

ANTITUBERCULAR AGENTS

Tuberculosis (TB) is a chronic infectious disease caused by various strains of *Mycobacterium* especially *Mycobacterium tuberculosis* which is an acid fast aerobic bacillus. It is transmitted via the respiratory route.

It mainly affects the lungs but can spread through blood stream and lymphatic system to the brain, bones, eyes and skin.

CLASSIFICATION

i) First line agents.

An effective bacterial agent, with an acceptable degree of toxicity.

Isoniazid, Ethambutol, Rifampicin, Streptomycin, Pyrazinamide, Rifabutin.

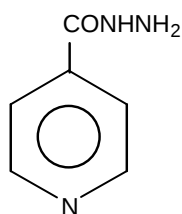
ii) Second line agents.

For microbial resistance or patient related factors.

Ethionamide, Aminosalicic acid, Cycloserine, Amikacin, Capreomycin.

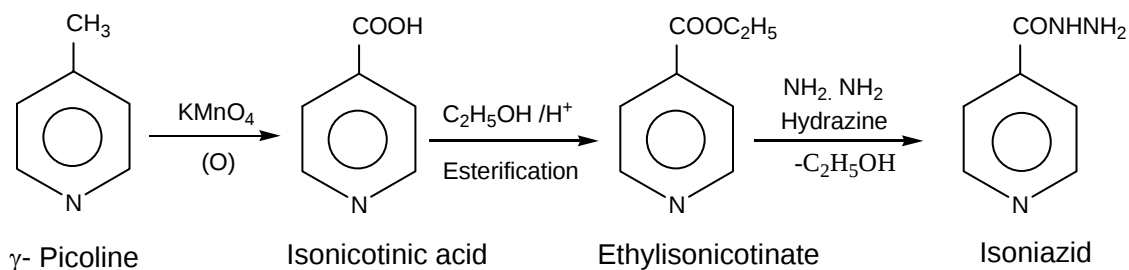
First Line Agents

Isoniazid (INH)



4 - Pyridinecarboxylic acid hydrazide

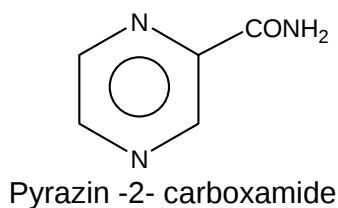
Synthesis



Food and various antacids, especially aluminium containing antacids interferes with absorption, therefore it is recommended that the drug to be taken on an empty stomach.

Use: Primary drug for treatment of *Mycobacterium tuberculosis*. It is most potent and selective of the known tuberculostatic antibacterial agent and it is regarded as the most effective agents in the therapy of tuberculosis.

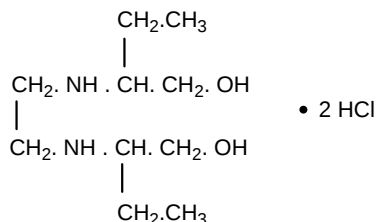
B. Pyrazinamide (Pyzid, Zypira)



Pyrazinamide is a bio-isomer of nicotinamide.

Use: It is a secondary tuberculostatic agent used in combination with other antitubercular drugs. It is an essential component of combination therapy.

Ethambutol Hydrochloride (Mycoback, Mycobutol, Mycobutol)

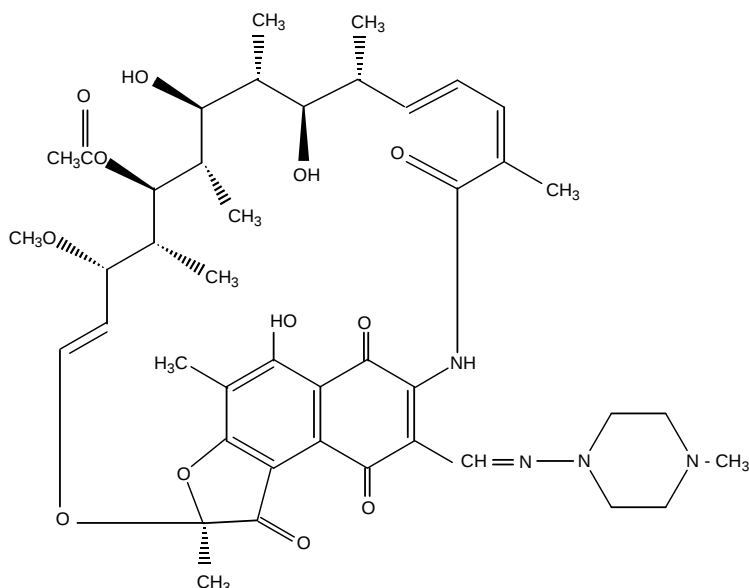


(+) 2,2' - (1,2 - Ethanediyl diamino) bis -1- butanol dihydrochloride

(+) Ethambutol is 200 to 500 fold more active than (-) enantiomer.

