**LEARNING MATERIAL**

**COURSE: B.PHARMACY, 6th Sem, Medicinal Chemistry, BP -601T**

# Module 03: Antitubercular agents

# UTI

# Antiviral Agents


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**Objectives:**

1. Understand the chemistry of Drugs.
2.Know the importance of SAR of drugs.
3.Know the Adverse effect and therapeuticvalue of drugs.

Learning Outcomes:

1.Student will learn about the Chemical structure and Medicinal uses of drugs.
2. Student will learn about the Relation of drug and its Activity.

# Antitubercular Drug

# Introduction

- Tuberculosis - most important communicable disease in the world.
- Mycobacteria are intrinsically resistant to most antibiotics
  - Grows more slowly than other bacteria – antibiotics active against **rapidly growing cells**
  - **lipid-rich mycobacterial cell wall** is impermeable to many agents
  - It grows inside macrophage – poorly penetrated by drugs
  - Excellent ability to develop resistance – Multiple Drug Resistant (MDR)

# Introduction

- Combinations of two or more drugs
  - to overcome these obstacles
  - to prevent emergence of resistance during the course of therapy
- The response of mycobacterial infections to chemotherapy is slow - treatment must be administered for months to years, depending on which drugs are used

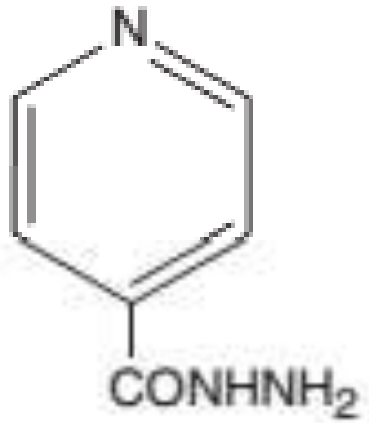
# Classification

- According to clinical utility the anti TB drugs can be divided into 2 groups
  - **First Line** : high antitubercular efficacy as well as low toxicity – routinely used
    - **Isoniazid (H) , Rifampin (R), Pyrazinamide (Z), Ethambutol (E), Streptomycin (S) - HRZES**
  - **Second Line** : low antitubercular efficacy or high toxicity
    - **Paraminosalicylic Acid, Cycloserine, Kanamycin, Amikacin, Ciprofloxacin, Olfloxacin, Clarithromycin, Azithromycin**

# First Line Drug

# ISONIAZID

- Isonicotinic acid hydrazide
- Most active drug for the treatment of tuberculosis
- freely soluble in water
- bactericidal for actively growing tubercle bacilli
- less effective against atypical mycobacterial species
- penetrates into macrophages and is active against both extracellular and intracellular organisms



Isoniazid

# Mechanism of Action & Basis of Resistance

- inhibits synthesis of mycolic acids - essential components of mycobacterial cell walls
- Higly selective for mycobacterium
- Resistance
  - Its prodrug – activated by enzyme catalase-peroxidase
  - Mutation causes inhibition of this enzyme
  - No cross resistance occurs with other antitubercular drug
  - Always given in combination

# RIFAMPIN

- Semisynthetic derivative of rifamycin -produced by ***Streptomyces mediterranei***
- Active in vitro against gram-positive and gram-negative cocci, some enteric bacteria, mycobacteria, and chlamydiae.
- Resistant mutants - approximately 1 in $10^6$ organisms
- Rapidly selected out if rifampin is used as a single drug – must be used in combination
- no cross-resistance to other classes of antimicrobial drugs

# Mechanism of Action & Resistance

- Binds to the bacterial DNA-dependent RNA polymerase - inhibits RNA synthesis
- Bactericidal for mycobacteria
- Readily penetrates most tissues and penetrates into phagocytic cells
- Can kill organisms that are poorly accessible to many other drugs
  - Intracellular organisms
  - sequestered in abscesses and lung cavities
- **Resistance:** mutations result in reduced binding of rifampin to RNA polymerase

# Clinical Uses

- 10 mg/kg/d O.D. for 6 months in combination with isoniazid or other **antituberculous** drugs to patient.
- Some **atypical mycobacterial infections** and in **leprosy**
- 600 mg twice daily for 2 days can eliminate **meningococcal carriage**
- 20 mg/kg/d for 4 days - prophylaxis in contacts of children with ***Haemophilus influenzae*** **type b disease**
- Serious staphylococcal infections **- osteomyelitis and prosthetic valve endocarditis**

# ETHAMBUTOL

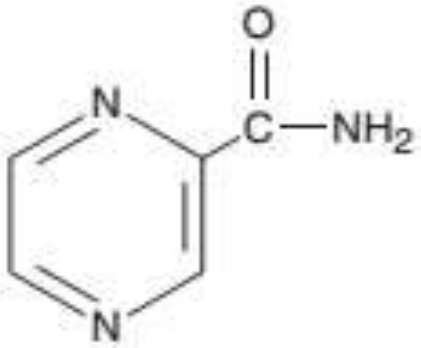
- Synthetic, water-soluble, heat-stable compound - dispensed as the dihydrochloride salt
- Bacteriostatic
- Additionally it slows the rate of sputum conversion
- Development of resistance
- Given in the combination with RHZ

# Mechanism of action

- Inhibits mycobacterial **arabinosyl transferases** - an essential component of the mycobacterial cell wall.
- Resistance – due to alteration in target gene
- No cross resistance with other drug
- Reesistance to ethambutol emerges rapidly when the drug is used alone - combination with other antituberculous drugs

# PYRAZINAMIDE

- Relative of nicotinamide
- Stable and slightly soluble in water but week drug
- Inactive at neutral pH, but at pH 5.5 it inhibits tubercle bacilli
- Taken up by macrophages and exerts its activity
- Highly effective during the first 2 month of therapy



Pyrazinamide (PZA)

# Mechanism of Action

- Pyrazinamide is converted to pyrazinoic acid (active form) - by mycobacterial pyrazinamidase.
- Disrupts mycobacterial cell membrane metabolism and transport functions
- Resistance
  - impaired uptake of pyrazinamide
  - mutations of enzyme causing conversion of pyrazinamide to its active form

# Clinical Use

- Used as front line drug for tuberculosis with rifampin and isoniazid
- **Normal Dose**: 40–50 mg/kg thrice weekly or twice-weekly treatment regimens for 6 months
- **Hemodialysis patients & creatinine clearance** less than 30 mL/min : 25–35 mg/kg three times weekly (not daily)

# Streptomycin

- Part of aminoglycosides antibiotic
- First clinically useful antitubercular drug, but less effective than INH or rifampin
- Acts only on extracellular bacilli – poor penetration into cells
- Doesn’t cross the BBB, but penetrates tubercular cavities

# Mechanism of action

- Irreversible inhibitors of protein synthesis,
- Bactericidal
- Inside the cell, aminoglycosides bind to specific 30S-subunit ribosomal proteins and inhibits protein synthesis
- **Resistance**
  - Inactivation by adenylylation, acetylation, or phosphorylation
  - impaired entry into the cell
  - receptor protein on the 30S ribosomal subunit - deleted or altered as a result of a mutation

# Clinical Use

- Treatment of infections resistant to other drugs
- Adults: 20–40 mg/kg/d daily for several weeks
  - Followed by 1–1.5 g two or three times weekly for several months
- Other drugs are always given in **combination** to prevent emergence of resistance
- Nontuberculosis species of mycobacteria other than *Mycobacterium avium* complex (MAC) and *Mycobacterium kansasii* are **resistant**
- Dose is reduced to half in hemodialysis patient

# Second Line Drugs

# Second Line Drugs

- This drugs are considered only when
  - resistance to first-line agents
  - failure of clinical response to conventional therapy;
  - Serious treatment-limiting adverse drug reactions
- Expert guidance to deal with the toxic effects is required
- Ex: **Paraminosalicylic Acid, Cycloserine, Kanamycin, Amikacin, Ciprofloxacin, Olfloxacin, Clarithromycin, Azithromycin**

# Para-aminosalicyclic Acid

– structural analogue of ***p*aminobenzoic acid (PABA)**

–**highly specific** for *M. tuberculosis* - not effective against other mycobacterium species

–Combined with isoniazid - **an alternative substrate** and **block hepatic acetylation of isoniazid-** increasing free isoniazid levels.

– limited to the treatment of **MDR tuberculosis**

–**Discouraged its use** : primary resistance, poor compliance due to GI intolerance, and lupus like reactions

# Ethionamide

- Blocks the synthesis of mycolic acids
- Chemically related to isoniazid
- Poorly water soluble and available only in oral form.
- Dosage of 15 mg/kg/d - initial dose of 250 mg once daily, which is increased in 250-mg increments to the recommended dosage
- Intense gastric irritation and neurologic symptoms as well as hepatotoxic

# Capreomycin

- **peptide protein synthesis** inhibitor antibiotic obtained from *Streptomyces capreolus*
- Daily injection of 15 mg/kg/d intramuscularly
- treatment of **drug-resistant tuberculosis**
- Strains of *M tuberculosis* that are **resistant to streptomycin or amikacin** - susceptible to capreomycin.
- Nephrotoxic and ototoxic - Tinnitus, deafness, and vestibular disturbances occur
- local pain, and sterile abscesses may occur

# Cycloserine

- inhibitor of cell wall synthesis
- 0.5–1 g/d in two divided oral doses
- Cleared renally - Dose is reduced to half in case of renal dysfunction
- peripheral neuropathy and central nervous system dysfunction, including depression and psychotic reactions.
- Pyridoxine, 150 mg/d given in addition to it

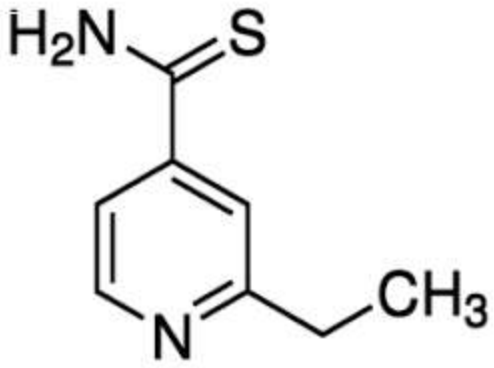
# Kanamycin & Amikacin

- Treatment of tuberculosis suspected or known to be caused by **streptomycin-resistant or multidrug-resistant strains**
- Kanamycin is more toxic comparatively – **absolute**
- Prevalence of **amikacin-resistant strains** is low (< 5%)
- Also active against atypical mycobacteria.
- 15 mg/kg intravenous infusion
- No cross-resistance between streptomycin and amikacin but it occurs with kanamycin
- used in combination with at least one and preferably two or three other drugs

