Development of Quality Control Method for Dissolution Analysis of Tapentadol and paracetamolin tablet

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Abstract

The aim of present study was to develop and validate a dissolution test method for film coated formulation containing tapentadol and paracetamol, using RP-HPLC method. The optimized dissolution conditions includes USP apparatus II at a paddle rotation rate of 50 rpm and 900 ml of 6.8 pH Phosphate buffer at 37°C± 0.5°C. Under these conditions, the *in vitro* release profiles of tapentadol and paracetamol showed good results. The drug release was estimated by RP-HPLC using column Hyperchrom ODS 5µ C18 (250 x 4.6mm, 100°A), detection wavelength 217 nm having the flow rate 1.0mL/min using ACN: Potassium dihydrogen phosphate buffer in the proportion of 35:65and adjusted pH to 2.8 with orthophosphoric acid. The method validation was carried out as per for USP guidelines and it was found that the results obtained by proposed method for dissolution test for tablet formulation containing Tapentadoland paracetamol are reliable, precise and accurate. Hence it was routinely adopted for dissolution analysis of the said drugs in the formulation.

Keywords: Dissolution testing, Tapentadol, Paracetamol, Validation, High performance liquid chromatography.

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Introduction

Dissolution is the process of dissolving solid drug substance in a solvent. The bioavailability and bioequivalence data obtained from dissolution testing can be utilized for the development of a new formulation and product development processes. It also ensures product optimization as well as continuing product quality and performance of the manufacturing process[1]. This is usually done in vitro, but by selecting the experimental parameters with utmost care a good in vivo correlation can be achieved. The dissolution testing methods for pharmaceutical preparations are both time-consuming as well as labor-intensive. From product development and quality control viewpoint, drug dissolution testing assist in evaluating the influence of formulation and manufacturing variations on drug release pattern in humans. The in vitro dissolution test relates to expected drug release features in vivo i.e. humans that helps to establish in vitro-in vivo correlation or IVIVC. IVIVC or bio-relevancy terms are used commonly in the literature interchangeably. Bio-relevancy has become a vital requirement during the product development stage or for its routine use as a QC test for an appropriate dissolution testing procedure[2].

Tapentadol[3](TAP) (Fig. 1) is chemically3-[(1R,2R)-3-(dimethyl amino)-1-ethyl-2-methylpropyl] phenol hydrochloride. It is centrally acting oral µ-opioid receptor agonist and also inhibits nor-epinephrine and serotoninreup take within the CNS. Paracetamol[4] (PCT)(Fig. 2) is chemically 4-Hydroxyacetanilide and widely used as Analgesic and Antipyretic.

Literature survey revealed that many analytical methods have been reported for the determination of Tapentadol and Paracetamol in pure drug, pharmaceutical dosage forms and in biological samples using liquid chromatography either in single or in combined forms, Gupta K[5] et al., Jain D[6] et al., Rao B[7] et al., Reddy T[8]. et al., spectrophotometric methods includes Khokhar V[9], Desai S. et al.,[10] but so far no method has been reported for their dissolution analysis. The present study describes the development and validation of a HPLC method for dissolution test analysis for simultaneous estimation of tapentadol and paracetamol.

Material and Method

Instrumentation

i. Dissolution apparatus USPXVIII, Model no. EF 1 W, Electrolab Pvt. Ltd
ii. Shimadzu HPLC series chromatograph equipped with binary pump LC 10ADvP, UV-Visible detector with manual injector 7725 I (Rheodyne) with 20µL loop and a reversed phase 5µ Hyperchrome ODS C18 column (250x4.6mm) used for the chromatographic study.

Reagents and Materials

Double distilled water was used for preparing various dissolution media and HPLC mobile phase. All other reagents and chemicals were of analytical or HPLC grade. Tablets containing 325mg of Paracetamol and 50 mg of Tapentadol was purchased from the local market.

Selection of Wavelength

The standard solutions Paracetamoland Tapentadol prepared were subjected to UV spectrophotometric study to determine wavelength. The wavelength was selected as 217 nm, such that both the drugs exhibit sufficient absorbance at the selected wavelength.

Preparation of mobile phase

Mobile phase comprises of ACN: Potassium dihydrogen phosphate buffer in the proportion of 35:65and adjusted pH to 2.8 with orthophosphoric acid.

Preparation of standard solutions

Mixed standard solution of PCT and TAP were prepared in mobile phase having concentration of 32.5µg/mL and 5µg/mL respectively.

Chromatographic conditions

Chromatography was achieved on a Hyperchrom ODS C_{18}column (250 x 4.6 mm). The mobile phase was a mixture of ACN: Potassium dihydrogen phosphate buffer in the proportion of 35:65and adjusted pH to 2.8 with orthophosphoric acid which was filtered (0.45µm) and degassed before use. All analysis was performed at room temperature at a flow rate of 1 mL/min. Detection was made at 217 nm. A 20 µL volume injection were utilized for triplicate analysis.

