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CEFPODOXIME PROXETIL: ANTIBACTERIAL ACTIVITY , PHARMACOKINETIC PROPERTIES AND THERAPEUTIC EFFICACY

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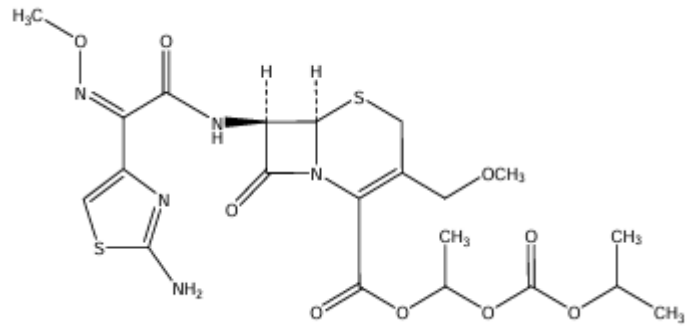
Abstract:
Cefpodoxime Proxetil is a broad-spectrum, orally administered third-generation cephalosporin that acts as a pro-drug. In the body, it is converted to cefpodoxime, which exhibits significant antibacterial activity. a third-generation antibiotic, is effective against various bacterial infections, including cerebral abscesses and bacterial meningitis. As part of the β-lactam antibiotic group, it is considered one of the safer options available[1]. Cefpodoxime proxetil has shown comparable clinical and bacteriological efficacy in treating lower respiratory tract infections, like pneumonia, when compared to cefuroxime axetil and amoxicillin/clavulanic acid in randomized controlled trials. It has also proven effective for skin and soft tissue infections in children. In studies involving both adults and children with various infections (such as abscesses, furuncles, cellulitis, and infected wounds),cefpodoxime proxetil's efficacy was similar to that of cefuroxime axetil and cefaclor.Additionally, cefpodoxime proxetil is generally well tolerated in pediatric patients, with adverse effects primarily involving gastrointestinal issues and skin rashes, which are consistent with those observed for other oral cephalosporins[2].

Keywords: : Cefpodoxime proxetil, Cephalosporin, Pharmacokinetic Properties ,Pharmacological applications

I. INTRODUCTION

II. Cefpodoxime proxetil is a broad spectrum third-generation cephalosporin, which reveals potent antibacterial activity against both Gram-positive and Gram-negative bacteria, and high stability in the presence of beta-lactamases[3-5]. Low concentrations of cefpodoxime inhibit most respiratory pathogens1. This drug has very good in-vitro activity against Enterobacteriaceae, Hemophilus spp. and Moraxella spp., including beta-lactamase producers and many strains resistant to other oral agents. It also has activity against Gram-positive bacteria, especially against streptococci. It has no activity against enterococci. It is well tolerated and is one of the first third-generation cephalosporins to be available in oral form2. It is used orally for the treatment of mild to moderate respiratory tract infections, uncomplicated gonorrhoea and urinary tract infections[6].



Structure of Cefpodoxime Proxetil

III. Mechanism of Action:

Cefpodoxime is a semi-synthetic third-generation cephalosporin, available as the prodrug cefpodoxime proxetil, which is well absorbed from the gut. It achieves concentrations in various body fluids that exceed the minimum inhibitory concentration (MIC) for most pathogens[7]. The drug is excreted unchanged by the kidneys, so dosage adjustments are necessary for patients with renal impairment[8].As a bactericidal agent, cefpodoxime works by inhibiting bacterial cell wall synthesis. After being converted by intestinal esterases, it penetrates bacterial cell walls through porins[9], reaches the periplasmic space, and binds to penicillin-binding proteins (PBP-1 and PBP-3) in the cell membrane[10]. This binding disrupts peptidoglycan synthesis, ultimately damaging the bacterial cell [11].Cefpodoxime is particularly effective against Enterobacteriaceae and streptococci, and it also inhibits Staphylococcus aureus[12]. Its antibacterial effect is primarily due to cell wall synthesis inhibition, and it is bactericidal against most strains at concentrations equal to or four times greater than the MIC[13].

IV. Pharmacokinetic Aspects of Cefpodoxime Proxetil

The pharmacokinetic characteristics of cefpodoxime proxetil, including absorption, distribution, metabolism, and elimination, are outlined below [14].

Absorption

Cefpodoxime proxetil is absorbed and converted in vivo to its active form, cefpodoxime, which has about 50% systemic availability. Peak plasma concentrations (Cmax) of cefpodoxime occur approximately 2.0 to 3.1 hours after oral administration. Cmax may be slightly elevated in patients with renal failure or elderly patients with respiratory issues[15]. Approximately 50% of the absorbed cefpodoxime is excreted unchanged in the urine within 12 hours, with about 29% to 33% of the administered dose eliminated.

Distribution

Cefpodoxime is widely distributed in the tissues and fluids of the respiratory tract. After a single oral dose of 100 or 200 mg, drug concentrations in upper (e.g., tonsils) and lower respiratory tract tissues (e.g., bronchial mucosa, lung parenchyma) remain above the MIC90 for common respiratory pathogens for 7-12 hours. Cefpodoxime has low binding to human plasma proteins (18% to 23%), indicating that it can easily penetrate capillary walls into tissues[16].

Metabolism

Once in systemic circulation, cefpodoxime undergoes minimal metabolism, with most of the drug eliminated via renal excretion.

Elimination

The clearance of cefpodoxime is inversely related to creatinine clearance (CLcr), necessitating dosage adjustments for patients with CLcr below 3.0 L/h. About 29% to 33% of the absorbed dose is excreted unchanged in the urine within 12 hours, with a half-life (t½) of 2.09 to 2.84 hours. In patients with renal impairment, the half-life increases while apparent plasma and renal clearance decrease. Unchanged cefpodoxime is primarily excreted through the urine[17].

Table 1: Pharmacokinetic profile of cefpodoxime proxetil

Parameters	Value
Bioavailability	50%
Average peak plasma concentration	1.0 to 4.5 mg/L
Time for peak plasma concentration	2.0 to 3.1 hr
Half-life ($t_{½}$)	1.9 to 2.8 hr
Elimination	Renal clearance

Drug interactions :The interactions of cefpodoxime proxetil with various interactants are summarized in Table .

Table 2: Drug interactions of cefpodoxime proxetil

Interactant	Interaction effect
Antacids or H_2 blockers	Reduced cefpodoxime proxetil peak blood levels and the extent of absorption
Probenecid	Effectively decreases excretion and increases systemic level of the drug
Potassium clavulanate	Showed higher clinical cure and improvement in the symptoms of lower respiratory tract infections
Propantheline	Causes slight delay in drug absorption; however, no effect on the extent of absorption
Anisotropine methylbromide	Slight increase in the extent of absorption
Metoclopramide	No effect on the extent or rate of cefpodoxime proxetil absorption

V.Conclusion

This paper has outlined significant pharmacological interventions, pharmacokinetic aspects, and clinical data related to cefpodoxime proxetil. Additionally, it has discussed various analytical methods for its determination and identification in different formulations and biological fluids[18-20]. Cefpodoxime proxetil has proven to be a promising and effective treatment option for various common bacterial infections. Further scientific advancements in pharmacology are emphasized as necessary for continued progress in this area[21-23].

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