MEDICINAL CHEMISTRY - III

UNIT 3 NOTES

ANTITUBERCULAR AGENTS

- SYNTHETIC
- ANTIBIOTICS

UTI AGENTS

- QUINOLONES
- MISCELLANEOUS

ANTIVIRAL AGENTS

IMPERFECT PHARMACY

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IMPERFECT PHARMACY APP

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ANTI TUBERCULAR AGENTS

- Antitubercular drugs are agents used to treat tuberculosis (TB), a serious infectious disease caused primarily by the bacteriam Mycobacterium Tuberculosis.
- These drugs either kill the bacteria or inhibit their growth.

TUBERCULOSIS

- Tuberculosis is a chronic infectious disease caused by its bacterium Mycobacterium Tuberculosis.
- It most commonly affects the lungs, but it can also spread to other body parts.

TYPES

It can be classified on the basis of two types :

① Based on site of .
② Based on Active state.

① BASED ON SITE OF

- Pulmonary TB (Lungs)
- Extrapulmonary TB (Lymph nodes, GIT, Bones & Joints, Brain, Kidneys, Skin)

② Based On Active State

- Latent TB (infected but no symptoms, may active later).
- Active TB (Bacteria are multiplying & cause symptoms).

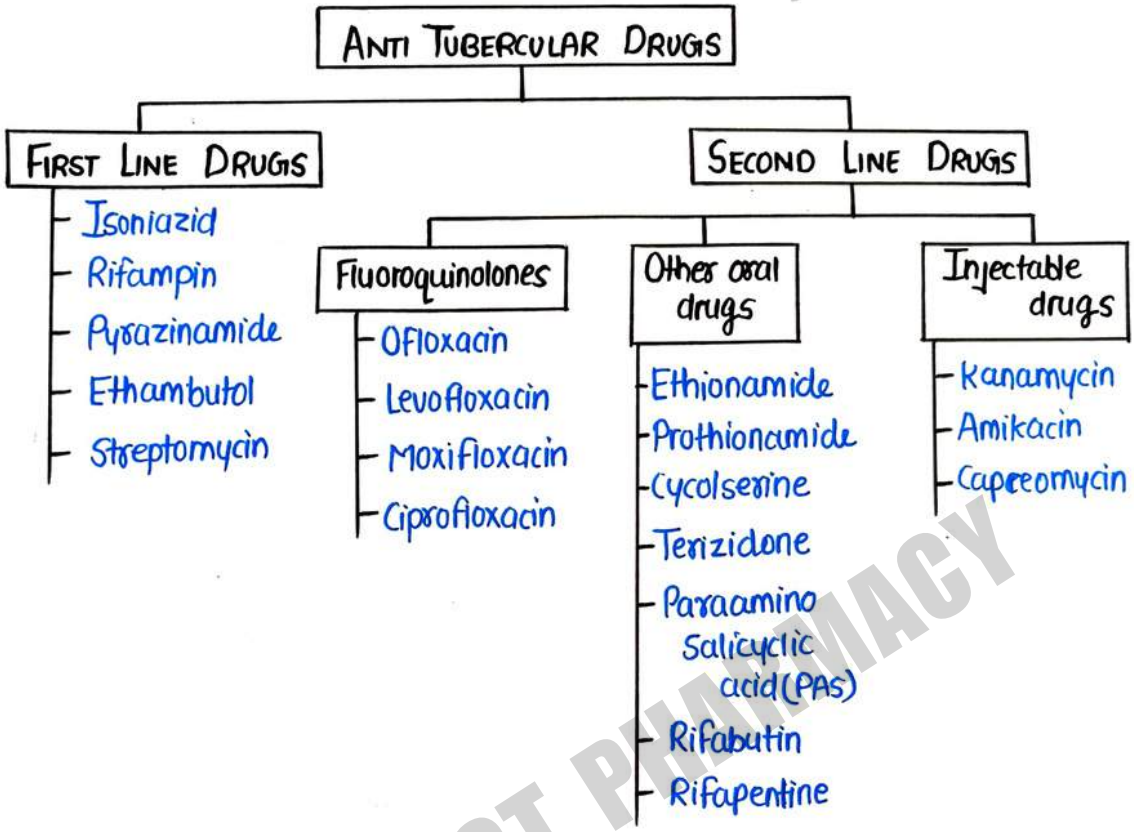
Mycobacterium Tuberculosis

- It is an acid-fast, aerobic, rod-shaped bacteria.
- Genus : Mycobacterium
- Species : Tuberculosis
- Family : Mycobacteriaceae
- It's cell wall is rich in Mycolic acids, making it waxy, thick and hydrophobic.
- It is a slow-growing bacteria (doubling time its about 15-20 hours).
- It spreads through airborne droplets when an infected person coughs, sneezes or talks.

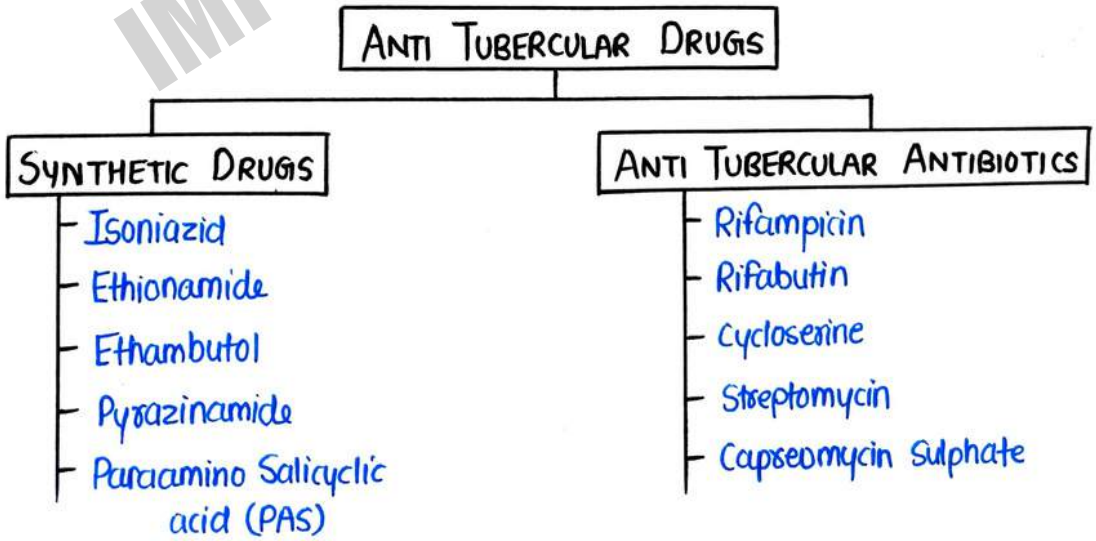
Symptoms

- fever
- Night sweats
- Fatigue
- Loss of Appetite
- Unexplained weight loss
- Persistant cough lasting more than 2-3 weeks
- Chest pain

Classification



Classification According To Our Syllabus

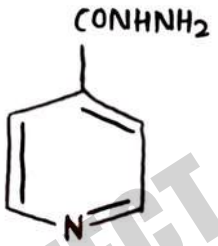


SYNTHETIC TUBERCULAR DRUGS

- These are Antitubercular drugs that are synthesized in laboratory to treat Tuberculosis (TB) caused by Mycobacterium Tuberculosis.

① ISONIAZID

- It is a first line synthetic antitubercular drug used to treat & prevent tuberculosis.
- It is one of the most effective & widely used medicine against M. Tuberculosis.
- Its chemical name is Isonicotinic Acid Hydrazide (INH).

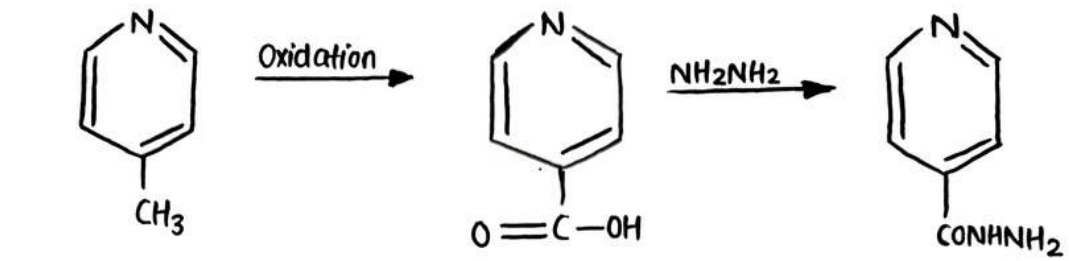


Isonicotinic acid hydrazide

MOA

- Isoniazid is a prodrug that gets activated by the KatG enzyme inside M. Tuberculosis.
- The active form inhibits the synthesis of Mycolic Acids, which are essential components of the Mycobacterial cell wall.
- This leads to bactericidal effects against actively dividing TB bacteria.

