ISSN: 0975-766X
Research Article
Available Online through
www.ijptonline.com

QUANTITATIVE SPECTROPHOTOMETRIC DETERMINATION OF CEFIXIME TABLET FORMULATION USING SODIUM TARTARATE AS HYDROTROPIC SOLUBILIZING AGENT

R.K. Maheshwari*, Shruti Moondra, Ms. Manoj More
Sita Prasad Prajapati, Shikhar Verma
Department of pharmacy, S.G.S.I.T.S., Indore, Madhya Pradesh, India.
E-mail: rkrkmaheshwari@yahoo.co.in

Received on 15-08-2010 ***Accepted on 30-07-2010***

ABSTRACT

Based on a large number of experiments on solubilization of poorly water-soluble drugs, the author is of the opinion that hydrotropy is another type of cosolvency and all water-soluble substances whether liquids, solids, or gases may act as solubilizers for poorly water-soluble drugs. In the present investigation, hydrotropic solution of sodium tartarate (2 M) was employed as solubilizing agent to solubilize the poorly water-soluble drug cefixime from fine powder of its tablet dosage form for spectrophotometric determination in ultraviolet region. Cefixime exhibits maximum absorbance at 288 nm and follows Beer's law in concentration range of 5-30 mcg/ml. Results of analysis were validated statistically and by recovery studies. The proposed method is new, simple, safe, environmentally friendly, accurate and cost-effective and can be successfully employed in routine to analyze cefixime tablets. Hydrotropic agent and commonly used tablet additives did not interfere in analysis. Just like cefixime as model drug, other poorly water-soluble drugs may be studied for the enhancement effect in solubility in hydrotropic solution of 2 M sodium tartarate for spectrophotometric analysis at a wavelength above 288 nm precluding the use of organic solvents (green chemistry)

KEYWORDS: Spectrophotometric, Validated, Hydrotropy, Sodium tartarate, Cefixime.

INTRODUCTION

Cefixime

chemically(6*R*,7*R*)-7-{[2-(2-amino-1,3-thiazol-4-yl)-2-(carboxymethoxyimino)acetyl]amino}-3-ethenyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid., it is an oral third generation cephalosporin antibiotic .used for treatment in gonorrhea. Literature survey reveals that HPLC method for the simultaneous determination of cefixime diasteriomers , HPTLC for estimation of Cefixime Flow injection chemiluminescent determination of Cefixime ,spectrophotometric determinations, and spectrofluorimetric determinations of cefixime have been developed. Here we have presented spectrophotometric methods, estimation and area under curve method by using hydrotropic agents for estimation of cefixime in pure and tablet dosage forms.Various concentrated aqueous solutions are used to increase the aqueous solubility of the poorly water soluble drugs and are called "hydrotropic agents". This is the phenomenon in which, "addition of second solute in large amount will increase the aqueous solubility of another solute (poorly water soluble drug). Hydrotropic agents have been observed to enhance the aqueous solubilties of poorly water-soluble drugs. Concentrated aqueous hydrotropic solutions of sodium benzoate, resorcinol, sodium glycinate, niacinamide, sodium citrate, sodium acetate and urea have been observed to enhance aqueous solubility of insoluble and slightly soluble drugs .Maheshwari has nicely applied the application of hydrotropy in titrimetric and spectrophotometric estimations of a large number of poorly water-soluble drugs precluding the use of organic solvents. He is of the opinion that hydrotopy is another type of cosolvency. In the present investigation, hydrotropic solubilization has been employed to analyze cefixime in the tablet dosage forms precluding the use of organic solvent (green chemistry). In the present investigation, hydrotropic solubilizing agent, 2M sodium tartarate was employed to solubilize cefixime from fine powder of its tablets to carryout spectrophotometric analysis .

MATERIALS AND METHODS

Shimadzu UV/Visible recording spectrophotometer (model-UV-160A) with 1cm matched silica cells was used for spectrophotometric analysis. Cefixime bulk drug sample was obtained as gift sample from M/s Alkem Laboratory Limited, Mumbai (India). The tablets of cefixime were procured from the local market. All other chemicals and solvents used were of analytical grade.

