EVALUATION OF THE QUALITY CONTROL PARAMETERS OF FIVE DIFFERENT BRANDS OF MONTELUKAST (10 MG) TABLETS AVAILABLE IN BANGLADESH

By

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A thesis submitted to the School of Pharmacy in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy (B. Pharm.)

School of Pharmacy
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Declaration

It is hereby declared that

1. The thesis submitted is my/our own 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/We have acknowledged all main sources of help.
5. **Student's Full Name & Signature:**

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Approval

The thesis titled "Evaluation of quality control parameters of five different brands of Montelukast (10mg) tablets available in Bangladesh" submitted by Abdus Samad Ahmed, of Summer, 2024 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy.

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Ethics Statement

No animals were used during experiments.

Abstract

Treatment of any disease can be failed by prescribing a substandard drug. Nowadays Montelukast is widely used in Bangladesh for the treatment of Prophylaxis and Chronic treatment of Asthma, Acute prevention of Exercise – Induced Bronchoconstriction, Relief of symptoms of Allergic Rhinitis: Seasonal and Perennial Allergic Rhinitis. Therefore, the goal of this study is to evaluate the competitive environment of the local market and evaluate the quality parameters with multiple Montelukast 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: Montelukast; 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. My advisor Dr.Raeed Jamiruddin sir has given me the idea of this project and has guided me throughout my project about how I can complete this perfectly and efficiently for which I greatly appreciate. Furthermore, I would like to thank lab officer Mebanin and Atikur Rahman for guiding me throughout my experiments and helping me performing them correctly.

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List of Acronyms

MTK	Montelukast
EIB	Exercise Induced Bronchoconstriction
PrP	Prophylaxis
AR	Allergic Rhintis

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. (Lehman et al.,2003) 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. (ICH,2009). 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.

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. (Eun & Hyung, 2021). 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 (Beer & Vervaet, 2011). The number of cases of asthma, nasal allergies, exercise induced breathing problem is increasing worldwide. The prevalence of asthma, nasal allergies, exercise induced breathing problem is much higher in countries with low and middle incomes than it is in countries with high incomes, about 60-80% of asthma patient have allergic rhinitis. The basis of treatment to control this problem is Montelukast. About 4-7% of population of Bangladesh has asthma and additional people suffers allergic rhinitis and about 5-10% of people could be benefited by Montelukast 10 mg excluded children. The cause of this problem can be significantly affected by factors related to Genetic predisposition, allergies (Triggers), Environmental irritants, infection, lifestyle. (Alamgir & Monjurul, 2008)

1.2 Chronic Asthma, EIB (Exercise Induced Bronchoconstriction), AR (Allergic Rhinitis)

Chronic Asthma is a long-term condition where the airways in the lungs become inflamed and narrow which makes breathing difficult. In chronic asthma the airways are chronically inflamed which leads it to constant swollen and irritation. Due to inflammation, it can lead to recurring episode of wheezing, coughing, chest tightness, and shortness of breath. Again, the airways become overly sensitive and reacts when different triggers emerge. Triggers which include allergens like pollen, dust mites, pet dander and irritants which also include smoke and pollution. This inflammation makes it harder for moving air in and out of the lungs (Sultana & Sayeed, 2014).

1.3 Symptoms

Now a days chronic asthma problems are growing rapidly, especially countries like China, India, Pakistan, Nepal and even Bangladesh. However, the exact cause isn't fully understood, factors that could be looked after like early exposure to smoking, family history of asthma or allergies. Again, environmental factors like dust mites, pollen, mold can also cause Asthma. Now if we look into the symptoms of asthma, we can find a couple of them like the common symptoms are a persistent coughing especially at night, wheezing when exhaling and sometimes inhaling, shortness of breath or difficulty while breathing. tightness of chest which makes it difficult to take deep breath. In winter asthma can become severe if the person having asthma catches cold. Triggers related to pollen, perfume, animal fur, smoke, dust all can lead to the symptoms (Beasley & Pearce, 2000)

Now for the symptoms of allergic Rhinitis we can find many of them and each are divided in to segments. Symptoms like runny nose, sneezing, itchy nose, watery eyes. Again, if we look into the nasal symptoms we can find sneezing, itchy eyes, Blocked nose, throat irritation and coughing. Then comes eye symptoms and we can find itchy eyes, red irritated eyes. Throat symptoms can also be seen like itchy throat, sore throat and an urge to clear throat (Greiner & Scadding, 2011). Finally for Exercise Induced Bronchoconstriction the following Symptoms are seen like coughing, wheezing shortness of breath or struggle for air, pain in chest or chest tightness like pressure or squeezing in chest. Fatigue can also be seen in people with EIB, Reduced endurance which leads to inability to keep up with exercise and physical activity like playing football or running. In case of children's they could face abdominal discomfort (Aggarwal & Berend, 2011).

1.4 Causes of Asthma, Allergic Rhinitis and EIB

Most importantly let us take a deep look at what causes these problems in us. Firstly, for asthma, it's not fully known exactly what causes asthma but deep studies shows that it can be caused due to genetic or hereditary factor and also environmental factors. Family history, genetic mutation, allergens, irritants like smoke and tobacco, air pollution and many more (Cockcroft et al., 2018). Secondly, Allergic rhinitis can be caused by dust mites, animal dander, mold spores, and our immune system mistakenly considers harmless substance called allergens as threat, release histamine which causes our nasal to inflammation and, mucus production (Bousquet & Toppila, 2020). Thirdly, Exercise induced bronchoconstriction can be seen when there is a increase in respiratory water loss, it can also be caused due to irritants during an intense training exercise and it can also be caused by airway cooling which leads narrowing of

airway and inflammation. People with asthma or have respiratory infection can also have EIB (Gotshall et al., 2002)

1.5 Treatment Strategies

Firstly, for the treatment of asthma we can find that quick relief process such as rescuing and a long-term control medication is used to deal with asthma. Regarding the quick relief process we use short acting beta agonist which open the air ways immediately and for long term we use inhaled corticosteroid which take time to reduce the airway inflammation. Strategies also involves avoiding triggers, quitting smoking and avoiding allergens (Barnes et al., 1989). Secondly, for the treatment of Allergic rhinitis mainly avoiding the allergen should do the trick, wearing mask, keeping windows closed, air filters and keeping pets at a distance. Medication can also be used to treat this problem like using intranasal corticosteroid and anti-histamines. Living and maintaining hygiene can also help to deal with AR (Sur & Scandale, 2010). Thirdly, to treat Exercise induced bronchoconstriction can be done by pharmacologically and non-pharmacologically and if we look deep into non -pharmacologically it can be dealt with if warm ups are done before exercise, breathing is done properly via nose and improving cardiovascular fitness. Again, through pharmacological treatment EIB can be dealt with by short acting beta agonist before exercise and in done cases inhaled corticosteroid can help for long term prevention (Backert & Porsbjerg, 2013).

1.6 Montelukast

Montelukast is a drug that is a selective and is commonly taken orally, this drug is orally active leukotriene receptor antagonist which inhibits cysteinyl leukotriene receptor (CyslT1). This CyslT1 is a material of arachidonic acid metabolism, which is released from various cell

including mast cells and eosinophils. There is a correlation of cysteinyl leukotrienes and leukotriene receptor occupation with asthma and allergic rhinitis including airway edema, smooth muscle contraction associated with inflammatory process which leads to the signs and symptoms of asthma (Markham & Faulds, 1998).

1.6.1 Discovery

Montelukast was first discovered my Merck & Co at Montreal, Canada. From 1970-1980 leukotrienes were identified as the key inflammatory agents in asthma, a long-targeted effort was done to find an oral medication that could block leukotrienes. Addition of Two parallel ways were used to block leukotrienes like 5-Lipoxygenase and Leukotriene D4 and after that early candidate was used and then refinement and setback were done then breakthrough came. Furthermore, in 1997 montelukast was submitted for global marketing and in 1998 it received FDA approval and Its discovery leads us towards a paradigm shift in asthma treatment because it was the first able to orally target the inflammatory process and made it simpler than inhaled corticosteroid (Young et al., 2012).

1.6.2 Chemistry

Montelukast is a quinoline-derived heteroaromatic compound with carboxylic acid, thioether, hydroxyl, and cyclopropyl groups, designed to antagonize leukotriene receptors useful in asthma, allergic rhinitis and EIB (Thun & Breu, 2009).

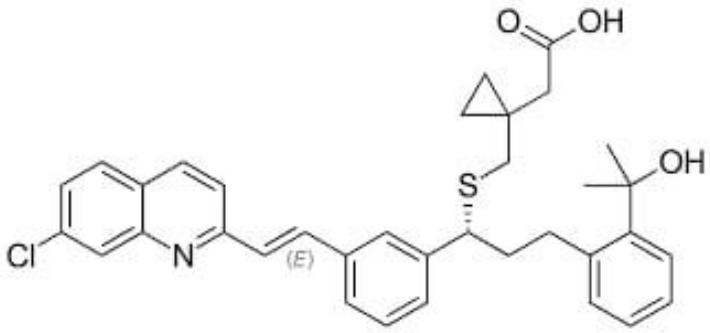

Figure 1.1: Structure of Montelukast

Table 1.2: Characteristics of Montelukast

Chemical Names	[R-(E)]-1-[[[1-[3-[2-(7-chloro-2quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propy]thio]methyl]cyclopropaneacetic acid, monosodium salt
Molecular Formula	$C_{35}H_{35}ClNNaO_3S$
Relative Molecular Mass	586.18 g/mol
Melting Point	115-148°C
Appearance	Often white or beige with round shaped or four-sided
Enantiomers	R/S because it has chiral center, but sold as R enantiomer

(ACS Publication)

Table 1.3: Solubility of Montelukast

Solvent	Relative Solubility
Water	**0.01 mg/mL to 0.05 mg/mL**
Ethanol	Freely soluble
DMSO	30 mg/ml
DMF	2 mg/ml

(*chemicalbook.Pdf*, n.d.)

1.6.3 Mechanism of action

Many cells, including mast cells and eosinophils, emit eicosanoids called cysteinyl leukotrienes (CysLT), which include LTC4, LTD4, and LTE4.3, 4, 5, 6, 7, 8, and 9 Activities that aid in the pathophysiology of asthma and allergic rhinitis are triggered when such CysLT bind to corresponding CysLT receptors, such as CysLT type-1 receptors found on respiratory airway smooth muscle cells, airway macrophages, and various pro-inflammatory cells like eosinophils and certain myeloid stem cells

Asthma-promoting effects include vascular permeability, occluding mucous secretion, eosinophil recruitment, and CysLT-mediated airway bronchoconstriction. A clogged nose and airway are among the symptoms of allergic rhinitis that are triggered by CysLTs, which are released by the nasal mucosa in response to allergen exposure during both early and late phase reactions. The leukotriene receptor antagonist montelukast then binds to the CysLT type 1 receptor with high affinity and selectivity, helping to block any physiological actions of CysLTs such as LTC4, LTD4, and LTE4 at the receptor that might exacerbate asthma or

allergic rhinitis (Allaf et al., 2023)

Again, by another source we can find the MOA of Montelukast:

A highly selective leukotriene receptor antagonist, montelukast (empirical formula C35H35ClNNaO3S) binds to the cysteinyl leukotriene receptor for leukotrienes D4 and E4 with great affinity. Numerous cells, including mast cells, release these leukotrienes, which contribute to the inflammatory process that might result in the symptoms of asthma and allergic rhinitis. Smooth muscle cells and macrophages are examples of airway cells that have leukotriene receptors. Without demonstrating any agonist activity, montelukast blocks leukotriene physiologic effects (including airway edema, smooth muscle contraction, and impairment of normal cellular activity) when it binds to leukotriene receptors. Low dosages of montelukast (5 mg) significantly reduce the bronchoconstriction brought on by leukotriene D4 in asthmatics. Additionally, in a crossover investigation, montelukast prevented 12 asthmatic patients from experiencing early and late-phase bronchoconstriction brought on by an antigen challenge. According to the majority of international asthma guidelines, montelukast should be used as an alternate therapy and daily low-to-moderate doses of inhaled corticosteroids (ICS) as the preferred controller for children with asthma who are ≤5 years old. According to controlled trials, montelukast significantly increases morning peak expiratory flow ($p=0.001$), decreases beta2-agonist use ($p<0.001$), blood eosinophils ($p=0.009$), and asthma symptoms ($p=0.001$). These metrics show that montelukast relieves clinical symptoms and reduces airway eosinophilic inflammation. Its impact on airway inflammation may contribute to its effectiveness in treating persistent asthma (Tintinger & Anderson, 2010).

1.6.4 Dosage and Administration

For Adult and adolescent 15 years of age and older who's with asthma and seasonal allergic rhinitis they are prescribed Montelukast 10 mg once daily. Now for Pediatric patients of 6 to 14 years of age are prescribed Montelukast 5 mg tablets once daily. Pediatric patients who are of 2 to 5 years of age are prescribed Montelukast 4 mg tablets once daily. Again, Pediatric Patients of 6 months to 5 years of age are prescribed Montelukast 4 mg oral granules once daily. Oral granules can be given directly in the mouth or mixed with spoonful of cold water or soft food at room temperature. For elderly patients the dose of a single montelukast 10 mg is similar in elderly and younger adults, the plasma half-life of montelukast is slightly longer in the elderly, no dose adjustment is required. For Renal impairment "No" dose adjustment is recommended and also for Hepatic impairment "No" dose adjustment is required. For Children the safety and efficacy of Montelukast have been established in adequate and well controlled studies in pediatric patients with asthma 6 months to 14 years of age. Safety and efficacy profile in this age group are similar to those seen in adults. (Markham & Faulds, 1998)

1.6.5 Side Effect

Regarding the side effect we can divide the side effect into common, uncommon and rare.

