AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: http://www.ajptr.com/

Newer HPTLC Method for Estimation of Cefixime, Cefpodoxime, Cefepime From Their Dosage Form

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ABSTRACT

Cefixime, cefpodoxime and cefepime are cephalosphrin antibiotics used widely in the different infectious diseases. Newer HPTLC methods were developed for their estimation from individual dosage forms due to versatile applications and advantages. The HPTLC chromatogram of cefixime was developed by using a mobile phase ethylene acetate: methanol: water (4.5:5:0.5%v/v) and scanning wavelength was 292nm. The Rf value was 0.58±0.02. The mobile phase optimized for cepodoxime was methanol: ethyl acetate: toluene (1.5:3:5.5% v/v), with the Rf value 0.53±0.02. The cefixime was retained using methanol :water : chloroform (6:3:1%v/v), on a silica gel G_{60} F_{254} aluminium sheet and scanning wavelength kept at 285nm. The Rf value was 0.44. The methods were optimized validated as per guidelines and successfully applied for individual dosage form containing of each of cephalosporin.

Keyword: HPTLC, Cefixime, Cepodoxime, Cefepime.

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Received 22 July 2018, Accepted 28 July 2018

Please cite this article as: Gandhimathi M *et al.*, Development of Naringenin Nanocrystals for Enhanced Solubility and Bioavailability . American Journal of PharmTech Research 2018.

INTRODUCTION

HPTLC[1,2] is a versatile technique that is explored for numerous drug analysis applications. It is cost effective and quicker chromatographic method when compared to others. Cephalosphorins[3] like cefixime, cefepime and cepodoxime were used as potential antibiotics. Cefixime is chemically, (6R,7R)-7-(2Z)-2-(2-amino-1,3-thiazol-4yl)-2-[(carboxymethoxy)imino]acetamido]-3-ethenyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid. It is a third generation cephalosporin drug. It used as an antibiotics by inhibiting biosynthesis and arresting cell wall assembly resulting in bacterial cell death. cepodoxime is chemically (6R,7R)-7-(2Z)-2-(-1,3-thiazol-4yl)-2-(methoxyimino)acetamido]-3-(methoxymethyl)-8-oxo-5-thia-1azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid. It is a third generation cephalosporin drug. It used as a antibiotics work by inhibition of bacterial cell wall synthesis. Cefepime is chemically, 1-{[(6R,7R)-7-(2Z)-2-(2-amino-1,3-thiazol-4yl)-2-[(carboxymethoxy)imino]acetamido]-2-carboxylato-8-oxo-5 thia 1 azabicyclo 4.2.0] oct-2-ene-3-yl]methyl}-1-methylpurrolidin-1-ium. It is a fourth generation cephalosporin drug. It provides bactericidal activity by interfering with bacterial cell wall synthesis and inhibiting cross linking of the peptidoglycan. Literature reveals few analytical works[4-9] for estimation of cefepime, cepodoxime and no HPTLC method available for cefixime. This paper describes development of HPTLC for determination cefixime, cepodoxime, cefepime for the bulk and pharmaceutical dosage form.

MATERIAL AND METHOD

Solvent and chemical used

Water, methanol, toluene, chloroform, ethyl acetate were supplied by S.D.Fine chemicals PVT Ltd., Maharashtra, India.

Materials Used

Pre-coated silica gel G_{60} F_{254} aluminium sheets were procured from Merck, Germany.

Instruments used

Shimadzu digital electronics balance, Camag HPTLC system (with TLC scanner-3, Win CATS software and Linomat 5 as a application device.

HPTLC METHOD

Method development

Cefexime, cepodoxime, cefepime they were retained on HPTLC plate with optimized mobile phase system.

Preparation of standard solutions

A quantity of 10 mg of cefixime, cepodoxime, cefepime were weighed into individual 10 ml volumetric flasks and dissolved in methanol, further diluted to the mark (1000 µg/ml). These were used as standard stock solutions. A working standard solution containing 100 µg/ml of each was prepared.

