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A Review Article On Azithromycin

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Abstract:
The azalide antibacterial agent azithromycin is a semisynthetic acid-stable erythromycin derivative with an expanded spectrum of activity and improved tissue pharmacokinetic characteristics relative to erythromycin. The drug is noted for its activity against some Gram-negative organisms associated with respiratory tract infections, particularly Haemophilus influenzae. Azithromycin has similar activity to other macrolides against Streptococcus pneumoniae and Moraxella catarrhalis, and is active against atypical pathogens such as Legionella pneumophila, Chlamydia pneumoniae and Mycoplasma pneumoniae. Once-daily administration of azithromycin is made possible by the long elimination half-life of the drug from tissue. Azithromycin is rapidly and highly concentrated in a number of cell types after absorption, including leucocytes, monocytes and macrophages. It undergoes extensive distribution into tissue, from where it is subsequently eliminated slowly. A 3-day oral regimen of once-daily azithromycin has been shown to be as effective as 5- to 10-day courses of other more frequently administered antibacterial agents [such as erythromycin, amoxicillin-clavulanic acid and phenoxymethylpenicillin (penicillin V)] in patients with acute exacerbations of chronic bronchitis, pneumonia, sinusitis, pharyngitis, tonsillitis and otitis media. Adverse effects of azithromycin are mainly gastrointestinal in nature and occur less frequently than with erythromycin. Azithromycin is likely to prove most useful as a 3-day regimen in the empirical management of respiratory tract infections in the community. Its ease of administration and 3-day duration of therapy, together with its good gastrointestinal tolerability, should optimise patient compliance (the highest level of which is achieved with once-daily regimens). Azithromycin is also likely to be useful in the hospital setting, particularly for outpatients and for those unable to tolerate erythromycin.

Keywords: *Azithromycin, Antibiotic, Immuno-Modulatory, Antiviral, Treatment, Pathogens, respiratory, toxicity, gastrointestinal, pathogens.*

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I. Introduction:

Azithromycin is an antibiotic since its discovery, it has been FDA-approved for Respiratory tract infections such as pneumonia, genitourinary infections such as chlamydia, and enteric infections such as typhoid, and has also been extensively studied with malaria . This drug has an absolute oral bioavailability of 35–42% in healthy volunteers and patients with cystic fibrosis. Upon administration of a single 500 mg oral dose, tissue concentrations exceed the minimum inhibitory concentration that would inhibit 90% of likely pathogens (MIC90), phagocytic concentrations can reach over 200 times serum concentrations and, due to a half-life of 68 h, such effective levels can be maintained for several days . Azithromycin's massive localisation to phagocytic cells and subsequent delivery to sites of infection as part of the innate immune system has enabled this macrolide to successfully mitigate a plethora of infections over the last 50 years and is a hallmark of this broad-spectrum therapeutic . As reviewed herein, these striking pharmacokinetic properties have also led to worldwide ongoing research into azithromycin's antiviral properties. Azithromycin is a macrolide antibiotic widely used to treat various bacterial infections due to its broad-spectrum activity and improved pharmacokinetics. It belongs to the azalide subclass of macrolides, characterized by a 15-member lactone ring structure, which provides enhanced stability and a longer half-life compared to traditional macrolides like erythromycin. Azithromycin works by binding to the 50S ribosomal subunit of bacteria, inhibiting protein synthesis and effectively halting bacterial growth. Azithromycin is employed to treat respiratory tract infections, including pharyngitis, bronchitis, and pneumonia, as well as skin and soft tissue infections. It is also a first-line treatment for sexually transmitted infections such as Chlamydia trachomatis and an alternative for patients allergic to penicillin. Its effectiveness against atypical pathogens like Mycoplasma pneumoniae and Legionella pneumophila makes it a valuable option for managing atypical pneumonia. One of Azithromycin's standout features is its extended half-life, allowing once-daily dosing and shorter treatment regimens, typically three to

five days. This convenience enhances patient compliance and reduces the risk of incomplete therapy. Additionally, Azithromycin achieves high tissue concentrations, making it particularly effective for infections in soft tissues and intracellular pathogens.

