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**Mechanism of antibiotics according to different target Classification one by one:**

Antibiotics are used in medicine and agriculture against bacterial infections and bacterial growth in food. There are several classes of antibiotic, and this article explains the bacteriocidal or bacteriostatic activity of each.

Inhibition of Cell Wall Synthesis (most common mechanism)

Inhibition of Protein Synthesis (Translation) (second largest class)

Alteration of Cell Membranes

Inhibition of Nucleic Acid Synthesis

Antimetabolite Activity

 **Inhibition of Cell Synthesis**

Beta-Lactams ---> Inhibition of peptidoglycan synthesis (bactericidal)

Resistance --->

(1) fails to cross membrane (gram negatives)

(2) fails to bind to altered PBP�s

(3) hydrolysis by beta-lactamases

Vancomycin ---> Disrupts peptidoglycan cross-linkage

Resistance --->

(1) fails to cross gram negative outer membrane (too large)

(2) some intrinsically resistant (pentapeptide terminus)

Bacitracin ---> Disrupts movement of peptidoglycan precursors (topical use)

Resistance ---> fails to penetrate into cell

Antimycobacterial agents ---> Disrupt mycolic acid or arabinoglycan synthesis (bactericidal)

Resistance --->

(1) reduced uptake

(2) alteration of target sites

 **Inhibition of Protein Synthesis**

 30S Ribosome site

Aminoglycosides ---> Irreversibly bind 30S ribosomal proteins (bactericidal)

Resistance --->

(1) mutation of ribosomal binding site

(2) decreased uptake

(3) enzymatic modification of antibiotic

Tetracyclines ---> Block tRNA binding to 30S ribosome-mRNA complex (b-static)

Resistance --->

(1) decreased penetration

(2) active efflux of antibiotic out of cell

(3) protection of 30S ribosome

 50S Ribosome site

Chloramphenicol ---> Binds peptidyl transferase component of 50S ribosome, blocking peptide elongation (bacteriostatic)

Resistance --->

(1) plasmid-encoded chloramphenicol transferase

(2) altered outer membrane (chromosomal mutations)

Macrolides ---> Reversibly bind 50S ribosome, block peptide elongation (b-static)

Resistance --->

(1) methylation of 23S ribosomal RNA subunit

(2) enzymatic cleavage (erythromycin esterase)

(3) active efflux

Clindamycin ---> Binds 50S ribosome, blocks peptide elongation; Inhibits peptidyl transferase by interfering with binding of amino acid-acyl-tRNA complex

Resistance ---> methylation of 23S ribosomal RNA subunit

 **Alternation of Cell membrane:**

Polymyxins (topical) ---> Cationic detergent-like activity (topical use)

Resistance ---> inability to penetrate outer membrane

Bacitracin (topical) ---> Disrupt cytoplasmic membranes

Resistance ---> inability to penetrate outer membrane

 **Inhibition of Nucleic acid synthesis**

 DNA Effects

Quinolones ---> Inhibit DNA gyrases or topoisomerases required for supercoiling of DNA; bind to alpha subunit

Resistance --->

(1) alteration of alpha subunit of DNA gyrase (chromosomal)

(2) decreased uptake by alteration of porins (chromosomal)

Metronidazole ---> Metabolic cytotoxic byproducts disrupt DNA

Resistance --->

(1) decreased uptake

(2) elimination of toxic compounds before they interact

 RNA Effects (Transcription)

Rifampin ---> Binds to DNA-dependent RNA polymerase inhibiting initiation & Rifabutin of RNA synthesis

Resistance --->

(1) altered of beta subunit of RNA polymerase (chromosomal)

(2) intrinsic resistance in gram negatives (decreased uptake)

Bacitracin (topical) ---> Inhibits RNA transcription

Resistance ---> inability to penetrate outer membrane

 **Antimetabolite Activity:**

Sulfonamides & Dapsone ---> Compete with p-aminobenzoic acid (PABA) preventing synthesis of folic acid

Resistance ---> permeability barriers (e.g., Pseudomonas)

Trimethoprim ---> Inhibit dihydrofolate reductase preventing synthesis of folic acid

Resistance --->

(1) decreased affinity of dihydrofolate reductase

(2) intrinsic resistance if use exogenous thymidine

Trimethoprim-Sulfamethoxazole synergism.

**TYPES OF Antibiotics**

**1)Penicillin:**

Penicillin was the first antibiotic to be discovered. Ernest Fleming discovered penicillin in 1928 when he accidentally left bacterial cultures uncovered near an open window.

This lead to the contamination of the cultures with mold spores, which produced a compound that killed the bacteria. This compound was later named penicillin by Fleming. Penicillin is part of a class of antibiotics called β-lactams. These antibiotics are characterized by a beta-lactam ring in the molecule’s center, and function by interfering with the synthesis of the bacterial cell wall.

β-lactams stop peptide chains from cross-linking during the formation of a new peptidoglycan chain which is a major component of the bacterial cell wall. Thus a bacterium cannot keep its structural integrity and will burst (lyse).

The structure of the β-lactam is similar to the subunits that make up peptidoglycan. It therefore acts as a competitive inhibitor to transpeptidase, an enzyme involved in the cross-linking of peptides, also called penicillin-binding protein.

**2)Cephalosporins:**

Cephalosporins also belong to the β-lactam group. They are very similar to penicillin but contain a different structure, which provides increased resistance to inactivation by an enzyme which can be produced by certain bacteria called beta-lactamase.

Cephalosporins antibiotic can, therefore, be used when penicillin is ineffective. β-lactams have R groups modify the antibiotic to give a different spectrum of activity. Cephalosporins have two R groups compared to one group in penicillin, creating more opportunities for chemical modification.

**3)Aminoglycosides:**

Aminoglycosides are bacteriostatic; they slow down the growth and reproduction of bacteria without killing them. These antibiotics inhibit the synthesis of proteins by binding to the 30S bacterial ribosome subunit. When these subunits bind together, they produce the proteins needed by the cell.

Ribosomes in animal cells are 80S, made of subunits of 40S and 60S, while bacterial ribosomes are 70S, so specific modification in bacterial ribosome can be achieved.

Aminoglycosides prevent effective proof-reading of the proteins produced by bacteria. They cause incorrect amino acids to be inserted into the peptide chain, creating misfolded and faulty proteins. their function. Many of these are structural proteins, so defect stops the bacterium repairing holes in the cell wall, undergoing cell growth or reproducing.

**4)Tetracyclines:**

Tetracyclines inhibit synthesis of proteins by binding to the 30S ribosome subunit but have a different method of action to aminoglycosides. Instead of preventing proof-reading of the peptide produced, they stop the binding of tRNA to the ribosome, stopping protein synthesis.

Preventing the binding of tRNA to the bacterial ribosome effectively prevents proteins being produced by the bacteria, leading to its death.

**5)Macrolides:**

Macrolides have a similar function to aminoglycosides and tetracyclines in that they inhibit the synthesis of proteins by binding to the bacterial ribosome, but they bind to the 50S subunit. Macrolides stop the formation of peptide bonds between amino acids, preventing protein synthesis.

**6)Fluroquinolones:**

Fluoroquinolones inhibit the activity of DNA gyrase, a type of topoisomerase found in prokaryotes, which prevents a harmful DNA modification called supercoiling.

Supercoiling occurs when DNA strands are wound together too tightly or not tightly enough. Undoing this supercoiling is essential for a bacteria’s ability to replicate, so DNA gyrase is a useful target for antibiotics. Human cells do not contain DNA gyrase and have a different type of topoisomerase instead.

**The End.**