Calibration curve

The standard stock solution (1000 mcg/ml) of cefixime trihydrate was prepared by solubilizing, accurately weighed 100 mg cefixime trihydrate in 25 ml volumetric with 20 ml of 2 M sodium titrate solution and furthur diluting with distilled water upto the mark. The stock solution was further diluted with distilled water to obtain various dilutions. Standard solutions of 5, 10, 15, 20 , 25 and 30 mcg/ml of drug were used to plot the calibration curve by taking the absorbance at 288 nm against corresponding reagent blanks. . A linear relationship was obtained.

Preliminary solubility studies-

Determination of solubility studies of cefixime in 2 M sodium tartarate and distilled water was carried out at 27±1°C. Sufficient amount of drug was added to screw capped 30 ml glass vials containing hydrotropic solution and distilled water. The vials were shaken mechanically for 12 hrs at 27±C in orbital flask shaker (Khera Instrument Pvt, Ltd, India). The solution were allowed to equilibrate for next 24 hrs and then centrifuged for 5 min at 2000 rpm . the supernatant was filtered through Whatmann filter paper #41 . Filtrate were diluted suitability and analyzed spectrophotometrically to determine the solubilites. The enhancement in solubility of cefixime in hydrotropic solution was found to be more than 45 folds as compared to distilled water .

Analysis of cefixime tablets using 2 M sodium tartarate solution

20 tablets were weighed and grounded to fine powder. Powder equivalent to 100 mg was solubilized in 20 ml of 2 M sodium tartarate solution, kept in 100 ml conical flask. The flask was shaken for about 10 min and the volume was made upto the mark by distilled water . The solution was filtered through Whatmann filter paper #41. Filtrate

was divided into two parts, A&B. Part A was kept at room temperature for 24 hours, to check the effect on stability the stability of the drug in the presence of sodium tartarate (2 M) and also to note the precipitation, if any, during this period. Part B filterate was appropriately diluted with distilled water and the absorbance was noted at 288 nm (λ max) against reagent blank and drug content was calculated drug content was calculated (Table No. 2). After 24 hours, part A filtrate was also appropriately diluted and the analyzed for drug content. There was no changed reflected in the drug content of filtrate within 24 hours. This period that the drug is stable for at least 24 hours in the presence of sodium tartarate (2 M). Also there no precipitation of drug is noted in the filtrate and during 24 hours. Same procedure was adapted from tablet II formulation and the drug content was calculated. and reported in Table No. 1

Recovery Studies

To study the accuracy reproducibility, precision of the proposed method recovery studies were carried out. 30 and 60 mg cefixime (pure bulk drug) were added to the pre analyzed tablet powdered equivalent to 100mg cefixime Each analysis was performed thrice (n=3) using 2M sodium tartrate solution and the drug content was calculated. and reported in Table No.2

RESULTS AND DISCUSSION

The preliminary solubility showed the progress of the proposed method by increasing the solubility of poorly water soluble drug cefixime in 2 M sodium tartarate solution by more than 45 folds. Therefore, hydrotropic solution is used to extract drugs into fine powder of tablet formulation. Table No. I reflects the percentage of label claim of proposed using 2 M sodium tartarate solution as 98.83±1.022 and 99.33±0.821, which is very close to 100 indicating the accuracy of proposed method. The accuracy, precision and reproducibility of proposed method is further confirmed by percentage recovery studies. The method is further validated by low values of standard error, percentage coefficient of variation and standard deviation. Table No. II indicated the percentage recovery ranged from 98.89±1.332 to 100.33±1.033, in case of 2 M sodium tartarate, which is very close to 100 indicates the accuracy of the proposed method.

Tabe 1 : Results of analysis of cefixime tablet formulations with statistical evaluation (n=3).

Tablet formulation	Label claim per tablet (mg)	%Label claim estimated (mean ± standard deviation)	% Coefficient of variation	Standard error
I	100	98.83± 1.022	0.978	0.590
II	200	99.33± 0.821	0.826	0.474

Tabe 2 : Recovery studies with statistical evaluation (n=3).

