



Therapeutical Activity of Cephalosporin Cefuroxime Broad-spectrum Antibiotic

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ABSTRACT

In the gastrointestinal tract, cefuroxime Axetil (CA), a broad-spectrum antibiotic with low solubility, is broken down by enzymes. Through an aminomethylation process, biologically active compounds with Cefuroxime axetil's heteroaromatic ring system have been created. Cefuroxime axetil was amino methylated using a range of physiologically potent sulphonamides / secondary amines. The resultant product was then characterized using elemental analysis and spectral studies (IR, ¹H-NMR, and ¹³C-NMR). Cefuroxime is present in cefuroxime axetil tablets as well. Cefuroxime axetil is an oral, broad-spectrum, semisynthetic cephalosporin antibiotic. Cefuroxime axetil is (RS)-1-hydroxyethyl (6R,7R) in chemical terms. Its molecular weight is 510.48, and its formula is C₁₈H₁₈N₂O₅S. The parent sulphonamides and derivatives of Cefuroxime axetil were compared for their antibacterial activity. The LD₅₀ test was used to determine the toxicity of synthetic derivatives of cefuroxime axetil. A broad-spectrum antibiotic of the second generation, cefuroxime has a poor absorption profile from the gastrointestinal tract. It resulted in the creation of cefuroxime's 1-acetoxyethyl ester, or cefuroxime axetil. A prodrug of cefuroxime that can be taken orally is cefuroxime axetil.

Keywords: Cefuroxime axetil, sulphonamides, LD₅₀, broad-spectrum.

Introduction

Since the first antibiotic, penicillin was introduced into medicine in 1942, researchers have been engaged in a perpetual "race" to develop new medications that target pathogenic bacteria. Every day, thousands of potentially harmful compounds are created in laboratories all over the world as a result of this particular "arms race". A sensible way to introduce a basic aminoalkyl chain into a variety of medications and compounds is through the Mannich reaction. A review of the literature in this area turned up several reports on the antimicrobial activity of N-Mannich bases. Acetil cefuroxime (CA). The orally absorbed pro-drug of cefuroxime, 1-acetoxyethyl ester of a β -lactamase-stable cephalosporin, is used to treat common community-acquired infections due to its in-vitro antibacterial activity against several gram-positive and gram-negative organisms. It has a methoxy-imino group that strengthens its resistance to β -lactamase attack and a carbamoyl group that contributes to its significant metabolic stability. These groups, along with the furyl ring, boost the molecule's ability to combat gram-negative bacteria, which is one way that they contribute to its antibacterial qualities. Furthermore, sulphonamides are widely recognized for their antimicrobial, anti-inflammatory, antiproliferative, carbonic anhydrase inhibitory, antitumor, and radiosensitizing properties.

The first second-generation oral antibiotic to be widely used in therapy that was commercially available was cefuroxime. According to Perry and Brogden (1996), it possesses broad-spectrum antibacterial activity against group A β -hemolytic streptococci, Haemophilus influenzae, methicillin-sensitive staphylococci, Streptococcus pneumoniae, and Moraxella (Branhamella) catarrhalis. It exhibits extensive efficacy against certain gram-positive respiratory pathogens that contain β -lactamase. Cefuroxime primarily acts by inhibiting the bacterial cell wall's peptidoglycan layer synthesis and transpeptidation.

Cefuroxime is primarily given parenterally in the form of salt because it is poorly absorbed when taken orally. Patient compliance is limited by the need for frequent dosing because of the medication's short elimination half-life (1.2–1.6 h). The cefuroxime molecule becomes a prodrug form (CA) when a 1-acetoxyethyl ester group is added. This increases the molecule's lipophilicity (logP~0.55), which improves oral absorption. Because of its higher pK_a value, CA also demonstrates gastric stability.

However, when taken orally, CA is mostly absorbed in the GI tract's proximal region, where it is rapidly hydrolyzed to produce cefuroxime in the presence of blood and intestinal mucosa-specific esterase enzymes. Low permeation across the intestinal mucosa is caused by de-esterification caused by esterase enzymes prior to absorption in the intestinal fluids. Because esterase enzymes in the intestine are less specific to CA, CA is poorly soluble and has a higher bioavailability when lipid-rich foods are present.



Figure 1: Cefuroxime tablets.

Physiochemical Properties

Property Name	Property Value
Molecular Weight	424.4 g/mol
XLogP3	-0.2
Hydrogen Bond Donor Count	3
Hydrogen Bond Acceptor Count	10
Complexity	798
Isotope Atom Count	0

Table I: Physiochemical properties.

