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DEVELOPMENT OF AN RP-HPLC METHOD FOR SIMULTANEOUS ESTIMATION AND FORCE DEGRADATION OF CEFIXIME AND MOXIFLOXACIN IN BULK AND PHARMACEUTICAL DOSAGE FORM

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Abstract

A simple, efficient, and reproducible RP-HPLC method for the simultaneous determination of Cefixime and Moxifloxacin in bulk and in pharmaceutical formulations has been developed and validated. The separation was carried out on Phenomix C18 (250×4.6 mm i.d, 5 µm) column using acetonitrile: 0.08M potassium dihydrogenortho phosphate (adjusted to pH 8 with NaOH) in the ratio of 40:60 v/v as eluent. The flow rate was 1 ml/min and effluent was detected at 290 nm. The retention time of Cefixime and Moxifloxacin were 2.157 and 3.570 min. respectively. The linear dynamic range was 20-80 µg/ml and 20-80 µg/ml for Cefixime and Moxifloxacin, respectively. Percentage recoveries for Cefixime and Moxifloxacin were 98.50 ± 0.25% and 99.00± 0.25%, respectively. All the analytical validation parameters were determined and found in the limit as per ICH guidelines, which indicates the validity of the method. The developed method is also found to be precise and robust for the simultaneous determination of Cefixime and Moxifloxacin in tablet dosage forms.

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INTRODUCTION

Cefixime Trihydrate (CEF), (6R,7R)-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 trihydrate (Figure 1), is third generation Cephelosporin antibiotic[1]. Moxifloxacin (MOX), 1-cyclopropyl-7-[(1*S*, 6S)-2,8-diazabicyclo[4.3.0]non-8-yl]-6-fluoro-8-methoxy-4-oxo- quinoline-3-carboxylic acid (Figure 2), is floroquinolone antibiotic[2]. This combination is used for treatment of lower Respiration tract infection in adult[3].Literature reveals Spectrophotometric[4], HPLC[8] methods for CEF in Pharmaceutical dosage forms and as well as biological fluids. Literature survey also reveals Spectrophotometric[14] and HPLC[18] methods for MOX in Pharmaceutical dosage forms and as well as biological fluids. The combination is not official in any pharmacopeia; hence no official method is available for the estimation of CEF and MOX in their combined dosage forms. Literature survey does not reveal any simple RP-HPLC method for simultaneous estimation of CEF and MOX in combined dosage forms. The present work describes simple, sensitive, rapid, accurate and economical RP-HPLC method for simultaneous estimation in their bulk and combined tablet dosage forms.

MATERIALS & METHODS

The HPLC system consisted of a solvent delivery module Rheodyne Injector Shimadzu liquid chromatograph pump with 20 µl loop UV- Visible detector. Cefixime powder was gifted by Kaptab Pharmaceuticals, Vadodara, India. Moxifloxacin powder was gifted by BDR Pharmaceutical International Pvt. Ltd., Mumbai, India. HPLC grade acetonitrile was procured from Rankem, Ahmedabad, Gujarat. NaOH (AR grade) was procured from SDFCL, Baroda, Gujarat, India. Potassium dihydrogenortho phosphate (AR Grade) was procured from SDFCL, Baroda, Gujarat, India.

CHROMATOGRAPHIC CONDITIONS:

Phenomix C18 column (250×4.6 mm, i.d, 5µ) was used for separation. The mobile containing acetonitrile and 0.08M of

potassium dihydrogenortho phosphate (adjusted to pH 8with NaOH) in the ratio of 40:60 v/v was delivered at a flow rate of 1.0 ml/min with detection at wavelength 290 nm. The Injection volume was 20 µl and the analysis was performed at ambient temperature.

STANDARD STOCK SOLUTION:

Stock solutions of Cefixime and Moxifloxacin (1 mg/ml) were prepared separately using mobile phase as solvent. From the standard stock solutions, mixed standard solutions of different concentrations ranging from 10 to 80 µg/ml of Cefixime and 10 to 80 µg/ml of Moxifloxacin were prepared by diluting with mobile phase. With the optimized chromatographic conditions, a steady base line was recorded. Twenty micro liters of each mixed standard solution was injected six times and chromatograms were recorded. The retention time of of Cefixime and Moxifloxacin were found to be 2.157 min 3.570 min, respectively. Calibration curves were constructed by plotting the average peak areas against the respective concentrations and found to be linear in the above range with the correlation coefficients (R^2) 0.9997 and 0.9988 for Cefixime and Moxifloxacin, respectively.

ANALYSIS OF CEFIXIME AND MOXIFLOXACIN IN COMBINED DOSAGE FORM:

Twenty tablets were weighed and average weight was determined and finely powdered. Tablet powder equivalent to 400 mg of Cefixime and 400 mg of Moxifloxacin was accurately weighed and transferred to 100 ml volumetric flask. The contents were sonicated after adding 5 ml of mobile phase and the volume were made up to the mark with mobile phase. The sample solution was filtered through whatmann filter paper and an appropriate volume of the aliquot was transferred to 10 ml volumetric flask and the volume was made up to the mark. Twenty micro liters of the solution was injected into the chromatographic system and the peak areas were measured and the quantitation was carried out by keeping these values to the regression equation of corresponding calibration curve.

VALIDATION[19, 20]:

The method was validated for accuracy, precision, linearity, limit of detection, limit

of quantitation and robustness as per ICH guidelines.

(1) Accuracy

For determination of accuracy, recovery study was carried out. The result of recovery study was found to 97.8% – 100.12% for CEF and 95.7% – 99.84% for MOX respectively (Table 7).

