# Comparative Study Different Brands Of Azithromycin Tablets



## B. Pharm. (Honors Project Report)

**A dissertation submitted to the Department of Pharmacy, Daffodil International University for the partial fulfillment of Bachelor of Pharmacy Degree**

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## APPROVAL

This Project, Enhance Performance and Salesmanship of marketing people in pharmaceutical company through Attitude submitted by **Most. Shahnaj Pervin** to the 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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Dedicated to……

MY PARENTS

# DECLARATION

I hereby declare that, this project report is done by us under the supervision of **Md. Al - Faruk Lecturer,** Department of Pharmacy, Daffodil International University, in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy. I am declaring that this Project is my original work. I am also declaring that neither this project nor any part thereof has been submitted elsewhere for the award of Bachelor or any degree.

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# ABSTRACT

Azithromycin belongs to the family of medications known as macrolide antibiotics. It is used to treat certain types of infections that are caused by bacteria. It is most commonly used to treat ear infections (e.g., otitis media), throat infections, lung infections (e.g., pneumonia), and skin infections. It can also be used to prevent mycobacterium avium complex (MAC) infections in people with HIV infection.The purpose of this study was to determine the pharmaceutical quality of the Azithromycin tablets dispensed in Bangladesh. The organoleptic and physicochemical properties of five different brands of Azithromycin tablets were assessed according to established methods. The results of weight variation, disintegration time, dissolution time, drug content and drug release of all marketed products comply with established limit.

The qualitative and quantitative parameters of all the tested samples complied with the USP reference standard which is a reflection of quality product of azithromycin in Bangladesh local market.

**Result:** The result showed that, five brands of Azithromycin tablets , meet a good result for weight variation, friability, disintegration time and dissolution rate. But one brand of tablets showed slow dissolution rate as compared to USP specificationailed to meet the USP specification.

**Conclusion:** The present study, Although performed on a limited scale yet on the basis of professional judgment the data reported in this study can help the Drug Control Authority to get an idea about the quality status of the marketed Azithromycin preparations in Bangladesh.

# ACKNOWLEDGEMENT

Nothing should be performed alone successfully. Contribution of other person must present behind every successful work as boost. So this successful research work is also not exceptional to this natural law. The success and final outcome required a lot of guidance and I am extremely fortunate to have got this all along the completion of my project work. Whatever I have done is only due to such guidance and I would not forget to thank them.

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# Chapter 1

# Introduction

# INTRODUCTION

## 1.1. Introduction.

The antimicrobial agents or antibiotics develops during the last 60 years are among the most dramatic examples of the advances of science. Azthromycin is a 15-atom lactone macrolide ring compound. Azithromycin is a semisynthetic derivative of Erythromycin obtained by the addition of methylated nitorgen into the lactone ring of Erythromycin. Azithromycin is effective against gram positive bacterias.

Azithromycin:
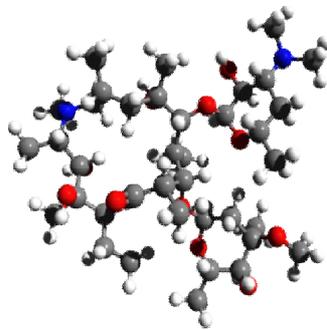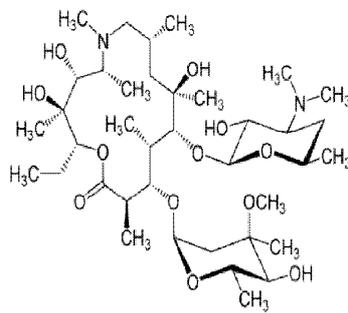
N-Methyl-11-aza-10-deoxo-10-dihydroerythromycin A

A team of researchers at the Croatian pharmaceutical company Pliva Gabrijela Kobrehel, Gorjana Radobolja-Lazarevski, and Zrinka Tambura, led by Dr. Slobodan Đokić — discovered azithromycin in 1980. It was patented in 1981. In 1986, Pliva and Pfizer signed a licensing agreement, which gave Pfizer exclusive rights for the sale of azithromycin in Western Europe and the United States. Pliva put its azithromycin on the market in Central and Eastern Europe under the brand name of Sumamed in 1988. Pfizer launched azithromycin under Pliva's license in other markets under the brand name Zithromax in 1991.

Pfizer's exclusive rights have since lapsed and Pliva-manufactured azithromycin is also marketed in the United States by generic drug maker Teva Pharmaceuticals (which now owns Pliva).

After several years, the U.S. Food and Drug Administration (FDA) approved AzaSite, an ophthalmic formulation of azithromycin, for the treatment of eye infections. AzaSite is marketed in the U.S. and Canada by Inspire Pharmaceuticals, a wholly owned subsidiary of Merck . In 2010 azithromycin was the most prescribed antibiotic in outpatients in the US, whereas in Sweden where outpatient antibiotic usage is a third macrolides are only on 4% of prescriptions.

The medicine is also used to treat some sexually transmitted diseases, including gonorrhea and chlamydia. Off-label azithromycin uses include preventing heart infections and treating acne .Azithromycin may also be used to treat a number of other more uncommon bacterial infections.

Following oral administration it is widely distributed throughout the body; its bioavailability is approximately 37% and is reduced by food. Small amounts are dimethylated in the liver but most is excreted unchanged in the bile. The plasma elimination half-life is 2 to 4 days.

Because of its exceptional therapeutic properties, azithromycin revolutionised antibiotic treatment and became one of the most successful drugs worldwide. From its early trials, it proved to be an extremely efficient antibiotic with expanded and enhanced antibacterial activity (particularly against gram-negative pathogens), prolonged and higher tissue concentration and a low incidence of gastrointestinal side effects compared to other similar antibiotics.

### 1.2. Mode of action

Azithromycin prevents bacteria from growing by interfering with their protein synthesis. It binds to the 50S subunit of the bacterial ribosome, and thus inhibits translation of mRNA. Nucleic acid synthesis is not affected.

**Spectrum of bacterial susceptibility and resistance medical:**

*Chlamydia pneumoniae, Chlamydia trachomatis, Eikenella corrodens, Escherichia coli, Haemophilus influenzae, Moraxella catarrhalis, Mycobacterium chelonae, Mycoplasma*

*fermentans, Neisseria gonorrhoeae* and *Ureaplasma urealyticum* are generally susceptible to azithromycin dihydrate, while *Pseudomonas aeruginosa, and Staphylococcus aureus* are resistant to azithromycin dihydrate. In general, Streptococcus pyogenes is susceptible. Some *Brevibacterium* spp., *Corynebacterium amycolatum, Haemophilus influenzae* and *Mycobacterium abscessus* have developed resistance to azithromycin dihydrate to varying degrees

The following represents azithromycin susceptibility data on medically significant organisms.

- · *Haemophilus influenzae* - 0.001 µg/mL - >256 µg/mL
- · *Streptococcus pneumoniae* - 0.004 µg/mL - >512 µg/mL
- · *Streptococcus pyogenes* - 0.001 µg/mL - >256 µg/mL

### 1.3. Pharmacological Properties

### 1.3.1 Pharmacodynamics Properties
Antibacterials for systemic use.

### 1.3.2 Pharmacokinetic properties

**Absorption**

Bioavailability after oral administration is approximately 37%. Peak plasma concentrations are attained 2-3 hours after taking the medicinal product.

**Distribution**

Orally administered azithromycin is widely distributed throughout the body. In pharmacokinetic studies it has been demonstrated that the concentrations of azithromycin measured in tissues are noticeably higher (as much as 50 times) than those measured in plasma, which indicates that the agent strongly binds to tissues.

Binding to serum proteins varies according to plasma concentration and ranges from 12% at 0.5 microgram/ml up to 52% at 0.05 microgram azithromycin/ml serum. The mean volume of distribution at steady state ($VV_{ss}$) has been calculated to be 31.1 l/kg.

**Elimination**

The terminal plasma elimination half-life closely reflects the elimination half-life from tissues of 2-4 days.

Approximately 12% of an intravenously administered dose of azithromycin is excreted unchanged in urine within the following three days. Particularly high concentrations of unchanged azithromycin have been found in human bile. Also in bile, ten metabolites were detected, which were formed through N- and O- dimethylation, hydroxylation of disosamine and a glycone rings and cleavage of cladinose conjugate. Comparison of the results of liquid chromatography and microbiological analyses has shown that the metabolites of azithromycin are not microbiologically active.

In animal tests, high concentrations of azithromycin have been found in phagocytes. It has also been established that during active phagocytosis higher concentrations of azithromycin are released from inactive phagocytes. In animal models this results in high concentrations of azithromycin being delivered to the site of infection.

## 1.4. Medical uses

Azithromycin is used to treat many different infections, including acute otitis media, nonstreptococcal bacterial pharyngitis, gastrointestinal infections such as traveler's diarrhea, respiratory tract infections such as pneumonia, cellulitis, babesiosis, *Bartonella* infection, chancroid, cholera, donovanosis, leptospirosis, Lyme disease, malaria, *Mycobacterium avium* complex disease, *Neisseria* meningitis, pelvic inflammatory disease, pertussis, scrub typhus, toxoplasmosis, and salmonellosis.It is used to prevent bacterial endocarditis and some sexually transmitted infections. It is also effective against localized dental infections, uncomplicated skin and skin structure infections, urethritis and cervicitis and also genital ulcer disease. Azithromycin is used as a second line treatment for strep throat and for those allergic to penicillin.[5] It has a similar antimicrobial spectrum to erythromycin, but is more effective against certain Gram-negative bacteria, in particular, *Haemophilus influenzae* (although it would not be the first choice of treatment in this infection).Azithromycin resistance has been described and is endemic in many areas. Long-term use in treating *Staphylococcus aureus* infections with azithromycin may increase bacterial resistance to this and other macrolide antibiotics.Azithromycin has been shown to be effective against malaria

when used in combination with artesunate or quinine; the optimal dose for this is not yet known.

