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Stability indicating simultaneous validation of Paracetamol, Phenylpropanolamine and Triprolidine with forced degradation behavior study by RP-HPLC in pharmaceutical dosage form

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ABSTRACT

A simple, precise, and accurate RP-HPLC method has been developed and validated for the simultaneous assay of Paracetamol, Phenylpropanolamine and Triprolidinein tablet dosage form. Isocratic RP-HPLC method was developed on BDS hypersil C18, (250mm×4.6mm internal diameter, 5µ particle size) using mobile phase as Water (pH-4.0): Methanol (70:30v/v) at a flow rate of 1.0 mL/min and the detection was carried out at 220nm using tunable absorbance detector (Waters 486). Forced degradation study was carried out by acid degradation, base degradation, thermal degradation, oxidation of the drug. The method was validated for linearity, precision, accuracy and robustness. It was found to ideally resolve the peaks with retention time (RT) 4.053min,5.603min and 11.083 min for Phenylpropanolamine, Paracetamol and Triprolidine respectively.The method was found to be linear in the concentration range of 50-150μg/mL with correlation coefficient of 0.9994 for Paracetamol,2.5-7.5μg/mL with correlation coefficient of 0.9995 for Phenylpropanolamineand 2.5-7.5μg/mLwith correlation coefficient of 0.9992 for Triprolidine. Degradation products produced as a result of stress studies did not interfere with the detection of Paracetamol, Phenylpropanolamine and Triprolidine; therefore, the assay can be considered to be stability indicating.

Keywords: HPLC, Paracetamol, Phenylpropanolamine, Triprolidine, Validation, Forced degradation.

Introduction

Paracetamol's empirical formula is $C_8H_9NO_2$and its IUPAC name is *N*-(4-hydroxyphenyl) ethanamide*N*-(4hydroxyphenyl) acetamide. Figure 1 shows chemical structure of Paracetamol. Paracetamol is organic compound containing an acetamide group conjugated to a phenyl group of Benzenoids group. Paracetamol is thought to act primarily in the CNS, increasing the pain threshold by inhibiting both isoforms of cyclooxygenase, COX-1, COX-2, and COX-3 enzymes involved in prostaglandin (PG) synthesis. Phenylpropanolamine's empirical formula is $C_9H_{14}NCl$ and its IUPAC name is (1S,2R)-2-amino-1-phenylpropan-1-ol.

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Figure 2 shows chemical structure of Phenylpropanolamine. Phenylpropanolamine is a drug with adrenergic agonist properties. Phenylpropanolamine acts directly on alpha- and, to a lesser degree, beta-adrenergic receptors in the mucosa of the respiratory tract. Stimulation of alpha-adrenergic receptors produces vasoconstriction, reduces tissue hyperemia, edema, and nasal congestion, and increases nasal airway patency. It indirectly stimulates beta-receptors, producing tachycardia and a positive inotropic effect. Triprolidine's empirical formula is $C_{19}H_{22}N_2$and its IUPAC name is 2-[(E)-1-(4-methylphenyl)-3-pyrrolidin-1-yl-prop-1-enyl] pyridine.Figure 3 shows the chemical structure of Triprolidine.Triprolidine is first generation histamine H1 antagonist used in allergic rhinitis; asthma; and urticaria. It is a component of cough and cold medicines and may cause drowsiness Triprolidine binds to the histamine H1 receptor. This blocks the action of endogenous histamine, which subsequently

leads to temporary relief of the negative symptoms brought on by histamine.

Literature survey reveals that quantitative analysis of Paracetamol, Phenylpropanolamine and Triprolidine have been done separately or in combination of two and in combination of other drugs but no method is reported for the simultaneous estimation of Paracetamol, Phenylpropanolamine and Triprolidinein combined dosage form. The present study involved the development and validation of RP-HPLC method for the estimation of Paracetamol, Phenylpropanolamine and Triprolidinein combined pharmaceutical dosage form (tablet) and their forced degradation study(1-3).

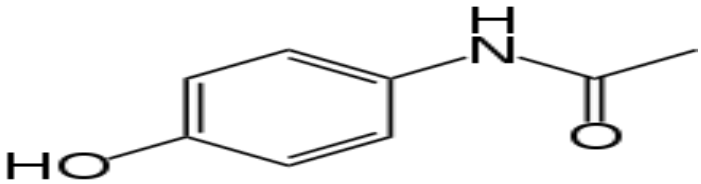


Fig 1: Structure of Paracetamol

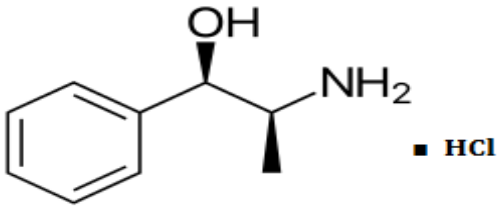


Fig 2: Structure of Phenylpropanolamine

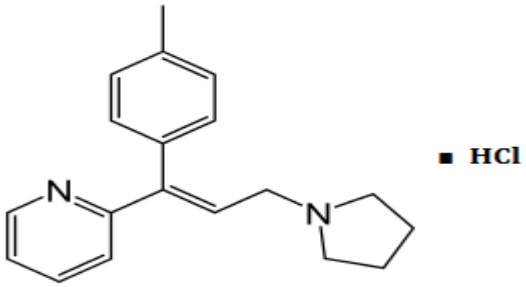


Fig 3: Structure of Triprolidine

Material and Methods

Instruments

The liquid chromatographic system consists of Waters series M510 equipped with a tunable absorbance detector (Waters 486), HPLC pump (Waters 510), and manual injector rheodyne valve with 20 μL fixed loop. The analytes were monitored at 220 nm. Chromatographic analysis was performed on Thermo scientific BDS hypersil C18, (250mm × 4.6mm internal diameter, 5µ particle size). All the drugs and chemicals were weighed on Citizen electronic balance. Chemiline India pH meter and Toshcon Ultrasonicator was used.

Chemicals and reagents

Methanolwas of HPLC grade obtained from Merck Ltd., Mumbai. Water was of HPLC grade prepared by triple distillation method. Sodium Hydroxide (NaOH), Hydrogen Peroxide (H_2O_2) and Hydrochloric Acid (HCl) were of AR grade and were obtained from Merck, Mumbai India. Paracetamol reference standard, Phenylpropanolamine and Triprolidine reference standards were procured from Yash Pharma. Actifed Plus containing 100 mg of Paracetamol, 5mg of Phenylpropanolamine and 0.5mg of Triprolidine manufactured by Glaxo SmithKline Pharmaceuticals Ltdwas procured from local market.

