STUDENT NAME	
CLASS	SUBJECT
ROLL NO.	DATE

Five modes of action with one example each

1) Inhibitor of cell membrane function

- Lipopeptides (Polypeptides)
  → Polymyxins
    - Polymyxin B
    - Colistin (colistimethate sulfate)
- Cyclic lipopeptides
  → Daptomycin

Polymixins

- Polymyxins are Bactericidal
- Polymixins classified as Polymixin A, B, C, D & E
- Polymixin B & E can be used therapeutically.
- Polymixin B - derived from Bacillus polymyxa var. aerosporus.
- Polymixin E - derived from Bacillus polymyxa var. colistinus (colistin)
- Colistin exists as 2 forms
  → Colistin Sulfate
  → Colistimethate Sodium

Polymyxin Mode of Action

- Polymyxins are positively charged molecules (cationic) which are attracted to the negatively charged bacteria.
- The antibiotic binds to the cell membrane (LPS (lipopolysaccaride) & Phospholipids).

alters its structure and makes it more permeable.

- This disrupts osmotic balance causing leakage of cellular molecules, inhibition of respiration & increased water uptake leading to cell death
- Gram-positives are naturally resistant

Cyclic Lipopeptides
Daptomycin (Cubicin)

- Bactericidal
- Got FDA approval on September 12, 2003
- Resistance rate appears to be low
- Active against
  - → Skin & Skin structure infections
  - → Beta-hemolytic Streptococci

Daptomycin's Mechanism of Action

- Irreversibly binds to cell membrane of Gram+ bacteria
  - → Calcium-dependent membrane insertion of molecule
  - → Rapidly depolarizes the cell membrane
    - Efflux of potassium
    - Destroys ion-concentration gradient
- Ultimately leading to loss of membrane potential & cell death

