"In vitro Quality Evaluation of Different Brands of Ebastine 10 mg Tablets Commercially Available in Bangladesh"

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DEDICATION

I would like to dedicate my work to my parents for their never-ending support in my life.

APPROVAL

This Project, **"In vitro Quality Evaluation of Different Brands of Ebastine 10 mg Tablets Commercially Available in Bangladesh"**, submitted by Dr. Mohammed Shafikur Rahman, Associate Professor, Department of Pharmacy, Daffodil International University, has been accepted as satisfactory for the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy and approved as to its style and contents.

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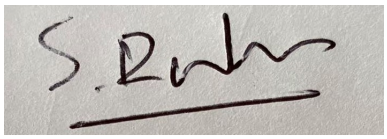

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ABSTRACT

The main purpose of this study was to evaluate and compare the quality control parameters of four different brands of Ebastine tablets available in Bangladesh. Different in vitro quality parameters including weight variation, friability, hardness, disintegration time, thickness, diameter, dissolution profile and potency were assessed according to the compendial procedures. According to BP specification, all tablets of each brand showed % weight variation within the range. All brands showed their friability within the USP designated limit of less than 0.5%. Within 30 minutes, tablets from all brands disintegrated completely which complies with BP and JP specifications and four brands could meet the first stage dissolution test. The study illustrates that all brands of Ebastine tablets showed acceptable results.

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CHAPTER ONE

INTRODUCTION

1.1: OVERVIEW

Ebastine is a low-potential H1 antihistamine for somnolence. The blood-brain barrier is not penetrated to a considerable extent and thus incorporates an effective block in the peripheral tissue of the H1 receptor with a low rate of core side effects, seldom leading to sedation or sleepiness. Almirall S.A's patent was issued in 1983 and medical application took place in 1990. Owing to the low water solubility, the material is also micronized.

Histamine is a core mediator of allergy symptoms and oral H1-antihistamines are among the most common therapies in disorders such as allergic rhinitis and chronic urticaria for symptomatic relief. Ebastine is an antihistamine of the second generation and has shown to be an effective therapy for allergic rhinitis both seasonally and perennially. In patients with other conditions such as cold urticaria, demographics hives, atopic asthma, mosquito dents, and common cold (compared to pseudoephedrine), small trials have shown beneficial effects of ebastine. A fast-dissolving tablet (FDT) formulation is also available in addition to the standard ebastine tablet. It dissolves in the mouth without the need for a drink. Ebastine has a fast onset of action that can be used with or without food once a day. Patients that are older who have mild to severe hepatic dysfunction do not need dose adjustments. Clinical trials have shown that ebastine is well tolerated at usual medicinal doses of 10 and 20 mg once daily. In addition to the standard tablet dosage, ebastine is now available as an FDT, giving patients a more flexible medication choice.

1.1.1: TABLET

Tablets are solid formulations that are obtained by compressing uniform particle volumes and each contains a single dose of one or more active ingredients. They are for oral administration purposes. Others are swallowed entirely, some are absorbed or scattered in water after chewing, others are kept in the mouth until the active ingredients are released.

Figure 1: Different types of Tablets

Tablets are generally spherical rigid disks, with smooth or convex end surfaces. They are the most often used solid-dose medications since they provide the user, the prescriber, the patient's

manufacturer, the pharmacist, and his production several advantages. Because of these advantages their popularity is continuously increasing day by day. "Welcome" in Britain first use the term 'tablet' to describe the compressed dosage form.

1.1.2: CLASSIFICATION OF TABLETS

Mainly tablets are classified into two classes

1. Compressed tablets
2. Molded tablets

1.1.3: COMPRESSED TABLETS

The compressed tablets usually prepared on large scale production methods, whereas the molded tablets are prepared extemporaneously on small scale. This two main type of tablet are further classified as follows :

1. Chewable tablets
2. Sublingual tablets
3. Effervescent tablets
4. Soluble tablets
5. Dispersible tablets
6. Gastro-resistant tablets
7. Modified release tablets
8. Implants
9. Soluble tablets
10. Layered tablets

1.1.4: MOLDED TABLETS

1.Hypodermic tablets

2.Dispensing tablets

1.1.5: PROPERTIES OF A GOOD TABLET

1. It should be precise and consistent in weight.
2. For simple management, scale and form should be appropriate.
3. The comprimés need not be too difficult to dissolve in the belly.
4. Incompatibilities do not occur.
5. During storage, they must be chemical and physically stable.
6. During transport, they do not crack or collapse in the patient's hands.
7. They should look attractive.
8. Fabrication faults such as splitting, chipping, or discoloration must not occur.

9. In manufacturing, it should be simple and economic.
10. It should easily disintegrate after administration.

1.1.6: ADVANTAGES

1. It's easy to swallow, to transport.
2. They look really attractive
3. Sugar can disguise a disgusting taste.
4. No dosage estimation is essential. The patient has made the procedure of taking the dose easier by the strip or blister packaging. It also provides a sealed cover that protects the tablets from ambient conditions such as air, moisture, and sun, etc.
5. Some tablets are delivered in half and quarters by drawing lines during production to make breakage easier when a fractional dosage is needed.
6. A precise quantity of a drug even though it is very small
7. Tablets give long medicinal stability

1.1.7: QUALITY AND ITS CRITERIA

For medicinal products, quality is an utter requirement. Drug consistency means care quality that guarantees patients' wellbeing. The manufactures must be responsible for the safety of the medicines they are producing according to the WHO (World Health Organization).

The principal criteria for a quality drug product are shown in the following figure:

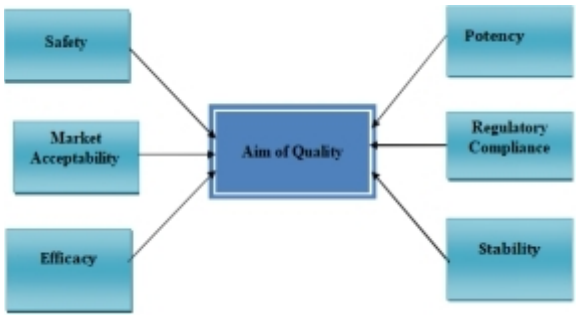

Figure 2: Aim of Quality of Tablets

SAFETY

Drug protection means that such safety standards related to its intended use must be met by the drug product. No medicine can be considered totally safe, especially prescription drugs. In real life, the drug complications (side effects) must be compared to the risk associated with the patient's benefit to assess the risk/benefit ratio. This ratio must be used to evaluate the medicinal effect of the drug.

Besides its dangerous side effect, such as teratogenicity, several additional factors including cross-contamination, contamination with pathogenic species and very high or low potential may cause a pharmaceutical product to become unhealthy.

POTENCY

A sufficient drug material in its active state shall be present in the product. Harmful materials for deterioration should be missing or under specified limits.

EFFICACY

The efficacy of a drug shows its biochemical function in animals or people. The active drug must be released from the dosage form properly.

STABILITY

Pharmaceutical preparations may exhibit chemical or physical instability. This may result in:

- Reduced activity of the drug.
- Formation of toxic degradation products and
- The drug may become inelegant and thus unacceptable.

The medicament must be safe enough and its dosage type to maintain its minimal potency criteria by the national or international pharmacopoeial monograph. In most western countries, 5% now is considered permissible above the labeled power unless the producer has sound reasons for a bigger variety. To guarantee its reliability for use under the prescribed conditions, the finished product must be sold inappropriate packs before their expiry.

ACCEPTABILITY

Acceptability refers to acceptability to the customer or the industry. This concerns organoleptic characteristics such as the flavor, odor, color, way of use and features not immediately apparent to patients, such as too high a degree of microbial pollution. For the acceptability of the industry, medication should have medicinal beauty.

REGULATORY COMPLIANCE

Each component unit package must be labeled clearly and accurately. Furthermore, the commodity shall comply with the rules of procedure. Various supporting facts such as power claims, indices and side-effects, warnings, conditions of storage, self-life, date of manufacture, batch number, guidelines for use, etc. must conform with the drug laws.

1.2 Antihistamines (H1-receptor antagonists)

Nowadays, the world's largest class of drugs used to cure allergic disorders and the most commonly used among all urticarial medications are more than 45 antihistamines (Mittal, Godse, & Patil, 2016). H1 antihistamines are essentially competitive reverse agonists, not receptor antagonists, since

antihistamines are believed to counteract H1 receptor effects (Simons & Simons, 2011). Traditionally, antihistamines are not called antagonists at other histamine receptors (Waller & Sampson, 2017). H1-antihistamines which are administered orally are well absorbed and metabolized by oxidation in the liver and removed through the kidneys only in unchanged traces (Goldstein, Weber-Schöndorfer, & Berkovitch, 2014).

