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SIMULTANEOUS DETERMINATION OF CHLORPHENIRAMINE MALEATE, PARACETAMOL AND PSEUDOEPHEDRINE HYDROCHLORIDE IN PHARMACEUTICAL PREPARATIONS BY HPLC

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ABSTRACT

A simple, precise and specific reverse-phase High performance liquid chromatography method was developed for identification and simultaneous determination of Chlorpheniramine maleate, Paracetamol and Pseudoephedrine Hydrochloride in capsules and liquids. The separation of three components was performed on C18, 150 x 4.6 mm, 5µ HPLC column using gradient mobile phase Methanol-Sodium Perchlorate (0.043M, 2 mLTriethylamine, pH 5.0) at a flow rate of 1.0 mL, detection was at 204nm for Chlopheniramine maleate, Pseudoephedrine and 300 nm for Paracetamol.Results have shown good separation of the three component:The recovery of the drugs ranged from 98 to 102%.Validation results showed that the method is selective, linear, accurate and precise.

Keywords: Chlorpheniramine maleate, Paracetamol and Pseudoephedrine Hcl, HPLC, UV detection.

INTRODUCTION

Many analytical methods are described for determination of Chlorpheniramine maleate, Paracetamol and Pseudoephedrine hydrochloride in pharmaceuticals like spectrophotometery, gas chromatography and liquid chromatography with ion pair reagents.

The aim of our study was to develop a simple, rapid and reverse phase HPLC method for simultaneous determination of Chlorpheniramine maleate, Paracetamol and Pseudoephedrine Hydrochloride by using easily available resources and to save time and high cost of ion pair reagents.

METHODOLOGY

Reagents:

1. Sodium Perchlorate (Make- BDH)
2. Triethylamine (Make-Spectrochem)
3. Orthophosphoric acid (Make-Scharlau)
4. Methanol (Make-Carlo Erba)

Secondary reference standards:

1. Chlorpheniramine maleate,
2. Paracetamol
3. Pseudoephedrine hydrochloride.

Preparation of mobile phase:

Phase A: Dissolve 6.0 gm of Sodium perchlorate in a 1000 ml of distilled water, add 2.0 ml of Triethylamine and mix well. Adjust pH 5.0 with Orthophosphoric acid, mix well, filter through 0.45µm nylon membren and degas.

Phase B: Methanol, filter and degas

Preparation of standard solution:

The mixture of three components was prepared by mixing the appropriate quantities of each standard and diluting with water to the working concentration: Paracetamol (5mg/ml), Pseudoephedrine hydrochloride (0.3mg/ml) and Chlorpheniramine maleate (0.02mg/ml)

Filter through 0.2-µm nylon membrane filter.

Sample preparation for capsule preparations:
Mixed powder of 20 capsules and accurately weighed the amount of sample powder so as to match the standard and test concentration and transferred into a 50 ml volumetric flask. Added about 30 ml distilled water and sonicated for 20 mins. to dissolve, cool and dilute to volume with distilled water and mix. Filter through 0.2-µm nylon membrane filter.

Sample preparation for liquid preparations:
Accurately weigh the amount of homogeneous liquid preparation so as to match the standard and test concentration and transfered into a 50 ml volumetric flask. Added about 30 ml distilled water and sonicated for 20 mins. to dissolve, cool and dilute to volume with distilled water and mix. Filter through 0.2-µ nylon membrane filter.

Apparatus and Chromatographic procedure:
A Shimadzu Class VP chromatographic system equipped with Quaternary pump, degasser, auto injector, UV-Vis detector, software for recording the chromatograms
Column : Phenomenex, Luna 5µ C18, 150 mm x 4.60 mm, 5 µ
P/N - 00F-4041-E0
Pump : Gradiant (Phase A: 85% and Phase B: 15%) (For Capsules preparations)
Pump : Gradiant (Phase A: 85% and Phase B: 15% up to 14 mins. then low pressure gradiant up to 35 mins with increase of phase B: 40%) (For Liquids preparations)
Flow rate : 1.0 ml/minute
Detector : UV
Detection wavelength : 204 nm and 300
(Wavelength program : 300 nm from 4 min. to 8.5 min for Paracetamol)
Injection volume : 20 µl
Run time : 18 minutes (For Capsule preparations)
Run time : 35 minutes (For Liquid Preparations)
Procedure:
Pre-equilibrate the column with mobile phase (Phase A: 85% and Phase B: 15%) for about 30 minutes or until a stable baseline is obtained. Separately injected equal volumes (20 µl) of water as blank, standard solution and sample solution into the chromatograph, record the chromatograms, and measure the responses for the major peaks.