The validation of the developed method was carried out in terms of linearity, accuracy, limit of detection(LOD), limit of quantification(LOQ), inter and intra day precision and stability studies as per ICH guidelines.

Linearity and range

A 100 µl/ml solution of cefixime, cepodoxime and cefepime were used for establishing the linearity and range. Aliquots of 2 - 4.5µl of cefixime, 1- 3 µl of cepodoxime and 5- 25µl of cefepime were applied were on individual HPTLC plates. The plates were developed with respective mobile phase, scanned and peak areas were noted. The linear regression data have shown a good relation correlation coefficient over a concentration range used for three drugs.

Accuracy

In order to ensure the suitability and reliability of proposed methods for three drugs, recovery studies were carried out. It was done by mixing known quantities of individual standard drug with their pre analysed sample formulation and the contents were reanalyzed by proposed method. Recovery studied were carried out at 80% and 120% levels.

Precision

It was demonstrated by Intra-day precision, Inter-day precision, Repeatability of sample application and repeatability of sample measurement.

Intra-day precision

Intra-day precision was studied by different concentration in linearity range of the drugs for several times on the same days and by calculating %RSD.

Inter-day precision

Inter-day precision was studied by standard drug at two concentration in the linearity range of the drug for three days over a period of one week and % RSD was calculated.

Repeatability

Repeatability of sample application was carried by spotting 3.5 µl of drug solution is six times on precoated TLC plate followed by development of plate and %RSD was calculated for three drugs.

Repeatability of measurement was determined by spotting 3.5µl of drug solution on a precoated TLC plate and developed the plate and scanned six times and %RSD was calculated.

Robustness

The robustness of the method is its ability to remain unaffected by small change in practical conditions. Here the effect of change in condition such as ratio of mobile phase (±0.5min) and saturation time (±5min) were studied to prove robustness

Limit of detection(LOD) and Limit of quantification(LOQ)

LOD and LOQ were determined by applying decreasing amount of the drug in triplicate on the plate. The lower concentration at which the peak is detected is called limit of detection. The lowest concentration at which the peak is quantified is called limit of quantification.

Stability of chromatographic plate

When the developed chromatographic plate is exposed to atmosphere the average are likely to decompose. Hence it is necessary to study the stability of drug on plate. It was studied by scanning the plate at different time intervals and peak areas were compared with the plate area of freshly scanned plate. The developed plate was found to be stable for 8 hour for cefexime, cefpodoxime.cefepime for about 24 hour.

Analysis of formulation

Twenty tablets each containing 200mg of cefixime were taken and average weight was calculated. They were finely pulverized and the quantity of homogenized powder equivalent to 10mg of cefixime was transferred to a 100ml volumetric flask, it was dissolved with methanol, sonicated and made up to volume with methanol. The solution was filtered. Similar procedure was employed for tablets containing 200 mg of cepodoxime. For cefepime ten formulation of powder for injection (1g/10ml) of cefepime was taken and the average weight was calculated, The quantity of homogenized powder equivalent to 10mg of cefepime was transferred to a 100ml volumetric flask and up to volume with methanol Then the solution was filtered using whattmann filter paper. All these three formulation solutions were applied on individual pre coated TLC plate. After developed the plate was scanned at 292nm for cefixime, cepodoxime and 285nm for cefepime the peak areas were noted. The amount of cefixime, cepodoxime, cefepime present in their respective formulation was calculated.

RESULTS AND DISCUSSION

Novel HPTLC method has been developed for three cephalosporins cefixime, cepodoxime, cefepime for their estimation from individual dosage form and validated as per guidelines[10] and ascertain the purpose.