Synthesis

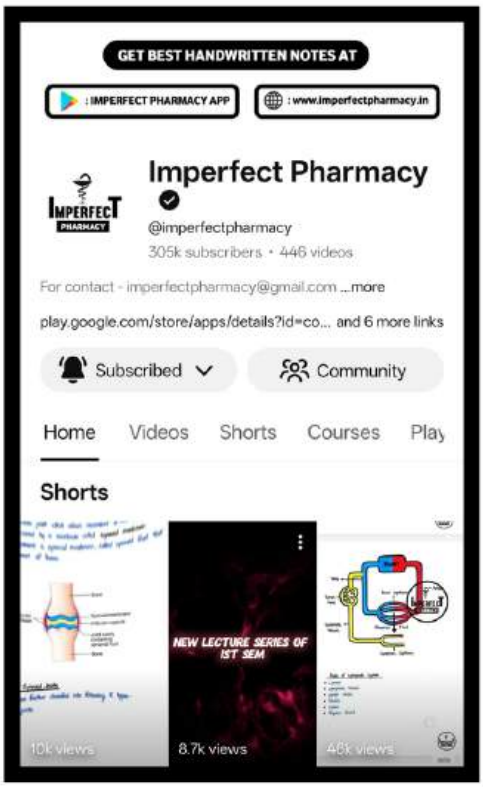


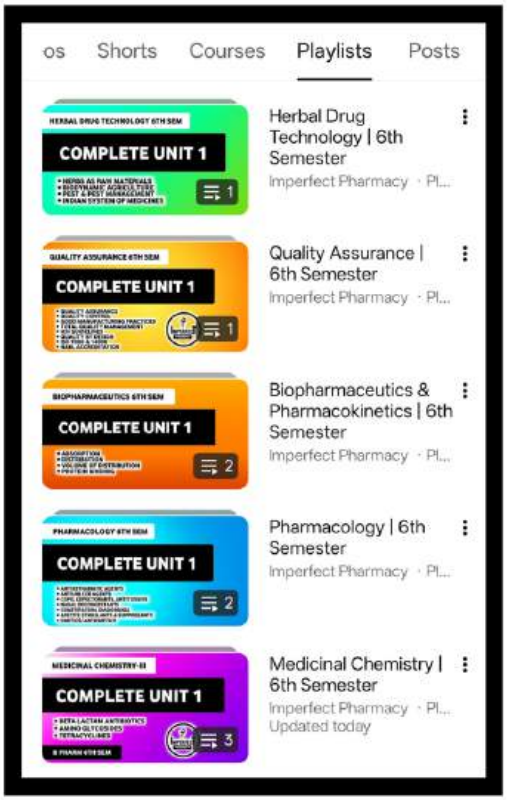
4-methyl Pyridine → Isonicotinic Acid → Isoniazid

Uses

- Active TB
- Latent TB

FOR LECTURE VIDEOS VISIT OUR CHANNEL

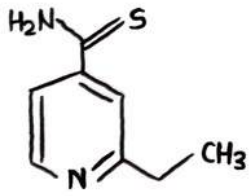




FOR MORE CONTENT : VISIT OUR APP

② ETHIONAMIDE

- It is a second-line drug used primarily to treat multidrug-resistant Tuberculosis (MDR-TB).



MOA

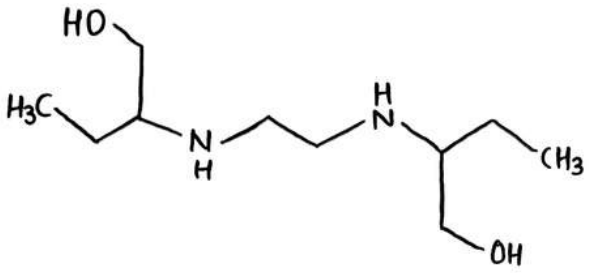
- Ethionamide is a prodrug that gets activated by bacterial enzymes.
- Its active form inhibits mycolic acid synthesis, a vital component of Mycobacterium Tuberculosis cell wall, leading to bacterial death.

Uses

- MDR-TB
- Leprosy (Rare)

③ ETHAMBUTOL

- It is first-line antitubercular drug used in combination therapy for tuberculosis.



MOA

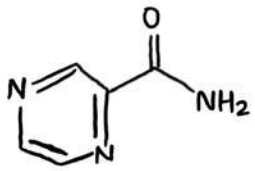
- Ethambutol inhibits arabinosyl transferase, an enzyme involved in the synthesis of the mycobacterial cell wall.
- This distrupt cell wall formation leading to bacteriostatic effect.

Uses

- Active TB

④ PYRAZINAMIDE

It's first line drug used in combination therapy of Tuberculosis.



MOA

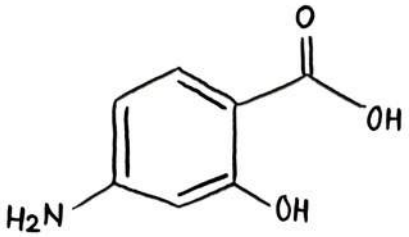
- Pyrazinamide is a prodrug converted to pyrazinoic acid by bacterial enzyme pyrazinamidase.
- It works best in acidic environments and distrupts membrane transport & energy production in Mycobacterium Tuberculosis.

Uses

- Active TB

⑤ PARA - AMINOSALICYCLIC ACID

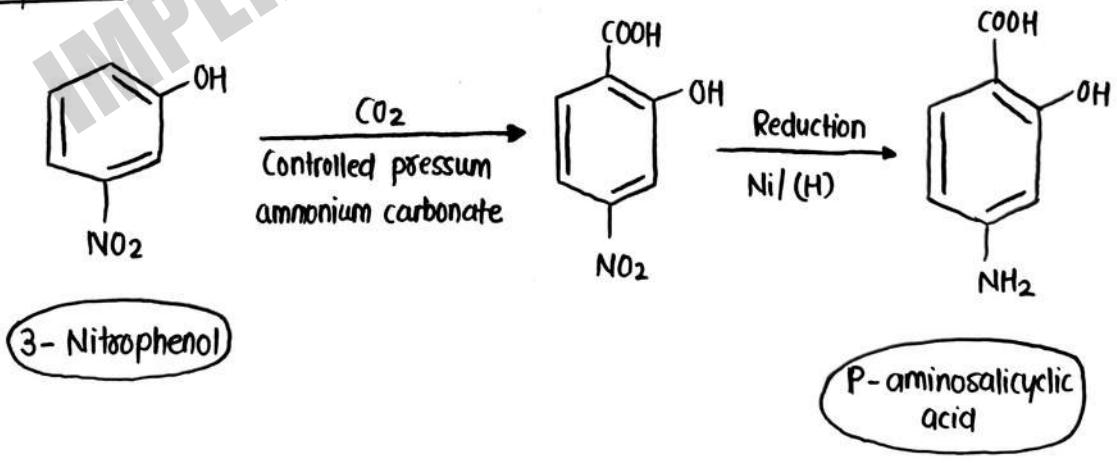
It's second line drug, mainly used when first line drugs failed.



MOA

- Its a folate synthesis antagonists.
- It resembles PABA (Para - aminobenzoic Acid), a key substrate in bacterial folic acid synthesis pathway.
- It inhibits dihydropteroate synthase, a key enzyme involved in folate synthesis, thereby blocking folic acid synthesis/production essential for bacterial growth.

Synthesis



Uses

- MDR - TB

ANTITUBERCULAR ANTIBIOTICS

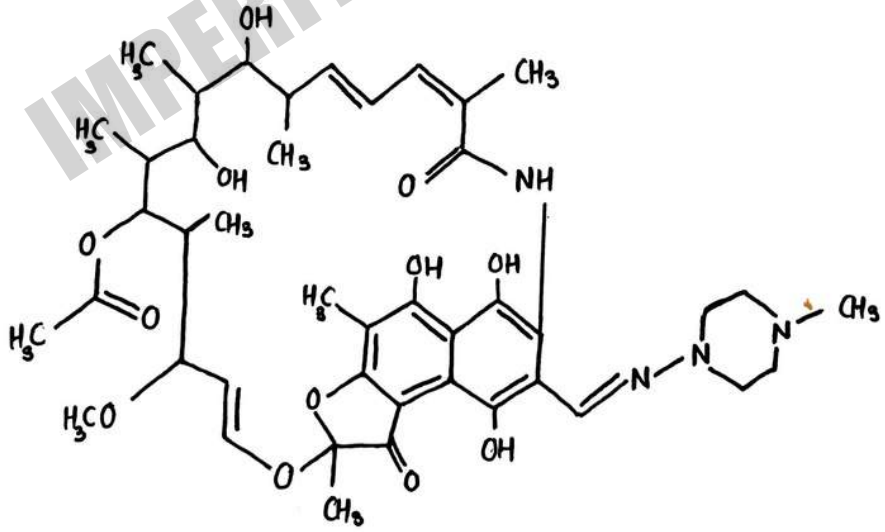
Antitubercular Antibiotics are medications that kill or inhibit the growth of Mycobacterium Tuberculosis, either by distrupting its cell wall, protein synthesis or vital metabolic process.

