Research
On

"Evaluation of Quality Control Parameters & in vitro Dissolution Test of Different Brands of Atenolol Available in Bangladesh"

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Subject: Submission of Research Paper on **"Evaluation of Quality Control Parameters & in vitro Dissolution Test of Different Brands of Atenolol Available in Bangladesh"**

Dear Sir,

I am pleased to submit my research paper on "Evaluation of Quality Control Parameters & in vitro Dissolution Test of Different Batches of Atenolol Available in Bangladesh" which you assigned to me as a requirement of Pharmacy program. It is great pleasure for me to present you this report.

I will be very glad if the report can serve its actual purpose. If you have any further enquiry concerning any additional information I would be very pleased to clarify that.

Sincerely yours

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Declaration

I am Subrota Ghosh, ID: -2006-2-70-050,student of Pharmacy Department of East West University do hereby declare that the Research Paper on **"Evaluation of Quality Control Parameters & in vitro Dissolution Test of Different Brands of Atenolol Available in Bangladesh"** has not been submitted before by me and any others one for any degree, diploma, title or recognition.

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Certificate

This is to certify that the research paper on **"Evaluation of Quality Control Parameters & in vitro Dissolution Test of Different Brands of Atenolol Available in Bangladesh"** has been prepared as a part of the Pharmacy program from East West University, carried out by Subrota Ghosh, ID: -2006-2-70-050 under my supervision. The paper or the information will not be used for any other purposes.

To the best of my knowledge this report is not submitted before to the award of any disclose.

Arindom Pal
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Firstly, I would like to express my gratitude to almighty God to give me the strength to complete the paper within the stipulated time.

Though the following research is an individual work, I could never have reached the heights or explored the depths without the help, support, guidance and efforts of a lot of people. I want to thanks my parents for making my studies possible and for their never ending support.

I have always had a great attraction with pharmacy related subjects, so it was obvious that the subject of my research would go in the same direction **"Evaluation of Quality Control Parameters & in vitro Dissolution Test of Different Brands of Atenolol Available in Bangladesh"** is a sounding title that was suggested to me by **Arindom Pal.** Special thanks go to him.

Finally I want to thanks the entire person who gave their full co-operation with the research s & the entire participants who take part in the experiment. Their contribution is highly appreciated.

Abstract

Atenolol is a very common and popular drug due to their availability in market and low cost. It is a very common drug to treat in cardiovascular disease and so on. Atenolol group of different brands of drug present in market .I would collect three (3) different brands of drug at different batches to measure their various quality control parameters such as weight variation, hardness, friability test, disintegration test and dissolution test.
I'll see that there are any batch variation occurs between three brands of drug by different test parameters. In my different test parameters I would see that there is no significant variation occurs between three brands of drug.

The Research on **"Evaluation of Quality Control Parameters & in vitro Dissolution Test of Different Brands of Atenolol Available in Bangladesh"** explains the various rules & procedure followed by ATENOLOL group.

Chapter 1 provides a review of the study and provides a background expression of the study. Define Pharmacokinetics, ADME, Fundamentals of Pharmacokinetics, Bioavailability, Factors Influencing Bioavailability, Bioequivalence, Beta- blocker, Adverse Effect. Define the limitation hindrances to make the research

Chapter 2 provides a complete profile of the ATENOLOL drug that covered the following topics- Chemistry, History, Mechanism of action, Categories, Pharmacokinetics & Metabolism, Absorption , distribution & Excretion, Indication, Pharmacokinetics data, Side effects, Warnings, Special precaution

Chapter 3 mention the overview of the Methods & materials of Atenolol drug that covered following topics- Experimental materials, Weight variation test of tablet, Hardness test of tablet, Friability test of tablet, Determination of disintegration time of tablet, Dissolution test of tablet.
Chapter 4 provides Result & Discussion -Table and figure of Tenoloc,Tenoren & Cardipro in Atenolol Group tablet.
Provide previous analysis covered various essential issues to action of the research- **"Evaluation of Quality Control Parameters & in vitro Dissolution Test of Different Brands of Atenolol Available in Bangladesh"**

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CHAPTER 01

INTRODUCTION

Introduction

1.1 Active Overview

Over the last 25 years, **Pharmacokinetics** has emerged as an integral part of drug development, especially when identifying a drug's biological properties. By pharmacokinetics, one means the application of kinetics to a Pharmakon, the Greek word used to specify drugs and poisons. The term thereby implies the time course and fate of drugs in the body. This general definition broadly embraces *absorption*, *distribution*, *metabolism* (biotransformation) and *excretion* (ADME). The linking of **Pharmacodynamics** (response) and pharmacokinetics offers a composite understanding both about how the drug affects the body and how the body affects the drug. The most comprehensive insight about a drug's inherent pharmacokinetic properties is gained by studying an intravenous dose.

This route of administration has the greatest quantitative potential, as it permits a mass balance approach to be applied to distribution, clearance and the body processes associated with excretion and metabolic elimination (e.g. renal, hepatic). The administration of a drug by other routes, notably oral, introduces an uncertainty that reflects the unknown fraction that is actually absorbed. Consequently, such doses alone cannot accurately identify the distribution and clearance processes.

The most important property of any non-intravenous dosage form, intended to treat a systemic condition, is the ability to deliver the active ingredient to the bloodstream in an amount sufficient to cause the desired response.

This property of a dosage form has historically been identified as physiologic availability, biologic availability or *bioavailability*. Bioavailability captures two essential features, namely *how fast*the drug enters the systemic circulation (rate of absorption) and *how much* of the nominal strength enters the body (extent of absorption). Given that the therapeutic effect is a function of the drug concentration in a patient's blood, these two properties of non-intravenous

dosage forms are, in principle, important in identifying the response to a drug dose. Onset of response is linked to the *rate* of drug absorption whereas the time-dependent extent of response is linked to the *extent* of drug absorption. While the bioavailability of each type of non-intravenous product (e.g. oral, inhalation, topical (e.g. patch), rectal, etc.) could be discussed, this chapter will of necessity focus only on orally administered products. They certainly represent the major pharmaceutical class in drug development and patient treatment. Bioavailability following oral doses may vary because of either patient-related or dosage-form-related factors.[17]

Patient factors can include the nature and timing of meals, age, disease, genetic traits and Gastrointestinal physiology. The dosage form factors include 1) the chemical form of the drug (e.g. salt vs. acid), 2) its physical properties (e.g. crystal structure, particle size), and 3) an array of formulation (e.g. non-active ingredients) and manufacturing variables. Not surprisingly, bioavailability is of clinical, academic, and regulatory interest.[16]

The latter includes agencies that approve the sale of products in their nation(s), as well as reimbursement agencies. Applications from manufacturers seeking regulatory approval for a new drug (e.g. New Drug Application (NDA)) must furnish exhaustive information about a drug's pharmacokinetics. Typically, such evidenceentails studies wherein the drug has been orally administered. While such trials may broadly be viewed as bioavailability studies, many are ostensibly designed to assess the drug's safety and efficacy via strategies of dose escalation and chronic administration. These studies will not be entertained in this chapter.[11]

The more pertinent interest in bioavailability relates to questions about absolute extent of absorption (absolute bioavailability), the importance of product formulation changes that are made duringa new drug's development process, the comparability of different oral dosage forms (e.g. modified-release versus conventional products), and whether the products can be administered with meals. These facets will receive attention in this chapter.[1]

Manufacturers seeking regulatory approval of competitive (generic) products (e.g. Abbreviated New Drug Application [ANDA]), must provide detailed bioavailability evidence showing head-to-head comparative performance of their product against the innovator's product. Such trials are

fundamentally designed to establish clinical equivalence particularly as it relates to interchangeability or substitutability.

1.2 Pharmacokinetics:

Pharmacokinetics may be simply defined as what the body does to the drug, as opposed to pharmacodynamics which may be defined as what the drug does to the body.

Pharmacokinetics, sometimes abbreviated as PK, (from Ancient Greek pharmakon "drug" and kinetikos "to do with motion"; see chemical kinetics) is a branch of pharmacology dedicated to the determination of the fate of substances administered externally to a living organism. The substances of interest include pharmaceutical agents, hormones, nutrients, and toxins.

Pharmacokinetics is often studied in conjunction with pharmacodynamics. Pharmacokinetics includes the study of the mechanisms of absorption and distribution of an administered drug, the rate at which a drug action begins and the duration of the effect, the chemical changes of the substance in the body (e.g. by metabolic enzymes such as CYP or UGT enzymes) and the effects and routes of excretion of the metabolites of the drug.

The most comprehensive insight about a drug's inherent pharmacokinetic properties is gained by studying an intravenous dose. This route of administration has the greatest quantitative potential, as it permits amass balance approach to be applied to distribution, clearance and the body processes associated with excretion and metabolic elimination (e.g. renal, hepatic). The administration of a drug by other routes, notably oral, introduces an uncertainty that reflects the unknown fraction that is actually absorbed. Consequently, such doses alone cannot accurately identify the distribution and clearance processes.[8] The most important property of any non-intravenous dosage form, intended to treat a systemic condition, is the ability to deliver the active ingredient to the bloodstream in an amount sufficient to cause the desired response. This property of a dosage form has historically been identified as physiologic availability, biologic availability or bioavailability. Bioavailability captures two essential features, namely how fast enters the body (extent of absorption). Given that the therapeutic effect is a function of the drug

concentration in a patient's blood, these two properties of non-intravenous dosage forms are, in principle, important in identifying the response to a drug dose. Onset of response is linked to the rate of drug absorption whereas the time-dependent extent of response is linked to the extent of drug absorption. While the bioavailability of each type of non-intravenous product (e.g. oral, inhalation, topical (e.g. patch), rectal, etc.) could be discussed, this chapter will of necessity focus only on orally administered products. They certainly represent the major pharmaceutical class in drug development and patient treatment.

Bioavailability following oral doses may vary because of either patient-related or dosage-form-related factors. Patient factors can include the nature and timing of meals, age, disease, genetic traits and gastrointestinal physiology. The dosage form factors include 1) the chemical form of the drug (e.g. saltvs. acid), 2) its physical properties (e.g. crystal structure, particle size), and 3) an array of formulation (e.g. On-active ingredients) and manufacturing (e.g. tablet hardness) variables. Not surprisingly, bioavailability is of clinical, academic, and regulatory interest.

1.3 ADME:

Pharmacokinetics is divided into several areas including the extent and rate of absorption, distribution, metabolism and excretion. This is commonly referred to as the ADME scheme:

Absorption - the process of a substance entering the blood circulation.

Distribution - the dispersion or dissemination of substances throughout the fluids and tissues of the body.

Metabolism (or Biotransformation) - the irreversible transformation of parent compounds into daughter metabolites.

Excretion - the removal of the substances from the body. In rare cases, some drugs irreversibly accumulate in body tissue.

1.4 Analysis:

Pharmacokinetic analysis is performed by noncompartmental or compartmental methods. Noncompartmental methods estimate the exposure to a drug by estimating the area under the curve of a concentration-time graph. Compartmental methods estimate the concentration-time graph using kinetic models. Noncompartmental methods are often more versatile in that they do not assume any specific compartmental model and produce accurate results also acceptable for bioequivalence studies.

Noncompartmental analysis:

Noncompartmental PK analysis is highly dependent on estimation of total drug exposure. Total drug exposure is most often estimated by area under the curve (AUC) methods, with the trapezoidal rule (numerical integration) the most common method. Due to the dependence on the length of 'x' in the trapezoidal rule, the area estimation is highly dependent on the blood/plasma sampling schedule.

Compartmental analysis:

Compartmental PK analysis uses kinetic models to describe and predict the concentration-time curve. PK compartmental models are often similar to kinetic models used in other scientific disciplines such as chemical kinetics and thermodynamics. The advantage of compartmental over some noncompartmental analyses is the ability to predict the concentration at any time. The disadvantage is the difficulty in developing and validating the proper model. Compartment-free modeling based on curve stripping does not suffer this limitation.

1.5 Fundamentals of Pharmacokinetics:

Pharmacokinetics can be described by the following three basic processes:

Absorption

Defined as the transfer of a drug from the site of administration to the site of measurement. This should not be confused with bioavailability, which is defined as the fraction of intact drug, or active moiety if a prodrug, reaching the systemic circulation. It is quite possible to have an oral drug that is 100% absorbed but with 0% bioavailability because, for example, due to high hepatic first pass metabolism.

Distribution

Defined as the reversible transfer of a drug to and from the site of measurement. In the majority of cases the concentration of a drug is measured in plasma, serum or blood but often the site of action is within other tissues. It is thus important to understand the factors governing the transfer of the drug to the desired site of action.

Elimination

Defined as the irreversible transfer of a drug from the site of measurement and includes drug metabolism, renal excretion, biliary excretion as well as several other minor routes. Drug metabolism is included in elimination since, if a drug is chemically modified, it is no longer the original compound and, unless the metabolism is reversible, has been irreversibly removed from the site of measurement. It is important, therefore, that any bio analysis of the drug is specific if a true understanding of the pharmacokinetics of a drug is to be obtained. If information is required on a metabolite because it is pharmacologically or toxicologically active, it should be studied separately, since invariably non-specific assays will lead to erroneous conclusions.

1.6 Bioavailability:

In pharmacology, bioavailability (BA) is a subcategory of absorption and is used to describe the fraction of an administered dose of unchanged drug that reaches the systemic circulation, one of the principal pharmacokinetic properties of drugs. By definition, when a medication is administered intravenously, its bioavailability is 100%.However, when a medication is administered via other routes

(such as orally), its bioavailability generally decreases (due to incomplete absorption and first-pass metabolism) or may vary from patient to patient. Bioavailability is one of the essential tools in pharmacokinetics, as bioavailability must be considered when calculating dosages for non-intravenous routes of administration.

Bioavailability is defined slightly differently for drugs as opposed to dietary supplements primarily due to the method of administration and Food and Drug Administration regulations.

In pharmacology, bioavailability is a measurement of the rate and extent to which a drug reaches the systemic circulation. It is denoted by the letter f (or, if expressed in percent, by F).

Absolute bioavailability:

Absolute bioavailability compares the bioavailability of the active drug in systemic circulation following non-intravenous administration (i.e., after oral, rectal, transdermal, subcutaneous, or sublingual administration), with the bioavailability of the same drug following intravenous administration. It is the fraction of the drug absorbed through non-intravenous administration compared with the corresponding intravenous administration of the same drug. The comparison must be dose normalized (e.g. account for different doses or varying weights of the subjects); consequently, the amount absorbed is corrected by dividing the corresponding dose administered.

In pharmacology, in order to determine absolute bioavailability of a drug, a pharmacokinetic study must be done to obtain a plasma drug concentration vs time plot for the drug after both intravenous (iv) and extravascular (non-intravenous, i.e., oral) administration. The absolute bioavailability is the dose-corrected area under curve (AUC) non-intravenous divided by AUC intravenous. For example, the formula for calculating F for a drug administered by the oral route is given below.

1.7 Relative bioavailability and bioequivalence:

In pharmacology, relative bioavailability measures the bioavailability (estimated as the AUC) of a formulation (A) of a certain drug when compared with another formulation (B) of the same drug, usually an established standard, or through administration via a different route. When the standard consists of intravenously administered drug, this is known as absolute bioavailability.

Relative bioavailability is one of the measures used to assess bioequivalence (BE) between two drug products. For FDA approval, a generic manufacturer must demonstrate that the 90% confidence interval for the ratio of the mean responses (usually of AUC and the maximum concentration, Cmax) of its product. While AUC refers to the extent of bioavailability, Cmax refers to the rate of bioavailability. When Tmax is given, it refers to the time it takes for a drug to reach Cmax.[10]

1.8 Factors influencing bioavailability:

The absolute bioavailability of a drug, when administered by an extravascular route, is usually less than one (i.e., F <100%). Various physiological factors reduce the availability of drugs prior to their entry into the systemic circulation. Whether a drug is taken with or without food will also affect absorption, other drugs taken concurrently may alter absorption and first-pass metabolism, intestinal motility alters the dissolution of the drug and may affect the degree of chemical

degradation of the drug by intestinal microflora. Disease states affecting liver metabolism or gastrointestinal function will also have an effect.

Other factors may include, but are not limited to:

a. Physical properties of the drug (hydrophobicity, pKa, solubility)

b.The drug formulation (immediate release, excipients used, manufacturing methods, modified release – delayed release, extended release, sustained release, etc.)

c. Whether the formulation is administered in a fed or fasted state

d. Gastric emptying rate

e. Circadian differences

f.Interactions with other drugs/foods:

f1. Interactions with other drugs (e.g., antacids, alcohol, nicotine)

f2. Interactions with other foods (e.g., grapefruit juice, pomello, cranberry juice, brassica vegetables)

f3.Transporters: Substrate of efflux transporters (e.g. P-glycoprotein)

f4.Health of the GI tract

g.Enzyme induction/inhibition by other drugs/foods:

g1.Enzyme induction (increased rate of metabolism), e.g., Phenytoin induces CYP1A2, CYP2C9, CYP2C19, and CYP3A4

g2.Enzyme inhibition (decreased rate of metabolism), e.g., grapefruit juice inhibits CYP3A → higher nifedipine concentrations

h.Individual variation in metabolic differences

h1. Age: In general, drugs are metabolized more slowly in fetal, neonatal, and geriatric populations

h3. Phenotypic differences, enterohepatic circulation, diet, gender

i. Disease state

E.g., hepatic insufficiency, poor renal function

Each of these factors may vary from patient to patient (inter-individual variation), and indeed in the same patient over time (intra-individual variation). In clinical trials, inter-individual variation is a critical measurement used to assess the bioavailability differences from patient to patient in order to ensure predictable dosing.

1.9 Bioequivalence:

Bioequivalence is a term in pharmacokinetics used to assess the expected in vivo biological equivalence of two proprietary preparations of a drug. If two products are said to be bioequivalent it means that they would be expected to be, for all intents and purposes, the same.

Birkett (2003) defined bioequivalence by stating that, "two pharmaceutical products are bioequivalent if they are pharmaceutically equivalent and their bioavailabilities (rate and extent of availability) after administration in the same molar dose are similar to such a degree that their effects, with respect to both efficacy and safety, can be expected to be essentially the same. Pharmaceutical equivalence implies the same amount of the same active substance(s), in the same dosage form, for the same route of administration and meeting the same or comparable standards.[10]

The United States Food and Drug Administration (FDA) has defined bioequivalence as, "the absence of a significant difference in the rate and extent to which the active ingredient or active moiety in pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site

of drug action when administered at the same molar dose under similar conditions in an appropriately designedstudy.

1.10 Beta-blocker:

Beta blockers (sometimes written as β-blockers) or beta-adrenergic blocking agents, beta-adrenergic antagonists, beta-adrenoreceptor antagonists or beta antagonists, are a class of drugs used for various indications. They are particularly used for the management of cardiac arrhythmias, cardioprotection after myocardial infarction (heart attack), and hypertension. As beta adrenergic receptor antagonists, they diminish the effects of epinephrine (adrenaline) and other stress hormones. In 1958, the first beta blocker, dichloroisoproterenol, was synthesized by Eli Lilly Laboratories, but Sir James W. Black in 1962, found the first clinically significant beta blockers - propranolol and pronethalol; it revolutionized the medical management of angina pectoris and is considered by many to be one of the most important contributions to clinical medicine and pharmacology of the 20th century.

Beta blockers block the action of endogenous catecholamines epinephrine (adrenaline) and norepinephrine (noradrenaline) in particular, on β-adrenergic receptors, part of the sympathetic nervous system which mediates the fight-or-flight response. Three types of beta receptors are known, designated β1, β2 and β3 receptors. β1-adrenergic receptors are located mainly in the heart and in the kidneys. β2-adrenergic receptors are located mainly in the lungs, gastrointestinal tract, liver, uterus, vascular smooth muscle, and skeletal muscle. β3-adrenergic receptors are located in fat cells.