RESULTS AND DISCUSSION

A reverse phase HPLC method was developed and validated for the simultaneous determination of Chlorpheniramine maleate, Paracetamol and Pseudoephedrine hydrochloride. Validation of the method was done for specificity, precision, linearity and accuracy.

SPECIFICITY
The specificity of an analytical method is its ability to measure accurately and specifically the analyte in the presence of components that may be expected to be present in the sample matrix.
In this study blank, placebo, standard and sample solutions were analyzed using the method of analysis.
Peak response due to blank and placebo was not observed at the retention time of Chlorpheniramine maleate, Paracetamol and Pseudoephedrine hydrochloride. **Table - I**

From the chromatogram shown in **Fig. I, II, III and IV**, it is evident, that under the proposed chromatographic conditions, Chlorpheniramine maleate, Paracetamol and Pseudoephedrine hydrochloride are completely separated from each other and there was no interference of excipents used in the formulation. This indicates that the method is selective and can be used for their identification and quantification simultaneously.

Table I

Parameters	Chlorpheniramine maleate	Paracetamol	Pseudoephedrine hydrochloride
Retention Time	2.33 min.	6.81 min	11.78 min
Tailing Factor	1.38	1.84	1.71
Theoretical Plate	3063	1862	1941
Resolution	-	11.22	5.84
Repeatability of the system (RSD %)	0.32%	0.51%	0.32%

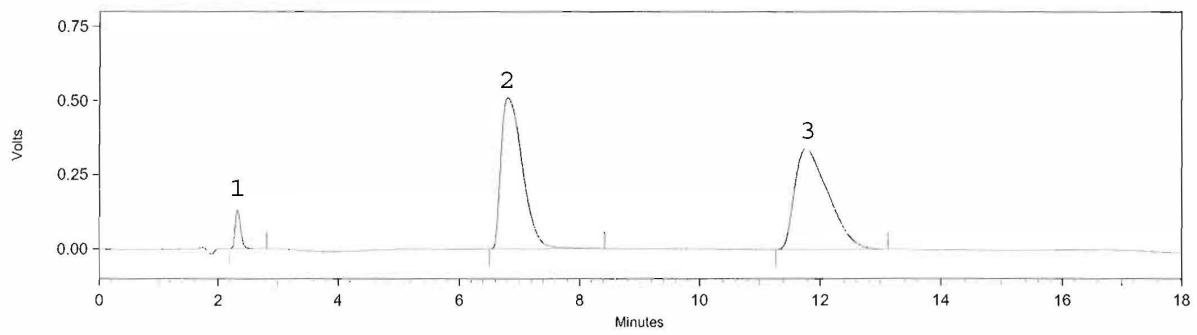

Fig. I: ***Chromatogram of standard solution in capsule preparation***.

