Evaluation of the Quality Control Parameters of Two Different Brands of Combined Atenolol (50mg) & Amlodipine (5mg) Tablets Available in Bangladesh

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Evaluation of the Quality Control Parameters of Two Different Brands of Combined Atenolol (50mg) & Amlodipine (5mg) Tablets Available in Bangladesh

A thesis report submitted to the Department of Pharmacy, East West University, in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy

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Declaration by the Research Candidate

I, Jinat Ashrafi, hereby declare that the dissertation entitled “Evaluation of the Quality Control Parameters of Two Different Brands of Combined Atenolol (50mg) & Amlodipine (5mg) Tablets Available in Bangladesh” submitted by me to the Department of Pharmacy, East West University, in the partial fulfillment of the requirement for the award of the degree Bachelor of Pharmacy is a bonafied record of original research work carried out by me. The thesis has not formed the basis for the award of any other degree or diploma or fellowship or other similar title to any candidate of any university.

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Dedicated
To
My Beloved Parents

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ABSTRACT

Hypertension is a very common disease. To treat this disease in short possible time combination drugs came in the market, because these are more efficacious and have low side effects. Amlodipine and Atenolol combination is widely used in Bangladesh for hypertension treatment. So quality control studies are performed in different marketed products in Bangladesh. The main objective of this study was to perform a comparative evaluation of the quality control parameters of two commercially available brands of combined atenolol (50mg) & amlodipine (5mg) tablets marketed by local pharmaceutical companies. Tablets from four batches of Camlodin® Plus and Amlovas® AT met the specification of USP for weight variation and thickness test. In hardness evaluation all four batches of two brands showed lower value than the specified range (4 to 8 or 10 kg). For disintegration test all batches met the specification of BP. In potency determining test for Amlodipine, only Batch-SGJ52 of Amlovas® AT (86%) did not met the specified range (90 to 110%) of BP. But in case of Atenolol all batches of two brand met the specification of BP. In dissolution study all batch of two brands met the specification of BP. Hardness and Potency of some batch did not met the specification due to formulation, processing or analytical error. Due to technical problem friability study could not be done. Further study needs to be conducted regarding the quality control parameters as these products are now becoming a potential choice of drugs for hypertension control.

Keywords: Atenolol, Amlodipine, weight variation, thickness, hardness, disintegration, potency, dissolution.

CHAPTER-1

INTRODUCTION

Chapter 1

INTRODUCTION

1.1 General

The huge cost and expenses in clinical trials for the development of novel drug by pharmaceutical companies is rewarded through achieving its drug patent for a certain period of time that protects the product from competition in the market. But, when the patent of innovator drug products expired, it gives an opportunity to several pharmaceutical companies to produce their own generic drug brands. Even though there are many drug brands available of same type of generic in the market, effective monitoring of the quality of products marketed are absent in many countries. This matter raises a few issues. One of it is the widespread distribution of substandard or counterfeit drug products. Substandard drug products can be defined as genuine drugs manufactured by authorized manufacturers but do not meet the quality specifications fixed for them by national standards. There are many causes and problems associated with substandard drugs. The common problems may include wrong concentration of active ingredient, poor quality of excipients and active ingredients, contamination of the product, problems in packaging as well as decomposition of active ingredients (Dharmalingam *et al*, 2014).

Thus, monitoring of drugs in the market is vital. WHO has issued many guidelines for global standard and requirements for the assessment, authorization, registration, marketing as well as quality assurance of the drug products. Monitoring marketed drugs can lessen a country's economic problem as well as health issues due to fraud and substandard drugs usage (Dharmalingam *et al*, 2014).

Here comes the importance of quality control of drugs. Quality control is a small part of quality assurance and it is concerned with sampling, testing, and documentation during manufacturing and also after completion of manufacturing that is used to ensure a certain level of quality in a product. Quality control is the monitoring process through which manufacturer measures actual quality performance of their product, comparing it with standards and also finds out the deviation from standard to ensure the equality of product. In general terms, quality control refers to a procedure or a set of steps taken during

manufacturing of a product to ensure that it meets requirements and the product is reproducible (Jim Heaphy, 2007).

So, Quality control methods of assessment are useful to monitor quality characteristics of various marketed brands and product consistency of batch to batch drug release. In addition, drugs that having three or more generic brand must be assessed and monitored to ensure its interchangeability with innovator brand (Jim Heaphy, 2007).

Hypertension is an increasingly important medical and public health problem. In Bangladesh, approximately 20% of adult and 40–65% of elderly people suffer from Hypertension. High incidence of metabolic syndrome and lifestyle-related factors like obesity, high salt intake, and less physical activity may play important role in the pathophysiology of Hypertension. The association of angiotensin-converting enzyme (ACE) gene polymorphism and low birth weight with blood pressure has been studied inadequately. Hypovitaminosis-D presumably plays role in the aetiopathogenesis of hypertension in patients. Treating hypertension is not an easy task because it does not related with only one kind of mechanism. There are several mechanisms in our body that enhance our blood pressure. So, a combination of therapy is suitable to control the hypertension. Studies suggested that the calcium channel blockers and beta-blockers have been found to be the most commonly prescribed antihypertensive drugs in Bangladesh. So, a product that is a combination of these blockers can be very helpful not only for the patient but also for treating the disease (Monwarul *et al*, 2012).

Now a day's, a product which is a combination of atenolol (beta-blocker) & amlodipine (calcium channel blocker) are widely prescribed for most of the hypertensive patient. It has the advantage of maintaining the blood pressure by functioning in two mechanisms. Thus it becomes a choice of drug for most of the physicians in recent times. This attracts most of the pharmaceutical company and now there are several brands available in Bangladesh pharma market (Monwarul *et al*, 2012).

1.2 Hypertension

Hypertension (HTN) or high blood pressure, sometimes called arterial hypertension, is a chronic medical condition in which the blood pressure in the arteries is elevated. Blood pressure is summarized by two measurements, systolic and diastolic, which depend on whether the heart muscle is contracting (systole) or relaxed between beats (diastole). This equals the maximum and minimum pressure, respectively. (Wikipedia, 2015)

Blood pressure (BP) is the pressure exerted by circulating blood upon the walls of blood vessels.

☐ Blood Pressure = Cardiac Output x Peripheral Vascular Resistance (PVR)

☐ Cardiac Output = Stroke Volume × Heart rate

1.3 Classification

The seventh report of the joint National committee classifies hypertension into four categories for the purpose of treatment management. The categories are shown in table 1.1

Table 1.1: Classification of hypertension

	Systolic mm Hg		Diastolic mm Hg
Normal	<120	and	<80
Prehyper-tension	120-139	or	80-89
Stage 1 (Mild hypertension)	140-159	or	90-99
Stage II	>160	or	>100

(Lippincott *et al*, 2009: p-225-226)

Hypertension puts strain on the heart, leading to hypertensive heart disease and coronary artery disease (Lewington *et al*, 2002). Hypertension is also a major risk factor for stroke, aneurysms of the arteries (e.g. aortic aneurysm), peripheral arterial disease and chronic kidney disease. (Wikipedia, 2015)

1.4 Symptoms

There is no guarantee that a person with hypertension will present any symptoms of the condition. About 33% of people actually do not know that they have high blood pressure, and this ignorance can last for years. For this reason, it is advisable to undergo periodic blood pressure screenings even when no symptoms are present. (Medicalnewstoday,2015)

Extremely high blood pressure may lead to some symptoms, however, and these include:

- Severe headaches
- Fatigue or confusion
- Dizziness
- Nausea
- Problems with vision
- Chest pains
- Breathing problems
- Irregular heartbeat
- Blood in the urine. (Medicalnewstoday,2015)

1.5 Causes of hypertension

1.5.1 Primary hypertension

Primary (essential) hypertension is the most common form of hypertension, accounting for 90–95% of all cases of hypertension.

- In almost all contemporary societies, blood pressure rises with aging and the risk of becoming hypertensive in later life is considerable. Hypertension results from a complex interaction of genes and environmental factors
- Insulin resistance, which is common in obesity and is a component of syndrome X (or the metabolic syndrome), is also thought to contribute to hypertension.
- Recent studies have also implicated events in early life (for example low birth weight, maternal smoking and lack of breast feeding) as risk factors for adult essential hypertension,
- Hypertension has also been associated with depression (Meng *et al*, 2012).

1.5.2 Secondary hypertension

Secondary hypertension results from an identifiable cause.

- Renal disease is the most common secondary cause of hypertension.
- Hypertension can also be caused by endocrine conditions, such as Cushing's syndrome, hyperthyroidism, hypothyroidism, Conn's syndrome or hyper aldosteronism, hyperparathyroidism.
- Other causes of secondary hypertension include obesity, sleep apnea, pregnancy, coarctation of the aorta, excessive liquorice consumption and certain prescription medicines, herbal remedies and illegal drugs (Grossman *et al*, 2012)

1.6 Treatment Strategies

The goal of antihypertensive therapy is to reduce cardiovascular adrenal morbidity and mortality. The relationship between blood pressure and the risk of cardiovascular events is continuous and thus lowering of even moderately elevated blood pressure significantly reduces cardiovascular disease. (Lippincott *et al*, 2009:p-227).

Prehypertension: recognizes this relationship and emphasizes the need for decreasing blood pressure in the general population by education and the adoption of blood pressure–lowering behaviors. For most patients, the blood pressure goal when treating hypertension is a systolic blood pressure of less than 140 mm Hg and a diastolic blood pressure of less than 90 mmHg (Lippincott *et al*, 2009:p-227).

Mild hypertension: can sometimes be controlled with mono therapy,but most patients require more than one drug to achieve blood pressure control. Current recommendations are to initiate therapy with thiazide diuretic, ACE inhibitor, angiotensin receptor blocker (ARB), or calcium channel blocker. If blood pressure is inadequately controlled, a second drug should be added, with the selection based on minimizing the adverse effects of the combined regimen and achieving goal blood pressure. (Lippincott *et al*, 2009:p-227).

Stage II Patients with systolic blood pressure greater than 160 mm Hg or diastolic blood pressure greater than 100 mm Hg (or systolic blood pressure greater than 20 mm Hg above goal or diastolic blood pressure more than 10 mm Hg above goal) should be started on two antihypertensive simultaneously (Lippincott *et al*, 2009:p-227).

1.7 Hypertension management

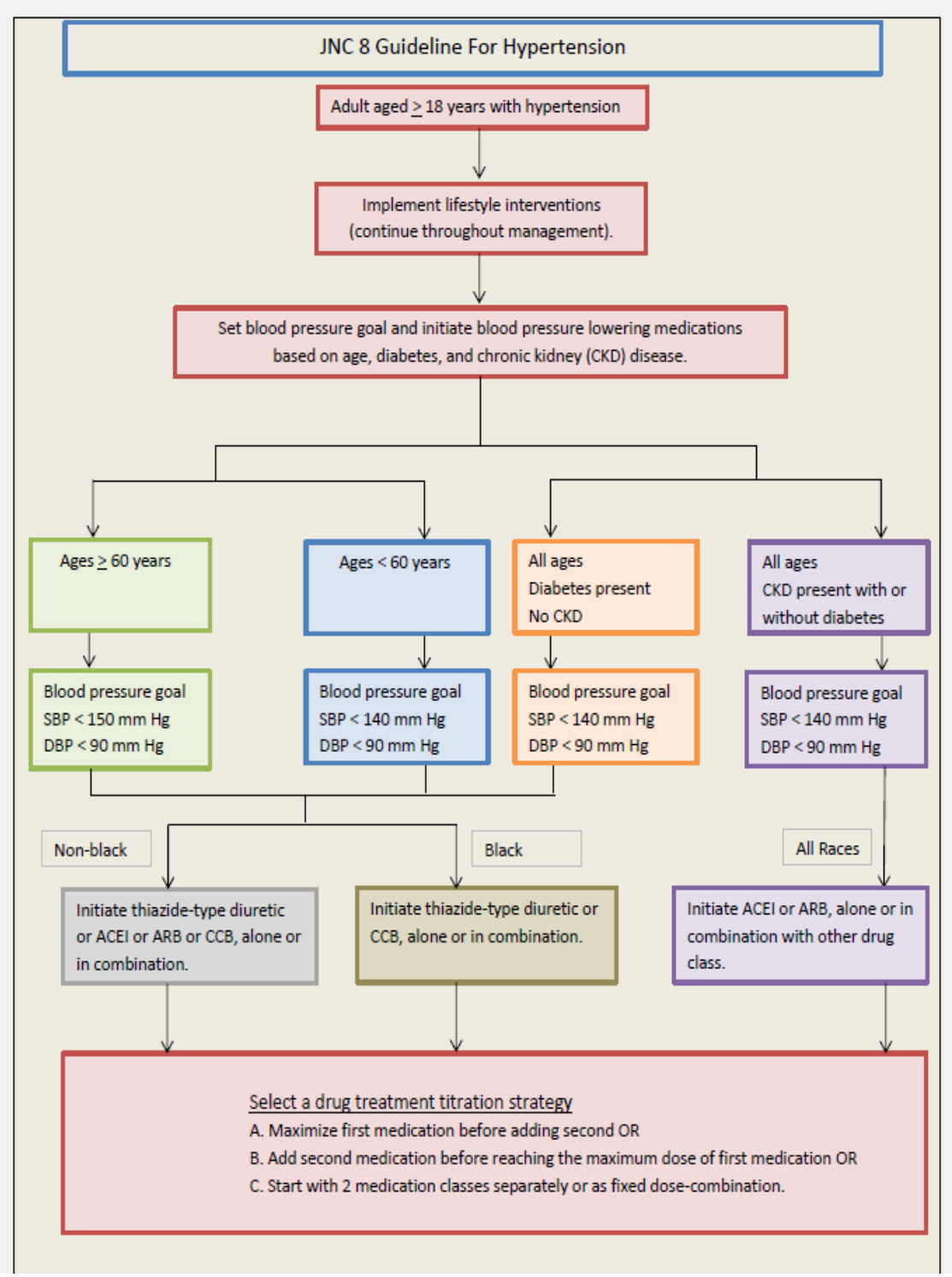


Fig 1.1: Hypertension Management (Pharmacyexam, 2015)

1.8 Classification for antihypertensive drug

Type	Mechanism of Action	Examples
Diuretics	Lowers BP initially by increasing sodium and water excretion	Amiloride Bumetanide Chlorthalidone Eplerenone Furosemide Hydrochlorothiazide Metolazone Spironolactone Triamterene
Beta-Blockers	Lowers BP by- • Decreasing cardiac output • Decrease sympathetic outflow from CNS • Inhibit the release of renin from kidney	Acebutolol Atenolol Carvedilol Labetalol Metoprolol Nadolol Nebivolol Propranolol Timolol
Angiotensin II Receptor Blockers	They block angiotensin-1 receptors, decrease the activation of receptor by angiotensin (II)	Azilsartan medoxomil Candesartan Eprosartan Irbesartan Losartan Olmesartan Telmisartan Valsartan
Renin Inhibitors	Directly inhibit renin	Aliskiren Ethacrynic acid Indapamide Torsemide Acebutolol Betaxolol Bisoprolol Penbutolol Pindolol Esmolol
ACE Inhibitors (Angiotensin converting enzyme)	By reducing peripheral vascular resistance without reflexively increasing cardiac output, rate or contractility	Benazepril Captopril Enalapril Fosinopril Lisinopril Moexipril Quinapril Perindopril Ramipril

Calcium Channel Blockers	1. Block the inward movement of calcium by binding to the calcium channel in heart and smooth muscle of coronary and periferal arteriolar vasculature 2. Dialets the arterioles	Amlodipine Diltiazem Felodipine Isradipine Nicardipine Nifedipine Nisoldipine Verapamil Clevidipine

(Lippincott *et al*, 2009: p-225-226)

1.9 Drug combinations

The majority of people require more than one drug to control their hypertension. In those with a systolic blood pressure greater than 160 mmHg or a diastolic blood pressure greater than 100 mmHg

(i) Acceptable combinations

The American Heart Association recommends starting both a thiazide and an ACE inhibitors (ACEI), angiotensin II receptor blocker (ARB) or calcium channel blocker(CCB). An ACEI and CCB. (Bauman *et al*, 2013)

(ii) Unacceptable combinations

- Non-dihydropyridine calcium blockers (such as verapamil or diltiazem) and beta-blockers,
- Dual renin–angiotensin system blockade (e.g. angiotensin converting enzyme inhibitor + angiotensin receptor blocker),
- Renin–angiotensin system blockers and beta-blockers,Beta-blockers and centrally acting medications.
- Combinations of an ACE-inhibitor or angiotensin II–receptor antagonist. (NPS, 2010)

1.10 Amlodipine

Amlodipine (as besylate, mesylate or maleate) is a medication used to lower blood pressure and prevent chest pain. It belongs to a group of medications known as long-acting dihydropyridine-type calcium channel blockers. Amlodipine relaxes (widens) blood vessels and improves blood flow. Widening of these blood vessels lowers blood pressure. In angina, amlodipine increases blood flow to the heart muscle to relieve pain

due to angina. It is on the World Health Organization's List of Essential Medicines, the most important medications needed in a basic health system (WHO, 2013).