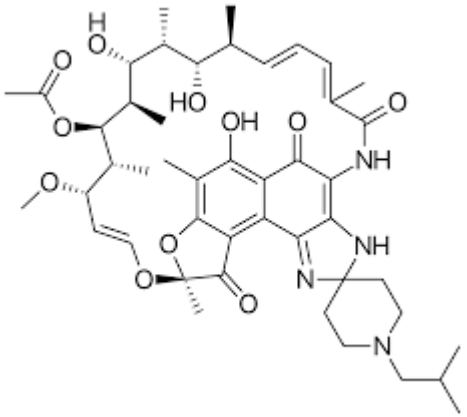
# Fluoroquinolones

- In addition to their activity against many gram-positive and gram-negative bacteria inhibit strains of *M. tuberculosis*
- Also active against atypical mycobacteria
- Standard dosage
  - **Ciprofloxacin:** 750 mg orally twice a day
  - **Levofloxacin:** 500–750 mg once a day
  - **Moxifloxacin:** 400 mg once a day

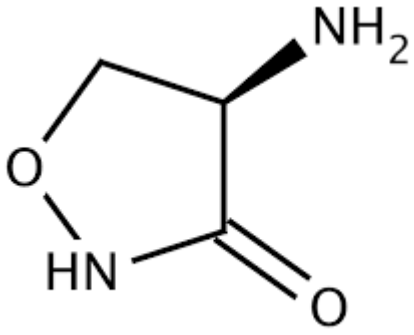
# Structures



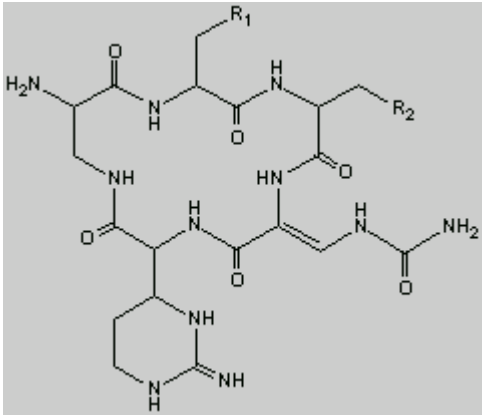

Ethionamide




Rifabutin




Cycloserine




Capreomycin

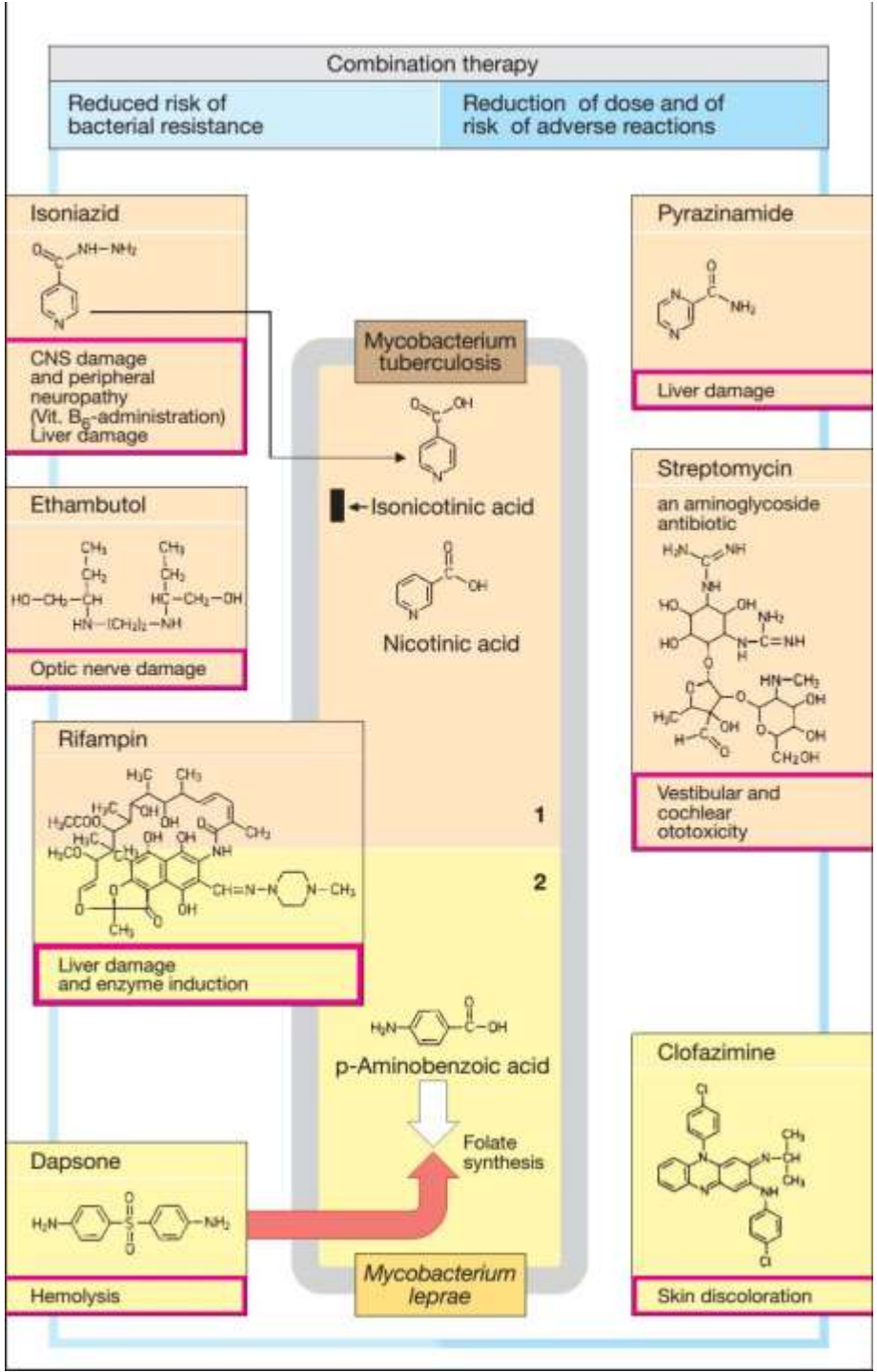
# Summary

| Subclass | Mechanism of Action | Effects | Clinical Applications | Pharmacokinetics, Toxicities, Interactions |
|---|---|---|---|---|
| **ISONIAZID** | Inhibits synthesis of mycolic acids, an essential component of mycobacterial cell walls | Bactericidal activity against susceptible strains of *M tuberculosis* | First-line agent for tuberculosis • treatment of latent infection • less active against other mycobacteria | Oral, IV • hepatic clearance (half-life 1 h) • reduces levels of phenytoin • *Toxicity:* Hepatotoxic, peripheral neuropathy (give pyridoxine to prevent) |
| **RIFAMYCINS** | | | | |
| • Rifampin | Inhibits DNA-dependent RNA polymerase, thereby blocking production of RNA | Bactericidal activity against susceptible bacteria and mycobacteria • resistance rapidly emerges when used as a single drug in the treatment of active infection | First-line agent for tuberculosis • atypical mycobacterial infections • eradication of meningococcal colonization, staphylococcal infections | Oral, IV • hepatic clearance (half-life 3.5 h) • potent cytochrome P450 inducer • turns body fluids orange color • *Toxicity:* Rash, nephritis, thrombocytopenia, cholestasis, flu-like syndrome with intermittent dosing |

- *Rifabutin: Oral; similar to rifampin but less cytochrome P450 induction and fewer drug interactions*
- *Rifapentine: Oral; long-acting analog of rifampin that may be given once weekly in the continuation phase of tuberculosis treatment*

# Summary

| | | | | |
|---|---|---|---|---|
| **PYRAZINAMIDE** | Not fully understood • pyrazinamide is converted to the active pyrazinoic acid under acidic conditions in macrophage lysosomes | Bacteriostatic activity against susceptible strains of *M tuberculosis* • may be bactericidal against actively dividing organisms | "Sterilizing" agent used during first 2 months of therapy • allows total duration of therapy to be shortened to 6 months | Oral • hepatic clearance (half-life 9 h), but metabolites are renally cleared so use doses 3 × weekly if creatinine clearance < 30 mL/min • *Toxicity:* Hepatotoxic, hyperuricemia |
| **ETHAMBUTOL** | Inhibits mycobacterial arabinosyl transferases, which are involved in the polymerization reaction of arabinoglycan, an essential component of the mycobacterial cell wall | Bacteriostatic activity against susceptible mycobacteria | Given in four-drug initial combination therapy for tuberculosis until drug sensitivities are known • also used for atypical mycobacterial infections | Oral • mixed clearance (half-life 4 h) • dose must be reduced in renal failure • *Toxicity:* Retrobulbar neuritis |
| **STREPTOMYCIN** | Prevents bacterial protein synthesis by binding to the S12 ribosomal subunit (see also Chapter 45) | Bactericidal activity against susceptible mycobacteria | Used in tuberculosis when an injectable drug is needed or desirable and in treatment of drug-resistant strains | IM, IV • renal clearance (half-life 2.5 h) • administered daily initially, then 2 × week • *Toxicity:* Nephrotoxic, ototoxic |


Combination therapy
Reduced risk of bacterial resistance
Reduction of dose and of risk of adverse reactions
Isoniazid
CNS damage and peripheral neuropathy (Vit. B6-administration) Liver damage
Ethambutol
Optic nerve damage
Rifampin
Liver damage and enzyme induction
Dapsone
Hemolysis
Mycobacterium tuberculosis
Isonicotinic acid
Nicotinic acid
1
2
p-Aminobenzoic acid
Folate synthesis
Mycobacterium leprae
Pyrazinamide
Liver damage
Streptomycin
an aminoglycoside antibiotic
Vestibular and cochlear ototoxicity
Clofazimine
Skin discoloration

# References


- **Basic & Clinical Pharmacology** Bertram G. Katzung Twelfth Edition
- Essential of medical pharmacology - K.D. Tripathi 6th edition
- Lippincott - Modern Pharmacology With Clinical Applications 6E
- Color Atlas Of Pharmacology, 2Nd Ed (Lüllmann, Thieme 2000)

# Quinolones

BY: Baljeet kaur

# DEFINITION:

The fluoroquinolones are a family of broad spectrum, systemic antibacterial agents that have been used widely as therapy of respiratory and urinary tract infections.

