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Hydrotropic Solubilization in Spectrophotometric Analysis of Cefixime in Solid Dosage Form

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Various techniques are employed to enhance the aqueous solubility of poorly water-soluble drugs and hydrotropic solubilization is one of them. In the present investigation, cefixime has been selected as a poorly water-soluble model drug. There were more than 120 and 240 fold enhancements in aqueous solubility of cefixime by 8 M potassium acetate and 6 M ammonium acetate solutions, respectively as compared to aqueous solubility. These hydrotropic agents were employed to solubilize the drug from the fine powder of tablet formulations. The selected λ_{max} for spectrophotometric estimation was 288 nm. The hydrotropic agents and the additives used in the manufacturing of tablets did not interfere in the analysis.

Key Words: Hydrotropy, Cefixime, Potassium acetate, Ammonium acetate, Spectroscopy.

INTRODUCTION

The term hydrotropy has been used to designate the increase in solubility of various poorly water-soluble compounds due to presence of a large amount of additives. Concentrated aqueous hydrotropic solutions of urea, nicotinamide, sodium benzoate, sodium salicylate, sodium acetate and sodium citrate have been observed to enhance the aqueous solubility of many poorly water-soluble drugs[1-14].

Maheshwari has analyzed several poorly water soluble drugs, *viz.*, frusemide[1], ketoprofen[2] and tinidazole[3] by use of hydrotropic solubilization technique. Maheshwari *et al.* have developed new analytical methods based on hydrotropic solubilization phenomenon for poorly water-soluble drugs like aceclofenec[5], metronidazole[6], norfloxacin[6], tinidazole[6], nalidixic acid[6] and hydrochlorthiazide[7].

There was tremendous increase in aqueous solubility of cefixime in 8 M potassium acetate and 6 M ammonium acetate solutions, respectively. Thus, it was thought worthwhile to solubilize the poorly water-soluble cefixime from fine powder of its tablets with the help of these solutions to carryout its spectrophotometric analysis. Chemically cefixime is, 7[2(2-amino-4-thiazolyl)-2-(carboxymethoxyimino)acetamido]-3-vinyl-3-cephem-4 carboxylic acid.

EXPERIMENTAL

Cefixime trihydrate drug sample was supplied by Alkem Laboratories Limited, Mumbai as gift sample. A Shimadzu UV-Visible recording spectrophotometer (model-UV 160A) with 1 cm matched silica cells was used for spectrophotometric analysis. Commercial tablets of cefixime were procured from the market. All chemicals used were of analytical grade.

Calibration curves: 100 mg cefixime trihydrate was accurately weighed and transferred to a 50 mL volumetric flask. To this, 10 mL of 8 M potassium acetate solution was added and flask was shaken to solubilize the drug. The volume was made up to the mark with distilled water. This stock solution (2000 mcg/mL) was further diluted with distilled water to obtain various dilutions containing 5, 10, 15, 20, 25 and 30 mcg/mL. Absorbances were noted at 288 nm (λ_{max}) against reagent blanks to get calibration curve. Similar method was used with 6 M ammonium acetate solution to get calibration curve.

Preliminary solubility studies of cefixime trihydrate: Determination of solubilities of the drug in 8 M potassium acetate, 6 M ammonium acetate solution and distilled water were carried out at 28 ± 1 ºC. Sufficient amount of drug was added to screw capped 30 mL glass vials containing hydrotropic solution and distilled water. The vials were shaken mechanically for 12 h at 28 ± 1 ºC in orbital flask shaker (Khera Instrument Pvt. Ltd., India). The solutions were allowed to equilibrate for next 24 h and then contrifuged for 5 min at 2000 rpm. The supernatant of each vial was filtered through Whatmann filter paper no. 41. Filtrates were diluted suitably and analyzed spectrophotometrically to determine the solubilities.

Analysis of tablet formulations of cefixime by the proposed method using 8 M potassium acetate solution: 20 Tablets were weighed and powdered. Powder equivalent to 100 mg cefixime was transferred to a 50 mL volumetric flask containing 10 mL of 8 M potassium acetate solution and shaken for about 5 min to solubilize the drug. The volume was then made up to the mark with distilled water. It was filtered through Whatmann filter paper no. 41. Filtered extract was appropriately diluted with distilled water and absorbance was noted at λ_{max} 288 nm against reagent blank and drug content was calculated (Table-1).

Recovery studies: To study the accuracy, reproducibility and the precision of the proposed method, recovery experiments were carried out. For recovery studies 10 and 15 mg of cefixime (pure drug) were added to tablet powder equivalent to 100 mg cefixime. Procedure of analysis was same using 8 M potassium acetate solution. The per cent recoveries were calculated and reported in Table-2.

