Evaluation of the Quality Control Parameters of Five Different Brands of Olmesartan Medoxomil (20 mg) Tablets Available in Bangladesh

By

Jaba Tahasin Samiha Treeno
19346018

A thesis submitted to the School of Pharmacy in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy

School of Pharmacy
Brac University
September 2024

Declaration

It is hereby declared that

1. The thesis submitted is my original work while completing degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I have acknowledged all main sources of help.
5. **Student's Full Name & Signature:**

Jaba Tahasin Samiha Treeno
19346018

Approval

The thesis titled "Evaluation of quality control parameters of five different brands of Olmesartan medoxomil (20mg) tablets available in Bangladesh", submitted by Jaba Tahasin Samiha Treeno, of Summer, 2024 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy.

Supervised By:

Mohd. Raeed Jamiruddin, PhD
Associate Professor
School of Pharmacy
Brac University

Approved By:

Dean:

A.F.M. Yusuf Haider, PhD
Acting Dean, School of Pharmacy
Professor, Department of Mathematics and Natural Sciences
Brac University

Ethics Statement

No animals were used during experiments.

Abstract

Treatment of any disease can be failed by prescribing a substandard drug. Nowadays Olmesartan Medoxomil is widely used in Bangladesh for the treatment of hypertension. Therefore, the goal of this study is to evaluate the competitive environment of the local market and evaluate the quality parameters with multiple Olmesartan Medoxomil brands. Five chosen brands experimented for physiochemical evaluation and in-vitro evaluation study as per USP. Experimented five brands met the weight variation USP range (differences % ±7.5) and specification of USP Hardness range (4 to 8 or 10 kg). The friability study also matches the USP criteria (mean weight loss ≤ 1%) and disintegration study parameters of BP. Dissolution study were within acceptable criteria according to BP and USP. Only one brand did not match the linearity criteria due to analytical error. Yet the marketed brands in Bangladesh could be prescribed equally as they met USP standard.

Keywords: Olmesartan Medoxomil; Weight variation; Hardness; Friability; Disintegration; Dissolution.

Dedication:

I would like to dedicate my work to my dearest parents who encouraged and supported me throughout my journey.

Acknowledgement

All praise to Almighty Allah for giving me the opportunity to complete my research work appropriately and patiently.

I would like to convey my deepest gratitude and pleasure to my supervisor Dr. Mohd. Raeed Jamiruddin (Associate professor, School of pharmacy, Brac University) for his constant guidance and continuous encouragements to implement the research work. His crucial suggestions and arrangements of important research facilities will be always remembered.

I am Indebted to Prof. Dr. A.F.M. Yusuf Haider, PhD (Acting Dean, School of Pharmacy) for his kind support and permission to use the available facilities at designated lab. I also offer my deepest gratitude to all my respected faculty members.

I also give my thanks to the Laboratory authority. I seek thankfulness to Ayesha Abed Library, Brac University and rest of the university facilities to allow me to conduct my experimental research works without hurdle.

At the last, I would like to thank my beloved family to give me moral support throughout my work.

Table of Contents

Declaration.....**ii**

Approval ..... **iii**

Ethics Statement.....**iv**

Abstract/ Executive Summary.....**v**

Dedication……**vi**

Acknowledgement……..**vii**

Table of Contents……**viii-xii**

List of Table ..... **xiiii-xvi**

List of Figures..... **xii-xiv**

Acronym……**xvii**

Chapter 1 Introduction.....**1**

1.1 General……..1-2

1.2 Hypertension…….2

1.3 Classification……....3

1.4 Symptoms…….....3-4

1.5 Causes of hypertension…….....4

1.5.1 Primary hypertension…… 4

1.5.2 Secondary hypertension……...4-5

1.6 Treatment strategies…….....5

1.7 Hypertension management…….....6

1.8 Classification of hypertension……...7

1.9 Olmesartan Medoxomil……8

1.9.1 Discovery……8

1.9.2 Chemistry…….. 8-10

1.9.3 Mechanism of action ……10-11

1.9.4 Dosage and administration ……11

1.9.5 Side effect ……11-12

1.9.6 Contraindication ……...12

1.9.7 Drug Interactions ……..13

1.9.8 Interaction with other medicinal products……13

1.10 Quality……...……..13-14

1.11 Quality control……..……...15-16

1.12 Quality of pharmaceutical product……...……....15-16

1.13 Quality assurance……..……16

1.14 Importance of quality control……...16-17

1.15 Quality control parameters of solid dosage form…….....17

1.15.1 Weight variation……17-18

1.15.2 Hardness test……18

1.15.3Friability test……...18-19

1.15.4 Disintegration test……..19

1.15.5 Dissolution test…….19-21

Significance of the study……...21

Aims and objective of the study……...…21-22

Chapter 2 Methodology…….....23

2.1 Sample……....23

2.2 Weight variation…….....24

2.2.1 Instrument…….....24

2.2.2 Method……24

2.2.3 Calculation…….24

2.2.4 Specification……...25

2.3 Hardness test…….....25

2.3.1 Method……25

2.3.2 Measurement unites……...25-26

2.3.3 Specification……26

2.4 Disintegration test……...26

2.4.1 Condition…….26

2.4.2 Method…….26

2.4.3 Specification……...26-27

2.5 Dissolution test…….....27

2.5.1 Condition…….27

2.5.2 Method…….27

2.5.3 Calculation……...27

2.5.4 Specification……...27-28

2.6 Friability test…….....28

2.6.1 Method…….28

2.6.2 Specification……28

Chapter 3 Result…….29

3.1 Weight variation……29-34

3.2 Hardness Test……34-37

3.3 Friability Test……..……38

3.2 Disintegration Test……..……..38-39

3.3 Dissolution Test……...……..39-41

Chapter 4 Discussion 42

4.1 Weight variation…….....42

4.2 Hardness test……...42

4.3 Friability test…….42-43

4.4 Disintegration test……...43

4.5 Dissolution test……...43

Chapter 5 Conclusion…….44

References……..45-49

List of Tables

Table 1.1: Classification of Hypertension……. 3

Table 1.2: Characteristics of Olmesartan medoxomil…… 9

Table 1.3: Solubility of Olmesartan Medoxomil……. 10

Table 2.1: Different brands along with their manufacturer names……...23

Table 2.2: Reagents & solvents…… 23

Table 2.3: List of Apparatus/ Glassware's used throughout this project…… 23

Table 2.4: Weight variation tolerance for tablet……25

Table 2.5: Acceptance criteria for Conventional-release dosage forms……...28

Table 3.1: Weight variation of (Olmesaf 20 mg) ……..30

Table 3.2: Weight variation of (Olmevas 20 mg) ……... 31

Table 3.3: Weight variation of (Olmesta 20 mg) ……..33

Table 3.4: Weight variation of (Olmecar 20 mg) ……34

Table 3.5: Weight variation of (Olmezest 20 mg) ……...36

Table 3.6: Hardness test of (Olmesaf 20 mg) …… 37

Table 3.7: Hardness test of (Olmevas 20 mg) …….....38

Table 3.8: Hardness test of (Olmesta 20 mg) ……..39

Table 3.9: Hardness test of (Olmecar 20 mg) ……...40

Table 3.10: Hardness test of (Olmezest 20 mg) ……41

Table 3.11: Friability test of different brands……43

Table 3.12: Disintegration test of different brands ……...44

Table 3.13: Dissolution test of (Olmesaf 20 mg)……...45

Table 3.14: Dissolution test of (Olmevas 20 mg) ……46

Tablet 3.15: Dissolution test of (Olmesta 20mg) ……..47

Table 3.16: Dissolution test of (Olmezest 20 mg) ……. ...48

Table 3.17: Dissolution test8 of (Olmecar 20 mg) ……. …..48

List of Figures

Figure 1.1: Olmesartan Medoxomil……9

Figure 3.1: Individual weight variation percentage of (Olmesaf 20 mg)…….30

Figure 3.2: Weight of individual tablet (Olmesafe 20 mg) …….. 31

Figure 3.3: Individual weight variation percentage of (Olmevas 20 mg) ……..32

Figure 3.4: Individual weight for (Olmevas 20 mg) …….32

Figure 3.5: Individual weight variation percentage of (Olmesta 20 mg) ……...33

Figure 3.6: Individual weight for (Olmesta 20 mg) …….,,,,,,34

Figure 3.7: Individual (%) weight variation of (Olmecar 20 mg) …….35

Figure 3.8: Individual weight variation for (Olmecar 20 mg) ……...35

Figure 3.9: Individual (%) weight variation of (Olmezest 20 mg) ……..36

Figure 3.10: Individual weight variation for (Olmezest 20 mg) ……37

Figure 3.11: Hardness of (Olmesaf 20 mg) ……...38

Figure 3.12: Hardness of (Olmevas 20 mg) ……..39

Figure 3.13: Hardness of (Olmesta 20 mg) ……...40

Figure 3.14: Hardness of (Olmecar 20 mg) ……..41

Figure 3.15: Hardness of (Olmezest 20 mg) …….42

Figure 3.16: Average hardness of Olmesartan Medoxomil 20 mg of different brands……..42

Figure 3.17: Weight loss tablets of different brand of Olmesartan Medoxomil (20mg)……43

Figure 3.18: Disintegration time of different brands of Olmesartan Medoxomil 20 mg……....44

Figure 3.19: Drug release of Olmesartan Medoxomil (Olmesaf 20 mg) ……...45

Figure 3.20: Drug release of Olmesartan Medoxomil (Olmevas 20 mg)……...46

Figure 3.21: Drug release of Olmesartan Medoxomil (Olmesta 20 mg) ……... ...46

Figure 3.22: Drug release of Olmesartan Medoxomil (Olmezest 20 mg) …….47

Figure 3.23: Drug release of Olmesartan Medoxomil (Olmecart 20 mg) …….48

Figure 3.24: Drug release of Olmesartan Medoxomil (standard) …….48

List of Acronyms

ACE	**Angiotensin-converting enzyme**
ARB	Angiotensin receptor blocker
BP	Blood pressure
CBC	Calcium Channel Blocker
CKD	Chronic kidney disease.
DBP	Diastolic blood pressure
HTN	High blood pressure
JNC 7	The seventh report of joint national committee.
OLM	Olmesartan
SBP	Systolic blood pressure

Chapter 1

Introduction

1.1 General

The pharmaceutical companies get paid for their significant costs and expenses in clinical trials for developing innovative drugs. Companies get drug patents for their innovation that further secure the product from competitors in the market for a certain period of time. By the time the patent expires on the innovator drug which opens the door for several companies to bring out their own generic drug. Although similar generic drugs are also available in the market, effective quality control is missing in many countries including Bangladesh. This situation arises many concerns and the most highlighted one is a prevalent dispensing of substandard or counterfeit drug products.

Drug items that are considered substandard are authentic and produced by licensed producers, but do not fulfill the quality requirements set out by national guidelines. Substandard drugs have a wide range of causes and complications. Incorrect active ingredient concentration, substandard excipients and active ingredients, product contamination, issues with packing, and active ingredient breakdown are some of the frequent issues (Dharmalingam, Madhappan, et al., 2014)).

Drug market surveillance is so essential. Several worldwide standards and recommendations have been released by WHO for the evaluation, approval, registration, marketing, and quality control of pharmaceutical products. Regulating pharmaceutical products that are on the market helps reduce health problems brought by improper use of drugs, as well as economic problems for a nation ((Dharmalingam, 2014)

The significance of drug quality control now becomes obvious. A smaller part of quality assurance, quality control deals with the sampling, testing, and documenting done both before and after manufacture to guarantee a particular degree of quality in a product. The monitoring process known as quality control is how manufacturers evaluate the actual performance of their products, compare them to standards, and identify any deviations from the standard to ensure product equality. In general, quality control refers to a process or a collection of actions made throughout a product's manufacture to guarantee that it meets specifications and can be produced again (Ashrafi, n.d.).

Thus, batch-to-batch drug release consistency and the quality attributes of several marketed brands may be monitored using quality control techniques of evaluation. Furthermore, medications with three or more generic brands need to be evaluated and monitored to make sure they can be replaced by innovator brands (Ashrafi, n.d.)

The amount of cases of hypertension is increasing worldwide. The prevalence of hypertension is much higher in countries with low and middle incomes than it is in countries with high incomes. The basis of treatment for control of hypertension is antihypertensive drugs. About 20% of adults and 40–65% of senior citizens in Bangladesh have hypertension. The cause of hypertension can be significantly affected by factors related to lifestyle, such as obesity, excessive salt consumption, and low physical activity, as well as by a high prevalence of metabolic syndrome (Islam & Majumder, 2012).

1.2 Hypertension

When the force of your blood hitting against the walls of your arteries is constantly excessive, you have high blood pressure. Over time, this causes damage to your arteries and raises the risk of major consequences, including heart attacks and strokes. Another term for this common disorder is "hypertension." The current criteria for hypertension (HTN) is 80 mm Hg (DBP)/130 mm Hg (SBP) or higher.

The definition of hypertension varies a little bit based on where you are located.

- Healthcare professionals in the United States describe hypertension, or high blood pressure, as: At least 130 mmHg for (SBP) and/or 80 mmHg for the (DBP) are minimum value.
- In Europe, hypertension is defined by medical professionals as: A minimum bottom measurement of 90 mmHg (SBP) and a minimum top measurement of 140 mmHg (DBP). (*High Blood Pressure*, n.d.)

1.3 Classification:

For the purpose of therapeutic management, hypertension is divided into four categories in the seventh report of the JNC 7. The categories are given in table 1.1 below:

Table 1.1: Classification of Hypertension: (*Ch32-Revised.Pdf*, n.d.)

	(SBP) mm Hg		(DBP) mm Hg
Normal	<120	and	<80
Pre-hypertension	120-139	or	80-89
Stage-I (Mild-hypertension)	140-149	or	90-99
Stage II	>160	or	>100

Heart strain from hypertension causes coronary artery disease and hypertensive heart disease (Lawes et al., 2003). Throughout the last century, hypertension has been extensively researched and has been identified as a major condition that increases the risk of stroke, myocardial infarction, heart failure, and renal failure (Hajar, 2017).

1.4 Symptoms

Healthcare practitioners call high blood pressure, a "silent killer" since there are usually no symptoms. It is possible to have high blood pressure for years without realizing it. According to estimates from the World Health Organization, 46% among people with hypertension are unawarethat they have the diseases. (*High Blood Pressure*, n.d.)