The validation parameters for three drugs are listed in table 1. The typical densitogram of cefixime, cepodoxime, cefepime are shown in fig 1-3. The result of analysis cefixime, cefpodoxime, cefipime in formulation by HPTLC analysis are shown in table 2

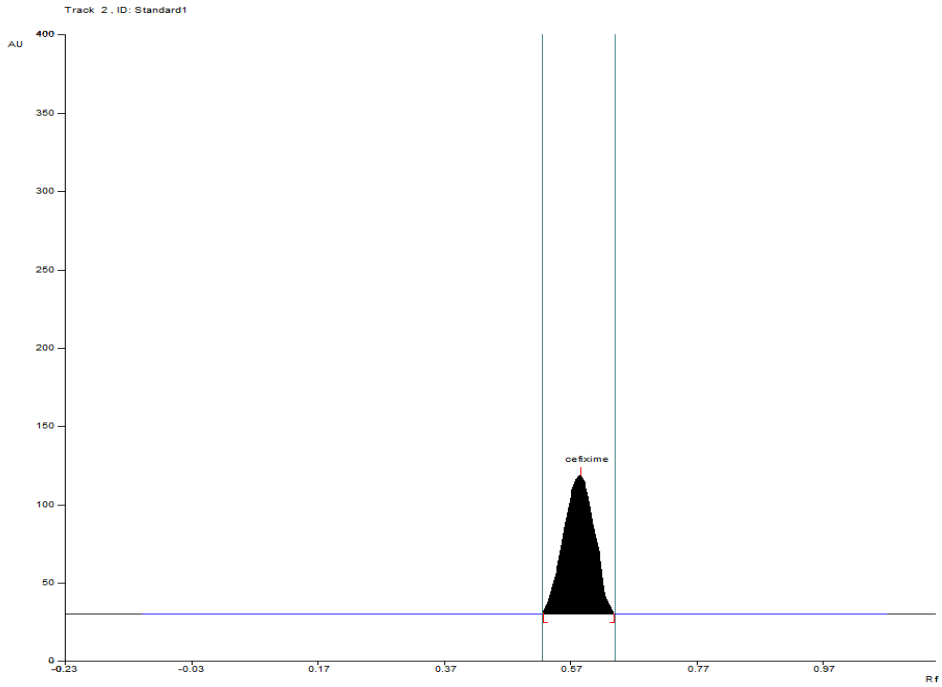

Figure 1: Densitogram of cefixime 200(ng/band)

