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Simultaneous RP-HPLC Determination of Nimesulide and Paracetamol in Tablets

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Abstract : A simple, specific, accurate and precise reverse phase high pressure liquid chromatographic method has been developed for the simultaneous determination of nimesulide and paracetamol from tablets by reverse phase C_{18} column (Inertsil C_{18}, 5µ , 150 mm x 4.6 mm). The sample was analyzed using Acetonitrile: Methanol: Water in the ratio of 40:40:20, (pH adjusted to 4.50 with orthophosphoric acid) as a mobile phase at a flow rate of 1.0 ml/min and detection at 276 nm. The retention time for paractetamol and nimesulide was found to be 2.04 and 4.67 min respectively, and recoveries from tablet were between 99 and 101 %. The method can be used for estimation of combination of these drugs in tablets.
Key words: Nimesulide, Paracetamol, RP-HPLC

Introduction

Nimesulide is an anti-inflammatory drug. Chemically, nimesulide is N-(4-nitro-2-phenoxyphenyl) methane sulphonamide.It is approved for used in treatment of musculoskeletal disorder, dyemenorrhoea, thrombophlebitis and dental pain, inflammation. Some HPLC[1, 2] and spectrophotometric[3, 4], methods have been reported in the literature for its estimation. Paracetamol is chemically N-(4-hydroxyphenyl) acetamide. It is a centrally and peripherally acting non-opioid analgesic and antipyretic. Many methods have been described in the literature for the determination of paracetamol with other drugs individually and in combination[5-13]**.** However there is no RP-HPLC method reported for the simultaneous estimation of these drugs in combined dosage forms.

Experimental

A High Performance Liquid Chromatograph system, with LC solutions data handling system (Shimadzu-LC2010) with an auto sampler was used for the analysis. The data was recorded using LC 2010 solutions software. The purity determination performed on a stainless steel column 150 mm long, 4.6 mm internal diameter filled with Octadecyl silane chemically bonded to porous silica particles of 5µm diameter (Inertsil C_{18}, 5µ , 150 mm x 4.6 mm, make: Shimadzu ltd, Japan). Optimized chromatographic conditions are listed in Table 1.

Materials and Chemicals

Pure samples of Nimesulide and Paracetamol were obtained from Granules India ltd. For the estimation of Nimesulide and Paracetamol in commercial formulations. HPLC grade Orthophosphoric acid, acetonitrile and 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 Nimesulide and Paracetamol were prepared by dissolving 25 mg of drug in 25 ml of acetonitrile, separately. The solutions were suitably diluted with mobile phase to get mixed standard solution containing 3 µg/ml of nimesulide and 15 µg/ml of paracetamol.

Twenty tablets (Nimupain plus Cipla laboratories). Each tablet was labeled contain 100 mg of Nimesulide and Paracetamol 325 mg were weighed, and powder equivalent to 25 mg of paracetamol was weighed accurately and taken into 25 ml volumetric flask. The drugs were extracted into acetonitrile; volume was adjusted to 25 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 3 µg/ml of nimesulide and 15 µg/ml of paracetamol. 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 nimesulide and paracetamol in the formulation were calculated by comparing AUC of sample with that of standard.

Results

Linearity and range of method was determined on standard solution by analyzing 70 to 130 % 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. Specificity was carried out by exposing the sample to different stress conditions for 24 hours, such as acidic (0.1 N HCl, 1 ml 40^{O}C), basic (0.1 N NaOH, 1 ml 40^{O}C), heat (60^{O}C), UV light (260 nm, 40^{O}C) and humidity (75 % RH, 40^{O}C), before analysis by proposed method. Ruggedness[14] 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 nimesulide was found to be 2.04 and 4.67 min respectively. Peaks were well resolved with resolution of 4.50 between the two drugs and were symmetrical in shape with asymmetry factor less than 1.20. Linearity was observed in the concentration range of 1.7-4.2 µg/ml for nimesulide and 9-20 µg/ml for paracetamol, with the correlation coefficient of 0.9996 for nimesulide and 0.9999 for paracetamol, respectively. Accuracy of the method was ascertained by recovery study (n=3). The concentration of standard spiked to the sample was 2.3-3.5 µg/ml for nimesulide and 12-15 µg/ml for paracetamol. Recovery data from the study are reported in table 3. The method was found to be accurate with percent recoveries between 99 and 101 %. There was good repeatability of proposed method with coefficient of variance of 0.80% for nimesulide and 0.60% for paracetamol. The results of specificity studies indicated no interference from excipients, impurities, and degradation products under various stress conditions and assured that the peak response was due to a single component only. Hence, the present method is cost-effective, faster and can be used for the routine analysis of these drugs from tablet formulations.

