International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Formulation and Evaluation of Azithromycin Tablet

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A B S T R A C T

Drugs can be administered through different routes; however, of all the routes of administration, oral route of administration is most convenient for administering drugs for systemic effect because of ease of administration and dosage adjustments. From the present work, it can be concluded that the results suggested that the prepared formulations were stable and globally acceptable. Azithromycin is the drug of choice in the treatment of several bacterial infections, most often those causing middle ear infection, bronchitis, pneumonia, typhoid and sinusitis. It's also effective against certain urinary tract infections and venereal diseases. This study was carried out to prepare an acceptable tablet preparation either as dry physical mixture powder or granules to be reconstituted, through studying the effect of various type of Lubricant (Magnesium Stearate), Wetting agent (Sodium lauryl Sulphate), Binder (Pregelatinized starch) etc. The research work was done with economical, commercial and regulatory point of view.

1. INTRODUCTION

The main aim of pharmaceutical formulation is to get better therapeutic activity in the shortest possible time by using smallest amount of drug administered by the most suitable route[1].

Drugs can be administered through multiples routes; however, of all the routes of administration, oral route of administration is most convenient for administering drugs for systemic effect because of ease of administration and dosage adjustments [2.] Parenteral route is not commonly used because of difficulty in self-administration and hospitalization may be required. Topical route is recent developed and is employed for only few drugs like scopolamine, nitroglycerine, for systemic effect[20]. Parenteral administration is employed in case of emergency and in which the subject is comatose or cannot swallow. However, it is possible that at least 90% of drug is administered by oral route to produce systemic effect Solid dosage forms of tablets and capsules are more commonly employed, the tablets have advantages than capsules in that they are tamper resistant and any adulterant of the tablet after its manufacture is almost certain to be observed. The adulteration can be easily found if it is done in either liquid form or solid form since deformation takes place, if it is done in liquid form and powders cannot be added to the tablet if once, they are formed. The main disadvantage of capsules over tablet is their higher cost. The capsules either hard capsule or soft capsule they are susceptible to breakage if they are not stored properly.

1.1 TABLETS [2,5,7,23,26]:

Tablets are solid pharmaceutical dosage forms that can be moulded or compressed, and they can contain medicinal ingredients with or without the proper diluents. Tablets are also described as "Solid preparations" in the European Pharmacopoeia, which are "obtained by compressing uniform volume of particles and each containing a single dose of one or more active components." Since the latter half of the 19th century, they have been used extensively, and their popularity has continueds[1,2].

Because of the benefits they provide both to the maker and the patient, including accuracy of dosage, compactness, post ability, blandness of taste, and ease of administration, tablets continue to be a preferred dosage form.

Although tablets are more frequently discoid in shape, they also may be round, oval, oblong, cylindrical or triangular. They may differ greatly in size and weight depending on the amount of drug substance present and the intended method of administration.

a) Properties of Tablets [1,26]:

The following characteristics of a suitable tablet must be present:

- The tablet must be sufficiently robust and resistant to stress and abrasion as well as handling during production, packing, shipping, and use. Tests for hardness and friability quantify this quality.
- Both the weight and medication content of each tablet must be the same. The weight variation and content uniformity tests are used to gauge this.

- The medicine in the pill needs to be bioavailable. The dissolving test is used to gauge this feature. After a medicine has been administered, the drug's levels can be used to determine the precise bioavailability.
- Tablets must have a classy design and distinctive shape, colour, and other characteristics to enable easy product identification.
- Tablets must maintain all of these functional characteristics, such as drug.

b) Advantages of Tablets [2,13,24,26]:

- They are easy to administer. They are unit dosage form, and they provide all oral dosage forms with higher capabilities for the most precise dosing and the least amount of content variability.
- They are the least expensive oral dose forms.
- Compared to other oral dosage forms, they are the lightest and most portable.
- They are generally the easiest and least expensive oral dose forms to package and ship.
- Product identification is possibly the simplest and least expensive, needing no additional processing steps when employing an embossed or monogrammed punch face. They may provide the greatest ease of swallowing with the least tendency for ―hang-up‖ above the stomach. Especially when coated, provided that tablet disintegration is not excessively rapid.
- In comparison to other unit oral forms, they are better suited to large-scale manufacture and have the best-combined features of chemical, mechanical, and microbiological stability.
- They also lend themselves to some unique release profile goods, such as enteric or delayed release products. One of the major advantages of tablet over capsules is that the tablet is essentially ―tamperproof dosage form‖.

