WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.63
Volume 15, Issue 13, 1702-1721. Review Article ISSN 2277–7105

TO STUDY THE PHARMACOLOGICAL PROFILE OF FOSFOMYCIN TROMETAMOL

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Article Received on 05 June 2026,
Article Revised on 25 June 2026,
Article Published on 01 July 2026,

https://doi.org/10.5281/zenodo.21155201

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How to cite this Article: Pravinya R. Sonkar*[1], Shubham V. Bhawar[2], Gauri N. Bhasme[3], Manva U. Bobde[4] Vedant D. Dhage[5], Dr. Manisha D. Kitukale[6]*. (2026). To Study The Pharmacological Profile of Fosfomycin Trometamol. World Journal of Pharmaceutical Research, 15(13), 1702-1721.

ABSTRACT

Urinary tract infections (UTIs) are among the most common bacterial infections worldwide and have become increasingly difficult to treat because of the growing problem of antimicrobial resistance. Fosfomycin Trometamol is a broad-spectrum phosphonic acid antibiotic that has gained renewed clinical importance due to its effectiveness against multidrug-resistant uropathogens. This review focuses on the pharmacological profile, mechanism of action, pharmacokinetics, therapeutic efficacy, safety, and clinical significance of Fosfomycin Trometamol. The drug acts by irreversibly inhibiting the MurA enzyme, thereby preventing bacterial cell wall synthesis and exhibiting potent bactericidal activity. Fosfomycin Trometamol demonstrates favorable pharmacokinetic properties, including good oral bioavailability and prolonged urinary concentrations, making it suitable for single-dose therapy in uncomplicated urinary tract infections. The review also discusses its activity against resistant organisms, including ESBL-producing bacteria, and compares its resistance profile with other commonly used antimicrobial agents. In addition, formulation aspects, adverse effects, drug interactions, and use in special populations such as pregnant women and pediatric patients are summarized. The findings indicate that Fosfomycin Trometamol remains a safe, effective, and valuable therapeutic option in the management of urinary tract infections and plays an important role in combating antimicrobial resistance.

KEYWORDS: Fosfomycin Trometamol, Urinary Tract Infection (UTI), Antimicrobial Resistance, MurA Enzyme, Broad-Spectrum Antibiotic, Multidrug-Resistant Bacteria, Pharmacokinetics, ESBL-Producing Organisms, Single-Dose Therapy, Uropathogens.

1. INTRODUCTION

1.1. GENERAL OVERVIEW OF URINARY TRACT INFECTION

The urinary system consists of the kidneys, ureters, bladder, and urethra, and its main function is to filter blood by removing waste products and excess water. The urinary system plays a key role in removing the waste products of metabolism from the bloodstream. Other important functions performed by the system are the normalization of the concentration of ions and solutes in the blood and the regulation of blood volume and blood pressure. In healthy people, urine is sterile or contains very few microorganisms that can cause an infection. Urinary tract infections (UTIs) are infections that can occur in the urethra (urethritis), bladder (cystitis), or kidneys (pyelonephritis) and are one of the world's most common infectious diseases, affecting 150 million people each year, with significant morbidity and high medical costs (e.g., it has been estimated that the economic burden of recurrent UTIs in the United States is more than $5 billion each year). Although symptomatology varies depending on the location of these infections, UTIs have a negative impact on patients' relationships, both intimate and social, resulting in a decreased quality of life. UTIs are classified as either uncomplicated (uUTIs) or complicated (cUTIs). uUTIs typically affect healthy patients in the absence of structural or neurological abnormalities of the urinary tract. cUTIs are defined as complicated when they are associated with urinary tract abnormalities that increase susceptibility to infection, such as catheterization or functional or anatomical abnormalities (e.g., obstructive uropathy, urinary retention, neurogenic bladder, renal failure, pregnancy, and the presence of calculi).

In both community and hospital settings, the Enterobacteriaceae family is predominant in UTIs, and the main isolated pathogen is uropathogenic Escherichia coli (UPEC). The latter is also the most common causative agent of cUTI. Antibiotic-resistant Gram-negative bacteria are more prevalent in hospitals than in community samples (e.g., carbapenemase-resistant Enterobacteriaceae). UTIs are mainly caused by bacteria, while the involvement of other microorganisms, such as fungi and viruses, is quite rare. Candida albicans is the most common type of fungus that causes UTIs. Common causes of viral UTI are cytomegalovirus, type 1 human Polyomavirus, and herpes simplex virus.

