Antibacterial Mode of Action

Microbiology Presentation

Members:
Blaismaidi Langthasa
Baishali Nath
Nikumani Choudhury
Jugasmita Goswami
Hannah Narjary

INTRODUCTION

ANTIBIOTICS

- **They are substances that either inhibit the growth or kill bacteria**
- **Used to treat bacterial infections in human ,animals and plants.**

Antibacterial agents work through various mechanisms such as -

- **Inhibitors of nucleic acid synthesis**
- **Inhibitors of cell wall synthesis**
- **Inhibitors of cell membrane function**
- **Inhibitors of protein synthesis**
- **Inhibitors of metabolism**

Examples of Antibacterial agents includes antibiotics ,antiseptics, disinfectants and Sanitizers.

INHIBITION OF CELL WALL BIOSYNTHESIS

- In bacteria, the cell wall is a rigid structure composed of peptidoglycan, which provides structural integrity and protection against osmotic lysis. The synthesis of peptidoglycan involves several enzymes, including transpeptidases (also known as penicillin-binding proteins, or PBPs).

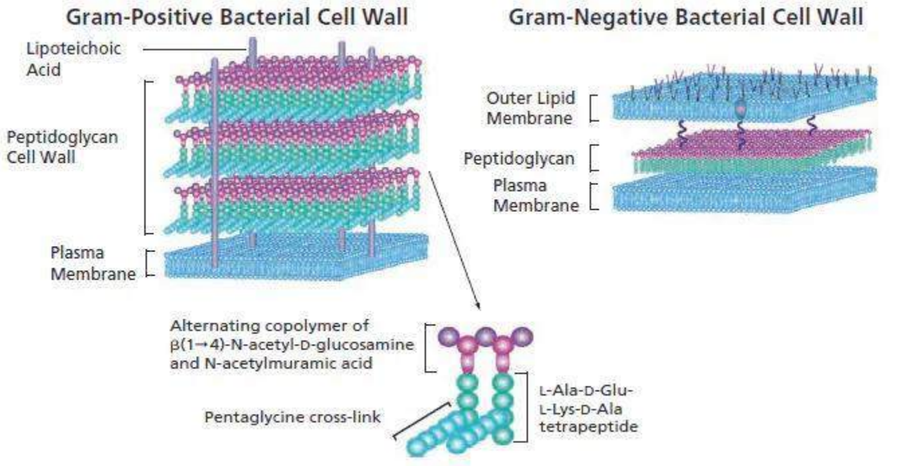
- Cell wall synthesis inhibitors work by interfering with the transpeptidase enzymes responsible for cross-linking the peptide chains in the peptidoglycan layer. This disruption of cross-linking prevents the formation of a complete, rigid cell wall, leading to a weakened and fragile cell wall structure.

- When the cell wall is weakened, the bacterium becomes susceptible to osmotic lysis.

INHIBITION OF CELL WALL BIOSYNTHESIS

Cell wall synthesis inhibitors encompass various classes of antibiotics targeting bacterial survival by disrupting peptidoglycan construction. The main types include:

- **β-lactam :** antibiotics such as penicillins and cephalosporins, which block peptidoglycan layer formation by inactivating penicillin-binding proteins.
- **Glycopeptides:** like vancomycin, which disrupt assembly of peptidoglycan precursors, crucial for cell wall integrity.
- **Miscellaneous inhibitors:** including fosfomycin and cycloserine, which interfere with different stages of peptidoglycan synthesis, contributing to bacterial lysis.



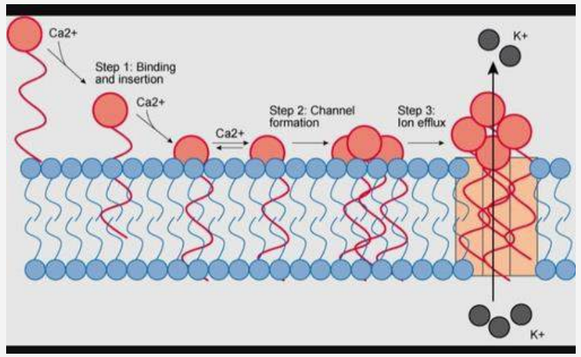
INHIBITION OF CELL MEMBRANE FUNCTION

- A disruption or damage to cell membrane could result in leakage of important solutes essential for the cells survival
- The action of this class of antibiotics are often poorly selective and can often be toxic for systemic use in the mammalian host
  Examples- Daptomycin, Polymyxin