(2) Precision

2.1) Intraday precision:

The result of intraday precision for Cefixime and Moxifloxacin was found to be 1.24% – 1.74% RSD for CEF and 1.45% – 1.62% RSD for MOX respectively (Table 4 and Table 5).

2.2) Interday precision:

The result of interday precision for Cefixime and Moxifloxacin was found to be 0.60% – 1.26% RSD for CEF and 1.09% – 1.74% RSD for MOX respectively (Table 4 and Table 5).

(3) Repeatability

Standard mixture solutions of CEF (20, 30, 40, 50, 60, 70, 80µg/ml) and MOX (20, 30, 40, 50, 60, 70, 80µg/ml) were prepared and chromatograms were recorded. Area was measured of the same concentration solution six times and RSD was calculated. (Table 6)

(4) Linearity and Range

The linearity of analytical method is its ability to elicit test results that are directly proportional to the concentration of analyte in sample within a given range. The range of analytical method is the interval between the upper and lower levels of analyte that have been demonstrated to be determined within a suitable level of precision, accuracy and linearity (Table 1 and Table 2).

(5) Solution stability

The solutions at analytical concentration (CEF 50 µg/ml and MOX 50 µg/ml) were prepared and stored at room temperature for 24hrs and analyzed at interval of 0, 6, 12 and 24hrs for the presence of any band other than that of CEF and MOX and the results were simultaneously compared with the freshly prepared CEF and MOX standard solution of the same concentration in the form of change in %RSD of the response obtained (Table 9).

(6) Robustness

For robustness of both the drug there was deliberate change was done which was change in pH, change in wavelength, change in flow rate, change in mobile phase

ratio and chromatogram obtained for these changes (Table 8).

(7) Limit of Detection

Limit of Detection for the CEF and MOX was found to be 1.2µg/ml and 0.5µg/ml respectively (Table 13).

(8) Limit of Quantitation

Limit of Detection for the CEF and MOX was found to be 3.96µg/ml and 1.65µg/ml respectively (Table 13).

(9) Forced degradation studies.

- **Alkali hydrolysis**

To the different 25 ml volumetric flask, 2.5 ml stock solutions of CEF and MOX were taken and 5 ml of 1N NaOH was added. In another volumetric flask from stock solution of formulation 2.5 ml solution was taken to obtain mixture and 5 ml of 1N NaOH was added to perform base hydrolysis. All flasks were heated at 80ºC for 1hrs and allowed to cool to room temperature. Solutions were neutralized with 1N HCl and diluted up to the mark with mobile phase. Appropriate aliquots were taken from the above solutions and diluted with mobile phase to obtain final concentration of 50µg mL^{-1} of CEF and 50µg mL^{-1} MOX separately and in the mixture (Fig 6).

- **Acid hydrolysis**

To the different 25 ml volumetric flask, 2.5 ml stock solutions of CEF and MOX were taken and 5 ml of 2N HCl was added. In another volumetric flask from stock solution of formulation 2.5 ml solution was taken to obtain mixture and 5 ml of 2N HCl was added to perform acid hydrolysis. All flasks were heated at 80ºC for 1hrs and allowed to cool to room temperature. Solutions were neutralized with 2N NaOH and diluted up to the mark with mobile phase. Appropriate aliquots were taken from the above solutions and diluted with mobile phase to obtain final concentration of 50µg mL^{-1} of CEF and 50µg mL^{-1} MOX separately and in the mixture (Fig 7).

- **Oxidative stress degradation**

To perform oxidative stress degradation, appropriate aliquots of stock solutions of CEF and MOX were taken in two different 25 ml volumetric flasks and 5 ml of 6% hydrogen peroxide was added. Similarly, appropriate aliquots of stock solutions from formulation were taken in the same 25 ml volumetric flaks and 5 ml 6% hydrogen peroxide was added. All the mixtures were heated in a water bath at 80°C for 1hrs and allowed to cool to room temperature and

diluted up to the mark with mobile phase. Appropriate aliquots were taken from above solutions and diluted with mobile phase to obtain final concentration of 50µg mL^{-1} of CEF and 50µg mL^{-1} MOX separately and in mixture (Fig 8).

- **Dry heat degradation**

Analytically pure samples of CEF, MOX and formulation were exposed in oven at 80°C for 1 hrs. The solids were allowed to cool and 25 mg each of CEF and MOX were weighed, transferred to two separate volumetric flasks (25 ml) and dissolved in few ml of methanol. In similar way formulation was also treated. Volumes were made up to the mark with the methanol. Solutions were further diluted by mobile phase taking appropriate aliquots in 10 ml volumetric flask to obtain final concentration of 50µg $mL^{-1}$of CEF and 50µg $mL^{-1}$of CEF (Fig 8).

All the reaction solutions were injected in the High performance Liquid Chromatographic system and chromatograms were recorded (Table 10).

RESULTS AND DISCUSSION

Calibration data for CEF and MOX are shown in (Table 1 and 2) respectively (Fig 5). The calibration curves for CEF and MOX were prepared by plotting area and concentration.

The following equations for straight line were obtained for CEF and MOX

Linear equation for CEF:

y = 36136x + 152030

Linear equation for MOX:

y = 13380x - 174567

The developed HPLC method was validated. The linear range, correlation coefficient, detection limit and standard deviation for CEF and MOX by HPLC method are shown in (Table 3) Accuracy were determined by calculating the recovery. The method was found to be accurate with % recovery 97.8% – 100.12% for CEF and 95.7% – 99.84% for MOX respectively (Table 7). Precision was calculated as repeatability and intra and Interday variation for both the drugs. The method was found to be precise with less than 2% RSD for Intraday (n=3) and less

than 2% RSD for Interday (n=3) for CEF and less than 2% RSD for intraday (n=3) and less than 2% RSD for Interday (n=3) for MOX respectively (Table 4 – 5). The method was found to be reproducible. The method was also found to be specific as no interference observed when the drugs were estimated in presence of excipients. The method was also rugged as there was no change in area up to 24 hours of preparation of solution in mobile phase (Table 9).The LOD for CEF and MOX was found to be 1.2µg/ml and 0.5µg/ml respectively (Table 13). Summary of validation parameters is tabulated in (Table 11).

