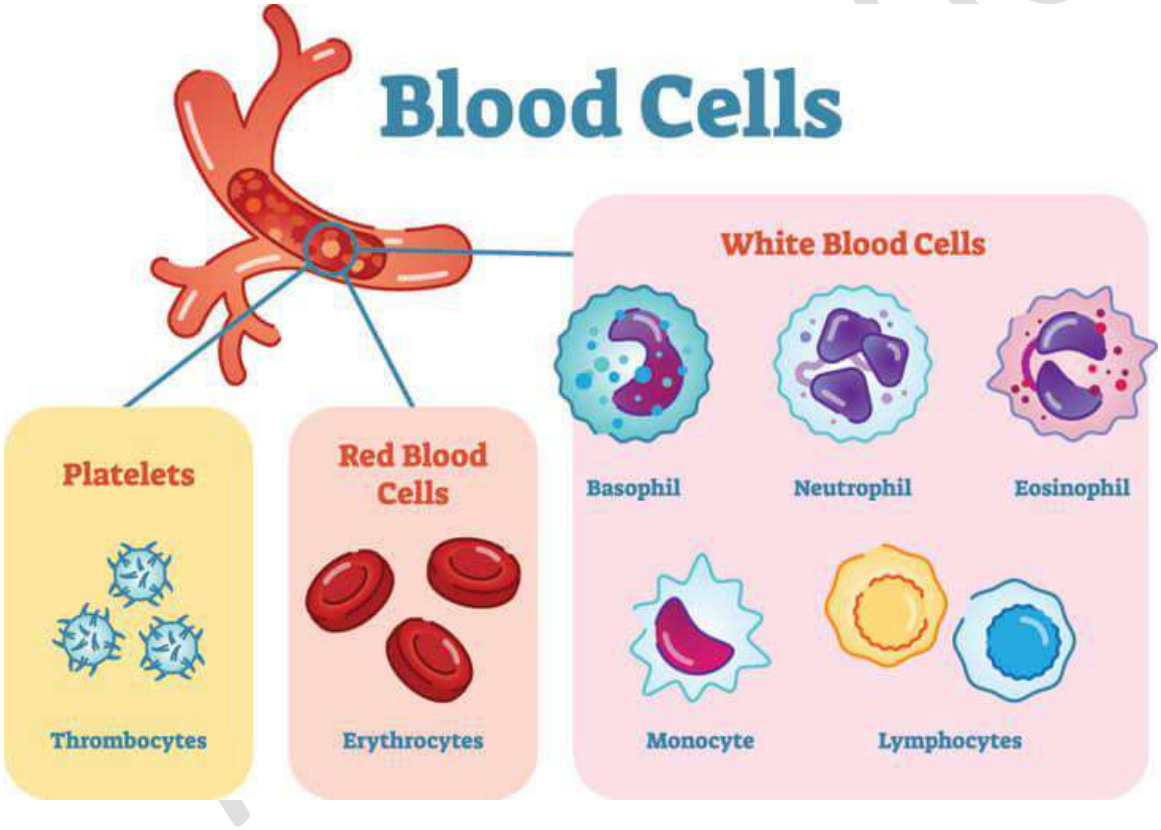
Anti-HIV Drugs:

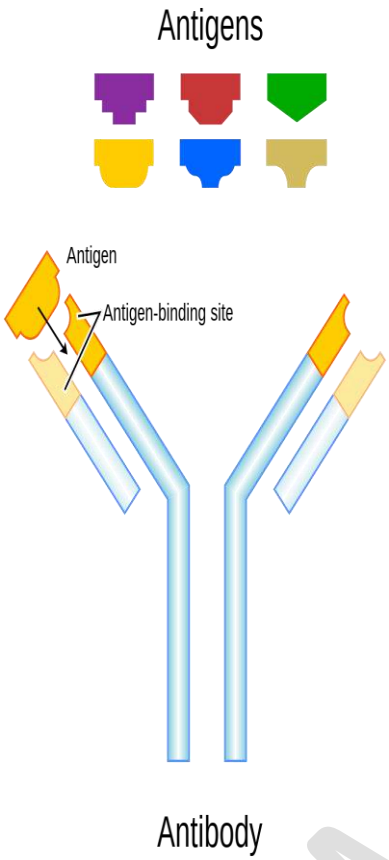
- The Human Immune Deficiency Virus infection causes AIDS (Acquired Immune Deficiency Syndrome)
- The infection causes the depletion of CD4 lymphocytes
- Lack of lymphocytes leads to immune deficiency



Antigen (**Ag**) is a molecule or molecular structure or any foreign particulate matter that can bind to a specific antibody or T-cell receptor.