HPLC Conditions

The mobile phase consisted of Water (pH-4.0): Methanol (70:30v/v).The mobile phase was prepared freshly and it was sonicated by using ToshconUltrasonicator for 5 min before use. BDS hypersil C18, (250mm×4.6mm internal diameter, 5µ particle size) was used and it was equilibrated for at least 30 min with the mobile phase flowing through the

system. The column and the HPLC system were kept at ambient temperature. The eluent was monitored by UV detection at 220 nm. Analysis was done at flowrate of 1.0ml/min with 20µl volume of injection. All data were analyzed by using Empower 3 software.

Preparation of Mobile Phase

The mobile phase was prepared by mixing Water (pH-4.0) and Methanol in the ratio of (70:30%v/v). The solution was then filtered through 0.45 microns membrane filter and degassed.

Preparation of standard stock solution

Standard stock solution of Paracetamol, Phenylpropanolamine and Triprolidinewere prepared by accurately weighing 100mg, 50mg and 50mg respectively and dissolving them separately in 100ml with methanol to prepare solution of 1000μg/ml, 50μg/ml and 50μg/ml.

Preparation of working standard solution

Add 1ml each of standard stock solution of Paracetamol, Phenylpropanolamine and Triprolidinein 10 ml volumetric flask and volume make up to 10ml with methanol.

Preparation of sample stock solution

Weigh tablet powder equivalent to 5mg of Phenylpropanolamine, 100mg of Paracetamol and 0.5mg of Triprolidine) into a 100ml volumetric flask. Add 60ml methanol andshake for 15 minutes. Make up volume with methanol upto 100ml. Filter this solution.

Preparation of sample working solution

Take 1ml from sample stock solution into a 10ml volumetric flask, add 1ml Triprolidine standard stock solution and make up with mobile phase to prepare a solution of Phenylpropanolamine 5mcg/ml, Paracetamol 100mcg/ml and Triprolidine 5.5mcg/ml (Triprolidine 0.5mcg+ Triprolidine standard 5mcg).

Forced Degradation Study

Preparation of solution for acid degradation

Acid decomposition study was performed by keeping the working solution of all three drugs (1 ml) in 2 ml of 0.1N HCl for 4 hrs. After 4hrs solution neutralized with 2ml 0.1N NaOH and finally made up to 10 ml volume with mobile phase, sonicated and filtered through 0.45µm membrane filter paper and injected in to HPLC system. Degradation samples were prepared as blank sample, separate standard samples and combined sample of all three drugs.

Preparation of solution for basic degradation

Alkali decomposition study was performed by keeping the working solution of all three drugs (1 ml) in 2 ml of 0.1N NaOH for 4 hrs. After 4hrs solution neutralized with 2 ml of 0.1N HCL and finally made up to 10 ml volume with mobile phase, sonicated and filtered through 0.45µm membrane filter paper and injected in to HPLC system. Degradation samples were prepared as blank sample, separate standard samples and combined sample of all three drugs.

Preparation of solution for oxidative degradation

Oxidative decomposition study was performed by keeping the working solution of all three drugs (1 ml) in 2 ml 3% H_2O_2 for 5 hrs. After 5hrs volume made up to 10 ml with mobile phase,sonicated and filtered through 0.45µm membrane filter paper and injected into HPLC system. Degradation samples were prepared as blank sample, separate standard samples and combined sample of all three drugs.

Preparation of solution for thermal degradation

Thermal decomposition study was performed by refluxing the working solution of all three drugs (1 ml) for 24hrs at 105 ºC. After 24hrs volume made up to 10 ml volume with mobile phase, sonicated and filtered through 0.45µm membrane filter paper and injected into HPLC system. Degradation samples were prepared as blank sample, separate standard samples and combined sample of all three drugs.

Preparation of solution for UV degradation

UV degradation was performed by exposing the working solution of all three drugs (1ml) to Sunlight for 24 hours. After 24 hours volume made up to 10 ml volume with mobile phase, sonicated and filtered through 0.45µm membrane filter paper and injected into HPLC system. Degradation samples were prepared as blank sample, separate standard samples and combined sample of all three drugs were prepared.

Determination of λ max

The UV spectra of standard stock solutions of Paracetamol, Phenylpropanolamine and Triprolidine were taken between the wave length range of 200-400nm using methanol as blank. The λ max was found to be 245.93nm, 232.95nm and 183.31nm for Paracetamol, Phenylpropanolamine and Triprolidine respectively. Overlay of the three spectra taken and iso-absorptive point was selected and it was found that all three drugs show appreciable absorbance at 220 nm, so it is used for the further study.

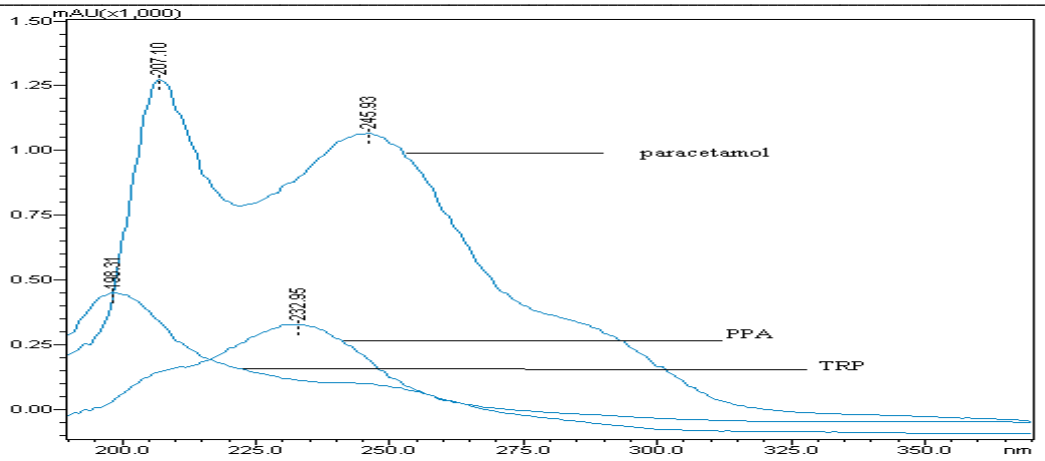


Fig 4: Overlay absorption spectrum for Paracetamol, Phenylpropanolamine and Triprolidine

Procedure of Analysis

1ml from Paracetamol Standard stock solution, 1ml from Phenylpropanolamine Standard stock solution and 1ml from Triprolidine Standard stock solution were taken and volume was make up to 10ml with Mobile phase to obtain Working standard solution containing Paracetamol (100μg/mL), Phenylpropanolamine (5μg/mL) and Triprolidine(5μg/mL). The contents of standard and sample solution were then filtered through 0.45 µm syringe filter. Chromatograms standard solution (six replicates) was recorded. A typical chromatogram of Paracetamol, Phenylpropanolamine and Triprolidineis presented in figure 5. The retention time of Paracetamol, Phenylpropanolamine and Triprolidinewere 5.603 min, 4.653 min and 11.083min respectively. The peak areas were measured and the quantitation was carried out by keeping these values to the regression equation of calibration curve.