Marketed formulation was analyzed by the proposed method and assay result of marketed formulation was shown in (Table 12).

CONCLUSION

Proposed study describes a new RP-HPLC method for the estimation of Cefixime and Moxifloxacin in combination using simple mobile phase. The method gives good resolution between the compounds with a short analysis time. The method was validated and found to be simple, sensitive, accurate, and precise.

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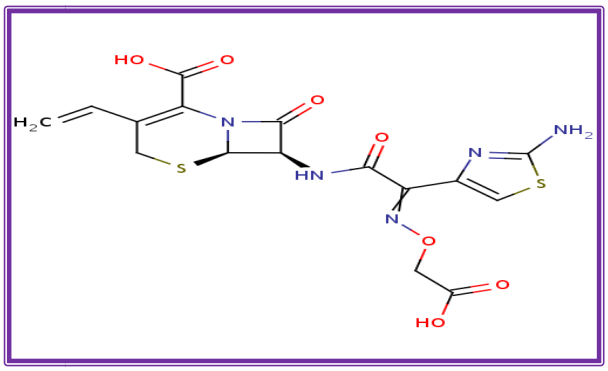

Figure 1. Structure of Cefixime.

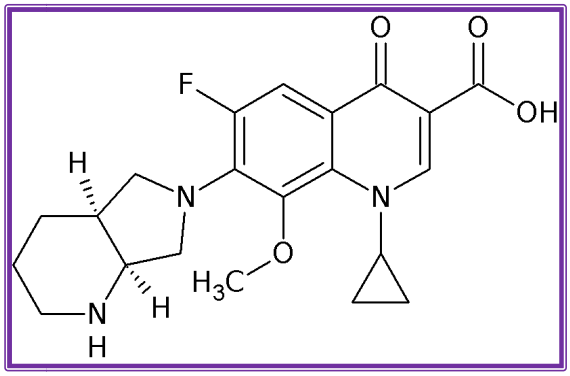

Figure 2. Structure of Moxifloxacin.

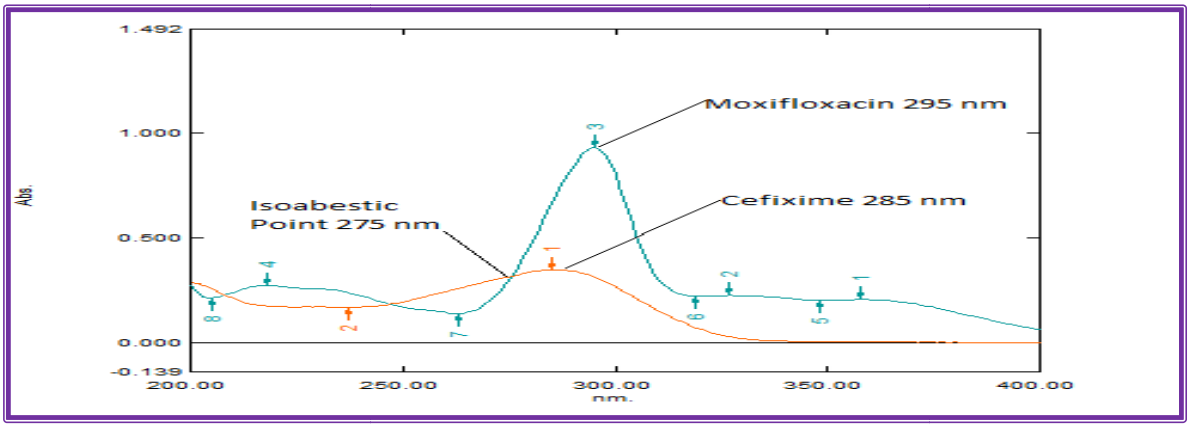

Figure 3. Overlay spectra of Cefixime and Moxifloxacin.