1.11 Indications for beta blockers include:

- Angina pectoris

-Atrial fibrillation

-Cardiac arrhythmia

-Congestive heart failure

-Essential tremor

-Glaucoma

-Hypertension

-Migraine prophylaxis

-Mitral valve prolapse

-Myocardial infarction

-Phaeochromocytoma, in conjunction with α-blocker

-Postural orthostatic tachycardia syndrome

-Symptomatic control (tachycardia, tremor) in anxiety and hyperthyroidism

1.12 Adverse effects:

Adverse drug reactions (ADRs) associated with the use of beta blockers include: nausea, diarrhea, bronchospasm, dyspnea, cold extremities, exacerbation of Raynaud's syndrome, bradycardia, hypotension, heart failure, heart block, fatigue, dizziness, alopecia (hair loss), abnormal vision, hallucinations, insomnia, nightmares, sexual dysfunction, erectile dysfunction and/or alteration of glucose and lipid metabolism. Mixed α1/β-antagonist therapy is also commonly associated with orthostatic hypotension. Carvedilol therapy is commonly associated with edema. Due to the high penetration across the blood–brain barrier, lipophilic beta blockers, such as propranolol and metoprolol, are more likely than other, less lipophilic, beta blockers to cause sleep disturbances, such as insomnia and vivid dreams and nightmares.

Adverse effects associated with β2-adrenergic receptor antagonist activity (bronchospasm, peripheral vasoconstriction, alteration of glucose and lipid metabolism) are less common with

β1-selective (often termed "cardioselective") agents; however receptor selectivity diminishes at higher doses. Beta blockade, especially of the beta-1 receptor at the macula densa, inhibits renin release, thus decreasing the release of aldosterone. This causes hyponatremia and hyperkalemia.

Hypoglycemia can occur with beta blockade because β2-adrenoceptors normally stimulate hepatic glycogen breakdown (glycogenolysis) and pancreatic release of glucagon, which work together to increase plasma glucose. Therefore, blocking β2-adrenoceptors lowers plasma glucose. β1-blockers have fewer metabolic side effects in diabetic patients; however, the tachycardia which serves as a warning sign for insulin-induced hypoglycemia may be masked. Therefore, beta blockers are to be used cautiously in diabetics.

A 2007 study revealed diuretics and beta blockers used for hypertension increase a patient's risk of developing diabetes, while ACE inhibitors and angiotensin II receptor antagonists (angiotensin receptor blockers) actually decrease the risk of diabetes.Clinical guidelines in Great Britain, but not in the United States, call for avoiding diuretics and beta blockers as first-line treatment of hypertension due to the risk of diabetes.

Nonselective agents:

- Alprenolol

-Bucindolol

-Carteolol

-Carvedilol (has additional α-blocking activity)

-Labetalol (has additional α-blocking activity)

-Nadolol

-Oxprenolol

-Penbutolol (has intrinsic sympathomimetic activity)

-Pindolol (has intrinsic sympathomimetic activity)

-Propranolol

-Sotalol

-Timolol

-Eucommia bark (herb)

-β1-Selective agents

-Acebutolol (has intrinsic sympathomimetic activity)

-Atenolol

-Betaxolol

-Bisoprolol

-Celiprolol

-Esmolol

-Metoprolol

-Nebivolol

-β2-Selective agents

-Butaxamine (weak α-adrenergic agonist activity) - No common clinical applications, but used in experiments.

-β3-Selective agents

-SR 59230A (has additional α-blocking activity) - Used in experiments.

CHAPTER 02

PROFILE Of ATENOLOL

PROFILE OF ATENOLOL

2.1 Atenolol:

Atenolol is a selective β1 receptor antagonist, a drug belonging to the group of beta blockers (sometimes written β-blockers), a class of drugs used primarily in cardiovascular diseases. Introduced in 1976, atenolol was developed as a replacement for propranolol in the treatment of hypertension. The chemical works by slowing down the heart and reducing its workload. Unlike propranolol, atenolol does not pass through the blood–brain barrier thus avoiding various central nervous system side effects.[15]

Atenolol is one of the most widely used β-blockers in the United Kingdom and was once the first-line treatment for hypertension. The role for β-blockers in hypertension was downgraded in June 2006 in the United Kingdom to fourth-line, as they perform less appropriately or effectively than newer drugs, particularly in the elderly. Some evidence suggests that even in normal doses the most frequently used β-blockers carry an unacceptable risk of provoking type 2 diabetes.

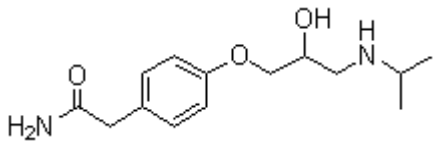
2.2 Chemistry

Atenolol may define by IUPAC nomenclature:

4-[2'-hydroxy-3'-[(1-methylethyl) amino]propoxy-benzeneacetamide

Benzeneacetamide, 4-[2'-hydroxy-3'-[(1-methylethyl) amino] propoxy]

Molecular Structure:



Molecular Formula: $C_{14}H_{22}N_2O_3$

Molecular Weight: 266.34

Melting range: between 152° and 156.5°.

Loss on drying: Dry it at 105° to constant weight: it loses not more than 0.5%of its weight.

Residue on ignition: not more than 0.2%.

It is a hydrophilic drug, with solubility in water equal to 26.5 mg/mL at 37ºC, with chemical formula C14H22N2O3 and

Molecular mass 266.34 gram/mole for the free base form. It is freely soluble in strongly acidic solution. Atenolol is a white or almost white powder. It is odorless or almost odorless.

2.3 History

Atenolol was developed by the Stuart Company which was a division of Imperial Chemical Industries (ICI). ICI was renamed Zeneca in 1992. Atenolol received approval in the United States August 19, 1981. According to drugstore.com, 90 days of generic 50 mg pills costs $17.99 in January, 2009.Generic atenolol was available in 1988.

Dosage forms:

Form	Route	Strength
Injection	Intravenous	0.5 mg/ml
Tablet	Oral	25 mg, 50 mg, 100 mg

2.4 Mechanism of action:

Atenolol competes with sympathomimetic neurotransmitters such as catecholamines for binding at beta (1)-adrenergic receptors in the heart and vascular smooth muscle, inhibiting sympathetic stimulation. This results in a reduction in resting heart rate, cardiac output, systolic and diastolic blood pressure, and reflex orthostatic hypotension. Higher doses of atenolol also competitively block beta (2)-adrenergic responses in the bronchial and vascular smooth muscles. Absorption Approximately 50% of an oral dose is absorbed from the gastrointestinal tract, the remainder being excreted unchanged in the feces.[12]

2.5 Categories

- Antihypertensive Agents
- Adrenergic Agents
- Adrenergic beta-Antagonists
- Sympatholytics
- Antiarrhythmic Agents
- Anti-Arrhythmia Agent

2.6 Pharmacokinetics and Metabolism:

Atenolol is incompletely absorbed (about 50%), but most of the absorbed dose reaches the systemic circulation. Peak blood levels are reached between two and four hours after ingestion. Unlike propranolol or metoprolol, atenolol undergoes little or no metabolism by the liver and the absorbed portion is eliminated by renal excretion. Over 85% of intravenous dose is excrete din urine within 24 hours compared with 50% for an oral dose Only a small amount (6-16%) is protein-bound resulting in

Relatively consistent plasma drug levels with about a four-foldinter-patient variation. The elimination half-life of atenolol is 6 to 7 hours and there is no alteration of kinetic profile of drug by chronic administration. Following intravenous administration peak plasma levels are reached within 5 minutes. Declines from peak levels are rapid (5 to 10 fold) during the first 7 hours. Following oral doses of50 mg or 100 mg both b-blocking and anti-hypertensive effects persist for at least 24 hours. The drug accumulates in patients with renal failure and dosage should be adjusted for patients whose creatinine clearance is less than 35 mL/min/1.73m2.

2.7 Absorption, Distribution and Excretion:

- In animals, atenolol is well distributed into most tissues and fluids except brain and /cerebrospinal fluid/. Unlike propranolol, only a small portion of atenolol is apparently distributed into the CNS.
- Approximately 5-15% of atenolol is bound to plasma protein.
- Atenolol readily crosses the placenta, and has been detected in cord blood. During continuous administration, fetal serum concentrations of the drug are probably equivalent to those in maternal serum. Atenolol is distributed into milk; peak milk concentrations of the drug are higher than peak serum concentrations after an individual dose, and the area under the milk concentration-time (AUC) is substantially greater than that of the serum AUC in lactating women receiving the drug continuously.

- Atenolol is rapidly but incompletely absorbed from the GI tract. Only about 50-60% of an oral dose of atenolol is absorbed. In healthy adults, peak plasma concentrations of 1-2 ug/ml are achieved 2-4 hours after oral administration of a single 200 mg dose of atenolol. An approximately fourfold interindividual variation in plasma concentrations attained has been reported with a specific oral dose of atenolol. Peak plasma atenolol concentrations are achieved within 5 minutes following direct IV injection of the drug, and decline rapidly during an initial distribution phase; after the first 7 hours, plasma concentrations reportedly decline with an elimination half-life similar to that of orally administered drug.[4]

- In patients with normal renal function, atenolol has a plasma half-life (t1/2) of 6-7 hours. Children with normal renal function may exhibit a shorter elimination half-life. In one study in children 5-16 (mean: 8.9) years of age with arrhythmias and normal renal and hepatic function, the terminal elimination half-life averaged 4.6 hours. Plasma t1/2 of the drug increases to 16-27 hours in patients with creatinine clearances of 15-35 ml/minute per 1.73 m2 and exceeds 27 hours with progressive renal impairment. Little or no metabolism of atenolol occurs in the liver. Approximately 40-50% of an oral dose of the drug is excreted in urine unchanged. The remainder is excreted unchanged in feces, principally as unabsorbed drug. About 1-12% of atenolol is reportedly removed by hemodialysis.

- The pharmacokinetics of atenolol enantiomers in 6 healthy male subjects (aged 23-65 yr.) who received a single oral tablet of 50 mg racemic atenolol and in rats who received an intravenous injection of 10 mg/kg of the racemic drug were studied. In humans the areas under the plasma concentration time curves were 1640 + or - 602 and 1860 + or - 652 (ng/ml) hr. for the S- and R-enantiomers, respectively. The small difference was due to a slight but statistically significant difference in the renal clearance of the enantiomers. The enantiomers did not differ from each other with respect to volume of distribution or terminal elimination rate constant. In rats, the area under the plasma concentration time

curves of the R-enantiomer was 4020 + or - 1080, compared with 3630 + or - 1040 for the S-enantiomer. As for humans, this difference was due to a stereoselective renal clearance in favor of the S-enantiomer. The elimination rate constant in rats was the same for both enantiomers.

2.8 Indication

- **Hypertension:**

50-100 mg daily, given orally as a single dose. It is unlikely that additional benefit will be gained by increasing the dose.

Atenolol is compatible with diuretics and other hypotensive agents. In refractory cases a further reduction of blood pressure may be achieved by combining atenolol with other antihypertensive agents for example, co-administration of a diuretic.[13]

Atenolol may exacerbate the rebound hypertension which can follow the withdrawal of clonidine. If the two medicines are co-administered, the atenolol should be withdrawn several days before discontinuing clonidine. If replacing clonidine by Atenolol therapy, the introduction of the latter should be delayed for several days after clonidine administration has stopped.

- **Angina Pectoris:**

The usual dose is 100 mg daily given as a single or divided dose. Additional benefit is not obtained from higher doses.

- **Patients with Renal Impairment:**

Since atenolol is eliminated predominantly via the kidneys, dosage should be adjusted in patients with severe renal impairment. Significant accumulation of atenolol occurs when creatinine clearance falls

below 35 mL/min/1,73 m^2 (normal range is 100-150 mL/min/1,73 m^2). The following maximum dosages are recommended for patients with renal impairment.

Patients on haemodialysis should be given 50 mg after each dialysis; this should be done under hospital supervision as marked falls in blood pressure can occur.

- **Acute myocardial infarction:**

Atenolol for acute myocardial infarction - meta-analysis of atenolol subgroup from larger meta-analysis by Brandler.Although atenolol is thought to be less effective than other beta-blockers for acute treatment according to systematic reviews of three randomized controlled trials. These reviews are dominated by the ISIS-1 study which found that atenolol reduced mortality, though not significantly so. However, atenolol was dosed at 100 mg per day and the Freemantel and co-meta-analysts studied the outcomes of the ISIS-1 at on year although the intervention lasted 7 days. The other two trials dose atenolol at twice a day. Cohort studies suggest that atenolol may or may not be better than other adrenergic beta-antagonists.

- **Heart failure:**

Although atenolol has not received indication in the United States for the treatment of heart failure, two cohort studies suggest that the beta-blockers atenolol and carvedilol may be more effect than metoprolol for the treatment of heart failure.

Children: There is no experience in children

2.9CONTRA-INDICATIONS:

Atenolol should not be used in the following instances:

1. Hypersensitivity to any of the ingredients.

2. Patients with bronchospasm or asthma, or patients with a history of obstructive airways disease.

3. In the presence of second degree or third degree heart block.

4. In patients with cardiogenic shock.

5. After prolonged fasting.

6. In patients with metabolic acidoses (e.g. in diabetes).

7. Special care should be taken with patients whose cardiac reserve is poor. Atenolol should be avoided in cardiac failure, unless or until signs of failure are controlled with digitalis or diuretics.

8. Uncontrolled cardiac failure, excluding that due to hypertrophic obstructive cardiomyopathy.

9. Pregnancy: Atenolol crosses the placental barrier and appears in cord blood. Administration to pregnant women has been associated with intra-uterine growth retardation. Administration of atenolol to pregnant mothers shortly before giving birth, or during labour may result in the newborn infants being born hypotonic, collapsed and hypoglycaemic.

10.There is significant accumulation in breast milk. Breastfeeding patients must not take atenolol.

11.Atenolol is not recommended for the emergency treatment of hypertensive crises.

2.10 Pregnancy

Atenolol is classified by FDA in pregnancy category D. This medication can cause harm to an unborn baby. Do not use atenolol if you are pregnant. Tell your doctor if you become pregnant during treatment. Use an effective form of birth control while you are using this medication. Atenolol if you are breast-feeding a baby. Can pass into breast milk and may harm a nursing baby. Do not use this medication without telling your doctor [2]

2.11 Other information should I know

Keep all appointments with your doctor. Your blood pressure should be checked regularly to determine your response to atenolol. Your doctor may ask you to check your pulse (heart rate). Ask your pharmacist or doctor to teach you how to take your pulse. If your pulse is faster or slower than it should be, call your doctor.

Do not let anyone else take your medication. Ask your pharmacist any questions you have about refilling your prescription.[3]

It is important for you to keep a written list of all of the prescription and nonprescription (over-the-counter) medicines you are taking, as well as any products such as vitamins, minerals, or other dietary supplements. You should bring this list with you each time you visit a doctor or if you are admitted to a hospital. It is also important information to carry with you in case of emergencies.

2.12 Important information about atenolol

Do not stop taking atenolol without first talking to your doctor. Stopping suddenly may make your condition worse.

If you need to have any type of surgery, you may need to temporarily stop using atenolol. Be sure the surgeon knows ahead of time that you are using atenolol.

Atenolol can cause side effects that may impair your thinking or reactions. Be careful if you drive or do anything that requires you to be awake and alert. Avoid drinking alcohol, which could increase drowsiness and dizziness while you are taking atenolol

2.13 Discuss with healthcare provider before taking atenolol

You should not use this medication if you are allergic to atenolol, or if you have certain heart conditions such as slow heartbeats, or heart block.

Before taking atenolol, tell your doctor if you have:

- asthma, bronchitis, emphysema;
- diabetes;
- low blood pressure;

- a heart problem such as heart block, sick sinus syndrome, slow heart rate, or congestive heart failure;
- depression;
- liver or kidney disease;
- a thyroid disorder;
- myasthenia gravis;
- pheochromocytoma; or
- problems with circulation (such as Raynaud's syndrome).

If you have any of these conditions, you may need a dose adjustment or special tests to safely take this medication.

2.14 Other drugs affect atenolol

Before taking atenolol, tell your doctor if you are using:

- allergy treatments (or if you are undergoing allergy skin-testing);
- amiodarone (Cordarone, Pacerone);
- clonidine (Catapres);
- digoxin (digitalis, Lanoxin);
- disopyramide (Norpace);
- guanabenz (Wytensin);
- an MAO inhibitor such as isocarboxazid (Marplan), tranylcypromine (Parnate), phenelzine (Nardil), or selegiline (Eldepryl, Emsam);

- a diabetes medication such as insulin, glyburide (Diabeta, Micronase, Glynase), glipizide (Glucotrol), chlorpropamide (Diabinese), or metformin (Glucophage);
- a heart medication such as nifedipine (Procardia, Adalat), reserpine (Serpasil), verapamil (Calan, Verelan, Isoptin), diltiazem (Cartia, Cardizem);
- medicine for asthma or other breathing disorders, such as albuterol (Ventolin, Proventil), bitolterol (Tornalate), metaproterenol (Alupent), pirbuterol (Maxair), terbutaline (Brethaire, Brethine, Bricanyl), and theophylline (Theo-Dur, Theolair); or
- Cold medicines, stimulant medicines, or diet pills.

If you are using any of these drugs, you may not be able to take atenolol, or you may need dosage adjustments or special tests during treatment.

There may be other drugs not listed that can affect atenolol. Tell your doctor about all the prescription and over-the-counter medications you use. This includes vitamins, minerals, herbal products, and drugs prescribed by other doctors. Do not start using a new medication without telling your doctor.

2.15 Adverse Reactions

Pronounced fatigue and cold extremities have been observed in 10 to 20% of the treated subjects. Complaints about bradycardia, dizziness and gastrointestinal symptoms are less frequent. Despite its relative selectivity, atenolol can cause bronchospasms in asthma patients.Amongst the many but rarely observed side-effects are sleep disturbances, depressions, paresthesiae, impotence, exanthema, psoriasis exacerbations and arthropathies. Clinically relevant changes in the blood sugar have hardly occurred. There is no clarity as to the practical significance of the above mentioned changes in the lipid metabolism.[14]

2.16 What should I do if I forget a dose?

Take the missed dose as soon as you remember it. However, if it is almost time for the next dose, skip the missed dose and continue your regular dosing schedule. Do not take a double dose to make up for a missed one.

2.17 Storage conditions

Keep this medication in the container it came in, tightly closed, and out of reach of children. Store it at room temperature and away from excess heat and moisture (not in the bathroom). Throw away any medication that is outdated or no longer needed. Talk to your pharmacist about the proper disposal of your medication .Keep out reach of children.

2.18 SIDE-EFFECTS

The most serious side-effects include heart failure, heart block and bronchospasm. Other side-effects include fatigue and coldness of the extremities. Cardiovascular effects include bradycardia and hypotension. Congestive heart failure may be precipitated in patients with underlying cardiac disorders.

Pneumonitis and pleurisy have been reported. Central nervous system effects include depression, confusion and sleep disturbances.

Fatigue is a common side-effect. Paraesthesia, peripheral neuropathy and myopathies have been reported. Gastro-intestinal side-effects include nausea, vomiting, diarrhoea, constipation and abdominal cramping.

Skin rash, pruritus and reversible alopecia have been reported.

Ocular symptoms experienced include decreased tear production, blurred vision and soreness.

Haematological reactions include non-thrombocytopenic purpura, thrombocytopenia and less frequently agranulocytosis. Transient eosinophilia can occur.

Metabolic changes can affect glucose control and cholesterol concentrations.

Other reported side-effects include a lupus-like syndrome, male impotence, sclerosing peritonitis and retroperitoneal fibrosis

Side Effects by Body System - for Healthcare Professionals

- **Cardiovascular**

Cardiovascular side effects occur in less than 3% of patients and include bradycardia, hypotension, precipitation of heart failure, and cold extremities. Less than 1% of patients report flushing symptoms. These side effects may require discontinuation of therapy or dosage reduction. The use of atenolol may be associated with reduced HDL cholesterol and increased total cholesterol. These changes may be deleterious in some patients with heart disease. Profound hypotension following atenolol administration for malignant hypertension has been reported.

- **Nervous system**

Nervous system side effects such as complaints of sleep disturbances, depression, and headache occur in up to 4% of patients. Nervous system side effects are less common than with some beta-blockers due to the more hydrophilic properties of atenolol. A single case of organic anxiety syndrome has been associated with rapid withdrawal of atenolol therapy.

Neurologic side effects are less common with atenolol than with some other beta-blockers because it is less lipophilic and, therefore, less able to penetrate the central nervous system. At least three cases of acute central nervous system disturbances have been attributed to atenolol therapy. In one case, the ratio of the serum to CSF atenolol levels was 2:1, which is much lower than previously reported ratios of 14:, 1 indicating that there was significant CSF penetration.

