Int J Pharm Bio Sci 2015 April; 6(2): (P) 183 - 193

Research Article **Analytical Chemistry**

International Journal of Pharma and Bio Sciences **ISSN 0975-6299**

STABILITY INDICATING HPLC METHOD DEVELOPMENT AND VALIDATION FOR THE SIMULTANEOUS DETERMINATION OF CEFPODOXIME PROXETIL AND OFLOXACIN IN ITS DOSAGE FORMS

PRASHANT D. GHODE*[1] AND DR. SUNIL P. PAWAR[2]

[1]JSPM's Rajarshi Shahu College of Pharmacy and Research, Tathawade, Pune 411033 Maharashtra India.
[2]P.S.G.V.P. Mandal's College of Pharmacy, Shahada, Nadurbar 425409 Maharashtra,India

ABSTRACT

A simple, precise, sensitive, reproducible stability indicating Reverse Phase High Performance Liquid Chromatographic method for determination of Cefpodoxime Proxetil and Ofloxacin in tablet dosage form was developed. Chromatographic separation was achieved on Hypersil-keystone RP C_{18} column maintained at 30ºC. Mobile phase consisting of buffer Potassium dihydrogenphosphate: Methanol: Acetonitrile (pH 3.0) in the ratio of 50:30:20v/v was pumped into the column at a flow rate of 1.2 ml/min. Determination was carried out at 235nm. Two peaks were obtained for Cefpodoxime at 13.1 min and 14.1 min and one peak for Ofloxacin at 5.11 min. The linearity was found to be 4-20 µg/ml and 10-50 µg/ml for Cefpodoxime for Ofloxacin respectively. Method was validated as per ICH guidelines. Cefpodoxime and Ofloxacin were subjected to various stress conditions including acidic, alkaline, oxidation, photolysis, reduction and thermal degradation. The proposed method can be extended to the analysis of Cefpodoxime and Ofloxacin in tablet dosage formulations.

KEYWORD: Cefpodoxime Proxetil, Ofloxacin, HPLC, Stability indicating, validation

PRASHANT D. GHODE
Research Scholar, P.S.G.V.P. Mandal's College of Pharmacy, Shahada, Nadurbar. 425409. Maharashtra. India.

***Corresponding author**

INTRODUCTION

Cefpodoxime Proxetil (CFP) is a broad spectrum, orally absorbed third generation cephalosporin antibiotic with chemical name (6R,7R)-7-[[(2Z)-(2-Amino-4-thiazolyl) (methoxyimino) acetyl] amino]-3-(methoxymethyl)-8-oxo-5-thia-1-azabicyclo [4.2.0] oct-2-ene-carboxylic acid 1-[[(1-methylmethoxy) carbonyl]]oxy]ethyl ester (Fig.1). It is used in the treatment of influenza, meningitis, gonorrhea, pneumonia, tuberculosis, acute otitis media, pharyngitis. Ofloxacin[OFL] is a broad spectrum fluorinated quinolones antibacterial with chemical name 9-Fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7H-pyridol[1,2,3-de]-1,4 benzoxazine -6-carboxylic acid (Fig.2). It is used in the treatment of respiratory tract infections, pharyngitis, community-acquired pneumonia, mild to moderate bacterial exacerbation, sexually transmitted diseases, acute and uncomplicated urethral and cervical gonorrhea, urethritis, complicated urinary tract infections, prostatitis, [1,2]. The combination of CFP and OFL has unique dual mode of action, OFL prevents nucleic acid synthesis, while CFP inhibits cell wall synthesis and work synergistically with improved patient compliance. The combined dosage forms of OFLO and CEFPO are available in the market and used as antibacterial drugs. The combination of these two drugs is not official in any pharmacopoeia; hence no official method is available for the simultaneous estimation of OFLO and CEFPO in their combined dosage forms[3]. Literature survey reveals that there are few reported methods to determine CFP[4-6] and OFL[7-9] alone and in combination with other drugs[10-16] in dosage forms by spectrometry and HPLC. Few spectrometry[3,17-20] and HPLC[21-24] methods are also available for the simultaneous determination of CEP and OFL, but no stability indicating method is available for CEP and OFL in combination. Therefore the purpose of this study is to develop stability indicating method for the simultaneous estimation of CFP and OFL in tablet dosage form.

MATERIALS AND METHODS

2.1 Chemicals and Reagents

CFP and OFL standards were obtained as a gift samples from Alkem Laboratories, Mumbai. Methanol and acetonitrile of HPLC grade (E. Merck) and potassium dihydrogenphosphate of AR grade (S.D. Fine Chemicals Ltd.) was purchased from local suppliers. Milli Q water was used. All the other reagents were of analytical grade. Marketed formulation Zedocef-O (Macleods Pharmaceutical Limited, India) was purchased from local pharmacy.