## 1.5. Dosage and administration

**Adults:**

For respiratory tract infections, otitis media and skin & soft tissue infections: 500 mg once daily for 3 days or an alternative to this as 500 mg once on day 1, followed by 250 mg once daily for next 4 days. For sexually transmitted diseases like genital ulcer, non-gonococcal urethritis and cervicitis due to Chlamydia trachomatis : a single 1 gm (1000 mg) dose. For the treatment of urethritis and cervicitis due to Neisseria gonorrhoeae : a single 2 gm (2000 mg) dose. In typhoid, 500 mg once daily for 7 days. In Cholera, a single 1 gm (1000 mg) dose. In Shigellosis, 500 mg once on day 1, followed by 250 mg once daily for next 4 days.

**Children:**

| Age/body weight | Daily dose | Duration |
|---|---|---|
| From 1month | 10mg/kg | 3 days |
| 15-25 kg | 200mg | 3 days |
| 26-35 kg | 300mg | 3 days |
| 36-45 kg | 400mg | 3 days |

Elderly:Same as adults.

## 1.6. Contraindications

Azithromycin is contraindicated in patients with known hypersensitivity to azithromycin, erythromycin, any macrolide or ketolide antibiotic. Azithromycin is contraindicated in patients with a history of cholestatic jaundice/hepatic dysfunction associated with prior use of azithromycin.

## 1.6.  Special warning for  use

**Hypersensitivity**

Serious allergic reactions, including angioedema, anaphylaxis, and dermatologic reactions including Stevens Johnson Syndrome and toxic epidermal necrolysis have been reported

rarely in patients on azithromycin therapy. Although rare, fatalities have been reported. Despite initially successful symptomatic treatment of the allergic symptoms, when symptomatic therapy was discontinued, the allergic symptoms recurred soon thereafter in some patients without further azithromycin exposure. These patients required prolonged periods of observation and symptomatic treatment. The relationship of these episodes to the long tissue half-life of azithromycin and subsequent prolonged exposure to antigen is unknown at present.

If an allergic reaction occurs, the drug should be discontinued and appropriate therapy should be instituted. Physicians should be aware that reappearance of the allergic symptoms may occur when symptomatic therapy is discontinued.

**Hepatotoxicity**

Abnormal liver function, hepatitis, cholestatic jaundice, hepatic necrosis, and hepatic failure have been reported, some of which have resulted in death. Discontinue azithromycin immediately if signs and symptoms of hepatitis occur.

**Clostridium Difficile-associated diarrhea**

Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including azithromycin, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C. difficile.

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of C. difficile cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibiotic use not directed against C. difficile may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of C. difficile, and surgical evaluation should be instituted as clinically indicated.

**QT Prolongation**

Prolonged cardiac repolarization and QT interval, imparting a risk of developing cardiac arrhythmia and torsades de pointes, have been seen in treatment with macrolides, including azithromycin. Cases of torsades de pointes have been spontaneously reported during post marketing surveillance in patients receiving azithromycin. Providers should consider the risk of QT prolongation which can be fatal when weighing the risks and benefits of azithromycin for at-risk groups including:

- Patients with known prolongation of the QT interval, a history of torsades de pointes, congenital long QT syndrome, bradyarrhythmias or uncompensated heart failure
- Patients on drugs known to prolong the QT interval
- Patients with ongoing proarrhythmic conditions such as uncorrected hypokalemia or hypomagnesemia, clinically significant bradycardia, and in patients receiving Class IA (quinidine, procainamide) or Class III (dofetilide, amiodarone, sotalol) antiarrhythmic agents.

Elderly patients may be more susceptible to drug-associated effects on the QT interval.

**1.8. Precautions**

Because azithromycin is principally eliminated via the liver, caution should be exercised when azithromycin is administered to patients with impaired hepatic function. Due to the limited data in subjects with GFR<10 mL/min, caution should be exercised when prescribing azithromycin in these patients.

Exacerbation of symptoms of myasthenia gravis and new onset of myasthenic syndrome have been reported in patients receiving azithromycin therapy.

Prescribing azithromycin in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

**1.9.Information for Patients**

Azithromycin tablets may be taken with or without food. However, increased tolerability has been observed when tablets are taken with food.

Patients should also be cautioned not to take aluminum- and magnesium-containing antacids and azithromycin simultaneously.

The patient should be directed to discontinue azithromycin immediately and contact a physician if any signs of an allergic reaction occur.

Patients should be counseled that antibacterial drugs including azithromycin should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When azithromycin is prescribed to treat bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by azithromycin or other antibacterial drugs in the future.

Diarrhea is a common problem caused by antibiotics which usually ends when the antibiotic is discontinued. Sometimes after starting treatment with antibiotics, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as two or more months after having taken the last dose of the antibiotic. If this occurs, patients should contact their physician as soon as possible.

**1.10.Drug Interactions**

**Aluminum- and magnesium-containing antacids**

May reduce the peak serum levels but not the AUC of azithromycin.

**Carbamazepine, hexobarbital, phenytoin**

Serum concentrations of these agents have been elevated by azithromycin, increasing the pharmacologic effects and risk of adverse reactions. Monitor serum concentrations of these agents and observe the patient for adverse reactions. Adjust the dose as needed.

**Cyclosporine, theophyllines**

Levels may be elevated by azithromycin, increasing the risk of toxicity. Monitor drug levels and adjust the dose as needed.

**Digoxin**

Digoxin plasma concentrations may be elevated, increasing the risk of toxicity. Monitor digoxin levels and observe the patient for signs of digoxin toxicity. Adjust the digoxin dose as needed.

**Dronedarone**

Dronedarone plasma concentrations and pharmacologic effects may be increased. Avoid coadministration.

**Ergot derivatives (eg, dihydroergotamine, ergotamine)**

Acute ergotism manifested as peripheral ischemia has been reported. Closely monitor for ergotism.

**Nelfinavir**

Azithromycin levels may be elevated, increasing the risk of adverse reactions (eg, abnormal LFTs, hearing impairment). Monitor for azithromycin adverse reactions.

**Nilotinib**

Increased nilotinib plasma concentrations with cardiotoxicity may occur. Avoid coadministration.

**Pimozide**

Pimozide plasma concentrations may be elevated, increasing the risk of cardiotoxicity. Coadministration is contraindicated.

QT prolonging drugs (eg, antiarrhythmic agents [class III (eg, dofetilide, sotalol) and class IA (eg, procainamide, quinidine)], arsenic trioxide, chlorpromazine, cisapride, dolasetron, droperidol, gatifloxacin, halofantrine, levomethadyl, lithium, maprotiline, mefloquine, mesoridazine, methadone, paliperidone, pentamidine, perflutren, pimozide, probucol, propafenone, sparfloxacin, tacrolimus, thioridazine, ziprasidone, quinolone antibiotics [eg, levofloxacin, moxifloxacin], tetrabenazine)

Risk of life-threatening cardiac arrhythmias, including torsades de pointes, may be increased. Use with caution. Avoid coadministration with paliperidone or propafenone. Close clinical and ECG monitoring is advised.

**Rifabutin**

Risk of neutropenia may be increased.

**Triazolam**

Plasma concentrations may be elevated by azithromycin, increasing the pharmacologic effect and risk of adverse reactions. Observe the clinical response of the patient and adjust the triazolam dose as needed.

**Warfarin**

The anticoagulant effect may be increased, increasing the risk of hemorrhage. Monitor anticoagulant parameters and adjust the warfarin dose as needed.

### 1.11.Side effects

A side effect is an unwanted response to a medication when it is taken in normal doses. Side effects can be mild or severe, temporary or permanent.The side effects have been reported by at least 1% of people taking this medication .The side effects include nausea, vomiting, abdominal discomfort (pain/cramps), flatulence, diarrhea, headache, dizziness, and skin rashes and are reversible upon discontinuation of therapy. Reversible elevations in liver transaminases have been observed occasionally. Transient mild reductions in neutrophil counts have occasionally been observed in clinical trials, although causal relationship to Azithromycin has not been established.

### 1.12.Adverse reactions

**Cardiovascular**

Chest pain, palpitations (1% or less); arrhythmias including ventricular tachycardia, hypotension, QT prolongation, syncope, torsades de pointes (postmarketing).

**CNS**

Dizziness, headache (1%); agitation, fatigue, hyperkinesia, insomnia, malaise, nervousness, somnolence, vertigo (1% or less); aggressive reaction, anxiety, asthenia, convulsions, hyperactivity, paresthesia (postmarketing).

**Dermatologic**

Rash (5%); dermatitis, pruritus (2%); eczema, fungal dermatitis, photosensitivity, swelling, urticaria, vesiculobullous rash (1% or less); erythema multiforme, Stevens-Johnson syndrome, TEN (postmarketing).

**EENT**Eye irritation with ophthalmic solution (1% to 2%); conjunctivitis, pharyngitis, rhinitis (1% or less); deafness, hearing disturbances including hearing loss, smell perversion or loss, taste perversion or loss, tinnitus (postmarketing).

**Ophthalmic**

Blurring vision, eye pain, eyelid swelling, itching eye, reduced visual acuity (postmarketing).

