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A Brief Review on Advances in Anti - Tubercular Agent

Miss. Payal Ashok Gaikwad, Prof. Poonam. P. Khade, Dr. Megha.T. salve

Abstract:
Tuberculosis (TB) is a disease that has affected mankind from very ancient times. anti–TB allopathic medications have been prescribed to control symptoms of this disease but results in to side effects like hepatitis, hypersensitivity reactions, nausea, vomiting etc. Effects of allopathic medicines. Medicinal plants form Ayurveda (India traditional medicine system) and form foreign origin have been successfully employed to treat TB. The aim of this review is to highlight the work on anti – tuberculararare identified form various sources in the literature. The present paper involves various plant drug along with their. Chemical constitution responsible for anti – tubercular activity. In 2023, the WHO reported that the south – East Asia Region had the highest number of new TB cases (45 %), followed by the African region (17%). India, Indonesia, china , the Philippines, Pakistan, Nigeria, Bangladesh, and the Democratic Republic of the congo accounted for over two – thirds of global TB cases

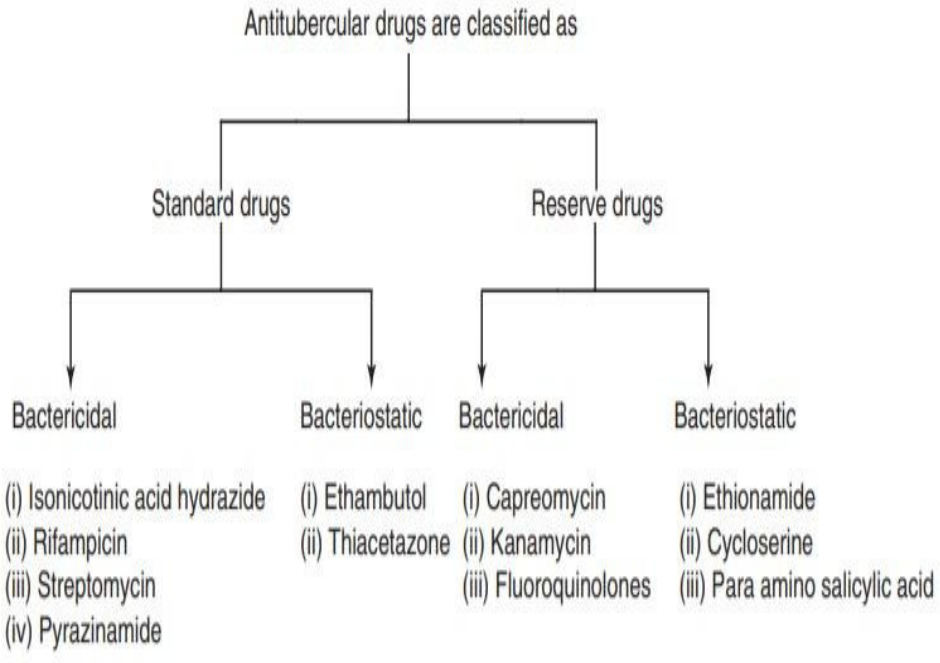
Keywords: Tuberculosis, Anti– Tubercular, Natural, Ayurveda

1.Introduction:

Tuberculosis (TB) is principally a disease of poverty, occurring in developing countries (1) Tuberculosis (TB) is a bacterial infection caused mainly mycobacterium tuberculosis (MTB).The development of paleopathology and paleopidemiology in infectious disease has proven the very ancient origin of this disease (2) The exact cause of this is unknown, although it is through that it could be because of the resurgence of TB due to HLV infection as well as multiple drug Resistant Tuberculosis (MDR – TB) due to inefficient management. Each year an estimated eight million new cases and two million deaths occur due to TB world wide 3 (3) In affected regions , the disease is recognized as serious impediment to economic and social development (4) Tuberculosis (TB) is a serious disease that kills about 2 million people every year. (5) In affected regions, the disease is seen as a major obstacle to economic and social progress (6).