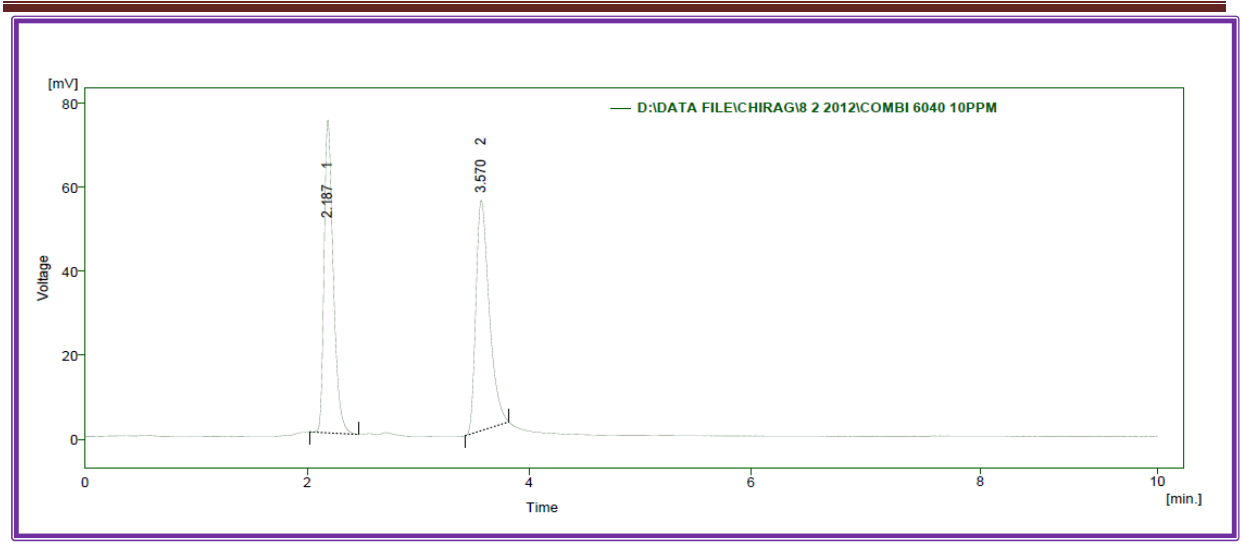

Figure 4 Chromatogram of mixed standard solution containing 10ppm of CEF and MOX Acetonitrile: Phosphate Buffer, pH was adjusted to 8 with NaOH, Flow rate 1.0 ml/min (40:60 v/v), Flow rate 1.0 ml/min of Proposed method.

Discussion: From the above chromatogram it was concluded that the Acetonitrile: Phosphate Buffer mobile phase was suitable because it showed good separation and resolution.

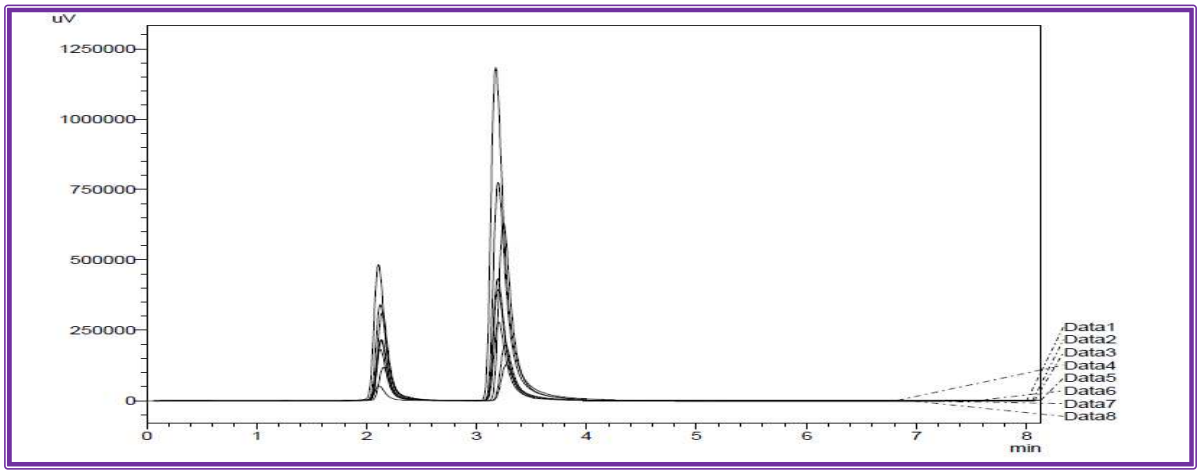

Figure 5 Chromatogram for linearity of both the drugs using mobile phase Buffer: ACN (60:40), pH was adjusted to 8 with 1N NaOH, Flow rate 1 ml/min.

Discussion: From the above chromatogram it was concluded that the chromatogram was linear.

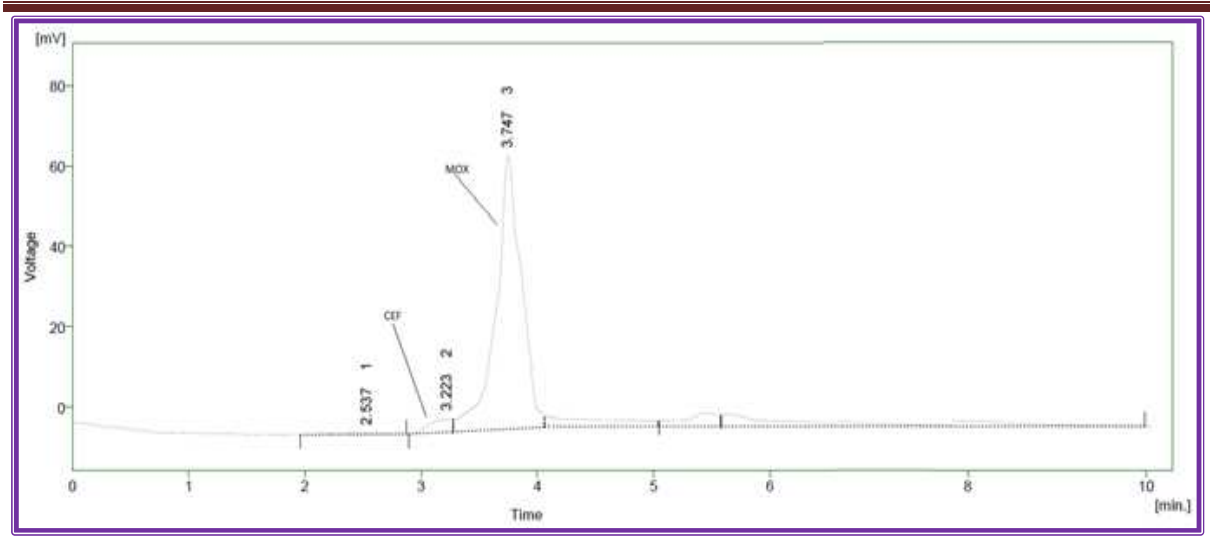

Figure 6 Chromatogram of base (1N NaOH) treated Cefixime (CEF) and Moxifloxacin (MOX) at 80°C for 1 hr.