Symptoms like headaches, heart palpitations, or nosebleeds if blood pressure is 180/120 mmHg or higher. This raised blood pressure is a hypertensive crisis that has to be treated medically right away. (*High Blood Pressure*, n.d.)

According to WHO (March 16,2023), Individuals who have extremely high blood pressure (which is typically 120/180 or greater) undergoes the listed consequences:

- severe headaches
- chest pain
- dizziness
- difficulty breathing
- nausea

- vomiting
- blurred vision or other vision changes
- anxiety
- confusion
- buzzing in the ears
- nosebleeds
- abnormal heart rhythm. (*Hypertension*, n.d.)

1.5 Causes of hypertension

1.5.1 Primary hypertension

90–95% of cases of hypertension are primary (essential) hypertension, which is the most typical kind of the disease:

- Aging causes blood pressure to increase in almost every modern country, increasing the danger the possibility of developing hypertension in the future is high.The cause of hypertension is a complex relationship between genetics and environment
- Insulin resistance, a feature of syndrome X and a common phenomenon in obesity (or the metabolic syndrome) may potentially have a role in the development of hypertension.
- Furthermore, early life experiences (such as low birth weight, maternal smoking, and lack of breastfeeding) are indicated as major risk factor in recent studies for essential hypertension,
- Moreover, depression have also been linked to hypertension (Meng et al., 2012).

1.5.2 Secondary hypertension

Secondary hypertension develops from a known reason:

- The most frequent secondary cause of hypertension is renal illness.
- Endocrine disorders such as hyperparathyroidism, Cushing's syndrome, hyperthyroidism, hypothyroidism, Conn's syndrome, or hyperaldosteronism can also result in hypertension.
- Obesity, sleep apnea, pregnancy, aortic coarctation, excessive alcohol consumption, some prescription medications, herbal treatments, and illicit substances are additional causes of secondary hypertension. (Grossman & Messerli, 2012)

1.6 Treatment Strategies

Antihypertensive medication helps to lower cardiovascular adrenal morbidity and mortality. Since there is a continuous correlation between blood pressure and the risk of cardiovascular events, reducing blood pressure, even to a modestly high level, can significantly minimize the risk of cardiovascular disease. (Pazdernik, 2009)

Pre-Hypertension: Emphasizes this link and highlights the necessity of reducing blood pressure in the general public via changes in behavior and education. A SBP of <140 mm Hg and a DBP of <90 mm Hg are the blood pressure goals for the majority of individuals receiving hypertension treatment. (Pazdernik, 2009)

Mild- Hypertension: It can sometimes be managed with monotherapy; however, the majority of patients need several medications to achieve blood pressure management. The current guidelines suggest starting treatment with an ACE inhibitor, CCB, ARB, or thiazide diuretic. (Pazdernik, 2009)

Stage II: Patients should begin taking two antihypertensive medications at the same time if their SBP is >160 mm Hg or their DBP >100 mm Hg (or if their SBP is > 20 mm Hg over target or their DBP >10 mm Hg above goal). (Pazdernik, 2009)

1.7 Hypertension management

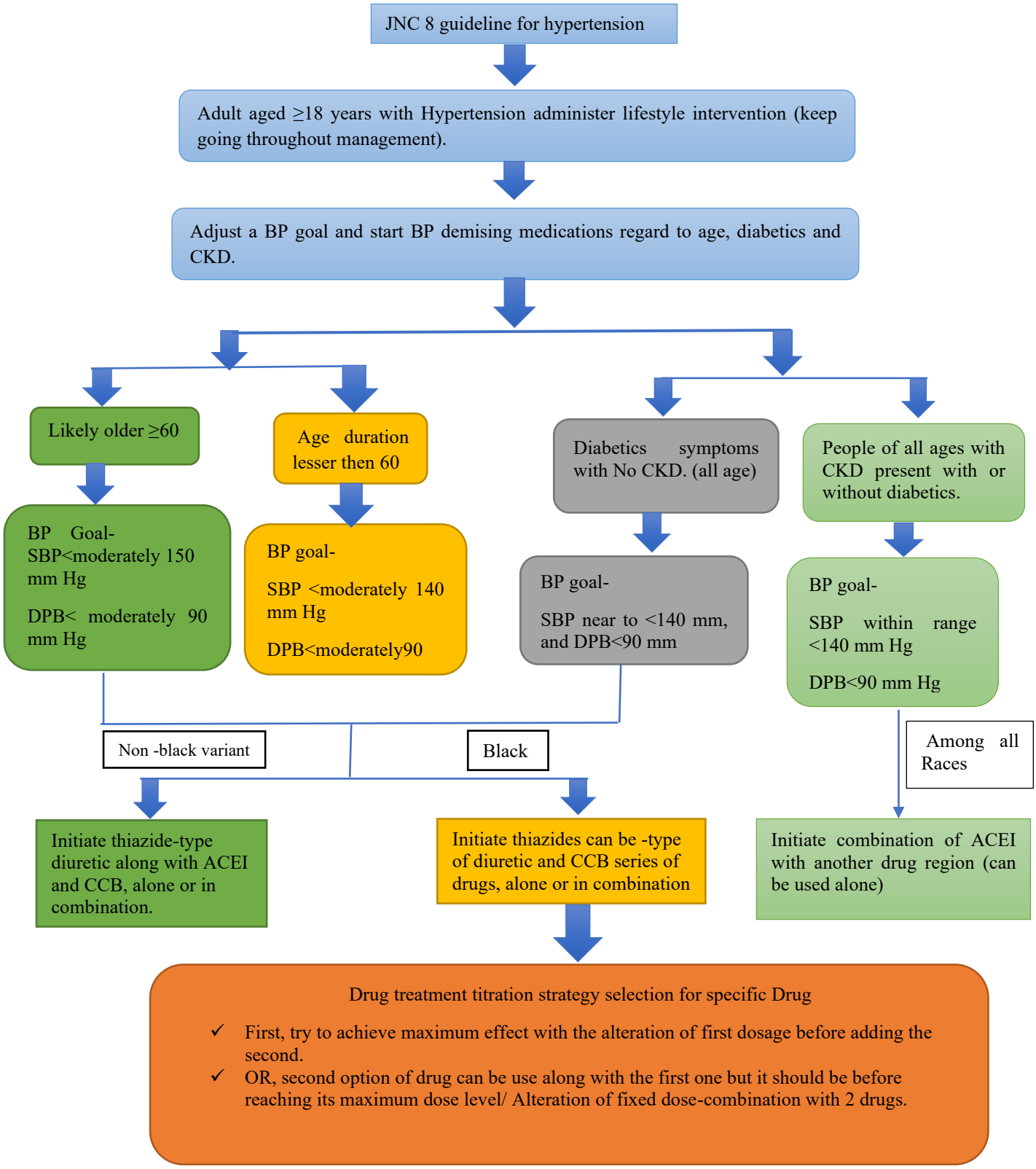

Figure 1.1: Hypertension Management (*JNC 8 Hypertension Guideline*, n.d.)

1.8 Classification for antihypertensive drug

Type	Mechanism of action	Example
Diuretics	Initially reduces blood pressure by increasing the elimination of water and sodium.	Amiloride, Bumetanide Chlorthalidone, Eplerenone Furosemide, Hydrochlorothiazide, Metolazone, Spironolactone, Triamterene
Beta-Blockers	Reduces blood pressure by: •Reducing cardiac output; • Reducing a sympathetic outflow from CNS; • Prevent the kidneys from releasing renin.	Acebutolol, Atenolol, Carvedilol, Labetalol, Metoprolol, Nadolol, Nebivolol, Propranolol, Timolol
Angiotensin II Receptor Blockers	They reduce the activation of the receptor by angiotensin II and block angiotensin-1 receptors.	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 lessening systemic vascular resistance without elevate cardiac output, rate or contractility.	Benazepril, Captopril, Enalapril, Fosinopril, Lisinopril, Moexipril, Quinapril, Perindopril, Ramipril
Calcium Channel Blockers	1.By attaching to the calcium channel into the heart and the smooth muscle of the coronary and peripheral arteriolar vasculature, block the inward transport of calcium. 2.The arterioles dilate.	Amlodipine, Diltiazem, Felodipine, Isradipine, Nicardipine, Nifedipine, Nisoldipine, Verapamil, Clevidipine

(Pazdernik, 2009)

1.9 Olmesartan Medoxomil

Olmesartan medoxomil known as a nonpeptide angiotensin II receptor antagonist which is selectively and competitively inhibits the type 1 angiotensin II receptor without interfering with other cardiovascular system-regulating receptors. Olmesartan is used to treat hypertension, or high blood pressure, either by itself or in combination with other medications. Elevated blood pressure increases the cardiac and vascular burden. Long-term continuation may cause abnormal heart and artery function. This may lead to a stroke, heart failure, or renal failure by damaging the blood vessel walls in the brain, heart, or kidneys. Lower blood pressure can decrease the chance of heart attacks and strokes. It functions by obstructing an internal chemical that tightens blood arteries. Olmesartan causes blood vessels to relax as a result. As a result, the heart receives more blood and oxygen and blood pressure is lowered. Compared to the other ARBs, it has a unique double-chain domain which lends it an efficient antihypertensive agent. (Warner & Jarvis, 2002)

1.9.1 Discovery

Olmesartan was unfolded firstly by Sankyo company limited in 1992 leading to the aim of a better oral bioavailability. But it was shown lower bioavailability which about 26% in human as the water solubility was low and efflux of the drug resistance pumps in the gastrointestinal tract. So, it needed an updated formulation technique which further improve the dissolution property. In 2007 Sankyo company limited released a formulation technique with improved dissolution properties which is procured by added at least one substance selected from a hydrophilic polymer, an acidic substance and a fluiziding agent. (Hedvati & Pilarsky, 2006)

1.9.2 Chemistry

Any drug's properties are essential to knowing both its chemical composition and the ensuing impact it has on the human body (Zhang et al., 2013). Olmesartan Medoxomil is a synthetic imidazole derivative prodrug with an antihypertensive property.

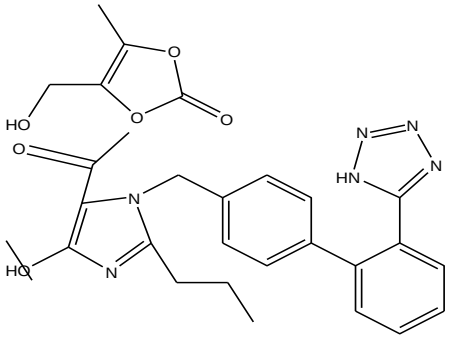

Figure 1.1: Olmesartan Medoxomil

Table 1.2: Characteristics of Olmesartan medoxomil (PubChem, n.d.)

Chemical Names	**(5-methyl-2-oxo-1, 3-dioxolen-4-yl) methyl 4-(1-hydroxy-1-methylethyl)-2-propyl-1-[[2'-(1H-tetrazol-5-yl)-1,1' –biphenyl-4-yl]methyl]-1Himidazole-5-carboxylate. Alternatively, it can be described as 2,3-dihydroxy-2-butenyl 4-(1- hydroxy-1-methylethyl)-2-propyl-1-[p-(o-1H-tetrazol-5-ylphenyl)benzyl]imidazole-5-carboxylate, cyclic 2,3-carbonate**
Molecular Formula	$C_{29}H_{34}N_6O_6$
Relative Molecular Mass	562.62
Melting Point	180℃
Appearance	white to light yellowish-white powder or crystalline powder
Enantiomers	both R/S and E/Z isomers are generated.

Table 1.3: Solubility of Olmesartan Medoxomil (*Solubility.Pdf*, n.d.)

Solvent	**Relative Solubility**
Water	0.00724 mg/ml
Ethanol	0.2 mg/ml
DMSO	20 mg/ml
DMF	30 mg/ml

1.9.3 Mechanism of action

Angiotensin II receptor blockers (ARBs), including Olmesartan medoxomil, are mainly used to treat hypertension. Analyzing the renin-angiotensin-aldosterone system (RAAS), which is essential for controlling blood pressure and fluid balance in the body, is necessary for understand its mode of action. (Kerndt & Soos, 2024)

Renin is an enzyme that the kidneys release when blood pressure lowers. The liver produces a protein called angiotensinogen, and renin then changes into angiotensin I. The enzyme angiotensin-converting enzyme (ACE) transforms the comparatively inert angiotensin I into angiotensin II. Being a strong vasoconstrictor, angiotensin II causes blood vessels to narrow, which raises blood pressure. Additionally, it causes the adrenal glands to secrete more

aldosterone, which encourages the kidneys to retain sodium and water and raises blood pressure even more. (*Mechanism of Action of Olmesartan*, n.d.)

The mechanism of action of Olmesartan medoxomil is to specifically prevent angiotensin II from attaching to AT1 receptors on smooth muscle cells in blood vessels and other tissues. Angiotensin II has the ability to constrict blood vessels and by promoting the production of aldosterone. So, it prevents the action of angiotensin II and help the vessel walls relax and dilate. As a result, blood pressure decreased. In addition, less aldosterone is secreted, which lowers water and salt retention and lowers blood pressure. (*What Is the Mechanism of Olmesartan Medoxomil?* n.d.)

Olmesartan Medoxomil is special since it's a prodrug. This indicates that it is inert when delivered and only turns active after it goes through a metabolic reaction. Olmesartan Medoxomil is quickly digested in the gastrointestinal system to produce Olmesartan, the active form, after ingestion. After entering the circulation, this active metabolite can successfully inhibit AT1 receptors. (*Mechanism of Action of Olmesartan*, n.d.) Olmesartan Medoxomil has a longer half-life of activity than other antihypertensive medications. Because of its comparatively lengthy half-life, a once-daily dosage can result in prolonged blood pressure management. In general, this can help manage hypertension more effectively and with more patient compliance. (Brunner, 2006)

1.9.4 Dosage and Administration

- ✓ **Adult**

For the adults, Olmesartan Medoxomil is normally recommended within 10-40 mg once in every day and the dose is adjusted according to the patient necessity.

- ✓ **Elder**

For elderly patients, there is no early adjustment in dose is recommended.

- ✓ **Renal impairment**

Patients with renal impairment should have a customized dosage of Olmesartan Medoxomil. The use of Olmesartan Medoxomil in dialysis patients has not been attempted before.

- ✓ **Hepatic impairment**

It is advised that individuals with mild to severe hepatic impairment avoid alter their original dosage.