NJS

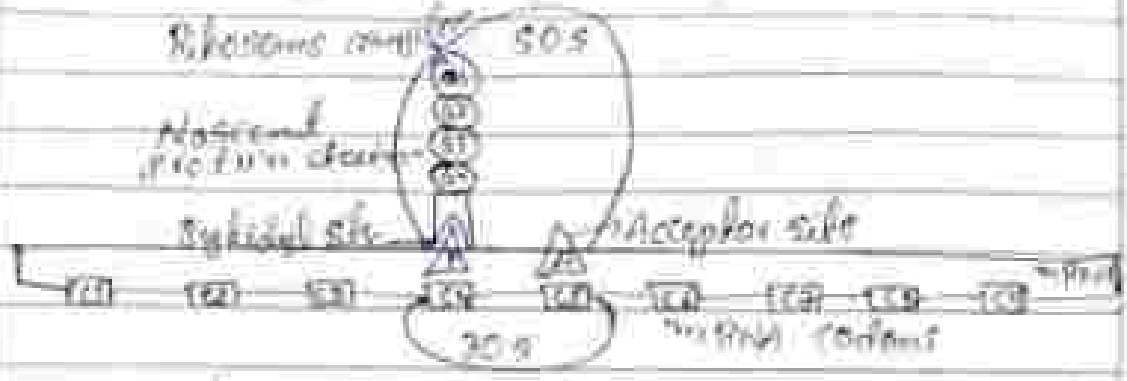
STUDENT'S NAME

CLASS	SUBJECT
ROLL NO	DATE

Protein Synthesis Inhibitors

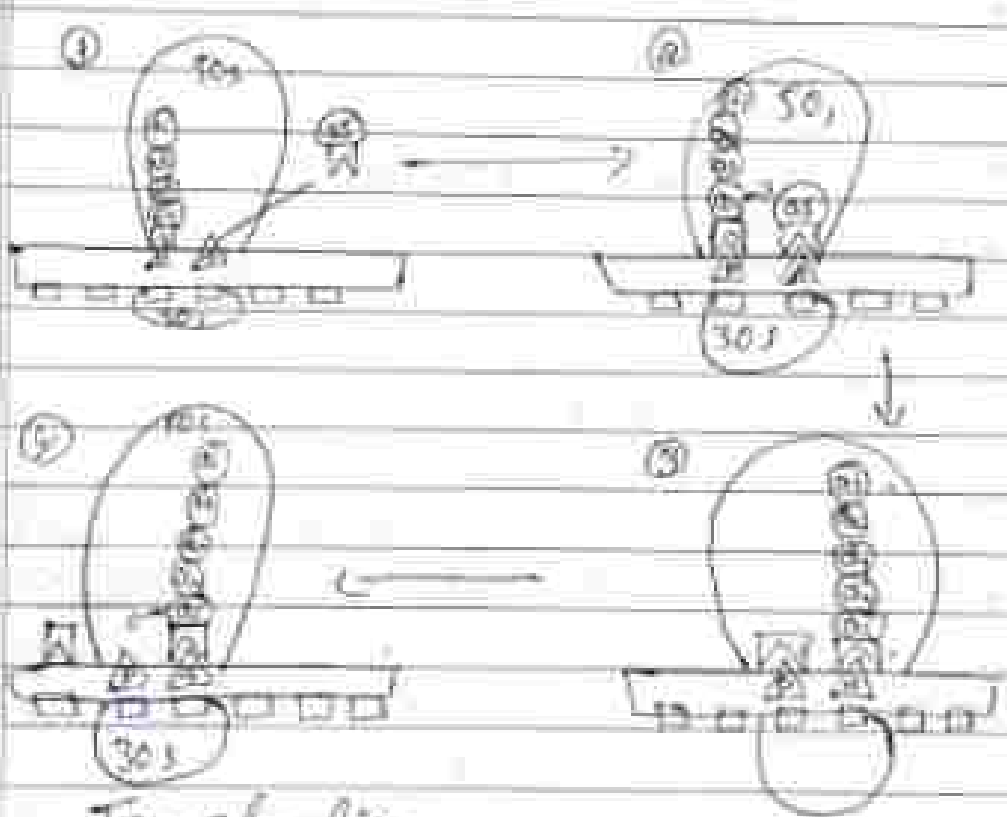
1) Aminoglycosides
2) Tetracyclines
3) Macrolides

Protein Synthesis mechanism



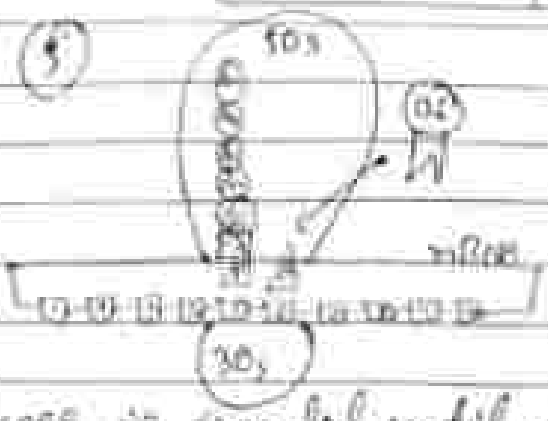
mRNA binding and protein being formed.

chain elongation



Translocation

↓



This process is repeated until ribosome encounters stop codon. Stop codon is a sign codon that signals the end of protein synthesis

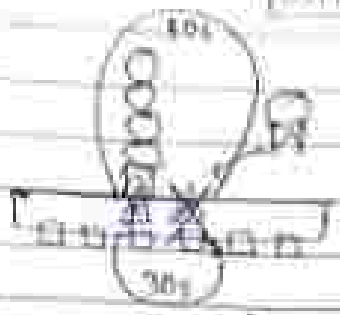
-2 Protein synthesis inhibitors act at a specific site on the ribosome to inhibit different steps in the protein synthesis

-3 Protein synthesis inhibitors can be divided into 2 groups
- 30S Subunit inhibitors
- 50S Subunit inhibitors

1) 30S subunit inhibitors
- Aminoglycosides
- Tetracyclines

* Aminoglycosides

Aminoglycosides work primarily by binding to an area adjacent to the decoding site on the 30S subunit of the ribosome where they interfere with the initiation of protein synthesis & cause misreading of the genetic code. This ultimately leads to either synthesis of nonfunctional proteins or premature termination of protein synthesis



Aminoglycosides binds 30s Subunit ribosome

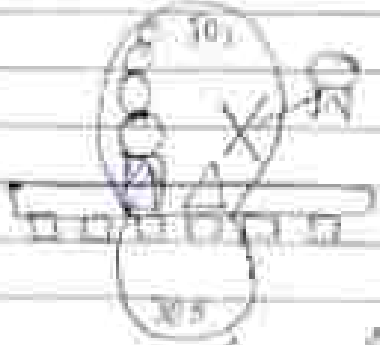
example of drugs

Neomycin, Amikacin, Gentamicin

Side effects are of Aminoglycosides ototoxicity, nephrotoxicity & neuromuscular blockage

* Tetracyclines

Tetracyclines also bind to the 30s ribosomal subunit however their primary mode of action is by blocking entry of aminoacyl tRNA molecules into the A site of the ribosome thus preventing introduction of new amino acids to the growing peptide chain this action is usually inhibitory & reversible upon withdrawal of the drug.