Discussion: From the above chromatogram it was concluded that the Cefixime was degraded in 1N NaOH

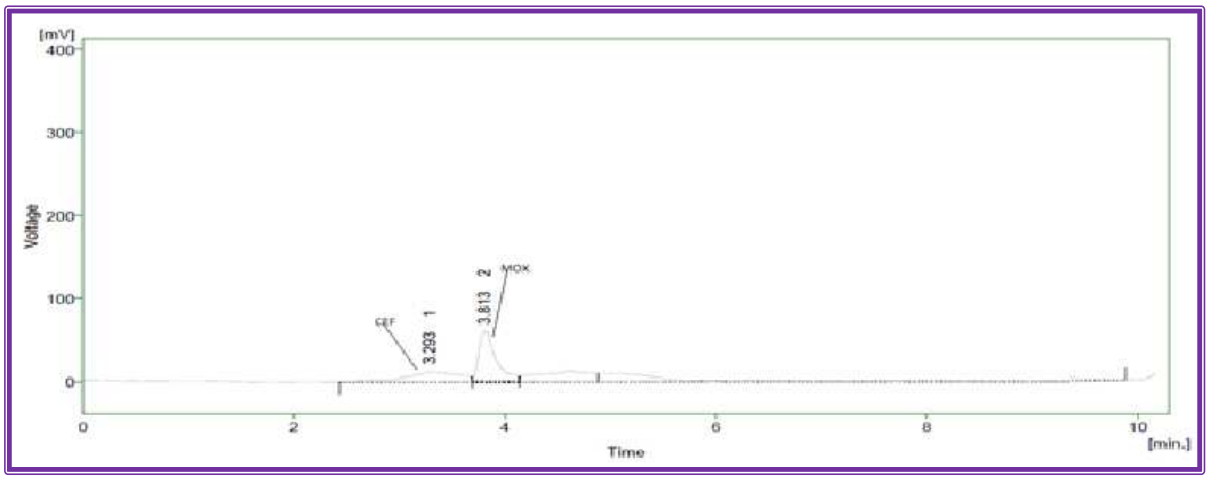

Figure 7 Chromatogram of acid (2N HCl) treated Cefixime (CEF) and Moxifloxacin (MOX) at 80°C for 1 hr.

Discussion: From the above chromatogram it was concluded that the Cefixime and Moxifloxacin both were degraded in 2N HCl.

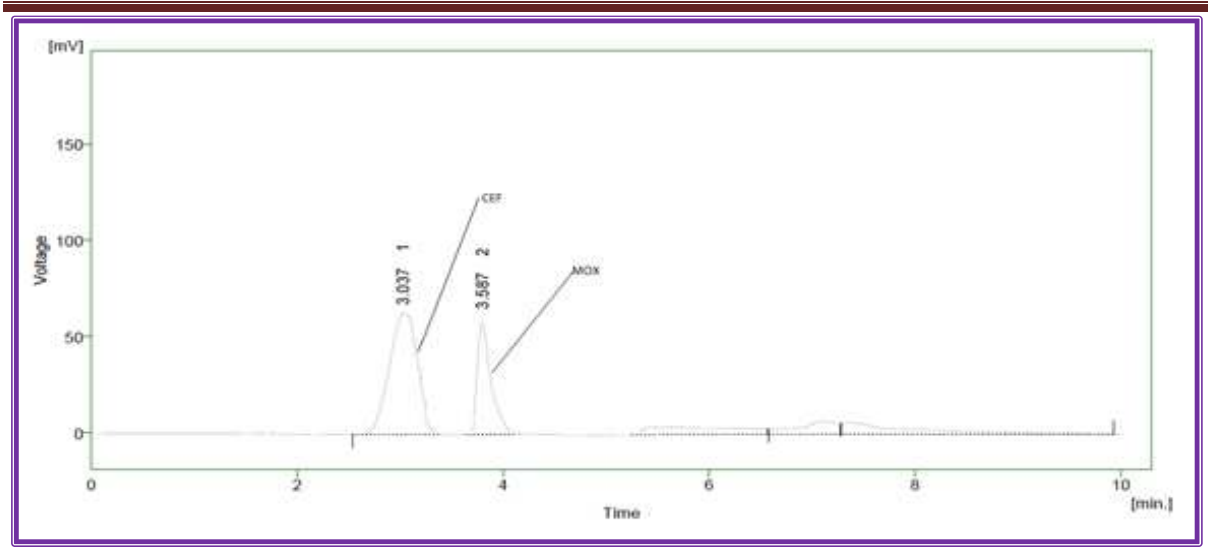

Figure 8 Chromatogram of 6% H_2O_2 treated Cefixime (CEF) and Moxifloxacin (MOX) at 80°C for 1 hr.

