for twelve different companies and their tablets.

**Procedure:**

Two vials containing standard solution and four vials containing sample solution were placed into the tray of the auto sampler of Shimadzu HPLC machine. The instrument was started to run and the chromatography was recorded.

**Calculation:**

The quantity of Prednisolone was calculated in sample using the following equation:

Prednisolone Content %:

$$\frac{\text{Peak area of sample solution} \times \text{weight of standard (mg)} \times \text{Potency of standard}}{\text{Peak Area of standard solution} \times \text{Weight of sample (mg)}}$$

## 2.3 In-vitro dissolution study

### Principle:

Release rate of Prednisolone tablet is carried on according to the general procedure of United States Pharmacopoeia (USP). Samples of dissolution fluid are withdrawn and analyzed by UV Spectrophotometer. The measurement is done at the wavelength at which the absorption is maximum. By comparing with absorbance of standard solution, the amount of active Prednisolone in tablets released is calculated.

### Conditions:

Apparatus	USP 2 Paddle
Dissolution medium	900ml pH 7, Distilled water
Temperature	37°C (±0.5)
Stirring Speed	50rpm
Time	30 minutes

### Preparation of Standard Solution:

50mg of working standard of Prednisolone was weighed and transferred into a clean and dry 100ml volumetric flask. Then 90ml of distilled water was added to the volumetric flask and shaken. The volumetric flask is put in the sonicator for 5 minutes and made up to the mark. From the above solution 10ml is taken in another clean and dry 100ml volumetric flask and 50ml distilled water is added to make the solution. The solution is put in sonicator for 5minutes and the volume is adjusted to make up the mark. Concentrations of 1mg/ml, 2mg/ml, 3mg/ml, 4mg/ml and 5mg/ml.

**Standard curve of Prednisolone:**

Concentration(mg/ml)	Absorbance
0	0
1	0.07
2	0.13
3	0.19
4	0.24
5	0.326

Table 2.4: Standard curve of Prednisolone

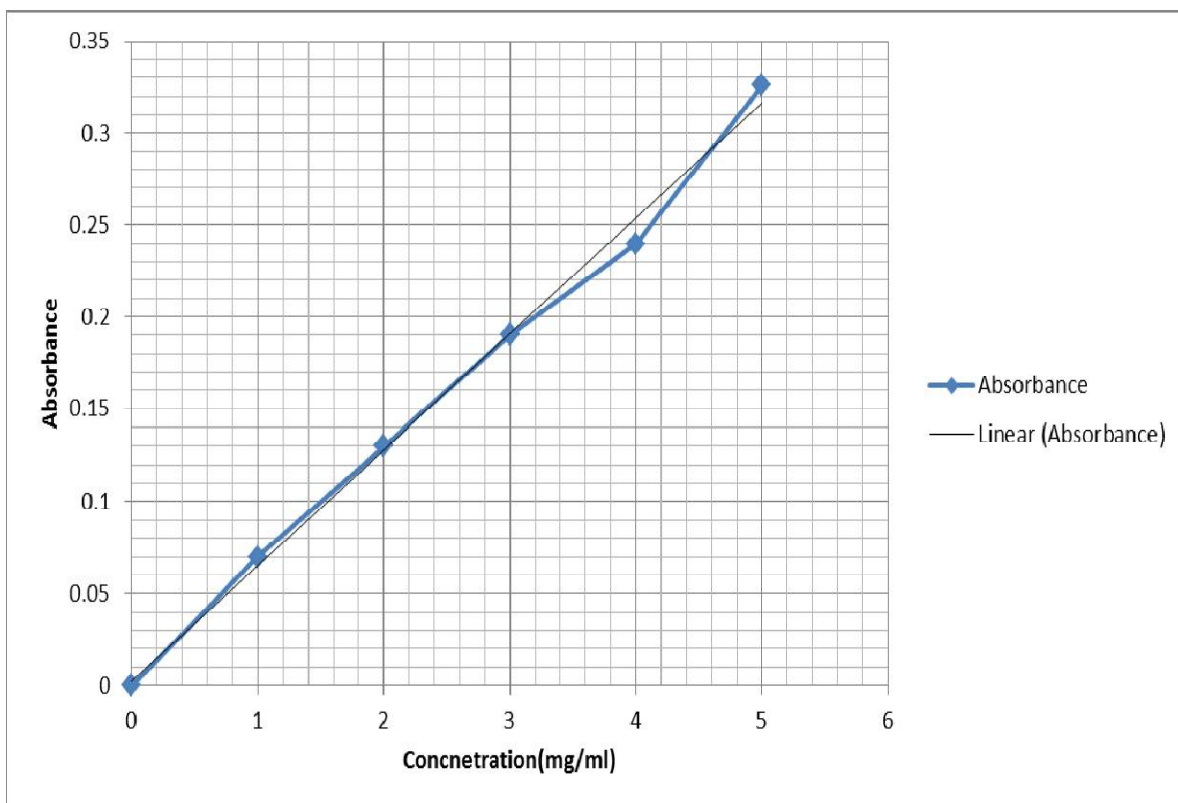


Figure 2.3.1: Standard curve of Prednisolone

**Preparation of sample solution:**

900ml of distilled water was placed into each of six dissolution vessels and the temperature was set to  $37^{\circ}\text{C}(\pm 0.5)$ . Weighed tablets of Prednisolone were transferred to each six baskets. The baskets were immersed into the medium to a distance  $25\pm 2$  mm between the basket and bottom of the vessel. The apparatus was started to operate at the specified rpm. At the end of 1<sup>st</sup> hour, 10ml samples were withdrawn from each vessel and filtered through Whatman filter paper discarding first few ml of filtrate. The withdrawn quantity of samples was replaced by fresh dissolution medium to maintain constant volume of dissolution medium. 4ml of the filtrate were diluted with distilled water into 10ml volumetric flask and mixed well.

Then the absorbance of the above solution in a 1cm silica cell were measured at the wavelength of maximum absorbance at 246nm by UV-visible spectrophotometer using distilled water as blank.

The amount of drug present in the samples was calculated with the help of straight-line equation obtained from the calibration curve of Prednisolone. The dissolution study was continued for 1 hour to get a simulated picture of the drug release in the in-vitro condition

## 2.4 Physical parameters of Prednisolone:

**Weight variation:** A fundamental quality attribute for all pharmaceutical preparations is the requirement for a constant dose of drug between individual tablets. Small variations between individual preparations are accepted.<sup>11</sup> The test for uniformity of weight is carried out by collecting sample of tablets, from a batch and determining their individual weight. The average weight of the tablets is then calculated. The sample complies with the standard if the individual weights do not deviate from the mean more than is permitted in terms of percentage.

**Thickness:** The thickness of a tablet is the only dimensional variable related to the process. At a constant compressive load, tablet thickness varies with changes in the die fill, with particle size distribution and packing of particle mix, being compressed and with tablet weight while with a constant die fill, thickness varies with variations in compressive load. Tablet thickness is consistent batch to batch or within a batch only if the tablet granulation or powder blend is adequately consistent in particle size and size distribution, if the punch tooling is of consistent length, and if the tablet press is clean and in good working order. The thickness of individual tablets can be measure with slide calipers which permits accurate measurements and provides information on the variation between tablets. Tablet thickness should be with in  $\pm 5\%$  variation of standard value.

**Hardness:** Tablets require a certain amount of strength or hardness and resistance to friability, to withstand mechanical shocks of handling in manufacture, packaging and shipping. Adequate tablet hardness and resistance to powdering and friability are necessary requisites for consumer and acceptance. Monitoring of tablet hardness is especially important for drug products that possess real or potential bioavailability problems or that are sensitive to altered dissolution release profiles as a function of the compressive force employed.