Blocking the entry of t RNA

STUDENT'S NAME	
CLASS	SUBJECT
ROLL NO	DATE

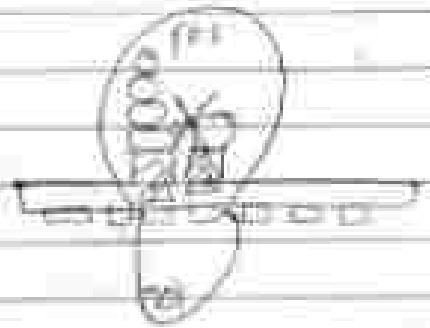
examples
• Doxycycline, Minocycline

Side effects
• GI disturbances photosensitivity, hepatotoxicity
• discoloration of teeth, inhibition of bone growth

B) 30 s Subunit inhibitors

Macrolides

This binds to 50s ribosomal subunit near the peptidyl transferase center where they the peptide exit tunnel that the newly assembled polypeptides pass through on their way out of the ribosome this results in inhibition of protein elongation process & thus bacterio static activity against most organism.



Inhibition of protein elongation

examples :- Azithromycin, Clarithromycin & Erythromycin

Side effects :- nausea, vomiting & diarrhea

N/S

Inhibitors of Nucleic acid synthesis

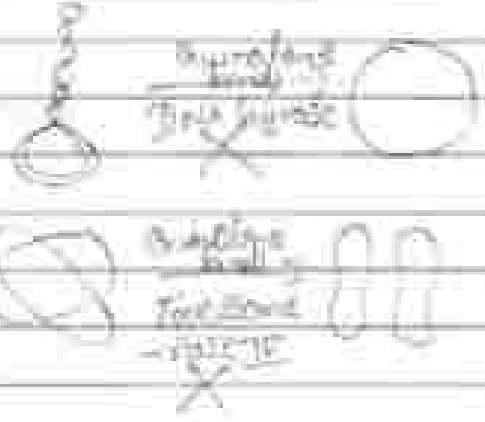
The various classes of nucleic acids are
1) DNA (Deoxyribonucleic acid)
2) RNA (Ribonucleic acid)

Bacteria like all other living organisms store their genetic information in the form of DNA the cell uses this like an instruction manual making it to find out what parts it needs to make further & replicate it before it can carry out their life processes bacteria must convert their genetic information into functional molecules this is done by using DNA as a template for the synthesis of RNA molecule a process known as transcription. Depending on the structure RNA can then perform their diverse or act as a blueprint for the synthesis of functional proteins in a process known as translation

The antimicrobial agents that primarily target nucleic acid synthesis include
→ Quinolones
→ Rifamycins

1. Quinolones

It involves interactions with topoisomerase type which are the enzymes responsible for the uncoiling & unlinking of DNA so in order for the bacterial cells to replicate highly coiled bacterial chromosome must unwound so that the DNA code can be accessed and copied like a principle topoisomerases that present this task are DNA gyrase which responds & relaxes supercoiled DNA & topoisomerase IV which facilitates separation of the linked daughter DNA molecules after replication so both both DNA gyrase & topoisomerase IV are the primary target of quinolone which bind to these enzymes and effectively inhibit their function thus in turn blocks DNA synthesis & cell growth ultimately leading to bacterial cell death.

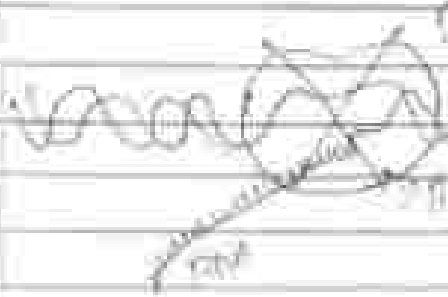


Majority of quinolones in clinical use are so called fluoroquinolones
ex:- Ciprofloxacin, levofloxacin & ofloxacin