POLYMYXIN

- Used to target gram negative cells
- Binds to lipopolysaccharides within outer membrane
- Once bound ,it disrupts its structure and permeability properties
- Disruption leads to leakage of intracellular contents, eventually leading to cell death

INHIBITION OF CELL MEMBRANE FUNCTION



DAPTOMYCIN

- **Used to target gram positive bacteria**
- **Binds with calcium ion to form a calcium complex**
- **Complexes aggregate within plasma membrane to form pore like structures ,eventually leading to cell death**

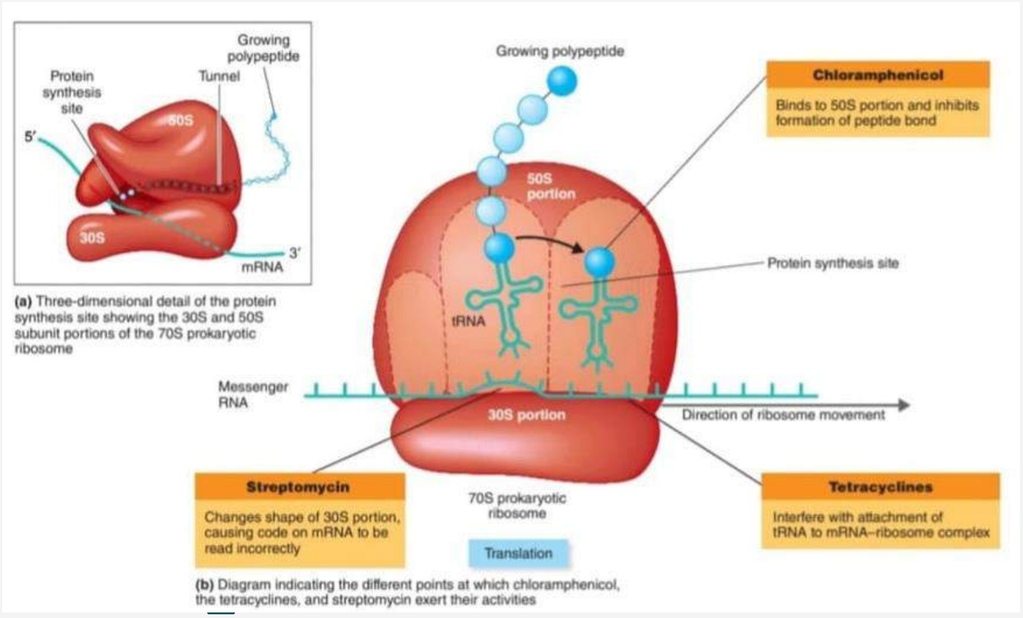
INHIBITION OF PROTEIN SYNTHESIS

* Protein synthesis inhibitors are the substances that stops or slow the process of translation (Protein synthesis)
* These inhibitors usually act at the ribosomal level.
* Ribosomes are the site of protein synthesis in prokaryotes and eukaryotes.
* These inhibitors work at different stages of translation such as initiation, elongation and termination.

INHIBITION OF PROTEIN SYNTHESIS

Name of some protein synthesis inhibitors that target the ribosomes:

* Tetracycline
* Streptomycin
* Chloramphenicol
* Erythromycin
* Rifamycin
* Actinomycin D

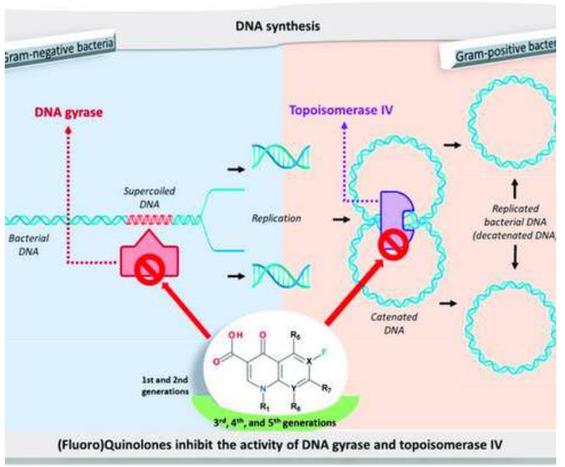


INHIBITION OF NUCLEIC ACID SYNTHESIS

••The antibacterial drugs inhibit nucleic acid synthesis function by inhibiting-

A) DNA replication inhibition

B) RNA transcription inhibition



(Fluoro)Quinolones inhibit the activity of DNA gyrase and topoisomerase IV

••DNA REPLICATION INHIBITION:

Quinolones

1) Quinolones act by inhibiting the bacterial DNA gyrase and topoisomerase IV.