The term *antigen* originally referred to a substance that is an antibody generator.

Antigens can be proteins, peptides (amino acid chains), polysaccharides (chains of monosaccharides/simple sugars), lipids, or nucleic acids, microorganisms including Virus, Bacteria.

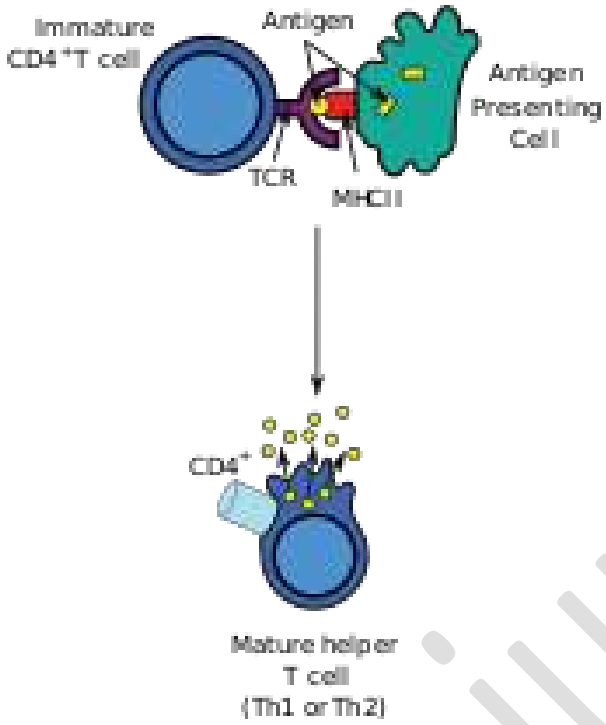


Antigen-presenting cells present antigens in the form of peptides on histocompatibility molecules.

The T cells selectively recognize the antigens; depending on the antigen and the type of the histocompatibility molecule.

An **antibody** (**Ab**), also known as an **immunoglobulin** (**Ig**),[1] is a large, Y-shaped protein used by the immune system to identify and neutralize foreign objects such as pathogenic bacteria and viruses.

