IJPSR (2017), Vol. 8, Issue 3 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 25 August, 2016; received in revised form, 26 November, 2016; accepted, 28 November, 2016; published 01 March, 2017

STABILITY INDICATING RP – HPLC METHOD FOR COMBINATION OF AMBROXOL HYDROCHLORIDE AND CEFADROXIL MONOHYDRATE IN PHARMACEUTICAL FORMULATION

J. A. Goswami [*1] and N. J. Shah [2]

Quality Assurance Department [1], School of Pharmacy, RK University, Rajkot, Gujarat, India.

Indubhai Patel College of Pharmacy and Research Centre [2], Dharmaj, Gujarat, India.

Keywords:

Ambroxol Hydrochloride (AMB), Cefadroxil Monohydrate (CEFXL), Stability indicating method, Reverse Phase - High performance liquid chromatographic (RP - HPLC), assay

Correspondence to Author:
Jigar A. Goswami

38, Ranna Park Society, Nr. Partheshvar Mahadev, Vatva Road, Isanpur, Ahmedabad – 382443, Gujarat, India.

E-mail: jigargoswami013@gmail.com

ABSTRACT: Reverse Phase - High performance liquid chromatographic (RP - HPLC) method was described for determination of Ambroxol Hydrochloride (AMB) and Cefadroxil Monohydrate (CEFXL). The chromatographic separation was achieved using mobile phase mixture of Acetonitrile and 0.05 M Dihydrogen Phosphate Buffer (pH 3.0 adjusted with Ortho Phosphoric Acid Solution) in the ratio of 40:60 (%v/v) and Eclipse Plus C_{18}, (150 x 4.6 mm i.d), Particle size 5 µm column at 1.0 ml/min flow rate. 20 µL of standard preparation containing 30 µg/ml AMB and 250 µg/ml CEFXL was injected into the column and the component was separated by carrying out elution for a run time of 15 minutes and detected at 230 nm wavelength. The described method shows excellent linearity over a range of 6 to 60 µg/ml and 50 to 500 µg/ml for AMB and CEFXL, respectively. AMB and CEFXL were subjected to stress degradation conditions of hydrolysis (acid and base), oxidation and thermal degradation. Stressed samples were analysed by the developed method. The proposed method was readily applied for the assay of pharmaceutical formulations and the results were found to be accepted, therefore the proposed method can be adopted for the routine analysis of any quality control laboratory.

INTRODUCTION: Ambroxol Hydrochloride with Cefadroxil Monohydrate is used for the prophylaxis and treatment of infections caused by bacteria. Ambroxol Hydrochloride is a Mucolytic agent. Its chemical name is Trans – 4- [(2-amino-3,5-dibromobenzyl) amino] cyclohexanol HCl. **(Fig. 1)**

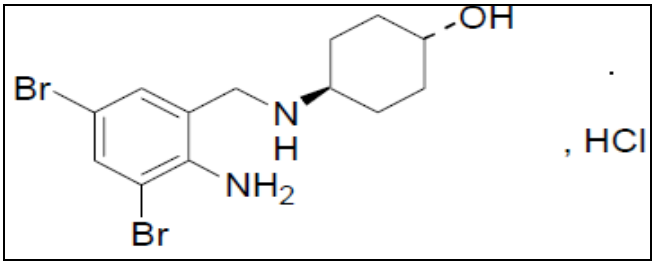

FIG. 1: AMBROXOL HYDROCHLORIDE

Cefadroxil Monohydrate is a Cephalosporin antibacterial agent. Its chemical name is (6R, 7R)-7-[(2R)-2-amino-2-(4-hydroxyphenyl) acetamido]-3-methyl-8-oxo-5-thia-1-azabicyclo [4.2.0] oct-2-ene-2-carboxylicacid monohydrate. **(Fig. 2)**

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.8(3).1220-28

Article can be accessed online on: www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.8 (3).1220-28

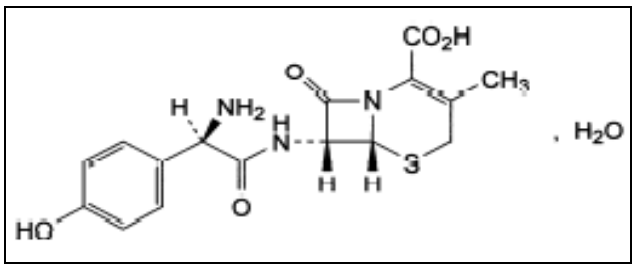

FIG. 2: CEFADROXIL MONOHYDRATE

This combination is available in 30 mg of Ambroxol Hydrochloride and 250 mg of Cefadroxil Monohydrate dose. Thus it is inevitable to develop such a sensitive, accurate, precise, rapid and economical method for routine analysis of this combination in pharmaceutical dosage form successfully.

MATERIALS AND METHODS:

Instrumentation: A high performance liquid chromatography system consisting of Agilent technologies 1260 infinity Module with Photo Diode Array detector was used. Chemicals were weighed using Analytical balance Mettler Toledo model MS105DU. All pH measurements were done on pH meter Systronics- model µpH System 361.

