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A Review on: Formulation and Evaluation of Levofloxacin Syrup

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ABSTRACT:

Levofloxacin, having completed its initial drug development phases in the mid-1990s, emerged as one of the first fluoroquinolones that could be reliably utilized for the treatment of respiratory tract infections. It subsequently became one of the most frequently prescribed antibiotics globally. Levofloxacin is the L-isomer of the fluoroquinolone antibacterial agent ofloxacin. In vitro studies have shown that levofloxacin possesses a broad spectrum of activity against both Gram-positive and Gram-negative organisms, as well as anaerobes. It exhibits greater efficacy against Gram-positive bacteria compared to ciprofloxacin, although it is less effective than newer fluoroquinolones like gatifloxacin. Notably, its effectiveness against Streptococcus pneumoniae remains intact even in the presence of penicillin resistance.

In clinical settings, sequential therapy with levofloxacin at a dosage of 500 mg twice daily for a duration of 7 to 14 days proved to be as effective as intravenous imipenem/cilastatin in patients suspected of having bacteraemia. Additionally, oral administration of levofloxacin at 500 mg once daily for 7 to 10 days was found to be an effective treatment for patients with uncomplicated skin and skin structure infections, as well as those with complicated urinary tract infections. Furthermore, a higher dosage of sequential levofloxacin at 750 mg once daily demonstrated comparable efficacy to intravenous ticarcillin/clavulanic acid (with an optional oral switch to amoxicillin/clavulanic acid) in managing complicated skin and skin structure infections.

Keywords:- fluroquinolones, penicillin , Levofloxacin streptococcus pneumoniae.

Introduction:

Syrup is a liquid dosage form administered orally, consisting of a viscous, concentrated solution of sucrose and other sugars, which may or may not include medicinal ingredients. It serves as a flavoring agent and vehicle, containing up to 85% sugar to inhibit bacterial growth, specifically designed for oral consumption. The preparation of syrup generally entails dissolving sugar in heated water, which can subsequently be enhanced with flavors derived from fruits, herbs, or spices. Depending on the intended application, syrups can vary in consistency from thick and viscous to light and fluid, with differing sugar concentrations to accommodate various dietary requirements.

Classification of Syrup:

- Simple Syrups: Composed solely of sugar and water (e.g., basic sugar syrup).

- Flavored Syrups: Enhanced with specific flavors (e.g., vanilla, mint).

- Herbal Syrups: Incorporate herbal extracts (e.g., elderberry syrup).

Levofloxacin belongs to the fluoroquinolone class of antibacterial agents, exhibiting microbiological activity against significant bacteria responsible for respiratory, skin, and genitourinary tract infections. It is utilized in the treatment of various bacterial infections, including acute bacterial sinusitis, pneumonia, H. pylori (in conjunction with other medications), urinary tract infections, Legionnaires' disease, chronic bacterial prostatitis, and certain types of gastroenteritis. In combination with other antibiotics, it may also be employed in the treatment of tuberculosis, meningitis, or pelvic inflammatory disease. Levofloxacin is available in oral, intravenous, and eye drop formulations. Recent studies have investigated higher-dose regimens of 750 mg administered over a shorter duration (5 days instead of 10 days) for patients with respiratory tract infections, recognizing the potential of this adjustment to positively influence drug resistance.

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Structure of Levofloxacin:

IUPAC name: for levofloxacin is (2S)-7-fluoro-2-methyl-6-(4-methylpiperazin-1-yl)-10-oxo-4-oxa-1-azatricyclo[7.3.1.05,13]trideca-5(13),6,8,11-tetraene-11-carboxylic acid.