c) Disadvantages of Tablets [24,26]:

- Due to their flocculent, low-density nature or amorphous nature, several medications defy compression into dense compacts.
- It may be difficult or impossible to formulate and manufacture a tablet for a drug with poor wetting, slow dissolution properties, intermediate to large dosages, optimal absorption high in the gastrointestinal tract, or any combination of these features while maintaining adequate or full drug bioavailability.
- Drugs that have an unpleasant taste, an offensive odour, or are sensitive to oxygen or moisture in the air may need to be encapsulated or coated with a unique material to make the most of the final tablets.

d) Types of Tablets [1,24,26]: [Classification of tablet]

The function or administration route of tablets determines their classification. The five primary classification categories are listed below:

- **Tablets ingested orally:**
  - Compressed tablets
  - Multiple compressed tablets
  - Multilayered tablets
- **Sustained action tablets**
  - Enteric coated tablets
  - Sugar coated tablets
  - Film coated tablets
  - Chewable tablets
- **Tablets used in the oral cavity:**
  - Buccal tablets
  - Sublingual tablets
  - Lozenge tablets and torches
  - Dental cones
- **Tablets administered by other routes:**
  - Implantation tablets

- Vaginal tablets

- **Tablets used to prepare solutions**:
  - Effervescent tablets
- **Molded tablets or tablet triturates (TT)**:
  - Dispensing tablets (DT)
  - Hypodermic tablets (HT)

1.2 TABLET MANUFACTURING [4,13,23]:

Tablets are compressed powders and their manufacturing is a complex, multistep process. The ultimate aim is to easily disperse in gastrointestinal fluid and in complete absorption of API and at the same time, offer stability to the formulation.

The production of tablets can be generally classified into:

a) Granulation method

1) Wet granulation method

2) Dry granulation method

b) Direct compression method

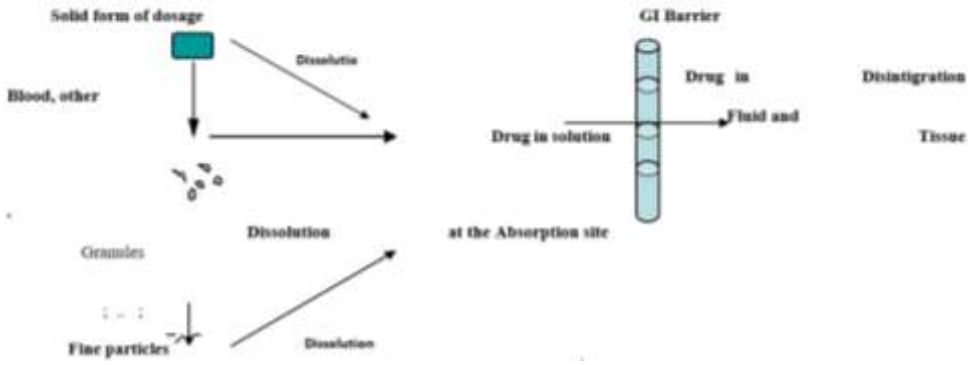


Fig No. 1: Absorption and Dissolution of Drugs from Solid Form Dosage (7)

When a drug is administered orally in a solid dosage form such as tablet, capsule it must be released from the dosage form and dissolved in the gastro intestinal fluid before it can be absorbed (3).

Numerous medications that are weakly water soluble have bioavailability restrictions due to their dissolution rates, which are in turn governed by the surface area they present for dissolution. 6. It is possible to separate the oral absorption of medicines from solid dosage forms into two sequential transport mechanisms.