# Background

- In 1962 nalidixic acid was discovered by George Lesher during synthesis of chloroquine and was named as Quinolone.

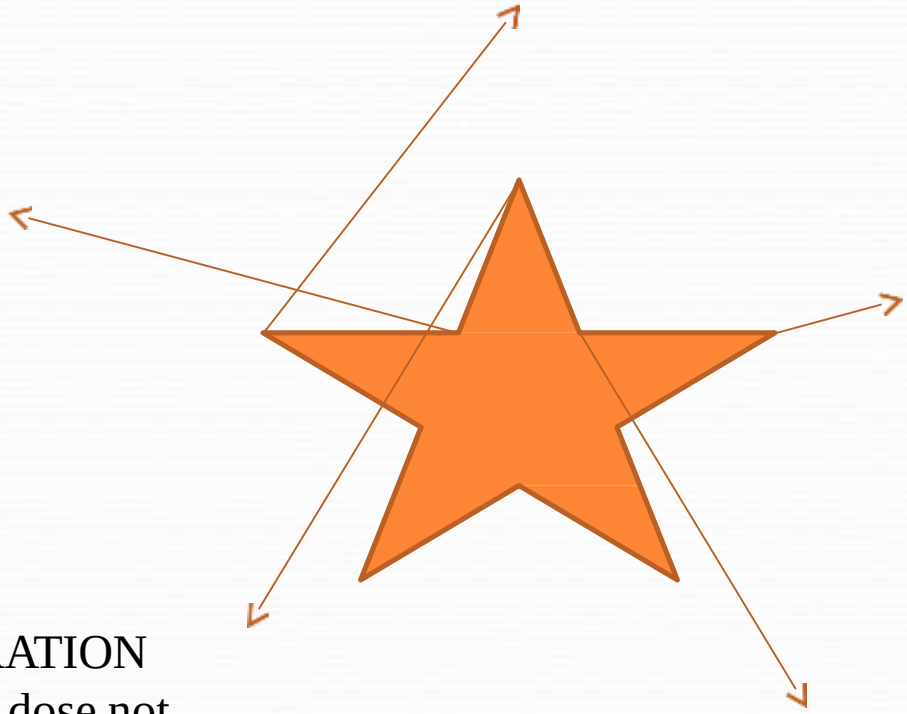
- Fluoroquinolones were derived by adding fluorine atom in nalidixic acid.

- Earlier quinolones were useful only for treatment of UTI.

- Fluorinated derivatives achieve bactericidal levels in blood and tissues so they have improved antibacterial spectrum.

# FLUOROQUINOLONES ARE FIVE STAR DRUGS !!!

1. SAFER TO USE



2.HIGH POTENCY

3.NEW FLUOROQUINOLONES ARE BROAD IN SPECTRUM

4.DEEP PENETRATION IN TISSUES (but dose not cross BBB. Can enter the cell i.e intracellular organism)

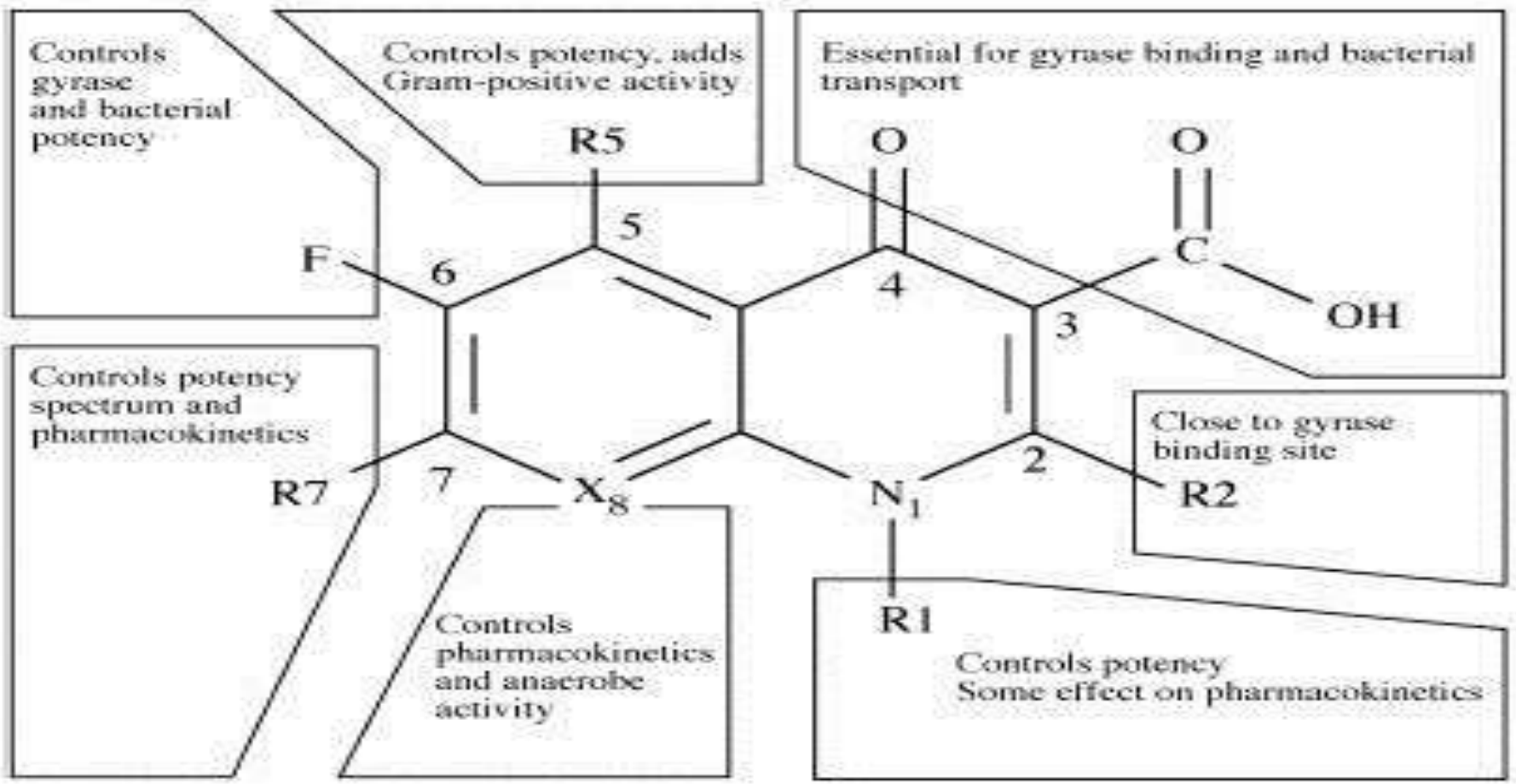
5.GOOD ORAL ABSORPTION

# CLASSIFICATION

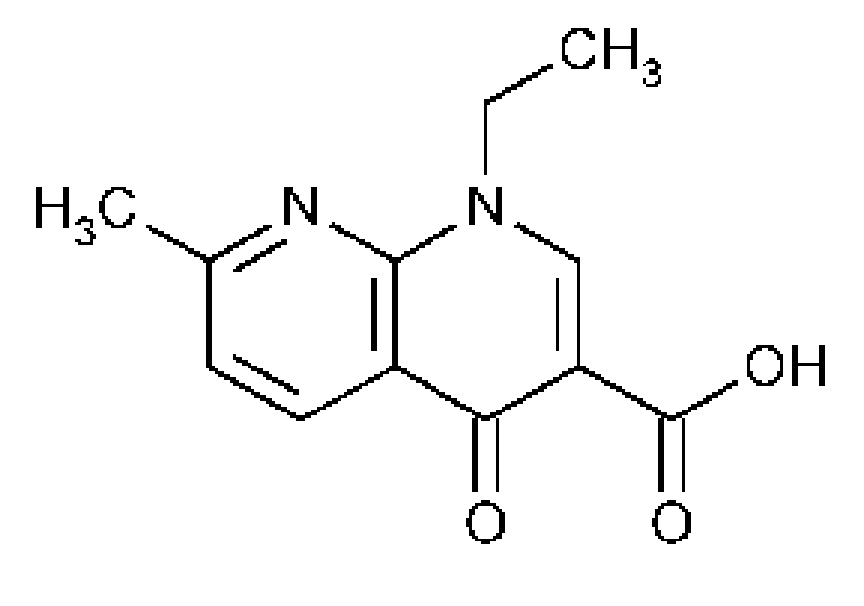
# Generations

| | Drugs | Spectrum |
|---|---|---|
| **1st (Quinolone)** | Nalidixic acid | Gram -ve but not Pseudomonas species |
| **2nd** | Norfloxacin<br>Ciprofloxacin<br>Ofloxacin | Gram -ve(including Pseudomonas species), some Gram+ (S. aureus) and some atypicals |
| **3rd** | Levofloxacin<br>Sparfloxacin<br>Moxifloxacin<br>Gatifloxacin | Same as 2nd generation with extended Gram +ve and atypical coverage |
| **4th** | *Trovafloxacin | Same as 3rd generation with broad anaerobic coverage |

