CEFPODOXIME PROXETIL: AN UPDATE ON ANALYTICAL, CLINICAL AND PHARMACOLOGICAL ASPECTS

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ABSTRACT

Cefpodoxime proxetil is an orally administered broad spectrum third-generation cephalosporin. It is a pro-drug that is de-esterified in-vivo to cefpodoxime, which has potent antibacterial activity. It is generally well tolerated and demonstrates good therapeutic potential in patients with various common bacterial infections. This compound has been used most widely in the management of infections of the respiratory and urinary tracts as well as those of the skin structure, acute otitis media, pharyngitis, tonsillitis etc. The present article describes pharmacology, pharmacokinetics, clinical aspects, adverse effects and interactions of cefpodoxime proxetil. Special emphasis is also laid on the determination of cefpodoxime proxetil in pharmaceutical dosage forms and biological fluids by employing different advanced analytical methodologies.

Key words: Cefpodoxime proxetil, Cephalosporin, Pharmacological aspects, Pharmacokinetics, Analytical reports.

INTRODUCTION

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. Low concentrations of cefpodoxime inhibit most respiratory pathogens. 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 form. It is used orally for the treatment of mild to moderate respiratory tract infections, uncomplicated gonorrhea and urinary tract infections.

Physicochemical aspects

Cefpodoxime proxetil is an orally absorbed prodrug of cefpodoxime, an extended spectrum, semi-synthetic cephalosporin. The chemical name is (RS)-1-(isopropoxycarbonyloxy)-ethyl (+)-(6R,7R)-7-[2-(2-amino-4-thiazolyl)-2-{(Z)-methoxy-imino} acetamido]-3-methoxymethyl-8-oxo-5-thia-1-azabicyclo[4.2.0] oct-2-ene-2-carboxylate. Its empirical formula is C_{21}H_{27}N_{5}O_{9}S_{2}. Its structural formula is represented in...
the following Fig. 1.

![Fig. 1: Structure of Cefpodoxime Proxetil](image)

**Description**

It is a white to light brownish-white powder, odourless or having a faint odour. It is very slightly soluble in water; freely soluble in dehydrated alcohol; soluble in acetonitrile and in methyl alcohol; slightly soluble in ether. It can be stored in airtight containers at a temperature not exceeding 25°C. Cefpodoxime proxetil is a pro-drug. It is cleaved enzymatically to 2-propanol, carbon dioxide, acetaldehyde and cefpodoxime in the gut wall.

**Mechanism of action**

Cefpodoxime is a semi-synthetic third generation cephalosporin. The drug is available for use as a prodrug—cefpodoxime proxetil which is absorbed readily from the gut. It reaches adequate levels exceeding the minimum inhibitory concentration (MIC) in most of the body fluids. It is excreted by kidneys, unchanged. Also, dose needs adjustment in compromised renal function. It is a bactericidal agent like rest of the cephalosporins. After de-esterification by the intestinal esterases, the drug acts by inhibiting the bacterial cell wall synthesis. The molecular weight of the active molecule is 557.6, which allows its free passage through the porins present in the bacterial cell wall. Then, it crosses the periplasmic space and binds with the penicillin binding proteins (PBP-1 and PBP-3) in the cell membrane. This binding then affects the peptidoglycan synthesis in cell membrane, which ultimately damages the cell. In addition to being highly active against Enterobacteriaceae and streptococci, it inhibits *Staphylococcus aureus*.

The antibacterial effect of cefpodoxime is based on inhibition of cell wall synthesis and the drug is bactericidal against most tested strains at a concentration equal to or 4-fold greater than the respective MIC.

**Analytical methodologies**

Various analytical techniques have been used for the determination of cefpodoxime proxetil in pharmaceutical dosage forms and biological fluids. Also, several analytical methodologies for simultaneous estimation of various cephalosporins have also been developed. Some important analytical procedures reported in scientific literature are summarized below.