Discussion: From the above chromatogram it was concluded that the Cefixime and Moxifloxacin both were degraded in 6% H_2O_2

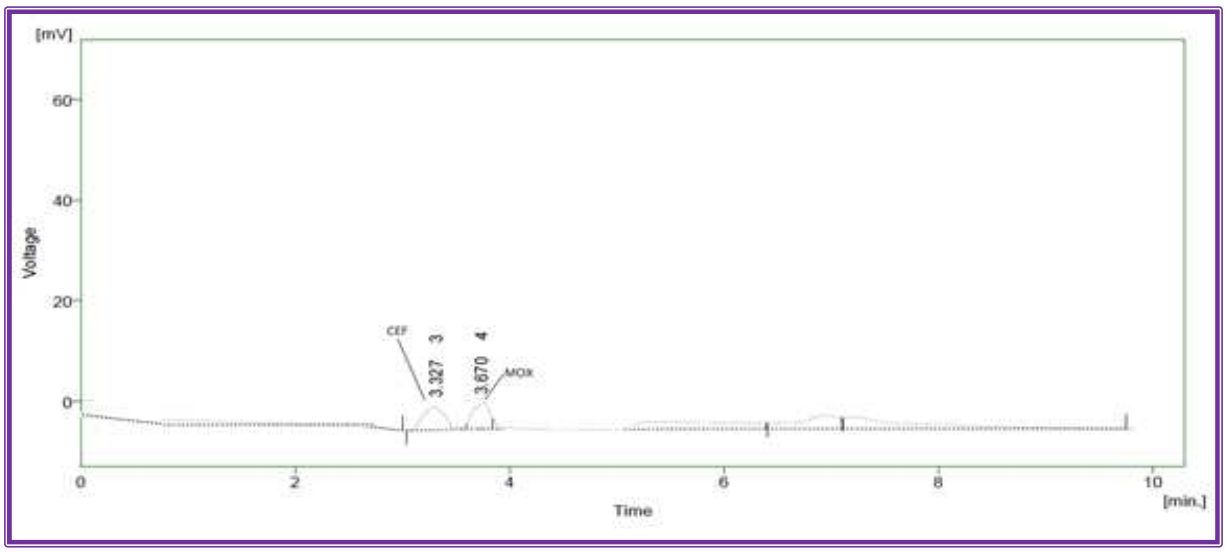

Figure 9 Chromatogram of dry heat degradation study of Cefixime (CEF) and Moxifloxacin (MOX) at 80°C for 1 hr.

Discussion: From the above chromatogram it was concluded that the Cefixime and Moxifloxacin both were degraded in dry heat.

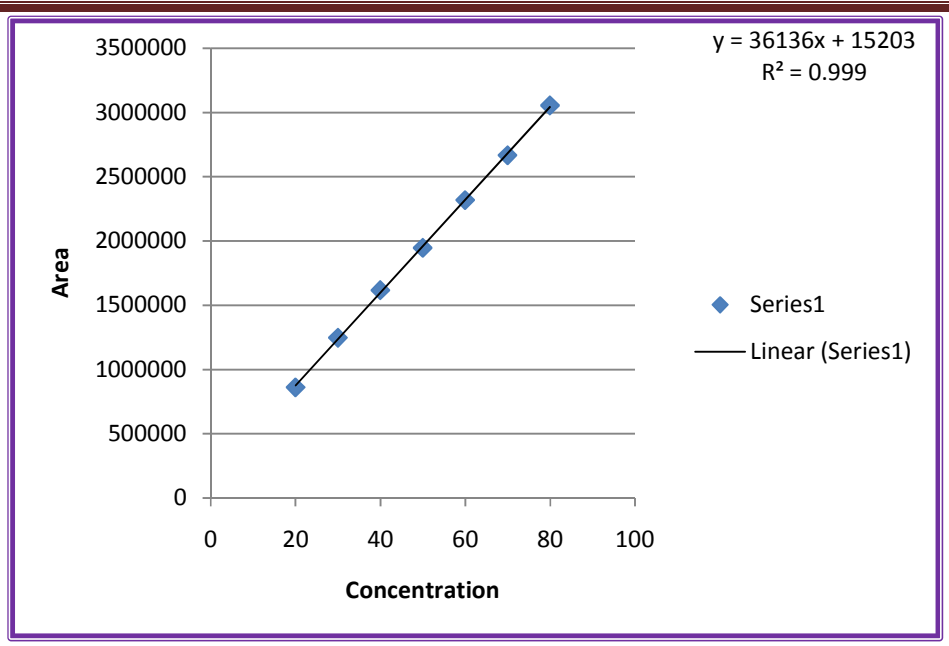

Figure 10. Calibration Curve of CEF by HPLC method

Discussion: From the above table and graph it was concluded that the graph was linear.

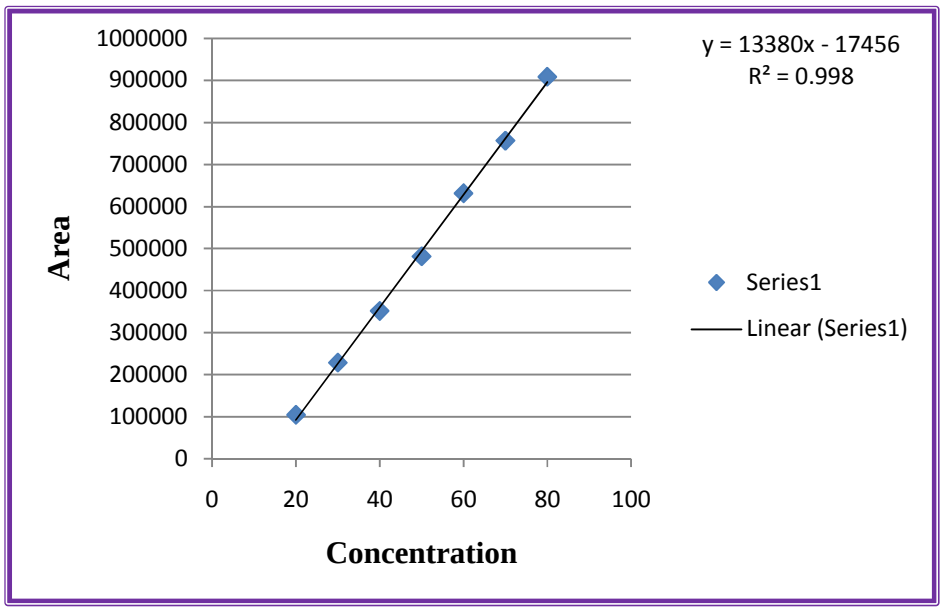

Figure 11. Calibration Curve of MOX by HPLC method

Discussion: From the above table and graph it was concluded that the graph was linea