Tablet formulation	Amount. of drug in preanalyzed tablet powder (mg)	Cefixime pure drug added (mg)	% Recovery estimated (mean ± standard deviation)	% Coefficient of variation	Standard error
I	100	30	100.33 ± 1.003	0.999	0.579
I	100	50	98.89 ± 1.332	1.347	0.769
II	100	30	99.44 ± 0.631	0.634	0.634
II	100	60	99.11 ± 1.010	1.019	0.583

CONCLUSION

The results conclude that the methods reflects the same result as reference method. The organic solvents such as ethanol, methanol, acetonitrile used widely in spectrophotometric analysis of poorly water soluble drugs are toxic in nature, costlier….. and responsible for pollution. Inaccuracy in spectrophotometric analysis due to volatility of organic solvents is the another drawback. Since sodium tartarate do not interfere at 288 nm, therefore, poorly water soluble drug having (λ max) above 288 nm can easily be estimated by proposed method, avoiding the use of organic solvents. It is concluded that the proposed method, is new, simple, cost effective, safe, accurate, precise and environment friendly. This method can be successfully employed in the routine analysis of cefixime in tablet dosage form and by this way we can reduce the cost of estimation of poorly water-soluble drugs.

ACKNOWLEDGEMENT

Authors are thankful to M/s Alkem Laboratory Limited, Mumbai (India).for providing the gift sample of drug.

BIBLIOGRAPHY

1. Tavaren NS, Jadhav VK. Separation through crystallization and hydrotropy : the 6-aminopenicillanic acid (6-APA) and phenoxyacetic acid (PAA) system. Journal of crystal growth 1999, Vol.198-99, pp1320-25
2. Agarwal, M, Gaikar, VG. Extractive separation using hydrotropes. Separations Technology 1992, Vol. 2, pp79-84.
3. Friberg SE, Yang J, Huang T. A reversible extraction process of phenyl ethyl alcohol, a fragrance. Industrial & Engineering Chemistry Research 1996, Vol.35, pp 2856-59.
4. Gaikar VG, Phatak PV. Selective solubilization of isomers in hydrotrope solution o-/p chlorobenzoic acids and o-/p-nitro anilines. Separation Science and Technology 1999, Vol.34, pp 439-59.
5. Friberg SE, Brancewicz C. O/W microemulsions and hydrotropes: the coupling action of a hydrotrope. Langmuir 1994, Vol.10, pp 2945-9.

6. Rigoli IC, Schmitt CC, Neumann MG. The hydrotrope effect on the photopolymerization of styrenesulfonate initiated by Ru complexes. Journal of Photochemistry and Photobiology A: Chemistry 2007, Vol.188, pp 329-33.
7. Dandekar DV, Jayaprakasha GK, Patil BS. Hydrotropic extraction of bioactive limonin from sour orange (Citrius aurantium L.) seeds. Food Chemistry 2008, Vol.109, 515-20.
8. Colonia EJ, Dixit AB, Tavare NS. Phase relations of o- and p-chlorobenzoic acids in hydrotrope solutions. Journal of Chemical & Engineering Data 1998, Vol. 43, pp 220-5.
9. Mansur CRE, Pires RV, Gonzalez G, Lucas EF. Influence of the hydrotrope structure on the physical chemical properties of polyoxide aqueous solutions. Langmuir 2005, Vol.21,pp 2696-703.
10. Ooya T, Moo HK, Saitoh M, Tamiya E, Park K. Self-assembly of cholesterol-hydrotropic dendrimers conjugates into micelle-like structure: preparation and hydrotropic solubilization of paclitaxel. Science and Technology of Advanced Materials 2005, Vol.6,pp 452-6.
11. Bauduin P, Renoncourt A, Kopf A, Touraud, D, Kunz W. Unified concept of solubilization in water by hydrotropes and cosolvents. Langmuir 2005, Vol. 21, pp 6769-75.
12. Balasubramanian D, Srinivas V, Gaikar VG, Sharma M. Aggregation beaviour of hydrotropic compounds in aqueous solutions. The Journal of Physical Chemistry 1989, Vol.93,pp 3865-70.
13. Maheshwari RK. Application of hydrotropic solubilization phenomenon in spectrophotometric estimation of norfloxacin in tablets. J Pharm Biomed Anal 2006, Vol.40,pp237-40.
14. Maheshwari RK. Application of hydrotropic solubilization in the analysis of aceclofenac. Asian J Chem 2006, Vol.18,pp1572-4.
15. Maheshwari RK. Solid dispersion and syrup formulation of poorly water soluble drug by hydrotropy. The Indian Pharmacist 2006, Vol.5,pp 87-90.
16. Maheshwari RK. Novel application of hydrotropic solubilization in the spectrophotometric analysis of piroxicam in solid dosage form. Indian Drugs 2006, Vol.43, pp 683-5.

