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Review Article

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Ultraviolet Spectrophotometric Determination of Mefenamic Acid in Pharmaceutical Preparations and Environmental Wastewater Sample: Application to Content Uniformity

Nief Rahman Ahmed

College of Environmental, University of Mosul-Iraq

***Corresponding author**
Nief Rahman Ahmed, College of Environmental, University of Mosul-Iraq.

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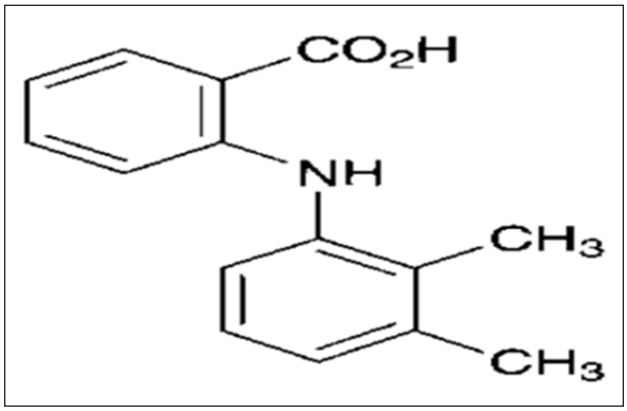
ABSTRACT
A simple, precise, accurate, rapid, economical and sensitive Uv spectrophotometric method has been developed for the determination of mefenamic acid in pharmaceutical preparations and environmental wastewater samples, which shows maximum absorbance at280 nm in a solution of hydrochloric acid in methanol (1 in 1000). Beer's law was obeyed in the range of 2-25µg/ ml, with molar absorptivity of 0.79 ×104 L.mol-1.cm-1, relative standard deviation of the method was less than 1.5%, and accuracy (average recovery %) was 100 ± 1.0. The method was successfully applied to the determination of mefenamic acid in some pharmaceutical formulations (tablets, capsules) and industrial wastewater samples. The proposed method was validated by sensitivity and precision which proves suitability for the routine analysis of mefenamic acid in true samples.

Keywords: Mefenamic Acid, Pharmaceutical, Spectrophotometry, Environmental Samples

Introduction

Mefenamic acid is chemically known as: N-2, 3-xylylanthranilic acid, is an analgesic, antipyretic with minor anti-inflammatory properties as shown in figure 1.



$C_{15}H_{15}NO_2$: 241.29
2-(2,3-Dimethylphenylamino) benzoic acid

Figure 1: Chemical Structure of Mefenamic Acid

Mefenamic acid is used in musculoskeletal and joint disorder such as rheumatoid arthritis, osteoarthritis and primary dysmenorrheal [1-4]. Different methods for the determination of mefenamic acid have been described, such as titrimetry (official method) for the assay of pure form and pharmaceutical preparation using sodium hydroxide as titrant and phenol red as indicator, HPLC, gas chromatography and cloud point extraction with spectrofluorimetry and spectrophotometry [5-9]. The most widely used methods for the determination of mefenamic acid are spectrophotometric methods [10-14]. However, all of these methods suffer from one or more disadvantage such as insufficient sensitivity, selectivity, tedious and use of complex solvent extraction procedures. Therefore, a simple method for assay of mefenamic acid is necessary for routine analysis and quality evaluation. It has the advantages of being rapid, sensitive, selective, accurate and reproducible. The present paper reports the development of a new UV method for determination of mefenamic acid in different type of tablets, capsules and environmental water samples.

Experimental

Apparatus

Shimadzu UV-1700 pharmaspec (double beam) spectrophotometer with 1.0 cm quartz cells was used for absorption measurement.

Reagents

All chemical used were of analytical or pharmaceutical grade and mefenamic acid standard material was provided from AL-hokamaa company for pharmaceutical industries (HPI) Mosul-Iraq.

HCL: Methanol ((1 in 1000) (v/v) was used as a solvent.

