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Application of Mixed Hydrotropic Solubilization in Spectrophotometric Estimation of Aceclofenac in Tablets.

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Abstract
Several techniques are used to increase the aqueous solubilities of poorly water-soluble drugs. Hydrotropic solubilization technique is one among them. In the present investigation mixed hydrotropic solubilization phenomenon was employed using the solution of 30% urea and 20% of sodium citrate to estimate poorly water-soluble drug aceclofenac from fine powder and its tablet dosage forms. The solubility of aceclofenac in distilled water was found to be 0.225mg/ml, whereas in the mixture of 30% urea and 20% sodium citrate, the solubility was found to be 19.64mg/ml. The increase in solubility of aceclofenac in the mixture was more than 100 folds. Aceclofenac showed maximum absorbance at 274.5nm. Beer's law was obeyed in the concentration range of 5-40 µg/ml. The estimated label claim was found to be 100.30±1.252mg. The recovery studies revealed that any small change in the drug concentration in the solution could be accurately determined by the proposed method. The co-efficient of variation were not more than 1.0% which confirmed good intermediate precision for the proposed method. The low values of LOD and LOQ indicated good sensitivity of proposed method. Thus the proposed method is new, simple, environmentally friendly, accurate and cost-effective which can be successfully employed in routine analysis of Aceclofenac in tablets.

Key Words
Hydrotropy, aceclofenac, urea, sodium citrate.

Introduction
Hydrotropes are a class of chemical compounds which affect an increased aqueous solubility by several folds to certain solutes which are sparingly soluble in water under normal conditions[1]. This phenomenon termed Hydrotropy can be considered to be a potentially and industrially attractive technique since the observed increase in solubility is much higher than that affected by other solubilization methods[2]. Easy recovery of dissolved solute and possible reuse of hydrotrope solutions makes this method the most attractive one particularly at industrial levels. Increasing the aqueous solubility of insoluble and slightly soluble drugs is major importance[3]. Solvents such as sodium benzoate, sodium salicylate, niacinamide, sodium hydroxide, sodium citrate, and urea have been employed to enhance the aqueous solubility of poorly water-soluble drugs. Most of these organic solvents are toxic, costlier and sources of pollution[4,5,6].

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Various techniques have been employed to enhance the aqueous solubility of poorly water-soluble drugs. Hydrotropic solubilization is one of them. In the present investigation, hydrotropic solubilising agent is 30% of Urea and 20% of Sodium Citrate was employed to solubilise Aceclofenac from its fine powder and tablet form to carry out Spectrophotometric analysis[7]. Most of the chemical entities that are been discovered are lipophilic and have poor aqueous solubility. Because of their low aqueous solubility and high permeability, dissolution from delivery systems forms the rate limiting step in their absorption and systemic bioavailability. Currently number of techniques addressed the poor solubility and dissolution rate of poorly soluble drugs[8]. Aceclofenac has been shown to have potent analgesic and anti-inflammatory activities and due to its preferential cox-2 blockade it has better safety than conventional NSAIDs with respect to adverse effects on gastrointestinal and cardiovascular system[9]. The purpose of this study was to develop a new, simple, accurate, environmental friendly, cost effective, safe, sensitive spectrophotometric method for estimation of aceclofenac in tablet dosage form using hydrotropic solution of mixture of 30 % urea and 20 % sodium citrate.

Materials and Method

Shimadzu UV/Visible recording spectrophotometer (model-UV-1601) with 1cm matched silica cells was employed. Aceclofenac bulk drug sample was purchased from Yarrow chem. Products Ltd, Mumbai. Tablets of aceclofenac were purchased from the local market. All other chemicals and solvents used were of analytical grade.

Experimental method

Preliminary solubility studies of the drug:

Solubility of aceclofenac was determined by saturation aqueous solubility method in mixture of 30 % urea and 20 % sodium citrate and distilled water. An excess amount of drug was added to the 100ml beakers containing mixture of 30 % urea and 20 % sodium citrate and distilled water. The beakers were shaken for 12 hours at 28±1^{0}C. The solutions were filtered through Whatman filter paper #.41, and the resulting filtrates were suitably diluted and analyzed spectrophotometrically against solvent blank.

Preparation of standard stock and calibration curve:

The standard stock solution of Aceclofenac was prepared by dissolving 50mg of drug in 50 ml of mixture (30 %urea and 20 % sodium citrate). From this solution 5ml of solution was taken and diluted to 100ml with distilled water to get a solution containing 50µg/ml and scanned in the entire UV range of 400-200 nm to determine the λ max of the drug. The λ max of aceclofenac was found to be 274.5 nm. Seven working standard solutions for the drug having concentration 5, 10,15,20,25,30 and 40 µg/ml was prepared with distilled water from the stock solution. The absorbances of resulting solutions for the drug were measured at λ max of 274.5nm and a calibration curve was plotted to get the linearity and regression equation.