1.10.1 Discovery

Amlodipine was discovered by a research team lead by Simon Campbell and developed by the Pfizer Corporation. Amlodipine was introduced in the US in 1992. Just two years after its discovery in 1994 the sale of amlodipine achieved a plateau of 2,000,000 new prescriptions per year (Richard F. Davies *et al*, 2005). The amlodipine has the longest half-life and the greatest bioavailability among all chemical abstract service for chemical information(CAs).This profile of amlodipine makes it suitable for convenient once-daily administration (NDA, 2007).

1.10.2 Chemistry

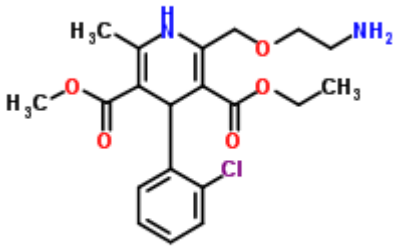
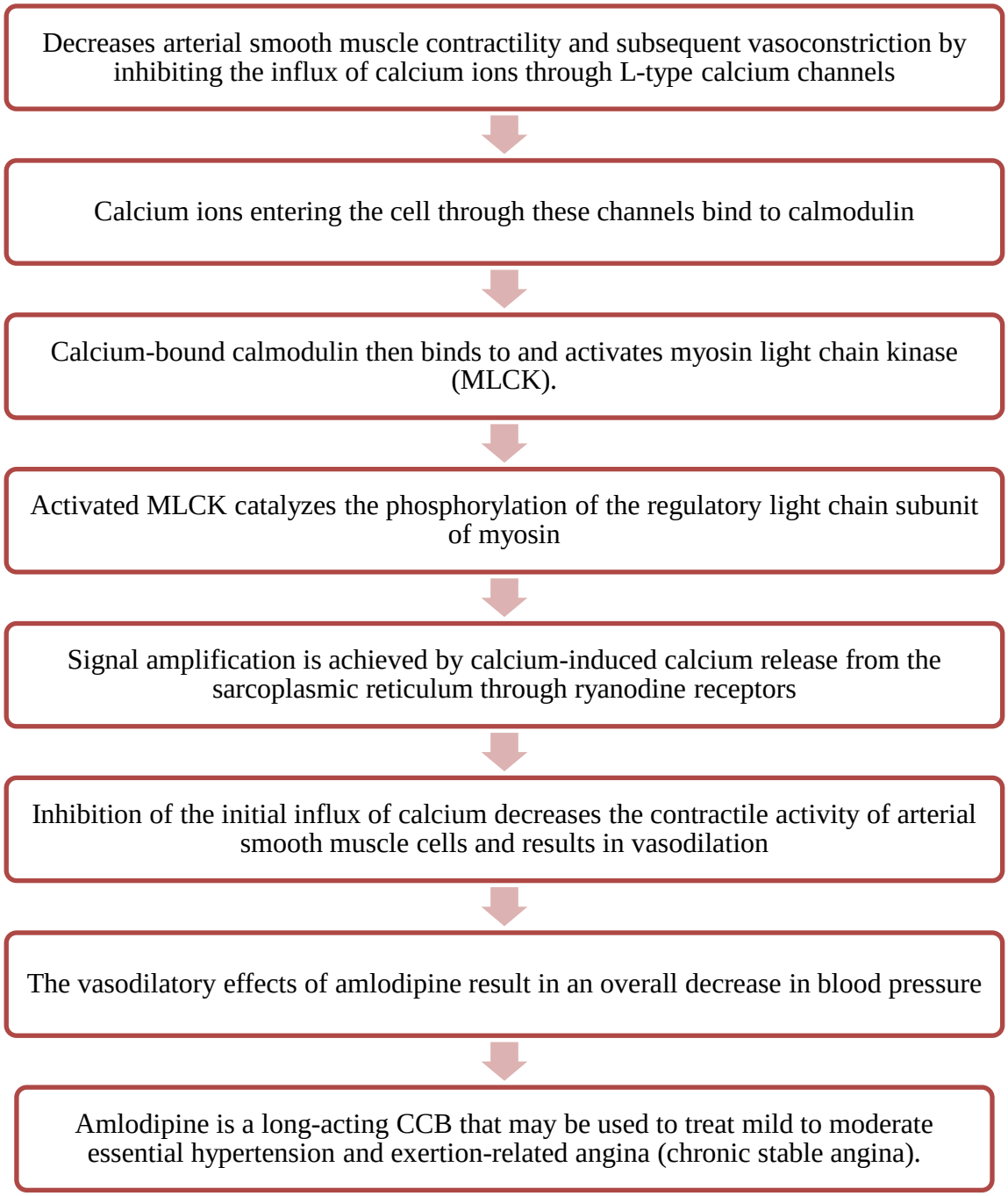


Fig 1.2: Molecular Structure of Amlodipine

- Molecular Formula: $C_{20}H_{25}ClN_2O_5$
- Average mass: 408.876 Da
- Monoisotopic mass: 408.145203 Da
- Systematic name: 3-Ethyl 5-methyl 2-[(2-aminoethoxy) methyl]-4-(2-chlorophenyl)-6-methyl-1,4-dihydro-3,5-pyridinedicarboxylate (Chemspider,2015)

1.10.3 Mechanism of action



(Zwieten et al,1994).

Another possible mechanism is that amlodipine inhibits vascular smooth muscle carbonic anhydrase I activity causing cellular pH increases which may be involved in regulating intracelluar calcium influx through calcium channels (Zwieten *et al*,1994).

1.11 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. It 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 (Agon *et al*, 1991).

1.11.1 Discovery

Atenolol was discovered by Imperical chemaical industries (ICI) in 1976, whilst searching for a specific Beta-1 cardioselective adrenoreceptor blocking agent. Though ICI's research was invaluable, atenolol may be seen as a drug evolved from the series of research being conducted into beta receptors during the late nineteen fifties. The first development of a chemical that acted to inhibit beta receptors was discovered by Slater, Powell and co-workers at Lilly in 1958. However the compound,3 ,4-dichloro isoproterenol only acted as a partial agonist that produced marked stimulation of cardiac beta receptors before inhibition. These inferences obviously contradicted the whole objective of their research, the milestone in the treatment of hypertension and angina came from a Scottish pharmacologist, Sir James Whyte Black (1924). (Ntlworld, 2004).

Atenolol soon followed in 1976, becoming the third best-selling drug in the world. Despite many companies having introduced the drug commercially, Atenolol began as the research molecule of ICI pharmaceuticals and is one of its major success stories till this day (Ntlworld, 2004).

1.11.2 Chemistry

The characteristics of any drug are crucial in the understanding of its chemical composition and the consequent effects it has on the human body. Atenolol has a diversity of attributes, which gives rise to both its physical and chemical behavior. (Ntlworld, 2004).

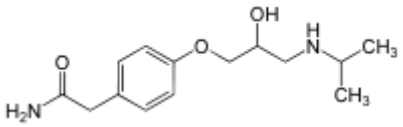


Fig 1.3: Molecular Structure of Atenolol

Table 1.2: Characteristic of Atenolol

Chemical Names	(RS)-4-(2-hydroxy-3-(isopropyl amino propoxy phenyl acetamide) 2-4-(2-Hydroxy-3-isopropyl amino propoxy phenyl acetamide) 4-(2-hydroxy-3-1-methyl ethyl amino propoxy benzeneacetamide).
Molecular Formula	$C_{14}H_{22}N_2O_3$
Relative Molecular Mass	266.3
Melting Point	152-154°C
Appearance	Atenolol is an odorless white powder
Enantiomers	YES R(+) and S(-)

(Ntlworld, 2004)

Table 1.3: Solubility of Atenolol

Solvent	**Relative Solubility**
Water	0.3 Mg/Ml
Ethanol	3.4 Mg/Ml
Dimethyl Sulfoxide(Dmso)	18 Mg/Ml
Ether	Practically Insoluble

(Ntlworld, 2004)

Enantiomers

Atenolol has two optical isomers. These mirror images are labelled the R (+) and S(-) enantiomers of Atenolol. By virtue of the chirality of the carbon, the molecule is able to exhibit optical isomerism. These are in the forms of the stereoisomers R+atenolol and S-atenolol. (Ntlworld, 2004)

1.11.3 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. (Lippincott *et al*, 2009:p-220)

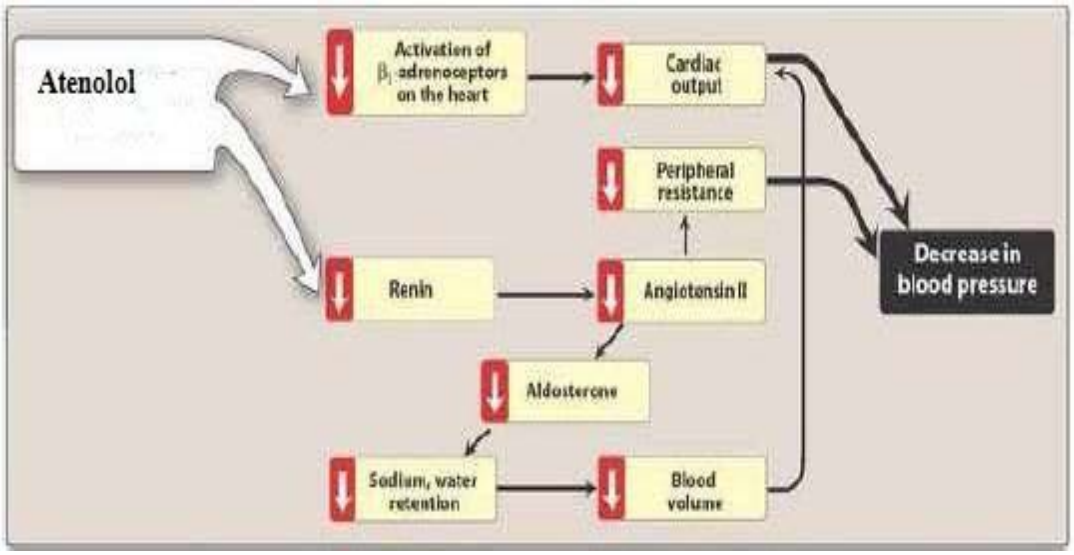


Figure 1.4: Atenolol (beta blocker) mechanism (Lippincott *et al,* 2009:p-220)

1.12 Amlodipine and Atenolol Combination

Fixed-dose combination of antihypertensive drugs can simplify dosing regimens, improve compliance, improve hypertension control, decrease dose-dependent side effects and reduce cost as the first-line treatment of hypertension (Prisant, 2002). These potential advantages make it recommendable for the combination antihypertensive therapy to be used as initial treatment, particularly in patients with target-organ damage or more severe initial hypertension (Moser, 1998; Moser and Black, 1998). Calcium antagonists are vasodilatory and tend to increase plasma renin, therefore combination with a β-blocker is theoretically sound (Waeber *et al.*, 1999). Amlodipine, with its intrinsically long half-life alone or together with β-blocker, is likely to produce superior ischaemia reduction in clinical practice when patients frequently forget to take medication or take doses irregularly (Deanfield *et al.,* 2002; Davies *et al.,* 1995). (Mettimano *et al.,* 2000) found that adding amlodipine to atenolol produced a significant reduction in blood pressure when compared with placebo in patients whose blood pressure was not controlled by atenolol alone. The reduction of side-effects, obtained by adding a dihydropyridine derivate to a *β*-blocker, confirms the effectiveness of this combination (Mettimano *et al.,* 2000). It is clearly demonstrated that the combination of atenolol and amlodipine is synergistic in lowering and stabilizing BP and this synergism is highest when the dose proportion of the two drugs is 10: 1 (Li-Ping *et al.,* 2005).

1.12.1 Pharmacokinetics of atenolol and amlodipine

	Atenolol	**Amlodipine**
Absorption	Bioavailability: 50–60% following oral administration. Onset: 1 hour following oral administration. Within 5 minutes following IV administration. Duration: At least 24 hours following oral administration (antihypertensive and β-adrenergic blocking effects). About 12 hours following IV administration (effect on heart rate). Special Populations: In geriatric patients, plasma concentrations are increased.	Plasma levels peak 6-12 hr after oral admin; absolute bioavailability is estimated to be 64-90%.

Distribution	Extent: Well distributed into most tissues and fluids except brain and CSF. Readily crosses the placenta, has been detected in cord blood. Distributed into milk in concentrations higher than those in serum. Plasma Protein Binding: Approximately 6–16%.	93% bound to plasma proteins
Elimination	Metabolism: Little or no hepatic metabolism. Elimination Route: 40–50% excreted unchanged in urine following oral administration. Remainder in feces, principally as unabsorbed drug. Half-life: 6–7 hours.	About 90% converted to inactive metabolites hepatically 10% of parent compound and 60% of the metabolites are removed in the urine; elimination from the plasma is biphasic with terminal half-life of about 30-50 hr.

(Drugsupdate,2015)

1.12.2 Dosage and Administration

Oral

Chronic stable angina, Hypertension

Adult: Per tablet contains atenolol 25 or 50 mg and amlodipine (as besylate) 5 mg: 1 tab once daily, may increase to 2 tablets daily if needed.

Elderly: Per tablet contains atenolol 25 mg and amlodipine (besylate) 5 mg: Initiate with 1 tablet daily.

Renal impairment: Per tablet contains atenolol 25 mg and amlodipine (besylate) 5 mg: Initiate with 1 tablet daily. (Drugsupdate,2015)

1.12.3 Uses of combination of atenolol and amlodipine

Patients with

- Essential hypertension
- Angina pectoris & hypertension as co-existing diseases
- Post MI
- Refractory angina pectoris where nitrate therapy has failed.

1.12.4 Side Effects of combination of atenolol and amlodipine

- Palpitations
- Flushing
- Oedema
- Dyspnoea
- Dyspepsia
- Cold Extremities
- Drowsiness
- Chest pain & Impotence Rarely
- Headache
- Hypotension
- Dizziness
- Breathlessness
- Fatigue
- Muscle Cramps
- Bradycardia
- Hypersensitivity Reactions (Drugsupdate,2015)

1.12.5 Precautions of combination of atenolol and amlodipine

Over dosage may cause hypotension and less commonly, congestive cardiac failure. Unabsorbed drug may be removed by gastric lavage or use of activated charcoal. Symptomatic treatment may be administered. (Drugsupdate,2015)

Excessive fall of BP may occur in elderly patients. Caution in patients with chronic obstructive pulmonary disease(COPD), thyrotoxicosis, congestive failure, hepatic & renal impairment. Caution in diabetic patients as beta-blockers may mask tachycardia occurring with hypoglycemia. Withdrawal should be gradual. Safety and efficacy have not been established in children. (Drugsupdate,2015)

1.12.6 Contraindications

- Pregnancy
- Lactation
- Hypotension
- Sinus bradycardia
- Second & third degrees of heart block
- Cardiogenic shock
- Overt congestive failure
- Poor left ventricular function
- Hypersensitivity (Drugsupdate,2015)

1.12.7 Drug Interactions

Additive effect when used with catecholamine depleting drugs; monitor for hypotension and/or marked bradycardia. If used with clonidine, clonidine withdrawal should occur a few days after withdrawal of the beta-blocker to prevent rebound hypertension, if replacing clonidine by beta-blocker, beta-blocker should be introduced only after clonidine administration has stopped for several days. Concurrent use with prostaglandin synthase inhibiting drugs (e.g. indomethacin) may reduce the hypotensive effects of beta-blockers. (Drugsupdate,2015)

1.13 Quality

Quality is essential for the survival and growth of any organization. Quality signifies excellence of the product or service, which is measured, based on the customer's experience with the product or service against his or her requirement. The quality of the product may be defined as its ability to fulfill the customer's needs and expectation. Quality needs to be defined firstly in terms of parameters or characteristics, which vary from product to product. For example, for pharmaceutical product, parameters such as physical and chemical characteristics, medical effect, toxicity, taste and shelf life etc, (Lachman, 2008). The quality, for a product or service, has two features, both of which together make for an appropriate definition of the term. The first relates to the features and attributes of the product or service. The second feature concerns the absence of deficiencies in the product (Mazumder *et al*., 2011).

