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SIMULTANEOUS ESTIMATION OF MEFENAMIC ACID AND PARACETAMOL IN SUSPENSION FORM BY USING UPLC

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ABSTRACT

A simple, fast, precise, specific, accurate reversed phase ultra performance liquid chromatographic (UPLC) method was developed and validated for the simultaneous determination of Mefenamic acid (MA) and paracetamol (PC) in suspension. The column used was acquity, BEH C_{18} 50 mm* 2.1 mm, 1.7 µm and a mobile phase composed of Acetonitrile : 0.1 % Formic Acid in water (95:05), The flow time was set at 0.6 mL/min. Analysis was performed using PDA detector, The column temperature was 35°C. The retention times of MA and PC were found to be 2.86 min and 1.03 min, respectively. Linearity was established for MA and PC in the range of 10-60 µg/mL and 10-60 µg/mL, respectively. Repeatability and intermediate precision were acceptable (RSD < 2%). The percentage recoveries of MA and PC were found to be in the range of 99.42% to 100.04% and 100.05% to 100.80%, respectively. The proposed method was validated and successfully used for estimation of Mefenamic acid and paracetamol in the pharmaceutical dosage form.

Key words: Mefenamic acid (MA), Paracetamol (PC), UHPLC, BEH C_{18}, Suspension.

INTRODUCTION

Mefenamic acid (MA) is 2-[(2, 3-dimethylphenyl) amino] benzoic acid. Mefenamic acid, an anthranilic acid derivative, is a member of the fenamate group of nonsteroidal anti-inflammatory drugs (NSAIDs). It exhibits anti-inflammatory, analgesic, and antipyretic activities. Similar to other NSAIDs, Mefenamic acid inhibits prostaglandin synthetase. Paracetamol (PC) is chemically N-(4-hydroxyphenyl) acetamide and is used as analgesic and anti-pyretic agent. Paracetamol has a narrow therapeutic index – the therapeutic dose is close to the toxic dose[1,2]. The chemical structure of Mefenamic acid and Paracetamol is shown in Figs. 1 and 2.

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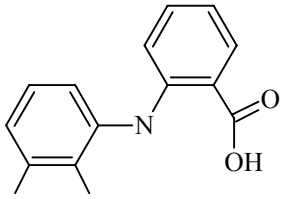

Fig. 1: Chemical structure of mefenamic acid

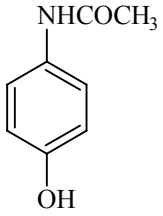

Fig. 2: Chemical structure of paracetamol

Literature survey reveals that various analytical techniques viz, UV spectrophotometry, spectroflurometry, high performance liquid chromatography (HPLC) and high performance thin layer chromatography (HPTLC)[3-9] were reported for the analysis of MA and PC in pharmaceuticals. Few HPLC methods have been reported for the simultaneous determination of MA and PC. Our aim was to develop proper method, which estimates both the analytes in a shorter time and to develop low cost method. The present study describes an isocratic, UPLC method using PDA detection for the determination of Mefenamic acid and Paracetamol from oral suspension form.

EXPERIMENTAL

Materials and method

Standard Mefenamic acid and Paracetamol was obtained from Versatile Pharma Pvt. Ltd., Hyderabad. Formic acid AR and ACN of HPLC grades were supplied by S.D. Fine Chemicals, Mumbai. Water HPLC grade was obtained from a milli-QRO water purification system.

A Ultra high-pressure liquid chromatography (Agilent Technology with DAD Model No- 1290 infinity-UPLC) with Binary Pumps; Pressure limit up 15000 psi, PDA Detector, auto Sampler and operating software Chemistation version-C.01.04 (35). The method was carried on a Acquity BEH C_{18} (50 mm* 2.1 mm i.d, 1.7 µ) column as a stationary phase. The mobile phase consisted of 0.1% of Formic acid in water as aqueous phase and acetonitrile.

The mobile phase was filtered through a 0.45 µ membrane filter and degassed before analysis. Acetonitrile and aqueous phase in the ratio of 95:05 v/v as the mobile phase flow rate of 0.6 mL/min. and separation was carried out at the column temperature is 35°.