- ✓ **Children**

Children's safety and effectiveness with Olmesartan Medoxomil have not been proven. (*ShowLabeling.Pdf*, n.d.)

1.9.5 Side Effect

The more common side effects that occur with Olmesartan include:

- back pain
- bronchitis
- diarrhea
- headache
- blood in your urine
- high blood sugar
- high triglycerides,
- flu-like symptoms, such as fever and body aches
- sore throat, runny nose, and sinus infection

There is also some serious side effect:

- Serious allergic reaction. Symptoms can be:
  - ❖ swelling of your face, lips, throat, or tongue
- Low blood pressure (hypotension). Symptoms can be:
  - ❖ faintness
  - ❖ dizziness
- Liver problems. Symptoms can be:
  - ❖ nausea
  - ❖ pain in the right upper part of your stomach
  - ❖ yellowing of the whites of your eyes and your skin
  - ❖ itchy skin
- Kidney problems. Symptoms can be:
  - ❖ swelling of your feet, ankles, or hands
  - ❖ weight gain

  (*Olmesartan*, 2017)

1.9.6 Contraindications

Patients who are hypersensitive to any of the tablet's components, including microcrystalline cellulose, low substituted hydroxypropylcellulose, lactose, hydroxypropylcellulose, magnesium stearate, talc, titanium dioxide, and hypromellose, should not use olemesartan medoxomil.When a patient becomes pregnant, they should stop using olmesartan medoxomil right away. When treating diabetic individuals, avoid co-administering aliskiren and olmesartan medoxomil. (*ShowLabeling.Pdf*, n.d.)

1.9.7 Drug Interaction

When digoxin or warfarin were given concurrently with Olmesartan medoxomil in healthy volunteers, no major pharmacokinetic interactions were discovered. Antacid (aluminum magnesium hydroxide) did not significantly impact the bioavailability of Olmesartan. As Olmesartan medoxomil does not affect P450 enzymes or metabolize through the cytochrome P450 system, interactions with medications that inhibit, induce, or are metabolized by these enzymes are not anticipated.

1.9.8 Interaction with other medicinal products

Interaction with other medicinal products;

- ✓ Use with Lithium
- ✓ Dual Blockade of the Renin-Angiotensin System (RAS)
- ✓ Use with Aliskiren
- ✓ Non-steroidal Anti-inflammatory Drugs (NSAIDs)
- ✓ Use with Colesevelam Hydrochloride (*Auspar-Olmesartan-Medoxomil-130226-Pi.Pdf*, n.d.)
- ✓

1.10 Quality

Any company that wants to survive and develop has to prioritize quality. The term "quality" refers to the ascendancy of the good or service, which is evaluated by comparing it to the customer's needs and experiences. The capacity of the product to meet the demands and expectations of the consumer may be used to describe its quality. Prioritizing the definition of quality in terms of statistics or features is necessary, as these differ depending on the product. For instance, when it comes to pharmaceutical products, factors like its taste, toxicity, physical

and chemical properties, and shelf life, among others, (*The Theory And-Practice-of-Industrial-Pharmacy-By-Lachman-and-Lieberman-3rd-Editn-SaMeep104-Pdf*, n.d.)

A product or service's quality consists of two characteristics that, are together, provide a suitable definition for the word. The first is concerned with the characteristics and aspects of the product or service. The product's lack of flaws is its second characteristic (Mazumder et al., n.d.)

1.11 Quality Control

The complete set of the actions made to guarantee the identification and purity of a certain medicine is referred to as quality control. These processes can be as basic as doing chemical studies (such as thin layer chromatography or infrared spectroscopy) to identify and screen for the presence of certain pharmaceutical substances, or they can be more complex and involve pharmacopoeial monograph requirements. The scope of activities includes quality control laboratories (good laboratory management practices, models, such as for analytical certificates and equipment lists, and an external assessment scheme). (WHO, 2015) (*Working Documents in Public Consultation*, n.d.)

The terms "quality" and "control" make into the phrase "quality control." Control is a procedure used in all regulations. It comes from satisfying standards in the sector. We refer to the procedure we use to set and adhere to standards as quality control. Quality control pertains to a framework that approves or disapproves of any actions that impact the quality and stops Inconsistency in the product or service's quality and a lack of quality (*The Theory And-Practice-of-Industrial-Pharmacy-By-Lachman-and-Lieberman-3rd-Editn-SaMeep104-Pdf*, n.d.)

Research and development are where the design of the product and process starts. Pre-formulation and physical, chemical, medicinal, and toxicological considerations are also included. The following features of medicine are guaranteed by quality control:

- ✓ Authentic quality
- ✓ It must be in a form that is effective after administration;
- ✓ it must be pure, both physically and chemically;
- ✓ it must have the same number of components as stated on the label;
- ✓ it must be high-quality in terms of shelf life and stability; and
- ✓ it must be free from harmful contaminants.

Quality is characterized by eight dimensions. They are vital to the success of the company.

They are as follows:

1. Performance: The main functional aspects of the product.
2. Characteristics: Enhancements to a product's fundamental operational characteristics.
3. Reliability: The likelihood that something won't go wrong within a given time frame.
4. Conformance: The extent to which a product's operational features and design adhere to predetermined standards.
5. Durability: An indicator of a product's lifespan.
6. Serviceability: It refers to the ease and quickness of repair.
7. Aesthetics: A product's appearance, texture, flavor, and aroma.
8. Perceived quality: A customer's perspective. (Mazumder et al., n.d.)

1.12 Quality of Pharmaceutical Product

The first requirement for every pharmaceutical company to remain in business is product quality. In pharmaceutical sector, quality is determined by a high level of technological, scientific, and managerial complexity. Any product must always have quality as a minimum requirement. When it comes to life-saving goods like medications, it takes center stage. It is truth that pharmacopoeia analysis of the finished product is insufficient to control the quality of pharmaceutical products, although being required by law and regulatory agencies. Today, a product's quality must be established from the beginning, and strict worldwide environmental, safety, and regulatory requirements must be adhered to. Validation has shown to be a valuable instrument for pharmaceutical quality control. (Mazumder et al., n.d.)

The majority of traditional pharmaceutical medications are very basic compounds that have been discovered to cure sickness or illness symptoms mostly via trial and error. These compounds were refined over decades to guarantee quality. There is a strong correlation between quality and any medicinal product. Pharmaceutical drugs of poor quality cannot be sold or promoted because they may result in overdose or subtherapeutic side effects. When prescribed to patients, medicine of any brand or firm that is not maintained may result in major issues. Because of its defective quality, the patient may experience negative consequences that occasionally prove to be deadly. (*The Theory And-Practice-of-Industrial-Pharmacy-By-Lachman-and-Lieberman-3rd-Editn-SaMeep104-Pdf*, n.d.)

1.13 Quality Assurance

In the pharmaceutical industry, designing, developing, and implementing quality assurance is the most important role. In pharmaceutical sector, quality is determined by a high standard of

technical, scientific, and management proficiency. The broad idea of quality assurance covers all factors that either alone or jointly affect the product's quality. It is the final stage of all the preparations done to guarantee that drugs meet the standards necessary for the purposes for which they are designed. (Mazumder et al., n.d.)

1.14 Importance of Quality

In the pharmaceutical field, quality matters for the following reasons:

- Manufacturing of safe, effective medicines; A medication must fulfill its designated quality requirements in order to be both safe and therapeutically effective. A medication that has been compromised may be hazardous or therapeutically ineffective. Thus, the highest attention to quality should be given to the manufacturing of pharmaceuticals in order to ensure patient safety.
- Prosperity and Longevity in a Competitive Sector; The pharmaceutical industry's main goal for survival and profitability is quality. For the pharmaceutical sector to thrive, high-quality products are necessary for consumer pleasure and eventual profit.
- In Order to Make Maximum Profit - A high-quality product can be used to increase profits. Low-quality products get bad reviews from customers, which lowers profitability. On the other hand, satisfied customers are the result of high-quality products. Increased client satisfaction boosts the business's profitability.
- Marketing strategy: The healthcare industry may effectively use the quality of its goods as a marketing strategy. (World Health Organization, 2007)

1.15 Quality control parameters of solid dosage form

Tablets are the most popular pharmaceutical dose type among healthcare providers, doctors, and patients alike. Tablets improve patient adherence. The physiochemical characteristics of these combination tablets were evaluated using the usual methodology for tablet weight uniformity, thickness, hardness, friability, disintegration, dissolution, and potency tests.

Generally, there are two types of tests:

1. Compendial tests &
2. Non-compendial tests,

Compendial tests: Compendial tests are those that follow the guidelines provided in pharmacopoeias such as the British Pharmacopoeia (BP), United States Pharmacopeia (USP),

and others.

They continue by the name of formal tests as well.

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

Non-compendial test: These tests are often known as unofficial tests as their methodologies are not specified in pharmacopeias. Among them are:

- Friability test
- Hardness test and
- Thickness test (Shohin et al., 2014)

1.15.1 Weight variation

A weight variation test is used to verify that the tablets are consistent. While some tablets are appropriately uniformed, others try hard to retain it. There are several explanations for why tablet weights differ from batch to batch. Variations in tablet weight might be brought on by,

- The vibration was brought on by distribution at Hoover. Because of the consolidation process, big granules will emerge first when smaller granules are pressed. Consequently, a homogeneous granule size must be used. Therefore, it would be wise to assess the particle size distribution before starting the compression process.
- The granule flow should be poor or non-free-flowing.
- If there is an abnormal particle distribution due to a variable specific gravity, this results in poor flow.
- If there is an uneven distribution of particle sizes. It is best to use a moderate number of granules and particles. Large particle diameter granules result in an uneven weight distribution in the tablet, whereas excessively tiny granules generate an uneven flow time.
- If the glidant or lubricant is not uniformly combined or is less.
- Adequate qualities of flow
- If there be any incorrect die cavity adjustments (Shohin et al., 2014)

1.15.2 Hardness test

To determine whether the tableting machine's pressure has to be adjusted, a hardness test is conducted. In order to handle mechanical shocks throughout the manufacture, packing, and shipment, hardness must be maintained. There are several kinds of hardness testers available, including the Erweka, Pfizer, Strong-Cobb, Monsanto, and Schleuinger testers (Shohin et al., 2014).

Hardness has an impact on how things break down. Therefore, if the pill is very firm, it could not break down in the allotted amount of time. Furthermore, if the tablet is too soft, it won't hold up to handling during further processing like coating or packing. The device used to measure hardness levels permitted values ranging from 8 to 12 kg. Tablet hardness typically impacts medication release and dissolution, and it may also impact bioavailability (*The Theory And-Practice-of-Industrial-Pharmacy-By-Lachman-and-Lieberman-3rd-Editn-SaMeep104-Pdf*, n.d.)

Factor influencing the tablet's hardness,

1. Compressive force and tablet compression.
2. Binder quantity; the more binder, the harder.
3. The granulation technique used to prepare the tablet (slugging approach yields the optimum hardness; wet method produces higher hardness than dry method) (Shohin et al., 2014)

1.15.3 Friability test

The friability test, which analyzes the tablet's resistance to abrasion during handling, packing, and shipping, is closely associated with tablet hardness. A percentage is used to express the value. During the friability test, a maximum weight loss of 1% of the weight of the tablets being tested is considered generally acceptable, and any broken or cracked tablets are not picked up (*The Theory And-Practice-of-Industrial-Pharmacy-By-Lachman-and-Lieberman-3rd-Editn-SaMeep104-Pdf*, n.d.)

1.15.4 Disintegration

The quality of the tablets can be determined by their disintegration. The purpose of the disintegration test is to measure how long it takes for a pill or capsule, or other solid oral dose form, to fully dissolve. One way to determine quality is to look at the disintegration time. This is due to the fact that, for instance, an excessively high disintegration time may indicate many

issues, such as an excessively compressed tablet. Additionally, non-uniform disintegration times in a group of tablets under analysis point to batch irregularities and a lack of batch homogeneity (*The Theory And-Practice-of-Industrial-Pharmacy-By-Lachman-and-Lieberman-3rd-Editn-SaMeep104-Pdf*, n.d.)

1.15.5 Dissolution test

Drug dosage forms are developed using dissolution testing, as are quality control guidelines for the production process. The in-vitro disintegrating test is an important test that may need the creation of certain methods and must correlate with in-vivo clinical research. In vitro, dissolution testing is used to evaluate batch-to-batch consistency, identify production errors, target crucial manufacturing parameters such as granulation procedure, coating parameters, mixing effects, binder effects, and excipient role in various dosage forms. (*The Theory And-Practice-of-Industrial-Pharmacy-By-Lachman-and-Lieberman-3rd-Editn-SaMeep104-Pdf*, n.d.)

The in vitro dissolution study serves an additional function. These are the following:

- Selecting formulations for additional development during the product development process.
- Determining if each batch meets specified in vitro release requirements during end-product quality control.
- Finding out if the in vitro release rate differs with a product age during stability testing.
- Assessing if changes impact in vitro release during the course of the market lifetime (Shohin et al., 2014)

Factor impacting the tablet's dissolution:
The rate at which the active component in a medicinal product dissolves can be directly impacted by a number of formulation-related factors. Following comprehensive characterization of these parameters, we may utilize this data to get personalized medication dissolution profiles.

- ✓ Excipients & additives: In addition to the active component in the formulation, the majority of solid dosage forms contain multiple excipients for different reasons. A pure drug's rate of dissolution can be dramatically changed by combining it with different

adjuncts. Diluents, binders, lubricants, granulating agents, disintegrants, and so forth are examples of these adjuncts.

- ✓ The size of Particle: Drugs in tablets will dissolve and absorb more readily if their particles are smaller. This is most likely related to the processes used in the manufacturing of tablets, which involve combining the medication with typically hydrophilic diluents and then granulating the mixture to produce a more hydrophilic surface, even for the drug particles that were initially hydrophobic.

- ✓ Granulating agent and binder: The dissolving properties of the medication from the dosage form can be significantly influenced by the binder and granulating agent used in tablet formulation and other solid dosage forms.
- ✓ Disintegrating Agents: Numerous studies that show how different disintegrating agents affect the pace at which tablets dissolve have been reported in the literature. It is important to remember that the type and quantity of disintegrating agent used in the formulation greatly affects how quickly the dosage form dissolves overall.
- ✓ Lubricants: Hydrophobic compounds are the main type of lubricants that are frequently used in the formulation of solid dosage forms. Thus, the kind, quality, and the amount of lubricant used can influence the rate of disintegration.