1.3 Functional classification of antihistamines

Antihistamines are divided into two functional groups:

1.3.1 First (old)–generation H1-antihistamines

The first-generation antihistamines are lipophilic, cross the blood-brain barrier and quickly cause side effects such as sedation, impaired vision, and sleepiness in the central nervous system. They are often short-lived and need several regular doses. They also have core antimuscarinic effects, which inhibit moving nausea (Waller & Sampson, 2017). Before any regulatory authority exists and before clinical pharmacology trials on novel medicines were required, most H1-antihistamines of the first generation were launched. Examples include Azelastine, Clemastine, Cyproheptadine, Dexchlorpheniramine, Dimethindene, Hydroxyzine, Mizo- lastine etc. (Goldstein et al., 2014).

1.3.2 Second (new)–generation H1-antihistamines

New antihistamines have been developed to minimize the side effects of medications of the first generation. A major increase in antihistamine expansion took place in the 1980s with the emergence of H1-antihistamine of second-generation (Mittal et al., 2016). Second-generation antihistamines are lipophobic and have a low blood-brain barrier, decreased sedation, and cognitive decline. For non-histamine receptors, their affinity is diminished and their binding specificity to H1 receptors is greater. You can have longer half-lifes, but you can take them once or twice a day (Waller & Sampson, 2017). They have very little antimuscarinic effect as well. The latest medicines in this category are active metabolites or optical isomers of second generation for instance desloratadine and levocetirizine (Mittal et al., 2016). Some widely used second-generation H1-receptor antagonists are desloratadine, fexofenadine, levocetirizine, bilastine, ebastine, rupatadine and olopatadine (Merlob & Weber-Schöndorfer, 2014).

1.4 General Ebastine Overview

In the second generation of antihistamines, low lipophilicity and higher molecular solubility have a reduced capacity to cross blood brain barrier and lower side effects, also seen in the first generation (Sastre, 2008). Ebastine is a sedative, long-acting second-generation histamine receptor antagonist with a structure dependent on oxypiperidine that selectively interacts with H1-peripheral receptors. Ebastine is readily consumed after oral dosage and is metabolized to carebastine, the active

metabolite, by a substantial first-pass metabolism. The chemical name of ebastine is 4-(4-benzhydryloxy-1-piperidyl)-1-(4-tert-butylphenyl) butan-1- one (Hurst & Spencer, 2000). It has antihistaminic, anti-allergic activity and avoids bronchoconstriction caused by histamine. It has no major sedative or antimuscarinic actions. It is commonly prescribed against allergic conditions (Frare & Singh, 2018). The ebastine is certified in many pharmacopeias, including British pharmacopeia ("The British pharmacopoeia," 2013), European Pharmacopeia (E. Pharmacopoeia, 2019), and Japanese Pharmacopeia XVI ("Japanese Pharmacopoeia XVII," 2017). Basically raw material and impurities are defined in the first two compendiums, while the Japanese Pharmacopeia provides a monograph on active drug ingredient of ebastine, ebastine tablets, and orally disintegrating tablets of ebastine (Frare & Singh, 2018). It is available as tablets of 10 and 20 mg, fast-dissolving tablets as well as pediatric syrup (1mg/ml). Ebastine is available commercially under different brand labels worldwide (Suratiya & Pancholi, 2014).

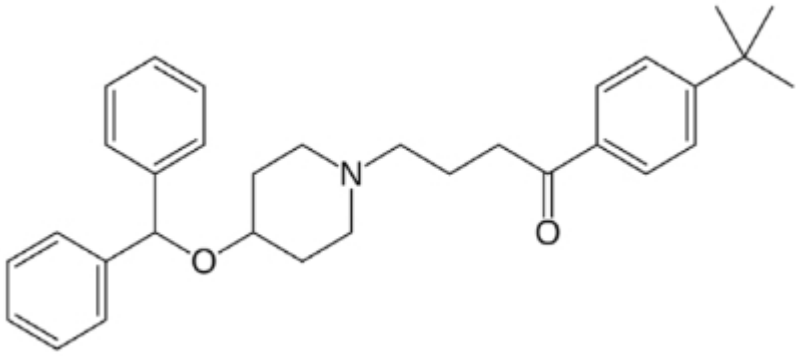

Figure 3: Chemical configuration of Ebastine (Frare & Singh, 2018).

1.5 Drug profile of Ebastine

1.5.1 Therapeutic class

Second generation non-sedating, long-lasting antihistamine (Ciprandi, 2010).

1.5.2 Mechanism of action

Ebastine is a second-generation piperidine H1-antihistamine. H1-antihistamine interferes with the agonizing activity of histamine on the H1 receptor and is used for the treatance of allergy, allergic conjunctivitis, and urticaria in inflammatory processes. Ebastine increases IFN-TM development in chronically allergic rhinitis patients and improves the prognosis of allergic conditions. Less activation through phospholipase C and phosphatidylinositol (PIP2) signaling pathway of the NF-μB

transcription factor often decreases the occurrence and activity of adhesion, pro-inflammatory cytokines, and the chemical factors of cellular adhesion molecules. Furthermore, reducing the concentration of calcium ion contributes to enhanced stability of the mast cell, which further decreases the release of histamine (Simons & Simons, 2011).

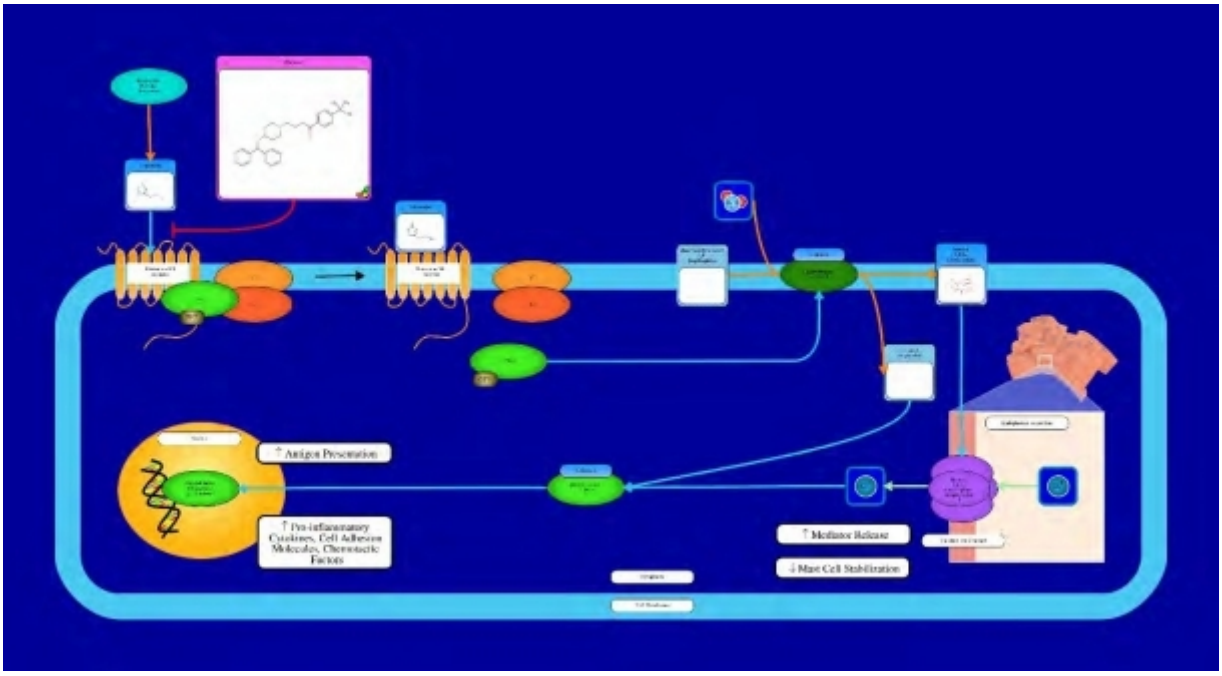

Figure 4: Mechanism of action of Ebastine (Simons & Simons, 2011).

1.5.3 Therapeutic indications

Ebastine 10 mg/20 mg tablet and syrup (1 mg/ml) are indicated for the symptomatic cure of:

- Allergic rhinitis (seasonal and perennial), whether or not linked with allergic conjunctivitis.
- Idiopathic chronic urticaria and in rare case Th-2 type autoimmune disease
- Allergic dermatitis and sometimes asthma
- In several countries for relief from mosquito bites or atopic dermatitis (Patel, 2018)

1.6 Pharmacokinetic properties

Ebastine is preferentially metabolized in the liver. The medicinal amount for normal adults is 10-20 mg, the operation begins for between 1 to 3 hours (Mittal et al., 2016). Routine administration of 10 mg ebastine results in a concentration of peak cubastine between 2.6-5.7 hours and a half-life range of 10.3- 19 hours in the pharmacokinetic examination. It strongly binds to plasma proteins (>95%), which are mostly excreted through urine. Gastrointestinal absorption and pharmacokinetics are not compromised if ebastine is taken with food. Pharmacokinetic parameters in children and aged volunteers are usually similar to those seen in healthy adults, although Cmax and AUC values are greater in children than in adults (Hurst & Spencer, 2000). Liver or serious kidney impairment patients (creatinine clearance <1.8 L/h/1.73m2) had considerably increased for t1⁄2 values compared

to those acquired from healthy volunteers. In healthful volunteers getting multiple doses of either ketoconazole or erythromycin (medicines that inhibit CYP metabolism), the metabolism of single doses of ebastine 20 mg was considerably affected (Adwi, Ahmed, & Osama, 2017). Cimetidine, on the other hand, had no major influences on the metabolism of a single dose of 20 mg of ebastine (Frare & Singh, 2018).

