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SIMULTANEOUS QUANTITATION AND VALIDATION OF CHLORPHENIRAMINE MALEATE, PHENYLPROPANOLAMINE HYDROCHLORIDE AND PARACETAMOL BY RP-HPLC IN BULK DRUG AND FORMULATION

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Keywords:

Chlorpheniramine Maleate; Phenylpropanolamine hydrochloride; Paracetamol; HPLC; Validation.

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ABSTRACT: A HPLC method has been described for simultaneous determination of Chlorpheniramine Maleate, Phenylpropanolamine Hydrochloride and Paracetamol in formulation. This method is based on HPLC separation of the three drugs on the Thermo Hypersil Gold C18 column (250mm ×4.6mm, 5.0µ), with isocratic conditions and mobile phase containing methanol: 0.01M disodium hydrogen phosphate dihydrate buffer pH 7 adjusted with Ortho Phosphoric Acid (OPA) (60: 40) at a flow rate of 1mL/min using UV detection at 217 nm. This method has been applied to formulation without interference of excipients of formulation. The linear regression analysis data for the calibration plots showed a good linear relationship over the concentration range of 0.5-3µg/mL for Chlorpheniramine Maleate, 7-12µg/mL for Phenylpropanolamine hydrochloride, and 0.4-1.4µg/mL for Paracetamol, respectively. The mean values of the correlation coefficient, slope and intercept were 0.999 ± 1.72, 28455 ± 1.01, 26185 ± 1.28 for Chlorpheniramine Maleate, 0.999 ± 0.34, 23604 ± 1.16, 73758 ± 1.49 for Phenylpropanolamine hydrochloride and 0.999 ± 0.80, 51233 ± 1.89, 5560 ± 1.62 for Paracetamol respectively. The method was validated for precision, robustness and recovery. The limit of detection (LOD) and limit of quantitation (LOQ) was 0.5µg/mL and 1µg/mL for Chlorpheniramine Maleate, 5µg/mL and 7µg/mL for Phenylpropanolamine hydrochloride and 0.2µg/mL and 0.4µg/mL for Paracetamol, respectively. Statistical analysis showed that the method is repeatable and selective for the estimation of, Chlorpheniramine Maleate, Phenylpropanolamine hydrochloride and Paracetamol.

INTRODUCTION: Chlorpheniramine Maleate **(Figure 1)** is chemically 1-(N, N-Dimethylamino)-3-(p-chlorophenyl) -3- (alpha-pyridyl) propane maleate.

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Chlorpheniramine maleate is a first-generation alkylamine antihistamine used in the prevention of the symptoms of allergic conditions such as rhinitis and urticaria. Its sedative effects are relatively weak compared to other first-generation antihistamines. Chlorpheniramine 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 [1].

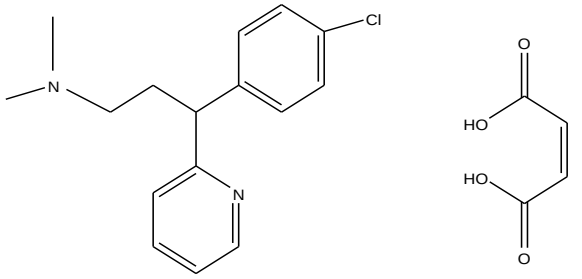

FIGURE 1 STRUCTURE OF CHLORPHENIRAMINE MALEATE

Phenylpropanolamine hydrochloride **(Figure 2)** is chemically (1S, 2R)-2-amino-1-phenylpropan-1-ol. It is a psychoactive drug of the phenethylamine and amphetamine chemical classes which is used as a stimulant, decongestant, and anorectic agent. It is commonly used in prescription and over-the-counter cough and cold preparations. Phenylpropanolamine acts as a potent and selective releasing agent of norepinephrine and epinephrine, or as a norepinephrine releasing agent (NRA). It also acts as a dopamine releasing agent (DRA) to a lesser extent. It works by mimicking the effects of endogenous catecholamines such as epinephrine and norepinephrine and to a lesser degree dopamine [2].