Firstly, for common side effect we can find Diarrhea, Gastrointestinal discomfort, upper respiratory infection, nausea. Secondly for uncommon side effect anxiety can be seen, abnormal behavior, sleep disorder, dizziness, drowsiness, depression and abnormal sensation can be seen. Thirdly, for rare side effect hallucination, memory disorder, hepatic disorder, tremor and suicidal tendencies (Calapai & Gangemi, 2014).

1.6.6 Contraindications

Montelukast is contraindicated in patients who have hypersensitivity to any component of this product. (Calapai, & Gangemi, 2014).

1.6.7 Drug Interaction

Montelukast can be taken with certain anti histamine like cetirizine, ebastine, fexofenadine. Montelukast is has been administered with other therapies in a daily bias with no apparent increase in adverse reaction. Montelukast is concomitantly with a wide range of commonly prescribed drugs in clinical studies without evidence of clinical adverse interactions. Medication which was used with monas are thyroid hormone, sedative hypnotic, NSAIDs, benzodiazepines, and decongestants. Phenobarbital a drug which induces hepatic metabolism decreases the AUC of montelukast by 40% following a single 10 mg dose. Further dose is not recommended, again it's important to employ appropriate clinical monitoring when potent cytochrome P450 enzyme inducer like rifampin is co administered with montelukast (Calapai, & Gangemi, 2014).

1.6.8 Interaction with other medicinal products

Montelukast can interact with different kinds of drug among them we can find montelukast has a interaction with certain antiepileptic drugs, certain antibiotic and fibrate for cholesterol. This kind of interaction is seen because of enzymes in our liver because they all are metabolized in our liver which make montelukast less effective. Interaction doesn't stop there; montelukast can also interact with antifungal drugs, HIV medications and Herbal supplements (Calapai, & Gangemi, 2014).

1.7 Quality

Prioritizing quality is a must for any company or business. The superiority of the product or service is referred to as "quality" and is assessed by contrasting it with the requirements and experiences of the client. One way to characterize the quality of a product is its ability to satisfy the needs and expectations of the customer. Since data and features vary depending on the product, it is essential to prioritize the quality of the definition. For Example, when it comes to pharmaceutical products, factors like its taste, toxicity, physical and chemical properties, and shelf life, appearance, Purity etc. This are the factors that determine the quality of a product. (Woodcock et al., 2004)

1.8 Quality Control

Quality control is a must in case of drug production, quality control is very important for the safety, efficacy and the consistency of the product. After many tests performed by the quality control department and if the raw material like API, Excipients and the finished product all pass the quality controls test then and then they are used for production and marketing. If quality control doesn't give any pass, then those raw materials and finished product will stay still until the pass is given by the quality control department. Tests that are performed in quality control are: Physical and chemical testing, Dissolution testing, Microbial testing, Stability testing. Testing of Raw Materials: Describe the significance of quality control in examining raw materials to make sure they are suitable for the production of pharmaceuticals.

In-Process Control: Talk about how quality control keeps an eye on important variables throughout the production process to preserve product quality. Both these tests done in quality control are very important for pharmaceutical product lifecycle. (Kumar & Rawal, 2018). 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. (Austin et al., 2006). A poor sampling strategy is very important because when test items are chosen in a way that does not fairly reflect all potential test items, this is known as an ineffective sampling design. Implementing statistically sound testing methods for all products produced, including units destined for final sale and samples for inspection, to enhance quality control in a business. Incorrect interpretation of the test findings should be given priority, it's crucial to employ a technique that can accurately evaluate your product when it's in evaluation process. This entails adhering to all the organization's standard operating procedures for planning, carrying out, and wrapping up testing. Inaccurate interpretation of test results can stem from poor test protocols. There are inherent chances for error at every stage of quality control, some more than others.

When conducting tests, reduction of human error by being aware of the steps that are most likely to occur. Inadequate record-keeping and documentation procedures is one of the most prevalent consequences of inadequate quality control is inadequate documentation and record-keeping. Accurate records are necessary for a strong quality control program in order to draw lessons from past performance and apply those lessons to new goods. Inadequate testing can result in a defective product, and proper testing methods are pointless if no one follows them. Consumers are unlikely to trust the brand again if a product fails quality control and is nevertheless distributed, which can negatively impact future sales and brand reputation.

Absence of a framework for managing quality is another problem, a set of protocols known as a quality management system guarantees that a company consistently and reliably addresses its quality control problems. minimization or even completely eradicating typical errors in any organization, such as improperly testing products, maintaining inaccurate records, or even selecting subpar suppliers, by including a clear quality control approach into workflow. Setting up a QMS is the most important thing you can do for your small business. Lack of one can quickly result in lost sales, clients, and even worse, long-term harm to one's reputation (Ott & Neubauer, 2005). Quality is characterized by eight dimensions. They are vital to the success of the company. They are as Performance which is the main functional aspects of the product. Characteristics which enhancements to a product's fundamental operational characteristics. Reliability which is most likely the likelihood that something won't go wrong within a given time frame. Conformance is the extent to which a product's operational features and design adhere to predetermined standards. Durability is an indicator of a product's lifespan. Serviceability refers to the ease and quickness of repair. Aesthetics is a product's appearance, texture, flavor, and aroma and Perceived quality is customer's perspective (Withrow et al., 2006)

1.9 Quality of Pharmaceutical Product

Product quality is the primary prerequisite for every pharmaceutical company to stay in operation. In the pharmaceutical industry, a high degree of administrative, scientific, and technological complexity determines quality. Quality is always a minimal criterion for every product. It takes center stage when it comes to life-saving products like pharmaceuticals. In the pharmaceutical industry, quality has grown to be a crucial issue. There has been an increase in awareness of the importance of pharmaceutical product quality since the FDA's current good

manufacturing practices, or cGMP, for the twenty-first century were introduced and the globe came together to standardize its methods and guidelines. The emergence of multiple criteria that specify precisely what the quality of the medication should be serves as a representation of this awareness (Woodcork et al., 2004). Most conventional pharmaceutical drugs are fairly simple substances that have been found via trial and error to treat disease or its symptoms. To ensure quality, these chemicals underwent decades of refinement. The quality of any medication is closely related to its quality. Because low-quality pharmaceuticals might cause overdose or subtherapeutic adverse effects, they cannot be marketed or sold. Medicines of any brand or company that are not maintained when prescribed to patients might cause serious problems. Because of its poor quality, the patient may suffer adverse effects, some of which can be fatal. (Lachman & Kanig,1976).

1.10 Quality Assurance

In the pharmaceutical industry, designing, developing, and implementing quality assurance is the most important role. In pharmaceutical sector, Reducing the likelihood of defects and, more crucially, fixing errors as early in the value chain as feasible are the main goals of quality assurance. As a result, fewer flaws are discovered during the final inspection step, when fixing them becomes challenging and expensive. Thanks to a well-managed quality assurance system, a defective piece can be found and fixed further upstream, saving time and effort, lowering costs, and protecting brand reputation (Swati & Ravindranath, 2011). In actuality, this entails implementing administrative and technical procedures to effectively track and enhance the caliber of goods and services. These procedures, such as equipment safety evaluations, personnel surveys, and product testing, are carried out with the help of a QA system. All of these components, when put into practice, will be focused on upholding and enhancing an

organization's quality standards. Additionally, QA gives businesses a competitive edge, guarantees adherence to rules and industry norms, and immediately boosts profitability. (Potdar et al., 2006).

1.11 Importance of Quality

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

Manufacturing of safe, effective medicines; For a drug to be both safe and therapeutically effective, it must meet its specified quality standards. Now a compromised medicine may be harmful or inefficient as a treatment. Therefore, in order to guarantee patient safety, pharmaceutical manufacture should get the utmost attention to quality. Furthermore, Prosperity and Longevity in a Competitive Sector; Quality is crucial to the pharmaceutical industry's existence and financial success. High-quality products are essential for consumer satisfaction and potential profit in order for the pharmaceutical industry to flourish. Moreover, In Order to Make Maximum Profit and Profits can be raised by using a high-quality product. Customers give low-quality products negative ratings, which reduces their profitability. On the other side, high-quality items lead to happy customers. Now A higher level of customer satisfaction increases the profitability of the company. Marketing strategy: The quality of its products can be a successful marketing tactic for the healthcare sector. (World Health Organization, 2007)

1.12 Quality control parameters of solid dosage form

The most common form of pharmaceutical dosage among physicians, patients, and healthcare providers is tablets. Tablets increase patient compliance. The physiochemical parameters of these combination tablets were examined using the normal approach for tablet weight uniformity, thickness, hardness, friability, disintegration, dissolution, and potency testing. Generally (Palemo et al., 2001). There are two types of tests: Compendial tests & 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 (Dasari & Nadendla, 2017).

1.12.1 Weight variation

The tablets' consistency is checked using a weight variation test. Some tablets make a concerted effort to keep it, while others are suitably uniformed. Tablet weights might vary from batch to batch for a number of reasons. Variations in tablet weight might be brought on by,

Distribution at Hoover was the cause of the vibration. When smaller granules are compressed, the consolidation process causes the larger granules to surface first. As a result, a uniform granule size needs to be employed. Therefore, before beginning the compression process, it would be prudent to evaluate the particle size distribution. The granule flow should be poor or non-free-flowing. If there is an abnormal particle distribution due to a variable specific gravity, this leads the results in a poor flow. If there is an uneven distribution of particle sizes. A moderate quantity of granules and particles is ideal. Granules with a large particle diameter cause an unequal weight distribution in the tablet, while granules with an excessively small particle diameter cause an uneven flow time. If the glidant or lubricant is not uniformly combined or is less that may lead to poor flow. Adequate qualities of flow If there be any

incorrect die cavity adjustments (Roberts et al., 1969).

1.12.2 Hardness test

A hardness test is performed to see if the pressure in the tableting machine has to be changed. Hardness must be preserved to withstand mechanical shocks during production, packaging, and shipping. Hardness testers come in a variety of forms, such as the Erweka, Pfizer, Strong-Cobb, Monsanto, and Schlesinger testers. Hardness affects the way things decompose. Therefore, an extremely solid pill will not be able to break down in the time provided. The tablet won't withstand handling during additional processing, such as coating or packing, if it is very soft. The hardness level measurement instrument allowed for readings between 8 and 12 kg. Generally speaking, tablet hardness affects how well medications dissolve and release, and it may also affect bioavailability. Factor influencing the tablet's hardness, Compressive force and tablet compression. Binder quantity; the more binder, the harder. The granulation technique used to prepare the tablet (slugging approach yields the optimum hardness; wet method produces higher hardness than dry method) (Dasari, & Nadendla, 2017).

1.12.3 Friability test

Tablet hardness is closely linked to the friability test, which evaluates the tablet's resistance to abrasion during handling, packing, and shipping. The value is represented as a percentage. No broken or fractured tablets are picked up during the friability test, and a weight loss of no more than 1% of the tested tablets' weight is deemed generally acceptable. (Dasari & Nadendla, 2017).

1.12.4 Disintegration

The disintegration of the tablets indicates their quality. The disintegration test is used to

determine how long it takes for a solid oral dose form, such as a pill or capsule, to completely dissolve. Examining the disintegration time is one method of assessing quality. These 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 (Lachman & Kanig, 1976).

1.12.5 Dissolution test

Dissolution testing is used to create drug dosage forms and to establish production process quality control standards. The in-vitro disintegration test is a crucial test that must be correlated with in-vivo clinical research and may require the development of specific techniques. Dissolution testing in vitro is used to assess consistency between batches, spot production faults, and target important manufacturing parameters such coating parameters, granulation process, mixing effects, binder effects, and excipient role in different dosage forms (Lachman & Kanig, 1976). Furthermore, 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 (Cardot, & Alric, 2007).Moreover, Factor impacting the tablet's dissolution can be of many formulation-related factors can directly affect how quickly the active ingredient in a medication dissolve. Now, we may use this information to obtain customized drug dissolving profiles when these parameters have been well characterized.

Excipients and additives: Most solid dosage forms include several excipients for various purposes in addition to the active ingredient in the formulation. Adding various adjuncts to a pure medication can significantly alter its rate of dissolution. These adjuncts include diluents, binders, lubricants, granulating agents, disintegrants, and so on.

The size of the particle: smaller particles in tablets will dissolve and absorb more easily. This probably has to do with the procedures used to make tablets, which include mixing the drug with diluents that are usually hydrophilic and then granulating the combination to create a surface that is more hydrophilic, even for the drug particles that were initially hydrophobic.

Granulating agent and binder: The binder and granulating agent used in tablet formulation and other solid dosage forms can have a major impact on the medication's ability to dissolve from the dosage form

Disintegrating Agents: Several studies have been published in the literature that demonstrate how various disintegrating agents impact the rate at which tablets dissolve. It is crucial to keep in mind that the kind and amount of disintegrating agent utilized in the formulation has a significant impact on the overall rate of dissolution of the dosage form.

Lubricants: The primary lubricant type commonly utilized in the creation of solid dosage forms is hydrophobic substances. Thus, the pace of disintegration can be affected by the type, quality, and quantity of lubricant utilized.

Surfactant: Drugs that are almost insoluble in aqueous solutions (<0.01%) are becoming more and more appealing from a therapeutic perspective due to problems with their bioavailability (Ghayas & Baig, 2013).

