

ECOFRIENDLY SPECTROPHOTOMETRIC ESTIMATION OF DICLOFENAC SODIUM IN TABLETS USING N, N-DIMETHYL UREA AS A HYDROTROPIC SOLUBILIZING AGENT

Maheshwari Rajesh Kumar^{*1}, Mathur Vineet², Satrawala Yamini¹, Rajput Mithun Singh³

¹Shri G.S. Institute of Technology and Science, 23-Park Road, Indore, M.P., India

²Niper, ITI Compound, Shri Bhawani Paper Mill Road, Rae Bareli, India

³College of Pharmacy, IPS Academy, Rajendra Nagar, A.B. Road, Indore, M.P., India

*Dr. R.K. Maheshwari, Professor and Head, Department of Pharmacy, Shri. G.S. Institute of Technology and Science, Indore - 452003, India, E-mail: rkrmaheshwari@yahoo.co.in

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ABSTRACT

A novel, safe and sensitive method of spectrophotometric estimation in ultraviolet region has been developed using 7.5M N,N-dimethylurea (an inexpensive hydrotropic agent) as hydrotropic solubilizing agent for the quantitative determination of diclofenac sodium, a poorly water soluble drug in tablet dosage form. Beer's law was obeyed in the concentration range of 10-60 µg/ml. N,N-dimethylurea does not interfere above 260 nm. There was more than a 11-fold enhancement in aqueous solubility of diclofenac sodium, in 7.5M N,N-dimethylurea solution as compared to the solubility in distilled water. Commonly used tablet excipients and N,N-dimethylurea did not interfere in spectrophotometric estimation. Results of the analysis were validated statistically and by recovery studies. The results of analysis obtained by the proposed method were very comparable with the results of analysis obtained by the Indian Pharmacopoeial method.

KEYWORDS: Hydrotropy, Diclofenac sodium, N,N-dimethylurea, Spectrophotometry

INTRODUCTION

It is well documented that concentrated aqueous solutions of a large number of hydrotropic agents viz. sodium gluconate, niacinamide, urea, sodium benzoate, sodium salicylate, sodium ascorbate and sodium glycinate, niacinamide have been employed to enhance the aqueous solubilities of poorly water-soluble drugs.¹⁻¹⁰ The primary objective of the present investigation was to employ a hydrotropic solution to extract the drug from the fine powder of diclofenac sodium tablets, precluding the use of costlier organic solvents for spectrophotometric analysis. Costlier organic solvents are more often employed to solubilize the poorly water-soluble drugs for spectrophotometric analysis. Volatility and pollution are drawbacks of such solvents. Various techniques are employed to enhance the aqueous solubility of poorly water-soluble drugs. Hydrotropic solubilization is one of them. Hydrotropes are a class of chemical compounds that cause a several fold increase in the solubility for sparingly soluble solute under normal conditions.

The present study aims to apply N,N-dimethylurea as a hydrotropic solubilizing agent to analyze a poorly water soluble drug diclofenac sodium in tablet dosage form, by spectrophotometric estimation. There was more than 11-fold increase in solubility of diclofenac sodium (a commonly used NSAID) in the hydrotropic solution. Therefore, it was thought worthwhile to solubilize the drug with the help of hydrotropy to carry out the estimation. Chemically, diclofenac is 2-(2,6-dichloranilino) phenylacetic acid.

MATERIALS AND METHODS

Diclofenac sodium tablets were procured from the local market. All other chemicals and solvents used were of analytical grade. Bulk drug (diclofenac sodium) was obtained as a gift sample from Shree

Pharmaceuticals, Indore. A spectrophotometer (Model UV-160A) with 1 cm matched silica cells was used for spectrophotometric analysis.

Preparation of calibration curve of diclofenac sodium: One hundred milligrams of diclofenac sodium standard drug was accurately weighed and transferred to a 100 ml volumetric flask. To this, 10 ml of 7.5M N,N-dimethylurea solution was added and flask was shaken to solubilize the drug. The volume was made up to the mark with distilled water. The stock solution was further diluted with distilled water to obtain various dilutions containing 10, 20, 30, 40, 50 and 60 $\mu\text{g/ml}$ of drug. The Beer's law range was 10-60 $\mu\text{g/ml}$ for diclofenac sodium. Absorbance was noted at 277 nm against reagent blanks to get the calibration curve.

Preliminary solubility study of diclofenac sodium: Solubility of diclofenac sodium was determined in distilled water and 7.5M N,N-dimethylurea solution at $27 \pm 1^\circ\text{C}$. Solubility was found to be increased by more than 11-fold in 7.5M N,N-dimethylurea solution as compared with the solubility in distilled water.

