RESEARCH ARTICLE

New quantitative estimation of benzoic acid bulk sample using calcium disodium edetate as hydrotropic solubilizing agent

R K Maheshwari *[1], Mithun Singh Rajput [2], Sampada Sinha [2]

[1]Department of Pharmacy, Shri G S Institute of Technology and Science, Indore – 452 003, India.
[2]College of Pharmacy, IPS Academy, Knowledge village, Rajendra Nagar, A B Road, Indore- 452012, India.

Address for correspondence: Dr. R K Maheshwari, Department of Pharmacy, Shri G S Institute of Technology and Science, Indore – 452 003, India. E-mail: rkrkmaheshwari@yahoo.co.in

In the present investigation, hydrotropic solubilization technique has been employed to solubilize the slightly water soluble topical antifungal drug, benzoic acid (by 1.0 M calcium disodium edetate solution), for its titrimetric analysis. There was more than 15 fold enhancement in aqueous solubility of benzoic acid in 1.0 M calcium disodium edetate solution as compared to the solubility in distilled water. The hydrotropic agent did not interfere in the analysis. The proposed method is new, simple, accurate and reproducible. Statistical data proved the accuracy, reproducibility and precision of the proposed method.

Keywords: *Hydrotropy, Benzoic acid, Calcium disodium edetate, Titrimetry*

INTRODUCTION

Increasing the aqueous solubility of insoluble and slightly soluble drug is of major importance. 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 ascorbate, niacinamide, sodium citrate, urea are the most popular examples of hydrotropic agents which have been used to solubilize a large number of poorly water-soluble compounds [1-19]. Hydrotropic solution of calcium disodium edetate was employed as solubilizing agent to analyze slightly water soluble drug, benzoic acid by titrimetric estimation.

There was tremendous increase in solubility of benzoic acid (a widely used topical antifungal drug) in 1.0 M calcium disodium edetate solution. Therefore, it was thought worthwhile to solubilize the drug with the help of calcium disodiun edetate solution to carry out the estimation.

MATERIALS AND METHODS

Benzoic acid was obtained as gift sample from Alkem Lab. Ltd., Mumbai. All other chemicals and solvents used were of analytical grade. A Shimadzu UV-Visible spectrophotometer (Model-UV 160A) with 1 cm matched silica cells was used for spectrophotometric analysis.

Preliminary solubility studies of drug

Solubility of benzoic acid was determined in distilled water and 1.0 M calcium disodium edetae solution at 27±1°C. Solubility was found to be increased by more than 15 fold in 1.0 M calcium disodium edetate solution as compared to the solubility in distilled water.

Analysis of benzoic acid bulk sample by I.P. (1996) method [20]

Accurately weighed (1.0 gm) benzoic acid bulk sample was dissolved in 15 ml of warm ethanol (95%) previously neutralized to phenolphthalein solution, 20 ml of distilled water was added to it and it was titrated with 0.5 M sodium hydroxide solution using phenolphthalein solution as indicator. Necessary blank determination was adjusted to get drug content (Table 1).

Table 1. Analysis data of benzoic acid bulk sample with statistical evaluation (n=3)

Amount of bulk drug taken (mg)	Method of analysis	Percent drug estimated (mean ± SD)	Coefficient of variation (%)	Standard error
1000.0	I.P.M.	101.32±1.082	1.067	0.625
200.0	P.T.M.	100.89±0.747	0.740	0.431

Where, I.P.M. - Indian Pharmacopoeial Method, P.T.M. - Proposed Titrimetric Method

Analysis of benzoic acid bulk sample by proposed titrimetric method

In the proposed method accurately weighed (200 mg) benzoic acid bulk sample was solubilized in 20 ml of 1.0 M calcium disodium edetate solution by shaking for about 5 minutes and it was titrated with 0.5 M sodium hydroxide solution using phenolphthalein solution as indicator. Necessary blank determination was adjusted to get drug content (Table 1).

RESULTS AND DISCUSSION

Results of solubility studies of benzoic acid revealed that enhancement in solubility in 1.0 M calcium disodium edetate solution was more than 15 fold as compared to its solubility in distilled water.

It is evident from Table 1 the values of mean percent of benzoic acid, estimated in the drug sample were 101.32 and 100.89 by the Indian Parmacopoeial and proposed titrimetric methods respectively. The amounts of drug estimated by Indian pharmacopoeial and proposed titrimetric methods (Table 1) are very close to each other and very near to 100.0, indicating the accuracy of the proposed method of analysis. This indicates the accuracy of the proposed method. Low values of standard deviation, percent coefficient of variation and standard error (Table 1), further validated the proposed titrimetric method.