Brand name: Levaquin

Molecular formula: C18H20FN3O4

Molecular weight:361.4g/mol

pka values:5.7 and7.9

category: fluoroquinolones

Mechanism of action:

LEVOFLOXACIN

↓

Bind to the A-subunit of DNA gyrase (topoisomerase II type) enzyme

↓

Prevents the binding of substrate to the active site of DNA gyrase

↓

Absence of formation of enzyme – substrate complex

↓

Blockade of unwinding of double-stranded DNA into a single stranded structure

↓

Prevention of synthesis of mRNA

↓

Inhibition of bacterial protein synthesis

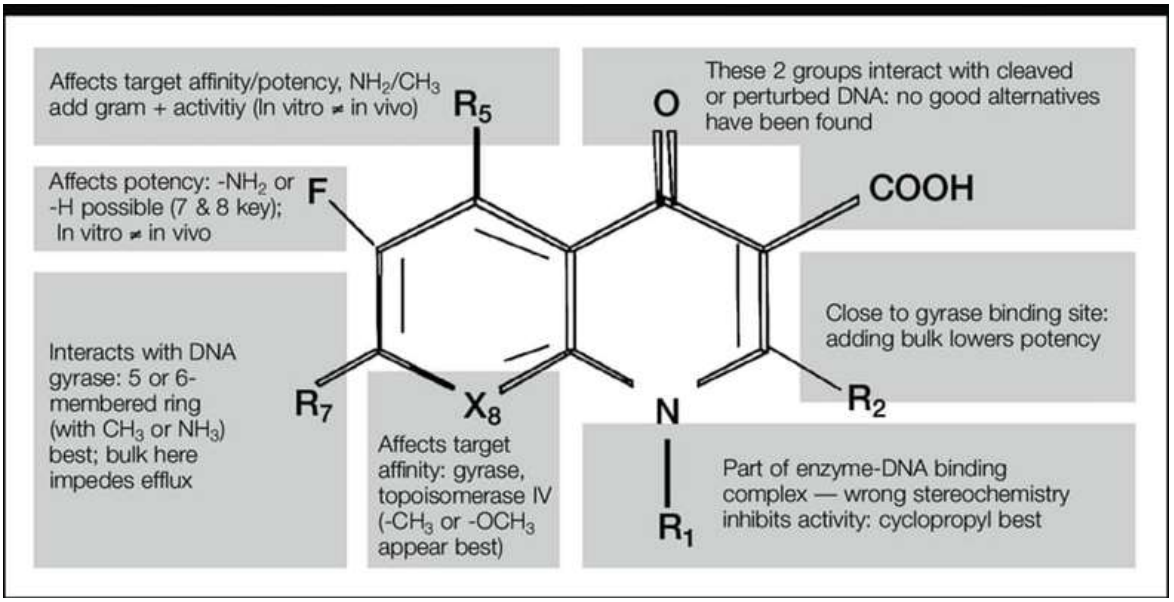
↓

Antibacterial activity

Levofloxacin, similar to other fluoroquinolone antibiotics, demonstrates its antimicrobial efficacy by inhibiting two critical bacterial enzymes: DNA gyrase and topoisomerase IV. Both of these enzymes are classified as type II topoisomerases, yet they perform distinct roles within bacterial cells. DNA gyrase, an enzyme exclusive to bacteria, introduces negative supercoils into DNA, which are vital for chromosome condensation and the initiation of transcription. This enzyme consists of four subunits, comprising two A subunits and two B subunits, with the A subunits being the primary targets for fluoroquinolone antibiotics. On the other hand, bacterial topoisomerase IV not only aids in the relaxation of positive supercoils but is also crucial during the final stages of DNA replication, functioning to separate newly replicated chromosomes to facilitate cell division.

The inhibition of these enzymes by levofloxacin is likely achieved through complex formation with the topoisomerase enzymes. Consequently, this leads to the obstruction of DNA replication, thereby hindering cell division and ultimately resulting in cell death.

Structure Activity Relationship of Levofloxacin:



Pharmacokinetics and Pharmacodynamics of Levofloxacin:

The pharmacokinetic characteristics of levofloxacin in humans have been thoroughly investigated and are comprehensively discussed in other sources. A summary of the pharmacokinetic parameters for levofloxacin at doses of 500 mg and 750 mg, administered either orally or intravenously in single or multiple doses, is presented in Table 1.

