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Review Article

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An Overview on Antimicrobial Activity of Cefixime

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Abstract Third-generation cephalosporins in oral formulations have become an increasingly important first-line option for common bacterial infections. Cefixime is one such agent that has excellent activity against a wide range of pathogens, including Haemophilus influenzae, Streptococcus pneumoniae, and Moraxella catarrhalis. Clinical success rates are similar to those of cefaclor, clarithromycin, and other cephalosporins. It should be noted that cefixime also has excellent activity against beta-lactamase-producing strains. The drug's pharmacodynamic properties include a half-life of 3 to 4 hours and a C_{max} of 4.4 µg/mL, which is well above the MIC 90 for susceptible pathogens and allows for once-daily dosing. In this brief summary, the bacteriological and clinical efficacy of cefixime and its indications are discussed.

Keywords Cefixime, Gram Negative Bacteria, Clinical Treatment, Facultative Anarobes

1. Introduction

Cefixime is a third-generation cephalosporin used to treat susceptible Gram negative and Gram-positive bacterial infections. Oral cephalosporins are available over 25 years. This is used extensively within the therapy of patient infections in adults and kids. Those agents are variably subject to hydrolysis by beta-lactamases. Cefixime is a new orally absorbed cephalosporin and it is initial oral one in the third generation. Cefixime is not hydrolysed by the common plasmid-mediated enzymes and by chromosomal 13-Lactamases because inactivate the now a day oral penicillin and cephalosporins, and for this reason it inhibits a good variety of gram-positive and Gram-negative aerobic bacteria together with Haemophilus influenzae, Moraxella catarrhalis, Neisseria gonorrhoea, Escherichia coli and klebsiella resistant to ampicillin, other oral cephalosporins and trimethoprim sulfamethoxazole.

Its broad-spectrum activity permits its use in respiratory and urinary tract infections. This paper is a review of chemical properties, antibacterial activity, pharmacokinetics, clinical pharmacology, indications and adverse effects of cefixime as compared to alternative orally absorbed cephalosporins and to amoxycillin or cotrimoxazole.

The treatment of typhoid fever with conventional agents can frequently result in clinical treatment failures or bacterial relapses. Frequencies of these strains, called MDR (multidrug-resistant), are reported to be 78% (1990) in India, 75% (1995) in Egypt, 77% (1995) in Pakistan and 86% (1995) in Vietnam. Reflecting this changing trend in antibiotic susceptibility of S. typhi, various new agents such as new quinolones and third-generation cephalosporins having strong in vitro activity have been tried clinically for the treatment of MDR S. typhi. The effectiveness of oral cefixime in the treatment of typhoid fever has also been reported clinically. In this study, the in vitro activity of cefixime against S. typhi including MDR strains were evaluated.

Antibacterial Activity

Most tested strains of Escherichia coli, Klebsiella pneumoniae, Klebsiella oxytoca, Proteus mirabilis, Proteus vulgaris, Citrobacter diversus and Providencia rettgeri were inhibited in vitro by cefixime 1 mg/L or less. Haemophilus influenzae, Branhamella catarrhalis and Neisseria gonorrhoeae were also inhibited by low concentrations of cefixime. A study of large numbers of Enterobacteriaceae conducted in the USA noted that the MIC_{50} was below 1 mg/L for most clinical isolates of all species other than Citrobacter freundii, Enterobacter cloacae, Hafnia alvei and Morganella morganii. Cefixime is more potent (MIC_{90} lower by 2 or more dilutions) in vitro than cefaclor and cephalexin against Enterobacteriaceae, but less potent than ciprofloxacin.

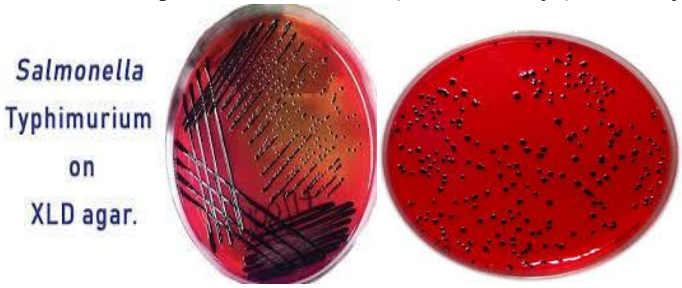
Cefixime is active against Streptococcus pyogenes, S. pneumoniae, S. agalactiae and most strains of streptococci belonging to Lancefield group C, but Lancefield groups F and G are only moderately sensitive and Staphylococcus aureus, S. epidermidis and Enterococcus faecal is are generally resistant. Pseudomonas aeruginosa is resistant to cefixime, as are most strains of the Bacteroides species, and many strains of Peptostreptococcus species and Flavobacterium species.