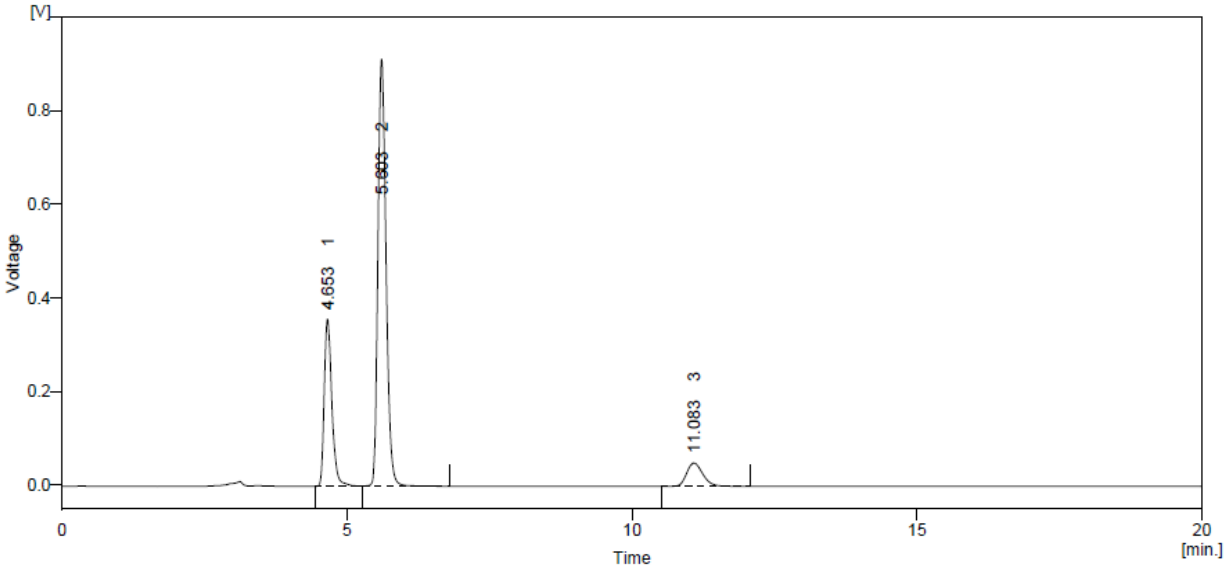


Fig 5: Standard Chromatograms of Paracetamol, Phenylpropanolamine and Triprolidine

Optimized Chromatographic Condition

Stationary phase: Thermo scientific BDS hypersil C_{18} (250mm × 4.6mm, 5µ).
Mobile phase **:** Water (pH 4.0): Methanol (70:30 v/v)
Flow rate **:** 1.0 ml/min
Run time (min) **:** 15min
Detection **:** At 220 nm
Injection (volume) **:** 20µl

Table 1: System suitability of proposed method

Parameters	Paracetamol	Phenylpropanolamine	Triprolidine
Theoretical plates	7398	5839	7396
Resolution	-	3.769	14.122
Asymmetry	1.398	1.563	1.366
Retention time	5.603 min	4.653 min	11.083 min

Method validation procedure

The developed method was validated for the parameters listed in ICH guidelines (4-7).

Linearity

The method was linear in the range of 50-150μg/mL, 2.5-7.5 μg/mL and 2.5-7.5μg/mL for Paracetamol, Phenylpropanolamine and Triprolidine respectively. The linear correlation coefficient for Paracetamol, Phenylpropanolamine and Triprolidine were found to be 0.9994, 0.9995 and 0.9992 respectively, and are recorded in table 2, 3 and 4. Calibration curve of Paracetamol, Phenylpropanolamine and Triprolidinewas obtained by plotting the peak area ratio versus the respective concentrations (Figure 6, 7 and 8).

Table 2: Linearity results of Paracetamol

Linearity Level	Concentration	Area
I	50 µg/ml	4633.059
II	75 µg/ml	7003.539
III	100 µg/ml	9079.044
IV	125 µg/ml	11424.241
V	150 µg/ml	13463.017
Correlation coefficient		0.9994

Table 3: Linearity of Phenylpropanolamine

Linearity Level	Concentration	Area
I	2.5 µg/ml	1706.569
II	3.75 µg/ml	2581.360
III	5 µg/ml	3336.578
IV	6.25 µg/ml	4209.745
V	7.5 µg/ml	4981.000
Correlation coefficient		0.9995

Table 4: Linearity of Triprolidine

Linearity Level	Concentration	Area
I	2.5 µg/ml	495.645
II	3.75 µg/ml	742.735
III	5 µg/ml	977.866
IV	6.25 µg/ml	1220.885
V	7.5 µg/ml	1430.128
Correlation coefficient		0.9992

