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Simultaneous Estimation of Paracetamol and Promethazine Hydrochloride in Pharmaceutical Formulations by a RP-HPLC Method

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Abstract: A rapid and sensitive high performance liquid chromatography method for determination of paracetamol and promethazine hydrochloride has been developed. The chromatography system used a reversed phase C18 column (HiQ Sil C18, 5µ, 250 mm x 4.6 mm). The sample was analyzed using Methanol: Water: Try ethyl amine, in the ratio of 90:10:0.1 v/v as a mobile phase at a flow rate of 1.0 ml/min and detection at 250 nm. The retention time for paracetamol and promethazine hydrochloride was found to be 2.853 and 5.107 min respectively, and recoveries from formulation were between 98 and 102 %. The method can be used for estimation of combination of these drugs formulations.
Key words: Paracetamol, Promethazine HCL, RP-HPLC

Introduction

Paracetamol (acetaminophen) is one of the most popular over-the-counter analgesic and antipyretic drugs. Paracetamol is available in different dosage forms: tablet, capsules, drops, elixirs, suspensions and suppositories. Dosage forms of paracetamol and its combinations with other drugs have been listed in various pharmacopoeias[1, 2].

The combination of paracetamol with promethazine HCL is used as antipyretic and antiemetic drugs. Numerous methods have been reported for the analysis of paracetamol and its combinations in pharmaceuticals or in biological fluids. Paracetamol has been determined in combination with other drugs using titrimetry,[3, 4] voltametry,[5] flourimetry,[6] Colorimetry,[6] uv-spectrophotometry,[7-9] quantitative thin layer chromatography(TLC),[10] High performance liquid chromatography(HPLC)[11-16] and gas chromatography(GC) [17] in pharmaceutical preparations.
Promethazine HCL is H_1 antagonist used as antiemetic in motion sickness also it is used as antipsychotic drug[18]. Numerous methods have been reported for analysis of promethazine HCL and its combination with other drug like HPLC, [19-22] UV- spectrophotometry, [23-25] nephelometry [26] and capillary isotachophoresis [27]

Experimental

LC system used consisted of pump (model JASCO; PU – 2080 plus) with universal loop injector (Rheodyne 7725 i) of injection capacity 20 µl. Detector consists of Photodiode array detector MD-2010 plus, JASCO; the column used was HiQ Sil C 18 (10 µm, 250 mm X 4.6 mm i.d.) Kya tech, Japan, at ambient temperature. Optimized chromatographic conditions are listed in Table 1.

Materials and Chemicals

Pharmaceutical grade paracetamol and promethazine HCL were kindly supplied as a gift sample by Umedica Labs Pvt. Ltd., Vapi, (G.S.), India,
HPLC grade methanol- procured from Merck, India. High pure water was prepared by using Millipore Milli Q plus purification system. Standard stock solution (1 mg/ml) of paracetamol and promethazine were prepared by dissolving 25 mg of drug in 25 ml of methanol separately. The solutions were suitably diluted with mobile phase to get mixed standard solution containing 80 µg/ml of paracetamol and 4 µg/ml of promethazine HCL.

Each ml (Kelvin- P, Leben Labs) was labeled contain 25 mg of paracetamol and 1.25 mg of promethazine HCL, were measured and syrup equivalent to 100 µg/ml of paracetamol and 5 µg/ml of promethazine HCL was taken and volume adjusted to 100 ml, vortexed and then filtered through 0.45 µ membrane filter. From this solution, further dilutions were made using mobile phase to get a final concentration of 80 µg/ml of paracetamol and 4 µg/ml of promethazine HCL. Twenty microliters of solution was injected into HPLC system to obtain chromatogram for standard drug solution (five replicates) and sample solution (five replicates). Concentrations of paracetamol and promethazine HCL in the formulation were calculated.