Bhandari and Khishi developed simple, specific, accurate and precise high-performance thin-layer chromatographic method for analysis of cefpodoxime proxetil in human plasma. This method has been successfully validated and applied for the analysis of drug in human plasma. The recovery of cefpodoxime proxetil from human plasma using the described precipitation procedure was about 94.75%. The method was validated for precision, accuracy, specificity, recovery and stability. Moreover, Date and Nagarsenkar developed a high-performance thin-layer chromatography method that coelutes both the isomers of cefpodoxime proxetil. The proposed method was successfully used to determine the amount of cefpodoxime...
proxetil present in the marketed tablets and self-nanoemulsifying systems. Furthermore, Darji et al. developed simple, precise, accurate and rapid high performance thin layer chromatographic method for the determination of cefpodoxime proxetil in dosage form. The method was validated in terms of linearity, accuracy, precision and specificity. The proposed method can be successfully used to determine the drug content in marketed formulation. Also a simple, selective, precise and stability-indicating high-performance thin-layer chromatographic method for analysis of cefpodoxime proxetil both in bulk and in pharmaceutical formulation has been developed and validated by Jain et al. They concluded that the method can be used to determine the purity of the drug available from various sources by detecting the related impurities.

Camus et al. described a selective HPLC method for the determination of cefpodoxime levels in plasma and sinus mucosa. The method was used to study the diffusion of cefpodoxime in sinus mucosa. Also, Papich et al. determined the effect of protein binding on the pharmacokinetics and distribution from plasma to interstitial fluid of cephalaxin and cefpodoxime proxetil in dogs. Plasma and interstitial fluid concentrations were analyzed with high-pressure liquid chromatography. Plasma protein binding was measured by use of a microcentrifugation technique. Beside this, other analytical method for the simultaneous determination of β-lactam antibiotics cefmetazole and cefpodoxime proxetil contaminants in non-β-lactam pharmaceuticals was developed by Fukutsu et al. using high performance liquid chromatography-tandem mass spectrometry. Results indicate that no contamination occurred in the manufacturing facility, suggesting that this method would be useful for detecting contamination of non-β-lactam pharmaceuticals with cefmetazole and cefpodoxime proxetil.

Swamy et al. developed three simple, sensitive, accurate and rapid UV/visible spectrophotometric methods for the estimation of cefpodoxime proxetil in bulk drug and pharmaceutical dosage form. Results of the analysis were validated statistically and by recovery studies. Also, Patel and Patel described simple, sensitive, rapid, accurate, precise and cost effective dual wavelength spectrophotometric method for the simultaneous determination of ofloxacin and cefpodoxime proxetil in combined tablet dosage form. Results of analysis have been validated statistically and by recovery studies. Furthermore, Asnani et al. developed and validated specific and accurate UV spectrophotometric method of cefpodoxime proxetil by using different hydrotropic solubilizing agents. The proposed method was new, simple, safe, eco-friendly, economic, accurate, and cost-effective and could be successfully employed in routine analysis. Also, Bicer et al. studied the anaerobic hydrolytic degradation of cefpodoxime proxetil in the presence of UV-light irradiation and in darkness at Britton-Robinson buffer solutions (pH 2.5-11) by cyclic and square-wave voltammetry techniques. They established the best pH storage conditions for cefpodoxime proxetil.

A new simple, precise, accurate and selective RP-HPLC method has been developed and validated for simultaneous estimation of cefpodoxime proxetil and ambroxol hydrochloride in tablet dosage form by Abirami and Vetrichelvan. They reported that the proposed method can be used for routine analysis of both these drugs simultaneously in their combined dosage form. The proposed method provided reliable assay results with short analysis time, using mobile phase acetonitrile: methanol: water pH-5 with orthophosphoric acid in the ratio of 30:50:20 v/v/v. In addition, Kotkar et al. developed and validated a new simple, precise, accurate and selective RP-HPLC method for simultaneous estimation of cefpodoxime proxetil and ambroxol hydrochloride in tablet dosage form. The proposed method could be used for routine analysis of both these drugs simultaneously in their combined dosage form. The method was validated as per ICH guidelines.