① RIFAMPICIN

Rifampicin is a first line antitubercular antibiotic used to treat tuberculosis & other bacterial infections.

MOA

- Rifampicin inhibits bacterial DNA-dependent RNA polymerase blocking RNA synthesis.
- This stops bacteria from making proteins, leading to bacterial death.



Uses

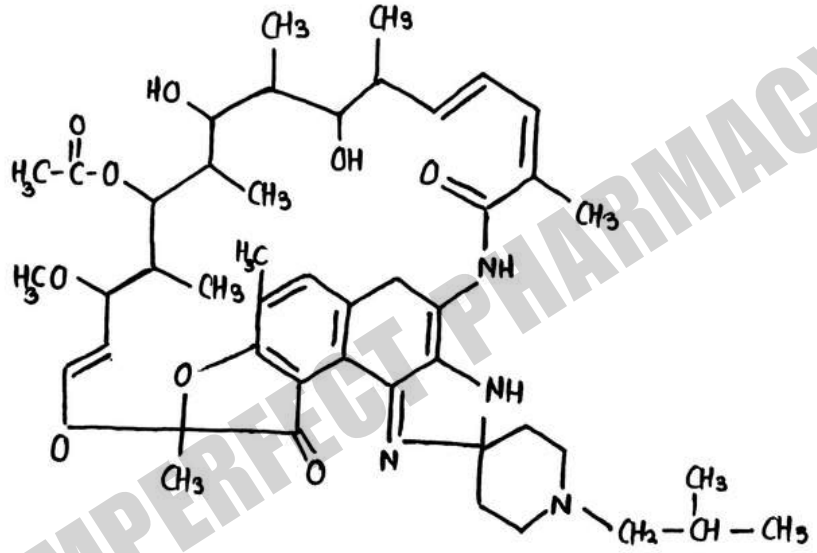
- Treatment of Tuberculosis

② RIFABUTIN

It is a rifamycin - class antibiotic similiar to Rifampicin, mainly used in bacterial infections, especially in HIV patients.

MOA

Same as Rifampicin

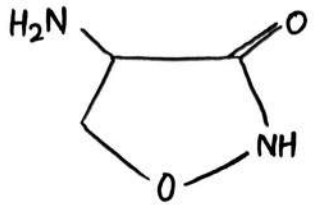


Uses

- Tuberculosis
- M. avium complex disease in AIDS patient

③ CYCLOSERIN

Cycloserin is a second-line antitubercular antibiotic, used mainly for drug-resistant TB.



MOA

- Cycloserin inhibits bacterial cell wall synthesis by blocking two enzymes:

① Alanine racemase

② D-alanine : D-alanine ligase

- They are essential for forming peptidoglycon, a key component of bacterial cell wall.

Uses

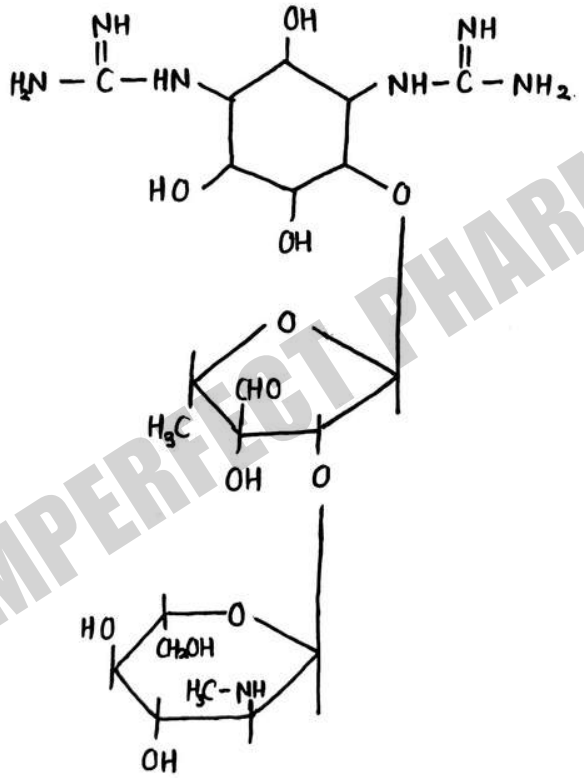
- MDR-TB
- Urinary Tract infections

④ STREPTOMYCIN

Its a first-gen aminoglycosides antibiotic & was the first effective antitubercular drug used in TB treatment.

MOA

Streptomycin binds to the 30s ribosomal subunits of bacteria, inhibiting protein synthesis by causing misreading of mRNA, leading to bacterial death.



Uses

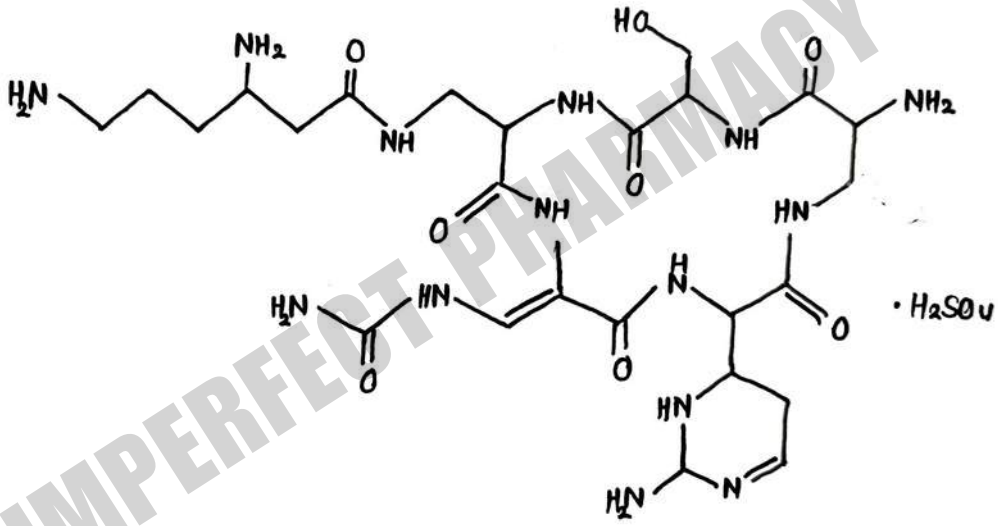
- Treatment of Tuberculosis
- Treatment of other bacterial infections

⑤ CAPREOMYCIN SULPHATE

It is a second line injectable antitubercular antibiotic mainly used for drug resistant TB.

MOA

- It inhibits protein synthesis by binding to the 70s ribosomal complex (likely at the 50s - 30s interface), distrupting translation in Tuberculosis.
- Depending on concentration, it acts on both bacteriostatic & bactesiocidal.



Uses

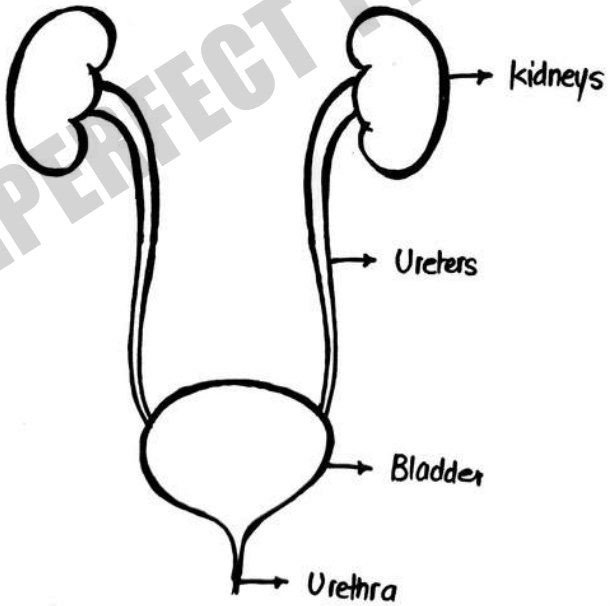
- MDR TB

Urinary Tract Anti Infective Agents

- Urinary Tract anti-infective agents are a group of medicine used to treat infections of urinary tract, including kidneys, bladder, ureters & urethra.
- These agents work by killing or inhibiting the growth of bacteria that cause urinary tract infections (UTIs).

UTIs

- Urinary Tract infections are infections that occur in any part of urinary system.
- Most UTIs are caused by bacteria, particularly E. coli, which normally live in the digestive tract but can enter the urinary tract.