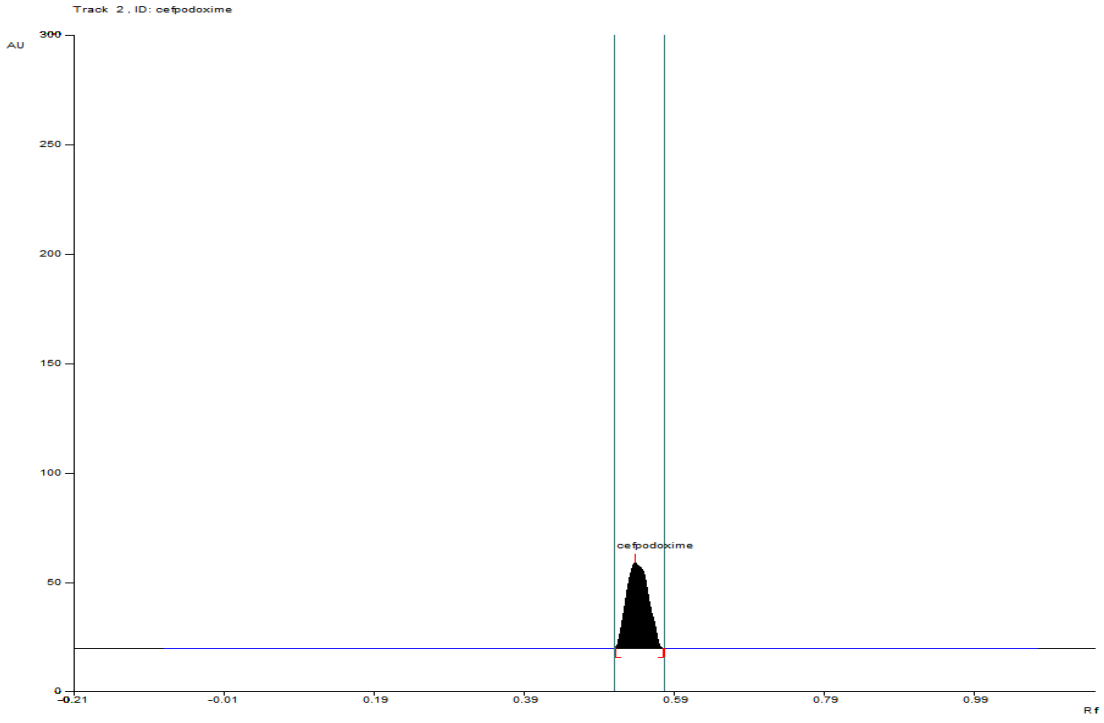

Figure 2: Densitogram of cefpodoxime 100(ng/band)

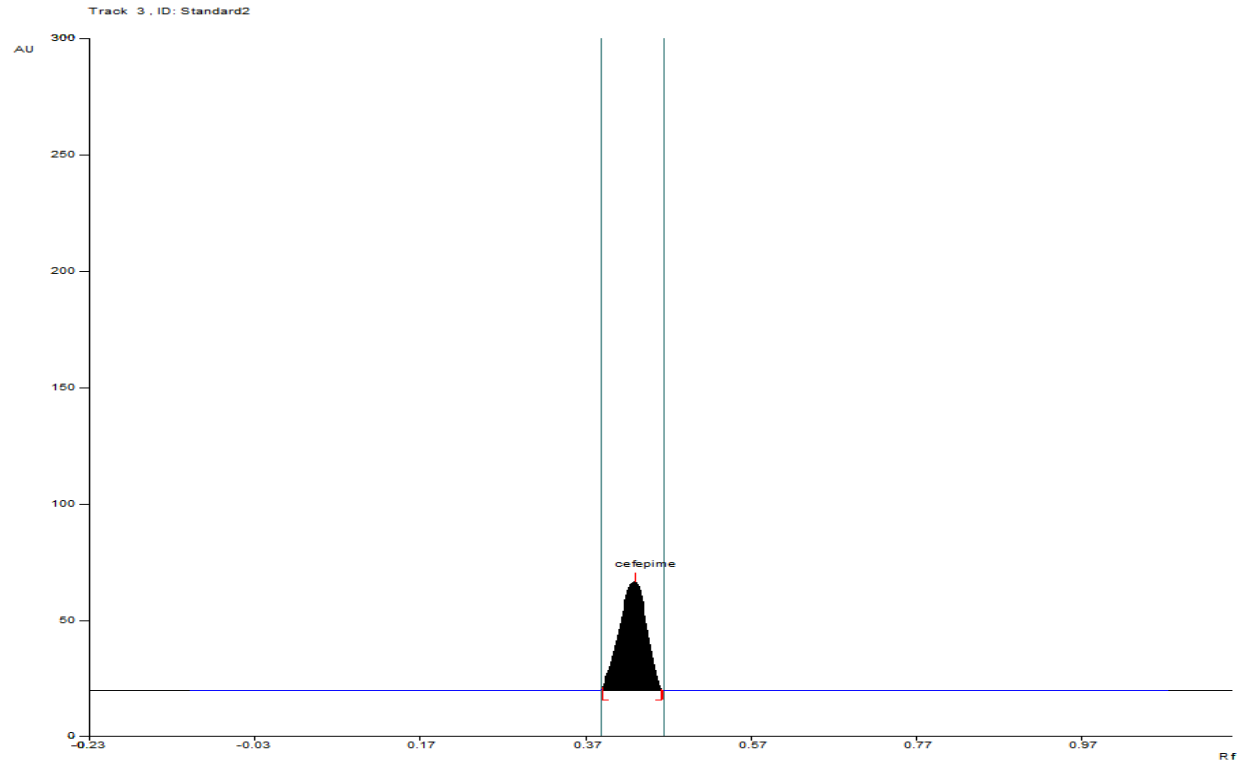

Figure 3: Densitogram of cefepime 1000(ng/band)