1. The drug's in-vivo dissolution to produce a solution
2. Moving the dissolved drugs across the GIT barrier.

Each process has a rate constant that can be used to describe it. If a drug's rate of dissolution is much slower than its rate of absorption, the drug's dissolution becomes the rate-limiting phase in the absorption process, and the drug's particle size is more crucial for transport from the GI tract to the site of action Most drugs are passively absorbed and their rates of absorption are dependent upon the concentration gradients in each case; by increasing the dissolution rate in GI tract, the absorption rate increases, so long as the dissolution rate is still the limiting step[5]. This commonly occurs for drugs with limited water solubility.

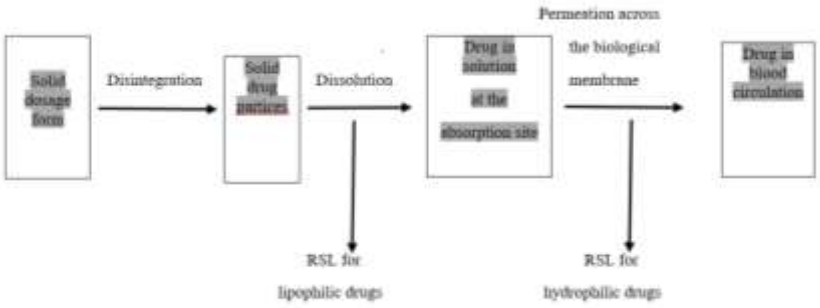


Fig No. 2: Drug Absorption from Orally Administered Formulations: The Two Rate Limiting Steps

1.3 FACTORS INFLUENCING DRUG ABSORPTION FROM ITS DOSAGE FORM (3,7,23):

a) Pharmaceutical factors: Take into account aspects of the drug's physicochemical nature, dosage form characteristics, and pharmaceutical constituents.

b) Physico-chemical property of the drug substance.

- ✓ Drug solubility and dissolution rate
- ✓ Particle size and effective surface area
- ✓ Polymorph and amorphism
- ✓ Pseudo polymorphism
- ✓ Salt form of the drug
- ✓ Lipophilicity of the drug
- ✓ P^{ka} of the drug and pH
- ✓ Drug stability

c) Dosage Form Characteristics

- ✓ Disintegration time
- ✓ Dissolution time
- ✓ Manufacturing variables
- ✓ Pharmaceutical ingredients (excipients / adjuvants)
- ✓ Nature and type of dosage form
- ✓ Product and storage conditions

2. **Patient-Related Factors:** Consider all aspects of the anatomical, physiological and pathological characteristics of the patient

- ✓ Age
- ✓ Gastric emptying time
- ✓ Intestinal transit time
- ✓ Gastro intestinal pH
- ✓ Disease states
- ✓ Blood flow through the GIT
- ✓ Gastrointestinal contents
- ✓ Pre-systemic metabolism

2.0 Macrolides antibiotics [6]:

Due to their potential use in human medicine, macrolides comprise a sizable family of protein synthesis inhibitors that are of great therapeutic interest.

Macrolides are made up of a macrocyclic lactone with one or more deoxy sugar or amino sugar residues attached. These residues might have varied ring diameters.

By attaching to the bacterial 50S ribosomal subunit and impeding protein synthesis, macrolides function as antibiotics.

Macrolides' broad-spectrum activity is compatible with their high affinity for bacterial ribosomes and the structure's high degree of conservation across almost all bacterial species.

Since the progenitor macrolide, erythromycin, was discovered in 1950, several derivatives have been synthesized, resulting in drugs with improved pharmacokinetics, acid stability, and bioavailability.

The second generation of macrolide, which includes well-known members like azithromycin and clarithromycin, is the result of these efforts.

The development of a third generation of macrolides with improved action against numerous strains that were resistant to macrolides was then undertaken to address the issue of rising antibiotic resistance.

However, these enhancements were accompanied by negative side effects that disappointed many researchers and led them to give up on macrolide derivative research, thinking that the process had reached its conclusion. On the other hand, a recent scientific discovery unveiled a fresh chemical framework for the synthesis and development of a wide variety of unique macrolide antibiotics.