2) DNA gyrase introduces negative twist in DNA and helps separate its strands and topoisomerase IV facilitate separation of linked daughter DNA molecule after replication is completed.

3) lnhibition of DNA gyrase amd topoisomerase IV disrupts DNA replication and repair, bacterial chromosome separation during division, and other processes involving DNA.

••EXAMPLE:

Majority of quinolones in clinical use are so called fluoroquinolones. Examples of fluoroquinolones includes-

Ciprofloxacin, levofloxacin, Moxifloxacin, Norfloxacin, ofloxacin

••SIDE EFFECTS:

Nausea, vomiting, diarrhoea, headache, insomnia etc

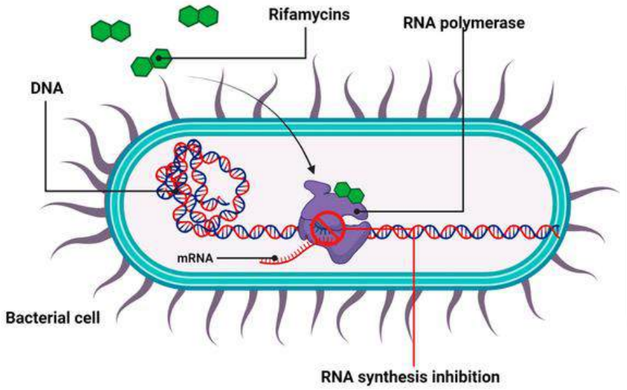
INHIBITION OF NUCLEIC ACID SYNTHESIS

••RNA TRANSCRIPTION INHIBITION

Rifamycin

1) Antibiotics such as rifampin bind to bacterial RNA polymerase, the enzyme responsible for transcribing DNA into RNA.

2) Bybinding to RNA polymerase, rifampin inhibits RNA synthesis, thereby preventing the production of essential RNA molecules needed for bacterial protein synthesis and other cellular functions.



••USES

Most important use of rifampin is against mycobacteria in the treatment of tuberculosis and leprosy.

••EXAMPLE:

Rifampin, Rifabulin, Rifapentine .

••SIDE EFFECT

1) Hepatotoxicity

2) Discoloration of body fluid including saliva, urine and tears from red to orange.

INTERFERENCE WITH METABOLIC PATHWAYS

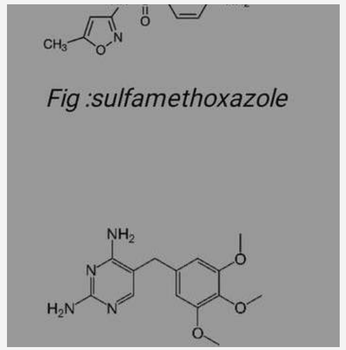
•Some antibiotics, such as sulfonamides and trimethoprim, target metabolic pathways essential metabolic growth.
•They inhibit enzymes involved in the synthesis of essential metabolites like folic acid (also known as folate synthesis) which bacteria need for DNA and RNA synthesis.
•Folate Synthesis involves a series of enzymatic reactions that ultimately produce tetrahydrofolate (THF), the biologically the active form of folate .

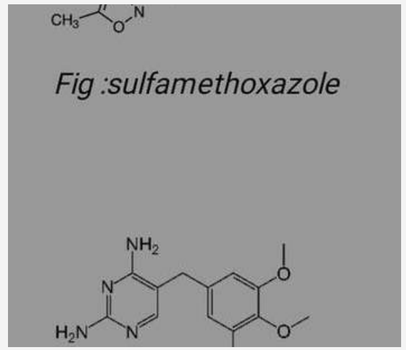
INTERFERENCE WITH METABOLIC PATHWAYS

•Lets us see how Sulfonamides and Trimethoprim cause interference with metabolic pathways:

1)Sulfonamides : Sulfonamide: Sulfonamide such as sulfamethoxazole competitively inhibit the enzyme dihydropteroate synthase, which catalyzes the conversion of PABA to dihydropteroate, a key step in folate synthesis, this prevents the synthesis of dihydropteroate and subsequently inhibiting folate production.

2)Trimethoprim: Trimethoprim inhibits the enzyme dihydrofolate reductase (DHFR), which catalyzes the conversion of dihydrofolate (DHF) to tetrahydrofolate (THF). By inhibiting DHFG, trimethoprim blocks the production of the THF, leading to a depletion of the folate pool in bacterial cells and inhibiting nucleotide synthesis.





THANK YOU.