In common with other cephalosporins such as cefotaxime and β-lactam antibacterial drugs such as latamoxef, cefixime is stable to hydrolysis by a wide range of β-lactamases. Its β-lactamase stability is greater than that of cephalexin, cephradine and cefadroxil and comparable to the profile of ceftizoxime.

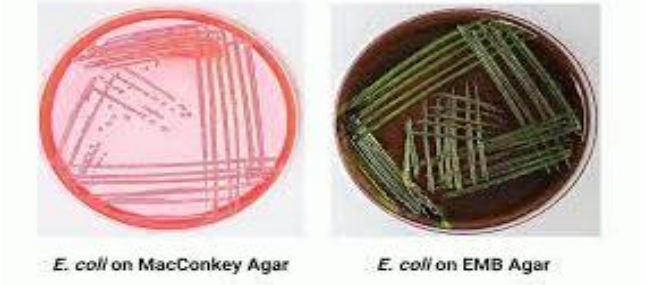
Cefixime has high affinity for penicillin-binding proteins 3, la and lb, and its affinity for the latter explains the rapid lytic activity of cefixime relative to that of the other orally active cephalosporins cefaclor and cephalexin.

Test organisms

Salmonella: Salmonella is a genus of rod-shaped (bacillus) gram negative bacteria of the family enterobacteriaceae. Salmonella species are non-spore-forming, predominantly motile enterobacteria with cell diameters between about 0.7 and 1.5 μm, lengths from 2 to 5 μm, and peritrichous flagella (all around the cell body, allowing them to move). They are chemotrophs, obtaining their energy from oxidation and reduction reactions, using organic sources. They are also facultative anaerobes, capable of generating adenosine triphosphate with oxygen ("aerobically") when it is available, or using other electron acceptors or fermentation ("anaerobically") when oxygen is not available.



E. Coli: *Escherichia Coli* is a gram- negative, facultative anaerobic, rod shaped, coliform bacterium commonly found in the lower intestines of warmblooded animals. Escherichia coli and other facultative anaerobic bacteria account for approximately 0.1% of infections, and oral infection is the main route of bacterial infections.



S. Aureus: Staphylococcus aureus is a Grampositive, spherical bacterium belonging to the genus Bacillus and a member of the human microbiota frequently found in the upper respiratory tract and skin. It is generally good for catalase and nitrate reduction and is a facultative anaerobic organism that does not need oxygen to grow. Although S. aureus is generally an integral part of the human microbiome, it can also become a common pathogen and a common cause of skin infections (e.g., abscesses), respiratory infections (such as sinusitis), and food poisoning. *Staphylococcus aureus* was found to be the second leading cause of antibiotic related deaths in 2019.

Therapeutic Trials

Cefixime has been studied by numerous groups of investigators in Japan prior to marketing, each of whom prescribed the drug for small numbers of patients with uncomplicated or complicated urinary tract infections, acute pharyngitis or tonsillitis or acute lower respiratory tract infections. To date there have been only a few controlled therapeutic trials comparing the clinical and bacteriological efficacy of cefixime with that of other orally active antibacterial drugs in adults, although several studies have compared cefixime with amoxycillin or cefaclor in children with acute otitis media with effusion.

Pooled data from non-comparative clinical studies of cefixime in uncomplicated urinary tract infection conducted in Japan, all of which utilised standard criteria devised by the Urinary Tract Committee in Japan, revealed overall therapeutic efficacy to be excellent in 67%, moderate in 30%, and poor in 3% of patients treated with the usual dose of cefixime 100mg daily (generally in 2 divided doses) for 3 to 7 days. Infecting pathogens, most often *E. coli*, were eradicated at the end of treatment in 97% of patients.

Adverse Effects

Clinical adverse experiences reported by investigators in patients treated with cefixime have usually been mild to moderate in severity, and transient. Diarrhoea and stool changes (as distinct from diarrhoea) have been the most commonly reported adverse effects, occurring in 13.8 and 13.5% of patients, respectively. Diarrhoea tended to be more frequent following once daily (15.3%) than twice daily (10.3%) administration in adults, but this trend was not apparent in children. In about two-thirds of instances diarrhoea and stool changes were evident within 4 days of beginning treatment, which is contrary to the pattern usually encountered with changes in bowel flora. Comparative trials conducted in the USA revealed a greater frequency of diarrhoea and stool changes with cefixime than with amoxycillin, while other gastrointestinal complaints occurred with similar frequency with both drugs.

Dosage and Administration

The usual adult dosage is 400mg daily administered as a single dose or in 2 equally divided doses. A lower dosage of 200mg daily has been used in uncomplicated urinary tract infections. In children, cefixime 8 mg/kg/day once daily or in 2 divided doses has been the most widely used dosage for treating acute otitis media, acute tonsillitis and

acute pharyngitis. In patients with severe renal dysfunction (creatinine clearance <20 ml/min) half the standard dose of cefixime should be administered once daily.

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