Table 1: Optimized Chromatographic conditions

Parameter	Optimized condition
Chromatograph	Shimadzu-HPLC
Column	Inertsil C_{18}, 5µ , 150 mm x 4.6 mm
Mobile phase*	Acetonitrile:methanoil:water (40:40:20) pH 4.5 (dil orthophosphoric acid)
Flow rate	1.0ml/min
Detection	UV at 276 nm
Injection volume	20µl
Temperature	Ambient
Reaction time-Paracetamol	2.04 min
Reaction time-Nimesulide	4.67 min

*Filtered through a 0.45µ membrane filter (Millipore), degassed and sonicated

Table 2. System Suitability Parameters

Parameter	Nimesulide	Paracetamol
Calibration range (µg/ml)	1.7 – 4.2	9 - 20
Theoretical plates	11532.75	6540.35
Resolution	-	4.50
Tailing factor	1.15	0.95
LOD (µg/ml)	0.050	0.025
LOQ (µg/ml)	0.150	0.090

Table 3.Analysis of Formulation and Recovery studies.

Drug	Label claim (mg/ml)	*Estimation		**Recovery	
		mg/tablet	% label claim	Amount added (μg/ml)	% Recovery
				2.4	99.80 (0.18)
Nimesulide	100	99.98	99.98(0.82)	3.0	99.70 (0.45)
				3.6	99.90 (0.39)
				12	100.02(0.54)
Paracetamol	325	325.5	100.2	14	100.15(0.84)
				16	99.90 (0.73)

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

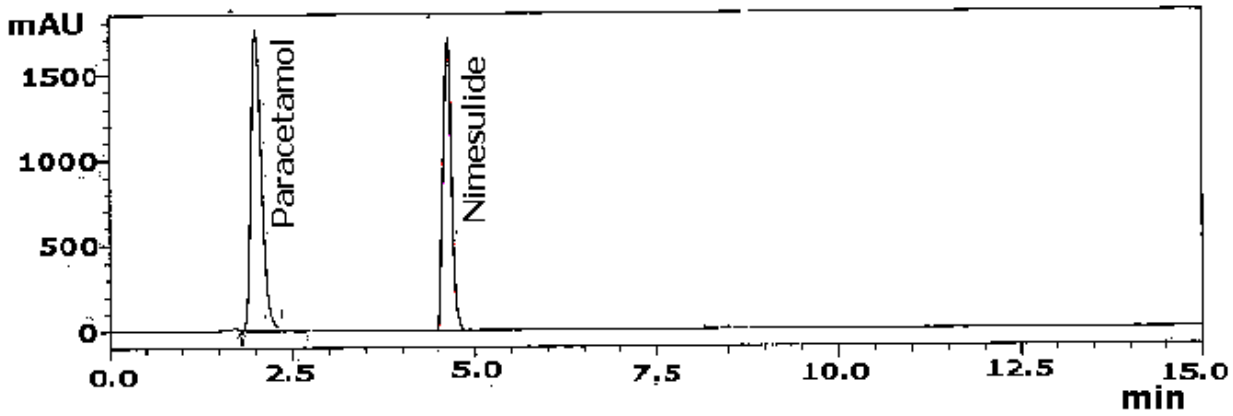

Figure 1: Typical chromatogram of Nimesulide and Paracetamol

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