A simple, rapid, accurate and precise spectrophotometric method has been developed by Patil and Chaudari for simultaneous estimation of cefpodoxime proxetil and ofloxacin from tablet dosage form. The proposed method was applied for pharmaceutical formulation and % label claim for cefpodoxime proxetil and ofloxacin was found to be 99.81 and 103.5, respectively. In addition, Patel and Patel described simple, sensitive, rapid, accurate, precise and economical first order derivative spectrophotometric method for the
simultaneous determination of dicloxacillin sodium and cefpodoxime proxetil in combined tablet dosage form. Result of the analysis of pharmaceutical formulation by the proposed method is highly reproducible and reliable and it was in good agreement with the label claim of the drug. The method can be used for the routine analysis of the dicloxacillin sodium and cefpodoxime proxetil in combined dosage form without any interference of excipients.

Fukutsu et al. demonstrated application of the HPLC hyphenated techniques of LC-MS, LC-NMR and solvent-elimination LC-IR by the identification of the degradation products of a third generation cephalosporin antibiotic, cefpodoxime proxetil in solid state, drug formulation and solution. The degradation products were successfully identified without complicated isolation or purification processes. Later, Singh et al. developed and validated simple, accurate, precise and sensitive ultraviolet spectrophotometric and reversed-phase high-performance liquid chromatography methods for simultaneous estimation of clavulanate potassium and cefpodoxime proxetil in combined tablet dosage form. Spectrophotometric and RP-HPLC methods have been successfully applied for the analysis of the drug in a pharmaceutical formulation and results of analysis were validated statistically and by recovery studies. Also, development of a sensitive and economic stability indicating high performance liquid chromatographic method for the determination of cefpodoxime proxetil as bulk drug and as pharmaceutical formulation was described by Mathew et al. The most interesting fact was that the method could separate the R and S isomers without the use of a chiral column or a chiral selector. In addition, Kakumanu et al. explained the development and validation of simple and reliable isomer specific liquid chromatographic method for the quantitative determination of cefpodoxime proxetil in rat in situ intestinal perfusate sample. Results of intra- and inter-day validation (n = 3) showed the method to be efficient and the same was applied in an in situ permeability study conducted for cefpodoxime proxetil in rats.

Patel and Patel described simple, sensitive, rapid, accurate, precise and economical Q-absorbance ratio method for the simultaneous determination of cefpodoxime proxetil and ofloxacin in combined tablet dosage form. Absorbance ratio method used the ratio of absorbances at two selected wavelengths, one which is an isoabsorptive point and other being the λ-max of one of the two components. In addition, Shah et al. developed an economically spectrophotometry method based on the simultaneous equations for analysis of cefpodoxime proxetil and ofloxacin using methanol as solvent. Also, Patel et al. described simple, sensitive, rapid, accurate, precise and economical first derivative spectrophotometric method for the simultaneous determination of ofloxacin and cefpodoxime proxetil in combined tablet dosage form. The derivative spectrophotometric method was based on the determination of both the drugs at their respective zero crossing point. Furthermore, Kavar et al. described simple, sensitive, rapid, accurate, precise and economical Q-absorbance ratio method for the simultaneous determination of ofloxacin and cefpodoxime proxetil in combined tablet dosage form. The developed spectrophotometric method was validated as per ICH guidelines. In addition two accurate, precise, sensitive and economical procedures for simultaneous estimation of cefpodoxime proxetil and potassium clavulanate in tablet dosage form have been developed by Gandhi et al. Estimation of potassium clavulanate has been carried out after correction for absorbance of cefpodoxime proxetil at 218 nm. The second method was based on first order derivative spectroscopy.