1.14 Quality Control

The term quality control refers to the sum of all procedures undertaken to ensure the identity and purity of a particular pharmaceutical. Such procedures may range from the performance of simple chemical experiments which determine the identity and screening for the presence of particular pharmaceutical substance (thin layer chromatography, infrared spectroscopy, etc.), to more complicated requirements of pharmacopoeial monographs. Activities extend to the area of quality control laboratories (good laboratory management practices, models, e.g. for certificate of analysis and lists of laboratory equipment, and an external assessment scheme. (WHO, 2015)

The term quality control comprises of two words quality and control. Control is a universal regulatory process. In the industry, it takes from of meeting standards. The process through which we establish and meet standards is called Quality control. Quality

control deals with a system which accepts or rejects any activities which affect the quality and prevents Quality deficiency and imports consistency in the quality of the product or service (Lachman, 2008). Quality is important in every product or service but it is vital in medicine as it involves life. Quality control is a concept which strives to produce a perfectly produced by a series of measure designed to prevent and eliminate errors at different stages of production. Although the responsibility for assuring product quality belongs principally to quality assurance personnel, it involves many departments and disciplines within a company. The quality of products is depending upon that of the participating constituents, some of which are sustainable and effectively controlled while others are not. To be effective, it must be supported by a team effort. Quality must be built into a drug product during product and process design, and it is influenced by the physical plant design, space, ventilation, cleanliness, and sanitation during routine production. The product and process design begins in research and development. It also includes pre-formulation and physical, chemical, therapeutic and toxicological consideration. Quality control ensures that a drug will have the following characteristics:

- Genuine Quality as well as good nature
- Physically and chemically pure
- It contains same amount of ingredients as mentioned on the label
- It must be in such a form that after administration it is effective
- Quality in terms of shelf life/stability
- No toxic impurities

The drug is tested for both qualities as well quantity by the quality control department. Every country will have an official pharmacopoeia which will give the standards of quality for all the medicines along with the methods to be used for quality control. Revised supplements are published periodically to stay up-to-date pertaining to drug quality, (Lachman, 2008). There are eight dimensions of quality. They are critically important for organizational success. (Mazumder *et al*., 2011)

They are:

1. Performance: Primary operating characteristics of product.

2. Features: Additions to a product basic functioning features.

3. Reliability: Probability of not malfunctioning during specified period.

4. Conformance: The degree to which a products design and operating characteristics meet established criteria.

5. Durability: A measure of product life.

6. Serviceability: The speed and ease of repair.

7. Aesthetics: Looks, feel, tastes and smells of a product.

8. Perceived quality: As seen by a customer (Mazumder *et al*., 2011).

1.15 Quality of Pharmaceutical Product

Quality of product is the main precursor for any pharmaceutical industry to maintain its existence. In the pharmaceutical industry, the quality is a measure of the high degree of managerial, scientific and technical sophistication. Quality is always an obligatory prerequisite when we consider any product. It becomes primary when it relates to life saving products like pharmaceuticals. Although it is mandatory for the government and regulatory bodies but it is also a fact that quality of pharmaceutical product cannot be adequately controlled solely by pharmacopoeia analysis of the final product. Today quality has to be built in to the product right from its inception and rigorous international environmental, safety and regulatory standards need to be followed. Validation had proven to be an important tool for quality management of pharmaceuticals (Mazumder *et al.*, 2011).

Most traditional pharmaceutical drugs are relatively simple molecules that have been found primarily through trial and error to treat the symptoms of a disease or illness. Over a period of time these molecules were perfected to ensure quality. The quality is very much related to every pharmaceutical product. Without quality pharmaceutical drug cannot be marketed or sold because it can cause many problems such as sub therapeutic or overdose. If a drug of any brand or company does not maintain it then may cause serious problems when prescribed to the patients. The patient may suffer from the adverse effects because of its faulty quality which may sometimes prove to be fatal, (Lachman *et al*, 2008).

1.16 Quality Assurance

Design, development and implementation of quality assurance are the most vital function in the pharmaceutical industry. In the pharmaceutical industry, the quality is a measure of high degree of managerial, scientific and technical sophistication. Quality assurance is a wide-ranging concept covering all matters that individually or collectively influence the quality of the product. It is the totality of arrangements made with the object of ensuring that pharmaceutical products are of the quality required for their intended use (Mazumder *et al*., 2011).

1.17 Importance of Quality

Quality is important in pharmaceutical industry due to the following reasons:

- Production of Therapeutically Active & Safe Drugs

For a drug to be safe and therapeutically active it is essential that it meets its specified quality. A drug deviated from its quality can be therapeutically inactive and toxic. Therefore, for during the production of drugs utmost care should be taken care of the quality for patient safety. (Quality assurance of pharmaceuticals, 2007).

- Prosperity and Survival as a Competitive Industry

Quality is the primary objective for prosperity and survival of a pharmaceutical industry. Quality pharmaceutical products are prerequisite to customer satisfaction and subsequent profit which is important for the industry to prosper. (Quality assurance of pharmaceuticals, 2007).

- To Gain Maximum Profit

Quality product is a tool for gaining profit. Products of poor quality yields negative customer feedback and as a result profitability decreases. On the contrary, high quality products yield positive customer feedback. Satisfied customers results in increased profitability for the company. (Quality assurance of pharmaceuticals, 2007).

- Marketing Tool

Quality of the products can also serve as a strong marketing tool for the pharmaceutical industry. (Quality assurance of pharmaceuticals, 2007).

1.18 Quality control parameters of solid dosage form

Most preferable dosage form in pharmaceutical, to clinician and physician and most importantly to patients is tablet. Tablets give good patient compliance. The physiochemical properties of this combination tablets were assessed through the evaluation of uniformity of tablet weight, thickness test, hardness test, friability test, disintegration test, dissolution test and potency test according to the standard method (Shohin *et al*, 2011). Generally there are two types of tests:

i. Compendial tests &

ii. Non-compendial tests

Compendial test: Compendial tests are test methods that are described in the pharmacopoeias like United States Pharmacopeia (USP), British Pharmacopoeia (BP) etc. They are also known as official tests. They include

- Weight variation test
- Disintegration test
- Dissolution test and
- Drug content test

Non-compendial test: These tests methods are not defined in the

pharmacopeias and so that are referred as Non Compendial Tests or unofficial

tests. They include:

- Friability test
- Hardness test and
- Thickness test (Shohin *et al*, 2011).

1.18.1 Weight variation

Weight variation test is done to check the uniformity of the tablets. Some tablet fails to maintain uniformity, some are properly uniformed. There are several reasons that the weight of tablets varies batch to batch (Shohin *et al*, 2011).

Tablet weight variation may be caused by

1. Distribution at Hoover caused the vibration. So, small granule pushed, large granules will come out first, because there is a process of consolidation. Therefore, needs to be put

a uniform granule size. So, before the compressing process begins better evaluation the particle size distribution first.

2. If the flow of granules is not good or not free-flowing granules.

3. If particle distribution is not normal, because the specific gravity is different, so that the flow is bad.

4. If particle size distribution is not uniformed. Not too many fines and not too many granules should be used. Granules with a large particle diameter which causes the resultant tablet has a variety of unsightly weight, while too fine granules which causes unsightly flow time.

5. If lubricant or glidant less or not mixed evenly.

6. Poor flow properties

7. If any improper adjustment of the die cavity (Shohin *et al*, 2011).

1.18.2 Hardness test

Hardness test is done to determine the need for pressure adjustment on the tableting machine. Hardness has to maintain to withstand mechanical shocks for handling in manufacturing, packing and shipping. There are different types of hardness tester are present like Monsanto tester, Strong-cobb-tester, Pfizer tester, Schleuinger tester and Erweka (Shohin *et al*, 2011).

Hardness can affect the disintegration. So if the tablet is too hard, it may not disintegrate in the required period of time. And if the tablet is too soft, it will not withstand the handling during subsequent processing such as coating or packaging. Hardness value differ with the instrument used allowed values 8-12 Kg. Tablet hardness usually affects drug dissolution and release, and it may affect bioavailability (Lachman *et al*, 2011).

Factor affecting the hardness of tablets,

1. Compression of the tablet and compressive force.

2. Amount of binder, more binder more hardness.

3. Method of granulation in preparing the tablet (wet method gives more hardness than dry method; slugging method gives the best hardness) (Shohin *et al*, 2011).

1.18.3 Thickness test

The thickness of tablet controlled carefully from the production run. Thickness can vary with no change in weight because of difference in the density of the granulation and the pressure applied to the tablets as well as the speed of tablet compression. Tablets thickness is determined with a caliper or thickness gauge that measures the thickness in millimeters (Lachman *et al*, 2011).

If the tablets are thicker than a specified given number no longer may be contained in the volume of a given size bottles. Tablet thickness also becomes an important characteristic in counting tablet using filling equipment. Some filling equipment uses the uniform thickness of the tablet as a counting mechanism. If thickness varies throughout the lot, the result will have variation in count. Other pieces of filling equipment can mal functioning because of variation in tablet thickness, since tablet above specified thickness may cause wedging of tablets in previously adjusted depth of the counting slots (Lachman *et al*, 2011).

1.18.4 Friability test

The friability test is closely related to tablet hardness and is designed to evaluate the ability of the tablet to withstand abrasion in packaging, handling and shipping. The value is expressed as a percentage. A maximum weight loss of not more than 1% of the weight of the tablets being tested during the friability test is considered generally acceptable and any broken or smashed tablets are not picked up (Lachman *et al*, 2011).

1.18.5 Disintegration test

Disintegration is a measure of the quality tablets. The disintegration test is performed to find out the time it takes for a solid oral dosage form like a tablet or capsule to completely disintegrate. The time of disintegration is a measure of the quality. This is because, for example, if the disintegration time is too high; it means that the tablet is too highly compressed or it may imply several other reasons. And also if the disintegration time is not uniform in a set of tablet being analyzed, it indicates batch inconsistency and lack of batch uniformity (Lachman *et al*, 2011)

1.18.6 Dissolution test.

Dissolution testing is used to formulate the drug dosage form and to develop quality control specifications for its manufacturing process. In-vitro dissolution test is a critical

test that has to correlate with in-vivo clinical studies and which could require specific method developments. In Vitro dissolution testing is used to assess batch to batch consistency and detect deviations of manufacturing, to identify critical manufacturing variables like binder effects, mixing effects, granulation Procedure, Coating Parameters, to assess excipients role in different dosage forms (Lachman *et al*, 2011).

There is some other purpose of in vitro dissolution study. These are:

1. During product development, selecting formulations for further development.

2. During end-product quality control, determining whether each batch meets predetermined in vitro release criteria.

3. During stability studies, determining whether in vitro release rate changes with product age.

4. During the market lifetime, determining whether variations affect in vitro release (Shohin *et al*, 2011).

Factor affecting dissolution of tablet:

A variety of factors concerning the formulation of a drug product can directly influence the dissolution rate of the active ingredient contained within it. Once these factors are completely characterized, we can use this information to achieve custom-tailored drug dissolution profiles.

- Excipients and additives: Most solid dosage forms incorporate more than one excipient for various purposes together with the active ingredient in the formulation. The dissolution rate of a pure drug can be altered significantly when mixed with various adjuncts. These adjuncts include diluents, binders, lubricants, granulating agents, disintegrants, and so on.
- Particle Size: Particle size of drugs contained in tablets will enhance dissolution and absorption. This can most likely be attributed to the procedures employed in tablet production that is, mixing the drug with usually hydrophilic diluents and subsequent granulation will result in a more hydrophilic surface, even for originally hydrophobic drug particles.

- ❖ Granulating agent and binder: Binder and granulating agent incorporated in tablet formulation and other solid dosage forms can markedly influence the dissolution characteristics of the drug from the dosage form.
- ❖ Disintegrating Agents: Several reports have been published in the literature demonstrating the effect of various disintegrating agents on the dissolution rate of tablets. It must be noted that the type and amount of disintegrating agent employed in the formulation significantly controls the overall rate of dissolution of the dosage form.
- ❖ Lubricants: Lubricants that are commonly incorporated in the formulation of solid dosage forms fall predominantly in the class of hydrophobic compounds. Consequently, the nature, quality, and quantity of the lubricant added can affect the dissolution rate.
- ❖ Surfactant: The drugs that are practically insoluble in aqueous medium (<0.01%) are of increasing therapeutic interest, particularly due to the problems associated with their bioavailability (Shohin *et al*, 2011).

1.18.7 Potency test

Potency is the strength of a dosage form. Potency determination is the chemical characteristic of a dosage form. Potency tests are assay to estimate the quality and quantity of active ingredient in the drug. Quantitative tests such as chemical, physical, pharmacological, biological or microbiological means yield the strength or potency of the drug substance. To assure uniformity, weight variation test is not sufficient. It is to determine the amount of a substance or the presence of a substance. It is actually do determine purity of a drug or drug dosage form. The test method and the acceptable limits are specified in the pharmacopoeias. Specified number of dosage units should be taken for analysis. Larger or smaller quantities from specified weight can be taken if the measurements are adjusted with equivalent accuracy and provided that any subsequent steps like dilutions are adjusted consequently to yield concentrations equivalent to those specified. Once the result is generated it is related to the amount of active ingredient per tablet by multiplying the result with the average tablet weight and dividing by the weight of portion taken for the assay. Impurity in the active ingredient or any weight variation may interact with the potency result of the drug. If a drug fails in potency test the patient may suffer under or over medication (Lachman *et al*, 2011).

Significance of the study

Hypertension is one of the most common diseases in our country. This is a kind of disease that cannot be easily cured but it can be controlled. Because of having a good number of pharmaceutical companies, our pharma market has a good competition. They launch numerous products on different diseases. And hypertension in respect of our country is one of the fields where every pharmaceutical has several products whether it is single drug product or combined drug product. That's why it is necessary to carry out a comparative study of the quality control parameters of different brands that are available in Bangladesh for the appropriate quality evaluation, therapeutic efficacy and safety of the tablets. It is because quality of the pharmaceutical product is uppermost important and they must be marketed as safe and therapeutically active formulation whose performance is consistent and not cause any kind of worse effect (Shohin *et al*, 2011).

The evaluation of quality control parameters (weight variation, hardness, thickness, disintegration, dissolution, potency determination) of the pharmaceutical product that are available in market is important ensure their quality. It also gives us an indirect idea about its bio-availability. The combination of atenolol (50mg) and amlodipine (5mg) is such a product which is increasing day by day in term of its use. The combination of atenolol (50mg) and amlodipine (5mg) is released by most of the pharmaceutical company under their cardiovascular management. At present there are many brands available of different pharmaceutical company in market. So, it is very important to evaluate the quality control parameters like weight variation, hardness, thickness, disintegration test, dissolution test, potency test of different brands and also to compare them with each other to find out an idea about which one is better in terms of quality as well as safety and which shows variation from the specification.

Aims and objectives of the study

The aim of this research paper were,

- To determine the quality control parameters of various brands (Camlodin® Plus & Amlovas® AT) of atenolol (50mg) and amlodipine (5mg) combination
- To make a comparison on different quality control parameters between brand to brand
- To determine the potency and dissolution of selected brands.

CHAPTER-2

LITERATURE REVIEW

Chapter 2

LITERATURE REVIEW

2.1 Simultaneous UV spectrophotometric methods for estimation of atenolol and amlodipine besylate in combined tablet dosage form

Two simple, rapid, accurate, precise, cost effective, and reproducible UV spectroscopic methods have been developed for the simultaneous estimation of atenolol and amlodipine besylate in bulk and combined tablet dosage form. The first method is based upon the simultaneous equation and second upon the determination of Q value. Atenolol and amlodipine have absorption maxima at 224.4 and 238.2 nm respectively. Beer's law obeyed in concentration range of 2-24 μg/ml and 2-34 μg/ml for ATN and AMN respectively. The method of Q analysis is based on measurement of absorptivity at 224.4 nm and at iso-isorptive point 232.2 nm. The recovery studies from tablet are indicative of accuracy of method and are found in between 99.87-101.43 % at three different levels of standard additions. Precision studies showed satisfactory results. A novel approach to use 0.02% SLS as solvent is proved to be beneficial with respect to cost, stability and avoidance of organic solvent (Sandip *et al*, 2010).

