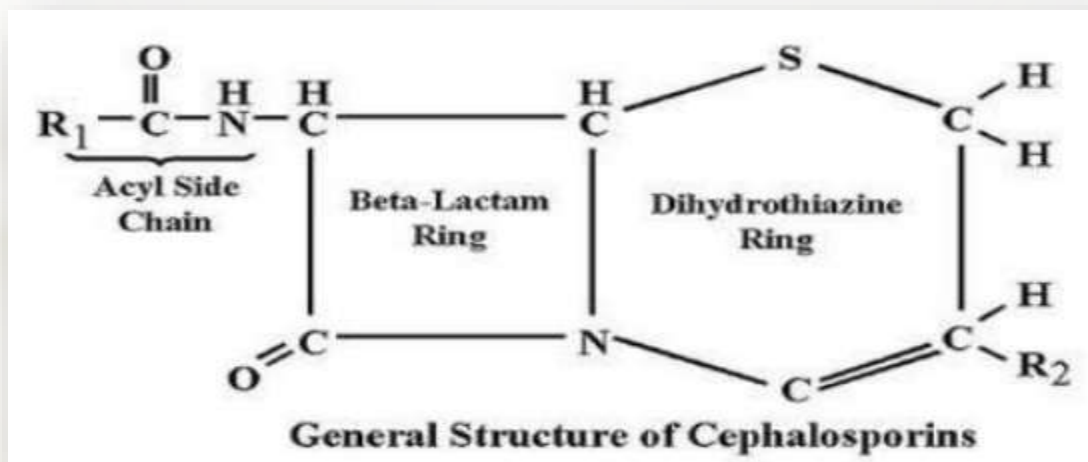


Cephalosporin

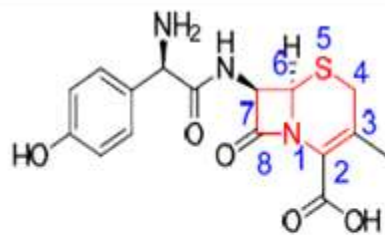
- It was isolated from fungus *Cephalosporium acremonium* in 1948 by an Italian scientist Giuseppe Brotzu.
- Cephalosporins are new and improved derivatives of the penicillins, They were actually discovered as naturally occurring substances separate from the penicillins.



Classification of Cephalosporin

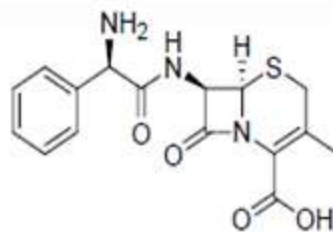
Based on generation:

- a) **First generation** : Cefazoline, Cefradine, Cefproxadine, Cefacetrole, Cefalexine, Cefadroxile, Cefalonium, Cefalotin, Cefaprin, Cefatrizine
- b) **Second generation** : cefuroxime, Cefprozil, Cefuzonam, Cefaclor, Cefotiamcefminox, Cefotetan, Cefoxitin.
- c) **Third generation** : Cefixime, Cefodizime, Cefoperazone, Cefteram, Ceftibuten, Ceftiofur, Cefpiramide, Cefdaloxime
- d) **Fourth generation**: Cefepime, Cefoselis, Cefozopran, Cefpirome, Cefquinome
- e) **Yet to be classified** : Cefaloram, Cefempidone, Cefetrizole, Cefivitril.



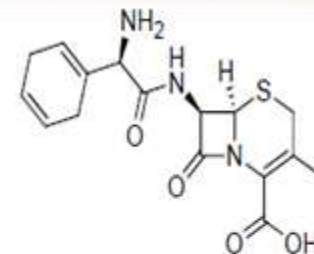
Cefadroxil

(6R,7R)-7-[(2R)-2-amino-2-(4-hydroxyphenyl)acetamido]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid



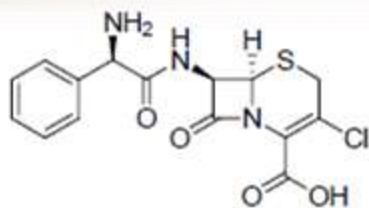
Cephalexin

(6R,7R)-7-[(2R)-2-amino-2-phenylacetamido]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid



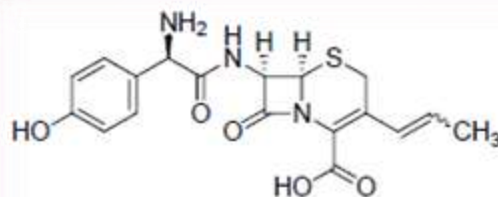
Cephadrine

(6R,7R)-7-[(2R)-2-amino-2-(cyclohexa-1,4-dien-1-yl)acetamido]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid



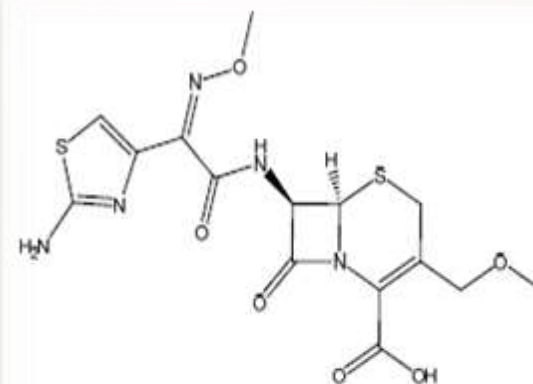
Cefactor

(6R,7R)-7-[(2R)-2-amino-2-phenylacetamido]-3-chloro-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid



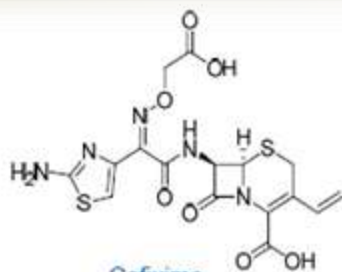
Cefprozil

(6R,7R)-7-[(2R)-2-amino-2-(4-hydroxyphenyl)acetamido]-8-oxo-3-(prop-1-en-1-yl)-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid



Cefpodoxime

(6R,7R)-7-[(2Z)-2-(2-amino-1,3-thiazol-4-yl)-2-(methoxyimino)acetamido]-3-(methoxymethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid

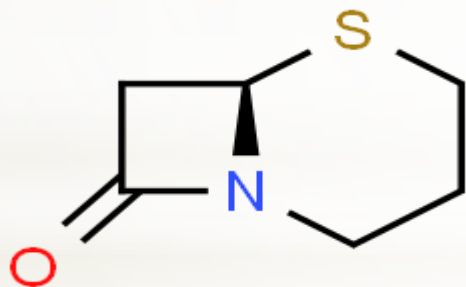


Cefixime

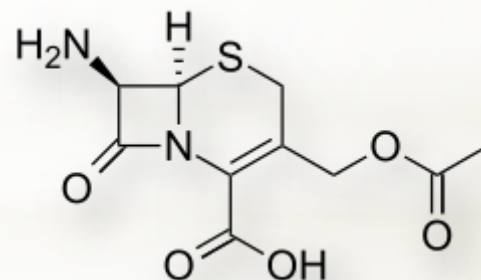
(6R,7R)-7-[(2Z)-2-(2-amino-1,3-thiazol-4-yl)-2-[(carboxymethoxy)imino]acetamido]-3-ethenyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid

Chemistry of Cephalosporin

- The core of the basic cephalosporin molecule consists of a two ring system which includes a β -lactam ring condensed with dihydrothiazine ring.
- Basic nucleus is made up of 7-amino cephalosporanic acid (7-ACA).
- Core ring present in cephalosporins 5-thia-1-aza-bicyclo [4.2.0] octanes.



