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# Spectrophotometric Analysis of Cefixime Trihydrate Tablets Using Metformin Hydrochloride as Hydrotropic Solubilizing Agent

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A new, simple, cost-effective, environment-friendly, safe, accurate and reproducible method was developed for quantitative analysis of cefixime trihydrate tablets. In the present investigation, 0.5 M metformin hydrochloride (an economic drug) was used as hydrotropic agent for solubilization of poorly water soluble drug cefixime trihydrate to carry out spectrophotometric analysis. The solubility of cefixime trihydrate increased to more than 18-folds. Accuracy and precision of proposed method were confirmed by recovery study. Percent recoveries estimated by proposed methods ranged from 98.33 ± 1.621 to 101.62 ± 2.002, which are very close to 100. Low values of standard deviation, percentage coefficient of variation and standard error further validated the proposed methods.

**Key Words: Hydrotropy, Cefixime trihydrate, Metformin hydrochloride.**

## INTRODUCTION

The term 'hydrotropy' has been used to designate the increase in solubility of various substances due to presence of large amount of additives. Various hydrotropic agents have been used to enhance the aqueous solubility of a large number of drugs[1-13]. Maheshwari[1] has analyzed cefixime (a poorly water-soluble drug) in tablet dosage forms using urea (8 M), sodium acetate (4 M) and sodium citrate (1.25 M) as hydrotropic solubilization agents. Frusemide (a poorly water soluble drug) is analyzed by titrimetric analysis[2] using hydrotropic solution of sodium benzoate (2 M). The same author[3] has developed titrimetric methods to analyze ketoprofen and salicylic acid. Hydrotropic solutions of sodium benzoate (2 M) sodium salicylate (2 M) and sodium acetate (2 M) were employed for ketoprofen. Hydrotropic solutions of urea (8 M), sodium citrate (1.25 M) and sodium benzoate (2 M) were employed in the estimation of salicylic acid. A spectrophotometric method to analyze ketoprofen in tablet dosage form using hydrotropic

solution of sodium acetate (4 M) is also reported in the literature[4]. Maheshwari *et al.*[5] used hydrotropic solution of sodium benzoate (2 M) as solubilizing agent to analyze a poorly water-soluble drug, ofloxacin by spectrophotometric estimation.

Cefixime, a widely used antibiotic, showed poor aqueous solubility. Application of 0.5 M metformin hydrochloride as a hydrotropic agent exhibited more than 18-folds increase in solubility of cefixime trihydrate. Therefore it was thought worthwhile to employ 0.5 M metformin hydrochloride to solubilize cefixime trihydrate for its quantitative estimation spectrophotometrically.

## EXPERIMENTAL

Shimadzu UV/Visible recording spectrophotometer (Model-UV-160A) was used in the spectrophotometric analysis with 1 cm matched silica cells. Gift samples of cefixime trihydrate were obtained from Alkem Laboratories Limited, Mumbai. Formulation I and II of cefixime trihydrate were procured from local market. All other chemicals were of analytical grade. Standard solutions were prepared with 100 mg cefixime, which was solubilized by 20 mL of 0.5 M metformin hydrochloride in a 100 mL volumetric flask. Distilled water was added to make up the volume. This stock solution was further diluted with distilled water to get various dilutions of 5, 10, 15, 20, 25 and 30 mcg/mL. Absorbances were noted at 288 nm against reagent blank. Enhancement in solubility of the drug was more than 18-folds in 0.5 M metformin hydrochloride as compared to its solubility in distilled water.

## RESULTS AND DISCUSSION

**Analysis of commercial tablets of cefixime trihydrate:** 20 Tablets of cefixime trihydrate (formulation-I) were weighed and finely powdered. Powder equivalent to 100 mg of cefixime was taken into 100 mL volumetric flask. 20 mL of 0.5 M metformin hydrochloride solution was taken and shaken properly for 10 min and the volume was made upto the mark with distilled water. The solution was filtered through Whatmann filter paper no. 41. The filtrate was divided into two parts A and B. Part A was kept at room temperature for 24 h to check for its chemical stability and precipitation, if any. Part B was diluted appropriately with distilled water and was analyzed on UV spectrophotometer at 288 nm against reagent blank. Drug content was calculated for part B. It is evident from Table-1 that the mean percentage label claim of formulation I was found to be 98.53. Standard deviation, coefficient of variation and standard error were found to be 2.950, 2.944 and 1.729 respectively. There was no precipitation in part A solution within 24 h. Also part A was analyzed in the same way as part B solution after 24 h. There was no difference in the drug content in part A solution (after 24 h)

and part B (fresh) solution. This study indicates that the solution can be analyzed within 24 h without having any adverse effect on the chemical stability of the drug in presence of metformin hydrochloride. Formulation II was treated in the same way and the mean percentage label claim was found to be 99.18. Standard deviation, co-efficient of variation and standard error was found to be 1.947, 1.963 and 1.124, respectively. The results are presented in Table-1.

TABLE-1
RESULTS OF ANALYSIS OF COMMERCIAL TABLETS OF CEFIXIME TRIHYDRATE WITH STATISTICAL EVALUATION

| Tablet formulation | Label claim tablet | % Label claim estimated (mean ± SD) | % Coefficient of variation | Standard error |
|---|---|---|---|---|
| I | 100 | 98.53 ± 2.950 | 2.994 | 1.729 |
| II | 100 | 99.18 ± 1.947 | 1.963 | 1.124 |

**Recovery study for spiked concentration of cefixime trihydrate added to preanalyzed powder:** In order to evaluate the accuracy, precision and reproducibility of the proposed methods, recovery experiments were carried out by adding a known quantity of cefixime trihydrate bulk drug sample to preanalyzed tablet powder at two levels (10 and 20 mg) and then analyzing them by the same proposed methods. The total amount of the drug was determined and the amount of the added drug was found by difference. The results of recovery studies are presented in Table-2.

TABLE-2
RECOVERY STUDY FOR SPIKED CONCENTRATION OF CEFIXIME TRIHYDRATE ADDED TO PREANALYZED TABLET POWDER

| Tablet formulation | Amount of drug in pre-analyzed tablet powder taken (mg) | Cefixime trihydrate drug sample added (spiked) (mg) | % Recovery estimated (mean ± SD) | % Coefficient of variation | Standard error |
|---|---|---|---|---|---|
| I | 100 | 10 | 98.33±1.621 | 1.648 | 0.936 |
| | | 20 | 99.02±0.984 | 0.994 | 0.568 |
| II | 100 | 10 | 98.77±0.884 | 0.854 | 0.487 |
| | | 20 | 101.26±2.002 | 1.997 | 1.156 |

The study indicates that there is a good agreement between the amounts found by the proposed method and the amounts claimed by the manufacturer. Mean percent label claims are very close to 100, indicating accuracy of the proposed methods. There was no interference of metformin hydrochloride

and commonly used additives used in tablet formulation. Accuracy and reproducibility of the proposed methods were confirmed by recovery studies. Percent recoveries estimated by proposed methods ranged from 98.33 ± 1.621 to 101.26 ± 2.002, which are very close to 100. Low values of standard deviation, percentage coefficient of variation and standard error further validated the proposed methods.

## Conclusion

The proposed method of analysis is new, simple, cost-effective, environmentally friendly, safe, accurate and reproducible. Thus, it also precludes the use of organic solvents, which are costly as well as environmentally unsafe. As there was no interference of metformin hydrochloride in the estimation and it has zero absorbance above 250 nm, there is a definite scope for its use as a solubilizing agent for other poorly water-soluble drugs having $\lambda_{max}$ above 250 nm.

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