This review pursues a twofold goal: the first is to provide an overview of the mechanisms underlying the pathogenesis of UTIs; the second is to provide an overview of recent advances in new strategies, as an alternative to antibiotics, to control the spread of multidrug-resistant UTI isolates.[01]

Classification of Urinary Tract Infections 1 Based on Anatomical Location

1.1 Upper Urinary Tract Infection

- Affects the kidneys and ureters
- Example: Pyelonephritis
- More serious; may cause kidney damage.

1.2 Lower Urinary Tract Infection

- Affects the bladder and urethra
- Examples: Cystitis, Urethritis
- Usually less severe but more common.

2 Based on Severity and Complexity

2.1 Uncomplicated UTI

- Occurs in healthy individuals
- No structural or functional abnormalities
- Common in young women.

2.2 Complicated UTI

Associated with:

- Urinary tract abnormalities
- Catheter use
- Kidney stones.

3 Based on Occurrence

3.1 Acute UTI

- Sudden onset of symptoms
- Short duration.

3.2 Chronic UTI

- Persistent or long-term infection

3.3 Recurrent UTI

- Repeated infections
- Defined as ≥2 infections in 6 months OR ≥3 infections in 1 year.

3.4 Special Types of UTI

- Catheter-Associated UTI (CAUTI)
- Pregnancy-associated UTI
- UTI in diabetic patients.

4. Causes of Urinary Tract Infections

1. Bacterial Causes

- ***Escherichia coli (E. coli)***
- Klebsiella species
- Proteus species
- Pseudomonas aeruginosa
- Staphylococcus saprophyticus
- Enterococcus species.

2. Poor Hygiene

- Improper cleaning after urination or defecation
- Using unclean public toilets
- Holding urine for long periods.

3. Low Water Intake

- Drinking less water reduces flushing of bacteria from the urinary tract.

4. Sexual Activity

- Frequent sexual intercourse can introduce bacteria into the urethra.

5. Urinary Obstruction

- Kidney stones
- Enlarged prostate[02]

OVERVIEW OF ANTIMICROBAL RESISTANCE AND NEED FOR NEW THERAPIES

Antimicrobial resistance (AMR) is a major global health problem in which microorganisms such as bacteria, viruses, fungi, and parasites become resistant to antimicrobial drugs that were previously effective in treating infections. Due to this resistance, medicines lose their effectiveness, infections become difficult to cure, and the risk of disease spread, severe illness, and death increases. Antimicrobial resistance mainly develops because of the overuse and misuse of antibiotics, incomplete treatment courses, self-medication, poor infection control practices, and excessive use of antibiotics in agriculture and animal farming. Microorganisms can develop resistance through mutation or by acquiring resistance genes from other microbes. Resistant organisms such as Methicillin-resistant Staphylococcus aureus (MRSA), Multidrug-resistant tuberculosis (MDR-TB), and Vancomycin-resistant Enterococci (VRE) are important examples of antimicrobial resistance.[03]

Microorganisms use several mechanisms to resist antimicrobial drugs. Some bacteria produce enzymes that destroy antibiotics, while others modify their target sites so that drugs cannot act effectively. Certain microorganisms reduce drug entry into the cell or actively pump drugs out through efflux mechanisms. Some also form biofilms that protect them from antimicrobial action. As a result, infections become harder to treat and may require stronger or multiple drugs. Antimicrobial resistance has serious health, economic, and clinical consequences. It increases mortality and morbidity, prolongs hospital stays, raises healthcare costs, and creates difficulty in performing surgeries, chemotherapy, organ transplantation, and other medical procedures safely.[04]

The rapid increase in resistant microorganisms has created an urgent need for newer therapies and advanced treatment approaches. Existing antibiotics are gradually losing their effectiveness, and the development of resistance is occurring faster than the discovery of new drugs. Therefore, researchers are focusing on the development of novel antimicrobial agents with unique mechanisms of action. Newer antibiotics such as oxazolidinones, lipopeptides, and glycylcyclines have shown effectiveness against resistant organisms. Combination therapy, in which two or more antimicrobial agents are used together, is also employed to improve therapeutic effectiveness and reduce resistance development.

Several alternative therapeutic approaches are being explored to combat antimicrobial resistance. Phage therapy uses bacteriophages, which are viruses that specifically infect and

destroy bacteria. Nanotechnology-based drug delivery systems improve targeted delivery and enhance antimicrobial activity.