Reagents and Chemicals: HPLC grade solvents Methanol, Acetonitrile and Water, Potassium Dihydrogen Phosphate were obtained from Merck Pvt. Ltd. India. Water was deionised and further purified by means of Milli-Q plus water purification system, Millipore Ltd (U.S.A). Hydrochloride acid AR, Sodium Hydroxide AR, Hydroxide Peroxide AR, Tetra butyl ammonium Hydrogen Sulphate AR Grade was obtained from Rankem Pharmaceuticals India Ltd. India.

Chromatographic Conditions and Measurement Procedure:

Preparation of Mobile phase: A mixture of 60 volume of 0.05 M Dihydrogen Phosphate Buffer (KH2PO4 Buffer = 6.8 gm KH2PO4 Buffer into 1000 ml Water and pH adjusted to 3.0 with Ortho Phosphoric Acid , filtered through 0.45 µm filter paper) and 40 volume of Acetonitrile, sonicated for 10 minutes to degas the mixture was used as mobile phase.

Standard Preparation: Accurately weighed AMB (30 mg) and CEFXL (250 mg) was transferred to a 100 ml volumetric flask and dissolved in 50 ml mobile phase. The flask was sonicated for 10 min. The flask was shaken and volume was made up to the mark with diluent to give a solution containing 300µg/ml AMB and 2500 µg/ml CEFXL. From this solution 5 ml was transfer to 50 ml volumetric flask. The volume was adjusted to the mark with the Diluent to give a solution containing 30µg/ml AMB and 250 µg/ml CEFXL.

Sample preparation: Twenty tablets were weighed and finely powdered. The powder equivalent to 30 mg AMB and 250 mg CEFXL was accurately weighed. These AMB and CEFXL powder was transferred to volumetric flask of 100 ml capacity and dissolved in 50 ml of Diluent. The flask was sonicated for 10 minute. The flask was shaken and volume was made up to the mark with mobile phase. The above solution was filtered through whatmann filter paper (0.45µ). This solution is expected to contain AMB – 300 µg/ml and CEFXL – 2500 µg/ml. From this, 5 ml of aliquot was taken and transferred to volumetric flask of 50 ml capacity and volume was made up to the mark with the Diluent to give a solution containing 30 µg/ml AMB and 250 µg/ml CEFXL. This solution was used for the estimation of AMB and CEFXL.

Selection of wavelength maxima: The sensitivity of HPLC method that uses UV detection depends upon proper selection of detection wavelength. An ideal wavelength is the one that gives good response for the drugs that are to be detected. In the present study individual drug solutions of 30µg/ml AMB and 100µg/ml CEFXL were prepared in solvent mixtures of 60 volume of Water and 40 volume of Acetonitrile. These drug solutions were than scanned in the UV region of 200-400 nm and the overlay spectrum was recorded **(Fig. 3).**

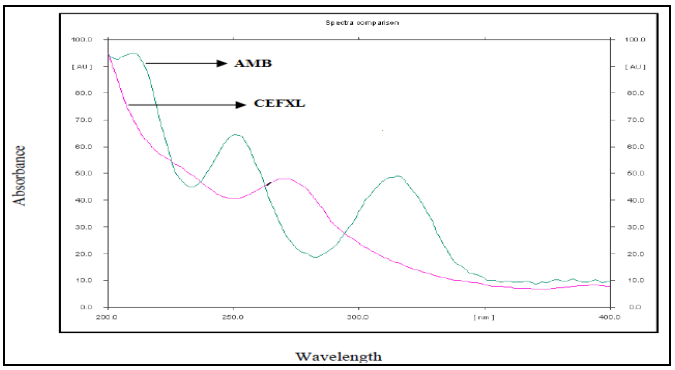

FIG. 3: OVERLAIN ZERO ORDER UV SPECTRUMS OF AMB AND CEFXL IN DILUENTS

Method Development: By using the chromatographic conditions that were used for assay of Anti – Histamine Drugs as reference, various trials were made. Each trial mixture of known components were injected and observed for resolution and tailing factor of the peaks. Various proportions of buffer, Methanol and Acetonitrile were tried as mobile phase and 60 volume of 0.05 M Dihydrogen Phosphate Buffer (KH_2PO_4 Buffer = 6.8 gm KH_2PO_4 Buffer into 1000 ml Water and pH adjusted to 3.0 with Ortho Phosphoric Acid) and 40 volume of Acetonitrile improved peak symmetry and resolution. Different flow rates of the mobile phase were tried for good resolution. Both the drugs AMB and CEFXL were found to be soluble and stable in a mixture of 60 volume of 0.05 M Dihydrogen Phosphate Buffer (KH_2PO_4 Buffer = 6.8 gm KH_2PO_4 Buffer into 1000 ml Water and pH adjusted to 3.0 with Ortho Phosphoric Acid) and 40 volume of Acetonitrile.