System suitability parameters

System suitability tests were carried out by making five replicate injections of mix standard solution containing PCT and TAP having concentrations 180.55 µg/mL and 27.77µg/mL was prepared in mobile phase. A 20µL of solution was injected through manual injector and chromatographed. Peak area, theoretical plates, RSD and tailing factor were noted. Results are shown in Table 1.

Table 1: Results of System Suitability test

Sr. No.	Standard weight taken (mg)		A.U.C of drug (mV)	
	PCT	TAP	PCT	TAP
1	~190.0	~ 30.0	4258.776	612.091
2			4252.083	611.912
3			4256.912	611.081
4			4256.690	612.516
5			4255.912	610.491
Mean			4255.474	611.617
±S.D.			2.6383	0.816959
%RSD			0.0619	0.13357
Theoretical plate/column			4640	6162
Retention time			3.757	4.443
Asymmetry			1.240	1.369
Resolution			-	3.105

Dissolution Test Conditions

Drug dissolution tests were carried out with USP apparatus II(paddle type) at 50 rpm and 75 rpm respectively with dissolution volume of 900mL.Thermostatic bath was used to maintain the temperature of the cell at 37°C±0.5°C.

Various dissolution media's were tried out of which 6.8 pH Phosphate buffer was selected. Weighed and dropped 1 tablet in each of the six dissolution vessel containing 6.8 pH Phospahte buffer for the drugs under analysis. Aliquots of 10.0 mL were withdrawn at 5, 10, 20, 30, 40, 50, 60 min and infinity time interval, used as sample and replaced with an equal volume of the fresh medium to maintain a constant total volume. After the end of each time point, sample aliquots were filtered and chromatographed. The percentage drug dissolved was estimated by validated HPLC method at each time point using the formula 1.

$$\%\,\text{Dissolved} = \frac{\text{Vol. of dissolution media}}{\text{Drug load}} \times \frac{A\,(\text{Sample})}{A\,(\text{Std})} \times \text{Conc (Std)} \times \text{Dilution factor} \times 100 \quad \text{—(1)}$$

Dissolution method parameter optimization

Various dissolutions were performed to optimize the parameters like dissolution media, dissolution media volume, apparatus and rpm, using the optimized chromatographic conditions and the solubility data of the drugs to select a set of parameter that will give maximum % release of the drug.

Change in Dissolution Media (Buffer)

Phosphate buffer pH5.0 and pH 6.8phosphate buffers were used as dissolution media, with a media volume of 900 mL was selected. The results were calculated using formula 1 and are shown in Table 2a and 2b for PCT and TAP respectively.

Change in the Volume of Dissolution Media

The dissolution media was kept constant, phosphate buffer pH 6.8 used in the above study whereas dissolution was performed using USP II with media volume varied from 900 mL to 1000 mL and 500 mL. The results were calculated using formula 1 and are shown in Table 3aand 3bfor PCT and TAP respectively

Change in USP Apparatus

Phosphate Buffer pH 6.8 was selected as dissolution media to study the effect of change in USP apparatus. A media volume of 900 mL was kept constant and the dissolution was performed on two different USP apparatus. The results were calculated using formula 1 and are shown in Table 4a and 4b for PCT and TAP respectively.

Model dependent release kinetics of dissolution test methods[12]

Model dependent methods are based on different mathematical functions, which describe the dissolution profile. The model dependent approaches included(zero order, first order, Higuchi, Korsmeyer-Peppas model).

The kinetics of % drug release was evaluated for all dissolution test methods. The plot of regression coefficient (r) obtained and the best fit observed indicates the order of reaction.

- Cumulative amount of drug released versus time (**Zero-order model**)
- Log cumulative percentage of drug remaining versus time (**First order model**)
- Cumulative percentage drug release versus square root of time (**Higuchi model**)
- Log cumulative percentage drug release versus log time (**Korsmeyer-Peppas model)**

Method Validation

The dissolution test method was validated to through the determination of linearity, precision, accuracy, solution stability, the column was equilibrated for at least 30 min with the mobile phase before injecting sample solutions into the system.

Linearity

The linearity for PCT and TAP with respect to concentration was demonstrated by considering the concentration of PCT and TAP as 100% target concentration (361.11 µg/mL PCT and 55.55µg/mL TAP) and preparing solutions in the mobile phase with concentration ranging from about 10% to 200% of the target concentration.

Precision

The precision of the method was evaluated by measuring the precision expressed as % RSD. Tablet samples were subjected to dissolution test conditions 900 mL of dissolution medium(6.8pH Phosphate buffer) pre-heated at 37°C±0.5°C, paddle with stirring rate of 50 rpm). The test sample were obtained by performing the dissolution of the respective drug which was under analysis using optimized dissolution parameters and were chromatographed by using optimized chromatographic parameters.

