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## Simultaneous Determination of Phenylpropanolamine Hydrochloride, Dextromethorphan Hydrobromide and Chlorpheniramine Maleate in Formulations by Reversed-phase Liquid Chromatography

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**A simple and cost effective reversed-phase high performance liquid chromatography method has been developed for the simultaneous determination of phenylpropanolamine hydrochloride, dextromethorphan hydrobromide and chlorpheniramine maleate in expectorant formulations. Water's symmetry C<sub>18</sub> column (5 µ, 4.6 x 250 mm) was used with a mobile phase consisting of water, methanol and glacial acetic acid in the ratio 70:30:1, with a flow rate of 1.0 ml/min isocratically. Linearity coefficients, assay values, recovery studies showed that the method is accurate and precise.**

Chlorpheniramine maleate (CPM) is official in IP<sup>1</sup>, BP<sup>2</sup> and USP<sup>3</sup>. Dextromethorphan hydrobromide (DMH) is official in IP<sup>4</sup>, BP<sup>5</sup> and USP<sup>6</sup>, While phenylpropanolamine hydrochloride (PPH) is official in BP<sup>7</sup> and USP<sup>8</sup>. Fixed dose combinations of PPH, DMH and CPM are widely used for the symptomatic treatment of cough and cold. Many methods have been reported in the literature for the determination of similar formulations with various other drugs using HPLC<sup>9-14</sup>, gas chromatography<sup>15</sup>, spectrophotometry<sup>16</sup> and thin layer chromatography<sup>17</sup>. However, a method for the simultaneous determination of PPH, DMH and CPM in formulations by HPLC has not been reported. In this present work efforts have been made to develop an isocratic method us-

ing a simple mobile phase and UV detection for the simultaneous determination of the above drugs.

A high performance liquid chromatographic system from Shimadzu, consisting of LC 10 AS Pump, SPD IOA UV Detector, C-R7A Integrator was used for the analysis. Analysis was carried out using Water's symmetry C<sub>18</sub> (5 µ, 4.6 x 250 mm) column with a flow rate of 1.0 ml/min. A Rheodyne 7725i injector with a 20 µl loop was used for injecting the samples. Detection was carried out at 250 nm for PPH and CPM and 280 nm for DMH.

Methanol HPLC grade (Merck), glacial acetic acid HPLC grade (Spectrochem), chloroform AR grade (Merck), and water collected from Millipore Milli Q system was used. Working reference standards of PPH, CPM and DMH were used

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for the analysis.

A mixture of water, methanol and glacial acetic acid in the ratio 70:30:1 was used as the mobile phase with a flow rate of 1.0 ml/min. The HPLC procedure was carried out at ambient temperature.

For standard solution about 125 mg of PPH, 20 mg of CPM and 100 mg of DMH were accurately weighed and dissolved in 50 ml water in a 100 ml volumetric flask. The solution was diluted to the mark with water and mixed thoroughly ( $S_1$ ). Into a 125 ml separator, 10 ml of ( $S_1$ ) was volumetrically transferred.

About 6 g of the sample was accurately weighed and transferred into another 125 ml separator. To this, 20 ml of water was added and mixed. The standard and sample solutions in the separators were made alkaline with 2 M sodium hydroxide and were extracted with 3x25 ml portions of chloroform AR. The combined chloroform extracts in each case were washed with 5 ml of water. The aqueous phase was discarded and the chloroform layer was passed through anhydrous sodium sulphate into the respective dried 100 ml volumetric flasks and finally made upto volume and mixed. Into two separate dried stoppered test tubes, 5 ml of each of the standard and sample chloroform extracts were volumetrically transferred and evaporated with the aid of nitro-

TABLE 1: ESTIMATION OF PPH, CPM AND DMH IN PHARMACEUTICAL PREPARATIONS.

Contents	Sample A			Sample B		
	Label claim [mg/5ml]	Found [mg/5ml]	% over label claim	Label claim [mg/5ml]	Found [mg/5ml]	% over label claim
PPH	12.5	12.5	100.0	12.5	12.7	101.6
CPM	2.00	2.02	101.0	2.00	2.05	102.5
DMH	10.0	10.2	102.0	10.0	10.07	100.7

\*Sample A and Sample B, both are in-house samples.

TABLE 2: RESULTS OF RECOVERY EXPERIMENTS FOR PPH, CPM AND DMH.

Product	Active Ingredients added over label claim (in %) to the PL	Percentage recovery (%)		
		PPH	CPM	DMH
PL	50	98.4	99.80	102.00
	75	100.00	99.70	99.03
	100	98.8	98.2	99.1
	150	99.1	98.8	99.3

PL: The formulation without active ingredients (PPH, CPM, DMH).

TABLE 3: METHOD VALIDATION AND SYSTEM SUITABILITY PARAMETERS.

Parameters	PPH	CPM	DMH
Linearity range ( $\mu\text{g/ml}$ )	60-300	10-50	25-125
Linearity coefficient (r)	0.9994	0.9998	0.9998
Precision of the method (% RSD) (n=5)	0.650	0.700	0.400
Resolution factor (RS)	-	7.47	7.79
Symmetry factor	1.0	1.0	1.1
Precision of the instrument (% RSD)	0.24	0.76	0.55

gen. To each test tube 5 ml of the mobile phase was volumetrically added, stoppered and mixed well. A volume of 20 µl each of standard and sample solutions were injected into the stabilised HPLC system. Detection was initially kept at 250 nm and changed to 280 nm after elution of CPM peak. The retention times for PPH, CPM, DMH were found to be approximately 2, 6 and 12 min, respectively. The respective peak areas of standard and sample for each ingredient were used for quantification.

The assays were carried out by the proposed method and the results are tabulated in Table 1. Accuracy of the method was established by spiking the placebo (PL) samples with active ingredients at four levels and the results are tabulated in Table 2. Linearity and range of the method was carried out by injecting five mixed standard solution containing 60-300 µg/ml for PPH, 10-50 µg/ml for CPM and 25-125 µg/ml for DMH. The calibration curves were plotted using peak areas versus concentration. Linearity coefficients obtained are given in Table 3. Precision of the method was demonstrated by repeatability studies. This was done by five replicate analysis of the composite sample. Percentage RSD was calculated and given in Table 3. The system suitability studies were carried out to determine resolution factor, symmetry factor and precision of the instrument. Results are tabulated in Table 3. The advantage of this extraction procedure is to avoid column loading, column contamination or interference of many excipients present in the formulation. Ruggedness of the method was confirmed by analysis of different batches (n=5) of the product on different instruments

(HP and Waters), by different analysts on different days. RSD was found to be 1.45, 1.49 and 1.77 for PPH, CPM and DMH, respectively.

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## Spectrophotometric Determination of Cefoperazone Sodium Using Imidazole-Mercury (II) Reagent

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**A rapid sensitive and simple spectrometric method is developed for the estimation of cefoperazone sodium. It is based on the reaction with imidazole-mercury (II) reagent in slightly acidic medium and heating at 83° for 20 min. The solution has an absorption maxima at 352 nm and obeyed Beer's law in the concentration range of 24-96 µg/ml. Result of analysis were validated statistically and by recovery studies.**

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