PHARMACOLOGY-III

UNIT 2 NOTES

CHEMOTHERAPY

- GENERAL PRINCIPLES
- SULFONAMIDES & COTRIMOXAZOLE
- ANTIBIOTICS

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CHEMOTHERAPY

- It is the type of cancer treatment that drugs to kill or slow down the growth of cancerous cells.
- They are derived from micro - organisms.
- They are also used to treat infectious disease which is caused by any type of micro - organisms.
- They are the treatment of any disease by synthetically and microbiologically, which killing microbes and cancer cells.
- Example - Cancer treatment, autoimmune disease, microbial infections etc.

GENERAL PRINCIPLE OF CHEMOTHERAPY

- Chemotherapy used to kill or stop growth of fast - deviding cells, like cancer cells.
- It works throughout the body to target cancer but also can affect healthy cells, causing side effects.
- The goal is to destroy cancer cells and treat infections disease with minimum harm to normal tissues or host cells (human body).

- **Antibiotics-** A natural substance produced by a micro-organisms to kill other micro-organisms.

- **Anti-infectives / Anti-microbials -** Antimicrobials are drugs that used to treat microbial disease. They are also derived from micro-organisms and treat micro-organisms which cause illness.

History Of Chemotherapy

- The Chemotherapy was discovered by Paul Ehrlich.
- In 1908, Ehrlich was awarded with Nobel Prize for medicine.
- In 1909, he and his student Sahachiro Hata developed Salvarsan (arsphenamine), treatment effective against syphilis (STD).
- The Golden Age of antimicrobial therapy began with the production of penicillin, which is discovered by Alexander Flaming in 1928.
- Penicillin inhibits the growth of staphylococci, which was growing by accident on a culture place.
- Penicillin was extracted for mass production in 1940 by the work of Florey & Chain.

Sulfonamides And Cotrimoxazole

Sulfonamides

- They are also known as Sulfa drugs, a group of synthetic antibiotics that contain sulfomide group/ Sulfonamide group.
- They are ~~pin~~ primarily used to treat bacterial infections.
- Sulfonamides were among the first anti-biotics discovered and have a historical role in the development of antibacterial treatment.

Classification

- Short Acting: Sulfadiazene
- Intermediate Acting: Sulfamethoxazole
- Long Acting: Sulfadoxine, Sulfamethopyrazine
- Special Puppose: Sulfacetamide sodium, Sulfasalazine, Mefiride etc.

General Mechanism Of Action Of Sulfonamides

Sulfonamides

↓

They looks like PABA and work together with PABA to bind to an enzyme called dihydropteroate synthase.

↓

Prevent the production of folic acid

↓

Bacteria unable to make DNA or protiens

↓

Stops bacterial growth/ Bacterial death

PHARMACOKINETICS

- Absorption - Orally administered and rapidly absorbed from GIT.
- Distribution - Widely distributed in body fluids and tissues, including the cerebrospinal fluid.
- Metabolism - Metabolized in liver through acetylation and conjugation.
- Excretion - Primarily excreted in the urine, both as unchanged drug and metabolites.

ADVERSE EFFECTS

- Anemia
- Vomitting
- Nausea
- Hepatitis
- Toxicity
- Leukopenia etc.

THERAPEUTIC EFFECTS

- UTIs
- Bronchitis
- Pneumonia
- Burns
- Meningitis
- Rheumatic fever etc.

COTRIMOXAZOLE

- Cotrimoxazole is a combination antibiotic consisting of two active ingredients : Sulfamethoxazole & Trimethaprim.
- It is used to treat a wide range of bacterial infections by inhibiting bacterial growth through a dual mechanism
- Where,
- Sulfamethoxazole - Inhibits bacterial folic acids synthesis by blocking the enzyme dihydropteroate synthase.
- Trimethaprim - A dihydrofolate reductase inhibitor that further prevents the conversion of folic acid into its active form, essential for bacterial DNA synthesis.

MECHANISM OF ACTION

- Co-trimoxazole works by blocking bacterial folic acid production, which is essential for bacterial growth and DNA synthesis. It has two steps here :

① Sulfamethoxazole - Stops bacteria from making folic acid by blocking an enzyme called dihydropteroate synthase.

