Online Available at www.thepharmaresearch.info

THE PHARMA RESEARCH, A JOURNAL

The Pharma Research (T. Ph. Res.), (2010), 3; 243-248.
Published on- 15 June 2010

ISSN 0975-8216

Original Article

APPLICATION OF MIXED-HYDROTROPIC SOLUBILIZATION CONCEPT IN SPECTROPHOTOMETRIC ANALYSIS OF FRUSEMIDE IN TABLET DOSAGE FORM

Rajesh k. Maheshwari*, chanpreet juneja and nitin juneja

Affiliated to:
Department of Pharmacy, Shri G.S. Institute of Technology and Science; 23, Park Road, Indore-452 003, India

ABSTRACT

In the present investigation, a poorly water-soluble drug, frusemide has been solubilized using hydrotropic blend containing 5 M urea, 1 M sodium acetate and 0.4 M sodium citrate for the spectrophotometric analysis precluding the use of organic solvents. These hydrotropes are economic and pollution-free. The mean percent frusemide estimated in frusemide tablets were 101.22 (formulation I) and 99.75 (formulation II). These values are very close to 100, indicating the accuracy of the proposed method. The proposed method was validated statistically by low values of statistical parameters viz. standard deviation, percent coefficient of variation and standard error. The proposed method is new, accurate, simple and economic.

Keywords: Frusemide, Mixed-Hydrotropy, Urea, Sodium Acetate, Sodium Citrate, Spectrophotometry

***Corresponding author:**
Rajesh k. Maheshwari

1.0 INTRODUCTION

Hydrotropy refers to the ability of a concentrated solution of a chemical compound to increase the aqueous solubility of another compound (usually a sparingly soluble organic compound). Compounds that have this property are called 'hydrotropes'. Sodium benzoate, sodium salicylate, sodium acetate, sodium glycinate, sodium ascorbate, niacinamide and sodium citrate are the most popular examples of hydrotropic agents which have been used to solubilize a large number of poorly water-soluble

compounds[1-26]. Maheshwari et al[1-21] analyzed various poorly water-soluble drugs, using hydrotropic solubilization phenomenon and mixed-solvency phenomenon including ibuprofen, salicylic acid aspirin, frusemide, tinidazole, ketoprofen, cefixime, hydrochlorothiazide, cephalexin and piroxicam.

There was tremendous increase in solubility of frusemide in hydrotropic blend containing 5 M urea, 1 M sodium acetate and 0.4 M sodium citrate in distilled water. Therefore, it was thought worthwhile to solubilize this drug in aforementioned hydrotropic blend to carry out the spectrophotometric analysis.

2.0 MATERIALS AND METHODS

All chemicals and solvents used were of analytical grade. Frusemide bulk drug was obtained as a gift sample from Alkem Laboratories Limited, Mumbai. Frusemide tablets were purchased from the local market.

2.1 Preliminary solubility studies of drug:

Solubility of frusemide was determined spectrophotometrically at 277 nm in distilled water and in blend of hydrotropic agents (5 M urea, 1 M sodium acetate and 0.4 M sodium citrate in distilled water) at 27±1 ˚C. There was more than 15 fold enhancement in the solubility of frusemide in hydrotropic blend containing 5 M urea, 1 M sodium acetate and 0.4 M sodium citrate in distilled water as compared to its aqueous solubility.

2.2 Preparation of calibration curve of drug:

Accurately weighed 50 mg of frusemide was transferred to a volumetric flask containing 20 ml of hydrotropic blend (containing 5 M urea, 1 M sodium acetate and 0.4 M sodium citrate in distilled water). The flask was shaken for 5 minutes to solubilize the drug and volume was made up to 25 ml using distilled water. Using this stock solution, various standard solutions of concentrations 4, 8, 12, 16 and 20 µg/ml were prepared using distilled water as diluents. Absorbances of these solutions were noted against

corresponding reagent blanks at 277 nm to obtain the calibration curve.