Types Of UTIs

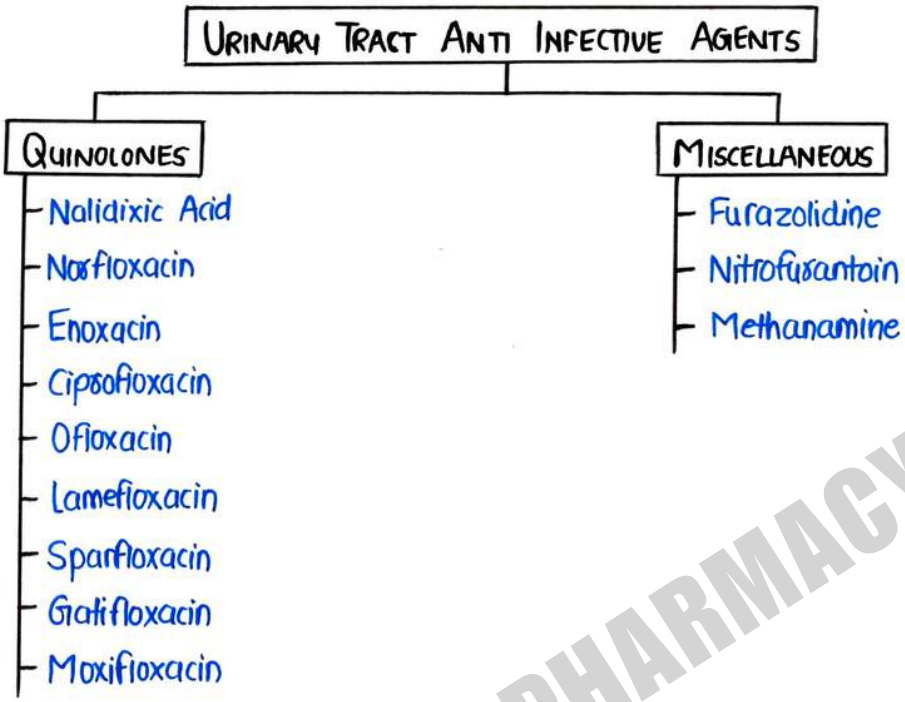
① Cystitis - Infection of Bladder (Most common form)
② Urethritis - Infection of urethera
③ Pyelonephritis - Infection of kidneys (more serious)
④ Ureteritis - Rare, infection of the ureters

Symptoms

- Burning or pain during urination.
- Frequent urge of urination.
- Increase urgency of urination.
- Clody or dark - coloured urine.
- Strong - smelling urine.
- Lower abdominal discomfort.
- Mild Fever

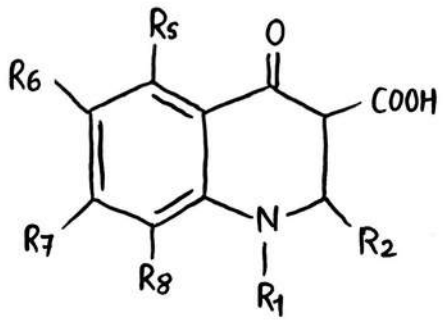
CLASSIFICATION

According to our syllabus :



QUINOLONES

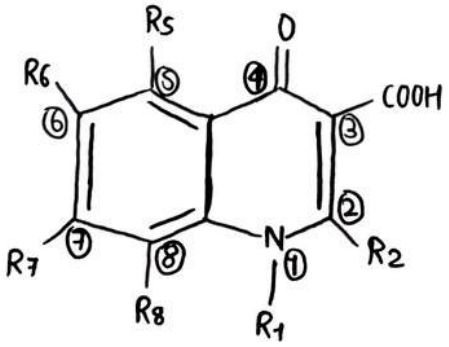
- Quinolones are class of synthetic broad-spectrum antibacterial agents that inhibit bacterial DNA replications.
- They are potent, broad spectrum antibacterial agents.



MOA

- Quinolones kills bacteria by interfering with DNA synthesis and inhibiting their replication pathway.
- During DNA synthesis, double-stranded DNA needs to unwind into two single-stranded structures to be used as the template, allowing the transcription complexes to proceed and complementary base pairing to occur.
- This unwinding process is done by the bacterial topoisomerase, II type enzymes, DNA gyrase and DNA topoisomerase IV.
- Quinolones exert their action by inhibiting these enzymes, thereby stopping the synthesis process.

SAR Of Quinolones



① Core Structure

- The basic quinolone nucleus (4-quinolone) is essential for activity.

② Position 1 (N-1 substitution)

- Alkyl groups (e.g. cyclopropyl) enhance activity, especially against Gram- negative bacteria.

③ Position 3 & 4 (Carboxylic acid & ketone group)

- This groups are crucial for binding to DNA - enzyme complexes.
- Any modification typically abolishes activity.

④ Position 6 (Fluorine Atom)

- Fluorination increases cell wall position / penetration and enhance activity, especially against Gram - negative bacteria.

⑤ Position 7 (Piperazine or similar ring)

- Affects spectrum and pharmacokinetics.
- Piperazine improves activity against Pseudomonas and increases CNS penetration (but may also increase side effects like siezures).

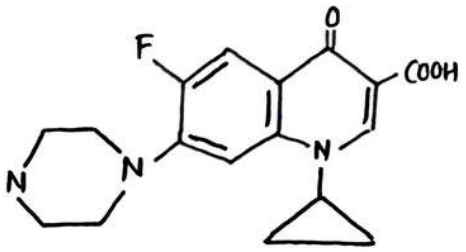
⑥ Position 8 (Substituents like methoxy)

- Methoxy or halogen at this position can reduce phototoxicity and enhance activity against anaerobes and Gram-positive bacteria.

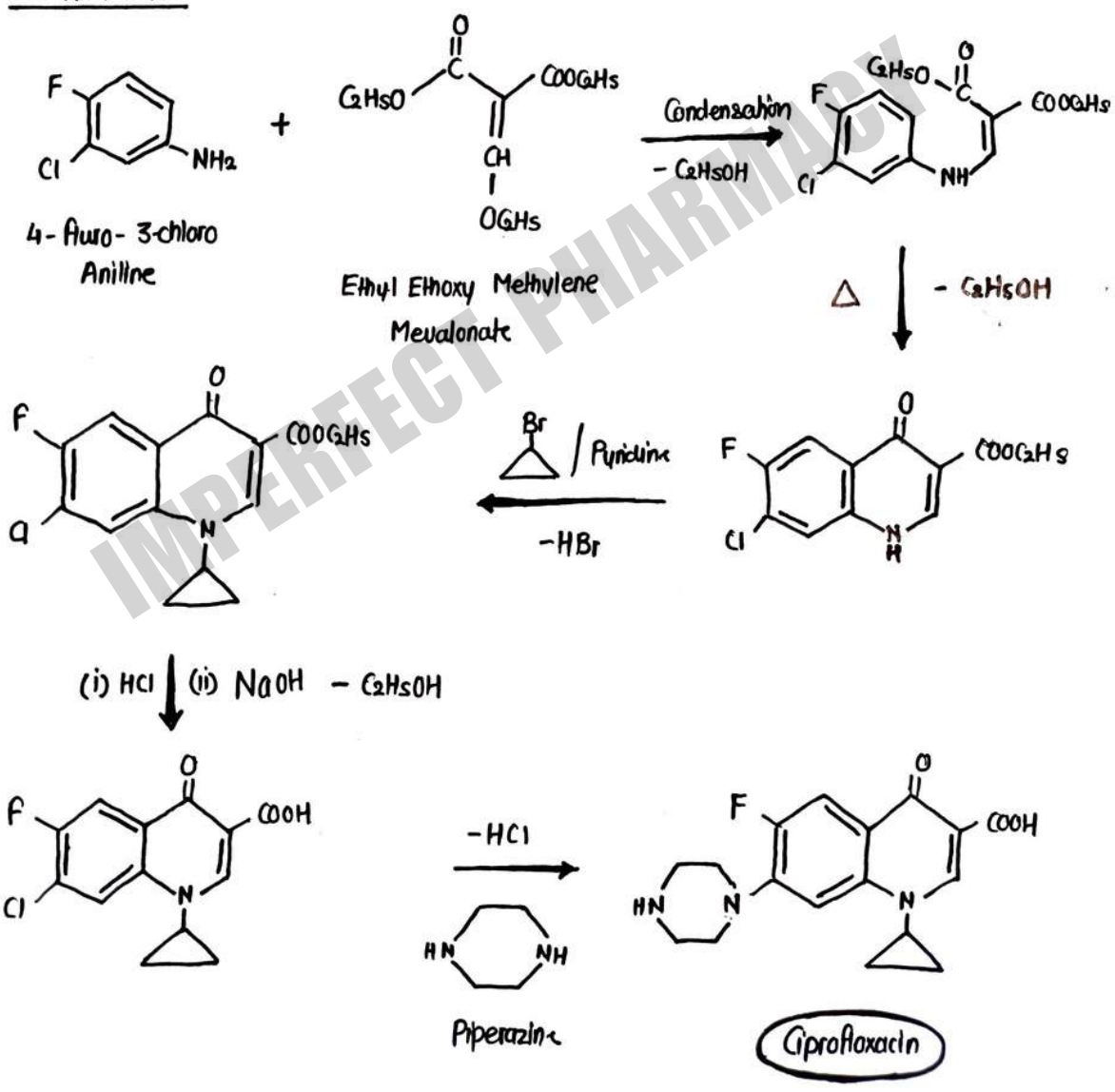
Drugs In Our Syllabus

- Nalidixic Acid
- Norfloxacin
- Enoxacin
- Ciprofloxacin*
- Ofloxacin
- Lamefloxacin
- Sparfloxacin
- Gatifloxacin
- Moxifloxacin