II. About Azithromycin:

Azithromycin Structure:

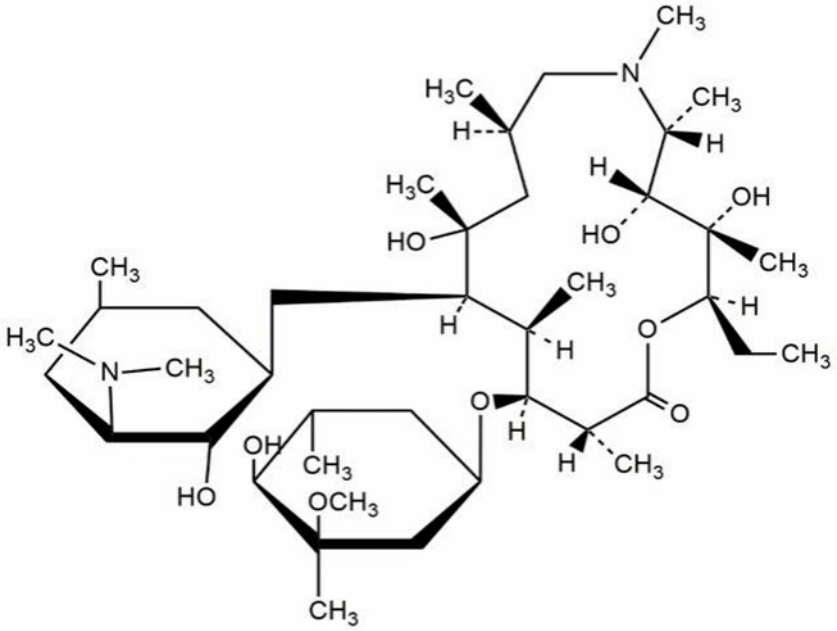

Figure 2: structure of Azithromycin

Azithromycin's Iupac Name:

(2R,3S,4R,5R,8R,10R,11R,12R,13S,14R)-2-ethyl-3,4,10-trihydroxy-3,5,6,8,10,12,14-heptamethyl-11-[(3,4,6-trideoxy-3-dimethylamino-β-D-xylo-hexopyranosyl)oxy]-1-oxa-6-azacyclopentadecan-15-one.[1]

Lactone Ring:

• Azithromycin contains a 15-membered lactone ring (instead of 14 in erythromycin).
• The nitrogen substitution in the lactone ring enhances its stability in acidic environments (e.g., the stomach), making azithromycin more bioavailable orally.[3]

Glycosidic Side Chains (Two Sugar Moieties):

• **Desosamine sugar:** Responsible for its interaction with bacterial ribosomal RNA, leading to inhibition of protein synthesis.
• **Cladinose sugar:** Imparts antibacterial specificity.

Methyl-Substituted Nitrogen (Azalide Group):

Provides resistance to acid degradation.
Extends its spectrum of activity and half-life, allowing once-daily dosing.

Hydroxyl Groups:

Multiple hydroxyl groups on the macrolide ring contribute to hydrophilic interactions with the bacterial ribosome.

Structure Formula:

Azithromycin has a molecular formula of C38H72N2O12, with a molecular weight of 748.98 g/mol.

III. Mechanism Of Action Of Azithromycin:

Azithromycin is a macrolide antibiotic that works by inhibiting bacterial protein synthesis, ultimately halting bacterial growth. It exhibits bacteriostatic activity at lower concentrations and bactericidal activity at higher concentrations against certain bacteria.[5]

Key Steps In Azithromycin's Mechanism:

Targeting The Bacterial Ribosome:

Azithromycin selectively binds to the 50S ribosomal subunit of bacterial ribosomes. Specifically, it interacts with the 23S ribosomal RNA (rRNA) within the 50S subunit.[3]

Inhibition Of Protein Synthesis:

Binding of azithromycin prevents the proper association of transfer RNA (tRNA) with the ribosome. This blocks the translocation step in protein synthesis, where the ribosome moves along messenger RNA (mRNA) to incorporate amino acids into a growing peptide chain.[4]

Disruption Of Bacterial Growth:

By halting protein synthesis, essential proteins required for bacterial cell growth and replication are not produced. This leads to the inhibition of bacterial growth (bacteriostatic effect) and, in some cases, bacterial cell death (bactericidal effect) depending on the concentration and type of bacteria.[17]