Arora et al. studied thermal and dissolution aspects of cefpodoxime proxetil drug and tablets. The thermal rate constant and dissolution rate constant were correlated graphically and found to have very good correlation. Moreover, four different, accurate, sensitive and reproducible stability-indicating methods for the determination of cefpodoxime proxetil in the presence of its acid and alkaline degradation products were presented by Laila et al. Results obtained by applying the proposed methods were statistically analyzed and compared with those obtained by the official method. The suggested methods was simple, fast and could be used in routine and quality control analysis of intact cefpodoxime proxetil in raw material and
pharmaceutical formulations without interference of degradation products or excipients. Also, Madgulkar et al.\textsuperscript{38} compared the \textit{in vitro} dissolution profiles of solid dispersion of cefpodoxime proxetil with PEG 6000, with those of pure drug and physical mixture of cefpodoxime proxetil and PEG 6000. Results showed that model-dependent methods were more discriminative than model-independent methods.

Electrochemical reduction behavior of cephalosporins, cefixime and cefpodoxime proxetil have been studied by Reddy et al.\textsuperscript{39} using different voltammetric techniques in Britton-Robinson buffer system. A differential pulse voltammetric method has been developed for the determination of these drugs in pharmaceutical formulations and urine samples. Moreover, Aleksic et al.\textsuperscript{40} studied adsorptive properties of cefpodoxime proxetil as a tool for a new method of its determination in urine. Validated adsorptive stripping differential pulse voltammetry was applied for the determination of low concentration of cefpodoxime proxetil at pH 3.5 and 9.0, where best pronounced adsorption effects were observed. The proposed method was tested for cefpodoxime proxetil determination in spiked urine samples, enabling determination of low concentrations of cefpodoxime proxetil.

**Pharmacokinetic aspects**

Pharmacokinetic characteristics namely absorption, distribution, metabolism and elimination of cefpodoxime proxetil are described in the following section.

**Absorption**

Cefpodoxime proxetil is absorbed and de-esterified \textit{in vivo} to release its active metabolite, cefpodoxime, which has $\approx 50\%$ systematic availability. Peak plasma concentration ($C_{\text{max}}$) of cefpodoxime were achieved approximately 2.0 to 3.1 h after oral administration of cefpodoxime proxetil to healthy volunteers; $C_{\text{max}}$ appears to be slightly higher in patients with renal failure or elderly patients with respiratory disease\textsuperscript{11}. Approximately 50\% of the administered cefpodoxime doses absorbed systemically, over the recommended dosing range (100 to 400 mg), approximately 29 to 33\% of the administered cefpodoxime dose excrete unchanged in the urine in 12 hrs\textsuperscript{2,41,42}.

**Distribution**

Cefpodoxime is extensively distributed throughout tissues and fluids of the respiratory tract; for 7-12 h after a single oral dose of cefpodoxime 100 or 200 mg, the concentrations of the drug achieved in upper (tonsils) or lower respiratory tract tissues (bronchial mucosa, lung parenchyma, pleural fluid), were greater than or equivalent to the MIC\textsubscript{90} for common respiratory tract pathogens\textsuperscript{11}. Binding of cefpodoxime to human plasma or serum protein is low (18 to 23\%), suggesting that cefpodoxime should readily transfer across the capillary lining into tissues\textsuperscript{43}. Cefpodoxime is generally well distributed to relevant tissues and fluids\textsuperscript{44}.

**Metabolism**

Once cefpodoxime reaches the systemic circulation, further minimal metabolism occurs and the drug is eliminated primarily by renal excretion\textsuperscript{11}.