Accuracy

The accuracy of the proposed method was evaluated by spiking method i.e. adding known amount of PCT and TAP standard drug (30%-125%) to that of target dissolution concentration[361.11µg/mL of PCT and 55.55 µg/mL TAP as 100% accuracy level] as per the labeled claim of 325 mg and 50 mg for PCT and TAP formulation respectively. Dissolution of the drugs were performed using optimized dissolution parameters along with the spiking of organic solution. The system was allowed to equilibrate with mobile phase for 30 minutes. After equilibration the test solution obtained from dissolution at different time intervals were filtered through 0.45 µ filter paper. A 2.0mL portion of test was diluted to 10.0mL with mobile phase, a 20µL volume of each sample was injected and chromatograms were recorded.

Total amount of drug estimated was calculated using following formula 1, 2, 3

$$\text{Amt Estimated} = \frac{A.t}{A.s} \times \text{Conc. of std} \times \text{dilution factor} \times \text{volume of stock}$$

$$\text{\% Amt. Recovered} = \text{Total amt of drug estimated} - \text{Label claim} \quad \ldots(2)$$

$$\text{\% Recovery} = \frac{\text{Amt recovered}}{\text{Amt of Std. drug added}} \times 100 \quad \ldots(3)$$

Where,

A.t = Peak area of test sample, A.s=Peak area of standard sample, Ws= Weight of standard

L=Label Claim

Range

Range of the Analytical procedure is the interval between the upper and the lower concentration (amounts) of analyze in the sample for which it has been demonstrated that the analytical procedure has a suitable level of precision, accuracy and Linearity. The plot of AUC vs % Target Concentration was plotted and is shown in Fig. 3a and3b for PCT and TAP respectively.

Ruggedness

The Ruggedness of the test method is the degree of reproducibility of the test results obtained by the analysis of the samples under variety of conditions. The ruggedness was performed for following two parameters.

- Different elapsed Assay Time
- Different Assay Temperature

Standard Solution stability

The standard solution stability was studied over a specified period of time and verifying the response of the standard solution. Five injections were injected at 0 h, 24 h and 48h, the chromatograms were recorded using final chromatographic conditions and dissolution method parameter. The relative standard deviation and the correlation were calculated for the area of standard.

Test Solution Stability

The test solution stability was studied over a specified period of time stored at bench top condition (25°C) and refrigeration (5°C), verifying the response of the sample solution. The chromatograms were recorded using final chromatographic conditions and dissolution method parameter. The % drug release was calculated.

Robustness of Test Method

The robustness of an analytical procedure is a measure of its ability to remain unaffected by small, but deliberate variations in method parameters and provides an indication of its reliability during normal usage. The robustness of test method was carried out for following parameters:

a) Change in flow rate
b) Change in pH of mobile phase
c) Change in detection wavelength
d) Change in mobile phase composition

Results and Discussion

HPLC Method development and validation

The final chromatographic conditions mentioned below were maintained throughout the experimentation. Stationary phase was allowed to equilibrate with mobile phase for about 30 min, indicated by a steady baseline.

Column - Hyperchrome ODS 5 µ C18 column (250 X 4.6mm)
Detection Wave length - 217.0 nm
Flow rate - 1.0 mL/min
Temperature: Ambient - (28-30^0 C)
pH - 2.8
Mobile Phase - ACN: 6.8 pH Phosphate buffer (35:65 v/v)

A standard chromatogram for both drugs so recorded in shown in Fig 4.

Optimization of dissolution method parameters for estimation of PCT and TAP

Various dissolutions were performed to optimize the parameters like dissolution media, dissolution media volume, apparatus and rpm, using the optimized chromatographic conditions and the solubility data of the drugs to select a set of parameter that will give maximum % release of the drug. The chromatograms of dissolution analysis of formulation under study at selected intervals recorded under optimized chromatographic parameters are shown in Fig. 4(a-f).

Change in dissolution media (buffer)

The result of % release is shown in Table 2(a) and 2(b) for PCT and TAP respectively. From the table, the release rate of the drug found for both drugs was less in 0.1N HCl and Phosphate buffer pH 5.0 compared to Phosphate buffer pH 6.8. Hence, phosphate buffer pH 6.8 was selected as finalized dissolution media and used further in the experimentation.