- **Gastrointestinal**

Gastrointestinal side effects have included diarrhea and nausea in 2% and 4% of patients, respectively. Retroperitoneal fibrosis has rarely been associated with atenolol.

A 68-year-old woman with hypertension developed vomiting, abdominal pain, and progressive renal failure associated with extensive retroperitoneal fibrosis and ureteral obstruction during atenolol therapy. While the patient was also taking oral iron preparations, metoclopramide, and ibuprofen, the authors of this case report implicate atenolol due to previous associations of the retroperitoneal fibrosis with other beta-blockers.

- **Hypersensitivity**

Hypersensitivity reactions are rare.

- Hepatic

Hepatic dysfunction has rarely been associated with atenolol. A single case of reversible liver dysfunction and a single case of cholecystitis have been associated with atenolol. The mechanism of toxicity is not known, and is considered to be idiosyncratic.

- Dermatologic

A 71-year-old woman with unstable angina developed multiple erythematous, subcutaneous nodules over the metacarpal-phalanx and interphalanx joints of both hands. The patient also developed an increase of CD8+ T lymphocytes (cytotoxic suppressor lymphocytes) and the presence of antinuclear antibodies. The lesions resolved by 90 days after atenolol was withdrawn. Subsequent use of atenolol lead to similar sequelae.Dermatologic side effects are rare. A case of septal panniculitis is reported, thought to be due to an immunologic mechanism.

- Endocrine

Endocrine side effects including slightly decreased T3 concentrations among patients with hyperthyroidism have been reported, although T4 concentrations were not affected.

- Genitourinary

Breast pain, swelling, and tenderness developed in a 54-year-old woman after starting therapy with atenolol 25 mg daily. Symptoms resolved following discontinuation of therapy.In one study, postmenopausal women reported a reduction in libido after receiving atenolol 50 to 100

mg daily.Genitourinary side effects have included decreased libido and at least one case of breast pain, swelling, and tenderness.

- Metabolic

The mechanism by which atenolol induces weight gain is unknown. Some investigators have reported a 4% to 9% reduction in total energy expenditure and a 25% reduction in thermogenic response to food during beta-blocker treatment.

2.19 WARNINGS:

While taking atenolol, patients with a history of anaphylactic reactions to a variety of allergens, may have a more severe reaction on repeated challenge. Such patients may be unresponsive to the usual dose of adrenaline used to treat allergic reactions. Particular caution should be exercised with patients suffering from the following:

Bradycardia of less that 50 pulse beats a minute

Peripheral vascular disease

Raynaud's phenomenon

The normal dose should be reduced in elderly patients, or in patients suffering from renal dysfunction. Elderly patients may not respond as well to atenolol as younger patients.

In the perioperative period it is generally unwise to reduce the dosage to which the patient is accustomed, as there may be danger of aggravation of angina pectoris or of hypertension. A patient's normal tachycardic response to hypovolemia or blood loss may be obscured during or after surgery. Particular caution should be taken in this regard.

2.20 INTERACTIONS

Anaesthetics: Care should be taken when anaesthetic agents are used with atenolol. The patient should be warned to inform the anaesthetist.

It can be dangerous to administer APO-ATENOLOL concomitantly with the following agents: hypoglycaemic agents, phenothiazines and Class 1 antiarrhythmic agents such as disopyramide. Such interactions can have life-threatening consequences.

It should be noted that digitalisation of patients receiving long term atenolol therapy may be necessary if congestive cardiac failure is likely to develop. This combination can be considered despite the potentiation of negative chronotropic effect of the two medicines. Careful control of dosages and of the individual patient's response (and notably pulse rate) is essential in this situation.

Combined use of atenolol and calcium channel blockers with negative inotropic effects such as verapamil and diltiazem can lead to an exaggeration of these effects, particularly in patients with impaired ventricular function and/or SA or AV conduction abnormalities. Neither medicine should be administered intravenously within 48 hours of discontinuing the other.

Patients with phaeochromocytoma require treatment with an alpha-adrenergic blocker.

If atenolol and clonidine are given concurrently, the clonidine should not be discontinued until several days after the withdrawal of the atenolol as severe rebound hypertension may occur.[14]

2.21 Overdose

Symptoms of overdose are due to excessive pharmacodynamics actions on β_1 and also β_2-receptors. These include bradycardia, severe hypotension with shock, acute heart failure,

hypoglycemia and bronchospastic reactions. Treatment is largely symptomatic. Hospitalization and intensive monitoring is indicated. In early cases emesis can be induced. Activated charcoal is useful to absorb the drug. Atropine will counteract bradycardia, glucagon helps with hypoglycemia, dobutamine can be given against hypotension and the inhalation of a β_2-mimetic as hexoprenalin or salbutamol will terminate bronchospasms. Blood or plasma atenolol concentrations may be measured to confirm a diagnosis of poisoning in hospitalized patients or to assist in a medicolegal death investigation. Plasma levels are usually less than 3 mg/L during therapeutic administration, but can range from 3–30 mg/L in overdose victims

Symptoms of overdose may include:

- lack of energy
- difficulty breathing
- wheezing
- slow heartbeat
- fainting
- swelling of the hands, feet, ankles, or lower legs
- unusual weight gain
- shakiness
- dizziness
- rapid heartbeat
- sweating or confusion
- blurred vision
- headache
- numbness or tingling of the mouth
- weakness
- excessive tiredness
- pale color
- sudden hunger

2.22 Pharmacokinetic data

- t_{cmax} = 2 to 4 hours after oral dosing (time elapsed before maximal concentration in the blood plasma is reached)
- The mean elimination halflife is 6 hours. However, the action of the usual oral dose of 25 to 100 mg lasts over a period of 24 hours.
- Atenolol is a hydrophilic drug. The concentration found in brain tissue is approximately 15% of the plasma concentration only. The drug crosses the placenta barrier freely. In the milk of breastfeeding mothers, approximately 3 times the plasma concentrations are measured.
- Atenolol is almost exclusively eliminated renally and is well removable by dialysis. A compromised liver function does not lead to higher peak-activity and/or a longer halflife with possible accumulation.
- Atenolol should not be taken with orange juice, which can interfere with its uptake. Generally, a 4-hour window is recommended in between the atenolol and orange juice intake.

2.23 FDA Requirements

- Atenolol, used as a beta adrenergic blocking agent, was approved by FDA for marketing in the United States 8/81.

- The Approved Drug Products with Therapeutic Equivalence Evaluations List identifies currently marketed drug products, incl atenolol, approved on the basis of safety and effectiveness by FDA under sections 505 and 507 of the Federal Food, Drug, and Cosmetic Act.

- Manufacturers, packers, and distributors of drug and drug products for human use are responsible for complying with the labeling, certification, and usage requirements as prescribed by the Federal Food, Drug, and Cosmetic Act, as amended (secs 201-902, 52 Stat. 1040 et seq., as amended; 21 U.S.C. 321-392). [

2.24 PRECAUTIONS

Patients with phaeochromocytoma should not receive atenolol without concomitant alpha-adrenoreceptor blocking therapy.

Bronchoconstriction may occur in patients suffering from asthma, bronchitis and other chronic pulmonary diseases.

Abrupt discontinuation of therapy may cause exacerbation of angina pectoris in patients suffering from ischaemic heart disease. Discontinuation of therapy should be gradual and patients should be advised to limit the extent of their physical activity during the period that the medicine is discontinued.

Atenolol may mask the symptoms of hyperthyroidism and of hypoglycaemia. Atenolol may unmask myasthenia gravis.

Psoriasis may be aggravated.

One of the pharmacological actions of atenolol is to reduce the heart rate. Bradycardia (usually less than 50-55 beats /minute) indicates that the dosage should not be further increased.

2.25 Special precautions

Before taking atenolol:

•tell your doctor and pharmacist if you are allergic to atenolol or any other medications.

•tell your doctor and pharmacist what prescription and nonprescription medications, vitamins, nutritional supplements, and herbal products you are taking. Be sure to mention any of the following: calcium channel blockers such as diltiazem (Cardizem, Dilacor, Tiazac, others) and verapamil (Calan, Isoptin, Verelan); clonidine (Catapres); nonsteroidal anti-inflammatory drugs (NSAIDs) such as indomethacin (Indocin); and reserpine (Serpalan, Serpasil, Serpatabs). Your doctor may need to change the doses of your medications or monitor you carefully for side effects.

•tell your doctor if you have or have ever had asthma or other lung disease; diabetes; severe allergies; an overactive thyroid gland (hyperthyroidism); pheochromocytoma; heart failure; a slow heart rate; circulation problems; or heart or kidney disease.

•tell your doctor if you are pregnant, plan to become pregnant, or are breast-feeding. If you become pregnant while taking atenolol, call your doctor immediately.

•if you are having surgery, including dental surgery, tell the doctor or dentist that you are taking atenolol.

•you should know that if you have allergic reactions to different substances, your reactions may be worse while you are using atenolol, and your allergic reactions may not respond to the usual doses of injectable epinephrine.

CHAPTER 03

OVERVIEW Of METHODS & METERIAL'S

3.1 Experimental materials:

Atenolol tablets were collected from local Pharmacy.Reagent used includes HCl, water etc. Materials also include in the various quality control test given as following

Table 1: Collection of sample

Brand name	Manufacturer	Price
Tenoloc 50 mg (100 tablet)	ACME Pharmaceutical Limited	**70Tk**
Tenoren 50 mg (100 tablet)	ACI Pharmaceutical Ltd.	**70Tk**
Cardipro 50 mg (100 tablet)	**Square pharmaceuticals Ltd.**	**70Tk**

3.2 Weight Variation Test of Tablets

Principle:

Weight variation test is the test by which variation of weight from tablet to tablet can be determined. The following formula is used,

Weight Variation = $\mathbf{(I_W\text{-}A_w)/A_w \times 100\%}$

Where,

Iw = Individual weight of tablet.

Aw = Average weight of tablet.

Acceptable range according to USP:-

Due to a variety of reasons tablets may be excessively overweight or underweight. To help alleviate this problem the United States Pharmacopoeia (USP) / National formulary (NF) provides limits for the permissible variations in the weight of individual tablets expressed as a percentage of the average weight of the sample. The USP weight variation test is run by weighting 20 tablets individually calculating the average weights and comparing the individual tablet weights to the average. The tablet meets the USP test if not more than 2 tablets are outside the percentage limit and if no tablet differs by more than two times the percentage limit. The weight variation tolerance for uncoated tablets differs depending on average tablet weight.[7]

Table 2: Weight Variation Tolerance

Weight Variation Tolerance For Uncoated	
Average Weight of Tablets (mg)	Maximum Percentage Difference Allowed
130 or Less	10%
130-324	7.5%
More than 324	5%

Fig. Electronic Balance.

Why is weight variation test done?

The weight of tablet is the quantity of granulation which contains the labeled amount of the therapeutic ingredient. The volumetric fill of the die cavity determines the weight of the compressed tablet. In setting up the tablet machine the fill is adjusted to give the desired tablet weight. After the tablet machine is operated the weight of the tablets are checked routinely either manually or electronically to ensure that proper weight tablets are being made. A large weight variation precludes good content uniformity. The patient receiving the tablet may be overdosed or under dosed resulting unpredictable.

Some possible reasons of weight variations:-

1) Erratic punch flight

2) Material loss or gain after proper die fills.

3) Feeder "starved" or "choked".

4) Dies not filling.

5) Lower punch starts pulling down without material coverage.

6) Bad scraps-Off

7) Die(s) projecting above die tablet.

Procedure:-

1) Each of the 20 tablets was weighed separately by using an electronic balance.
2) All of the 20 tablets was weighed together and average weight was calculated Individually by dividing it with 20.
3) Weight variation of each tablet was calculated individually by using the formula
4) These procedures were followed to determine weight variation of each brand of Atenolol tablets.

3.3 Hardness Test of Tablets

Hardness

Tablet Hardness testing is also called tablet breaking force and measures the tablet mechanical integrity. The acceptable hardness of a tablet is 4kg/cm2.

Principle:-

Tablets require a certain amount of strength, or hardness to withstand mechanical shocks of handling in manufacturing, packaging, and shipping. In addition, tablets should be able to withstand reasonable abuse when in the hands of consumers. Adequate tablet hardness and

resistance to powdering are necessary requisites for consumer acceptance. More recently, this relationship of hardness to tablet disintegration, and perhaps more significantly, to the drug dissolution release rate, has become apparent. The 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 compressive force employed.[6]

Importance:-

Hardness determinations are made throughout the tablet runs to determine the need for pressure adjustments on the tableting machine.

- It may not disintegrate in the required period of time or,
- Meet the dissolution requirements if the tablet is too soft.
- It will not withstand the handling during subsequent processing such as coating or packaging and shipping operations.

Factors effecting hardness of tablets:

Die fill and compression force:-

At a constant die fill, the hardness value increases and thickness decrease as additional compression force is applied. The relationship holds up to a maximum value for hardness and minimum value for thickness, beyond which increases in pressure cause the tablet to laminate or cap, thus destroying the integrity of the tablet. At a constant compression force hardness increases with increases die fills and decreases with lower die fills.

Lubricants:-

Lubricants affect the tablet hardness when they are used in too high a concentration or mixed for too long a period.

Tablet Size:-

Large tablets require a greater force to cause fracture and are therefore harder than smalltablets.

Tool Shape:-

For a given granulation, a flat beveled too produces a tablet harder than a deep cup tool.

Materials and Reagents:

Mainly two materials are needed –

1)Tablet to be tested 2)Tablet Hardness Tester

Description of tester

To evaluate the tablet hardness we use Ketan tablet hardness tester, which is a type of Monsanto hardness tester. It is developed approximately fifty years ago. The tester consists of a barrel containing a compressible spring held between two plungers.

Procedure:-

- The lower plunger is placed in contact with the tablet and zero reading was taken.
- The upper plunger is then forced against a spring by turning a threaded bolt until thetablet fractures.
- As the spring is compressed, a pointer rides along a gauge in the barrel to indicate theforce.
- The force of fracture is recorded.
- These procedures were followed to determine hardness of each brand of atenolol tablets.

3.4 FRIABILITY TEST OF TABLETS

Principle:-

Friability of tablet is defined as the capacity to withstand shock and abrasion in packaging, handling and shipping. It is determined by the following formula -

Friability = $(I_w-F_w)/I_w \times 100\%$

Where,

$\mathbf{I_w}$ = Individual weight of tablets.

$\mathbf{F_w}$ = Total final weight of tablets.

Acceptable range according to USP:-

Conventional compressed tablets that loss less than 0.5% to l% (after 100 revolutions) of their weight are generally considered acceptable

Why is Friability test done?

Friability test is done due to the following reasons:

- Friable tablets no longer have sharp edges, consequently pharmaceutical elegance andpatient acceptance is diminished.
- Tablet friability results in weight loss of tablets owing to partial chipping orfragmentation.
- Weight loss due to excessive friability may affect therapeutic response.

Some possible causes of friability:

1. Excessive moisture content.

2. Over dried granulation.

3. Inadequate amount of binder.

Description of the Machine:

Tablet friability is related to tablet hardness, and the measurement is made by use of a friabilator rather than a measure of the force required to crush a tablet. The instrument is designed to evaluate the ability of the tablet to withstand abrasion in packaging, handling and shipping.

The device has two circular plastic chambers that revolve at 30rpm, dropping the tablets at a distance of 6 inches with each revolution. This device facilitates time setting or no of revolution setting and stops automatically. A number of tablets are weighed and placed in the tumbling apparatus where they are exposed to rolling and repeated shocks resulting from free-falls within the apparatus where they are exposed to rolling and repeated shocks tablets are weighed and loss in weight indicates the ability of the tablets to withstand this type of wear.

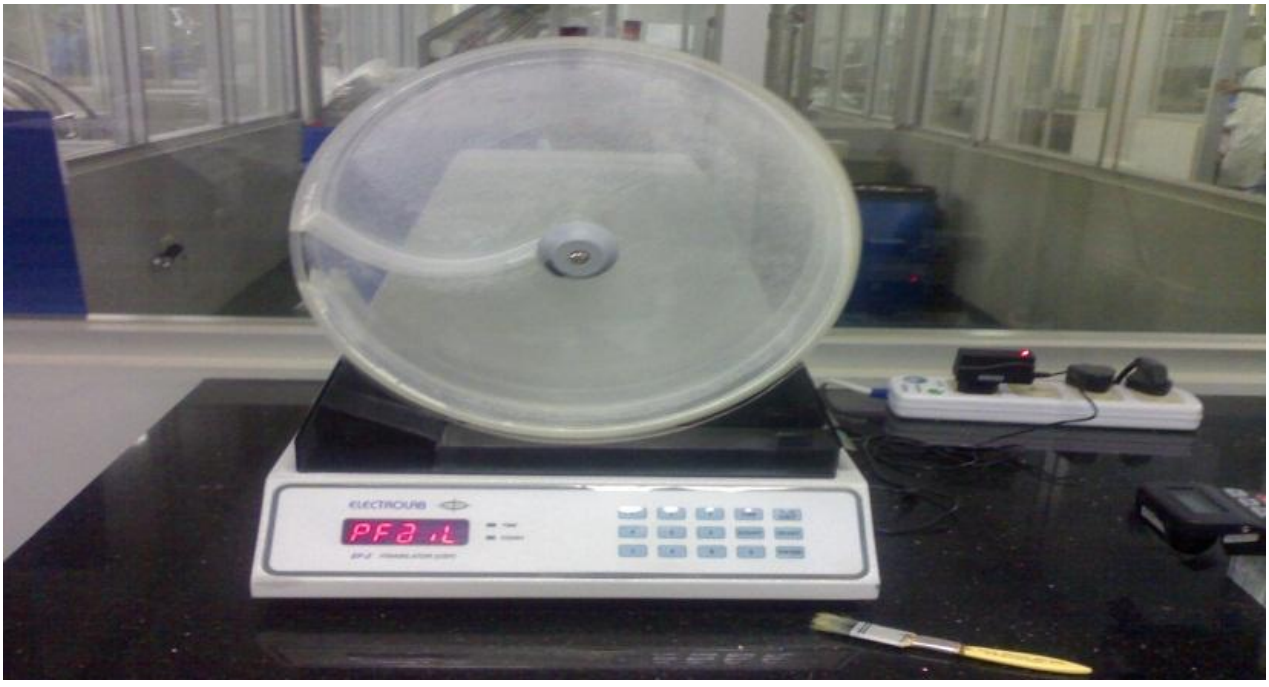


Fig. Friability Tester

Procedure:-

1. Each of the 10 tablets was weighed separately by using an electronic balance.
2. The friabilator was then set for 5min of 150 revolutions and all the tablets are placed in the apparatus and it was turned on.
3. During this period the tablets were exposed to rolling and repeated shocks resulting from free-fall within the apparatus.
4. When the device stops automatically the tablets was collected and weighed again and calculated individually by using the formula.

3.5 Determination of Disintegration Time of Tablets.

Principle:-

Before absorption of a drug takes place to the body, it must be in solution. For most tablets the first important step toward solution is breakdown of the tablet into smaller particles or granules, a process known as disintegration. The time that takes a tablet to disintegrate is measured in a device described in the USP/NF.

Factors affecting disintegration:-

- Tablet hardness too high. This can he reduced by reducing machine pressure for acceptable tablet.
- Over lubrication. These can also cause waterproofing. Tb is can be reduced by blending lubricant only 5-10 mines in final mix and replacing metallic steerages with satiric acid.
- Lack of disintegrates.

- P^H of the medium such as in gastric fluid, intestinal fluid.

Description the machine:-

The USP device to lest disintegration uses six glass tubes that arc 3 inches long, open at the sop and held agonist a 10 mesh screen at bottom end to the basket rack assembly.

