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ESTIMATION OF MEFENAMIC ACID IN PHARMACEUTICAL DOSAGE FORMS BY RP-HPLC

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ABSTRACT

A simple and precise RP-HPLC method was developed and validated for the determination of mefenamic acid in pharmaceutical dosage forms. Chromatography was carried out using an ODS packing L_1, 250 x 4.6 mm, 5 µ,column at 27°C with a mobile phase acetonitrile : 0.05 M monobasic ammonium phosphate buffer : tetrahydrofuran (46 : 40 : 14) at a flow rate was 1.0 mL/min and UV detection wavelength was 254 nm. The retention time of the drug was 10.583 min. The proposed method was found to have linearity in the concentration range of 5-30 µg/mL with correlation coefficient of $r^2 = 0.99954$. The developed method has been statistically validated and was found simple and accurate. The limit of detection and limit of quantification for mefenamic acid was found to be 0.12 and 0.36 µg/mL, respectively. The proposed method is accurate, precise, specific and rapid for estimation of mefenamic acid in tablet dosage form.

Key words: Mefenamic acid, RP-HPLC, Tablet.

INTRODUCTION

High performance liquid chromatography (HPLC) is the fastest growing analytical technique for the analysis of drugs. The technique of HPLC is developed from advances made in column chromatography. The technique is based on the same modes of separation mentioned above. It differs from conventional column chromatography in the sense that the mobile phase is pumped through the packed column under high pressure. Because of the relatively high pressure necessary to perform this type of chromatography, a more elaborate experimental set up is required[1-6].

Mefenamic acid (MEF) is 2-(2,3-dimethyl phenyl) aminobenzoic acid. It has analgesic, anti-inflammatory and anti-pyretic properties. It works by blocking the action of

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a substance in the body called cyclooxygenase which is responsible for production of prostaglandians[7-8]. It is white or almost white microcrystalline powder[9].

Only very few HPLC methods have been reported in the literature for the estimation of MEF alone (or) combination with other drug is reported. The present paper describes a precise, accurate, specific and sensitive RP-HPLC method for estimation of MEF in tablet dosage forms.

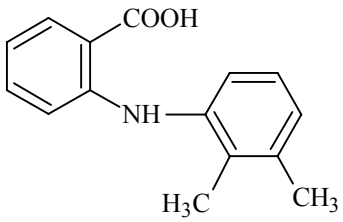

Fig. 1: Mefenamic Acid

EXPERIMENTAL

Material and methods

Instrumentation

An isocratic HPLC system (Shimadzu) consisting of LC-20AT VP liquid pump, rheodyne injector loop, SPD-20A, UV/Vis detector, an ODS packing L_1 column, Hamilton injecting syringe and window based spin chrome software was used.

Chemicals and reagents

Mefenamic acid was obtained as a gift sample from Martin and Harris Loborataries Ltd. Mefthal with a labeled claim at 250 mg of mefenamic acid was obtained from local drug stores. Acetonitrile (HPLC grade), 0.05 M monobasic ammonium phosphate buffer (5.7515 g of monobasic ammonium phosphate dissolved in 100 mL water adjusted to a pH of 5.0 with 3M ammonia) and tetrahydrofuran were used.

Chromatographic conditions

Mobile phase consists of acetonitrile : 0.05 M monobasic ammonium phosphate buffer: tetrahydrofuran (46 : 40 : 14). Buffer was prepared by weighing accurately and dissolving 5.7515 g of monobasic ammonium phosphate in 100 mL water and adjusting to a pH of 5.0 with 3M ammonia and filtered through 0.45 µm nylon membrane filter. The mobile phase was pumped from the solvent reservoir to the column at a flow rate of 1.0

mL/min. The column was maintained at 27°C and the volumn of each injection was 20 µL. The eluents were monitored at 254 nm.

Standard preparation

Weigh accurately 28.0 mg of mefenamic acid for working standard and transferred into a 100 mL clean dry volumetric flask. About 70 mL of mobile phase was added, sonicated for 5 minutes and volume was made up with mobile phase.

Sample preparation

Accurately powder equivalent to 100 mg of mefenamic acid was weighed and transferred in to a 100 mL volumetric flask, 60 mL of mobile phase was added, kept on rotary shaker for 30 min, sonicated 5 min with occasional shaking in between. The volume made up with mobile phase and mixed well.

