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Eco-friendly spectrophotometric estimation of cefixime tablets using water as solvent and sodium lauryl sulphate as wicking and solubilizing agent

***Tarkase K. N., Tarkase. M. K., Deshpande. A. P, Wagh. V. S and Dokhe M. D.**

**Department of Quality Assurance Technique, Padmashree Dr. Vithalrao Vikhe Patil Foundation's, College of Pharmacy, Viladghat, Ahmednagar. Maharashtra, INDIA*

ABSTRACT

The objective of the current study is to develop a simple, sensitive ultraviolet absorption spectrophotometric method for the estimation of poorly water soluble drugs like Cefixime, norfloxacin, tinidazole, and metronidazole in pharmaceutical formulations and to evaluate the increased solubility of cefixime in the prepared formulation. Aqueous solubilities of these selected model drugs were enhanced to a great extent (5 to 98 fold) in distilled water, SGF and SIF along with 0.2 M phosphate buffer. The various hydrotropic agents that can be used include ammonium acetate (6M), Potassium acetate (5M),Potassium citrate (0.5 M), Sodium citrate (1.25 M) , Urea (8M). 2.0 M sodium benzoate, and the most affordable and safe solubilizing agent that has been used here ie. Sodium lauryl sulphate. The primary objective of the present investigation is to employ this solubilising agent to extract and dissolve the drugs from their dosage forms, precluding the use of costlier organic solvents. The selected λmax for Cefixime is 288 nm and Sodium lauryl sulphate did not show any absorbance at 288 nm, and therefore, no interference in the estimation is seen. The results of analysis have been validated statistically, and by recovery studies. The proposed method is new, simple, economic, accurate, safe and precise. Increasing the aqueous solubility of insoluble and slightly soluble drugs, is of major importance. Various organic solvents like methanol, chloroform, alcohol, dimethyl formamide, and benzene have been employed for the solubilization of poorly water soluble drugs for spectrophotometric estimations. Drawbacks of organic solvents include higher cost, toxicity, pollution, and error, in analysis due to volatility. In the preliminary solubility studies, it was found that there was considerable enhancement in the aqueous solubilities .

Keywords: Hydrotropic, Spectrophotometric estimation, Cefixime, Sodium lauryl sulphate.

INTRODUCTION

Cefixime trihydrate is chemically(6R,7R)-7-[[(Z)-2-(2-aminothiazol-4-yl)-2- [(carboxymethoxy) imino] acetyl]amino]-3ethenyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid trihydrate. Cefixime is a β-lactam third-generation antibiotic used in treatment of various infections caused by gram negative bacteria like Haemophilius influenzae, Moraxella catarrhalis, Escherichia coli, Klebsiella spp. Literature survey revealed HPTLC determination of Cefixime , Reversed phase HPLC determination of Cefixime are the few methods available for it's estimation. Cefixime is poorly soluble in water. Special techniques are required to solubilize poorly water-soluble drugs .Several methods have been reported in the literature to enhance the aqueous solubilites of poorly water-soluble drugs. Hydrotropic solubilization is one of them. It is a phenomenon where addition of large amount of second solute results in an increase in aqueous solubility of another solute. Concentrated aqueous hydrotropic solutions of sodium benzoate, niacinamide, sodium citrate, sodium glycinate and urea have been observed to enhance aqueous solubility of insoluble and slightly soluble drugs . Hydrotropic solutions can be employed to replace organic solvents employed in analysis of poorly water-soluble drugs. The primary objective of the present investigation is to employ the solubilising agent in the tablet formulation and in analytical stock solutions to a poorly

water-soluble drug, Cefixime, from its dosage form, is well dissolved precluding the use of costlier organic solvent. Results of analysis by the proposed method compared with results obtained by United states Pharmacopoeial method. The solubilising hydrotropic agent, sodium lauryl sulphate and commonly used tablet excipients did not interfere in spectrophotometric determination at λ_{max} 288nm. Beer's law was obeyed in the concentration range of 5-30µg/ml. The results of analysis have been validated statistically. The proposed method is advantageous in a way that organic solvents (costlier and toxic) are avoided in the analysis with an economic agent sodium lauryl sulphate, but not at the expense of accuracy. The proposed method was found to be new, simple, ecofriendly, accurate, safe, reproducible and cost-effective and can be successfully employed in routine analysis of Cefixime tablets. Certainly, there is further scope of 10 %sodium lauryl sulphate as solubilizing agent for the spectrophotometric analysis of other poorly water-soluble drugs . The proposed method is The proposed method was optimized and validated in accordance with International Conference on Harmonization (ICH) guidelines and is worth adopting in respective pharmacopoeia.