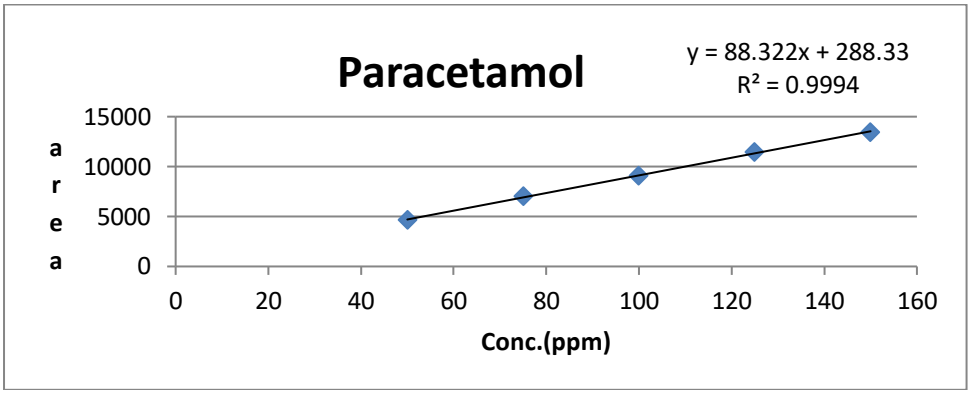


Fig 6: Calibration curve of Paracetamol

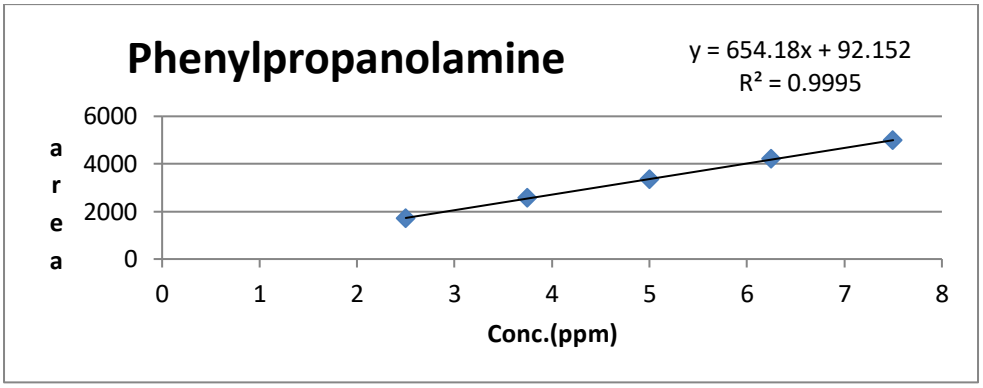


Fig 7: Calibration curve of Phenylpropanolamine

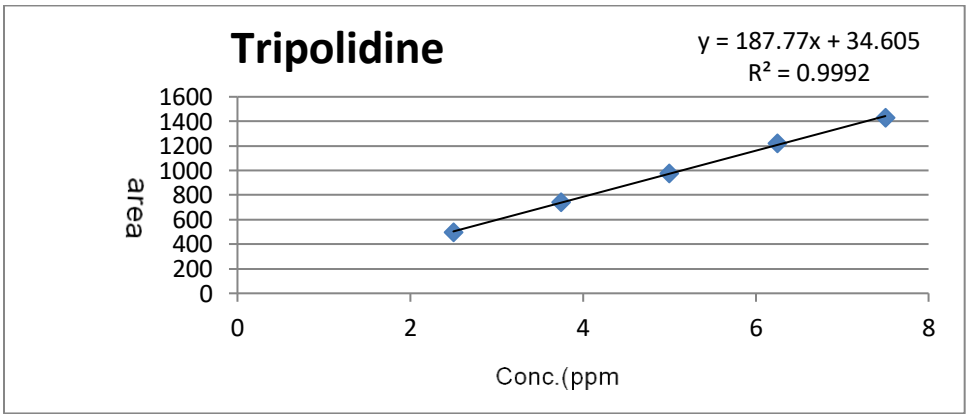


Fig 8: Calibration curve of Triprolidine

Accuracy

The accuracy of the method was determined by recovery experiment and known concentration of working standard was added to the fixed concentration of the pre-analyzed tablet solution. Percent recovery was calculated by comparing the area before and after the addition of working standard and recovery was performed in the same way for all the three drugs. The recovery studies were performed in triplicate and results are recorded in table 5. This standard addition method was performed at 80%, 100%, 120% level and the percentage recovery was calculated. Percent recovery was within the range of 99.206-100.578 for Paracetamol, 98.923-99.943 for Phenylpropanolamine and99.727-100.308 for Triprolidinewhich indicates that the method was accurate.

Table 5: Results of Accuracy

Sample	Accuracy	Standard Drug(µg/ml)	Sample Drug (µg/ml)	% of recovery	S.D.
Paracetamol	80%	40	50	100.578	0.522
	100%	50	50	99.206	1.504
	120%	60	50	100.136	0.264
Phenylpropanolamine	80%	2	2.5	99.943	0.971
	100%	2.5	2.5	98.923	1.268
	120%	3	2.5	99.894	0.439
Triprolidine	80%	4	0.25	100.288	1.013
	100%	5	0.25	99.727	0.504
	120%	6	0.25	100.308	0.265

Precision

For the precision study, repeatability study was carried out for short time interval under the same chromatographic condition. The sample was injected in six replicates and peak area for all the six replicates was recorded. The mean and % relative standard deviation (%RSD) was calculated and the results are shown in table 6. The %RSD for Paracetamol, Phenylpropanolamine and Triprolidine were found to be 0.778%, 0.869% and 0.924 % respectively. From the data obtained the developed RP-HPLC method was found to be precise. For interday and intraday precision three different concentrations (50%, 100% and 150% of analyte) of standard solutions were injected on same day and three consecutive days in three replicates and results were recorded in table 7 & 8.

Table 6: Results of Precision

Injection	Area of Paracetamol	Area of Phenylpropanolamine	Area of Triprolidine
Injection 1	9122.124	3359.548	978.816
Injection 2	9076.541	3335.379	975.895
Injection 3	9017.960	3321.314	967.660
Injection 4	9000.116	3309.954	967.635
Injection 5	8999.830	3302.161	956.177
Injection 6	8918.921	3275.594	958.962
Average	9022.582	3317.325	967.524
S.D.	70.156	28.811	8.941
% RSD	0.778	0.869	0.924

Table 7: Result of Interday Precision

Conc. (µg/ml)			Area			% RSD		
Paracetamol	Phenylpropanolamine	Triprolidine	Paracetamol	Phenylpropanolamine	Triprolidine	Paracetamol	Phenylpropanolamine	Triprolidine
50	2.5	2.5	4528.097	1662.431	485.395	0.849	1.321	0.759
100	5	5	9008.891	3312.439	969.738	0.579	0.607	0.554
150	7.5	7.5	13594.07	4994.392	1461.311	1.034	1.144	0.902

Table 8: Result of Intraday Precision

Conc. (µg/ml)			Area			% RSD		
Paracetamol	Phenylpropanolamine	Triprolidine	Paracetamol	Phenylpropanolamine	Triprolidine	Paracetamol	Phenylpropanolamine	Triprolidine
50	2.5	2.5	4528.097	1662.431	485.395	0.849	1.321	0.759
100	5	5	9008.891	3312.439	969.738	0.579	0.607	0.554
150	7.5	7.5	13594.07	4994.392	1461.311	1.034	1.144	0.902

Limit of Detection (LOD) and Limit of Quantification (LOQ)

The limit of detection and quantification were calculated using standard deviation of response and slope of the calibration curve and results are recorded table 9. The LOD for Paracetamol, Phenylpropanolamineand Triprolidine was found to be 3.716 µg/ml, 0.174 µg/ml and 0.210 µg/ml respectively. The LOQ is the smallest concentration of the analyte, which gives response that can be accurately quantified. The LOQ for Paracetamol, Phenylpropanolamine and Triprolidinewas 11.261 µg/ml, 0.529 µg/ml and 0.638µg/ml.