This chemical synthesis breakthrough has raised hopes for new, risk-free therapeutic medicines to treat important human infectious diseases by reducing side effects, or "Ketek effects," and expanding the use of macrolides.

3.0 Azithromycin profile

Azithromycin is one of macrolide antibiotic it has been used for more than a decade to treat various infections, particularly those of the urinary tract, bronchial tract, lungs, sinuses, and the middle ear.

The unique pharmacokinetics of azithromycin— rapid oral absorption, extensive distribution into tissues, and a long serum half-life of ~68 hours1— allows for a short 3-day (500 mg/day for 3 days) or 5-day (500 mg on day 1 followed by 250mg on days 2–5) course of therapy.

AUC/MIC ratio has been linked to azithromycin efficacy in preclinical trials, and giving the therapeutic courses all simultaneously as a single dose may boost efficacy. (i.e., ‘front loading’ or one dose only)2.

A single-day therapy would also have the advantage of improved patient compliance. However, side effects, such as nausea, vomiting, and diarrhea, limit the maximum dose of azithromycin that can be administered.

Thus, the aim of this work was to develop a new formulation of azithromycin that would allow administration of a full course of therapy in a single dose without compromising toleration.

Three factors were considered in the design of the 2-g single-dose azithromycin formulation:

(i) improving gastrointestinal (GI) toleration,

(ii) minimizing loss of bioavailability because of an absorption window, and

(iii) masking azithromycin's unpleasant taste.

The GI side effects associated with azithromycin increase with the increase in dosage, and previous studies with intravenous administration have indicated that they are not related to systemic drug levels but to the local drug concentration in the GI tract, possibly because of the action of azithromycin on motilin receptors located in theupper GI tract.

Intubation studies suggested that improved toleration would result when azithromycin was delivered directly to the ileum versus the duodenum.

Preclinical models indicate that azithromycin may have poor colonic absorption. Clinical studies with formulations having very long delivery durations confirmed that azithromycin had an absorption window, that is, poor absorption in the colon leading to low relative bioavailability compared to an immediate release formulation

. Thus, a 2-g dose of azithromycin delivered over a relatively short duration could result in improved toleration without significantly lowering the relative bioavailability. Particle size has an effect on palatability (bitterness, mouth feel, and texture), and to have acceptable palatability, azithromycin release in the mouth has to be minimized and to avoid a gritty mouth feel, the microspheres' particle size must be tiny. Conventional sustained release tablets and capsules were eliminated from consideration as the 2-g dose could not be formulated in a single unit of reasonable size.

Consistent with dose-solubility map for technology selection6, sustained release multi particulates given as an oral powder for constitution were selected because they provide a means for delivering a large dose as well as other components such as flavors, sweetener, and buffers.

Furthermore, multi particulates have the advantage of being rapidly emptied from the stomach, thereby minimizing drug release in the upper duodenum. The delivery duration would be designed such that the drug would be absorbed prior to the multi particulates reaching the colon. Several methods exist to prepare multi particulates including extrusion–spheronization, balling (spherical agglomeration), spray congealing, and cryopelletization8.

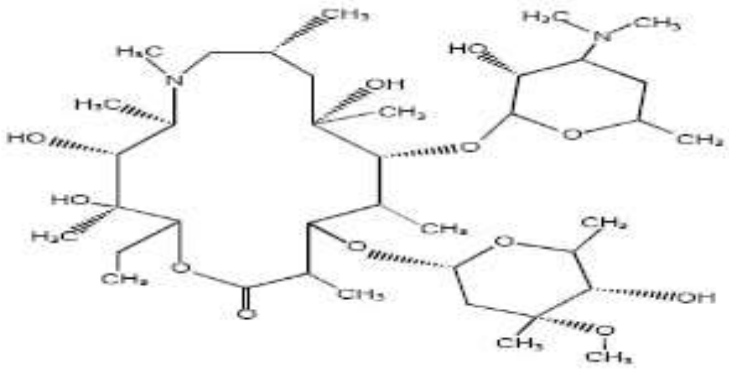
The small particle size of microspheres from spray congealing offers the advantage in formulating a suspension.