The significance of the study

Now a days Asthma, Allergic Rhinitis and EIB has become an alarming problem in our own country due to increase of pollution. 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, Asthma, Allergic rhinitis 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. 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. In terms of use, Montelukast 10mg is one of the popular drugs to deal with Asthma, Allergic rhinitis in the current market. Because of its low risk profile, most of the pharmaceutical companies are marketed this drug under their general 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 Montelukast 10mg

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 Montelukast (MLT): In Bangladesh several brands are available of MLT. Among them 5 brands were selected randomly and collected them from the different medicine shop in Dhaka. This tablet was randomly coded by MLT-1, MLT-2, MLT-3, MLT-4, MLT-4, MLT-5, MLT-6, MLT-7, MLT-8, OLM-9, MLT-10, 10 Mg of MLT was analyzed during the study.

Table 2.1: Different brands along with their manufacturer names

Tablet	Pharmaceutical name
Montelukast (Monas 10 mg	ACME Pharmaceuticals
Montelukast (Aeron 10 mg)	Healthcare Pharmaceuticals
Montelukast (Trilock 10 mg)	Opsonin Pharmaceuticals
Montelukast (Montex 10 mg)	Ibn Sina Pharmaceuticals
Montelukast (Monalast 10 mg)	Ziska 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 a crucial consideration when discussing a typical pharmaceutical product, and it is closely related to content consistency when creating a solid dosage form. A significant weight variance is indicative of good content consistency, whereas a modest weight variation is necessary to provide good content uniformity. A number of factors influence the variation in tablet weight: An uneven die fill is a result of poor granulation flow properties.

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.

Lower punch length dissimilarities can be result different size (Roberts et al., 1969).

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 (Mulloy, B., Heath, A., Shriver, Z., Jameison, F., Al Hakim, A., Morris, T. S., & Szajek, A. Y. (2014). USP compendial methods for analysis of heparin: chromatographic determination of molecular weight distributions for heparin sodium.)

2.2.3 Calculation: Percentage of weight variation was calculated by following formula:

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

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

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

(*USP Weight Variation_25_feb_2011.Pdf*, n.d.)

2.3 Hardness test:

When discussing a tablet's mechanical stability during packaging and shipping, tablet hardness is an essential metric. Therefore, the load required to crush the tablet on its edge is the conventional definition. Tablet density and porosity are also influenced by tablet hardness. A tablet's friability and disintegration time may also be impacted by this attribute. It also impacts bioavailability, solubility, and release (Dasari & Nadendla, 2017).

2.3.1 Method:

The hardness tester's slide scale was set to zero. Between two jaws, one tablet was positioned vertically. A screw thread and spring were used to apply force until the tablet broke. The sliding scale was used to get the reading in kilograms (Dasari & Nadendla, 2017).

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: Oral tablets typically have a hardness of 4 to 8 or 10 kg. Since hypodermic and chewable pills are softer than regular ones, their hardness is 3 kg. Some sustain-released pills are considerably tougher and have a hardness of 10–20 kg (Goodhart & Ninger, 1973)

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.)

Condition is Distilled water and 37º C temperatures to maintain body temperature (Gousous & Langguth, 2015).

2.4.1 Condition: Distilled water and 37º C temperatures to maintain body temperature (Disintegration Test BP 2019.Pdf, n.d.)

2.4.2 Method

Before the test the disintegration tester was correctly assembled.

Then following the specification, the time and temperature was set.

The 1000 ml beaker then filled with 600 ml of distilled water.

The liquid maintained at 37º C temperature.

One tablet was placed in each of the 6 tubes.

The machine started according to the listed period.

the entire tablet was disintegrated within the listed time (Gousous & Langguth,2015).

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 (Schmid & Löbenberg,2010).

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:

Level	Sample tested	Acceptance criteria
S1	6	Each value is not less than Q + 5%
S2	6	Average value of the 12 dosage units (S1 + S2) is equal to or greater than Q and no unit is less than Q-15%
S3	12	Average value of 24 dosage units (S1 + S2 + S3) is equal to or greater than Q; not more than 2 units are less than Q - 15%; no unit is less than Q - 25%.

(*Dissolution Testers – USP Guidelines - Total Laboratory Services - ERWEKA UK - Dissolution Testers*, 2024)

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 Montelukast (10mg) tablets are given below.

Table 3.1: Weight variation of (Monas 10 mg)

Number of tablets	Weight of individual tablets (g)	Average weight (g)	Individual weight Variation (%)	Highest weight variation (%)	Lowest Weight variation (%)
3	0.20		5.820		
4	0.17		-10.052		
5	0.19		0.529		
6	0.19		0.529	5.820	-10.052
7	0.18		-4.761		
8	0.19		0.529		
9	0.19		0.529		
10	0.19		0.529		

Standard deviation of individual weight is 0.008755.

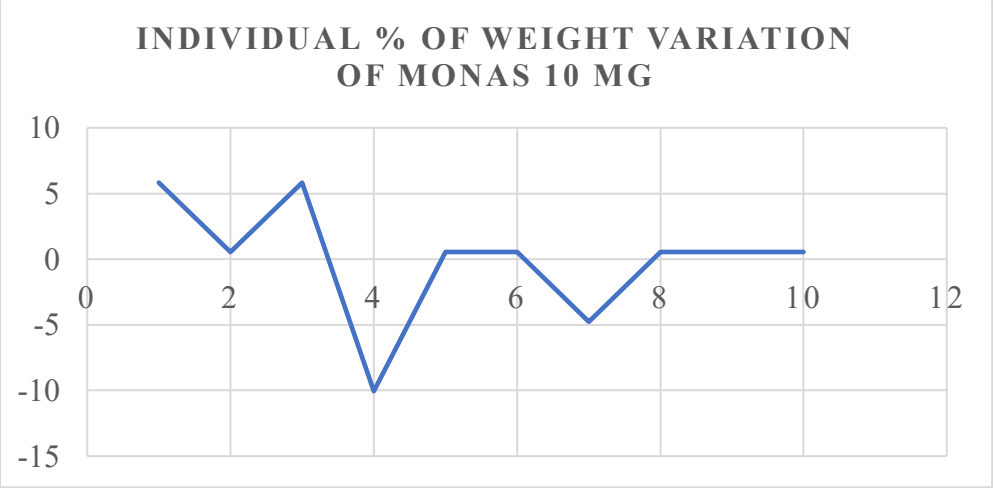

Figure 3.1: Individual weight variation percentage of (Monas 10 mg).

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.

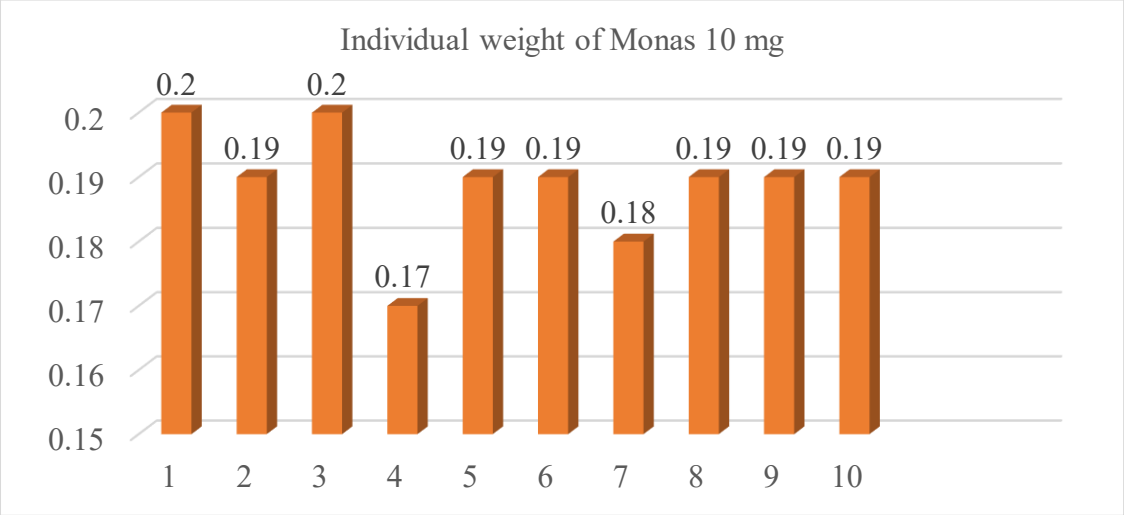

Figure 3.2: Weight of individual tablet (Monas 10 mg).

The X-axis indicate the numbers of tablet used for test and the Y- axis indicate weight variation of individual tablet. This figure shows the individual weight of 10 tablets of Monas 10 mg which consists of different individual weight.

Table 3.2: Weight variation of (Aeron 10 mg)

Number of tablets	Weight of individual tablets (g)	Average weight (g)	Individual weight Variation (%)	Highest weight variation (%)	Lowest Weight variation (%)
1	0.25	0.245	2.040	2.040	-2.04
2	0.25		2.040		
3	0.24		-2.040		
4	0.25		2.04		
5	0.24		-2.04		
6	0.24		-2.04		
7	0.24		-2.04		
8	0.24		-2.04		
9	0.24		-2.04		
10	0.26		-2.04		

Standard deviation of individual weight is 0.007071.

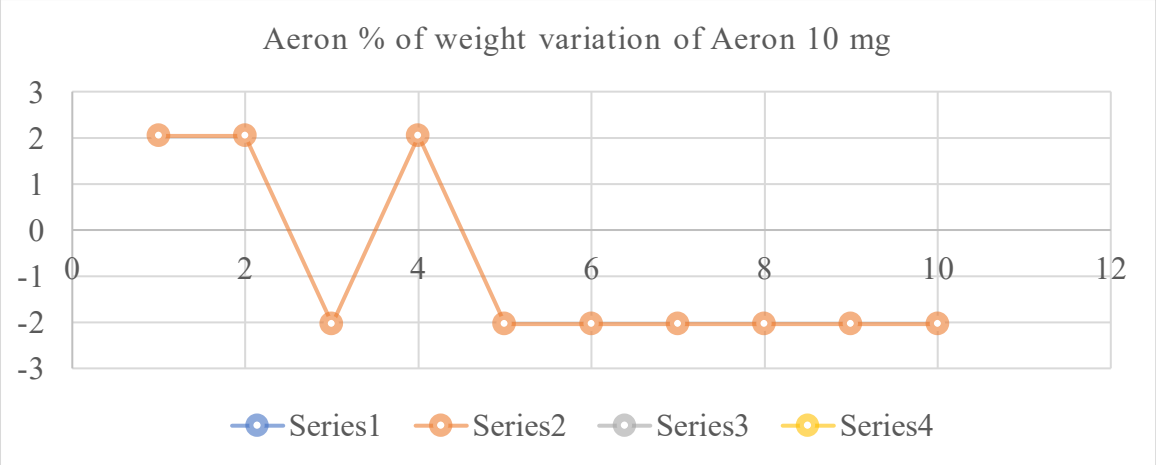

Figure 3.3: Individual weight variation percentage of (Aeron 10 mg).

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. This figure shows the individual percentage of weight of 10 tablets of Aeron 10 mg which consists of different individual % of weight.

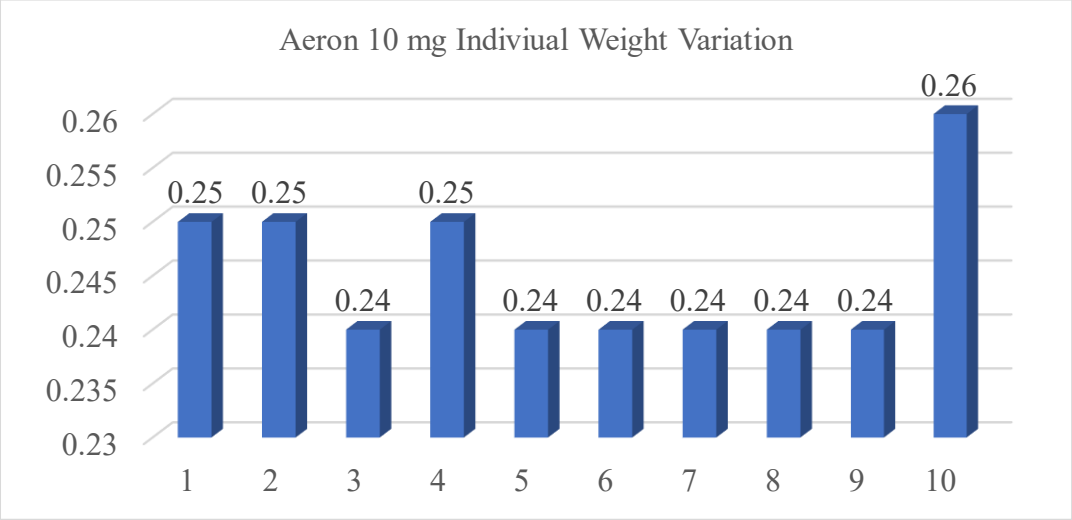

Figure 3.4: Individual weight for (Aeron 10 mg).

The X-axis indicate the numbers of tablet used for test and the Y-axis indicate weight variation of individual tablet. This figure shows the weight of 10 tablets of Aeron 10 mg which consists of different individual weight.

Table 3.3: Weight variation of (Trilock 10 mg).

Number of tablets	Weight of individual tablets (g)	Weight of individual tablets (g)	Individual weight Variation (%)	Highest weight variation (%)	Lowest Weight variation (%)
1	0.18	0.177	1.694	1.694	-15.254
2	0.18		1.694		
3	0.18		1.694		
4	0.18		1.694		
5	0.18		1.694		
6	0.15		-15.254		
7	0.18		1.694		
8	0.18		1.694		
9	0.18		1.694		
10	0.18		1.694		

Standard deviation of individual weight is 0.009486.