2.2 HPLC instruments and analytical conditions

The separation was carried out on HPLC system (Waters) with binary HPLC pump, Waters 2998 PDA detector, Data Ace software. The chromatographic column used in this study was Hypersil-keystone RP18, (250 mm×4.6 mm×5µ). The column was maintained at 30°C. The mobile phase consisting of buffer (20 mM potassium dihydrogenphosphate): methanol: acetonitrile (pH 3.0 adjusted with orthophosphoric acid) was filtered through 0.45µ membrane filter before use, degassed and was pumped from the solvent reservoir in the ratio of 50:30:20v/v at a flow rate of 1.2 ml/min. The detection was monitored at 235 nm and the run time was 25min. The volume of injection loop was 10µl. Prior to injection of the drug solution the column was equilibrated for at least 15 min. with the mobile phase flowing through the system. The mobile phase was used as a diluent in the present study.

2.3 Standard and sample preparation

Accurately 200.0 mg of OFL and CEF was weighed and transferred into separate 100 ml volumetric flask containing 30 ml of mobile phase sonicate for 15 min until dissolved. The volume made up to 100 ml with diluent (Stock A of 2000 ppm). Solutions were further diluted with diluent. Twenty tablets of Zedocef-O were accurately weighed and crushed to fine powder. Powdered sample equivalent to 200 mg of CFP (200 mg of OFL) was accurately weighed and transferred into 100 ml

volumetric flask. The sample was dissolved in 100 ml of diluents by sonication for 25 min with intermittent vigorous shaking, cooled to room temperature and volume was made up with diluent. The solution was filtered through 0.45µ Teflon filter syringe and 5 ml of this solution was further diluted to 50 ml with diluent and mixed.

2.4 Method Validation

The method was validated for the parameters such as system suitability, selectivity, linearity and range, precision (interday and intraday), accuracy, robustness, ruggedness limit of quantitation (LOQ) and limit of detection (LOD) [25]. For the system suitability study, the solutions containing 10µg/ml each for OFL and CEF standards were prepared and diluted with diluent. The column efficiency, resolution and peak asymmetry were calculated for the standard solutions. During mobile phase optimization Buffer: Methanol: Acetonitrile (50:30:20), pH 3 at λ_{max}235 nm was found to be satisfactory for both drugs. After mobile phase selection, effect of pH and flow rate was studied on resolution of peaks of both the drugs from each other. It was found that pH 3 and flow rate1.2 ml/min. was suitable for both drugs. To determine the linearity of the method different concentration levels were prepared from standards stock solutions and each solution was injected into the HPLC system. The peak area of the chromatogram obtained was noted and calibration curve was constructed by plotting response factor against concentration of drugs. The precision of the method was established by carrying out intra-day and inter-day analysis and relative standard deviation (%RSD) was calculated. The intra-day precision was studied by performing analysis at regular interval in a day, while inter-day precision was performed on three different days (day 1, 2, and 3). The accuracy study of the method was performed by the addition of standard drug to the pre-analyzed sample at three different levels 80 %, 100 % and 120 % and mean percentage recovery was determined. Effect of small changes in the HPLC conditions such as change of pH, change in temperature & change in flow rate was studied to evaluate robustness of the method while ruggedness was studied by a change in analyst. The LOD and LOQ were determined based on the standard deviation of the response and the slope of the calibration curve.

2.5 Forced Degradation

Forced degradation studies were performed to evaluate the stability indicating properties (specificity) of the proposed method. Samples were subjected to stress conditions such as acid hydrolysis, base hydrolysis, heat or thermal, photolytic, oxidation and reduction. Individual drug solutions, standard mixture and sample solution were subjected to the same stress conditions to ensure the effective separation of degradation peaks and main peaks. Standard stock and sample stock solution (stock B) was further diluted to get the concentration 10µg/ml for CEP and OFL in individual solutions and in sample solution. Acid degradation was carried using 2 ml of 0.1N hydrochloric acid; alkali degradation was carried out in 2 ml of 0.1N sodium hydroxide. The stressed solutions were neutralized and then diluted with diluent. Oxidation degradation was performed by adding 2 ml of 30% H2O2 and then diluted with diluent. For the thermal degradation study solid samples (equivalent to 10 mg) were kept in oven at 80ºC for 24 hrs which were further diluted and chromatographed. Photolytic degradation was carried out in by exposing to UV radiations (1.2 million lux hrs) and reduction was carried out using 10% sodium metabisulphate

RESULTS AND DISCUSSION

3.1 Method Development

Chromatographic separation was achieved by using Hypersil- keystone RP18 with a flow rate of 1.2 ml/min. The optimized mobile phase was buffer: methanol: acetonitrile (50:30:20), 3 pH at λ_{max} 235nm was found satisfactory for both drugs out of various combinations of mobile phase tried. The chromatogram of standard CFP showed two peaks at 13.11 and 14.12 min which are due to *R* and *S* isomers respectively present in the recimic mixture[5]. Similarly chromatogram of standard OFL showed peak at 5.01 min. Representative chromatograms for single standard CFP, OFL and formulation are shown in Fig. 3 & 4.