Table 9: Results of LOD and LOQ

Parameter	Paracetamol (µg/ml)	Phenylpropanolamine (µg/ml)	Triprolidine(µg/ml)
LOD	3.716	0.174	0.210
LOQ	11.261	0.529	0.638

Robustness

Robustness of the method was checked by making slight deliberate changes in chromatographic conditions like flow rate, mobile phase ratio and pH of buffer and the result were recorded in table 10. It was observed that there were no marked changes in chromatograms and % relative standard deviation was found below 2%, which demonstrated that the developed RP-HPLC method is robust.

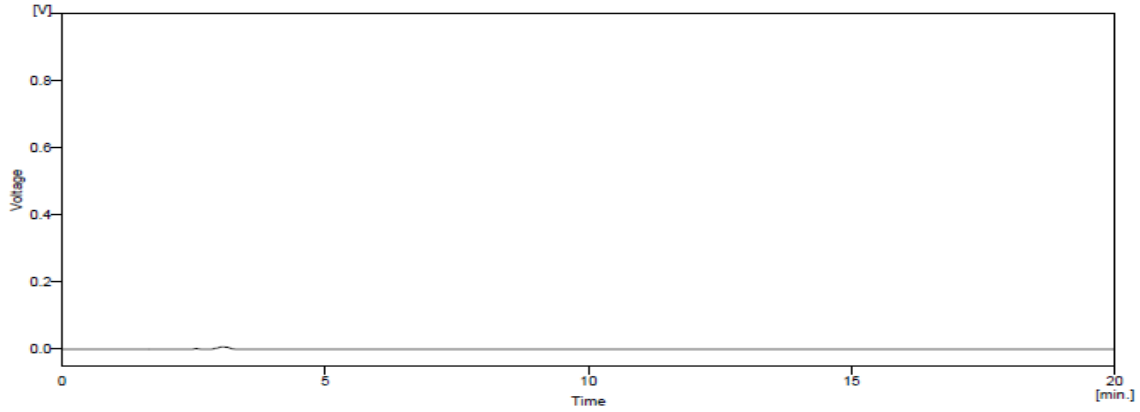
Table 10: Results of Robustness

Condition	Variation	Average Area			% RSD		
		Paracetamol	Phenylpropanolamine	Triprolidine	Paracetamol	Phenylpropanolamine	Triprolidine
Flow rate	0.8 min	9546.055	3510.605	1022.257	0.216	0.332776	0.711444
	1.2 min	8691.59	3188.266	932.7417	0.251	0.62451	0.265757
Mobile phase	Water (pH 4.0): Methanol (72:28 v/v)	8836.413	3247.385	947.9253	0.221	0.289671	0.541888
	Water (pH 4.0): Methanol (68:32 v/v)	9366.981	3445.988	1004.45	0.694	0.885241	0.795956
pH	6.2	9056.592	3322.327	973.375	0.352	0.633679	0.299421
	5.8	8877.534	3264.259	951.1223	0.462	0.423682	0.886248

Specificity

The specificity of proposed method is justified by the chromatograms of blank, placebo, standard and sample solutions under same chromatographic conditions shown in figure 9. The placebos did not interfere in determination of Paracetamol, Phenylpropanolamine and Triprolidinein commercial tablet. Specificity of the developed method was also evaluated by applying different stress conditions (oxidation, acid, base, thermal and photolytic) to Paracetamol, Phenylpropanolamine and Triprolidine tablet.

(a)



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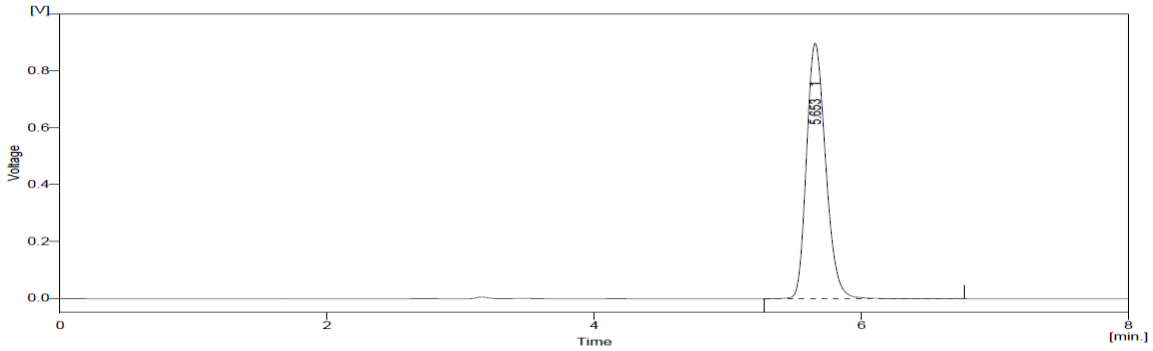

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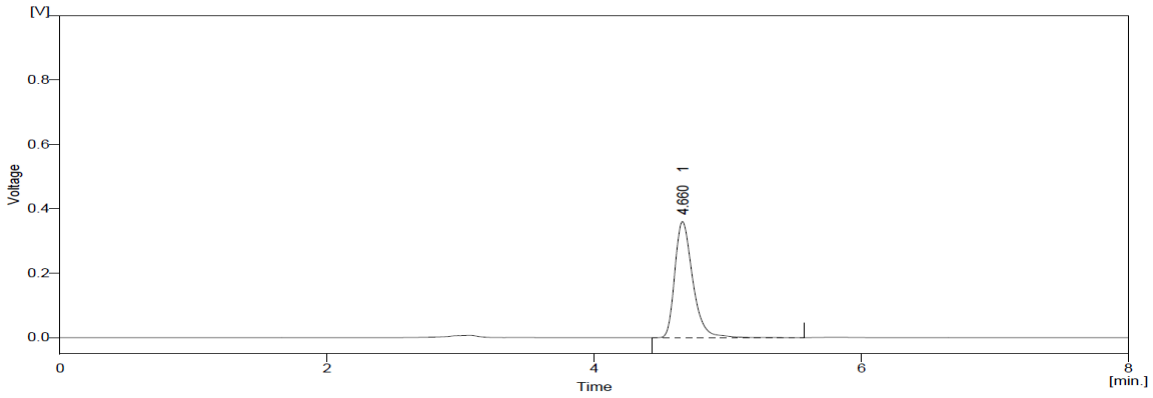