1.7 Pharmacodynamic properties

Instead of an H1-receptor antagonist, Ebastine is called an inverse agonist of histamine. Its antagonistic influence keeps histamine running repeatedly, particularly in instantaneous hypersensitivity (Ciprandi, 2010). This is primarily used to inhibit or reduce movement disease, seasonal rhinitis, and allergy dermatitis on bronchitis, capillaries, and various other smooth muscles (Adwi et al., 2017). A single dose of ebastine (10 mg or more) is significantly greater than a placebo by inhibiting histamine-induced wheal and flare. Single or repeated doses of ebastine do not interfere with the operation of a psychomotor or volunteer driving capacity. Thus far, the literature has not defined any crucial cardiovascular effects of ebastine (Hurst & Spencer, 2000). Furthermore, ebastine therapy, 20 mg daily for 1 week, did not induce the psychomotor performance diminishing effects or the depressive implications of ethanol of diazepam (Frare & Singh, 2018).

1.8 Safety and tolerability

Ebastine tablet is given orally once daily (10 mg/20 mg). Ebastine is generally well tolerated and beneficial in alleviating allergic rhinitis and chronic idiopathic urticaria symptoms. Headache, somnolence and dry mouth are the most common cases. Co-administration of ketoconazole or erythromycin is not clinically essential for heart adverse reactions. Ebastine 10 mg and 20 mg are not sedating and does not affect cognitive or psychomotor capacity, including driving skills (Ciprandi, 2010). No significant differences in the QTc interval with ebastine were found in doses up to 5 times the recommended clinical dosage.

1.9 Dosage and administration

Ebastine tablets and syrup are for oral administration. For orodispersible (Fast dissolving tablet) tablet it should be placed on the tongue where the drug will release, no water or other fluid is needed for this. Ebastine may be administered with or without food as there is no effect of food on drug (Sastre, 2019).

- **Children between 2 and 5 years:** 2.5 ml (half teaspoonful) once a day (in severe situations such as perennial allergic rhinitis up to 5 ml)
- **Children between 6 and 12 years**: 5 ml (one teaspoonful) or 5 mg (half tablet) once a day (up to 10 ml in serious conditions such as perennial rhinitis)

- **Adults and older children more than 12 years old:** Once daily 10 mg (1 tablet) or 10 ml (2 teaspoonful) ("Ebastine Drug Information - Indications, Dosage, Side Effects and Precautions," 2019).

1.10 Drug interactions and precautions

Pharmacokinetic interactions with CYP3A4 metabolized medicines such as ketoconazole, itraconazole, or erythromycin contribute to increased amounts of ebastine or carebastin plasma, causing QTc to extend. Rifampin (rifampicin) pharmacokinetic activity that leads to a lower concentration of carebastine plasma. Ebastine does not interfere with theophylline, warfarin, cimetidine, diazepam, or alcohol kinetics. Improved effects on alcohol and diazepam sedation (Sastre, 2019). Caution should also be recommended when ebastine is administered with other medications.

1.11 Contraindications

Ebastine is contraindicated in patients with diarrhea, cardiac arrhythmias and recognized hypersensitivity to ebastine or to any of its excipients, in hepatic impairment, renal insufficiency, special caution is advised (Adwi et al., 2017).

1.12 Use of Ebastine during pregnancy and lactation

1.12.1 Pregnancy

Data from the use of ebastine in pregnant females are limited. Animal studies do not show detrimental effects on reproductive toxicity, either directly or indirectly. As a precautionary measure, the use of ebastine during pregnancy should be avoided (Ciprandi, 2010).

1.12.2 Lactation

Whether ebastine is excreted in human milk is not known. High protein binding (>97%) of ebastine and its active metabolite, carebastine, does not suggest drug excretion and drug excretion into breast milk. It is preferable to avoid using ebastine during lactation as a precautionary measure ("Information on Ebastine and its use," 2018) .

1.13 Side effects

Headache, dry mouth and drowsiness are the most prevalent side effects. Pharyngitis, abdominal pain, dyspepsia, asthenia, epistaxis, rhinitis, sinusitis, nausea, and insomnia are less frequently reported side effects ("Information on Ebastine and its use," 2018).

1.14 Physicochemical properties

1.14.1 Molecular formula and molecular mass

C32H39NO2 and 469.7 g/mol (Frare & Singh, 2018).

1.14.2 Appearance & physical state

non-hygroscopic, white to off-white crystals or crystalline powder (Hurst & Spencer, 2000)

1.14.3 Melting point

80 – 82ºC (Frare & Singh, 2018)

1.14.4 Boiling Point

596.3ºC ("Ebastine - Chemical Book," 2017)

1.14.5 Solubility

It is easily soluble in acetic acid, in methanol it is also soluble, in water practically insoluble, partially soluble in ethanol ("Japanese Pharmacopoeia XVII," 2017)

1.14.6 Storage Condition

25ºC ("Information on Ebastine and its use," 2018)

1.14.7 l_{max}

252 nm (wavelength of maximum absorption) ("Ebastine - JP XVII - Ultraviolet-visible Reference Spectra," 2017)

1.15 Conventional oral dosage forms

Tablets that are the most significant and meaningful in all pharmaceuticals are the most popular mode of oral administration. The strong oral dosage types are more relevant in the pharmaceutical industry. Tablets are stable dosages commonly achieved by single or repeated compressions of powder or granules. In certain cases, tablets can be obtained by molding or extrusion processes. You may have one or two active ingredients in tablets uncoated, or covered (Ansel, 2015). Tables may include diluents, disintegrants, gliders, lubricants which may modify the action of dosage types and gastrointestinal active content, dyed content, and flavoring materials licensed by an appropriate national or regional authority. Tables may be complementary for use throughout the gastrointestinal tract. The durability, dissolution rate, bioavailability, purity or efficacy of the active ingredient must be guaranteed when using such excipients (Ansel, 2015). Tablets are single dose prepared for oral administration. Others should be swallowed fully. Others should be spread or dissolved in water, others after the crushing and some should be retained in the oral cell in which the active medicinal product is published ('The International Pharmacopoeia, Eighth Edition, 2018).

1.16 Advantages of conventional oral dosage forms

- Tablets are a drug-form unit that offers the maximum dose and latest difference of active product of all medication types.
- The price of both medication formulations is cheaper than the price.
- They are the easiest and strongest type of all oral dosage types.
- They are usually the simplest and inexpensive to package and transport of all oral dose shapes.
- Product identification should be the simplest and cheapest, and no more operational measures are necessary if a punch face is printed or single graphics.
- They may possibly deliver the supreme ease of swallowing with the slightest possibility to remain above the stomach, especially when coated, as long as the disintegration of the tablet is not too fast.
- Tablets offer themselves to specialized release profile medications such as enteric or delayed-release tablets.
- Tablets are more appropriate for large-scale manufacturing than other oral forms of units.
- They have the best overall characteristics of all oral forms of chemical, mechanical and microbiological stability (Aulton, 2005).

1.17 Disadvantages of conventional oral dosage forms

- Some medicines block compression into dense compacts due to their amorphous existence or flocculent low density feature.
- Drug substances with minimal weighting, sluggish dissolving properties, mild to bulky doses, optimum elevated absorption in or compiling these characteristics can be hard to produce or unfeasible as a tablet but still gives enough or full bioavailabilité of medicinal products. The use of these characteristics can be difficult.
- Medications that are bitterly tasting or that have undesirable smells or are vulnerable to oxygen or moisture can need encapsulation or trap until they are compressed or tablet compressions may need coating (Ansel, 2015).

1.18 In vitro study vs. in vivo study

1.18.1 In vitro study

In vitro (Latin for glass inside) refers to the process of conducting a certain process in a sterile environment outside a live organism. Often experiments in cell biology are conducted beyond animals and cells. One of the repeated shortcomings of in vitro studies is that the exact cellular circumstances of an organism, particularly the microbe, are not imitated. For instance, one estimation

shows that 99.6% of human microbiota species have not or cannot be identified in vitro. A therapy, for instance, can provide a short-term benefit, but a long-term damage (Etman, Shekedef, Nada, & Ismail, 2017).

1.19 In vitro quality control parameters and tests for tablets

A medicine must meet the physical specifications, compendial criteria, and quality guidelines prescribed and defined in various pharmacopeial monographs during manufacture to be considered a finished product and released into the market, and certain critical factors must be regulated during the manufacturing process. They're also known as quality performance checks and in-process quality control criteria. There is a risk that mistakes will occur during the manufacturing phase; thus, it is critical to monitor any defects that might arise during the manufacturing process, and stringent quality control checks must be conducted to determine the product's consistency. To meet the criteria and to pass and qualify finished product quality management checks and ensure the quality of the products, finished products must even go through certain strict quality tests and guidelines, so that they cannot be considered misbranded or under standard pharmaceuticals and medicines. There is also an important necessity to ensure optimal product consistency during the process and completed product quality testing (Shabana, 2016). In order to know how important they are, the following are some main (official and non-official) quality assurance checks for the tablets.