TABLE-1
ANALYSIS DATA OF CEFIXIME TABLET FORMULATIONS WITH STATISTICAL EVALUTION

Tablet formulation	Label claim / tablet (mg)	Method	Per cent label claim estimated* (mean ± SD)	Per cent coefficient of variation	Standard error
I	100	PAM	100.21 ± 1.507	1.504	0.615
	100	AAM	99.47 ± 2.236	2.248	0.913
II	200	PAM	99.36 ± 1.598	1.548	0.632
	200	AAM	99.57 ± 1.681	1.688	0.686

*Average of six determinations; PAM = Potassium acetate method; AAM = Ammonium acetate method

TABLE-2
RECOVERY STUDY FOR SPIKED CONCENTRATION OF CEFIXIME ADDED TO THE PREANLYZED TABLET POWDER

Tablet formulation	Amount of cefixime present in preanalyzed tablet powder taken (mg)	Amount of pure cefixime added (mg)	Method	Per cent recovery estimated* (mean ± SD)	Per cent coefficient of variation	Standard error
I	100	10	PAM	99.33 ± 1.223	1.231	0.499
	100	15	PAM	98.76 ± 0.902	0.913	0.368
	100	10	AAM	99.04 ± 1.296	1.308	0.529
	100	15	AAM	100.73 ± 0.887	0.881	0.362
II	100	10	PAM	101.26 ± 2.013	1.988	0.822
	100	15	PAM	99.77 ± 0.808	0.810	0.330
	100	10	AAM	100.67 ± 1.839	1.827	0.751
	100	15	AAM	98.75 ± 0.938	0.950	0.383

*Average of six determination; PAM = Potassium acetate method; AAM = Ammonium acetate method

Analysis of tablet formulations of cefixime by the proposed method using 6 M ammonium acetate solution: Powder equivalent to 100 mg cefixime was transferred to a 50 mL volumetric flask containing 10 mL of 6 M ammonium acetate solution and shaken for about 5 min to solubilize the drug. Then volume was made up to the mark with distilled water. It was filtered through Whatmann filter paper no. 41. Filtered extract was appropriately diluted with distilled water and absorbance was noted at λ_{max} 288 nm against reagent blank and drug content was calculated (Table-1).

Recovery studies: To study the accuracy, reproducibility and the precision of the proposed method, recovery experiments were carried out. For recovery studies 10 and 15 mg of cefixime (pure drug) were added to tablet powder equivalent to 100 mg cefixime. Procedure of analysis was same using 6 M ammonium acetate solution. The percent recoveries were calculated and reported in Table-2.

RESULTS AND DISCUSSION

In solubility determination studies, it was found that there were more than 120 and 240 fold enhancement in the solubility of cefixime in 8 M potassium acetate and ammonium acetate solution as compared to solubility in distilled water. Therefore these hydrotropic solutions were used to extract out cefixime from fine powders of tablet formulations. Table-1 shows that per cent label claims were 100.21 ± 1.507 and 99.36 ± 1.548 in case of proposed method employing 8 M potassium acetate solution and per cent label claims were 99.47 ± 2.236 and 99.57 ± 1.681 in case of proposed method employing 6 M ammonium acetate solution. Since per cent label claims are very close to 100 and values of standard deviation, per cent coeffcient of variation and standard error are satisfactorily low, therefore, these indicate the accuracies of the proposed methods.

Accuracy, precision and reproducibility of the proposed methods were further confirmed by per cent recovery studies.The results of recovery studies, presented in Table-2 indicated that per cent recoveries ranged from 98.75 ± 0.902 to 101.26 ± 2.013 and 98.75 ± 0.938 to 100.73 ± 0.887 in case of proposed method employing 8 M potassium acetate and 6 M ammonium acetate solutions, respectively.

Per cent recoveries estimated in recovery studies were also very close to 100 indicating the accuracy of the proposed methods. Values of standard deviation, per cent coefficient of variation and standard error were satisfactorily low and confirmed the accuracy.

Conclusion

Most of the organic solvents like ethanol, methanol, acetonitrile, hexane, cyclohexane, diethyl ether, chloroform and toluene find wide use in spectrophotometic analysis of poorly water-soluble drugs. Most of these organic solvents are toxic in nature, costlier and responsible for pollution. Inaccuracy in spectrophotometric estimation due to volatility is another drawback of organic solvents. Since potassium acetate and ammonium acetate do not interfere above 245 nm, therefore poorly water-soluble drugs having λ_{max} above 245 nm, can be easily estimated by the proposed method, avoiding the use of organic solvents. It is, thus, concluded that the proposed method is new, simple, cost-effective, safe, accurate, precise and environmentally friendly. This method can be successfully employed in the routine analysis of cefixime in tablet dosage form.

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