Analysis of aceclofenac in tablets using mixture of 30 %urea and 20 % sodium citrate:

Twenty tablets were weighed and powdered. Powder equivalent to 100 mg aceclofenac was transferred to a 50 ml volumetric flask containing 40 ml of mixture of 30 %urea and 20 % sodium citrate solution. The flask was shaken for about 5 min to solubilize the drug. Then volume was made up to the mark with distilled water. Solution was filtered through Whatman filter paper #41. Filtrate was divided into two parts, A and B. Part A was kept at room temperature for 24 hours to check the effect on stability of drug in presence of urea and also to note precipitation, if any, during this period. Part B filtrate was appropriately diluted with distilled water and absorbance was noted at 274.5 nm against solvent blank and drug content was calculated. After 48 hours, filtrate of part A was also appropriately diluted with distilled water and analyzed for drug content. There was no precipitation in the filtrate in 48 hours.

Validation of the proposed method Recovery studies:

In order to check the accuracy and reproducibility of the proposed method, recovery studies were conducted. Tablet powder equivalent to100 mg of aceclofenac was transferred to a 50 ml volumetric flask containing 40 ml of mixture of 30 %urea and 20 % sodium citrate solution. Pure aceclofenac drug sample (20 mg) was added to the same volumetric flask. The flask was shaken for 5 mins to solubilize the drug. Then solution was filtered through Whatman filter paper #41. The filtrate was diluted with distilled water appropriately and absorbance was measured at 274.5nm against corresponding reagent blank. Drug content was calculated and % recovery was calculated. Similar procedure was repeated using 40 mg and 80 mg of pure aceclofenac as spiked concentration. The drug contents were determined and % recoveries were estimated.

Precision:

Precision was determined by studying the repeatability and intermediate precision. The standard deviation, coefficient of variance and standard error were calculated for the drug.

Inter- day and Intra- day precision:

The intra-day concentration of the drug was calculated on the same day at an interval of one hour. Whereas the inter day concentration of drug was calculated on three different days within the laboratory conditions.

Linearity:

Appropriate dilutions of standard stock solutions were assayed as per the developed methods. The Beer- Lambert's concentration range was found to be 5-40 µg/ml for the drug. The linearity data was given in Table 3.

Limit of detection (LOD) and Limit of Quantitation (LOQ):

The LOD and LOQ of aceclofenac by the proposed method were determined using calibration standards. LOD and LOQ were calculated as 3.3σ /S and 10σ/S, respectively, where S is the slope of the calibration curve and σ is the standard deviation of response. The result was shown in Table 3.

Results and Discussion

The results of solubility studies indicated that aqueous solubility of aceclofenac was enhanced in hydrotropic mixture solution of 30% urea and 20% sodium citrate as compared to solubility in distilled water. The solubility of pure aceclofenac in distilled water was found to be 0.225mg/ml, whereas in the mixture of 30% urea and 20% sodium citrate, the solubility was found to be 19.64mg/ml. The increase in solubility was more than 100 folds. So it was optimized to employ this mixture solution in the analysis of the tablet formulation. A part of the solution was kept at room temperature for 24 hours to check the effect on stability of drug in presence of urea and for precipitation. The study revealed that estimations of aceclofenac can be done within 24 hours without any detrimental effect on drug stability. The Beer-Lambert's concentration range was found to be 5-40 µg/ml for aceclofenac at the wavelength of 274.5 nm. The drug showed good regression value at this wave length. It was evident that there is good correlation between the amounts estimated and the label claim. The estimated label claim was found to be 100.30±1.252mg and low values of standard error (Table 1). Accuracy and reproducibility of the proposed method were further confirmed by the recovery studies. The results of recovery study revealed that any small change in the drug concentration in the solution could be accurately determined by the proposed method (Table 2). The low values of LOD and LOQ indicated good sensitivity of proposed method. Repeatability results indicated the precision under the same operating conditions over a short interval time and inter- assay precision. Intermediate precision study expresses within laboratory variation in different days. In both intra and inter-day precision study for the method co-efficient of variation were not more than 1.0% indicates good intermediate precision. The value of LOD was 0.2129µg/ml and LOQ were 0.6451µg/ml respectively (Table 3).

Conclusion

It is thus concluded that the proposed method is a new, simple, cost effective, accurate, safe, free from pollution and precise method. This method can be successfully adopted for routine analysis of aceclofenac in tablet dosage form.

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Table 1: Analysis of tablet formulations of aceclofenac.

Tablet formulation	Label claim (mg)	% Label claim Estimated*(mean ±S.D.)	Standard error
Commercial Tablet I	100	100.30±1.252	0.687

***** Average of six determinations

Table 2: Result of recovery studies.

Formulation	Amount of aceclofenac tablet powder	Amount of standard drug added (mg)	% recovery estimated* (mean ±S.D.)	Standard error
Commercial Tablet I	100	20	100.67±1.49	1.060
	100	40	100.23±0.74	0.530
	100	80	99.45±0.45	0.325

***** Average of six determinations

Table 3: Optical characteristics data and validation parameters.

Parameters	Values for aceclofenac
Working λ_{max} (nm) in 30 % urea and 20 % sodium citrate solution	274.5nm
Beer's law limit (µg/ml)	5-40
Molar Absorptivity	11.40 X 10^3
Correlation coefficient*	0.9955
Intercept*	0.0014
Slope*	0.0217
LOD* (µg/ml)	0.2129
LOQ* (µg/ml)	0.6451
Intra-day* (precision) (Co-eff. of variation)	0.3169
Inter-day*(precision) (Co-eff. of variation)	0.2425
Robustness	Robust

***** Average of 6 determinations

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