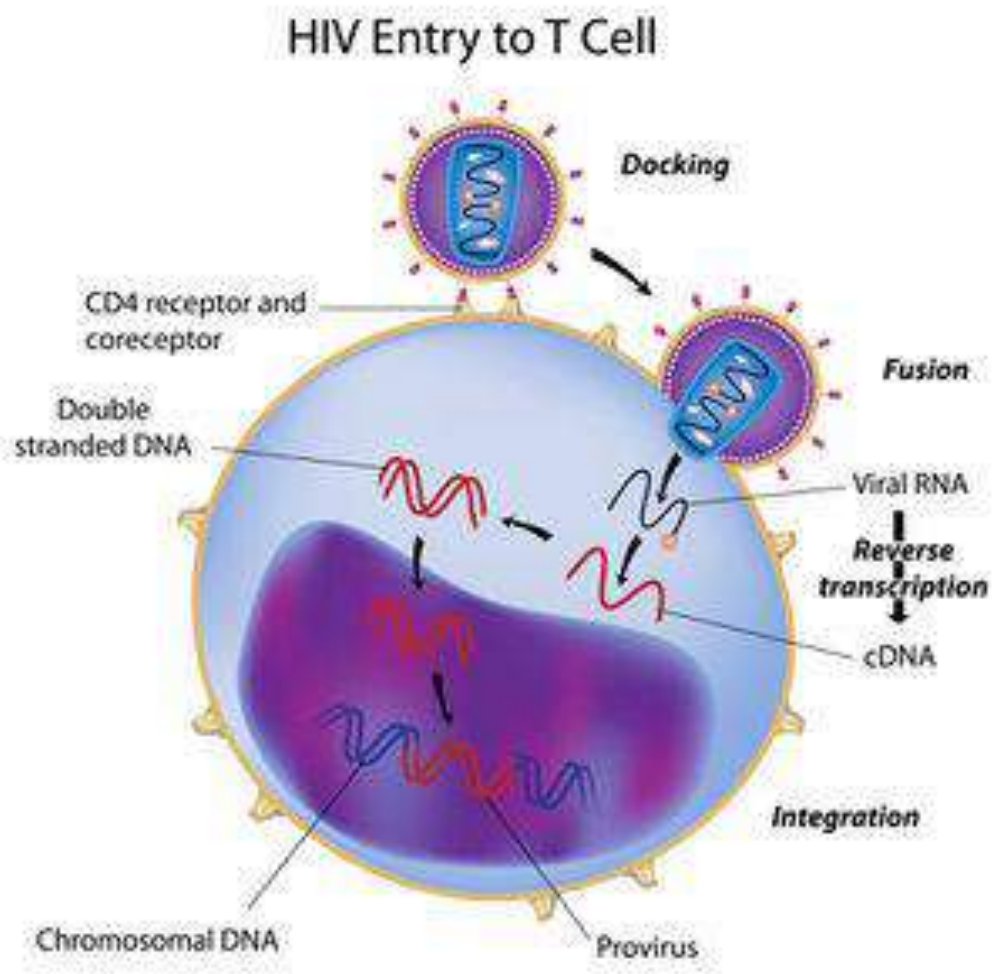
Immunity:



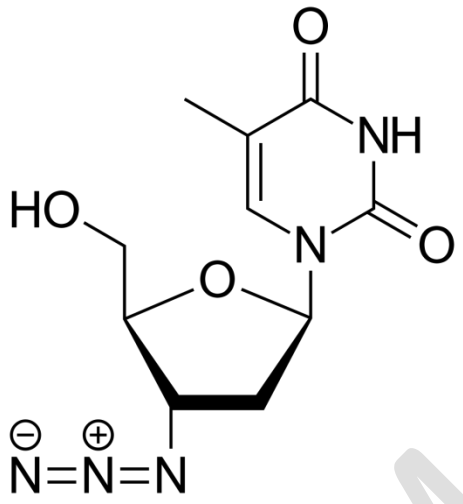
-
- **CD4 (cluster of differentiation 4) is a glycoprotein that serves as a co-receptor for the T-cell receptor (TCR).**
- **CD4 is a co-receptor of the T cell receptor (TCR) and assists the latter in communicating with antigen-presenting cells (APC).**
- **APCs process antigens and present them to T-cells.**

Types of HIV drugs:

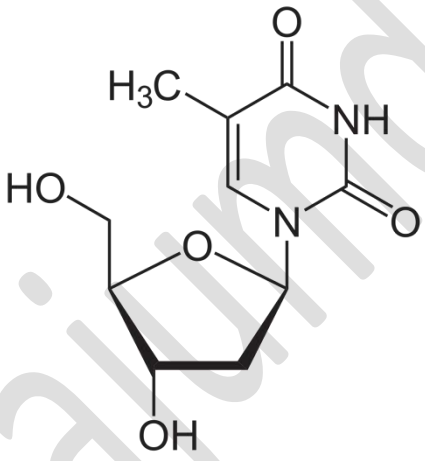
- **Reverse Transcriptase Inhibitors**
- **HIV Protease Inhibitors**



Anti HIV Drug: Zidovudine
AZidoThymidine (AZT)