3.2 Method Validation

In system suitability the values obtained demonstrated the suitability of the system for

the analysis of these drugs combination. The values for resolution, capacity factor, theoretical plate, HETP and asymmetric factor were given in Table 1. The values were found well within the acceptable limit. Linearity was observed over the concentration range 4 – 20 µg/ml for CFP and 10 – 50 µg/ml for the OFL. The correlation coefficients (r^2) were found to be 0.997 & 0.999 for OFL and CFP respectively. The result showed that an excellent correlation exists between responses and concentration of drugs (Table 2). The calibration curves are shown in Fig. 6 & 7. Intra-day and inter-day analysis was performed for precision study. Repeatability or intra-day precision was investigated by injecting six replicate sample solutions on the same day. Inter-day precision was assessed in triplicate over three consecutive days. The relative standard deviation (%RSD) was found to be well within the acceptable limit. The % RSD for inter-day study was 0.552 and 0.508 for CFP and OFL respectively, and for intra-day it was 0.671 and 0.1002 for CFP and OFL respectively and the results of precision study are given in Table 3. The results implied that the method developed was precisely for the determination. The recovery study at three different levels 80, 100 and 120 % was performed to asses the accuracy of the method. The results of the recovery study are shown in table no. 4. % recovery for CFP was found to be 99.59 –.99.78% and 99.59–99.75% for OFL. The LOQ & LOD was found to be 0.00635µg/ml, 0.002096µg/ml respectively for OFL. For CFP the LOQ & LOD was found to be 0.0008560 µg/ml and 0.000282494 µg/ml respectively. The % RSD in robustness and ruggedness was found well within the acceptable limit and mentioned in Table no. 5. The proposed method was applied for the determination of CFP and OFL in tablet dosage form. The % assay for CFP and OFL was found to be 99.8% & 99.2% respectively. Assay determination was carried in five replicates and %RSD was found less than 2% (Table 6).

3.3 Forced Degradation

Forced degradation studies were performed on standard drug alone, mixture of standard drugs and their formulation. From the degradation of these solutions under the same stress condition gives us an idea about the origin of degradent products. Peak purity study was performed by using purity angle and purity threshold parameters. Degradants did not show any interference with the elution of drug peaks as the peak purity of CFP and OFL was well within acceptance criteria for stressed samples. Hence, the method is stability indicating.

3.3.1 Acid degradation

Degradation of CFP was found to be 91.54% and degradant peak appeared at 11.189 min while the drug peaks at 13.098 and 14.124 min. Degradation of OFL was found to be 49.99% when treated with 0.1 N hydrochloric acid. A degradant was observed with OFL at 4.338, whereas sample solution the CFP was degraded by 91.364% when treated with acid and OFL was 50.02%. The degradant peak of CFP appeared at 11.187min and degradent peak of OFL was obtained at 4.338 min. The peaks of drugs and degradation products were confirmed by comparing them with the individual chromatograms of the drugs under the same stress conditions. (Fig. no. 8, 9, 10 & 11). The degradents appeared in the formulation and standard mixtures were identified by correlating their retention time.

3.3.2 Alkali degradation

CFP gets 91.248% degraded and form degradant at 11.903 with drug peaks at 13.113 and 14.131 while OFL was degraded 25.02% when treated with sodium hydroxide alkali and degradant was observed with OFL at 4.241. In formulation the CFP was 91.628% degraded when treated with alkali and OFL was 25.02%. The degradant peaks of CFP and OFL are 4.242, 5.113, 12.903, 13.112 and 14.129. Degraded peak of OFL was observed at 5.113. The peaks were confirmed by comparing them with the individual chromatograms of the drugs.

3.3.3 Peroxide degradation

No degradation was observed when treated with hydrogen peroxide (oxidation) for CFP, whereas OFL was partially degraded (19.789%) when treated with hydrogen peroxide.

3.3.4 Reduction

No degradation was observed when treated with sodium bi sulphite for CFP and OFL in standard and sample too.

3.3.5 Photolytic degradation

No degradation was observed when treatment with UV light for CFP, whereas OFL was partially degraded (16.457%) when treated with UV light.

3.3.6 Thermal degradation

29.6% degradation was observed for CFP when treated with dry heat and OFL was degraded 26.81% when treated with dry heat. A degradant was observed with OFL at 4.197.