1.19.1 Weight variation test

This test is a formal tablet test (United states pharmacopoeial commission, 2016). The weight uniformity test is used to check if each tablet contains the amount of drug material listed in a batch with a little difference from the tablets. The purpose of this test is to assess the consistency of dose-based tablet weights. The average weight of 20 tablets is registered, the percentage difference or percent deviation of the average or mean weight of each tablet is determined, the percentage weight variance must be within the percentage range specified in USP, BP, and IP for tests (Chaplain, August 2014). Only apparatus that is needed for this procedure is an analytical balance.

1.19.2 Tablet thickness test

For very few tablets, thickness testing is performed as it is not an official test to conduct. Venire caliper or screw gauge is used to measure tablet thickness (Ansel, 2015).

1.19.3 Content uniformity test

This is an official quality control test (Pharmaceutical Commission of the United States, 2016) The content uniformity test has been developed in a restricted range across the product assertion to ensure accuracy of active drug ingredients on dosage units. This test is essential for comprimés of less than 25 mg or less than 25% of the total tablet weight of the medication. The trial is carried out using 30

tablets, 10 tablets are individually assayed as prescribed in the individual monograph. The procedure is considered and the tablets pass, as it is observed that the quantity of the active substance persists within a range of 85% to115% in each dosage device. Remaining 20 tablets are used when this experiment fails to comply (Kongsuk, 2011).

1.19.4 Content of active ingredient (Assay)

This is also an official test described in individual drug monograph of pharmacopeia. The objective of this experiment is quantitative and qualitative analysis of active contents in tablets. The requirement of this test is to confirm and check whether labeled amount of active drug is present in the given dosage form. This is calculated from a sample of 20 tablets that should be chosen casually from a tablet batch (Savale, Laboratories, Nasik, & Estimation, 2018). The tablets are weighed and crushed with just a pestle in a mortar. In an analytical balance, a quantity equivalent to the theoretical content of each tablet or the average crushed tablet is weighed out in the balance. The weighted sample is dissolved either in a solvent where the active drug is readily soluble or in a solvent prescribed in the individual compendial monograph then the resultant solution is filtered and the stipulated assay procedures are subjected to an aliquot of the resulting supernatant (Gupta, 2017). Spectrophotometry or High-Performance Liquid Chromatography (HPLC) is generally used to analyze the active drug (Allen, Bassani, Elder, & Parr, 2014).

1.19.5 Hardness test

The purpose of this test is to check whether or not the tablets can withstand extreme handling and pressure by measuring the crushing strength property which is defined as the compressional force applied to a tablet along the diameter (Savale et al., 2018). Most of the time, the test is carried out to satisfy the need for pressure adjustments on the tablet machine. Hardness influences the test for disintegration. The newton, as accepted by the SI system, is the recommended unit of force. However, the kilogram may also be used as the measuring unit for hardness test. But newton will be the unit that should be used to measure the tablet crushing strength, 1 kilogram 9.807 newton (Gupta, 2017). Hardness tester is used to measure the degree of force for crushing the tablets (Shabana, 2016).

1.19.6 Friability test

The aim of this test is to see how long tablets last (physical strength) and how well they withstand abrasion during handling, coating, packaging, shipping, and other processing steps (Shabana, 2016). A tumble movement is used to do a test friabilator or friction test. Weight loss of 10 tablets is the

point after a fixed amount of time of the test. Frabilator has a revolving drum that rotates for 4 minutes at 25 rpm (S. Interim, Announcement, & Friability, 2016). Initial weight of 10 tablets is calculated and after the rotation 10 tablets are weigh again for final weight and from that % weight loss is measured (Ansel, 2015).

1.19.7 Disintegration test

The aim of this test is to see whether tablets break down into small parts when placed in a liquid medium under laboratory conditions within the recommended time frame ("The British pharmacopoeia," 2013). This is an important first step toward opioid dissolution (T. I. Pharmacopoeia, 2011). This is an official measure that shows how long it takes to dissolve a tablet into fine particles and tiny fragments, increasing the tablet's solvent solubility ("The International Pharmacopoeia, Eighth Edition," 2018). The disintegration process can be combined with the dissolution process, which involves breaking down a solid ingredient into small parts and dispersing it in a liquid until a homogeneous solution of the solute and the solvent forms. Disintegration has an effect on the dissolution measure. Both tablets must pass a disintegration examination, which is done in vitro using a disintegration test system (T. I. Pharmacopoeia, 2016). A basket-rack configuration with 6 USP-specified dimensional open-ended transparent tubes mounted vertically on a 10-mesh scale (2 mm) stainless steel wire mesh makes up the USP disintegration system (Pharmacopeia, 2008). For the duration of experimentation, a tablet is put in every single of the basket's 6 chambers and the basket is lifted and dropped in a fluid reservoir for example, water (most of the time) or any other solvent recommended in the individual monograph at 29 to 32 cycles per minute by using a mechanical device (T. I. Pharmacopoeia, 2016). The wire screen should always be below the level of the fluid. The temperature of the immersion medium should be maintained at 37º ± 2ºC and media volume should be 600 ml in each 1000 ml beaker (Pharmacopeia, 2008). Disintegration is considered to be achieved if there are no residue or fragments (other than coating fragments adhered to the lower surface of the disk) on the screen or if there are particles left, they are soft mass without any palpably firm, un-moistened core (T. I. Pharmacopoeia, 2016). Disintegration procedure helps to understand the solubility of the API (active pharmaceutical ingredient) in the digestive system's gastric fluid or in the intestinal fluid (Assembly, 2019).

1.19.8 Dissolution test

The dissolution test is an official test that determines the percentage release of drug material from dosage forms by measuring the amount of active substance dissolved in the medium over a specified period of time. Normal dissolution is the process of dissolving solid, gaseous, or liquid products in a solvent to form a solution. However, in order to create a solution, the solvent must be consistent with the materials; the solution formed by the process of dissolution is often homogeneous. Since dissolution is a kinetic process, the kinetic energy released by a high temperature can hasten the cycle of solute dissolution in a liquid. Dissolution is a kinetic process, so that kinetic energy emerging from high temperature will accelerate the mechanism of dissolving a solute in a liquid. Dissolution testing is an in vitro procedure which defines how an API is extracted out of a solid dosage unit into a solution within the gastrointestinal tract ("In Vitro Dissolution Testing for Solid Oral Dosage Forms," 2010). The FDA instruction on dissolution testing for types of immediate release solid oral dosage involves the execution of the Biopharmaceutical Classification System (BCS) guidelines and criteria for bio-relevant dissolution studies and that is based on the solubility and permeability of the API ("Biopharmaceutical Classification System and Formulation Development," 2011). In vitro dissolution testing may be a useful method for predicting in vivo drug material efficacy and reducing the amount of bioavailability or bioequivalence studies needed. The 2 most important considerations are the choice of suitable dissolution medium and the medium temperature. In vitro conditions must imitate in vivo conditions to improve in vivo dissolution (United States Pharmacopeial Convention, 2011). Therefore, the tablet dissolution rate is a very important factor for drug absorption inside the body as increased the dissolution rate → increased the absorption rate→ increased bioavailability of drug (Shargel, Leon & B.C. Yu, 2017). USP apparatus I (basket) and USP apparatus II (paddle) remain the most widely operated dissolution-testing instrument. 37º ± 0.5ºC is the optimum temperature condition that is maintained mostly and paddle rotation may vary from 25, 50, 75 or 100 rpm. 1000 ml beaker is used in the apparatus and in each 1000 ml of beaker 900 ml of media volume is generally placed to perform the method (F. Interim & Announcement, 2016).

1.20 Aim of the study

This study aimed at evaluating some relevant in vitro quality control parameters to correlate and compare the quality of different brands of ebastine 10mg tablets available in the Bangladesh market. The study also focuses on determining whether these tablets comply with the physical specifications and compendial (pharmacopeial) requirements as claimed by the manufacturing companies or not.

1.21 Objectives of the study

In the pharmaceutical industry, total product quality must be assured to remove the product that does not fulfill the standards and specifications specified in the Pharmacopoeias. There are many brands of Ebastine BP tablets available all around the Bangladesh. Therefore, it is quite difficult to select the most effective and the safest one within the affordable price range. Objectives of this study are as follows:

- To determine safety and efficacy of the tablets.
- To find out the tablets with flaws, defects, errors, and the tablets which will fail to pass the quality standards and measurements.
- To find out the dosage forms that will not meet the compendial requirements of tablets among these four brands.
- To find out the misbranded (mislabeled), sub-standard and counterfeit (falsified) tablets.
- To compare and correlate the quality of the four brands of ebastine tablets.
- To find out the safest and the most effective brand within an affordable price.
- To establish possible equivalence among the brands of ebastine tablets.