# Structural relativity of quinolones

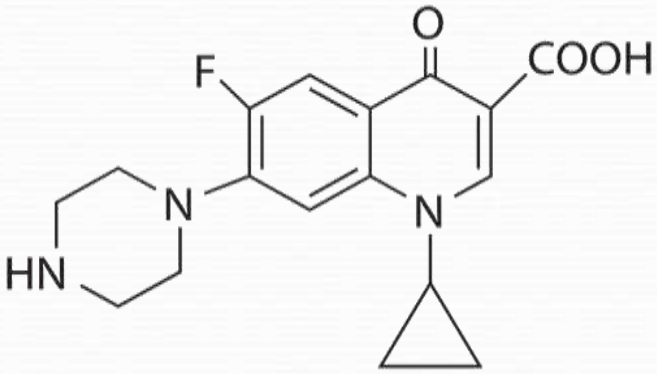


# First generation quinolones

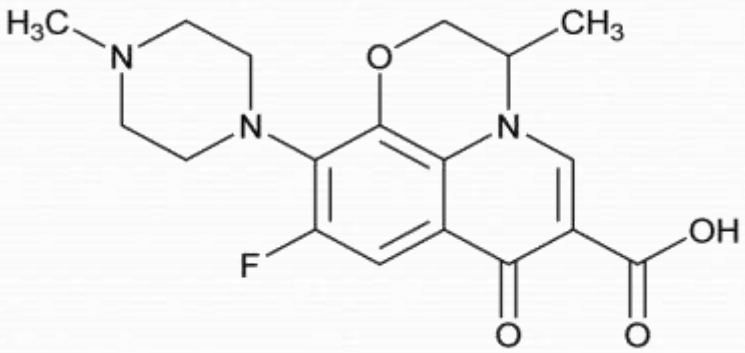



Nalidixic acid

# Second generation quinolones



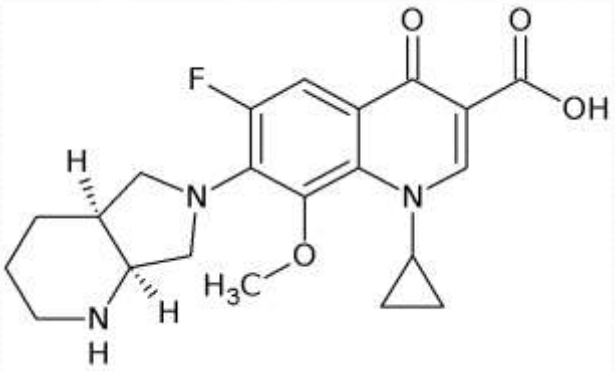

ciprofloxacin



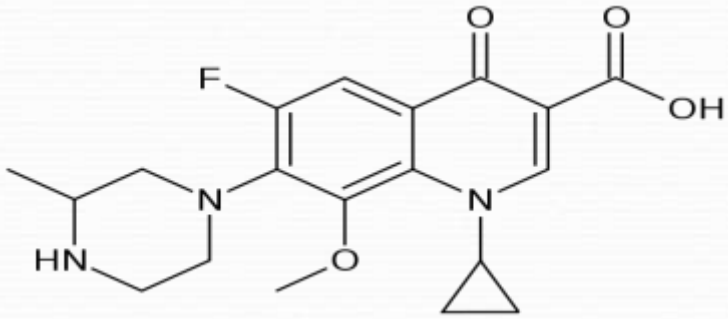

Ofloxacin

Norfloxacin

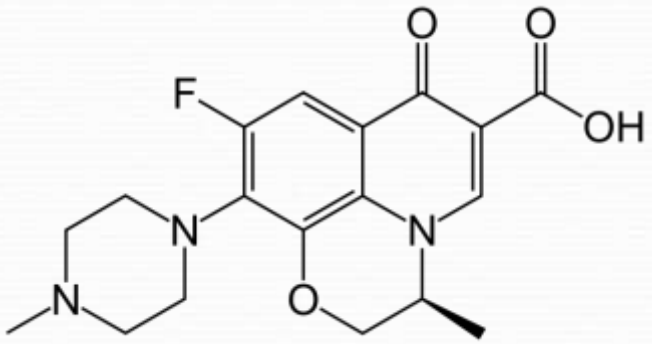
# Third generation of quinolones



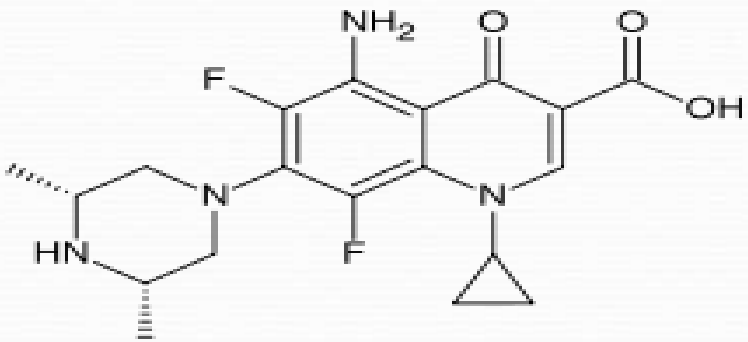

Moxifloxacin



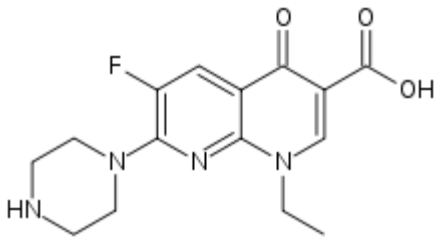

Gatifloxacin



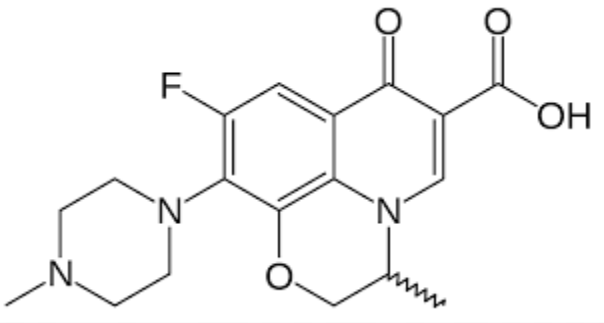

Levofloxacin



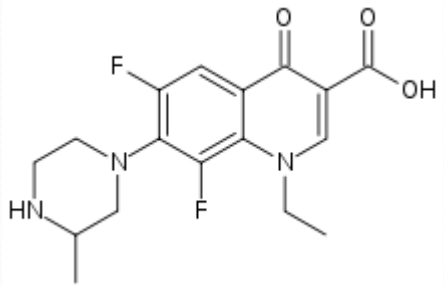

Sparfloxacin




Enoxacin



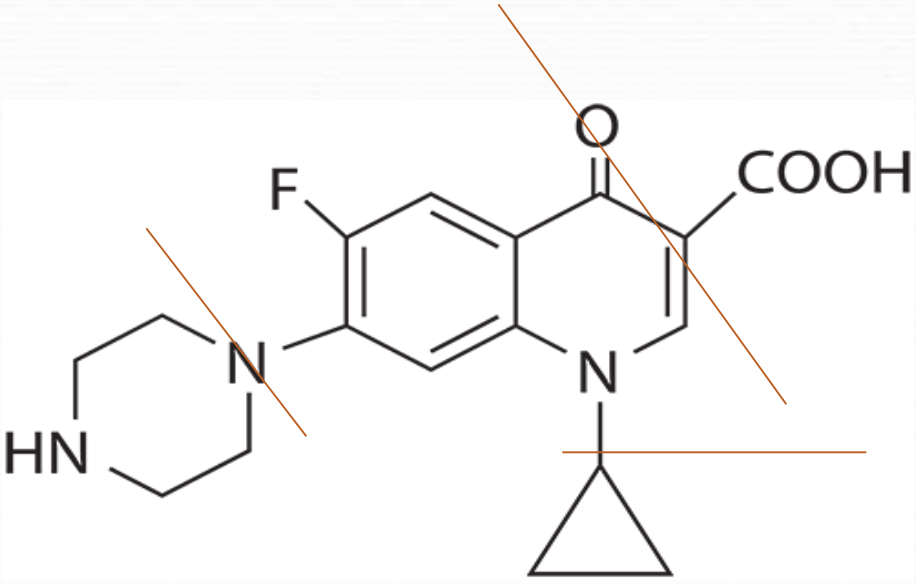

Ofloxacin



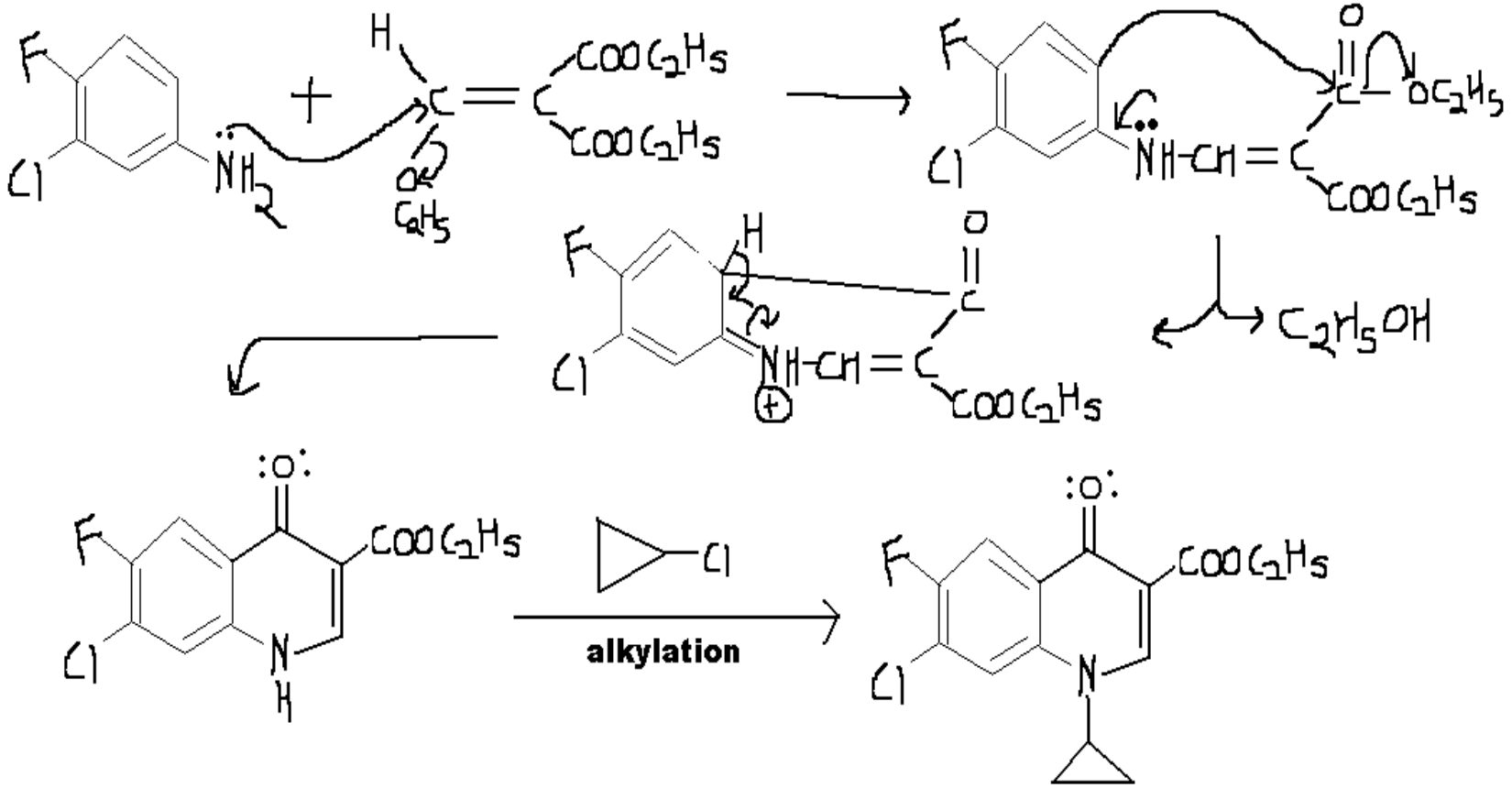

Lomefloxacin

# SYNTHESIS OF CIPROFLOXACIN

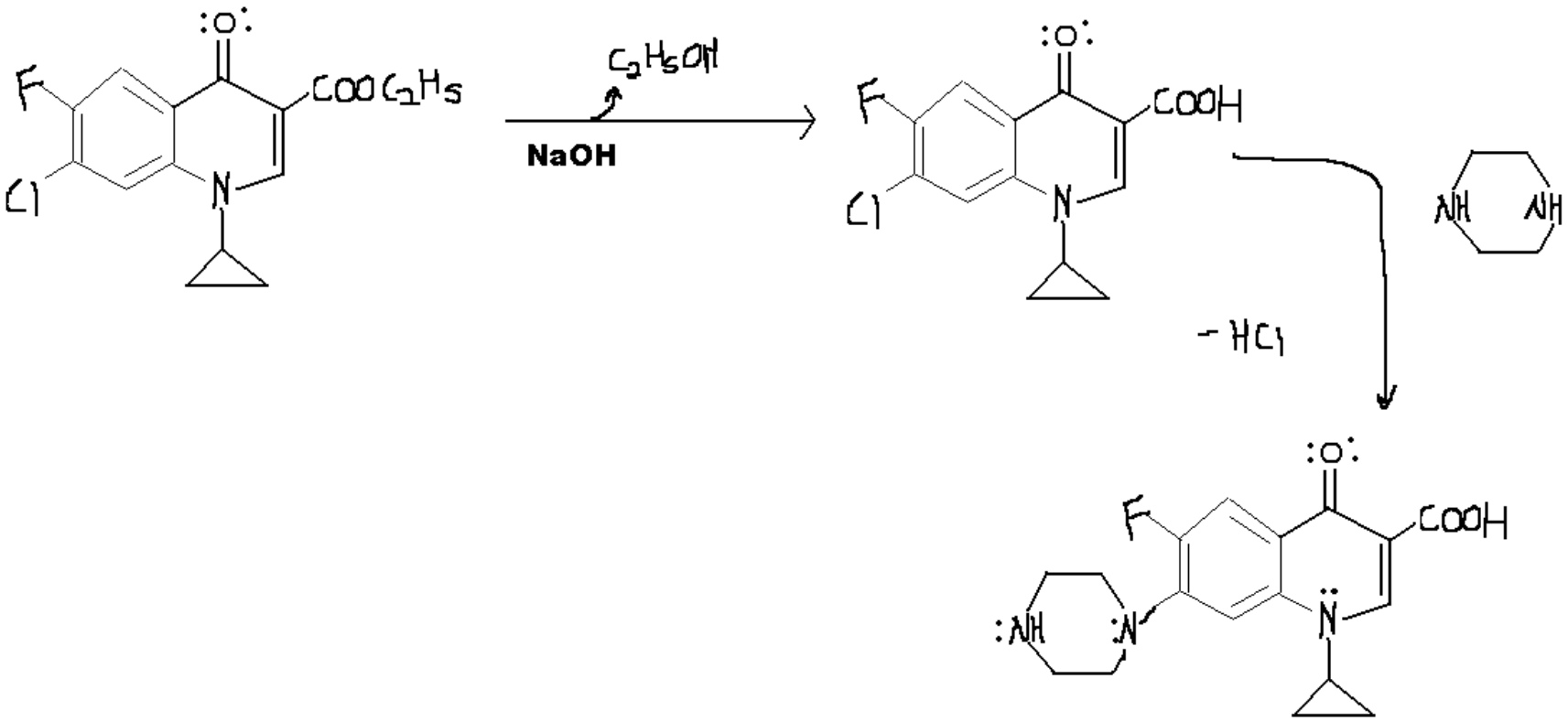
*USE RETROSYNTHESIS TECHNIQUE IT WOULD MAKE YOUR LIFE EASY..* !



