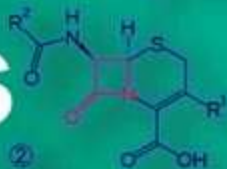
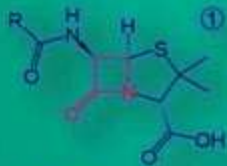




β -Lactam Antibiotics





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Key Words

Brief Introduction

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- History of β lactam Antibiotics

Cell wall synthesis inhibitors

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 - Cephalosporins
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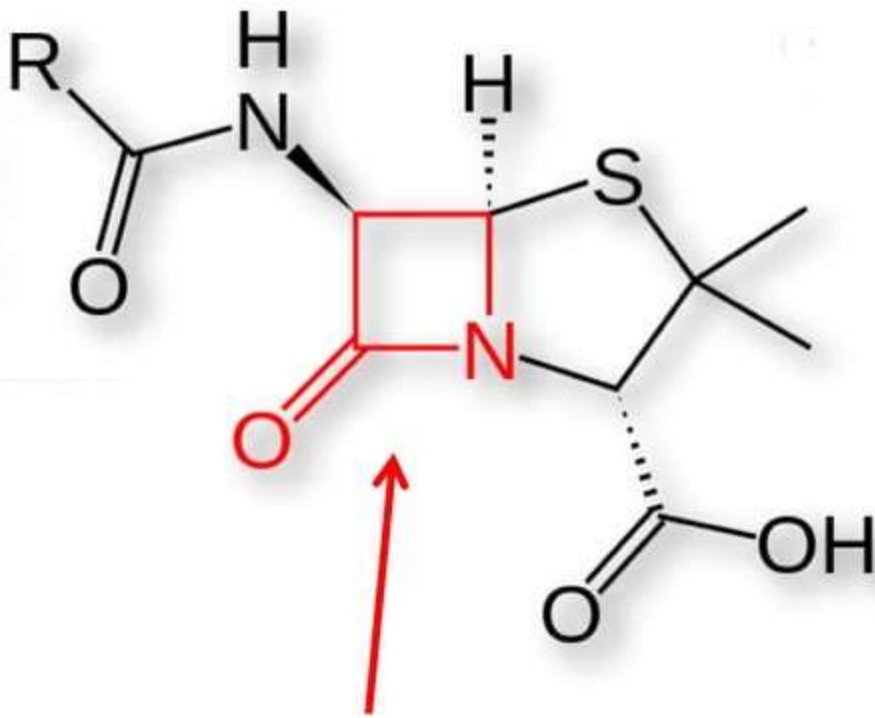


Introduction



What is β lactam ring?

- The β -lactam ring is part of the core structure of several antibiotic families
- Nearly all of β lactam antibiotics work by inhibiting bacterial cell wall biosynthesis
- This has a lethal effect on bacteria (bactericidal)



Structure of β lactam ring

History of β lactam Antibiotics

Alexander Fleming accidentally discovered the first antibiotic in **1928**. He found that a green mold called ***Penicillium notatum*** had contaminated Petri dishes in his lab ... and were killing some of the bacteria he'd been growing.