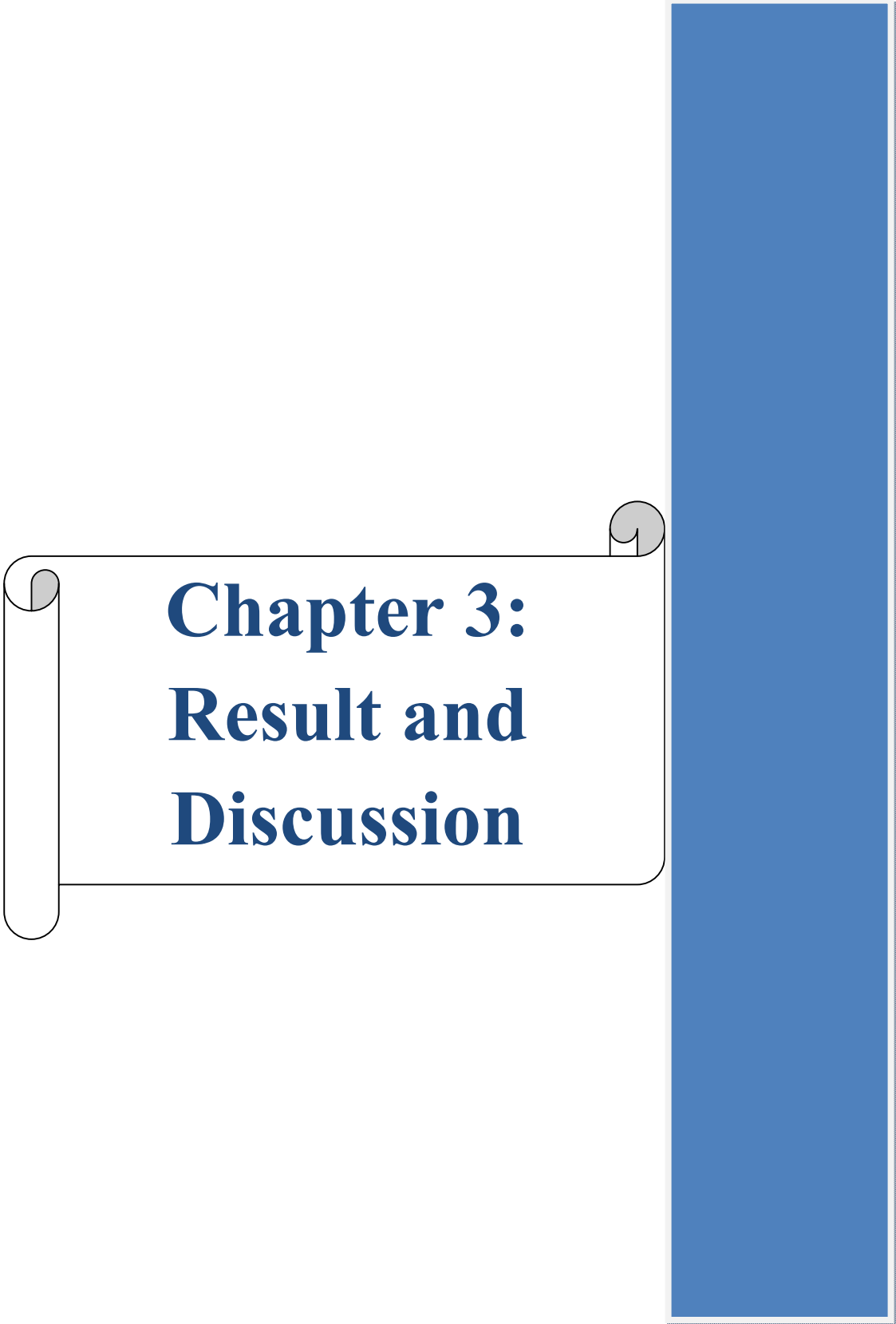
**Friability:** The laboratory friability tester is known as Roche friabilator. This device subjects a number of tablets to the combined effects of abrasion and shock by utilizing a plastic chamber that revolves at 25rpm dropping the tablets a distance of six inches with each revolution. Normally a reweighed tablet sample is placed in the friabilator which is then operated for

100 revolutions. The tablets are then dusted and reweighed. Conventional compressed tablets that lose less than 0.5 to 1.0% of their weight are generally considered acceptable.

**Disintegration:** The first important step toward solution is breakdown of the tablet into smaller particles or granules a process known as disintegration. The time that it takes a tablet to disintegrate is measured in a device described in the USP. The USP device to test disintegration uses 6 glass tubes that are 3 inches 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 is placed in each tube and the basket rack is positioned in a 1 liter beaker of water, at  $37 \pm 2^\circ\text{C}$  such that the tablets remain 2.5cm below the surface of the liquid on their upward movement and descend not closer than 2.5cm from the bottom of the beaker. A standard motor driven device is used to move the basket assembly containing the tablets up and down through a distance of 5 to 6 cm at a frequency of 28 to 32 cycles per minute. Perforated plastic discs may also be used in the test. These are placed on top of the tablets and impart an abrasive action to the tablets.

## 2.5 Collection of sample

The samples for this project were purchased from different retail pharmacies from the following areas: Mohakhali wireless gate, Banani road 11, Kallynpur bus stand and Gulshan. All the purchased samples were stored in the favorable conditions and away from direct sunlight. The samples were taken and verified before carrying out any type of experiment on them.



**Chapter 3:  
Result and  
Discussion**

**Chemical analysis:**

**3.1 HPLC assay values of Prednisolone tablets of different samples -**

<b>% Prednisolone content</b>												
<b>Tablet number</b>	<b>Sample 1 (local)</b>	<b>Sample 2 (local)</b>	<b>Sample 3 (local)</b>	<b>Sample 4 (local)</b>	<b>Sample 5 (multi-national)</b>	<b>Sample 6 (Multi-national)</b>	<b>Sample 7 (local)</b>	<b>Sample 8 (local)</b>	<b>Sample 9 (local)</b>	<b>Sample 10 (local)</b>	<b>Sample 11 (local)</b>	<b>Sample 12 (local)</b>
1	99.66	79.98	82.83	83.28	96.03	97.81	95.65	93.36	91.85	82.37	76.89	76.22
2	97.62	77.93	81.52	80.52	97.78	97.43	97.38	99.92	91.75	82.32	76.87	75.76
3	97.98	78.3	66.52	84.02	93.75	96.34	93.38	95.73	91.8	82.23	74.64	75.96
4	96.74	77.05	60.64	83.34	93.57	95.72	93.20	95.37	91.75	82.16	73.88	75.72
5	95.9	76.21	52.49	83.71	92.43	94.98	92.06	96.55	91.72	82.09	72.75	75.59
6	95.06	75.37	44.33	84.08	91.29	94.25	90.93	97.74	91.7	82.02	71.63	75.46