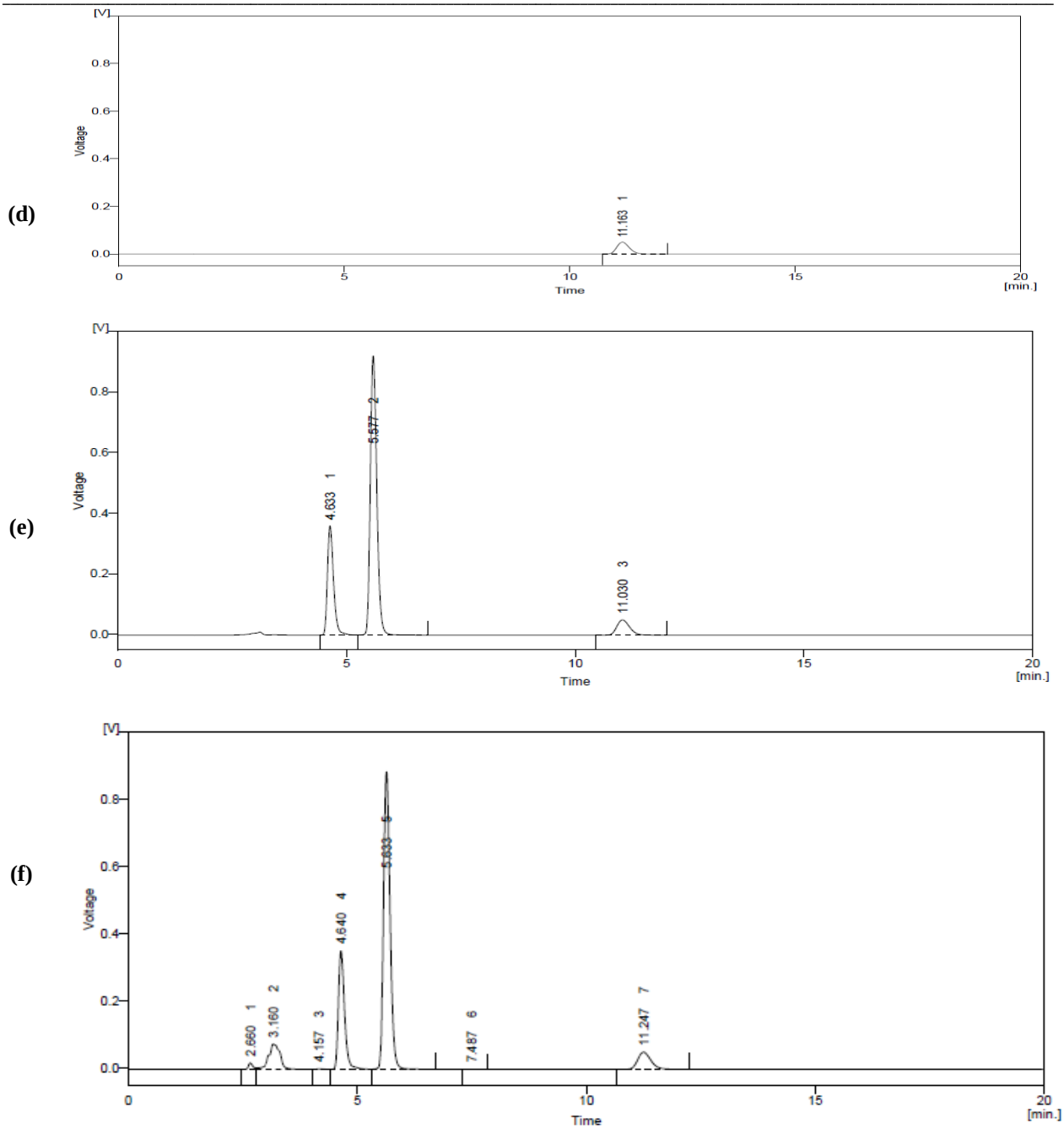


Fig 9: Chromatograms of (a) Blank, (b) Paracetamol, (c) Phenylpropanolamine,(d) Triprolidine, (e) Standard mixture and (f) Sample mixture

Degradation Study

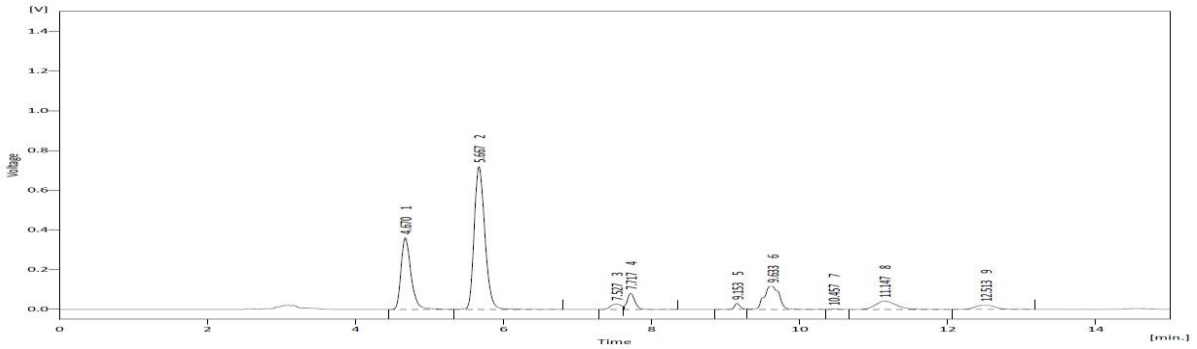
From the results of forced degradation studies showed that these components do not remained intact under stressed conditions and hence special storage conditions should be provided for the dosage form. The specificity studies showed that the principle peaks were well resolved (peak purity 99.99%) and free from any interference from the degradation product. The stress conditions were applied and degraded products of all three drugs are compared and showed in table 11 and

chromatograms are in figure 10. From the stress studies it is concluded that substantial degradation of Paracetamol, Phenylpropanolamine and Triprolidine occurred in acid, basic, oxidative thermal and photolytic stress conditions. The degradation products (impurities) in addition to percent degradation under acid, base, oxidation, thermal and photolytic stresses have unique retention times (RT) to acidic stress (9 impurities, RT: 4.670 min, 5.667 min, 7.527 min, 7.717 min, 9.153 min and 9.633min, 10.457 min, 11.147 min and 12.513 min), basic stress (8 impurities, RT: 4.650 min, 5.667 min, 6.807 min and 7.900 min, 9.647 min, 10.487 min, 11.160 min and 12.653 min), oxidative stress (8impurities, RT: 3.810 min, 4.673 min, 5.627 min, 7.840 min, 8.420 min, 9.623 min, 10.193 min and 11.217 min), thermal stress (7 impurities, RT: 4.653 min, 5.643 min, 7.027 min, 8.367 min. 9.490 min, 10.007 min and 11.183 min) and photolytic stress (12 impurities, RT: 4.650 min, 5.670 min, 6.443 min, 6.873 min, 7.703 min, 8.300 min, 8.750 min, 9.777 min, 10.540 min, 11.197 min, 12.740 minand 14.193 min). Degradation studies justified the method specificity for its intended application.