Table 2a: Effect of Change in Dissolution Medium on PCT analysis

PCT	Dissolution Media Volume: 900 mL Apparatus: USP-II											
	% Release at RPM											
	Phosphate Buffer pH 6.8				0.1N HCl				Phosphate Buffer pH 5.0			
Time points	50		75		50		75		50		75	
	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD
5	19.84	0.30	25.92	0.32	13.99	0.40	17.52	0.34	16.19	0.12	20.32	0.22
10	54.56	0.10	60.59	0.12	19.72	0.05	25.42	0.18	29.25	0.10	33.46	0.17
20	70.62	0.10	76.55	0.34	29.51	0.12	33.60	0.19	55.49	0.19	58.95	0.21
30	78.81	0.40	81.15	0.27	44.12	0.15	49.65	0.12	77.07	0.07	81.05	0.07
40	84.25	0.29	83.59	0.10	57.85	0.19	61.90	0.22	79.09	0.23	83.11	0.14
50	93.37	0.12	86.67	0.29	68.46	0.32	72.54	0.31	82.03	0.17	84.65	0.08
60	100.43	0.19	88.85	0.09	77.57	0.14	79.65	0.15	84.51	0.21	85.90	0.13
Infinity	100.88	0.24	91.59	0.11	78.78	0.29	82.37	0.12	85.89	0.18	86.59	0.11

Table 2b: Effect of Change in Dissolution Medium on TAP analysis

TAP	Dissolution Media Volume: 900 mL								Apparatus : USP-II			
	% Release at RPM											
	Phosphate buffer pH 6.8				0.1N HCl				Phosphate buffer pH 5.0			
Time points	50		75		50		75		50		75	
	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD
5	26.23	0.20	30.71	0.12	18.90	0.32	24.12	0.34	16.19	0.19	22.91	0.23
10	55.90	0.15	61.96	0.22	26.12	0.09	29.30	0.18	29.25	0.19	40.77	0.19
20	72.52	0.12	76.19	0.42	42.32	0.10	46.32	0.19	55.49	0.11	67.91	0.11
30	87.91	0.24	88.45	0.20	69.70	0.10	72.65	0.12	77.07	0.27	81.52	0.42
40	95.12	0.39	99.12	0.14	75.12	0.12	78.32	0.22	79.09	0.33	84.62	0.24
50	97.67	0.32	100.15	0.21	86.31	0.26	88.60	0.31	82.03	0.19	86.59	0.32
60	102.21	0.15	100.59	0.11	90.43	0.34	93.20	0.15	84.51	0.31	88.12	0.14
Infinity	102.57	0.20	100.52	0.19	93.12	0.39	95.64	0.12	85.89	0.17	89.12	0.31

Change in the volume of dissolution media

The result of % release is shown in Table 3(a) and 3(b) for PCT and TAP respectively. From the table, the percent drug release in a media volume using 1000 mL and 500 mL was less as compared to a media volume of 900 mL for both PCT and TAP. Hence dissolution media volume of 900 mL was selected as one of the finalized dissolution parameter and used further in the experimentation.

Table 3a: Effect of Change in Volume of Dissolution Media on PCT Analysis

PCT	Dissolution Media: Phosphate Buffer pH 6.8								Apparatus: USP-II			
	900mL				500mL				1000mL			
	% Release at RPM											
Time points	50		75		50		75		50		75	
	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD
5	19.20	0.09	25.92	0.30	14.53	0.25	20.21	0.08	20.61	0.33	25.21	0.32
10	55.22	0.14	60.59	0.05	36.26	0.09	48.52	0.25	34.47	0.12	39.62	0.09
20	71.25	0.32	76.55	0.08	46.49	0.13	55.91	0.15	57.83	0.24	65.21	0.16
30	78.21	0.23	81.15	0.23	61.88	0.19	68.21	0.17	81.73	0.31	86.27	0.07
40	83.65	0.36	83.59	0.20	71.24	0.26	75.52	0.11	84.40	0.22	88.21	0.24
50	95.40	0.44	86.67	0.33	73.66	0.33	76.90	0.09	86.91	0.11	89.12	0.21
60	100.90	0.26	88.85	0.14	79.15	0.11	82.21	0.23	89.61	0.25	90.27	0.28
Infinity	101.20	0.13	91.59	0.19	85.54	0.22	86.12	0.33	90.21	0.23	91.68	0.12

Change in USP apparatus

The result of % release is shown in Table 4(a) and 4(b) for PCT and TAP respectively. From the table, the release of drug in USP I was slow as compared to USP II. Also the release of drug at 50 rpm was found to be optimum as compared to other RPM conditions; therefore USP II and 50 RPM were selected as one of the finalized dissolution parameter and used further in the experimentation.

The finalized dissolution parameter selected for the dissolution analysis of PCT and TAP are shown in Table 5 and percent release of drugs under final chromatographic and final dissolution parameters on formulation are shown in Table 6a and 6b for PCT and TAP.