Table 3.1: Percentage of Prednisolone content of tablets of different samples



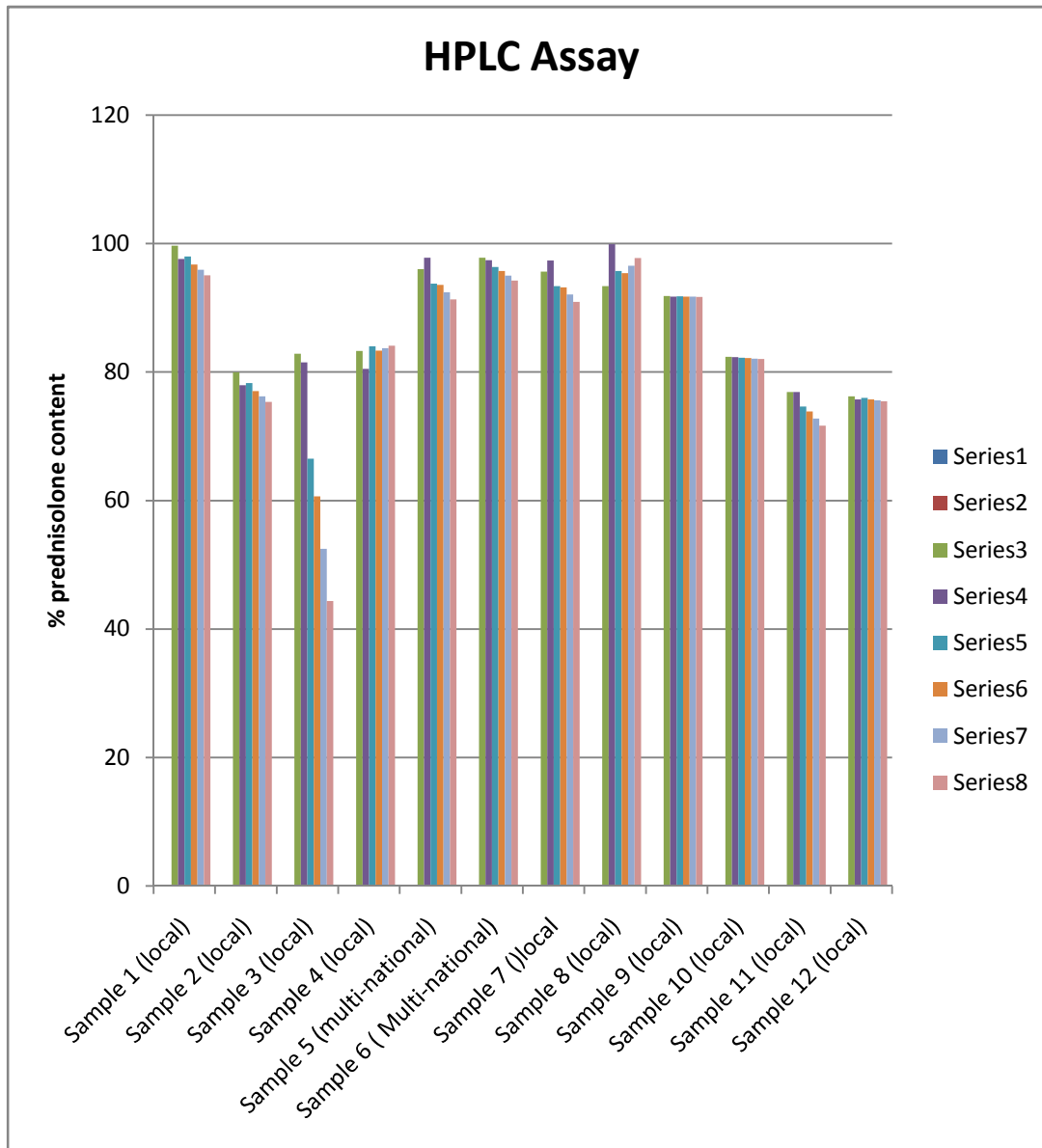


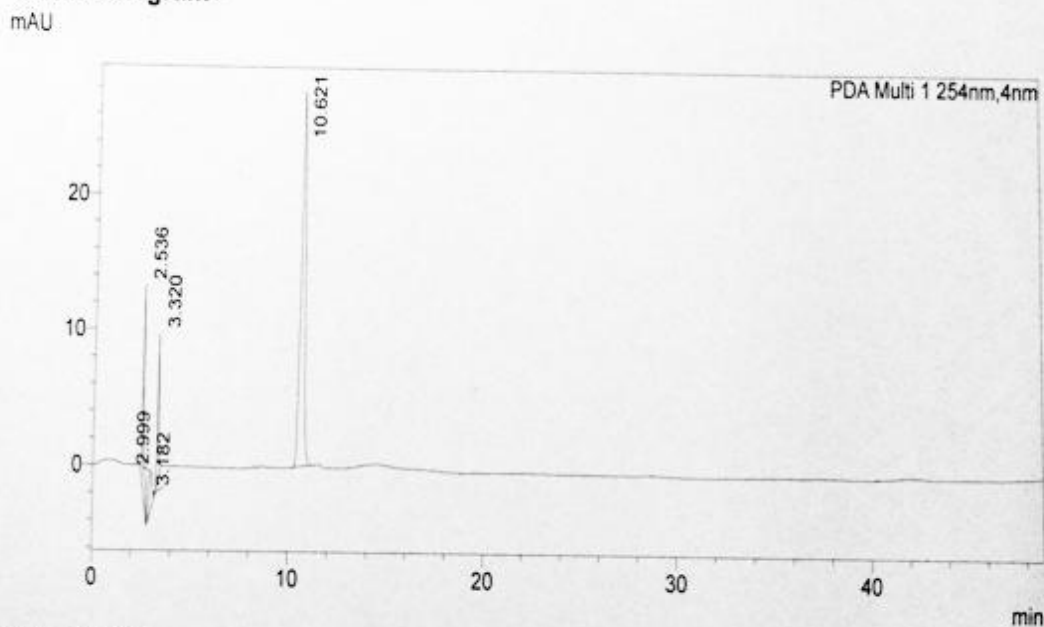
Figure 3.1: Bar chart showing percentage of Prednisolone content of tablets of different The results of HPLC analysis are presented in the bar chart above, from the above bar chart we can see that the percentage of Prednisolone content varies from one sample to another. The lowest percentage content of Prednisolone was found of sample 12 was 75.21%. The highest percentage content of Prednisolone was found for sample 6 and that was 97.81%. According to USP monographs HPLC assay should be within 90%-110%, from the result above we observe six samples give HPLC assay more than 90% the rest of the six samples are below 90% HPLC assay.

SHIMADZU  
LabSolutions Analysis Report

<Sample Information>

Sample Name	: Prednisolone	Sample Type	: Unknown
Sample ID	: Pred 1 checking	Level	: 1
Data Filename	: std2.lcd	Acquired by	: System Administrator
Method Filename	: Prednisolone tablet.lcm	Processed by	: System Administrator
Batch Filename	:		
Vial #	: 1-1		
Injection Volume	: 10 uL		
Date Acquired	: 11/19/2014 1:10:12 PM		
Date Processed	: 11/19/2014 1:59:04 PM		

<Chromatogram>



<Peak Table>

PDA Ch1 254nm							
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	2.536	71536	14346	0.000			
2	2.999	34809	2958	0.000			
3	3.182	1343	392	0.000		V	
4	3.320	51660	11153	0.000			
5	10.621	416537	27800	0.000			
Total		575885	56648				

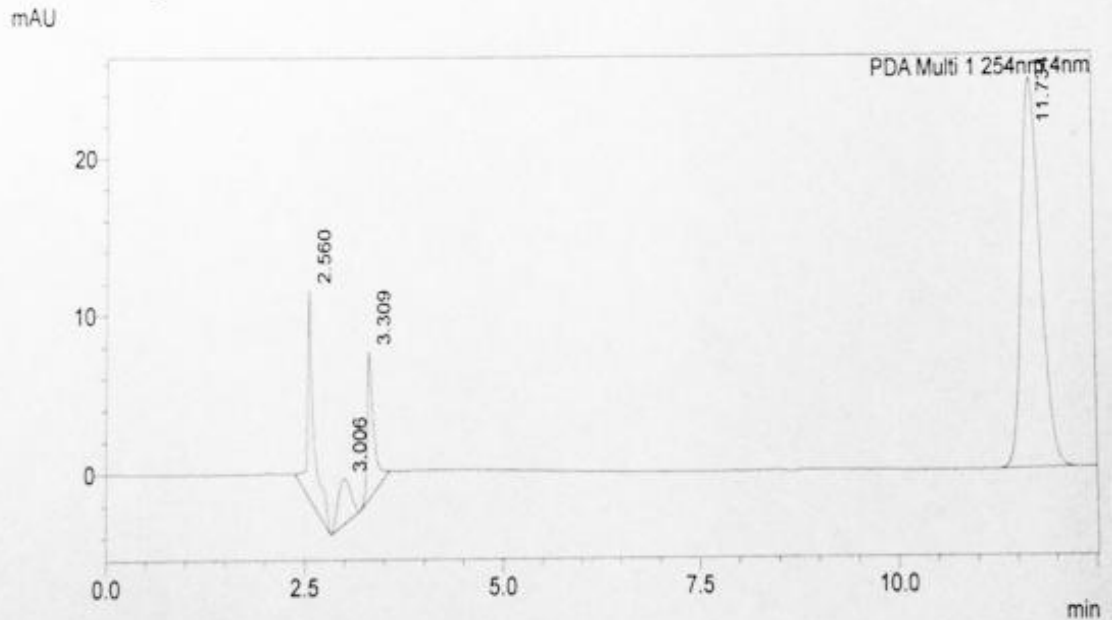
Figure 3.1.1: HPLC report of Prednisolone standard 1



## <Sample Information>

Sample Name : Prednisolone  
Sample ID : Pred 1 checking  
Data Filename : std3.lcd  
Method Filename : Prednisolone tablet.lcm  
Batch Filename :  
Vial # : 1-1  
Injection Volume : 10  $\mu$ L  
Date Acquired : 11/19/2014 1:59:39 PM  
Date Processed : 11/19/2014 2:12:13 PM  
Sample Type : Unknown  
Level : 1  
Acquired by : System Administrator  
Processed by : System Administrator

## <Chromatogram>



## <Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	2.560	72794	13103	0.000			
2	3.006	31956	2814	0.000			
3	3.309	53516	9305	0.000			
4	11.734	414900	24781	0.000			
Total		573166	50004				

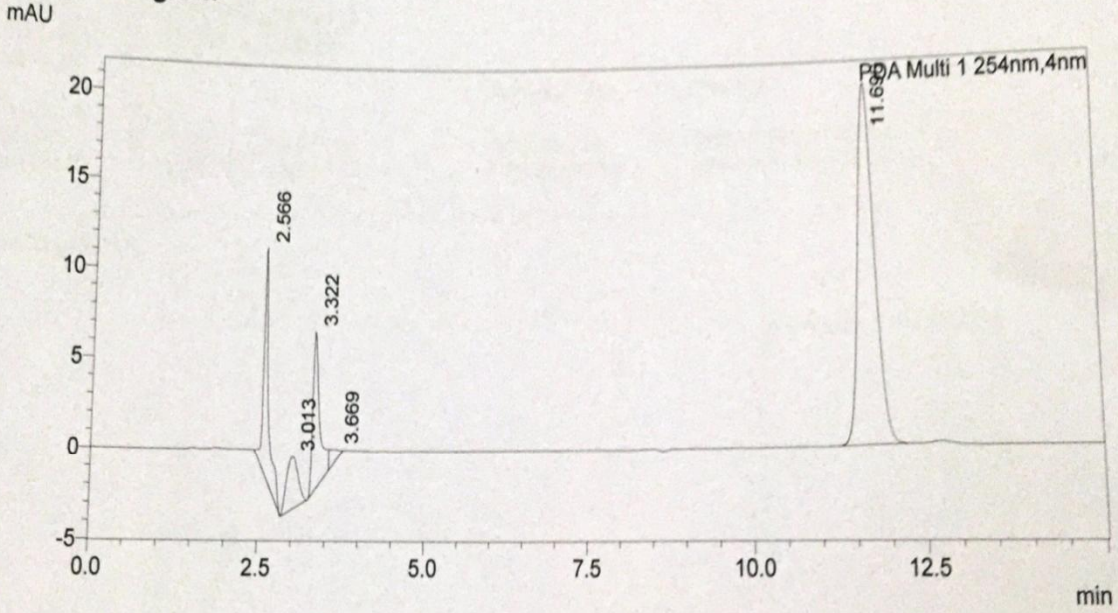
Figure3.1.2: HPLC report of Prednisolone standard 2

# SHIMADZU LabSolutions Analysis Report

## <Sample Information>

Sample Name : Sam. sqr 2  
Sample ID :  
Data Filename : Sam\_11.lcd  
Method Filename : Prednisolone tablet.lcm  
Batch Filename : Prednisolone tablet.lcm.lcb  
Vial # : 1-1  
Injection Volume : 10 uL  
Date Acquired : 11/22/2014 1:16:03 PM  
Date Processed : 11/22/2014 1:31:06 PM  
Sample Type : Unknown  
Acquired by : System Administrator  
Processed by : System Administrator

## <Chromatogram>



## <Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	2.566	66014	12496	0.000			
2	3.013	34931	2925	0.000			
3	3.322	63670	9001	0.000			
4	3.669	7828	568	0.000		V	
5	11.696	341251	20256	0.000			
Total		513694	45245				