Finally the chromatographic conditions were optimized at flow rate 1.0 ml/min, injection volume of 20 µL, run time of 15 minutes, at column oven temp 30°C with mobile phase (sonicated and degased) as diluent in a Eclipse Plus C_{18}, (150 x 4.6 mm i.d), Particle size 5 µm. The %RSD for both the drugs AMB and CEFXL were found to be 0.10 and 0.02 respectively and tailing factor was 1.54 and 1.503 for AMB and CEFXL respectively. **(Table 1)**

TABLE 1: SYSTEM SUITABILITY TEST PARAMETER

System Suitability Parameters	Proposed Method	
	AMB	CEFXL
Retention times (R_t) (min)	7.750 ± 0.01	2.912 ± 0.01
Theoretical plates (N)	3183.15 ± 18.08	2300.11 ± 13.72
Resolution (R_S)	12.247 ± 0.26	
Tailing factor (A_S)	1.54 ± 0.01	1.503 ± 0.002
RSD of all Replicates area of Standard Solution	0.10 %	0.02 %

The retention time for AMB and CEFXL was found to be 2.91 minutes and 7.75 minutes respectively. Absorption maximum was found to be 230 nm. And peaks shape was good.
The method was further validated under the chromatographic conditions.

Method Validation: Once chromatographic conditions were established, the method was validated in compliance with ICH guidelines. The following parameters like system suitability along with specificity, linearity, precision and accuracy, limits of detection and limit of quantification were performed for validation. The specificity of the method was described as the ability to discriminate the analyte from all potential interfering substances (i.e. excipients) in the tablet dosage form. This test was performed by recording chromatograms of placebo blank solution and drug mixture spiked in the placebo solution. The placebo blank solution was prepared by mixing the corresponding tablet excipients It can be seen from the chromatogram, that no peaks were observed in the placebo blank solution and percentage recovery of drugs spiked in placebo blank solution indicating that no interference due the excipients for the recovery of the analytes occurred. A study to evaluate the interference of placebo was conducted. Samples were prepared in duplicate by taking placebo equivalent to the weight present in portion of test preparation as per the test method and injected into the HPLC system. It was observed that there were no peaks interfering with the analyte peak. The chromatogram indicates that the peak is homogeneous, there is no interference from the excipients at the retention time of analyte peak and has no co-eluting peaks indicating specificity of the method. For the analytical method, determination of assay specificity was also demonstrated by performing force degradation study of placebo and drug product under various stress conditions like Acid degradation, Alkali degradation, Oxidative degradation, Photolytic degradation and Thermal degradation.

Forced degradation studies:

Degradation with 3% H_2O_2: Weighed and transferred about 500 mg of sample (Average Weight of Tablet) in to 100 mL volumetric flask. Add 5.0 mL 3% v/v Hydrogen peroxide to the flask. Reflux the solution for 1 hour at 80 ºC. Allow to cool the solution at room temperature.

Add about 50 ml of Diluent and sonicated to dissolve it completely and make volume up to the mark with Diluent. Dilute 5 ml of this solution to 50 ml with the Diluent (250 µg/ml CEFXL and 30 µg/ml AMB). **(Fig. 4)**