1.2. INTRODUCTION TO FOSFOMYCIN AND ITS SALT DERIVATIES (TRAMETAMOL/CALCIUM SODIUM)

Fosfomycin is a broad-spectrum bactericidal antibiotic belonging to the phosphonic acid derivative class. It was first discovered in 1969 from strains of Streptomyces species and is widely used for the treatment of bacterial infections, especially urinary tract infections (UTIs). Fosfomycin exhibits activity against both Gram-positive and Gram-negative bacteria, including multidrug-resistant organisms. The drug acts by inhibiting bacterial cell wall synthesis through irreversible inhibition of the enzyme UDP-N-acetylglucosamine enolpyruvyl transferase (MurA), which plays an important role in the early stage of peptidoglycan synthesis. Due to its unique mechanism of action, fosfomycin shows minimal cross-resistance with other classes of antibiotics and is considered an important therapeutic option for resistant infections.

To improve its pharmacokinetic properties and therapeutic effectiveness, fosfomycin is available in different salt derivatives such as fosfomycin trometamol, fosfomycin calcium, and fosfomycin sodium. These salt forms differ in their absorption, solubility, route of administration, and clinical applications. Fosfomycin trometamol, also known as fosfomycin tromethamine, is the most commonly used oral formulation. Trometamol enhances the oral bioavailability and gastrointestinal absorption of fosfomycin, making it highly effective for oral administration. It is mainly prescribed as a single-dose therapy for uncomplicated urinary tract infections caused by susceptible bacteria such as Escherichia coli and Enterococcus faecalis. Because of its convenient dosage regimen and good patient compliance, fosfomycin trometamol is widely preferred in clinical practice.

Fosfomycin calcium is another oral salt derivative of fosfomycin. Although it possesses antibacterial activity similar to fosfomycin trometamol, its oral absorption is comparatively lower, resulting in reduced bioavailability and serum concentration. Therefore, fosfomycin calcium is less commonly used than fosfomycin trometamol. However, it still remains effective against various urinary pathogens and is used in some countries for the treatment of mild urinary tract infections.[05]

Fosfomycin sodium, also referred to as fosfomycin disodium, is a highly water-soluble salt

form mainly intended for intravenous administration. It is commonly used in hospitals for severe systemic infections, complicated urinary tract infections, sepsis, meningitis, bone infections, and infections caused by multidrug-resistant bacteria. Intravenous fosfomycin sodium provides high plasma concentrations and rapid therapeutic action, making it useful in critically ill patients. However, this formulation is not suitable for oral administration because it is unstable in acidic gastric conditions.

2. DRUG PROFILE

2.1 Generic Name

Fosfomycin Trometamol (also known as Fosfomycin Tromethamine).

2.2 Brand Names

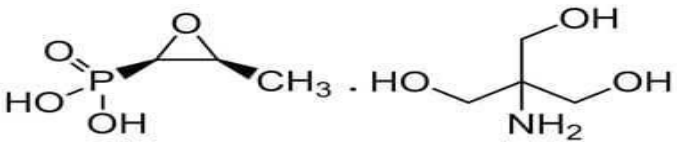
Commonly used brand names include:

- Monurol
- Monuril
- Fosfocin
- Fosirol[08]

2.3 Drug Class

Broad-spectrum antibiotic (Phosphonic acid derivative)