Cell Wall Synthesis Inhibitors



Penicillins



β Lactamase-sensitive Penicillins

- Penicillin G/V
- Ampicillin
- Amoxicillin

Anti-staphylococcal Penicillins

- Oxacillin
- Nafcillin
- Dicloxacillin

Anti-pseudomonal Penicillins

- Ticarcillin
- Piperacillin



Penicillin G/V

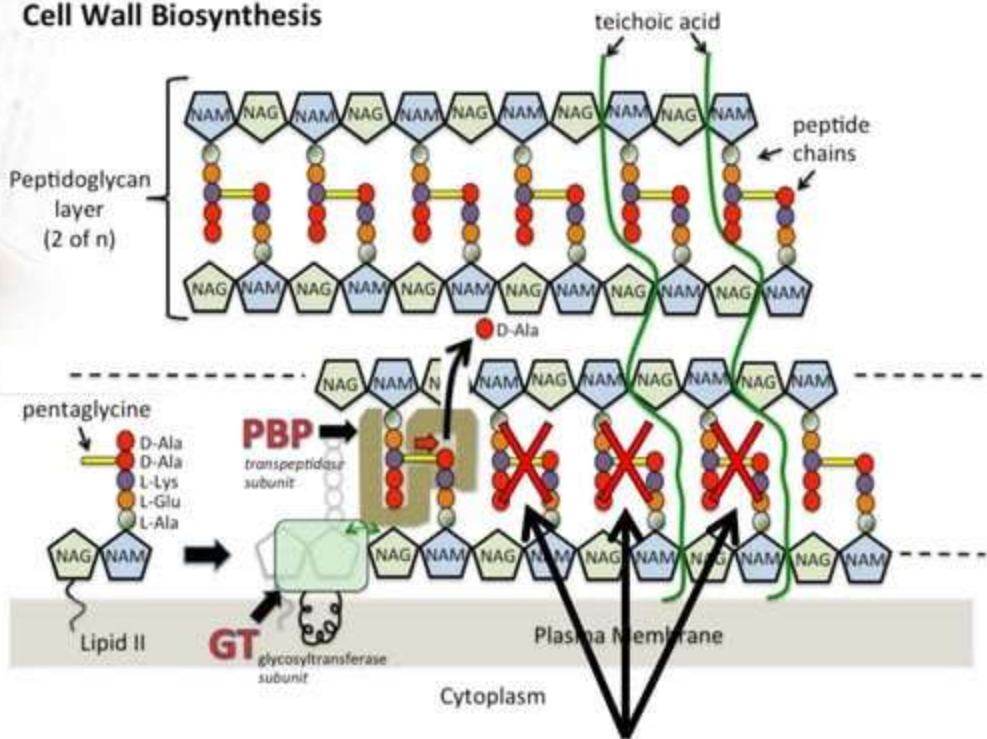
❖ Mechanism of Action:

Bacterial cell wall is cross-linked polymer of polysaccharides and peptides.

Penicillins interact with cytoplasmic membrane-binding proteins (PBPs) to inhibit transpeptidation reactions involved in cross-linking, the final steps in cell-wall synthesis.



Cell Wall Biosynthesis



Penicillin



Penicillin G/V

❖ Indications:

- Gram +ve organisms (*S. pneumoniae*, *S. pyogenes*, *Actinomyces*)
- Gram –ve organisms (*N. meningitidis*)
- Spirochetes (*T. pallidum*)

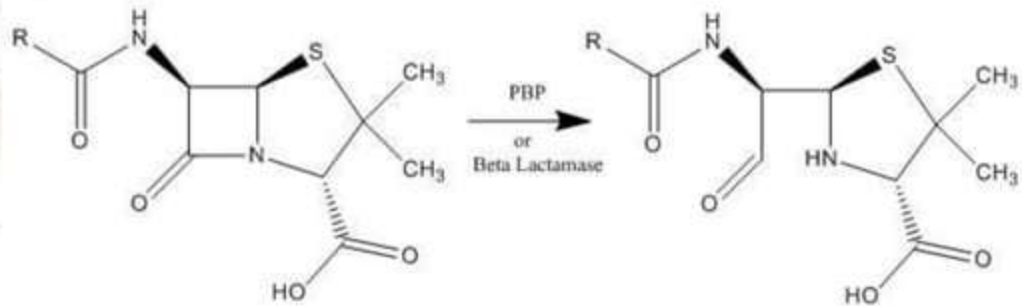


Penicillin G/V

❖ Mechanism of Resistance:

Bacteria produce an enzyme called penicillinase (B lactamase) which breaks the β lactam ring structure, rendering the drug ineffective.