- ✓ Surfactant: Because of issues with their bioavailability, medications that are nearly insoluble in aqueous media (<0.01%) are becoming increasingly attractive from a therapeutic standpoint. (Shohin et al., 2014)

The significance of the study

The prevalence of hypertension is among the highest in our own country. This type of disease is difficult to treat, but it is manageable. Our pharmaceutical industry is competitive since there are a considerable number of pharmaceutical businesses operating in it. They introduce a number of products for various ailments. Furthermore, hypertension is one of the medical specialties in our nation where pharmaceutical companies provide a variety of goods, whether they are independent or combination medications. For the proper quality evaluation, therapeutic efficacy, and safety of the tablets, a comparative analysis of the quality control characteristics of several brands that are sold in Bangladesh is thus required. This is due to the fact that pharmaceutical products must be of the highest quality and advertised as safe,

therapeutically effective formulations with constant performance that do not have any negative side effects (Shohin et al., 2014)

The assessment of quality control measures, such as weight variation, hardness, thickness, disintegration, dissolution, and friability determination, is crucial in maintaining the quality of pharmaceutical products that are marketed. It also provides us with a blurry understanding of its bioavailability. In terms of use, Olmesartan medoxomil 20mg is one of the popular anti-hypertensive drugs in the current market. Because of its low risk profile, most of the pharmaceutical companies are marketed this drug under their cardiovascular management. Therefore, it is crucial to assess the quality control parameters, such as weight variation, hardness, thickness, disintegration test, dissolution test, and potency test, of various brands and to compare them with one another in order to determine which exhibits variation from the specification and which is superior in terms of both quality and safety.

Aims and objectives of the study

The aim of this research paper was,

- To determine the quality control parameters of various brands of Olmesartan Medoxomil 20mg
- To make a comparison on different quality control parameters between brand to brand
- To determine the disintegration and dissolution of selected brands.

Chapter 2

Methodology

2.1 Samples

Tablet selection for testing and reference standard collection of Olmesartan Medoxomil (OLM): In Bangladesh 14 brands are available of OLM. Among them 5 brands were selected randomly and collected them from the different medicine shop in Dhaka. This tablet was randomly coded by OLM-1, OLM-2, OLM-3, OLM-4, OLM-4, OLM-5, OLM-6, OLM-7, OLM-8, OLM-9, OLM-10. 20 Mg of OLM was analyzed during the study.

Table 2.1: Different brands along with their manufacturer names

Tablet	Pharmaceutical name
Olmesartan medoxomil (Olmesaf 20 mg	Orin Pharmaceuticals
Olmesartan medoxomil (Olmevas 20 mg)	Popular Pharmaceuticals
Olmesartan medoxomil (Olmesta 20 mg)	Eskafey Pharmaceuticals
Olmesartan medoxomil (Olmezest 20 mg)	Sun Pharmaceuticals
Olmesartan medoxomil (Olmecar 20 mg)	Square Pharmaceuticals

Table 2.2: Reagents & solvents

Potassium Dihydrogen Phosphate	Use to make buffer solution for the dissolution test.
Dipotassium Hydrogen Phosphate	Use to make buffer solution for the dissolution test.
Sodium Chloride Hydrogen	Use to make buffer solution for the dissolution test.
Hydrochloric Acid (0.1N HCL)	Use to make buffer solution for the dissolution test.
Distilled Water	Use to make buffer solution for dissolution test. Also use to do disintegration test.

Table 2.3: List of Apparatus/ Glassware's used throughout this project

Container	Stop watch
Test tubes	Measuring Cylinders
Volumetric Flasks	Pipettes
Beakers	Glass rod
Droppers	Filter paper

2.2 Weight variation:

Weight variation is an important point while talking about the standard pharmaceutical product and it has a strong connection with content uniformity for the preparation of a solid dosage form. For ensuring a good content uniformity the weight variation need to be small, while large weight variation stand of good content uniformity. There are several factors which has impact in tablet weight variation:

1. An uneven die fill is a result of poor granulation flow properties.
2. Variation in die fill density can happen as a factor of particle size and size distribution in various point while the production is run because of a wide variation in granulation particle size.
3. Lower punch length dissimilarities can be result different size die cavities. (Dharmalingam, Ramamurthy, et al., 2014)

2.2.1 Instrument: Analytical Balance, Model-902

2.2.2 Method:

Calculated average weight of 10 tablets and weighed 10 whole tablets individually. Then observed weight of individual tablets was within the range or not (*USP Weight Variation_25_feb_2011.Pdf*, n.d.)

2.2.3 Calculation: Percentage of weight variation was calculated by following formula (Dharmalingam, Ramamurthy, et al., 2014)

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

2.2.4 Specification:

In USP (2011), it is pointed that the difference must not more than two table in case of individual variation from the average weights and percentage given below:

Table 2.4: Weight variation tolerance for tablets. (*USP Weight Variation_25_feb_2011.Pdf*, n.d.)

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

2.3 Hardness test:

Tablet hardness is a necessary parameter while talking about the mechanical stability of a tablet during packaging and shipment. So, it is commonly defined as the load needed while crushing the tablet on its edge. Tablet hardness also create impact in tablet density and porosity. This parameter may also have an effect on friability and disintegration time of a tablet. It also affects dissolution and release as well as on bioavailability. (Dharmalingam, Ramamurthy, et al., 2014)

2.3.1 Method:

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, Ramamurthy, et al., 2014)

2.3.2 Measurement Units: The international system of units is commonly used for testing of most materials. The most approached unite in SI system for force is Newton. Kilogram (Kg) is another system also used and it is known as the primary unite mass (*Tablet Breaking Force | USP-NF*, n.d.)

2.3.3 Specification: The hardness of an oral tablet usually 4 to 8 or 10 kg. in case of hypodermic and chewable tablets hardness is 3kg as these tablets are soft then the normal one. There are some sustain released tablets and their hardness is (10-20kg) and they are much harder. (*Tablet Breaking Force | USP-NF*, n.d.)

2.4 Disintegration test

For getting better dissolution of a drug, disintegration is a vital and mandatory step. To get a better therapeutic action and absorption, the breakdown of drug in optimum time is prerequisite. What type of disintegrator is used in a drug may control the disintegration time.

The higher the disintegration time, the lower the dissolution rate, and it gives poor absorption as well. So, disintegration is an emergent part of a drug for better therapeutic action (*Disintegration Test BP 2019.Pdf*, n.d.)

2.4.1 Condition

- Distilled water
- 37º C temperatures to maintain body temperature (*Disintegration Test BP 2019.Pdf*, n.d.)

2.4.2 Method

1. Before the test the disintegration tester was correctly assembled.
2. Then following the specification the time and temperature was set.
3. The 1000 ml beaker then filled with 600 ml of distilled water.
4. The liquid maintained at 37º C temperature.
5. One tablet was placed in each of the 6 tubes.
6. The machine started according to the listed period.
7. the entire tablet was disintegrated within the listed time (*Disintegration Test BP 2019.Pdf*, n.d.)

2.4.3 Specification:

For the uncoated tablet the disintegration time is 15 minutes, for coated one is 30 minutes, for film coated tablet is 30 minutes and for enteric coated, it is 60 minutes or 1 hour (*Disintegration Test BP 2019.Pdf*, n.d.)

2.5 Dissolution Test

2.5.1 Condition

- Medium: 900ml Phosphate buffer
- Apparatus: USP dissolution apparatus type-II
- Speed: 50rpm
- Temp: 37.5°
- Time: 30 min

2.5.2 Method

The water tank of the dissolution tester was filled with water and set the temperature 37.5° C. Then 900 ml of phosphate buffer was poured into the vessels and were run till the set temperature was acquired. The rotation of the paddle was set at 50 revolution per minutes. Then one tablet was placed into the vessel and tart the run of the paddle. The test was run about 30 minutes and dilution performed according to the requirement. At the last, the absorbance was taken at 257 nm for OLM and the analysis was performed by UV-visible spectrophotometer.

2.5.3 Calculation:

$$\%\ dissolution = \frac{\text{Absorbance(a)} \times \text{Dilution factor} \times 900}{1000}$$

2.5.4 Specification:

Immediate dosage release forms:

The criteria are satisfied if the amounts of active ingredients dissolved in dosage forms match with the given table or noted in the specific monograph. If the findings do not match at S1 or S2, the test needs to be continued till the level three. 5%, 15%, and 25% numbers in the acceptance table are percentages of a labeled content, therefore these values and Q are in the same terms. The quantity, Q, is the prescribed amount of dissolved active ingredient represented as a percentage of the labelled content. (WHO,2014)

Table 2.5: Acceptance criteria for Conventional-release dosage forms: (*Dissolution Testers – USP Guidelines - Total Laboratory Services - ERWEKA UK - Dissolution Testers*, 2024)

Level	Sample tested	Acceptance criteria
S_1	6	Each value is not less than Q + 5%
S_2	6	Standard value of 12 dosage unites (S1+S2) ≥Q; any unite is unacceptable for ≤ Q-15
S_3	12	Standard value of 24 dose unites (S1+S2+S3) ≥Q; the range of < Q - 15% is acceptable for (not more than 2 units) where, less than Q - 25% is unacceptable for any unit.

2.6 Friability

2.6.1 Method

Tablets from each brand which are chosen for the test had a unit weight about less than 650 mg. So, for the friability test, the total tablet weight needs close to 6.5 g. A randomly chosen tablet from each brand weighed and placed to the friability drum of a friability tester (Electro lab EF-2) For this test, the drum adjusted to rotate at 25 rpm, about 4 minutes with a total 100 rotations. After this, the tablet needed to be removed from the drum, dusted and finally weighed. For each brand the mean percentage of weight loss was noted.

2.6.2 Specification

The maximum mean weight loss is not more than 1.0% and it is deliberated as satisfactory. This tablet can counteract diverse mechanical stress and prevent chipping as well as surface abrasion combat during packaging, storage, shipment, and other steps in the distribution cycle. (USP)

Chapter 3

Result

3.1 Weight Variation test

Percentage of variation of 5 different brands of Olmesartan medoxomil (20mg) tablets are given below.

Table 3.1: Weight variation of (Olmesaf 20 mg)

Number of tablets	Weight of individual tablets (g)	Average weight (g)	Individual weight Variation (%)	Highest weight variation (%)	Lowest Weight variation (%)
1	0.13	0.128	1.5625	1.5625	-6.25
2	0.12		-6.25		
3	0.13		1.5625		
4	0.13		1.5625		
5	0.13		1.5625		

Standard deviation of individual weight is 0.004472.

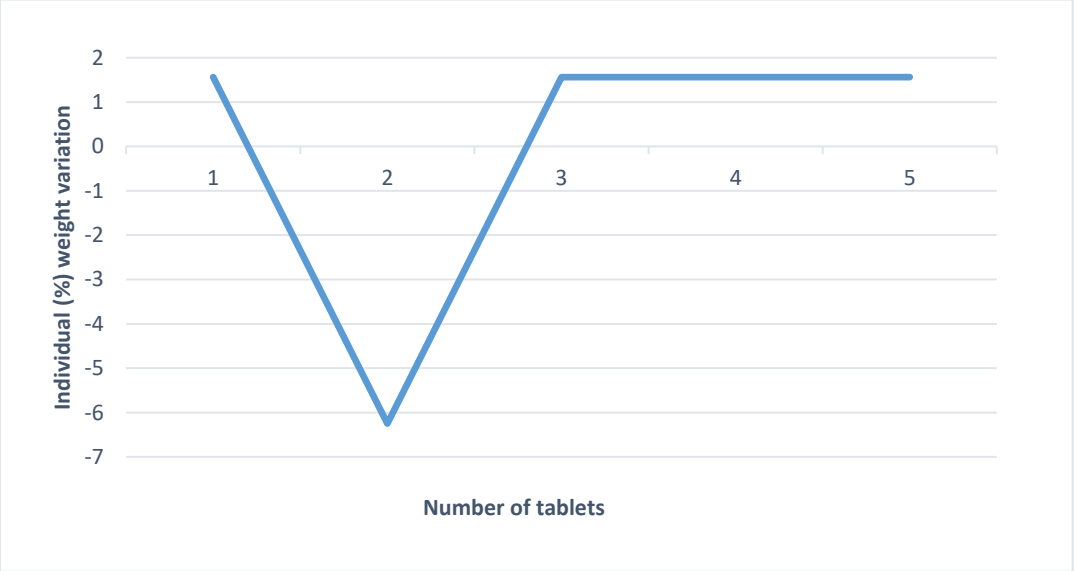

Figure 3.1: Individual weight variation percentage of (Olmesaf 20 mg).

The x-axis indicates the number of the tablets used for test and the y-axis indicate the percentage of weight variation detected for each marketed tablet.

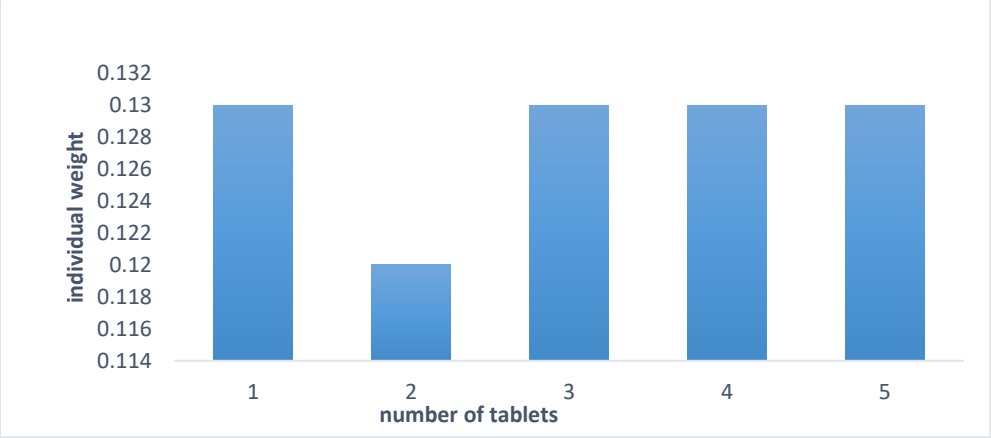

Figure 3.2: Weight of individual tablet (Olmesafe 20 mg).

The X-axis indicate the numbers of tablet used for test and the Y-axis indicate weight variation of individual tablet.