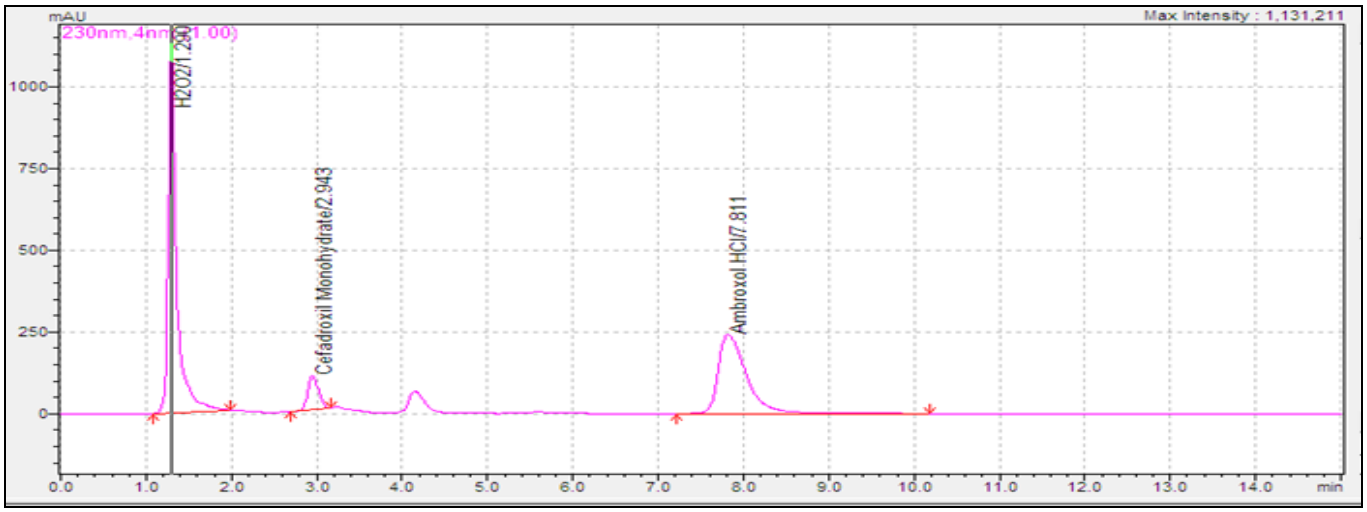

FIG. 4: CHROMATOGRAPH OF FORCED DEGRADATION STUDY ON SAMPLE SOLUTION CONTAINING AMB AND CEFXL USING 3 % H_2O_2 SOLUTION

Degradation with 0.1M HCl: Weighed and transferred about 500 mg of sample (Average Weight of Tablet) in to 100 mL volumetric flask. Add 5.0 mL 0.1 M Hydrochloric acid to the flask. Reflux the solution for 1 hour at 80 ºC. Allow to cool the solution at room temperature. Add 5.0 mL 0.1 M Sodium hydroxide. Add about 50 ml of Diluent and sonicated to dissolve it completely and make volume up to the mark with Diluent. Dilute 5 ml of this solution to 50 ml with the Diluent. (250µg/ml CEFXL and 30µg/ml AMB). **(Fig. 5)**

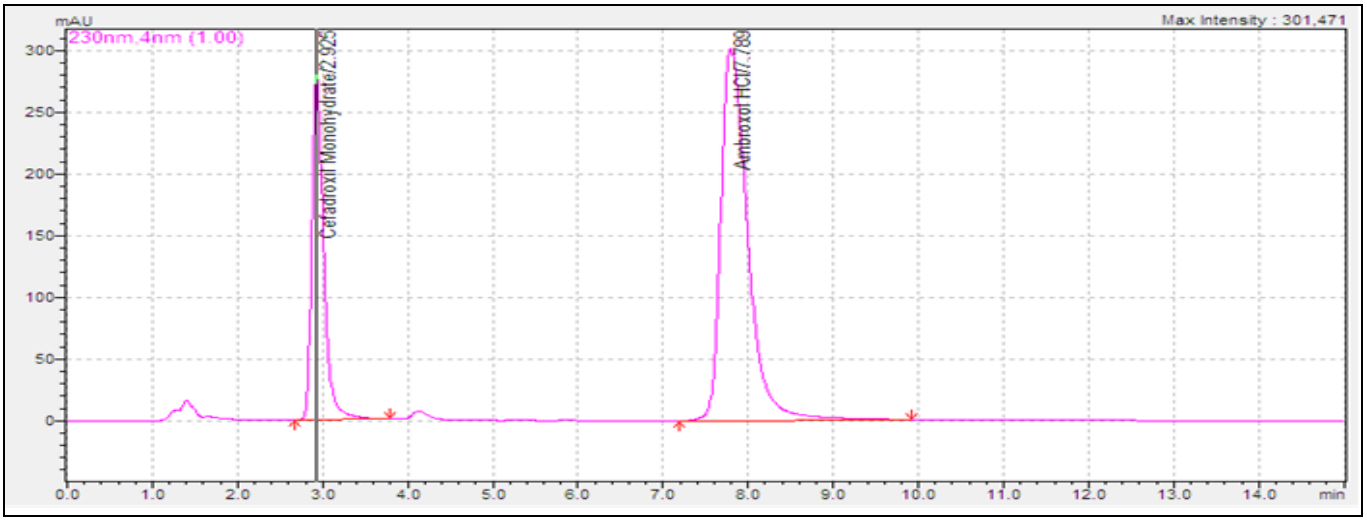

FIG. 5: CHROMATOGRAPH OF FORCED DEGRADATION STUDY ON SAMPLE SOLUTION CONTAINING AMB AND CEFXL USING 0.1 M HCL SOLUTION

Degradation with 0.1M NaOH: Weighed and transferred about 500 mg of sample (Average Weight of Tablet) in to 100 mL volumetric flask Add 5.0 mL 0.1 M Sodium hydroxide to the flask. Reflux the solution for 1 hour at 80 ºC. Allow to cool the solution at room temperature. Add 5.0 mL 0.1 M Hydrochloric acid. Add about 50 ml of Diluent and sonicated to dissolve it completely and make volume up to the mark with Diluent. Dilute 5 ml of this solution to 50 ml with the Diluent. (250µg/ml CEFXL and 30 µg/ml AMB). **(Fig. 6)**