Penicillin G/V



Breaking of the beta lactam ring



Penicillin G/V

❖ β lactamase sensitive

To overcome this sensitivity, they are used in combination with β lactamase inhibitors, to protect the antibiotic from destruction by the B lactamase:

- Clavulanic acid
- Sulbactam



Penicillin G/V

❖ Adverse Effects:

- Hypersensitivity reaction (skin rash, anaphylaxis)
- Hemolytic anemia
- Diarrhea (superinfection)
- Nephritis



Ampicillin and Amoxicillin

❖ Mechanism of Action:

- Same as Penicillin. Wider spectrum, β lactamase sensitive. Also used in conjunction with clavulanic acid to prevent destruction by B lactamase.
- Amoxicillin has greater oral bioavailability than Ampicillin.



Ampicillin and Amoxicillin

❖ Indication:

- Extended-Spectrum penicillin:
Listeria monocytogenes, *Salmonella*,
Enterococci, *E. coli*, *H. pylori*.



Ampicillin and Amoxicillin

❖ Adverse Effects:

- HSR
- Skin rash
- Pseudomembranous colitis



Anti-staphylococcal Penicillins (Oxacillin, Nafcillin, Dicloxacillin)

❖ Mechanism of Action:

- Same as Penicillin. Narrow spectrum; β lactamase resistant.



Anti-staphylococcal Penicillins

❖ Indication:

- *Staphylococcus aureus* (except MRSA)



Anti-staphylococcal Penicillins

❖ Adverse effects:

- HSR
- Interstitial nephritis



Anti-staphylococcal Penicillins

❖ Mechanism of resistance:

- MRSA has altered Penicillin-binding protein target site



Anti-pseudomonal Penicillins (Piperacillin, Ticarcillin)

❖ Mechanism of action:

- Same as Penicillin, extended spectrum. β lactamase sensitive, used with β lactamase inhibitor.



Anti-pseudomonal Penicillins

❖ Indication:

- *Pseudomonas* spp. and Gram -ve organisms



Anti-pseudomonal Penicillins

❖ Adverse effects:

- HSR

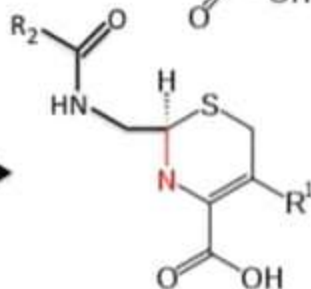
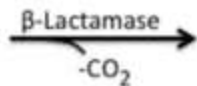
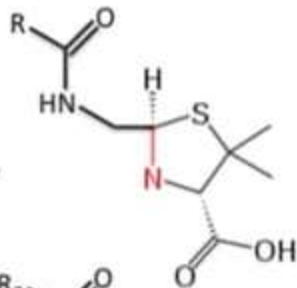
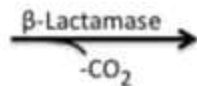


Cephalosporins

Cephalosporins

They have structural similarities to Penicillins

Penicillin



Cephalosporin

inactive metabolites



Cephalosporins

❖ Mechanism of Action & Resistance:

Are β lactam antibiotics that are structurally and functionally related to Penicillins.

Cephalosporins have the same mechanism of action as Penicillins and are affected by the same the same resistance mechanism



Cephalosporins

- **First generation** (Moderate spectrum)
 - Cefazolin · Cephalexin
- **Second generation** (Moderate spectrum)
 - Cefaclor · Cefuroxime
- **Third generation** (Broad spectrum)
 - Cefixime · Cefotaxime · Ceftriaxone
Ceftazidime
- **Fourth generation** (Broad spectrum)
 - Cefipime

First Generation

This is the prototype of first-generation, oral cephalosporins. Oral administration twice daily is effective against pharyngitis.

Cephalexin

Second Generation

Administered twice daily, this drug is well absorbed and is active against β -lactamase-producing organisms.

**Cefuroxime
axetil**

❖ Indications:

Third Generation

**Cefdinir
Cefixime**

These are administered orally once daily.

Cefotaxime

This penetrates well into the CSF.

Ceftazidime

This is active against *Pseudomonas aeruginosa*.

Ceftriaxone

This drug has the longest half-life of any cephalosporin (6 to 8 hours), which permits once-a-day dosing. High levels of the drug can be achieved in blood and CSF. It is effective against genital, anal, and pharyngeal penicillin-resistant *Neisseria gonorrhoeae*. The drug is excreted in bile and may be used in patients with renal insufficiency. It has good penetration into bone.