MATERIALS AND METHODS

JASCO UV/Visible recording spectrophotometer (JASCO-v-630) with 1cm matched quartz cells is employed. Cefixime bulk drug sample was obtained as gift sample from "CONCEPT Laboratories Limited", Aurangabad. The tablets of Cefixime (Formulation-II) of CPOP developed with 1:1.5 ratio of osmogents to drug and constituting 3.6 % w/w of SLS with respect to drug were used as formulation. All other chemicals and solvents used were of analytical grade.

Calibration Curve in Presence and Absence of sodium lauryl sulphate

For preparation of calibration curve of Cefixime, 10 mg cefixime is transferred to a 100 ml volumetric flask. To this flask, 20 ml of AR Methanol was added and the flask was sonicated to solubilize the drug. Rest of methanol was used to make up the volume up to the mark to give a stock solution (100 mcg/ml). This stock solution was diluted suitably with methanol to produce various standard solutions containing 5, 10, 15, and 20µg/ml of drug. Also similarly stock solution is prepared with same quantity of drug and distilled water with 5% & 10% of Sodium lauryl sulphate with respect to drug, instead of methanol as solvent Absorbance's of these solutions were observed at 288 nm against corresponding reagent blanks. (Fig.no.i & ii).

Preliminary Solubility Studies of Cefixime

In the solubility studies, it was found that there was more than 3 fold enhancement in the solubility of Cefixime in distilled water with 5% & 10% of Sodium lauryl sulphate with respect to drug ,at 28±1ºC (in comparison to solubility in distilled water).(Table no.iii,iv & v)

Analysis of Cefixime in Tablets using United States Pharmacopoeial Method

For analysis of Cefixime in tablets using United States Pharmacopoeial method, twenty tablets were weighed and powdered finely. A portion of this powder containing 10 mg Cefixime was accurately weighed and transferred to a 100 ml volumetric flask. Methanol (30 ml) was added and sonicated for 5 minutes. After, it was diluted to 100 ml with methanol and filtered through a sintered glass funnel (G-3). The filtrate was diluted suitably with methanol to produce a solution containing 15µg/ml of Cefixime. The absorbance of this solution was noted at 288 nm and the drug content was determined (Table ii).

Analysis of Cefixime in Tablets by the Proposed Method

For the analysis of Cefixime in tablets by the proposed method, 20 tablets were powdered and tablet powder equivalent to 10 mg Cefixime (27.5 mg) was transferred to a 100 ml volumetric flask containing 20 ml of distilled water with 0.5mg and 1.00 mg of sodium lauryl sulphate solution separately. Flasks were sonicated for about 10 minutes to solubilize the drug present in tablet powder and volume was made up to the mark with distilled water. After filtration through sintered glass funnel (G-3), the filtrate (tablet extract) was appropriately diluted with distilled water containing 5% & 10% of SLS to produce a solution containing 15µg/ml of Cefixime and absorbance was noted at 288 nm against reagent blank. Table no.vii & viii.

Accuracy/Recovery Studies

To study the accuracy of the proposed methods in both Spectrophotometric and chromatographic methods, recovery study were carried out by addition of known amount of bulk drug to solution. To perform recovery studies, Cefixime bulk drug sample was added (13.5 mg) to the pre-analyzed tablet powder (equivalent to 5 mg of Cefixime) and drug content was determined by the proposed method. The results of recovery studies were presented in (Table no.x). which shows 100.97 & 100.29 % recovery respectively.

Effect of SLS Concentration:-
To elucidate the concentration dependent solubilising effect of SLS the three stock solutios with plain disilled water and with distilled water having 5% & 10% of SLS solution as solvent were prepared to get 100µg/ml stock solution .This was further diluted with respective solution to yield 15 ppm solution and absorbance at 288 nm was reported as shown in (table no.iii,iv & v)

Limit of detection (LOD) and limit of quantitation (LOQ)
The detection limit and quantitation limit were computed to assess quantity of analyte which can be detected and minimum quantity of analyte which can be determined quantitatively by proposed UV- spectrophotometric and chromatographic methods. The LOD and LOQ of Cefixime Trihydrate were estimated from the standard deviation of the response and the slope of the calibration curve by using following formula.

$$LOD = \frac{3.3 \times \sigma}{S}$$

$$LOQ = \frac{10 \times \sigma}{S}$$

Where σ = the standard deviation of the response

S = the slope of the calibration curve
LOD and LOQ were found to be 0.1980 µg / ml and 0.0287 µg / ml respectively with USP method while , LOD and LOQ were found to be 0.0151 µg / ml and 0.0458 µg / ml respectively with the proposed method .