Figure3.1.3: HPLC report of Prednisolone sample 1

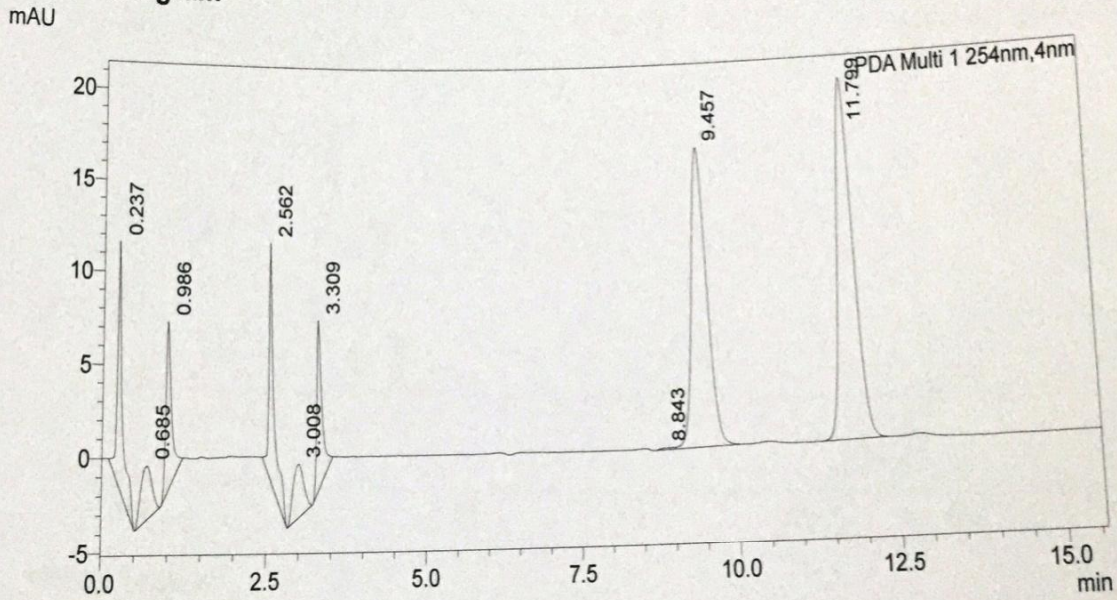
SHIMADZU  
LabSolutions Analysis Report

<Sample Information>

Sample Name : Prednisolone  
 Sample ID : Sam  
 Data Filename : Sam.Opso 5mg004.lcd  
 Method Filename : Prednisolone tablet.lcm  
 Batch Filename : seq.lcb  
 Vial # : 1-1  
 Injection Volume : 10 uL  
 Date Acquired : 11/19/2014 3:28:58 PM  
 Date Processed : 11/19/2014 3:44:36 PM

Sample Type : Unknown  
 Acquired by : System Administrator  
 Processed by : System Administrator

<Chromatogram>



<Peak Table>

PDA Ch1 254nm						
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	0.237	67403	12824	0.000		
2	0.685	33640	2859	0.000		
3	0.986	52990	9214	0.000		
4	2.562	66281	12753	0.000		
5	3.008	33462	2864	0.000		
6	3.309	52118	9282	0.000		
7	8.843	1703	108	0.000		
8	9.457	282741	16620	0.000		V
9	11.799	340252	20031	0.000		
Total		930589	86555			

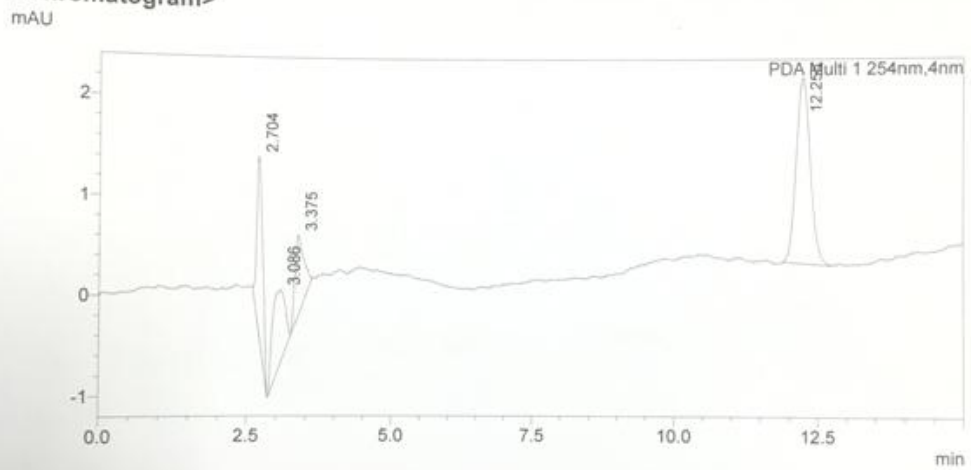
Figure3.1.4: HPLC report of Prednisolone sample 2

**SHIMADZU**  
**LabSolutions Analysis Report**

**<Sample Information>**

Sample Name	: Prednisolone 5 mg	Sample Type	: Unknown
Sample ID	: Sample 6d	Acquired by	: System Administrator
Data Filename	: Sam_18.lcd	Processed by	: System Administrator
Method Filename	: Prednisolone tablet.lcm		
Batch Filename	: seq.lcb		
Vial #	: 1-4		
Injection Volume	: 1 uL		
Date Acquired	: 3/7/2015 3:29:20 PM		
Date Processed	: 3/7/2015 3:44:22 PM		

**<Chromatogram>**



**<Peak Table>**

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	2.704	12572	1746	0.000			
2	3.086	11812	733	0.000			
3	3.375	8145	817	0.000		V	
4	12.255	31966	1874	0.000			
Total		64496	5170				

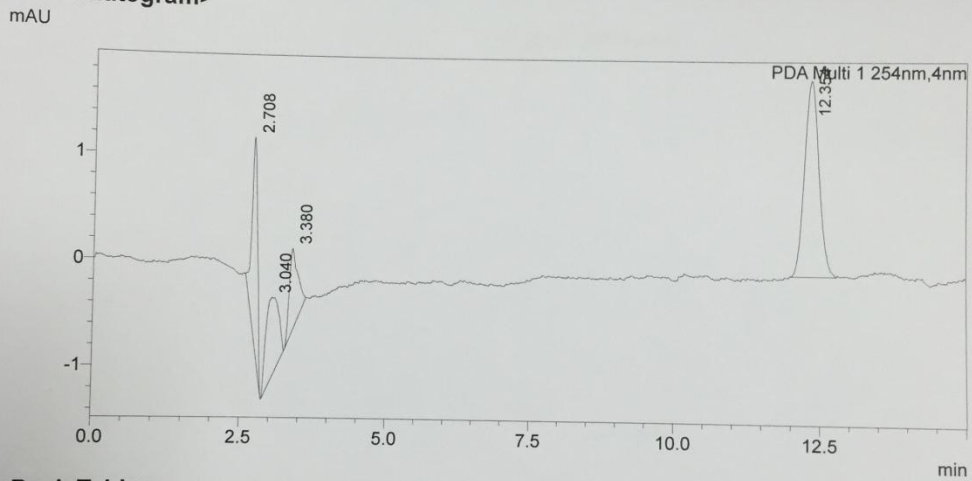
Figure 3.1.5: HPLC report of Prednisolone sample 3

**SHIMADZU**  
**LabSolutions Analysis Report**

**<Sample Information>**

Sample Name	: Prednisolone 5 mg	Sample Type	: Unknown
Sample ID	: Sample 6c	Acquired by	: System Administrator
Data Filename	: Sam_17.lcd	Processed by	: System Administrator
Method Filename	: Prednisolone tablet.lcm		
Batch Filename	: seq.lcb		
Vial #	: 1-3		
Injection Volume	: 1 uL		
Date Acquired	: 3/7/2015 3:13:53 PM		
Date Processed	: 3/7/2015 3:28:55 PM		

**<Chromatogram>**



**<Peak Table>**

PDA Ch1 254nm							
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	2.708	13178	1809	0.000			
2	3.040	11174	761	0.000			
3	3.380	7828	797	0.000			
4	12.354	31958	1856	0.000			
Total		64139	5222				

Figure 3.1.6: HPLC report of Prednisolone sample 4



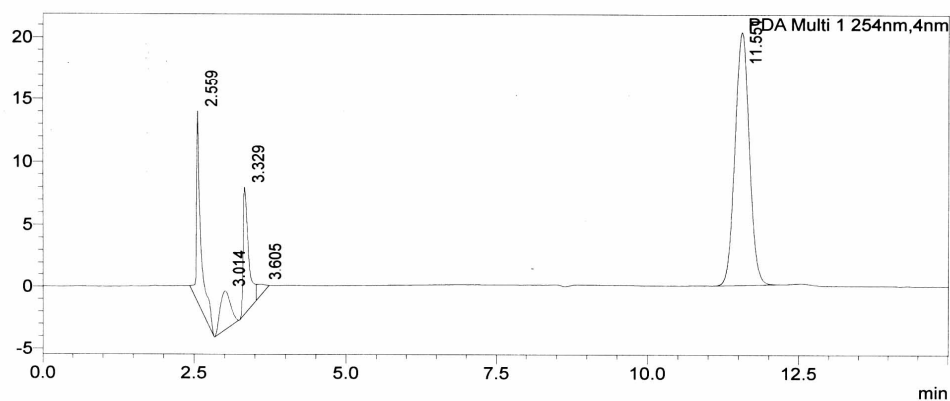
# Analysis Report

**<Sample Information>**

Sample Name	: Sam.GSK 2	Sample Type	: Unknown
Sample ID	:	Acquired by	: System Administrator
Data Filename	: Sam_7.lcd	Processed by	: System Administrator
Method Filename	: Prednisolone tablet.lcm		
Batch Filename	: Prednisolone tablet.lcm.lcb		
Vial #	: 1-6		
Injection Volume	: 10 uL		
Date Acquired	: 11/22/2014 12:08:13 PM		
Date Processed	: 11/22/2014 12:29:12 PM		