**Elimination**

Clearance of cefpodoxime is reduced in proportion to creatinine clearance (CL\textsubscript{cr}) and dosage restrictions may be necessary in patients with CL\textsubscript{cr} values below 3.0 L/h\textsuperscript{11}. About 29\% to 33\% of the absorbed dose is excreted unchanged in the urine in 12 h. The $t_{1/2}$ is 2.09 to 2.84 h\textsuperscript{42}. As expected for a drug eliminated primarily by renal excretion, the disposition of cefpodoxime is altered in patients with impaired renal function; the half-life increases, while apparent plasma clearance and renal clearance decrease\textsuperscript{43}. Excretion of unchanged cefpodoxime in the urine is the primary route of elimination of the drug.
of cefpodoxime appears to be age-dependent, with mean clearance values higher (0.57 L/h/kg) in children less than 5 years of age than in older children (0.36 L/h/kg). Various pharmacokinetic profile of cefpodoxime proxetil are summarized in Table 1.

Table 1: Pharmacokinetic profile of cefpodoxime proxetil

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bioavailability</td>
<td>50%</td>
</tr>
<tr>
<td>Average peak plasma conc.</td>
<td>1.0 to 4.5 mg/L</td>
</tr>
<tr>
<td>Time for peak plasma conc.</td>
<td>2.0 to 3.1 hr</td>
</tr>
<tr>
<td>Half-life (t½)</td>
<td>1.9 to 2.8 hr</td>
</tr>
<tr>
<td>Elimination</td>
<td>Renal clearance</td>
</tr>
</tbody>
</table>

Clinical aspects

Cefpodoxime proxetil is a semi-synthetic antibiotic of the cephalosporin class. Important findings from various clinical studies have been summarized here.

Eugenie et al. investigated oral cephalosporin, cefpodoxime proxetil, which possesses characteristics of the third-generation cephalosporins, in large numbers of patients with upper and lower respiratory tract infections, urinary tract infections or skin and soft tissue infections. The international clinical experience with this drug has confirmed its efficacy in treating pharyngotonsillitis with 97% to 100% success rates in adults, and 92% to 100% in pediatric patients. In 7351 patients in the international experience, cefpodoxime proxetil has proven efficacious and well tolerated, and therefore, should be added to the antibacterial armamentarium for use in community-acquired infections and in hospitals for follow-up treatment after initial parenteral therapy. Also, Sarubbi et al. studied in vitro activity of cefpodoxime proxetil against clinical isolates of Branhamella catarrhalis. Moreover, the pharmacokinetics, bacteriological and clinical efficacy, and safety of the suspension formulation of cefpodoxime proxetil, an oral cephalosporin antibacterial were evaluated in paediatric patients with various infections by Fujii. With single doses of 3 and 6 mg/kg (cefpodoxime equivalent) a dose response was evident in the serum concentration values. Side effects occurred in 17 (2.29%) patients, and transient and reversible abnormal laboratory values were found in a few patients. Furthermore, Muller-serieys C et al. investigated penetration of cefpodoxime proxetil in lung parenchyma and epithelial lining fluid of noninfected patients. The pulmonary disposition of cefpodoxime was studied in 12 patients with pulmonary opacities after a single oral dose of 260 mg of cefpodoxime proxetil, which is equivalent to 200 mg of cefpodoxime. Concentrations in lung parenchyma 6 h after dosing were at least equal to or above the MICs for 90% of the strains of most organisms commonly found in respiratory tract infections, whereas data for epithelial lining fluid suggest levels of drug insufficient to inhibit bacteria.

Shakur et al. evaluated clinical and bacteriological efficacy of cefpodoxime proxetil in typhoid fever in comparison to cefixime. They assessed 140 children with suspected typhoid fever. Fulfilling inclusion criteria finally 40 culture confirmed typhoid fever were allocated in randomized double blind clinical trial to receive therapy with either oral cefpodoxime proxetil or oral cefixime for 10 days. The clinical efficacy was similar in the two groups with only 2 (one in each group) clinical failures and all showing bacteriological eradication on subsequent blood culture. Cefpodoxime proxetil reduced the treatment cost by 33% in comparison to cefixime. They suggested that cefpodoxime proxetil is effective, safe and cheaper oral option for treatment of typhoid fever in children. Beside this, Takasugi et al. evaluated the
usefulness of cefpodoxime proxetil in the treatment of puerperal infection. Results suggested that cefpodoxime proxetil, with its good transfer to the lochia and its potent antimicrobial activity is a promising drug for the prophylactic and therapeutic treatment of puerperal infections caused by susceptible organisms. As well Hendrickson and North\textsuperscript{51} carried out studies to evaluate the economic benefit associated with the early conversion of therapy from intravenous ceftriaxone to the comparable oral third-generation cephalosporin, cefpodoxime proxetil. Pharmacist intervention and cefpodoxime step-down therapy were associated with decreased overall antibiotic costs in our intravenous-to-oral program.