2.4 Chemical Structure



2.5 Chemical Information

2.5.1 IUPAC Names

2.5.1.1 Fosfomycin: (2R,3S)-3-methyloxiran-2-ylphosphonic acid

2.5.1.2 Trometamol (Tromethamine): 2-amino-2-(hydroxymethyl)propane-1,3-diol.

2.5.2 Molecular Formulae

2.5.2.1 Fosfomycin: $C_3H_7O_4P$

2.5.2.2 Trometamol: $C_4H_{11}NO_3$

2.5.2.3 Combined (Fosfomycin Trometamol): $C_7H_{18}NO_7P$.

2.5.3 Molecular Weight

2.5.3.1 Fosfomycin Trometamol: ≈ 259.2 g/mol.

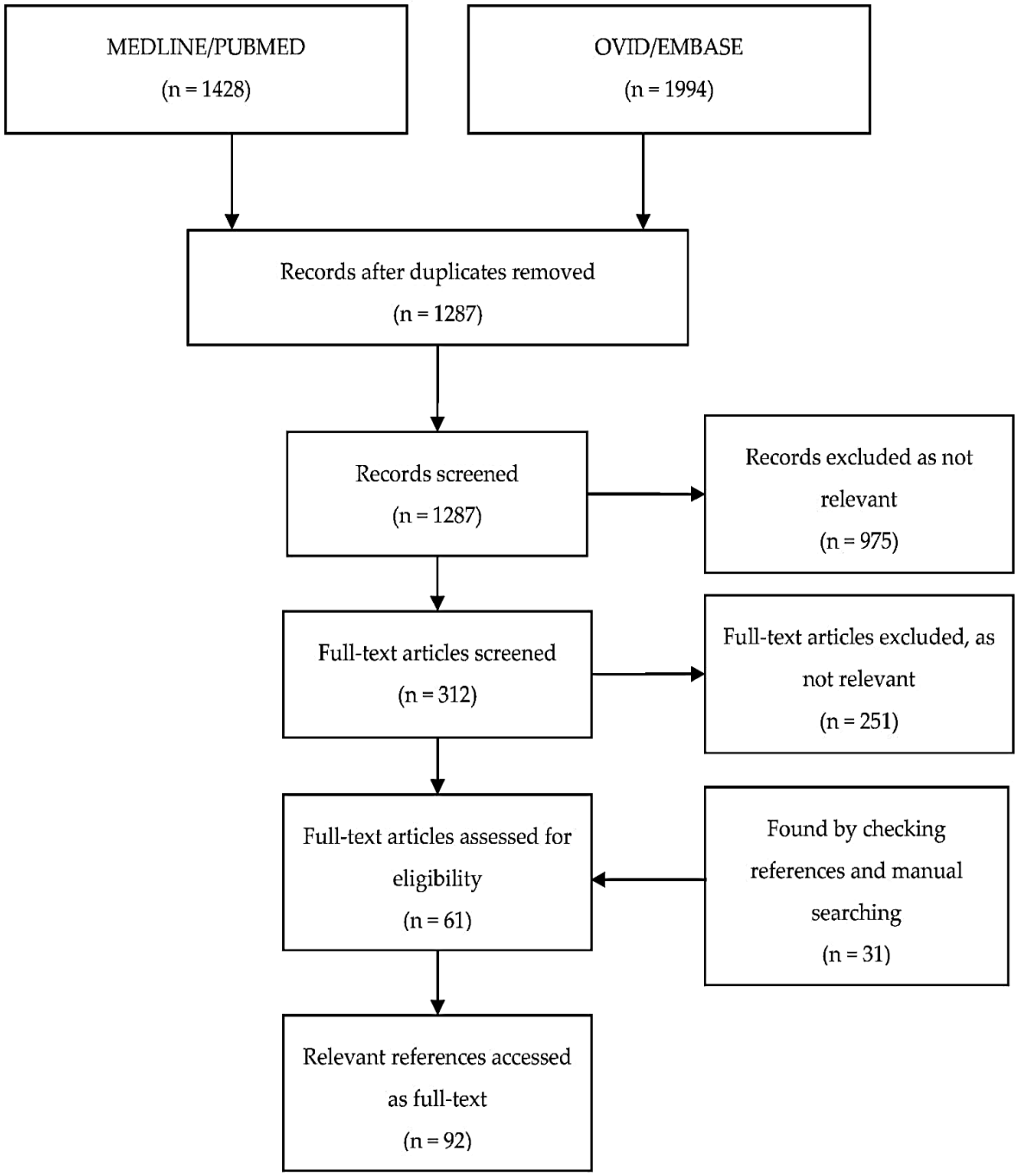
2.5.4 Solubility

2.5.4.1 Freely soluble in water

2.5.4.2 Slightly soluble in alcohol

2.5.4.3 Practically insoluble in non-polar solvents.[09]

2.6 MECHANISM OF ACTION[10]



2.7 PHARMACOKINETICS (ADME)[11]

PHARMACOKINETICS OF FOSFOMYCIN

Parameter	Details
Absorption	Rapidly absorbed after oral administration.
Oral Bioavailability	Approximately 34–58% (fosfomycin trometamol).
Peak Plasma Time (Tmax)	2 – 2.5 hours after oral dose.
Distribution	Widely distributed in tissues, kidneys, bladder and urine.
Protein Binding	Very low (<5%).
Volume of Distribution	Moderate to high.
Metabolism	Not significantly metabolized.
Excretion	Mainly excreted unchanged in urine.
Elimination Half-life (t½)	Approximately 4 – 6 hours.
Route of Elimination	Renal excretion via glomerular filtration.
Urinary Concentration	High urinary concentrations maintained for 24 – 48 hours.
Crosses Placenta	Yes.
Blood–Brain Barrier Penetration	Limited penetration.