Table 1

Result of calibration readings for CEF by HPLC method

Concentrations (µg/ml)	Area Mean ± S.D. (n=6)	% RSD
20	868348.2	1.490754
30	1243849	0.471028
40	1610545	0.981811
50	1939078	1.122568
60	2313995	0.46801
70	2674738	0.474243
80	3070215	1.130087

Table 2

Result of calibration readings for MOX by HPLC method

Concentrations (µg/ml)	Area Mean ± S.D. (n=6)	% RSD
20	104540.8	0.202128
30	228684.3	0.151018
40	356266	1.970721
50	482778.2	0.343634
60	638641.8	1.010715
70	752687.7	1.016915
80	909924.3	0.462946

Table 3

Statistical data for CEF and MOX by HPLC method

Parameter	CEF	MOX
Linearity (µg/ml)	20-80	20-80
Correlation coefficient (r)	0.9997	0.9988
Slope of Regression	36136	13380
Standard deviation of slope	125.4	53.2
Intercept of Regression	152030	174567
Standard deviation of intercept	34.6	65.2

Table 4

Precision data for CEF

Conc. µg/ml	Intraday (n=3)	% RSD	Inter day (n=3)	% RSD
40	1633349	1.746878	1324366	0.637311
50	1959635	1.191444	1625685	0.603495
60	2335456	1.243861	2311588	1.263022

Discussion: From the above table was concluded that the Precision data of CEF was less than 2% RSD.

Table 5

Precision data for MOX

Conc. µg/ml	Intraday (n=3)	% RSD	Inter day (n=3)	% RSD
40	354668.3	1.626395	315023	1.744394
50	486274.3	1.492442	428841	1.33806
60	639029	1.456823	592393.7	1.091456

Discussion: From the above table was concluded that the Precision data of MOX was less than 2% RSD.

Table 6

Repeatability of sample application data for CEF and MOX

Concentration	CEF 50µg/ml	MOX 50 µg/ml
Area	1907635	482608
	1906937	483267
	1901748	496693
	1907945	499392
	1907012	486106
	1946379	491238
Mean.	1912943	489884
Std. Dev.	16539.03	7065.352
% RSD	0.864586	1.44225

Discussion: From the above table was concluded that the Repeatability data of CEF and MOX was less than 2% RSD.

Table 7

Accuracy study of CEF and MOX by the proposed HPLC method

Amount of sample taken (µg/ml)		Amount of standard drug added (µg/ml)		Amount of drug recovered (µg/ml)		% recovery ± %RSD(n = 3)	
CEF	MOX	CEF	MOX	CEF	MOX	CEF	MOX
25	25	0.0	0.0	25.03	24.96	100.12+0.21	99.84+0.45
25	25	15	15	39.49	39.04	98.73+0.18	97.6+1.53
25	25	25	25	48.9	47.85	97.8+0.25	95.70+0.82
25	25	35	35	59.38	59.85	98.96+0.27	99.75+0.77

Discussion: From the above table, it was concluded that the Method was Accurate.

Table 8

Robustness results of CEF and MOX in given formulations

Parameter	Method condition	CEF		MOX	
		Mean	**% RSD**	**Mean**	**% RSD**
Flow rate	0.8 ml/min	1324366	0.637311	315023	1.744394
	1.0 ml/min	1625685	0.603495	428841	1.33806
	1.2 ml/min	2311588	1.263022	592393.7	1.091456
Mobile phase ratio	42 : 58	1257699	1.769896	335023	1.639715
ACN : Phosphate	40 : 60	1425685	0.688155	424507.7	1.745958
Buffer	38 : 62	2294921	0.884428	698894	1.568214
Wavelength change	287	1634077	1.709505	355019.7	1.546251
	290	1972424	1.164062	486626	1.419667
	293	2348618	1.102345	645112	1.136803
pH change	7.8	1321032	0.950198	325023	1.690164
	8.0	1665685	0.589002	445507.7	1.459695
	8.2	2338254	1.744891	609060.3	0.372438

Discussion: From the above table, it was concluded that the method was Robust for CEF and MOX when change in Flow Rate, Wavelength, pH change, Mobile phase ratio respectively.

Table 9

Solution stability study

Time (Hrs.)	Area		RESULT %	
	CEF 50 (µg/ml)	**MOX 50 (µg/ml)**	**CEF**	**MOX**
0	1959635	486674.3	100	100
4	1959019	486626	99.96	100
8	1952424	482174.3	99.63	99.15
24	1945685	481507.7	99.28	99.02

Discussion: From the above table, it was concluded that both the solution were stable for 24 hrs.

Table 10

Forced degradation study of CEF and MOX.

Conditions	Time (min)	Area		Retention time of degradation products	
		CEF	**MOX**	**CEF**	**MOX**
Base 1N NaOH	10	44.129	1064.422	3.223	3.747
Acid 2N HCl	10	435.513	708.769	3.293	3.813
6% hydrogen peroxide	10	837.321	765.552	3.037	3.587
Dry heat	10	70.096	107.313	3.327	3.670

Discussion: From the above table it was concluded that the Area of both the drug was decreased during force degradation study.