1.22 Thickness test

The thickness of the tablet is calibrated with the diameter of the die, the filling quantity allowed into the die cavity, the compaction features of the substance of fill, and the pressure or force used during compression. The same fill, die, and pressure parameters have to be used to produce tablets of consistent thickness during and between batch manufacturing for the same formulation.

Hardness is perhaps the most essential factor as it may affect disintegration and dissolving, not just the thickness but also the hardness of the tablet. Therefore, it is doubly crucial to managing pressure for tablets of consistent thickness and hardness. Tablet thickness also becomes an important characteristic in packing operations and in counting of tablets using filling equipment which uses the uniform thickness of the tablets as a counting mechanism. Tablet thickness is measured with a vernier caliper, thickness gauge or automated equipment (Automatic weight, hardness, thickness, and tablet diameter test instrument). The thickness of a tablet should be controlled within ±5% variation of a standard value depending on the size of the tablet.

Chapter 2

Materials and methods

2.1 Materials

2.1.1 Study samples

Samples of this study were film-coated ebastine BP tablets (containing 10 mg API in each tablet) of four different brands and all of them are immediate release solid oral dosage forms.

2.1.2 Sample collection and identification

All the tablet samples were purchased from different local registered drug stores of Dhanmondi, Basabo and Pranthapath of Dhaka city. Before purchasing, all the samples were accurately verified for their price, manufacturing and expiry dates. All the sample brands were given a brand code assigned to each one of them from S1-S4 randomly to hide their identity. Label information of the purchased four different brands of ebastine tablets is given below.

Table 1: Label information of randomly selected four different brands of Ebastine tablets (10 mg)

Brand Code	Strength/ Dose	Dosage form	Company Name	Mfg. Date	Exp. Date	Batch No
S1	10 mg	Tablet	Popular Pharmaceuticals Ltd	Dec 2020	Nov 2022	SLC81
S2	10 mg	Tablet	ACI Pharmaceuticals Ltd	Dec 2020	Dec 2022	TK041
S3	10 mg	Tablet	Delta Pharmaceuticals Ltd	Feb 2021	Feb 2023	006
S4	10 mg	Tablet	Square Pharmaceuticals Ltd	Jan 2021	Dec 2023	IA03594

2.1.3Reference standard drug

Standard ebastine drug was a kind gift from one of the leading pharmaceutical companies of Bangladesh, Popular Pharmaceuticals Ltd.

2.1.4 Glassware and paper materials

Table 2: Glassware and paper materials used in the experiment

Serial No.	Name	Specification
1	Volumetric flask	10ml, 50ml, 100ml
2	Pipette	2ml, 5ml, 10ml
3	Beakers	50ml, 100ml, 500ml
4	Funnel	Medium
5	Measuring cylinder	50ml, 100ml
6	Pipette filler	Medium
7	Filter paper	Whatman Grade 41
8	Mortar and pestle	Large
9	Glass rod	Small, medium
10	Spatula	Small, medium
11	Weighing paper	Small, medium
12	Test tube	Small
13	Aluminum foil paper	Medium

2.1.5 Solvents and reagents

Table 3: Solvents and reagents used in the experiment

Serial No.	Name	Purpose
1	Hydrochloric acid	Dissolution test and Disintegration test
2	Distilled Water	Dissolution test and Disintegration test

2.1.6 Equipment and instruments

Table 4: Equipment and instruments used in the experiment

Serial no.	Equipment Name
1	Electronic Balance
2	Tablet Friability Tester
3	Tablet Disintegration Tester
4	Hardness Tester
5	UV Spectrophotometer
6	USP Dissolution Apparatus II

2.2 Methods

2.2.1 Weight variation test

With the help of a digital analytical equilibrium The average weight was determined after 20 tablets from each brand were correctly measured and chosen at random. The following calculation was used to calculate the percentage deviation of actual tablet weight from the average weight:

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

Not more than two of the individual tablet weights would deviate from the mean weight more than the percentage limit range recommended by USP, IP and BP that is listed below and none should deviate from the mean weight more than twice the percentage limit range (Kumar, 2013). Furthermore, average weight of 10 tablets from each brand was noted with standard deviation.

Table 5: USP, BP and IP acceptance limits of maximum weight variation (%) (Kumar, 2013).

BP/IP standards of average weight	Maximum allowed % variation limit	USP standards of average weight
80 mg or less	± 10 %	130 mg or less
80 mg – 250 mg	± 7.5 %	130 mg – 324 mg
More than 250 mg	± 5 %	More than 324 mg

2.2.2 Hardness test

The hardness tester was used to calculate the crushing strength of 10 randomly chosen tablets from each brand. The strength measuring machine was newton (N), and the pressure used to smash the tablets was measured for ten tablets separately from each one of the 12 labels by placing each punch between the top punch and the bottom punch and then smashing each tablet, and a standard deviation was observed for the average durability. The normal intensity range is from 39.24 to 78.48 N (Karmoker J, Joydhar P, Sarkar S, 2016). (Kumar, 2013).

2.2.3 Friability test

For this test, ten tablets were chosen at random from each brand, and the test was conducted in a system known as the Roche friabilator. The initial weight of 10 tablets was recorded after they were weighted together before being placed inside the transparent drum of the USP friability tester. Then, after 4 minutes of tumbling or rotating the drum at 25 ± 1 rpm, the final weight of the same 10 tablets in the drum was recoded to calculate any percent loss of weight of these 10 tablets after 4 minutes. The USP advises that the weight loss of the tablets does not exceed 1%, with less than 0.5 percent being the most common (S. Interim et al., 2016). The % weight loss is calculated by the following equation:

$$\% \text{ Weight loss} = \frac{(\text{Initial weight} - \text{Final weight})}{\text{Initial weight}} \times 100$$

2.2.4 Disintegration test

For this test 6 tablets from each brand were chosen at random and were placed inside the six open-ended transparent tubes of the disintegration device's basket and then the basket was reassembled with the rack of the device as this tester is known as basket-rack assembly (Assembly, 2019). Finally, discs were put on top of each six tablets as it was specified in individual monograph of USP, BP and JP for disintegration of film-coated tablet (Al- Gousous & Langguth, 2015). IP, JP, Ph. Eur. and BP prescribed in their individual monograph about the conditions for plain-coated or film-coated tablet disintegration:

Table 6: Disintegration test conditions of film coated tablets according to IP, JP, BP and Ph. Eur. (Al-Gousous & Langguth, 2015), (Savale et al., 2018).

Immersion medium	Temperature	Time Limit
Water with discs	37° ± 2° C	Not more than 30 minutes

However, JP suggested a different media condition for the disintegration of ebastine film coated tablet and that is using of 0.1M HCl (pH 1.2) as the immersion fluid or medium with discs, rest of the parameters are the same as BP, IP and Ph. Eur. recommended (Al-Gousous & Langguth, 2015), (Kumar, 2013). So, for this test USP GSF (gastric simulated fluid) was used as medium as it was recommended by JP ("Japanese Pharmacopoeia XVII," 2017). 600 ml of immersion medium was prepared using 0.1 M HCl for 6 tablets from each brand and the medium was transferred into the 1000 ml beaker of the device and the temperature was maintained at 37º ± 2ºC using the device's thermostat.

The machine was turned on with a timer after placing the tablets into the 6 tubes of the basket and reassembling it with the rack of the device, which had 1000 ml of beaker containing 600 ml of immersion fluid. The basket was continuously raised and lowered from and into the medium until all six tablets were completely broken down into small fragments and there was no residue left on the medium (Pharmacopeia, 2008). When all the 6 tablets were broken into small particles and all the particles passed from tube mesh to outer beaker that time was recoded and average time was noted with standard deviation for future analysis and it was carried out for each of the brands. It was made sure before closing the test that all the ebastine tablets were disintegrated within the specified time.

2.2.5 In vitro dissolution test

Ebastine is a Class II drug which means that it has high permeability but low solubility in accordance with BCS (Biopharmaceutical Classification System) (Kamisetti & Gupta, 2017). The active ingredient, ebastine, is not water soluble. Therefore, this dissolution process requires a particular procedure and system to be used for this sort of active medicine. The standard release tablets (BCS classes II and IV) are prepared on a case-by-case basis on the proper experimental conditions for formulations consisting of poorly water soluble active materials. Normally, a single-point dissolution test is used. Due to the low aqueous solubility, it may be necessary to dissolve the drug in dissolution volume of 900 ml and add a surfactant to increase its solubility in water (I. Pharmacopoeia, 2015).

For immediate dosage formulations, the time of the dissolution is normally between 30 and 60 minutes, and if device II (paddle) is used, the rotary velocity is 50 and 75 rpm. Ebastine tablet dissolution is defined in Japanese Pharmacopeia. According to the current monographs, dissolution can be performed by means of a paddle technique: 900 ml of 0.2% sodium chloride, with a pH set of 1.2, with HCl replicating gastric fluid of the human stomach in swift mode (SGF). Ebastine tablet dissolution rates are not below 75% in 30 minutes ("Japanese Pharmacopoeia XVII," 2017). Based

on the findings, the writers recommended a procedure of dissolution using apparatus II with a 900 ml (acidic) medium at 75 rpm (Arend, 2010). BP and USP do not have any official monograph for ebastine tablet dissolution.