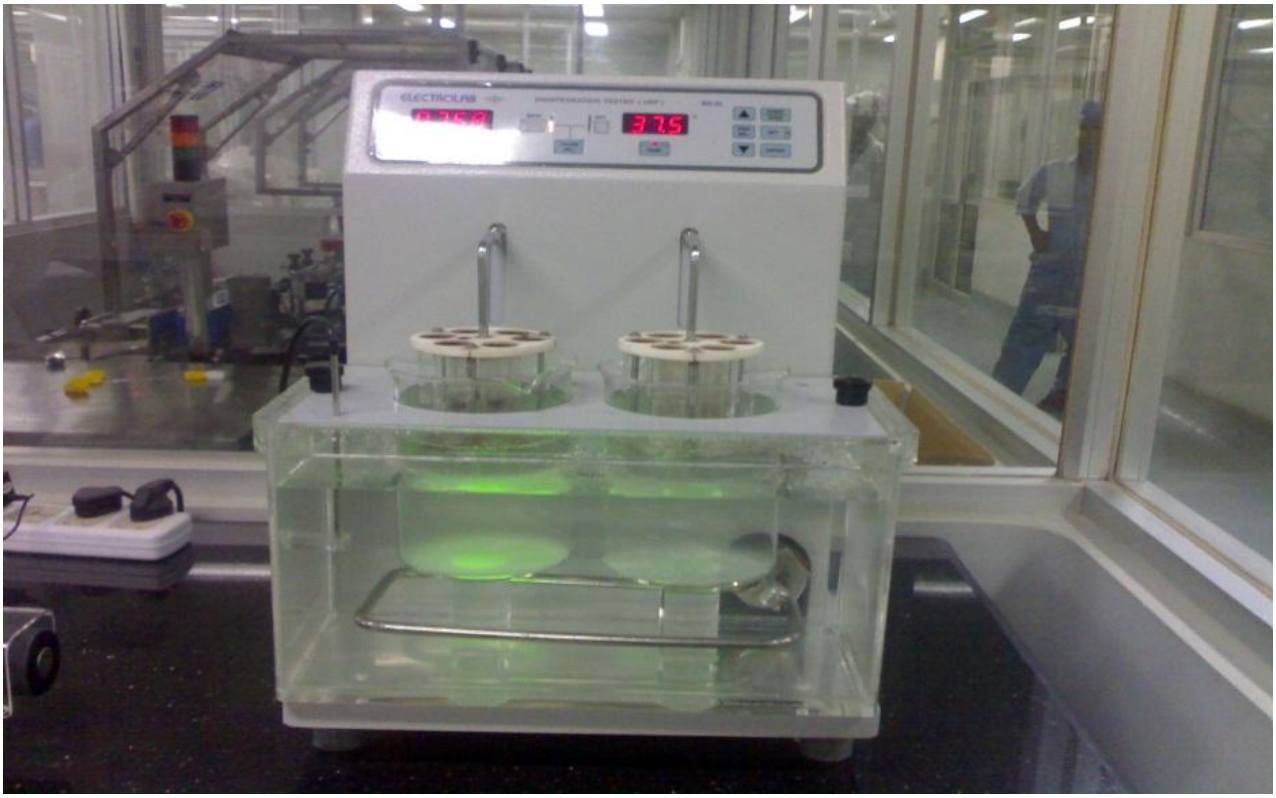


Fig. Disintegration Machine.

Procedure:-

This was determined at 37° C using veego disintegration testing apparatus until no particle remained on the basket of the system.To test for disintegration time one Atenolol tabletis placed in each tube, and the basket rack is positioned in a 1-L beaker of water at 37° C, such that the

tablets remain 2.5 cm below the surface of the liquid on their upward movement and descent not closer than 2.5 cm from the bottom of the beaker.

A standard motor driven device is used to move the basket assembly coating the tablets up and down through a distance of 5 to 6cm at a frequency of 28 to 32 cycles per minute. Perforated plastic discs may also be used in the test.

These are placed on the top of tablets and impart an abrasive action to the tablets. The discs may not be meaningful or impart more sensitivity to the test, but they are useful for tablets that float. To create an acidic media we used O.01N HCl solution

3.6 Dissolution Test of Tablets

What is the definition of Dissolution?

Dissolution is pharmaceutically defined as the rate of mass transfer from a solid surface into the dissolution medium or solvent under standardized conditions of liquid/solid interface, temperature and solvent composition. It is a dynamic property that changes with time and explains the process by which a homogenous mixture of a solid or a liquid can be obtained in a solvent. It happens to chemically occur by the crystal break down into individual ions, atoms or molecules and their transport into the solvent.

Fig. Dissolution Machine

Why dissolution testing is used for pharmaceuticals?

Dissolution testing is a critical reformulation solubility analysis research tool in the process of drug discovery that entails measuring the stability of the investigational product, achieving uniformity in production lots and determining it's in vivo availability. Thus this Dissolution testing is an essential requirement for the development, establishment of in vitro dissolution and in vivo performance (IVIVR), registration and quality control of different dosage forms.[9]

What are the applications of dissolution testing?

Dissolution testing is widely used in the pharmaceutical industry for optimization of formulation and quality control.It is useful in the pharmaceutical and biotechnology industry to formulate drug dosage forms and to develop quality control specifications for

its manufacturing process.To identify the critical manufacturing variable, like the binding agent effect, mixing effects, granulation procedure, coating parameters and comparative profile studies.

- To comply with guidelines set in the scale up and post approval changes (SUPAC) and ICH.
- To select candidate formulation
- To simulate food effect on bio availability.
- To support waiver for bio equivalence requirements.
- In the study of Bio waivers.
- As a Surrogate for invivo studies.

Calculation for determination of dissolution of atenolol tablet:

$$\%\text{Dissolution} = \frac{\text{Absorbance of sample} \times \text{Total volume of the dissolution medium} \times \text{Dilution factor}}{\text{Concentration factor (mg/100ml)} \times \text{weight of the tablet}} \times 100$$

N.B: Concentration is calculated from the equation of standard curve ($y = 0.0455x + 0.009$)

CHAPTER 04

ANALYSIS & RESULT DISCUSSION

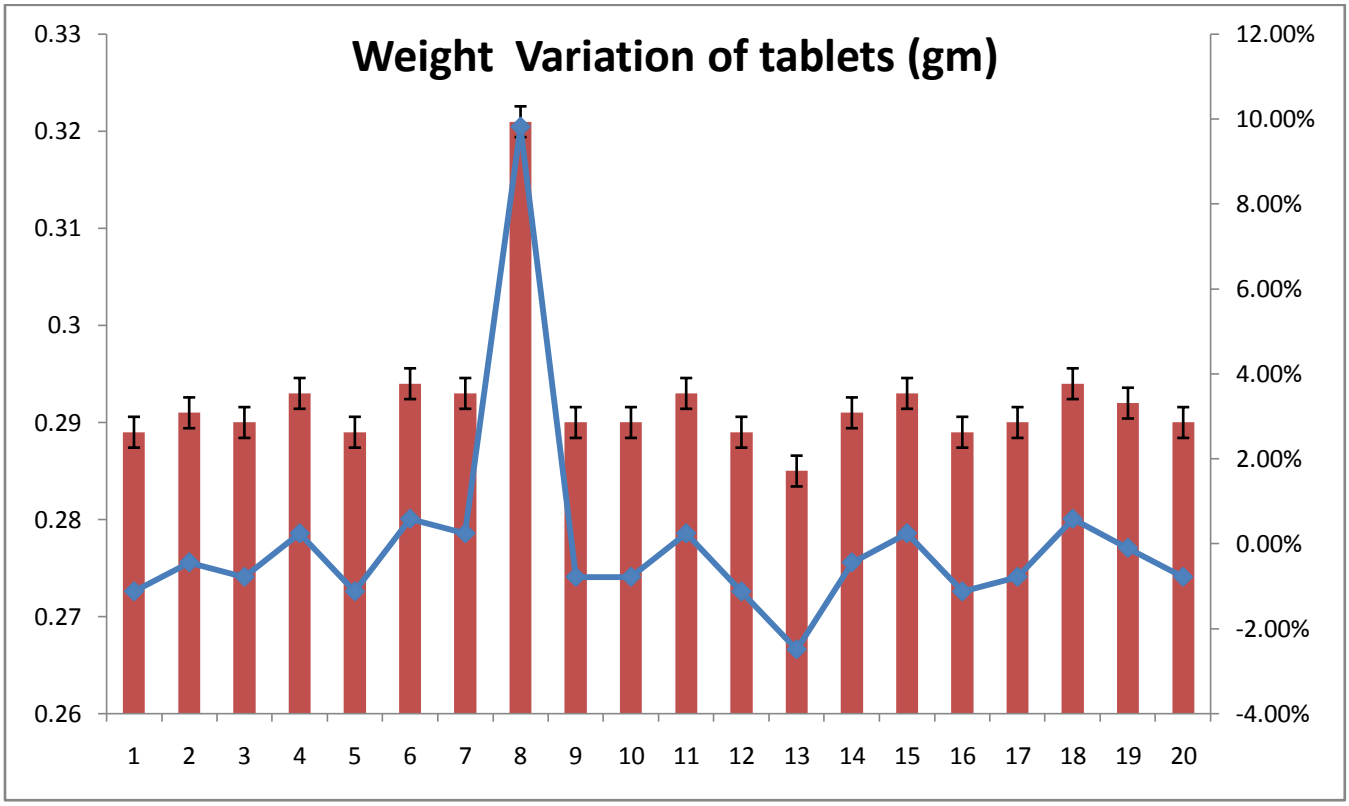
ANALYSIS & RESULT DISCUSSION

4.1.1 Data

Generic name: Atenolol
Brand name: TENOLOC 50 mg
Batch No. : V01125
Manufacturer: ACME Pharmaceutical Limited.

Table 4.1.1: Weight Variation Result

Tablet No.	Initial Weight of each tablet(gm)	Total Weight of 20 tablets(gm)	Average Weight(gm)	Weight Variation(%)	Average Weight Variation(%)
1	0.289	5.85	0.2923	-1.129	.0011
2	0.291			-0.445	
3	0.29			-0.787	
4	0.293			0.239	
5	0.289			-1.129	
6	0.294			0.582	
7	0.293			0.239	
8	0.321			9.819	
9	0.29			-0.787	
10	0.29			-0.787	
11	0.293			0.239	
12	0.289			-1.13	
13	0.285			-2.497	
14	0.291			-0.445	
15	0.293			0.24	
16	0.289			-1.13	
17	0.29			-0.787	
18	0.294			0.58	
19	0.292			-0.103	
20	0.29			-0.787	



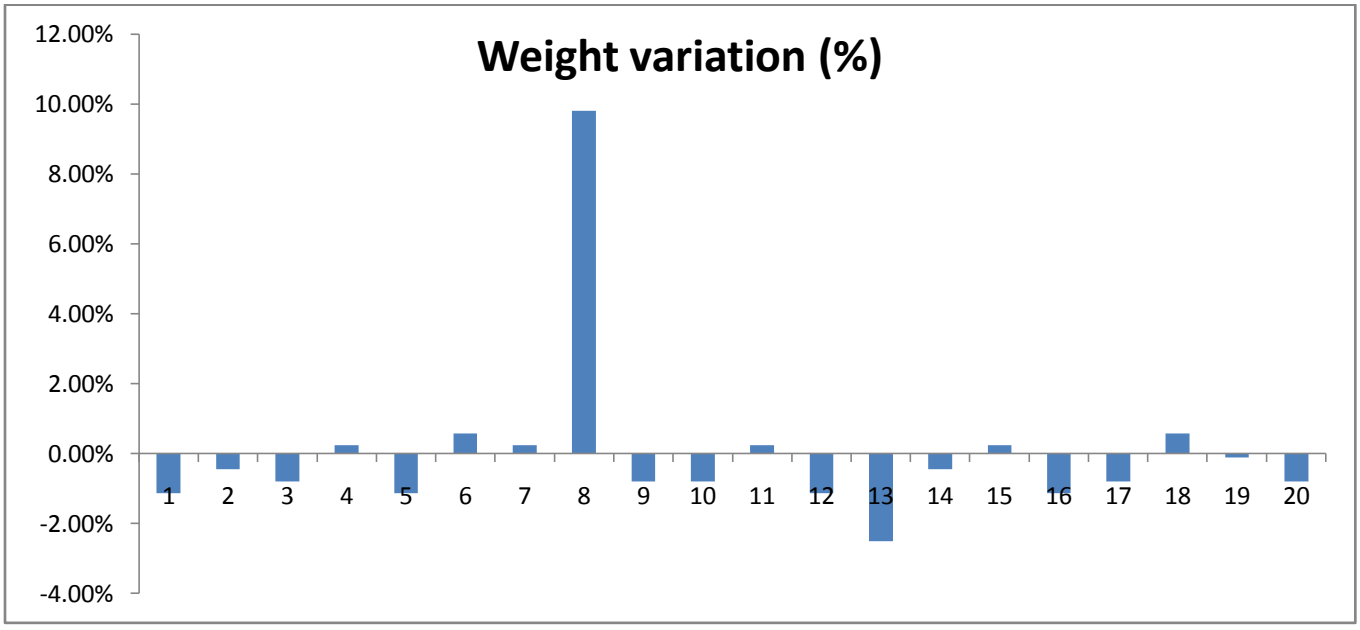
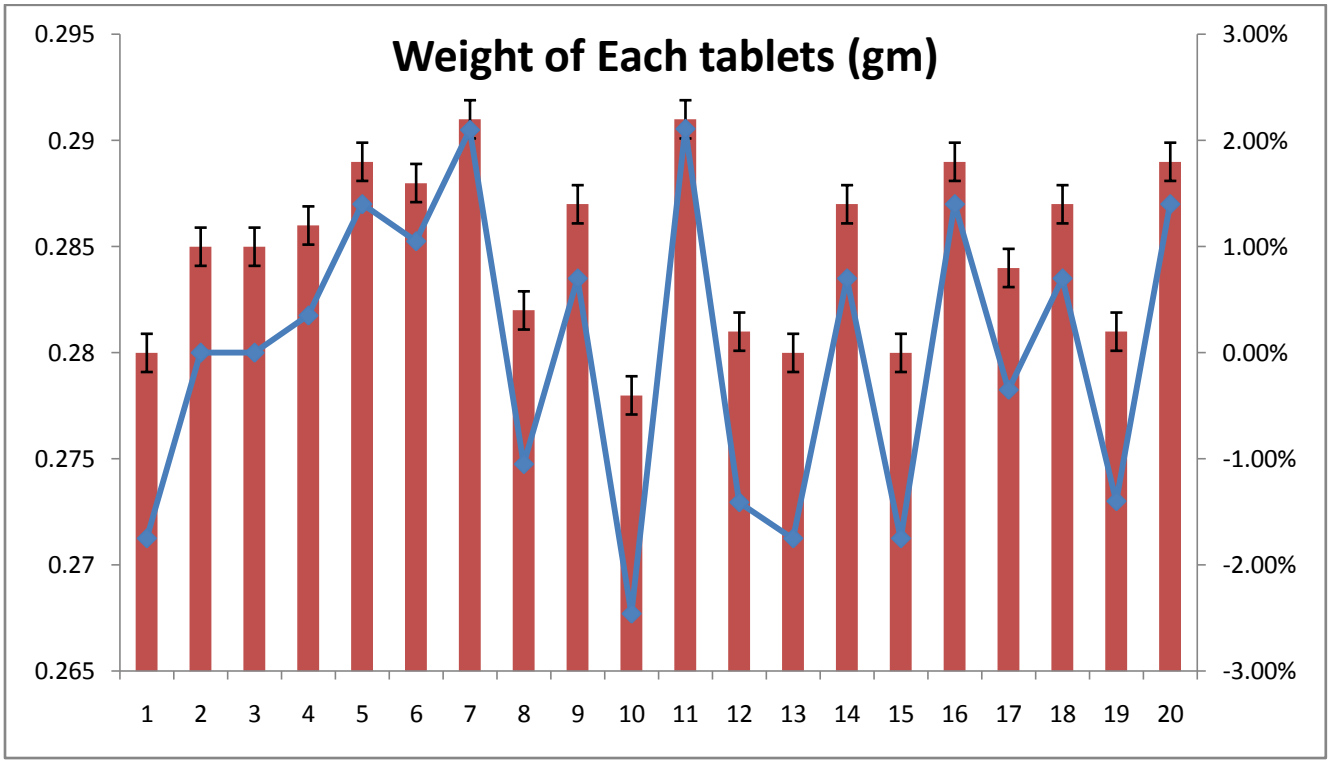


Figure 4.1.1: Bar chart to show weight variation of TENOLOC Batch#V01125

Generic name: Atenolol
Brand name: TENOLOC 50 mg
Batch No. : V01182
Manufacturer: ACME Pharmaceutical Limited.

Table 4.1.2: Weight Variation Result

Tablet No.	Initial Weight of each tablet(gm)	Total Weight of 20 tablets(gm)	Average Weight(gm)	Weight Variation (%)	Average Weight Variation(%)
1	0.28	5.7	0.285	-1.75	0.00015
2	0.285			0	
3	0.285			0	
4	0.286			0.35	
5	0.289			1.4	
6	0.288			1.053	
7	0.291			2.11	
8	0.282			-1.05	
9	0.287			0.7	
10	0.278			-2.46	
11	0.291			2.11	
12	0.281			-1.41	
13	0.28			-1.75	
14	0.287			0.7	
15	0.28			-1.75	
16	0.289			1.4	
17	0.284			-0.35	
18	0.287			0.7	
19	0.281			-1.4	
20	0.289			1.4	



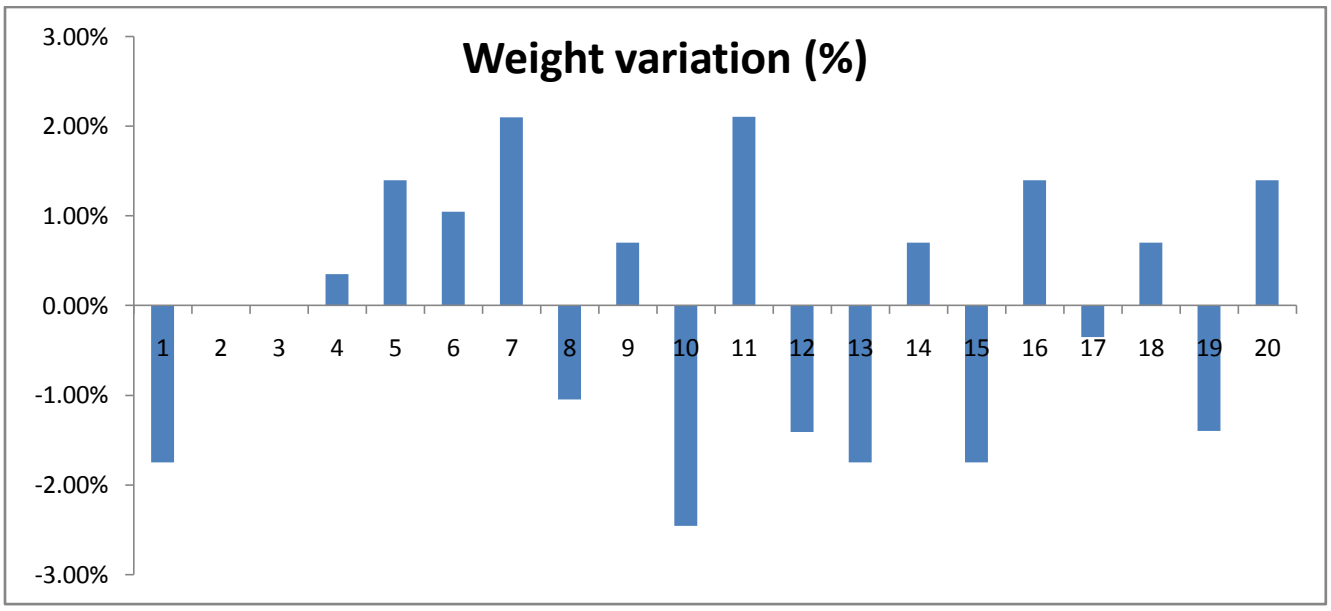


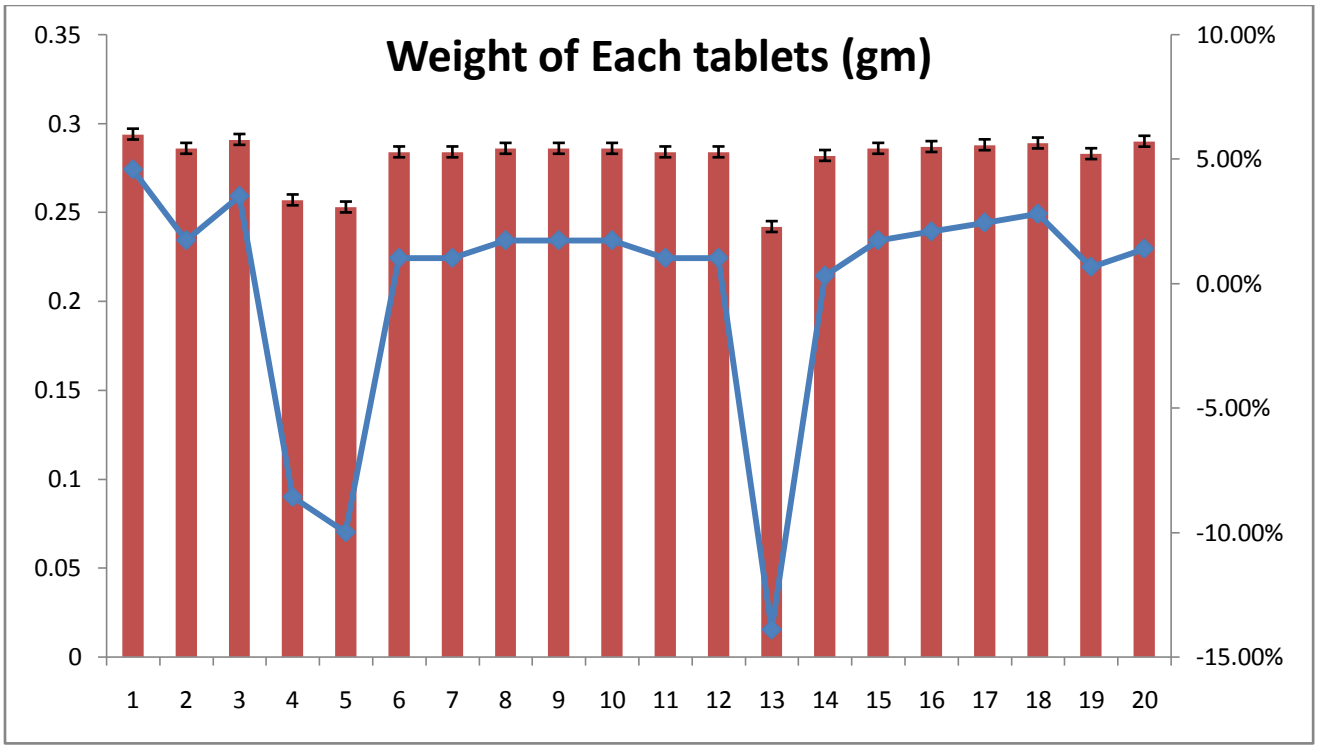
Figure 4.1.2: Bar chart to show weight variation of TENOLOC Batch#V01182

Generic name: Atenolol
Brand name: TENOLOC 50 mg
Batch No. : V01186
Manufacturer: ACME Pharmaceutical Limited.

