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A Novel Spectroscopic Method for the Estimation of Ketoprofen in Tablet Dosage Form Using Hydrotropic Solubilization Phenomenon

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Abstract: A new, simple, environment friendly, cost-effective, safe and sensitive spectrophotometric method for the estimation of ketoprofen in tablet dosage form using hydrotropic solution 2.0 M potassium acetate as solubilizing agent was developed and statistically validated as per designed protocol. The potassium acetate, a hydrotropic agent increases the solubility of ketoprofen (more then 210 folds) and hence was used for the solubilization of poorly water-soluble drugs. Ketoprofen is nonsteroidal anti-inflammatory drug used in acute pain and rheumatoid arthritis and shows maximum absorbance at 260 nm. Beer's law was obeyed in the concentration range of 4-20 µg/ml. Proposed method is new, accurate and reproducible. Accuracy, reproducibility and precision of the proposed method was validated statistically.

Key words: Hydrotropy · Ketoprofen · Potassium Acetate · Spectrophotometry.

INTRODUCTION

Various techniques have been employed to enhance the aqueous solubility of poorly water-soluble drugs, hydrotropic solubilization is one of them. Concentrated aqueous hydrotropic solution of sodium benzoate, sodium salicylate, sodium acetate, urea and niacinamide have been found to enhance solubility of large number of drugs [1-21] by using this technique the aqueous solubility of various (poorly insoluble substance) increases many folds. Maheshwari *et al.* analyzed various poorly water-soluble drugs, using hydrotropic solubilization phenomenon *viz.* cefixme [1], frusemide [2], salicylic acid [3], ketoprofen [3-4], tinidazole [5] and aceclofenac [6]. Further Maheshwari *et al.* have developed various analytical techniques employing hydrotropic solubilization phenomenon, to analyze poorly water-soluble drugs, hydrochlorthiazide [7] ofloxacin [8] and aceclofinac [9].

Various organic solvents like methanol, benzene, chloroform, alcohol and dimethyl formamide, have been employed for the solubilization of poorly water-soluble drugs for spectrophotometric estimation. Some distinguished drawbacks using organic solvents include higher cost, toxicity, pollution and error in analysis due to volatility. The primary objective of this study was to employ hydrotropic solubilizing agent (potassium acetate) for the selected model drug to preclude the use of organic solvent (methanol). In the preliminary solubility studies it was found that there was considerable enhancement in the aqueous solubility of ketoprofen in 2.0 M potassium acetate solution. Since potassium acetate does not absorb above 245 nm it was thought worthwhile to use this hydrotropic agent, to extract out drug (poorly soluble) from their corresponding solid dosage forms. Recovery studies and statistical analysis were used for the validation of the method.

MATERIALS AND METHODS

The analysis was carried out using Shimadzu UV/Visible recording spectrophotometer (Model-UV-160A) with 1 cm matched quartz cells. Ketoprofen bulk drug and ketoprofen tablets (two batches) were procured from Ranbaxy Laboratories Limited, Dewas, India as a gift samples. Other chemicals used were of analytical grades.

Calibration curve method was used for the estimation of ketoprofen. The ketoprofen (100 mg) was weighed and transferred to a 100 ml volumetric flask. To this, 20 ml of 2.0 M potassium acetate solution was added and drug

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was dissolved by shaking for about 5 min. Then volume was made up to the mark by distilled water. This stock solution (1000µg/ml) was further diluted with distilled water to obtain various dilutions 4, 8, 12, 16 and 20 µg/ml. Absorbance's of these solutions were noted at 260 nm ($ë_{max}$) against respective blanks to get calibration curve.

Preliminary Solubility Studies of Ketoprofen: The solubility of ketoprofen was determined in distilled water and 2.0 M potassium acetate solution at 27 ± 1°C. The enhancement in the solubility of ketoprofen in 2.0 M potassium acetate solution was more then >210 folds (as compared its solubility in distilled water).

Analysis of Tablet Formulations of Ketoprofen by Proposed Method: Two different batches of ketoprofen tablets were used in the present investigation. Twenty tablets of ketoprofen (formulation-I) were weighed and ground to a fine powder. An accurately weighed powder sample equivalent to 100 mg of ketoprofen was transferred in a 100 ml volumetric flask and 20 ml of 2.0 M potassium acetate solution was added the flask was shaken for about 5 minutes to solubilize the drug and the volume was made up to the mark with distilled water. The solution was filtered through Whatman filter paper No. 41. The filtrate was divided in two parts A and B. Part A was kept at room temperature for 48 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. The drug content of tablet formulation was then calculated (Table 1, 2). After 48 h, part A solution was analyzed in the same way as part B solution. The tablet formulations of batch II were also treated in the same way as above.