In this procedure, azithromycin dihydrate was suspended in the molten carrier matrix to create microspheres. Using a spinning-disk atomizer, this suspension was sprayed to create droplets, which then solidified into microspheres after cooling. Typical low melting point matrix materials that have been mentioned in the literature are waxes, fatty acids, glycerides, stearic acid, and stearyl alcohol, and other materials are solids at normal temperature and melt without decomposition. In addition to the microspheres, the final powder for oral suspension also contained a vehicle blend containing taste-masking components (sweetener and flavors), colorants, and suspending agents.

Additionally, the vehicle also contained alkalizing agents, which were designed to keep a high pH of the constituted suspension to prevent drug release while in suspension and for taste masking. The alkalizing agents also reduced the frequency of GI side effects by increasing the gastric Ph for a short period of time and further reducing the rate of drug release in the stomach10. The choice and quantity of alkalizing agents were optimized in a clinical study. The final formulation is conveniently administered after constituting with 60 mL of water; the entire contents are orally administered as a single dose.

0bb It should be used within 12 hours of mixing and taken 1 hour before or 2 hours after a meal. The formulation was approved in the United States by the FDA in 2005 and this commercially available as Zmax™ (Pfizer Inc., New York, NY, USA). Several clinical studies have been conducted with this novel formulation to evaluate its pharmacokinetics and tolerability and to demonstrate safety and efficacy in a variety of indications, for example, respiratory tract infections, community-acquired pneumonia, acute bacterial rhinosinusitis, and chronic bronchitis

A) Structure of Azithromycin:



B) Laboratory Chemical Safety Summary(11):

C) Physical and chemical properties:

Mol. Formula Anhydrous Dihydrate	C38H72N2O12 C38H72N2O12. 2H2O
Mol. Wt Anhydrous Dihydrate	748.98 785.0
% Composition	C- 60.94% H- 9.69% N-3.74% O- 25.63%
State	solid (crystalline power)
Odor	Odorless
Taste	not available
M.P	113- 115 ºC (for anhydrous) 126 ºC (for dihydrate)
Color	white
pH	9.0 to 11.0
Solubility	Almost insoluble in water, readily soluble in methylene chloride and anhydrous ethanol.
Specific optical rotation	-45 to -49 (anhydrous substance)
Water contain	1.8% to 6.5% determined on 0.200g
Sulphate ash	maximum 0.2%, determined on 1.0gm
Heavy metals	maximum 25 ppm

4.0 Azithromycin Tablet [9]:

Azithromycin Tablet contains not less than 90.0% of the labelled amount of Azithromycin and not more than 110.0% of the labelled amount of Azithromycin.

1) Description:

White tablet or film coated tablets with Coarse white or nearly white.

2) Identification:

Dissolve quantity of the powder tablets in ethanol to form a solution of 10mg of Azithromycin/ml and filter, using successive filtrate as a test solution. Dissolve a quantity of Azithromycin LRS in ethanol to produce a reference solution of 10mg of Azithromycin/ml, the solution comply with test (1) for identification describe under Azithromycin.

3) Dissolution:

Carryout the dissolution test (method-2) using a phosphate BS (to 6000ml of 0.1mol/L solution of disodium hydrogen phosphate add 40ml of hydrochloric acid, adjust the ph value to 6.0) 900ml as the dissolution medium, adjust the rotation speed of the paddle to 100 rpm. Withdraw the solution after exact 45 minute and filter.

Dilute an accurately measured quantity of the successive filtrate with the same solvent to form a solution of 55µg per ml, as test solution.

Triturate 10 tablets to an accurately weight quantity equivalent to about the average wt of one tab add a quantity of ethanol (using 1ml of ethanol for 2mg of the given amount of Azithromycin) and the dissolution medium,

shake for 30 minutes or ultrasonic ate for 10 minutes to dissolve Azithromycin. Dilute an accurately measured quantity of the successive filtrate with the dissolution medium to form a solution of 55µg per ml and filter, using the successive filtrate as the reference solution.