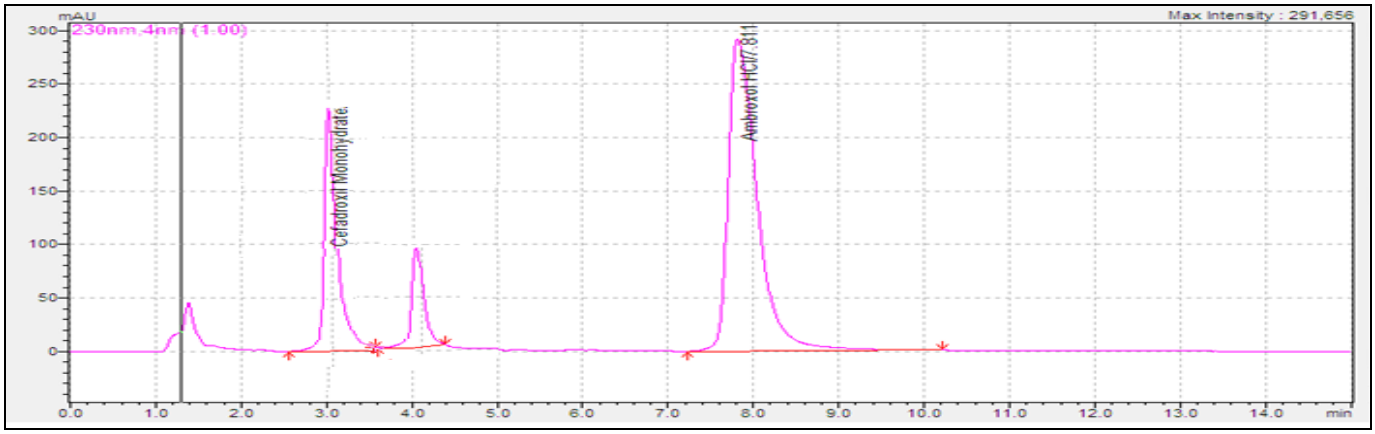

FIG. 6: CHROMATOGRAPH OF FORCED DEGRADATION STUDY ON SAMPLE SOLUTION CONTAINING CEFXL AND AMB USING 0.1 M NAOH

Exposed to Heat: Weighed and transferred about 500 mg of sample (Average Weight of Tablet) exposed under heat at 80ºC for 1 hour in 100 ml volumetric flask. Add about 50 ml of Diluent and sonicated to dissolve it completely and make volume up to the mark with Diluent. Dilute 5 ml of this solution to 50 ml with the Diluent. (250µg/ml CEFXL and 30 µg/ml AMB). **(Fig. 7)**

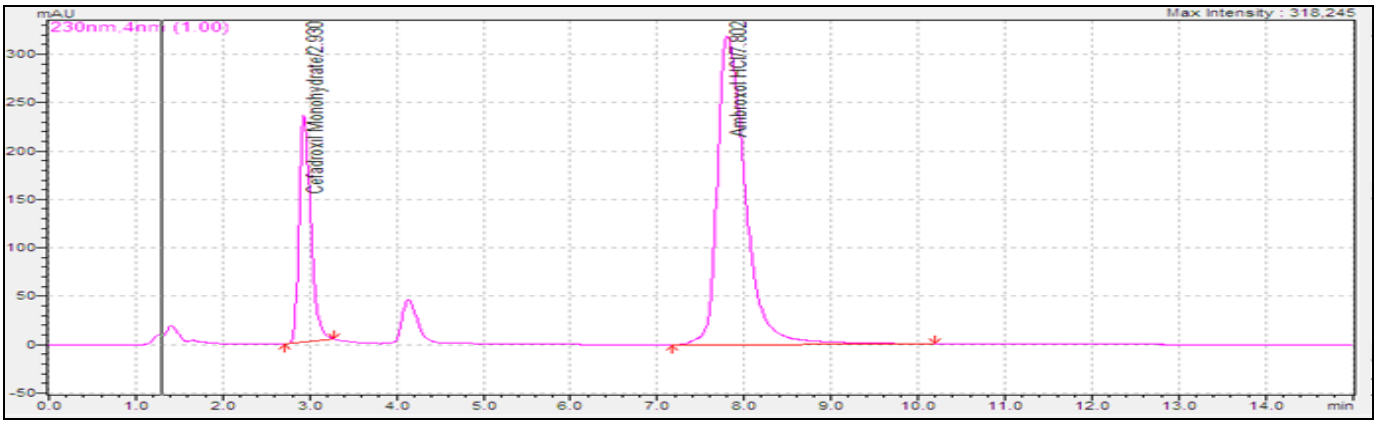

FIG. 7: CHROMATOGRAPH OF FORCED DEGRADATION STUDY ON SAMPLE SOLUTION CONTAINING AMB AND CEFXL USING HEAT TREATMENT AT 80ºC 1 HOUR

Exposed to UV light: Weighed and transferred about 500 mg of sample (Average Weight of Tablet) exposed UV radiation for 12 hour in 100 ml volumetric flask. Add about 50 ml of Diluent and sonicated to dissolve it completely and make volume up to the mark with Diluent. Dilute 5 ml of this solution to 50 ml with the Diluent. (250 µg/ml CEFXL and 30 µg/ml AMB). **(Fig. 8)**