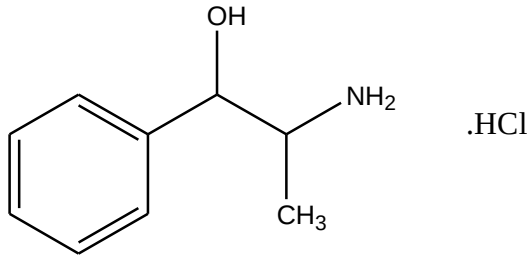

FIGURE 2 STRUCTURE OF PHENYLPROPANOLAMINE HYDROCHLORIDE

Paracetamol **(Figure 3)** is chemically N-(4-hydroxyphenyl)acetamide. It is a widely used over-the-counter analgesic (pain reliever) and antipyretic (fever reducer). It is commonly used for the relief of headaches, other minor aches and pains, and is a major ingredient in numerous cold and flu remedies. The onset of analgesia is approximately 11 minutes after oral administration of paracetamol. It is the active metabolite of phenacetin, once popular as an analgesic and antipyretic in its own right, but unlike phenacetin and its combinations, paracetamol is not considered to be carcinogenic at therapeutic doses. Paracetamol is considered to be the inhibitor of cyclooxygenase (COX), and recent findings suggest that it is highly selective for COX-2. While it has analgesic and antipyretic properties comparable to those of aspirin or other NSAIDs, its peripheral anti-inflammatory activity is usually limited by several factors, one of which is high level of peroxides present in inflammatory lesions[1].

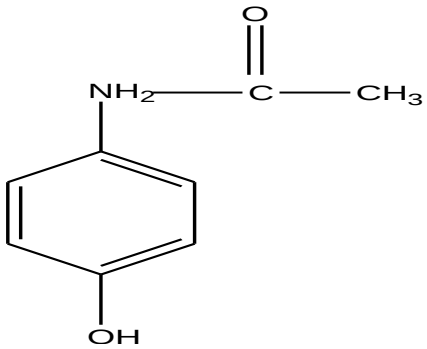

FIGURE 3 STRUCTURE OF PARACETAMOL

Literature review reveals that methods have been reported for analysis of Chlorpheniramine Maleate, Phenylpropanolamine Hydrochloride and Paracetamol either alone or in combination with other drugs. UV Spectrophotometric method [3], HPLC method [4, 5, 6, 7, 8, 9], stability indicating HPLC method[10] in combination with other drugs is reported for Chlorpheniramine Maleate. Similarly HPLC method have been reported for Phenylpropanolamine hydrochloride alone [11, 12], HPLC method in combination with other drugs [13, 14, 15, 16, 17].

Capillary electrophoretic method has also been reported for simultaneous determination of Cetirizine dihydrochloride, Paracetamol and Phenylpropanolamine in tablets [18]. Similarly UV Spectrophotometric method [19, 20], HPLC method [21, 22, 23, 24, 25, 26, 27, 28, 29], stability indicating HPLC method [30, 31], and some bioanalytical work by capillary electrophoresis [32] and HPLC [33] alone or in combination with other drugs is reported for Paracetamol.

To date, there have been no published reports about the simultaneous quantitation of, Chlorpheniramine Maleate, Phenylpropanolamine hydrochloride, and Paracetamol by chromatographic method in bulk drug and in tablet dosage form. This present study reports for the first time simultaneous quantitation

of the same drugs by RP-HPLC in bulk drug and in tablet dosage form. The proposed method is validated as per ICH guidelines [34].

MATERIALS AND METHODS:

Working standards of pharmaceutical grade, Chlorpheniramine Maleate (Batch no. 581/03) Phenylpropanolamine hydrochloride (Batch no. 16043/01) and Paracetamol (Batch no. 260738) were obtained as generous gifts from AGIO Pharma Limited, MIDC, (Pune, Maharashtra, India).