Table 1
Description of System suitability

S.No.	Parameters	Cefpodoxime Proxetil		Ofloxacin
		1	2	
1.	Resolution (Rs)	6.8716	6.5743	9.4652
2.	Capacity Factor (k´)	4.609	4.422	5.0903
3.	Theoretical Plate	213988.5732	213950.4271	125706.54
4.	HETP	0.1246	0.1059	0.0548
5.	Tailing Factor	1.0759	1.0763	1.0697
6.	Retention time	13.112	14.231	5.012
7.	Asymmetry	1.049	1.103	1.4251

Table 2
Standard Curve of Ofloxacin and Cefpodoxime Proxetil

S.No.	Conc.(µg/ml)	Area	Conc.(µg/ml)	Area
1	10	50027.90494	4	197022.3937
2	20	98038.03621	6	295533.2376
3	30	151814.2378	8	404045.0734
4	40	210487.7318	10	492556.4015
5	50	250091.8838	20	982112.951

Table 3
Intra- day and Inter-day Precision

Parameters	Intra-day Precision		Inter-day Precision	
Observations	CEFO	OFLO	CEFO	OFLO
Mean % Label Claim	99.38	99.35	99.13	99.8
SD	0.549	0.504	0.665	0.1
%RSD	0.552	0.508	0.671	0.100

Table 4 ***Recovery Studies***

Recovery Level (%)	80		100		120	
	CEFO	OFLO	CEFO	OFLO	CEFO	OFLO
Amount Present (mg)	200	200	200	200	200	200
	200	200	200	200	200	200
	200	200	200	200	200	200
Amount of Std. Added (mg)	160	160	200	200	240	240
	160	160	200	200	240	240
	160	160	200	200	240	240
Amount Recovered (mg)	158.968	159.832	199.79	198.62	239.844	239.62
	159.904	159.112	198.89	198.79	239.976	239.94
	159.192	159.984	199.92	199.88	238.62	238.66
% Recovery	99.355	98.895	99.895	99.31	99.935	99.845
	99.94	99.99	99.445	99.395	99.99	99.975
	99.495	99.885	99.96	99.94	99.425	99.445
Mean Recovery	**99.59**	**99.59**	**99.76**	**99.54**	**99.78**	**99.75**
SD	0.305	0.604	0.28	0.341	0.311	0.276
%RSD	0.306	0.606	0.281	0.343	0.312	0.276

Table 5
Robustness and Ruggedness

Sr.No.	Validation Parameter	Changeinchromatographic conditions	SD*			%RSD*		
			CFP1	CFP2	OFL	CFP1	CFP2	OFL
1	Robustness	Effect of pH	14.658	26.81	1.62	0.00585	0.011	0.0032
		Effectof temperature	18.52	26.81	4.01	0.0074	0.011	0.008
		Effect of flow rate	17.02	26.81	2.29	0.006	0.112	0.004
2	Ruggedness	Analyst to Analyst	0.579		0.46	0.581		0.46

n=3 (average of Three determinations)

Table 6
Assay of CFP and OFL in Tablet Formulation

Brand Name	CFP		OFL	
	Label Claim (mg)	% Assay	Label Claim (mg)	% Assay
Zedocef-O	200	99.8	200	99.6
	200	99.9	200	98.9
	200	99.8	200	99.5
	200	99.7	200	98.3
	200	99.8	200	99.7
Mean		99.8		99.2
SD		0.070710678		0.591607978
%RSD		0.070852383		0.59637901