Standard stock solution of the drug was prepared by dissolving each 25 mg of Mefenamic acid and Paracetamol in a mixture of acetonitrile: water (1:1 v/v) and made up to with 25 mL with the same (1000 µg/mL). Working standard solution was prepared by diluting 1 mL of the stock solution to 10 mL with acetonitrile: water (1:1 v/v) (100 µg/mL). The gradient dilution were prepared by taking 1, 2, 3, 4, 5 and 6 mL of solution and made up to 10 mL with acetonitrile: water (1:1 v/v) solution; 0.5 micro liter of the solution from each flask to use for experiment. Calibration curve was constructed by plotting mean peak area against the corresponding drug concentration (Figs. 3 and 4).

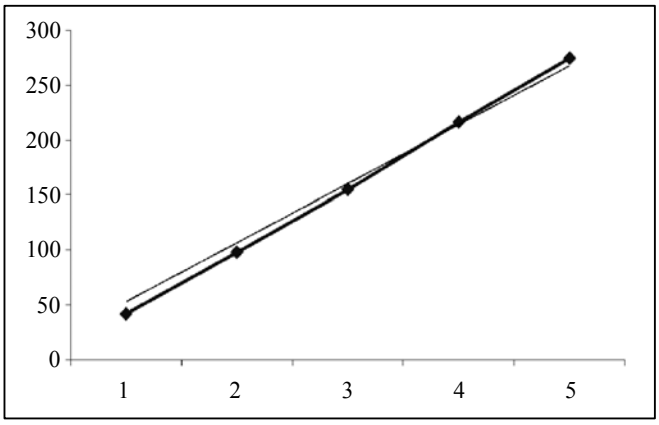

Fig. 3: Mefenamic acid standard plot (Concentration vs area) Y = 53.39 x (R^2 = 0.99)

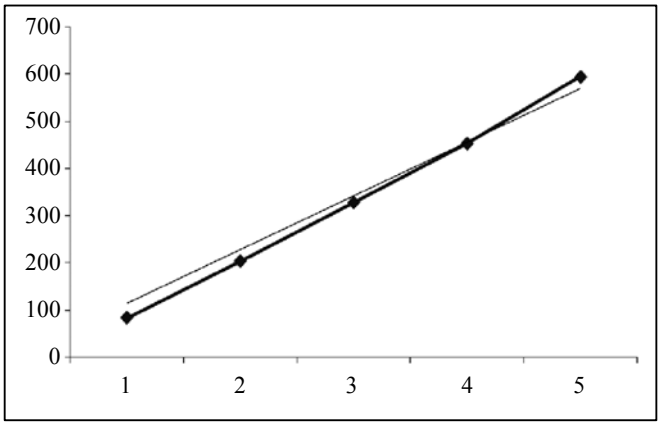

Fig. 4: Paracetamol Standard plot (Concentration vs Area) Y = 113.7 x (R^2 = 0.99)

The detector response was found to be liner in the concentration range of 10-60 µ/mL (Table 1). The typical chromatogram of Mefenamic acid Standard drug solution (Fig. 5), Paracetamol standard drug solution (Fig. 6) and Mefenamic acid, Paracetamol standard drug solution shows Fig. 7. Calibration curves could be represented by the following equation Y = 53.39 x (R^2 = 0.99), Y = 113.7 x (R2 = 0.99). This equations was used for the determination of Mefenamic acid and Paracetamol from suspension.

Table 1: Detector response (concentration vs area)

Concentration (µg/mL)	Mefenamic acid				
	10	**20**	**30**	**40**	**50**
1	42.074	98.826	154.816	216.080	278.386
2	42.042	98.762	154.032	215.696	280.032
3	42.152	97.131	155.006	216.119	278.601
Average	42.080	98.240	154.618	215.965	279.023
	Paracetamol				
1	83.547	201.825	327.165	452.483	592.969
2	83.122	203.249	326.982	453.346	594.981
3	83.200	201.083	327.674	452.730	594.953
Average	83.289	202.719	327.273	452.853	594.301