Table 4.1.3: Weight Variation Result

Tablet No.	Initial Weight of each tablet(gm)	Total Weight of 20 tablets (gm)	Average Weight (gm)	Weight Variation (%)	Average Weight Variation (%)
1	0.294			4.589	
2	0.286			1.743	
3	0.291			3.522	
4	0.257			-8.573	

5	0.253	5.622	0.2811	-9.994	-0.088
6	0.284			1.032	
7	0.284			1.032	
8	0.286			1.743	
9	0.286			1.743	
10	0.286			1.743	
11	0.284			1.032	
12	0.284			1.032	
13	0.242			-13.91	
14	0.282			0.32	
15	0.286			1.743	
16	0.287			2.099	
17	0.288			2.455	
18	0.289			2.81	
19	0.283			0.676	
20	0.29			1.404	



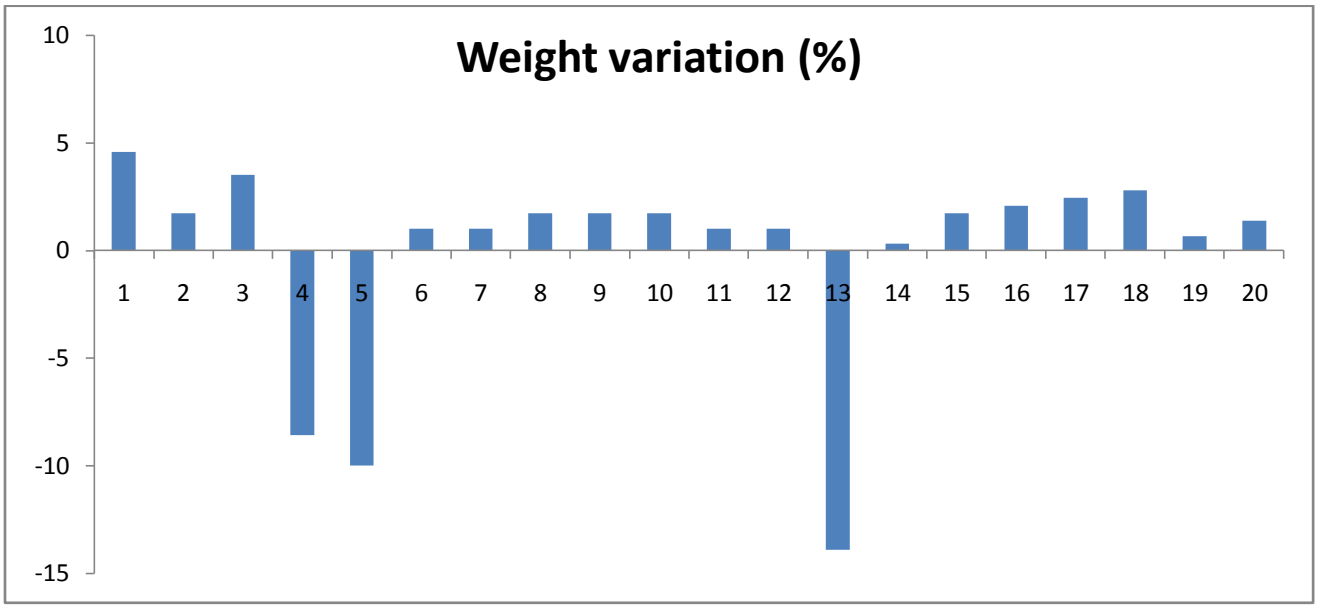


Figure 4.1.5: Bar chart to show weight variation of TENOLOC Batch#V01186

Table 4.1.4: Disintegration Time test Result TENOLOC

DISINTEGRATION			
Tablet sample	**Batch no.V01165**	**Batch no.V01182**	**Batch no.V01186**
1	1.13	2.23	2.53
2	1.75	3.33	3.19
3	1.44	2.2	3.35
4	1.79	3.17	3.26
5	1.83	2.45	3.65
6	1.65	2.17	3.13

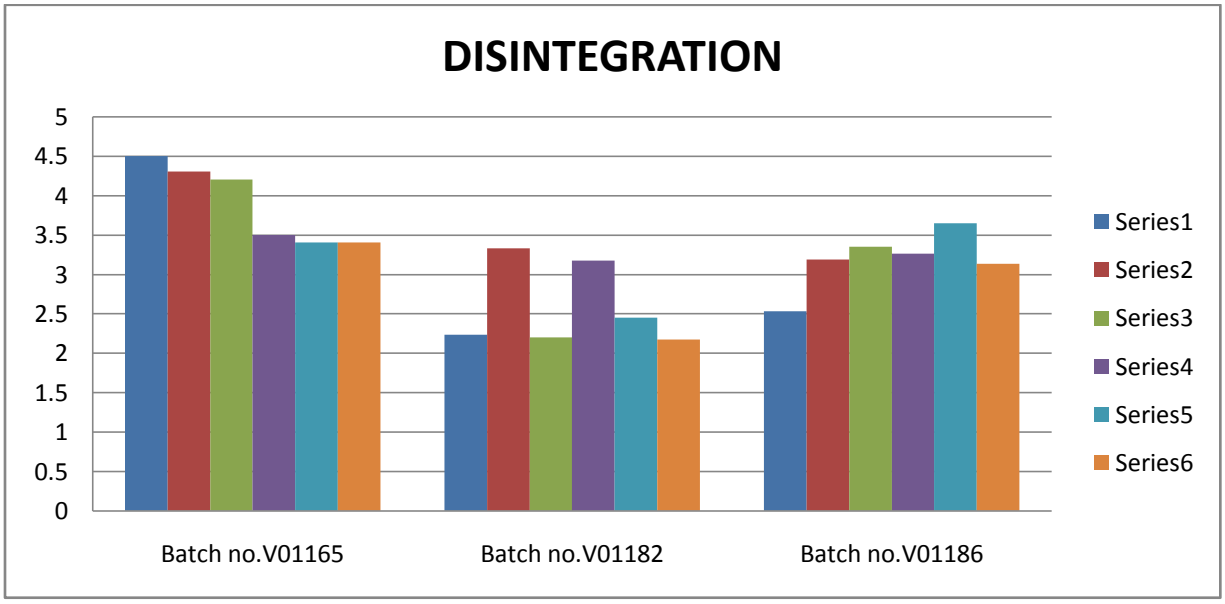


Figure 4.1.4: Bar chart to show Disintegration Time test Result TENOLOC

Table 4.1.5: Hardness test Result TENOLOC

Hardness kg/cm2			
Tablet sample	**Batch no.V01165**	**Batch no.V01182**	**Batch no.V01186**
1	4.5	5.2	5
2	4.3	5	5
3	4.2	4.7	5.3
4	3.5	5.7	4.9
5	3.4	5	5.6
6	3.4	5	5.2

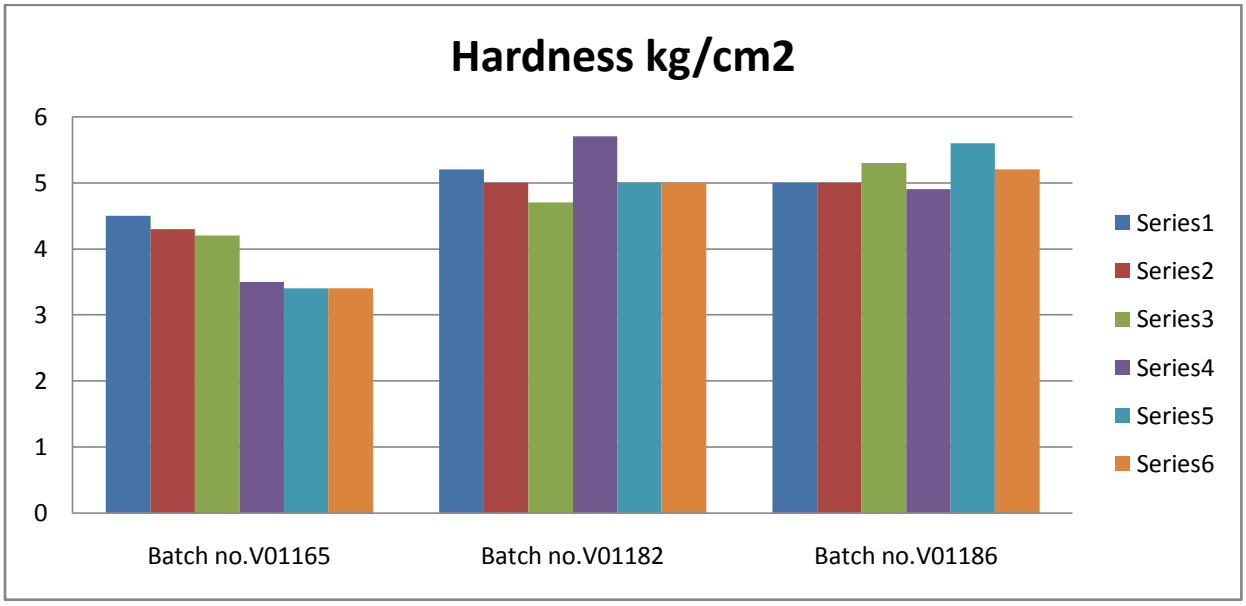


Figure 4.1.5: Bar chart to show to Hardness variation test of TENOLOC

Table 4.1.6: Comparative Friability Test Result

Brand name	Initial Weight of 10 tablet (gm)	Final weight of 10 tablet (gm)	Friability(%)
TENOLOC	3.145	2.904	7.663
	3.097	2.86	7.653
	3.13	2.89	7.668

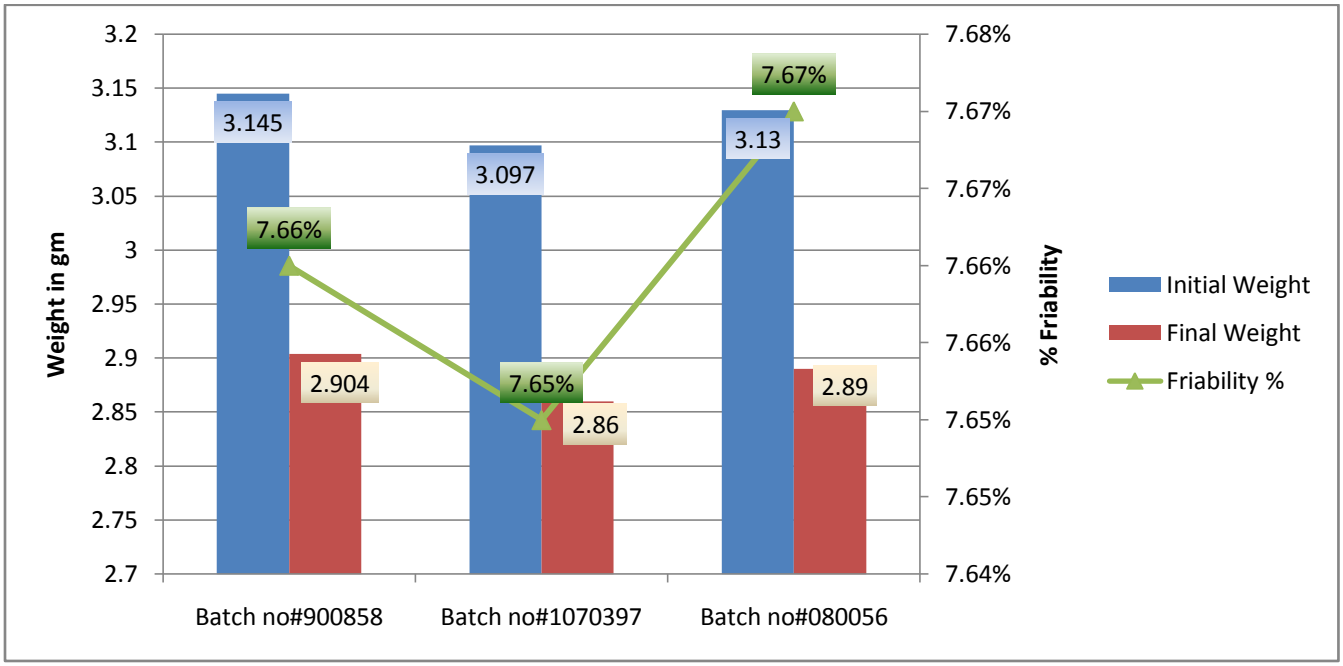


Figure 4.1.6:Bar chart to show percentage friability of TENOLOC

Absorbance

Concentration mg/100 ml	Absorbance (275nm)
4	0.2
5	0.24
10	0.46
20	0.92

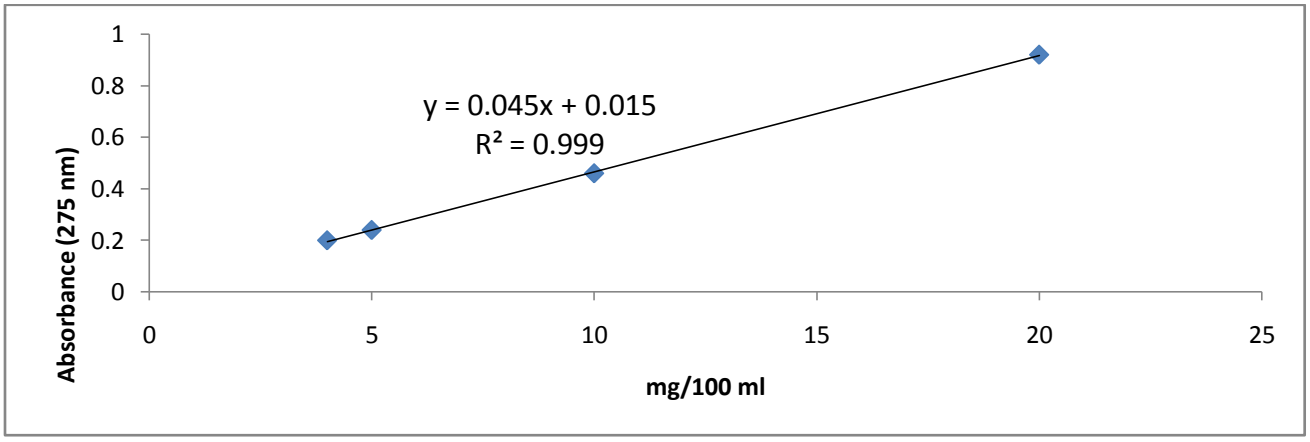


Table 4.1.7:Dissolution test of TENOLOC Tablet

Tenoloc			
Sample	Absorbance	Con. Mg/100ml	% release
1	0.526	11.33	113.30
2	0.48	10.31	102.22
3	0.468	10.04	100.44
4	0.476	10.22	102.22
5	0.469	10.07	100.67
6	0.497	10.69	106.87

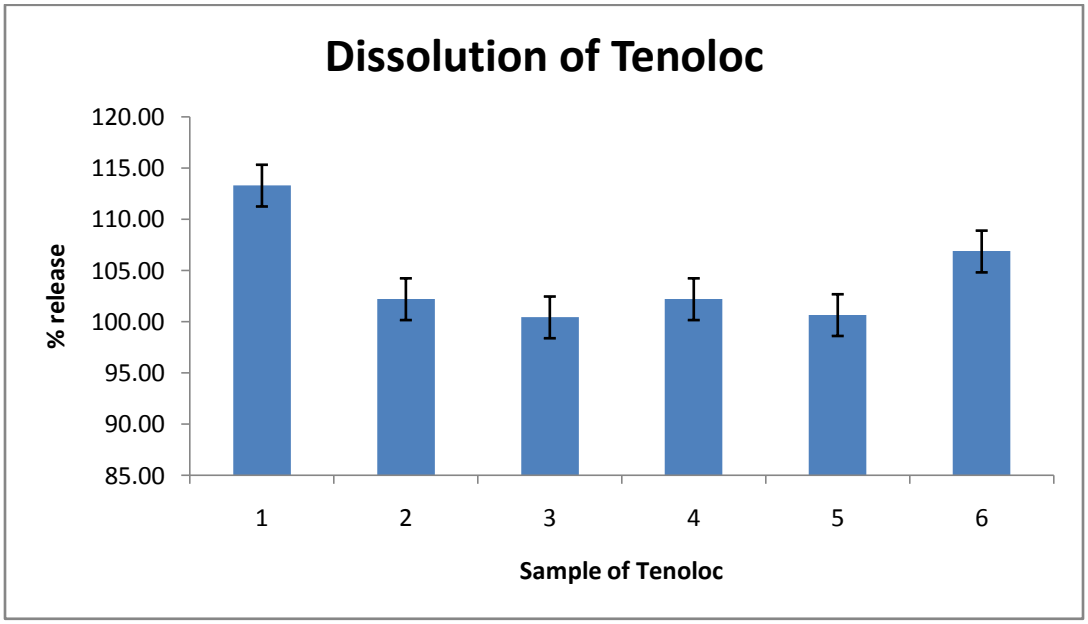


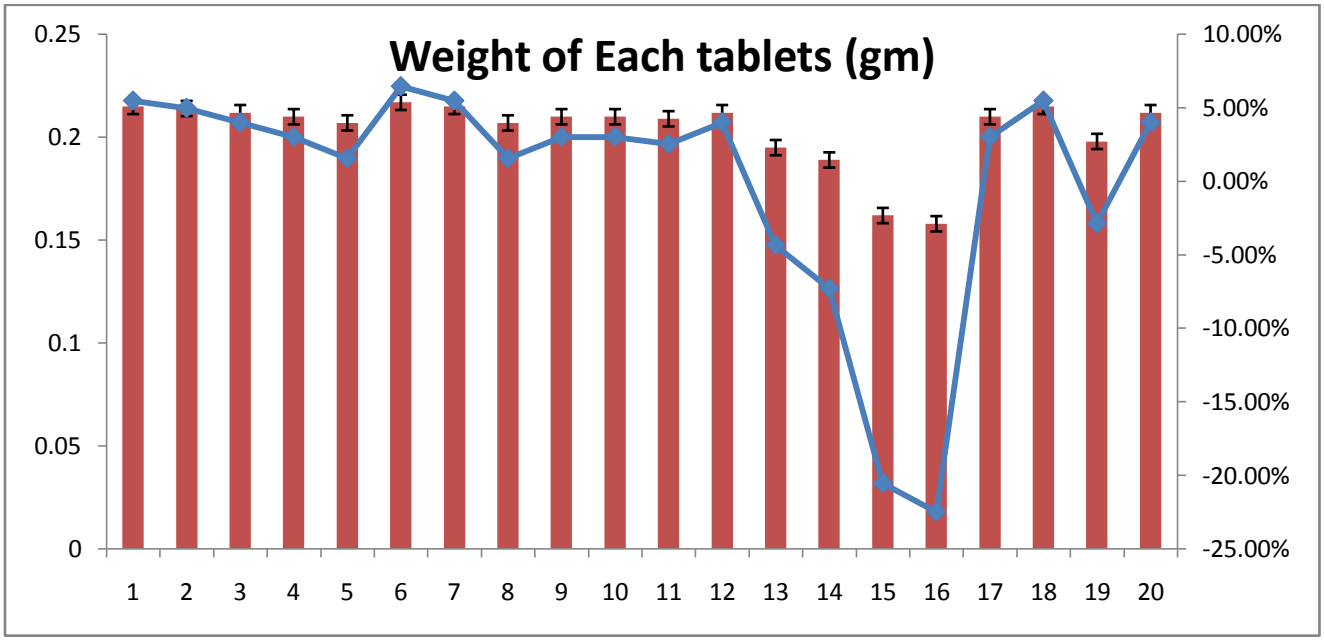
Figure 4.1.7: Bar chart to show dissolution of TENOLOC

4.2.1. Data

Generic name: Atenolol
Brand name: TENOREN 50 mg
Batch No. : V0116
Manufacturer: ACI Pharmaceutical Limited.