② Trimethaprim - prevents the making of folic acid by inhibiting dihydrofolate reductase, stopping form DNA in bacteria.

- This dual action kills bacteria more effectively than using either drug alone.

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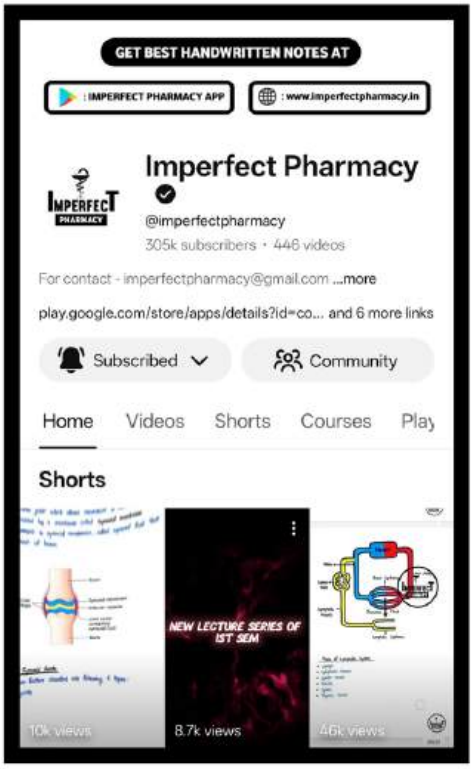

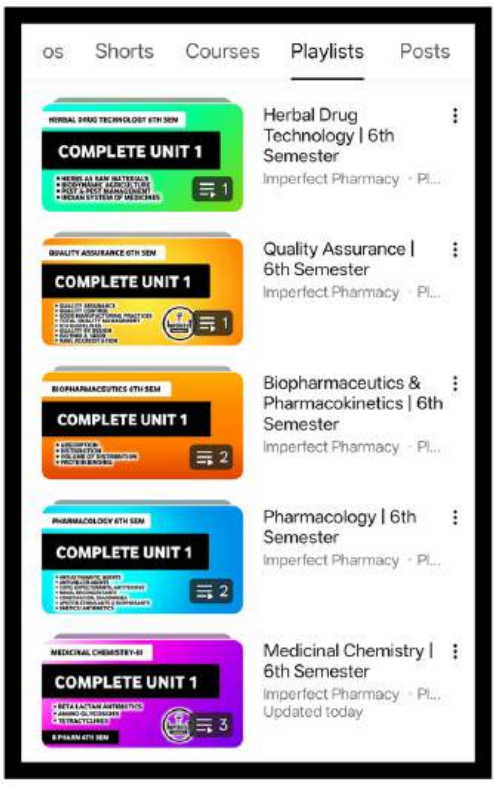

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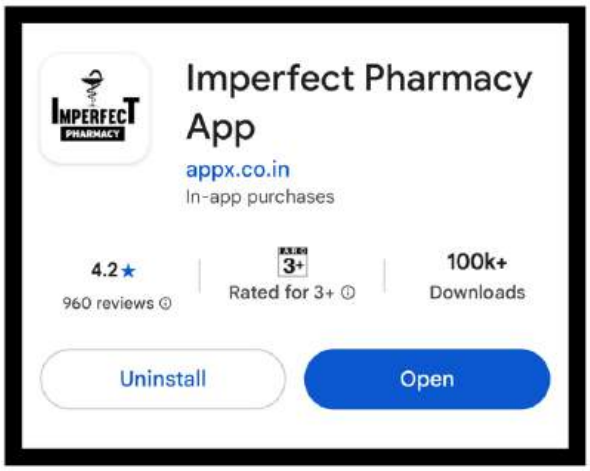


PHARMACOKINETICS

- Absorption - Well absorbed orally, reaching peak level in 1-4 hours.
- Distribution - Widely distributed including lungs, kidneys and cerebrospinal fluid.
- Metabolism - Mainly metabolized in liver.
- Excretion - Primarily excreted via the kidneys.

ADVERSE EFFECTS

- Anemia
- Leukopenia
- Hepatitis
- Thrombocytopenia
- Crystelluria
- Vomitting, Nausea
- Toxicity etc.