They were used without further purification and certified to contain 99.21 %, 99.62 % and 99.79 % on dry weight basis for, Chlorpheniramine Maleate, Phenylpropanolamine hydrochloride and Paracetamol, respectively. Fixed dose combination tablet RINOSTAT PLUS (RPG Life Sciences Ltd) Batch no. 3345 (Exp date Mar 2012), containing, 4 mg Chlorpheniramine Maleate, 25 mg Phenylpropanolamine hydrochloride and 500 mg Paracetamol was purchased from local market, Pune, Maharashtra, India. All the chemicals were of HPLC grade, purchased from Merck Chemicals, India. Water used was double distilled and filtered through 0.45µm filter.

Instrumentation

The HPLC system consisted of Intelligent HPLC pump model (Jasco PU 2080 Plus) with sampler programmed at 20µL capacity per injection was used. The detector consisted of a UV/ VIS (Jasco UV 2075 Plus). Another system consisted of Intelligent HPLC pump (Jasco PU 1580) with detector (Jasco UV-1575) and auto sampler. Data was integrated using Jasco Borwin version 1.5, LC-Net II/ADC system. The column used was, Thermo Hypersil Gold C18 column (250mm×4.6mm, 5.0µ), with isocratic conditions. Mobile phase consisted of a mixture of methanol: 0.01 M phosphate buffer pH 7 adjusted with OPA (60: 40) at flow rate of 1mL/min using UV detection at 217 nm. The mobile phase was filtered through a 0.45micron membrane filter and degassed. The injection volume was 20µL and analysis was performed at ambient temperature.

Preparation of Standard Stock Solutions

Standard solutions for both drugs were prepared by dissolving 10mg of CPM, 10 mg of PPA and 10 mg of PCM separately in 10mL water (1000µg/mL). From the standard stock solution, the mixed standard solution was prepared using water to contain 10µg/mL of each drug for HPLC experiment. The stock solutions were stored at 2-8 °C protected from light. The standard stock solution was stable for three days.

Optimization of HPLC Method

The three drugs were subjected to chromatographic analysis using mobile phases of different flow rate, pH, strength and composition. The changes in the retention time of all drugs were noted as a function of changing mobile phase, pH, flow rate, strength and selectivity. Initially methanol: water in the ratio of 70: 30 was tried but splitting of paracetamol peak was observed. Then acetonitrile: water in the ratio of 70: 30 was tried but all the three peaks of drug got merged into each other. Later methanol: 0.01 M disodium hydrogen phosphate dihydrate buffer pH 7 adjusted with OPA in various ratios were tried.

It was found that methanol: 0.01 M disodium hydrogen phosphate dihydrate buffer pH 7 adjusted with OPA in the ratio of 60: 40 at flow rate of 1mL/min gave acceptable retention time of 2.5, 3.10 and 4.00 and plate count was 4878, 5067, and 5623 with good resolution (2.37 between Chlorpheniramine maleate and Paracetamol and 2.748 between Paracetamol and Phenylpropanolamine hydrochloride) for Chlorpheniramine maleate, Phenylpropanolamine hydrochloride and Paracetamol respectively **(Figure 4)**.

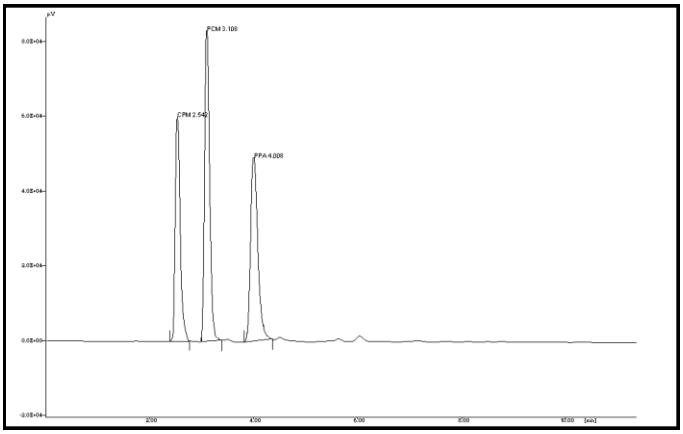

FIGURE 4: CHROMATOGRAM OF STANDARD CHLORPHENIRAMINE MALEATE R_t (2.54) PHENYLPROPANOLAMINE HYDROCHLORIDE R_t (4.008) AND PARACETAMOL R_t (3.108).