Table 4.2.1: Weight Variation Result

Tablet No.	Initial Weight of each tablet(gm)	Total Weight of 20 tablets(gm)	Average Weight(gm)	Weight Variation (%)	Average Weight Variation (%)
1	0.215	4.077	0.20385	5.47	-0.0002
2	0.214			4.98	
3	0.212			3.991	
4	0.21			3.017	
5	0.207			1.55	
6	0.217			6.451	
7	0.215			5.47	
8	0.207			1.545	
9	0.21			3.017	
10	0.21			3.017	
11	0.209			2.526	
12	0.212			3.998	
13	0.195			-4.341	
14	0.189			-7.286	
15	0.162			-20.529	
16	0.158			-22.492	
17	0.21			3.017	
18	0.215			5.47	
19	0.198			-2.87	
20	0.212			3.998	



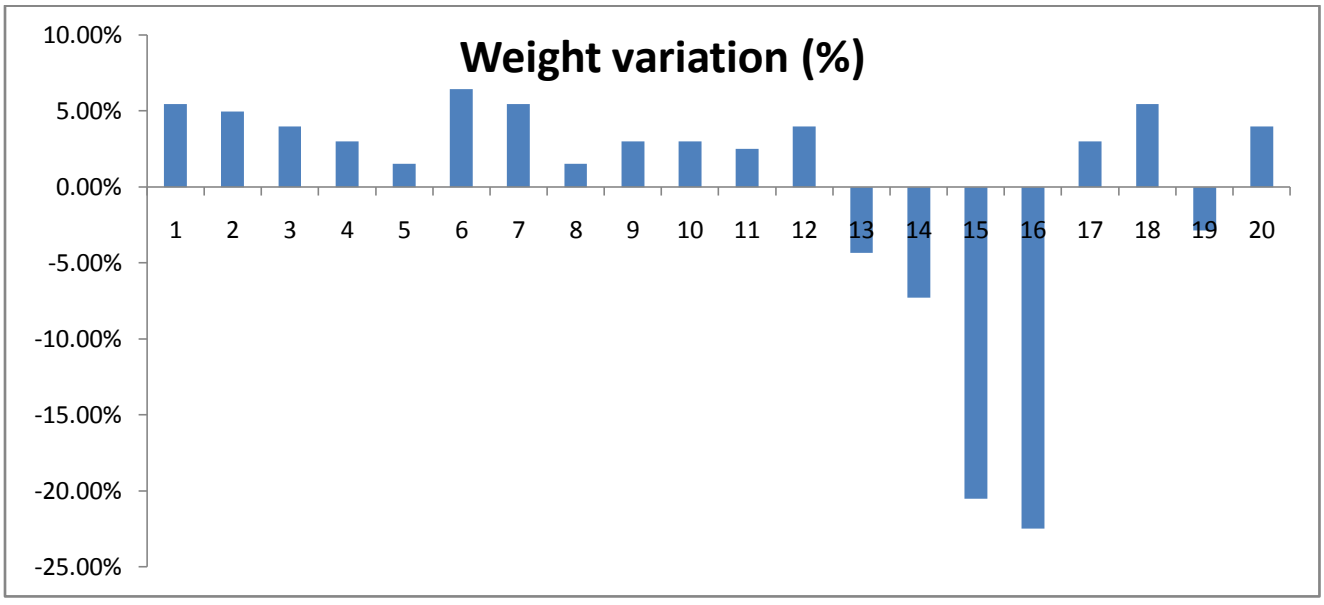


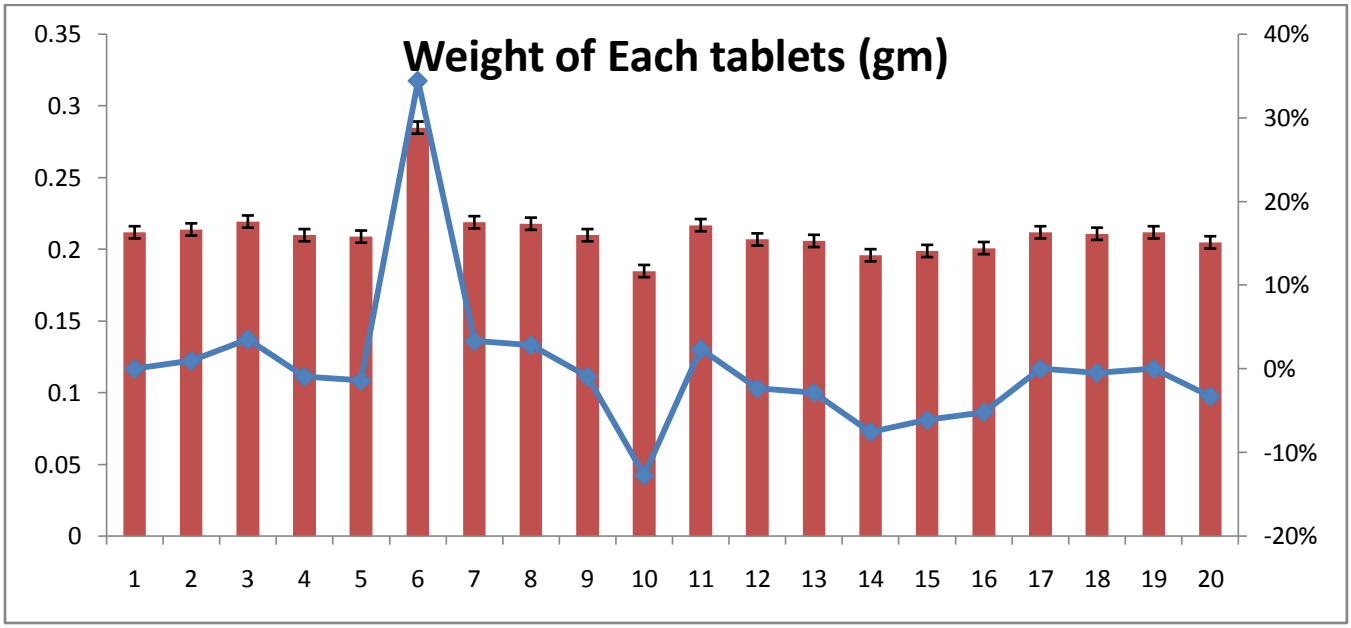
Figure 4.2.1: Bar chart to show weight variation of TENOREN Batch#0116

Generic name: Atenolol

Brand name: TENOREN 50 mg
Batch No. : V0118
Manufacturer: ACI Pharmaceutical Limited.

Table 4.2.2: Weight Variation Result

Tablet No.	Initial Weight of each tablet(gm)	Total Weight of 20 tablets(gm)	Average Weight(gm)	Weight Variation (%)	Average Weight Variation (%)
1	0.212	4.505	0.20385	0	.177
2	0.214			0.943	
3	0.2195			3.538	
4	0.21			-0.94	
5	0.209			-1.42	
6	0.285			34.434	
7	0.219			3.302	
8	0.218			2.830	
9	0.21			-0.943	
10	0.185			-12.74	
11	0.217			2.358	
12	0.207			-2.358	
13	0.206			-2.830	
14	0.196			-7.547	
15	0.199			-6.132	
16	0.201			-5.189	
17	0.212			0	
18	0.211			-0.472	
19	0.212			0	
20	0.205			-3.302	



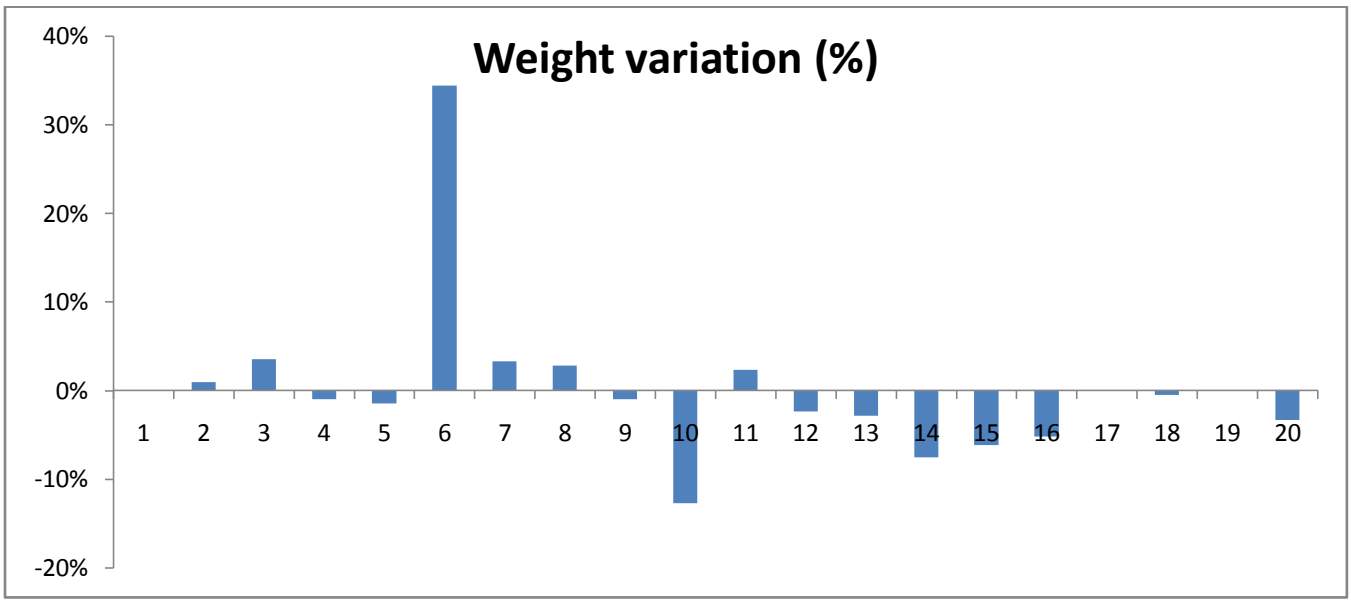
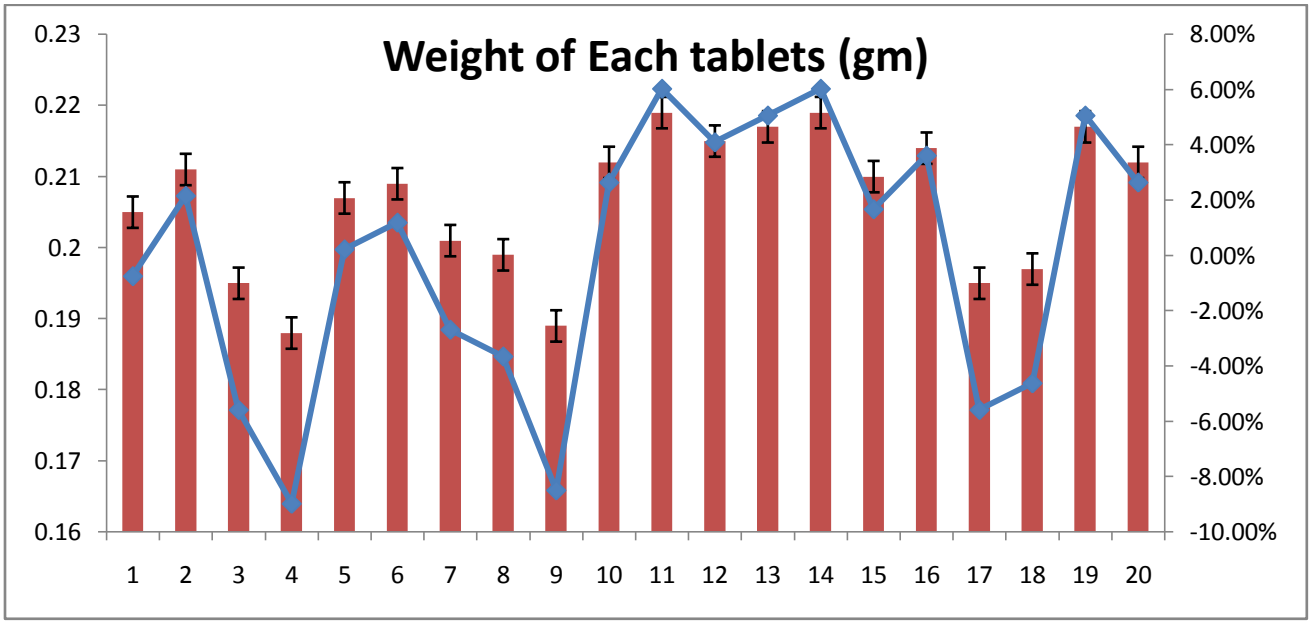


Figure 4.2.2: Bar chart to show weight variation of TENOREN Batch#118

Generic name: Atenolol
Brand name: TENOREN 50 mg
Batch No. : V0117
Manufacturer: ACI Pharmaceutical Limited.

Table 4.2.3: Weight Variation Result

Tablet No.	Initial Weight of each tablet(gm)	Total Weight of 20 tablets(gm)	Average Weight(gm)	Weight Variation(%)	Average Weight Variation (%)
1	0.205	4.425	0.20655	-0.750	0.00025
2	0.211			2.154	
3	0.195			-5.591	
4	0.188			-8.980	
5	0.207			0.218	
6	0.209			1.186	
7	0.201			-2.687	
8	0.199			-3.655	
9	0.189			-8.497	
10	0.212			2.639	
11	0.219			6.028	
12	0.215			4.091	
13	0.217			5.06	
14	0.219			6.028	
15	0.21			1.670	
16	0.214			3.607	
17	0.195			-5.59	
18	0.197			-4.624	
19	0.217			5.059	
20	0.212			2.639	



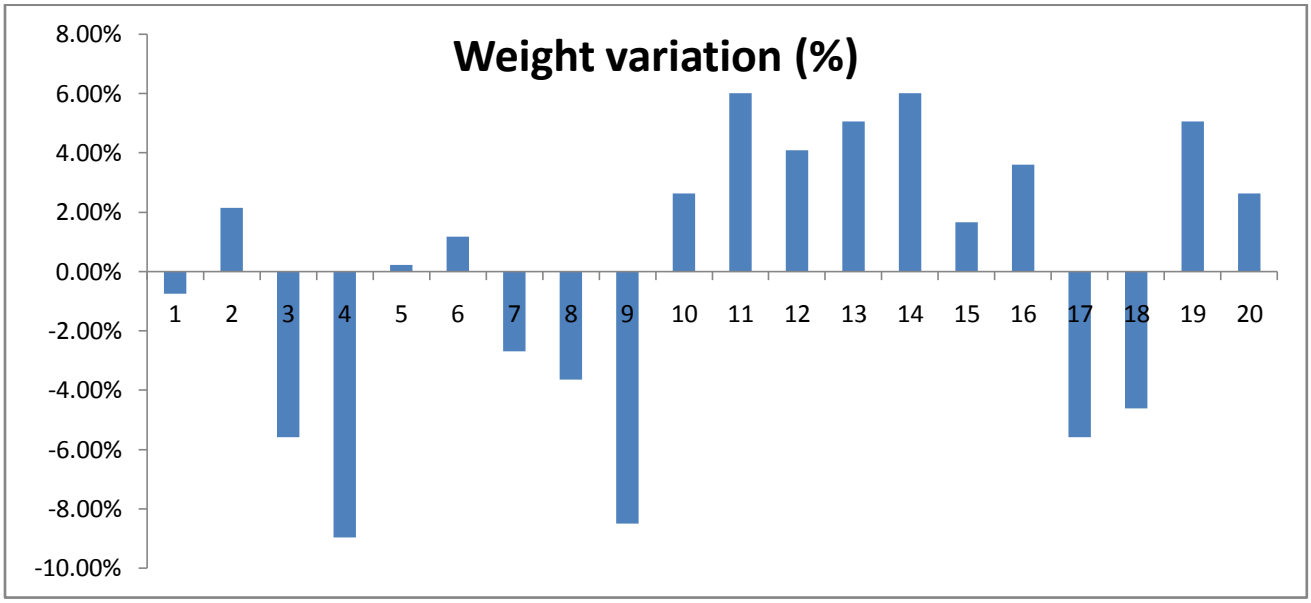


Figure 4.2.3: Bar chart to show weight variation of TENOREN Batch#0117

Table 4.2.4: Disintegration Time test Result of Tenoren:

DISINTEGRATION			
Tablet sample	**Batch no.0116**	**Batch no.118**	**Batch no.117**
1	2.36	1.43	2.36
2	2.41	1.1	2.18
3	2.05	0.59	2.22
4	2.18	1.31	2.33
5	2.27	1.35	2.39
6	2.47	1.18	2.1

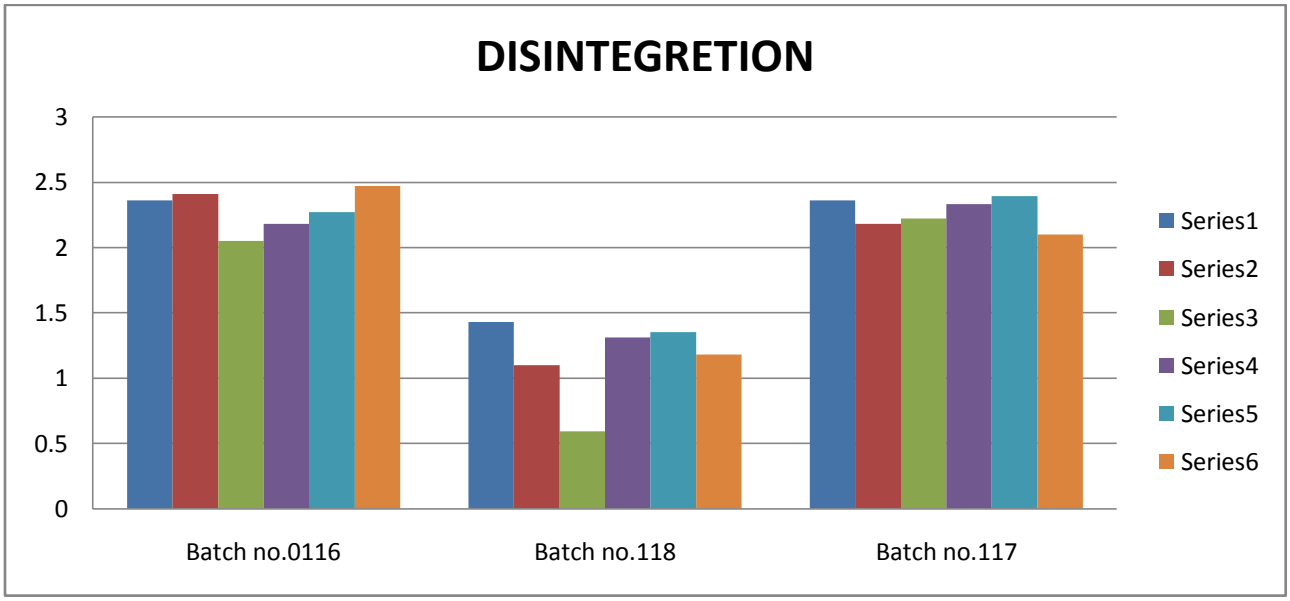


Figure 4.2.4: Bar chart to show Disintegration test Result of TENOREN

Table 4.2.5: Hardness test Result of Tenoren:

Hardness kg/cm2			
Tablet sample	**Batch no.0116**	**Batch no.118**	**Batch no.117**
1	5	5.2	5.2
2	5	5.5	5
3	5.3	5.4	5
4	4.9	5	4.9
5	5.6	5.3	4.8
6	5.2	4.9	4.9

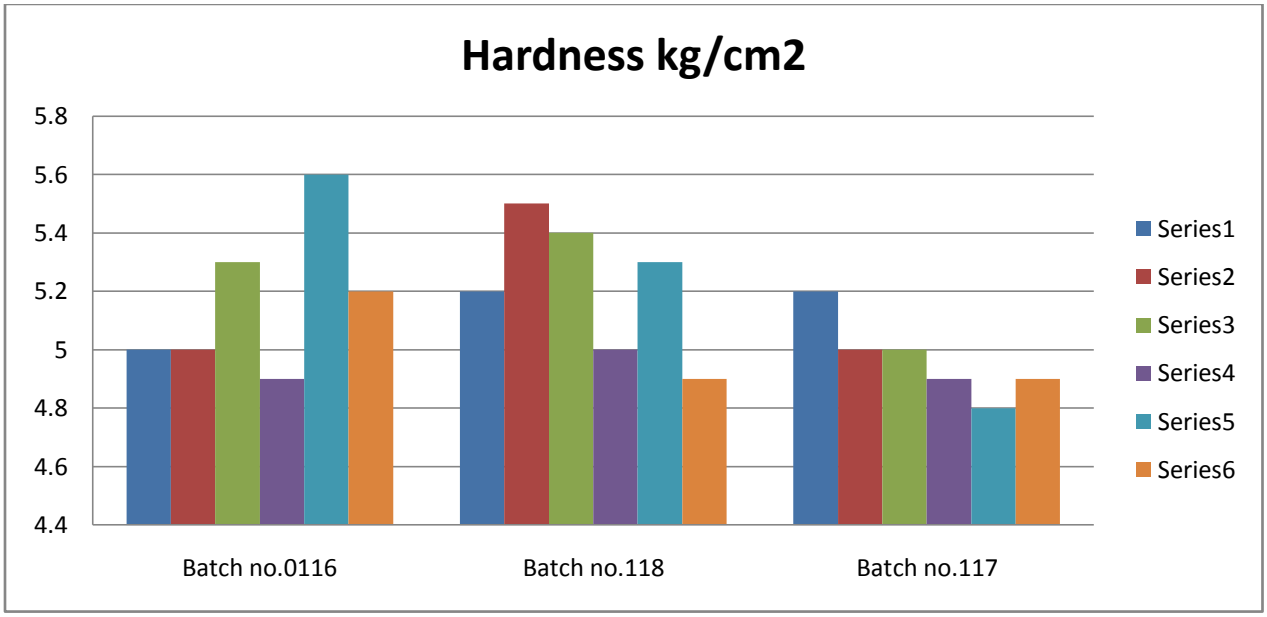


Figure 4.2.5: Bar chart to show Hardness test Result of TENOREN

Table 4.2.6: Comparative Friability Test Result of Tenoren

Brand name	Initial Weight of 10 tablet (gm)	Final weight of 10 tablet (gm)	Friability (%)
TENOREN	2.13	2.02	5.164
	2.23	2.11	5.381
	2.19	2.05	6.393

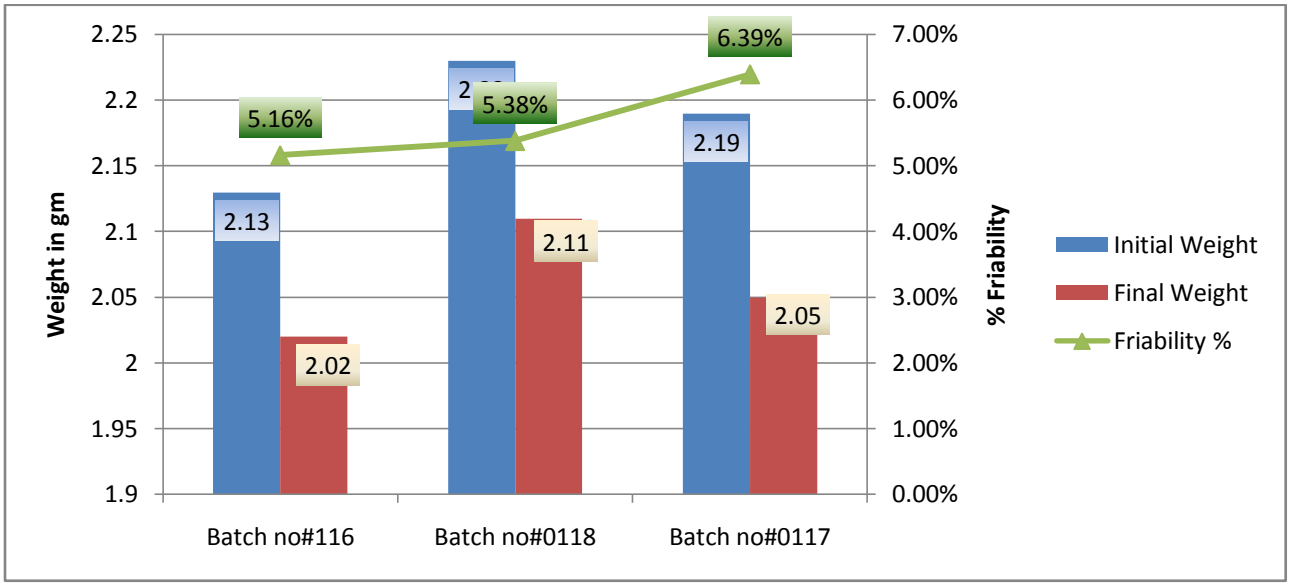


Figure 4.2.6: Bar chart to show percentage friability of TENOREN

Table 4.2.7: Dissolution of TENOREN Tablet

Tenoren			
Sample	**Absorbance**	**Con. Mg/100ml**	**% release**
1	0.512	11.02	110.20
2	0.504	10.84	108.43
3	0.501	10.78	107.76
4	0.507	10.91	109.09
5	0.495	10.64	106.43
6	0.496	10.67	106.65

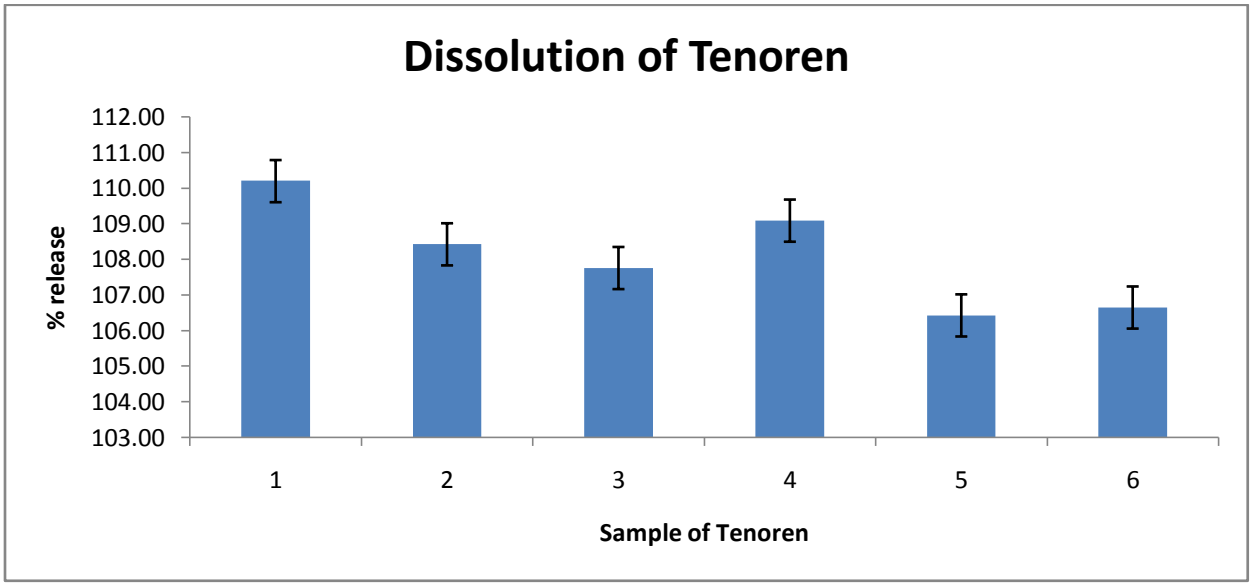


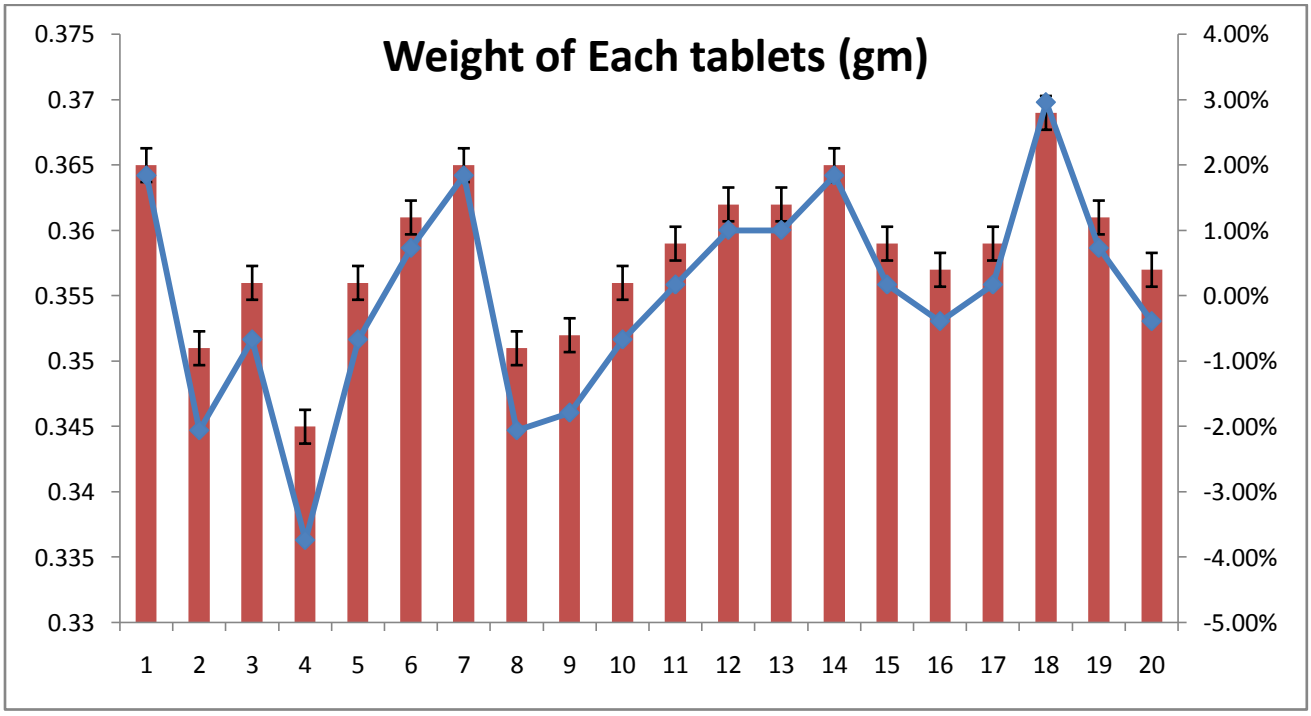
Figure4.2.7: Bar chart to show dissolution of TENOREN

Data 4.3

Generic name: Atenolol
Brand name: CARDIPRO 50 mg
Batch No. : 202001
Manufacturer: Square Pharmaceutical Limited.

TABLE 4.3.1: Weight Variation Result

Tablet No.	Initial Wait of each tablet(gm)	Total Weight of 20 tablets(gm)	Average Weight(gm)	Weight Variation (%)	Average Weight Variation (%)
1	0.365	7.168	0.3584	1.84	.0009
2	0.351			-2.06	
3	0.356			-0.67	
4	0.345			-3.74	
5	0.356			-0.67	
6	0.361			0.73	
7	0.365			1.84	
8	0.351			-2.06	
9	0.352			-1.79	
10	0.356			-0.67	
11	0.359			0.17	
12	0.362			1.004	
13	0.362			1.004	
14	0.365			1.84	
15	0.359			0.17	
16	0.357			-0.39	
17	0.359			0.17	
18	0.369			2.96	
19	0.361			0.73	
20	0.357			-0.39	



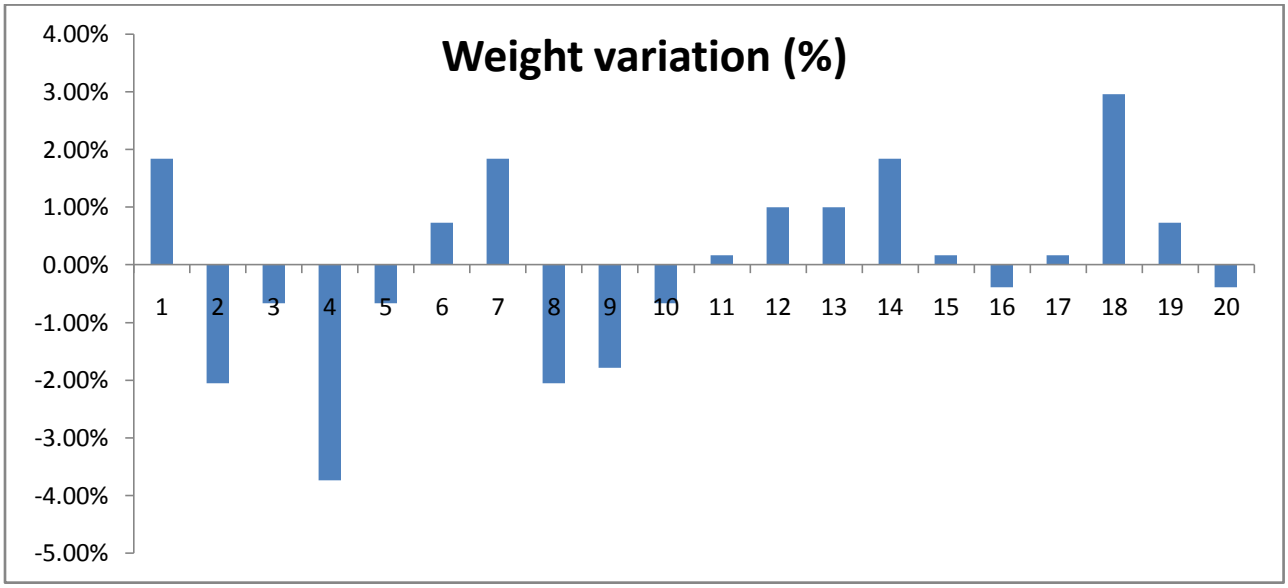
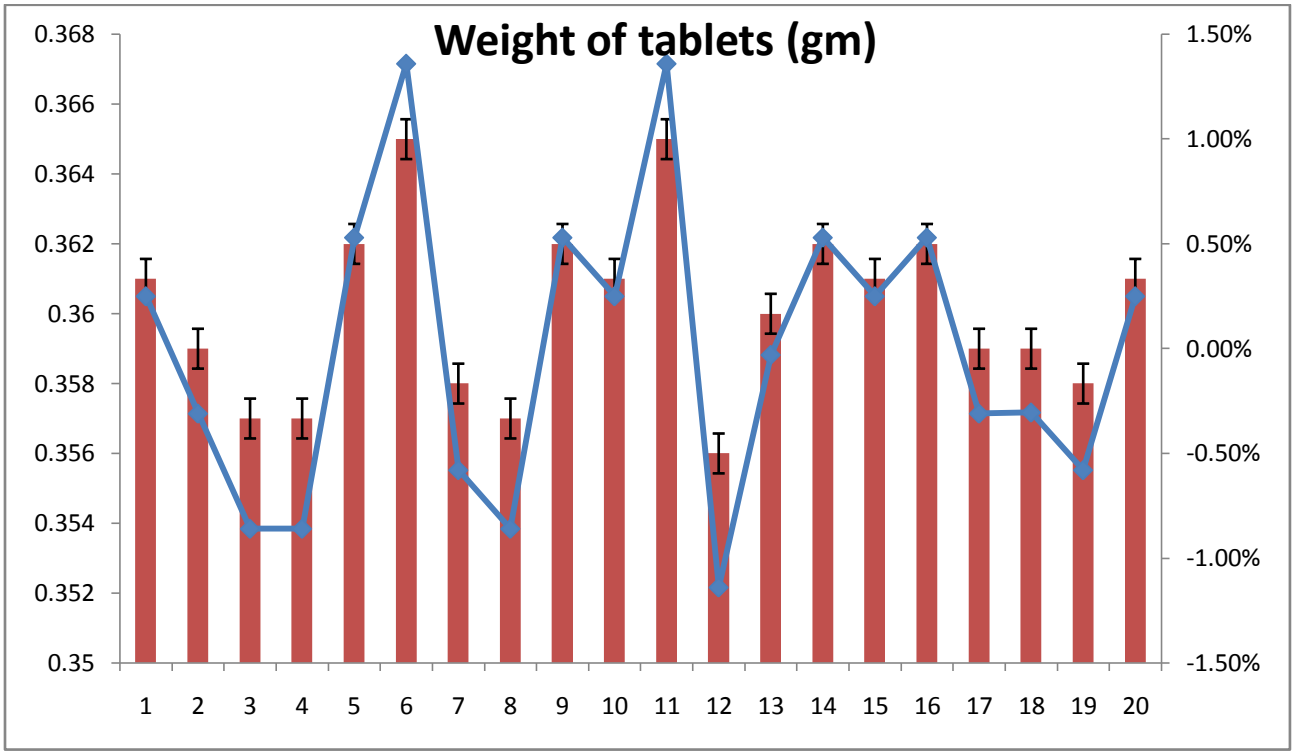


Figure 4.3.1: Bar chart to show weight variation of CARDIPRO Batch#202001

Generic name: Atenolol
Brand name: CARDIPRO 50 mg
Batch No. : 1070194
Manufacturer: Square Pharmaceutical Limited.

