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Novel Spectrophotometric Estimation of Frusemide Using Hydrotropic Solubilization Phenomenon

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Maheshwari, *et al.*: Spectrophotometric Estimation of Frusemide

A novel, safe and sensitive method of spectrophotometric estimation in ultraviolet region has been developed using 0.5 M ibuprofen sodium solution as hydrotropic solubilizing agent for the quantitative determination of frusemide, a poorly water-soluble diuretic drug in tablet dosage form. Frusemide shows maximum absorbance at 330 nm. Beer's law was obeyed in the concentration range of 20 to100 µg/ml. Ibuprofen sodium does not absorb above 300 nm. Commonly used tablet excipients and ibuprofen sodium did not interfere in spectrophotometric estimation. Results of the analysis were validated statistically and by recovery studies. Using 0.5 M ibuprofen sodium solution for analysis of two different tablet formulations of frusemide, the percent label claims and percent recoveries estimated were close to 100 with low values of standard deviation, percent coefficient of variation and standard error.

Key words: Frusemide, hydrotropy, ibuprofen sodium, spectrophotometry

Increasing the aqueous solubility of insoluble and slightly soluble drugs is of major importance. Various techniques have been employed to enhance the aqueous solubility of poorly water-soluble drugs. Hydrotropic solubilization is one of them. The term hydrotropy has been used to designate the increase in solubility in water of various substances due to the presence of large amounts of additives. Sodium salicylate, sodium benzoate, urea, nicotinamide, sodium citrate and sodium acetate are the most common examples of hydrotropic agents[1-15]. Maheshwari has analyzed various poorly water-soluble drugs using hydrotropic solubilization phenomenon viz. ketoprofen[1], frusemide[4], cefixime[5], salicylic acid[1], tinidazole[6] and amoxycillin[7]. Maheshwari *et al,* have developed various analytical techniques employing hydrotropic solubilisation phenomenon to analyze poorly water-soluble drugs like hyrochlorthiazide[8], aceclofenac[9] and ofloxacin[10].

Various organic solvents such as methanol, chloroform and dimethyl formamide, have been employed for solubilization of poorly water-soluble drugs to carry out spectrophotometric analysis. Drawbacks of organic solvents include their higher cost, toxicity and pollution. Hydrotropic solution may be a proper choice to preclude the use of organic solvents.

Frusemide (4-chloro-N-furfuryl-5-sulphamoylanthranilic acid) is a widely used diuretic drug. In the preliminary solubility studies there was more than 105 fold enhancement in the solubility of frusemide in 0.5 M ibuprofen sodium solution. Therefore, it was thought worthwhile to employ this hydrotropic solution to extract out the drug from fine powder of tablets to carry out spectrophotometric estimation.

There is broad scope for hydrotropic agents in quantitative estimations of other poorly water-soluble drugs. Shimadzu UV/Vis recording spectrophotometer (Model UV160A) with 1 cm matched silica cell was employed. Frusemide was obtained from M/s Alkem Lab Ltd, Mumbai. All other chemicals were of analytical grade.

For the preparation of 0.5 M ibuprofen sodium solution, 10 g of sodium hydroxide was dissolved in 200 ml of distilled water. Ibuprofen (51.6 g) was added little at a time and stirred to dissolve. After complete addition of ibuprofen, the pH was adjusted to remain between 7.5 to 8.0 with sodium hydroxide to assure the complete neutralization of ibuprofen. Then the volume was made up to 250 ml with distilled water.

For the preparation of a calibration curve, 100 mg of the drug was dissolved in 10 ml of 0.5 M ibuprofen sodium solution and diluted up to 100 ml with distilled water. The standard solution (1000 µg/ml) was further diluted with distilled water to obtain

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TABLE 1: RESULTS OF ANALYSIS OF FRUSEMIDE TABLET FORMULATIONS

Amount of drug in tablet powder taken (mg)	Amount found (mg)		Percentage estimated	
	Formulation 1	Formulation 2	Formulation 1	Formulation 2
100	97.36	99.11	97.36	99.11
100	98.59	98.86	98.59	99.86
100	101.30	98.22	101.30	98.22

Formulation 1 is Lasix, Aventis Pharma Limited, Ankleshwar and Formulation 2 is Frusenex-100 of Geno Pharmaceuticals Limited, Goa

TABLE 2: STATISTICAL EVALUATION OF ANALYSIS OF TABLETS

Tablet formulation	Mean % estimation	Standard deviation	%coefficient of variation	Standard error
1	99.08	2.016	2.035	1.164
2	98.73	0.458	0.464	0.264

Formulation 1 is Lasix, Aventis Pharma Limited, Ankleshwar and Formulation 2 is Frusenex-100 of Geno Pharmaceuticals Limited, Goa.