**GI**

Nausea (18%); diarrhea/loose stools, vomiting (14%); abdominal pain (5%); anorexia (2%); dyspepsia (1%); constipation, enteritis, flatulence, gastritis, melena (1% or less); oral candidiasis, pancreatitis, pseudomembranous colitis, tongue discoloration (postmarketing).

**Genitourinary**

Vaginitis (3%); monilia, nephritis (1% or less); acute renal failure, interstitial nephritis (postmarketing).

**Hematologic-Lymphatic**

Decreased lymphocytes, decreased neutrophils, increased eosinophils, increased lymphocytes, increased neutrophils, increased platelet count (at least 1%); anemia, leukopenia (1% or less); thrombocytopenia (postmarketing).

**Hepatic**

Cholestatic jaundice, jaundice (1% or less); abnormal liver function including hepatic failure, hepatic necrosis, hepatitis (postmarketing).

**Hypersensitivity**

Angioedema (1% or less); anaphylaxis (postmarketing).

**Ophthalmic**

Allergic reactions including facial swelling, hives, periocular swelling, rash, and urticaria (postmarketing).

**Local**

Pain at injection site (7%); local inflammation (3%).

**Musculoskeletal**

Arthralgia (postmarketing).

**Respiratory**

Cough, pleural effusion (1% or less).

**Miscellaneous**

Fever (2%); face edema, fungal infection, pain (1% or less); edema (postmarketing).

## 1.13. Pregnancy and lactation

**Pregancy:**

Teratogenic Effects:Pregnancy Category B**:**Animal reproduction studies have been performed at doses up to moderate maternally toxic dose concentrations. In these studies, no evidence of harm to the foetus was found. There are no adequate and well controlled studies in pregnant women. Since animal studies are not necessarily predictive of human response azithromycin should be used in pregnancy only if clearly needed.

**Lactation:** No data on secretion of azithromycin in breast milk are available. As many drugs are excreted in human milk, Zithromax (azithromycin) should not be used in the treatment of lactating women unless the physician feels that the potential benefits justify the potential risks to the infant, and were adequate alternatives are not available.

## 1.14. Overdose

Adverse events experienced in higher than recommended doses were similar to those seen at normal doses. In the event of overdosage, general symptomatic and supportive measures are indicated as required**.**

## 1.15.Preparations

- · Tablets: 250 mg,500mg.
- · Capsule:250mg,500mg.
- · Suspension: 15ml,30ml,35ml,50ml power for  suspention.
- · Injection: 500 mg/5ml(IV) vial

## 1.16. Shelf life

2 years

## 1.17.Storage

Tablets should be stored at room temperature between 15 C to 30 C (59 C to 86 F). Store away from heat, moisture, and light. Do not store in the bathroom. Keep azithromycin tablets out of the reach of children and away from pets.

## 1.18. Evaluation of Tablets

Tablets are evaluated by a variety of methods.

## 1.18.1. Weight variation of tablets:

In the process of compressing a tablet, of course there are problems, one of them is theweight variation. Usually, the range is still tolerable for large-sized tablets (diameter> 10mm) was 3%, while for small tablet (diameter <7mm) is 5%. However, this specificationranges vary

depending on the respective industry and the active ingredient of the drug. If the active ingredient is an extremely potent drug, in terms of the number of doses are very small(microgram scale) has a large effect, then the range specifications for tablet weight variationwould be minimized.



Fig 3.Analytical balance

Tablet weight variation in compressing process is not a trivial thing. Moreover, whenaffecting the uniformity of dosage units.

**Tablet weight variation may be caused by:**

Distribution at However caused the vibration. So, small granule pushed, large granules willcome out first, because there is a process of consolidation. Therefore, needs to be put auniform granule size. So, before the compressing process begins better evaluation the particlesize distribution first.

The flow of granules is not good / not free-flowing granules particle distribution is notnormal, because the specific gravity is different, so that the flow is bad.Granules with a large particle diameter which causes the resultant tablet has a variety ofunsightly weight, while too fine granules which causes unsightly flow time.

### 1.18.1. How to overcome the weight variation of tablets:

### 1. Particle size distribution is uneven

At first the particle size is evaluated.

- Ø If too many fines, then need to do are create a number of more granular. This case is commonly found on the direct compression process. This need not happen if are careful in choosing excipient for direct compression. The problem is excipient for direct compression is usually relatively more expensive.
- Ø If the active ingredient of the drug is stable to heat and humidity, then an easier way is to produce by wet granulation. Through granulation, drying and sifting, which formed granules can be more evenly? Critical points that need more attention is the moisturecontent and size of mesh used at the time of sifting.
- Ø If the active ingredients of drugs are not stable to heat and humid, then try to dry granulation, compaction with the compactor machine or slugging. Note the size ofmesh used to sift.

### 2. Lubricant or glidant less or not mixed evenly

To solve tablet weight variation, excipient Aerosil or colloidal Silicon Dioxide can be added. This excipient was added to the external phase. The amount used is usually 1-2% of the total weight of the tablet. Mix them for 10-15 minutes.

### 3. Specific gravity too different

This case often occurs in the manufacture of tablets that contain more than one type of granules. Two or more active ingredients each made in separate granules (usually because of incompatible) then at the time of compression into one, and coupled with the outer phase. Or two granules remain separate, but when compression using two different hopper, then compress into one tablet-

**Requirement:**

Requirement is met if the weight variation of tablets is of no more than 10 tablets differs from average weight by more than percentage given below-

**Acceptable percentage difference of tablet**

| Average weight of tablets | Percentage of difference |
|---|---|
| 130mg or less | 10% |
| 130-324mg | 7.5% |
| More than 324 mg | 5% |

### 1.18.2. Tablet Friability

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

Friability= (Iw-Fw)/Iw x 100

Where,

  Iw = Total initial weight of tablets

  Fw = Total final weight of tablets



**Fig 4:Tablet Friability Machine**

### 1.18.2.1. Acceptable range of friability:

Conventional compressed tablets that loss than 0.5% to 1% (after 100 revolutions) of their weight are generally acceptable.

### 1.18.2.2. Purpose of friability:

Tablet friability results in weight loss of tablet in packaging containers owing to chipping or fragmentation of the tablet to alteration of wear. Weight loss due to excessive friability causes the loss of dose which may cause loss of therapeutic activity. So friability study is essential.

Tablets are chipped or mechanically ended and no longer have sharp edges are of reduced pharmaceutical elegance and reduced quality. Friability often reflects lacks of cohesiveness on comparison of the drug granulation from which the tablets are made.

### 1.18.2.3. Possible causes of friability problem:

· Excessive moisture content.
· Over dried granulation.
· Inadequate amount of binder.
· Excessive pressure.

### 1.18.2.4. Remedy of friability:

1. Sufficient quantity of binder should be used.
2. Optimum drying is needed.
3. Proper pressure should be used.
4. Excess moisture should be removed.

### 1.18.3. Tablet disintegration

There are commercially available disintegration and dissolution apparatus. Most pharmacists will not have this equipment. However, a simple disintegration apparatus can be made. Start by supporting a 10 mesh screen about 2 inches above the bottom of a 1000 ml beaker. Fill the beaker with 900 ml of phosphate buffer, add a stirring bar, and place the beaker on a magnetic stirring plate. Stir at a moderate speed. Drop the tablets onto the mesh screen and record the time needed for the tablets to disintegrate. A reasonable disintegration time should be between 15 and 30 minutes, although the time will depend on the product, the stirring speed, etc.

**Fig 5 : Disintegration Apparatus**

The disintegration test for each dosage form is given in the pharmacopoeia. There are some general tests for typical types of dosage forms. However, the disintegration test prescribed in the individual monograph of a product is to be followed. If the monograph does not specify any specific test, the general test for the specific dosage form may be employed. Some of the types of dosage forms and their disintegration tests are:

**1.Uncoated tablets-** Tested using distilled water as medium at 37+/-2 C at 29-32 cycles per minute; test is completed after 15 minutes. It is acceptable when there is no palpable core at the end of the cycle (for at least 5 tablets or capsules) and if the mass does not stick to the immersion disc.

**2.Coated tablets-** the same test procedure is adapted but the time of operation is 30 minutes.

**3.Enteric coated/ Gastric resistant tablets-** the test is carried out first in distilled water (at room temperature for 5 min.; USP and no distilled water per BP and IP), then it is tested in 0.1 M HCL (upto 2 hours; BP) or Stimulated gastric fluid (1 hour; USP) followed by Phosphate buffer, pH 6.8 (1 hour; BP) or Stimulated intestinal fluid without enzymes (1 hour; USP).

**4.Chewable tablets-** exempted from disintegration test (BP and IP), 4 hours (USP).

These are a few examples for illustration. The disintegration tests for capsules, both hard and soft gelatin capsules are also performed in a similar manner. Also, the USP also provides disintegration tests for suppositories, peccaries etc

### 1.18.3.1. Purpose of disintegration:

It is directly influence the-

- · Dissolution of the tablet
- · Onset of the drug
- · Rate of absorption of the drug
- · Rate of bioavailability of the drug

### 1.18.3.2. Factors affecting the disintegrating time

- · Disintegrating agent
- · Binder
- · Particle size
- · Drying of powder
- · Mixing of powder

### 1.18.3.3Advantages of Disintegration tests:

- Ø This test is simple in concept and in practice.
- Ø It is very useful in pre-formulation, optimization and in quality control.