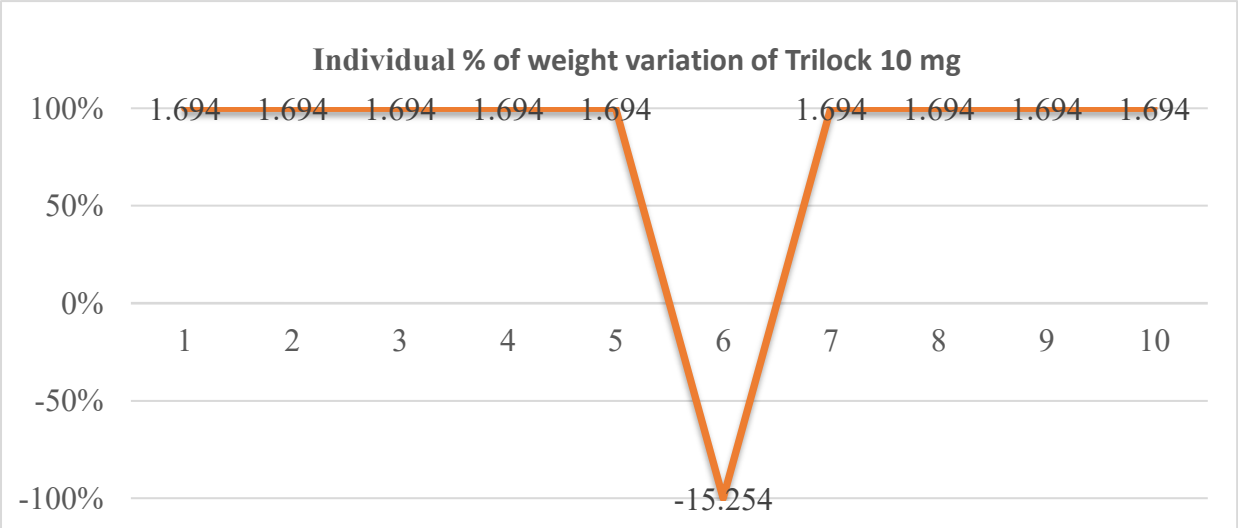

Figure 3.5: Individual weight variation percentage of (Trilock 10 mg).

In the graph X-axis represent the tablet count for the test and Y-axis shows the individual weight variation percentage of tablets. This figure shows the individual percentage of weight of 10 tablets of Trilock 10 mg which consists of different individual % of weight.

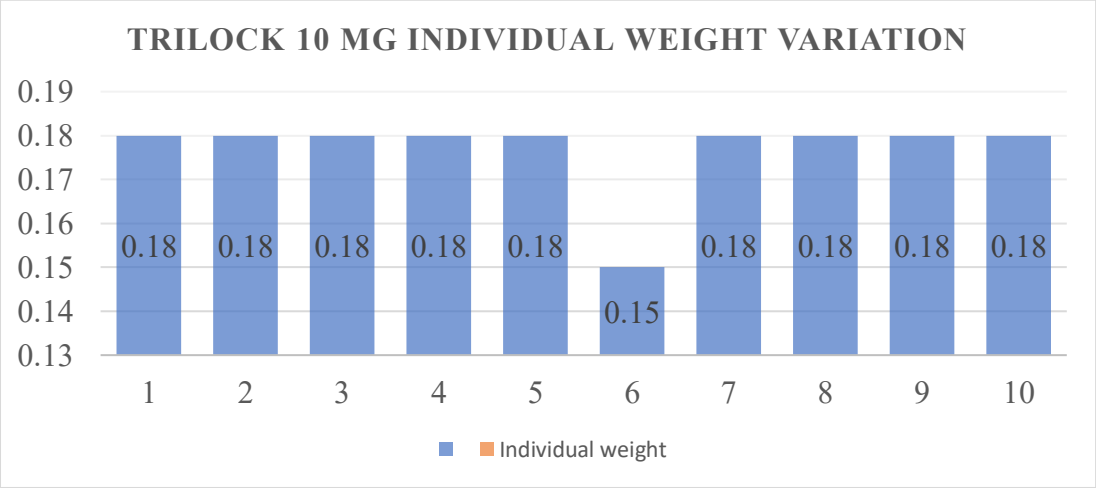

Figure 3.6: Individual weight for (Trilock 10 mg).

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. This figure shows the individual weight of 10 tablets of Trilock 10 mg which consists of different individual weight.

Table 3.4: Weight variation of (Montex 10 mg).

Number of tablets	Weight of individual tablets (g)	Weight of individual tablets (g)	Individual weight Variation (%)	Highest weight variation (%)	Lowest Weight variation (%)
1	0.29	0.288	0.694	4.166	-2.777
2	0.29		0.694		
3	0.28		-2.777		
4	0.29		0.694		
5	0.29		0.694		
6	0.28		-2.777		
7	0.30		4.166		
8	0.28		-2.777		
9	0.29		0.694		
10	0.29		0.694		

Standard deviation of individual weight is 0.006324.

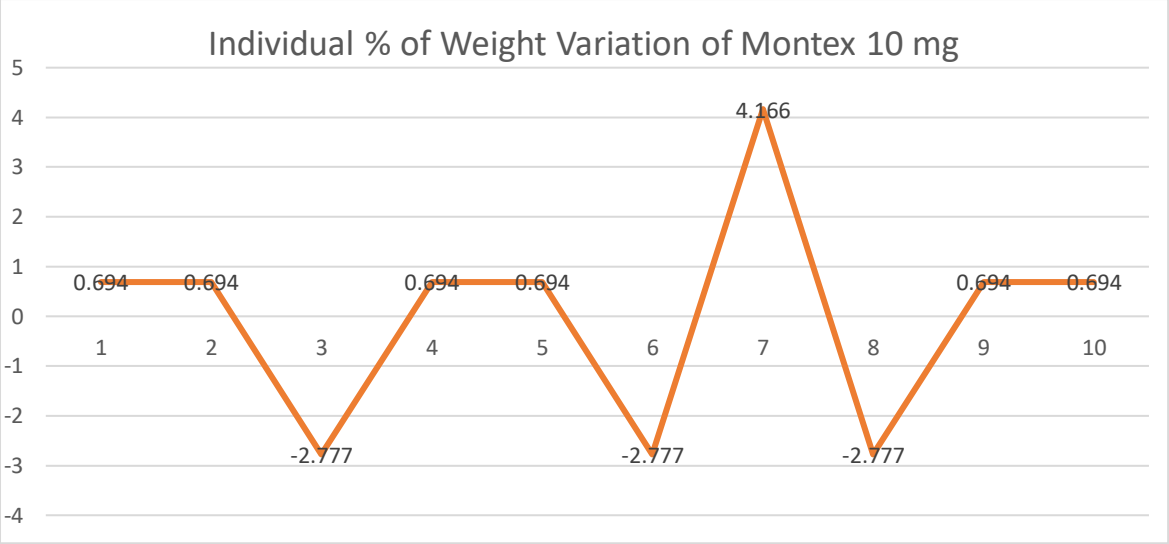

Figure 3.7: Individual (%) weight variation of (Montex 10 mg).

In the graph X-axis reflects counting of the tablets and Y-axis indicates individual weight variation percentage of the tablets. This figure shows the percentage of weight of Montex 10mg detected in market.

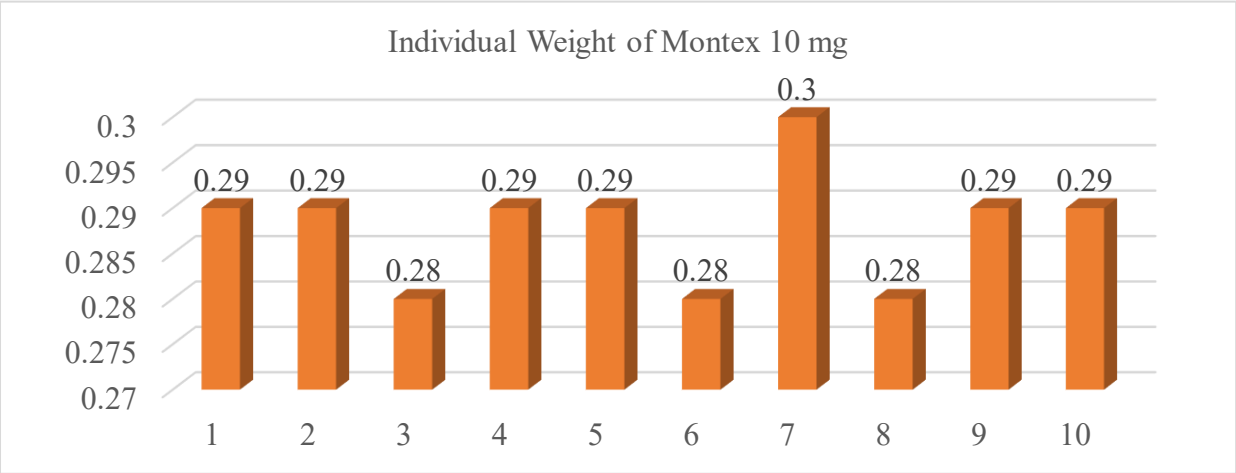

Figure 3.8: Individual weight variation for (Montex 10 mg).

The X-axis indicate same as the previous graph. Y- axis the shows single weight variation of tablets. This figure shows the individual weight of 10 tablets of Montex 10 mg which have different individual weight.

Table 3.5: Weight variation of Monalast 10 mg.

Number of tablets	Weight of individual tablets (g)	Weight of individual tablets (g)	Individual weight Variation (%)	Highest weight variation (%)	Lowest Weight variation (%)
1	0.17	0.233	0.705	0.764	0.647
2	0.17		0.705		
3	0.18		0.647		
4	0.17		0.705		
5	0.17		0.705		
6	0.17		0.647		
7	0.16		0.764		
8	0.17		0.647		
9	0.17		0.705		
10	0.17		0.705		

Standard deviation of individual weight is 0.004690.

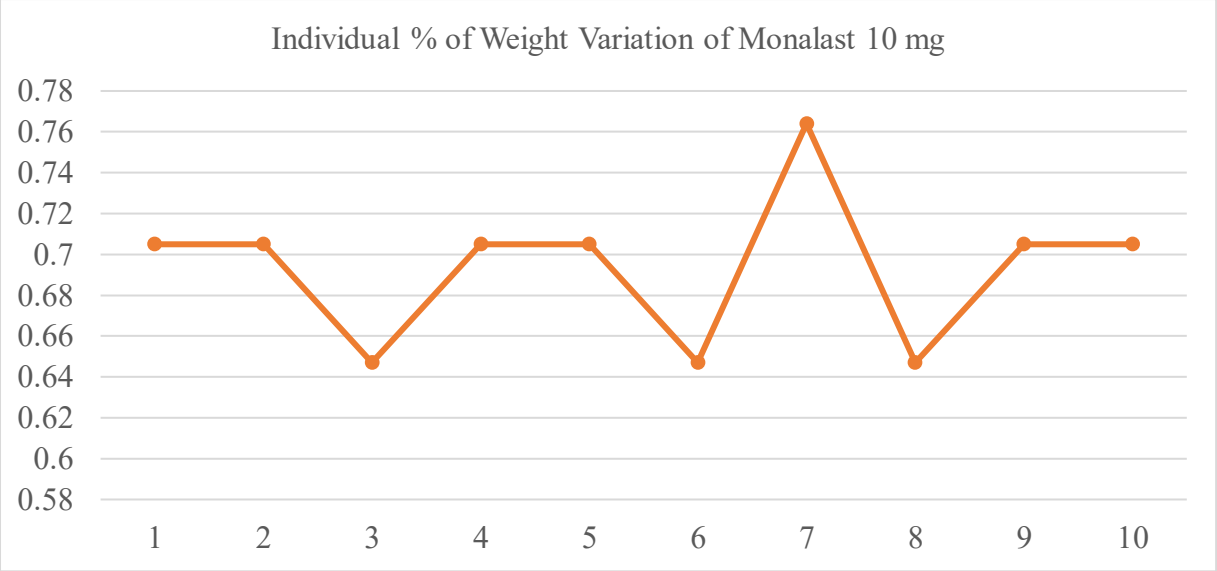

Figure 3.9: Individual (%) weight variation of (Monalast 10 mg).

In the graph X-axis shows counting of the tablets and Y- axis reflect weight variation percentage of marketed product.

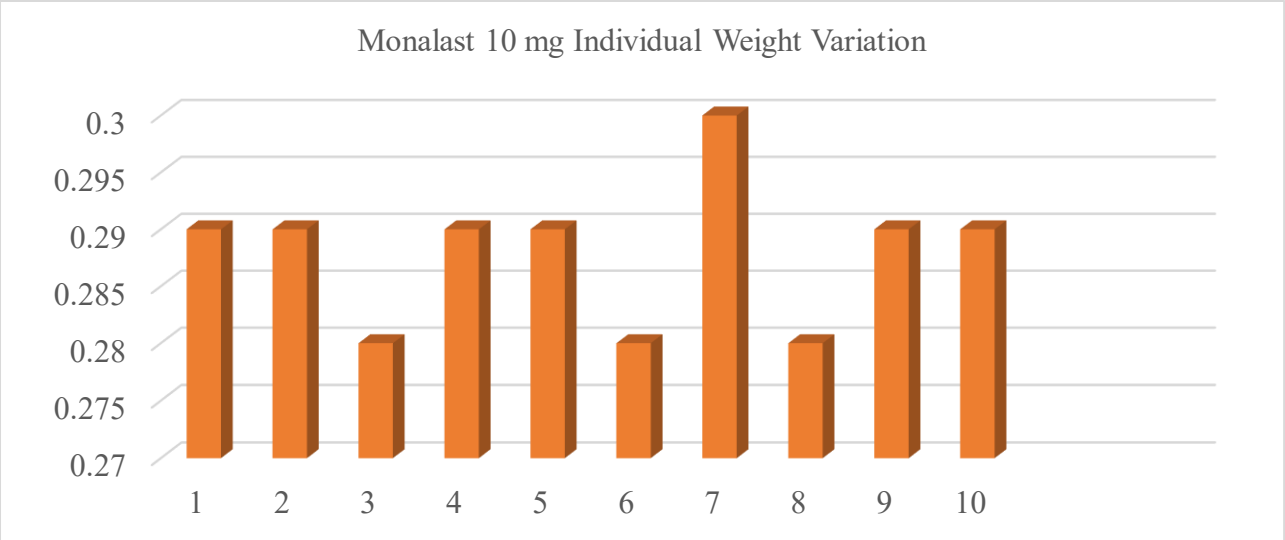

Figure 3.10: Individual weight variation for (Monalast 10 mg).