Fourth Generation

Cefepime

This is active against *Pseudomonas aeruginosa*.



Cephalosporins

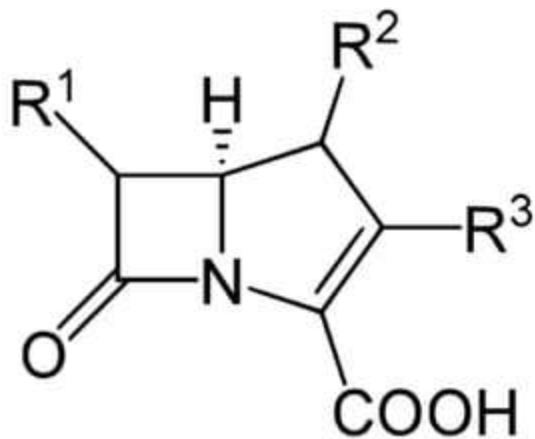
❖ Adverse effects:

Similar to Penicillins.

Patients who have anaphylactic response to penicillins should NOT consume cephalosporins due to cross reactivity.



Carbapenems





Carbapenem (Imipenem & Meropenem)

❖ Mechanism of action:

- Same as penicillin and cephalosporin.
- Broad spectrum, resistant to B lactamase.
- Imipenem is quickly degraded by renal dehydropeptidase . So it's always administered with cilastatin (inhibitor of renal dehydropeptidase) to prevent the degradation of imipenem.



Carbapenem (Imipenem & Meropenem)

❖ **Indications:**

- Gram +ve cocci.
- Gram – ve rods
- Anaerobes



Carbapenem (Imipenem & Meropenem)

❖ **Indications cont'd:**

- Are important for use in severe life-threatening infection or when other drugs have failed.
- Meropenem has decreased risk of seizures and is stable to renal dehydropeptidase.



Carbapenem (Imipenem & Meropenem)

❖ Mechanism of resistance:

- Inactivated by carbapenemases produced by certain types of bacteria like:

- *E.coli* , *Klebsiella pneumonia*



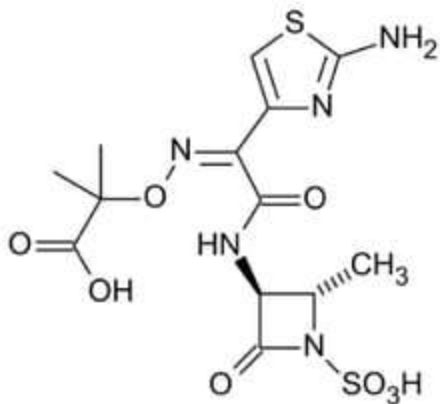
Carbapenem (Imipenem & Meropenem)

❖ Adverse Effects:

- GI distress
- Rash
- CNS toxicity (seizures) at high doses.



Monobactams





Monobactam (Aztreonam)

❖ Mechanism of action:

- Prevents peptidoglycan cross linking like penicillins & cephalosporins.
- Resistant to B-lactamase.
- Synergistic with aminoglycosides.
- NO cross-allergenicity with penicillins.



Monobactam (Aztreonam)

❖ Indication:

- Gram –ve rods only. (e.g. *Pseudomonas aer.*)
- No activity against gram +ve rods or anaerobes.
- Use for patients with penicillin allergy or those with renal insufficiency who can't tolerate aminoglycosides.



Monobactam (Aztreonam)

❖ Adverse effects:

- Usually non-toxic , occasional GI upset.



Sources:

❖ Books:

- Lippincott's Illustrated Reviews: Pharmacology, 6th Edition, by Karen Whalen, 2014
- Kaplan Medical, USMLE Step 1 Lecture Notes 2018, Pharmacology
- Handbook of First Aid drugs



Sources:

❖ Websites:

- www.Wikipedia.com
- www.google.com/images
- www.ncbi.nlm.nih.gov
- www.sciencedirect.com



**Thanks for your
attendance**



Any Questions?