2. Classification

Fig 1: Classification of anti – Tuberculosis drug



3.New structural classes of Anti – Tuberculosis Drug:-
Table: 1

Drugs	AntiTuberculosis efficacy	Toxicity	Side effects
		First Line	
Isoniazid (INH)	High	Low	Peripheral neuritis, mental disturbances, rarely convulsion.
Rifampicin (RIF)	High	Low	Hepatitis, heamolysis, shock, renal failure.
Pyrazinamide (PYZ)	High	Low	Hepatotoxicity, hyperuricemia.
Ethambutol (E)	High	Low	Nausea, rashses, fever, neurological changes.
Streptomycin (S)	High	Low	Ototoxicity,nephrotoxicity.
		Second Line	
Thiacetazone (Tzn)	Low	High	Hepatitis, dermatitis.
Para-amino salisylic acid (PAS)	Low	High	Anorexia, epigastric pain
Ethionamide	Low	High	Impotence, Optic neuritis
Cycloserine (CYS)	Low	High	Tremors, psychosis, tremors.
		New Drugs	
Ciprofloxacin	Low	High	Anorexia, dermatitis.
Clarthromycin	Low	High	Ototoxicity
Azithromycin	Low	High	Epigastric pain, impotence

Limitations of Conventional Therapy

1. Poor penetration.
2. Systemic toxicity.
3. Higher dosing.
4. Failure rates are high.
5. Drug resistance is the main problem.
6. Poor patient compliance.
7. Non-specific drug delivery.

- **Synthetic drugs :-**

1. **First line Drugs**

First- line anti – Tuberculosis drugs are essential in treating. Tuberculosis (7) these drugs are usually taken together to prevent drug resistance and to make the treatment more effective(8)

2. **Isoniazid (INH)**

- **Mechanism of action**

The drug specifically targets and inhibits the inhA enzyme, which is crucial for mycolic acid production, an important part of the cell wall of mycobacteria(9)

- **Adverse effects**

It mentions unusual blending, which implies blending that occurs unexpectedly or in atypical situations

3. **Rifampicin (RIF)**

Rifampicin originates form rifamycin B, which is a metabolite produced Naturally by the bacteria Nocardia mediterranel (10) Rifampicin , also known as Rifampin , is a term mentioned in the text (11) Rifampicin has been crucial in treating Tuberculosis (Tb) since 1968 because it can sterilize the bacteria and reduces treatment duration of high doses (12)

Mechanism of action

The text explains that a certain process inhibits the Enzyme DNA – dependent RNA polymerase in mycobacteria, which stop RNA production and result in cell death.

Adverse effects

The text describes urine, sputum, sweet and faces that are orange – red in color

Pyrazinamide (PZA)

Mechanism of action

The drug interferes with how mycobacterium cell members transport substances and metabolize . It turns pyrazinoicacid , which reduces the PH of the environment (13)

Adverse effect

Yellow eyes or skin can indicate jaundice a condition often linked to liver problem

Ethambutol

Mechanism of action

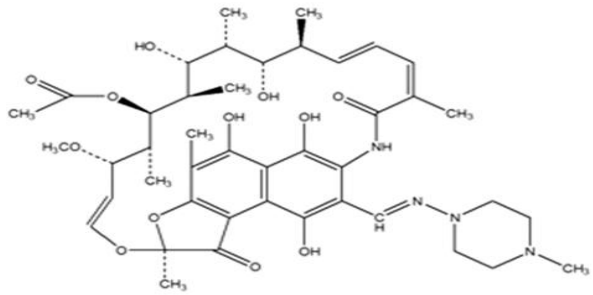
A drug stop the formation of arabinogalactan , a key part of the mycobacterial cell wall by blocking the Arabinosyl transfence enzyme . This prevent the synthesis of the cell wall (14)

Adverse effect

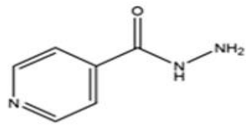
Red – green blindness is a type of color vision deficiency where it is hard to distinguish between red and green color.

GI disturbance cover Several issues related to eyesight, including blurriness difficulty seeing

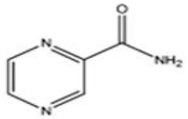
Rifampicin



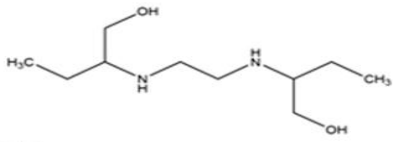
Isoniazid



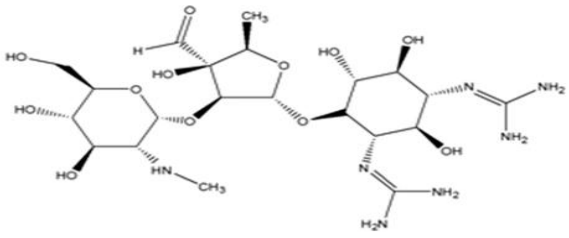
Pyrazinamide



Ethambutol



Streptomycin



Second line Drugs

Second – line Anti – TB drug have more serious side effects than first – line drug (15)

