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Novel Application of Hydrotropic Solubilization in the Spectrophotometric Analysis of Cephalexin in Solid Dosage Form

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In the present investigation, cephalexin has been selected as a poorly water-soluble model drug. There was more than 6-fold enhancement in aqueous solubility of cephalexin by 8.0 M urea solution (as compared to aqueous solubility). This hydrotropic agent was employed to solubilize the drug from the fine powder of tablet formulations. The selected λ_{max} for spectrophotometric estimation was 262 nm. The hydrotropic agent and the additives used in the manufacture of tablets did not interfere in the analysis. Proposed method is new, rapid, simple, accurate and reproducible. Statistical data prove the accuracy, reproducibility and the precision of the proposed method.

Key Words: Hydrotropy, Cephalexin, Urea, Spectrophotometry.

INTRODUCTION

In hydrotropic solubilization phenomenon, addition of a large amount of a second solute results in an increase in the aqueous solubility of another solute. Concentrated aqueous hydrotropic solutions of urea, nicotinamide, sodium benzoate, sodium salicylate, sodium acetate and sodium citrate have been observed to enhance the aqueous solubilities of many poorly water-soluble drugs.[1-15] Maheshwari *et al.* has developed new analytical methods based on hydrotropic solubilization phenomenon for poorly water-soluble drugs cefixime[1], frusemide[2], ketoprofen[3, 5], salicylic acid[3], tinidazole[4], ofloxacin[6], metronidazole[7], norfloxacin[7], nalidixic acid[7], tinidazole[7] and aceclofenac[8].

There was considerable increase in the solubility of cephalexin (a widely used antibiotic drug) in 8.0 M urea solution (a hydrotropic solution). Therefore, it was thought worthwhile to solubilize the drug present in its tablet powder with the help of 8.0 M urea solution to carry out its spectrophotometric analysis. Chemically, Cephalexin is 7-α-D-phenylglycylamino-3-cephem-4-carboxylic acid monohydrate.

EXPERIMENTAL

Cephalexin was a generous gift by Plethico Pharmaceuticals Ltd., Indore (India). All chemicals used were of analytical grade. A Shimadzu UV-Visible recording spectrophotometer (model-UV 160 A) with 1 cm matched silica cells was used for spectrophotometric analysis. Commercial tablets of cephalexin were procured from the market.

Calibration curve

The standard solution (300 μg/mL) of cephalexin was prepared in distilled water. The standard solution was diluted with distilled water to obtain various dilutions (15, 30, 45, 60, 75, 90 μg/mL). A linear relationship was obtained over the range of 15 to 90 μg/mL for cephalexin (λ_{max} 262 nm).

Preliminary solubility studies of drug

Solubility of cephalexin was determined in distilled water and 8.0 M urea solution at 27 ± 1°C. Enhancement in the solubility of cephalexin in 8.0 M urea solution was more than 6-fold (as compared to its solubility in distilled water).

Analysis of tablet formulations of cephalexin by the proposed method using 8.0 M urea solution

Twenty tablets of cephalexin (formulation-I) were weighed and ground to a fine powder. An accurately weighed powder sample equivalent to 100 mg of cephalexin was transferred to a 100 mL volumetric flask containing 20 mL of 8.0 M urea solution. The flask was shaken for about 10 min to solubilize the drug and the volume was made up to 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 its chemical stability and precipitation, if any. Part B was diluted sufficiently with distilled water and was analyzed on UV spectrophotometer against reagent blank. Drug content of tablet formulation was then calculated (Table-1). After 24 h, the Part A solution was analyzed in the same way as the Part B solution. Same procedure was followed for formulation-II.

TABLE-1
RESULTS OF ANALYSIS OF COMMERCIAL TABLET FORMULATIONS WITH STATISTICAL EVALUATION

Tablet formulation	Label claim (mg)	Per cent label claim estimated* (mean ± S.D.)	Per cent coefficient of variation	Standard error
I	100	98.76 ± 0.875	0.885	0.505
II	100	98.58 ± 1.178	1.180	0.680

*Average of three determimations

Recovery studies

For recovery studies 20 and 50 mg of cephalexin pure drug were added to tablet powder equivalent to 100 mg cephalexin. Procedure of analysis was same using 8.0 M urea solution. The per cent recoveries were calculated and reported in Table-2.

TABLE-2
RECOVERY STUDY FOR SPIKED CONCENTRATION OF CEPHALEXIN ADDED TO THE PREANALYZED DOSAGE FORM

Tablet formulation	Amount standard of drug (mg)	Pure cephalexin added (mg)	Per cent recovery estimated* (mean ± S.D.)	Per cent coefficiant of variation	Error
I	100	20	100.12 ± 2.440	2.430	1.408
	100	40	99.61 ± 0.605	0.607	0.349
II	100	20	98.89 ± 1.290	1.220	0.698
	100	40	99.21 ± 0.926	0.933	0.534

*Average of three determinations.

RESULTS AND DISCUSSION

Results of solubility studies indicate that enhancement in aqueous solubility of cephalexin in 8.0 M urea solution was more than 6-fold as compared to solubility in distilled water. Therefore, this solution was employed to extract out cephalexin from fine powder of tablet formulation. It is evident from Table-1 that per cent label claims ranged from 98.58 ± 1.178 to 98.76 ± 0.875 in case of proposed method employing 8.0 M urea solution. Per cent label claims are very close to 100 with low values of standard deviation, per cent coefficient of variation and standard error, showing the accuracy of the proposed methods.

Accuracy, reproducibility and precision of the proposed methods were further confirmed by per cent recovery values. As evident from Table-2, per cent recovery values ranged from 98.89 ± 1.290 to 100.12 ± 2.440 in case of proposed method employing 8.0 M urea. Per cent recovery values were close to 100 with low values of standard deviation, per cent coefficient of variation and standard error. These results validated the proposed method.

The drug contents in extracts of hydrotropic solution (8.0 M urea) were nearly same during 24 h and also there was no precipitation in 24 h. This indicates that extracts can be analyzed with sufficient accuracy.

Conclusions

Ethanol, methanol, acetonitrile, hexane, cyclohexane, diethyl ether, chloroform, carbon tetrachloride, toluene and acetone have been employed for solubilization of poorly water-soluble drugs for their spectrophotometric analysis. Most of the organic solvents are toxic, costlier and are responsible for pollution. Inaccuracy due to volatility is another drawback of organic solvents. Using poorly water-soluble cephalexin, as a model drug, the present researchers want to

emphasize on the use of hydrotropic solutions as solubilizing agents. Urea does not interfere in the specterophotometric estimation of drugs having λ_{max} above 250 nm. Thus, other poorly water-soluble drugs can be checked for their solubilities in this hydrotropic solution. If they have good solubilities, they can be easily estimated excluding the use of organic solvents provided their λ_{max} is above 250 nm. It is concluded that the proposed method is new, simple cost effective, accurate, safe, free from pollution and precise and can be successfully employed in the routine analysis of cephalexin tablets.

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