1. Chlopheniramine maleate peak
2. Paracetamol Peak
3. Pseudoephedrine hydrochloride

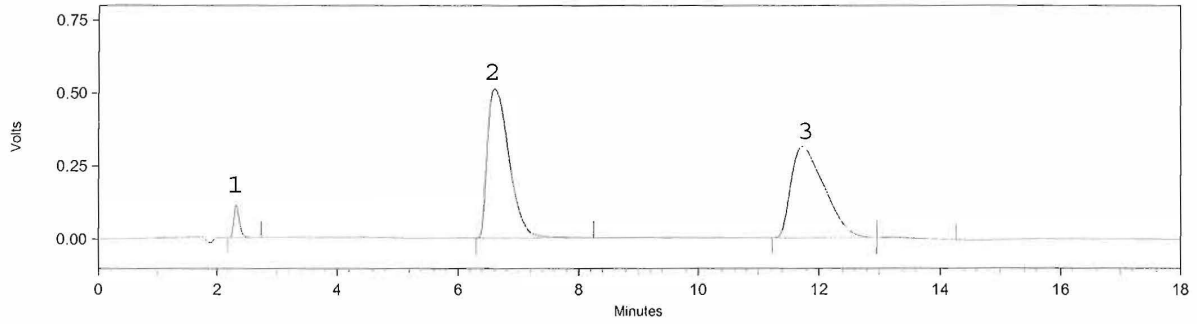

Fig. II: ***Chromatogram of sample solution in capsule preparation.***

1. Chlopheniramine maleate peak
2. Paracetamol Peak
3. Pseudoephedrine hydrochloride

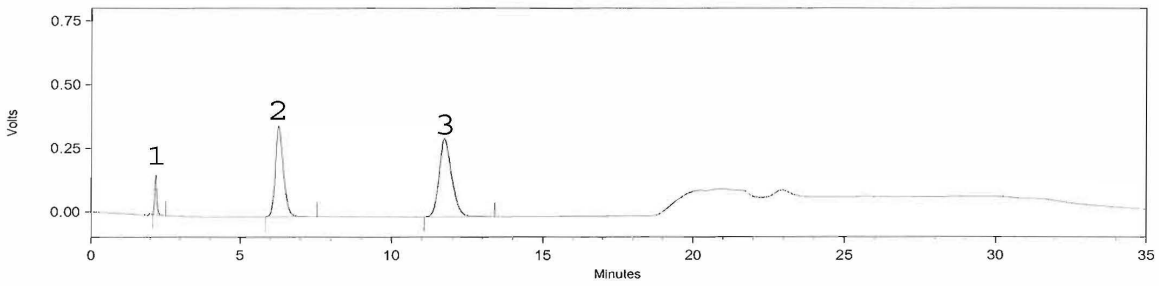

Fig. III: ***Chromatogram of standard solution in liquid preparation.***

1. Chlopheniramine maleate peak
2. Paracetamol Peak
3. Pseudoephedrine hydrochloride

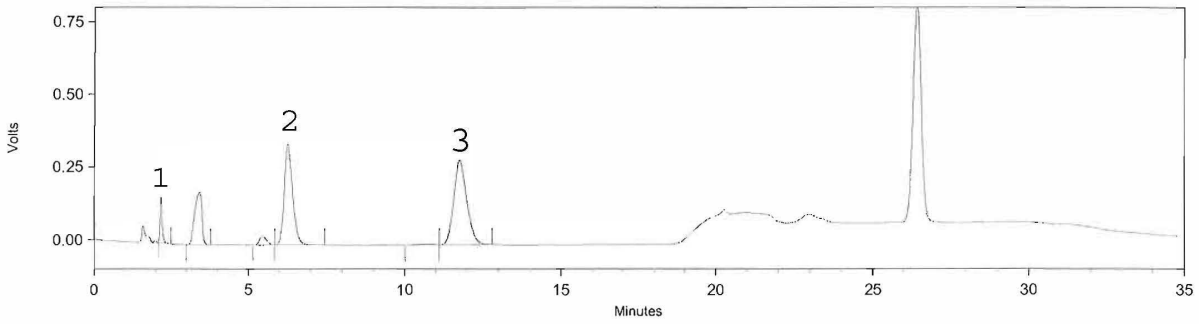

Fig. IV: ***Chromatogram of sample solution in liquid preparation.***

1. Chlopheniramine maleate peak
2. Paracetamol Peak
3. Pseudoephedrine hydrochloride

PRECISION

Precision of the method was determined by comparing the results obtained from six quantitative determinations, performed on two different days and by two analysts. The % relative standard deviation of assay result from six quantitative determinations were found well within acceptance criteria (RSD ≤2.0) and % variance between two analysts performed on two different day were also found within acceptance criteria (± 2.0), confirms the reproducibility of the proposed method. For capsule preparation refer **Table II** and for liquid preparation refer **Table III**

Table II*: Capsule preparation*

Content	Chlorpheniramine Maleate	Paracetamol	Pseudoephedrine hydrochloride
Declared mg	2	500	30
Determined mg	2.02	496.49	30.06
Determined %	101.0	99.3	100.2
Sd	0.04	2.56	0.36
% RSD of six Determinations	1.80	0.51	1.19
% variance	-0.50	0.25	0.49