### 1.18.4. Tablet dissolution:

Disintegration time determination is a useful tool for production control, but disintegration of a tablet does not imply that the drug has dissolved. A tablet can have a rapid disintegration time yet be biologically unavailable. The dissolution rate of the drug from the primary particles of the tablet is the important factor in drug absorption and for many formulations is the rate-limiting step. Therefore, a dissolution time is more indicative of the availability of a drug from a tablet than the disintegration test.

Fig 6-Dissolution apparatus.

**Necessity of dissolution study**

1. For selection of the formulation in the development phase

- § By comparison of the dissolution profiles of innovator product with those of formulations
- § This should be a basic strategy in R&D to maximize the chances of bioequivalence

2. It is a requirement for comparative dissolution data for the bio-batch and innovate or batch

- § Same batches as used in bioequivalence study
- § Submit report with data, profile comparison & discussion (see report requirements)
- § This report forms part of pharmaceutical development report

3. Demonstration of in vivo bioequivalence of one or more of the lower strength(s) of an FPP may be waived based on-

- § An acceptable in vivo BE study of the highest strength against the comparator product
- § Demonstration of similarity of dissolution profiles,
- § If the lower strength is proportionally similar in formula to the higher strength (bio-
- § batch) and
- § If all pharmacokinetic requirements are met

4. Comparison of the release properties of pivotal batches

- § To demonstrate *in vitro* similarity of such batches.

§    The studies should be submitted in dossier as part of the FPP development report.

5. Selection of the dissolution specifications for product release & stability purposes

§    Conditions and acceptance criteria to be set

§    The dissolution profiles of the bio-batch should be used for this purpose

§    A dissolution specification should be able to detect inadequate release properties of the commercial batches

6. Post-approval amendment application

§    Assessment of formulation changes to demonstrate that the profiles of the amendment batch and the current batch are similar

**Variables affecting dissolution:**

§    Characteristics of the API  e.g., particle size, crystal form, bulk density

§    Product composition e.g., drugs loading, and the identity, type, and levels of excipients.

§    Manufacturing process e.g., compression forces, equipment

§    Effects of stability storage conditions e.g., temperature, humidity

**Mechanism of dissolution:**

Dissolution test determines the cumulative amount of drug that goes into solution as a function of time. Following steps involved

§    Liberation of the solute or drug from the formulation matrix (disintegration)

§    Dissolution of the drug (solubilization of the drug particles) in the liquid medium

§    The overall rate of dissolution depends on the slower of these two steps

**First Step**

Cohesive properties of the formulated solid dosage form drug play a key role disintegration and erosion semi- solid or liquid formulations, the dispersion of lipids or partitioning of the drug from the lipid phase is the key factor If the first step of dissolution is rate-limiting, then the rate of dissolution is considered to be disintegration controlled.

**Second Step**

Solubilization of the drug particles depends on the physicochemical properties of the drug such as its chemical form (*e.g.,* salt, free acid, free base) and physical attributes.

**Dosage form type and design affect dissolution testing**

For intrinsic dissolution-limited absorption (i.e., the disintegration of the dosage form is rapid, but dissolution is slow) the particle size of the API reduces. Small particle size creates challenges as they can pass through filters and subsequently dissolve. For solubility-limited absorption (intrinsic- solubility controlled) the transient solubility of the API enhances.

- § Different salt forms of the API
- § Surfactants in the formulation
- § Solubilized liquid formulations in hard or soft gelatin capsules.
- § Non-crystalline materials

**Media selection**

For batch-to-batch quality testing medium selection may be based on the solubility data and the dose range of the drug product to ensure that sink conditions are met. .The term sink conditions is defined as the volume of medium at least greater than three times that required to form a saturated solution of a drug substance. When the dissolution test is used to indicate the biopharmaceutical properties - closely simulate the environment in the GIT than sink conditions.
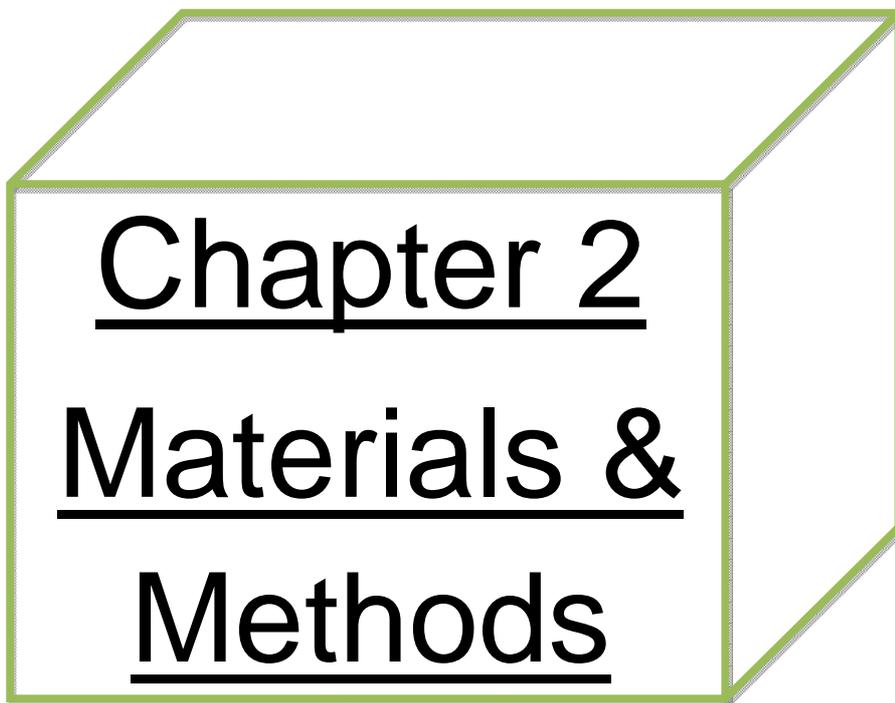
# Chapter 2
# Materials & Methods

## 2.MATERIALS AND METHODS

### Table No. 1. Instruments

| Sr. no. | Instruments | Make |
|---------|-------------|------|
| 1 | Electronic balance | Elder |
| 2 | Vernier Calliper | Mitutoyo |
| 3 | Friability test apparatus | Roche |
| 4 | Disintegration test apparatus | Magumps |
| 5 | Dissulotion test apparatus USP | Electrolab |
| 6 | UV Visible Spectrophotometer | Shimadzu |

**2.1. Others:** Micropipette, Measuring Cylinder, Beaker, Spatula, Alluminum Foil Paper,Pipette,Glass Rods,Water bath,Volumetric flask, Conical flask, Test tubes,pH Meter.

## 2.2. Material:

## 2.2.1. Chemicals:

- · 0.1M Phosphate buffer solution.
- · Azithromycin.
- · Distilled Water

**Table No. 2. Different brand name of Azithromycin in this study**

| Brand Name | Contains | Dosage Form | Manufacturer |
|---|---|---|---|
| TRIDOSIL | doTridosil 250mg tablet | Tablet | INCEPTA Pharmaceutical Ltd. |
| ROZITH | Rozith 250mg tablet | Tablet | HEALTHCARE Pharmaceuticals Ltd. |
| AZIMEX | Azimex 250mg tablet | Tablet | DRUG INTERNATIOL  Bangladesh. |
| ZITHRIN | Zithrin 250mg tablet | Tablet | RENETA  Ltd. |
| AZ | AZ 250mg tablet | Tablet | ARISTOPHARMA Ltd. |

For the analytical studies, the sample products of Azithromycinwere collected from local market. The samples were properly checked for their batch number and expiry date. The quantity of the sample purchased was  different batches of the different company. These are also of different strengths and dosage forms.

**Table No. 3. Samples designed in the study**

| No | Sample Name | Company Name | Brand Name | Color | Shape | Flim Coating | Dosage Form |
|---|---|---|---|---|---|---|---|
| 1 | A | Incepta | Tridosil 250 mg | Pink | Caplet | Flim | Tablet |
| 2 | B | Healthcare | Rozith 250 mg | White | Caplet | Flim | Tablet |
| 3 | C | Drug International | Azimex 250 mg | Blue | Round | Flim | Tablet |
| 4 | D | Reneta | Zithrin 250 mg | White | Caplet | Flim | Tablet |
| 5 | E | Aristopharma | AZ 250 mg | White | Caplet | Flim | Tablet |

## 2.3. Preparation of 0.1 M Phosphate buffer

Added 11.8gm KH2PO4 and  2.3gm K2HPO4 in 100 ml water .Then adjusted the pH 6 of solution .This is the procedure to prepare 100 ml 0.1M phosphate buffer. But to perform a complete procedure different volume of phosphate buffer was prepared .

## 2.4. Preparation of standard solution

Azithromycin 0.1 gm was taken in a 100 ml volumetric flask added with 0.1M phosphate buffer pH 6 and dissolved it. The volume was adjusted to 100 ml  and then 1 ml of the solution was taken and further diluted to 100 ml to make concentration of  100 μg/ ml. Then a series of standard solution of standard azithromycin  eg,  10μg/ml,  20μg/ml,  30μg/ml,  40μg/ml, 50μg/ml,60μg/ml,  70μg/ml,  80μg/ml,  90μg/ml, 100μg/ml etc.  were check for Absorbance at 298nm against a blank for each solution by UV-spectrophotometer (Shimadzu). The measured absorbance's were plotted against the respective concentration of the standard solutions which give a straight line.