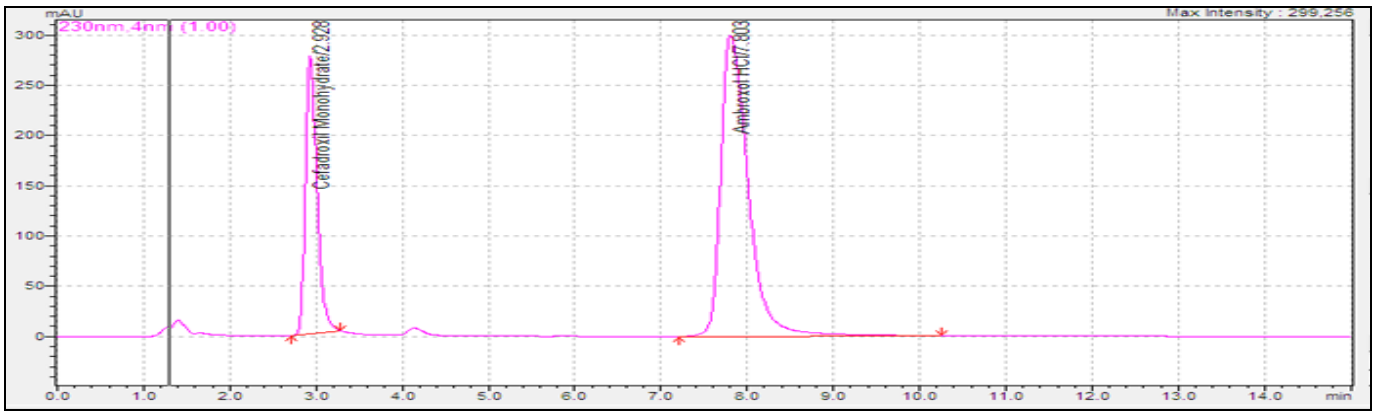

FIG. 8: CHROMATOGRAPH OF FORCED DEGRADATION STUDY ON SAMPLE SOLUTION CONTAINING AMB AND CEF USING UV LIGHT TREATMENT FOR 12 HOURS

RESULTS AND DISCUSSION:

System Suitability: The standard solution was prepared by using working standard as per the method. For six replicate injections system suitability parameters like number of theoretical plates, USP Tailing and % RSD were found to be within specified limits. **(Table 2)**

TABLE 2: SYSTEM SUITABILITY TEST PARAMETER

System Suitability Parameters	Proposed Method	
	AMB	CEFXL
Retention times (R_t) (min)	7.750 ± 0.01	2.912 ± 0.01
Theoretical plates (N)	3183.15 ± 18.08	2300.11 ± 13.72
Resolution (R_S)	12.247 ± 0.26	
Tailing factor (A_S)	1.54 ± 0.01	1.503 ± 0.002
RSD of all Replicates area of Standard Solution	0.10 %	0.02 %

Specificity: A study was carried out by determining peak purity. It observed that there were no peaks interfering with the analyte which was evident from the purity data.

Linearity: Linearity of detector response was established by plotting graph between concentrations versus average area counts of the analytes. Data shown in **Table 3** and represented graphically in Graph **(Fig. 9 and Fig. 10)** indicate that the response is linear over the specified range.

TABLE 3: LINEARITY

Linearity Level (%)	Final conc. (µg/mL)		Mean Area ± SD (n = 3)	
	CEFXL	AMB	CEFXL	AMB
20	50	6	456353 ± 69.05	1150970 ± 450.32
50	125	15	1235073 ± 659.48	2898038 ± 547.24
80	200	24	1979102 ± 458.32	4544172 ± 675.34
100	250	30	2466041 ± 563.72	5786622 ± 476.49
150	375	45	3690488 ± 493.26	8468042 ± 578.96
200	500	60	4915346 ± 359.76	11538951 ± 657.47

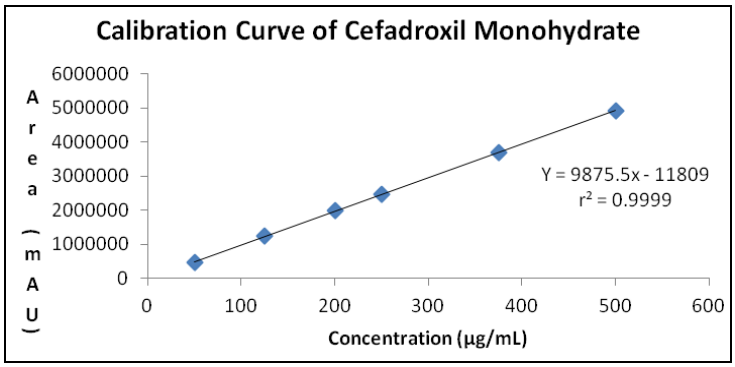

FIG. 9: CALIBRATION CURVE OF CEFADROXIL MONOHYDRATE

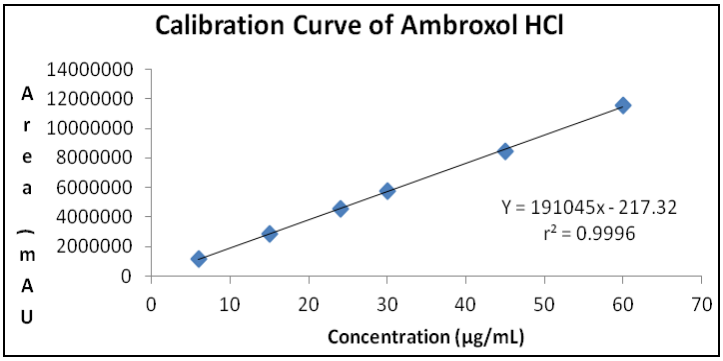

FIG. 10: CALIBRATION CURVE OF AMBROXOL HCL

Accuracy: A study of accuracy (recovery) was performed on known amount of placebo by spiking active pharmaceutical ingredient. Samples were prepared as per the proposed method at 80% to 120% of the sample concentration. Data shown in **Table 3** indicate that the method has an acceptable level of accuracy.