THERAPEUTIC USES

- UTIs
- Pneumonia
- Bronchitis
- Meningitis
- Cholera
- HIV - related infections etc.

ANTIBIOTICS

- Antibiotics are a class of medicines used to treat infections caused by bacteria.
- They either kill bacteria (bacteriocidal) or inhibit their growth (bacteriostatic).
- Antibiotics are among the most widely used medications in medicines, particularly for treating bacterial infections.
  e.g. - Penicillins, Cephalosporins etc.

HISTORY OF ANTIBIOTICS

- In ancient times, difficult to treatment of infections or infectious disease or bacterial disease (used moldy bread for wound healing).
- Then Ist antibiotic discovered by scientist Alexander Flaming is name Penicillin in 1928.
- Chain and Florey, discovered penicillin into a usable drug during world war II, leading to its mass production & saving countless lives.
- Selman Waksman discovered streptomycin in 1942, effective against Tuberculosis.
- Paul Ehrlich father of mordern chemotherapy, discovered treatment for Syphillis in 1909.

CLASSIFICATIONS

- Based on Mechanism of Actions
- Based on spectrum
- Based on chemical structure
- Based on Natural sources
- Based on Bacteriocidal / Bacteriostatic Actions.

① Based On MOA :

a) Inhibitors of cell wall synthesis - Penicillins, Cephalosporins, Carbapenems, Vancomycin etc.

b) Inhibitors of Protien synthesis - Aminoglycosides, Macrolides, Tetracyclines, Chloramphenicol etc.

c) Inhibitors of Nucleic Acid synthesis - Floroquinolones, Metronidazole, Rifamycine etc.

d) Inhibitors of Folic Acid synthesis - Sulfonamides, Trimethaprim etc.

e) Distruptors of cell membrane - Polymyxin, Daphomycin etc.

② Based On Specturum :

a) Broad Specturum - Tetracyclines, Fluoroquinolones, Carbapenems etc.

b) Narrow Specturum - Penicillin G (Gram +ve), Isoniazid etc.

③ Based On Chemical Structure :

a) β - lactam antibiotics - Penicillin, Cephalosporins, Carbapenems, Monobactams

b) Aminoglycosides - Gentamycin, Amikacin, Streptomycin etc.

c) Macrolides - Erythromycin, Azithromycin, Clarithromycin etc.

d) Tetracyclines - Doxycyclines, Minocyclines etc.

e) Fluoroquinolones - Ciprofloxacin, Levofloxacin etc.

f) Sulfonamides - Sulfamethoxazole, Trimethaprim etc.

g) Miscellaneous - Vancomycin, Polymyxin B, Rifampin, Ethambutol, Fluconazole, Nystatin etc.

④ Based On Natural Sources :

a) Natural Antibiotics - Derived from micro-organisms like Penicillins, Tetracyclines etc.

b) Semi-synthetic antibiotics - Modified natural antibiotics like Amoxicillin, Penicillin V etc.

c) Synthetic antibiotics - Fully lab-made like Sulfonamides, Isoniazid etc.

⑤ Based On Bactericidal / Bacteriostatic Action :

a) Bactericidal - Penicillins, Cephalosporins, Fluoroquinolones, Aminoglycosides etc.

b) Bacteriostatic - Tetracyclines, Macrolides, Sulfonamides etc.

PENICILLIN

- Penicillin is a group of antibiotics derived from Penicillium Mold, widely used to treat bacterial infections.
- Penicillin is a β-lactam antibiotics that inhibits bacterial cell wall synthesis, leading to bacterial cell death.
- It was the first antibiotic discovered in 1920 and remains widely used for bacterial infections.
- Penicillin is now obtained from fungus Penicillium notatum for therapeutic use but the present source of penicillin is the high-yielding Penicillium chrysogenum.
- They contain Lactam ring and Thiazolidine ring:

CLASSIFICATIONS

① Natural Penicillins - Benzyl Penicillin (Penicillin G)

