Anti-tubercular Agents

Tuberculosis (TB)

What is Tuberculosis?

- Tuberculosis (TB) is a bacterial infection caused by Mycobacterium tuberculosis.
- While it primarily affects the lungs, it can also spread to other parts of the body, such as the kidneys, spine, and brain.

How is TB Spread?

- TB is an **airborne disease**, meaning it spreads when an infected person **coughs or sneezes**, releasing bacteria into the air.
- It can also be transmitted through **sharing needles** or other injection equipment contaminated with infected blood.

Symptoms of Tuberculosis

- Symptoms of TB can vary but commonly include:
  - **Persistent cough** (lasting more than three weeks)
  - **Chest pain**
  - **Coughing up blood**
  - **Fatigue**
  - **Fever**
  - **Night sweats**
  - **Unexplained weight loss**
- However, not everyone infected with TB develops symptoms.
- The bacteria can **remain dormant** in the body for years, a condition known as **latent TB infection (LTBI)**.

TB Treatment

- Tuberculosis is treatable with antibiotics, but treatment is long and complex, typically lasting six to nine months or longer.
- It involves a combination of several medications to prevent the development of drug-resistant TB strains.

Importance of Completing Treatment

- Even if symptoms improve, it is essential to complete the full course of treatment to ensure complete eradication of the bacteria.
- Incomplete treatment can lead to drug resistance, making TB harder to treat and more dangerous.

Prevention of Tuberculosis

- Prevention strategies include:
  - **Avoiding close contact** with infected individuals
  - **Vaccination** (*BCG vaccine*) in high-risk populations
  - **Early diagnosis and treatment** to prevent the spread of TB

Screening and High-Risk Groups

- **Screening for TB is recommended for individuals at higher risk, including:**
  - People with weakened immune systems (e.g., HIV patients)
  - Those who have had close contact with an infected person

Anti-Tubercular Agents

- Anti-tubercular agents are medications used to treat **tuberculosis (TB)**, a potentially serious and contagious bacterial infection that primarily affects the lungs but can also involve other parts of the body.
- These medications work by **killing or inhibiting the growth of Mycobacterium tuberculosis**, the bacteria responsible for TB.

Factors Influencing Treatment Selection

- The choice of anti-tubercular agents and the duration of treatment depend on several factors, including:
  - The **severity** of the disease
  - The **patient's age and overall health**
  - The **drug susceptibility** of the TB bacteria

Treatment Duration and Importance

- Tuberculosis treatment typically involves a combination of multiple drugs taken for several months to ensure complete eradication of the bacteria and prevent the development of drug resistance.
- Adherence to the prescribed regimen is crucial to achieving successful treatment outcomes.

Classification of Anti-Tubercular Agents

- Anti-tubercular agents are used to treat infections caused by ***Mycobacterium tuberculosis*** and can be classified based on their mechanism of action and chemical structure.
- They are often categorized into first-line and second-line drugs, and further grouped into two main types:

1. Synthetic Anti-Tubercular Agents

- These are chemically synthesized drugs that target various biochemical pathways in M. tuberculosis.
- Examples:
    1. Isoniazid
    2. Ethionamide
    3. Ethambutol
    4. Pyrazinamide
    5. Para-aminosalicylic acid

2. Anti-Tubercular Antibiotics

- These agents are naturally derived or semi-synthetic and work by inhibiting mycobacterial growth through mechanisms such as interfering with bacterial RNA synthesis, protein synthesis, or cell wall formation.
- Examples:
    1. Rifampicin
    2. Rifabutin
    3. Cycloserine
    4. Streptomycin
    5. Capreomycin sulphate

Brand Names Of Important Marketed Products

Used for the treatment of tuberculosis (TB). Often used in combinations.

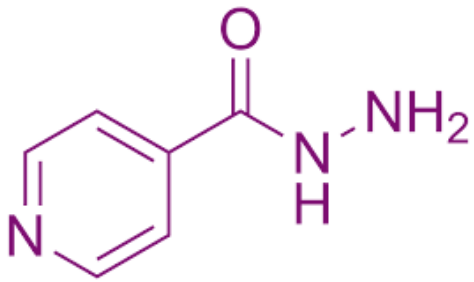
Drug Name	Brand Name(s)	Formulation	Use
Isoniazid (INH)	**Isonex, Nydrazid**	Tablet	First-line TB drug
Rifampicin	**R-cin, Rifadin, R-cinex**	Capsule, Tablet	Bactericidal in TB
Pyrazinamide	**PZA, Zinamide**	Tablet	First 2 months of therapy
Ethambutol	**Myambutol, Combutol**	Tablet	Prevent resistance
Streptomycin	**Streptomycin injection**	Injection	Severe TB, 2nd line
Fixed Dose Combinations (FDCs)	**R-cinex, Forecox, AKT-4**	Tablet	Combination for compliance

Various Synthetic Anti-Tubercular Agents Drugs

1. Isoniazid (INH)*

Chemical Structure / Formula

- **Formula:** C6H7N3O
- **Structure:** Pyridine ring with a hydrazide (-CONHNH$_2$) group.