Following oral administration, levofloxacin exhibits rapid and nearly complete absorption, with a bioavailability of 99%. This absorption is not significantly influenced by food intake. Both oral and intravenous forms of levofloxacin demonstrate linear pharmacokinetics, as evidenced by the dose-proportional increases in maximum plasma concentration (Cmax) and area under the concentration-time curve (AUC). Due to its relatively extended half-life of 7 to 9 hours and the resulting plasma concentration profile, once-daily dosing of levofloxacin in patients with normal renal function achieves sufficient AUC to meet the AUC:MIC (minimum inhibitory concentration) ratios necessary for the clinical eradication of a wide range of bacterial infections. It is important to note that children, particularly those under the age of 5, exhibit significantly different pharmacokinetic profiles compared to adults. Young children may eliminate levofloxacin at nearly double the rate of adults, which suggests that applying adult dosing regimens based solely on weight may lead to suboptimal drug exposure in pediatric patients, potentially falling short of the pharmacodynamic targets linked to therapeutic efficacy.

Uses:

Respiratory Infections: Effective against pneumonia and bronchitis.

Urinary Tract Infections (UTIs): Used for complicated and uncomplicated UTIs.

Skin Infections: Treats skin and soft tissue infections.

Prostatitis: Effective in treating bacterial prostatitis.

Sinusitis: Can be used for acute bacterial sinusitis.

Inhalational Anthrax: Used as part of post-exposure prophylaxis.

Marketed formulation of levofloxacin:

Markted formulation of levofloxacin in tablet dosage form:-

Brand name	Formulation	Labeled amount (mg)	Manufacturer
Glevo	Tablets	Levofloxacin -500 mg	Glenmark Pharmaceuticals Ltd., Mumbai, India.
Pruflox	Tablets	Prulifloxacin- 600 mg	Cipla Ltd., Mumbai, India.
Segat	Tablets	Gatifloxacin- 400 mg	Secure health care Inc. India.
Sparcip	Tablets	Sparfloxacin – 100 mg	Cipla Ltd., Mumbai, India.
Moxicip	Tablets	Moxifloxacin–400 mg	Intralabs, Bangalore, India.
Balox-100	Tablets	Balofloxacin -100 mg	Lupin Ltd., Mumbai, India.

Method of Preparation Levofloxacin syrup:-

Determine the necessary quantities of each ingredient or the overall amount to be prepared. Carefully weigh or measure each component. Grind the specified number of tablets into a fine powder, or utilize the powder directly. Introduce a small amount of Ora-Plus to create a smooth paste. Gradually incorporate the remaining Ora-Plus and mix thoroughly. Add the Strawberry Syrup incrementally to achieve the desired final volume, ensuring to mix well after each addition. Finally, package and label the product.

Evaluation criteria for the syrup:

Color: Assess clarity and viscosity. The syrup should be uniform without any sediment or cloudiness.

Aroma: Analyze the fragrance. It should be pleasant and representative of the syrup type (e.g., maple, fruit).

Flavor: Sample the syrup to evaluate sweetness, balance, and specific flavor characteristics. It should not be excessively sweet or possess any undesirable flavors.

Texture: Evaluate the mouthfeel; it should be smooth and pour easily, avoiding excessive thickness or stickiness.

Sugar Content: Determine the Brix level (sugar concentration) using a refractometer to assess quality and sweetness.

pH Level: Testing the acidity can provide insights into stability and the potential for fermentation.

Shelf Stability: Assess how well the syrup maintains its flavor and appearance over time.

Packaging: Review the packaging for functionality and safety, ensuring it effectively protects the syrup from contamination.

Conclusion :-

Levofloxacin syrup is a potent antibiotic utilized for the treatment of a range of bacterial infections. As a member of the fluoroquinolone class, it functions by obstructing the synthesis of bacterial DNA. Although it provides extensive coverage and is generally well-accepted by patients, it is crucial to be aware of possible side effects, such as gastrointestinal issues and the potential for tendon damage. Continuous monitoring of both effectiveness and adverse reactions is essential, and its administration should adhere to antibiotic stewardship guidelines to mitigate the risk of resistance. In summary, levofloxacin syrup represents a significant therapeutic option for specific infections when prescribed judiciously.

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