② Semisynthatic Penicillins -
- Acid-resistant alternative to Penicillin G - Phenoxymethy Peniallin (Penicillin V)
- Penicillinase resistant penicillins - Methicillin, Cloxacillin, Dicloxacillin
- Extended spectrum penicillins -
  - Aminopenicillins: Ampicillin, Becampicillin, Amoxicillin
  - Carboxypenicillins: Carbenicillin, Ticarcillin
  - Uriedo penicillins: Piperacillin, Mezlocillin

③ β-Lactamase inhibitors - Clavulanic Acid, Sulbactam, Tazobactam

Mechanism Of Action

Penicillin enters into bacterial cells

↓

Bind with PBP Protien - Binding Protiens (PBPs)

↓

PBPs are enzyme involved in forming bacterial cell wall

↓

Inhibits PBPs from linking peptidoglycon layers

↓

Cell wall synthesis distrupted

↓

Bacterial cell death

Pharmacokinetics

- Absorptions - Rapidly absorbed from GIT (orally), affected in blood.
- Distribution - Widely distributed, crosses placenta and blood-brain barier.
- Metabolism - Minimal haptic metabolism, primarily excreted unchanged.
- Elimination - Primarily renal excretion via glomerular filtration and active secretion.
- Half-life - Short (30-60 minutes), prolonged in renal impairement.

Adverse Effects

- Allergy
- Nausea
- Vomitting
- Anemia
- Siezures
- Urticaria etc.

Therapeutic Uses

- Pneumonia
- Syphillis
- Meningitis
- Gonorrhea
- Infections
- Endocarditis etc.

CEPHALOSPORINS

- They are group of antibiotics derived from the mold Acremonium (cephalosporium).
- They are the part of β- Lactamase class of antibiotics.
- They work by inhibiting bacterial cell wall synthesis and distrupt bacterial cell integrity and leads to bacterial death.

CLASSIFICATION

① First Generation
- Oral - Cefuroxime , Cefoxitin
- Parenteral - Cefazolin

② Second Generation
- Oral - Cefactor , Ceforoximeaxetil , Cefprozil
- Parenteral - Cefuroxime , Cefoxitine

③ Third Generation
- Oral - Cefixime, Cefdinir, Ceftibuten, Ceftamet pivoxil, Cefpodoxime proxetil
- Parenteral - Cefotaximine, Ceftriaxone, Ceftizoxime, Ceftazidime, Cefoperazone

④ Fourth Generation
- Parenteral - Cefepime , Cefpirome

⑤ Fifth Generation
- Parenteral - Ceftaroline fosamil , Ceftobiprole medocaril

Mechanism Of Action

- They binds with PBPs and inhibit PBPs, which distrupts cell wall synthesis and due to this lysis of bacterial cell wall by osmotic pressure occurs and bacterial cell died.

Pharmacokinetics

- Absorption - Generally well - absorbed orally; food may reduce absorption.
- Distribution - Widely distributed; crosses blood - brain barrier (3rd and 4th gen).
- Metabolism - Minimal hepatic metabolism and primarily excreted unchanged.
- Elimination - Renal excretion (glomerular filtration and tubular secretions).
- Half - life - Range from 0.5 to 2 hours and extended in renal dysfunction.

Adverse Effects

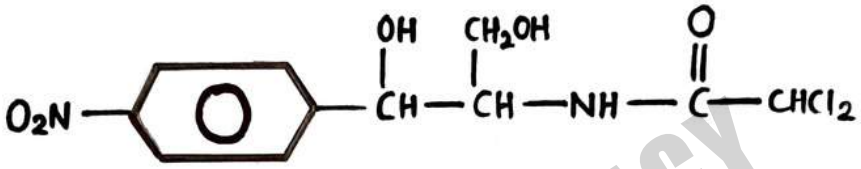
- Allergy
- Diarrhea
- Hepatotoxicity
- Nausea
- Headache
- Bleeding etc.

Therapeutic Uses

- Pneumonia
- Meningitis
- UTIs
- Sinusitis
- Gonorrhea
- Sepsis etc.

CHLORAMPHENICOL

- Chloramphenicol is broad spectrum antibiotic used to treat variety of bacterial infections.
- It was discovered in 1947 and was one of the first antibiotics to be produced synthetically.
- It is highly effective against a wide range of gram +ve and gram -ve bacteria.