# SYNTHESIS OF CIPROFLOXACIN

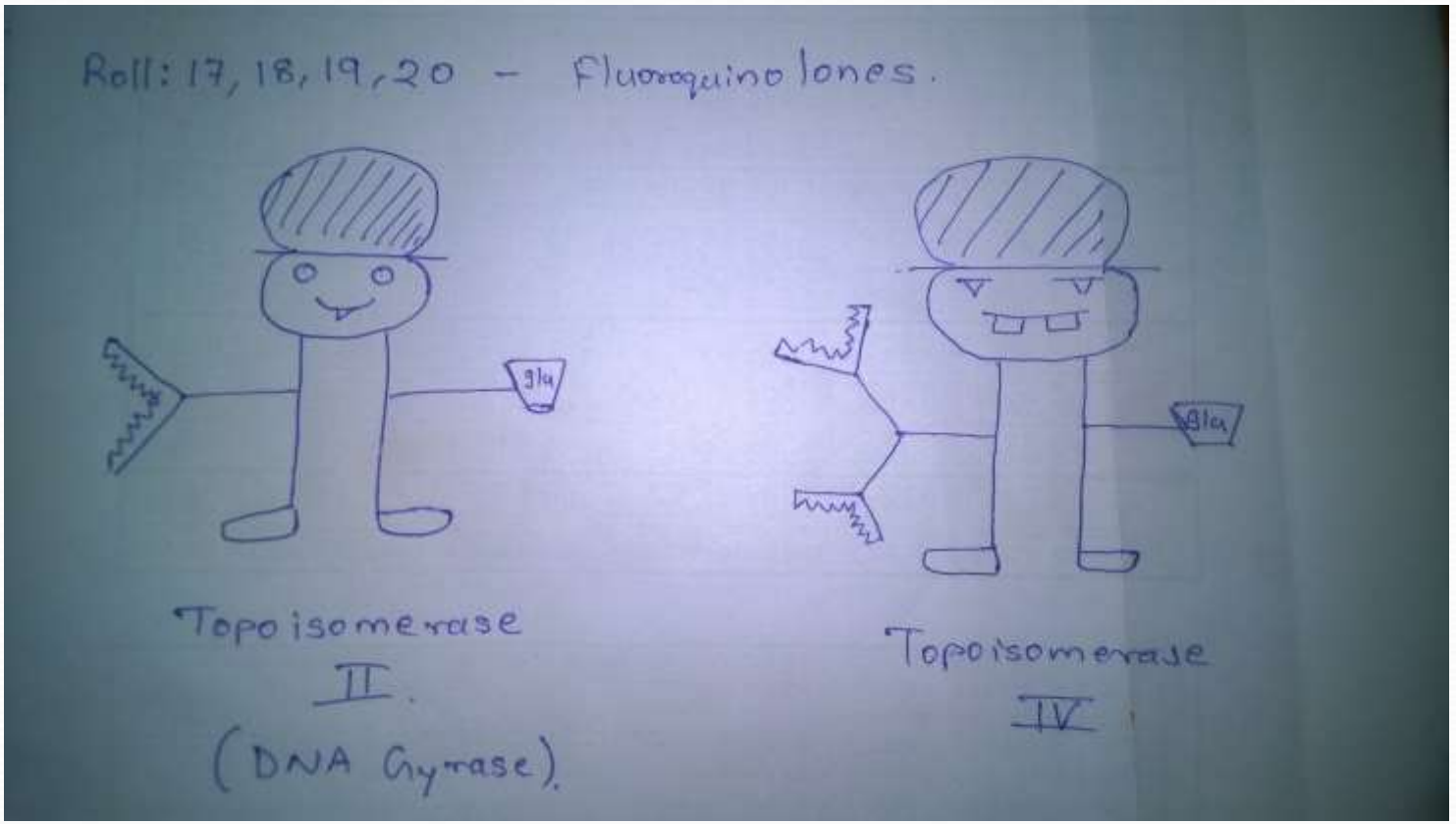


# SYNTHESIS (CONT..)



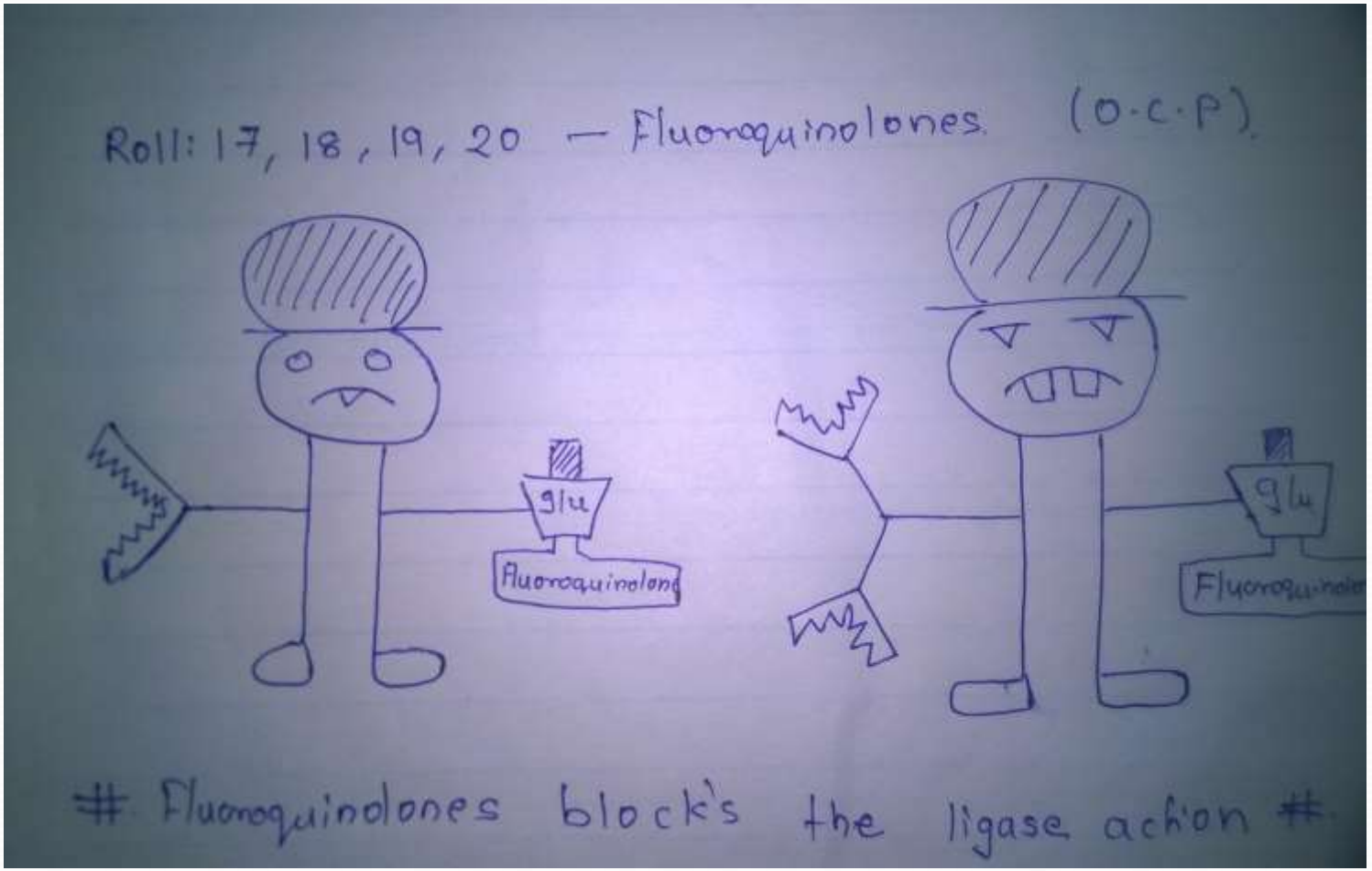

CIPROFLOXACIN

# MECHANISM OF ACTION




Topoisomerase II : to convert the +ve supercoiling to –ve supercoiling. There by allowing the process of replication or the allows the action of DNA helicase to proceed.

Topoisomerase IV: to separate the entangled DNA so that its expression could be proceeded.




Fluoroquinolones blocks the ligase action where in has no effect on endoneuclease action of the enzyme. Thus what the bacteria left with is fragments of DNA which cannot be expressed.

# MECHANISM OF ACTION (cont..)

- quinolones are bactericidal agents
- They block bacterial DNA synthesis by inhibiting bacterial DNA gyrase and topoisomerase IV.
- Inhibition of DNA gyrase prevents the relaxation of positively supercoiled DNA that is required for normal transcription and replication

## Cont….

- Inhibition of topoisomeraseIV interferes with separation of replicated chromosomal DNA into the respective daughter cells during cell division.

- They can enter cells easily via porins and are used to treat intracellular pathogens (*Legionella, pneumophila* and *Mycoplasma)*

# Adverse effects.

- Generally safe antibiotics
- G.I.T-nausea,vomiting,diarrhea and antibiotic associated colitis have been reported.
- CNS-confusion,insomnia,dizziness,anxiety,and seizures(displacement of GABA from its receptors).
- CVS-torsade de pointes,prolonged QTc interval.
- May damage growing cartilage resulting in arthropathy(but that's reversible so may b used in psudomonal infections in C.F where benefit outweighs the risk.)

# Ciprofloxacin

- 2nd generation fluoroquinolone
- **Mainly effective against G –ve bacteria :**

Enterobacteriacae H. influenzae M. catarrhalis
Campylobacter Pseudomonas N. gonorrheae

**Intracellular pathogens**

M. Tuberculosis Mycoplasma Chlamydia
Legionella Brucella

- Not effective against G+ and anaerobes

# Clinical uses

1. Urinary tract infections (G- bacteria)
2. Osteomyelitis due to P. aeruginosa
3. Gonorrhea
4. Travellers' diarrhea- ciprofloxacin commonly used
5. Tuberculosis
6. Prostatitis
7. Community- acquired pneumoniae
8. Diabetic foot infections ( P. aeruginosa )
9. Anthrax

# Levofloxacin

- 3rd generation fluoroquinolone

- **Spectrum:** Gram-ve, Gram+ve (S. aureus including MRSA & S. pneumoniae) and Legionella pneumophila, atypical resp. pathogens, Mycobacterium tuberculosis

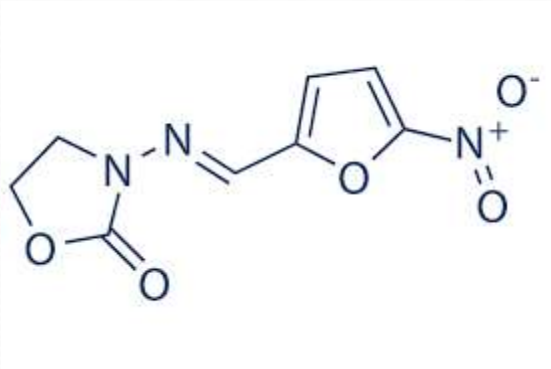
- **Indications:**
  - Chronic bronchitis and CAP
  - Nosocomial pneumonia
  - Intra-abdominal infections

# Cont.

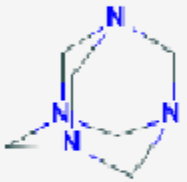
**Adverse reaction.**

- Blood glucose disturbances in DM patients
- QTC prolongation, torsades de pointes, arrhythmias
- Nausea, GI upset
- Interstitial nephritis

# Miscellaneous

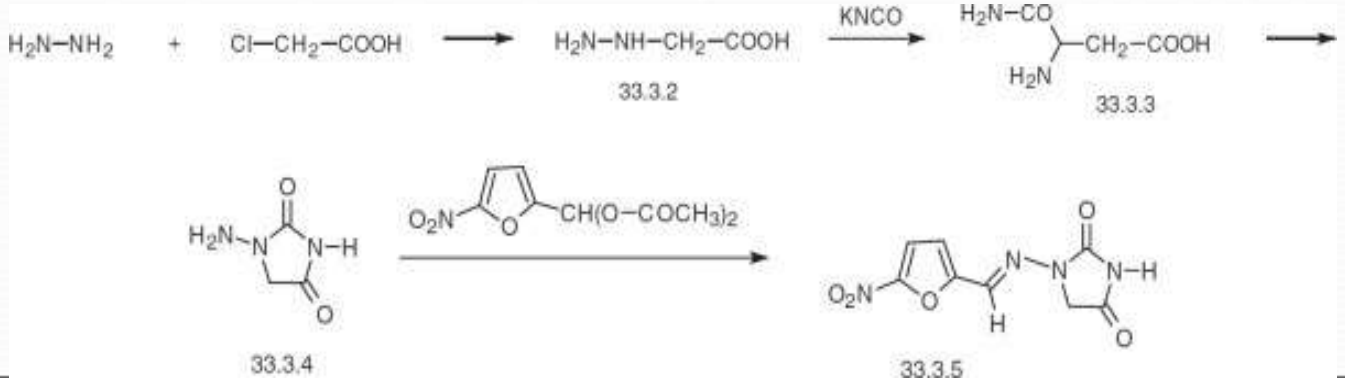


Furazolidine



Methanamine

Synthesis and Structure of Nitrofurantoin



# THANKYOU !!

# Antiviral agents

**By Baljeet kaur**

# Antiviral agents

- Antiviral drugs are available to treat **only a few viral diseases**.

- The reason for this is the fact that viral replication is so intimately associated with the host cell that any drug that interferes significantly with viral replication, is likely to be **toxic to the host**.

- Antiviral agents are totally different from antibacterial drugs and antiprotozoan drugs.

- Since viruses are obligate intracellular parasite therefore, antiviral agents must be capable of selectively inhibiting viral functions without damaging the host cell.