Table 4.3.2: Weight Variation Result

Tablet No.	Initial Wait of each tablet(gm)	Total Weight of 20 tablets(gm)	Average Weight(gm)	Weight Variation(%)	Average Weight Variation(%)
1	0.361	7.202	0.3601	0.25	0.00025
2	0.359			-0.31	
3	0.357			-0.86	
4	0.357			-0.86	
5	0.362			0.53	
6	0.365			1.36	
7	0.358			-0.58	
8	0.357			-0.86	
9	0.362			0.53	
10	0.361			0.25	
11	0.365			1.36	
12	0.356			-1.14	
13	0.36			-0.03	
14	0.362			0.53	
15	0.361			0.25	
16	0.362			0.53	
17	0.359			-0.31	
18	0.359			-0.305	
19	0.358			-0.58	
20	0.361			0.25	



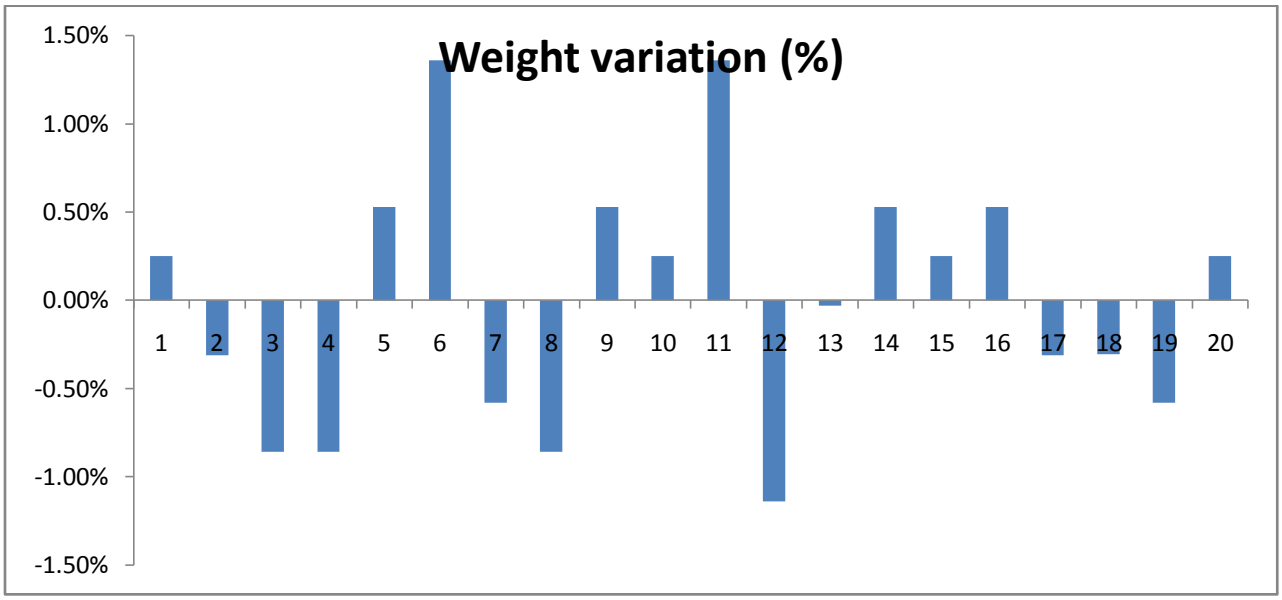
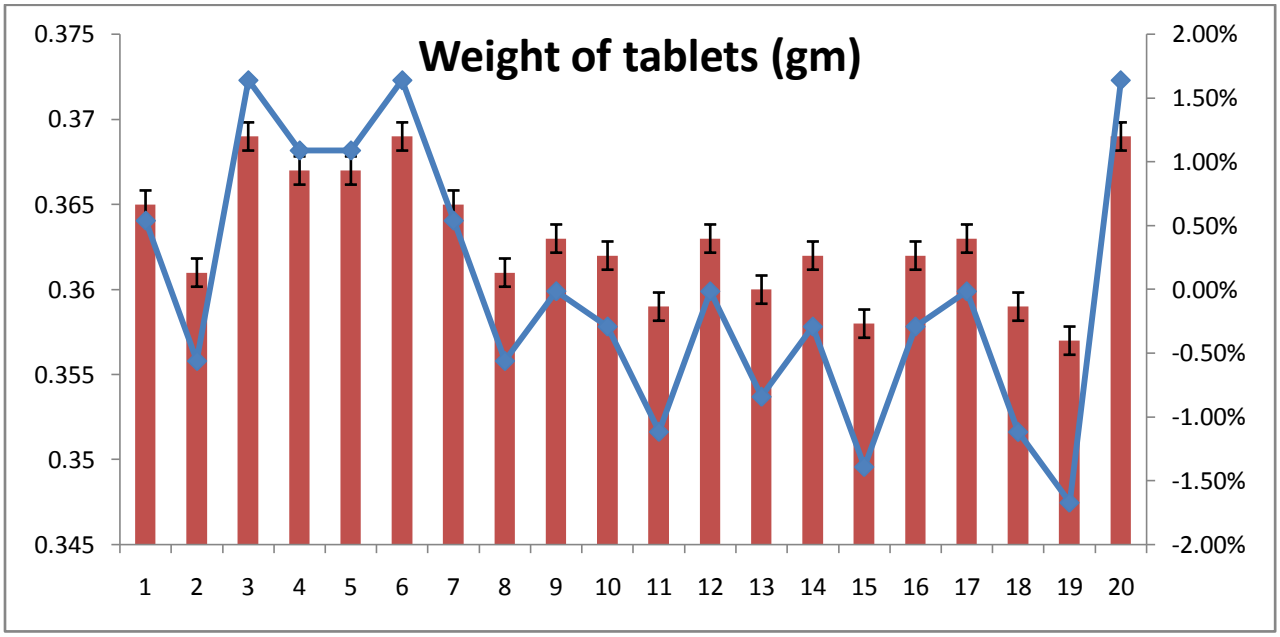


Figure 4.3.2: Bar chart to show weight variation of CARDIPRO Batch#1070194

Generic name: Atenolol
Brand name: CARDIPRO 50 mg
Batch No. : 202002
Manufacturer: Square Pharmaceutical Limited.

Table 4.3.3: Weight Variation Result

Tablet No.	Initial Weight of each tablet(gm)	Total Weight of 20 tablets(gm)	Average Weight(gm)	Weight Variation (%)	Average Weight Variation (%)
1	0.365	7.261	0.36	0.54	1.689
2	0.361			-0.56	
3	0.369			1.64	
4	0.367			1.09	
5	0.367			1.09	
6	0.369			1.64	
7	0.365			0.54	
8	0.361			-0.56	
9	0.363			-0.013	
10	0.362			-0.29	
11	0.359			-1.115	
12	0.363			-0.014	
13	0.36			-0.840	
14	0.362			-0.29	
15	0.358			-1.390	
16	0.362			-0.29	
17	0.363			-0.014	
18	0.359			-1.116	
19	0.357			-1.67	
20	0.369			1.64	



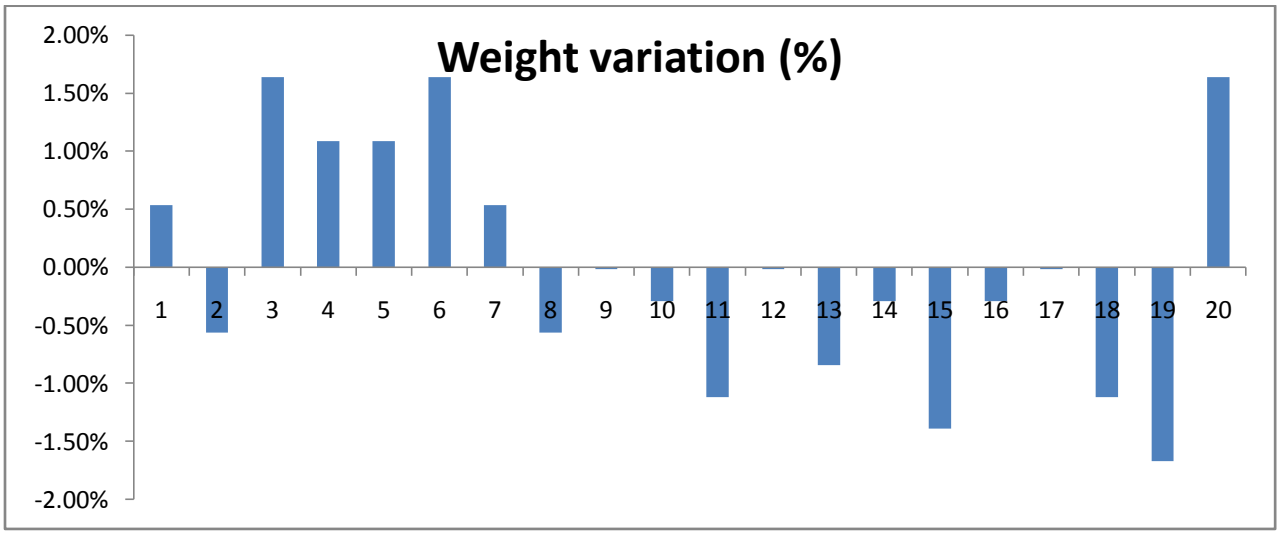


Figure 4.3.3: Bar chart to show weight variation of CARDIPRO Batch#201002

Table 4.3.4: Disintegration of Cardipro

DISINTEGRATION			
Tablet sample	**Batch no.202001**	**Batch no.1070194**	**Batch no.202002**
CARDIPRO	7.24	10.33	8.6
	1.45	9.24	10.2
	2.02	7.57	7.9
	5.58	10.24	7.8
	3.1	10.54	8.1
	5.28	9.47	8.3

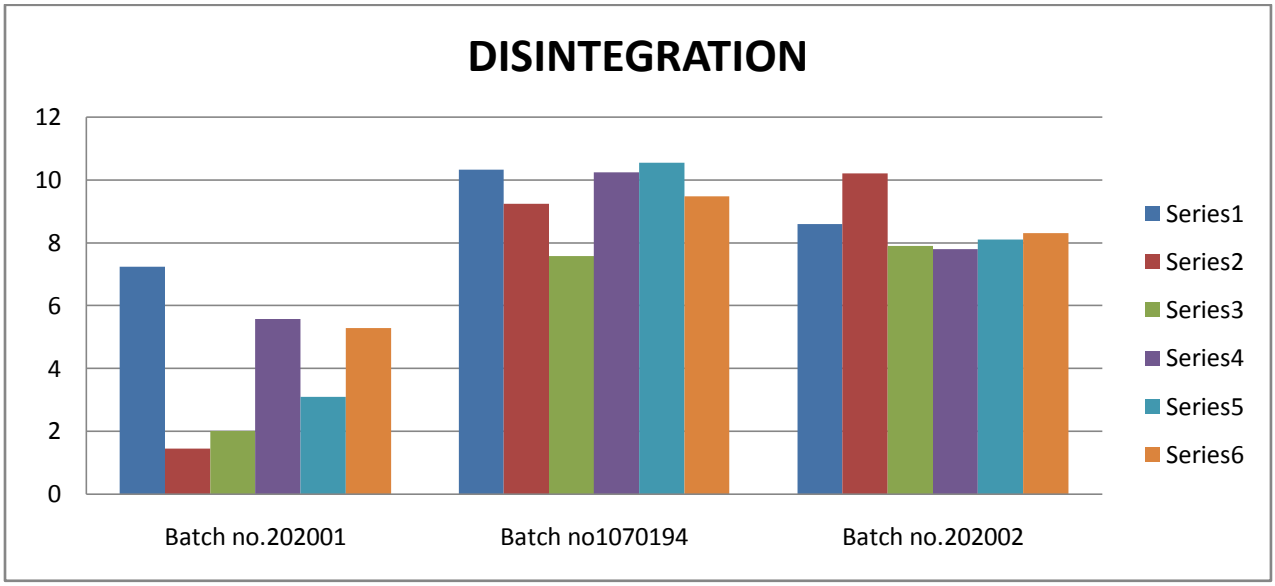


Figure 4.3.4: Bar chart to show Hardness test Result CARDIPRO

Table 4.3.5: Hardness test Result of Cardipro

HARDNESS			
Tablet sample	**Batch no.202001**	**Batch no.1070194**	**Batch no.202002**
CARDIPRO	5.9	6.1	5.9
	5.8	6.1	6
	6.2	6	5.9
	6	6.4	6.3

	6	5.9	6.2
	6.1	6.2	6

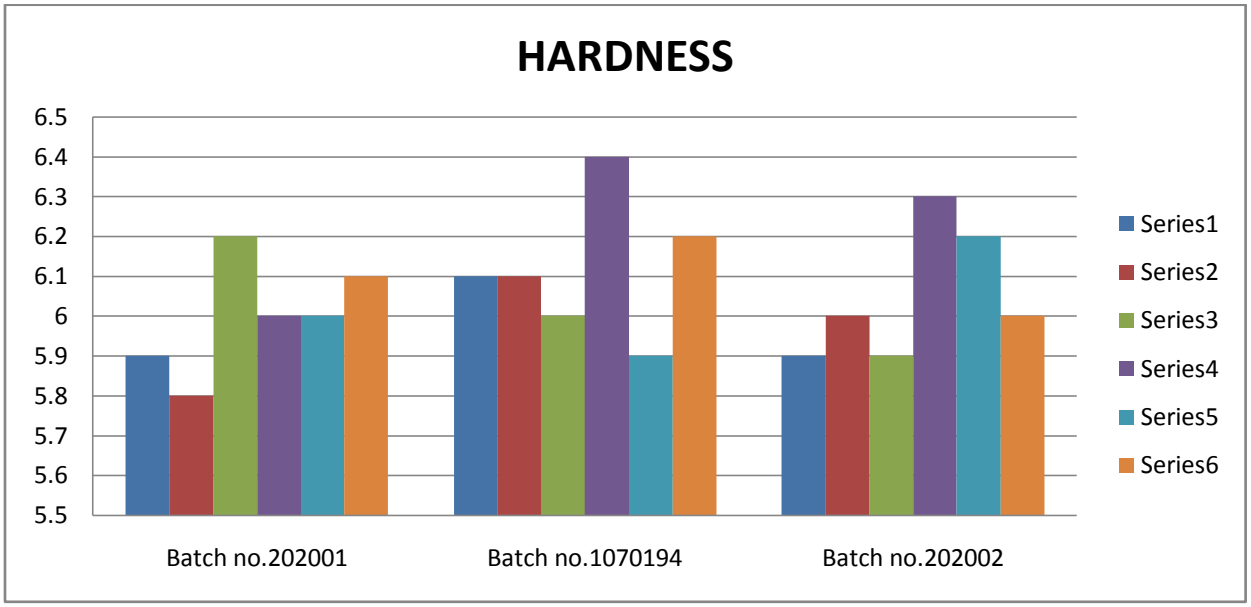


Figure 4.3.5: Bar chart to show Hardness test Result CARDIPRO

Table No 4.3.6: Friability test of CARDIPRO Tablet

Brand name	Initial Weight of 10 tablet (gm)	Final weight of10 tablet (gm)	Friability(%)
CARDIPRO	3.6	3.41	5.278
	3.62	3.45	4.696
	3.71	3.59	3.235

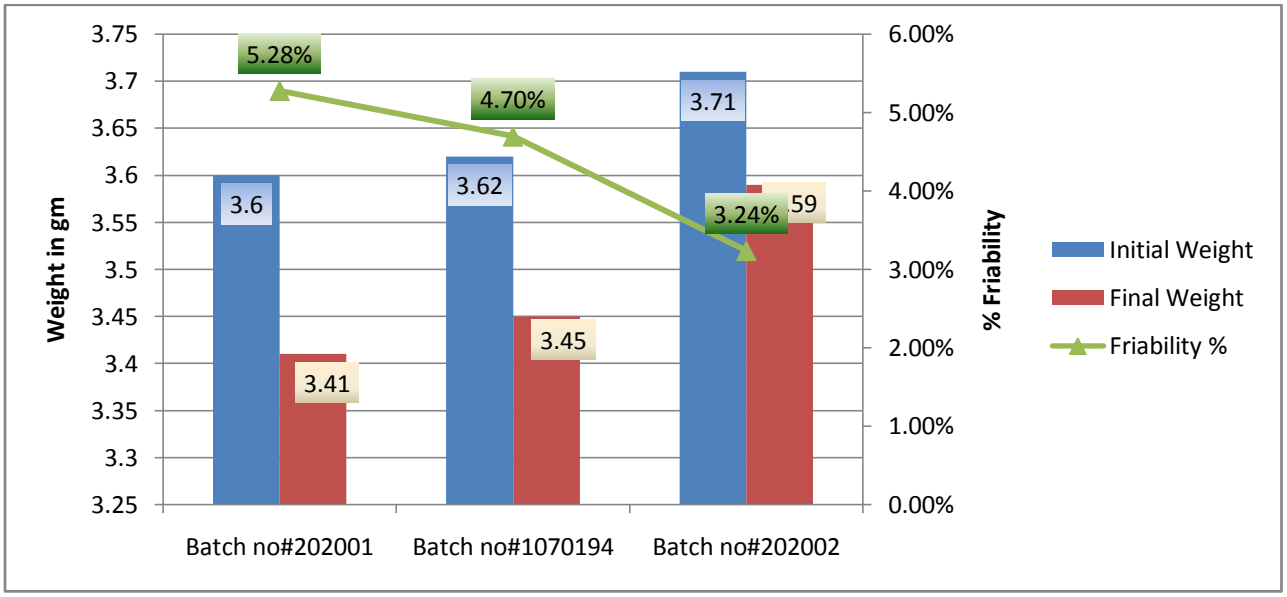


Figure 4.3.6 : Bar chart to show percentage friability of CARDIPRO

Table 4.3.7 : Dissolution of CARDIPRO Tablet

Cardipro			
Sample	**Absorbance**	**Con. Mg/100ml**	**% release**
1	0.501	10.78	107.76
2	0.523	11.26	112.64
3	0.51	10.98	109.76
4	0.53	11.42	114.19
5	0.621	13.44	134.37
6	0.537	11.57	115.74

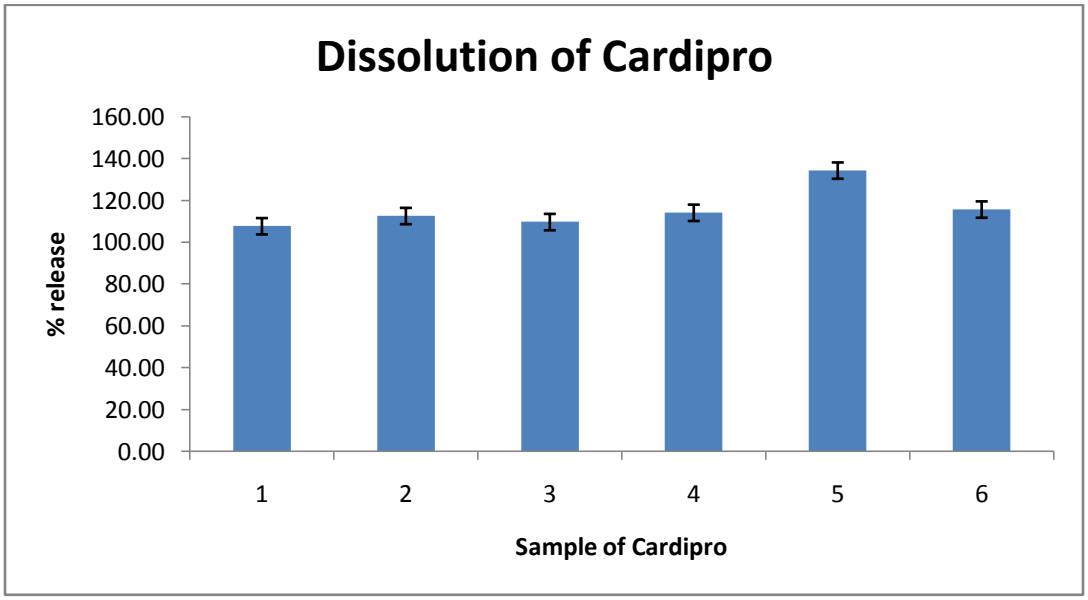


Figure 4.3.7: Bar chart to show dissolution of CARDIPRO

4.4. Discussion

The weight variation for all the tablets with in USP specification i.e not deviated by up to 5% for their average weight.

The hardness test all tablets (both generics ATENOLOL and the TENOLOC, TENOREN, CARDIPRO brand) were done to assess the ability of tablets withstands handling without facture or ATENOLOL. A force about 4kg/cm2 is the minimum requirement for satisfactory hardness of tablets.

The result of hardness testing should that hardness of all generic ATENOLOL tablets that's brand-

TENOLOC were within the range between 3.88 mg to 5.1 mg.

TRNOREN were within the range between 4.97 mg to 5.22 mg.

CARDIPRO were within the range between 6 mg to 6.12 mg.

So the results say that all brands have the satisfactory hardness.

The result of friability for ATENOLOL of all tablets is very satisfactory

TENOLOC-from 7.653 to 6.668 are less than 10%w/w

TENOREN-from 5.381 to 6.393 are less than 10%w/w

CARDIPRO-from 3.235 to 5.278 are less than 10%w/w

Which indicate all tablets meets the requirements for friability.

The USP specification for uncoated tablets should disintegrate within 15 minutes. All the generic ATENOLOL tablets including-

TENOLOC brand 1.598 to 3.185 minute

TENOREN brand 1.16 to 2.29 minute

CARDIPRO brand 4.11 to 9.565 minute

Which is satisfactory result.

Conclusion & Reference

Conclusion:

In this study we have observed that in the quality control parameter testing study most case the three batches have passed. In weight variation test all the tablets have passed but there is batch to batch variation may occur due changes in the formulation. May be due changes of diluents. All the three batches have passed hardness test, friability test.There is no significant variation into the thickness of batches. Disintegration time of the tablets is almost similar. Dissolution profile of three batches is very good and there is no batch to batch variation. So more care should be given by the Pharmaceutical Company during the production and marketing of medicine because pharmaceutical companies are dealing with the life of human.

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