**<Chromatogram>**

mAU

**<Peak Table>**

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	2.559	75884	15263	0.000			
2	3.014	37357	3117	0.000			
3	3.329	63933	10226	0.000			
4	3.605	8689	849	0.000		V	
5	11.551	336098	20326	0.000			
Total		521960	49781				

C:\LabSolutions\Data\Project-SHN-Nabila\Sam\_7.lcd

Figure 3.1.7: HPLC report of Prednisolone sample 5

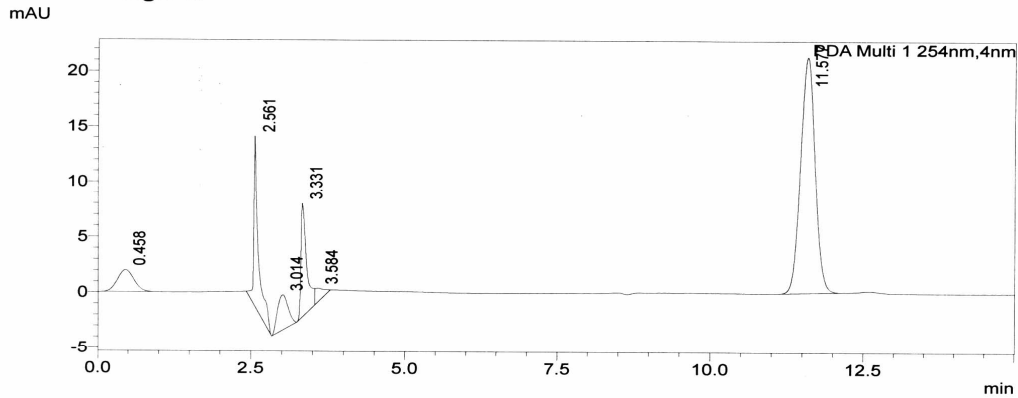


**SHIMADZU**  
**LabSolutions Analysis Report**

**<Sample Information>**

Sample Name	: Sam.GSK 1	Sample Type	: Unknown
Sample ID	:	Acquired by	: System Administrator
Data Filename	: Sam_6.lcd	Processed by	: System Administrator
Method Filename	: Prednisolone tablet.lcm		
Batch Filename	: Prednisolone tablet.lcm.lcb		
Vial #	: 1-5		
Injection Volume	: 10 uL		
Date Acquired	: 11/22/2014 11:52:46 AM		
Date Processed	: 11/22/2014 12:07:49 PM		

**<Chromatogram>**



**<Peak Table>**

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	0.458	37390	1973	0.000			
2	2.561	77412	15375	0.000			
3	3.014	38369	3166	0.000			
4	3.331	66594	10223	0.000			
5	3.584	11632	1242	0.000		V	
6	11.577	350716	21279	0.000			
Total		582112	53257				

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Figure 3.1.8: HPLC report of Prednisolone sample 6

### 3.2 In-vitro dissolution study results

% Drug Released												
Sample Number	Sample 1 (local)	Sample 2 (local)	Sample 3 (local)	Sample 4 (local)	Sample 5(Multi-national)	Sample 6 (Multi-national)	Sample 7 (local)	Sample 8 (local)	Sample 9 (local)	Sample 10(local)	Sample 11 (local)	Sample 12 (local)
1	79.40	61.78	12.20	11.45	70.74	78.56	94.14	76.58	76.34	56.58	46.75	48.25
2	74.82	62.29	11.54	10.85	79.57	79.85	90.74	75.95	78.38	55.95	48.71	49.78
3	72.46	60.08	10.86	12.47	72.46	72.35	92.10	76.75	74.82	56.75	49.57	48.62
4	71.95	69.57	12.56	12.32	76.85	75.27	95.84	75.85	78.81	55.85	48.35	49.35
5	78.67	60.76	11.65	10.75	71.65	72.85	92.65	72.59	78.65	52.59	47.65	48.25
6	79.67	61.61	12.45	11.95	72.21	70.32	93.52	73.85	77.52	54.81	49.25	48.72
7	70.65	60.25	10.98	10.85	75.85	71.20	92.85	75.25	70.95	55.25	48.45	49.65
8	72.45	60.59	11.54	11.35	78.65	79.85	91.65	79.57	72.56	59.57	49.51	50.25

Table 3.2: Table of in-vitro dissolution of Prednisolone tablets of different samples

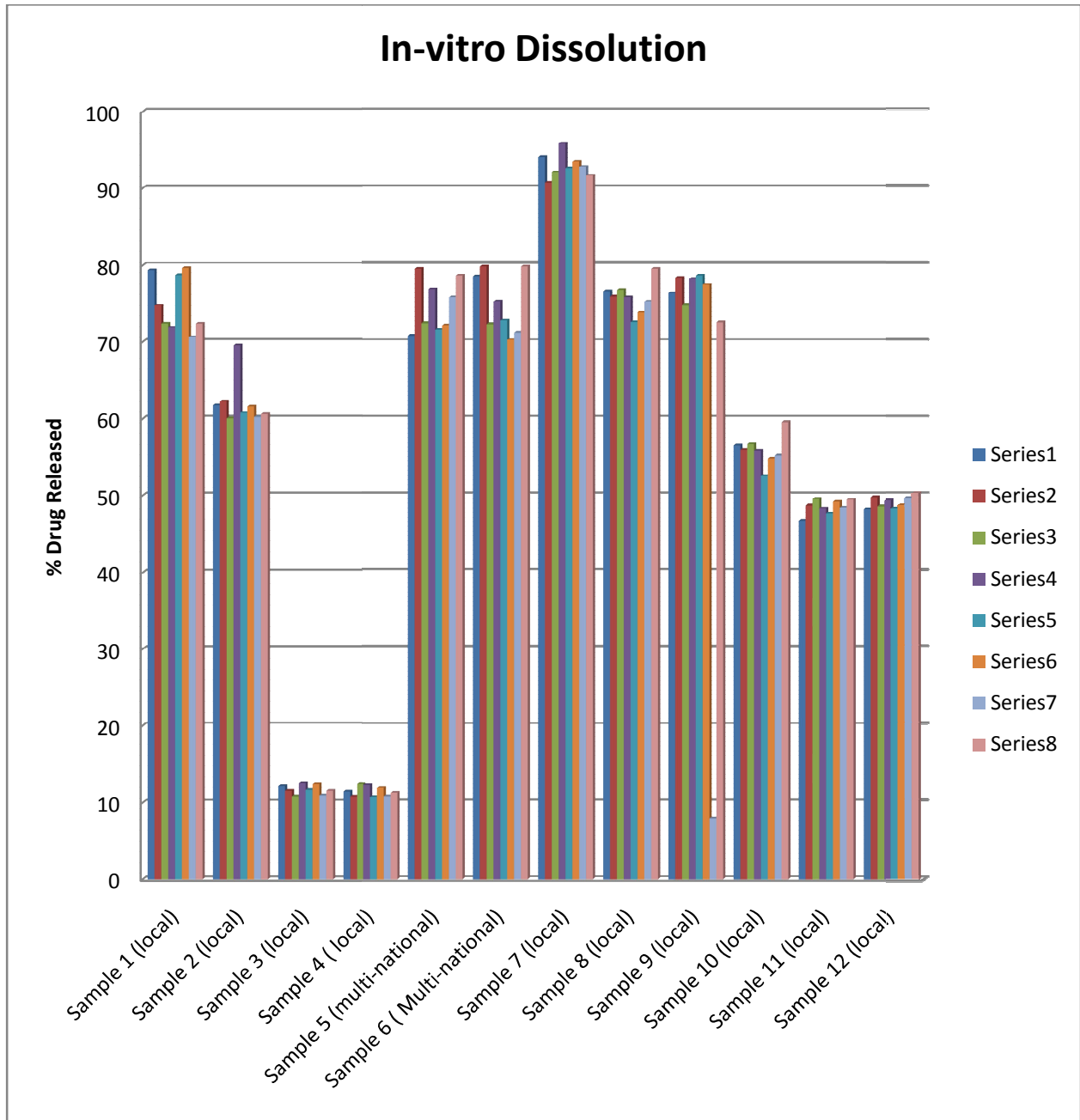


Figure 3.2: Bar chart of in-vitro dissolution of Prednisolone tablets of different companies

According to USP not less than 75% of the labeled amount of Prednisolone should be dissolved in 30 minutes, whereas the results show only six samples are above 75%. Tablets require undergoing dissolution in order to be absorbed in the gastro-intestinal tract. If tablets do not undergo dissolution no absorption will take place. Only six brands passed the dissolution test, samples of six brands were below 75%.

### 3.3 Physical analysis:

All physical tests parameters for the tablets are done according to USP (United States Pharmacopeia) and BP(British Pharmacopeia). The parameters are shape, color, appearance and size.