The X-axis indicate same as previous graph. Y-axis shows single weight variation of tablets. This figure shows the individual weight of 10 tablets of Monalast 10 mg and all don't have same weight.

3.2 Hardness test

Hardness test of 5 brands of Montelukast 10 mg tablets are given below:

Table 3.6: Hardness test of Monas 10 mg.

Number of tablets	Hardness (Kg)	Average (kg)
1	7.45	5.541
2	3.21	
3	6.30	
4	5.39	
5	7.03	
6	4.35	
7	7.47	
8	6.50	
9	4.48	
10	3.23	

Standard deviation 1.156806.

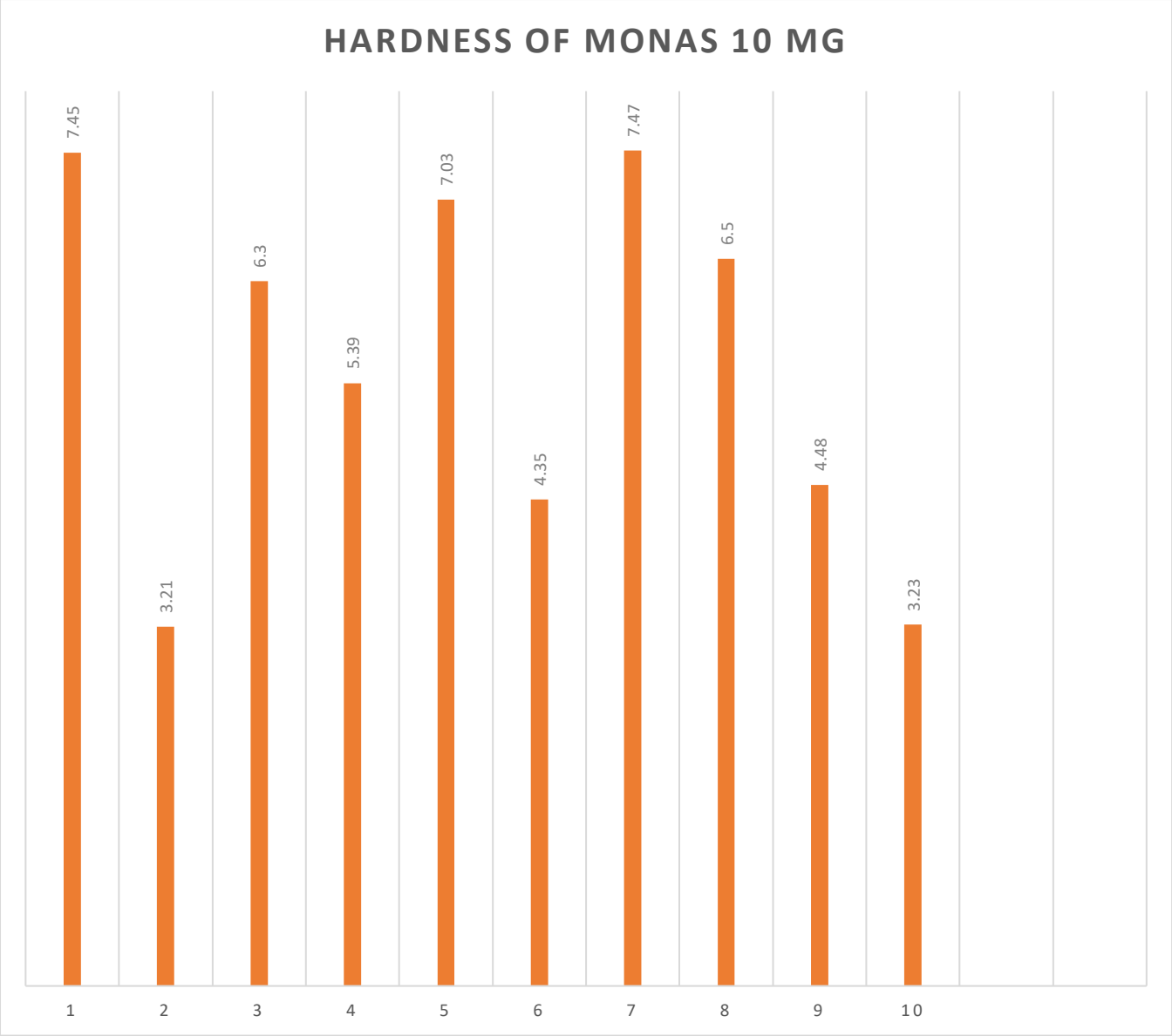

Figure 3.11: Hardness of (Monas 10 mg).

X-axis represent numbers of tablet used in experiment. Y- axis shows the hardness of the tablets. This figure shows the hardness of 10 tablets of Monas 10 mg which were marketed.

Table 3.7: Hardness test of Aeron 10 mg

Number of tablets	Hardness (Kg)	Average (kg)
1	10.16	9.126
2	9.97	
3	10.13	
4	9.25	
5	9.10	
6	8.94	
7	7.55	
8	8.92	
9	8.78	
10	8.46	

Standard deviation is 0.564154.

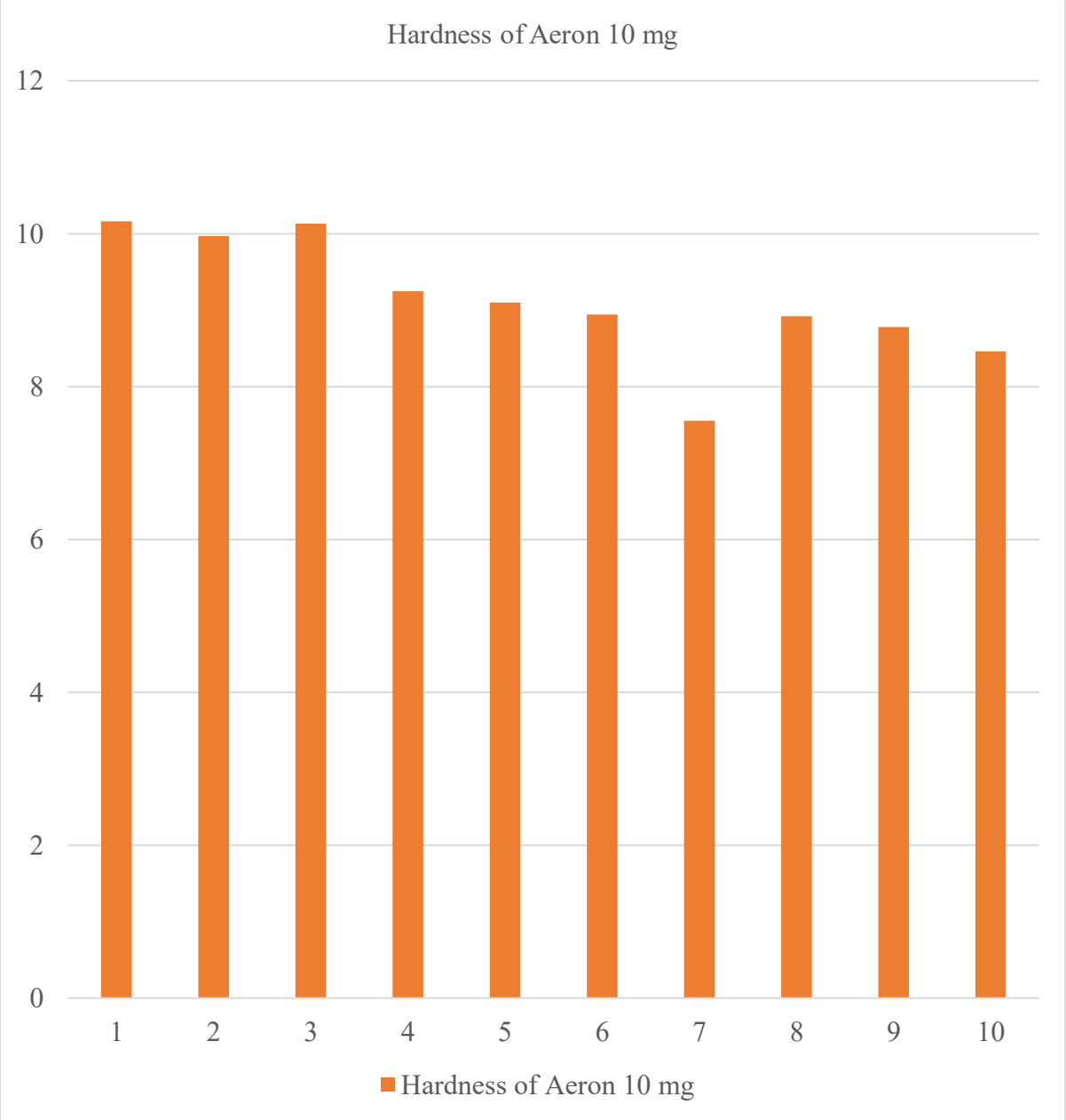

Figure 3.12: Hardness of (Aeron 10 mg).

X-axis indicates numbers of tablet used in test. Y- axis shows about hardness of the tablets.

This figure shows the hardness of 10 tablets of Aeron 10 mg which were marketed.

Table 3.8: Hardness test of Trilock 10 mg.

Number of tablets	Hardness (Kg)	Average (kg)
1	6.93	6.797
2	7.12	
3	6.17	
4	6.66	
5	6.71	
6	6.76	
7	7.37	
8	6.65	
9	7.15	
10	6.45	

Standard deviation is 0.968359.

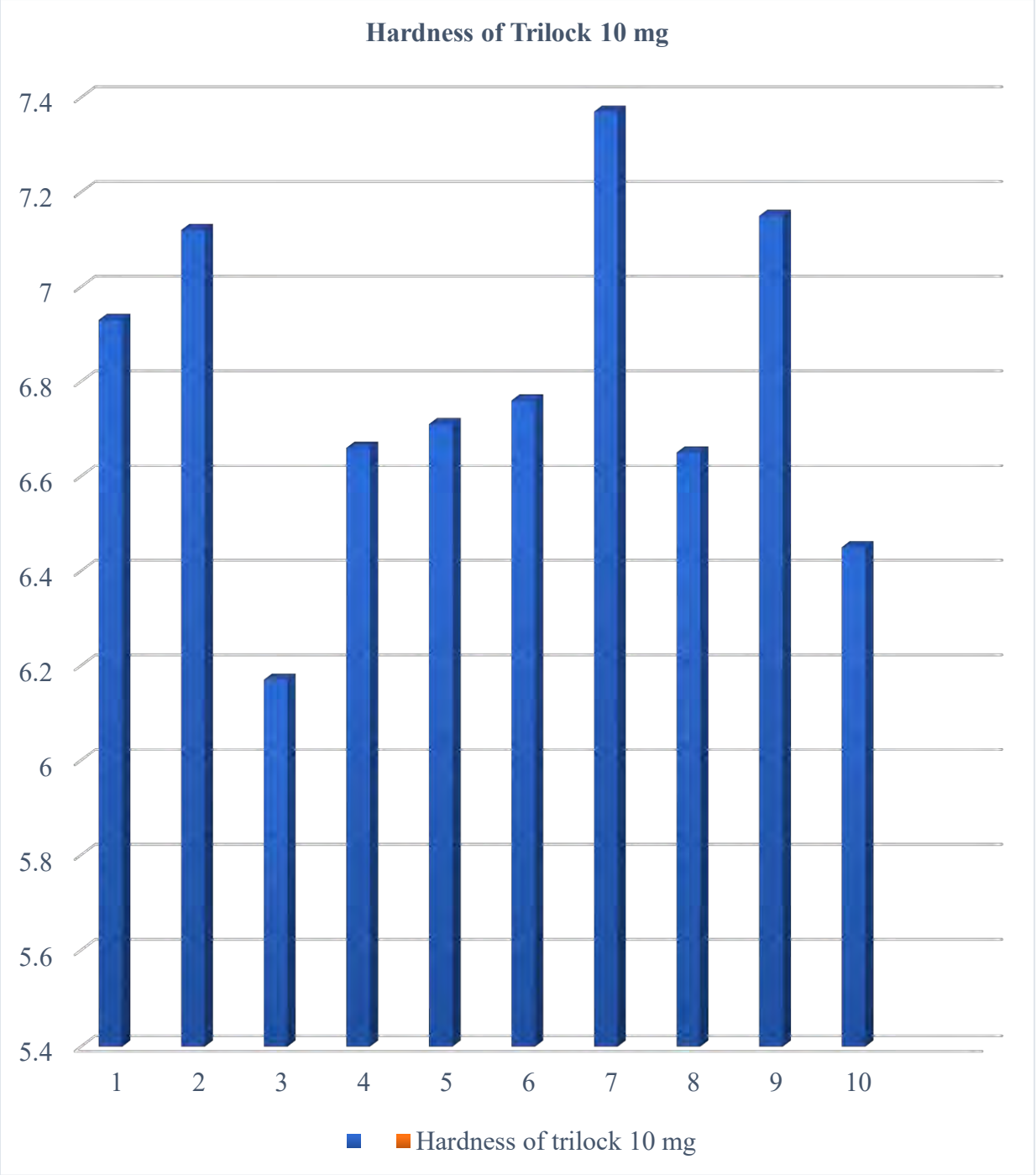

Figure 3.13: Hardness of (Trilock 10 mg) X-axis tells numbers of tablet used in test. Y-axis shows about hardness of the tablets. This figure shows the hardness of 10 tablets of Trilock 10 mg which were marketed.