Mechanism of Action

- **Prodrug** that is activated by **KatG enzyme** (catalase-peroxidase) in *Mycobacterium tuberculosis*.
- Once activated, it forms **isonicotinoyl radical**, which inhibits:
    1. **Enoyl-acyl carrier protein reductase (InhA)** → prevents mycolic acid synthesis (essential for the mycobacterial cell wall).
    2. **Dihydrofolate reductase** → interferes with nucleic acid synthesis.

Uses

- **First-line treatment for tuberculosis (TB)**.
- Used **alone** for **latent TB infection** (LTBI).
- Combined with **rifampicin, ethambutol, and pyrazinamide** for active TB.

Side Effects

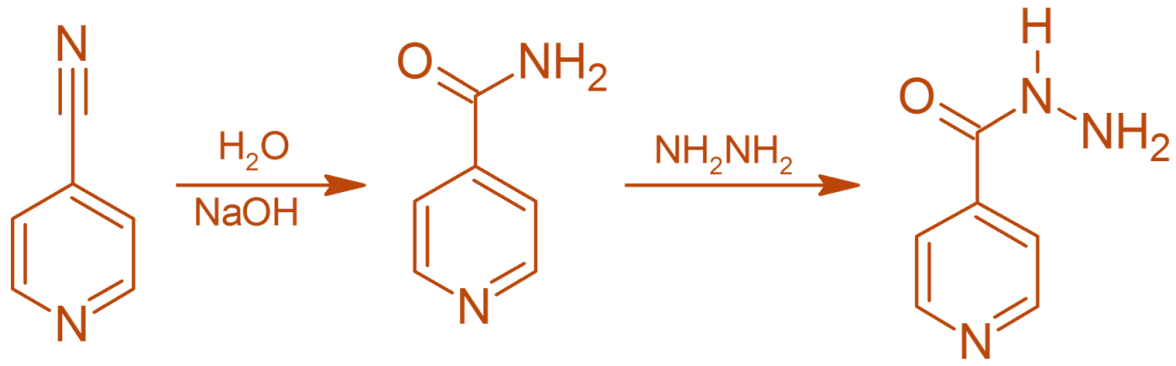
- **Hepatotoxicity** (elevated liver enzymes, hepatitis).
- **Peripheral neuropathy** (due to pyridoxine deficiency – prevented by vitamin B6 supplementation).
- **Neurotoxicity** (seizures, ataxia, dizziness).
- Hemolysis in G6PD-deficient patients.
- Drug-induced lupus (rare).

Structure-Activity Relationship (SAR) of Isoniazid

Structural Feature	SAR Insight

Isonicotinic acid hydrazide core	Essential for activity. Modifications to the hydrazide group generally reduce or eliminate activity.
Hydrazide (-$CONHNH_2$) group	Important for activation by the bacterial catalase-peroxidase enzyme (KatG). Oxidation is necessary for its prodrug activation.
Free –NH_2 group	Critical for forming the isonicotinoyl radical that inhibits InhA (mycolic acid synthesis enzyme).
Substitutions on pyridine ring	Generally, reduce antitubercular activity.
Electron-donating groups	Usually decrease activity by altering binding or red

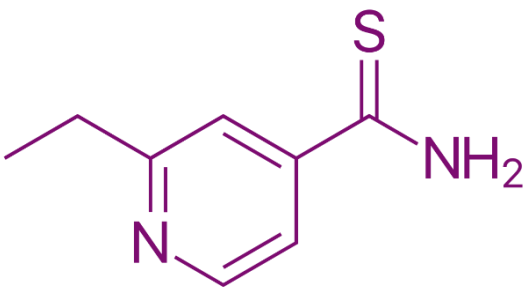
Synthesis of Isoniazid



2. Ethionamide

Chemical Structure / Formula

- **Formula:** C8H10N2S
- **Structure:** Similar to isoniazid but contains a **thioamide (-$CSNH_2$) group** instead of a hydrazide.



Mechanism of Action

- **Prodrug**, activated by mycobacterial **EthA enzyme**.
- Inhibits InhA enzyme, blocking mycolic acid synthesis, disrupting the bacterial cell wall.

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