Validation of the method

Validation of the optimized HPLC method was carried out with respect to the following parameters.

Linearity and range

The mixed standard stock solution (100µg/mL of Chlorpheniramine Maleate, 100µg/mL Phenylpropanolamine hydrochloride and 100µg/mL of Paracetamol) was further diluted to get these drug concentrations in the range of 0.5-3.0µg/mL, 7–12µg/mL, and 0.4-1.4µg/mL, respectively. Linearity of the method was studied by injecting six concentrations of the drug prepared in the mobile phase in triplicate into the LC system keeping the injection volume constant. The peak areas were plotted against the corresponding concentrations to obtain the calibration graphs.

Precision:

The precision of the method was verified by repeatability and intermediate precision studies. Repeatability studies were performed by analysis of three different concentrations, 0.5, 1.5, 2.5µg/mL for Chlorpheniramine Maleate, 7, 9, 11µg/mL for Phenylpropanolamine hydrochloride and 0.4, 0.8, 1.2µg/mL for Paracetamol six times on the same day. The intermediate precision of the method was checked by repeating studies on three different days.

Limit of detection and limit of quantitation

Limits of detection (LOD) and quantification (LOQ) represent the concentration of the analyte that would yield signal-to-noise ratios of 3 for LOD and 10 for LOQ, respectively. To determine the LOD and LOQ, serial dilutions of mixed standard solution of, Chlorpheniramine Maleate, Phenylpropanolamine hydrochloride and Paracetamol was made from the standard stock solution. The samples were injected in LC system and measured signal from the samples was compared with those of blank samples.

Robustness of the method

To evaluate robustness of the HPLC method, few parameters were deliberately varied. The parameters included variation of flow rate, percentage of methanol in the mobile phase and solvents from different lot. Robustness of the method was checked at three different concentration levels 0.5, 1.5, 2.5µg/mL, 7, 9, 11µg/mL and 0.4, 0.8, 1.2µg/mL for Chlorpheniramine Maleate, Phenylpropanolamine hydrochloride and Paracetamol, respectively.

Specificity

The specificity of the method towards the drug was established through study of resolution factor of the drug peak from the nearest resolving peak. The peak purity of, Chlorpheniramine Maleate, Phenylpropanolamine hydrochloride and Paracetamol was determined by comparing the spectrum at three different regions of the peak i.e. peak start (S), peak apex (M) and peak end (E). Effect of excipients of formulation was studied for whether it interfered with the assay.

Accuracy

Accuracy of the method was carried out by applying the method to pre-analyzed drug sample (Chlorpheniramine Maleate, Phenylpropanolamine hydrochloride and Paracetamol combination tablet) to which known amount of, Chlorpheniramine Maleate, Phenylpropanolamine hydrochloride and Paracetamol standard powder corresponding to 80, 100 and 120 % of label claim had been added (Standard addition method), mixed and the powder was extracted and analyzed by running chromatogram in optimized mobile phase.

Analysis of a marketed formulation

To determine the content of Chlorpheniramine Maleate, Phenylpropanolamine hydrochloride and Paracetamol in conventional tablet (Brand name: Rinostat Plus, Label claim: 4mg Chlorpheniramine Maleate, 25mg Phenylpropanolamine hydrochloride and 500 mg Paracetamol, and per tablet, Expiry Date Mar. 2012), twenty tablets were weighed, their mean weight determined and finely powdered.

The weight of the tablet triturate equivalent to 4 mg of CPM, 25mg of PPA and 500mg of PCM was transferred into a 50mL volumetric flask containing 30mL water sonicated for 30 min and diluted up to 50mL with water. The resulting solution was centrifuged at 3000 rpm for 5min and the drug content of the supernatant was determined ((80, 500, 10000µg/mL for Chlorpheniramine Maleate, Phenylpropanolamine hydrochloride and Paracetamol respectively). For Chlorpheniramine Maleate 1mL from the supernatant was diluted to produce final concentration of 10µg/mL, for

Phenylpropanolamine Hydrochloride 0.2mL of from the supernatant was diluted to produce final concentration of 10µg/mL and for Paracetamol 0.1mL from the supernatant was diluted to produce 100µg/mL concentrations and from this solution 1mL was taken and further diluted to 10mL with water to make final concentration of 10µg/mL.