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Mefenamic Acid Standard Solution 25 ppm

This solution was prepared by dissolving 25 mg of mefenamic acid in 1000 ml of a solution of hydrochloric acid in methanol (1 in 1000) in calibrated flask.

Determination of Absorption Maxima

The standard solution of mefenamic acid (15µg/ml) was scanned in the range of 220-400 nm which shows maxima located at 280 nm (Figure 2). Therefore, 280 nm wavelength was selected for the construction of calibration curve.

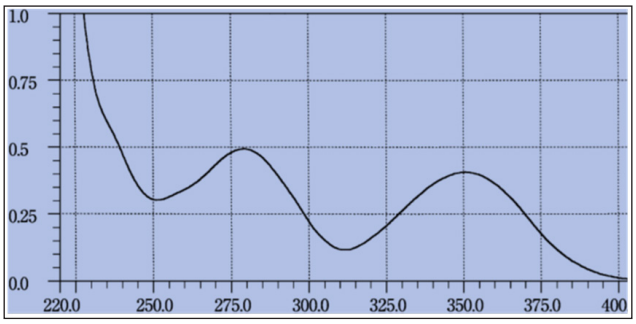

Figure 2: Absorption spectra of 15µg/ml mefenamic acid

Recommended Procedure

From the absorption maxima, calibration curve was prepared in the concentration range of 2-25 µg/ml. The absorbance was measured at 280 nm against HCL: Methanol (1 in 1000) as a blank. The concentration of the sample solution can be determined by using the calibration curve.

Analysis of Pharmaceutical Preparations

Tablets

Weigh and powder 10 tablets. Dissolve a quantity of the powdered tablets containing 0.01 g of mefenamic acid in about 100 ml of HCL: Methanol (1 in 1000). It was shaken thoroughly for about 10-15 min, and filtered. The filtrate was made up to 1 L with the same solvent. Treated this solution as mentioned under recommended procedure.

Capsules

Dissolve a quantity of the mixed contents of 10 capsules containing 0.01 g of mefenamic acid in 100 ml of HCL: Methanol (1 in 1000) solution and mixed for 10-15 mint and then filtered. The filtrate was made up to 1L with the same solvent. Treated this solution as described under recommended procedure.

Procedure for Real Water Samples

To demonstrate the practical applicability of the proposed method, real water samples were analyzed by this method. Industrial waste water from AL-hokamaa company for pharmaceutical industries (HPI) Mosul-Iraq, were fortified with the concentrations in the range of 5, 15, 20 µg/ml of mefenamic acid. The fortified water samples were analyzed as described above for recommended procedure and the concentration was calculated by using the calibration curve of this method.

Result and Discussion

The method used for the determination of mefenamic acid in pharmaceutical preparations and environmental wastewater samples was found to be sensitive, simple, accurate, and reproducible. Beer s law was obeyed in the concentration range of 2-25µg/ ml (Figure 3) with correlation coefficient of 0.9995, intercept of 0.012 and slope of 0.0329. The conditional molar absorptivity was found to be 0.79×10^4 l/mol.cm.

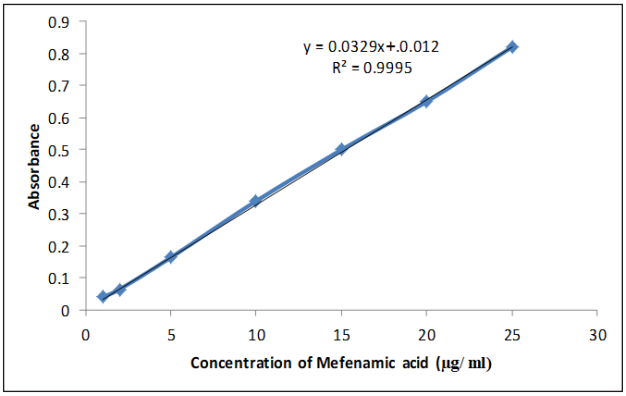

Figure 3: Calibration curve for mefenamic acid

The accuracy and precision of the method, a pure drug solution was analyzed at three different concentrations, each determination being repeated six times. The relative error (%) and relative standard deviation values are summarized in (Table 1). From (table 1) the values of standard deviation were satisfactory and the recovery studies were close to 100%. The RSD% value is less than1.6 indicative of accuracy of the method.