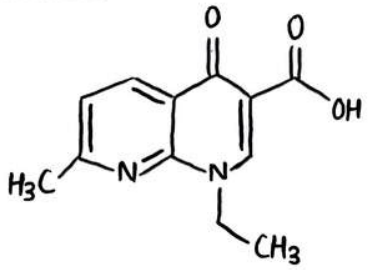
① CIPROFLOXACIN*



SYNTHESIS



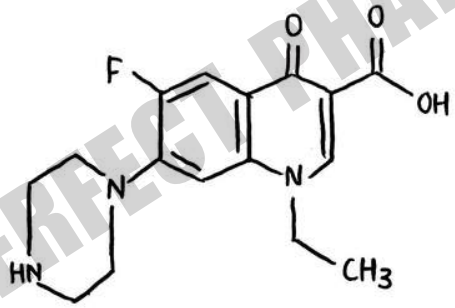
② Nalidixic Acid



Uses

- UTIs
- Diarrhea
- Dysentery

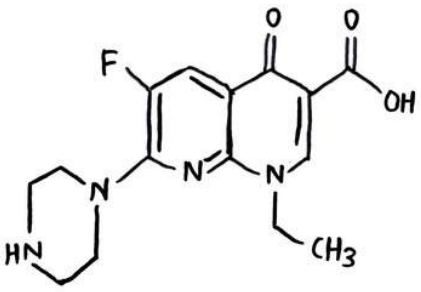
③ Norfloxacin



Uses

- Gonnorhea
- Syphillis
- UTIs.

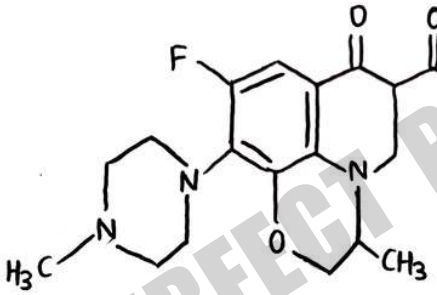
④ Enoxacin



Uses

- UTIs

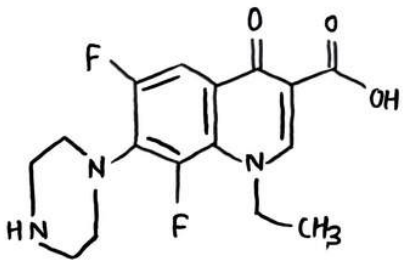
⑤ Ofloxacin



Uses

- Sinusitis
- Chlamydia
- UTIs

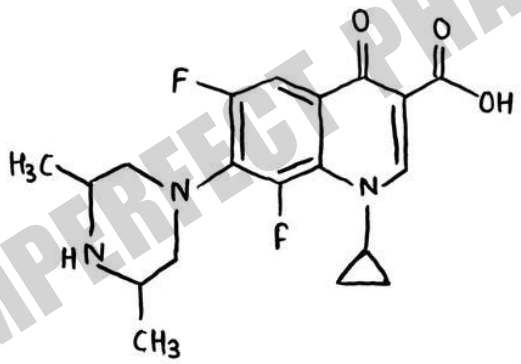
⑤ LOMEFLOXACIN



Uses

- Pneumonia
- UTIs
- Gonorrhea

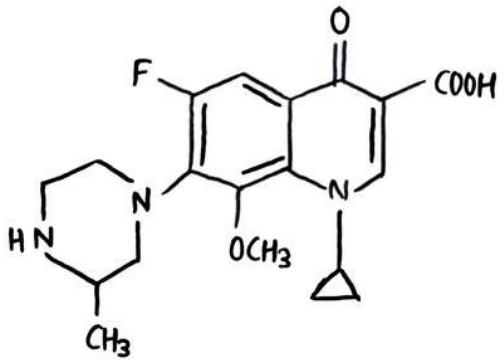
⑥ SPARFLOXACIN



Uses

- Pneumonia
- Sinusitis
- Gonorrhea

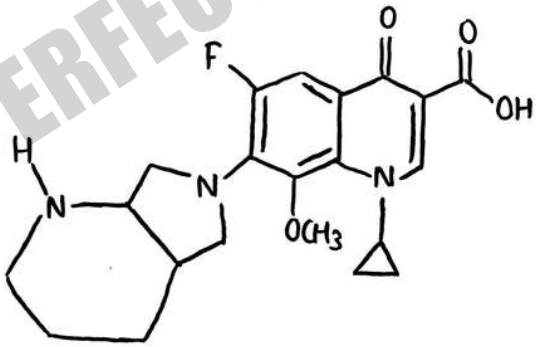
⑦ Gatifloxacin



Uses

- Sinusitis
- UTIs
- Gonorrhea.

⑧ Moxifloxacin

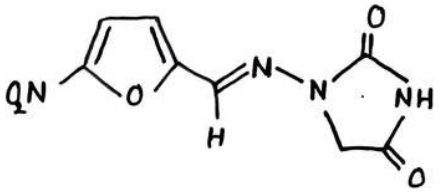


Uses

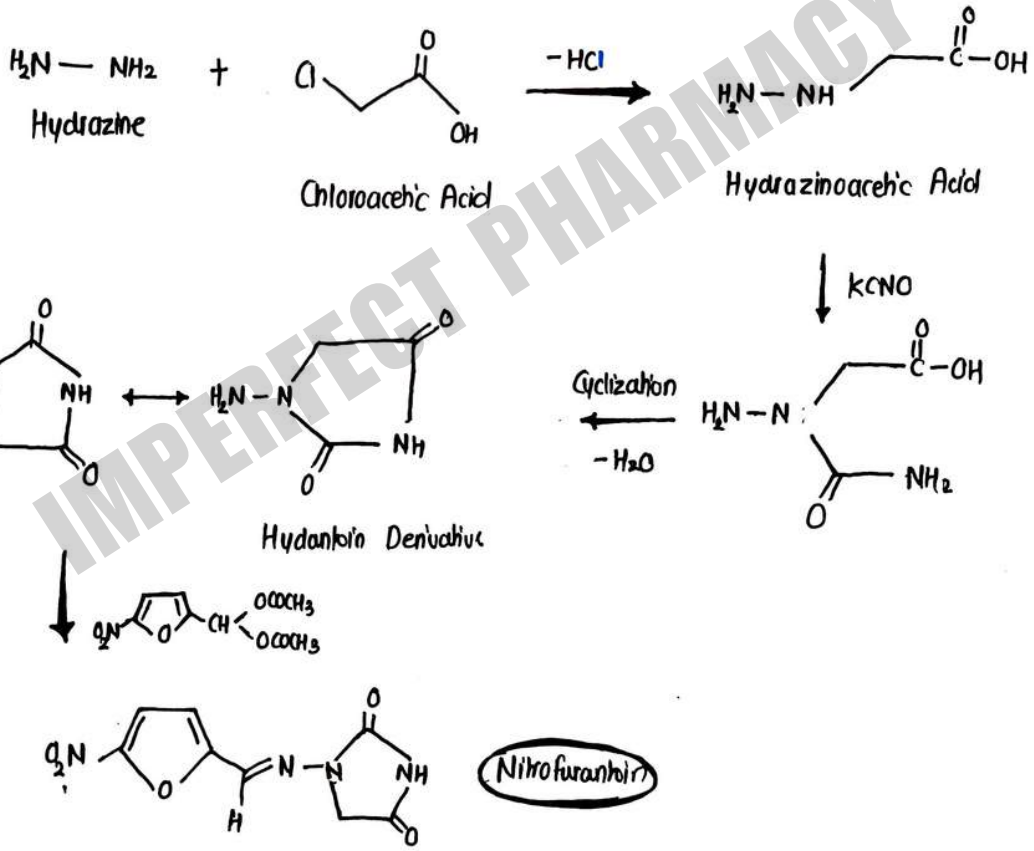
- Pneumonia
- TB
- Sinusitis

MISCELLANEOUS

① NITROFURANTOIN



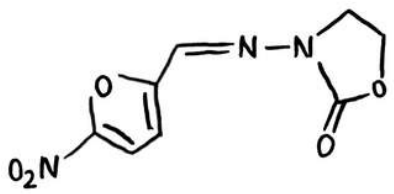
SYNTHESIS



Uses

- Typhoid
- Cholera etc.