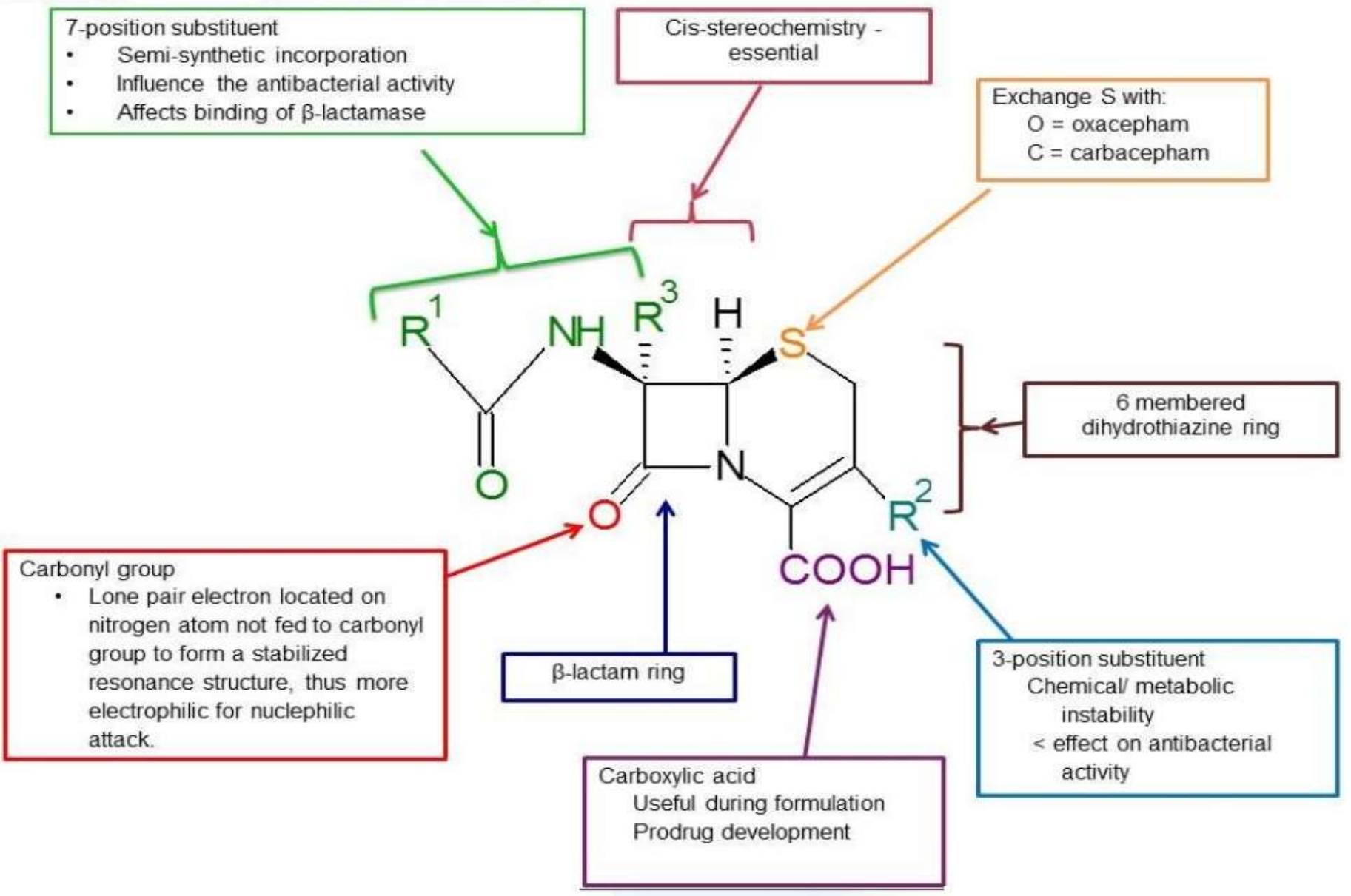
(Cepham)



Mechanism of action of Cephalosporin

- Cephalosporins have same mode of action as other beta lactam antibiotics.
- It disrupt the synthesis of peptidoglycan layer of bacterial cell wall.
- The peptidoglycan layer is important for cell wall structural integrity.
- The final transpeptidation step in the synthesis of peptidoglycan is facilitated by transpeptidase known as penicillin binding protein.
- Prevents new cell wall formation in bacteria

SAR of Cephalosporin



Adverse effect

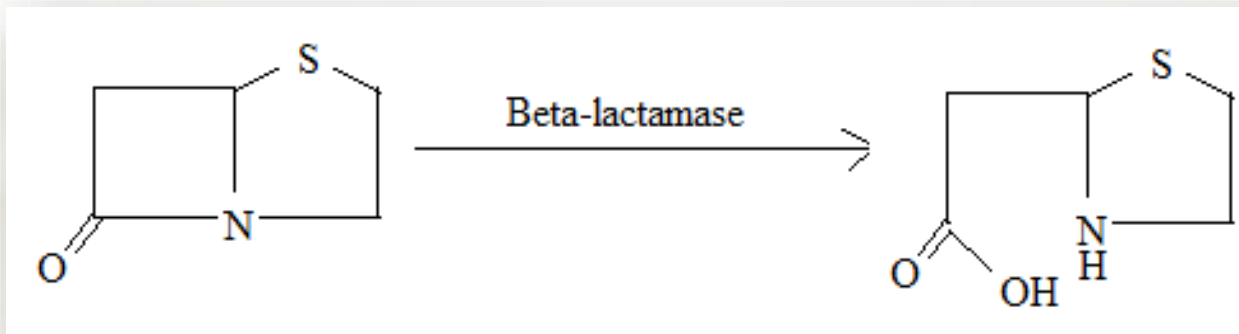
- Stomach upset
- Nausea
- Vomiting
- Diarrhea
- Dizziness