<b>Sample number</b>	<b>Shape</b>
Sample 1(local)	Oval
Sample 2(local)	Arc triangle
Sample 3(local)	Arc triangle
Sample 4(local)	Round
Sample 5(multi-national)	Round
Sample 6 (multi-national)	Round
Sample 7(local)	Round
Sample 8(local)	Oval
Sample 9 (local)	Oval
Sample 10( local)	Oval
Sample 11( local)	Oval
Sample 12 (local)	Oval

Table 3.3: Table showing shapes of different company tablets

### 3.4 Weight Variation:

Weight (gm)												
Tablet number	Sample 1(local)	Sample 2 (local)	Sample 3 (local)	Sample 4 (local)	Sample 5 (multi-national)	Sample 6 ( Multi-national)	Sample 7 (local)	Sample 8 (local)	Sample 9 (local)	Sample 10 (local)	Sample 11 (local)	Sample 12 (local)
1	0.138	0.131	0.18	0.18	0.101	0.098	0.066	0.066	0.151	0.154	0.151	0.148
2	0.133	0.142	0.173	0.177	0.100	0.100	0.066	0.065	0.147	0.151	0.152	0.155
3	0.134	0.134	0.181	0.179	0.100	0.098	0.067	0.066	0.156	0.154	0.146	0.158
4	0.136	0.131	0.179	0.176	0.100	0.100	0.065	0.067	0.148	0.151	0.144	0.154
5	0.134	0.138	0.175	0.179	0.098	0.101	0.065	0.065	0.153	0.153	0.153	0.152
6	0.138	0.134	0.179	0.175	0.100	0.098	0.065	0.063	0.152	0.152	0.157	0.149
7	0.131	0.136	0.176	0.179	0.102	0.100	0.065	0.065	0.151	0.153	0.154	0.152
8	0.142	0.134	0.179	0.181	0.100	0.100	0.065	0.068	0.154	0.148	0.154	0.153
9	0.134	0.138	0.177	0.173	0.098	0.098	0.063	0.067	0.154	0.147	0.152	0.157
10	0.131	0.135	0.180	0.180	0.100	0.097	0.066	0.064	0.151	0.152	0.154	0.158

Table 3.4: Table showing weight variation of ten tablets from different samples

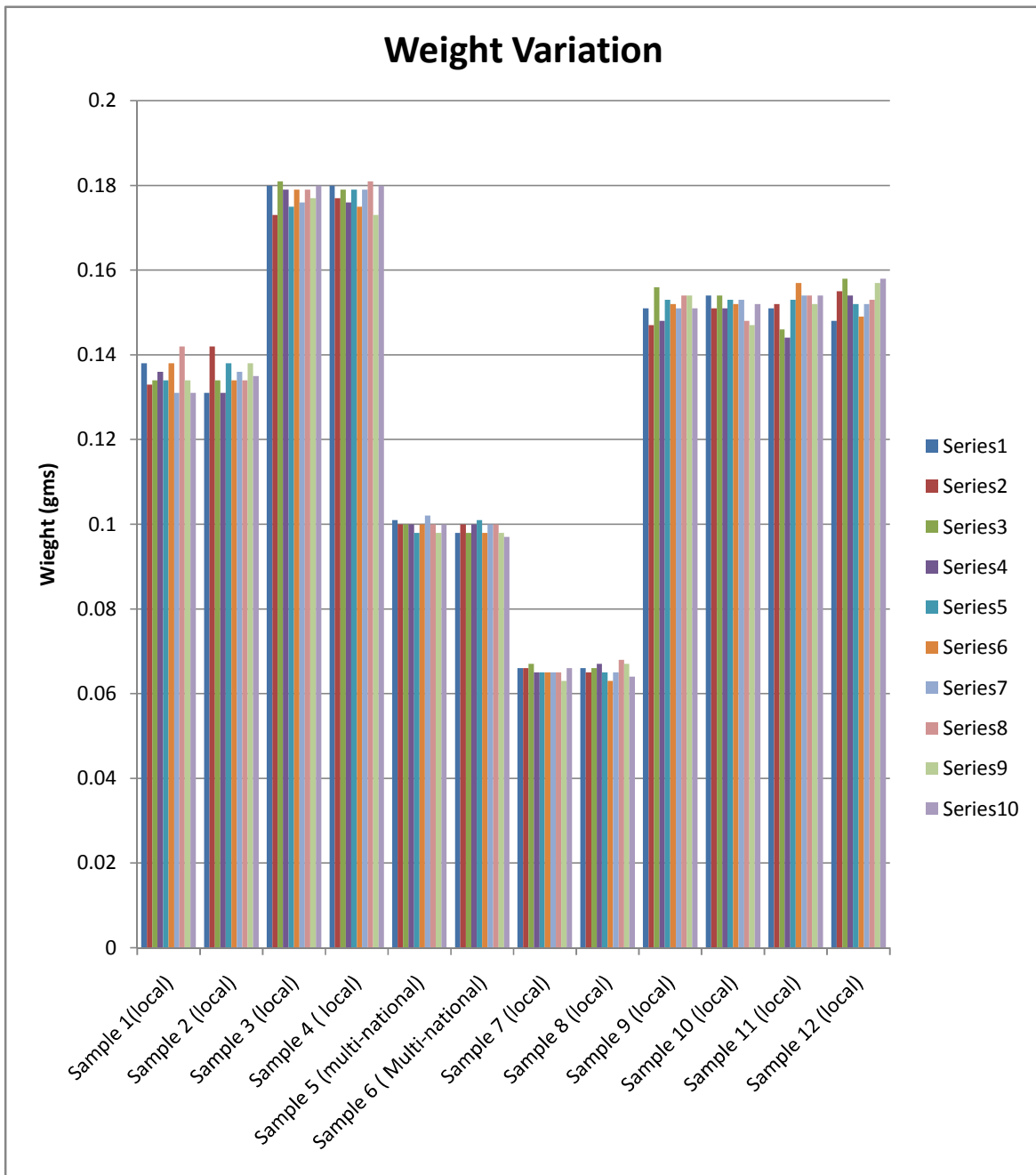


Figure 3.3: Bar chart showing weight variation of different samples

From the bar chart of weight variation it can be concluded that all the tablets are of uniform weight. The average weight of all tablets of each sample is in the same range.

### 3.5 Thickness:

Thickness( cm)												
Tablet number	Sample 1(local)	Sample 2 (local)	Sample 3 (local)	Sample 4 (local)	Sample 5 (Multi-national)	Sample 6 (Multi-national)	Sample 7 (local)	Sample 8 (local)	Sample 9 (local)	Sample 10 (local)	Sample 11 (local)	Sample 12 (local)
1	0.3	0.3	0.35	0.35	0.2	0.2	0.2	0.2	0.31	0.31	0.33	0.31
2	0.3	0.3	0.35	0.35	0.2	0.2	0.2	0.2	0.31	0.32	0.32	0.33
3	0.3	0.3	0.35	0.35	0.2	0.2	0.2	0.2	0.31	0.31	0.31	0.32
4	0.3	0.3	0.35	0.35	0.2	0.2	0.2	0.2	0.32	0.32	0.33	0.31
5	0.3	0.3	0.35	0.35	0.2	0.2	0.2	0.2	0.33	0.3	0.32	0.32
6	0.3	0.3	0.35	0.35	0.2	0.2	0.2	0.2	0.31	0.3	0.3	0.33
7	0.3	0.3	0.35	0.35	0.2	0.2	0.2	0.2	0.33	0.34	0.32	0.31
8	0.3	0.3	0.35	0.35	0.2	0.2	0.2	0.2	0.32	0.32	0.33	0.32
9	0.3	0.3	0.35	0.35	0.2	0.2	0.2	0.2	0.31	0.32	0.32	0.33
10	0.3	0.3	0.35	0.35	0.2	0.2	0.2	0.2	0.33	0.31	0.33	0.3

Table 3.5: Table showing thickness variability of different samples

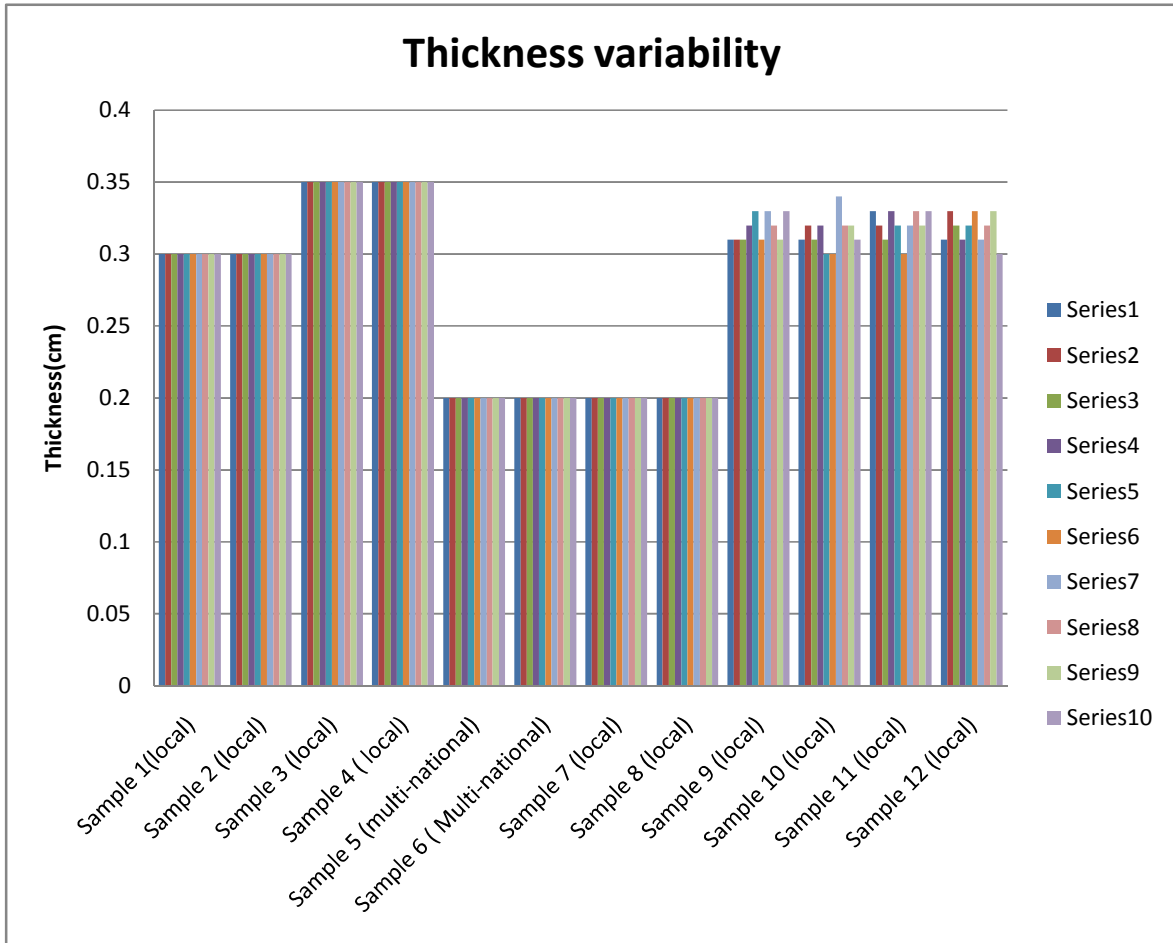


Figure3.4: Bar chart showing thickness variability of different samples

All the tablets of different companies have a uniform thickness. There is no major variability in their thickness. There is only variation from one sample to another