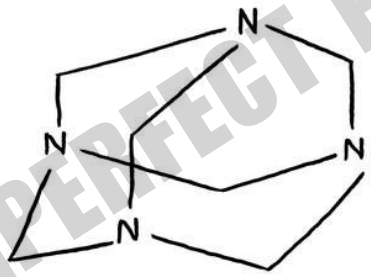
② FURAZOLIDINE



Uses

- Typhoid
- Diarrhea
- Cholera

③ METHENAMINE



Uses

- Urethritis
- Pyelonephritis
- Cystitis

ANTIVIRAL AGENTS

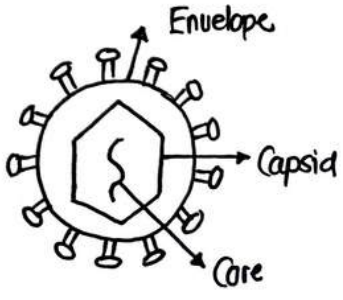
- Antiviral drugs are class of medications designed to prevent the replication of viruses by interfering with various stages of the viral life cycle.
- These medications are used to treat various viral disease such as:

- HIV/ AIDS
- Hepatitis
- Influenza etc.

VIRUSES

- Viruses are microscopic infections agents that can only replicate inside the living cells of an organism.
- They are not living organisms, that rely on host cells machinery to reproduce.
- They contain either DNA or RNA as their genetics material, but never both.

STRUCTURE OF A VIRUS



① Core : It is the genetic material either DNA or RNA.

② Capsid: It is the protein shell sorrounding the genetic material.

③ Envelope : Some viruses have additional lipid envelope sorrounding the capsid derived from host membrane.

VIRAL REPLICATION

The viral replication known as life cycle of virus is complex process that involves several stages:

① **Attachment**

- In this, virus binds to specific receptors on host cell using proteins or glycoproteins on its surface.

② **Entry**

- The virus or its genetic material enters the host cell.
- This can happen through direct fusion or endocytosis.

③ **Uncoating & Replication**

- After entry, the viral capsid is removed, exposing the viral genome.
- Viral genome starts replicating, using host cell machinery.

④ **Biosynthesis**

- Viral proteins are synthesized using host ribosomes.

⑤ **Assembly / Maturation**

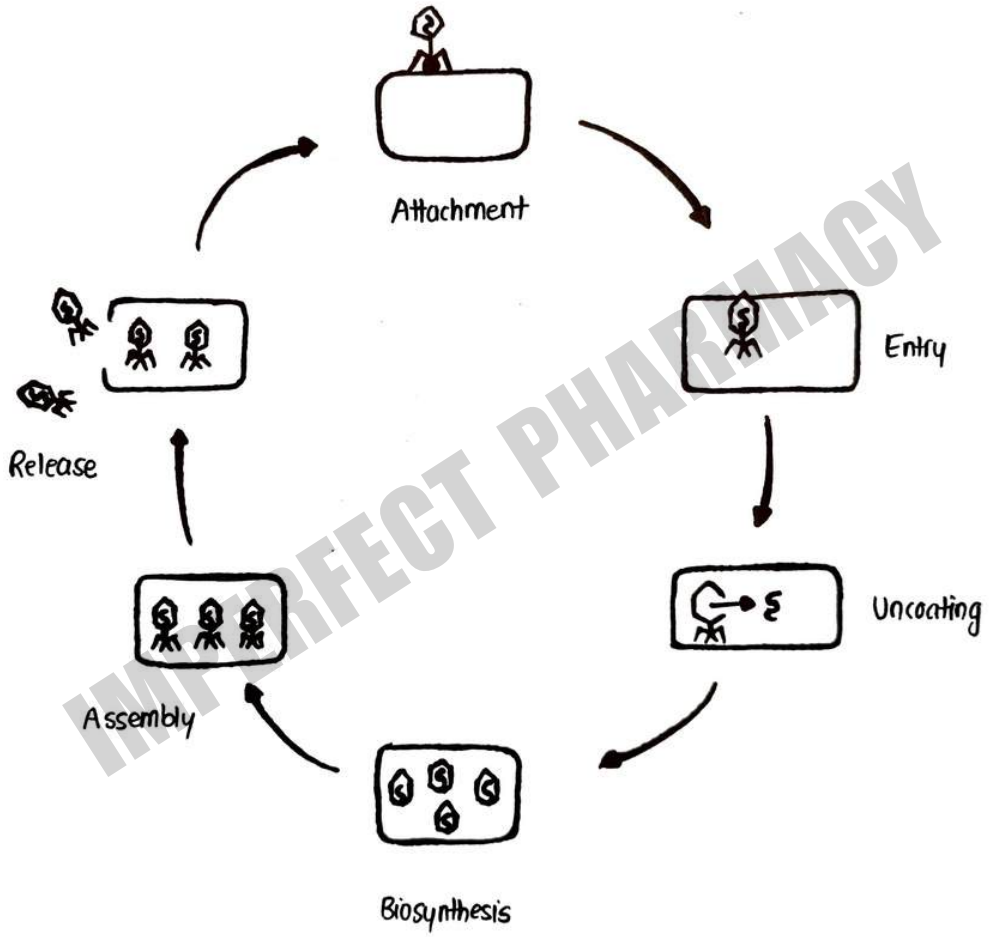
- Newly synthesized viral genomes and protein are assembled into new viral particles (virions).

⑥ Release

- The newly synthesized viruses exit the host cell to infect their other cells by two ways :

(a) Budding : Enveloped Viruses

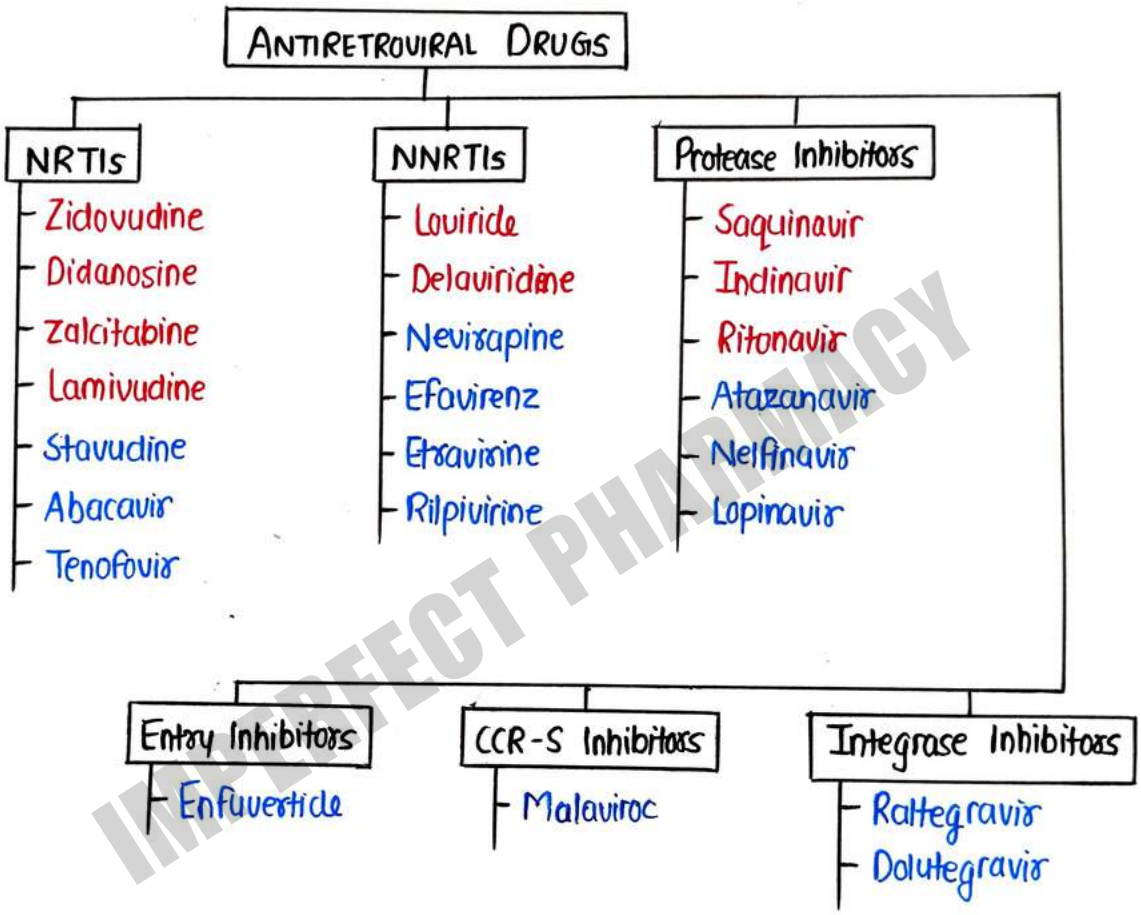
(b) Cell lysis : Non - enveloped viruses