ADME SUMMARY

ABSORPTION

- Well absorbed from the gastrointestinal tract.
- Food may slightly reduce absorption.
- Oral bioavailability 34–58%.

DISTRIBUTION

- Widely distributed in kidneys, bladder wall, prostate, urine and soft tissues.
- Very low protein binding increases free drug availability.

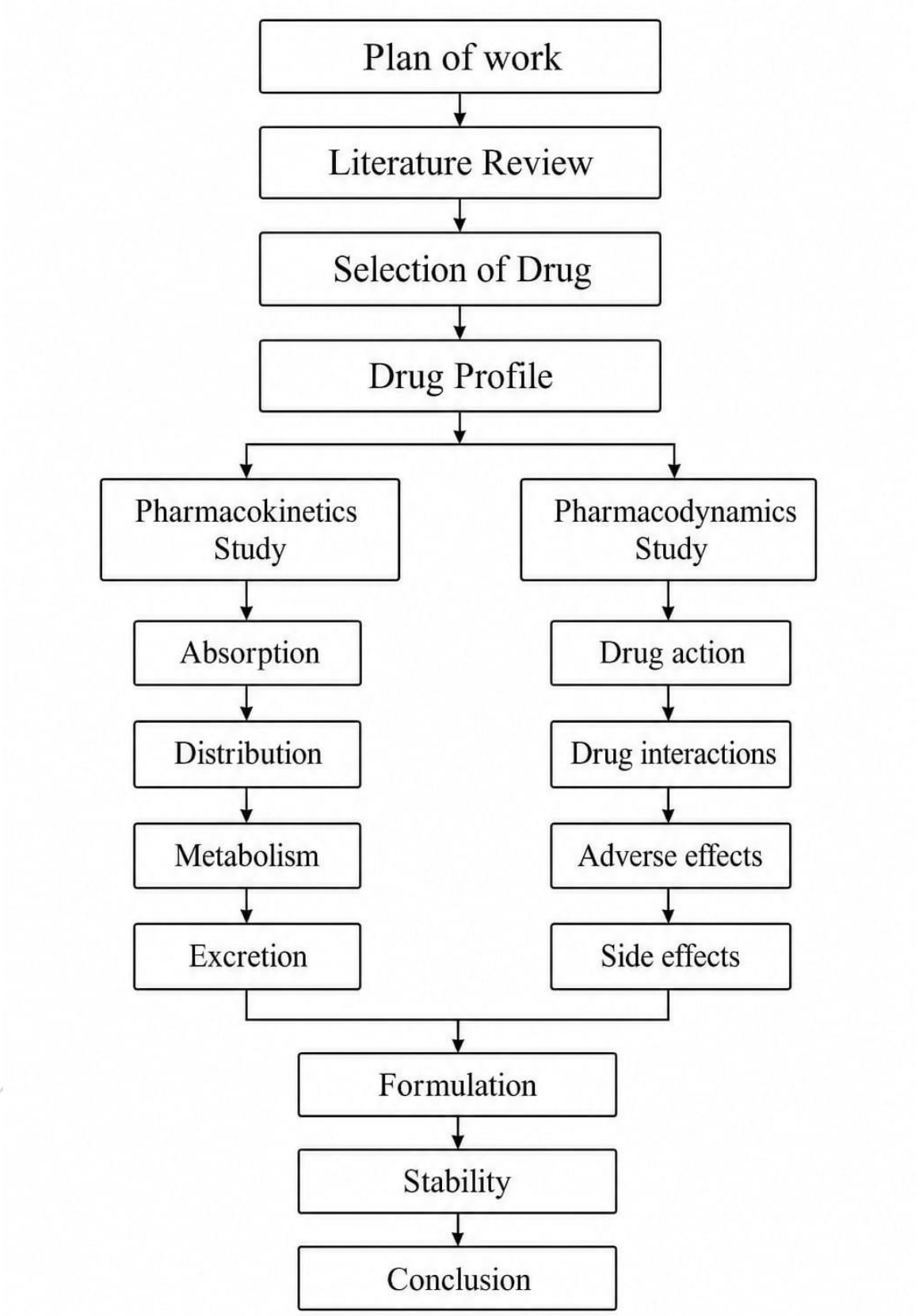
METABOLISM

- Undergoes minimal or no metabolism.
- Remains mostly unchanged after administration.