2.2 Formulation development and in-vitro evaluation of orally disintegrating tablets of amlodipine besylate

An attempt has been made for the development of orally disintegrating tablets of amlodipine besylate prepared by direct compression method by using super disintegrants like cross povidone, cross caramellose sodium and sodium starch glycolate. Effect of different super disintegrants on disintegration behaviour of tablets was evaluated. All the formulations were evaluated for pre compression, post compression parameters and in-vitro dissolution. Wetting time of formulations containing cross carmellose sodium was least and tablets showed fast disintegration. Of the nine formulations studied 9th showed short dispersion time with maximum drug release 99.59% in 20 minutes. Combinations of super disintegrants were found to be better in the formulation of fast dissolving tablets of amlodipine besylate rather than using alone (Bharathi *et al*, 2012).

2.3 Simultaneous estimation of atenolol and amlodipine besylate in tablets formulation by Vierodt's method using UV spectrophotometry

A UV- spectrophotometric method has been developed for the simultaneous estimation of atenolol and amlodipine besylate in tablet dosage forms using 0.1N hydrochloric acid (pH 1.2). The method is based on simultaneous equation or Vieordt's method. The valus for atenolol and amlodipine besylate were found to be 224.6 nm and 239.6 nm respectively. The system obey Beer's law in the range of 4-28 μg/ml and 4-32 μg/ml with correlation coefficient of 0.9991 and 0.9932 for atenolol and amlodipine besylate respectively. Intraday and interday precision were found to be 0.08577-1.4682, 0.1080-1.71138, 0.2525-1.6080 and 0.2599-1.3906 respectively. The developed method can be successfully employed for the assay of atenolol and amlodipine besylate in different formulations (Girdhari *et al*, 2012).

2.4 Assessment of pharmaceutical quality control and equivalence of various brands of amlodipine besylate (5 mg) tablets available in the pakistani market under biowaiver conditions.

The dissolution profiles of amlodipine besylate tablets under biowaiver condition were evaluated in four different media (distill water, buffer pH 1.2, buffer pH 4.5 and buffer 6.8) using US Pharmacopoeia dissolution apparatus II. Among them dissolution either single point or multiple point including release profile comparison is the most important tool. Quality control tests were satisfactory and within the limits for all amlodipine besylate brands. The results obtained for disintegration test, assay, hardness and friability were less than 15 minutes, 98.96-100.76 %, 1.53-8.77 kg/cm2 and less than 1% respectively. The physico-chemical characteristics of the five generic brands tested were comparable with the innovator brand. They were all within the BP limits as specified for immediate release dosage forms; these assure pharmaceutical equivalence of generics tested with the innovator. The evaluated drugs were "very rapidly dissolving" because the active pharmaceutical ingredient release at time point 15 min was more than 85% so no statistical treatment is required hence are considered to be in- vitro equivalent without in - vivo evaluation. The percent relative standard deviation (% RSD) for all time points fulfills all requirements (≤20% for 15 min, ≤10% for other time points), so results are valid. Under the biowaiver conditions, all the generics are interchangeable with the innovator; they are therapeutically equivalent. The generic substitutions for the innovator are appropriate despite the high price differential (Mahwish *et al*, 2014).

2.5 Biowaiver Studies of Atenolol Tablets (100mg) - An Alternative to In Vivo Bioequivalence Studies.

Four brands of atenolol 100 mg tablets have been evaluated using some quality control parameters, such as weight variation, hardness, content assay, disintegration and dissolution test. In vitro dissolution testing can be used in some cases not only to determine the quality of the pharmaceutical products but also to demonstrate bioequivalence to the generic product. Similarity factor (f2) and Difference Factor (f1) were used to assess bioequivalency among four products. The FDA recommended dissolution medium for atenolol is 0.1N HCl but it shows a good releasing pattern in water also. The dissolution profiles of Aten-4 and Aten-2 in pH 1.2 is rapid and good, only Aten -3 failed to cross the similarity factor but f1 is within limit. In pH 4.5 and 6.8 all brands fulfilled biowaiver requirements, except Aten-2 in pH 6.8 that may be due to manufacturing process difference. In the same time Aten-2 has f1 value 12 that is within the limit. Therefore, generic drugs with differing in vitro dissolution will not necessarily exhibit different in vivo performance. The results suggest that the formulation and/or the manufacturing process affect the dissolution and thus the bioavailability of the drug products. Thus the significance of the observed in-vitro differences must be confirmed by an in-vivo bioequivalence study. (Usman *et al*,2014)

2.6 Comparative quality control evaluation of atenolol tablets marketed in kuala lumpur, Malaysia

The main objective of this study is to perform a comparative evaluation of the physicochemical properties of five commercially available leading brands of Atenolol tablets marketed in Kuala Lumpur. The quality control parameters of five different brands of atenolol tablets were atenolol tablet assessed included uniformity of content, uniformity of weight, friability, crushing strength, disintegration and dissolution tests as well as content uniformity of the tablets. All the tablets were assessed for conformity with British Pharmacopoeia (BP) standards.All the five brands of the tablets passed the British Pharmacopoeia (BP) standards for weight uniformity, disintegration, friability, content uniformity and hardness tests.The quality control parameters of all five top selling brands of atenolol tablets marketed in Kuala Lumpur analyzed passed all the BP and USP quality specifications and were physically and chemically equivalent (Dharmalingam *et al*, 2014).

2.7 Simultaneous estimation of amlodipine besylate and atenolol in combined dosage forms marketed in pakistan by Vierodt's method using U.V. spectroscopy

Spectroscopic studies were carried out using double beam U.V spectrophotometer model JASCO. The marketed combination of atenolol and amlodipine besylate that is primol-AT 10 TAB Madley pharma and 0.1N HCL used as solvent. Then spectra of amlodipine and atenolol exhibit λmax of 239nm and 228nm resepectively. Additionaly one isoprtive point was observed at 233nm this wavelength were selected for simultaneous estimation of amlodipine and atenolol and standard calibration curves for amlodipine and atenolol were linear with correlation coefficient 0.996 and 0.993 at all selected wavelengths. This method was found to be applicable over a range of 4-24 µg/ml for amlodipine and atenolol. This method can be used as alternative for rapid and routine determination of bulk sample and tablets (Pawar *et al*, 2013).

2.8 Formulation and evaluation of fast dissolving tablets atenolol

Administration of conventional tablets of atenolol in has been reported to exhibit fluctuations in plasma drug levels, resulting either in manifestation of side effects or reduction in drug concentration at the receptor sites. The half-life of atenolol is 6-7 hours hence multiple doses of the drug are needed to maintain a constant plasma concentration for a good therapeutic response, and improve patient compliance, hence the objective of the study was made to develop fast dissolving tablet of atenolol. Conventional atenolol tablets available in market are not suitable where quick onset of action is required. Besides, the conventional tablets also show poor patient compliance particularly by the geriatric and pediatric patients who experience difficulty in swallowing, and by those who are bed ridden or who are traveling and do not have an easy access of water. In this studies using polymer like AC-DI-SOL, Sodium starch glycolate and which will quickly the release of drug, increasing the bioavailability of the drug and thus decreasing the dosing frequency of the drug. The description and appearance, melting point and solubility were also performed for further characterization & it was found that all results are satisfactory. Atenolol was estimated by UV/VIS spectrophotometry in 0.1N HCl. The in vitro dissolution study was also carried out in 0.1N HCl (PH 1.2) and B7 is the best formulation among of that and it release 99.5% (Praveen khirwadkar *et al*, 2013).

CHAPTER-3

METHODOLOGY

Chapter 3

METHODOLOGY

3.1 Samples

40 tablets of 2 different brands of atenolol (50mg) & amlodipine (5mg) combinational tablets were collected from different pharmacy shops.

Table 3.1: Different brands along with their manufacturer names

Tablet	**Pharmaceutical name**
Amlovas® AT	Popular
Camlodin® Plus	Square Pharmaceuticals Ltd.

Table 3.2 Reagents and solvent

Hydrochloric Acid (0.1N HCL)
Distilled water

Table 3.3: List of Apparatus/ Glassware's used throughout this project

Serial No.	**Name**	**Serial No.**	**Name**
1	Several Containers	5	Measuring Cylinder
2	Mortar & Pastels	6	Pipette
3	Test tubes	7	Beakers
4	Volumetric Flasks	8	Filter Papers

3.2 Weight variation test

Weight variation test is most significant because it has a relationship with content uniformity of a solid dosage forms. A small weight variation does not ensure good content uniformity between dosage units; a large weight variation precludes good content uniformity. Any of the following factors, can produce excessive tablet variations:

1. Poor granulation flow properties, resulting in uneven die fill.
2. A wide variation in granulation particle size, which result in a variation in die fill density as a function of particle size and particle size distribution at different points in the production run.
3. Differences in lower punch length which result in different size die cavities (Dharmalingam *et al*, 2014).

3.2.1 Instrument: Analytical Balance (AY220, Shimadzu, Japan)

Figure 3.1: Analytical Balance (AY220, Shimadzu, Japan)

3.2.2 Method: Calculated average weight of 20 tablets and weighed 20 whole tablets individually. Then observed weight of individual tablets was within the range or not (USP, 2007).

3.2.3 Calculation: Percentage of weight variation was calculated by following formula (Dharmalingam *et al*, 2014)

$$\text{Weight variation} = \frac{\text{Tablet weight - Average Weight}}{\text{Average Weight}} \times 100$$

3.2.4 Specification: According to the USP (2007), the individual variation from the average weights must not differ for more than two tablets than percentage listed below:

Table 3.4: Weight variation tolerance for tablets

Average weight of the tablet	**Percentage of difference**
130 mg or less	±10
From 130 mg through 324 mg	±7.5
More than 324 mg	± 5

3.3 Thickness test

3.3.1 Instrument: Vernier Calipers (Shimadzu, Japan)

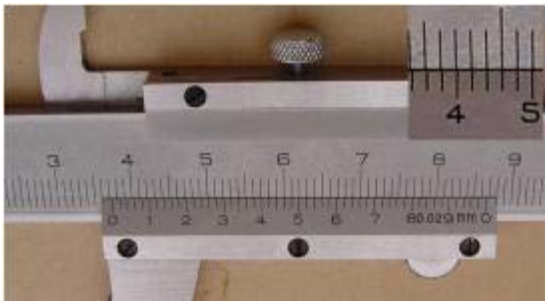


Figure 3.2: Vernier Calipers (Shimadzu, Japan)

3.3.2 Method: 20 tablets were individually placed horizontally between two jaws of the calipers. The caliper scale was run to hold the tablet which gave a visual reading of tablet thickness (Dharmalingam *et al,* 2014).

3.3.3 Calculation: Thickness was calculated by using the following formula:

Thickness: = Main scale reading + vernier scale reading X vernier constant ± Vernier error (Dharmalingam *et al*, 2014).

3.3.4 Specification: According to the USP (2007), tablets should have thickness about ± 5mm.

3.4 Hardness test

Tablet hardness is usually expressed as the load required crushing a tablet placed on its edge. Hardness is thus sometimes termed the tablet crushing strength. The suitability of tablet in regard to mechanical stability during packaging and shipment can usually be predicted on the basis of hardness. Tablet hardness, in turn, influences tablet density and porosity. It may affect tablet friability and disintegration time. It usually affects drug dissolution and release and it may affect bioavailability (Dharmalingam *et al*, 2014).

3.4.1 Instrument: Hardness tester (Veego, India)

Figure 3.3: Hardness tester (Veego, India)

3.4.2 Method:

- The slide scale of the hardness tester was made zero
- One tablet was placed vertically between two jaws.
- Force was applied with a screw thread and spring until the tablet fractured.
- Reading in Kg was taken from the sliding scale (Dharmalingam *et al*, 2014).

3.4.3 Measurement Units: Most materials testing are performed using the International System of Units. The Newton is the preferred unit of force as is recognized by the SI system. However the Kg can also be used. Kilogram (Kg) – The Kilogram is recognized by the SI system as the primary unit of mass (USP, 2007).

3.4.4 Specification: According to USP (2007), oral tablets normally have a hardness of 4 to 8 or 10 kg; however, hypodermic and chewable tablets are much soften (3 kg) and some sustained release tablets are much harder (10-20 kg).

3.5 Disintegration test

Disintegration is the most important step of a drug being better dissolution. The breakdown of a drug within its optimum time is the prerequisite for better absorption and consequently better therapeutic action. Disintegration time may vary considering to its disintegrator used. Higher the disintegration time required lower the dissolution rate and followed to poor absorption. So disintegration is the crucial part of a drug for therapeutic action (BP, 2009).

3.5.1 Condition:

- Distilled water
- 37° C temperatures to maintain body temperature (BP, 2009).

3.5.2 Instrument: Disintegration tester (Vanguard Pharmaceutical Machinery INC)

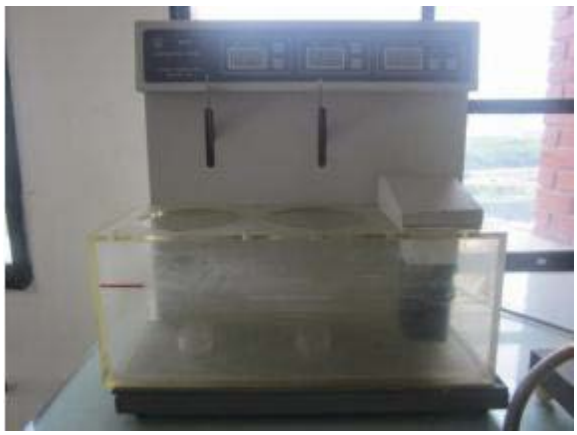


Figure 3.4: Disintegration tester (Vanguard Pharmaceutical Machinery INC)

3.5.3 Method:

1. The disintegration tester was assembled.
2. Then the time and temperature was set at prescribed in specification.
3. 600ml of the distilled water was placed in each 1000ml beaker.
4. The temperature of the liquid was maintained at 37° C.
5. In each of the 6 tubes one tablet was placed.
6. The machine was then operated for the prescribed period.
7. The entire tablet was disintegrated within the prescribed time (BP, 2009).

3.5.4 Specification:

According to BP (2009), the disintegration time for uncoated tablet is 15 minutes, for coated tablet is 30 minutes and for enteric coated tablet is 60 minutes or 1 hour.

3.6 Potency Test

3.6.1 Material: Analytical balance, mortar & pestle, spatula, volumetric flask, funnel, filter paper, pipettes, pipette pumper, tablets.

3.6.2 Method: 10 tablets from each batch were weighed and ground into a fine powder. Powder equivalent to 50 mg and 5 mg of atenolol and amlodipine was transferred into 100 ml volumetric flasks and dissolved in 25 ml of 0.1 N hydrochloric (PH 1.2). The solution was sonicated for 20 mintues and was filtered through Whatman No. 40 filter paper. The residue was washed with hydrochloric acid buffer and washing were added to the filtrate. The volume was made up to the mark with 0.1N hydrochloric acid buffer. From this solution, 1 ml was pipette out into 10 ml volumetric flask and diluted up to the mark with 0.1N hydrochloric acid buffer (PH 1.2). The absolute values were measured at 223.5 nm and 237.5 nm respectively (Girdhari *et al*, 2012).

3.6.3 Calculation: Using the following formula we can measure the measure amount of the active in sample,

$$\% \text{ potency} = \frac{A_{Sample}}{A_{STD}} \times \frac{Weight_{STD}}{Weight_{Sample}} \times \frac{Potency_{STD} \times Dilution\ Factor \times Avg\ Wt_{Sample}}{Label\ Claimed} \times 100$$

3.6.4. Specification: According to BP (2009), in order to pass the potency test, tablets contain not less than 90.0% and not more than 110.0% of atenolol and amlodipine.

3.7 Dissolution Test

3.7.1 Instrument: Dissolution Apparatus (LABINDIA DS 8000)

Fig 3.5: Dissolution Tester (LABINDIA DS 8000, India)

3.7.2 Condition:

Medium: 900ml 0.1N HCL

Apparatus: USP dissolution apparatus type-II

Speed: 50rpm

Temp: 37.5°

Time: 30 min (Vuyyala, 2014)

3.7.3 Method: On the dissolution test apparatus the water tank was filled and the temp was set. Then 900 ml of 0.1N HCL was poured into one of the vessels and instrument were run till the set temp was attained. One of the tables was placed into the vessels and starts the run. Rotate the paddle at 50 revolutions per min. Run the test for 30 min. Dilution was performed wherever necessary. (Vuyyala, 2014). Finally the absorbance's were taken at 237.5 nm for amlodipine and at 223.5 nm for atenolol. Analysis was performed by UV-visible spectrophotometer.