Novak et al.\textsuperscript{52} studied orally administered cefpodoxime proxetil for treatment of uncomplicated gonococcal urethritis in males. An open-label, dose-response study of cefpodoxime proxetil, an expanded-spectrum cephalosporin was conducted with 58 males with uncomplicated \textit{Neisseria gonorrhoeae} infections with single doses of 600, 400, 200, 100, or 50 mg of cefpodoxime proxetil administered orally by tablet. Results revealed that single oral doses of cefpodoxime proxetil are effective and well-tolerated treatment for uncomplicated \textit{Neisseria gonorrhoeae} infection in males at doses as low as 50 mg. Furthermore, clinical efficacy was examined by Kasagi et al.\textsuperscript{53} for oral cepham antibiotic, cefpodoxime proxetil dry syrup in the treatment of various acute infections in the field of pediatrics. Furthermore, pharmacokinetic and clinical studies on cefpodoxime proxetil dry syrup in the field of pediatrics were carried out by Motohiro \textit{et al}.\textsuperscript{54}. Also, a multicentre open-label, randomized trial was performed by Macloughlin et al.\textsuperscript{55} to compare the efficacy and safety of cefpodoxime proxetil (bd) and cefaclor (tds) in the treatment of acute otitis media in children. The less frequent dosing schedule of cefpodoxime (bd) compared with cefaclor (tds) appears to be more convenient for the treatment of the infections in children.

Clinical studies were also carried out by Portier et al.\textsuperscript{56}, where a total of 220 adults and children > 10 years old (mean 29.5 ± 11.7 years) with pharyngitis/tonsillitis were randomized to receive either cefpodoxime proxetil 100 mg bid for 5 days (\(n = 113\)) or phenoxy methyl penicillin, 600 mg tid for 10 days (\(n = 107\)). At the end of treatment of 166 evaluable patients, a satisfactory clinical response was obtained in 85/88 (96.6\%) patients treated with cefpodoxime proxetil and in 75/78 (96.1\%) treated with phenoxy methyl penicillin. The shorter duration of therapy, in conjunction with demonstrated clinical and bacteriological efficacy that is equivalent to standard therapy, make cefpodoxime proxetil an acceptable alternative for the treatment of group A \(\beta\)-hemolytic streptococci pharyngitis/tonsillitis. Furthermore, clinical studies were carried out by Cherni \textit{et al}.\textsuperscript{57} in which one hundred fifty-seven dogs with bacterial pyoderma were allocated randomly to receive 5 mg/Kg oral cefpodoxime proxetil once daily or 26.4 mg/Kg oral cephalaxin twice daily for 28 or 42 days. One hundred twenty-nine dogs (63 cefpodoxime proxetil, 66 cephalaxin) were included in the efficacy evaluation. Cefpodoxime proxetil administered once daily for 28 or 42 days was safe and effective against canine bacterial pyoderma. Moreover, Awad\textsuperscript{58} evaluated the efficacy and safety of fixed dose combination of cefpodoxime proxetil and potassium clavulanate in comparison with cefuroxime axetil in patients with lower respiratory tract infections. The fixed dose combination of cefpodoxime proxetil 200 mg and potassium clavulanate 125 mg in comparison with cefuroxime axetil 500 mg showed improvement in the cure of respiratory tract infections.