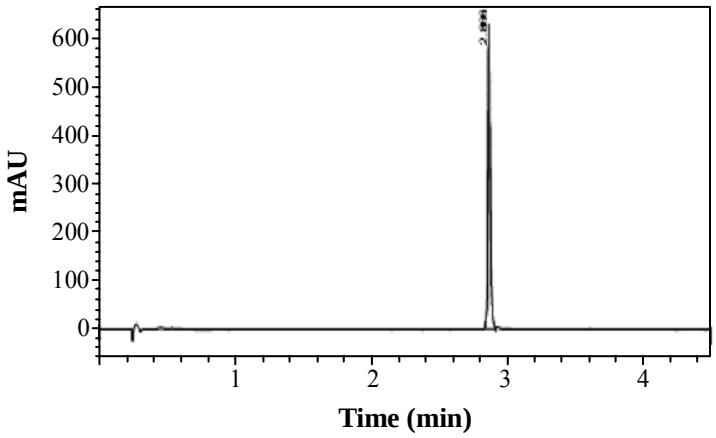

Fig. 5: Chromatogram of mefenamic acid drug solution

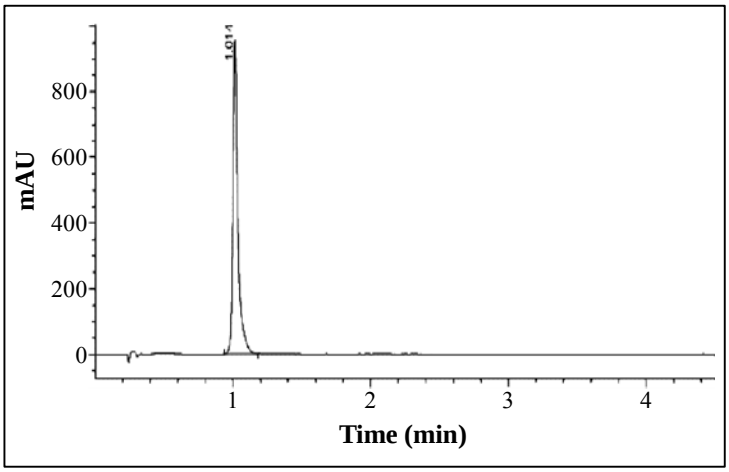

Fig. 6: Chromatogram of paracetamol drug solution

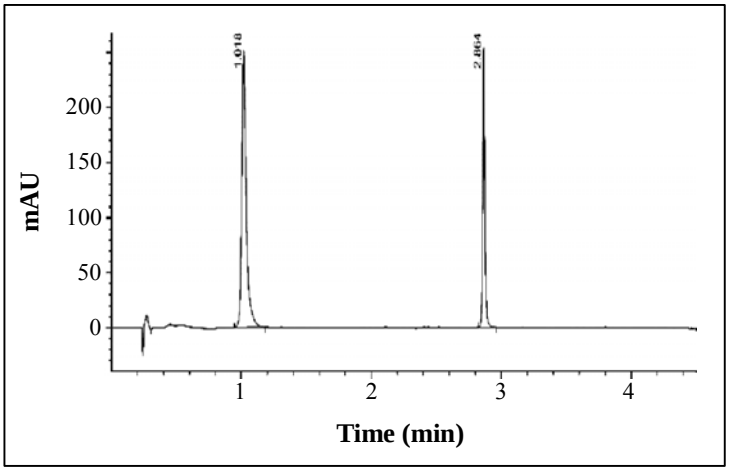

Fig. 7: Chromatogram of mefenamic acid and paracetamol drug solution

For the estimation of drug from commercial formulation, 60 mL of two brands-Meftagesic-P suspension (Blue Cross Laboratories Ltd., Nashik) and Nimucet MF Suspension (Intas Laboratories Pvt. Ltd., Ahmedabad). Each 5 mL contained 125 mg of Paracetamol and 50 mg of Mefenamic acid, respectively. A quantity equivalent to 125 mg of Paracetamol and 50 mg of Mefenamic acid was transferred in to 100 mL volumetric flask, dissolved and made up to acetonitrile: water (1:1 v/v) solution. The solution filtered through a 0.45 µ membrane filter. One milliliter of the resulting solution was then diluted to 10 mL with an about used solution. From this 0.5 and 1 mL sample was taken and their volume was made up to 10 mL each.