MECHANISM OF ACTION

Chloramphenicol

↓

Binds reversibly to 50s ribosomal subunit

↓

Prevents the formation of peptide bond

↓

Inhibit Protien synthesis

↓

Bacterial Death

PHARMACOKINETICS

- Absorption - Well absorbed orally, rapidly absorbed IM.
- Distribution - Widely distributed and cross Placenta & Blood-brain barrier.
- Metabolism - Hepatic metabolism
- Excretion - Renal and hepatic excretion.
- Half-life - 1.5 hours - 4 hours.

ADVERSE EFFECTS

- Nausea
- Vomitting
- Headache
- Rash
- Hepatotoxicity
- Allergy etc.

THERAPEUTIC USES

- Meningitis
- Typhoid
- Plague
- Anemia
- H. pylori etc.

MACROLIDES

- They are the class of antibiotics that characterized by large macrocyclic lactom ring structure and obtained from streptomyces erythreus.
- They are primarily used to treat variety of infections and are effective against gram +ve and gram-ve bacteria.
- They are widely used to treating respiratory infections, skin infections, and sexually transmitted disease.
- Example - Erythromycin, Clarithromycin etc.

CLASSIFICATION

① First Generation - Erithromycin, Clarithromycin
② Second Generation - Azithromycin, Roxithromycin
③ Third Generation - Telithromycin (ketolide)

MECHANISM OF ACTION

Macrolides enters into bacterial cells
↓
Binding with 50_S ribosomes subunit of bacterial ribosome
↓
Inhibits of protien synthesis by translocation of peptides
↓
Reduce protien synthesis
↓
Bacteriostatic effect
(Inhibition of bacterial growth)

PHARMACOKINETICS

- Absorption - Well absorbed orally and food may reduce absorption.
- Distribution - Widely distributed and crosses placenta barrier.
- Metabolism - Hepatic metabolism.
- Excretion - Renal and biliary excretion.
- Half-time - 1-4 hours (erythromycin), 60 hours (azithromycin).

ADVERSE EFFECTS

- Diarrhoea
- Hepatotoxicity
- Allergy
- Hearing
- Superinfections etc.

THERAPEUTIC USES

- Pneumonia
- Bronchitis
- Gonorrhea
- Whooping
- H. pylori etc.

QUINOLONES

- They are class of synthetic quinolones antibiotics that are primarily used to treat bacterial infections.
- Quinolones works by inhibiting bacterial DNA replication and transcription, results cell death or inhibition of bacterial cell growth.
- They are known for their broad specturum activity against various bacterial infections, they are high potency and ability to peneterate tissues and fluids well, making them effective for treating infections in various parts of body.
- Example - Nalidixic Acid, Balofloxacin, Pazufloxacin etc.

CLASSIFICATION

① Nonfluoronated quindone – Nalidixic Acid

② Fluoroquinolones

First generation - Norfloxacin, Ciprofloxacin, Ofloxacin, Pefloxacin

Second generation - Levofloxacin, Moxifloxacin, Gemifloxacin, Prulifloxacin etc.

MECHANISM OF ACTION

- Quinolones enters into bacterial cell ⟶ They binds to and inhibits the bacterial enzymes DNA gyrase and topoisomerase IV ⟶ Distruption of DNA replication ⟶ This leads to bacterial death / bactericidal effect.

PHARMACOKINETICS

- Absorption - Well absorbed orally.
- Distribution - Widely distributed and crosses placenta and blood-brain barrier.
- Metabolism - Hepatic metabolism (primarily for ciprofloxacin, norfloxacin)
- Excretion - Renal and biliary excretion
- Half life - 3-12 hours.

ADVERSE EFFECTS

- Nausea
- Diarrhea
- Headache
- Dizziness
- Allergy etc.

THERAPEUTIC USES

- UTI
- Pneumonia
- Sinusitis
- Prostatitis
- Gastroenteritis etc.

FLUOROQUINOLONES

- They are class of synthetic antibiotics that are part of broad quinolones family.
- They are modified quinolones with fluorine atom at 6th position.
- They are effective against gram +ve, gram -ve and atypical bacteria.
- Example - Ciprofloxacin, Moxifloxacin etc.