TABLE 4: ACCURACY

Accuracy Level	Theoretical amount (ppm)		Practical amount (ppm)		% Recovery		Mean	
	AMB	CEFXL	AMB	CEFXL	AMB	CEFXL	AMB	CEFXL
80 % Set - 1	24.04	200.05	24.09	200.55	100.2	100.2		
80 % Set - 2	24.18	200.12	24.07	200.39	99.6	100.1	100.1	100.3
80 % Set - 3	24.02	200.08	24.12	200.86	100.4	100.4		
100 % Set - 1	30.11	250.32	30.13	249.48	100.1	99.7		
100 % Set - 2	30.25	250.20	30.12	250.02	99.6	99.9	100.0	99.8
100 % Set - 3	30.08	250.18	30.18	249.86	100.3	99.9		
120 % Set - 1	36.05	300.10	36.26	299.74	100.6	99.9		
120 % Set - 2	36.12	300.13	36.13	299.50	100.0	99.8	100.2	99.8
120 % Set - 3	36.20	300.27	36.25	299.65	100.1	99.8		

Precision:

System precision: Six replicate injections of standard solution were injected into the HPLC system. The %RSD for six replicated injections was found to be in the limits.

Method precision: The precision of test method was evaluated by analysing assay for six individual samples prepared from same batch by the proposed method. The average %Assay and the relative standard deviation for the six sample preparation were found to be in the specified limits. **Table 5**

TABLE 5: METHOD PRECISION

	Injections	Mean Area ± SD (n = 3)		% Assay	
		AMB	CEFXL	AMB	CEFXL
Concentration	1	5784721 ± 358.21	2489312 ± 273.43	100.1	100.8
AMB	2	5793454 ± 273.43	2483245 ± 383.43	100.3	100.6
(30 ppm)	3	5783532 ± 283.72	2479204 ± 493.21	99.9	100.2
CEFXL	4	5761399 ± 482.85	2465483 ± 384.35	99.6	99.7
(250 ppm)	5	5774975 ± 492.74	2495231 ± 237.45	99.8	100.9
	6	5786584 ± 374.54	2474294 ± 283.46	100.1	100.1
		Mean		100.0	100.4
		% RSD		1.19	1.12

Intermediate precision (Ruggedness): The ruggedness of method was verified by conducting the precision study by using different HPLC, different columns of same make by different analyst on different days. Six samples of same batch were prepared and analysed by the proposed method. The mean, standard deviation, and %RSD for the two sets of data are shown in **Table 6.** Ruggedness of the method is indicated by the overall RSD between the two sets of data.

TABLE 6: INTERMEDIATE PRECISION

	Injections	Mean Area ± SD (n = 3)		% Assay	
		AMB	CEFXL	AMB	CEFXL
Concentration	1	5690572 ± 345.32	2459036 ± 385.31	99.8	99.4
AMB	2	5704493 ± 395.21	2461927 ± 340.65	100.1	99.5
(30 ppm)	3	5680492 ± 214.65	2466123 ± 254.67	99.7	99.7
CEFXL	4	5698481 ± 385.12	2465176 ± 286.94	100.0	99.6
(250 ppm)	5	5689831 ± 295.36	2461964 ± 228.64	99.8	99.5
	6	5680382 ± 356.31	2460379 ± 342.65	99.7	99.4
		Mean		99.9	99.5
		% RSD		0.17	0.11
% Difference between Method Precision and Intermediate Precision				0.1	0.9

Robustness: Robustness of the method was investigated **Table 7** by varying the instrumental conditions such as flow rate (±0.2), column oven temperature (±2%), organic content in mobile phase (±1.75) and pH of buffer in mobile phase (0.2). Standard solution was prepared and analysed as per the test procedure monitored the system suitability results.

TABLE 7: ROBUSTNESS STUDY FOR AMB AND CEFXL

Factors		Retention time (min)		Asymmetry (A_s)		Resolution
		AMB	CEFXL	AMB	CEFXL	
pH of mobile phase	2.9	7.743	2.908	1.605	1.523	12.200
	3.0	7.750	2.912	1.544	1.503	12.247
	3.2	7.745	2.910	1.621	1.519	12.598
	Mean ± SD	7.746 ± 0.004	2.910 ± 0.002	1.590± 0.041	1.515± 0.011	12.348 ± 0.217
Temp (^oC)	28	7.718	2.894	1.619	1.389	13.241
	30	7.750	2.912	1.544	1.503	12.247
	32	7.802	2.945	1.694	1.793	11.485
	Mean ± SD	7.757 ± 0.042	2.917 ± 0.026	1.619 ± 0.075	1.562 ± 0.208	12.324 ± 0.881
Flow rate	0.8	8.021	3.143	1.365	1.386	13.07
	1.0	7.750	2.912	1.544	1.503	12.247
	1.2	7.72	2.724	1.643	1.683	11.98
	Mean ± SD	7.830 ± 0.166	2.926 ± 0.210	1.517 ± 0.141	1.524 ± 0.150	12.429 ± 0.567
Mobile Phase Ratio	ACN: Buffer (38.25:61.75)	7.864	3.143	1.582	1.564	12.090
	ACN: Buffer (40:60)	7.750	2.912	1.544	1.503	12.247
	ACN: Buffer (41.75:58.25)	7.742	2.895	1.428	1.468	12.430
	Mean ± SD	7.785 ± 0.068	2.983 ± 0.139	1.518 ± 0.080	1.512 ± 0.049	12.259 ± 0.173