- Making such drugs is very difficult.

- Most antiviral are targeted towards viral encoded enzymes or towards the structures of virus that are important for replication.
- Most of these are chemical compounds or biochemical inhibitors of viral encoded enzymes.
- Unlike antibacterial drugs antiviral are limited to specific family of the viruses.
- Molecular virology studies are succeeding in identifying virus specific functions that can serve as antiviral therapy.
- The most important stages to target in viral infections are of progeny virus particles. **attachment of virus to host cell, uncoating of viral genome, regulation of viral reverse transcription, replication of viral nucleic acid, translation of viral proteins, assembly ,maturation and release.**

- Resistance to antiviral drugs has become problematic because of high rates of mutations.

- Future researches are necessary to learn how to minimize the emergence of drug resistant variant viruses and to design more antivirals based on molecular insight into the structure and replication of different classes of agents.

- **Stages in virus replication which are possible targets for chemotherapeutic agents:**
- Attachment to host cell
- Uncoating - (Amantadine)
- Synthesis of viral mRNA - (Interferon)
- Translation of mRNA - (Interferon)
- Replication of viral RNA or DNA - (Nucleoside analogues)
- Maturation of new virus proteins (Protease inhibitors)
- Budding, release

- Two useful antivirals are:

  the nucleoside analogues and
  the interferons

- Diseases for which effective therapy is available:

  **Herpes Simplex virus** (Acyclovir)
  **Varicella-Zoster virus** (Acyclovir)
  **Cytomegalovirus** (Gancyclovir, Foscarnet)
  **AIDS** (Zidovudine, Lamivudine[3TC], Protease inhibitors; in combination)
  **Respiratory Syncitial virus** (Ribavirin)
  **Influenza** (Amantadine)

- **Nucleoside analogue**
- Most of the antiviral drugs are Nucleoside analogues.
- These are limited in inhibitory activity to use against herpes viruses and HIV.
- These inhibit the nucleic acid replication by inhibition of enzymes Of metabolic pathways for purines or pyremidines .

- Sometimes some analogues are incorporated into the nucleic acid and block further synthesis or alter its function.

- Drug can bind better to viral DNA polymerase,rather than cellular DNApolymerase.
- Ex. Acyclovir, Valacyclovir,penciclovir,famciclovir lamivudine,and zydovudine.

- Penetration and uncoating of virus are required to deliver the viral genome into cytoplasm of the host cell.
- Arildone,disoxaril,and pleonaril, are the compounds which block uncoating of picornaviruses.

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- Amantadine,rimantidine also inhibit penetration.

- **Nucleotide analogues**
- These are **synthetic compounds which resemble nucleosides**, but have an incomplete or abnormal deoxy-ribose /or ribose group.
  These compounds are **phosphorylated** to the tri-phosphate form within the infected cell.
- In this form, **the drug competes with normal nucleotides** for incorporation into viral DNA or RNA.
- Incorporation of drug into the growing nucleic acid chain results in irreversible association with the viral polymerase and chain termination.

- **Interferon:**
- There are three classes: ***alpha- beta-*** and ***gamma-***
- ***The alpha and beta Interferon***
  are **cytokines** which are **secreted by virus infected cells**.