Uses

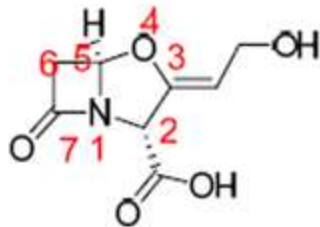
- Skin or soft tissue infections
- Urinary tract infections (UTIs)
- Strep throat
- Ear infections
- Pneumonia
- Sinus infections
- Meningitis
- Gonorrhoea

β -lactamase inhibitor

- These are a family of enzymes involved in bacterial resistance to beta-lactam antibiotics.
- They act by breaking the beta-lactam ring that allows penicillin-like antibiotics to work.
- Drug substance that inhibit the enzyme Beta-lactamases are called betalactamase inhibitors.

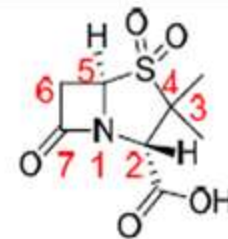


- β -lactamase inhibitors have little antibiotic activity of their own
- They are co-administered with beta-lactam antimicrobials to prevent antimicrobial resistance.
- Beta-lactamase inhibitors are primarily indicated for infections by gram negative bacteria, as they produce this enzyme.



Clavulanic acid

(2R,3Z,5R)-3-(2-hydroxyethylidene)-7-oxo-4-oxa-1-azabicyclo[3.2.0]heptane-2-carboxylic acid



Sulbactam

(2S,5R)-3,3-dimethyl-4,4,7-trioxo-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid

Beta lactam antibiotic + Beta-lactamase inhibitor



Complex



Effectiveness of beta lactamase is diminished



Enhance the activity of Beta-lactam antibiotics

Adverse effect

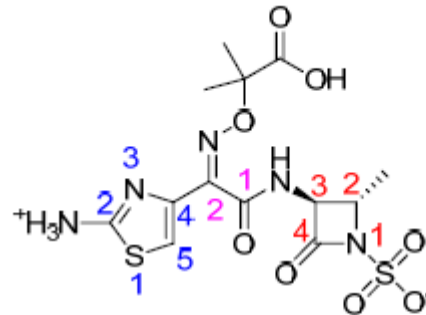
- Gastrointestinal **side effects**, such as diarrhea, nausea, and constipation.
- Nervous system **effects** such as headaches, insomnia, and seizures.
- hematological **effects** such as impaired platelet function

Uses

- A **beta lactamase inhibitor** used to enhance the effectiveness of **beta lactam** antibiotics.
- A **non- β -lactam β -lactamase inhibitor** used in combination with ceftazidime for the treatment of complicated intra-abdominal infections, complicated urinary tract infections, and hospital or ventilator-acquired pneumonia.

Monobactam

- Monobactams are monocyclic β -lactam antibiotics.
- The β -lactam ring is not fused to another ring, in contrast to most other β -lactams.
- Monobactams are effective only against aerobic Gram-negative bacteria (e.g., *Neisseria*, *Pseudomonas*).



Aztreonam

(2S,3S)-3-[(2Z)-2-(2-azaniumyl-1,3-thiazol-4-yl)-2-[(1-carboxy-1-methylethoxy)imino]acetamido]-2-methyl-4-oxoazetidine-1-sulfonate

Mechanism of action of Monobactam

The antibacterial activity of monobactam is due to inhibition of penicillin binding protein 3 (PBP3), interfering with peptidoglycan synthesis and cell wall formation.

Uses

- It is used primarily to treat infections caused by gram-negative bacteria such as *Pseudomonas aeruginosa*.
- This may include bone infections, endometritis, intra abdominal infections, pneumonia, urinary tract infections, and sepsis.

Adverse effects

- Skin rash and occasional abnormal liver functions.