RESULTS AND DISCUSSION

Several systematic trials were performed to optimize the chromatographic conditions for developing a sensitive, precise and accurate RP-HPLC method for the analysis of mefenamic acid in pharmaceutical dosage forms. The present method contains mobile phase acetonitrile : 0.05 M monobasic ammonium phosphate buffer : tetrahydrofuran (46 : 40 : 14), which was found to be the most suitable as the peak obtained with good peak shape and symmetry. Hence, this method was finalized for the estimation of MEF.

Table 1: System suitability, precision and accuracy of the proposed methods for MEF

Parameter	Results
Retention time (Rt) min	10.583
Theoretical (n)	2641.53
Tailing factor	0.852
Linearity range (µg/mL)	5-30
Limit of detection (µg/mL)	0.12
Limit of quantification (µg/mL)	0.36
Regression eqation (y = mx + c)	Y = 508189.2 x – 7067.8
Slope (m)	508189.2
Intercept (c)	– 7067.8

Cont…

Parameter	Results
Correlation coefficient (r)	0.99954
% Relative standard deviation*	
Retention time	0.076
Peak area	0.049
* Average of six determinations	

Linearity

A series of dilutions were prepared using MEF working standard (250 µg/mL) at concentration levels from 5%-30% of target concentration (5%, 10%, 15%, 20%, 25% and 30%). The peak response of solution was measured.

Accuracy

A study of accuracy was conducted. Drug assay was performed in triplicate as per test method with equivalent amount of MEF into each volumetric flask for each spike level to get the concentration of MEF equivalent to 80%, 100% and 120% of the labeled amount as per the test method. The average % recovery of mefenamic acid was calculated.

Table 2: Accuracy (recovery) data for MEF

Sample	Concentration (µg/mL)	Area	Percentage recovery	Mean percentage recovery	Standard deviation	Relative standard deviation
1	80%	3967.089	100.90			
2	80%	3966.712	100.94	100.98	1.18	0.122
3	80%	3964.872	101.10			
4	100%	7609.835	100.40			
5	100%	7610.943	100.30	100.20	1.734	0.143
6	100%	7613.251	100.12			
7	120%	11254.756	100.80			
8	120%	11251.089	101.00	100.80	2.91	0.200
9	120%	11256.881	100.60			

Table 3: Assay and recovery results of MEF in pharmaceutical formulations

Method	Pharmaceutical formulation	Labeled amount (mg)	Amount found (mg)	% Recovery	% RSD*
RP-HPLC	Tablet	250	248.54	99.27	0.143

* Average of five determinations

Precision

The system precision was performed by analyzing a standard solution of MEF at working concentration level for 6 times.

Robustness

Robustness of the proposed method was evaluated by making changes in flow rate, temperature and pH of the buffer solution. The results were found to be not affected by these small alterations.

