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PHARMACOLOGY - III

UNIT 3

TOPIC :

- **Chemotherapy**
 - a. Antitubercular agents



Chemotherapy

Antitubercular Agents

- Antitubercular agents are the drugs used for the prevention, treatment, and control of tuberculosis (TB), a chronic infectious disease mainly caused by *Mycobacterium tuberculosis*.
- These drugs either kill the tubercle bacilli (bactericidal action) or inhibit their growth (bacteriostatic action). Antitubercular therapy always involves the use of multiple drugs together to prevent the development of drug resistance.

Introduction to Tuberculosis (TB)

Tuberculosis is a contagious bacterial disease that commonly affects the lungs, but it can also involve:

- Bones
- Kidneys
- Intestines
- Brain
- Lymph nodes

Causative Organism

- *Mycobacterium tuberculosis*

Mode of Transmission

- Spread through airborne droplets during:
 - Coughing
 - Sneezing
 - Talking

Symptoms of TB

- Persistent cough
- Fever
- Night sweats
- Weight loss
- Chest pain
- Blood in sputum

Classification of Antitubercular Drugs

1. First-Line Antitubercular Drugs

→ These are highly effective and less toxic drugs used routinely for TB treatment.

Drugs

- Isoniazid (INH)
- Rifampicin
- Pyrazinamide
- Ethambutol
- Streptomycin

2. Second-Line Antitubercular Drugs

→ Used in resistant TB or when first-line drugs cannot be used.

Drugs

- Ethionamide
- Cycloserine
- Para-aminosalicylic acid (PAS)
- Kanamycin
- Amikacin
- Capreomycin
- Levofloxacin
- Moxifloxacin

Ideal Properties of Antitubercular Drugs

An ideal antitubercular drug should:

- Be effective against mycobacteria
- Penetrate tissues properly
- Produce minimal toxicity
- Be inexpensive
- Have low resistance potential
- Be easy to administer

1. First-Line Antitubercular Drugs

1. Isoniazid (INH)

→ Isoniazid is the most important first-line antitubercular drug with strong bactericidal activity against rapidly dividing tubercle bacilli.

Mechanism of Action

Isoniazid inhibits the synthesis of **mycolic acid**, an essential component of the mycobacterial cell wall.

This leads to:

- Defective cell wall formation
- Death of bacteria

Pharmacokinetics

- Well absorbed orally
- Widely distributed in body tissues and CSF
- Metabolized in liver
- Excreted through kidneys

Uses

- Pulmonary TB
- Extrapulmonary TB
- TB prophylaxis

Adverse Effects

- Peripheral neuropathy
- Hepatitis
- Skin rash
- CNS toxicity

2. Rifampicin

→ Rifampicin is a broad-spectrum bactericidal antibiotic used as a key component in antitubercular therapy.

Mechanism of Action

- It inhibits bacterial DNA-dependent RNA polymerase, thereby preventing RNA synthesis.

Pharmacokinetics

- Well absorbed orally
- Widely distributed
- Metabolized in liver
- Excreted through bile and urine

Uses

- Tuberculosis
- Leprosy
- Meningococcal carrier state

Adverse Effects

- Hepatotoxicity
- Orange-red discoloration of urine, sweat, and tears
- Flu-like syndrome

Drug Interaction

Rifampicin is a strong enzyme inducer and decreases the action of many drugs.

3. Pyrazinamide

→ Pyrazinamide is a synthetic antitubercular drug mainly used during the intensive phase of TB therapy.

Mechanism of Action

- It disrupts mycobacterial membrane metabolism and transport functions.

Pharmacokinetics

- Good oral absorption
- Wide tissue distribution
- Metabolized in liver
- Excreted by kidneys

Uses

- Combination therapy for TB

Adverse Effects

- Hepatotoxicity, Hyperuricemia
- Joint pain, Nausea

4. Ethambutol

→ Ethambutol is a bacteriostatic antitubercular drug used in combination therapy.

Mechanism of Action

- It inhibits arabinosyl transferase, leading to impaired cell wall synthesis.

Pharmacokinetics

- Well absorbed orally
- Distributed widely
- Excreted through kidneys

Uses

- Pulmonary TB
- Drug-resistant TB

Adverse Effects

- Optic neuritis
- Blurred vision

- Red-green color blindness

5. Streptomycin

→ Streptomycin is an aminoglycoside antibiotic used as a first-line antitubercular drug.

Mechanism of Action

- It binds to the 30S ribosomal subunit and inhibits protein synthesis.

Pharmacokinetics

- Poor oral absorption
- Given intramuscularly
- Excreted unchanged in urine

Uses

- Severe TB
- TB meningitis

Adverse Effects

- Ototoxicity
- Nephrotoxicity
- Allergic reactions