Table 11

Summary of Validation Parameters of HPLC

Parameters	**CEF**	**MOX**
Range	20-80	20-80
Retention time (min)	2.187	3.570
Tailing factor	1.5	1.8
Resolution	5.311	
Theoretical Plates	3250	5081
Detection limit (µg/ ml)	1.2	0.5
Quantitationlimit (µg/ ml)	3.96	1.65
Accuracy(%)	97.8-100.12%	95.70-99.84%
Intra-day (n=3)	1.19-1.74	1.45-1.62
Inter-day (n=3)	0.60-1.26	1.09-1.74
Specificity	Specific	Specific

Table 12

Analysis of marketed formulation

Formulation	Labeled Amount (mg)		Amount found (mg)		% of drug found ±RSD	
	CEF	**MOX**	**CEF**	**MOX**	**CEF**	**MOX**
1	400	400	394	397	98.5 ± 0.97	99.25 ± 0.83
2	400	400	395	396	98.75 ± 1.37	99.00± 1.63

Discussion: From the above table, it was concluded that the Method could be applied to marketed formulation

Table 13

LOD and LOQ of CEF and MOX

Parameter	CEF (µg ml^{-1})	MOX (µg ml^{-1})
SD	125.4	53.2
LOD (µg ml^{-1})	1.2	0.5
LOQ (µg ml^{-1})	3.96	1.65

Discussion: From the above table, it was concluded that the LOD of CEF was 1.2µg $ml^{-1}$and LOQ was 3.96µg ml^{-1} and LOD of MOX was 0.5µg $ml^{-1}$and LOQ was 1.65µg ml^{-1}.

REFERNCES

1. Maryadele JO: The Merck Index: Encyclopedia of Chemicals, drugs and biological, 14th Ed. New Jersey: Published by Merck Research Laboratories, Division of Merck and Co., Inc. Whitehouse station: **2006**: 1924.

2. Budavari S: The Merck Index: Encyclopedia of Chemicals, drugs and biological, 13th Ed. New Jersey: Published by Merck Research Laboratories, Division of Merck and Co., Inc. Whitehouse station: **2001**: 1097 and 1125.

3. http://meherpharmainnovation.blogspot.com/2010/07/moxifloxacincefixime.html

4. Dhoka MV: Simultaneous Estimation of Cefixime Trihydrate and Erdosteine in Pharmaceutical Dosage form by RP-HPLC method. International Journal of Chem Tech Research. 2010; 2: 79-87.

5. Gandhi Santosh V: A simple and sensitive RP-HPLC method for simultaneous estimation of Cefixime and Ofloxacin in combined tablet dosage form",International Journal of Pharmacy and Pharmaceutical Science. 2011; 3: 46-48.

6. Kumar Rajnish: Development of colorimetric method for the analysis of pharmaceutical formulation containing both Ofloxacin and Cefixime", International Journal of Pharmacy and Pharmaceutical Sciences. 2011; 3: 178-179.

7. Patel Satish: Simultaneous Spectrophotometric Determination of Cefixime Trihydrate and Ofloxacin in Tablet Dosage form. IRJPS. 2011: 105-108.

8. Pareek V: Role of Different Hydrotopic Agents in Spectrophotometric and Chromatographic estimation of Cefixime. International Journal of Pharma and Bio Science. 2010.

9. Kumar Hemanth AK: Simple and rapid liquid chromatography method for determination of moxifloxacin in saliva. Journal of Chromatography B. 2011: 3663-3667.

10. Rathinavel G: A Validated RP – HPLC Method for Simultaneous Estimation of Cefixime and Cloxacillin in Tablets. Journal of Chemistry. 2008; 5: 648-651.

11. Kumudhavalli MV: Development and Validation of Rp-Hplc Method For Simultaneous Determination Of Cefixime And Potassium Clavulanate In Tablet Dosage Form" International Journal of Pharma Recent Research. 2010; 2: 57-60.

12. Motwani Sanjay K: Validated spectrophotometric methods for the estimation of moxifloxacin in bulk and pharmaceutical formulations" Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy. 2007: 250-256.

13. Gandhi LR: Absorption Ratio method for estimation of Moxifloxacin HCl & Ketorolac Tromethamine in their combined dosage form by UV-Visible Spectroscopy"

International Journal of Pharmaceutical Research and Development. 2011: 21-26.

14. Mishra M: Simple and Validated UV-Spectroscopic method for estimation of Moxifloxacin HCl in bulk and formulation. Journal of Global Pharma and Technology. 2010**.**

15. Sahu: Spectrophotometric Estimation of Moxifloxacin in Bulk and its Pharmaceutical Formulations. Pharmacology online. 2011: 491-502.

16. Nimmagadda Srinivas: Development and validation of a HPLC method for simultaneous quantitation of gatifloxacin, sparfloxacin and moxifloxacin using levofloxacin as internal standard in human plasma. Wiley. 2008: 1288-1295.

17. Kumar Hemanth AK: Simple and rapid liquid chromatography method for determination of moxifloxacin in plasma. Journal of Chromatography B, 2009: 1205-1208.

18. Rama Subbaiah: Method Development and Validation for estimation of Moxifloxacin HCl in tablet dosage form by RP-HPLC method. Pharmaceutica Analytica Acta. 2010.

19. Q2 (R1), Text on Validation of Analytical Procedures, International Conference on Harmonization, Geneva, November **2005**, pp. 8-17.

20. Robert A. Nash and Alfred HW: In Pharmaceutical Validation, 3rd Edn, Informa Publishers, **2003**: 693-99.

21. Beckett AH and Stenlake JB: Practical pharmaceutical chemistry, 4th ed., Delhi: CBS publishers and distributors; **1997**.