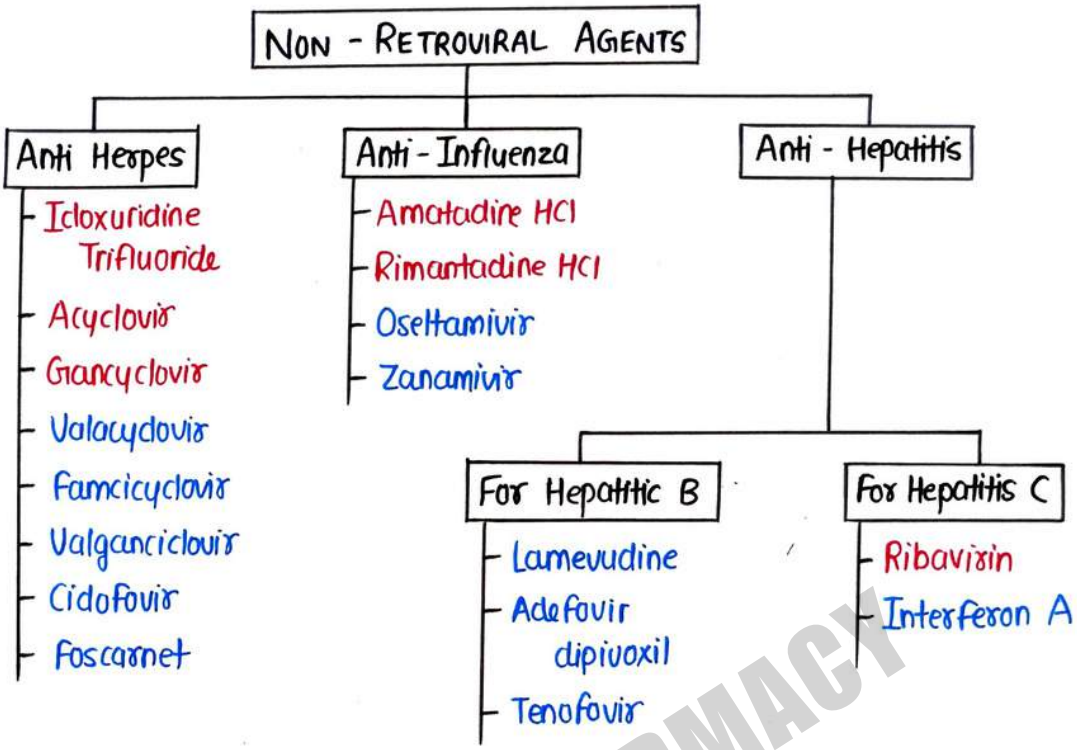


Classification Of Antiviral Agents

It can be classified on two types :

1. Antiretroviral drugs
2. Non- retroviral drugs





ANTIRETROVIRAL DRUGS

- Antiretrouiral drugs are a group of medications used to treat infections caused by retrouiruses, primarily HIV.
- They work by inhibiting various stages of the HIV life cycle to prevent the virus from multiplying in the body.

NRTIs

Nucleosid Reverse Transcriptase Inhibitors (NRTIs) are class of antiretroviral drug used in the treatment of HIV infection.

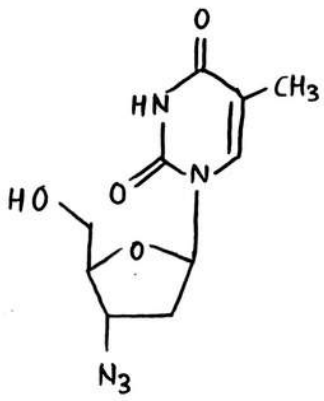
MOA

- They mimic natural nucleoside (building blocks of DNA).
- After entering the host cell they are phosphorylated to their active triphosphate form.
- During reverse transcription they get incorporated into the viral DNA.
- Now NRTIs are basically faulty nucleosides (they lack 3'-OH group, neccessary for completion of DNA synthesis).
- This prevents the completion of viral DNA synthesis thereby inhibiting viral replication.

Drugs in Our syllabus

- Zidovudine
- Didanosine
- Zalcitabine
- Lamivudine

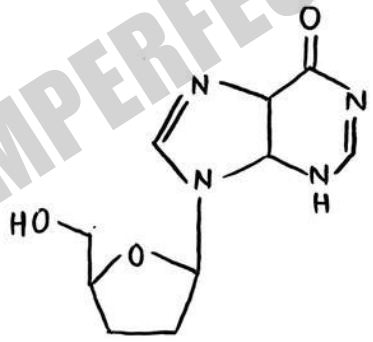
① Zidovudine



Uses

- HIV
- AIDS
- Leukemia

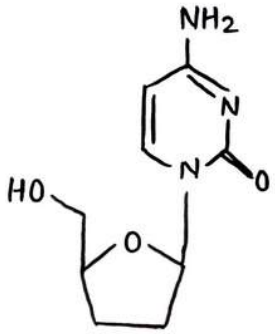
② Didanosine



Uses

- HIV/ AIDS

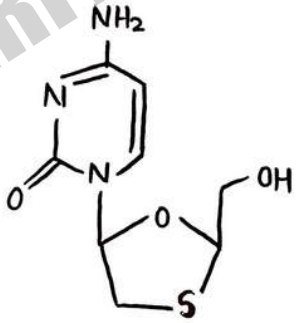
③ ZALCITABINE



Uses

- HIV / AIDS
- Immunodeficiency
- Neuropathy

④ LAMIVUDINE



Uses

- HIV
- Hepatitis B

NNRTIs

- Non Nucleoside reverse transcriptase inhibitors are class of Antiretroviral drug used in treatment of HIV.
- Unlike NRTIs, NNRTIs do not mimic nucleosides, Instead they bind directly to a specific site on HIV-1 reverse transcriptase enzyme.

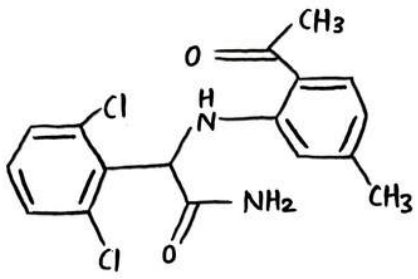
MOA

- NNRTIs binds non-comptitively to the allosteric site on reverse transcriptase enzyme.
- This binding causes a conformational change in the enzyme, reducing its activity & preventing the conversion of viral RNA into DNA.

Drugs

- Loviride
- Delavirdine

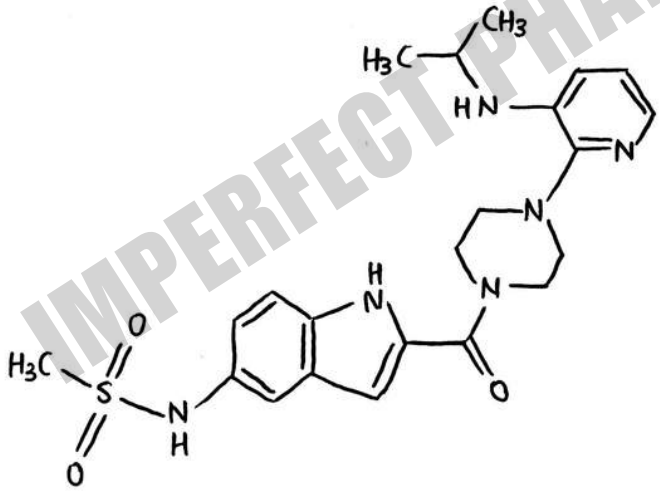
① LOVIRIDE



Uses

- HIV/AIDS
- Immunodeficiency

② DELAVIRDINE



Uses

- HIV-1
- AIDS

PROTEASE INHIBITORS

- Protease Inhibitors are class of antiretroviral drugs used in the treatment of HIV infections.

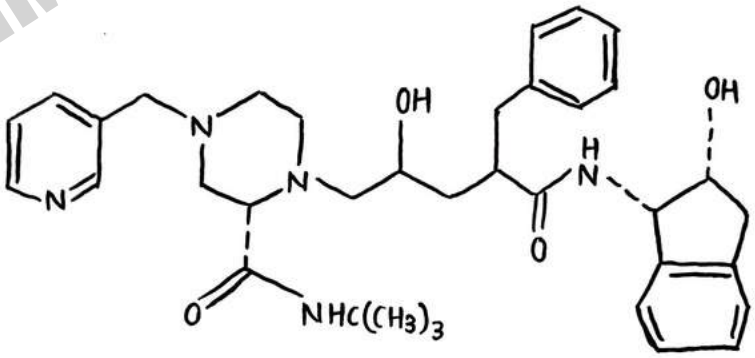
MOA

- Protease Inhibitors bind to the active site of the HIV protease enzyme, preventing it from cleaving the viral polyprotein precursors into functional viral proteins.
- As a result, immature, non-infectious viral particles are produced.