BCS Class	Solubility	Permeability	Oral Dosage Form Approach
1	High	High	Simple solid oral dosage form
2	Low	High	• Techniques to increase surface area like particle size reduction, solid solution, solid dispersion • Solutions using solvents and/ or surfactants
3	High	Low	Incorporate permeability enhancers, maximize local lumenal concentration
4	Low	Low	Combine 2 and 3

Figure 5: Approaches to enhance solubility and permeability for BCS class I – IV drugs ("Biopharmaceutical Classification System and Formulation Development," 2011).

So, methods prescribed and described in individual monograph of Japanese pharmacopeia about ebastine dissolution was followed during this experiment. Here, the alternative method of ebastine tablet dissolution was implemented using 0.1M HCl as the dissolution media as 0.1M at 75 rpm showed highest amount of active drug getting dissolved and giving highest percentage of drug release and pH was maintained between 2 – 2.5 using HCl (Arend, 2010). The conditions of this dissolution experiment were as follows:

Table 7: Dissolution test conditions of Ebastine tablets

Equipment	USP II (paddle)
Dissolution media	900 ml, 0.1M Hydrochloric acid
Temperature	37º ± 0.5ºC
pH	2
Rotation	75 rpm
Time	30 minutes

Preparation of stock solution and standard curve: Accurately weighed 5 mg of pure drug was taken in a 50 ml of volumetric flask and dissolved in acidic medium (pH 2) up to the mark. For better dissolution of the pure drug in the acidic medium, the solution was taken in a beaker with a magnet

and it was put on the hot plate with magnetic stirrer and it was kept there for 30 minutes at 40ºC. 0.1M HCL Acidic medium or fluid was made by using V1 × C1 = V2 × C2 equation and the pH was adjusted to 2 using further HCl if needed. So, the concentration of the solution was 0.1 mg/ml or 100 µg/ml and from this 100 µg/ml solution, 20 µg/ml of solution of 100 ml was prepared and this was used as stock solution. Using this stock solution, solutions of concentration ranging from 2 – 14 µg/ml were prepared as working standard solutions by using this V1 × C1 = V2 × C2 equation. After that absorbance of each of the solutions of pure drug was measured and noted at 252 nm (wavelength of maximum absorption of ebastine) using UV-spectrometer against a suitable blank solution of acidic fluid then a calibration curve or standard curve (absorbance vs. concentration graph) of ebastine was constructed according to Beer-Lambert's law.

In vitro dissolution test procedure: The dissolution test was carried out with a dissolution tester using USP II. A 900 ml acidic fluid prepared by the use of 0.1M HCl (pH 2) has been employed as the dissolution medium for determining medication release from the dosage type. After just 30 minutes, a single point dissolution trial was conducted, which means that 30 minutes were determined as the sample time. The sampling was conducted manually, since the apparatus does not have a mechanical sampler. At 37º ± 0.5ºC auto heater, the temperature has been held, and the paddle is rotated at a speed of 75 rpm. After 30 minutes, 10 ml of sample was withdrawn and then it was filtered with whatman (grade 41) filter paper of pore size 20 µm and the filtrate was diluted 5 times with fresh acidic solvent. 2 ml from that 10 mL of sample was taken in a separate volumetric flask of 10 ml and fresh acidic fluid was added up to the mark to dilute 5 times. Amount of dissolved ebastine was determined by using UV-spectrometer by taking absorbance values at about 252 nm (λmax) against the blank solvent of dissolution medium. After that by using the linear equation of the standard calibration curve of ebastine in acidic medium (pH 2), concentration of drug from the dosage form was calculated by using the absorbance values. This process was done for all brands by using 3 tablets from each brand and putting each tablet in one beaker thus using 3 beakers at a time of the dissolution tester device (United States Pharmacopeial Convention, 2011). Average percentage drug release was calculated by using 3 tablets from each brand. Amount of released drug was calculated by the following equation:

$$\% \text{ Drug release} = \frac{\text{Amount of released drug}}{\text{Labeled Amount}} \times 100$$

Table 8: Acceptance criteria for in vitro dissolution test of immediate release tablet (WHO Department of Essential Medicines and Health, 2018).

Level	Samples tested	Acceptance criteria
S_1	6	Each magnitude is not less than Q + 5%
S_2	6	The mean magnitude of the twelve units of dosage (S1 + S2) is equal to or higher than Q and no unit is less than Q-15%
S_3	12	The mean magnitude of twenty four units of dosage (S1 + S2 + S3) is equal to or higher than Q; not more than two units are less than Q-15% ; not less than Q-25%

Q (dissolution limit) is the stated amount of dissolved active ingredient expressed as a percentage of the labeled amount. Here for Ebastine 10 mg tablet, Q value is not less than 75% according to JP (Frare & Singh, 2018). 5%, 15% and 25%; these percentages in the acceptance criteria are percentages of the labeled amount so as to these magnitudes and Q are in the similar forms (WHO Department of Essential Medicines and Health, 2018).

Chapter 3

Results

3.1 Average weight and weight variation test

The weight variations of four brands of Linagliptin were determined and the observed results are shown in the following table.

USP specification of weight variation:

- ±10% for 130mg or less average weight of tablet.
- ±7.5% for more than 130mg average weight of tablet.

Table 9: Measured weight and average weight of Ebastine 10 mg tablet

Tablet No	S1	S2	S3	S4
1	120	163	123	102
2	123	164	120	102
3	129	160	126	104
4	121	169	121	101
5	126	164	123	101
6	120	167	121	103
7	127	166	124	102
8	122	169	129	104
9	126	164	128	104
10	117	165	124	102
Average	123.35	164.00	123.95	103.35

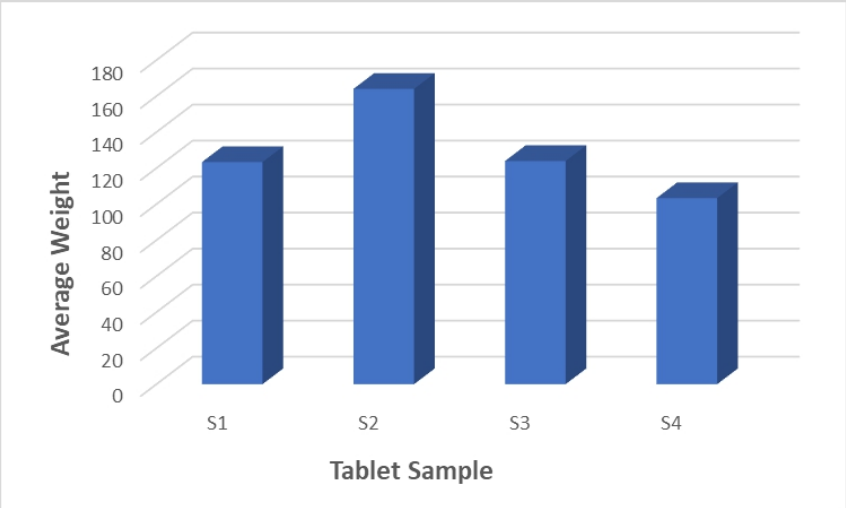

Figure 6: Average weight of different brands of Ebastine tablets

Table 10: Results of %weight variation

Tablet No	S1	S2	S3	S4
1	-2.72	-0.61	-0.77	-1.31
2	-0.28	0	-3.19	-1.31
3	4.58	-2.44	1.65	0.63
4	-1.91	3.05	-2.38	-2.27
5	2.15	0	-0.77	-2.27
6	-2.72	1.83	-2.38	-0.34
7	2.96	1.22	0.04	-1.31
8	-1.09	3.05	4.07	0.63
9	2.15	0	4.88	0.63
10	5.15	0.61	0.04	-1.31
% Average weight	±2.571%	±1.281%	±2.017%	±1.201%

Result: From the above tables, it is appeared that all brands of Ebastine tablets complied with the specification of weight variation.