## 2.5. Preparation of sample solution

The water bath was checked, added water to maintain desired water level. Then 900 ml of phosphate buffer pH 6 in each of the six vessels of the apparatus was taken, thermostat was adjusted at $37 \pm 0.5°C$. After attaining this temperature the rotation was adjusted at 75 rpm. One Tablet was placed in each of the five vessels. The apparatus were operated for 45 minutes. Then 5 ml of samples from each of the vessels was withdrawn and 5ml filled by 0.1M phosphate buffer pH 6 into each of the vessels. Filtered and collected the filtrate. Diluted 1ml of this solution to 100 ml with 0.1M  phosphate buffer pH 6.

## 2.6. Evaluation Test:

1. Weight Variation Test.
2. Disintegration Test.
3. Dissolution Studies.
4. Friability Test.

## 2.7. Methods

## 2.7.1. Weight variation procedure:

Ten tablets were taken and weighted individually by an analytical balance. The average weight of the tablets was calculated. Then % of weight variation is calculated by using the following formula:

% of weight variation = {(individual weight –average weight)/average weight} × 100.

Then RSD% was calculated.

## 2.7.2. Friability test procedure:

Friability test can be performed to evaluate the ability of the tablets to withstand abrasion in packing, handling and transporting. The Friabulator consists of a plastic chamber divided into two parts and revolves at 25 rpm. A fixed number of tablets are weighed, placed in the tumbling chamber and rotated for four minutes of 100 revolutions. During each revolution the tablets fall from a distance of six inches to undergo shock. After 100 revolutions the tablets are again weighed. The loss in weight indicates the friability. The acceptable limits of weight loss should not be more than 0.5-1% . The friability (f) is given by:

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

## 2.7.3.Disintegration test procedure:

About 700ml distilled water was taken in 1000ml beaker and the beaker was placed into the device.  One Azithromycin was placed in each tube of basket rack &plastic disk is placed over each tablet & the basket rack is accurately positioned into the beaker. The temperature was maintained as a motor driven device helps to move the basket up  down through a distance of 5-

6cm at a rate of 28-32 cycles per minutes. The time at which all the azithromycin tablets passed through the sieve was the disintegration time & the average disintegration time were calculated.

## 2.7.4. In-vitro dissolution test procedure:

About 900 ml of 0.1M phosphate buffer was filled into 1000ml beaker of dissolution apparatus. One Azithromycin tablet was placed into each beaker. The dissolution medium was heated up to 37±5 degree c by an auto heater & 75 r.p.m was adjusted.5ml solution were withdrawn from beaker at 10 minutes interval which was replaced with another 5ml distilled water & then withdrawn solution was filtered through filter paper. The withdrawn solution of the sample was suitably diluted & absorbance was measured at 298 nm by using UV-visible spectrophotometer. Finally the percent release of Azithromycin tablet was determined.

## 2.7.5.Assay of Potency:

The potency of five brands of Azithromycin tablets were determined as following-

- § Average weights of five tablets were determined.
- § Five tablets were crushed.
- § Tablet powder equivalent to 0.1gm of Azithromycin was taken.
- § It was dissolved in distilled water.
- § Then it was shaken for genteelly.
- § The filtrate was suitably diluted.
- § Absorbance was taken at 298 nm by using UV-visible spectrophotometer.
- § Finally the potency of Azithromycin tablet was determined.

# Chapter 3
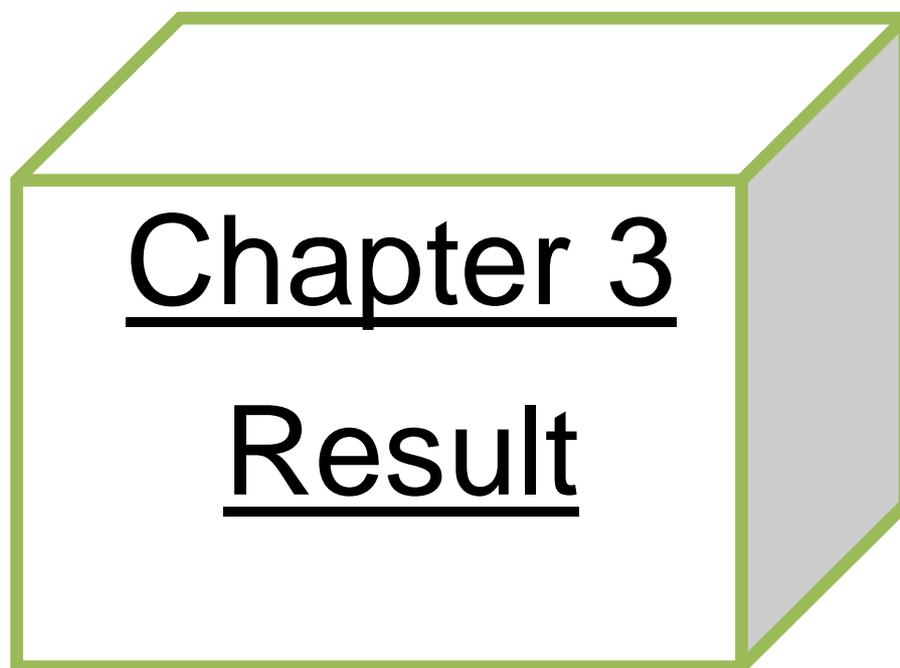
# Result

## RESULT

### 3.1. Weight Variation of each brand

**Table No. 5. Weight Variation of Sample A**

| Tablet number | Wt. of tablet (mg) | Average wt. (mg) | Wt. Variation (%) | RSD% |
|:---:|:---:|:---:|:---:|:---:|
| 1 | 424 | | 0.700 | |
| 2 | 427 | | 0.630 | |
| 3 | 424 | | 0.700 | |
| 4 | 423 | | 0.300 | |
| 5 | 426 | 424.3 | 0.400 | 0.187 |
| 6 | 422 | | 0.540 | |
| 7 | 425 | | 0.160 | |
| 8 | 424 | | 0.700 | |
| 9 | 426 | | 0.400 | |
| 10 | 422 | | 0.540 | |

**Table No. 6. Weight Variation of Sample B**

| Tablet number | Wt. of tablet (mg) | Average wt. (mg) | Wt. Variation (%) | RSD% |
|:---|:---|:---|:---|:---|
| 1 | 676 | | 0.547 | |
| 2 | 673 | | 0.311 | |
| 3 | 676 | | 0.134 | |
| 4 | 668 | | 0.875 | |
| 5 | 684 | **673.9** | 1.498 | 0.547 |
| 6 | 684 | | 1.498 | |
| 7 | 665 | | 1.320 | |
| 8 | 677 | | 0.460 | |
| 9 | 665 | | 1.320 | |
| 10 | 671 | | 0.430 | |

**Table No. 7. Weight Variation of Sample C**

| Tablet number | Wt. of tablet (mg) | Average wt. (mg) | Wt. Variation (%) | RSD% |
|---|---|---|---|---|
| 1 | 630 | | 3.261 | |
| 2 | 617 | | 1.130 | |
| 3 | 620 | | 1.622 | |
| 4 | 655 | | 7.359 | |
| 5 | 603 | | 0.163 | |
| 6 | 588 | **610.1** | 1.623 | 1.878 |
| 7 | 600 | | 1.655 | |
| 8 | 597 | | 2.174 | |
| 9 | 598 | | 1.983 | |
| 10 | 593 | | 1.622 | |

**Table No. 8. Weight Variation of Sample D**

| Tablet number | Wt. of tablet (mg) | Average wt. (mg) | Wt. Variation (%) | RSD% |
|---|---|---|---|---|
| 1 | 456 | | 1.03 | |
| 2 | 447 | | 0.68 | |
| 3 | 461 | | 0.89 | |
| 4 | 458 | | 0.54 | |
| 5 | 446 | | 1.59 | |
| 6 | 450 | **456.5** | 1.77 | 0.962 |
| 7 | 469 | | 1.21 | |
| 8 | 465 | | 0.68 | |
| 9 | 455 | | 0.33 | |
| 10 | 458 | | 0.85 | |

**Table No. 9. Weight Variation of Sample E**

| Tablet number | Wt. of tablet (mg) | Average wt. (mg) | Wt. Variation (%) | RSD% |
|---|---|---|---|---|
| 1 | 383 | | 0.674 | |
| 2 | 392 | | 1.659 | |
| 3 | 385 | | 0.155 | |
| 4 | 389 | | 0.881 | |
| 5 | 389 | **385.6** | 0.881 | 0.674 |
| 6 | 389 | | 0.881 | |
| 7 | 377 | | 2.230 | |
| 8 | 387 | | 0.363 | |
| 9 | 385 | | 0.155 | |
| 10 | 380 | | 1.452 | |

