Original Article

Development and validation of spectrophotometric method of cefpodoxime proxetil using hydrotropic solubilizing agents

Abstract

Purpose: To develop and validate specific and accurate UV spectrophotometric method of cefpodoxime proxetil by using different hydrotropic solubilizing agents. **Materials and Methods:** The present study deals with spectrophotometric analysis of cefpodoxime proxetil by utilizing 4 different hydrotropic agents such as ammonium acetate (6 M), sodium citrate (1.25 M), sodium gycinate (1 M), sodium chloride (1 M), and urea (1 M). **Results**: From different hydrotropic agents, urea showed best aqueous solubility of cefpodoxime proxetil. The linearity was observed in the concentration range of 10-120 μg/ml. The method was validated and found to be precise. Accuracy (percent recovery) for cefpodoxime proxetil was found to be 99.82 ± 0.106. **Conclusion:** Urea as hydrotropic agent showed best aqueous solubility of cefpodoxime proxetil, which can be used as solubilizing agent. The proposed method is new, simple, safe, eco-friendly, economic, accurate, and cost-effective and can be successfully employed in routine analysis.

Key words: Eco-friendly, hydrotropic solubilization, safe, spectrophotometric, urea

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INTRODUCTION

Cefpodoxime proxetil is an orally-absorbed prodrug of cefpodoxime, an extended-spectrum, semi-synthetic cephalosporin developed by Sankyo Co. Ltd Japan. Cefpodoxime proxetil, chemically a relatively new broad-spectrum third-generation cephalosporin, has very good *in vitro* activity against *Enterobacteriaceae, Hemophilus spp.*, and *Moraxella spp.*, including fl-lactamase producers and many strains resistant to other oral agents. It also has activity against gram-positive bacteria, especially against streptococci. Cefpodoxime proxetil [Figure 1] chemically is (RS)- 1-(isopropoxycarbonyloxy)-ethyl- (+)-(6R,7R)-7-[2-(2-amino-4-thiazolyl-2- { (Z)-methoxy-imino} acetamido]-3-methoxymethyl-8-oxo-5-thia-l-azabicyclo- [4.2.0]oct-2-ene-2-carboxylate.[1]

It is very soluble in acetonitrile or methanol, freely soluble in dehydrated ethanol, slightly soluble in ether and very slightly soluble in water. Literature survey revealed that RP HPLC[2] and HPTLC[3] re the methods available for its estimation. Cefpodoxime proxetil is slightly soluble in water. Thus, hydrotropy can be used to increase the solubility. The proposed methods utilize solutions of non-toxic, non-volatile hydrotropic agents, which are the substitutes and minimizes the use of organic solvents, which are costlier, toxic, and source of pollutant.

The term "Hydrotropy" has been used to designate the increase in aqueous solubility of various poorly water-soluble compounds due to presence of a large amount of additives. Still the mechanism of hydrotropy is not understood very clearly. The concept of hydrotropy was first introduced in 1916 by Neuberg. According to his definition, hydrotropes are metal salts of organic acids, which at fairly high concentration increase the solubility of poorly water-soluble compounds.[4] On the other hand, Poochikian, Gradock (1979)

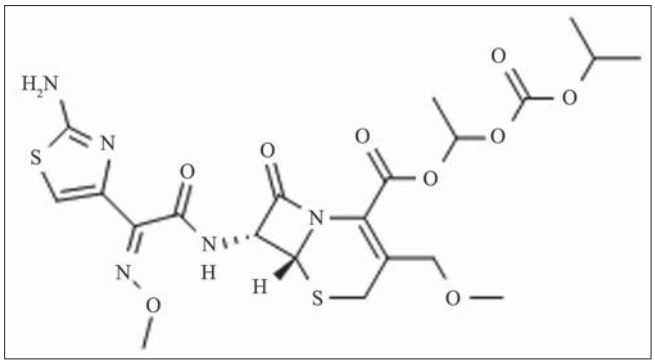

Figure 1: Structure of Cefpodoxime proxetil

studied that planarity of the hydrophobic part has been emphasized as an important factor in the mechanism of hydrotropic solubilization.[5] Hence, it seems rational to propose that molecules with a planar hydrophobic part and a polar group, which is not necessarily anionic, can act as hydrotropic agents. Saleh *et al*, in 1985, extended the definition of a hydrotrope and said that it can be cationic, anionic, or a neutral molecule, provided it has a hydrophobic as well as a hydrophilic group.[6] Coffman and Kildsig studied the mechanism of hydrotropic solubilization using the riboflavin–nicotinamide system. They concluded that the complexation of nicotinamide and riboflavin did not occur because nicotinamide is not able to quench riboflavin fluorescence and does not produce significant UV- spectral changes.[7] Literature survey revealed that the hydrotropes can be used to enhance the solubility of poorly-soluble drugs, same as that of surfactants forming a term critical hydrotrope concentration (CHC) has been used in consonant with the critical micelle concentration.[8-13] Hydrotropic solutions can also be used as co-solvents, in solid dispersion technology,[14] nanotechnology, parentral preparations,[15] extraction purpose for solubilize[16] poorly water-soluble drugs. When hydrotropes are added to aqueous surfactants or to polymer solutions, they produce strong synergistic effects.

MATERIALS AND METHODS

Pharmaceutical grade cefpodoxime proxetil was kindly supplied as a gift sample by Orchid Pharmaceutical, Chennai. Tablets of cefpodoxime proxetil were procured from local market. Hydrotropic agents used were ammonium acetate, sodium citrate, sodium glycinate, sodium chloride and were of analytical grade.

Instrument

Instrument used were Schimadzu 1800 double beam UV/Visible Spectrophotometer and schimadzu 1600 analytical balance, Japan

Preliminary solubility study of cefpodoxime proxetil

In the solubility studies, it was found that there was more than 5-fold enhancement in the solubility of cefpodoxime proxetil in 1 M urea solution in comparison to its solubility in distilled water, ammonium acetate (6 M), sodium Citrate (1.25 M), sodium glycinate (1 M), sodium chloride (1 M).

Preparation of standard stock solution

Standard drug solution of cefpodoxime proxetil was prepared by dissolving 10 mg cefpodoxime proxetil in 10 ml 1 M urea. This solution was then sonicated for 15 mins and filtered through Whatmann filter Paper≠41.

Preparation of calibration curve

Aliquots of 1–12 ml portion of stock solutions were transferred to series of 100 ml volumetric flasks, and volume made up to mark with distilled water. Solutions were scanned in the range of 400-200 nm against blank. The absorption maxima were found to be at 231 nm against blank. The calibration curve was plotted. The optical characteristics are summarized in Table 1.

Preparation of sample solution

The proposed method was applied to analyze commercially available cefpodoxime proxetil tablet. Ten tablets were weighed and powdered. The amount of tablet powder equivalent to 10 mg of cefpodoxime proxetil was weighed accurately and transferred to 10 ml volumetric flask, and then, 10 ml 1 M urea was added and kept for sonication for 15 min. The solution was then filtered through

Table 1: Calibration curve of cefpodoxime proxetil

Concentration (µg/ml)	Absorbance
10	0.13
20	0.20
30	0.32
40	0.45
50	0.56
60	0.68
70	0.74
80	0.81
90	0.97
100	1.04
110	1.17
120	1.28