  They bind to specific receptors on adjacent cells and protect them from infection by viruses.

  They form part of the **immediate protective host response** to invasion by viruses.

  **In addition to these direct antiviral effects, alpha and beta interferon also enhance the expression of class I and class II MHC molecules on the surface of infected cells, in this way, enhancing the presentation of viral antigens to specific immune cells.**

Their presence can be demonstrated in body fluids during the acute phase of virus infection.

- **Recombinant alpha and beta interferon** are now available and have been used for the treatment of Chronic hepatitis B and C virus infections.
- However, **side effects** such as fever, malaise and weight loss have limited the use.
- ***gamma Interferon*** (immune interferon) is a **cytokine secreted by TH1 CD4 cells**. Its function is to enhance specific **T cell mediated** immune responses.

- **Mechanism of action of the interferons :**
- Enhancement of the specific immune response.
  **By increasing the expression of MHC class I molecules on the surface of infected cells, the interferon increase the opportunity for specific cytotoxic T cells to recognize and kill infected cells.**
- Direct antiviral effect
  a) degradation of viral mRNA
  b)inhibition of protein synthesis
  Prevents the infection of new cells

- **Immunoglobulin Therapy**
- **Passive Immunisation**
- **Passive immunisation** is the transfer of immunity to a host by means of immunoglobulins (preformed antibodies).
- These immunoglobulins are typically prepared by cold ethanol fractionation as a 16% solution of gammaglobulin from large pools of serum obtained from the blood donations of at least 1000 donors.
- Immunoglobulin from immune individuals can be used as prophylaxis to prevent viral infections in exposed, but non immune individuals.
- It works by binding to extra-cellular virions and preventing them from attaching to and entering susceptible cells. The protective effect is short lived (up to three months) because the antibodies are metabolized by the host.

- **"Normal" Immune globulin**

  **This is a pooled product, prepared from the serum of normal blood donors. It contains low titres of antibody to a wide range of human viruses. It is mainly used as prophylaxis against:**
- **hepatitis A virus infection,**
- **parvovirus infection, and enterovirus infections (in neonates).**

- **Hyper-immune globulin**

  **Immunoglobulin may be prepared from the serum of selected individuals who have high titres of antibody to particular viruses. Examples include:**
- **Zoster immune globulin**

  **Prevention of Varicella in immunocompromised children and neonates.**
- **Human Rabies immunoglobulin**

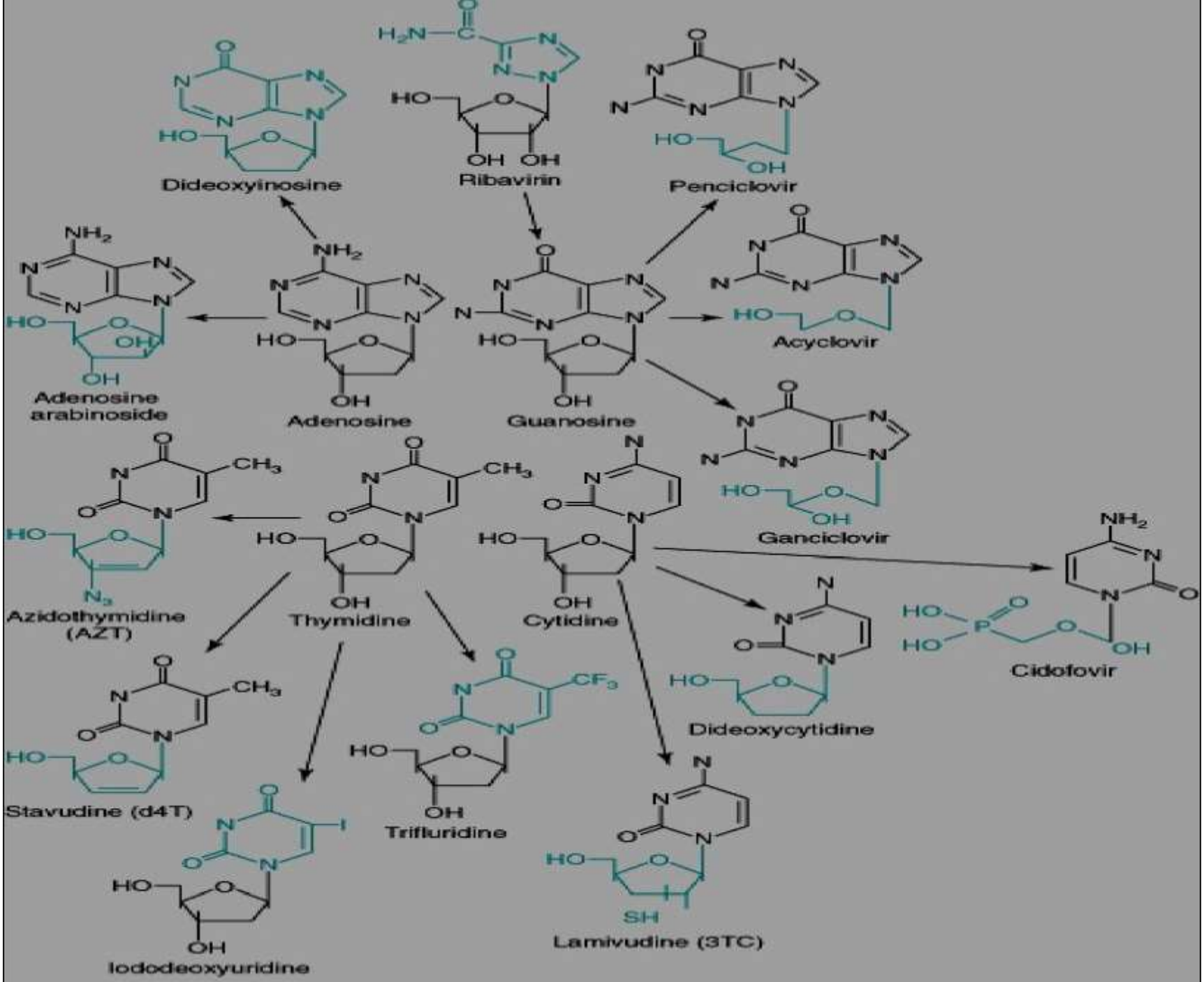
  **Post-exposure prophylaxis in an individual who has been bitten by a rabid animal.**
- **Hepatitis B Immune globulin**

  **Non-immune individual who has been exposed to HBV.**

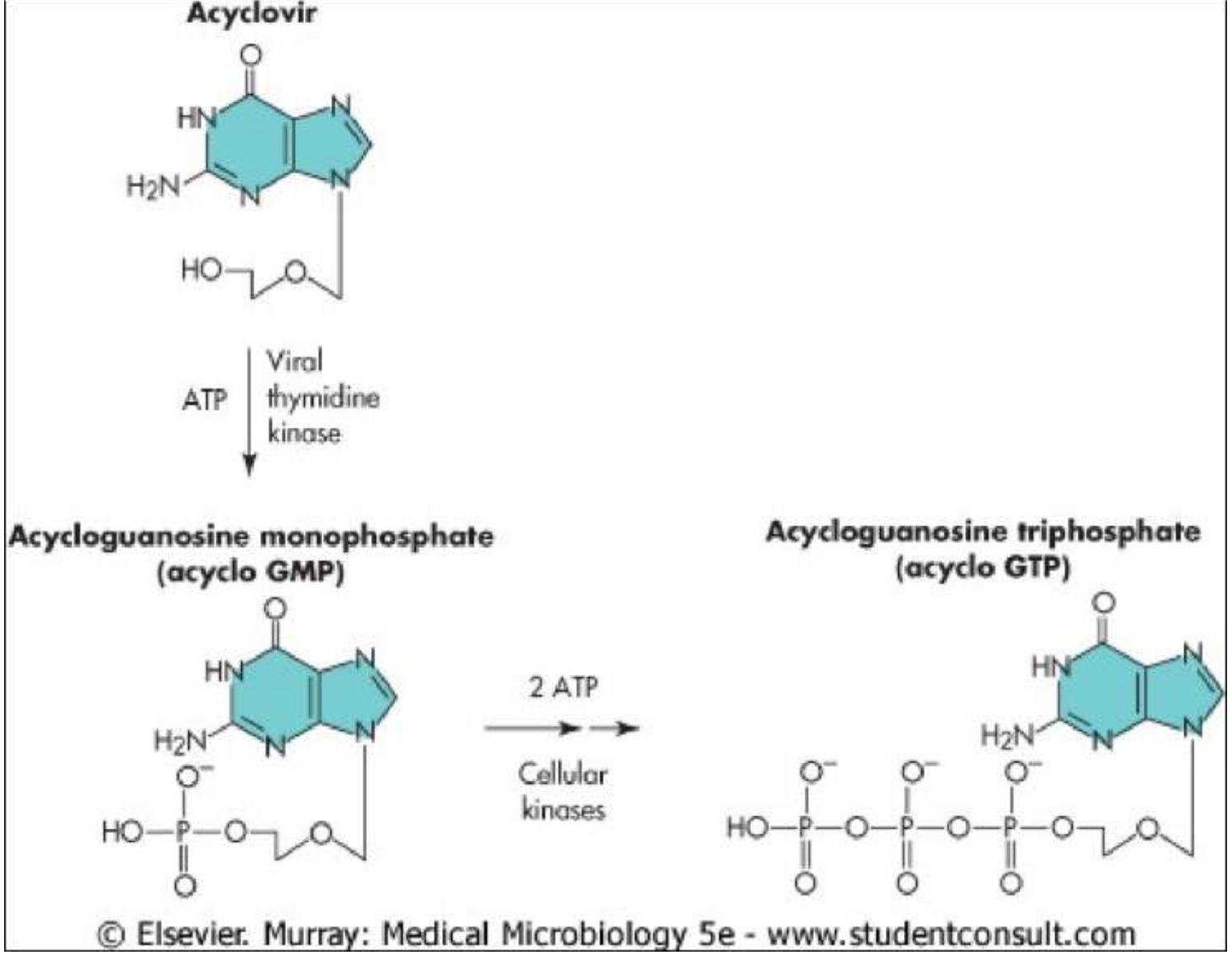
# DESCRIPTION OF THE FIGURE 1

Structure of the most common nucleoside analogues that are antiviral drugs.

The chemical distinctions between the natural deoxynucleoside and the antiviral drug analogues are highlighted. Arrows indicate related drugs. Valacyclovir (not shown) is the l-valyl ester of acyclovir. Famciclovir (not shown) is the diacetyl 6-deoxyanalogue of penciclovir. Both of these drugs are metabolized to the active drug in the liver or intestinal wall.