EXCRETION

- Primarily excreted unchanged in urine by glomerular filtration.
- Therapeutic concentrations persist in urine for up to 24–48 hours after a single dose.

3. PLAN OF WORK



3.1. METHODS

1. Literature Review and Data Collection

A detailed review of published research articles, review papers, clinical studies, pharmacopoeias, and standard textbooks will be carried out to collect information related to Fosfomycin Trometamol. Scientific databases and journals will be referred to for updated pharmacological and clinical data.

2. Study of Pharmacological and Mechanistic Profile

The chemical structure, classification, and mechanism of action of Fosfomycin Trometamol will be studied in detail. Special emphasis will be given to its irreversible inhibition of the MurA enzyme and its role in blocking bacterial cell wall synthesis. The pharmacokinetic properties such as absorption, distribution, metabolism, and excretion will also be analyzed.

3. Evaluation of Antibacterial Spectrum and Therapeutic Efficacy

The antibacterial activity of Fosfomycin Trometamol against common uropathogens, especially Escherichia coli and Enterococcus faecalis, will be reviewed. Its effectiveness in the treatment of uncomplicated and complicated urinary tract infections (UTIs) will also be evaluated using available clinical literature and research findings.

4. Comparative Resistance Profiling

Comparative analysis will be performed between Fosfomycin Trometamol and other commonly used antimicrobial agents such as nitrofurantoin and trimethoprim-sulfamethoxazole. The prevalence of bacterial resistance and the effectiveness of fosfomycin against multidrug-resistant (MDR) and extended-spectrum beta-lactamase (ESBL)-producing strains will be assessed from available resources.

5. Safety and Clinical Tolerability Assessment

The safety profile, adverse drug reactions, tolerability, and patient compliance associated with Fosfomycin Trometamol therapy will be reviewed. Particular attention will be given to gastrointestinal side effects and the advantages of single-dose therapy.

6. Assessment in Special Populations

Clinical use and safety of Fosfomycin Trometamol in special populations such as pregnant women and pediatric female patients (under age of 12) will be studied using available clinical evidence and treatment guidelines.

7. Compilation and Interpretation of Findings

All collected information and study findings will be systematically compiled, analyzed, and interpreted to provide a comprehensive understanding of the pharmacological profile, therapeutic effectiveness, resistance pattern, and clinical significance of Fosfomycin Trometamol.

4. FORMULATION AND PHARMACOLOGICAL ASPECTS

Selection of drug

Tromethamine, also called trometamol, is an alkaline organic compound widely used in pharmaceutical preparations as a buffering and stabilizing agent. It helps maintain an appropriate pH environment and improves the stability of acid-sensitive drugs.

In fosfomycin formulations, trometamol plays an essential role in protecting the drug and improving its therapeutic performance.[12]

Reasons for Using Trometamol in Fosfomycin

- **Enhancement of Oral Bioavailability**

One of the major purposes of adding trometamol to Fosfomycin is to improve oral bioavailability. Fosfomycin alone is not absorbed efficiently from the gastrointestinal tract. When formulated as fosfomycin trometamol, the absorption of the drug increases considerably.

Trometamol improves drug absorption by:

- Increasing stability of fosfomycin in the stomach
- Promoting better dissolution in gastrointestinal fluids
- Facilitating absorption through the intestinal wall

As a result, higher concentrations of active drug reach systemic circulation and urine.

- **Protection Against Acidic Degradation**

The stomach contains highly acidic gastric fluid, which can degrade fosfomycin before it is absorbed. Trometamol acts as a buffering agent and creates a less acidic microenvironment around the drug.

This protective effect

- Reduces degradation of fosfomycin.
- Preserves the active form of the antibiotic

- Improves the amount of drug available for absorption

Therefore, trometamol helps maintain the chemical integrity of fosfomycin during passage through the stoma.[13]

➢ **Improvement of Water Solubility**

Fosfomycin trometamol possesses excellent water solubility. Trometamol helps the drug dissolve rapidly in aqueous media, which is important for oral formulations such as sachets.