When fist - line TB medications are not suitable due to resistance or intolerance, Second- line medications are used, mainly for treating multi – drug – resistance TB (16)

Fluoroquinolones (e.g. Levofloxacin, Moxifloxacin)

Mechanism o action

The text discusses the treatment of several infection such as puniomonia , Tuberculosis (TB) , sinusitis and endocarditis by treating specific bacterial enzymes. It highlights how inhibing the Enzymes topoisomerase IV and DNA gyrase prevent bacterial DNA transcription, replication, and repair , effectively stopping bacterial DNA synthesis (17)

Adverse effect

Tendinitis, QT Prolongation

Aminoglycosides (e.g. Aminkacin , kanamycin)

Mechanism of action

The Bacterial cell dies because a substance bind to its 30S ribosomal subunits. The binding causes mRNA to be misred , preventing the production of necessary proteins

Adverse effect

Ototoxicity , nephrotocity

Capreomycin

A polypeptide antibiotic

Mechanism of action

The text explains a Mechanism by which certain substances attach to ribosome, stopping protein production in a way similar to Aminoglycosides. This process ultimately results in the death of bacterial cell .(18)

Adverse effect

Ototoxicity, nephrotocity

Ethionamide

Mechanism o action

It inhibits mycolic acid synthetics, similar to Isoniazid with with discrubs the cell wall of mycobacteria. This interference with the cell wall is crucial for its effectiveness .(19)

Adverse effect

Neurotoxicity , psychisis , seizures

Para – amino salicylic acid (PAS)

Mechanism of action

The text explain that a process inhibits the production of folate ,which a crucial for making DNA and for cell replication. This is done by a substance that competes with para- minobenzoic acid, or PABA

Bedaquiline

An Diqrylquinolic antibiotic

Mechanism of action

The drug blocks an important enzyme that helps make ATP , which the bacteria need for energy.

Delamanid

A Nitro – dihydro – imidazole oxazole derivative

Mechanism of action

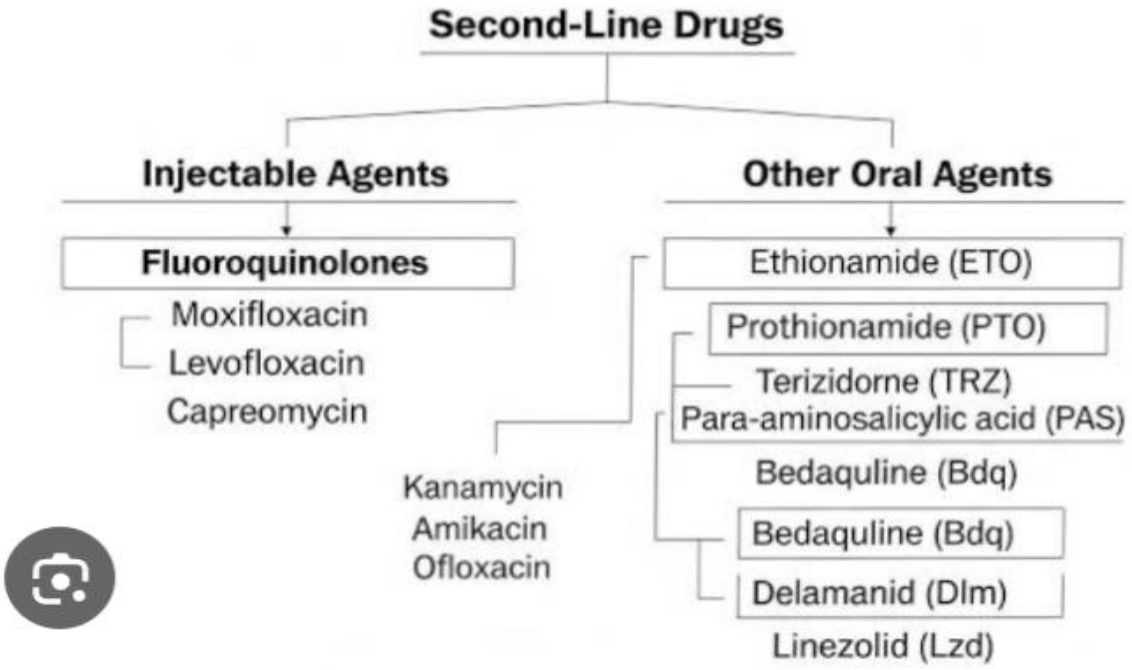
A drug stop the production of mycolic acid, which is important for building the bacteria cell Wall . Without mycolic acid, the bacteria die because they can maintain their cell walls .(20)