The dilutions were done individually due to the large differences in LOD and LOQ values as well as label claim. After the dilutions the sample solution was filtered using 0.45-micron filter (Millipore, Milford, MA). A 20µL volume of sample solution was injected into HPLC, six times, under the conditions described above. The peak areas were measured at 217nm and concentrations in the samples were determined using multilevel calibration developed on the same HPLC system under the same conditions using linear regression equation.

RESULTS AND DISCUSSIONS:

The results of validation studies on simultaneous estimation method developed for, Chlorpheniramine Maleate, Phenylpropanolamine hydrochloride and Paracetamol in the current study involving mobile phase methanol: 0.01 M disodium hydrogen phosphate dihydrate buffer at pH 7 adjusted with OPA (60: 40) are given below.

Linearity

Chlorpheniramine Maleate, Phenylpropanolamine hydrochloride and Paracetamol showed good correlation coefficient (r^2=0.999 for Chlorpheniramine Maleate, 0.999 for Phenylpropanolamine hydrochloride and 0.999 for Paracetamol) in given concentration range (0.5-3 µg/mL for Chlorpheniramine Maleate, 7-12µg/mL for Phenylpropanolamine hydrochloride and 0.4-1.4µg/mL for Paracetamol). The mean values of the slope and intercept were, 28455, 26185 for Chlorpheniramine Maleate, 23604, 73758 for Phenylpropanolamine hydrochloride and 51233, 5566 for Paracetamol respectively.

Precision

The results of the repeatability and intermediate precision experiments are shown in **Table 1**. The developed method was found to be precise as the RSD values for repeatability and intermediate precision studies were < 2 %, respectively as recommended by ICH guidelines.

TABLE 1: PRECISION STUDIES

Conc. (µg/mL)	Repeatability (n=6)			Intermediate precision (n=6)		
	Measured conc. (ng/spot) ±SD	(%) RSD	Recovery (%)	Measured conc. (ng/spot) ±SD	(%) RSD	Recovery (%)
Chlorpheniramine Maleate						
0.5	0.495±0.064	1.30	99.00	0.503±0.004	0.98	100.6
1.5	1.489±0.021	1.47	99.26	1.502±0.007	0.52	100.13
2.5	2.499±0.026	1.05	99.96	2.496±0.024	0.99	99.84
Phenylpropanolamine Hydrochloride						
7	7.09±0.06	0.89	101.28	6.985±0.132	1.89	99.78
9	8.98±0.065	0.73	99.77	8.967±0.109	1.22	99.63
11	10.99±0.121	1.11	99.90	11.05±0.113	1.02	100.45
Paracetamol						
0.4	0.398±0.0049	1.23	99.5	0.397±0.001	0.33	99.25
0.8	0.802±0.018	0.23	100.25	0.801±0.001	0.21	100.12
1.2	1.210±0.02	1.29	100.83	1.193±0.006	0.57	99.41

LOD and LOQ

Signal-to-noise ratios of 3:1 and 10:1 were obtained for the LOD and LOQ respectively. The LOD and LOQ were found to be, 0.5µg/mL and 1µg/mL for Chlorpheniramine Maleate, 5µg/mL and 7µg/mL for Phenylpropanolamine hydrochloride and 0.2µg/mL and 0.4µg/mL for Paracetamol, respectively.