2.3 Analysis of frusemide tablets by the proposed method:

Marketed tablets (formulation I) of frusemide were analysed by the proposed method. To do this, 20 tablets were weighed accurately and were finely powdered. Tablet powder equivalent to 50 mg of frusemide was transferred to a volumetric flask containing 20 ml of hydrotropic blend containing 5 M urea, 1 M sodium acetate and 0.4 M sodium citrate in distilled water. The flask was shaken for 5 minutes to solubilize the drug and the volume was made up to 25 ml using distilled water. After filtration, the filtrate was appropriately diluted with distilled water and the absorbance of this solution was noted at 277 nm against corresponding reagent blank. The results of analysis are presented in Table 1. Each type of analysis was performed in triplicate. The same procedure was repeated for formulation II of the frusemide tablets.

Table 1. Results of analysis of marketed tablets of frusemide tablet formulations

Tablet formulation	Label claim (mg per tablet)	% drug estimated * (mean±S.D.)	% Coefficient of variation	Standard error
I	40	101.22±0.907	0.896	0.524
II	40	99.75±1.623	1.627	0.937

* Mean of three determinations. S.D- Standard deviation

2.4 Recovery studies:

To evaluate the validity and reproducibility of the proposed method, recovery studies were carried out by adding known quantities of frusemide bulk drug sample in the preanalyzed tablet powder containing known amounts of drug and performing the analysis using the same procedure and percent recoveries were calculated (Table 2). Each type of analysis was performed in triplicate for both formulations of frusemide tablets.

3.0 Results and Discussion

From the solubility studies, it was found that there was more than 15 fold enhancement in

the solubility of frusemide in hydrotropic blend containing 5 M urea, 1 M sodium acetate and 0.4 M sodium citrate in distilled water (as compared to its solubility in distilled water). As evident from Table 1, the mean per cent drug estimated were 101.22 (formulation I) and 99.75 (formulation II). These values are very close to

100, indicating the accuracy of the proposed method. The values of standard deviation (0.907 and 1.623), % coefficient of variation (0.896 and 1.627) and standard error (0.524 and 0.937) were satisfactorily low and validated the proposed method.

The values of the mean per cent recoveries (Table 2) were 100.84 and 100.92 in case of formulation I and 101.55 and 99.69 in case of formulation II. The values are close to 100, indicating the accuracy of the proposed method. Low values of standard deviation (0.942 to 1.339), % coefficient of variation (0.933 to 1.319) and standard error (0.544 to 0.773) further validated the proposed method.

Table 2. Recovery study for spiked concentration of frusemide added to the preanalyzed tablet powders

Tablet formulation	Drug present in preanalyzed tablet powder taken (mg)	Pure drug taken (mg)	% Recovery estimated* (mean±S.D.)	% Coefficient of variation	Standard error
I	50	10	100.84±1.246	1.236	0.719
I	50	20	100.92±0.942	0.933	0.544
II	50	10	101.55±1.339	1.319	0.773
II	50	20	99.69±1.008	1.011	0.582

* Mean of three determinations. S.D- Standard deviation

4.0 Conclusions

It is, thus, concluded that the proposed method is new, simple, accurate, cost-effective, safe, economic, precise and can be successfully employed in the routine analysis of frusemide in bulk and tablets. There is definitely further scope of hydrotropic blend containing 5 M urea, 1 M sodium acetate and 0.4 M sodium citrate as a hydrotropic solubilizing agent for the spectrophotometric analysis of other poorly water-soluble drugs precluding the involvement of organic solvents.

5.0 Acknowledgements

Authors are thankful to Alkem Laboratories Limited, Mumbai for providing a gift sample of frusemide bulk drug.