Table 3.2: Weight variation of (Olmevas 20 mg)

Number of tablets	Weight of individual tablets (g)	Average weight (g)	Individual weight Variation (%)	Highest weight variation (%)	Lowest Weight variation (%)
1	0.14	0.134	4.478	4.478	-2.985
2	0.14		4.478		
3	0.13		-2.985		
4	0.13		-2.985		
5	0.13		-2.985		

Standard deviation of individual weight is 0.005477.

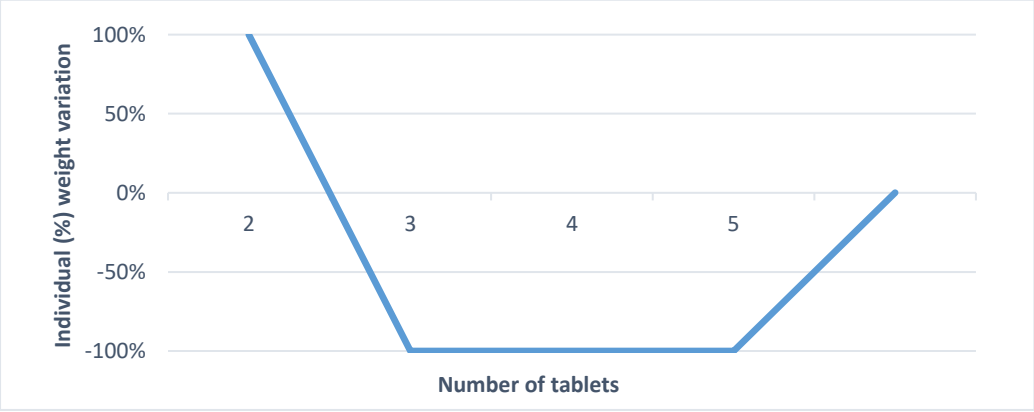

Figure 3.3: Individual weight variation percentage of (Olmevas 20 mg).

The x-axis indicates the number of the tablet used for test and the y-axis shows what percentage of weight variation each tablet had.

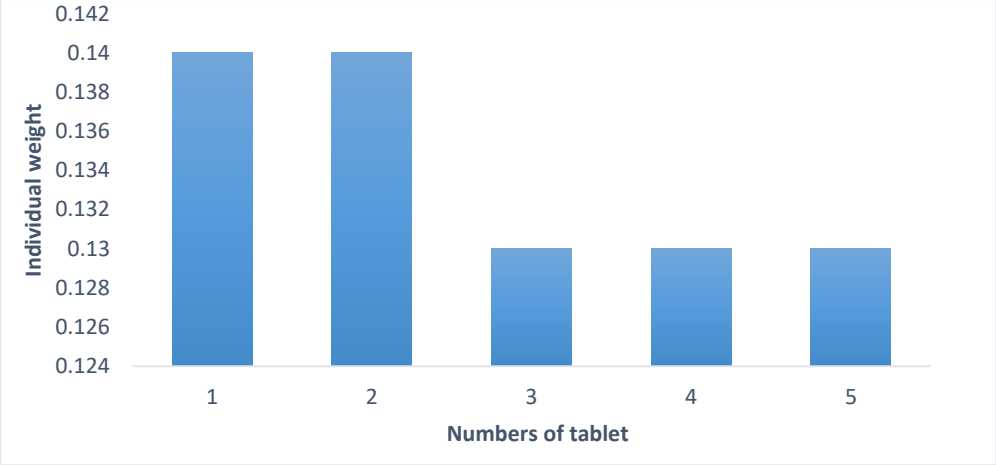

Figure 3.4: Individual weight for (Olmevas 20 mg).

The X-axis indicate the numbers of tablet used for test and the Y-axis indicate weight variation of individual tablet. Three tablet shows same weight variation.

Table 3.3: Weight variation of (Olmesta 20 mg).

Number of tablets	Weight of individual tablets (g)	Weight of individual tablets (g)	Individual weight Variation (%)	Highest weight variation (%)	Lowest Weight variation (%)
1	0.14	0.136	2.941	2.941	-11.765
2	0.12		-11.765		
3	0.14		2.941		
4	0.14		2.941		
5	0.14		2.941		

Standard deviation of individual weight is 0.008944

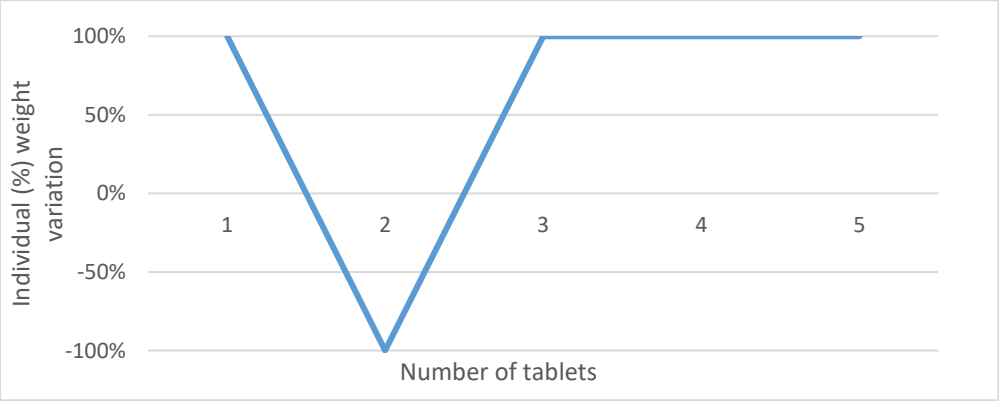

Figure 3.5: Individual weight variation percentage of (Olmesta 20 mg). In the graph X-axis represent the tablet count for the test and Y-axis shows the individual weight variation percentage of tablets. All most four tablet shows the same percentage of weight variation.

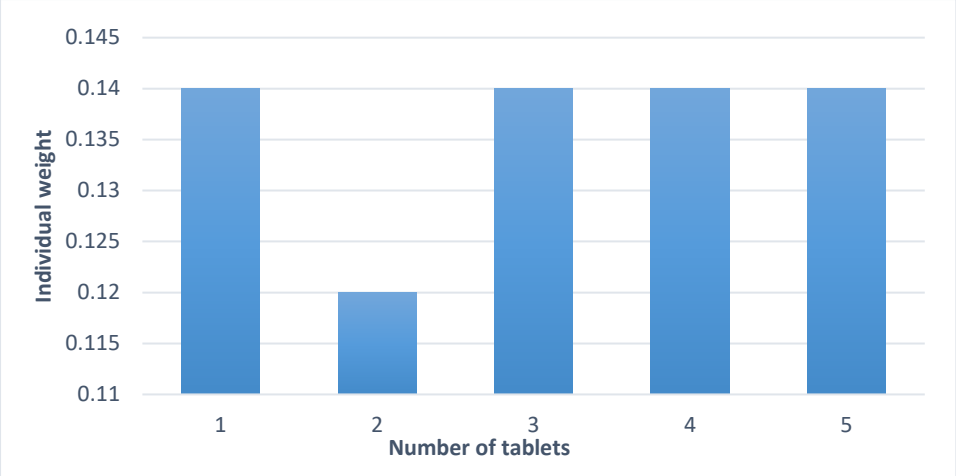

Figure 3.6: Individual weight for (Olmesta 20 mg).

The X-axis specify the numbers of tablet used for the test and the Y-axis shows percentage of individual weight variation of the tablets. A single tablet has the lowest weight.

Table 3.4: Weight variation of (Olmecar 20 mg).

Number of tablets	Weight of individual tablets (g)	Weight of individual tablets (g)	Individual weight Variation (%)	Highest weight variation (%)	Lowest Weight variation (%)
1	0.20	0.208	-3.846	0.962	-3.846
2	0.21		0.962		
3	0.21		0.962		
4	0.21		0.962		
5	0.21		0.962		

Standard deviation of individual weight is 0.004472.

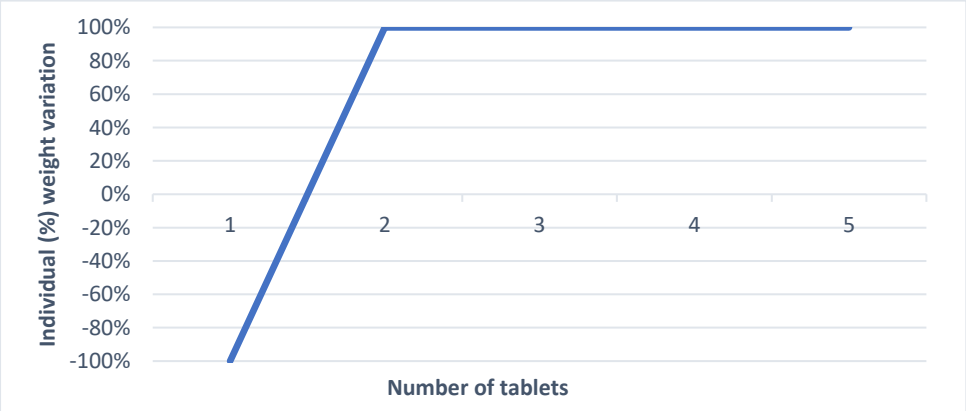

Figure 3.7: Individual (%) weight variation of (Olmecar 20 mg).

In the graph X-axis reflects counting of the tablets and Y-axis indicates individual weight variation percentage of the tablets.

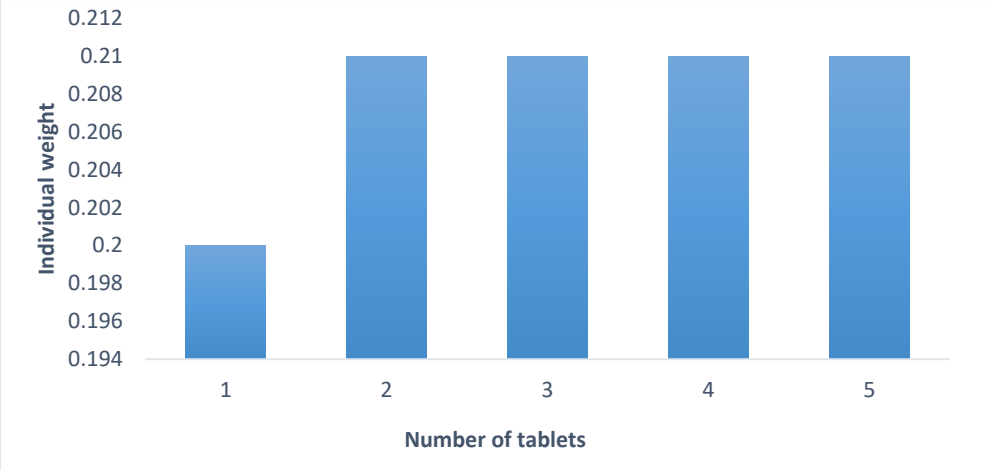

Figure 3.8: Individual weight variation for (Olmecar 20 mg).

The X-axis indicate same as the previous graph. Y-axis the shows single weight variation of tablets and one tablet has less weight than other tablets.

Table 3.5: Weight variation of Olmezest 20 mg.

Number of tablets	Weight of individual tablets (g)	Weight of individual tablets (g)	Individual weight Variation (%)	Highest weight variation (%)	Lowest Weight variation (%)
1	0.15	0.148	1.351	1.351	-5.405
2	0.15		1.351		
3	0.15		1.351		
4	0.15		1.351		
5	0.14		-5.405		

Standard deviation of individual weight is 0.004472.

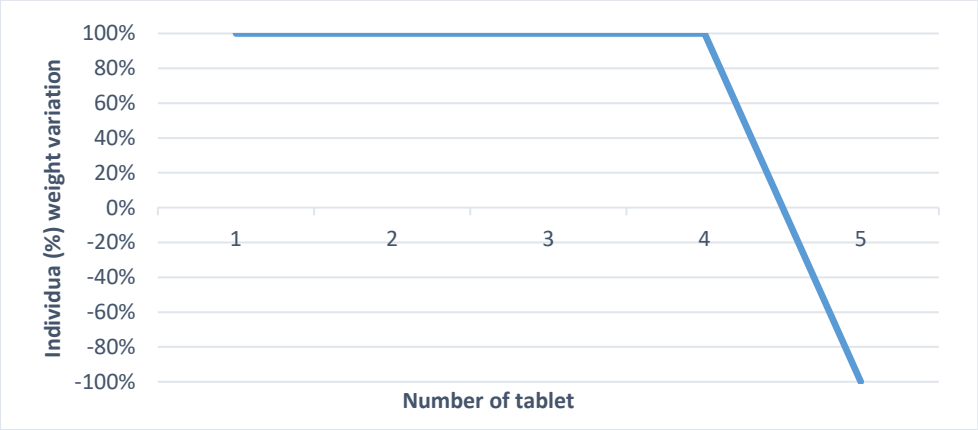

Figure 3.9: Individual (%) weight variation of (Olmezest 20 mg).

In the graph X-axis shows counting of the tablets and Y-axis reflect weight variation percentage from one tablet to another.

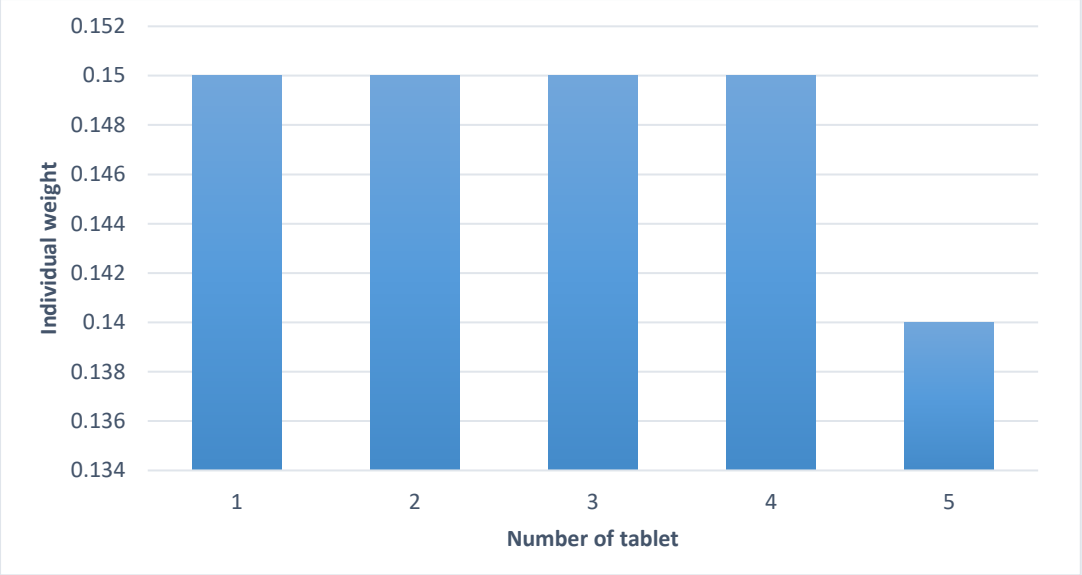

Figure 3.10: Individual weight variation for (Olmezest 20 mg).