Robustness of the method

Each factor selected (except columns from different manufacturers) was changed at three levels (−0.1, 0 and 0.1). One factor at the time was changed to estimate the effect. Thus, replicate injections (n = 6) of mixed standard solution at three concentration levels were performed under small changes of three chromatographic parameters (factors). Insignificant

differences in peak areas and less variability in retention time were observed **(Table 2).**

Table 2 Robustness Testing

TABLE 2.1: ROBUSTNESS TESTING FOR CHLORPHENIRAMINE MALEATE (n = 6)

Factor[a]	Level	Retention time	Retention factor	Asymmetry
A: Flow rate (mL/min)				
0.9	-1	2.589	0.0356	1.23
1.0	0	2.542	0.0168	1.50
1.1	+1	2.509	0.0036	1.45
Mean ± SD (n = 3)		2.546±0.065	0.0186±0.061	1.39±0.076
B: % of methanol in the mobile phase (v/v)				
59	-1	2.565	0.026	1.19
60	0	2.542	0.0168	1.17
61	+1	2.501	0.0004	1.02
Mean ± SD (n = 3)		2.536±0.078	0.0144±0.091	1.12±0.034
C: Solvents of different lots				
First lot		2.542	0.0168	1.12
Second lot		2.578	0.026	1.13
Mean ± SD (n = 3)		2.51±0.021	0.0214	1.125±0.021

[a] Three factors were slightly changed at three levels (-0.1, 0, 0.1)

TABLE 2.2: ROBUSTNESS TESTING FOR PHENYLPROPANOLAMINE HYDROCHLORIDE (n = 6)

Factor[a]	Level	Retention time	Retention factor	Asymmetry
A: Flow rate (mL/min)				
0.9	-1	4.012	0.605	1.13
1.0	0	4.008	0.603	1.11
1.1	+1	4.005	0.602	1.07
Mean ± SD (n = 3)		4.008 ± 0.063	0.603± 0.043	1.10 ± 0.05
B: % of methanol in the mobile phase (v/v)				
59	-1	4.013	0.605	1.14
60	0	4.008	0.603	1.11
61	+1	4.000	0.600	1.09
Mean ± SD (n = 3)		4.007 ± 0.078	0.603 ± 0.049	1.11 ± 0.05
C: Solvents of different lots				
First lot		4.008	0.6032	1.11
Second lot		4.014	0.6056	1.10
Mean ± SD (n = 3)		4.011 ± 0.003	0.6044 ± 0.001	1.10 ± 0.01

[a]Three factors were slightly changed at three levels (-0.1, 0, 0.1)

TABLE 2.3 ROBUSTNESS TESTING FOR PARACETAMOL (n = 6)

Factor[a]	Level	Retention time	Retention factor	Asymmetry
A: Flow rate (mL/min)				
0.9	-1	3.112	0.2448	1.12
1.0	0	3.108	0.2432	1.10
1.1	+1	3.104	0.2416	1.09
Mean ± SD (n = 3)		3.108 ± 0.004	0.2432 ± 0.0016	1.10 ± 0.01
B: % of methanol in the mobile phase (v/v)				
59	-1	3.110	0.244	1.11
60	0	3.108	0.2432	1.10
61	+1	3.005	0.202	1.10
Mean ± SD (n = 3)		3.074 ± 0.06	0.229 ± 0.024	1.10 ± 0.01
C: Solvents of different lots				
First lot		3.108	0.2432	1.10
Second lot		3.111	0.2444	1.13
Mean ± SD (n = 3)		3.1095 ± 0.002	0.2438 ± 0.0008	1.11 ± 0.01

[a] Three factors were slightly changed at three levels (-0.1, 0, 0.1)

Specificity studies

The peak purity of Chlorpheniramine Maleate, Phenylpropanolamine hydrochloride and Paracetamol was assessed by comparing their respective spectra at the peak start, apex and end positions i.e., r (S, M) = 0.999 and r (M, E) = 0.999. A good correlation (r = 0.999) was also obtained between the standard and sample spectra of Chlorpheniramine Maleate, Phenylpropanolamine hydrochloride and Paracetamol respectively. Also, excipients from formulation were not interfering with the assay.

Recovery

As shown from the data in **Table 3** good recoveries of the Chlorpheniramine Maleate, Phenylpropanolamine hydrochloride and Paracetamol in the range from 98.9 to 101.45% were obtained at various added concentrations.