## 3.2.Disintegration test

**Table 10: Disintegration time of 5 brands of Azithromycin tablets**

| Serial no. | Marketed sample | Average disintegration time min |
|---|---|---|
| 1 | Sample A | 7 |
| 2 | Sample B | 8 |
| 3 | Sample C | 11 |
| 4 | Sample D | 9 |
| 5 | Sample E | 14 |
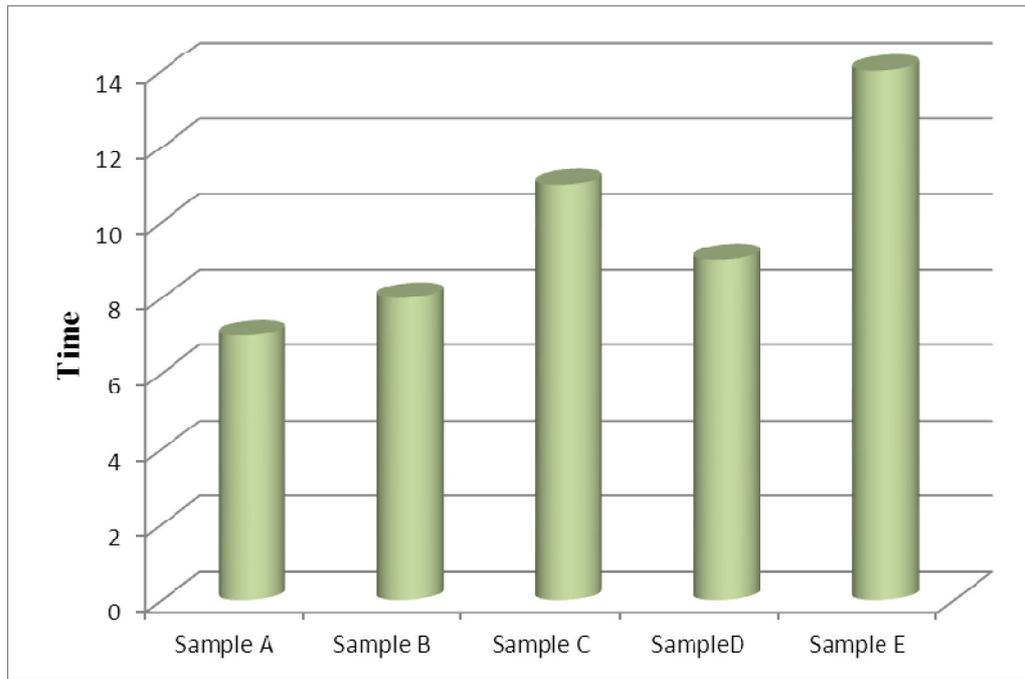
**Fig: 3.1.1-Bar Diagram of Average Disintegration time (min) of different Marketed Sample:**

### 3.3.Potency test:

The potency of five Brands of Azithromycin tablets was determined.  The obtained results were shown in the Table11.

**USP specification**:

Azithromycin tablets contain an amount of Azithromycin equivalent to not less than 90.0 persent & not more than 110.0percent.of the labeled amount of Azithromycin.. From the result, it is evident that 4 out of five brands of Azithromycin tablet meet the specification of potency whereas only Brand 5 was more potent than the USP range.

Potency of 5 brand samples .

| SI NO. | Marketed sample | Potency% |
|--------|-----------------|----------|
| 1 | Sample A | 102 |
| 2 | Sample B | 99.08 |
| 3 | Sample C | 106.3 |
| 4 | Sample D | 101 |
| 5 | Sample E | 88 |
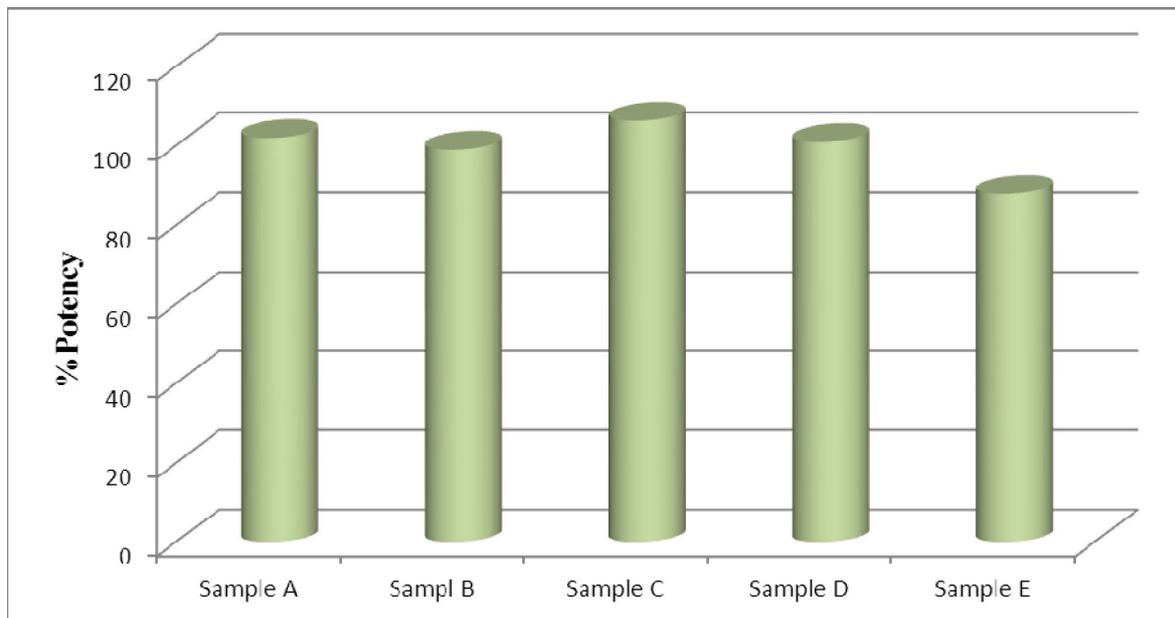


**Fig: 3.1.2-Bar Diagram of Average Potency of different Marketed Sample**

**Preparation of standard curve for Azithromycin.**

A series of standard solution of standard azithromycin eg, 10µg/ml, 20µg/ml, 30µg/ml, 40µg/ml, 50µg/ml,60µg/ml, 70µg/ml, 80µg/ml, 90µg/ml, 100µg/ml etc. were check for Absorbance at 298nm against a blank for each solution by UV-spectrophotometer (Shimadzu). The measured absorbance's were plotted against the respective concentration of the standard solutions which give a straight line.
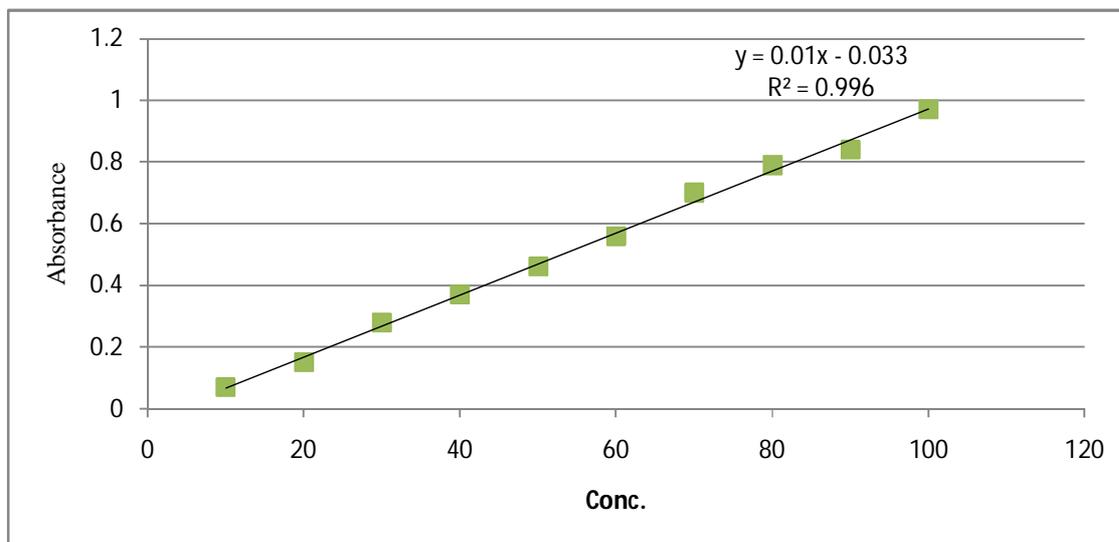


**3.4.Dissolution test:**

The dissolution rate of five brands of Azithromycin tablets was determined. The observed results were shown in table. The drug release% was plotted against the times, which give dissolution curve.

**Table No. 12. Dissolution Test of Sample A**

| NO. | Time min | Absorbance | percent of drug release% |
|-----|----------|------------|--------------------------|
| 1 | 10 | 0.015 | 77 |
| 2 | 20 | 0.142 | 90 |
| 3 | 30 | 0.211 | 99.92 |
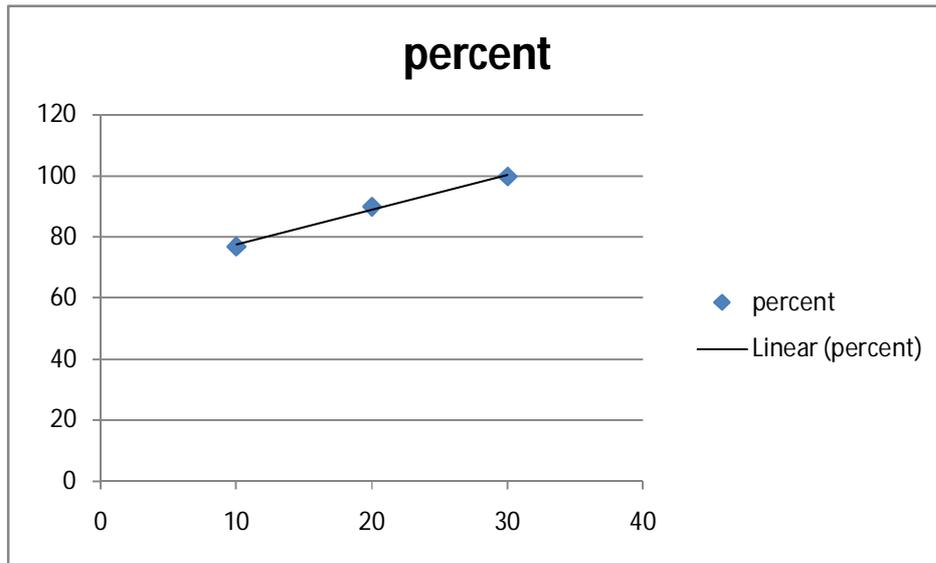
**Fig. Release curve of sample A**