The X-axis indicate same as previous graph. Y-axis shows single weight variation of tablets and one tablet has less weight than other tablets.

3.2 Hardness test

Hardness test of 5 brands of Olmesartan Medoxomil tablets are given below:

Table 3.6: Hardness test of Olmesaf 20 mg.

Number of tablets	Hardness (Kg)	Average (kg)
1	7.63	6.6
2	5.23	
3	6.70	
4	7.81	
5	5.63	

Standard deviation 1.156806.

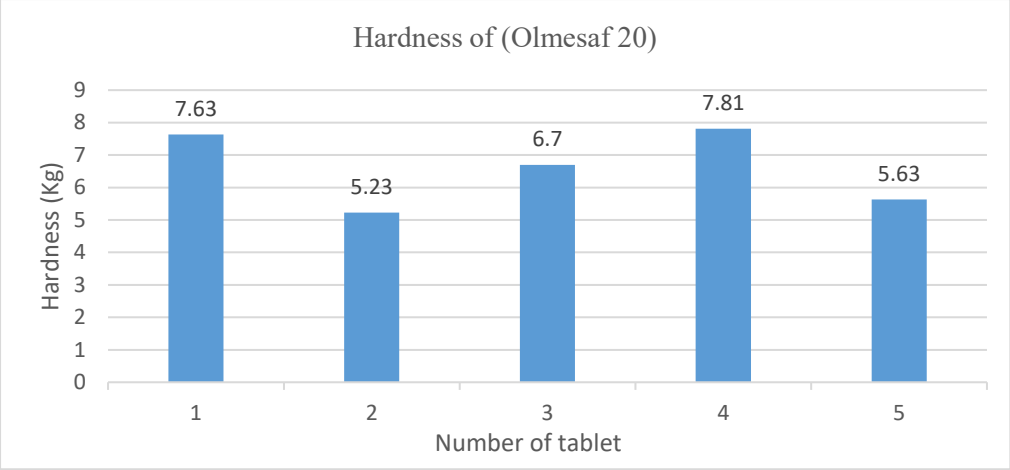

Figure 3.11: Hardness of (Olmesaf 20 mg).

X-axis represent numbers of tablet used in experiment. Y-axis tells about hardness of the tablets and One tablet shows less hardness than other four tablet.

Table 3.7: Hardness test of Olmevas 20 mg

Number of tablets	Hardness (Kg)	Average (kg)
1	10	10.31
2	10.83	
3	10.84	
4	10.35	
5	9.53	

Standard deviation is 0.564154.

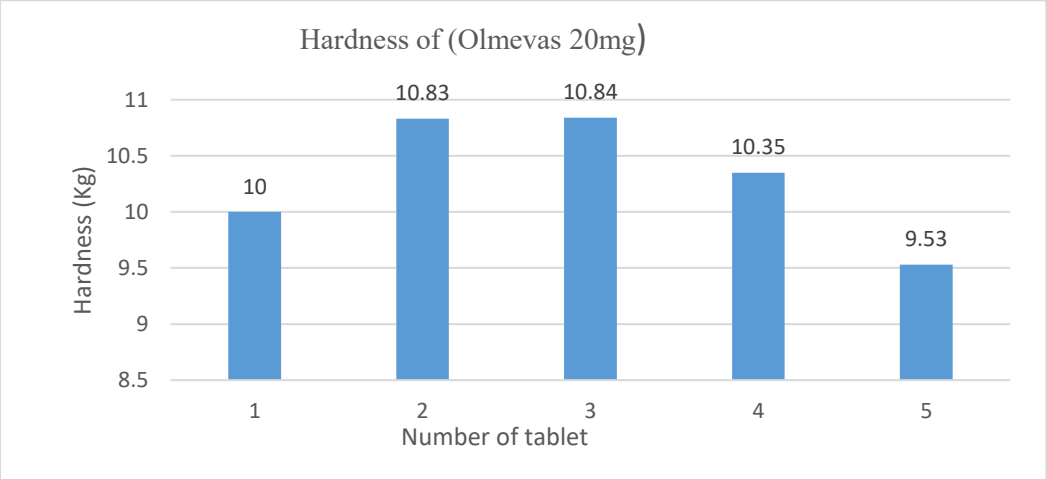

Figure 3.12: Hardness of (Olmevas 20 mg).

X-axis indicates numbers of tablet used in test. Y-axis shows about hardness of the tablets and One tablet shows little less hardness than other four tablet but in range.

Table 3.8: Hardness test of Olmesta 20 mg.

Number of tablets	Hardness (Kg)	Average (kg)
1	9.75	9.018
2	8.02	
3	10.22	
4	8.14	
5	8.96	

Standard deviation is 0.968359.

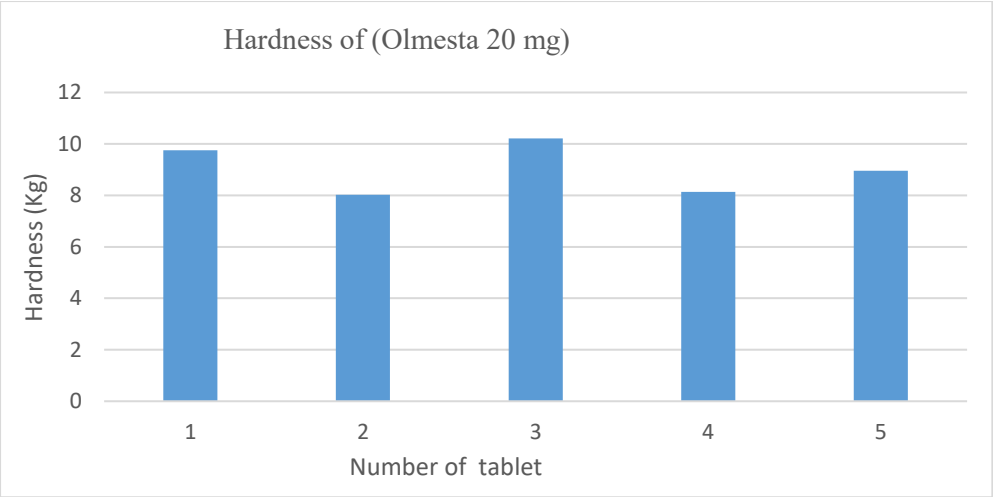

Figure 3.13: Hardness of (Olmesta 20 mg)

X-axis tells numbers of tablet used in test. Y-axis shows about hardness of the tablets and One tablet shows highest hardness than other four tablet.

Table 3.9: Hardness test of Olmecar 20 mg.

Number of tablets	Hardness (Kg)	Average (kg)
1	9.04	10.262
2	10.60	
3	10.21	
4	9.77	
5	11.69	

Standard deviation is 0.986342

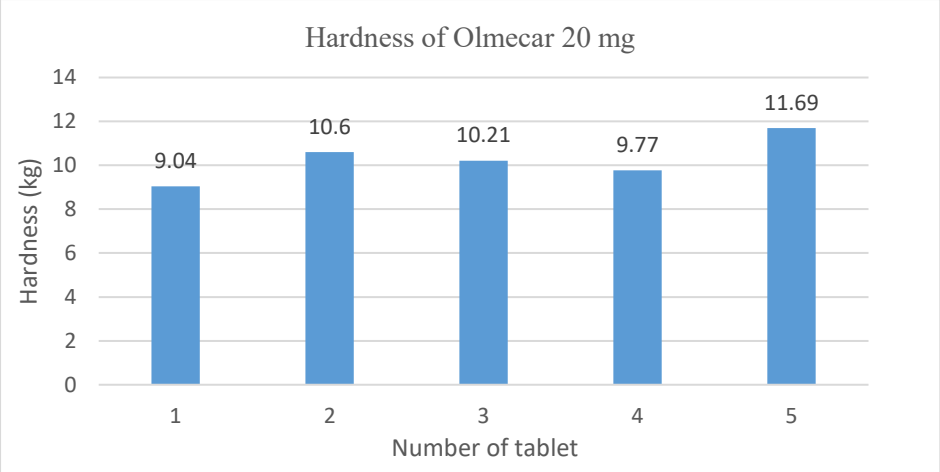

Figure 3.14: Hardness of (Olmecar 20 mg)

X-axis tells numbers of tablet used in test. Y-axis shows about hardness of the tablets which are in range and One tablet shows highest hardness.

Table 3.10: Hardness test of Olmezest 20 mg.

Number of tablets	Hardness (Kg)	Average (kg)
1	4.90	6.16
2	5.80	
3	6.84	
4	7.16	
5	6.10	

Standard deviation is 0.892079.

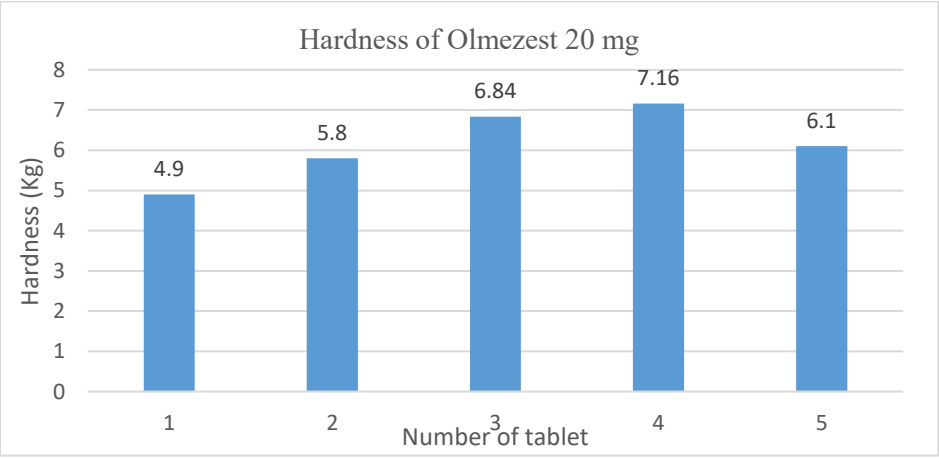

Figure 3.15: Hardness of (Olmezest 20 mg)

X-axis indicates numbers of tablet used in experiment. Y-axis shows about hardness of the tablets and all tablets had hardness in range.

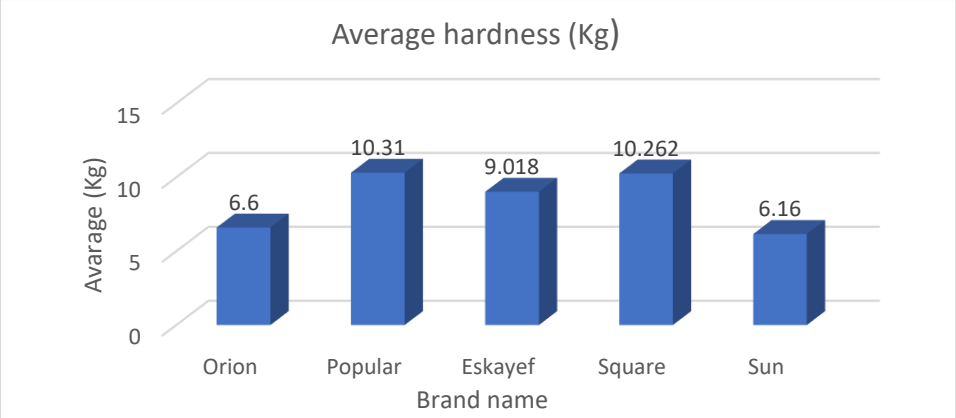

Figure 3.16: Average hardness of Olmesartan Medoxomil 20 mg of different brands.

It shows the average hardness of different brand and also indicate among the five brands which one shows more rigidity during manufacturing, shipping and transporting.

3.3 Friability test

The weight loss of randomly chosen 5 tablets from each brand was given below:

Table 3.11: Friability test of different brands.

Brand name	Before test	After test
Olmesaf 20 mg	0.68 g	0.67 g
Olmevas 20 mg	0.68 g	0.68 g
Olmesta 20 mg	0.71 g	0.70 g
Olmecar 20 mg	1.04 g	1.03 g
Olmezest 20 mg	0.76 g	0.76 g
Mean	0.774	0.766

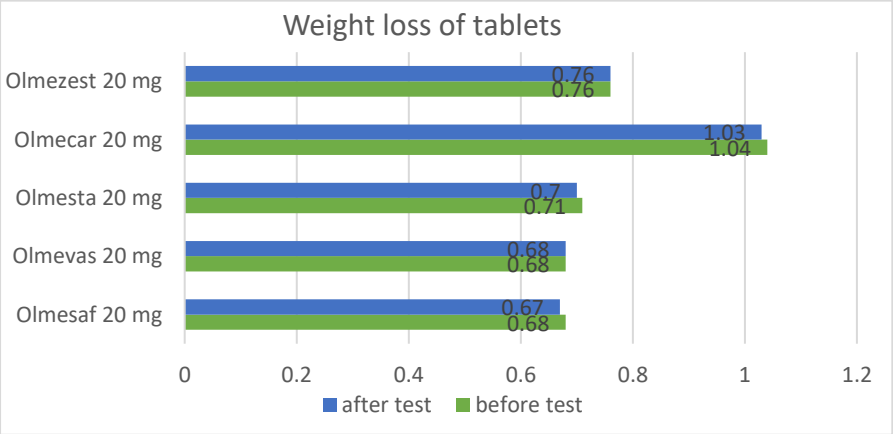

Figure 3.17: Weight loss tablets of different brand of Olmesartan Medoxomil (20mg). The graph shows weight loss of different brand. Olmesaf 20mg, Olmesta 20mg and Olmecar 20mg shows

1% weight loss during test. But Olmevas 20 mg and Olmeszest 20 mg did not show any weight loss.

3.4 Disintegration test

Disintegration test of 5 brands of Olmesartan Medoxomil tablets are given below:

Table 3.12: Disintegration test of different brands.

Brand Name	Disintegration time (minute)
Olmesaf 20 mg	1 min. 50 sec.
Olmevas 20 mg	2 min. 21 sec.
Olmesta 20 mg	7 min. 37 sec.
Olmecar 20 mg	3 min. 53 sec.
Olmezest 20 mg	6 min. 41 sec.