Table 3b: Effect of change in volume in Dissolution medium on TAP analysis

TAP	Dissolution Media: Phosphate Buffer pH 6.8 Apparatus: USP-II											
	900mL				500mL				1000mL			
	% Release at RPM											
Time points	50		75		50		75		50		75	
	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD
5	25.50	0.05	30.71	0.31	23.80	0.26	27.45	0.23	29.58	0.24	31.32	0.42
10	54.12	0.16	62.65	0.35	37.92	0.09	45.52	0.26	50.48	0.15	63.91	0.10
20	72.32	0.24	75.40	0.12	57.37	0.06	65.20	0.18	64.91	0.12	77.79	0.09
30	86.95	0.33	87.54	0.25	72.76	0.24	77.20	0.42	78.73	0.32	82.27	0.32

40	96.35	0.14	98.20	0.16	80.13	0.18	84.49	0.19	82.40	0.25	86.21	0.28
50	98.15	0.08	99.20	0.19	84.66	0.25	89.12	0.23	84.91	0.28	89.12	0.31
60	101.24	0.15	100.20	0.24	86.89	0.09	91.38	0.19	87.61	0.32	92.27	0.19
Infinity	102.10	0.28	100.60	0.14	87.08	0.34	92.01	0.32	89.51	0.22	93.68	0.21

Table 4a: Effect of Change in USP Apparatus on PCT Analysis

PCT	**Dissolution Medium: Phosphate Buffer pH 6.8 Dissolution Volume: 900 mL**							
Time points Mins	**Apparatus: USP-I**				**Apparatus: USP-II**			
	% Release at RPM							
	50		**75**		**50**		**75**	
	Mean	**±SD**	**Mean**	**±SD**	**Mean**	**±SD**	**Mean**	**±SD**
5	15.61	0.15	22.47	0.32	20.20	0.29	25.92	0.06
10	25.87	0.36	31.92	0.21	53.14	0.23	60.59	0.33
20	59.18	0.24	66.27	0.28	69.20	0.38	76.55	0.28
30	64.20	0.29	70.09	0.39	79.54	0.11	81.15	0.09
40	69.89	0.17	77.37	0.27	85.65	0.17	83.59	0.13
50	75.57	0.34	82.10	0.31	94.39	0.21	86.67	0.21
60	79.94	0.22	88.47	0.25	100.05	0.34	88.85	0.10
Infinity	81.52	0.23	90.25	0.12	100.65	0.23	91.59	0.38

Table 4b: Effect of Change in USP Apparatus on TAP Analysis

TAP	**Dissolution Medium: Phosphate Buffer pH 6.8 Dissolution Volume: 900 mL**							
Time Points Mins	**Apparatus: USP-I**				**Apparatus: USP-II**			
	% Release at RPM							
	50		**75**		**50**		**75**	
	Mean	**±SD**	**Mean**	**±SD**	**Mean**	**±SD**	**Mean**	**±SD**
5	24.39	0.12	29.81	0.32	27.50	0.27	30.71	0.23
10	40.51	0.15	46.28	0.39	56.42	0.42	61.96	0.37
20	55.95	0.07	61.37	0.15	74.59	0.15	76.19	0.17
30	67.68	0.29	73.38	0.09	88.95	0.14	88.45	0.15
40	74.83	0.19	77.37	0.19	93.20	0.29	99.12	0.33
50	82.57	0.13	85.21	0.16	97.15	0.36	100.15	0.13
60	87.29	0.36	89.41	0.41	101.90	0.17	100.59	0.41
Infinity	93.19	0.31	95.99	0.12	102.12	0.19	100.32	0.19

Table 5: Final Dissolution Method Parameters for PCT and TAP Analysis

Drugs	**Dissolution**	**Media Volume**	**USP Apparatus**	**Agitation/ Rotation(RPM)**	**Temp**
PCT and TAP	Phosphate Buffer pH 6.8	900 mL	II	50	37°C±0.5°C

Table 6(a) Results showing effect of optimized parameters for PCT analysis for formulation

PCT			**6.8 pH Phosphate buffer**							
			Time Points (in min; % Release)							
USP II	**Media Volume 900 mL**	**RPM**	**5**	**10**	**15**	**20**	**30**	**45**	**60**	**Infinity**
	Sample	50	20.20	53.14	69.20	79.54	85.65	94.39	100.05	100.65

Table 6(b) Results showing effect of optimized parameters for TAP analysis for formulation

TAP			**6.8 pH Phosphate buffer**							
			Time Points (in min; % Release)							
USP II	**Media Volume 900 mL**	**RPM**	**5**	**10**	**15**	**20**	**30**	**45**	**60**	**Infinity**
	Sample	50	27.80	56.42	74.59	88.95	93.20	97.15	101.90	102.12

Model Kinetics

The data obtained as percent release of drugs at different time intervals were utilized for applying the model dependent kinetic release of each drug. The best fit model for PCT and Tap was found to be Korsmeyer Peppas.

Validation parameters

The peak area of linearity solutions noted was plotted against the corresponding concentrations to obtain the calibration graphs and was shown in Fig. 5a and 5b. The coefficient of correlation for PCT and TAP was found to be 0.997 and 0.998 respectively.