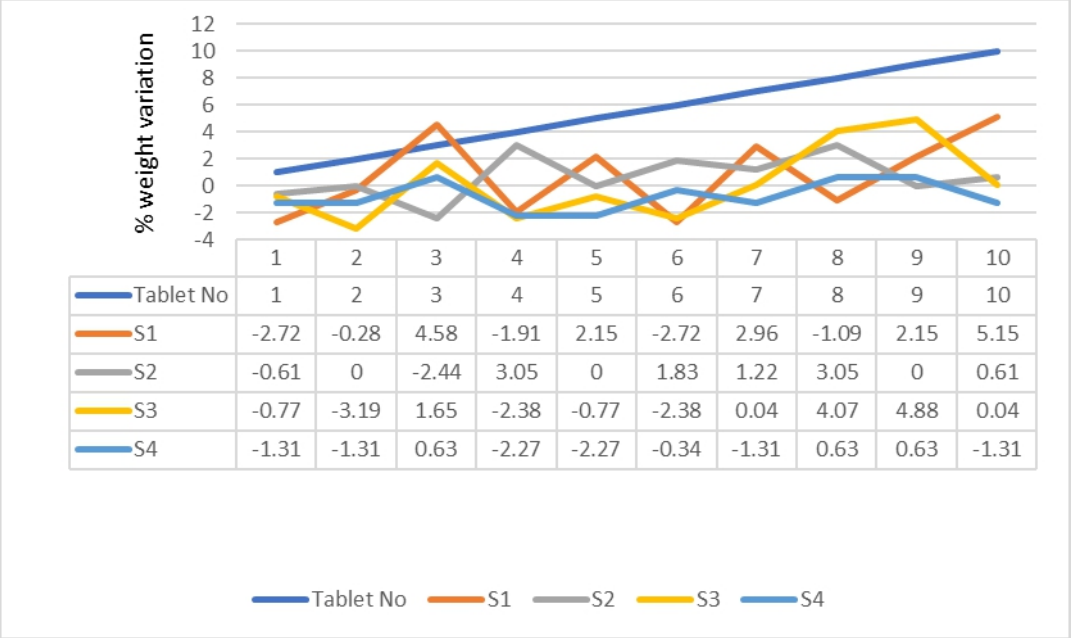

Figure 7: Results of %weight variation of different brands of Ebastine tablet

3.2 Hardness test

The hardness of four brands of Evastine tablet was determined and the observed results are shown in the following table.

Table 11: Results of hardness test

Tablet Brands	T1(kg/cm2)	T2(kg/cm2)	T3(kg/cm2)	T4(kg/cm2)	Avg.(kg/cm2)
S1	4	3.5	4	3.7	3.8
S2	4.5	4.9	4.2	4.5	4.5
S3	3.5	4	3.4	3.8	3.6
S4	3.5	4.1	3.8	3.5	3.7

Result: From the above tables, it is appeared that all brands of Ebastine tablets complied with the specification of hardness.

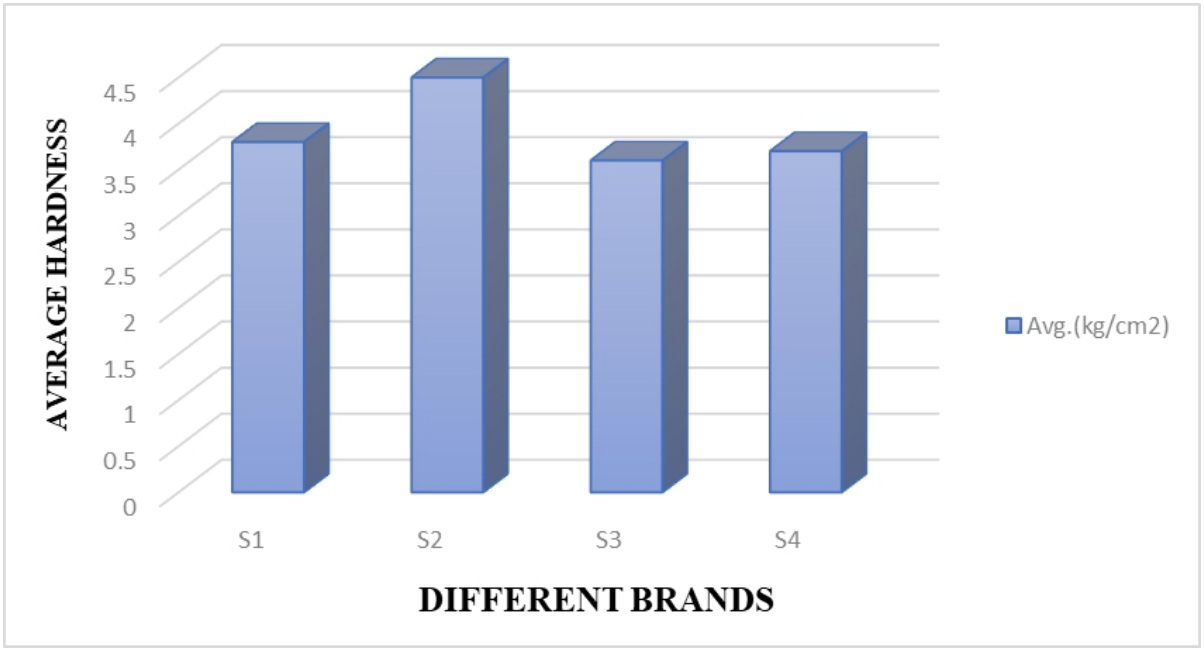

Figure 8: Comparison of hardness test of different brands of Ebastine tablets

3.3 Friability test

Results of friability test of 10 tablets from each brand had been tabulated and the table has been given below:

Table 12: Results of friability test

Brands	Initial Weight (mg)	Final Weight (mg)	% Weight loss
S1	1234	1233	0.08
S2	1631	1631	0
S3	1564	1562	0.13
S4	1369	1367	0.14

Result: From the above tables, it is appeared that all brands of Ebastine tablets performed good friability.

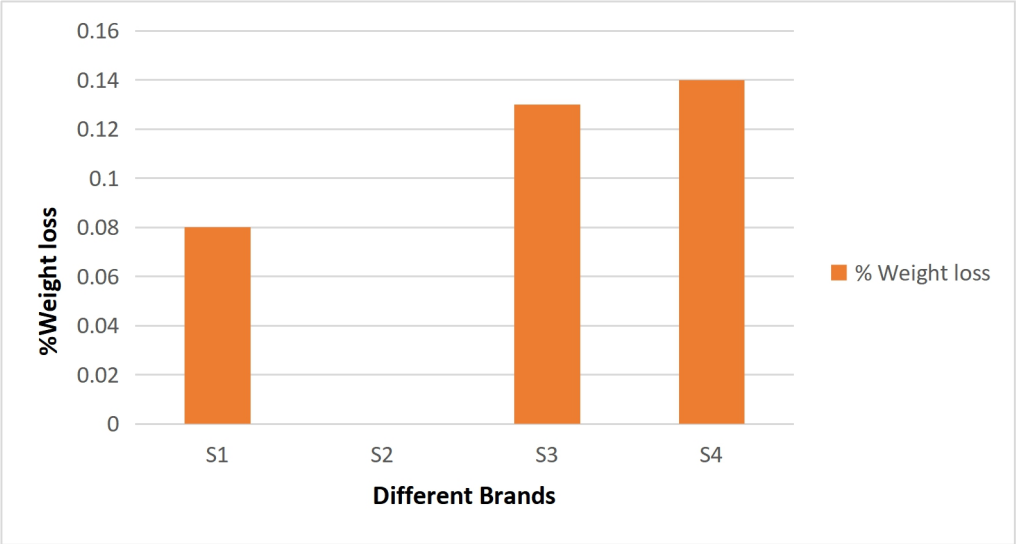

Figure 9: Comparison of friability test of different brands of Ebastine tablets

3.4 Disintegration test

Results of disintegration test (measuring unit of time was minute) of 6 tablets from each brand had been tabulated and the table has been given below:

Table 13: Results of Disintegration test

Brands	T1	T2	T3	T4	T5	T6	Average
S1	1.58	1.51	1.59	1.55	1.57	1.53	1.55
S2	1.17	1.10	1.03	1.27	1.01	1.2	1.13
S3	1.59	1.48	1.53	1.45	1.37	1.41	1.47
S4	1.15	1.11	1.04	1.29	1.07	1.11	1.12

Result: From the above tables, it is appeared that all brands of Ebastine tablets complied with the specification of disintegration.

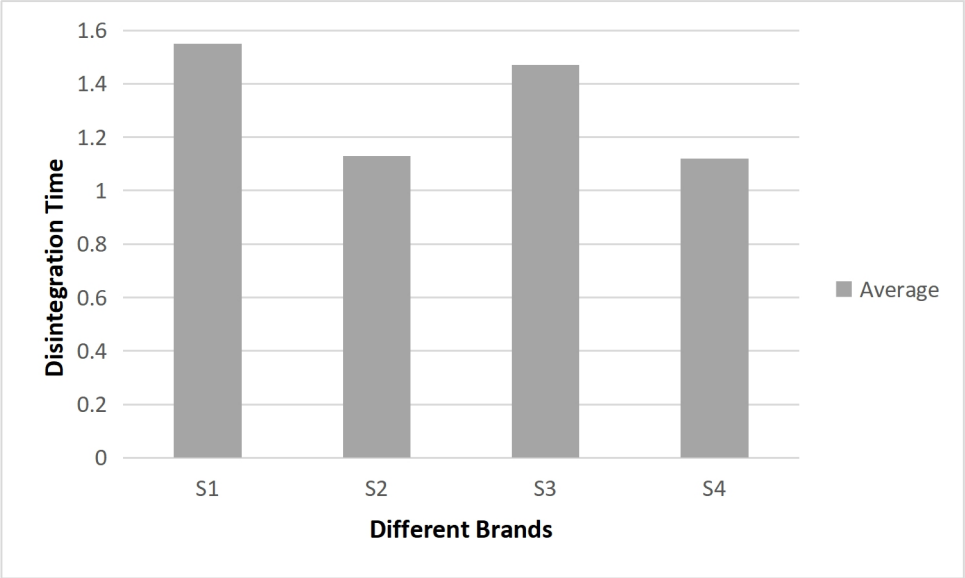

Figure 10: Comparison of disintegration test of different brands of Ebastine tablets