3.7.4 Calculation

$$\% \text{ dissolution} = \frac{\text{Absorbance (a)}}{\text{A (1\%, 1cm)}} \times \frac{\text{diluation factor x 900}}{\text{tablet weight (gm)}}$$

3.7.5 Specification:

Conventional-release (or immediate-release) dosage forms

Unless otherwise specified in the individual monograph the requirements are met if the quantities of active ingredient(s) dissolved from the dosage forms tested conform to Table 3.5. Continue testing through the three levels unless the results conform at either S_1 or S_2. The quantity, *Q*, is the specified amount of dissolved active ingredient expressed as a percentage of the labelled content; the 5%, 15% and 25% values in the acceptance table are percentages of the labelled content so that these values and *Q* are in the same terms. (WHO,2014)

Table 3.5: Acceptance criteria for Conventional-release dosage forms

Level	Samples tested	Acceptance criteria
S_1	6	Each value is not less than *Q* + 5%
S_2	6	Average value of the 12 dosage units (S_1 + S_2) is equal to or greater than *Q* and no unit is less than *Q*-15%
S_3	12	Average value of 24 dosage units (S_1 + S_2 + S_3) is equal to or greater than *Q*; not more than 2 units are less than *Q* - 15%; no unit is less than *Q* - 25%.

(WHO,2014)

CHAPTER-4

RESULTS

Chapter 4

RESULTS

4.1 Weight Variation test

Percentage of variation of 4 batches of 2 different brands of combined atenolol and amlodipine tablets are given below.

Table 4.1: Weight variation of Camlodin® Plus (406003)

Number of tablets	Weight of individual tablets (g)	Average weight (g)	Individual weight Variation (%)	Highest weight variation (%)	Lowest Weight variation (%)
1	0.1838	0.1804	1.884701	2.7161	-5.9312
2	0.1810		0.332594		
3	0.1796		-0.44346		
4	0.1787		-0.94235		
5	0.1819		0.831486		
6	0.1768		-1.99557		
7	0.1697		-5.93126		
8	0.1789		-0.83149		
9	0.1825		1.16408		
10	0.1814		0.554324		
11	0.1815		0.609756		
12	0.1836		1.773836		
13	0.1833		1.607539		
14	0.1805		0.055432		
15	0.1819		0.831486		
16	0.1780		-1.33038		
17	0.1819		0.831486		

18	0.1776		-1.55211		
19	0.1853		2.716186		
20	0.1817		0.720621		

Standard deviation of individual weight is 0.0033

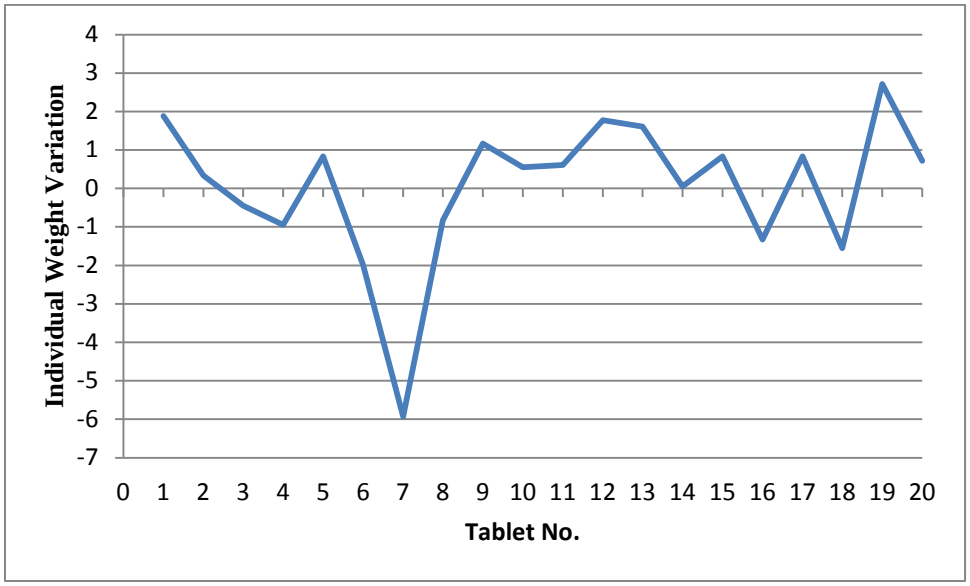


Fig 4.1: Individual weight variation of Camlodin® Plus (406003)

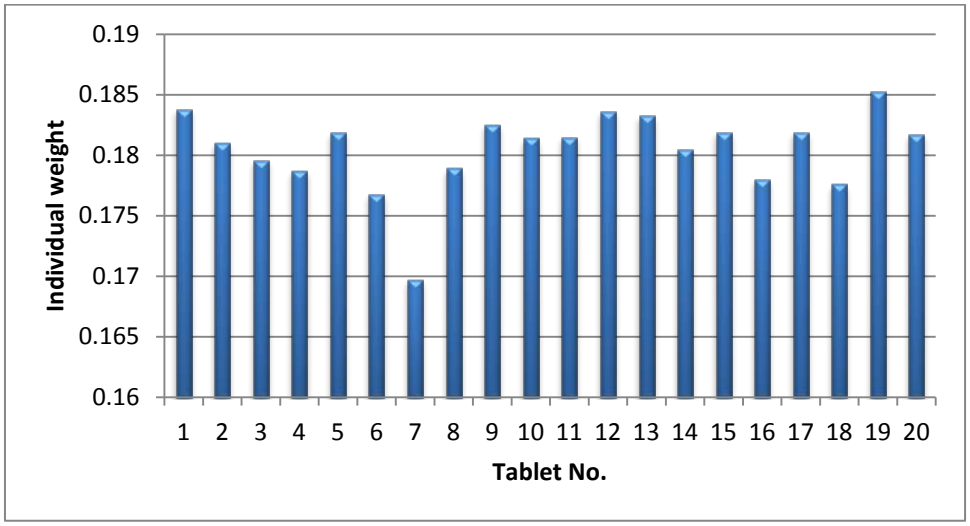


Fig 4.2: Weight of individual Tablets for Camlodin® Plus (406003)

Table 4.2: Weight variation of Camlodin® Plus (411002)

Number of tablets	Weight of individual tablets (g)	Average weight (g)	Individual weight Variation (%)	Highest weight variation (%)	Lowest weight variation (%)
1	0.1777	0.1764	0.736961	1.6439	-1.6439
2	0.1755		-0.5102		
3	0.1770		0.340136		
4	0.1735		-1.64399		
5	0.1744		-1.13379		
6	0.1775		0.623583		
7	0.1763		-0.05669		
8	0.1773		0.510204		
9	0.1782		1.020408		
10	0.1763		-0.05669		
11	0.1774		0.566893		
12	0.1740		-1.36054		
13	0.1760		-0.22676		
14	0.1769		0.283447		
15	0.1735		-1.64399		
16	0.1793		1.643991		
17	0.1777		0.736961		
18	0.1785		1.190476		
19	0.1748		-0.90703		
20	0.1775		0.623583		

SD of individual weight is 0.0016

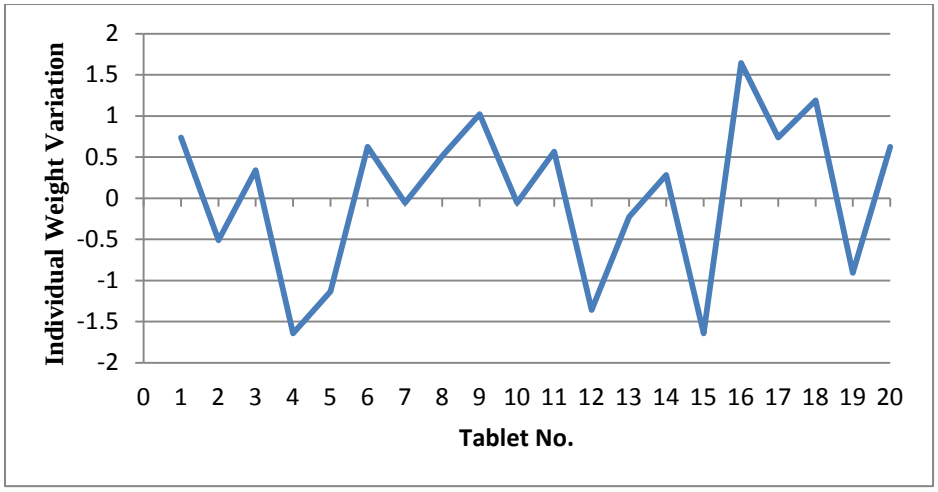


Fig 4.3: Individual weight variation of Camlodin® Plus (411002)

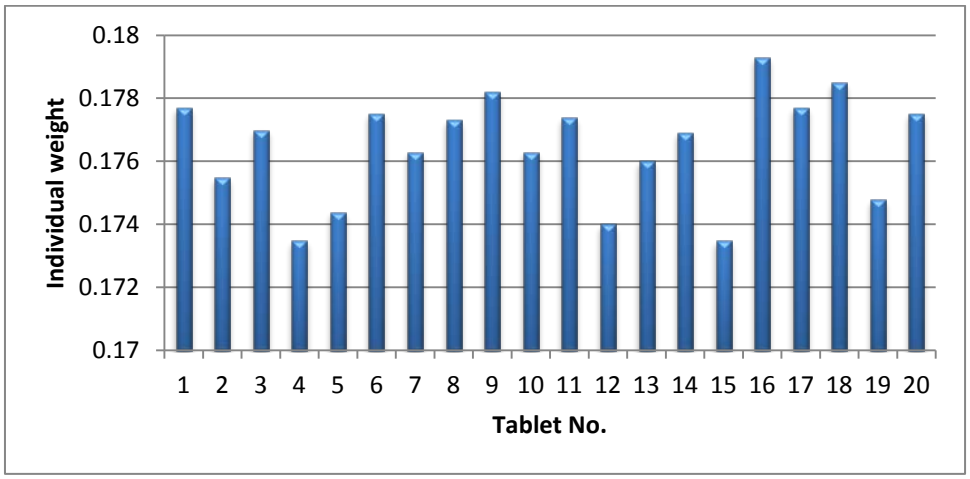


Fig 4.4: Weight of individual tablets for Camlodin® Plus (406003)

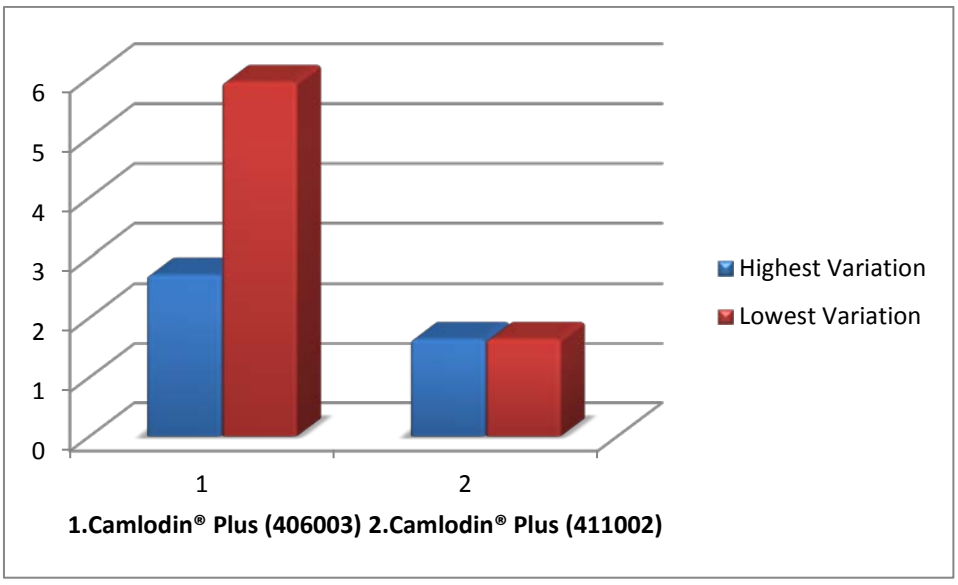


Fig 4.5: Comparison between two batches highest and lowest variations

Table 4.3: Weight variation of Amlovas® AT (SJJ58)

Number of tablets	Weight of individual tablets (g)	Average weight (g)	Individual weight Variation (%)	Highest weight variation (%)	Lowest weight variation (%)
1	0.2720	0.2730	-0.39184	1.8420	-1.9299
2	0.2680		-1.85667		
3	0.2764		1.219468		
4	0.2712		-0.68481		
5	0.2678		-1.92991		
6	0.2765		1.256088		
7	0.2690		-1.49046		
8	0.2729		-0.06226		
9	0.2776		1.658915		
10	0.2682		-1.78343		
11	0.2729		-0.06226		
12	0.2726		-0.17212		
13	0.2726		-0.17212		
14	0.2729		-0.06226		
15	0.2762		1.146226		
16	0.2733		0.084227		
17	0.2755		0.889882		
18	0.2732		0.047607		
19	0.2781		1.842019		
20	0.2745		0.523675		

SD of Individual weight is 0.0031

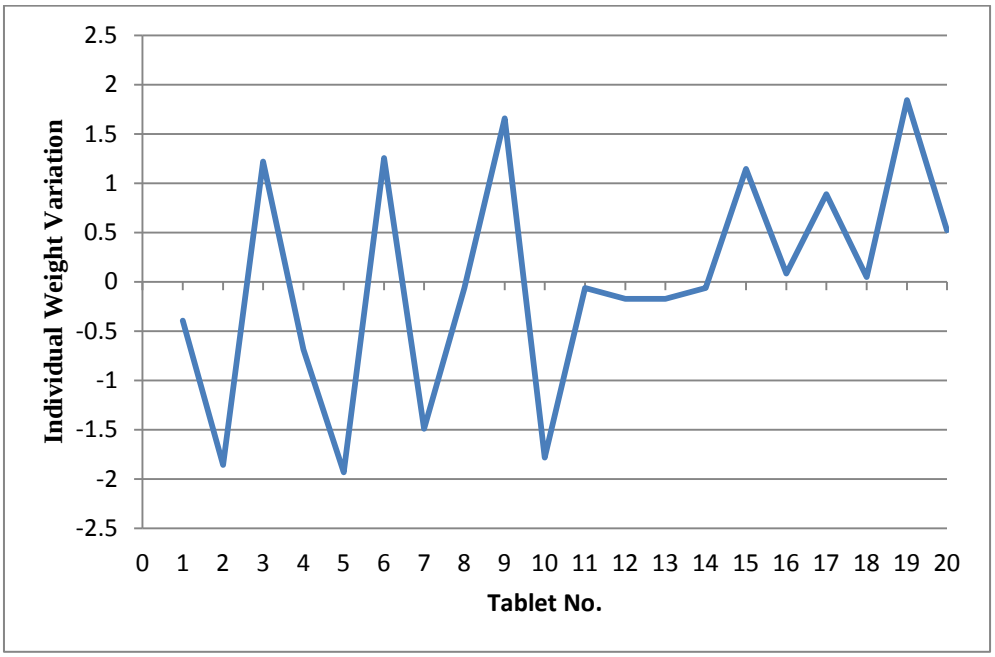


Fig 4.6: Individual weight variation of Amlovas® AT (SJJ58)

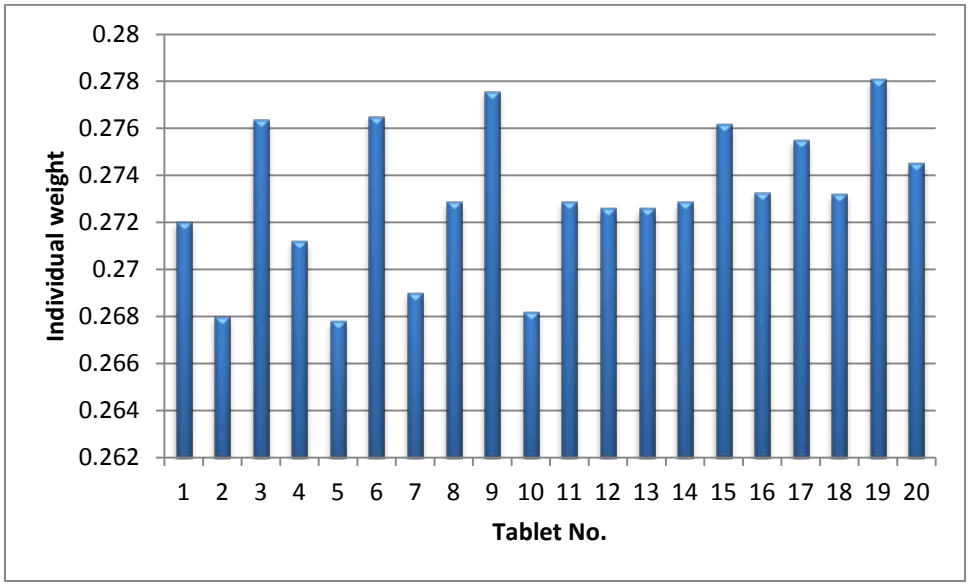


Fig 4.7: Weight of individual tablets for Amlovas® AT (SJJ58)