References

1. Maheshwari RK, Khera C, Lovlekar A. Novel method of analysis for ibuprofen and flurbiprofen bulk drugs using ibuprofen sodium solution as hydrotropic solubilizing agent. The Pharma Review 2007;22:167-9.
2. Maheshwari RK, Kumar S, Ramchandani U, Sahoo K, Khera C, Varghese S. The Indian Pharmacist 2006;13:124-6.
3. Maheshwari RK. Analysis of frusemide by application of hydrotropic solubilization phenomenon. Indian Pharmacist 2005;34:55-8.
4. Maheshwari RK. Novel application of hydrotropic solubilization in spectrophotometric analysis of tinidazole in dosage form. Asian J Chem 2006;18:640-4.
5. 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.
6. Maheshwari RK. Spectrophotometric determination of cefixime in tablets by hydrotropic solubilization phenomenon. Indian Pharmacist 2005;4:63-8.
7. Maheshwari RK. New application of hydrotropic solubilization in the spectrophotometric estimation of ketoprofen in tablet dosage form. Pharma Rev 2005;3:123-5.
8. Maheshwari RK, Jain NK, Chaturvedi SC. Titrimetric analysis of aceclofenac in tablets using hydrotropic solubilization technique. Indian Drugs 2006;43:516-8.
9. Maheshwari RK, Chaturvedi SC, Jain NK. Application of hydrotropic solubilization phenomenon in spectrophotometric analysis of hydrochlorothiazide tablets. Indian Drugs 2005;42:541-4.
10. Maheshwari RK, Pandey SP, Lovlekar A, Chavda V, Ajmera A, Gupta HM, *et al*. Novel application of hydrotropic solubilization in the spectrophotometric analysis of cephalexin in solid dosage form. Asian J Chem 2006;18:1451-4.
11. Maheshwari RK. Novel application of hydrotropic solubilization in the spectrophotometric analysis of piroxicam in solid dosage form. Indian Drugs 2006;43:683-5.
12. Maheshwari RK, Maheshwari RB, Bhatt P. Simultaneous spectrophotometric estimation of norfloxacin and tinidazole in two component tablet formulations. Asian J Chem 2006;18:1481-6.
13. Maheshwari RK, Ajmera A. A novel application of hydrotropic solubilization in the quantitative analysis of bulk sample of ketoprofen and frusemide. Asian J Pharm 2006;1:60-2.

14. Maheshwari RK, Chavda V, Sahoo K, Varghese S. Novel application of hydrotropic solubilization in the spectrophotometric analysis of diclofenac sodium in solid dosage form. Asian J Pharm 2006;1:30-2.
15. Gaikar VG, Latha V. Hydrotropic properties of sodium salt of ibuprofen. Drug Develop Ind Pharm 1997;23:309-12.
16. Maheshwari RK, Chaturvedi SC, Jain NK. Application of hydrotropic solubilization phenomenon in spectrophotometric analysis of hydrochlorothiazide tablets. Indian Drugs 2005;42:541-4.
17. Maheshwari RK. Application of hydrotropic solubilization in the analysis of aceclofenac. Asian J Chem 2006;18:1572-4.
18. Maheshwari RK. Spectrophotometric analysis of amoxycillin in tablets using hydrotropic solubilization technique. Asian J Chem 2006;18:3194-6.
19. Maheshwari RK. Mixed hydrotropy in spectrophotometric analysis of aceclofenac. The Indian Pharmacist 2007;6:67-9.
20. Maheshwari RK. Solubilization of ibuprofen by mixed solvency approach. The Indian Pharmacist 2009;8:81-4.
21 Maheshwari RK. Mixed-Solvency- A novel concept for solubilization of poorly water-soluble drugs. Delving J. Technology and Engineering Sciences 2009;1,1: 39-43.
22 Jain NK, Agrawal RK, Singhai AK. Hydrotropic solubilization of nifedipine. Pharmazie 1990;45:221-5.
23 Da Silva RC, Spitzer M, Da Silva LHM, Loh W. Investigations on the mechanism of aqueous solubility increase caused by some hydrotropes, Thermochimica Acta 1999;328:161-7.
24 Etman MA, Hada AH. Hydrotropic and cosolvent solubilization of indomethacin, Acta Pharm 1999; 49:291-8.
25 Poochikian GD, Cradock JC. Enhanced chartreusin solubility by hydroxyl benzoate hydrotropy, J Pharm Sci 1979; 68:728-32.
26 Darwish A, Florence AT, Saleh AM**,** Novel application of hydrotropic solubilization in the spectrophotometric analysis, J Pharm Sci 1989; 78:577-81.