Bairamis \textit{et al}.\textsuperscript{59} studied concentrations of cefpodoxime in plasma, adenoid, and tonsillar tissue after repeated administrations of cefpodoxime proxetil in children. Cefpodoxime proxetil was administered to 36 children undergoing tonsillectomy, adenoidec tomy or both. It was very well tolerated and also it was suggested the possibility of twice-daily administration. Another clinical study was performed by Kavatha \textit{et al}.\textsuperscript{60} on cefpodoxime proxetil versus trimethoprim-sulfamethoxazole for short-term therapy of uncomplicated acute cystitis in women. One hundred sixty-three women with uncomplicated acute lower urinary tract infections were included in a multicenter randomized study comparing cefpodoxime-proxetil (one 100-mg tablet twice daily) with trimethoprim-sulfamethoxazole (one double-strength tablet [160/800
mg] twice daily) for 3 days. It was concluded that cefpodoxime proxetil treatment for 3 days was as safe and effective as trimethoprim-sulfamethoxazole for 3 days for the treatment of uncomplicated acute cystitis in women. Also, the effect of food on absorption of cefpodoxime proxetil oral suspension in adults was studied by Borin and Forbes. The effect of a high-fat meal on absorption of a 200-mg dose of cefpodoxime proxetil oral suspension was evaluated in 20 healthy, male volunteers in a randomized, two-way crossover study.

**Drug interactions**

The interactions of cefpodoxime proxetil with various interactants are summarized in Table 2.

**Table 2: Drug interactions of cefpodoxime proxetil**

<table>
<thead>
<tr>
<th>Interactant</th>
<th>Interaction effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antacids or H₂ blockers</td>
<td>Reduced cefpodoxime proxetil peak blood levels and the extent of absorption</td>
</tr>
<tr>
<td>Probenecid</td>
<td>Effectively decreases excretion and increases systemic level of the drug</td>
</tr>
<tr>
<td>Potassium clavulanate</td>
<td>Showed higher clinical cure and improvement in the symptoms of lower respiratory tract infections</td>
</tr>
<tr>
<td>Propantheline</td>
<td>Causes slight delay in drug absorption; however, no effect on the extent of absorption</td>
</tr>
<tr>
<td>Anisotropine methylbromide</td>
<td>Slight increase in the extent of absorption</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>No effect on the extent or rate of cefpodoxime proxetil absorption</td>
</tr>
</tbody>
</table>

**Adverse effects**

The use and specifically overuse of cephalosporins has been associated with adverse drug reactions, ranging from rashes and diarrhea to anaphylaxis, serious cutaneous adverse reactions, hemolytic anemia, nephropathy, *Clostridium difficile* infection, and death. Renal dysfunction has been reported after cephalosporin use, with transient increases in blood urea nitrogen and serum creatinine levels. Adverse events thought possibly or probably related to cefpodoxime proxetil that occurred in less than 1% of patients includes fungal infections, abdominal distention, malaise, fatigue, asthenia, fever, chills, generalized pain, abnormal microbiological tests, allergic reaction, facial edema, bacterial infections, parasitic infections, localized edema and localized pain. Some of the other possible adverse effects caused by cefpodoxime proxetil are vomiting, dyspepsia, dry mouth, flatulence, decreased appetite, constipation, oral moniliasis, anorexia, gastritis, mouth ulcers, gastrointestinal disorders, increased thirst, oral lesions, dry throat etc.

**CONCLUSION**

Significant pharmacological interventions, pharmacokinetic aspects along with clinical data of cefpodoxime proxetil have been described in this paper. Various important analytical methodologies for its determination or identification in different formulations and biological fluids have also been discussed. Cefpodoxime proxetil has emerged as a promising and efficacious drug in the management of various common bacterial infections. It is emphasized that further scientific advancements in pharmacology,
pharmaceutical technology and analytical techniques are still needed to optimally harness the therapeutic benefits of this third generation cephalosporin.

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