17. Maheshwari RK. Mixed hydrotropy in spectrophotometric analysis of aceclofenac. The Indian Pharmacist 2007,Vol.6, pp 67-9.
18. Maheshwari RK, Chaturvedi SC, Jain NK. Novel spectrophotometric estimation of some poorly water soluble drugs using hydrotropic solubilizing agents. Indian J Pharmaceu Sci 2006, Vol.68,pp195-8.
19. Jain NK and Patel. Hydrotropic solubilization. The Eastern Pharmacist 1986,Vol.29,pp 51.
20. Maheshwari RK .Spectrophotometric analysis of Amoxicillin in Tablets using hydrotropic solubilisation technique. Asian J.Chem.2000,Vol.18,pp 3194
21. Coffman,RE., and Kidsig, DF.O., hydrotropic solubilization-mechanistic studies.Pharma.Res.1996,Vol.13,pp 1460.
22. Maheshwari RK. A novel application of hydrotropic solublization in the analysis of bulk samples of ketoprofen and salicylic acid. Asian JChem 2006,Vol.8,pp 393-6.
23. Maheshwari RK. Novel application of hydrotropic solubilization in the spectrophotometirc analysis of tinidazole in dosage form. Asian J Chem 2006,Vol.18,pp 640-4.
24. Maheshwari RK. Application of hydrotropic solubilization in the analysis of aceclofenac Asian J . Chem 20061,Vol.81,pp 572-4.
25. MaheshwariRK Novel application of hydrotropic solubilisation in the spectrophotometric analysis of piroxicam in solid dosage form. Indian Drugs 200,Vol.68,pp 683.
26. Maheshwari RK. A novel application of hydrotropic solubilization in spectrophotometric estimation of frusemide in tablets. Pharma Rev 2006,Vol.4,pp148-9.
27. Jain NK, Patel VV. Hydrotropic solubilization. Eastern Pharmacist. 1986,Vol.29,5.
28. Saleh AM.El- Khordagui LK. Hydrotropic agents: a new definition. Int.J.Pharm. 1985, Vol . 24, pp 231.
29. SablePN, Chaulang GM and Bhosale AV. Novel spectrophotometric estimation of izetemib, lsorton and simvastatinusing hydrotropic solubilizing agents. International Journal of ChemTech Research 2009

,Vol.1,pp 1393-1397

30. Sharma M.C.,Sharma Smita and Sharma A. D. Novel application and spectrophotometric estimation of Melitracen HCl tablet dosage form using Niacinamide as hydrotropic solubilizing agent.J. Chem. Pharm. Res 2(2);2010 : 416-420

31. Sable.P.N,ChaulangG.M.,BhosaleA.V.,and ChaudhariP.D, Novel Spectrophotometric estimation of Olanzepine Using Hydrotropic Solubilizing Agents. Research J. Pharm. and Tech.2009,Vol.2,pp297-300

Address for correspondence:

Dr. R. K. Maheshwari,
Department of Pharmacy,
Shri G.S.Institute of Technology and Science;
23, Park Road,
Indore-452 003, India.
E-mail: r*krkmaheshwari@yahoo.co.in*