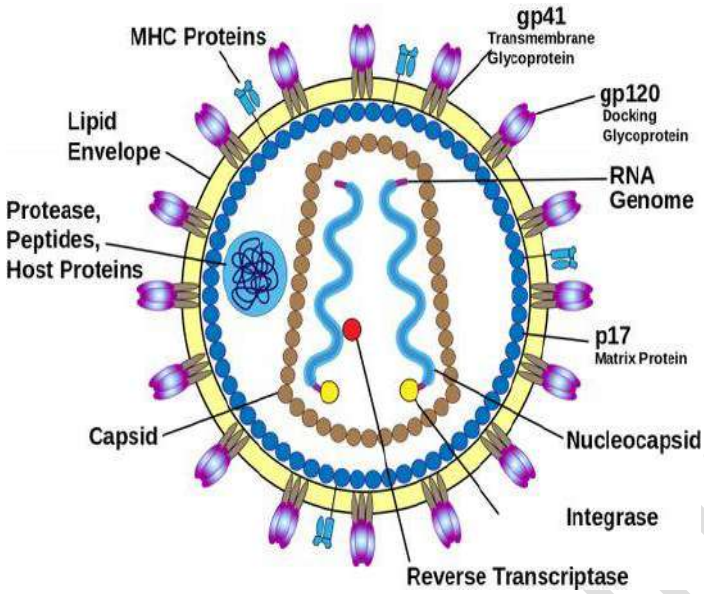
Zidovudine



Thymidine

Zidovudine is structurally similar to Thymidine

Retro virus and RNA Virus

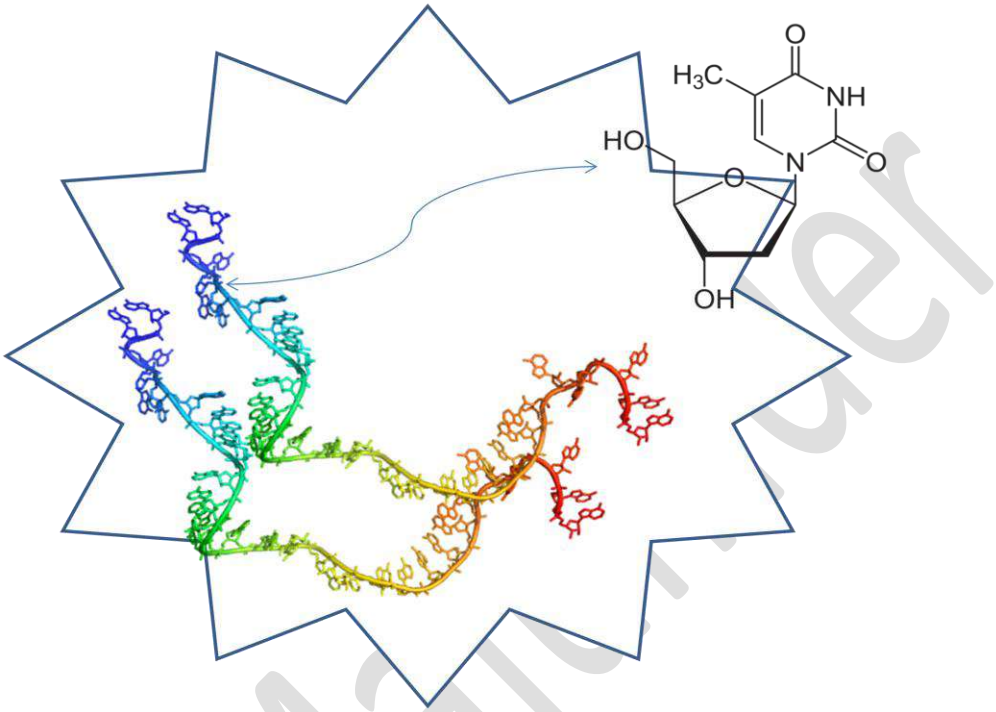


Most RNA viruses reproduce by inserting RNA into the host cell. The RNA contains the instructions for making copies of the virus.

A retrovirus is an RNA virus, but instead of inserting the RNA directly into the cell, it first converts it into DNA.