Table 4.4: Weight variation of Amlovas® AT (SGJ52)

Number of tablets	Weight of individual tablets (g)	Average weight (g)	Individual weight Variation (%)	Highest weight variation (%)	Lowest weight variation (%)
1	0.2746	0.2736	0.365497	2.5219	-2.8508
2	0.2792		2.046784		
3	0.2775		1.425439		
4	0.2749		0.475146		
5	0.2727		-0.32895		
6	0.273		-0.2193		
7	0.2805		2.52193		
8	0.2773		1.352339		
9	0.278		1.608187		
10	0.2676		-2.19298		
11	0.2725		-0.40205		
12	0.2718		-0.65789		
13	0.2715		-0.76754		
14	0.2802		2.412281		
15	0.2699		-1.35234		
16	0.2716		-0.73099		
17	0.2658		-2.85088		
18	0.2705		-1.13304		
19	0.2721		-0.54825		
20	0.2708		-1.02339		

SD of individual weight is 0.0040

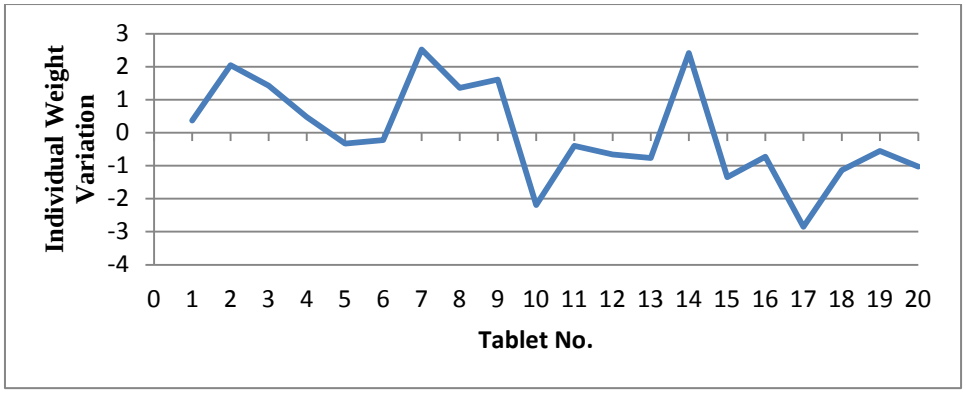


Fig 4.8: Individual weight variation of Amlovas® AT (SGJ52)

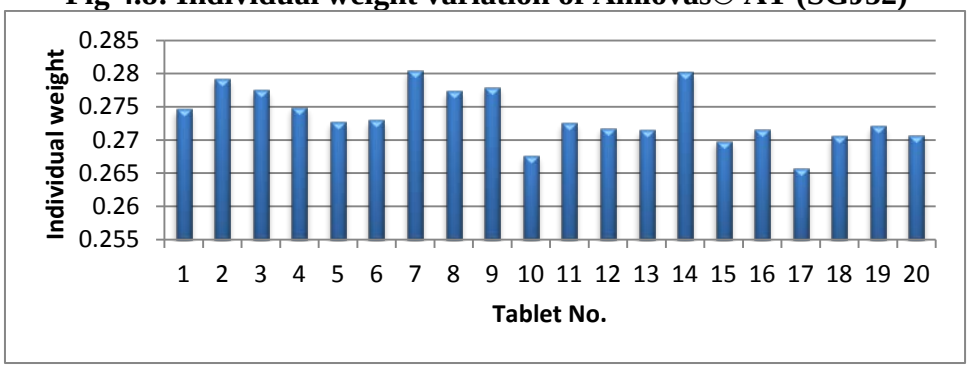


Fig 4.9: Weight of individual tablets for Amlovas® AT (SGJ52)

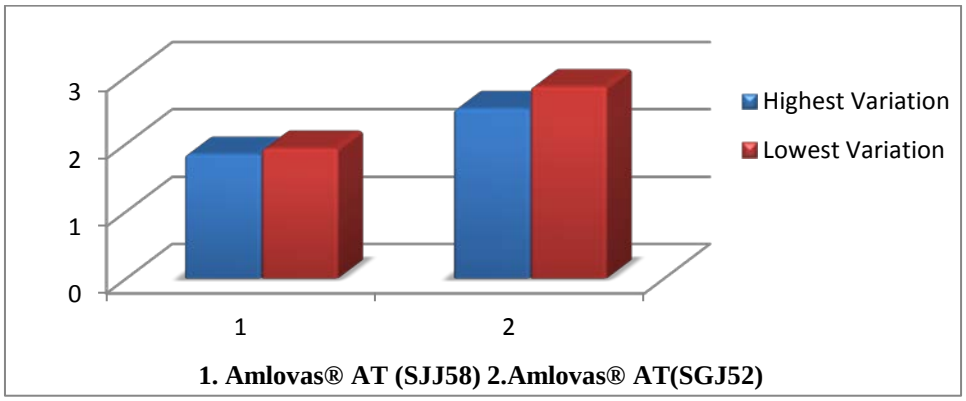


Fig 4.10: Comparison between two batches highest and lowest variations

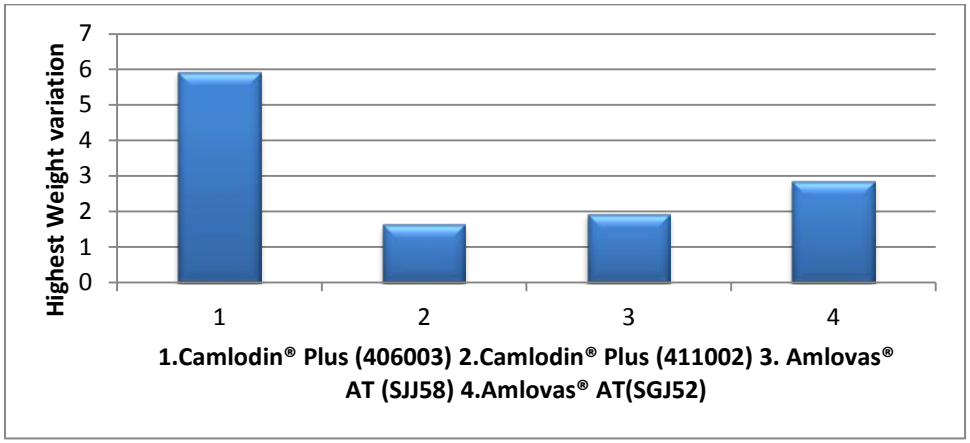


Fig 4.11: Comparison between the highest weight variations of 4 batches

4.2 Thickness test

Thickness test of 2 brands of combined atenolol and amlodipine tablets are given below.

Table 4.5: Thickness test of Camlodin® Plus (406003)

Number of tablets	Reading of main scale(mm)	Reading Of vernier scale	Vernier constant	Vernier error	Thickness (mm)	Average (mm)
1	3.5	5	0.1	0.05	4.05	4.12
2	3.5	6			4.15	
3	3.5	5.5			4.1	
4	3.5	7			4.25	
5	3.5	6.5			4.2	
6	3.5	5			4.05	
7	3.5	5			4.05	
8	3.5	6			4.15	
9	3.5	5			4.05	
10	3.5	6			4.15	

SD of Thickness=0.0714

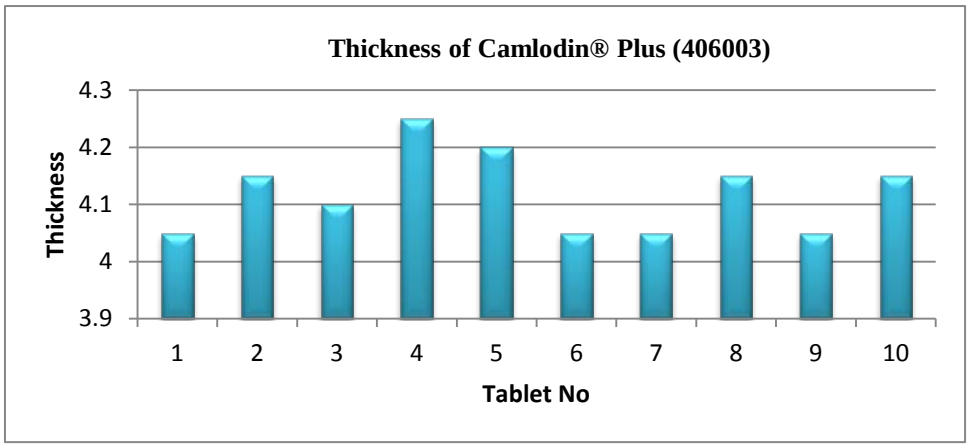


Fig 12: Thickness of tablets of Camlodin® Plus (406003)

Table 4.6: Thickness test of Camlodin® Plus (411002)

Number of tablets	Reading of main scale(mm)	Reading Of vernier scale	Vernier constant	Vernier error	Thickness (mm)	Average (mm)
1	3.5	5	0.1	0.05	4.05	4.1
2	3.5	6			4.15	
3	3.5	6			4.15	
4	3.5	5			4.05	
5	3.5	6			4.15	
6	3.5	6			4.15	
7	3.5	5			4.05	
8	3.5	5			4.05	
9	3.5	5			4.05	
10	3.5	6			4.15	

SD of Thickness=0.0527

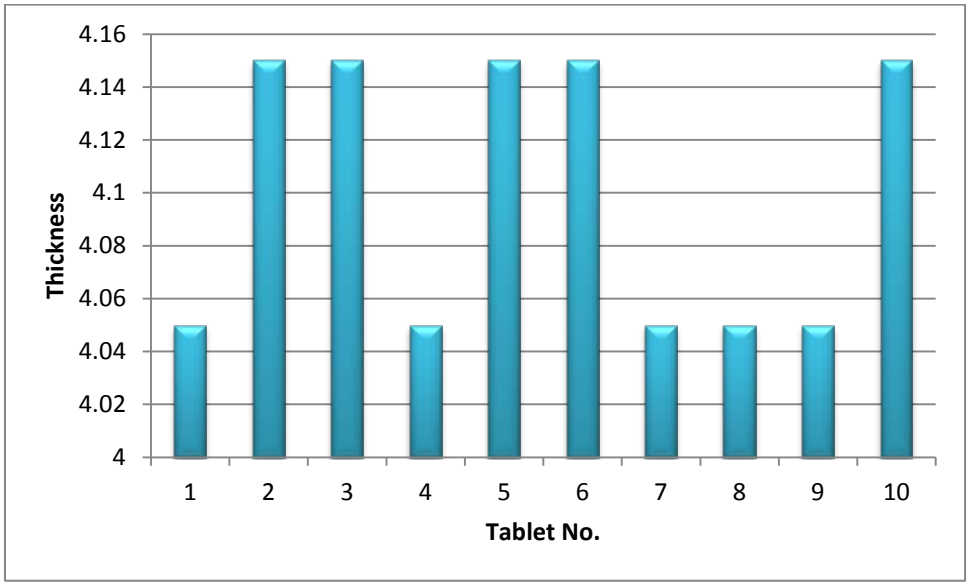


Fig 4.13: Thickness of tablets of Camlodin® Plus (411002)

Table 4.7: Thickness test of Amlovas® AT SJJ58

Number of tablets	Reading of main scale(mm)	Reading Of vernier scale	Vernier constant	Vernier error	Thickness (mm)	Average (mm)
1	3	2	0.1	0.05	3.25	3.3
2	3	3			3.35	
3	3	2.5			3.3	
4	3	3			3.35	
5	3	3			3.35	
6	3	2.5			3.3	
7	3	2			3.25	
8	3	2			3.25	
9	3	3			3.35	
10	3	2			3.25	

SD of Thickness=0.0471

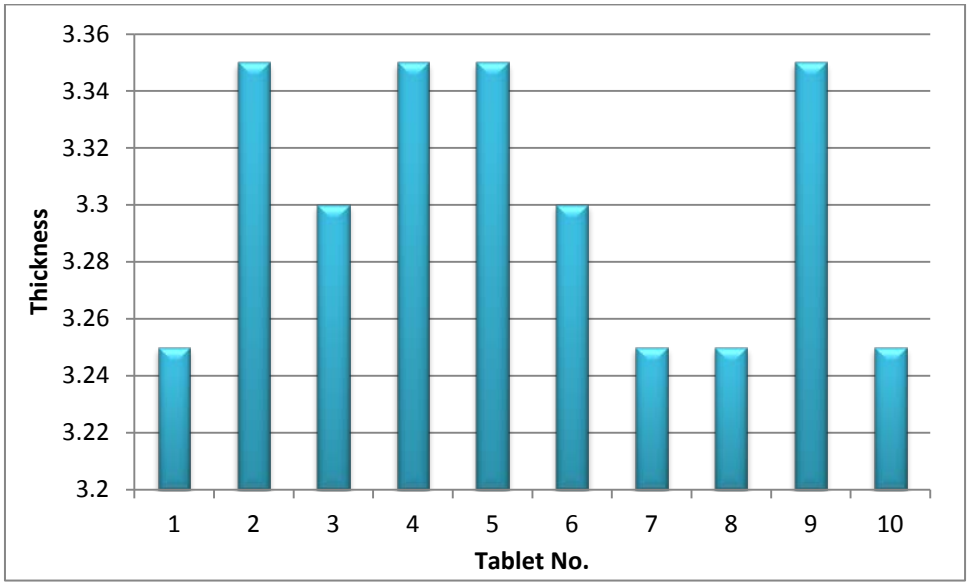


Fig 4.14: Thickness of tablets of Amlovas® AT SJJ58

Table 4.8: Thickness test of Amlovas® AT SGJ52

Number of tablets	Reading of main scale(mm)	Reading Of vernier scale	Vernier constant	Vernier error	Thickness (mm)	Average (mm)
1	3	2	0.1	0.05	3.25	3.215
2	3	1.5			3.2	
3	3	2			3.25	
4	3	1.5			3.2	
5	3	2			3.25	
6	3	1.5			3.2	
7	3	1.5			3.2	
8	3	1.5			3.2	
9	3	1			3.15	
10	3	2			3.25	

SD of Thickness=0.0337

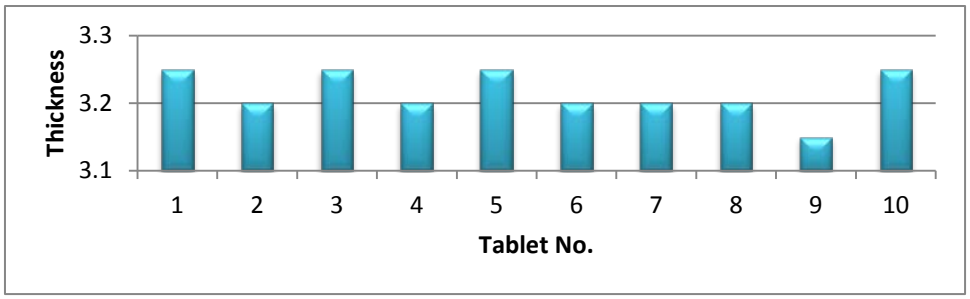


Fig 4.14: Thickness of tablets of Amlovas® AT SJJ58

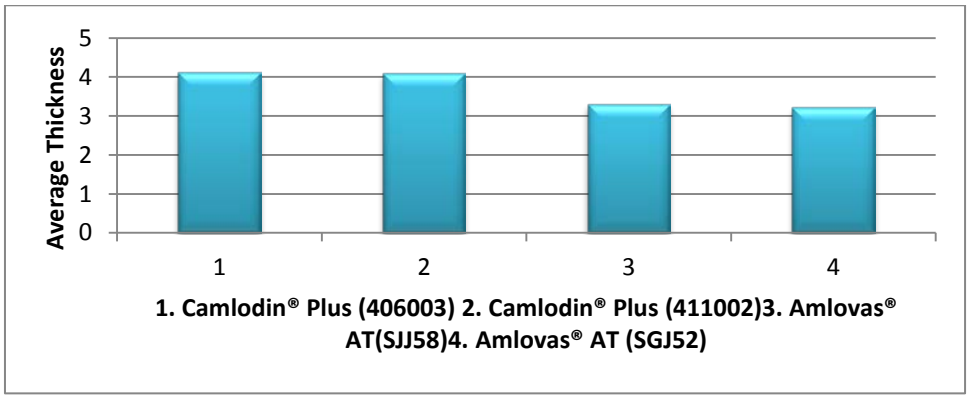


Fig 4.15: Comparison of average thickness of 4 batches

4.3 Hardness test

Hardness test of 2 brands of combined atenolol and amlodipin tablets are given below:

Table 4.9: Hardness test of Camlodin® Plus (406003)

Number of tablets	Hardness (Kg)	Average (kg)
1	2.5	2.35
2	2.5	
3	2	
4	2.5	
5	2	
6	2.5	
7	2.5	
8	2.5	
9	2	
10	2.5	

SD of Hardness=0.2415

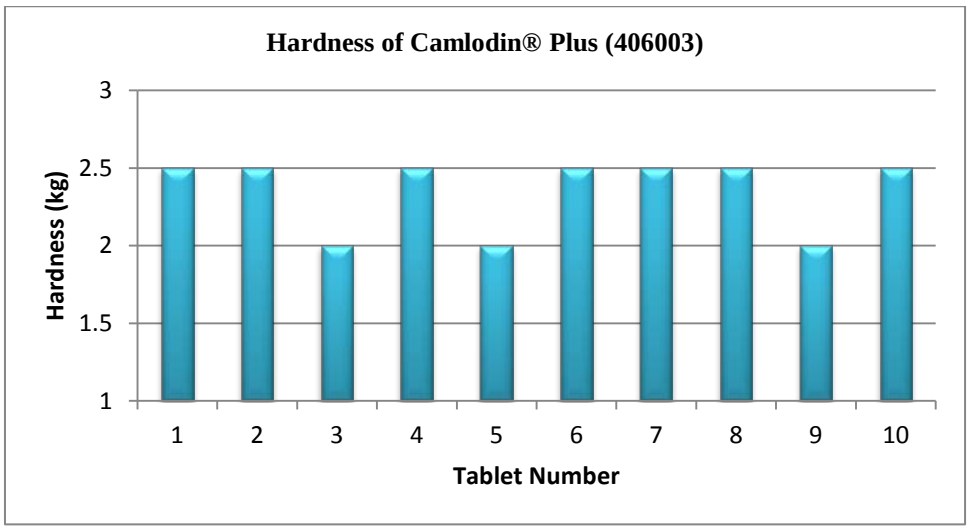


Fig 4.16: Hardness of Camlodin® Plus (406003)

Table 4.10: Hardness test of Camlodin® Plus (411002)

Number of tablets	Hardness (Kg)	Average (kg)
1	2.5	2.05
2	2	
3	2	
4	2	
5	2	
6	2	
7	2.5	
8	2	
9	2	
10	1.5	

SD of Hardness=0.2838

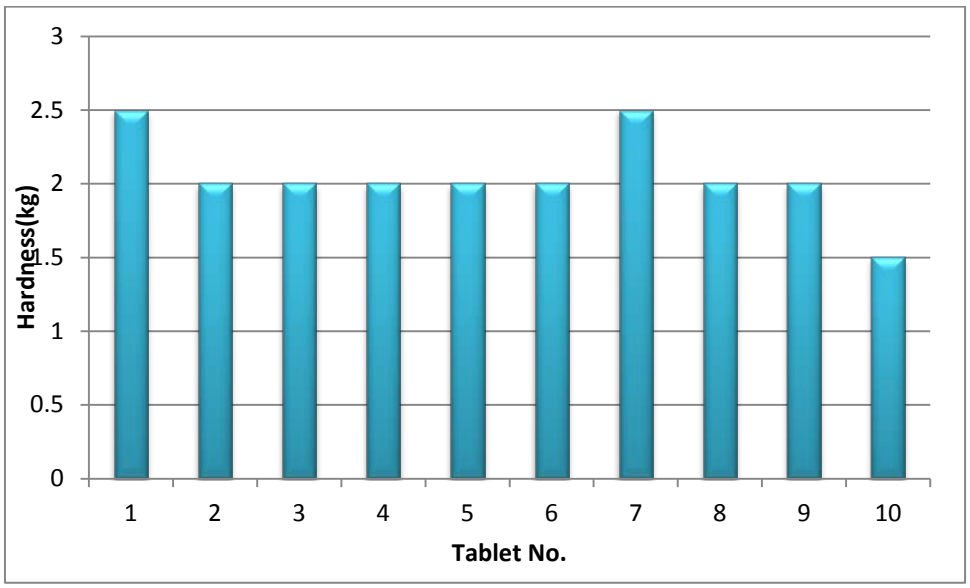


Fig 4.17: Hardness of Camlodin® Plus (411002)

Table 4.11: Hardness test of Amlovas® AT SJJ58

Number of tablets	Hardness (Kg)	Average (kg)
1	2.5	2.35
2	2.5	
3	2	
4	2.5	
5	2	
6	2.5	
7	2.5	
8	2.5	
9	2	
10	2.5	

SD of Hardness=0.2415

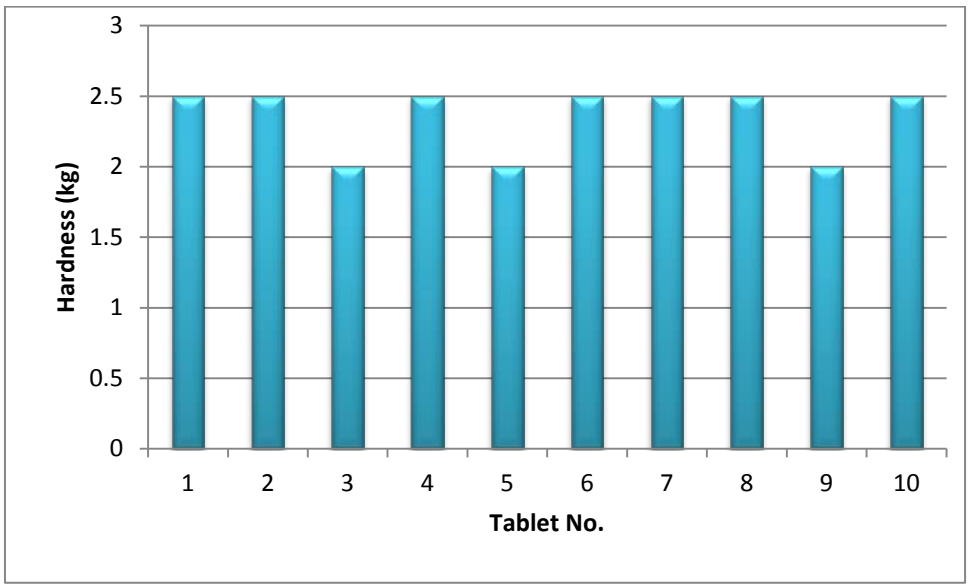


Fig 4.18: Hardness of Amlovas® AT (SJJ58)

Table 4.12: Hardness test of Amlovas® AT SGJ52

Number of tablets	Hardness (Kg)	Average (kg)
1	3	3.55
2	3	
3	4	
4	3.5	
5	4	
6	3.5	
7	3	
8	3.5	
9	4	
10	4	

SD of Hardness=0.4377

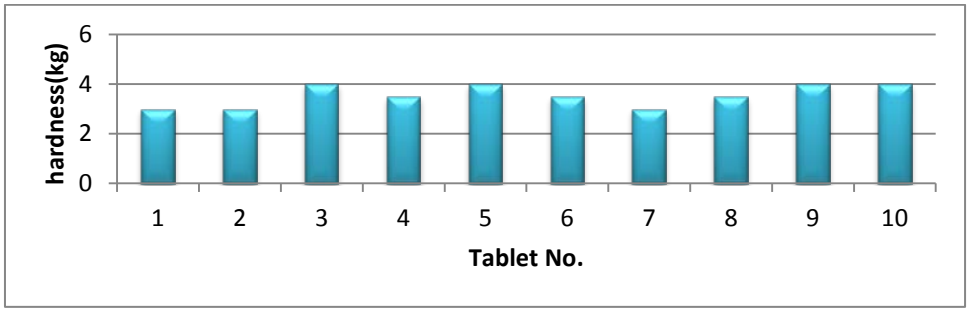


Fig 4.19: Hardness of Amlovas® AT (SGJ52)

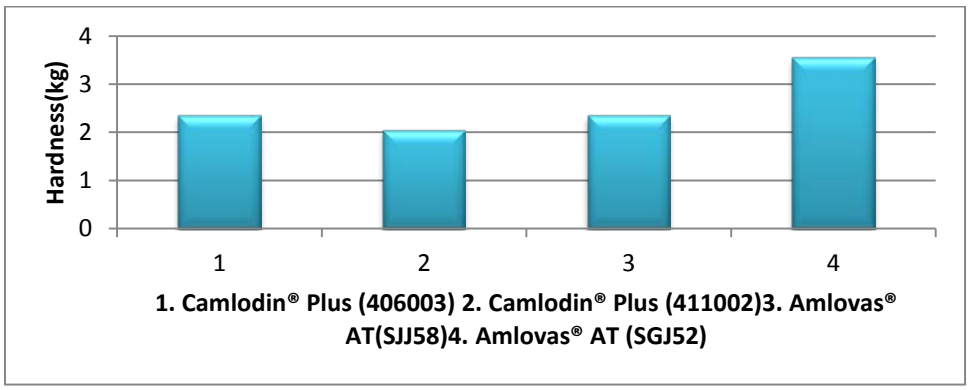


Fig 4.20: Comparison of average hardness (kg) of 4 batches

4.4 Disintegration test

Disintegration test of 2 brands of combined atenolol and amlodipine tablets are given below:

Table 4.13: Disintegration test Camlodin® Plus 41002 & Camlodin® Plus 406003

Number of tablets	Disintegration time (min) of Camlodin® Plus 411002	Average (min)	Disintegration time (min) of Camlodin® Plus 406003	Average (min)
1	3.54	4.08	3	3.27
2	3.55		3.01	
3	3.54		3.13	
4	4.35		3.11	
5	4.47		3.32	
6	5.04		4.07	

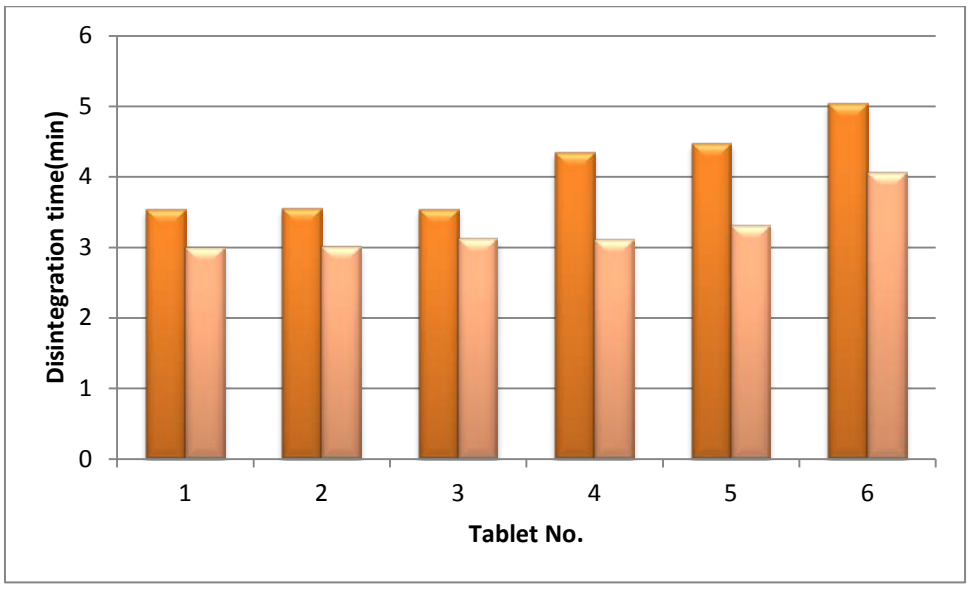


Fig 4.21: Comparison of disintegration time between two batches of Camlodin® Plus

Table 4.14: Disintegration test of Amlovas® AT SJJ58 & SGJ52

Number of tablets	Disintegration time (min) of Amlovas® AT SJJ58	Average (min)	Disintegration time (min) of Amlovas® AT SGJ52	Average (min)
1	14.00	15.01	12.44	13.63
2	14.56		13.13	
3	15.43		13.58	
4	15.34		14.07	
5	15.56		14.18	
6	16.25		14.39	

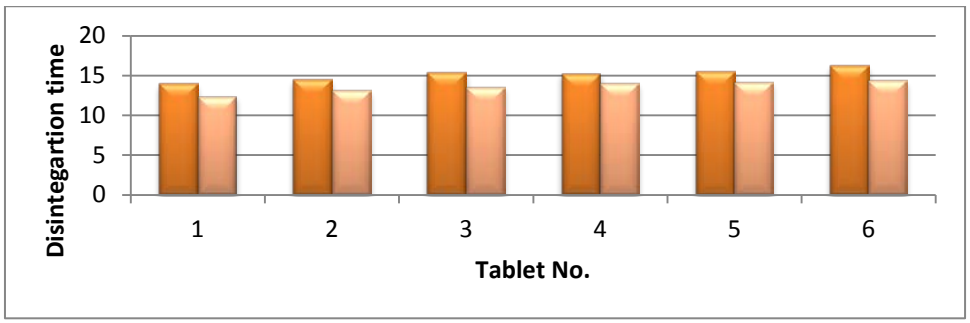


Fig 4.22: Comparison of disintegration time between two batches of Amlovas® AT

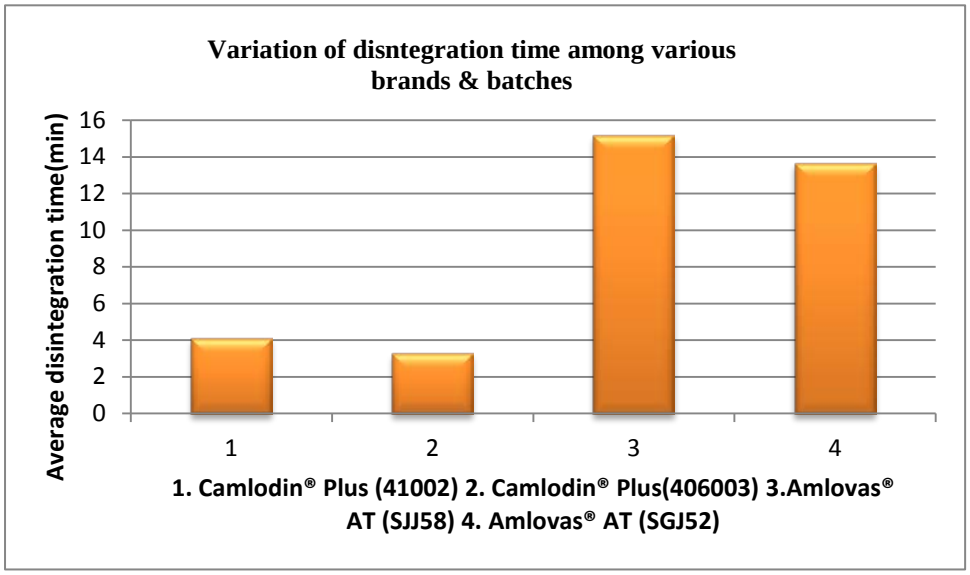


Figure 4.23: A comparison of average disintegration time among various brands

4.5 Potency test

Potency test of 2 brands of combined atenolol and Amlodipine tablets are given below:

4.15: Potency test of 2 brands for Amlodipine:

Name of brand	Concentration	Absorbance at 237.5 nm	Absorbance of pure amlodipine at 237.5 nm wavelength	% Potency
Camlodin® Plus 406003	5 µg/ml	0.805	0.521	110
Camlodin® Plus 411002		0.681		94
Amlovas® AT SJJ58		0.655		90
Amlovas® AT SGJ52		0.628		86