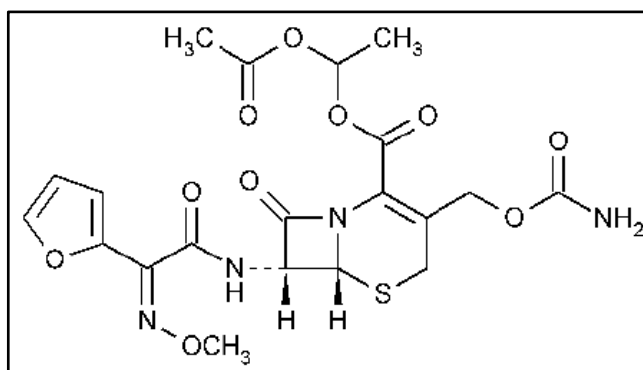
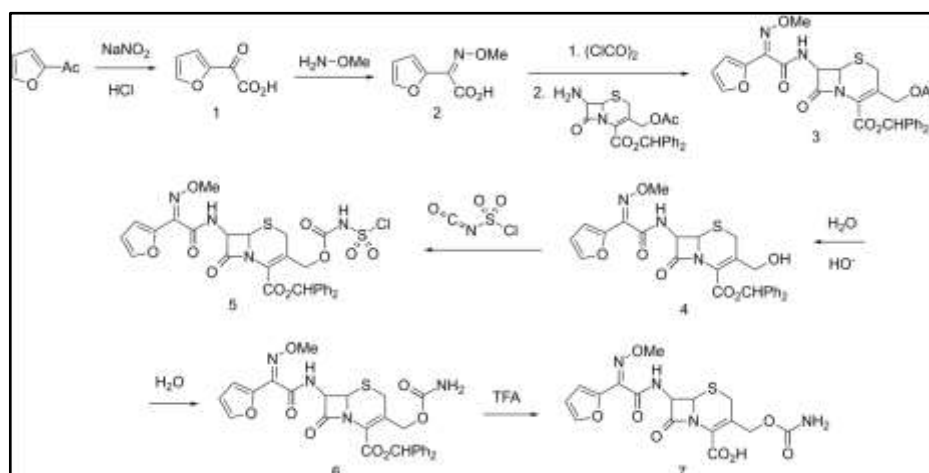


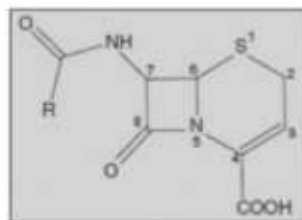
Figure 2: Chemical Structure of Cefuroxime

Synthesis of Cefuroxime



Structural Active Relationship of Cephalosporin

SAR of cephalosporins

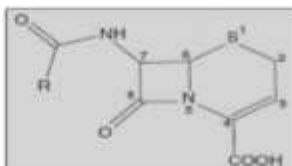


1. 7-Acylamino substituents:

- Acylation of amino group generally increases the potency against gram-positive bacteria, but it is accompanied by a decrease in gram-negative potency.
- High antibacterial activity is observed only when the new acyl groups are derived from carboxylic acids for gram-positive bacteria.
- Substituents on the aromatic ring that increases lipophilicity provide higher gram-positive activity and generally lower gram-negative activity.
- The phenyl ring in the side-chain can be replaced with other heterocycles with improved spectrum of activity and pharmacokinetic properties, and these include thiophene, tetrazole, furan, pyridine, and aminothiazoles

- C-3 substituents:** The nature of C-3 substituents influences pharmacokinetic and pharmacological properties as well as antibacterial activity. Modification at C-3 position has been made to reduce the degradation (lactone of desacetyl cephalosporin) of cephalosporins.

SAR of cephalosporins



- Pyridine and imidazole-replaced acetoxy groups show improved activity against *P.aeruginosa*. Displacement of acetoxy group by azide ion yields derivatives with relatively low gram-negative activity.
- Displacement with aromatic thiols of 3-acetoxy group results in an enhancement of activity against gram-negative bacteria with improved pharmacokinetic properties.
- Replacement of acetoxy group at C-3 position with $-\text{CH}_2\text{Cl}$ has resulted in orally active compounds.
- Oxidation of ring sulphur to sulphoxide or sulphone greatly diminishes or destroys the antibacterial activity.
- Replacement of sulphur with oxygen leads to oxacepam (latamoxef) with increased antibacterial activity, because of its enhanced acylating power.
- Similarly, replacement of sulphur with methylene group (loracarbef) has greater chemical stability and a longer half-life.
- The carboxyl group of position-4 has been converted into ester prodrugs to increase bioavailability of cephalosporins, and these can be given orally as well. Examples include cefuroxime axetil and cefodoxime proxetil
- Olefinic linkage at C 3-4 is essential for antibacterial activity. Isomerization of the double bond to 2-3 position leads to great losses in antibacterial activity.