Table III: *Liquid preparation*

Content	Chlorpheniramine Maleate	Paracetamol	Pseudoephedrine hydrochloride
Declared mg	1	120	10
Determined mg	0.98	118.65	9.66
Determined %	98.0	98.9	96.6
Sd	0.01	0.60	0.07
% RSD of six determinations	0.75	0.50	0.76
% variance	1.02	0.16	0.41

LINEARITY AND RANGE:

Linearity of the method was determined for each component separately using a calibration curve, of the peak area relative to the concentration in the range of 50 – 150% of the target concentration. In this study the solution of secondary reference standard at five different levels was prepared by dilution of stock solution and analyzed. The readings were noted and correlation co-efficient (r 2) was calculated.

The correlation coefficient was found well within the acceptance criteria ≥0.995 as per ICH guidelines. Confirms the proposed method is linear. Refer **Table IV**

Table IV: *Capsule preparation*

Content	Correlation coefficient in capsule preparation	Correlation coefficient in liquid preparation
Chlorpheniramine maleate	0.9998	0.9996
Paracetamol	0.9979	0.9998
Pseudoephedrine hydrochloride	1.0000	0.9997

ACCURACY/RECOVERY:

The accuracy of the method was determined by the method of standard addition. The known quantities of standard were added to the placebo at three different levels in triplicate, so as to obtain final concentration at the level of 80 %, 100 %, and 120% of the target concentration. All individual recoveries and overall recovery was calculated. The percentage recovery was found within acceptance criteria (98.0 to 102.0%) as per ICH guidelines. For capsule preparation refer **Table V** and for liquid preparation refer **Table VI**

Table V: ***Capsule preparation:***

Content	Amount added (mg)	Amount recovered (mg)	% Recovery
Chlorpheniramine maleate			
Recovery 80%	0.8	0.797	99.63
Recovery 100%	1.0	1.014	101.4
Recovery 120%	1.2	1.218	101.5
Paracetamol			
Recovery 80%	206.4	209.7	101.6
Recovery 100%	249.9	247.8	99.2
Recovery 120%	289.9	285.0	98.3
Pseudoephedrine hydrochloride			
Recovery 80%	12.0	12.0	100.0
Recovery 100%	15.0	15.1	100.7
Recovery 120%	18.0	18.1	100.6

Table VI: ***Liquid preparation***

Content	Amount added (mg)	Amount recovered (mg)	% Recovery
Chlorpheniramine maleate			
Recovery 80%	0.8	0.806	100.8
Recovery 100%	1.0	0.992	99.2
Recovery 120%	1.2	1.200	100.0
Paracetamol			
Recovery 80%	98.5	100.1	101.6
Recovery 100%	119.7	117.7	98.3
Recovery 120%	136.3	134.1	98.4

Pseudoephedrine hydrochloride			
Recovery 80%	8.0	7.92	99.0
Recovery 100%	10.0	9.95	99.5
Recovery 120%	12.0	11.92	99.3

CONCLUSION

A reverse phase HPLC method, using gradient elution for the separation of basic compounds, Chlorpheniramine maleate, Paracetamol and Pseudoephedrine Hydrochloride has been developed.The method was found selective for Chlorpheniramine maleate, Paracetamol and Pseudoephedrine Hydrochloride in the presence of common excipients like colour, flavor, sugar and other which are commonly used in pharmaceutical formulations. Based on the above data it was concluded that the method for assay of Chlorpheniramine maleate, Paracetamol and Pseudoephedrine Hydrochloride in capsules and liquid preparation is Specific, Precise, Accurate, and Linear in the range of 50 to 150 % of target concentration.

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REFERENCES

1. US pharmacopoeia
2. ICH guidelines
3. Department of Analytical Chemistry, Faculty of Pharmacy, University of Ankara, 06100 Tandoğan, Ankara, Turkey-M.Palabiyik and F.Onur – [Springerlink]
4. Bulletin of the Chemists and Technologists of Macedonia, Vol. 22, No. 1, pp. 33–37 (2003) - Katerina Milenkova, Aneta Dimitrovska, Liljana Ugrinova, Suzana Trajkovi}-Jolevska, Institute of Drug Quality Control, Faculty of Pharmacy, The "Sv. Kiril i Metodij" University,Vodnjanska 17, MK-1000 Skopje, Republic of Macedonia