Table1.validation parameters of cephalosporins

Parameter	**cefixime**	**cefpodoxime**	**Cefepime**
Linearity (ng/band)	200 - 450	100 – 300	500 – 2500
Correlation coefficient	o.998	0.999	0.998
Slope	11.21	8.124	1.2
Intercept	593.815	293.581	85.12
Precision (% RSD)			
Interday precision(n=3)	1.4 – 1.9	1.2 – 1.6	0.4 - 0.6
Intraday precision(n=3)	0.2 – 0.9	1.4 – 1.6	0.3 – 0.8
Repeatability of peak area (n=6)	0.6	1.4	1.1
Accuracy			
% recovery method(% RSD)	0.78 – 0.87	0.51 – 0.82	0.27 – 054
Limit of detection (LOD) (ng/band)	40	60	120
Limit of quantification (LOQ) (ng/band)	100	100	250
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Table 2. Result of formulation analysis of cephalosporins

Label amount	Amount found	% label claim	Formulation	% RSD
200 mg/tablet	195.2mg/tablet	97.6	cefixime	0.6
200 mg/tablet	195.2mg/tablet	97.6	cefpodoxime	0.96
1gm/10ml vial	997.2gm/10ml	99.7	cefepime	0.37

CONCLUSION

Novel newer HPTLC methods were developed for the estimation of cefixime, cefpodoxime, cefepime and successfully applied to their formulation.

There were no interference found from matrix during analysis and linearity accuracy and precision of the method were good.

The method developed for cephalosporin (cefixime, cefpodoxime, cefepime) can be used in industry for routine analysis to check the amount of the drug present in pharmaceutical dosage form.

ACKNOWLEDGEMENT

The author thank SNR sons charitable trust, Coimbatore for providing facility to carry out the research work.

REFERENCES

1. Sethi PD, HPTLC: High Performance Liquid Chromatography. Quantitative Analysis of Pharmaceutical Formulations. New Delhi: CBS publishers and distributers; 1997. p.3- 92.
2. SethiPD. Quantitative analysis of drugs in pharmaceutical formulation. 3rd ed. New Delhi: CBS Publishers and Distributers; 1997. p. 1-56.
3. The United States Pharmacopoeia, 2nd Edn.,Rockivile. United States Pharmacopoeial Convention, 2004, 354- 357,359-361, 378-379.

4. Azmi S.N.H, Iqbal B, Mamari.J.K, AlHattali,K.A., Hadhrami W.N.AI. Method development and validation for determination of cefixime in pure and commercial dosage form by spectrophotometry, 2014,8(6), 595-601.
5. Deepshikah Patle, HPTLC method Development and validation of cepodoxime proxetil and ofloxacin in bulk and combination tablet dosage form, Current Trends in Biotechology and Phamrmacy, 2016,10(1),56-63.
6. Smita J Pawar, Amol P Kale, Manoj P Amrutkar, Jyotsna J Jagade, Nikhil S Pore and Asok V, HPTLC estimation estimation cefixime and cloxacillin in tablet dosage form, Asian J Resear. I Chem., 2010, 3(2), 299-301.
7. Pritam Jain, Amar Chaudhari, Anup Bang and OsanjaySurana, validated stability indicating HPTLC method for determination of cefpodoximeproxetil in bulk and in pharmaceutical formulation according to ICH guidelines.J. Pharm Bioallied.Sci; 2012;4(2), 101-106.
8. Laxman Prajapati, HPTLC method for simultaneous estimation of cefepimeHCL and sulbactum sodium. Asian Journal of Pharmaceutical Sciences; 2016;6(4).
9. ICH harmonized tripartite guideline, validation of analytical procedures: text and methodology. Q2 (R1), (November 2005). Geneva. Switzerland