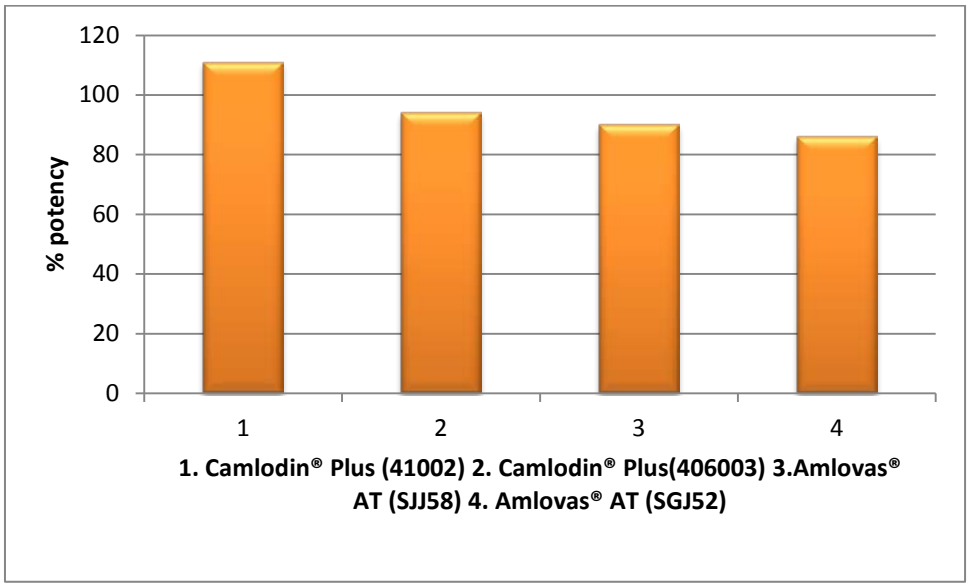


Fig 4.24: Comparison of %Potency of Amlodipine among various brands

4.16: Potency test of 2 brands for Atenolol:

Name of brand	Concentration	Absorbence at 223.5 nm	Absorbence of pure atenolol at 223.5 nm wavelength	% Potency
Camlodin® Plus 406003	5 µg/ml	0.483	0.264	91
Camlodin® Plus 411002		0.473		90
Amlovas® AT SJJ58		0.477		90
Amlovas® AT SGJ52		0.479		90

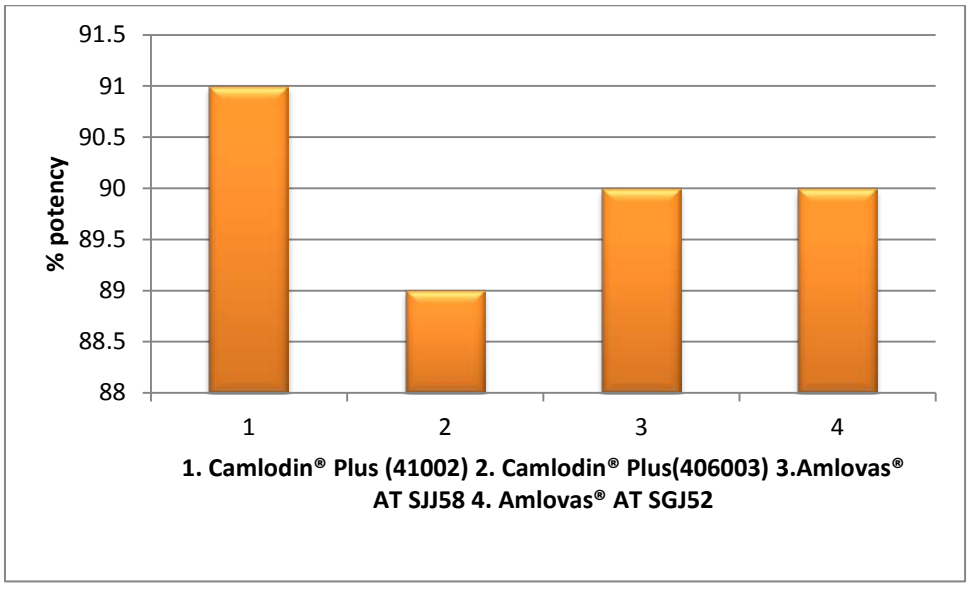


Fig 4.25: Comparison of %Potency of Atenolol among various brands

4.6 Dissolution Test

Table 4.17: Dissolution test of Camlodin® Plus (411002)

Amlodipine				Atenolol			
Drug	**Absorbance (237.5 nm)**	**Conc.**	**% dissolved**	**Drug**	**Absorbance (223.5 nm)**	**Conc.**	**% dissolved**
1	0.800	5 µg/ml	100	1	0.465	5 µg/ml	132
2	0.772		96	2	0.454		129
3	0.770		96	3	0.383		109
4	0.784		98	4	0.441		125
5	0.793		99	5	0.618		194
6	0.770		96	6	0.410		116
Average			97.5	Average			134.16

Table 4.18: Dissolution test of Camlodin® Plus (406003)

Amlodipine				Atenolol			
Drug	**Absorbance (237.5 nm)**	**Drug**	**Absorbance (237.5 nm)**	**Drug**	**Absorbance (237.5 nm)**	**Drug**	**Absorbance (237.5 nm)**
1	0.743	5 µg/ml	93	1	0.404	5 µg/ml	115
2	0.820		102	2	0.451		128
3	0.828		103	3	0.456		126
4	0.773		96	4	0.441		125
5	0.775		96	5	0.423		120
6	0.812		101	6	0.440		125
Average			98.5	Average			123.16

Table 4.19: Dissolution test of Amlovas® AT (SJJ58)

Amlodipine				Atenolol			
Drug	**Absorbance (237.5 nm)**	**Drug**	**Absorbance (237.5 nm)**	**Drug**	**Absorbance (237.5 nm)**	**Drug**	**Absorbance (237.5 nm)**
1	0.720	5 µg/ml	90.14	1	0.375	5 µg/ml	106
2	0.719		90.01	2	0.421		119
3	0.662		82.88	3	0.356		101
4	0.689		86.26	4	0.370		105
5	0.723		90.51	5	0.424		120
6	0.779		97.53	6	0.409		116
Average			89.55	Average			111.16

Table 4.20: Dissolution test of Amlovas® AT (SGJ52)

Amlodipine				Atenolol			
Drug	**Absorbance (237.5 nm)**	**Drug**	**Absorbance (237.5 nm)**	**Drug**	**Absorbance (237.5 nm)**	**Drug**	**Absorbance (237.5 nm)**
1	0.736	5 µg/ml	92.13	1	0.436	5 µg/ml	124.48
2	0.752		94.15	2	0.528		150.48
3	0.728		91	3	0.478		136.23
4	0.774		97.03	4	0.477		135.94
5	0.763		95.52	5	0.481		137.08
6	0.780		97.65	6	0.407		115.99
Average			94.58	Average			133.36

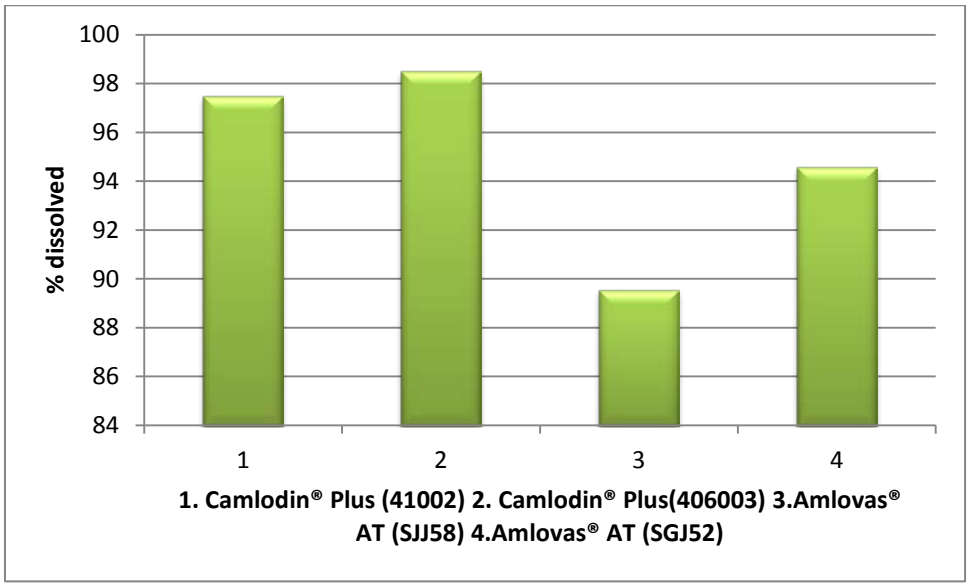


Fig 4.26: Comparison of %Dissolved of Atenolol among various brands

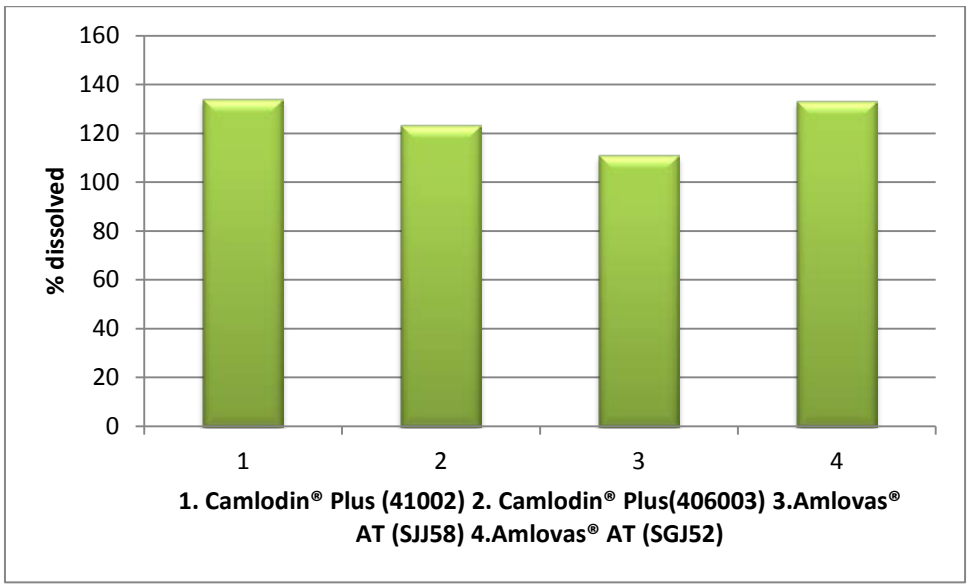


Fig 4.27: Comparison of %Dissolved of Amlodipine among various brands

CHAPTER-5

DISCUSSION

Chapter 5

DISCUSSION

5.1 Weight variation

The % weight variation for Camlodin® Plus ranged from 2.7161% to -5.9312% (Batch no 406003) with a Standard deviation of 0.0033 for individual weights and 1.6439% to -1.6439% (Batch no 411002) with a Standard deviation of 0.0016 for individual weights. The % weight variation for Amlovas® AT ranged from 1.8420% to -1.9299% (Batch no. SJJ58) with a Standard deviation of 0.0031 for individual weights and 2.5219% to -2.8508% (Batch no. SGJ52) with a Standard deviation of 0.0040 for individual weights.

Average weights of tablets were in between 130 mg to 324 mg so, according to the USP specification, the range of weight variation is ±7.5%. All 4 batches of tablets from the two brands complies with U.S.P specification and signifies that there is uniformity in flow of powder blend which leads to uniform die fill.

5.2 Thickness test

According to the USP specification, the range for tablet thickness is ±5mm. All the brands of combined atenolol and amlodipine, Camlodin® Plus (Batch-411002) with an average thickness of 4.1mm and standard deviation of 0.0527, Camlodin® Plus (Batch-406003) with an average thickness of 4.12mm and standard deviation of 0.0714, Amlovas® AT (Batch-SJJ58) with an average thickness of 3.3mm and standard deviation of 0.0471, Amlovas® AT (Batch-SGJ52) with an average thickness of 3.215mm and standard deviation of 0.0337, met the specification of USP for tablet thickness.

5.3 Hardness test

According to the USP specification, the minimum tablet hardness is 4kg and the range of hardness is 4 to 8 kg or 10kg for oral tablets. All the batches, Camlodin® Plus (Batch-411002) with an average hardness of 2.05 kg and standard deviation of 0.2838, Camlodin® Plus (Batch-406003) with an average hardness of 2.35 kg and standard

deviation of 0.2415, Amlovas® AT (Batch-SJJ58) with an average hardness of 2.35 kg and standard deviation of 0.2415 and Amlovas® AT (Batch-SGJ52) with an average hardness of 3.55 kg and standard deviation of 0.4377 of both the brands falls short on the range, none even comes close except Amlovas® AT (Batch no. SGJ52).

5.4 Disintegration test

According to BP limit of disintegration time for, uncoated tablet is 15 minutes; coated tablet is 30 minutes enteric coated tablet is 60 minutes or 1 hour. Both Camlodin® Plus and Amlovas® AT are uncoated tablets and all the bathes, Camlodin® Plus (Batch-411002) with an average disintegration time of 4.08 min, Camlodin® Plus (Batch-406003) with an average disintegration time of 3.27 min, Amlovas® AT (Batch-SJJ58) with an average disintegration time of 15.01 min, Amlovas® AT (Batch-SGJ52) with an average disintegration time of 13.63 min met the specification.

5.5 Potency test

According to BP, in order to pass the potency test, tablets should not contain less than 90.0% and not more than 110.0% of atenolol and amlodipine. For atenolol all four batches; Camlodin® Plus (Batch-406003) with a potency of 91%, Camlodin® Plus (Batch-411002) with a potency of 90%, Amlovas® AT Batch-SJJ58 with a potency of 90% and Amlovas® AT (Batch-SGJ52) with a potency of 90% met the specification except. For amlodipine three batches; Camlodin® Plus (Batch-411002) with a potency of 94%, Camlodin® Plus (Batch-406003) with a potency of 110% and Amlovas® AT (Batch-SJJ58) with a potency of 90% met the specification, only Amlovas® AT (Batch-SGJ52) with a potency of 86% didn't met the specification. This was may be due to the error of formulation or processing or analytical error or Personal error.

5.6 Dissolution Test

According to WHO for sample of six tablets, the % release of tablet should be 85% within 30 minute (WHO, 2014). For Camlodin® Plus (411002), % dissolved of Amlodipine ranged from 96-100% with an average of 97.5% and Atenolol ranged from 109-194% with an average of 134.16. For Camlodin® Plus (406003), % dissolved of

Amlodipine ranged from 93-103% with an average of 98.5% and Atenolol ranged from 115-128% with an average of 123.16. For Amlovas® AT (SJJ58), % dissolved of Amlodipine ranged from 82.88-97.53% with an average of 89.55% and Atenolol ranged from 101-120% with an average of 111.16. For Amlovas® AT (SGJ52), % dissolved of Amlodipine ranged from 91-97.65% with an average of 94.58% and Atenolol ranged from 115.99-150.48% with an average of 133.36.Thus all 4 batch met the specification.

CHAPTER-6

CONCLUSION

Chapter 6

CONCLUSION

Combination of atenolol and amlodipine is a good therapeutic class in terms of treating blood pressure and its related disease. Hence it is important to maintain its quality to give the specified and expected effect. In this study it was observed that the two brands of combined atenolol and amlodipine have passed most of the quality control parameter tests with the specifications described in USP and BP. In weight variation test a comparison among the two brands revealed that Camlodin® Plus had the highest weight variation. In thickness test a comparison among two brands clearly shows that Amlovas® AT has a more consistence thickness than Camlodin® Plus. In the hardness test all batch of both brand shows lower value than the specified range (4 to 8 or 10 kg). Both batches of Camlodin® Plus had a very low hardness value. Rapid disintegration time is seen among both batches of Camlodin® Plus due to its poor hardness value and comparatively Amlovas® AT had a higher disintegration time. This low hardness value signifies that it is not hard enough to withstand mechanical shocks during manufacturing, packaging, shipping and could face reasonable abuse by the consumer. In the potency test for Atenolol all batches met the specification but in case of Amlodipine Amlovas® AT (Batch-SGJ52) shows a lower potency (86%) than the specified range (90 to 110%). This may occur due to formulation or processing error or may be due to the analytical error or personal error. Due to some technical problem friability study was not carried out. So, further study needs to be conducted regarding the quality control parameters as these products are now becoming a potential choice of drugs for hypertension control.

CHAPTER-7

REFERENCES

Chapter 7

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