Figure 3 & 4: SAR of Cephalosporin

Mechanism of Action

A second-generation cephalosporin with the traditional β -lactam ring structure is cefuroxime axetil. Its binding to vital target proteins found in the bacterial cell wall—referred to as the penicillin-binding proteins—causes bactericidal activity in vivo. Bacterial cell wall elongation and leakage result from the inhibition of these proteins, which prevents the bacteria from dividing and maturing.

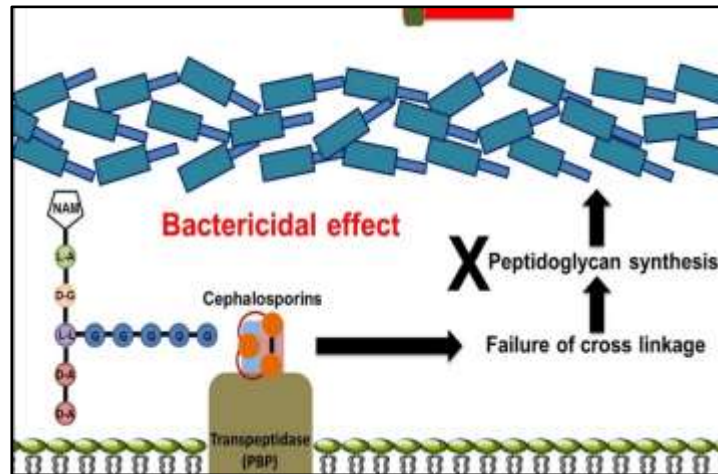


Figure 5: Mechanism action of cephalosporin.

Medical Use

Cefuroxime exhibits antibacterial activity against a variety of bacteria, including sensitive strains of Streptococci and Staphylococci, in addition to gram-negative organisms. It is susceptible to beta-lactamase, just like the other cephalosporins, albeit less so as a second-generation variety. Therefore, it might be more effective against Lyme disease, Neisseria gonorrhoeae, and Haemophilus influenzae. Cefuroxime can pass through the blood-brain barrier, in contrast to other second-generation cephalosporins.

Side Effects

Cefuroxime is usually well tolerated, and most of its negative effects are momentary. Compared to most antibiotics in its class, this one is better absorbed and less likely to cause the most common side effects of diarrhea, nausea, vomiting, headaches/migraines, dizziness, and stomach pain if taken after food.

Indication & Usage

Cefuroxime is a cephalosporin antibacterial medication prescribed to treat the infections caused by susceptible bacteria listed below:

- Tonsillitis/pharyngitis (both in adults and children)
- Pediatric patients with acute bacterial otitis media
- Adults and pediatric patients experiencing acute bacterial maxillary sinusitis
- In adults and pediatric patients 13 years of age and older, acute bacterial exacerbations of chronic bronchitis and secondary bacterial infections of acute bronchitis
- Simple infections of the skin and its structure (adults and pediatric patients 13 years and older)
- Simple urinary tract infections (in patients 13 years of age and older, both adults and pediatric).
- Simple gonorrhea in adults and children (13 years of age and up)
- Adults and pediatric patients 13 years of age and older with early Lyme disease
- Impetigo in young patients

Dosage & Administration

Oral suspension and tablets are not milligram-for-milligram interchangeable since they are not bioequivalent.

- You can take tablets with or without meals.

- Give the oral suspension while eating.
- As directed by the dosage guidelines, administer Cefuroxime tablets for oral suspension.
- Adults and pediatric patients 13 years of age and older with early Lyme disease.
- Impetigo in young patients.

Infection	Dosage	Duration (Days)
Adults and Adolescents (13 years and older)		
Pharyngitis/tonsillitis (mild to moderate)	250 mg every 12 hours	10
Acute bacterial maxillary sinusitis (mild to moderate)	250 mg every 12 hours	10
Acute bacterial exacerbations of chronic bronchitis (mild to moderate)	250 or 500 mg every 12 hours	10 ^a
Secondary bacterial infections of acute bronchitis	250 or 500 mg every 12 hours	5 to 10
Uncomplicated skin and skin-structure infections	250 or 500 mg every 12 hours	10
Uncomplicated urinary tract infections	250 mg every 12 hours	7 to 10
Uncomplicated gonorrhea	1,000 mg	single dose
Early Lyme disease	500 mg every 12 hours	20
Pediatric Patients younger than 13 years (who can swallow tablets whole)^b		
Acute bacterial otitis media	250 mg every 12 hours	10
Acute bacterial maxillary sinusitis	250 mg every 12 hours	10

Figure 6: Dosage.

Conclusion

A broad-spectrum 13-lactam antibiotic is cefuroxime axetil. Despite having numerous approved indications, it is regarded as a secondary treatment option. It is not the recommended medication for any type of infection, especially those found in obstetrics and gynecology. Although it has a low adverse effect profile and is safe to use during pregnancy, it should only be used in specific situations because of its high acquisition cost and superior therapeutic alternatives.

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