Analysis of diclofenac sodium tablet formulations by the IP (2007) method:¹¹ Twenty tablets of diclofenac sodium (formulation I) were weighed and ground to a fine powder. An accurately weighed powder sample equivalent to 50 mg of diclofenac sodium was transferred to a 200 ml volumetric flask. Sixty milliliters of methanol was added, the flask was shaken for about 10 min to dissolve the drug and the volume was made up to the mark with methanol. Five milliliters of the solution was diluted to 100 ml with methanol. The absorbance of the resulting solution was measured at a maximum at 285 nm. The drug content of the tablet formulation was then calculated [Table 1]. The same procedure was followed for formulation II [Table 1].

Analysis of diclofenac sodium tablet formulations by the proposed method: Twenty tablets of diclofenac sodium (formulation I) were weighed and ground to a fine powder. Tablet powder equivalent to about 100 mg of diclofenac sodium was accurately weighed and transferred to a 100 ml volumetric flask containing 10 ml of 7.5M N,N-dimethyl urea solution. Flask was shaken for about 10 min to solubilize the drug present in tablet powder and volume was made up to the mark with distilled water. After filtration through Whatmann filter paper no. 41. the filtrate was appropriately diluted with distilled water and absorbance was noted at 277 nm against reagent blank. The drug content of the tablet formulation was then calculated [Table 1]. The same procedure was followed for formulation II [Table 1].

Recovery studies: To evaluate the validity and reproducibility of the proposed method, recovery experiments were carried out. For recovery studies, in preanalyzed tablet powder equivalent to 100 mg diclofenac sodium, bulk drug samples 20 and 40 mg were added as spiked concentrations and drug contents were determined by the proposed analytical method. The results of analysis of recovery studies are presented in Table 2.

RESULTS AND DISCUSSION

Results of solubility studies of diclofenac sodium revealed that enhancement in solubility in 7.5M N,N-dimethylurea solution was more than 11-fold as compared to its solubility in distilled water. It is evident from Table 1 that the values of mean percent drug (diclofenac sodium) estimated by IP and the proposed method are 99.33 and 100.75, respectively, for formulation I and the values of mean percent drug (diclofenac sodium) estimated by IP and proposed method are 98.79 and 99.82, respectively, for formulation II. The results of the analysis by the proposed method are comparable to the results obtained from the IP method. The amounts of drug estimated by the IP and the proposed methods [Table 1] are very close to each other and are very close to 100.0, indicating the accuracy of the proposed method of analysis. Low values of standard deviation, percent coefficient of variation and standard error [Table 1] further validated the proposed method.

The values of mean percent recoveries estimated were 99.72 and 100.55 for formulation I and 98.65 and 98.91 for formulation II. The values are close to 100 indicating the accuracy of the proposed method. The values of standard deviation, percent coefficient of variation and standard error are statistically low and thus validate the proposed method [Table 2].

CONCLUSION

It is thus, concluded that the proposed method is new, simple, environment friendly, accurate and reproducible. The proposed method can be successfully employed in the routine analysis of diclofenac sodium in tablets. Decided advantage is that the organic solvent is precluded but not at the expense of accuracy. There is a good scope for other poorly water soluble drugs which may be tried to get solubilized by suitable hydrotropic agents to carry out their titrimetric/spectrophotometric analysis precluding the use of costlier and unsafe organic solvents.

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Table 1: Analysis Data of Diclofenac Sodium Tablet Formulations with Statistical Evaluation (N=3)

Tablet formulation	Label claim per tablet (mg)	Method of analysis	Percent drug estimated (mean±SD)	% Coefficient of variation	Standard error
I	100	P.M	100.75 ± 1.201	1.192	0.693
I	100	I.P.M	99.33 ± 1.877	1.890	1.084
II	50	P.M	99.82 ± 0.830	0.831	0.479
II	50	I.P.M	98.79 ± 1.555	1.574	0.898

P.M. = Proposed Method, I.P.M. = Indian Pharmacopoeial Method.

Table 2: Recovery Studies Using Proposed Analytical Method with Statistical Evaluation (N=3)

Tablet formulation	Drug present in pre analyzed tablet powder	Pure drug added (spiked) (mg)	Percent recovery estimated (mean±SD)	% Coefficient of variation	Standard error
I	100	20	99.72 ± 1.297	1.301	0.749
I	100	40	100.55 ± 1.547	1.539	0.893
II	100	20	98.65 ± 0.982	0.995	0.567
II	100	40	98.91 ± 1.602	1.620	0.925

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