Table 3.9: Hardness test of Montex 10 mg

Number of tablets	Hardness (Kg)	Average (kg)
1	12.13	10.52
2	10.83	
3	7.04	
4	9.97	
5	9.83	
6	9.62	
7	10.54	
8	11.35	
9	11.72	
10	12.17	

Standard deviation is 0.986342

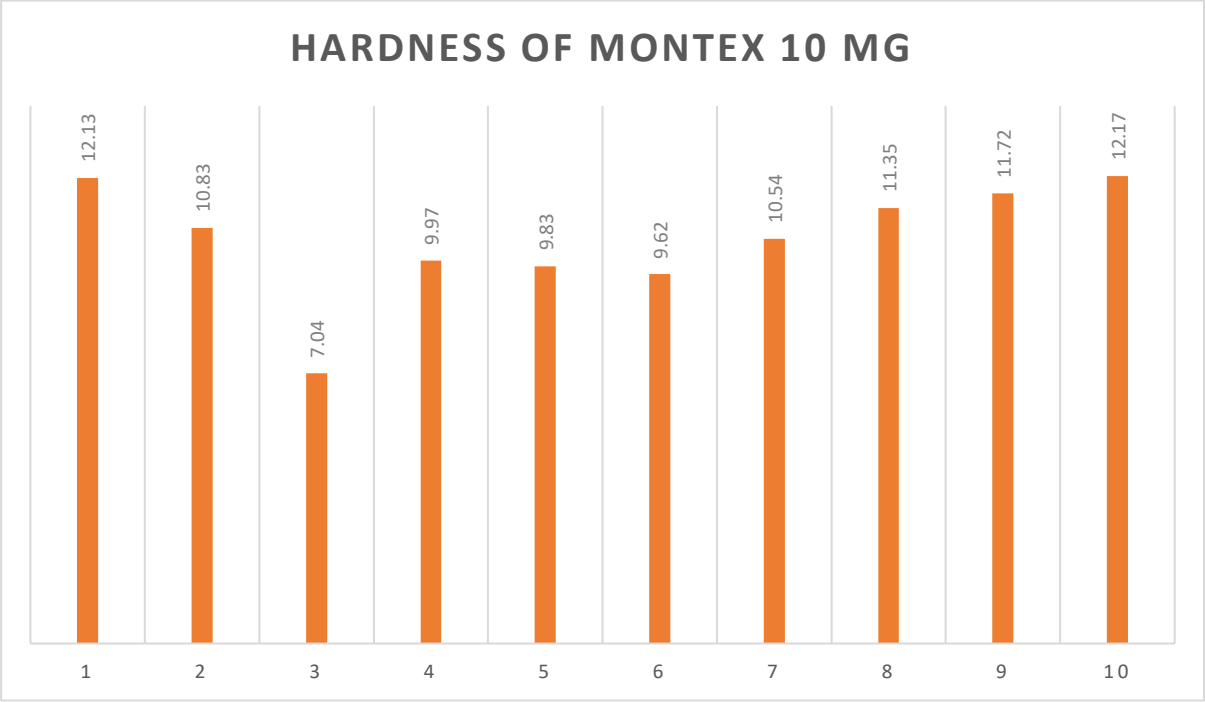

Figure 3.14: Hardness of (Montex 10 mg)

X-axis tells numbers of tablet used in test. Y-axis shows about hardness of the tablets. This figure shows the hardness of 10 tablets of Montex 10 mg which were marketed.

Table 3.10: Hardness test of Monalast 10 mg.

Number of tablets	Hardness (Kg)	Average (kg)
1	8.9	7.443
2	7.94	
3	8.71	
4	8.26	
5	7.29	
6	5.26	
7	7.26	
8	9.26	
9	6.26	
10	5.29	

Standard deviation is 0.892079.

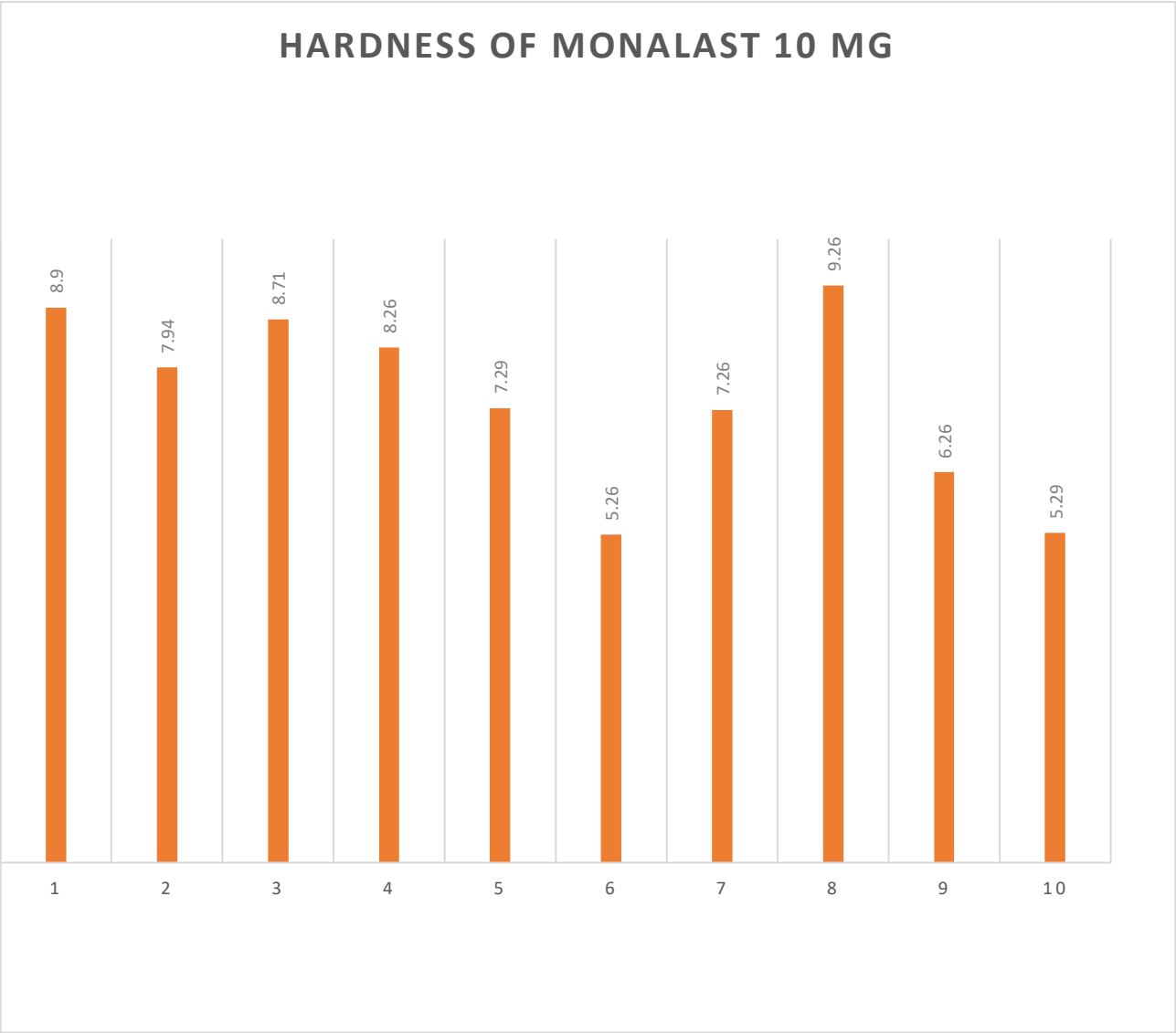

Figure 3.15: Hardness of (Monalast 10 mg) X-axis indicates numbers of tablet used in experiment. Y- axis shows about hardness of the tablets. This figure shows us the hardness of 10 tablets of Monalast 10 mg which were marketed.

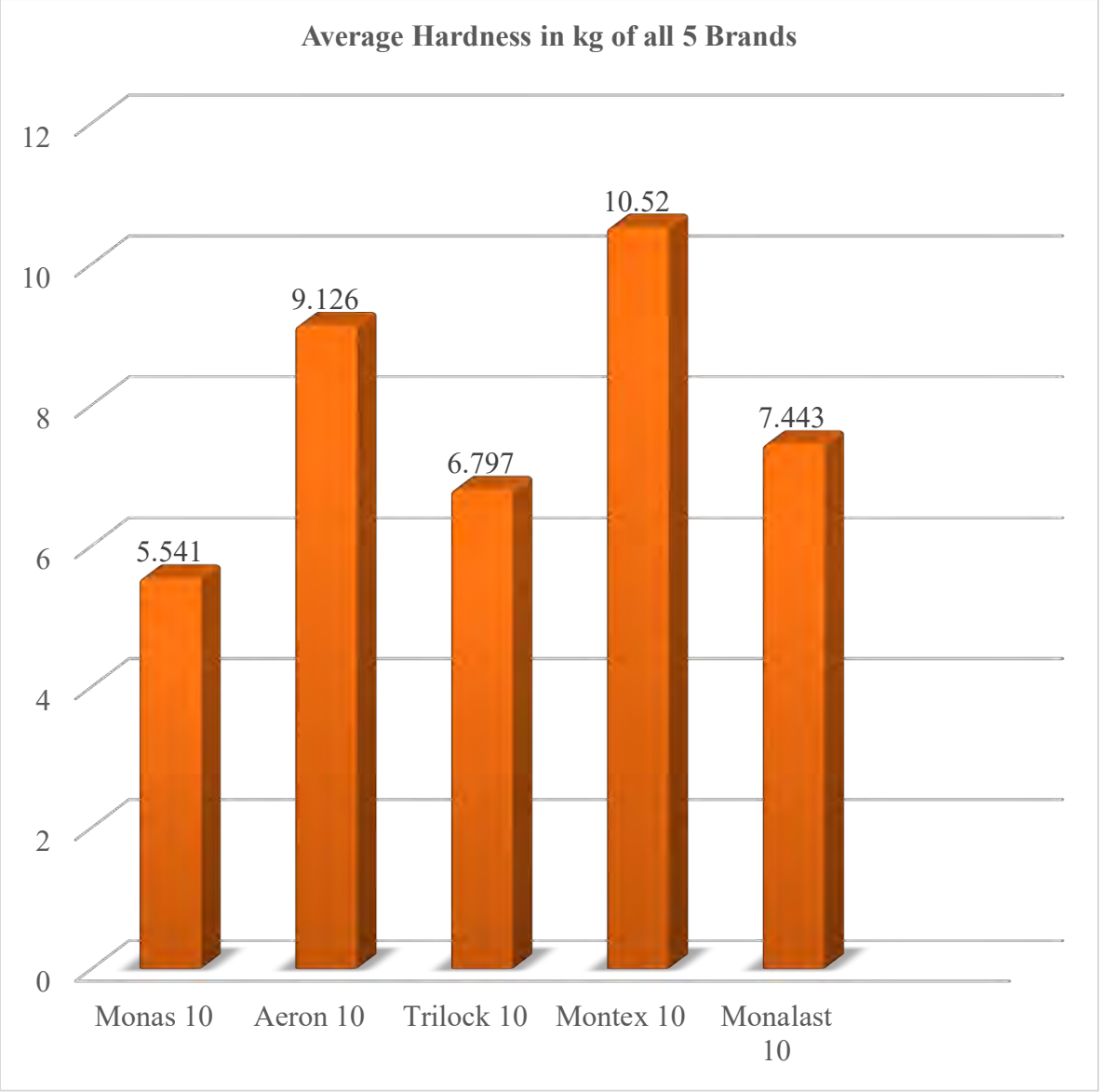

Figure 3.16: Average hardness of Montelukast 10 mg of different brands.

X- axis shows the brand and Y- axis shows the average hardness. This figure 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 10 tablets from each brand was given below:

Table 3.11: Friability test of different brands.

Brand name	Before test	After test
Monas 10 mg	1.94 g	1.94 g
Aeron 10 mg	2.49 g	2.48 g
Trilock 10 mg	1.85 g	1.85 g
Montex 10 mg	3.06 g	2.88 g
Monalast 10 mg	2.23 g	2.23 g
Mean	2.314	2.296

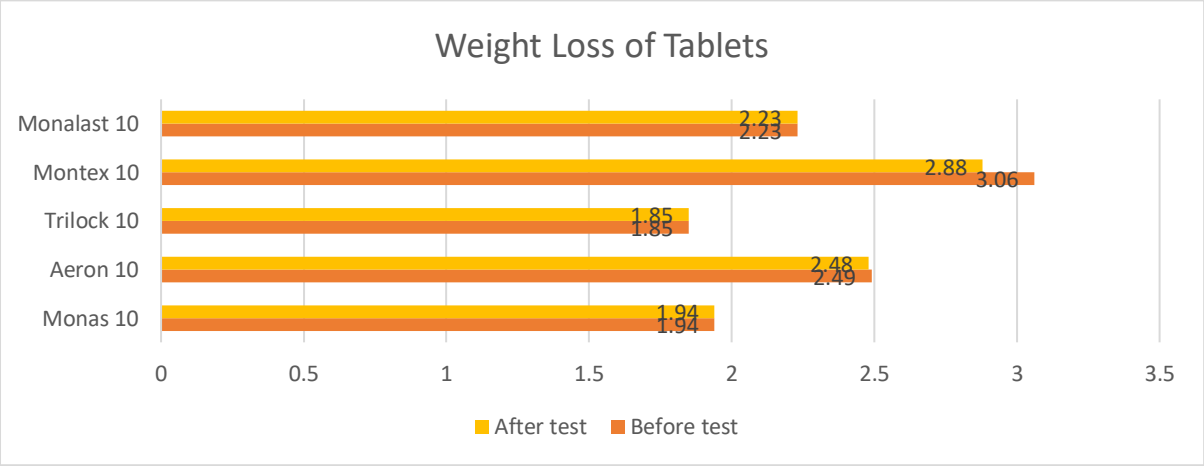

Figure 3.17: Weight loss tablets of different brand of Montelukast (10mg).