PRECISION:
Precision of the method reported as % RSD, was estimated by repeatability, reproducibility and intermediate precision by measuring absorbance of three replicates of 10 µg / ml of Cefixime Trihydrate. % RSD values as in Table no.8 is less than 2% that illustrate the good precision of the analytical method.

RESULTS AND DISCUSSION

The mean percent label claims (Table ix) of formulation II, estimated by United States Pharmacopoeial Method (a standard analytical method) and proposed method were 100.86 and 99.97, respectively. Also, the mean percent label claims (Table viii) of formulation II, estimated by United States Pharmacopoeial Method and proposed method were 100.86 and 99.97, respectively. The results of analysis of the proposed method compared very well with the results of analysis of Pharmacopoeial method, indicating the accuracy (Recovery study table no.x) of the proposed analytical method. The low values of statistical parameters, viz standard deviation, percent coefficient of variation and standard error (Table viii & ix) further validated the method. From Table no.x, it is evident that the values of the mean percent recoveries (ranged from 99.38 to 100.33) are very close to 100. This together with the low values of statistical parameters viz standard deviation, percent coefficient of variation and standard error (Table no.viii) further validated the proposed method.

Fig.No.I Linearity of API in methanol

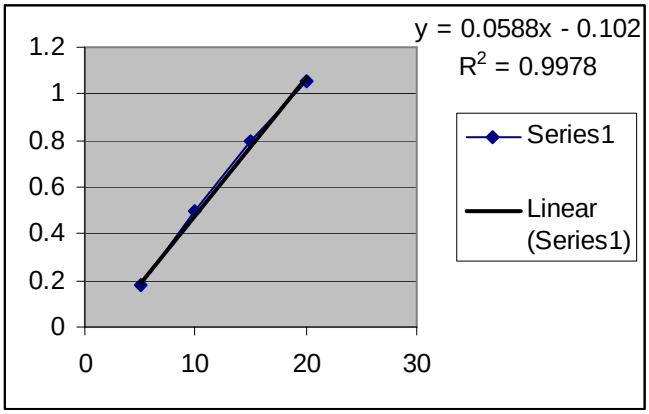

Fig.no.ii Linearity of tablet in methanol

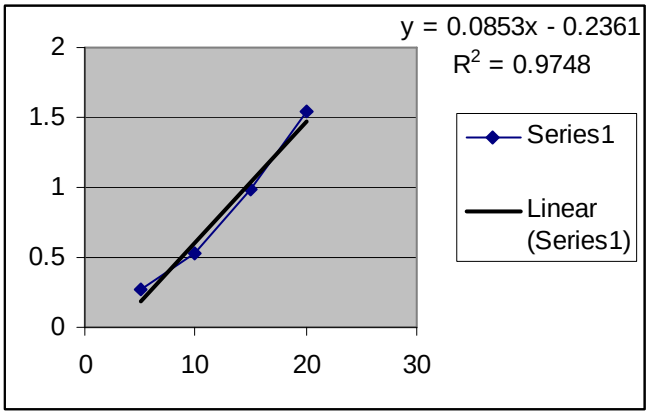

Table no. i Absorbance of API dissolved in Methanol at 288 nm.

Sr.no.	Conc.taken	Abs. I	Abs. II	Abs. III	Abs. Mean	±S.D.
1	5	0.178	0.180	0.176	0.178	0.0888
2	10	0.4980	0.499	0.4973	0.4984	0.2490
3	15	0.7989	0.7899	0.7994	0.7980	0.3980
4	20	1.0580	1.0601	1.0589	1.0590	0.5295

N=3 SD=standard deviation

Table no.ii Concentration of API & Tablet in methanol at 288 nm

Sr no.	Conc.taken	Solvent	Abs.288 nm API	Con.obtained	Abs. 288 nm Tablet	Conc.obtained
1	5 ppm	Methanol	0.178	4.761-95.23%	0.173	4.676-93.52%
2	10 ppm	Methanol	0.4980	10.20-102.04%	0.4900	10.12-100.60%
3	15 ppm	Methanol	0.7989	15.32-102.14%	0.7880	15.75-100.90%
4	20 ppm	Methanol	1.0580	19.72-98.63%	1.05321	19.64-98.23%

N=3 *SD=standard deviation*

Table no.iii Absorbances of TABLET in Methanol at 288 nm.