Linezolid

An oxazolidinone antibiotic

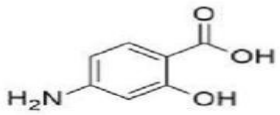
Mechanism of action

The text explains that a certain substances attaches to the 50S part of a ribosome . This action stop the starting step needed for making proteins. As a result, it prevents proteins form being produced. (20)

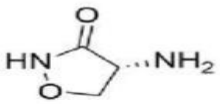


Structure

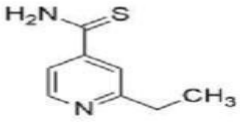
Second-line anti-TB drugs



Para-amino salicylic acid (4)

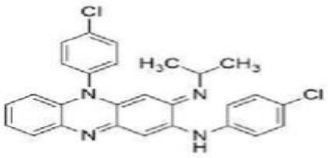


cycloserine (5)

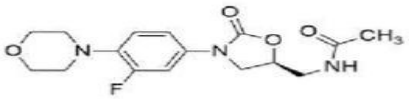


Ethionamide (6)

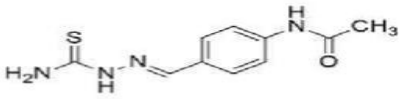
Drugs used for MDR-TB



Clofazimine (7)

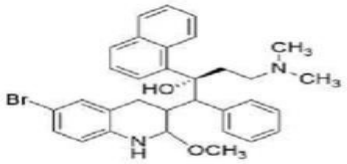


Linezolid (8)

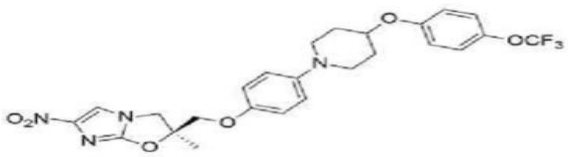


Thioacetazone (9)

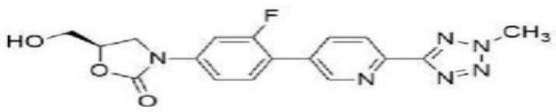
New Drugs for TB



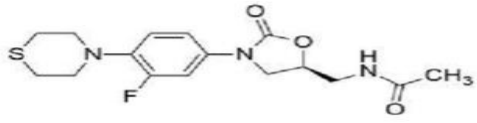
Bedaquiline (10)



Delamanid (11)



Tedizolid (12)



Sutezolid (13)

Medicinal Herbs proved to cure TB

Herbal drug have various natural components that are being researched for their possible effectiveness against Tuberculosis .(21)

Garlic has antibacterial properties that can protect against mycobacterium TB and other infection .(22)

Catechins can fight against mycobacterium tuberculosis. (23)

The text provide a list of specific herbs known for their anti – Tubercular properties.

Novel anti – tubercula agents

New discoveries in Tuberculosis (TB) research are needed to meet global targets and achieve the sustainable development golas and the end TB strategy. After nearly four decades of research, about 13 new compounds have been discovered, through no. New TB medications have been approved. (24)

Essential oils form plants as anti – tuberculosis agents

Essential oils from plants can fight mycobacterium tuberculosis in lab tests. These olis have many chemical that might help , with eugenol being studied for its effects.(25)

The Essential oil form murraya koenigli shown strong ability to inhibit bacteria such as corynebactrium tuberculosis, pseudimonas areuginosa , streptococcus pyogenes ,klebsiella pneumoniae , and Enterobacter aerigenes (26)

Table : 2

S.No	Plant name	Activity/Microbe inhibited	
1	*Pulicaria gnaphalodes* and *Perovskia abrotanoides* (Essential oils)	*Mycobacterium tuberculosis*	35
2.	Essential oils from different plants	*Mycobacterium tuberculosis*	36
3.	Essential oil from *Murraya koenigii* (L.)	*Corynebacterium tuberculosis, Pseudomonas aeruginosa, Streptococcus pyogenes, Klebsiella pneumonia* and *Enterobacter aerogenes*	37

Conclusion

Current efforts to develop new drugs of repurpose existing ones to tackle drug resistance in TB are praiseworthy . Bedaquiline and damanid are promising drugs with unique action that might avoid common

TB drug resistance. More work is needed to develop new anti – TB medications and repurpose drugs used for other resistant bacteria. Additionally, Expiring new therapeutic targets and innovative drug delivery techniques could improve treatment effectiveness, reduce dosage , and minimize side effects.

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