### 3.6 Hardness:

Hardness(kg)												
Tablet number	Sample 1(local)	Sample 2 (local)	Sample 3 (local)	Sample 4 (local)	Sample 5 (multi-national)	Sample 6 (Multi-national)	Sample 7 (local)	Sample 8 (local)	Sample 9 (local)	Sample 10 (local)	Sample 11 (local)	Sample 12 (local)
1	2.68	2.92	8.25	9.21	5.62	5.65	4.65	4.73	2.75	2.78	3.65	3.27
2	3.48	2.24	10.47	12.56	5.18	5.43	4.81	4.15	2.98	2.54	3.74	3.45
3	2.63	2.84	10.55	11.65	6.06	5.34	3.8	4.69	2.56	2.89	3.42	3.86
4	2.02	3.67	12.25	10.85	5.38	4.17	3.84	4.28	2.78	2.84	3.21	3.92
5	3.72	2.48	9.10	10.31	5.86	4.72	4.73	4.95	2.68	2.57	3.52	3.84
6	2.26	2.95	8.77	9.45	5.42	4.38	4.16	4.75	2.49	2.82	3.58	3.73
7	2.67	2.98	10.11	9.87	4.81	4.24	4.77	4.64	2.65	2.92	4.57	3.41
8	2.39	2.52	10.55	10.75	4.41	5.81	3.96	3.97	2.58	2.71	3.81	3.25
9	4.21	2.54	8.21	11.85	4.85	5.63	3.15	4.27	2.48	2.82	3.72	4.85
10	2.55	3.24	9.1	12.34	5.54	4.97	4.37	4.87	2.29	2.45	3.14	3.24

Table 3.6: Table showing hardness variability of different samples

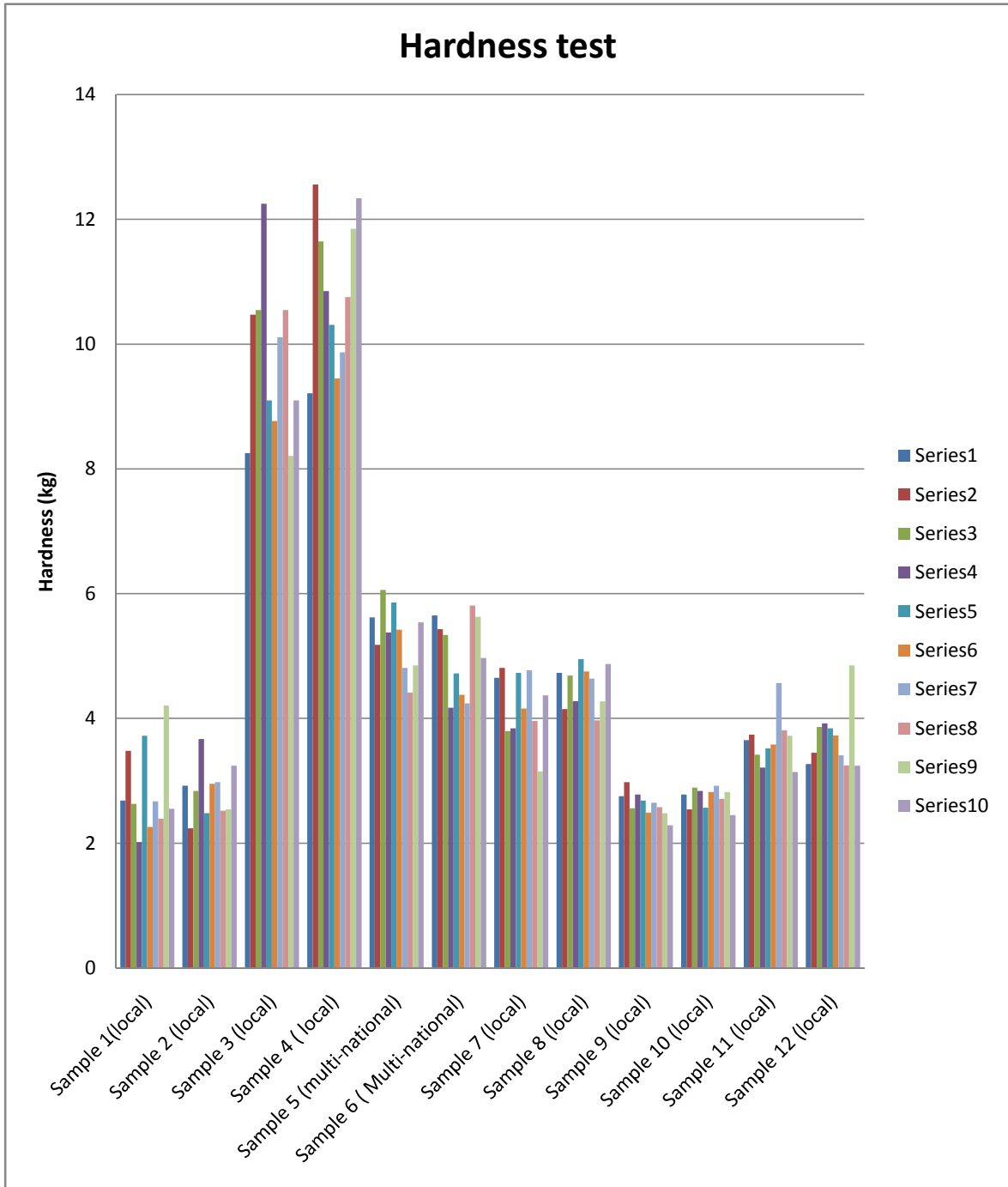


Figure 3.5 Hardness variability of ten tablets of different samples

Hardness of each tablet of each company varies with tablets, but they are in the same range.

Only two samples show very high hardness around the range of 10-12 kg.

### 3.7 Friability:

Total weight of 10 tablets (gm)												
	Sample 1(local)	Sample 2 (local)	Sample 3 (local)	Sample 4 (local)	Sample 5 (Multi-national)	Sample 6 (Multi-national)	Sample 7 (local)	Sample 8 (local)	Sample 9 (local)	Sample 10 (local)	Sample 11 (local)	Sample 12 (local)
before	1.352	1.452	1.785	1.654	0.99	1.102	0.654	0.665	1.513	1.515	1.518	1.52
after	1.351	1.452	1.785	1.654	0.99	1.102	0.653	0.665	1.512	1.515	1.518	1.52

Table 3.7: Friability test of different samples and their total weight before and after the test

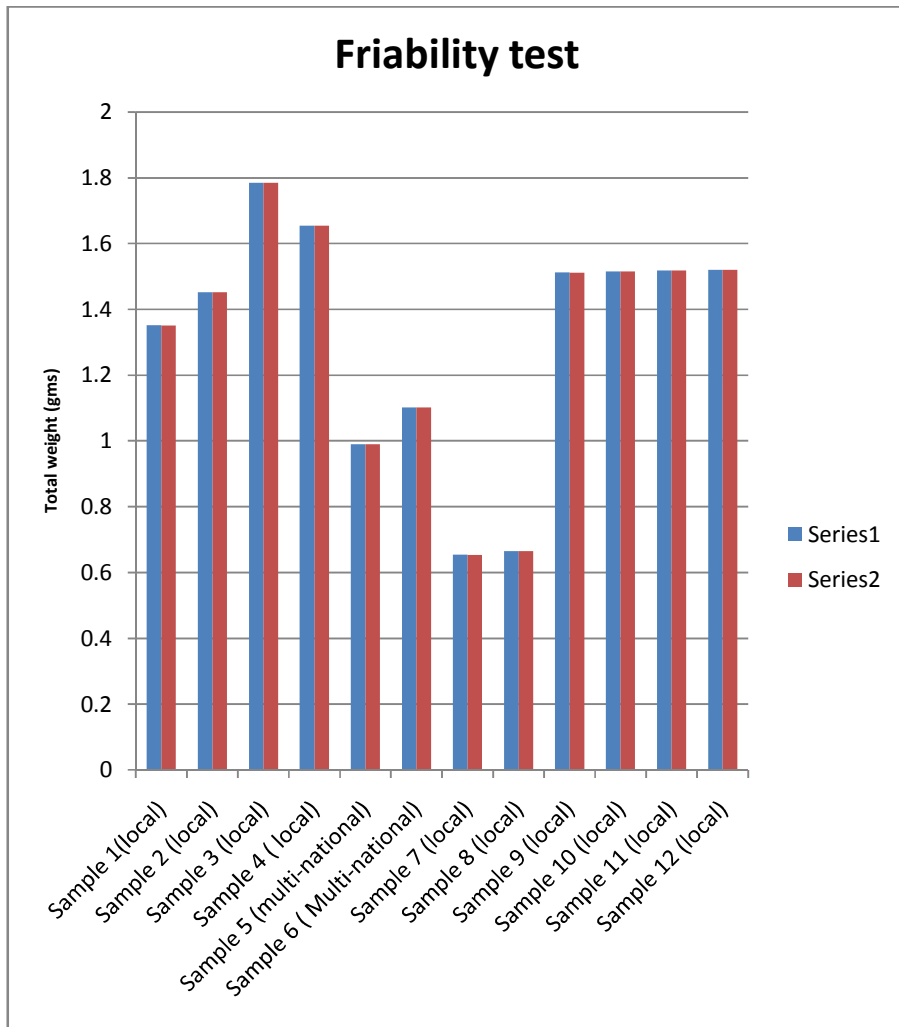


Figure 3.6: Bar chart of friability test of different samples and their total weight before and after the test