The % recoveries of drugs at each accuracy level were found to be in the range of 98.35%-101.69% (acceptance range of 95%-105%). The results of accuracy studies at each level are shown in Table 7.

The precision of proposed method evaluated by repeatability of measurements was determined as percent dissolution which should not be less than 75% release at 45 minutes and % RSD should not be more than 5.0% for each drug under analysis. The % release was found to be above the acceptance level and % RSD of drugs was found to be 0.41 and 0.56 respectively ascertaining the precision of method. The observation and the result of precision study for drugs are summarized in the Table 8.

Standard solutions of PCT, TAP and its formulation under study are stable for the period of upto 48 hrs. The relative standard deviation for peak areas of replicate injections of mix standard solution under varied condition should not be more than 5.0%. Hence, proposed method was found to be robust.

Table 7: Observation and Results of Recovery Studies

Spike Level	Amt. of pure drug added (mg)		Amt. Recovered		% Recovery		
	PCT	TAP	PCT	TAP	PCT	TAP	
30%	96.95	14.60	95.85	14.36	98.86	98.35	
50%	162.10	24.95	161.17	24.80	99.42	99.39	
60%	194.50	29.90	194.73	29.83	100.11	99.76	
75%	242.95	40.10	242.19	40.19	99.68	100.22	
100%	325.50	50.50	326.51	51.28	100.32	101.56	
125%	406.10	61.45	406.04	62.49	99.98	101.69	
					Mean	99.72	100.16
					±SD	0.531	1.291
					% RSD	0.532	1.288

Table 8: Observation & Result for precision Study

S. No	AREA (mV)		% Dissolution	
	PCT	TAP	PCT	TAP
1	3944.420	570.013	101.30	102.66
2	3902.615	567.981	99.34	102.30
3	3899.986	568.156	99.28	101.08
4	3916.512	565.402	99.70	102.55
5	3924.450	568.397	99.90	102.37
		Mean	99.70	102.192
		%RSD	0.4126	0.5582