Improved solubility offers several advantages:

- Faster dissolution in gastrointestinal fluid
- Rapid absorption

➢ **Achievement of High Urinary Drug Concentration**

After oral administration, fosfomycin trometamol produces high concentrations of the drug in urine for an extended period. Since UTIs occur in the urinary tract, maintaining high urinary levels is essential for successful treatment.

The improved absorption produced by trometamol allows:

- Greater drug delivery to the kidneys
- Sustained urinary concentration
- Effective elimination of pathogenic bacteria.

This is one reason why fosfomycin trometamol is commonly administered as a single-dose therapy.[14]

➢ **Better Patient Compliance**

Due to its enhanced absorption and prolonged urinary activity, fostomycin trometamol is usually given as a single oral dose for uncomplicated UTIs.

This provides several clinical benefits:

- Reduced dosing frequency
- Easier treatment schedule
- Improved patient adherence
- Lower possibility of missed doses

Single-dose therapy also improves convenience and patient satisfaction.

2. Bioavailability and pharmacokinetic

The oral bioavailability of fosfomycin trometamol is approximately 34-58%. This means that nearly one-third to one-half of the orally administered dose is absorbed into the bloodstream.

Reasons for Good Bioavailability

Fosfomycin is combined with trometamol (tromethamine) to improve

- Water solubility
- Gastrointestinal absorption
- Stability in acidic gastric conditions

The trometamol salt form shows much higher absorption compared to fosfomycin calcium.[15]

Pharmacokinetic Features

After oral administration

- Rapid absorption occurs mainly in the small intestine
- Peak plasma concentration is reached within about 2 hours
- High urinary concentrations are maintained for 24-48 hours
- About 35-60% of the dose is excreted unchanged in urine[16]

Effect of Food

Food decreases the rate and extent of absorption:

- Bioavailability under fasting conditions: about 37%
- Bioavailability with food: about 30%

Therefore, fosfomycin trometamol is usually recommended to be taken on an empty stomach for better absorption.

5. ADVERSE EFFECTS

1. Common side effect

1) Gastrointestinal Effects (Most Common)

- Diarrhea
- Nausea
- Abdominal pain

Indigestion (dyspepsia)

2) **Headache**

- Mild to moderate headache may occur.

3) **Dizziness**

- Some patients may feel lightheaded or dizzy

4) **Vaginitis**

- Vaginal irritation or infection (due to change in normal flora)

5) **Skin Reactions**

- Rash
- Itching (pruritus).[17]

Less common and serious side effect

1) Severe Diarrhea

May indicate Clostridioides difficile infection

Symptoms

- Persistent watery diarrhea
- Blood/mucus in stool

Requires immediate medical attention

3) Food Interaction

- Food may delay absorption
- Best taken on empty stomach 4)Combination with Other Antibiotics
- Can be used with:
- Beta-lactams
- Aminoglycosides
- Effect: May show synergistic action, especially in resistant infections 5)Anticoagulants (Rare Interaction)
- May alter gut flora → possible effect on vitamin K levelsCould influence anticoagulant response (rare but monitor)[18]

2. DRUG INTERACTION

Drug Interaction

1) Metoclopramide

Effect: Decreases absorption of fosfomycin Result: Reduced therapeutic effect

Advice: Avoid taking both together

2) Other Gastrointestinal Motility Drugs Examples: prokinetic agents

Effect: Faster gastric emptying → reduced drug absorption

3. Food Interaction

Food may delay absorption Best taken on empty stomach

4) Combination with Other Antibiotics Can be used with

Beta-lactams

Aminoglycosides

Effect: May show synergistic action, especially in resistant infections

5) Anticoagulants (Rare Interaction)

May alter gut flora → possible effect on vitamin K levels Could influence anticoagulant response (rare but monitor).

6. DISCUSSION

The review project focused on the formulation, pharmacological properties, and clinical significance of Fosfomycin Trometamol in the treatment of urinary tract infections and antimicrobial-resistant bacterial infections. Based on the reviewed literature, Fosfomycin Trometamol has emerged as an important antibacterial agent because of its broad-spectrum activity, unique mechanism of action, and effectiveness against multidrug-resistant microorganisms. The increasing prevalence of antimicrobial resistance has reduced the effectiveness of many commonly used antibiotics, creating a need for alternative therapeutic agents. In such situations, Fosfomycin Trometamol has regained considerable attention in modern clinical practice.[19]