The HIV genome consists of **two identical single-stranded RNA molecules** that are enclosed within the core of the virus particle

HIV virus structure



Thymidine in the virus

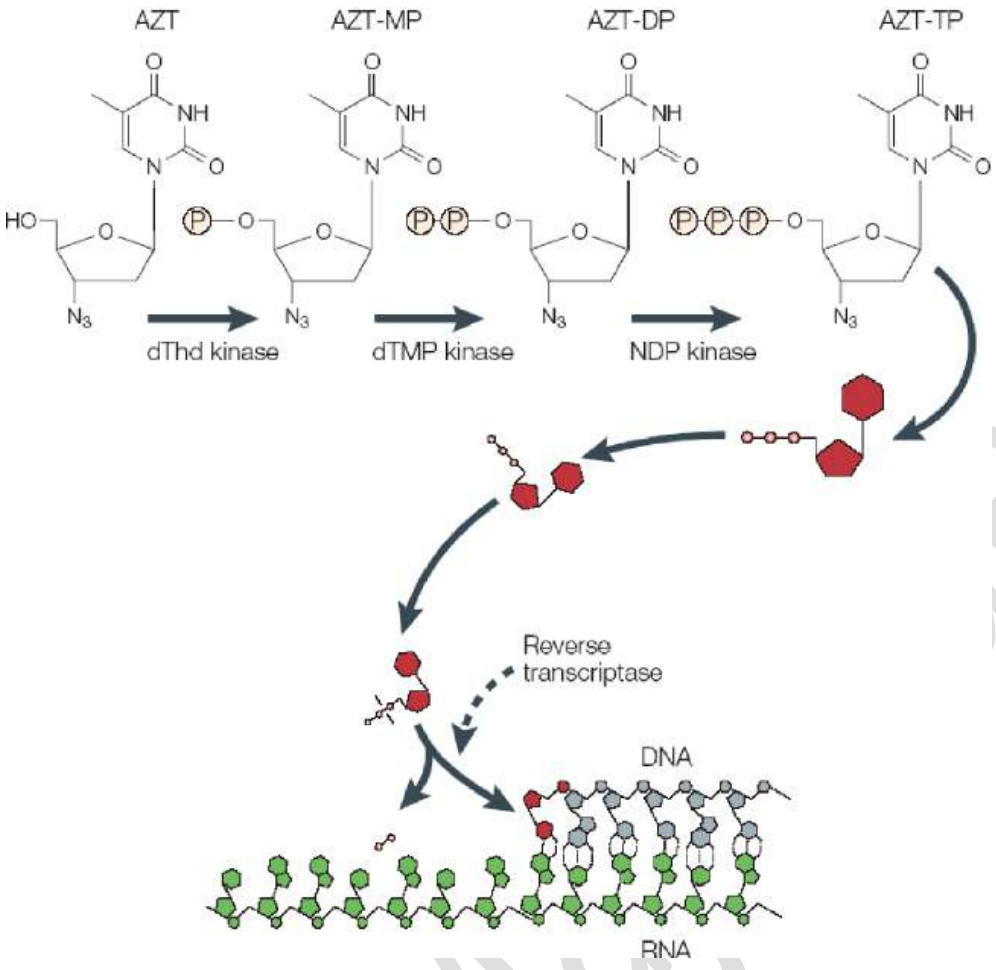
Mechanism of action of AZT Zidovudine

AZT is a thymidine analogue.