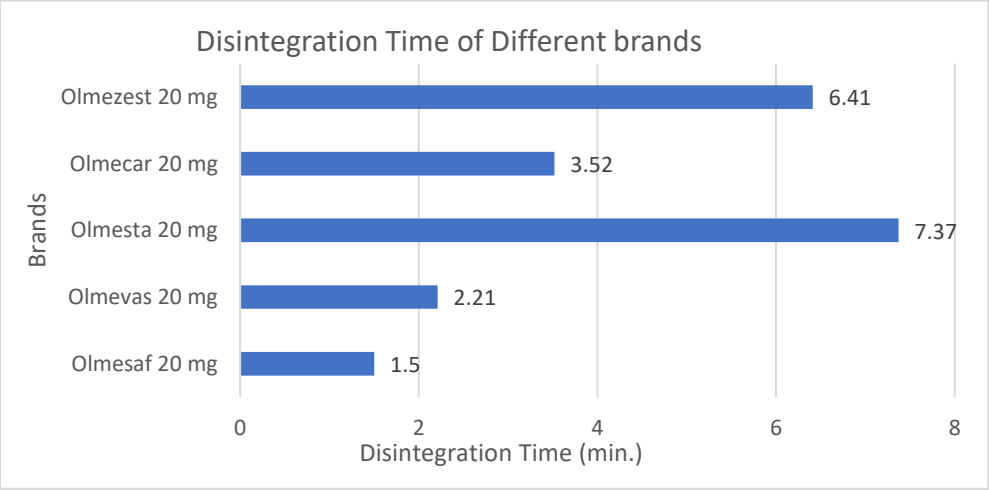

Figure 3.18: Disintegration time of different brands of Olmesartan Medoxomil 20 mg.

For all the brand disintegration time was in range. Olmesaf 20 mg shows lowest disintegration time where Olmesta 20 mg shows highest disintegration time.

3.5 Dissolution Test

Table 3.13: Dissolution test of (Olmesaf 20 mg)

time	Tbl-1	Tbl-2	Tbl-3	Tbl-4	Tbl-5	Tbl-6	Tbl-7	Tbl-8	Tbl-9	Tbl-10
5	0.010	0.023	0.023	0.015	0.026	0.021	0.023	0.010	0.019	0.020
10	0.011	0.024	0.024	0.017	0.028	0.022	0.024	0.011	0.025	0.021
15	0.015	0.027	0.025	0.020	0.032	0.024	0.024	0.013	0.026	0.022
20	0.017	0.028	0.028	0.024	0.033	0.026	0.026	0.013	0.034	0.026

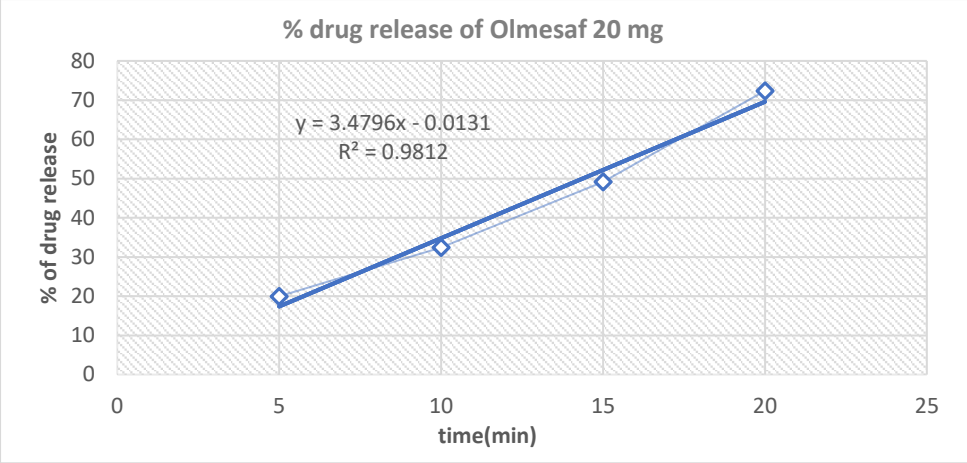

Figure 3.19: Drug release of Olmesartan Medoxomil (Olmesaf 20 mg).

The graph shows drug release of the tablet on time and also indicate linier equation and r^2 value. These values identify the percentage of drug release compare to the standard.

Table 3.14: Dissolution profile of Olmevas 20 mg.

time	Tbl-1	Tbl-2	Tbl-3	Tbl-4	Tbl-5	Tbl-6	Tbl-7	Tbl-8	Tbl-9	Tbl-10
5	0.006	0.012	0.011	0.013	0.009	0.011	0.010	0.011	0.023	0.022
10	0.015	0.015	0.012	0.013	0.010	0.015	0.010	0.012	0.024	0.024
15	0.018	0.016	0.017	0.014	0.011	0.016	0.011	0.015	0.025	0.025
20	0.018	0.017	0.019	0.016	0.019	0.017	0.019	0.017	0.029	0.034

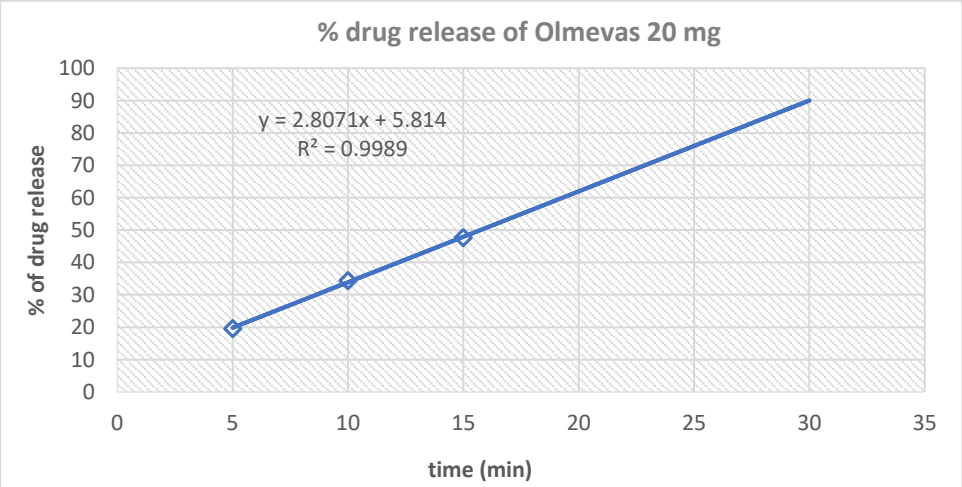

Figure 3.20: Drug release of Olmesartan Medoxomil (Olmevas 20 mg).

The graph shows drug release of the tablet on time and also indicate linier equation and r^2 value. The tablet in graph shows almost close drug release as standard.

Tablet 3.15: Dissolution test of Olmesta 20mg

time	Tbl-1	Tbl-2	Tbl-3	Tbl-4	Tbl-5	Tbl-6	Tbl-7	Tbl-8	Tbl-9	Tbl-10
5	0.007	0.004	0.001	0.012	0.019	0.019	0.007	0.016	0.005	0.014
10	0.007	0.010	0.010	0.016	0.019	0.021	0.014	0.019	0.007	0.016
15	0.008	0.016	0.013	0.018	0.020	0.034	0.014	0.019	0.012	0.020
20	0.012	0.021	0.013	0.020	0.021	0.036	0.026	0.023	0.014	0.025

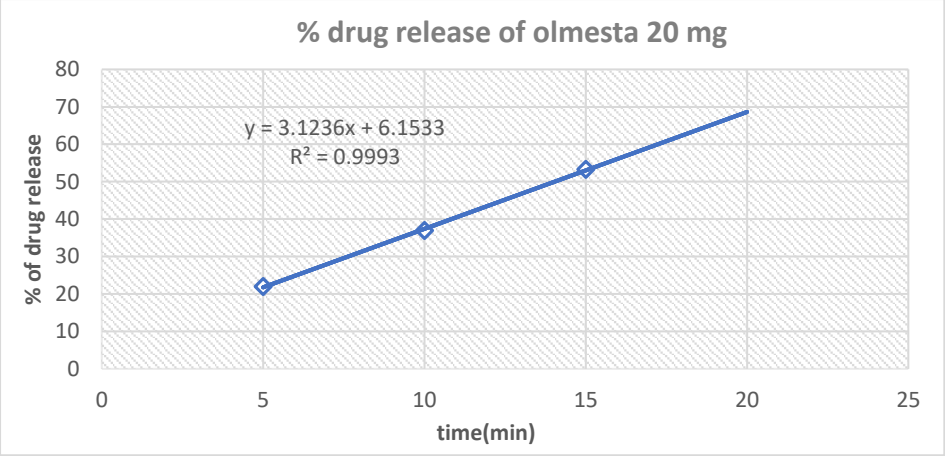

Figure 3.21: Drug release of Olmesartan Medoxomil (Olmesta 20 mg).

The graph indicates drug release profile of the tablet on time and also indicate the linier equation and r^2 value. Tested tablet shows almost similar drug release profile as standard.

Table 3.16: Dissolution test of Olmezest 20 mg

time	Tbl-1	Tbl-2	Tbl-3	Tbl-4	Tbl-5	Tbl-6	Tbl-7	Tbl-8	Tbl-9	Tbl-10
5	0.004	0.008	0.014	0.014	0.011	0.015	0.023	0.011	0.017	0.018
10	0.009	0.016	0.015	0.015	0.014	0.019	0.025	0.015	0.019	0.025
15	0.010	0.022	0.015	0.023	0.017	0.022	0.028	0.015	0.019	0.028
20	0.011	0.028	0.017	0.037	0.018	0.022	0.030	0.018	0.020	0.030

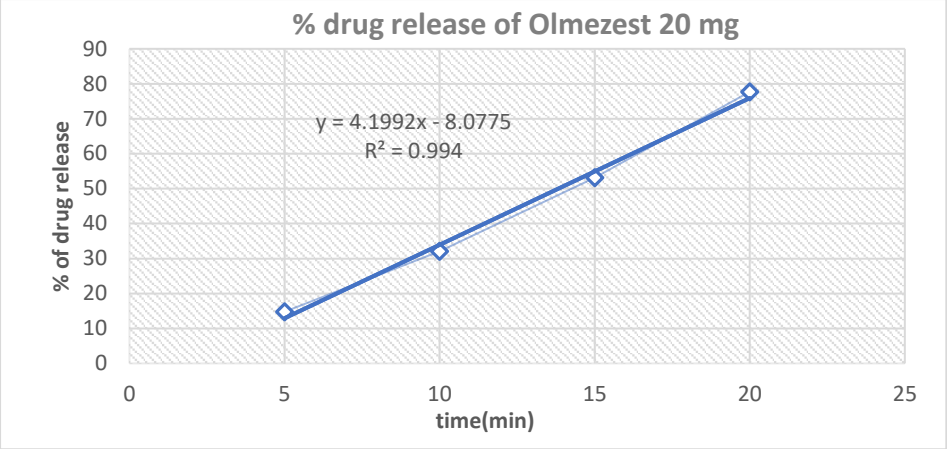

Figure 3.22: Drug release of Olmesartan Medoxomil (Olmezest 20 mg).

The graph tells drug release profile of tablet on time and also indicate linier equation and r^2 value. Tested tablet indicates similar release as standard.

Table 3.17: Dissolution profile of (Olmecar 20 mg).

time	Tbl-1	Tbl-2	Tbl-3	Tbl-4	Tbl-5	Tbl-6	Tbl-7	Tbl-8	Tbl-9	Tbl-10
5	0.016	0.009	0.002	0.013	0.009	0.002	0.009	0.011	0.010	0.018
10	0.017	0.013	0.006	0.015	0.011	0.013	0.013	0.017	0.013	0.020
15	0.020	0.014	0.011	0.016	0.015	0.015	0.026	0.024	0.015	0.021
20	0.029	0.022	0.019	0.018	0.027	0.022	0.036	0.064	0.018	0.027

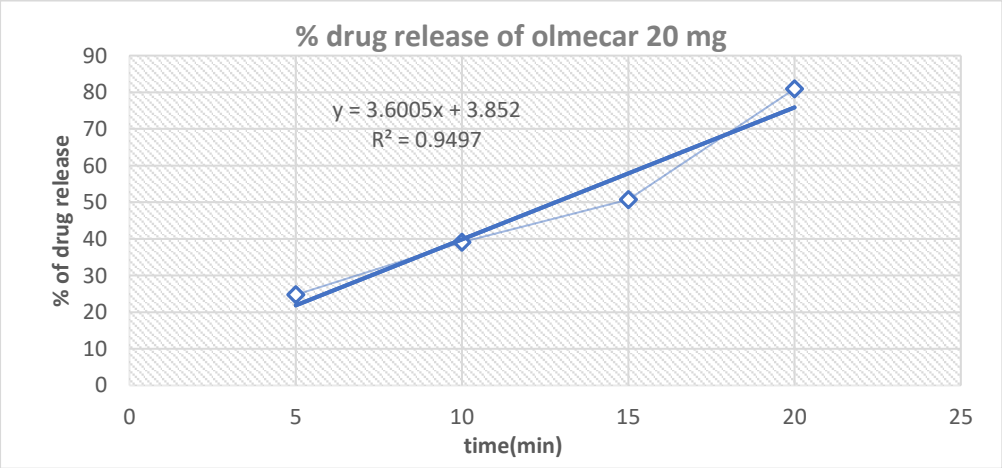

Figure 3.23: Drug release of Olmesartan Medoxomil (Olmecart 20 mg).

The graph shows drug release profile of tablet on time and also indicate linier equation and r^2 value. Tested tablet tells the drug had less release of drug compare to the standard.