Selective Toxicity:

Azithromycin specifically targets bacterial ribosomes, which are structurally distinct from mammalian ribosomes. This selective binding minimizes its effects on human cells, ensuring effective antibacterial action with relatively low toxicity.[9]

Spectrum Of Activity:

- **Gram-Positive Bacteria:** Effective against pathogens like Staphylococcus aureus and Streptococcus pneumoniae.
- **Gram-Negative Bacteria:** Active against Haemophilus influenzae and Neisseria gonorrhoeae.
- **Atypical Bacteria:** Works against intracellular organisms such as Chlamydia trachomatis and Mycoplasma pneumoniae.

Anti-Inflammatory Effects:Azithromycin exhibits mild anti-inflammatory properties by modulating cytokine production, which can be beneficial in respiratory infections.

IV. Calibration Curve Of Azithromycin In Phosphate Buffer (Ph 6.8):

The calibration curve is an essential analytical tool for determining the concentration of a substance in a solution by measuring its absorbance at a specific wavelength. For azithromycin in phosphate buffer (pH 6.8), the following points summarize the key aspects of the linearity study:[6]

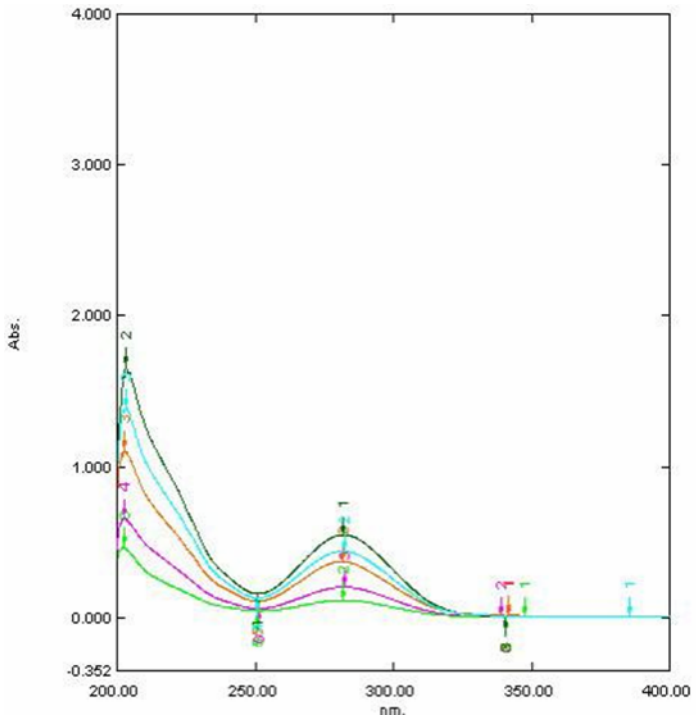

Figure 2: Azithromycin linearity absorbance spectrum The calibration curve of azithromycin in phosphate buffer pH 6.8 was found to be linear in the concentration range 10-50 µg/ml.

Principle:

Azithromycin's absorbance spectrum is measured using UV-visible spectrophotometry. The absorbance at a specific wavelength is proportional to its concentration, following Beer-Lambert's law:

$A=\epsilon \cdot c \cdot l$

Where:

- A: Absorbance (no units)
- ϵ: Molar absorptivity (L mol^{-1} cm^{-1}
- c: Concentration (mol/L)
- l: Path length (cm)

Wavelength For Azithromycin Absorbance:

- Azithromycin typically shows maximum absorbance (λmax) around **210–220 nm** in UV-visible spectrophotometry.
- The exact λmax depends on the solvent and pH.

Calibration Curve Setup:

- **Solvent:** Phosphate buffer (pH 6.8).
- **Concentration Range:** 10–50 µg/mL.
- **Preparation of Standards:** Serial dilutions of azithromycin are prepared in the buffer to achieve the desired concentrations.

Experimental Steps:

- **Stock Solution:** Prepare a stock solution of azithromycin (e.g., 100 µg/mL) in phosphate buffer.
- **Dilutions:** Prepare working standards in the range of 10–50 µg/mL by serial dilution.
- **Measurement:** Measure the absorbance of each standard solution at Max Using a UV-visible spectrophotometer.
- **Blank:** Use phosphate buffer (pH 6.8) as the blank to zero the spectrophotometer.

