

* Antimicrobial Drugs main modes of Action:

1] Inhibitors of cell wall synthesis:

a) Penicillins:

β -aminopenicillanic acid. + Differ in the Side chain Attached to the aminogroup.

* The main active ingredient and the Bioactive material $\Rightarrow \beta$ -lactam Ring.

+ Penicillin Resistant Bacteria Produce an enzyme called β -lactamase $\rightarrow$ Hydrolyse the Bond in the Ring of β -lactam.

$\rightarrow$ What is the mode of Action for penicillin?

$\rightarrow$ Blocking the enzyme that catalyzes Transpeptidation $\rightarrow$ (Peptide Bonds in the cell wall) $\Rightarrow$ No Peptide Bonds will be formed.

$\rightarrow$ Prevent the complete synthesis of cell wall.

$\rightarrow$ Binds to Penicillin-Binding Proteins.

* Naturally occurring penicillin $\rightarrow$ Produced by microorganisms.

* Penicillin G + V $\rightarrow$ Gram Positive Resistance $\rightarrow$ Narrow spectrum

* Semisynthetic penicillins $\rightarrow$ Broad spectrum + it has **Polka Side** $\rightarrow$ makes it more difficult to β -lactamase to destroy it.

* Aminopenicillin (Ampicillin) $\rightarrow$ Gram Neg Resistance.

b) Cephalosporins: Has the Same structure and function of Penicillin.

$\rightarrow$ used for Patients that are allergic to Penicillin. + for species that are Resistant to Peni

c) Vancomycin: MRSA - Meticillin Resistant **S. Aureus** $\rightarrow$ Resistance to most of Antibiotics. + used orally + last Drug choice.

glycopeptide antibiotic + Important for the treatment of antibiotic Resistant *Staphylococcus* + *enterococci*.

2] Protein Synthesis Inhibitors: the main thing for protein is the Ribosome, so this type of antibiotics interferes with the Ribosomal function and units.

$\rightarrow$ Bind specifically to the Bacterial Ribosome and target different steps: i) Translocation ii) Peptide Bond Formation iii) mRNA Reading iv) Aminoacyl-tRNA Binding

a) Aminoglycosides: $\rightarrow$ Cyclohexene Ring + aminogroups.

$\rightarrow$ Bind to 30s Ribosomal subunit + interferes with Protein Synthesis by directly inhibiting the Process. $\rightarrow$ Misreading of the mRNA.

b) Tetracyclines: 4 Rings and it may have side chains.

Broad spectrum + Bacteriostatic (inhibition) + target 30s Ribosomal unit.

c) Macrolides: 12 - 22 Carbon lactone linked to one or more Sugars (Erythromycin)

Broad Spectrum + Bacteriostatic + 50s Ribosomal unit (inhibit Protein elongation) + for Patients that are allergic to Penicillin

d) Chloramphenicol: Chemically synthesised + 50s Ribosomal subunit

Inhibition of Bacterial Protein synthesis + **Serious**

3] Metabolic Antagonistic $\rightarrow$ Produce metabolite that are structurally the same in eukaryotes.

$\rightarrow$ Acts As Antimetabolite, Antagonize / Block the function of metabolic pathway (inhibit the use of metabolites).

a) Sulfonamids OR Sulfonamides: looks similar to compounds used for the synthesis of folic acid. + Para-aminobenzoic acid Analogue.

PARA $\rightarrow$ used for synthesis of folic acid + made by many pathogens

* Selectively toxic $\rightarrow$ Competitive inhibition of folic acid synthesis enzymes.

b) Trimethoprim: interferes with folic acid production. + Broad

can be combined to Sulfonamides $\rightarrow$ increase efficacy of treatment. (the combination blocks 2 pathways for the production of folic acid)

4] Nucleic acid synthesis Inhibition: + Inhibit DNA Polymerase + topoisomerase. + RNA Polymerase. (Not as effective as others).

a) Fluoroquinolones: Effect DNA synthesis (unwinding of DNA strand)

Contains the 4 quinolone + Inhibit Bacterial DNA Gyrase + topoisomerase.

$\rightarrow$ Broad spectrum - Ciprofloxacin.

Because Bacteria + eukarya do not differ greatly in the way of synthesizing nucleic acids.

* Antiviral Drugs:

- Once viruses enter a host cell they start replicating and making their own structures, so these Antiviral Drugs are challenging because viruses are obligating organisms.
- So the antiviral drugs only limit the duration of illness. (Inhibit viruses specific enzymes + life cycle process).
- * they are not preferred because they also affect the host cell.

1] Antiviral Drugs for Influenza:

- a) **Oseltamivir** Anti-influenza agent / neuraminidase inhibitor - Shorten course of illness.
- b) **Acyclovir + Vidarabine**: Herpes infection + shingles.
- c) **Ganciclovir**: treat systemic cytomegalovirus illness.
- d) **Foscarnet**: for the resistance of acyclovir + ganciclovir. → **DNA Genome**.
↳ Herpes + cytomegaloviruses.

* Broad Spectrum Antiviral Drugs:

- **Cidofovir**: (inhibits viral DNA Polymerase)

* Anti HIV Drugs:

1) Nucleoside Reverse transcriptase inhibitors:

Interfere with critical steps in the replication process.

2) Protease inhibitors (PIs):

Block activity of HIV Protease for producing the viral proteins.

3) Nucleoside Reverse transcriptase inhibitors:

Prevent HIV DNA synthesis → by binding to and inhibiting the viral Reverse Transcriptase enzyme.

4) Integrase inhibitors:

Prevent incorporation of HIV Genome to the host's cell genome

5) Fusion inhibitors:

Prevent the entry of HIV into the host cell.

* **Antifungal Drugs**: least effective because the similarity of the eukaryot + fungal cells.
Used on outside + we may use combination of drugs.

Treating Mycoses:

1) Superficial Mycoses (External)

Candida (oral + intestinal tract).

- topical + oral.

Disrupt permeability + inhibit cell synthesis → Disrupts mitotic spindle + may inhibit Protein-DNA system

2) Systemic Mycoses (Internal)

Difficult to be controlled

a) **Amphotericin B**: bind to sterol membrane

b) **5-Fluorouracil**: RNA function disruptor.

c) **Itraconazole**: low side effects

* Drug Resistance by Microbs types:

1] Intrinsic:

Mycoplasma lack the cell wall. So it's Resistance to the β -lactam antibiotic.

2] Acquired:

When there is change in the Genome that Converts it from one that is sensitive to one that is Resistant.

3] Drug Tolerant Bacteria:

Ignore the Presence of Antibiotic $\rightarrow$ embedded in Biofilm so cannot Penetrate the organisms.

* What are the mechanisms for Drugs Resistance:

- Modify the target of antibiotic
- inactivation
- Minimizing Con.
- Increase Production of metabolites.

* How the Resistance is detected

- 1) color change $\rightarrow$ when β -lactam is acts upon chromopore
- 2) PCR.

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