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PHARMACOLOGY - III

UNIT 2

TOPIC :

- b. Sulfonamides and cotrimoxazole.



Sulfonamides

- Sulfonamides are synthetic antimicrobial drugs used for the treatment of bacterial infections. They were the first effective chemotherapeutic agents used in medicine.
- These drugs are mainly bacteriostatic, meaning they inhibit the growth and multiplication of bacteria.

Definition

- Sulfonamides are synthetic antibacterial agents that inhibit bacterial folic acid synthesis by acting as competitive antagonists of para-aminobenzoic acid (PABA).

History

- First sulfonamide discovered: Prontosil
- Developed from azo dye research
- Opened the modern era of antimicrobial chemotherapy

Chemical Nature

Sulfonamides contain:

- Sulfonamide group (SO_2NH_2)
- Similar structure to PABA

Because of structural similarity, bacteria mistakenly use sulfonamides instead of PABA during folic acid synthesis.

Mechanism of Action

Sulfonamides inhibit bacterial folic acid synthesis.

They competitively inhibit the enzyme:

- Dihydropteroate synthase

This blocks formation of:

- Dihydrofolic acid

As a result:

- DNA synthesis decreases
- Bacterial growth stops

Simple Mechanism

PABA → Folic Acid → DNA synthesis

Sulfonamides block this pathway.

Classification of Sulfonamides

1. Short-acting Sulfonamides

Duration: 4–8 hours

Examples:

- Sulfisoxazole
- Sulfadiazine

2. Intermediate-acting Sulfonamides

Duration: 10–24 hours

Examples:

- Sulfamethoxazole

3. Long-acting Sulfonamides

Duration: More than 24 hours

Examples:

- Sulfadoxine

4. Topical Sulfonamides

Used externally

Examples:

- Silver sulfadiazine
- Sulfacetamide

Pharmacological Actions

- Inhibit bacterial multiplication
- Broad-spectrum antibacterial activity
- Effective against Gram-positive and Gram-negative bacteria

Uses of Sulfonamides

1. Urinary Tract Infections (UTI)

- Sulfisoxazole

2. Respiratory Infections

- Sulfamethoxazole

3. Gastrointestinal Infections

- Shigellosis

4. Eye Infections

- Sulfacetamide eye drops

5. Burns

- Silver sulfadiazine cream

6. Malaria

Combination:

- Sulfadoxine + Pyrimethamine

7. Pneumocystis Pneumonia

Combination:

- Sulfamethoxazole + Trimethoprim

Combination Therapy

Cotrimoxazole

Combination of:

- Sulfamethoxazole
- Trimethoprim

Advantages

- Synergistic action
- Broader antibacterial effect
- Reduced resistance

Adverse Effects

Common Side Effects

- Nausea
- Vomiting

- Headache

Serious Side Effects

- Crystalluria
- Hypersensitivity reactions
- Stevens–Johnson syndrome
- Hemolytic anemia
- Photosensitivity

Contraindications

Sulfonamides should be avoided in:

- Pregnancy
- Neonates
- Liver disease
- Kidney disease
- Patients allergic to sulfa drugs

Advantages

- Broad-spectrum activity
- Low cost
- Oral administration possible

Disadvantages

- Drug resistance common
- Allergic reactions
- Not effective against all bacteria

Cotrimoxazole

- Cotrimoxazole is a combination antibacterial drug containing:
 - Sulfamethoxazole
 - Trimethoprim
- It is a broad-spectrum antimicrobial agent used to treat various bacterial infections.
- The combination produces synergistic action by blocking two sequential steps in folic acid synthesis.

Definition

- Cotrimoxazole is a fixed-dose combination of sulfamethoxazole and trimethoprim used as a bactericidal antibacterial agent.

Composition

Ratio

- Sulfamethoxazole : Trimethoprim = 5 : 1

Example:

- 400 mg Sulfamethoxazole
- 80 mg Trimethoprim

Classification

- Sulfonamide combination antibiotic
- Broad-spectrum antibacterial agent

Mechanism of Action

- Cotrimoxazole inhibits bacterial folic acid synthesis at two different steps.

Step 1 – Action of Sulfamethoxazole

Sulfamethoxazole inhibits:

- Dihydropteroate synthase

This blocks conversion of PABA into dihydrofolic acid.

Step 2 – Action of Trimethoprim

Trimethoprim inhibits:

- Dihydrofolate reductase

This prevents formation of tetrahydrofolic acid.

Result

- DNA synthesis is inhibited
- Bacterial growth stops
- Bacteria die

Because two steps are blocked, the combination becomes bactericidal.

Simple Flow of Action

PABA → Dihydrofolic acid → Tetrahydrofolic acid → DNA synthesis
Cotrimoxazole blocks both steps.

Spectrum of Activity

Effective against:

- Gram-positive bacteria
- Gram-negative bacteria
- Some protozoa

Examples:

- E. coli, Salmonella, Shigella, Klebsiella, Pneumocystis jirovecii

Pharmacological Actions

- Broad-spectrum antibacterial action
- Bactericidal effect in combination
- Prevents bacterial multiplication

Uses of Cotrimoxazole

1. Urinary Tract Infections (UTI)

2. Respiratory Tract Infections

- Bronchitis
- Pneumonia

3. Gastrointestinal Infections

- Typhoid
- Shigellosis
- Traveler's diarrhea

4. Pneumocystis Pneumonia (PCP)

5. Ear Infections

- Otitis media

Dosage Forms

- Tablets
- Syrup
- Injection

Adverse Effects

Common Side Effects

- Nausea
- Vomiting
- Loss of appetite
- Skin rash

Serious Side Effects

- Stevens–Johnson syndrome
- Bone marrow suppression
- Hemolytic anemia
- Crystalluria
- Hyperkalemia

Contraindications

Avoid in:

- Pregnancy
- Neonates
- Severe liver disease

Drug Interactions

Cotrimoxazole may interact with:

- Warfarin
- Phenytoin
- Methotrexate

Advantages

- Broad-spectrum activity
- Synergistic action

Disadvantages

- Hypersensitivity reactions

- Resistance may occur