Use: It is a tuberculostatic drug that is effective against tubercle bacilli resistant to Isoniazid or Streptomycin.

Rifampicin (Rifampin) (LS Rif, Rimpacin)



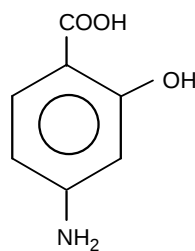
It inhibits bacterial DNA-dependent RNA polymerase (DDRP) and blocks the chain formation of RNA synthesis. It has been suggested that the aromatic naphthalene ring (π - π) bonds to the DDRP

Use: A broad spectrum antibiotic effective against most of the Gram positive bacteria and variably active against Gram negative organisms. Both *Mycobacterium tuberculosis* and *Mycobacterium leprae* are very susceptible to this drug. Its clinical

use is mainly in the treatment of tuberculosis. It is not recommended in the treatment of HIV-infected patients, since it decreases the effectiveness of protease inhibitors.

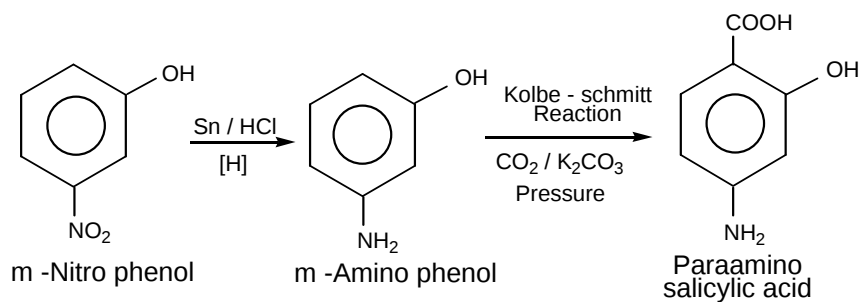
Second Line Agents

Para Amino Salicylic Acid (Sodium - PAS)



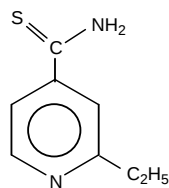
4 - Amino - 2- hydroxy benzoic acid.

Synthesis



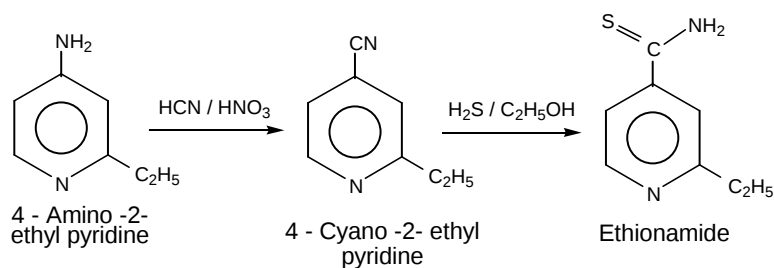
Use: It is used in the treatment of tuberculosis. PAS is a bacteriostatic agent, so it only arrest but does not eradicate the *tubercle bacilli*. Therefore PAS is always used in combination with one or two other antitubercular drugs.

Ethionamide (Ethide, Mycotuf)



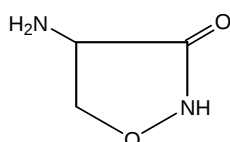
2-Ethyl - 4- pyridine carbothioamide

Synthesis



Use: It is less potent and more toxic than INH, so its general use should be avoided. It should be used only when the usual combination of Streptomycin, PAS and INH are ineffective or cannot be tolerated.

Cycloserine (Cycloko, Cyclocline, Seromycin)



4 - Amino -3- isoxazolidinone.

It is an antibiotic, isolated from *Streptomyces* species. The compound slowly dimerizes on standing or in solution.

Use: It is useful in the therapy of tuberculosis resistant to other drugs. It is always combined with other anti-tubercular drug.