Sr.no.	Conc.taken	Abs. I	Abs. II	Abs. III	Abs. Mean	±S.D.
1	5	0.172	0.175	0.172	0.173	0.0865
2	10	0.4910	0.4885	0.4905	0.4900	0.2450
3	15	0.7889	0.7870	0.7886	0.7881	0.3940
4	20	1.0580	1.0585	1.0576	1.05803	0.5290

N=3 SD=standard deviation

Table no.iv Absorbances of API in distilled water without SLS at 288 nm.

Sr.no.	Conc.taken	Abs. I	Abs. II	Abs. III	Abs. Mean	±S.D.
1	5	0.0588	0.0597	0.0568	0.0584	0.280
2	10	0.162	0.158	0.161	0.1603	0.0801
3	15	0.461	0.498	0.475	0.478	0.1994
4	20	0.501	0.506	0.494	0.500	0.250

N=3 SD=standard deviation

Table no.v Absorbances of API in distilled water with 5% SLS at 288 nm.

Sr.no.	Conc.taken	Abs. I	Abs. II	Abs. III	Abs. Mean	±S.D.
1	5	0.0865	0.0868	0.0870	0.0869	0.407
2	10	0.3054	0.3046	0.3045	0.3048	0.1524
3	15	0.6364	0.6357	0.6362	0.6361	0.3180

N=3 SD=standard deviation

Table no.vi Absorbance's of API in distilled water with 10% SLS at 288 nm.

Sr.no.	Conc.taken	Abs. I	Abs. II	Abs. III	Abs. Mean	±S.D.
1	5	0.173	0.172	0.177	0.174	0.0780
2	10	0.4910	0.4900	0.4890	0.4900	0.2450
3	15	0.7828	0.7826	0.7836	0.7830	0.3915
4	20	1.0541	1.0540	1.0539	1.0540	0.5270

N=3 SD=standard deviation

Table no.vii Absorbances of tablet in distilled water at 288 nm.

Sr.no.	Conc.taken	Abs. I	Abs. II	Abs. III	Abs. Mean	±S.D.
1	10	0.4849	0.4856	0.4848	0.4851	0.242
2	15	0.7826	0.7830	0.7830	0.7828	0.3914

N=3 SD=standard deviation

Table no.viii Analysis of tablet by both methods

Sr.no.	Tablet label claim	Method	Absorbance 288 nm	Conc.mean ±SD	SE	LOD	LOQ
1	200 mg-10	USP Method	0.4905	100.76±0.2450	0.1416	0.1980	0.0287
2	200 mg-15	USP Method	0.7886	100.97±0.3940	0.2277	0.0152	0.0017
3	200 mg-10	Proposed Method	0.4851	99.63±0.242	0.1398	0.1598	0.0283
4	200 mg-15	Proposed Method	0.7828	100.31±0.3914	0.2262	0.0151	0.0458

N=3 SE=stand. Error LOD=limit of detection LOQ=limit of quantitation

Table no.ix Comparison of both methods of estimation of cefixime.

Tablet formulation	Label claim/ tablet (mg)	Method of analysis	% Label claim estimated*(Mean±S.D.)	% Coefficient of variation	Standard error
II	200	USP	100.86±1.119	1.1094	0.6468
II	200	PM	99.97±1.414	1.4144	0.8173

Table no.x Recovery study

SR NO.	Stock.sol.+spiking	Method	Abs.at 288	Conc.	%Recovery
1	10+5 ppm	USP	0.7880	15.22	100.97
2	10+5 ppm	PM	0.7826	15.04	100.296

CPOP- *controlled porosity osmotic pump*
SLS- *sodium lauryl sulphate*
RSD- *relative standard deviation*
SD- *standard deviation*
SGF- *simulated gastric fluid*
SIF- *simulated intestinal fluid*

CONCLUSION

There was no interference of SLS and the commonly used additives present in the tablet formulation in the estimation by proposed method. It is, thus, concluded that the proposed method of analysis is new, simple, cost-effective, environmentally friendly, safe, accurate and reproducible. Decided advantage is that organic solvent (methanol) is precluded but not at the expense of accuracy. The proposed method is The proposed method was optimized and validated in accordance with International Conference on Harmonization (ICH) guidelines and is worth adopting in respective pharmacopoeia.

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