CLASSIFICATION

① First Generation - Norfloxacin, Ciprofloxacin, Ofloxacin, Pefloxacin

② Second Generation - Levofloxacin, Moxifloxacin, Gemifloxacin, Poulifloxacin, Lomefloxacin, Sparfloxacin etc.

MECHANISM OF ACTION

- They inhibit DNA gyrase and topoisomerase IV, essential enzymes for bacterial DNA replication and leads to bacteriocidal effects / bacterial death.

PHARMACOKINETICS

- Absorption - Well absorbed orally.
- Distribution - Widely distributed, and crosses placenta & blood-brain barrier.
- Metabolism - Hepatic metabolism (mainly for moxifloxacin, levofloxacin).
- Excretion - Renal and biliary excretion.
- Half time - 4 - 12 hours.

Adverse Effects

- Photosensitivity
- Headache
- Dizziness
- Allergy
- Nausea
- Diarrhea etc.

Therapeutic Uses

- UTI
- Pneumonia
- Sinusitis
- Prostatitis
- Anthrax
- Sepsis etc.

TETRACYCLINES

- Tetracyclines are group of broad-spectarum antibiotics that are derived from streptomycin bacteria or synthetically produced.
- They are used to treat a variety of bacterial infections and are effective against a wide range of gram +ve, gram -ve & atypical bacteria.
- Example- Doxycycline, Oxytetracycline, Tetracycline etc.

CLASSIFICATION

- Tetracyclines
  - Oxytetracycline
  - Tetracycline
  - Demeclocycline
  - Doxycycline
  - Minocycline
- Glycyclines
  - Tigecycline

MECHANISM OF ACTION

Tetracyclines enters into bacterial cell

↓

Binds with 30s ribosomes subunit of bacterial ribosomes

↓

Prevents the attachment of aminoacyl-tRNA to the ribosomes

↓

Thereby inhibit protien synthesis

↓

Bacteriostatic effect

PHARMACOKINETICS

- Absorption- Well absorbed orally.
- Distribution- Widely distributed and crosses placenta & blood-brain barrier.
- Metabolism- Hepatic metabolism mostly for (doxycycline, tetracyclines)
- Excretion- Renal and fecal excretion.
- Half time- 6- 22 hours.

ADVERSE EFFECTS

- Nausea
- Vomitting
- Photosensitivity
- Hepatotoxicity
- Allergy
- Dizziness etc.

THERAPEUTIC USES

- Acne
- Pneumonia
- Malaria
- Sinusitis
- Prostatitis etc.

AMINOGLYCOSIDES

- Aminoglycosides are group of antibiotics derived from bacteria such as streptomyces & micromonospara.
- They are primarily used to treat serious bacterial infections, especially gram -ve bacteria.
- They are bactericidal, kill the bacteria not inhibiting bacterial growth.
- They work by interfering with protein synthesis in bacteria.

CLASSIFICATION

Systemic		Topical
Gentamycin	Streptomycin	Neomycin
Tobramycin	kanamycin	Framycin
Sisomycin	Amikacin	
Netilmicin	Paromycin	

MECHANISM OF ACTION

They binds with 30s ribosomes subunit of the bacterial ribosomes

↓

Causes misleading of mRNA & leading to the production of abnormal protiens

↓

Inhibition of protien synthesis

↓

Bactericidal effect / Bacterial cell death

PHARMACOKINETICS

- Absorption - Poorly absorbed orally, given parenterally.
- Distribution - Widely distributed and Poor CNS peneteration, crosses placenta.
- Metabolism - Minimal hepatic metabolism, primarily excreted unchanged.
- Excretion - Renal excretion (glomerular filtration).
- Half time - 2-3 hours.

ADVERSE EFFECTS

- Nephrotoxicity
- Neurotoxicity
- Allergy
- Nausea
- Rash
- Dizziness
- Headache etc.

THERAPEUTIC USES

- Pneumonia
- Meningitis
- Osteomyelitis
- Endocarditis
- Typhoid
- Plague etc.

THANK YOU

FOR CHOOSING IMPERFECT PHARMACY AS YOUR STUDY PARTNER

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