COMPARISON BETWEEN FOSFOMYCIN TROMETAMOL POWDER FORMULATION AND PESSARY FORMULATION

PARAMETER	FOSFOMYCIN TROMETAMOL POWDER FORMULATION (For Oral Solution)	FOSFOMYCIN TROMETAMOL PESSARY FORMULATION
Dosage Form	Oral powder sachet	Vaginal pessary
Route of Administration	Oral	Vaginal
Purpose / Indication	Treatment of urinary tract infection (UTI)	Treatment of vaginal / genitourinary infections
Drug Release Site	Systemic circulation through GIT	Local effect in the vaginal area
Main Objective	Achieve systemic antibacterial effect	Achieve localized antibacterial effect
Main Base / Vehicle	Sucrose, Mannitol (diluents)	Cocoa butter (pessary base)
Major Excipients	Sweeteners (Saccharin sodium), Flavors (Orange / Mandarin), Diluents (Sucrose / Mannitol), Glidant (Silica – optional)	Cocoa butter (base) (No sweetener or flavor required)
Taste Masking Required	Yes (Sweetener and flavors used)	No
Patient Compliance	Easy oral administration	Useful for localized therapy
Preparation Method	Sieving and blending of powders	Hand rolling (molding) method
Manufacturing Complexity	Simple	Moderate
Stability Concerns	Moisture sensitive	Melting at high temperature
Drug Release Pattern	Rapid dissolution in water	Slow melting and local release
Packaging	Sachets (Aluminum laminated)	Aluminum foil / Wax paper
Storage Condition	Store in a dry place	Store in a cool / refrigerated place
Advantages	Convenient single-dose therapy, Systemic effect, Widely accepted	High local concentration, Prolonged retention, Fewer systemic side effects
Disadvantages	Gastrointestinal side effects possible	Patient discomfort during insertion possible

The comparison between Fosfomycin Trometamol powder formulation and pessary formulation shows that both dosage forms are designed for different therapeutic purposes and routes of administration. The powder formulation is mainly prepared for oral use in the treatment of urinary tract infections (UTIs). It provides a systemic antibacterial effect after absorption through the gastrointestinal tract. It contains excipients such as sucrose, mannitol, sweeteners, and flavoring agents to improve taste and patient acceptability. The formulation process is simple and involves sieving and blending of powders. However, it is moisture sensitive and may cause gastrointestinal side effects in some patients.[20]

On the other hand, the pessary formulation is intended for vaginal administration and is mainly used for localized treatment of vaginal or genitourinary infections. It provides a local antibacterial effect directly at the site of infection, which helps reduce systemic side effects. Cocoa butter is commonly used as the pessary base because it melts at body temperature and ensures slow local drug release. Unlike the oral powder, taste masking is not required. The preparation method generally involves hand rolling or molding techniques and requires cool storage conditions to prevent melting.[21]

Overall, the powder formulation is more convenient for systemic therapy and widely accepted for single-dose treatment, whereas the pessary formulation is more suitable for localized therapy with prolonged retention and fewer systemic adverse effects. Both formulations have unique advantages and limitations depending on the therapeutic requirement and route of administration.

7. CONCLUSION

Fosfomycin trometamol occupies a unique and increasingly important position in modern antimicrobial therapy. Its distinctive mechanism of action, broad-spectrum activity, favorable pharmacokinetic profile, single-dose convenience, and excellent safety record collectively make it a first-line treatment option for uncomplicated urinary tract infections.

In the current era of escalating antimicrobial resistance, fosfomycin trometamol stands out as a reliable alternative when conventional antibiotics are no longer effective. Its documented activity against ESBL- producing and other drug-resistant organisms positions it as a critical agent in the management of difficult-to-treat infections.

From a formulation perspective, the oral powder sachet remains the gold standard for UTI management, offering systemic efficacy with a single-dose regimen. The pessary formulation represents an innovative approach for localized genitourinary infections, offering direct drug delivery with reduced systemic exposure.

Regarding analytical methodology, both reviewed HPLC methods are validated and reliable. For routine quality control, the simple direct UV method is preferred due to its speed and simplicity. For research settings requiring detailed stability data and high sensitivity, the derivatization-based method is more appropriate.

Future research should focus on novel formulation strategies to improve bioavailability and tissue distribution, extended therapeutic indications beyond UTIs, and comprehensive analytical validation studies conforming to international regulatory standards (ICH, IP, BP, USP). Fosfomycin trometamol's profile as a safe, effective, and patient-friendly antibiotic makes it a subject of enduring relevance in pharmaceutical and clinical science.

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