Results And Linearity:

- **Plot:** A graph is plotted with concentration (µg/mL) on the x-axis and absorbance on the y-axis.
- **Linearity Range:** The absorbance values are found to be linear within the concentration range of 10–50 µg/mL.
- **Regression Equation:** The calibration curve typically follows the linear regression equation:

$y=mx+c$

Where:

- y: Absorbance
- m: Slope of the line
- x: Concentration (µg/mL)
- C: Intercept
- **Correlation Coefficient (R^2):** A value close to **1** (e.g., $R2 \geq 0.99 R^2 \geq 0.99$) confirms good linearity.

V. Calibration Curve (Quantification):

Typical concentration range: 10–50 µg/mL in buffer solutions (e.g., phosphate buffer, pH 6.8).[14]

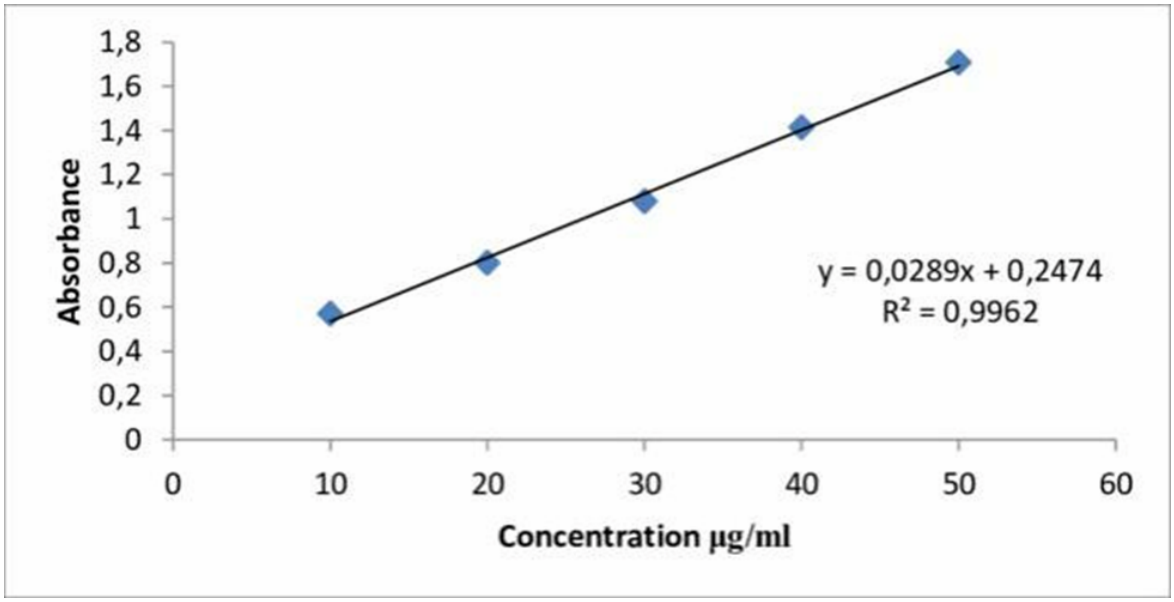

Figure 3: Calibration Curve of Azithromycin (Figure 3) having R 2 value 0.997.

VI. Observations:

A straight-line calibration curve confirms the proportional relationship between concentration and absorbance, validating Beer-Lambert's law. The linear range (10–50 µg/mL) ensures accurate quantification within this interval. Intrapartum administration of azithromycin to the mother does reduce maternal postpartum infections in low-income countries. The impact on maternal mortality showed both clear benefit and substantial harm, and thus conclusions as to the effect of azithromycin on maternal mortality remains undecided. Azithromycin does not reduce neonatal adverse outcomes. Further studies are needed in different settings and countries to better estimate the implication of this finding in each region before introducing it into wider use.[OBSERVATION]

VII. Conclusion:

Azithromycin exerts its antibacterial effects by binding to the 50S ribosomal subunit, halting protein synthesis, and thereby inhibiting bacterial growth. It is effective against a wide range of bacteria, particularly those causing respiratory, gastrointestinal, and sexually transmitted infections.

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