The graph shows weight loss of different brand of montelukast by comparing the initial weight and the final weight after test.

3.4 Disintegration test

Disintegration test of 5 brands of Montelukast 10mg tablets are given below:

Table 3.12: Disintegration test of different brands.

Brand Name	Disintegration time (minute)
Monas 10 mg	6 min. 05 sec.
Aeron 10 mg	2 min. 57 sec.
Trilock 10 mg	5 min. 58 sec.
Montex 10 mg	15 min. 00 sec.
Monalast 10 mg	2 min. 57 sec.

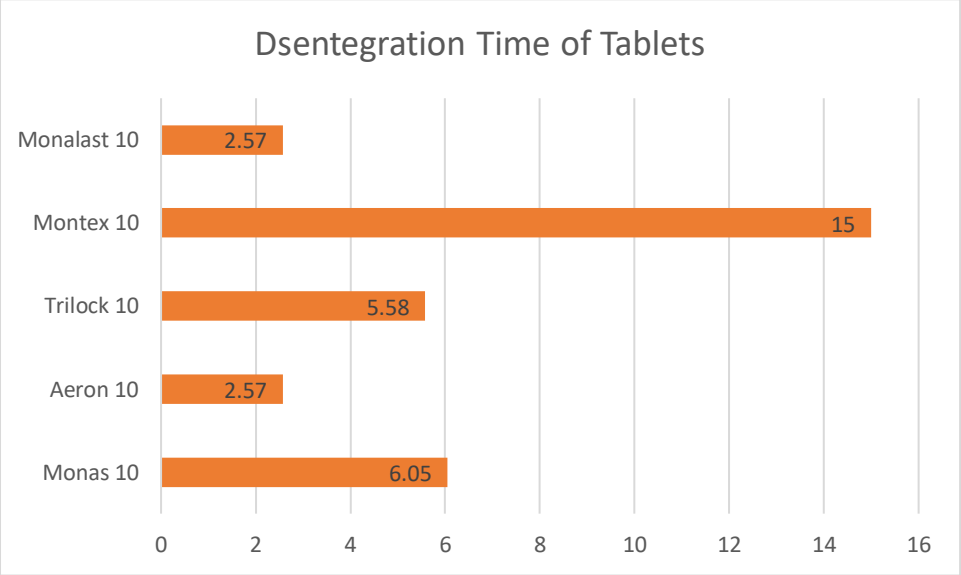

Figure 3.18: Disintegration time of different brands of Montelukast 10 mg.

This graph shows the disintegration time of all the 5 brands of Montelukast compared with the disintegration time of international standard of 15 minute.

3.5 Dissolution Test

Table 3.13: Dissolution test of (Monas 10 mg)

Time	T 1
5	0.016
10	0.019
15	0.025
20	0.029

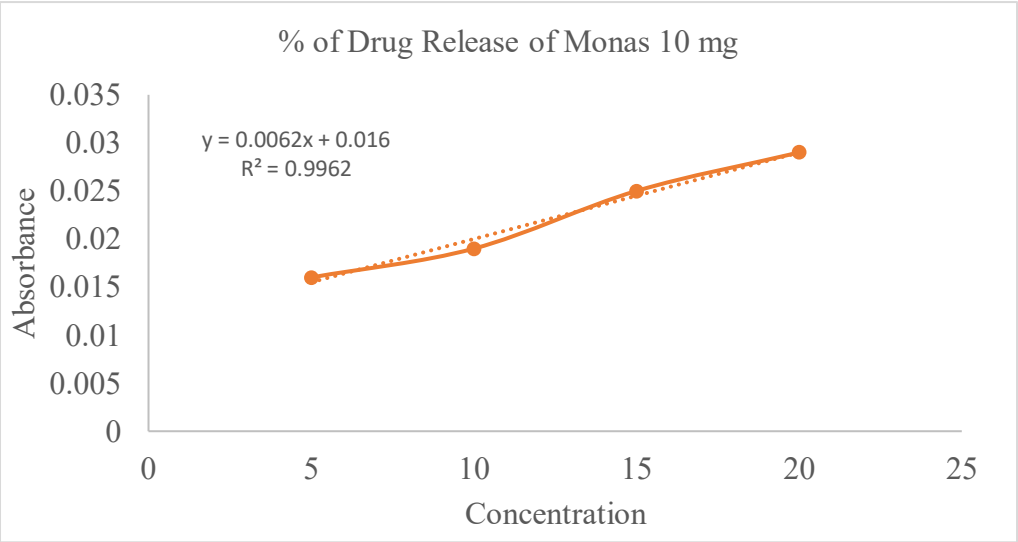

Figure 3.19: A: Drug release of Monas 10 mg.

X- axis shows the concentration and Y- axis shows absorbance and 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 and it almost shows a straight line.

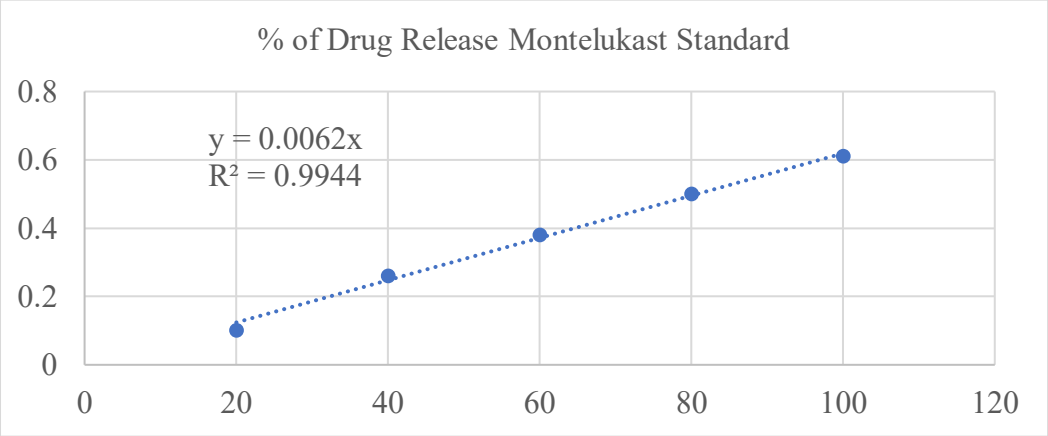

Figure 3.19: B: Drug release of Monas 10 mg. X- axis shows the concentration and Y- axis shows absorbance The graph shows drug release of the tablet on time and also indicate linier equation and r^2 value. These values identify the percentage of drug release similar to the standard.

Table 3.14: Dissolution profile of Aeron 10 mg.

Time	T1
5	0.015
10	0.017
15	0.020
20	0.024

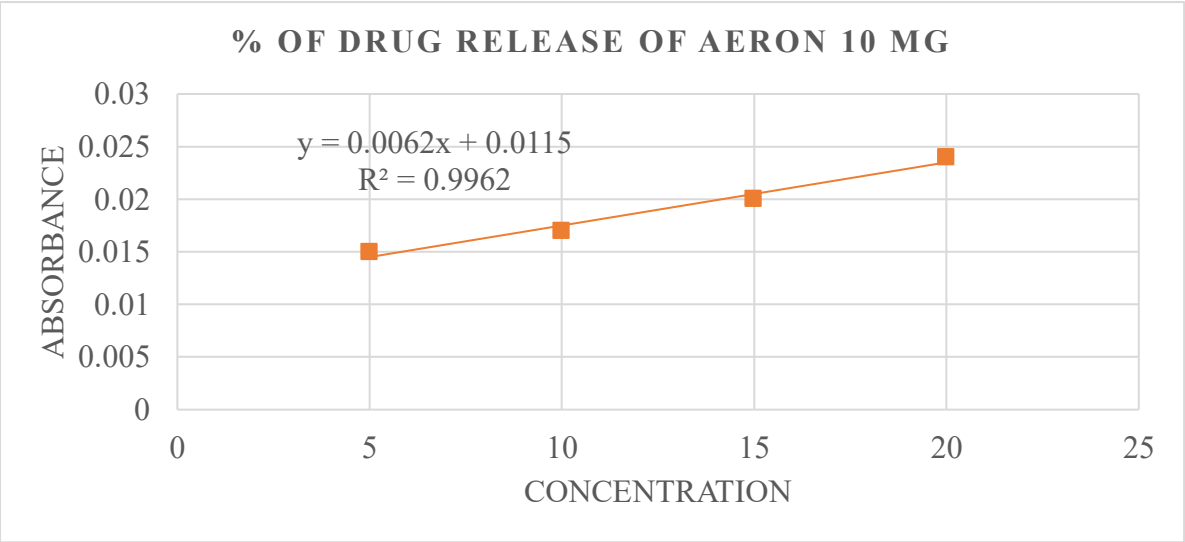

Figure 3.20: A: Drug release of Montelukast (Aeron 10 mg). X- shows the concentration and Y- axis shows the absorbance and the graph shows drug release of the tablet on time and also indicate linier equation and r^2 value. The tablet in graph shows almost close drug release compared towards standard and almost makes a straight line.

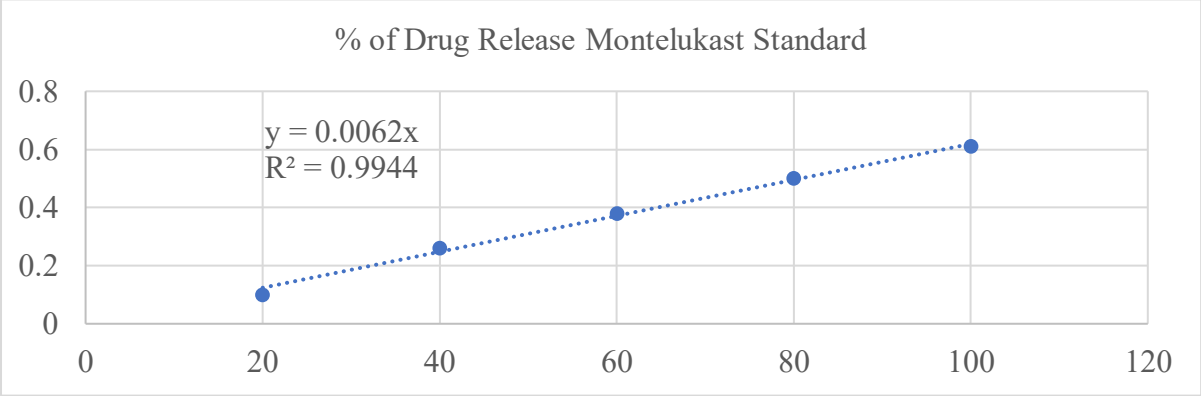

Figure 3.20: B: Drug release of Montelukast (Aeron 10 mg). X- axis shows the concentration and Y- axis shows the absorbance. The graph shows drug release of the tablet on time and also indicate linier equation and r^2 value. The tablet in graph shows almost close drug release as standard

Tablet 3.15: Dissolution test of Trilock 10mg

Time	T1
5	0.012
10	0.015
15	0.017
20	0.019

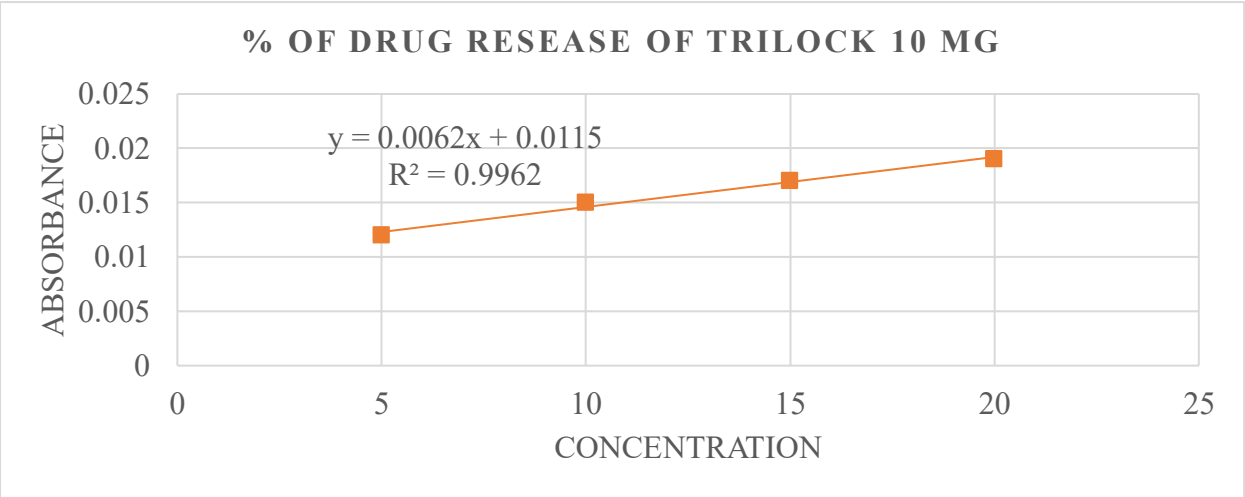

Figure 3.21: A: Drug release of Montelukast (Trilock 10 mg).

X- axis shows the concentration and the Y- axis shows the absorbance. 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 compared to standard and almost shows a straight line.