NAME	
CLASS	SUBJECT
ROLL NO.	DATE

① Rifamycins

Rifamycins interfere with transcription of bacterial DNA into RNA. Specifically Rifamycins target enzyme responsible for translating DNA into RNA called DNA polymerase by combining with α-subunit of the bacterial DNA-dependent RNA polymerase Rifamycins bring all synthesis of RNA to a halt without RNA the bacteria cannot make proteins that are essential for survival so the cell dies eventually results



ex:- Rifampin, Rifabutin & Rifapentine

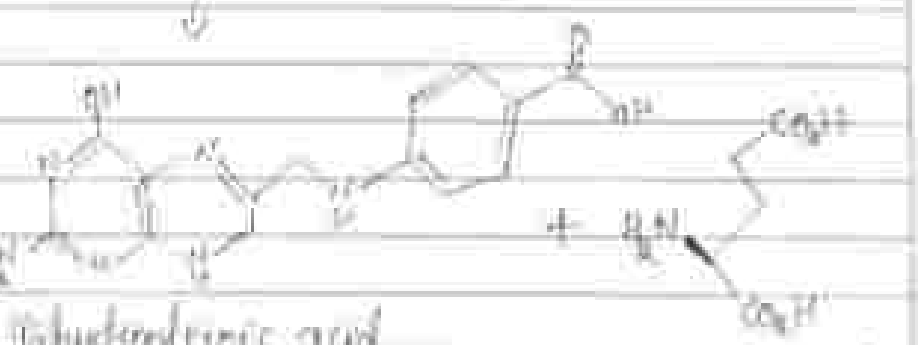
Metabolic Pathway inhibitors

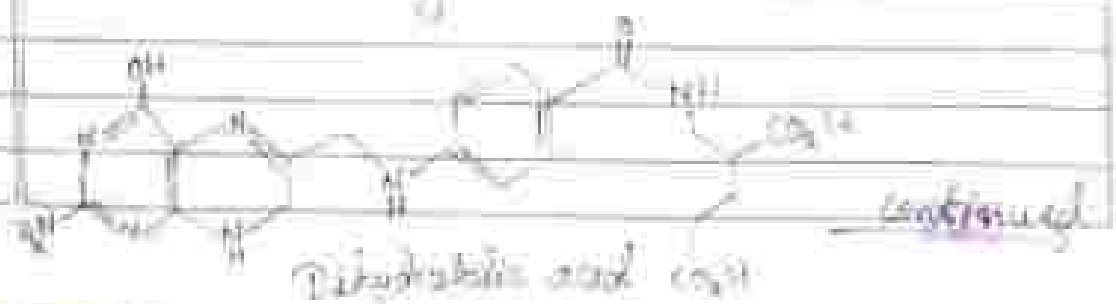
The primary target of metabolic pathway inhibitors is the pathway that bacteria use to synthesize folic acid.

folic acid is an important vitamin that bacteria as well as humans need in order to make nucleotides and some amino acids so as you can imagine without folic acid DNA replication & cellular growth would be disrupted new

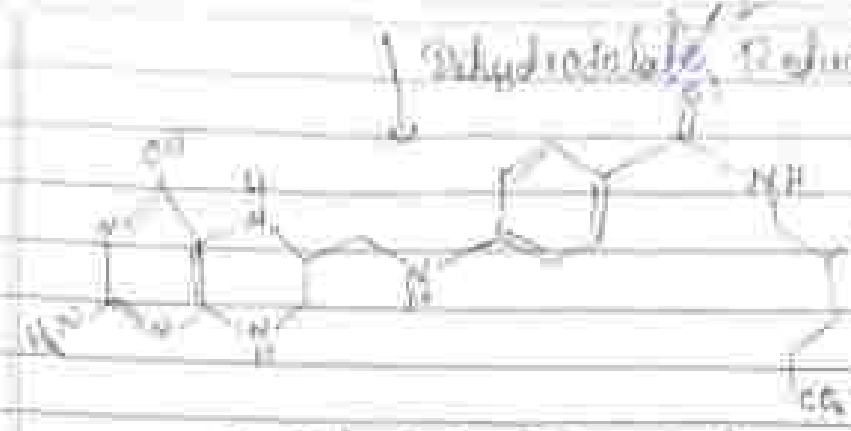
unlike us humans who obtain folic acid from the diet bacteria must make folic acid on their own.

Bacteria synthesize folic acid by taking para-aminobenzoic acid (PABA) & adding a compound called pteridine in the presence of enzyme dihydropteroate synthase to form dihydropteric acid then they add glutamate to make dihydrofolic acid & use an enzyme called dihydrofolate reductase to make tetrahydrofolic acid. tetrahydrofolic acid is the metabolically active form of folic acid which acts as a coenzyme for a number of key biochemical reactions.