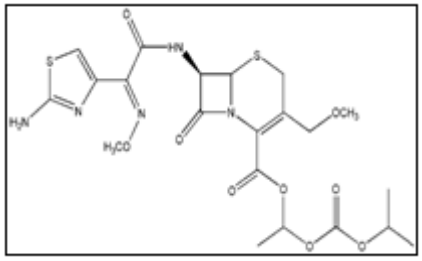

Figure 1 ***Cefpodoxime Proxetil***

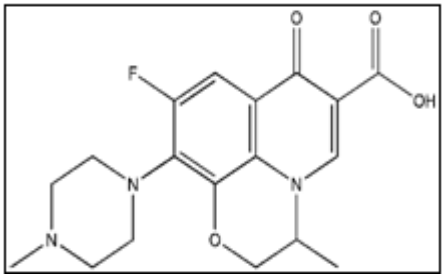

Figure 2 ***Ofloxacin***

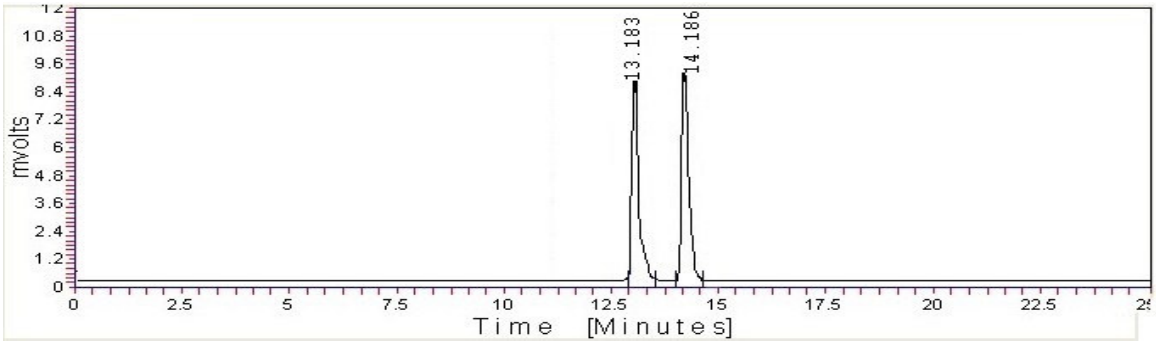

Figure 3
Chromatogram of Cefpodoxime Proxetil

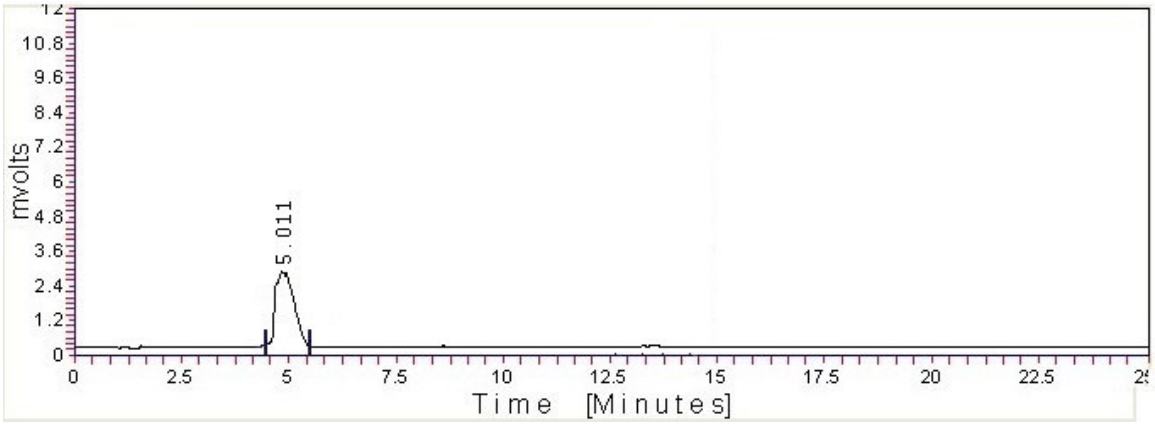

Figure 4
Chromatogram of Ofloxacin

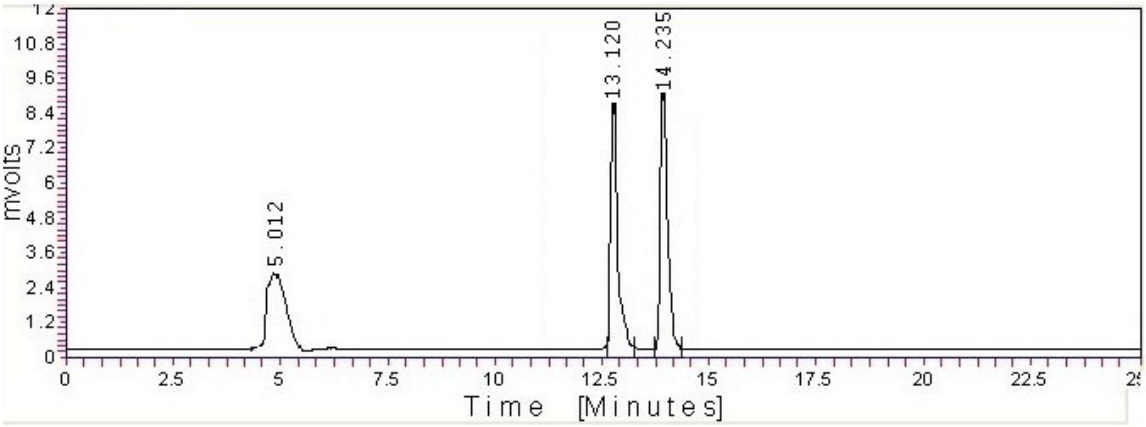

Figure 5
Chromatogram of mixture

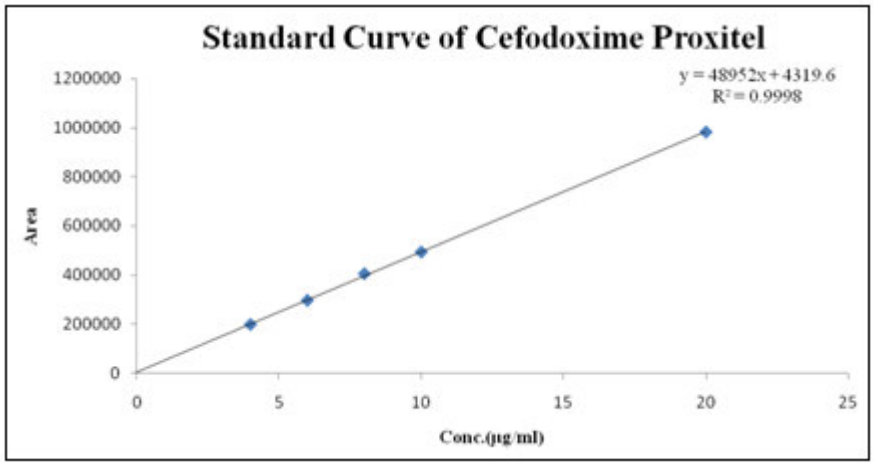

Figure 6
Calibration curve of Cefpodoxime Proxetil

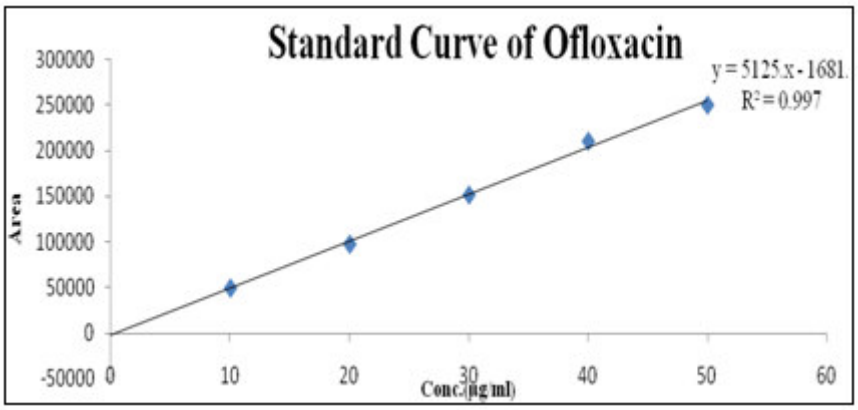

Figure 7
Calibration curve of Ofloxacin

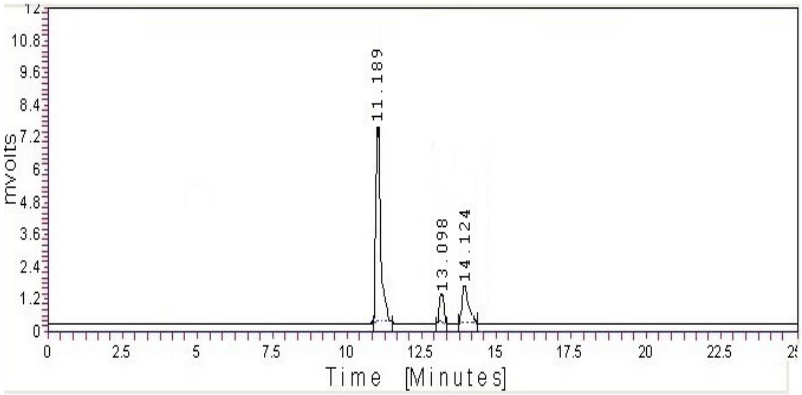

Figure 8
Cefpodoxime Proxetil Acid Degradation

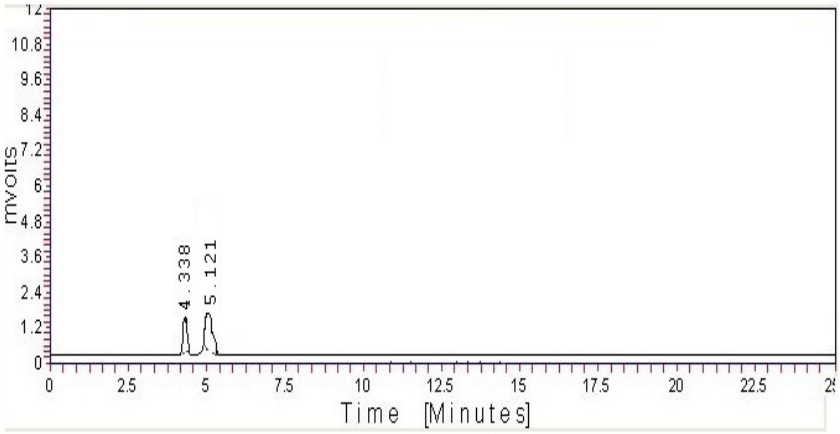

Figure 9
Ofloxacin with Hydrochloric Acid

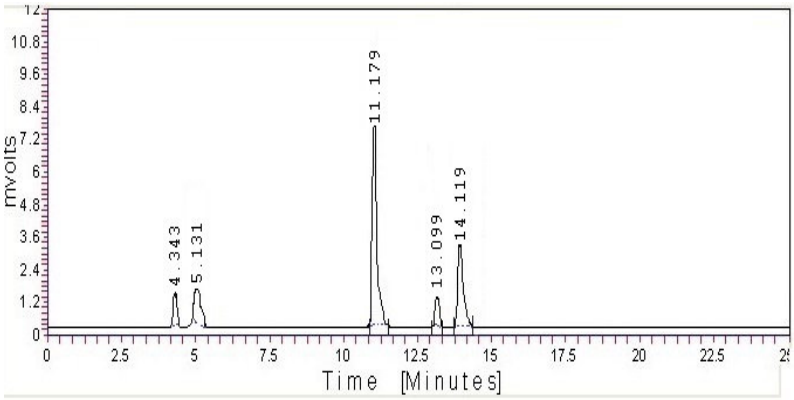

Figure 10