Measure accurately 5ml each of the two solutions separately to two tubes with stoppers respectively and accurately 5ml of sulfuric acid solution (75→100) mix well, allow to stand for 30 minutes, cool determine the absorbance of the resulting solution at 482nm. Calculate the dissolution of Azithromycin form each tablet 75% or greater dissolve.

4) Assay:

Weigh accurately and triturates 10 tablets dissolve accurately weighed quantity equivalent to 0.25gm Azithromycin in 125ml of ethanol, dilute with sterile water to form a solution of 1000unit per ml, mix well, carry out the assay describe under Azithromycin using the supernatant liquid.

5) Storage:

Preserve in tightly closed container stored in dry place.

3.1 Pharmacokinetics [10,12,14,19]: -

By replacing the carbonyl group at the 9a position of the aglycone ring with a methyl-substituted nitrogen, azithromycin (9-deoxo-9a-aza-9a-methyl-9a-homoerythromycin) is created. It is fairer to refer to the resultant dibasic 15-membered ring macrolide derivative as a "azalide." When compared to erythromycin, the compound has greater activity against gram-negative organisms and decreased activity against a few gram-positive bacteria due to this structural alteration, which also boosts the product's stability in acid, serum half-life, and tissue penetration.

Azithromycin is available as 250-, 500-, or 600-mg tablets; oral suspension (100–200 mg per 5 mL); and intravenous preparation (lyophilized 500 mg per10 mL vial).

1) Absorption:

Azithromycin given orally is about 40% bioavailability absorption from capsule, but not tablet is reduced by food. Peak plasma concentration are achieved 2-3 hours after a dose but Azithromycin extensively distributed to the tissue and tissue concentration subsequently remain much higher than these in the blend. In contrast to other antibacterial plasma concentration is therefore, a little value as a guide to efficacy. High concentrations are taken of in to add blood cell.

At stomach pH, azithromycin is more stable than erythromycin. The fast and widespread absorption from the circulation into the intracellular compartment is shown in the pharmacokinetic properties of azithromycin, followed by a slow release. It has been demonstrated that azithromycin swiftly and deeply penetrates tissues, steady- state levels were 0.64µg/ml at 2 to 4hr,0.1µg/ml at 10 to 12hr, and 0.012µg/ml at 72 to 96hr.Azithromycin remains in human polymorph nuclear leukocyte in vitro for several hr even after extra cellular drug has been removed, and its release can be stimulated by phagocytosis. With a mean tissue half-life of 2 to 4 days, azithromycin levels are persistently elevated in tonsillar tissue, polymorphonuclear leukocytes, vaginal or pelvic tissue, pulmonary macrophages, and these tissues' other tissues as well.

2) Distribution:

Azithromycin is distributes widely throughout the body, except to the brain and CSF. Azithromycin has unique pharmacokinetic properties include extensive tissue distribution and high drug concentration within cells (including phagocytes) resulting in much greater drug concentration in tissue or secretion compared to simultaneous serum concentration. Tissue fibroblast acts as the natural reservoir for the drug in vivo. Protein binding is 50% at very low plasma concentration and less at higher concentration.

3) Metabolism and Excretion:

A small amount of Azithromycin are demethylated in the liver and it is excreted in bile as unchanged drug and metabolites. About 6.0% of oral dose (representing about 20% of the amount in the systemic circulation) is excreted in urine. Due to significant tissue sequestration and eating, the terminally elimination half life, which is 40 to 68 hours, is extended.

3.2 Resistance[17]:

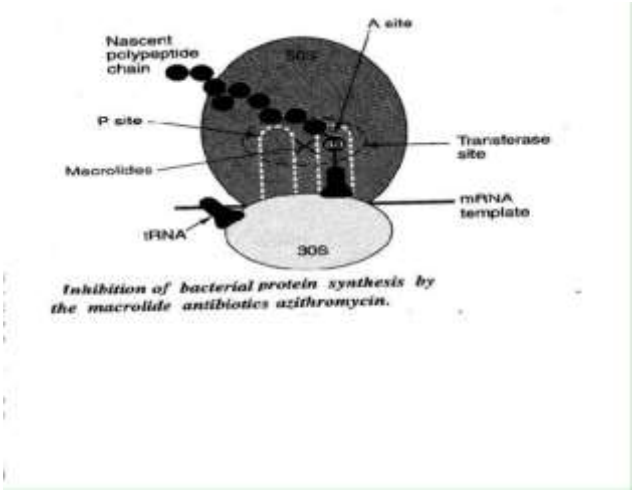
Resistance to macrolides usually results from one of four mechanisms

- Drug efflux by an active pump mechanism (en coded by mrsA, mefA, or mefE in staphylococci, group A. streptococci, or S.pneumoniae, respectively.