Drugs

- Saquinavir
- Indinavir
- Ritonavir

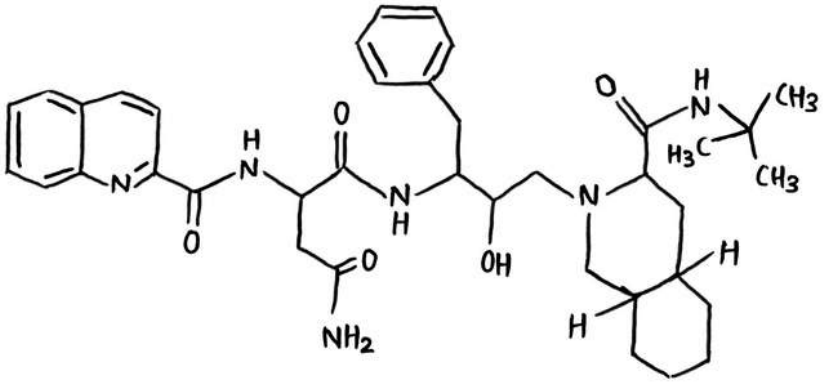
① INDINAVIR



Uses

- HIV/AIDS
- Immunodeficiency

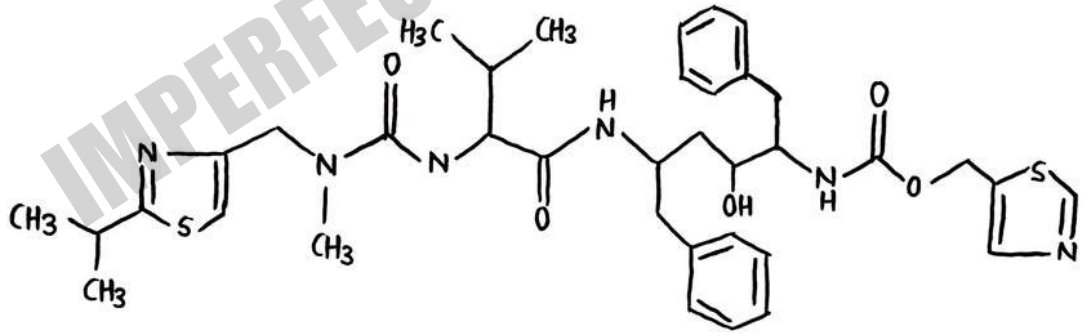
② SAQUINAVIR



Uses

- HIV/AIDS
- Immunodeficiency

③ RITONAVIR



Uses

- HIV/AIDS
- COVID-19
- Hepatitis C
- SARS

NON RETROVIRAL AGENTS

- Non-Retroviral agents are antiviral drugs used to treat infections caused by non-retroviruses (viruses that do not use reverse transcriptase as part of their replication cycles).

ANTI HERPES DRUGS

- These are antiviral drug used to treat infections caused by Herpes virus.

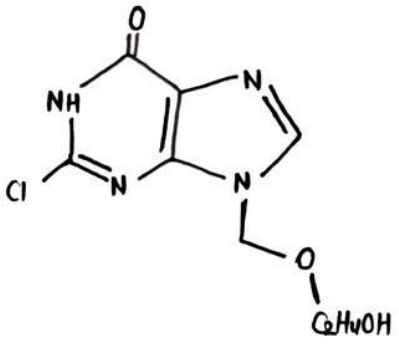
MOA

- These are nucleoside analogues.
- They are first activated by viral enzymes.
- Once activated to their triphosphate form, they compete with natural nucleotides.
- They are incorporated into the viral DNA during replication.
- Due to their faulty structure, they cause premature chain termination, halting DNA synthesis.

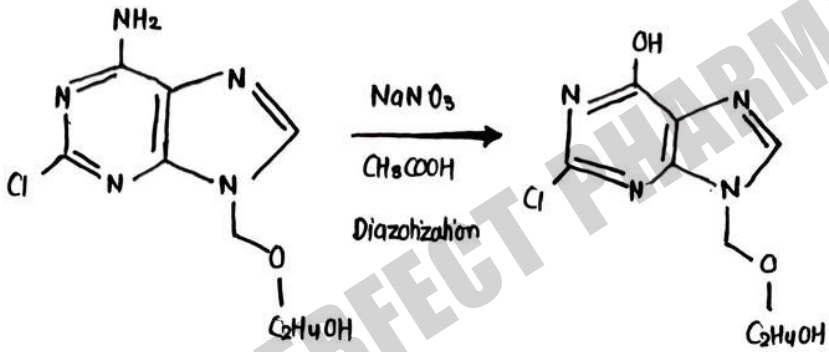
Drugs

- Acyclovir*
- Giancyclovir
- Idoxuridine Trifluoride

① Acyclovir

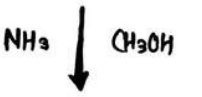


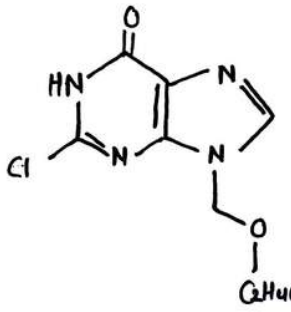
Synthesis



2-Chloro-6-aminopurine derivative

2-Chloro-6-hydroxypurine derivative



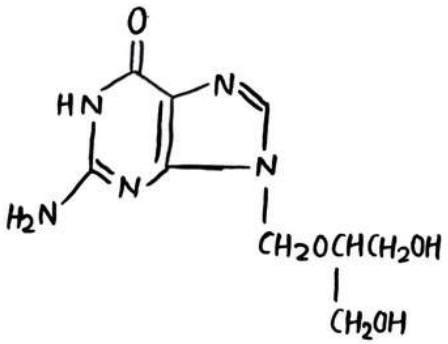


Acyclovir

Uses

- Herpes Simplex Virus

② GANCYCLOVIR

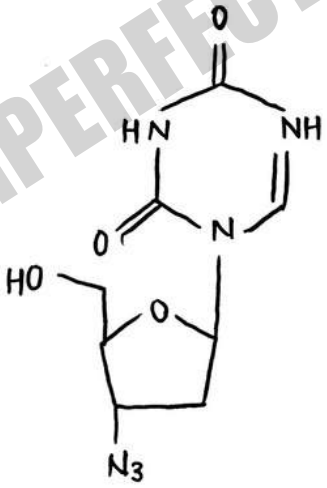


Uses

- CMV - Pneumonitis
- CMV - esophagitis etc

[CMV - Cytomegalovirus]

③ IDOXURIDINE TRIFLUORIDE



Uses

- Herpes
- Conjuctivitis

ANTI INFLUENZA VIRUS DRUGS

Anti - Influenza drugs are antiviral medications used to treat or prevent influenza (flu) caused by Influenza A or Influenza B viruses.

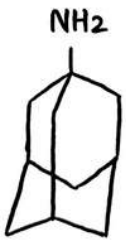
MOA (M_2 Ion Channel Blockers)

- These drugs blocks the M_2 proton channel of the influenza A viruses.
- This inhibiting coating of the virus inside host cells, preventing the release of viral RNA into cytoplasm of host cells.

Drugs

- Amantadine HCl
- Rimantdine HCl

① AMANTADINE HYDROCHLORIDE

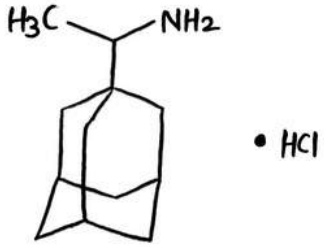


- HCl

Uses

- Influenza - A
- Tremor
- Depression

② RIMANTADINE HYDROCHLORIDE



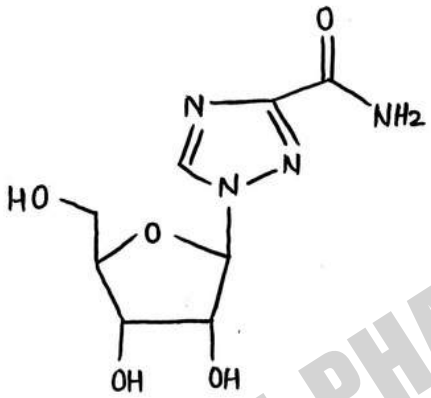
Uses

- Influenza
- Parkinson's disease

ANTI HEPATITIS C VIRUS DRUGS

Anti-HCV drugs are antiviral drugs used to treat infections caused by Hepatitic C virus, a blood born virus that primarily affects the lives.

① RIBAVIRIN



MOA

- It is synthetic guanosine analogues that:
- Inhibits RNA synthesis by interfering with viral RNA Polymerase.
- Inhibits inosine monophosphate, dehydrogenase, reducing GTP levels needed for RNA synthesis.
- Causes lethal mutagenesis in Hepatitis Virus.
- Enhances hosts immune response against viruses.

Uses

- Hepatitis - C
- RSV (Respiratory Syncytial Virus)
- COVID-19

THANK YOU

FOR CHOOSING IMPERFECT PHARMACY AS YOUR STUDY PARTNER

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