Total weight of 10 tablets before and after the friability test is found the same. There was no significant loss in weight of the tablets after the test for all the samples.

### 3.8 Disintegration time:

Disintegration time (minutes)												
Tablet number	Sample 1(local)	Sample 2 (local)	Sample 3 (local)	Sample 4 ( local)	Sample 5 (multi-national)	Sample 6 ( Multi-national)	Sample 7 (local)	Sample 8 (local)	Sample 9 (local)	Sample 10 (local)	Sample 11 (local)	Sample 12 (local)
1	8	7	Did not disintegrate	Did not disintegrate	2	2	3	3	6	6	8	8
2	8	7	Did not disintegrate	Did not disintegrate	2	2	3	3	6	6	8	8
3	8	7	Did not disintegrate	Did not disintegrate	2	2	3	3	6	6	8	8
4	8	7	Did not disintegrate	Did not disintegrate	2	2	3	3	6	6	8	8
5	8	7	Did not disintegrate	Did not disintegrate	2	2	3	3	6	6	8	8
6	8	7	Did not disintegrate	Did not disintegrate	2	2	3	3	6	6	8	8

Table 3.8: Table showing the disintegration time of different samples

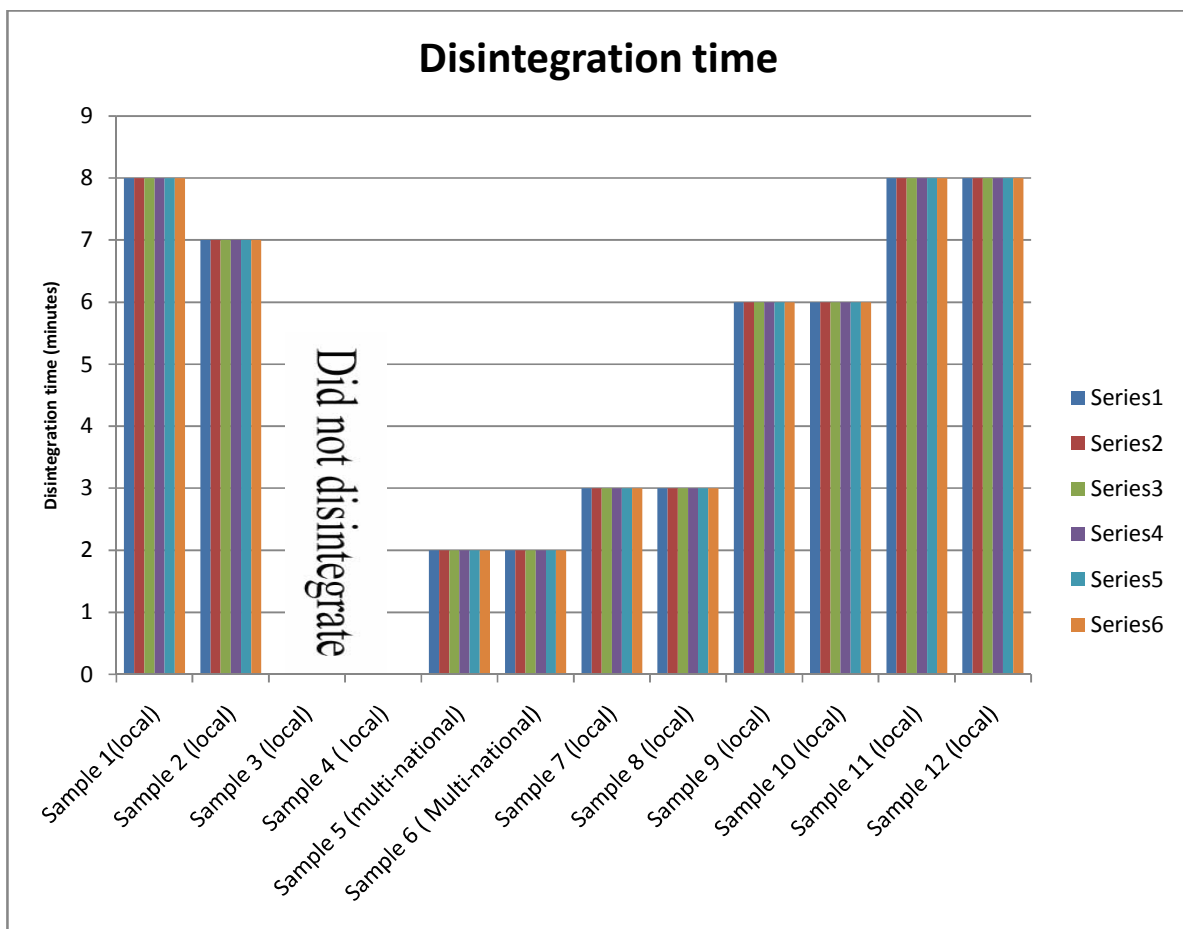


Figure 3.7: Bar chart showing the different disintegration time of different samples

Disintegration could be related to dissolution and similarly availability of drug to body (absorption) and finally the therapeutic efficacy of product. The result showed that disintegration time of all the selected tablets was found to be within specified limits of USP and BP. According to USP, uncoated tablets have disintegration time standards as low as 5 minutes. For sample 3 and 4 it is seen no disintegration takes place. Which shows the drug does not undergo dissolution and is substandard.

## 4. Conclusion

Although a wide range of synthetic glucocorticoids are now available, prednisolone still remains the most popular choice in glucocorticoid therapy, especially for oral administration.<sup>15</sup>

Falsified and substandard drugs may contain toxic ingredients; some of the most compelling stories of pharmaceutical crime are of frank poisoning. By far the more common problem however, is medicine that simply does not work. Poor quality medicines cause treatment failure, but doctors do not generally suspect medicines as a cause of disease progression. Lifesaving medicines can be of poor quality, which may be an uncouneted root cause of high mortality in low- and middle-income countries. No class of drug is immune to being compromised. Medications for chronic and infectious diseases alike have been found falsified and substandard. A considerable body of research indicates that inexpensive antimicrobial drugs in low- and middle-income countries are frequently poor quality. This not only put patients at risk, but encourages drug resistance, thereby threatening population health for future generations. Falsified and substandard drugs increase costs to patients and health systems. Medicines are expensive; patients and governments waste money on ineffective ones. Lingering illnesses decrease productivity, causing workers to forgo pay and spend more on treatment. Through encouraging antimicrobial resistance, illegitimate medicines reduce the effective life of a drug. Society must bear the cost of drug development, an expense that increases as drugs become more complex.

Close monitoring of different process in pharmaceutical industries will reduce the production time and cost, as well as will improve the quality of the product. It was found that dissolution was the critical parameter where problem exist among different brands. Only six brands passed the dissolution test, tablets of six brands where below 50% as well as in HPLC assay shows some of the companies are below 90%. Two samples did not undergo disintegration at all that shows that the tablets are substandard. However, no major problem was found in tablet variation, thickness, friability and hardness. From the experiment we can conclude that 50% of the companies in the urban area are substandard, whereas 50% companies provide standard drugs. It was noted that some of the local companies has very low price as compared to the multi-national companies having the same good quality but some local companies has nearly the same price as that of multi-national with low price.

The drug administration should make new policy and drug acts to stop adulteration and control substandard drugs. Extend their regulatory mandate to cover manufacturers of marketed pharmaceutical product particularly with regard to inspection of GMP compliance, and impose rigorous requirements for labeling and certificates of analysis for consignments moving in international commerce. Introduce regulations that require APIs and all other starting materials intended for the formulation of medicinal products to be clearly labeled “for pharmaceutical use” or with a suitable pictogram. Establish within the regulatory authority a multidisciplinary group to investigate illicit activities promptly and professionally. Monitor free ports and strengthen collaboration with law enforcement agencies including customs officials, and offices of criminal investigation, at national and international level. Seek to enact legislation that permits sequestration of assets gained by unlawful activity and seizure and destruction of products involved.

In conclusion it can be said that the different brands of well reputed local pharmaceutical companies can be compared with that of multi-national companies. As in Bangladesh not only in rural areas but also in urban areas more medicine is required of high standard as more patients require better healthcare. However, products of some less known local pharmaceutical industry needs improvements in quality and should be strictly monitored for manufacturing of substandard dosage forms.



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