**Table No. 13. Dissolution Test of Sample B.**

| NO. | Time min | Absorbance | percent of drug release% |
|-----|----------|------------|--------------------------|
| 1 | 10 | 0.101 | 70 |
| 2 | 20 | 0.143 | 90 |
| 3 | 30 | 0.246 | 102 |
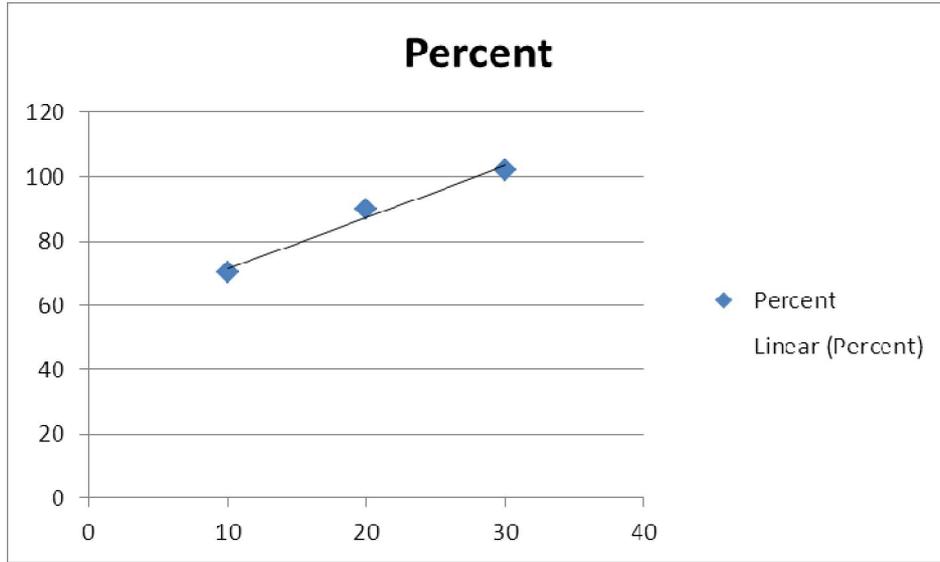
**Fig. Release curve of sample B**

**Table No. 14. Dissolution Test of Sample C**

| NO. | Time min | Absorbance | percent of drug release% |
|-----|----------|------------|--------------------------|
| 1 | 10 | 0.102 | 75.05 |
| 2 | 20 | 0.142 | 90 |
| 3 | 30 | 0.198 | 98.95 |
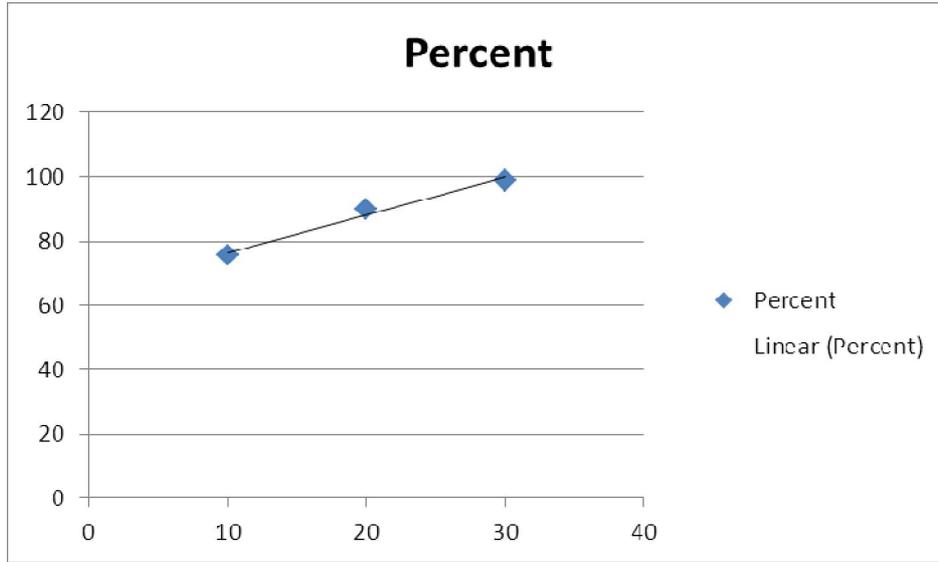
**Fig. Release curve of sample C**


**Table No. 15. Dissolution Test of Sample D**

| NO. | Time min | Absorbance | percent of drug release% |
|-----|----------|------------|--------------------------|
| 1 | 10 | 0.101 | 75 |
| 2 | 20 | 0.142 | 90 |
| 3 | 30 | 0.267 | 106 |
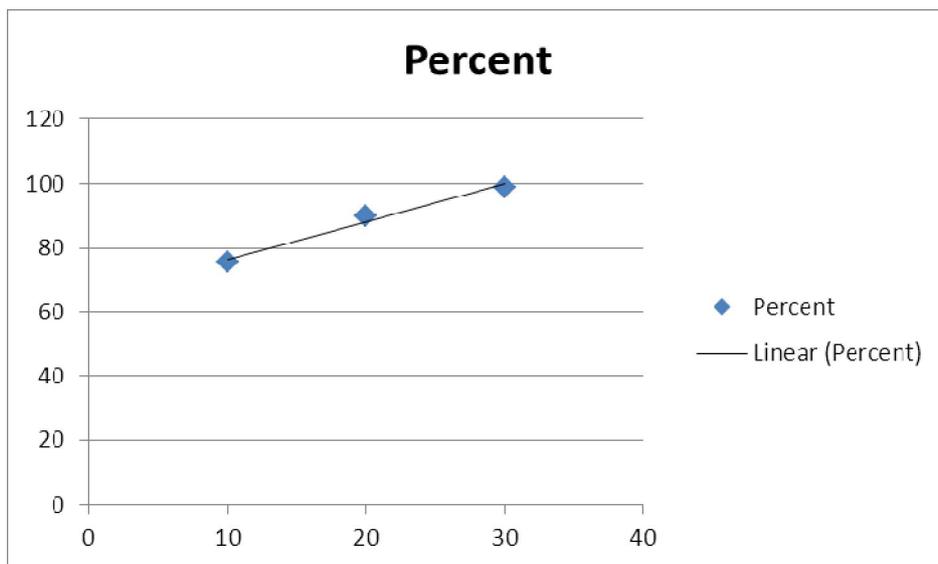
**Fig. Release curve of sample D**

**Table No. 16. Dissolution Test of Sample E**

| NO. | Time min | Absorbance | percent of drug release% |
|-----|----------|------------|--------------------------|
| 1 | 10 | 0.065 | 60.75 |
| 2 | 20 | 0.102 | 71.05 |
| 3 | 30 | 0.225 | 87 |
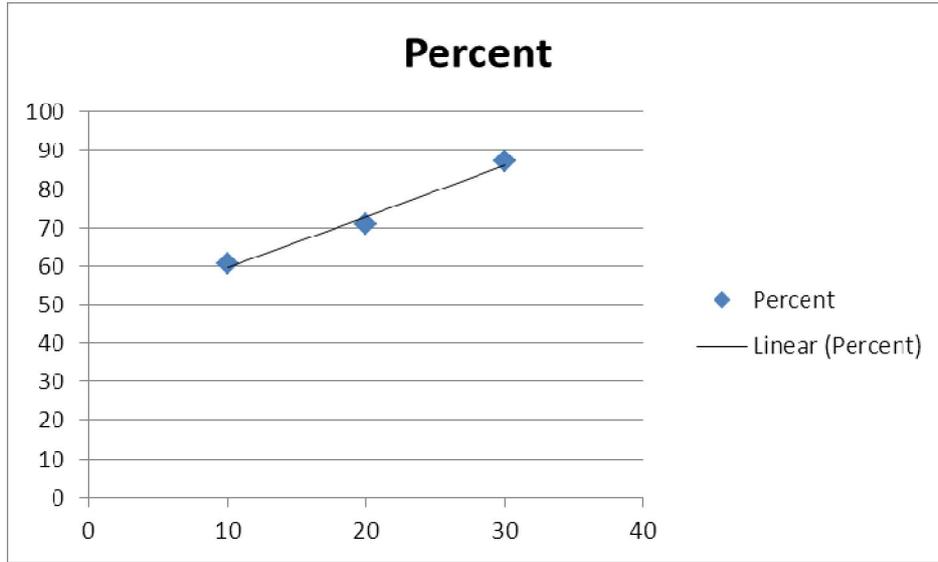
**Fig. Release curve of sample E**

## 3.5. Friability Test:

**Table No. 23.  Friability Test of  5 Brand samples.**

| No. | Marketed Sample | Friability (%) |
|---|---|---|
| 1 | Sample A | 0.659 |
| 2 | Sample B | 0.503 |
| 3 | Sample C | 0.512 |
| 4 | Sample D | 0.793 |
| 5 | Sample E | 0.464 |