CONCLUSION

It was, thus, concluded that the proposed method is new, simple, cost effective, accurate, safe and precise. It can be successfully employed in the routine analysis of benzoic acid in bulk drug sample. No organic solvent were employed. There is good scope for other poorly water-soluble drugs which may be tried to get solubilized in 1.0 M calcium disodium edetate solution (as hydrotropic agent) to carry out their titrimetric and/or spectrophotometric analysis excluding the use of costlier and unsafe organic solvents. The proposed method is worth adopting in the respective pharmacopoeia.

ACKNOWLEDGEMENT

The authors are thankful to Alkem Labs Ltd., Mumbai for supplying benzoic acid as gift sample.

REFERENCES

1. Maheshwari RK, Maheshwari RB, Bhatt P. Simultaneous spectrophotometric estimation of norfloxacin and tinidazole in two component tablet formulations. Asian Journal of Chemistry 2006; 18:1481-6.
2. Maheshwari RK, Pandey SP, Lovlekar A, Chavda V, Ajmera A, Gupta HM. Novel application of hydrotropic solubilization in the spectrophotometric analysis of cephalexin in solid dosage form. Aaian Journal of Chemistry 2006; 18:1451-4.
3. Maheshwari RK. Application of hydrotropic solubilization in the analysis of aceclofenac. Asian Journal of Chemistry 2006; 18:1572-4.
4. Maheshwari RK, Chaturvedi SC, Jain NK. Novel spectrophotometric estimation of some poorly water soluble drugs using hydrotropic solubilizing agents. Indian Journal of Pharmaceutical Science 2006; 68:195-8.
5. Maheshwari RK, Dewangan A, Soni PK, Kansagra PK, Jain SK. Novel application of hydrotropic solubilization in the spectrophotometric analysis of paracetamol tablet. Asian Journal of Chemistry 2006; 18:2879-82.
6. Maheshwari RK. Solid dispersion and syrup formulation of poorly water soluble drug by hydrotropy. The Indian Pharmacist 2006; 5:87-90.
7. Maheshwari RK. Novel application of hydrotropic solubilization in the spectrophotometric analysis of piroxicam in solid dosage form. Indian Drugs 2006; 43:683-5.
8. Maheshwari RK, Chaturvedi SC, Jain NK. Novel application of hydrotropic solubilizing additives in the estimation of aspirin in bulk sample and tablets. International Journal of Pharmaceutical Excipients 2005; 4:84-8.
9. Maheshwari RK. Application of hydrotropic solubilization phenomenon in spectrophotometric estimation of norfloxacin in tablets. Indian Journal of Pharmaceutical Education and Research 2006; 40:237-40.
10. Maheshwari RK, Gupta HM, Singh M, Ramchandani U, Pandey SP. A novel application of hydrotropic solubilization in the spectrophotometric analysis

of gatifloxacin in solid dosage form. Asian Journal of Chemistry 2008; 20:241-5
11. Maheshwari RK, Pandey, SP, Gupta HM, Ramchandani U. Analysis of frusemide by application of hydrotropic solubilization phenomenon in solid dosage form. Asian Journal of Chemistry 2008; 20:277-281.
12. Maheshwari RK, Dubey N, Singh M. Hydrotropic solubilization in spectrophotometric analysis of cefixime in solid dosage form. Asian Journal of Chemistry 2008; 20:375-9.
13. Maheshwari RK. Mixed hydrotropy in spectrophotometric analysis of aceclofenac. The Indian Pharmacist 2007; 6:67-9.
14. Maheshwari RK, Deswal S, Tiwari D, Ali N, Pothen B, Jain S. Novel spectrophotometric estimation of frusemide using hydrotropic solubilization phenomenon. Indian Journal of Pharmaceutical Science 2007; 69:822-6.
15. Maheshwari RK, Singh M. Quantitative determination of ketoprofen bulk drug using sodium salt of aspirin as hydrotropic solubilizing agent. Asian Journal of Chemistry 2008; 20:4922.
16. Maheshwari RK, Shukla RS. Quantitative spectrophotometric estimation of famotidine using hydrotropic solubilization technique. Asian Journal of Chemistry 2008; 20:4221-4.
17. Maheshwari RK, Kinariwala M, Saxena M, Gahlot M, Chaki R, Jagwani Y. Spectrophotometric analysis of cefixime trihydrate tablets using metformin hydrochloride as hydrotropic solubilizing agent. Asian Journal of Chemistry 2008; 20:6047-50
18. Maheshwari RK, Arif D, Mittal P, Manchandani P, Indurkhya A, Jawade S. A novel method for quantitative determination of aceclofenac in bulk drug and tablets using ibuprofen sodium as a hydrotropic solubilizing agent. Journal of Applied Chemical Research 2008; 5:63-8.
19. Maheshwari RK, Patidar V, Maliwal D, Jain A. Simultaneous spectrophotometric estimation of metronidazole and norfloxacin in combined tablet formulations using hydrotropy. Research Journal of Pharmacy and Technology 2008; 1:357-61.
20. Indian Parmacopoeia, Fourth edition, Delhi: Controller of Publications; Vol. I, 1996, 93.