TABLE 3 RECOVERY STUDIES (N = 6)

Label claim (mg/tablet)	Amount added (mg)	Total amount (mg)	Amount Recovered (mg) ± % RSD	% Recovery
Chlorpheniramine Maleate				
4	3.2 (80%)	7.2	7.19± 1.52	99.86
4	4 (100%)	8	7.95± 0.64	99.37
4	4.8 (120%)	8.8	8.801± 1.56	100.01
Phenylpropanolamine Hydrochloride				
25	20 (80%)	45	44.85 ± 1.32	99.67
25	25 (100%)	50	49.45 ± 1.16	98.90
25	30 (120%)	55	55.8 ± 1.40	101.45
Paracetamol				
500	400 (80%)	900	907.7 ± 1.41	100.85
500	500 (100%)	1000	995.0 ± 0.89	99.50
500	600 (120%)	1100	1093.0 ± 0.90	99.36

Analysis of a formulation

Experimental results of the amount of Chlorpheniramine Maleate, Phenylpropanolamine hydrochloride and Paracetamol in tablets, expressed as a percentage of label claims were in good agreement with the label claims thereby suggesting that there is no interference from any of the excipients which are normally present. The dilutions were done individually due to the large differences in LOD and LOQ values as well as label claim. The drug content was found to be 99.8 % (± 0.09), 100.04 % (± 0.23) and 100.1 % (± 0.12) for Chlorpheniramine Maleate, Phenylpropanolamine hydrochloride and Paracetamol. Two different lots of Chlorpheniramine Maleate, Phenylpropanolamine hydrochloride and Paracetamol combination tablets were analyzed using the proposed procedures as shown in **Table 4**.

TABLE 4: ANALYSIS OF COMMERCIAL FORMULATION

Drug	Lot	Drug found (mg per tablet)	
		Mean ± SD (n= 6)	Recovery (%)
Chlorpheniramine Maleate (4 mg)	1st Lot	4.05±1.27	100.5
	2nd Lot	3.97±1.61	99.25
Phenylpropanolamine Hydrochloride (25 mg)	1st Lot	25.04±0.98	100.16
	2nd Lot	24.98±0.65	99.92
Paracetamol (500 mg)	1st Lot	500.99±0.87	100.19
	2nd Lot	500.08±1.49	100.01

Renostat Plus (Chlorpheniramine Maleate 4 mg, Phenylpropanolamine hydrochloride 25 mg and Paracetamol 500 mg, Batch no.3345).

CONCLUSIONS: HPLC method was developed and validated as per ICH guidelines. UV detection allowed an accurate quantitation of chromophoric compounds. The drug was analyzed by HPLC method using Thermo Hypersil Gold C18 column (250mm ×4.6 mm, 5.0µ), with isocratic conditions and mobile phase containing methanol: 0.01M disodium hydrogen phosphate dihydrate buffer at pH 7 adjusted with OPA (60: 40) at a flow rate of 1mL/min using UV detection at 217nm. The procedure has been evaluated for the linearity, accuracy, precision and robustness in order to ascertain the suitability of the analytical method.

The method was also applied to marketed samples. It has been proved that the method is selective and linear between concentration range of 0.5-3µg/mL for Chlorpheniramine Maleate, 7-12µg/mL for Phenylpropanolamine hydrochloride, and 0.4-1.4µg/mL for Paracetamol. LOD and LOQ was found to be, 0.5µg/mL and 1µg/mL for Chlorpheniramine Maleate, 5µg/mL and 7µg/mL for Phenylpropanolamine hydrochloride and 0.2µg/mL and 0.4µg/mL for Paracetamol, respectively.

Statistical analysis proves that the method is suitable for the analysis of Chlorpheniramine Maleate, Phenylpropanolamine hydrochloride and Paracetamol as bulk drug and in pharmaceutical formulation without any interference from the excipients. It may be extended to study the degradation kinetics of Chlorpheniramine Maleate, Phenylpropanolamine hydrochloride and Paracetamol and also for its estimation in plasma and other biological fluids.

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