Linearity curve for mefenamic acid

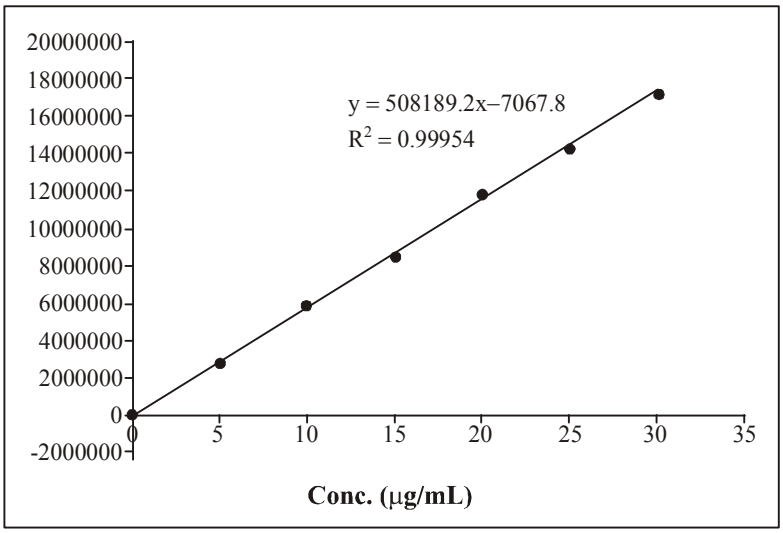

Fig. 2: Linearity curve for mefenamic acid

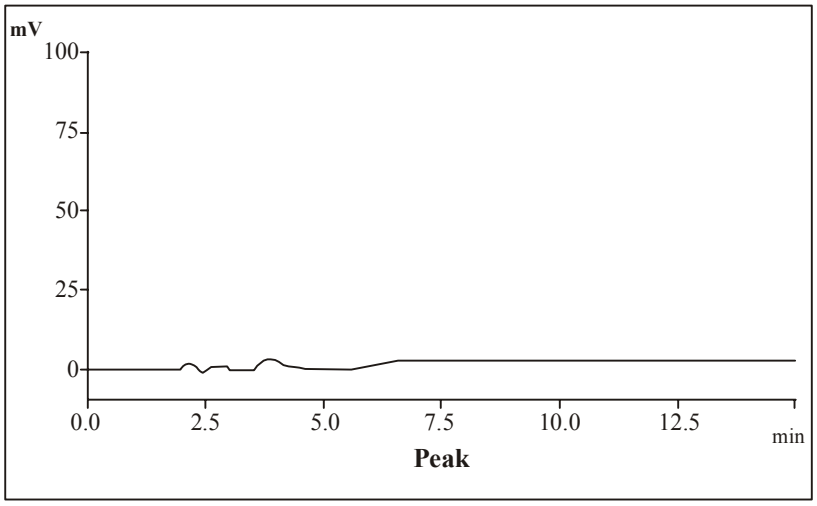

Fig. 3: Chromatogram of blank

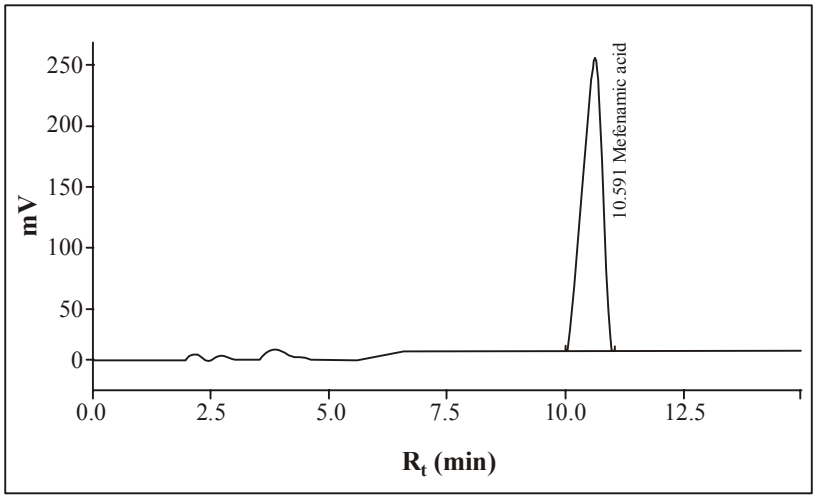

Fig. 4: Chromatogram of standard

Table 4: Peak table

Peak#	Name	Ret. time	Area	Area %	Tailing factor	Theoretical plate#
1	Mefenamic acid	10.591	7688496	100.000	0.854	2641.530
Total			7688496	100.000		

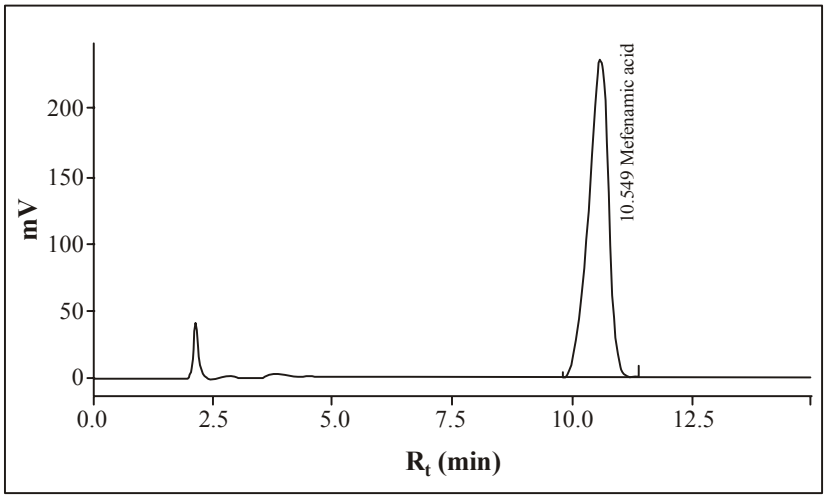

Fig. 5: Chromatogram of sample

Table 5: Peak table

Peak#	Name	Ret. time	Area	Area %	Tailing factor	Theoretical plate#
1	Mefenamic acid	10.549	7000936	100.000	0.875	2677.299
Total			7000936	100.000		

CONCLUSION

From these results, it can be concluded that the proposed method is quite precise and accurate. The absence of additional peaks in the chromatogram indicated that there is no interference of the common excipients used in the tablets. The proposed HPLC method is sensitive and reproducible for the analysis of MEF in tablet dosage forms. The method was duly validated by using required statistical perameters.

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