RESULTS AND DISCUSSION

A chromatogram of these solutions was obtained by injecting 0.5 µL of each sample in to the chromatographic system (Fig. 8). There was no interference from diluents and excipients. The retention time of the drugs Paracetamol and Mefenamic acid was 1.01 min and 2.86 min. To study the accuracy, reproducibility, precision of the proposed method and recovery experiments were carried out. A fixed amount of the pre analyzed sample was taken and standard were added at three different levels. Each level was repeated at five times. The summaries of recovery studies are reported in Table 2.

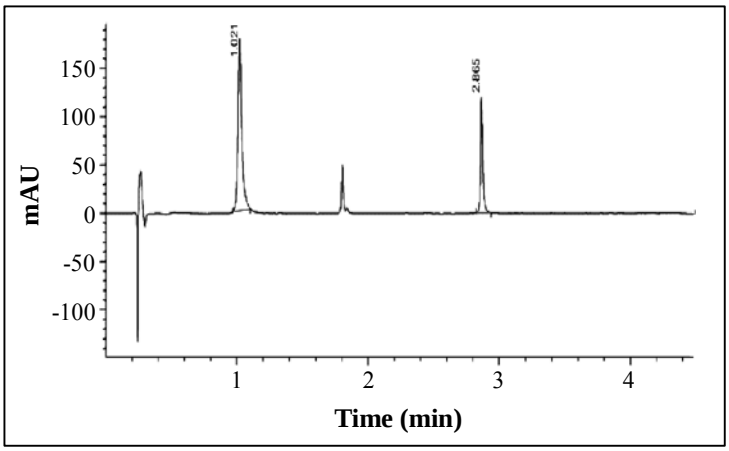

Fig. 8: Chromatogram of the sample oral suspension solution

Table 2: Summary of recovery studies

Suspen-sions	Drug	Label claim (5 mL/mg)	Amount found (mg)	Recovery studies		
				Amount added (mg/5 mL)	Amount recovery (mg/5 mL)	Percentage recovery (%)
A	Paracetamol	125	125.07 ± 0.024	50	175.09 ± 0.05	100.05
				100	225.04 ± 0.04	100.04
	Mefenamic acid	50	49.97 ± 0.025	50	99.98 ± 0.08	99.94
				100	149.99 ± 0.04	99.99
B	Paracetamol	125	126.01 ± 0.021	50	176.04 ± 0.02	100.59
				100	226.03 ± 0.05	100.45
	Mefenamic acid	50	50.02 ± 0.01	50	99.89 ± 0.02	99.89
				100	149.94 ± 0.02	149.94

Suspension A is Mefetagesic-P (Blue Cross Laboratories Ltd, Nashik) and
Suspension B is Nimucet MF (Intas Laboratories Pvt. Ltd., Ahmedabad)

The present study comprises a ultra performance liquid chromatography method to determine Mefenamic acid and Paracetamol from oral suspension dosage form. Experiment was carried out to establish the method. The mobile phase, bearing acetonitrile: 0.1% formic acid in water proportion of (95:05) was found to be idle. The retention time of Mefenamic acid and Paracetamol were found 2.86 and 1.01 min. the value of percent recovery and standard deviation indicate that method is accurate, reproducible, and precise. The summaries of final result are illustrated in Table 3.

Table 3: Summaries of final result

Brand Name	Drugs	Amount found (mg/5 mL)	% RSD	Percentage assay
Meftagesic-P (Blue cross Laboratories Ltd., Nashik)	Paracetamol	125.07 ± 0.024	0.241	100.05
	Mefenamic acid	49.71 ± 0.025	0.211	99.42
Nimucet MF (Intas Laboratories Pvt. Ltd., Ahmedabad)	Paracetamol	126.01 ± 0.021	0.262	100.80
	Mefenamic acid	50.02 ± 0.01	0.247	100.04

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