Standard Mixture (Cefpodoxime and Ofloxacin) with Hydrochloric acid

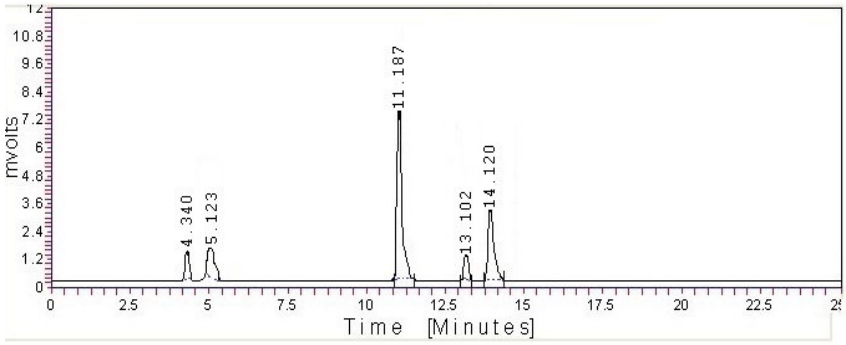

Figure11
Formulation (Cefpodoxime and Ofloxacin) with Hydrochloric acid

CONCLUSION

A simple and precise stability indicating HPLC method has been developed for estimation of CFP and OFL in tablet dosage form. The %RSD values in precision, recovery studies, robustness and ruggedness studies was found to be less than 2.0%, indicating that the method is precise, accurate and robust. The LOQ & LOD was found to be 0.00635µg/ml, 0.00209 µg/ml respectively for OFL. For CFP the LOQ & LOD was found to be 0.00085 µg/ml and 0.000282 µg/ml respectively. The % assay was found to be well within the acceptable limit. In degradation studies, it was found that CFP was more sensitive to acidic and alkali degradation, while OFL showed degradation in acidic, alkali, peroxide, photolytic thermal conditions. The peaks of the degradants in each condition were well separated from main peaks. Purity plot confirmed that there is no interference of any degradants at the retention time of the main peaks indicates that the developed method is stability indicating. The proposed method can be used as an alternative method for the analysis of CEP and OFL in its dosage forms.

ACKNOWLEDGEMENT

The authors are thankful to the Alkem Laboratories, Mumbai for providing the gift samples of the drugs.

REFERENCES

1. O'Neil MJ, The Merck Index, An Encyclopedia of Chemicals Drugs and Biological. 14th Edn, Merck Research Laboratories, Merck and Company, Inc.,Whitehouse station, NJ, USA: 1941,6771:319 1170, (2006).