Stability of sample solution: The sample solution was stable up to 36 hours and did not show any appreciable change in sample area. **Table 8**

TABLE 8: SOLVENT SUITABILITY

Time points (hour)	AMB % Difference		CEFXL % Difference	
	Standard Preparation	Test Preparation	Standard Preparation	Test Preparation
0 Hours	NA	NA	NA	NA
12 Hours	0.06	0.09	0.36	0.40
24 Hours	0.16	0.26	0.83	0.96
36 Hours	0.24	0.50	1.14	1.29

Forced degradation Study: The Data for Forced degradation are tabulated in **Table 9**. There was no interference of any peak at the retention time of analyte peaks from blank and placebo, Peak purity of all forced degradation treated samples were passed.

TABLE 9: FORCED DEGRADATION STUDY

Sr. No.	Condition applied	Area		% Assay		% Degradation	
		AMB	CEFXL	AMB	CEFXL	AMB	CEFXL
1	Untreated Sample	5784721	2489312	100.1	100.8	---	---
2	0.1 M HCl 80º C 1 Hour	5557848	2367845	96.2	95.9	3.8	4.1
3	0.1 M NaOH RT 1 Hour	5387082	2033865	93.2	82.4	6.8	17.6
4	3 % H_2O_2 RT 1 Hour	5589696	2105947	96.7	85.3	3.3	14.7
5	Heat Treatment	5703364	2200545	98.7	89.1	1.3	10.9
6	UV light treatment	5725598	2459681	99.1	99.6	0.9	0.4

Summary of Validation Parameters are tabulated in **Table 9**.

TABLE 10: SUMMARY OF VALIDATION PARAMETERS OF RP-HPLC

Parameters	AMB	CEFXL
Recovery %	99.6 – 100.6	99.7 – 100.4
Method precision	0.25	0.46
Intermediate precision	0.17	0.11
Specificity	Specific	Specific
Solvent suitability	Solvent suitable for 36 hours	Solvent suitable for 36 hours

Estimation of Marketed Formulation: Estimation of Marketed Formulation was carried out in **Table 11.** From this study it has been concluded that the proposed method is specific and stability indicating for the estimation of PSE and FEX, in the tablet dosage form.

TABLE 11: ASSAY RESULTS OF MARKETED FORMULATION

Formulation	Drug	Label claim (mg)	Amount Taken (µg/ml) (n = 3)	Amount Found (µg/ml) (n = 3)	% Label claim ± S.D
KEFDIL-AX	AMB	30	30	29.97	99.9 ± 0.02
	CEFXL	250	250	249.50	99.8 ± 0.06

CONCLUSION: This intended study can be concluded as the proposed method is simple, highly fast, economical, sensitive and reliable and is found to be more precise, accurate, specific, stability indicating, rugged and robust. Hence it can be employed for routine estimation of tablets containing AMB and CEFXL. Conventional reported chromatographic methods may be replaced by the proposed stability indicating HPLC method because of its superiority in cost effectiveness, short analysis time per sample and better detection. For faster samples testing routinely in QC lab the validated method may be used.

ACKNOWLEDGMENT: The authors wish to thank the management of Advanced Analytical Research and Technical Institute, Ahmedabad, India for providing laboratory facility for this work.

REFERENCES:

1. Indian pharmacopoeia, - Ambroxol Hydrochloride, Govt. of India, "ministry of health and family welfare", controller and publication, Delhi; volume 2, 2007-83.
2. http://www.chemicalland21.com/lifescience/phar/AMBROXOL%20hydrochloride.htmChemicalland21 – Ambroxol Hydrochloride;[cited 2012 Sept 28],
3. Indian pharmacopoeia – Cefadroxil Govt. of India, "ministry of health and family welfare", controller and publication, Delhi, volume 2, 2007-250.
4. http://www.drugbank.ca/drugs/DB01140 Drug Bank – Open Data Drug and Drug Target Database, Cefadroxil; [cited 2012 Oct 5].

How to cite this article:
Goswami JA and Shah NJ: Stability indicating RP – HPLC method for combination of ambroxol hydrochloride and cefadroxil monohydrate in pharmaceutical formulation. Int J Pharm Sci Res 2017; 8(3): 1220-28.doi: 10.13040/IJPSR.0975-8232.8(3).1220-28.