Table 1: Accuracy and precision of the proposed method

Mefenamic acid taken (µg/ml))	Er (%)[a]	RSD (%)
5	1.1	1.5
15	1.2	1.6
20	1.2	1.5

a: Mean of six determinations.

The limit of detection (LOD) and limit of quantitation (LOQ) were calculated using the standard deviation of the intercepts(σ) and the mean slope(s) of the calibration curves. LOD=3.3σ/s and it was 1.2 µg/ml. and LOQ=10 σ/s and it was 3.6µg/ml. [15-16]. The results are compiled in Table 2.

Table 2: Optical characteristics and statistical data for regression equation of the proposed method

Parameters	Value
λ max (nm)	280
Beer´s law limit (µg .ml^{-1})	2-25
Molar absorptivity (l.mol^{-1}.cm^{-1})	0.79×10^4
Correlation coefficient (r^2)	0.9995
Regression equation (Y= a × + b)	
Slope (a)	- 0.012
Intercept (b)	0. 329
Recovery %	100±0.5
Relative standard deviation (%)	< ±2
Limit of detection, (µg\ml)	1.2 µg/ml
Limit of quantification, (µg\ml)	3.6µg/ml

Application of the Proposed Method

The proposed method was satisfactorily applied to the determination of Mefenamic acid in its pharmaceutical preparations tablets,

capsules and wastewater samples, the results of the assay of the pharmaceutical preparations revels that there is close agreement between the results obtained by the proposed method and the label claim Table 3. And the results of water samples table 4 show that the recovery values obtained were close to 100%.

Table 3: Assay of mefenamic acid in pharmaceutical formulations

Label amount	Amount of mefenamic acid*	Pharmaceutical formulations
Ponstadin capsules (250 mg/capsule) (HPI)	250. 06	250 mg/capsule
Ponstadin capsules (500 mg/capsule) (HPI)	500.01	500 mg/tablets

*Mean of five determinations

Table 4: Determination of mefenamic acid in industrial wastewater samples

Wastewater samples	Added µg/ml	Found* µg/ml	Recovery %(n=10)
Industrial wastewater	5	5.02	100.4
	15	15.05	100.1333
	20	20.06	100.3

*Mean value of ten determinations

Application of the proposed method to content uniformity [17]

Content uniformity or the Uniformity of dosage unit was defined as the degree of uniformity in the amount of active substance among dosage units. The risk assessment strategy underlying content uniformity testing is the assumption that some pre-specified limits exist where safety and efficacy outcomes may change if content uniformity fails. The proposed method proved to be suitable for the content uniformity test, where a great number of assays on individual tablets are required. Data presented in table 5 indicate that the proposed method cans accurately and precisely quantitative of mefenamic acid in its commercially available tablets. The mean percentage (with RSD) of the labeled claim found in ten tablets was 100.1 (0.1176%) which fall within the content uniformity limits specified by the USP Pharmacopoeia [19].

Table 5: Content uniformity testing of mefenamic acid tablets using the Proposed method

Parameter	% of the label claim
Table No.1	100.13
Table No.2	99.97
Table No.3	100.20
Table No.4	100.20
Table No.5	99.96
Table No.6	100.10
Table No.7	99.98
Table No.8	100.20
Table No.9	100,21
Table N0.10	99.98
Mean(X)	100.093
%RSD	0.1176
Max. allowed unit value [18]	±15%

Conclusion

The spectrophotometric method proposed is simple, sensitive, rapid, low-cost, does not involve solvent extraction steps and gives precise and accurate results. The proposed method was successfully applied to analysis of mefenamic acid in tablets, capsules and environmental wastewater samples.

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