TABLE 3: RESULTS OF RECOVERY STUDIES OF TABLET FORMULATION WITH STATISTICAL EVALUATION

Tablet formulation	Drug present in preanalysed tablet powder(mg)	Pure drug added (mg)	% recovery estimated*(mean±SD)	% coefficient of variance	Standard error
1	100	20	98.33±1.231	1.252	0.711
	100	40	98.76±0.813	0.823	0.469
2	100	20	99.30±0.922	0.928	0.532
	100	40	97.58±1.008	1.033	0.582

Formulation 1 is Lasix, Aventis Pharma Limited, Ankleshwar and Formulation 2 is Frusenex-100 of Geno Pharmaceuticals Limited, Goa. *(n=3).

20, 40, 60, 80 and 100 µg/ml. Absorbances were noted against respective reagent blanks to plot the calibration curve.

In the preliminary solubility studies the solubility of frusemide was determined in distilled water and 0.5 M ibuprofen sodium solution at 27±1º. Enhancement in the solubility of frusemide in 0.5 M ibuprofen sodium solution was more than 105 folds (as compared to its solubility in distilled water).

Analysis of tablet formulation of frusemide by the proposed method was done by a method in which two different marketed tablet formulations of frusemide were used. Twenty tablets of frusemide from formulation 1 (Lasix, Aventis Pharma Limited, Ankleshwar) were weighed and ground to a fine powder. An accurately weighed powder sample equivalent to l00 mg of frusemide was transferred to a l00.0 ml of volumetric flask containing l0 ml of 0.5 M ibuprofen sodium solution. The flask was shaken for about 5 min to solubilize the drug and the volume was made up to mark with distilled water. The solution was filtered through Whatmann filter paper No 41. The filtrate was diluted appropriately with distilled water and was analyzed on UV spectrophotometer against reagent blank. Drug content of tablet formulation was then calculated (Table 1). Tablet formulation 2 (Frusenex-100, Geno Pharmaceuticals Limited, Goa) was treated in the same way.

Recovery studies were performed adding pure drug in the preanalysed tablet powder and following the same method of analysis. All types of analysis were performed in triplicate. Percent label claims estimated by the proposed method were 99.08±2.016 and 98.73±0.458 (Table 2), which were near to 100, indicating the accuracy of the proposed method. Low values of standard deviation, percent coefficient of variation and standard error further validated the proposed method. Percent recoveries ranged from 97.58±1.008 to 99.30±0.922 (Table 3). All these values were very close to 100. Also the values of standard deviation, percent coefficient of variation and standard error were satisfactorily low. This further confirmed the accuracy, reproducibility and validity of the proposed method.

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REFERENCES

1. Maheshwari RK. A novel application of hydrotropic solubilization in the analysis of bulk samples of ketoprofen and salicylic acid. Asian J Chem 2006;18:393-6.
2. Maheshwari RK. New application of hydrotropic solubilization in the spectrophotometric estimation of ketoprofen in tablet dosage form. Pharma Rev 2005;3:123-5.
3. Maheshwari RK. Application of hydrotropic solubilization in the analysis of aceclofenac. Asian J Chem 2006;18:1572-4.
4. Maheshwari RK. Analysis of frusemide by application of hydrotropic

solubilization phenomenon. Indian Pharmacist 2005;4:55-8.
5. Maheshwari RK. Spectrophotometric determination of cefixime in tablets by hydrotropic solubilization phenomenon. Indian Pharmacist 2005;4:63-8.
6. Maheshwari RK. Novel application of hydrotropic solubilization in the spectrophotometric analysis of tinidazole in dosage form. Asian J Chem 2006;18:640-4.
7. Maheshwari RK. Spectrophotometric analysis of amoxycillin in tablets using hydrotropic solubilization technique. Asian J Chem 2006;18:194-6.
8. Maheshwari RK, Chaturvedi SC, Jain NK. Application of hydrotropic solubilization phenomenon in spectrophotometric analysis of hydrochlorothiazide tablets**.** Indian Drugs 2005;42:541-4.
9. Maheshwari RK, Chaturvedi SC, Jain NK. Titrimetric analysis of aceclofenac in tablets using hydrotropic solubilization technique. Indian Drugs 2006;43:516-8.
10. Maheshwari RK, Chaturvedi SC, Jain NK. Application of hydrotropy in spectrophotometric determination of pharmaceutical dosage forms. Indian Drugs 2005;42:760-3.
11. Jain NK, Agrawal RK, Singhai AK. Hydrotropic solubilization of nifedipine. Pharmzie 1990;45:221-5.
12. Jain NK, Patel VV. Hydrotropic solubilization. Eastern Pharmacist 1986;29:51-3.
13. Etman MA, Hada AH, Hydrotropic cosolvent solubilization of indomethacin. Acta Pharm 1999;49:291-8.
14. Poochikian GD, Cradock JC. Enhanced chartreusin solubility by hydroxyl benzoate hydrotropy. J Pharm Sci 1979;68:728-32.
15. Saleh AM, Daabis NA. Study of interaction of menadione with hydrotropic salts. Pharmazie 1974;29:525-7.
16. British Pharmacopoeia, London: Her Majesty's Stationary Office; 2002. p. 340.

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