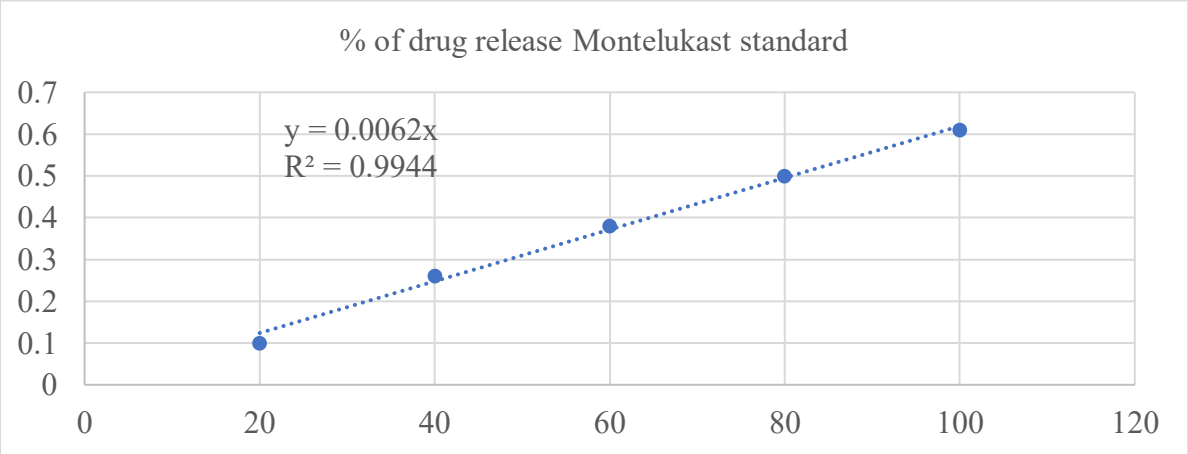

Figure 3.21: B: Drug release of Montelukast (Trilock 10 mg).

X- axis shows the concentration and Y- axis shows the absorbance.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 Montex 10 mg

Time	T1
5	0.012
10	0.016
15	0.018
20	0.020

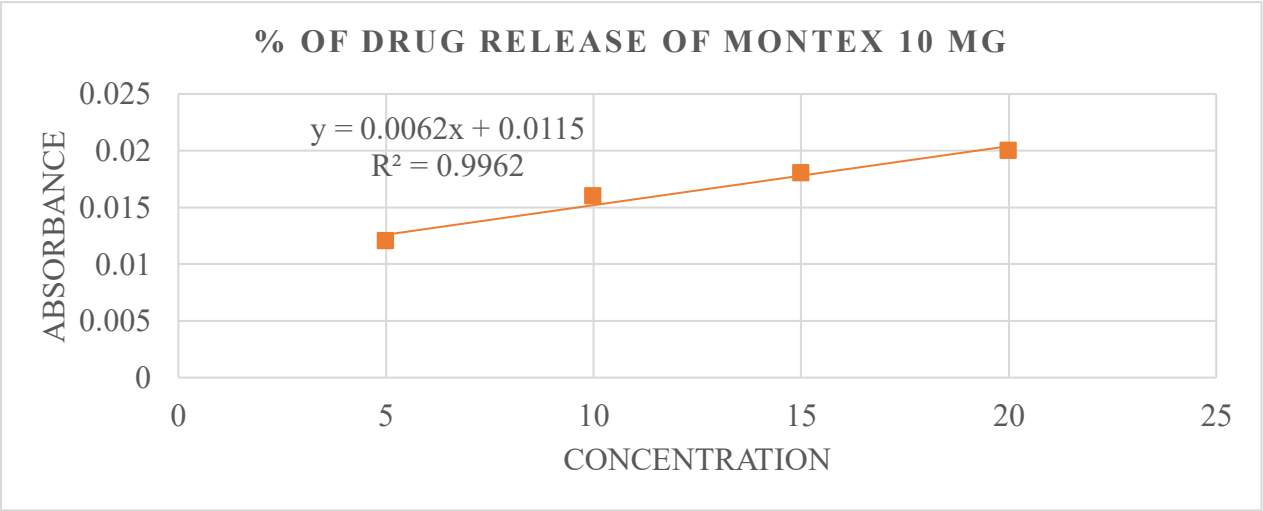

Figure 3.22: A: Drug release of Montelukast (Montex10 mg).

X- axis shows concentration and the Y- axis shows absorbance. The graph tells drug release profile of tablet on time and also indicate linier equation and r^2 value. Tested tablet indicates the result compared to standard and almost shows a straight line.

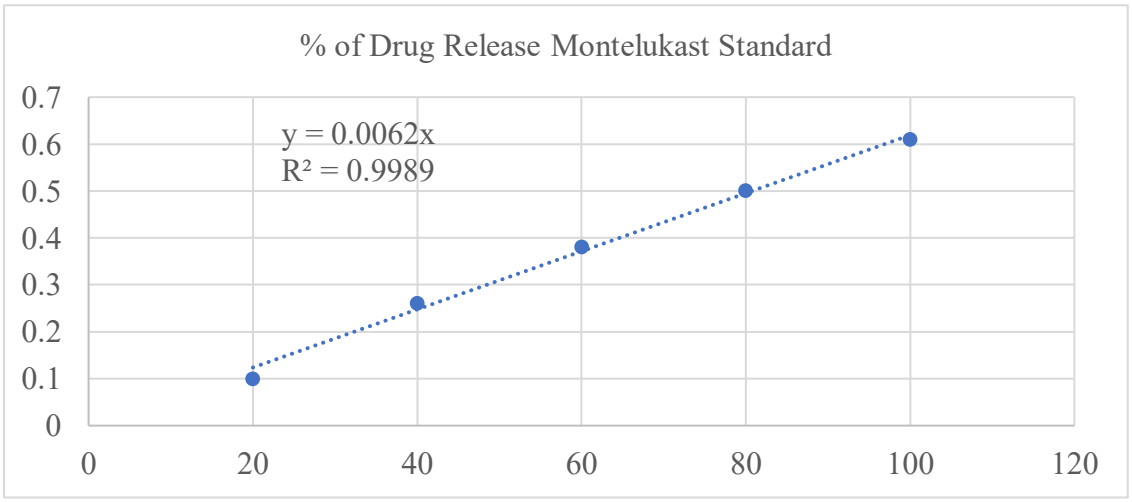

Figure 3.22: B: Drug release of Montelukast (Montex10 mg).

X-axis shows concentration and Y-axis shows absorbance 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 (Monalast 10 mg).

Time	T1
5	0.011
10	0.014
15	0.016
20	0.018

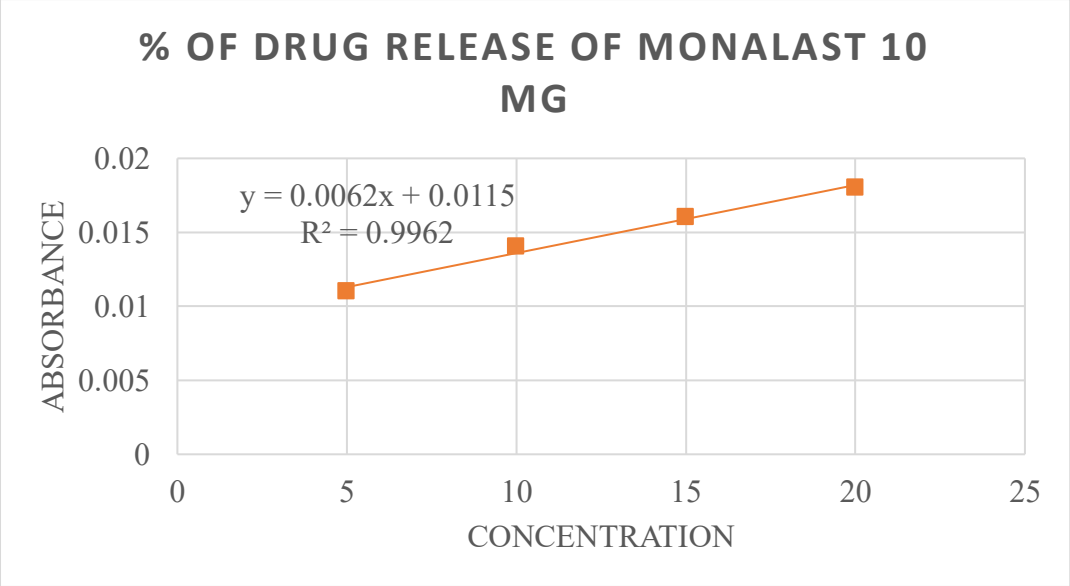

Figure 3.23: Drug release of Montelukast (Monalast 10 mg). X- axis shows concentration and Y-axis shows absorbance. The graph shows drug release profile of tablet on time and also indicate linier equation and r^2 value. Tested tablet tells the drug had less release of drug compare to the standard.

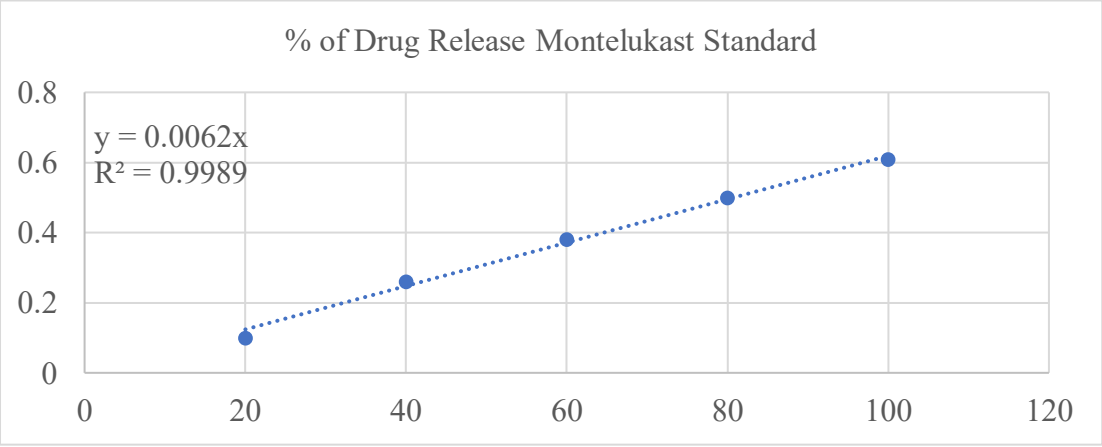

Figure 3.24: Drug release of Montelukast (standard)

X- axis shows the concentration and Y- axis shows the absorbance. The r^2value is close to one and the equation is a linier equation.

Chapter 4

Discussion

4.1 Weight variation

For individual weights, the % of weight variation of Monas 10 mg percentage difference is ranged to 0.529% to 5.820% and the standard deviation for individual weights is 0.008755. For Aeron 10 mg the % of weight variation ranged from 6.122% to -2.04% and the standard deviation is 0.007071. The % weight variation of Trilock 10 mg ranged from 1.694 to -15.254% where the standard deviation found 0.009486. For Montex 10 mg the weight variation ranged from 4.166 to - 2.777% where the standard deviation is 0.006324. The % of weight variation of Monalast 10 mg ranged from 5.882 to -5.882% and standard deviation is 0.004690 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 Montelukast 10 mg from different brands are goes under the test and for Monas 10 mg the average hardness of 5.541 kg and standard deviation 1.581138. The average hardness for Aeron 10 mg is 9.126 and standard deviation is 0.712066. For Trilock 10 mg the average hardness is 6.797 kg and standard deviation is 0.353553. Another brand Montex 10 mg has the average hardness 10.52 kg with standard deviation 1.511952. The Monalast 10 mg has hardness 7.443 kg with 1.444991 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 Monas 10 mg weighted 1.94g and after the test it has 1.94g that means the mean weight loss is 0%. For Aeron 10 mg the mean weight loss is 0%. For Trilock 10 mg the result before test is 1.85g and after the test 1.85g and mean weight loss is 0%. Montex 10 mg has a mean weight loss 0.062% as before the test weight was 3.06g and after the test the weight was 2.88g. Monalast 10 mg also have 0% mean weight loss. So, all the tablet meets the criteria of USP.

4.4 Disintegration test

As per USP, 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 Montelukast 10 mg are the film coated tablet. So, the average disintegration time of Monas 10 mg 6.05 minutes. For Aeron 10 mg the average disintegration time is 2.57 minutes. The average disintegration time of Trilock 10 mg is 5.58 minutes. For Montex 10 mg the average disintegration time is 15.00 minutes and for Monalast 10 mg the average disintegration time is 2.57 minutes. All the batches of Montelukast 10 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 Monas 10 mg, % dissolved of Montelukast ranged from 61.44% to 111.36% and Aeron 10 mg ranged from 44.43% to 71%. Again, for Trilock 10 mg ranaged from 49.20% to 77.91%, for

Montex 10 mg it ranged 30.24% to 50.40% and Monalast 10 mg ranged from 34.26% to 56%. 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 Montelukast 10 mg. Another criterion is r^2 value. The accepted r^2 value for Montelukast is very High ranger up to 0.995 to 0.999. After conducting the experiment, we were able to form a standard curve where we got r^2 value of the five brand (Monas 10 mg, Aeron 10mg, Trilock 10 mg, Montex 10 mg, Monalast 10 mg) and values are all similar as 0.996. After analysis, it is found that some results provide unusual. 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, Usage of Expired GSF or ISF, Error during Measurements, Error in time management

Chapter 5: Conclusion

In case of Dealing with Asthma, Allergic rhinitis and EIB Montelukast 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 Montelukast has pass most of the quality control parameters which were given by USP and BP. In comparison among five brands, Montex 10 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 to 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 Asthma, allergic rhinitis and EIB.

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