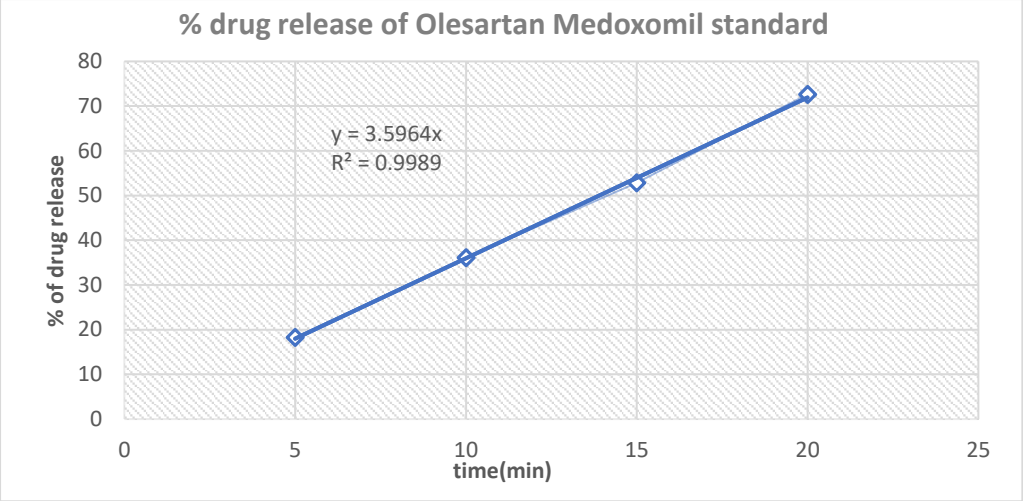

Figure 3.24: Drug release of Olmesartan Medoxomil (standard)

The r^2value is close to one and the equation is a linier equation.

(Patel et al., 2011)

Chapter 4
Discussion

4.1 Weight variation

For individual weights, the % of weight variation of Olmesafe 20 mg ranged from 1.5625% to -6.25% and the standard deviation for individual weights is 0.004472. For Olmevas 20 mg the % of weight variation ranged from 4.478% to -2.985 and the standard deviation is 0.005477. The % weight variation of Olmesta 20 mg ranged from 2.941 to -11.765 where the standard deviation found 0.008944. For Olmescar 20 mg the weight variation ranged from 0.962 to -3.846 where the standard deviation is 0.004472. The % of weight variation of Olmezest 20 mg ranged from 1.351 to -5.405.

The average weight for the tablets in between 130 mg to 324 mg. Following to the USP, ±7.5% is the range for weight variation. 5 brands concur with the U.S.P requirement and denotes that the flow of powder blend is uniform, which means the die fill is also uniform.

4.2 Hardness test

In accord to USP, the minimum hardness for a tablet is 4kg and for oral tablet the range is 4 to 8 kg or 10 kg. All the batches of Olmesartan Medoxomil from different brands are goes under the test and for Olmesafe 20 mg the average hardness of 6.6 kg and standard deviation 1.156806. The average hardness for Olmevas 20 mg is 10.31 and standard deviation is 0.564154. For Olmesta 20 mg the average hardness is 9.018 kg and standard deviation is 0.968359. Another brand Olmecar 20 mg has the average hardness 10.262 kg with standard deviation 0.986342. The Olmezest 20 mg has hardness 8.16 kg with 0.892079 standard deviation.

4.3 Friability Test

As per USP 2006, 1.0% is the maximum weight loss and tagged as satisfactory while doing storage, shipping etc. Before the test, 10 tablets of Olmesafe 20 mg weighted 0.68g and after the test it has 0.67g that means the mean weight loss is 1%. For Olmevas 20 mg the mean weight loss is 0%. For olmesta 20 mg the result before test is 0.71g and after the test 0.70g and

mean weight loss is 1%. Olmecar 20 mg has a mean weight loss 1% as before the test weight was 1.06g and after the test the weight was 1.05g. Olmezest is also have 0% mean weight loss. So, all the tablet meets the criteria of USP.

4.4 Disintegration test

As per BP, for film coated tablet the disintegration time is 30 minutes; for uncoated tablet the time is 15 minutes; for coated tablet the time is 30 minutes and for enteric coated tablet the time is 60 minutes or 1 hour. All the batches of Olmesartan Medoxomil 20 mg are the film coated tablet.

So, the average disintegration time of Olmesafe 20 mg 1.50 minutes. For olmevas 20 mg the average disintegration time is 2.21 minutes. The average disintegration time of Olmesta 20 mg is 7.37 minutes. For Olmecar 20 mg the average disintegration time is 3.53 minutes and for Olmezest, the average disintegration time is 6.41 minutes. All the batches of Olmesartan Medoxomil 20 mg batches meet the specification.

4.5 Dissolution test

According to USP, the % release of tablet should be 80% within 30 minutes (USP,2019). For Olmesaf 20 mg, % dissolved of Olmesartan Medoxomil ranged from 19.96% to 72.36% and Olmevas 20 mg ranged from 19.58% to 73.65%. % dissolved of Olmesartan Medoxomil for Olmesta 20 mg ranaged from 22% to 72.62%, for Olmezest 20 mg it ranged 14.77% to 70.29% and Olmecar 20 mg ranged from 24.75% to 80.90%. As the experiment was conducted for 20 minutes and evaluated the dissolution profile, it can be claimed that the drug is meet up the acceptable criteria of dissolution of Olmesartan Medoxomil.

Another criterion is r^2 value. The accepted r^2 value is ≥ 0.995. After conducting the experiment, we were able to form a standard curve where we got r^2 value of the five brand (Olmesaf 20 mg, Olmevas 20mg, Olmesta 20 mg, Olmezest 20 mg, Olmecar 20 mg) and values are 0.9812, 0.9989, 0.9993, 0.994, 0.9998. After analysis, it is found that the value for Olmesafe 20 mg is not meet the acceptable criteria. There can be many reasons for this;

- ✓ There may be an error while conducting the test.
- ✓ While undo the solution for dilution, the time may be not maintained properly.
- ✓ An unwanted particle may be mixed while using UV spectrometry so the reading is not perfect.

Chapter 5

Conclusion

In case of treating hypertension with fast acting profile Olmesartan Medoxomil is a decent therapeutic class. Yet it is necessary to maintain the quality to get the exact therapeutic effect. In this study it was examined and noticed that Olmesartan Medoxomil has pass most of the quality control parameters which were given by USP and BP. In comparison among five brands, Olmevas 20 mg showed the highest weight variation. In case of hardness test all brands are meet the exact range (4 to 8or 10 kg). So, the integration time of all the brands met the specification of BP (uncoated tablets within 15 mins). A good hardness value shows a strong withstand during manufacturing, packaging, shipping and protected from consumer abuse. In friability study, all brands showed good result and no brand showed weight loss more than 1%. The percentage of drug release of all brands were varying, but close to the standard drug. The variation may occur while conducting the test or may be personal or analytical error. An extended study needs to be conducted regarding the quality control parameters as this drug are now potential choice in the treatment of hypertension.

References:

1. Ashrafi, J. (n.d.). Evaluation of the Quality Control Parameters of Two Different Brands of Combined Atenolol (50mg) & Amlodipine (5mg) Tablets Available in Bangladesh.

2. Auspar-olmesartan-medoxomil-130226-pi.pdf. (n.d.). Retrieved 27 September 2024, from https://www.tga.gov.au/sites/default/files/auspar-olmesartan-medoxomil-130226-pi.pdf

3. Brunner, H. R. (2006). Olmesartan medoxomil: Current status of its use in monotherapy. Vascular Health and Risk Management, 2(4), 327–340. https://doi.org/10.2147/vhrm.2006.2.4.327

4. Ch32-Revised.pdf. (n.d.). Retrieved 26 September 2024, from https://download.lww.com/downloads/thePoint/9780781731935_Smeltzer/Content_Updates/Ch32-Revised.pdf

5. Dharmalingam, S. (2014). Comparative Quality Control Evaluation of Atenolol Tablets Marketed in Kuala Lumpur, Malaysia. British Journal of Pharmaceutical Research, 4(13), 1688–1695. https://doi.org/10.9734/BJPR/2014/8813

6. Dharmalingam, S., Madhappan, R., Ramamurthy, S., Chidambaram, K., Srikanth, M., Shanmugham, S., & Kumar, S. (2014). Investigation On Antidiarrhoeal Activity Of Aristolochia Indica Linn. Root Extracts In Mice. African Journal of Traditional, Complementary and Alternative Medicines, 11(2), 292. https://doi.org/10.4314/ajtcam.v11i2.11

7. Dharmalingam, S., Ramamurthy, S., Chidambaram, K., & Nadaraju, S. (2014). A Simple HPLC Bioanalytical Method for the Determination of Doxorubicin

Hydrochloride in Rat Plasma: Application to Pharmacokinetic Studies. Tropical Journal of Pharmaceutical Research, 13(3), 409. https://doi.org/10.4314/tjpr.v13i3.15

8. Disintegration test BP 2019.pdf. (n.d.). Retrieved 27 September 2024, from https://www.usp.org/sites/default/files/usp/document/harmonization/gen-chapter/april-2019-m99460.pdf

9. Dissolution Testers – USP Guidelines—Total Laboratory Services—ERWEKA UK - Dissolution Testers. (2024, January 24). https://www.totallaboratoryservices.co.uk/dissolution-testers-usp-guidelines/

10. Grossman, E., & Messerli, F. H. (2012). Drug-induced Hypertension: An Unappreciated Cause of Secondary Hypertension. The American Journal of Medicine, 125(1), 14–22. https://doi.org/10.1016/j.amjmed.2011.05.024

11. Hajar, R. (2017). Risk Factors for Coronary Artery Disease: Historical Perspectives. Heart Views : The Official Journal of the Gulf Heart Association, 18(3), 109–114. https://doi.org/10.4103/HEARTVIEWS.HEARTVIEWS_106_17

12. Hedvati, L., & Pilarsky, G. (2006). Preparation of olmesartan medoxomil (World Intellectual Property Organization Patent No. WO2006029056A1). https://patents.google.com/patent/WO2006029056A1/en

13. High Blood Pressure: What You Need To Know. (n.d.). Cleveland Clinic. Retrieved 26 September 2024, from https://my.clevelandclinic.org/health/diseases/4314-hypertension-high-blood-pressure

14. Hypertension. (n.d.). Retrieved 26 September 2024, from https://www.who.int/news-room/fact-sheets/detail/hypertension

15. Islam, A. K. M. M., & Majumder, A. A. S. (2012). Hypertension in Bangladesh: A review. Indian Heart Journal, 64(3), 319–323. https://doi.org/10.1016/S0019-4832(12)60096-0

16. JNC 8 Hypertension Guideline. (n.d.). Retrieved 26 September 2024, from https://www.studocu.com/en-us/document/university-of-memphis/adult-health-nursing/jnc-8-hypertension-guideline-algorithm/57504521

17. Kerndt, C. C., & Soos, M. P. (2024). Olmesartan. In StatPearls. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK544367/

18. Lawes, C. M. M., Bennett, D. A., Lewington, S., & Rodgers, A. (2003). Blood Pressure and Coronary Heart Disease: A Review of the Evidence. Seminars in Vascular Medicine, 02, 355–368. https://doi.org/10.1055/s-2002-36765

19. Mazumder, B., Bhattacharya, S., & Yadav, A. (n.d.). Total Quality Management in Pharmaceuticals: A Review.

20. Mechanism of action of Olmesartan. (n.d.). Retrieved 27 September 2024, from https://go.drugbank.com/drugs/DB00275

21. Meng, L., Chen, D., Yang, Y., Zheng, Y., & Hui, R. (2012). Depression increases the risk of hypertension incidence: A meta-analysis of prospective cohort studies. Journal of Hypertension, 30(5), 842–851. https://doi.org/10.1097/HJH.0b013e32835080b7

22. Olmesartan: Side Effects, Dosage, Uses, and More. (2017, November 25). Healthline. https://www.healthline.com/health/olmesartan-oral-tablet

23. Patel, J., Kevin, G., Patel, A., Raval, M., & Sheth, N. (2011). Development of the UV spectrophotometric method of Olmesartan medoxomil in bulk drug and pharmaceutical

formulation and stress degradation studies. Pharmaceutical Methods, 2(1), 36–41. https://doi.org/10.4103/2229-4708.81092

24. Pazdernik, T. (2009). Lippincott's Illustrated Reviews: Pharmacology, 4th Edition. Medicine & Science in Sports & Exercise, 41(7), 1531. https://doi.org/10.1249/MSS.0b013e3181a21294

25. PubChem. (n.d.). Olmesartan Medoxomil. Retrieved 27 September 2024, from https://pubchem.ncbi.nlm.nih.gov/compound/130881

26. Shohin, I. E., Kulinich, J. I., Ramenskaya, G. V., Abrahamsson, B., Kopp, S., Langguth, P., Polli, J. E., Shah, V. P., Groot, D. W., Barends, D. M., & Dressman, J. B. (2014). Biowaiver Monographs for Immediate Release Solid Oral Dosage Forms: Piroxicam. Journal of Pharmaceutical Sciences, 103(2), 367–377. https://doi.org/10.1002/jps.23799

27. ShowLabeling.pdf. (n.d.). Retrieved 27 September 2024, from https://labeling.pfizer.com/ShowLabeling.aspx?id=9909

28. Solubility.pdf. (n.d.). Retrieved 27 September 2024, from https://cdn.caymanchem.com/cdn/insert/11614.pdf

29. Tablet Breaking Force | USP-NF. (n.d.). Retrieved 27 September 2024, from https://www.uspnf.com/notices/general-chapter-prospectus-tablet-breaking-force-1217

30. The Theory and-Practice-of-Industrial-Pharmacy-By-Lachman-and-Lieberman-3rd-Editn-SaMeep104-pdf. (n.d.).

31. USP weight variation_25_feb_2011.pdf. (n.d.). Retrieved 27 September 2024, from https://www.usp.org/sites/default/files/usp/document/harmonization/gen-method/q0304_stage_6_monograph_25_feb_2011.pdf

32. Warner, G. T., & Jarvis, B. (2002). Olmesartan Medoxomil: Drugs, 62(9), 1345–1353. https://doi.org/10.2165/00003495-200262090-00005

33. What is the mechanism of Olmesartan Medoxomil? (n.d.). Retrieved 27 September 2024, from https://synapse.patsnap.com/article/what-is-the-mechanism-of-olmesartan-medoxomil

34. Working documents in public consultation. (n.d.). Retrieved 27 September 2024, from https://www.who.int/teams/health-product-and-policy-standards/standards-and-specifications/norms-and-standards-for-pharmaceuticals/guidelines/quality-control

35. World Health Organization. (2007). Quality assurance of pharmaceuticals: A compendium of guidelines and related materials. Good Manufacturing Practices and Inspection. https://iris.who.int/handle/10665/43532

36. Zhang, P., Wang, F., Hu, J., & Sorrentino, R. (2013). Exploring the Relationship Between Drug Side-Effects and Therapeutic Indications. AMIA Annual Symposium Proceedings, 2013, 1568–1577. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3900166/