Analysis of Ketoprofen Tablet Formulations (Standard Method): Indian pharmacopoeia (1996) [22] describes a method to analyze ketoprofen capsules by spectrophotometric method. Same procedure was applied to analyze ketoprofen tablet formulations (I and II). Tablet powder equivalent to 100 mg ketoprofen was shaken with 150 ml of methanol (75%) for 10 minutes and diluted to 250 ml with methanol (75%) after allowing to stand for some time, 2.5 ml of supernatant liquid was diluted to 100 ml with methanol (75%) and absorbance of resulting solution was measured at the wavelength maximum of about 258 nm. Drug content was calculated taken 662 as the value of A (1%, 1 cm) at the wavelength maximum of about 258 nm (Table 1, 2).

Recovery Studies Using Proposed Method : For recovery studies of tablet formulation I, tablet powder equivalent to 100 mg was taken in two separate volumetric flasks of 100 ml capacity. In first flask 30.0 mg and in second, 50.0 mg of pure drug (spiked drug) was transferred and 20 ml of 2.0 M potassium acetate solution (in each flask separately) was added in each flask and then flasks were shaken for about 10 minutes. The volume was made up to the mark with the distilled water and filtered through Whatman filter paper No. 41.The solutions were diluted appropriately with distilled water and analyzed for drug contents and percent recoveries were estimated (Table 3).

Table 1: Analysis Data of Ketoprofen Tablet Formulations

		Amount found (mg)				Percent estimated			
		Formulation I		Formulation II		Formulation I		Formulation II	
S.No.	Amount of drugpresent in tablet powder analyzed (mg)	S.M.	P.M.	S.M.	P.M.	S.M.	P.M.	S.M.	P.M.
1	100	99.36	98.34	100.88	98.58	99.36	99.34	100.88	98.58
2	100	98.73	99.72	99.18	99.96	98.73	99.72	99.18	99.96
3	100	99.89	97.33	97.08	97.54	99.89	97.33	97.08	97.54
4	100	97.77	98.49	98.22	98.67	97.77	98.49	98.22	98.67
5	100	98.04	97.54	98.91	97.83	98.04	97.54	98.91	97.83
6	100	99.54	98.84	101.86	99.16	99.54	98.84	101.86	99.16

Table 2: Statistical Evaluation of Analytical Data of Ketoprofen Tablet Formulations

		S.M.*				P.M.*			
S.No.	Tablet Formulation	Mean% Estimated	S.D.	% Coef. of Variation	Std. Err.	Mean% Estimated	S.D.	% Coef. of Variation	Std. Err.
1	I	98.89	0.853	0.862	0.348	99.38	0.875	0.889	0.357
2	II	99.35	1.749	1.760	0.714	98.62	0.881	0.893	0.360

* P.M.- Proposed method, S.M.- Standard method, S.D.- Standard deviation

Table 3: Recovery Studies for Spiked Concentration of Drug Added to the Pre-analyzed Dosage Form

Tablet formulation	Drug present in preanalyzed tablet powder (mg)	Pure drug added	%Recovery estimated* Mean ± S.D.	%Coeff. of variation	Standard error
I	100	30	98.92± 1.311	1.325	0.535
	100	50	99.08± 0.866	0.874	0.353
II	100	30	98.82± 1.227	1.242	0.501
	100	50	99.38± 0.638	0.642	0.260

*Mean of six determinations.

RESULTS AND DISCUSSION

Results of solubility studies indicated that, enhancement in aqueous solubility in 2.0 M potassium acetate solution, as compared to solubility in distilled water, was more than 210 folds for ketoprofen due to hydrotropic solubilization phenomenon. Part A solutions of drug were kept at room temperature for 48 h. There was no precipitation of drugs in Part A solutions within 48 hours. In addition, drug contents of Part A solutions (after 48 h) were same as those of Part B solutions (fresh solutions). This study reveals that the estimations can be done within 48 h at least, without having any detrimental effect on drug stability. From (Table 1), it is evident that there is good agreement between the amounts estimated and those claimed by the manufacturers. The mean percent label claims estimated by standard method are 98.89% and 99.35% and those estimated by proposed method are 99.38% and 98.62%, which are closed to 100 indicating the accuracy of proposed method. Low values of standard deviation, % coefficient of variation and standard error (Table 2) further validate the proposed method. The results of analysis by the proposed method compares very well with the results of analysis by the standard method. Accuracy, reproducibility and precision of the proposed methods, were further confirmed by percent recovery values, which were close to 100 with low values of standard deviation, % coefficient of variation and standard error (Table 3). From this study, it is obvious that there was no interference of potassium acetate and commonly used tablet excipients in the estimation of ketoprofen (λ_{max} 260 nm). Potassium acetate solution (2.0 M) is economic, safe and eco-friendly and it is a better substitute for toxic, pollutant and volatile organic solvents, methanol to carry out spectrophotometric estimation of ketoprofen tablets. Like this study the solubility study of other poorly water-soluble drugs may be conducted. If the enhancement in the solubility in 2.0 M potassium acetate is large enough and drugs have λ_{max} above 245 nm they can be estimated by use of this hydrotropic agent.

CONCLUSIONS

In present study authors emphasize on the application of various hydrotropic solutions to estimate various poorly water-soluble drugs precluding the use of organic solvents, which may be expensive, toxic, pollutant and volatile. 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 these drugs in pharmaceutical dosage forms.

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