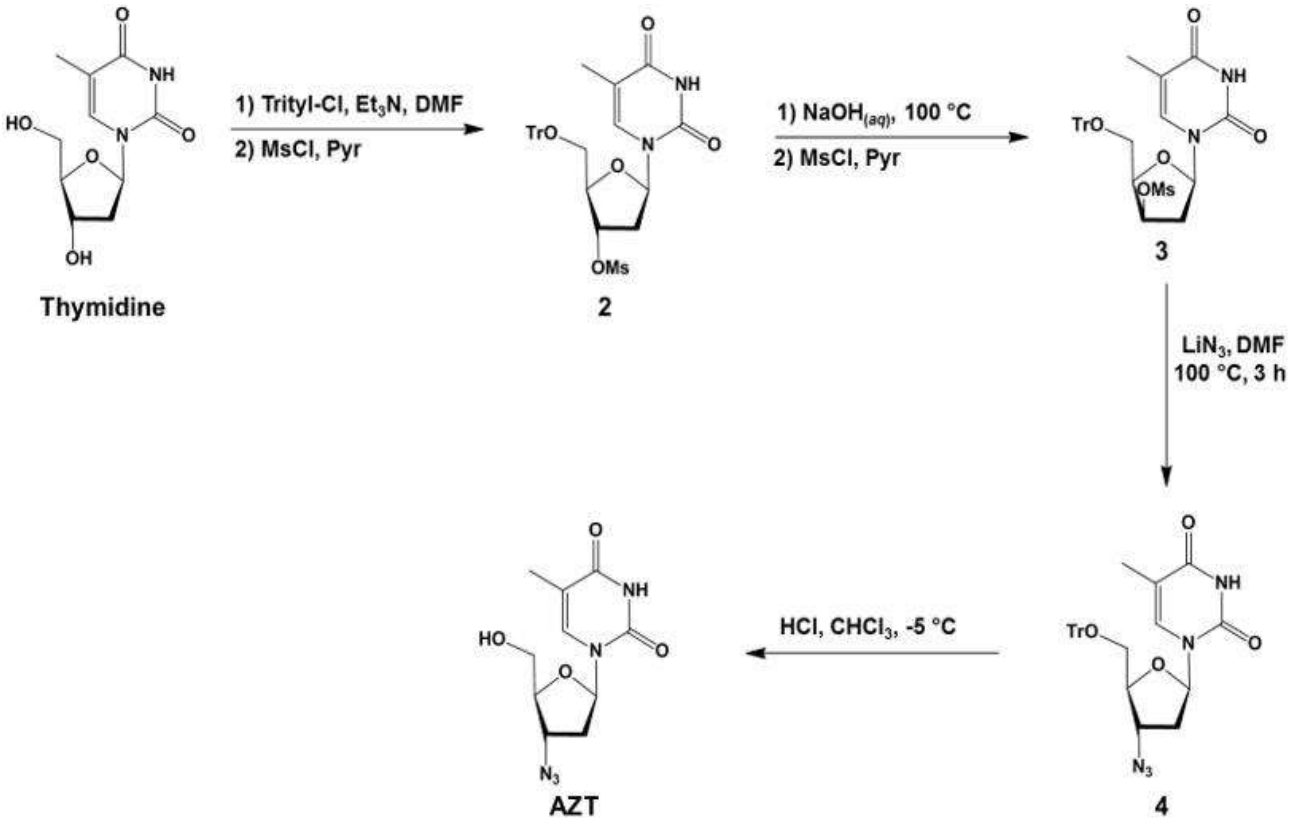
It is well absorbed by oral intake and is converted to triphosphate.

AZT works by **selectively inhibiting HIV's reverse transcriptase**, the enzyme that the virus uses to make a DNA copy of its RNA.

It halts the DNA synthesis



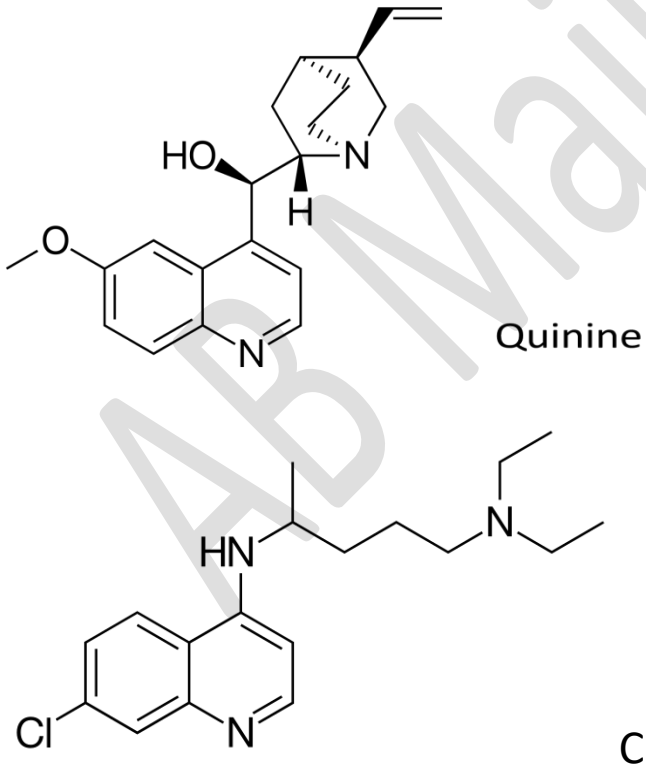
Synthesis of AZT Zidovudine:


Thymidine
1) Trityl-Cl, Et_3N, DMF
2) MsCl, Pyr
2
1) $NaOH_{(aq)}$, 100 °C
2) MsCl, Pyr
3
LiN_3, DMF
100 °C, 3 h
4
HCl, $CHCl_3$, -5 °C
AZT

Anti Malarial Drug

Quinine is **used to treat malaria caused by *Plasmodium falciparum*.** It is the only natural drug that can treat malaria.

Plasmodium falciparum is a parasite that gets into the red blood cells in the body and causes malaria. Quinine works by killing the parasite or preventing it from growing.



Quinine

Chloroquinine

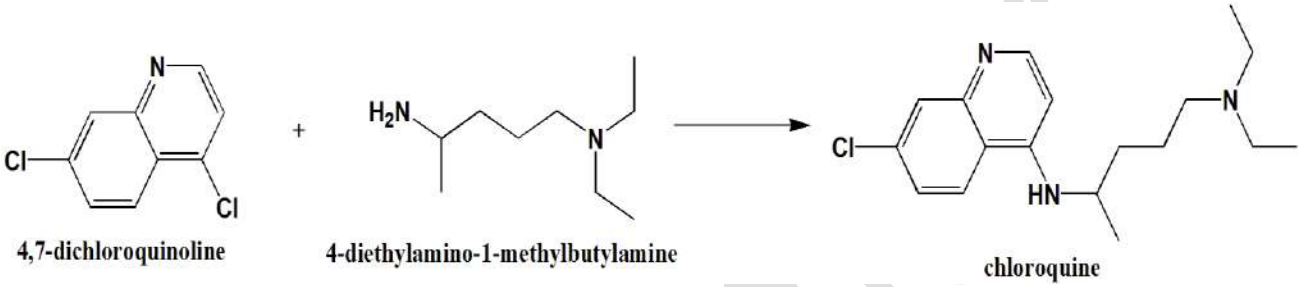
Natural source: Parthenium integrifolium (wild quinine)

Quinine: Mechanism

- It enters red blood cells and binds with heme through complex formation
- This heme-quinine complex inhibits the metabolic process of the parasite.
- Chloroquine accumulates in the food vacuole of the Plasmodia parasite
- It prevents the conversion of Heme to Hemozoin
- Accumulation of Heme is toxic to the parasite and kills it

Synthesis:

N-C Coupling:



4,7-dichloroquinoline

4-diethylamino-1-methylbutylamine

chloroquine

Antibiotics

Compounds that Kill the microbial cells (Germs) by inhibiting its protein synthesis

History: Antibiotics have been used for millennia to treat infections, although until the last century or so people did not know the infections were caused by bacteria. Various moulds and plant extracts were used to treat infections by some of the earliest civilisations – the ancient Egyptians, for example, applied mouldy bread to infected wounds. Nevertheless, until the 20th century, infections that we now consider straightforward to treat – such as pneumonia and diarrhoea – that are caused by bacteria, were the number one cause of human death in the developed world.

It wasn't until the late 19th century that scientists began to observe antibacterial chemicals in action. Paul Ehrlich, a German physician, noted that certain chemical dyes coloured some bacterial cells but not others. He concluded that, according to this principle, it must be possible to create substances that can kill certain bacteria selectively without harming other cells. In 1909, he discovered that a chemical called arsphenamine was an effective treatment for syphilis. This became the first modern antibiotic, although Ehrlich himself referred to his discovery as 'chemotherapy' – the use of a chemical to treat a disease. The word 'antibiotics' was first used over 30 years later by the Ukrainian-American inventor and microbiologist Selman Waksman, who in his lifetime discovered over 20 antibiotics.