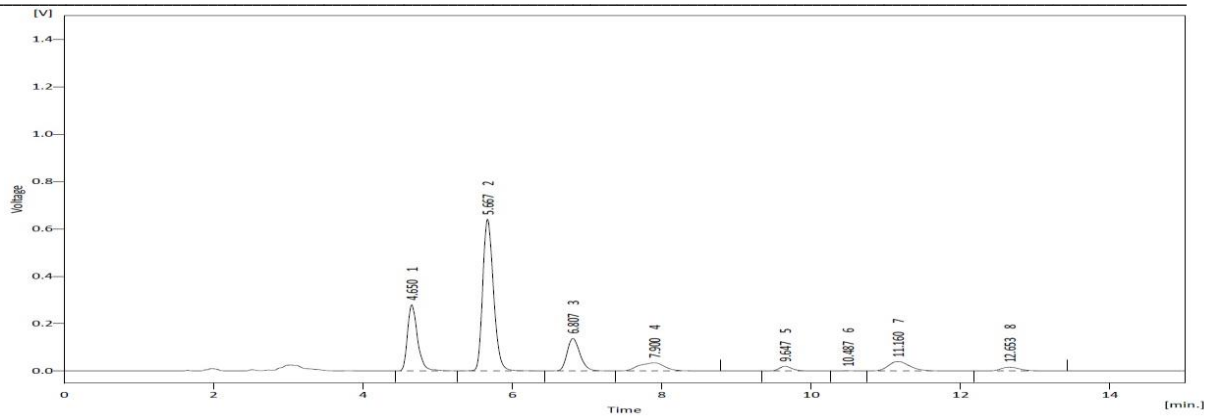
Table 11: Stability study results

Type of degradation	Drug	Peak Area of Standard	Conditions	Peak area			
				Standard		Sample	
				Area	% Deg.	Area	% Deg.
Acid degradation	Paracetamol	9085.492	4 hours at Room Temperature	7142.284	21.38803	7184.386	20.92463
	Phenylpropanolamine	3346.163		2778.715	16.96	2768.554	17.26
	Triprolidine	974.959		793.635	18.59812	801.740	17.767
Base degradation	Paracetamol	9085.492	4 hours at Room Temperature	6301.313	30.64423	6394.391	29.61976
	Phenylpropanolamine	3346.163		2653.422	20.70	2594.504	22.46
	Triprolidine	974.959		780.623	19.93274	779.570	20.041
Oxidative degradation	Paracetamol	9085.492	5 hours at Room Temperature	6136.852	32.45438	6288.912	30.78072
	Phenylpropanolamine	3346.163		2446.238	26.89	2478.91	25.92
	Triprolidine	974.959		745.265	23.55935	754.969	22.564
Thermal degradation	Paracetamol	9085.492	24 hours at 105^0C	6331.444	30.31259	6372.831	29.85706
	Phenylpropanolamine	3346.163		2152.561	35.67	2192.828	34.47
	Triprolidine	974.959		623.33	36.06603	626.050	35.787
Photolytic degradation	Paracetamol	9085.492	24 hours in UV chamber	7290.649	19.75504	7358.982	19.00293
	Phenylpropanolamine	3346.163		2818.476	15.77	2855.725	14.66
	Triprolidine	974.959		782.466	19.7437	775.488	20.459

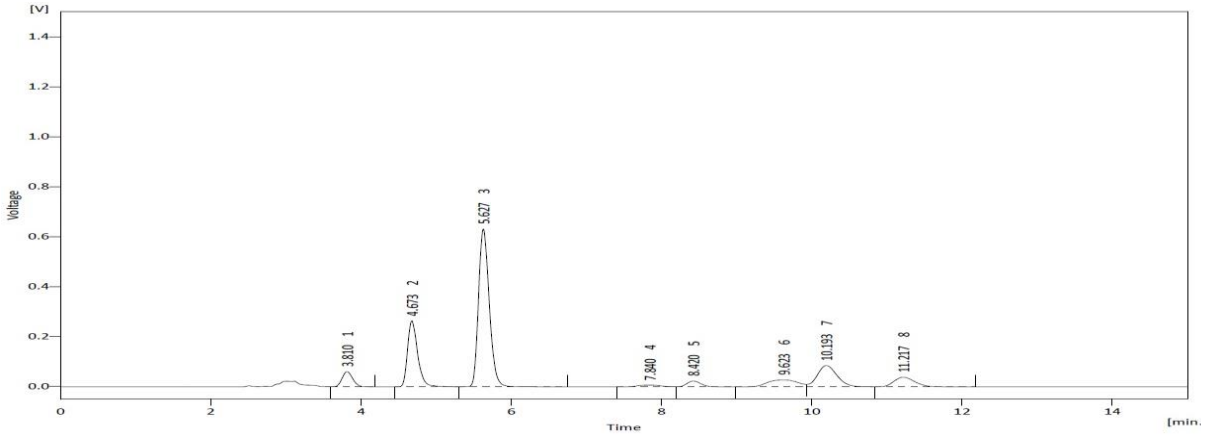
(a)