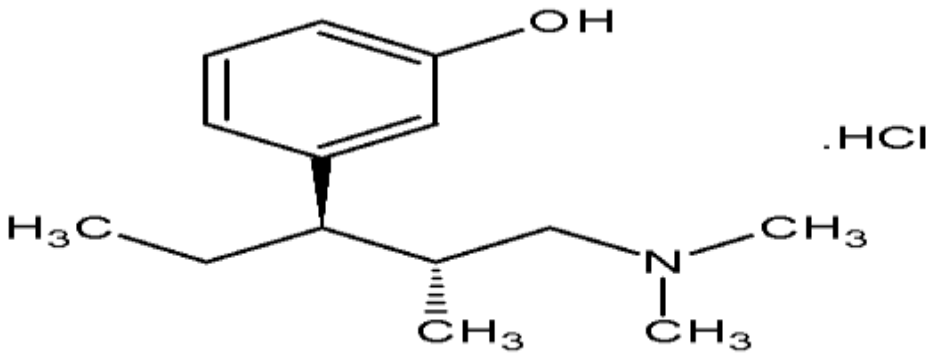


Fig 1: Structure of Atenolol

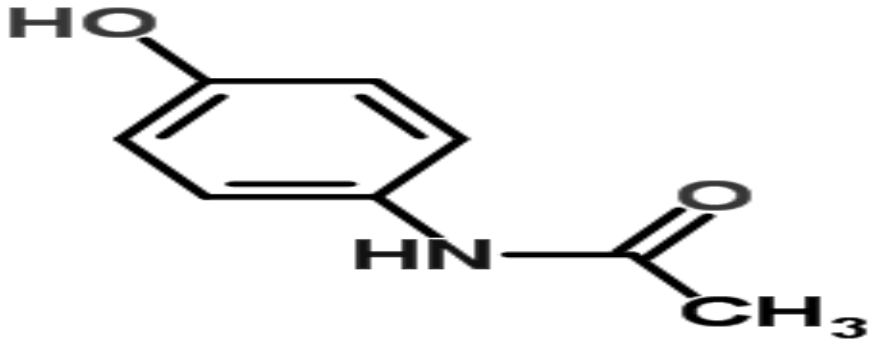


Fig 2: Structure of Paracetamol

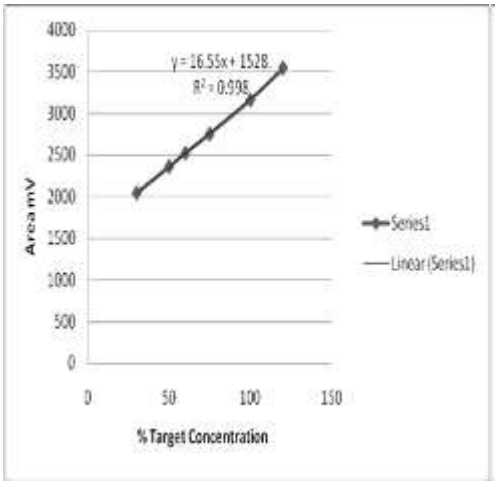


Fig 3a: Range study for PCT

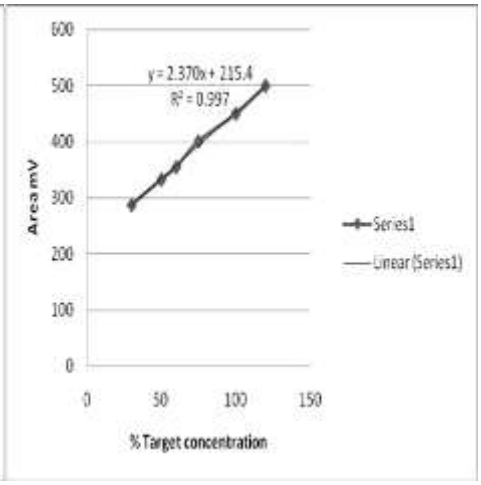


Fig 3b: Range study for TAP

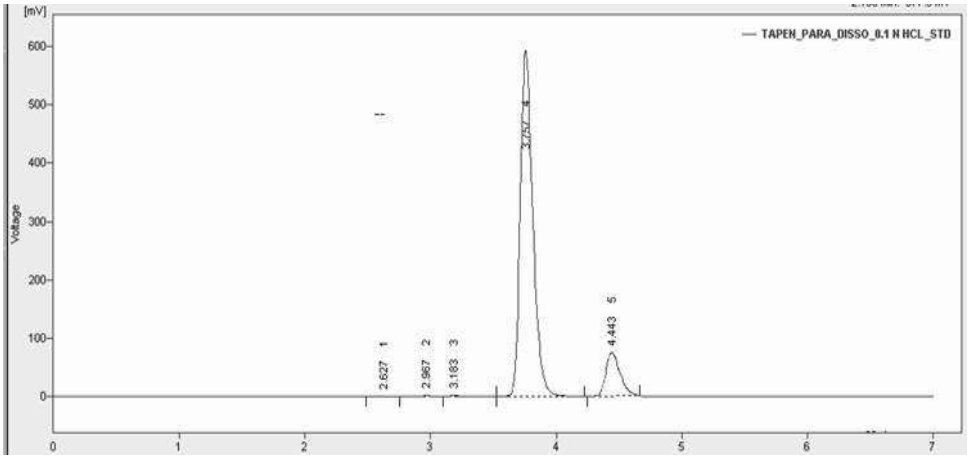
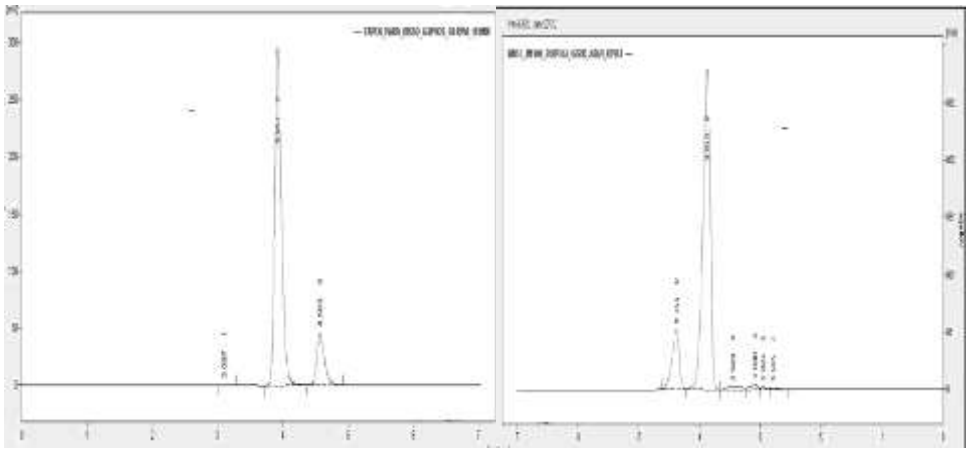
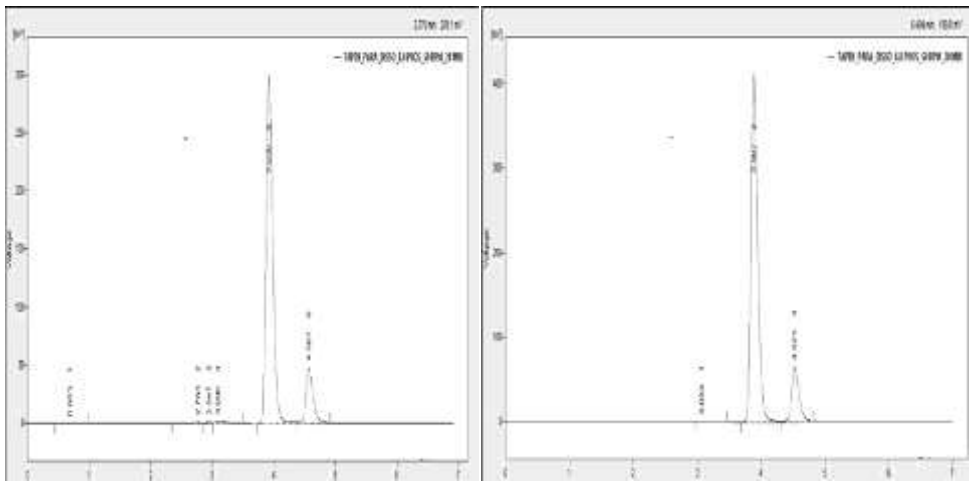