3.5 In vitro dissolution test

3.5.1 Standard curve of Ebastine in 0.1N HCl

Table 14: Absorbance of Ebastine standard solutions of various concentrations at 252 nm

Concentration	Absorbance at 252 nm
0	0
2	0.061
4	0.11
6	0.162
8	0.209
10	0.268
12	0.318
14	0.368

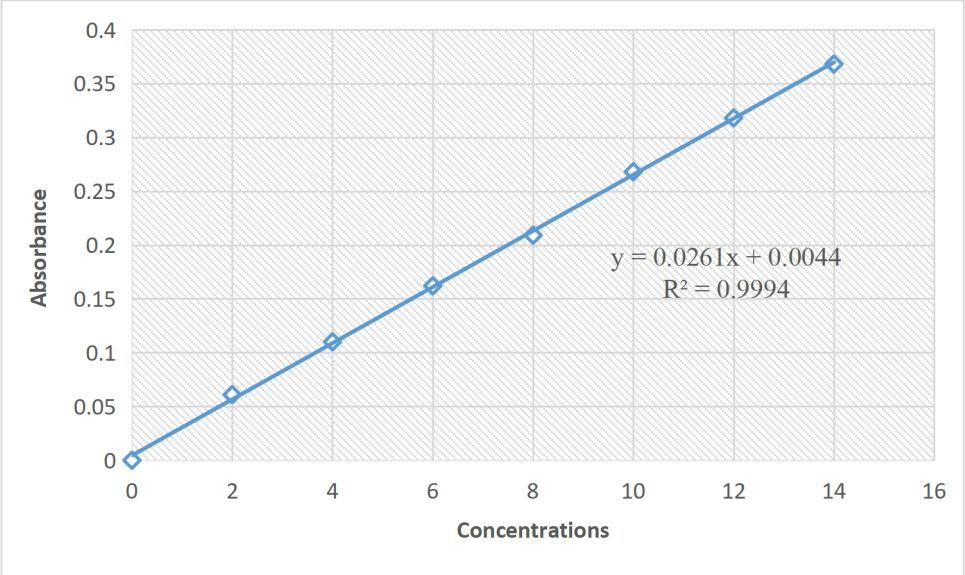

Figure 11: Standard curve of Ebastine in 0.1N HCl

3.5.2 Results of dissolution test

Results of dissolution study of ebastine tablets are obtained by using linear equation of the standard calibration curve of ebastine in acidic medium (pH 2 – 2.5). With the help of absorbance values acquired from the test, the concentration of ebastine is determined from the standard curve, thus amount of released drug or dissolved drug and percentage drug release is determined using the equations mentioned earlier. As the coefficient of determination of this curve (R2 value) is close to 1, all the values obtained from this graph would be more accurate and more valid and close to the values of pure ebastine in acidic medium. Results had been tabulated and the table is given below:

Specification: Not less than 75% in 0.1M HCl of the labeled amount of Ebastine to be dissolved in 30 minutes.

Table No. 15: Dissolution rate of S1

SI. No.	Time interval	Drug release %			Average %
		Sample 1	Sample 2	Sample 3	
01	After 10 min	65.7	60.3	62	62.66
02	After 20 min	84.8	79.3	81.3	81.8
03	After 30 min	98.6	93.1	100	97.23

Table No. 16: Dissolution rate of S2

SI. No.	Time interval	Drug release %			Average %
		Sample 1	Sample 2	Sample 3	
01	After 10 min	75.86	70.68	68.96	71.83
02	After 20 min	89.65	94.82	81.03	88.5
03	After 30 min	98.27	96.55	91.37	95.39

Table No. 17: Dissolution rate of S3

SI. No.	Time interval	Drug release %			Average %
		Sample 1	Sample 2	Sample 3	
01	After 10 min	62.03	54.72	65.7	60.81
02	After 20 min	81.37	84.82	79.31	81.83
03	After 30 min	93.18	94.83	98.93	95.64

Table No. 18: Dissolution rate of S4

SI. No.	Time interval	Drug release %			Average %
		Sample 1	Sample 2	Sample 3	
01	After 10 min	74.13	77.58	81.03	77.58
02	After 20 min	89.65	94.82	93.79	92.75
03	After 30 min	96.55	98.27	99.93	98.25

Result: All the brands meet the specification of the U.S.P standard as they release in cases of all brands more than 75% within 30 minutes in 0.1 M HCl dissolution medium.

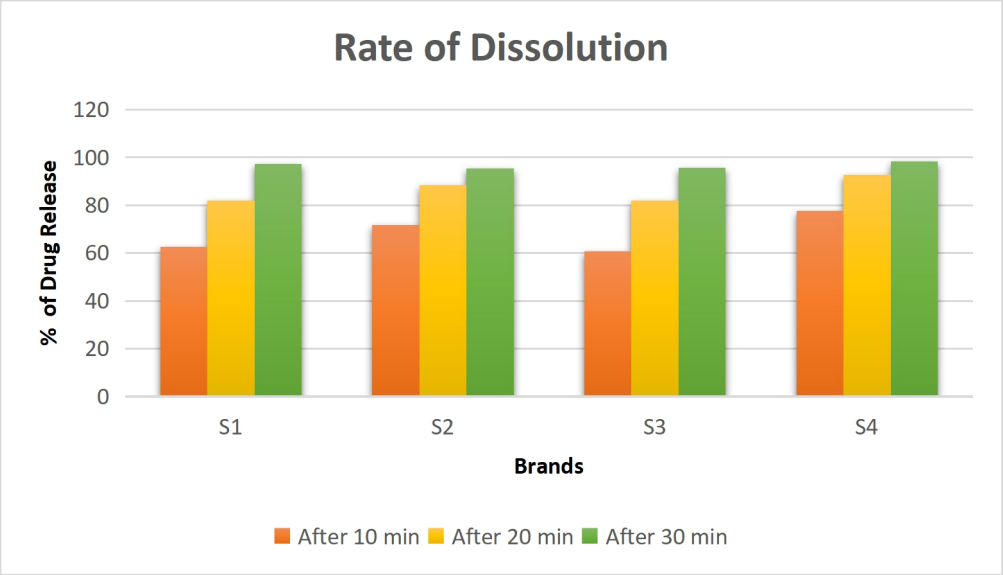

Fig. 12: Dissolution rate of four brands of Ebastine tablet

3.6 Thickness Test

Results of thickness test of 10 tablets from each brand had been tabulated and the table has been given below:

Table 19: Results of Thickness Test

Brands	T1	T2	T3	T4	T5	T6	T7	T8	T9	T10	Average
S1	3.1	3.1	3.0	3.1	3.1	3.1	3.0	3.1	3.1	3.1	3.0
S2	3.0	3.0	3.1	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
S3	2.8	2.8	2.6	2.8	2.8	2.8	2.7	2.8	2.8	2.8	2.7
S4	3.7	3.7	3.7	3.7	3.7	3.7	3.7	3.7	3.8	3.7	3.7

Result: From the above tables, it is appeared that all brands of Ebastine tablets complied with the specification of Thickness.

3.7 Tablet Diameter Test

Results of tablet Diameter test of 10 tablets from each brand had been tabulated and the table has been given below:

Table 20: Results of tablet diameter Test

Brands	T1	T2	T3	T4	T5	T6	T7	T8	T9	T10	Average
S1	7.1	7.1	7.0	7.1	7.1	7.1	7.0	7.1	7.1	7.1	7.0
S2	7.8	7.8	7.7	7.8	7.8	7.8	7.8	7.8	7.7	7.8	7.7
S3	7.8	7.8	7.6	7.8	7.8	7.8	7.7	7.8	7.8	7.8	7.7
S4	7.1	7.1	7.1	7.1	7.1	7.1	7.0	7.1	7.1	7.1	7.1

Result: From the above tables, it is appeared that all brands of Ebastine tablets complied with the specification of tablet Diameter.

Chapter 4

Conclusion

Conclusion:

In the existing industrial practice, in-vitro tests play a vital role in comparing with multi- brand generic molecules and providing adequate therapeutic activity of the dosage form which may eventually reflect in vivo functioning of the drug. Although in the field of most of the cases, in vitro-in vivo relation of a specific drug is hard to establish. The physical and chemical study of chosen commercial brands of ebastine tablet marketed in Bangladesh has displayed quality and effectiveness in accordance with the compendial standards and requirements. Since the parameters of quality control are associated to each other from the early step to the drug's pharmacological action, a high-quality tablet must fulfill all established quality parameters to achieve its required therapeutic action. Since all the formulations except satisfy compendial specifications. So, we can say they will produce the desired antihistaminic effect. However, all the brands exhibit results good % weight variation, excellent disintegration, 90% drug release after 30 minutes. Moreover, its unit price is also minimum. Considering these points, S1 may be regarded as the best brand among these four brands in Bangladesh.

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