Results

Linearity and range of method was determined on standard solution by analyzing 0 to 100 % of test concentration, and the calibration curve was plotted using AUC versus concentration of standard solution. Accuracy of method was ascertained by recovery study by adding a known amount of standard drug (±20% of test concentration) to preanalysed sample and reanalyzing the samples by proposed method. Precision was studied by analyzing five replicates of sample solution. Before analysis by proposed method ruggedness of method was evaluated by performing the assay with different analysis and on different days. The chromatographic parameters were also validated by system suitability studies (Table 2), which were carried out on freshly prepared standard stock solutions. The typical chromatogram obtained from the formulation is presented in fig 1. The retention time for paracetamol and promethazine HCL was found to be and 2.853 and 5.107 min respectively. Peaks were well resolved with resolution of 2.17 between the two drugs and were symmetrical in shape with asymmetry factor less than 2.1. Linearity was observed in the concentration range of 50-500 µg/ml for paracetamol and 1-10 µg/ml for promethazine HCL, with the correlation coefficient of 0.999 for paracetamol and 0.9995 for promethazine HCL respectively. Accuracy of the method was ascertained by recovery study (n=3). The concentration of standard spiked to the sample was 0-80 µg/ml for paracetamol and 0-4 µg/ml for promethazine HCL. Recovery data from the study are reported in table 3. The method was found to be accurate with percent recoveries between 98 and 102 %. There was good repeatability of proposed method with coefficient of variance of 0.80% for paracetamol and 0.60% for promethazine HCL. The present method is cost-effective, faster and can be used for the routine analysis of these drugs from formulations.

Table 1. Optimized Chromatographic condition

Parameter	Optimized condition
Chromatograph	Jasco- HPLC
Column	HiQ SiL C18, 5µ , 250 mm x 4.6 mm
Mobile phase*	Methanol: Water: Try ethyl amine (90:100:0.1)
Flow rate	1.0 ml/ min
Detection	UV at 250 nm
Injection volume	20µl
Temperature	Ambient
Retention time Paracetamol	2.853
Retention time Promethazine HCL	5.107

Table 2. System Suitability Parameter

Parameter	Paracetamol	Promethazine HCL
Calibration Range µg/ml	50 -500	2-10
Theoretical Plates	7381.10	3132.45
Resolution	----	2.17
Tailing Factor	1.42	2.06
LOD (µg/ml)	2.61	1.3
LOQ (µg/ml)	7.92	4.08

Table 3. Analysis of Formulation and Recovery studies.

Drug	Label claim (mg/ml)	*Estimation		**Recovery	
		mg/ml	% label claim	Amount added (µg/ml)	% Recovery
				0	99.2 (0.1)
Paracetamol	25	24.8	99.2	12.5	98.10 (0.2)
				25	98.00 (0.50)
Promethazine HCL	1.25	1.23	98.4	0	98.4 (0.63)
				0.625	102.5 (0.97)
				1.25	99.31 (0.5)

*mean (%RSD) of five observations, **mean (%RSD) of three determinations

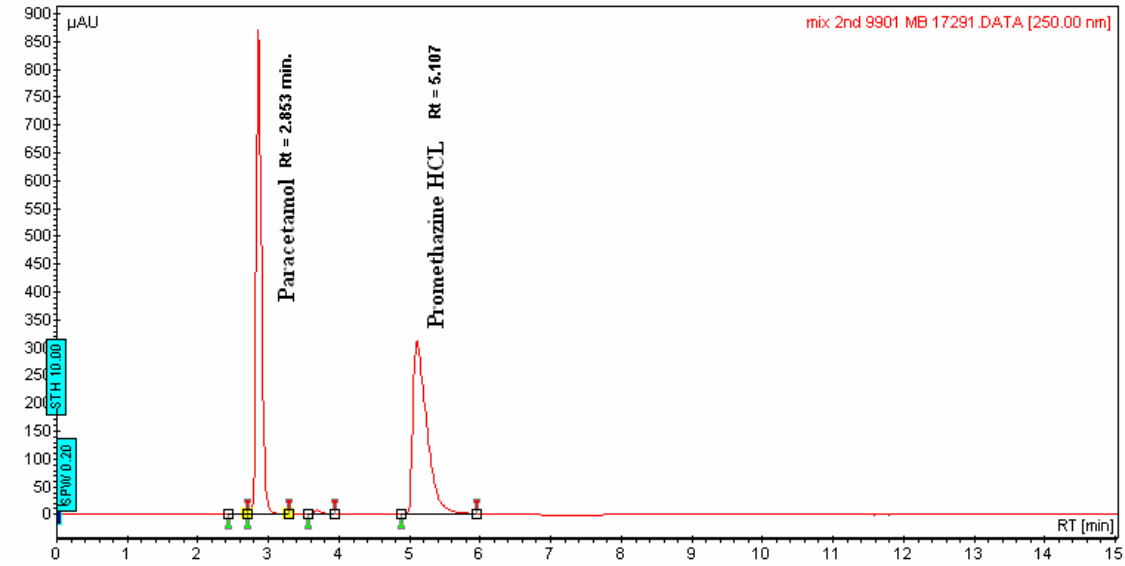

Figure 1: A typical chromatogram of paracetamol and promethazine hydrochloride

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