Chromatographic Estimation of Dextromethorphan Hydrobromide, Pseudoephedrine Hydrochloride and Triprolidine Hydrochloride from Multicomponent Tablets

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A simple, precise and accurate reverse phase high performance liquid chromatographic method for simultaneous estimation of triprolidine hydrochloride, pseudoephedrine hydrochloride and dextromethorphan hydrobromide from tablets, has been developed. This chromatographic method utilises a 12.5 cm Nucleosil 100-5C_{18} bonded phase column with a mobile phase containing methanol:acetonitrile:0.1 M potassium dihydrogen phosphate (75:15:10), adjusted to pH 6.8 with sodium hydroxide. The standard deviation values obtained from the results of analysis of commercial formulations were below 1.6 and recovery study values were between 97.84 and 101.64 per cent. Thus this method is suitable for routine analysis of multicomponent formulations of these three drugs.

Triprolidine hydrochloride (TPH) is a potent antihistaminic with a moderate sedative action. Dextromethorphan hydrobromide (DMH) is a cough suppressant and antitussive agent while pseudoephedrine hydrochloride (PEH) is a bronchodilator. Each of these drugs is used in many other multicomponent formulations for symptomatic treatment of common cold. BP and IP describe a spectrophotometric method[1,2] for the estimation of TPH in tablets while a high performance liquid chromatographic (HPLC) method[3] is described in the USP for analysis of syrups and tablets containing TPH. HPLC methods are official in the IP, BP and USP for the estimation of PEH from its various formulations. IP and USP describe a HPLC method[2,3] for the analysis of DMH in syrup. A derivative difference spectrophotometric method[4] for the simultaneous analysis of PEH, DMH and TPH has been reported. Few HPLC methods[5,6,7] have been reported for the simultaneous analysis of PEH with TPH and other drugs. One derivative spectrophotometric method[8] and three HPLC methods[9,10,11] have been cited in the literature for estimation of DMH with various other drugs in multicomponent formulations.

In the present work an attempt has been made to develop a simple HPLC method for simultaneous analysis of TPH, PEH and DMH from their multicomponent formulations.

An isocratic Spectra Physics HPLC system with a 5µ Nucleosil 100-C_{18} (125 x 4 mm) column was used for this work. All reagents used for this work were of analytical reagent grade and all the mobile phase components were of chromatographic grade.

Separation of TPH, DMH and PEH along with the internal standard caffeine (CF) was achieved using a 5µNucleosil 100-C_{18} (125 x 4 mm) column and a mobile phase consisting of methanol:acetonitrile:0.1M potassium dihydrogen phosphate (75:15:10), adjusted to pH 6.8 with sodium hydroxide. The ultraviolet detector was monitored at 262 nm. Using a flow rate of 1.0 ml/min CF, PEH, TPH and DMH were eluted at 1.50, 2.25, 3.22 and 4.70 min. respectively. Standard curves for TPH in the concentration range of 100 to 500 µg/ml, for DMH in the range of 500 to 2500 µg/ml and for PEH in the range of 1000 to 5000 µg/ml were generated by plotting the peak area ratio (area of drug peak/area of internal standard peak) against the concentration of the respective drugs in their standard solutions.

For preparation of formulation sample solution twenty tablets were crushed and ground to a fine powder. Powder equivalent to 1.25 mg of TPH was transferred to a

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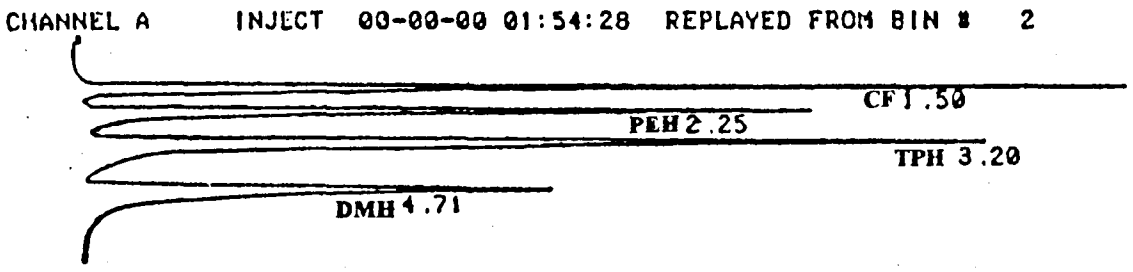

Fig. 1 : Chromatogram of the Formulation Sample Solution

TABLE 1 : RESULTS OF ANALYSIS OF FORMULATIONS

Sample	Label Claim (mg/tab)			% of Label Claim Estimated*±95% Confidence Limits		
	PEH	DMH	TPH	PEH	DMH	TPH
Batch-I	30	10	1.25	97.94±1.76	99.60±1.73	100.91±1.28
Batch-II	30	10	1.25	100.66±1.95	99.94±1.69	101.23±1.22