Trimethoprim



Tetrahydrofolic Acid

Host metabolic pathway inhibitors work by interfering with bacterial synthesis of tetrahydrofolic acid thus include family of drugs called
1) Sulfonamides or Sulfa drugs
2) Trimethoprim

1) Sulfonamides

They acts through competitive inhibition of dihydropteroate synthase, this is due to their structural resemblance to para-aminobenzoic acid, the enzyme that normally converts PABA to the precursor of folic acid combines with the sulfonamide instead the dihydrofolic prevents Tetrahydrofolic acid synthesis & thereby stops the growth of the bacteria
ex- Sulfamethoxazole & Sulfacetamide

2) Trimethoprim

It targets the second key enzyme in the folic acid synthesis pathway that is dihydrofolate reductase as our

analog of dihydrofolic acid. Terconil potent competitively inhibits the enzyme thus effectively disrupting production of tetrahydrofolic acid.

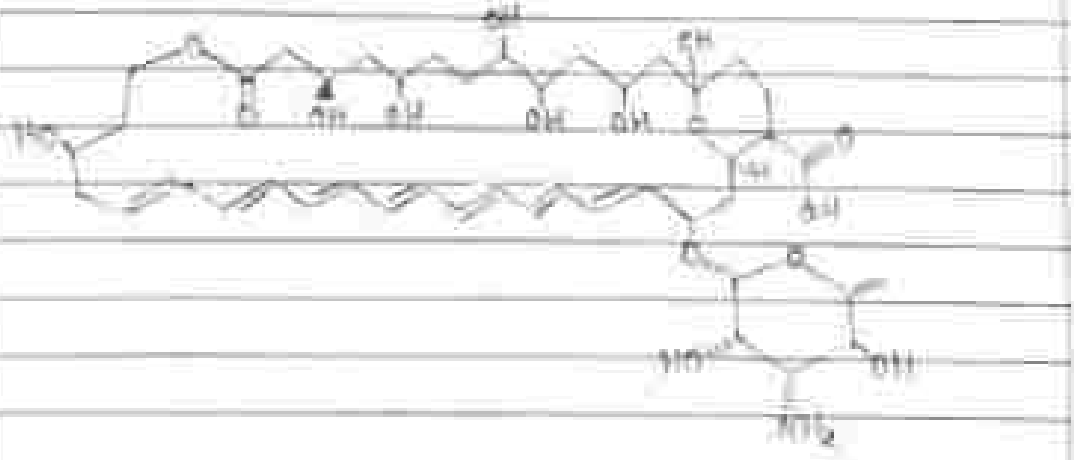
Antifungal Agent

An antifungal Agent is a drug that selectively eliminates fungal pathogens from a host with minimal toxicity to the host.

Classification

1) Antifungal Antibiotics
   - → Amphotericin B
   - → Nystatin
2) Synthetic Antifungal Agents
3) Azole antifungal Agents

1) Amphotericin B



Ergosterol :- It is an essential component of fungal cell membrane, so Amphotericin B have high affinity towards the ergosterol

Amphotericin B

↓

Binds exposed in fungal cell membrane

↓

Forms pores in cell membrane

↓

Cell contents leak out

↓

Cell death

① Amphotericin B interacts hydrophobically with ergosterol in the fungal cell membrane, forming a pore

② Potassium & other small molecules are lost through the pore, causing cell death.

A) Echinocandins

Echinocandins

↓ binds to

Fungal 1,3 β-D-glucan synthase

↓ inhibiting

Fungal cell formation

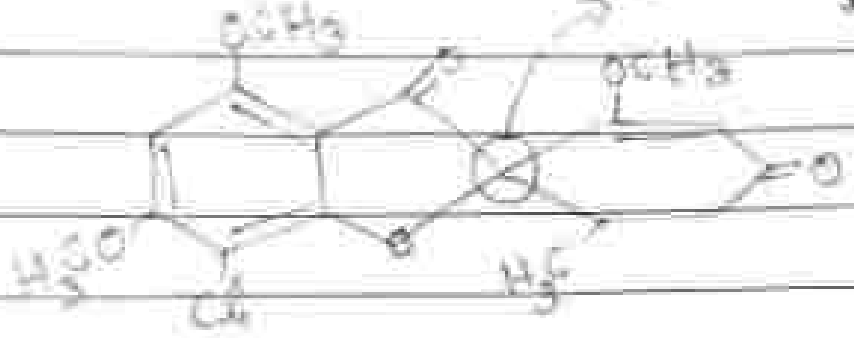
↓ resulting in

Inhibition of synthesis of fungal cell wall

↓

Fungicidal effect

STUDENT'S NAME	
CLASS	SUBJECT
ROLL NO.	DATE



griseofulvin