- Methylase enzyme protection for ribosomes by inducible or constitutive synthesis, mediated by expression of ermA, ermB, and ermC, which alters the ribosomal target and reduces drug binding..
- Macrolides hydrolysis by esterase's produced by Enterobacteriaceae.
- Chromosomal mutation that alter a 50s ribosomal protein (found in B .sub ilis, campylobacter spp, mycobacteria and gram-positive cocci.

3.3 Mode of action (16):

Macrolide antibiotic are bacteriostatic substances that prevent the production of proteins by forming reversible bonds with the 50s ribosomal subunit of susceptible organisms. As the nascent peptide chain is temporarily located at the a site of the transferase reaction, Azithromycin appears to prevent the translocation step where the peptide chain fails to move to the P or donor site. Alternatively, macrolides could bind and lead to a conformational change that inhibits transpeptidation and translocation by indirectly terminating protein synthesis. Fig no.1



Inhibition of bacterial protein synthesis by the macrolide antibiotics azithromycin.

3.4 Side Effects:

Minor: Abdominal pain, diarrhea, dizziness, headache, nausea, or vomiting. These effects should disappear as your body adjusts to Azithromycin.

Azithromycin can cause increased sensitivity to sunlight. It is important to avoid prolonged exposure to sunlight and sunlamps. Wear protective clothing, and use an effective sunscreen.

If you feel dizzy or light-headed, sit or lie down for a while; get up slowly from a sitting or reclining position; and be careful on stairs.

Major: palpitations, rash, rectal or vaginal itching, shortness of breath, swelling of the face or neck, sore throat, unusual bruising or bleeding, or yellowing of the eyes or skin. If your symptoms of infection seem to be getting worse rather than improving, you should contact your doctor.

3.4 Drug- Interactions(18):

Azithromycin interacts with several medications:

- Azithromycin may increase blood levels of aminophylline, theophylline, carbamazepine, cyclosporine, tacrolimus, disopyramide, phenytoin, digoxin, triazolam, phenobarbital, ergotamine, dihydroergotamine, or oral anticoagulants (blood thinners, such as warfarin) when they are used concurrently; this may lead to serious side effects.
- Antacids containing aluminum or magnesium will decrease the efficacy of Azithromycin. Take antacids 1 hour before / 2 hours after your dose of Azithromycin.
- Avoid using azithromycin if you're also taking pimozide since it could cause more heart-related adverse effects.

3.5 Adverse reactions(18):

Most of the negative effects that were documented during clinical trials were low to moderate in severity & were curable by stopping the medication. About 0.7% of patients in the multiple-dose clinical studies who were taking azithromycin stopped their treatment as a result of side effects.. Most of the side effects leading to discontinuation were related to the GI tract, e.g., nausea, vomiting, diarrhea, or abdominal pain. Rarely but potentially serious side effects were angioedema and cholestatic jaundice.

- **Storage :**

to store this medicine:

1. Keep out of children's reach.

2. Do not Store in heat and direct light.
3. Store the pediatric suspension form of azithromycin in the refrigerator.
4. Do not store in the bathroom, near the kitchen sink, or in other damp places. Heat or moisture may cause the medicine to break down.
5. Do not keep expired or no longer needed medications. Make certain that any discarded medication is out of children's reach..

- **Azithromycin tablet sold under brand name;**

4. Formulation of Azithromycin

- **Objective [7]:**

To develop a non-infringing formulation of Azithromycin, which is stable and bioequivalent to Zithromax of Pfizer and being marketed in domestic.