2. Goodmann & Gilman's, The Pharmacological Basis of Therapeutics, 11th Edn, McGraw- Hill companies Inc., USA: 1148–1149 (2006).
3. Patel SA, Patel SA, Simultaneous spectrophotometric determination of cefpodoxime proxetil and ofloxacin in tablets. Journal of Applied Pharmaceutical Science, 01 (07): 141-144, (2011).
4. Subbayamma AV, Rambabu C, Spectrophotmetric determination of cefpodoxime proxetil in tablets. Asian Journal of Chemistry, 22 (5): 3345-3348 (2010).
5. Mathew C, Ajitha M, Sathesh Babu PR, Cefpodoxime proxetil: A new stability indicating RP-HPLC method. ISRN Chromatography, 328157: 1-8 (2013).
6. Fattaha LA, Weshahyb SA, Hassana NY, Mostafaa NM, Boltia SA, Stability indicating methods for the determination of cefpodoxime Proxetil in the presence of its acid and alkaline degradation products. International Journal of Pharmaceutical and Biological Research, 3(6): 223-239 (2013).
7. Prashanth KN, Basavaiah K, Raghu MS, Simple and selective spectrophotometric determination of ofloxacin in pharmaceutical formulations using two sulphonphthalein acid dyes. ISRN Spectroscopy, 357598: 1-4 (2013).
8. Vinay KB, Revanasiddappa HD, Divya MR, Rajendraprasad N, Spectrophotometric determination of ofloxacin in pharmaceuticals and human urine. Ecletica Quimica, 34(4) :65-78(2009).
9. Fabre D, Bressolle F, Kinowski JM, Bouvet O, Paganin F, Galtier M, A reproducible, simple and sensitive HPLC assay for determination of ofloxacin in plasma and lung tissue: Application in pharmacokinetic studies. J. Pharm Biomed Anal, 12(11) :1463-9 (1994).
10. Malathi S, Dubey RN, Venkatnarayanan R, Simultaneous RP-HPLC estimation of cefpodoxime proxetil and clavulanic acid in tablets. Indian J Pharm Sci, 71(1) 102–105: (2009).
11. Singh S, Dubey N, Jain DK, Tyagi LK, Singh M, Spectrophotometric and RP-HPLC methods for simultaneous determination of cefpodoxime proxetil and clavulanate potassium in combined tablet dosage form. American- Eurasian Journal of Scientific Research, 5(2): 88-93(2010).
12. Rote AR, Kande SK, Development of HPTLC method for determination of cefpodoxime proxetil and ambroxol hydrochloride in human plasma by liquid–liquid extraction. Pharm Methods, 2(4): 242–246 (2011).
13. Hassan EM, Mahrous MS, Shdeed RN, Stability indicating spectrophotometric methods for the determination of ofloxacin and ceftriaxone and their degradation products. Journal of Pharmaceutical and Biomedical Sciences, 18(18): 1-13(2012).
14. Dharuman J, Vasudevan M, Somasekaran KN, Dhandapani B, Ghode PD, Thiagarajan M, RP-HPLC method development and validation for the simultaneous estimation of ofloxacin and tinidazole in tablets. International Journal of Pharm Tech Research,1(2):121-124 (2009).
15. Ghosh SJ, Darbar S, Chowdhury PP, Chattopadhyay SP, Chakraborty MR, Simultaneous determination and validation of ofloxacin and ornidazole in combined dosage pharmaceutical formulation. International Journal of Pharm Tech Research, 2(1):367-374 (2010).
16. Rege PV, Mapari R, Simultaneous quantification of ofloxacin and ornidazole from combined pharmaceutical drug formulation by HPLC. International Journal of Pharma and Bio Sciences,2(4) :51-58(2011).
17. Patel SA, Patel SA, Dual wavelength spectrophotometric method for simultaneous estimation of Ofloxacin and cefpodoxime proxetil in tablet dosage form. Asian Journal of Pharmacy and Life Science, 1 (3): 261-268 (2011).
18. Patel SA, Patel SA, Development and validation of first order derivative spectrophotometric method for simultaneous estimation of ofloxacin and cefpodoxime proxetil in tablet dosage form. Journal of Pharmaceutical science and Bioscientific Research, 1(2): 108-112 (2011).

19. Kalsariya NM, Chodavadia RM, Patel PB, Mevada ZN, Marolia BP, Shah SA, Simultaneous estimation of cefpodoxime proxetil and ofloxacin in combined dosage form by UV Spectrophotometric method. Asian Journal of Research in Chemistry, 4(12): 1836-40 (2011).
20. Patil VD, Chaudari RY, Spectrophotometric method for estimation of cefpodoxime proxetil and ofloxacin in tablet dosage form by simultaneous equation method. Int. J. of Pharm. & Life Sci, 3 (9): 1982-1984 (2012).
21. Shah D, Talaviya S, Patel M, Simultaneous estimation of cefpodoxime proxetil and ofloxacin in pharmaceutical dosage form by RP-HPLC. International Journal of Pharmacy and Pharmaceutical Sciences, 4(3): 627-630 (2012).
22. Chiranjeevi A, Srinivas M, Simultaneous estimation of cefpodoxime proxetil and ofloxacin in tablet dosage form using RP-HPLC. Journal of Applied Pharmaceutical Science, 4 (5): 46-50 (2014).
23. Kumar KS, Srinivas R, Rao VJ, Rani SS, Kumar DK, Rajesh Babu KB, Development and validation of a RP-HPLC method for simultaneous estimation of cefpodoxime proxetil and ofloxacin in bulk drugs and in pharmaceutical dosage forms. Journal of Pharmacy Research, 5 (7): 3904 (2012).
24. Patel SA, Patel SA, development and validation of RP-HPLC method for simultaneous estimation of cefpodoxime proxetil and ofloxacin in tablet dosage form. International Journal of Institutional Pharmacy and Life Sciences, 2(2): 535-543 (2012).
25. International Conference on Harmonization. Harmonized Tripartite Guideline, Validation of analytical procedures: Text and Methodology Q2 (R1): 1-17 (2005).