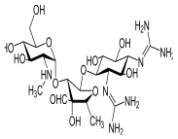
Alexander Fleming was, it seems, a bit disorderly in his work and accidentally discovered penicillin. Upon returning from a holiday in Suffolk in 1928, he noticed that a fungus, *Penicillium notatum*, had contaminated a culture plate of *Staphylococcus* bacteria he had accidentally left uncovered. The fungus had created bacteria-free zones wherever it grew on the plate. Fleming isolated and grew the mould in pure culture. He found that *P. notatum* proved extremely effective even at very low concentrations,

preventing *Staphylococcus* growth even when diluted 800 times, and was less toxic than the disinfectants used at the time.

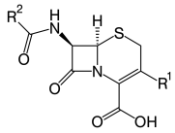
After early trials in treating human wounds, collaborations with British pharmaceutical companies ensured that the mass production of penicillin (the antibiotic chemical produced by *P. notatum*) was possible. Following a fire in Boston, Massachusetts, USA, in which nearly 500 people died, many survivors received skin grafts which are liable to infection by *Staphylococcus*. Treatment with penicillin was hugely successful, and the US government began supporting the mass production of the drug. By D-Day in 1944, penicillin was being widely used to treat troops for infections both in the field and in hospitals throughout Europe. By the end of World War II, penicillin was nicknamed 'the wonder drug' and had saved many lives.

Scientists in Oxford were instrumental in developing the mass production process, and Howard Florey and Ernst Chain shared the 1945 Nobel Prize in Medicine with Alexander Fleming for their role in creating the first mass-produced antibiotic.

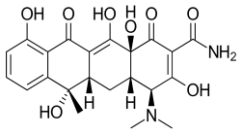
Types of antibiotics



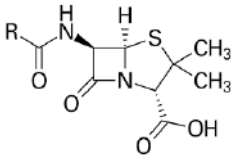
Aminoglycosides



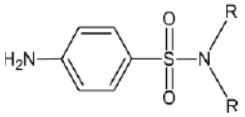
Cephalosporins



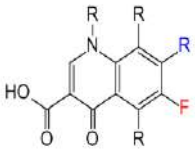
Tetracyclins



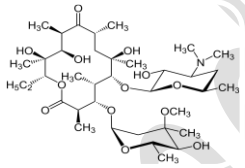
Penicillins



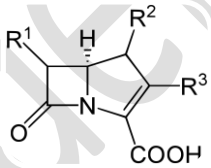
Sulphonamides



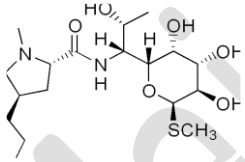
Fluoroquinolones



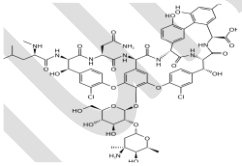
Macrolides



Carbapenems



Lincosamides



Glycopeptides

Aminoglycosides	The name ends with “mycin”: e.g. Streptomycin, Gentamycin	Used for infection in blood streams and in severe abdominal infections: bacteremia These inhibit the protein synthesis in gram negative bacteria.

Cephalosporins	The name of drugs starts with " ceph" of "Cef" For example: Cefixime	Used for Skin, Urinary and respiratory infections. Attacks both gram positive and gram negative bacteria.
Tetracyclins	These drugs ends with the name " cycline" For Example: Doxycycline, Methacycline	Used for Lyme Disease, Pulmonary inflammatory diseases and STDs (Sexually Transmitted Diseases)
Carbapenems	Name ends with "penems". Examples are like Meropenem, Ertapenem	Inhibits bacterial cell wall synthesis Used for UTI and Abdomen infections
Fluoroquinolones	Drug name ends with "floxacin". For example: Ciprofloxacin, Levofloxacin	Inhibits bacterial DNA replication Used for respiratory and UTI
Macrolides	Ends with the name : "thromycin". For example , Azethromycin, Erythromycin	Used for pneumonia, sinucites, UTI, inner throat infection, STD.
Lincosides	Ends with mycin : Gentamycin	Used for skin, bone and lung infections
Glycopeptides	This also ends with mycin: For example Vancomycin	Inhibits bacterial cell wall synthesis Used for skin and cardioinfections