The strength to be developed is 250 mg.

Qualitative composition of the formulation with respect to the Excipients would be same as that of the innovator.

Quantitative composition would be derived by trials, to ensure a drug product having similar physico-chemical properties as that of the innovator.

- **Manufacturing Process:**

The same manufacturing process and the equipment's used during development would be similar to the intended commercial scale equipment's.

- **Selection of Excipients Sourcing**

The excipients used during development were procured from qualified vendors.

4.1 Function and Justification

a) Diluents: In view of drug dose it is essential to add bulking agents or diluents to increase the weight of the tablet. Microcrystalline cellulose was selected as the main diluent.

b) Disintegrant: Cross Carmel lose sodium we selected as super disintegrant. The strong correlation of disintegration time to bioavailability. Thus, it is important to optimize the disintegration time in order to enhance in vivo dissolution of the drug. In order to release the active ingredient from a solid dosage form matrix as efficiently as possible, disintegrate is often used in the formulation, especially when the dosage forms are compressed with binder. Disintegrates help rupturing the dosage form matrix by swelling or capillary action when moisture is absorbed into the dosage form.

c) Binder: As a tablet binder, pregelatinized starch in concentrations ranging from 0.5 to 5% was employed. Expert formulators can choose the level of binder in their formulations, however binder usage levels of 2-25% in tablet formulations are typical.

d) Lubricants: Magnesium Stearate is widely used as Tablet and Capsule lubricant. It is generally used in concentrations between 0.25 – 5.0 %.

e) Glidant: Colloidal Anhydrous Silica is widely used as Tablet and Capsule Glidant. It is generally used in the concentrations between 0.25 – 3.0 %.

f) Lubricants: Magnesium Stearate is widely used in Tablet and Capsule as a lubricant. It is generally used in the concentrations between 0.25 – 5.0 %.

g) Film former: Hypromellose is broadly used in oral and topical pharmaceutical formulation. It is generally used in coating suspension in the concentrations between 50- 30.0 %.

h) Coating agent: Titanium dioxide is frequently used in pharmaceutical formulations for oral dose. as white pigment and as opacifier in film coating. it is generally used in the concentrations b/w 10.0 – 30.0 %.

i) Plasticizer: polyethylene glycol 6000 is widely used as plasticizer in film coating of tablet. It is generally used in concentrations b/w 5.0 – 20.0 %.

j) Granulation vehicle: Water is widely used for granulating Agent because of no any toxic effect and for non- aqueous solvent we widely use Isopropyl alcohol.

k) Wetting agent: Sodium lauryl sulfate is mainly used as wetting agent. It is generally used in the concentrations b/w 1.0 – 2.0 %.

4.2 Components and composition of the final Formula Strength: 250 mg

Sr.No	Ingredients	Function	Qty/tablet(m g)	% w/w
1	Azithromycin (as dehydrate)	Active	262.00*	81.88
2	Microcrystalline cellulose	Diluent	19.06	5.96
3	Croscarmellose sodium	Disintegrant	2.90	0.91
4	Pregelatinized starch	Binder	12.00	3.75
5	Sodium lauryl Sulphate	Wetting agent	0.64	0.20
6	Purified water	Granulating fluid	Qs	Qs
7	Syloid 244 FP	Glidant	4.80	1.81
8	Magnesium Stearate	Lubricant	4.80	1.50
9	Hypromellose	Film former	6.05	1.89
10	PEG-6000	Plasticizer	0.85	0.27
11	Titanium di oxide	Opacifier	0.50	0.16
12	Quinoline yellow	Colorant	0.10	0.03

CONCLUSION

Azithromycin's pharmacokinetics and tolerability make it particularly useful in the treatment of sexually transmitted infections, intracellular enteric pathogens and for prophylaxis of mycobacterial disease. it also included advantages and disadvantages of azithromycin with its mechanism of action and its pharmacokinetics. It is also useful for treating a range of respiratory diseases. Unfettered use of azithromycin, particularly for its immunomodulatory properties, is of concern in light of macrolide resistance. Novel non-antibiotic macrolides may be used for this role in future.

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