*Average of five estimations TPH : Triprolidine hydrochloride DMH : Dextromethorphan hydrobromide PEH : Pseudoephedrine hydrochloride

10 ml volumetric flask containing about 5 ml of the mobile phase. To this volumetric flask 2 ml of standard solution of CF (1mg/ml) was added. The powder mixture was dissolved and the volume was made upto the mark with the mobile phase. This solution was first filtered through Whatman filter paper no. 41 and then through a 0.4 micron membrane filter.

After setting the chromatographic conditions and stabilising the instrument to obtain a steady baseline, 10 µl of the sample solution was injected and a chromatogram was recorded. The concentrations of the three drugs were obtained from the standard curves using the peak area ratio of each drug to the internal standard. A resolved chromatogram of the sample solution is given as figure-1. Results of analysis of the formulations are tabulated in table-1. Recovery studies were performed for TPH, DMH and PEH by addition of fixed quantities of the standard solutions of the three drugs to the pre-analysed tablet sample solution. Recovery studies gave results between 97.84 to 101.64 per cent for all the three drugs. The regression parameters (slope and intercept) and Pearson's correlation coefficient for linearity test are 0.9888, 0.0180 and 0.9997 for TPH, 0.9850, 1.3736 and 0.9997 for PEH and 0.9863, 0.5040 and 0.9998 for DMH, respectively.

The proposed method for simultaneous estimation of TPH, PEH and DMH from multicomponent tablets was found to be simple and rapid. This HPLC method is very rapid as the three drugs in the formulation along with the internal standard are separated and eluted in less than seven minutes. Values of standard deviation for the method were satisfactorily low and recovery was close to 100%, indicating high reproducibility and accuracy. This method can thus be conveniently adopted for routine quality control analysis of formulations containing TPH, DMH and PEH.

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Synthesis and Evaluation of Some Novel 2-Mercapto-3-(substitutedmethyl amino)quinazolin-4(3H)-ones as Analgesic, Antiinflammatory and Antibacterial Agents

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In view of the potent analgesic, antiinflammatory and antimicrobial activities exhibited by quinazolin-4(3H)-ones, a series of novel 2-mercapto-3-(substitutedmethyl amino)quinazolin-4(3H)-ones have been synthesized. When these compounds were evaluated for their analgesic, antiinflammatory and antibacterial activities, the compounds, I, II, III, IV, V and X exhibited comparable analgesic activity with the standard diclofenac sodium and it was found to be significant as compared to control.

Bacterial infections often produce inflammation and pain. In normal practice, two groups of agents (chemotherapeutic, analgesic and antiinflammatory) are prescribed simultaneously. The compounds possessing all three activities are not common. Quinazolines and condensed quinazolines received the attention of medicinal chemists due to its wide range of biological activities which include analgesic and antiinflammatory[1-3], antibacterial[4-7], antiviral[8-9], antihistaminic[10], antihypertensive[11-12] and anticancer[13] activities. Mannich bases were reported to possess potent antibacterial activity[14]. In the present study it was envisaged that a drug molecule possessing the above mentioned pharmacophore could be of advantage since it might possess analgesic antiinflammatory and antibacterial activities. The target compounds, 2-mercapto-3-(substitutedmethyl amino)quinazolin-4(3H)-ones [Mannich bases of 3-amino-2-mercaptoquinazolin-4(3H)-one] were synthesized by condensing the active hydrogen atom of 3-amino of 3-amino-2-mercapto quinazolin-4-(3H)-one(3), with formaldehyde and the desired amines [Mannich reaction]. The starting material (3) was synthesized from anthranilic acid by a novel innovative route (Scheme I). All compounds (Table - I) gave satisfactory elemental analysis. IR and NMR spectra consistent with the assigned structure. All the synthesized compounds were tested for analgesic antiinflammatory and antibacterial activities.

Melting points were taken in open capillary tubes on a Thomas Hoover melting point apparatus and are uncorrected. IR spectra were recorded in KBr on Perkin Elmer-841 grating spectrometer (γ max in cm^{-1}, mass spectra on Varian Atlas CH-7 mass spectrometer at 70 eV and NMR spectra on Varian A-60 or EM-360 spectrometer at 60 MHZ, using TMS as internal standard.

The compound 3-amino-2-mercapto quinazolin-4-(3H)-one (3) was synthesized by adding carbondisulphide (1.6 ml, 0.026 mol) and aqueous sodium hydroxide

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