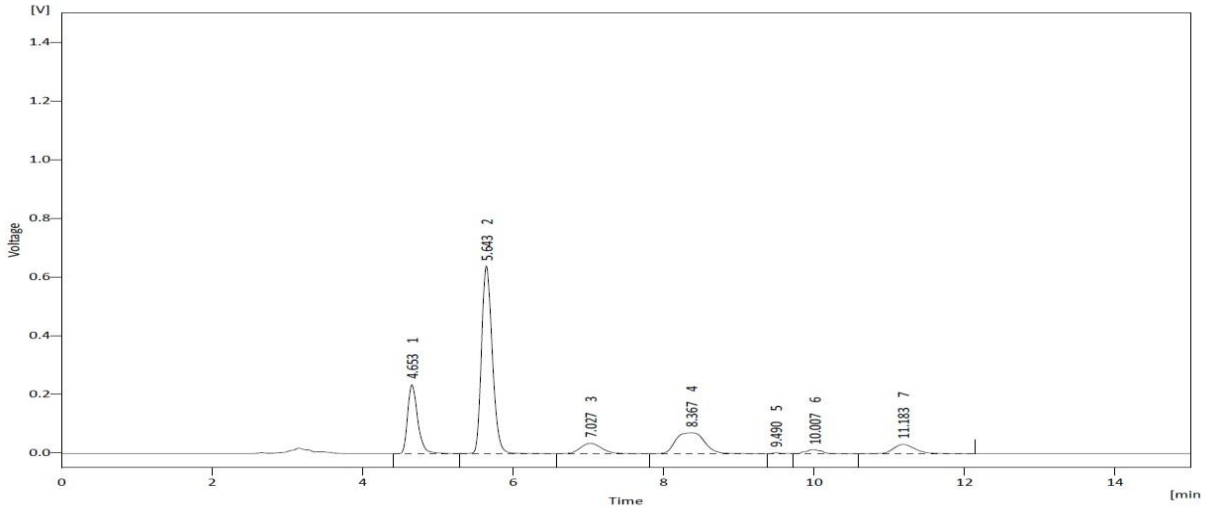
(b)


[V]
Voltage
4.650 1
5.667 2
6.807 3
7.900 4
9.647 5
10.487 6
11.160 7
12.653 8
Time
[min.]

(c)


[V]
Voltage
3.810 1
4.673 2
5.627 3
7.840 4
8.420 5
9.623 6
10.193 7
11.217 8
Time
[min.

(d)


[V]
Voltage
4.653 1
5.643 2
7.027 3
8.367 4
9.490 5
10.007 6
11.183 7
Time
[min

(e)

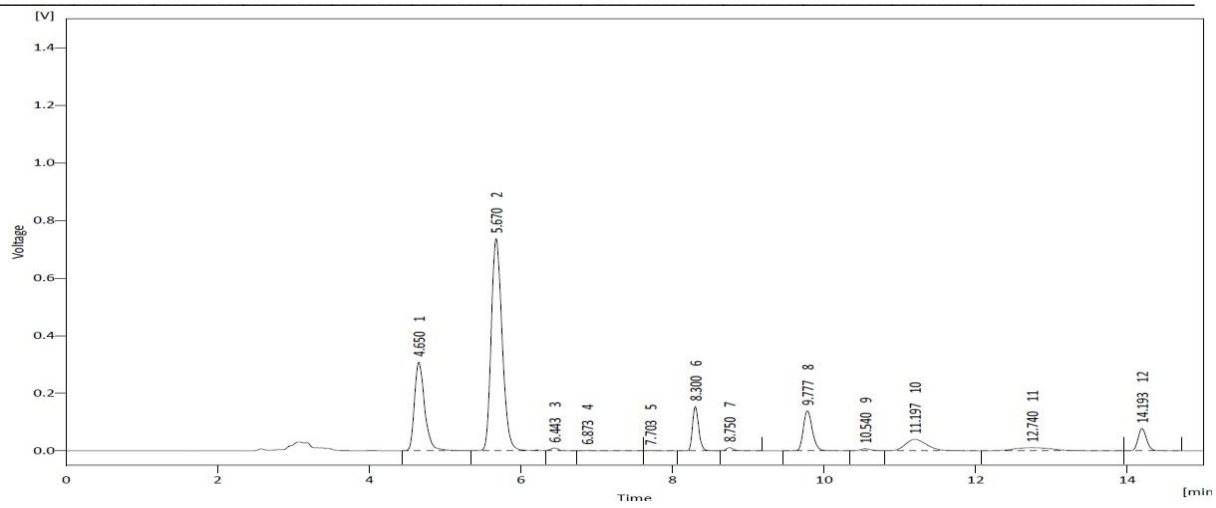


Fig 10: Chromatograms of (a) Acid Degradation, (b) Base Degradation (c) Oxidative Degradation, (d) Thermal Degradation, (e) Photolytic Degradation

Results and Discussion

To develop a new RP-HPLC method, several mobile phase compositions were tried. A satisfactory separation and good peak symmetry was obtained with BDS hypersil C_{18}, 250mm×4.6mm internal diameter, 5µ particle size or equivalent column and mobile phase comprising of Water (pH 4.0): Methanol (70:30v/v) at a flow rate of 1.0 ml/min to get better reproducibility and repeatability. Quantification was achieved with UV detection at 220nm based on peak area. The retention time for Paracetamol, Phenylpropanolamine and Triprolidine were found to be 5.603 min, 4.653 min and 11.083 min respectively.

The optimized method was validated as per ICH guidelines. The system suitability parameters observed by using this optimized condition were reported. The method was found to be linear in the concentration range of 50-150 µg/mL with correlation coefficient of 0.9994 for Paracetamol, 2.5-7.5 µg/mL with correlation coefficient of 0.9995 for Phenylpropanolamine, and 2.5-7.5µg/mL with correlation coefficient of 0.9992 for Triprolidine. The results of recovery study (99.206% for Paracetamol,98.923% for Phenylpropanolamine and 99.727% for Triprolidine) suggest that the method has good recovery. The precision of the proposed method was carried in terms of the repeatability. The low% RSD (<2) values of 0.778%, 0.869% and 0.924% variation for Paracetamol, Phenylpropanolamine and Triprolidine, respectively, reveals that the proposed method is precise. The LOD and LOQ values for Paracetamol were found to be 3.716µg/ml and 11.261µg/ml, for Phenylpropanolamine were 0.174µg/ml and 0.529µg/ml and for Triprolidine were 0.210µg/ml and 0.638µg/ml. The results of robustness in the present method showed no significant changes. The results of analysis of drop indicated that no interference due to common excipients was observed with the developed method. Degradation studies justified the method specificity for its intended application. Therefore, the proposed method can be used for routine analysis of three drugs in their combined pharmaceutical dosage form.

Conclusion

A simple, precise, accurate and rapid method was developed for simultaneous estimation of Paracetamol, Phenylpropanolamine and Triprolidinefrom pure and its dosage forms. The mobile phase is simple to prepare and economical. The sample recoveries in the formulation were in good agreement with their respective label claims. Hence, this method can be easily and conveniently adopted for routine analysis of Paracetamol, Phenylpropanolamine and Triprolidinein pure form and its dosage form.

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