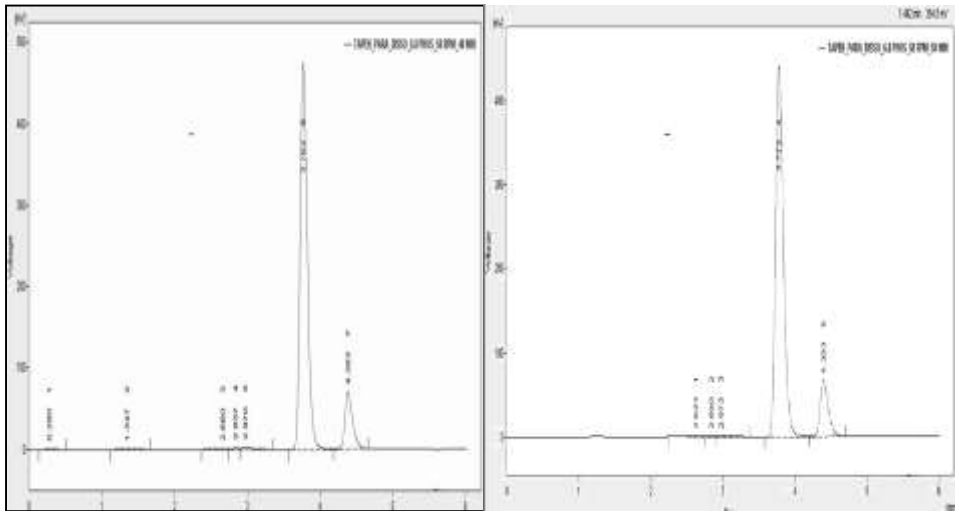
Fig 3: Chromatogram of mix standard (PCT and TAP)



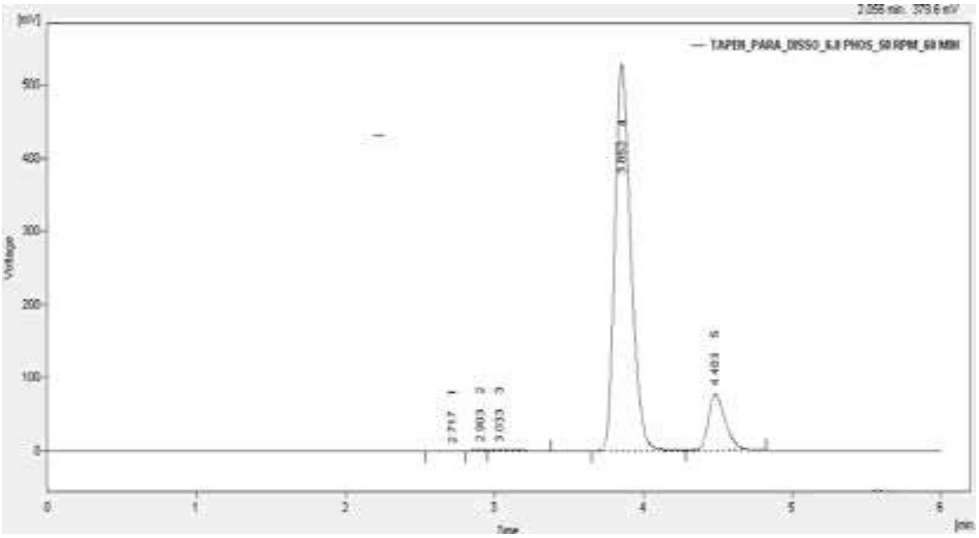
(a) Test sampleat 5 min (b) Test sampleat 10 min



(c) Test sample at 20 mins(d) Test sample at 30 min



(e) Test sample at 40 min (f) Test sample at 50 min



(g) Test sample at 60 min

Fig. 5a-g: Chromatograms of sample for dissolution analysis at various time intervals

Conclusion

The results obtained by RP-HPLC method for dissolution test of tablet formulation containing PCT and TAP are reliable, precise and accurate. Hence, it can be routinely adopted as a quality control test for dissolution analysis of the said drugs in their formulation.

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