# Chapter 4
# Discussion
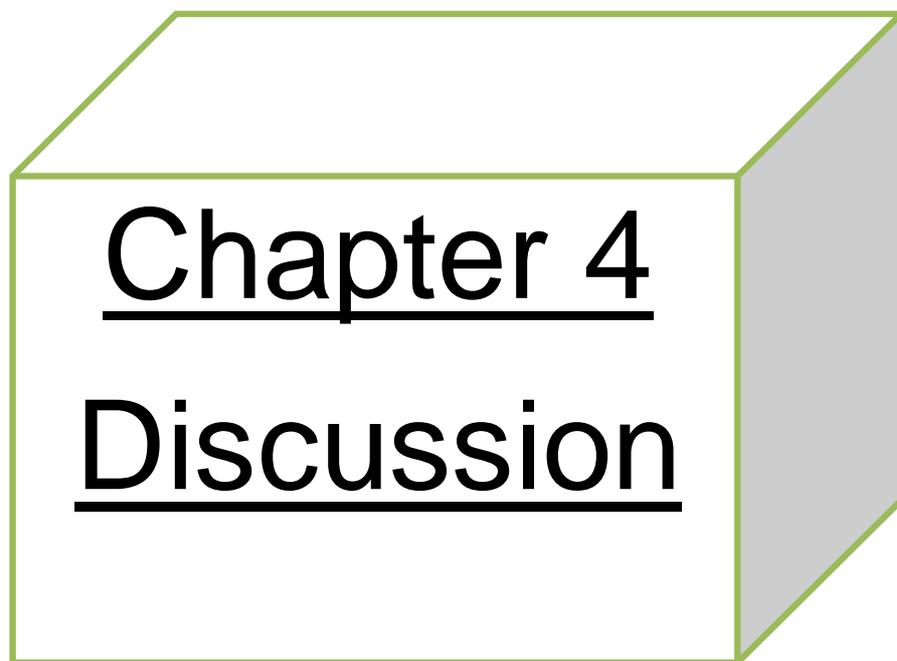
## DISCUSSION

All the samples used for the study were within their shelf life at the time of investigation. All brands showed acceptable uniformity of weight as none had percent deviation in weight greater than 5% as stipulated by the USP .The significance of this test is to ensure that the tablets in each Lot are within the appropriate size range.

The crushing strength of the tablets is an essential criterion in the determination of the ability of the tablets to resist chipping, abrasion or breakage under conditions of storage, transportation and handling before storage.

The dissolution test is a measure of the amount of the drug released into the dissolution medium with time. In case of dissolution the results of product Azithromycin, Sample **A**77%(after 10 min), 90%(after 20 min), 99.92%(after 30 min). Sample **B** 70%(after 10 min), 90%(after 20 min), 102%(after 30 min). Sample **C** 75.05%(after 10 min), 90%(after 20 min),98.95%(after 30 min). Sample **D**75%(after 10 min),90%(after 20 min),106%(after 30). Sample **E**60.75%(after 10 min),71.05%(after 20 min),87%(After 30 min) respectively. All the brands passed the dissolution test except in buffer medium. This may be due to the nature of excipients used or the formulation process. This implies that the product may not release a significant amount of the drug on absorption into the systemic circulation and thus leading to therapeutic failure.

Disintegration cannot be explained by any particular theory. It occurs according to the disintegrates used in the formulation. In case of disintegration, the results were from 7 , 8, 11, 9, minutes to 14 minutes. Disintegrates can act by swelling in the pressure of water to make the tablet burst in the gastrointestinal medium. Starch in the commonest disintegrates used in tablet formulation and is believed to act by swelling. However other effective disintegrants do not swell in contact with water and the mechanisms by which they act is the subject of some controversy. It is believed that disintegrants that do not swell exert their disintegrating action by capillary action. Liquid is drown up through capillary pathways within the tablet and ruptures the inter-particulate bond. This action serves to break the tablet apart. Such tablet fragmentation may be critical to the subsequent dissolution of the drug and to the attainment of satisfactory drug bioavailability.

Disintegration is the pre step of dissolution. The most important step for a solid dosage from is dissolution through which a solid drug within the dosage from enters into solution and related in the surrounding liquid medium.

Disintegration is a process which causes the tablet to break rapidly so as to increase the surface area of the tablet fragments and promote rapid release of the drug.

The disintegration test measures the time required for tablets to disintegrate into particles. This is a necessary condition for dissolution and could be the rate-determining step in the process of drug absorption. The USP stipulates a disintegration time of not less than 45min for enteric coated tablets. The results of the disintegration test are showed above.The results showed that brands Sample A, Sample B, Sample C and Sample E conformed to the required standard for disintegration, while brands Sample D failed to comply. This failure could have resulted from the use of excess amountof binding agent during formulation, excess moisture content during compression.

Release rate of drug is greater from disintegrated particles than from the intact tablet or tablet fragments. For this disintegration is an important step for tablet doses from Disintegration test, included in all pharmacopeias, is used as an important quality assurance tool to indicate not only the time required for the breakdown of a tablet but also batch to batch consistency.

It is well recognized that dissolution is facilitated by disintegration and any factor which affects disintegration also influence dissolution. Several factors such as selection of disintegrates, binders, lubricants, tablet hardness, manufacturing procedure etc. can significantly affect the disintegration time of compressed tablets.

# Chapter 5
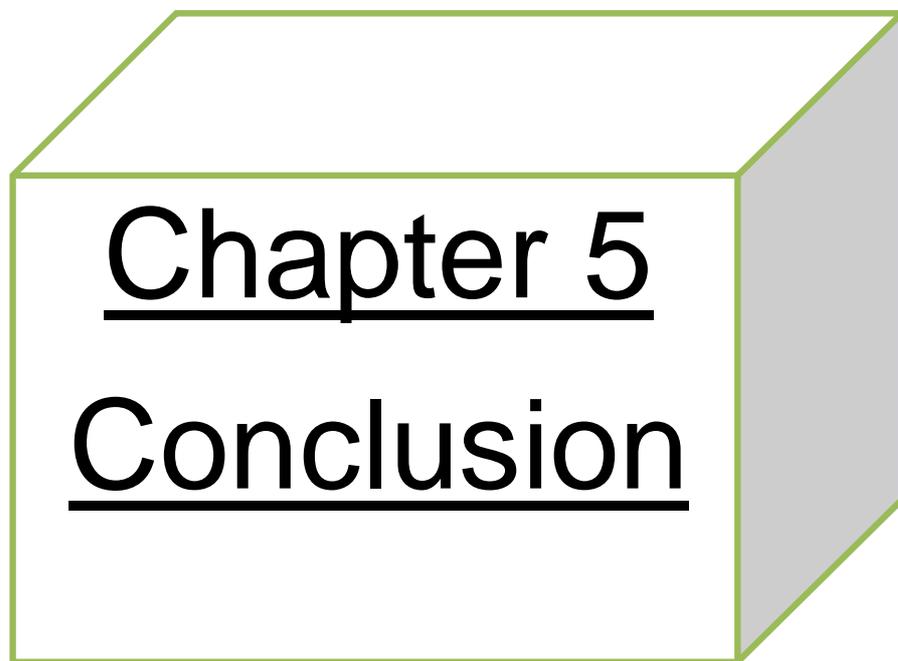
# Conclusion

# CONCLUSION

The five brands of Azithromycin Flim coated tablets evaluated in this study therefore be freely interchanged. The disintegration test of Azithromycin conformed to the required standard for disintegration.

The study demonstrates clearly the divergences in the dissolution behavior of azithromycin release sufficient amount after 10 and 20 minutes but after 30 minutes it release drug more than after 10 and 30 minutes.

The present work reports the comparative study and quality evaluation of tablets formulated by five different pharmaceutical companies ,it was observed that there was some variation in the dissolution rates and weight variation but there was no much variation in the pattern of friability of tablets of the five companies. It need high sophisticated machine for which we could not found the final findings so its need further study.

# Chapter 6
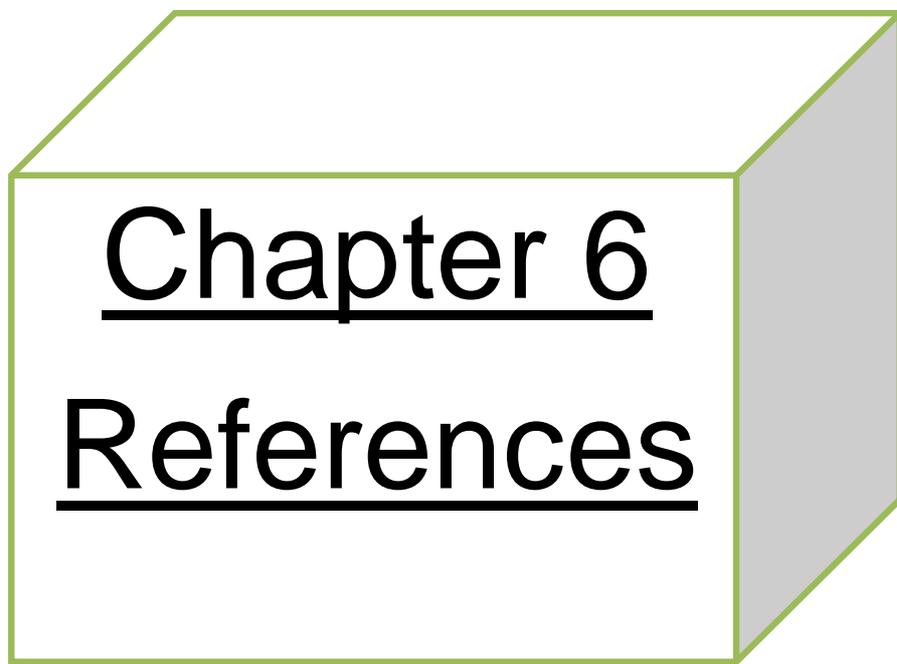
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