- Figure 2
- Activation of ACV (acycloguanosine) in herpes simplex virus-infected cells.
- ACV is converted to acycloguanosine monophosphate (acyclo GMP) by herpes-specific viral thymidine kinase, then to acycloguanosine triphosphate (acyclo GTP) by cellular kinases.



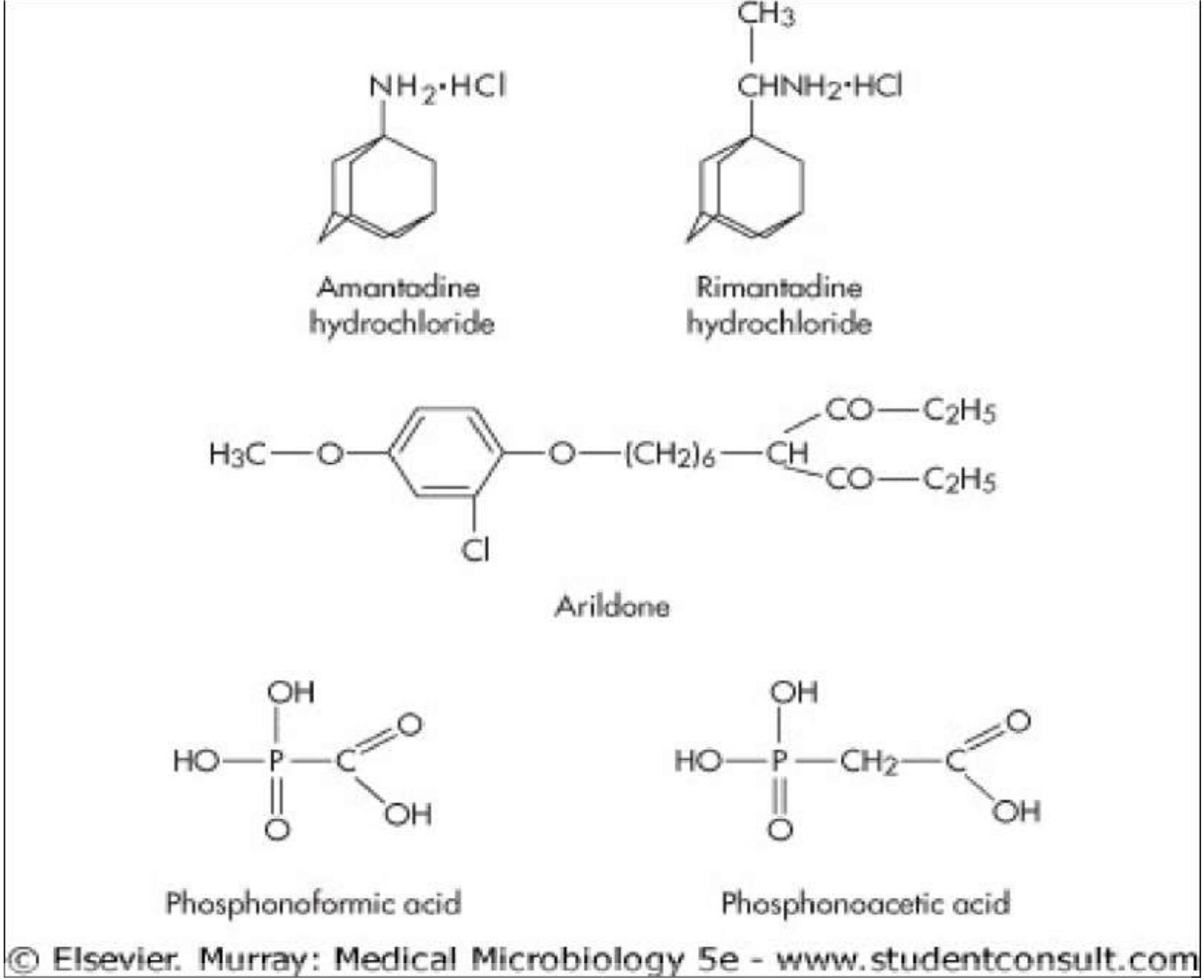
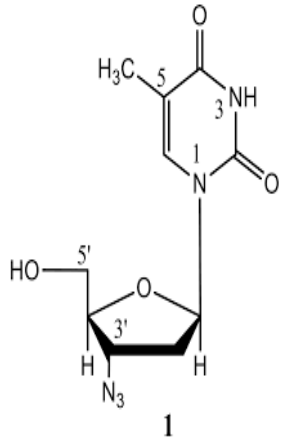
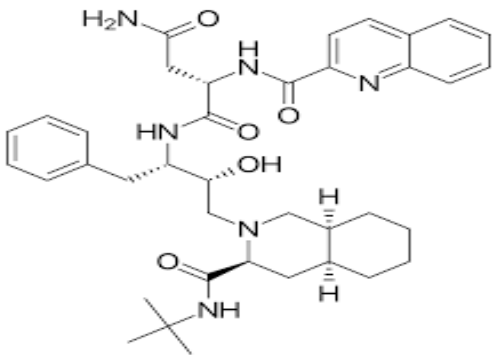


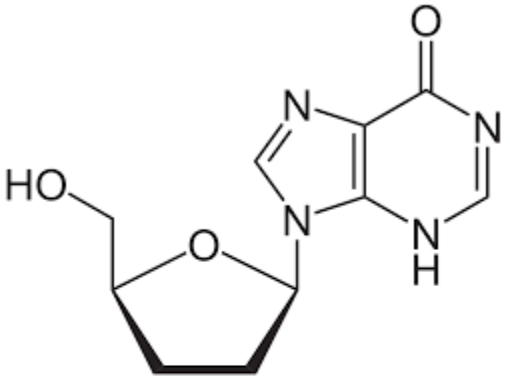

Figure 3 Structures of non-nucleoside antiviral drugs.



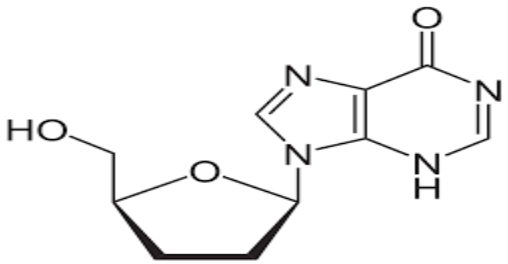

zidovudine



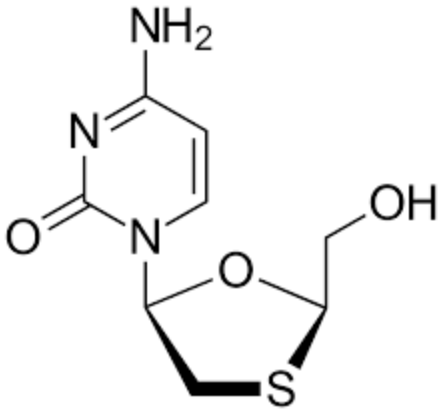

saquanavir



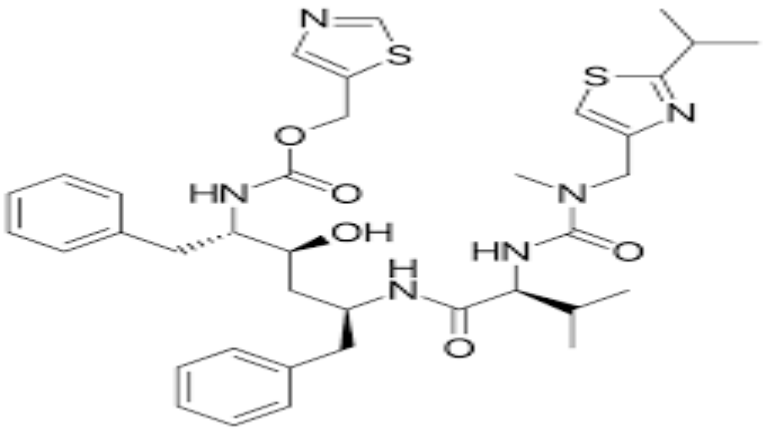

Didanosine



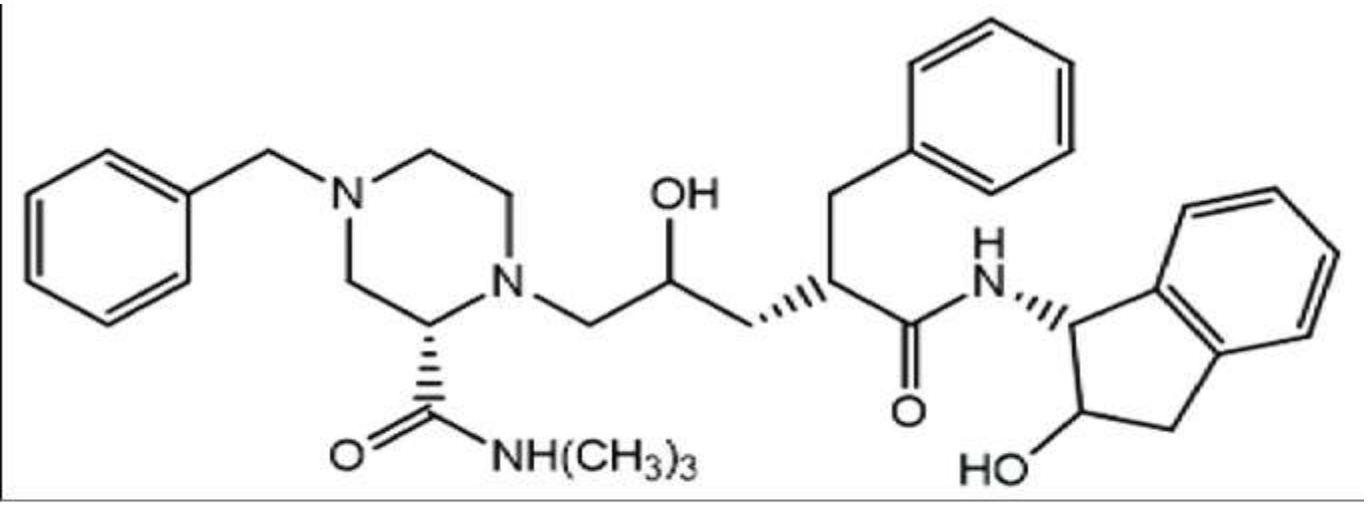

Zalcitabine




Lamivudine




Ritonavir




Indinavir