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Simultaneous Determination of Mefenamic Acid and Ethamsylate by Area Under Curve Spectrophotometric Method

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Abstract

The method for the simultaneous determination of Mefenamic acid and Ethamsylate by spectroscopy has been developed. The simple, accurate and precise method includes Area Under the Curve (AUC) method. From a solvent effect studies and the spectral behaviours of Mefenamic acid and Ethamsylate, methanol was selected as solvent. Mefenamic acid shows maximum absorbance at 337 nm and Ethamsylate shows maximum absorbance at 306 nm. For the AUC method, the wavelength ranges between. 337-344 nm and 300-306 nm were selected with reference to the absorbance curves plotted between the wavelengths of 200-400 nm. This method allows rapid analysis of two drug combination. The results of analysis were validated statistically and by recovery studies by following ICH method validation guideline. Tablet containing both drugs was assayed using the methods developed, showing a good accuracy and precision.

Keywords: Spectroscopy; Mefenamic acid; Ethamsylate; Area Under Curve Method;

INTRODUCTION

Ethamsylate (ETH); *2,5-Dihydrobenzene sulphonic acid* is haemostatic drug. It reduces capillary bleeding when platelets are adequate; exerts antihyaluronidase action-improves capillary wall stability but does not stabilize fibrin (not an antifibrinolytic). It inhibits PGI2 synthesis and hence promotes platelet aggregation. It has been used in the prevention and treatment of capillary bleeding in menorrhagia, after abortion, PPH, epistaxis, malena, hematuria and after tooth extraction.

Mefenamic acid (MEF); *N-(2,3-Xylyl)-2-aminobenzoic acid* is analgesic, antipyretic and weaker non-steroidal anti-inflammatory drug used as combination drug therapy for treatment of painful

menstruation. It inhibits COX and antagonises certain actions of PGs. It inhibits leukotriene level as well, by inhibiting phospholipase A2. It exerts peripheral as well as central analgesic action. [1,2]

Recently, the combination of MEF and ETH has demonstrated significant activity against painful menstruation.

The aim of this work is to develop a simple, rapid, selective and low cost method for the simultaneous determination of MEF and ETH by Area under Curve Spectrophotometric Method. For the individual determination of MEF and ETH the methods were available such as Area under Curve, Dual Wavelength and Simultaneous Spectrophotometer Methods, but for the combination of both the drugs the method was available which was Estimation of MEF and ETH by simultaneous equation and dual wavelength method. Hence this method was developed and validated for determination of MEF and ETH in tablets. The proposed method was applied in pharmaceutical formulations. [3,5]

MATERIALS AND METHODS

Experimental

Instruments

An UV-Visible double beam spectrophotometer (Varian Cary 100) with 10MM matched quartz cells was used for spectrophotometric measurements. All weighing were done on electronic balance (Model Shimadzu AUW-220D).

Reagents

Spectroscopy grade methanol was used through out the study. Pure drug sample of MEF and ETH were kindly supplied as a gift sample by Emcure Pharmaceuticals Pvt. Ltd. Pune, India. It was used without further purification. Tablets were purchased from local market; containing MEF 500 mg and ETH 500 mg. Tablet used for analysis were of brand Sylate-M form batch (Batch No. ECA09001) manufactured by Emcure Pharmaceuticals Pvt. Ltd. Pune, India and E-sylate M manufactured by Saf Fermion Ltd. Kolkata, India.

Preparation of Stock Solutions and Sample solution:

Stock solution of 100 µg/ml of both the drugs ware prepared separately in methanol. For verification of Beer`s Law, a series of diluted solutions of MEF and ETH ranging from 5-25 µg/mL (series A) and 5-25 µg/ml (series B), respectively were prepared and mixture of both the drugs in (series C) in same concentration range were prepared. [6,7]

Twenty tablets were weighed accurately and a quantity of tablet powder equivalent to 100 mg of MEF (100 mg of ETH) was weighed and dissolved in the 80 mL of methanol with ultrasonication for 5 min and solution was filtered through Whatman paper No. 41 into a 100 mL volumetric flask. Filter paper was washed with methanol, adding washings to the volumetric flask and volume was made up to the mark with methanol. The solution was suitably diluted further to get required final concentration 15 µg mL^{-1} of both the drugs.

Method

Area under curve method:

For the simultaneous determination using the area under the curve method, suitable dilutions of the standard stock solutions (100 µg/ml) of both the drugs were prepared separately. The solution of drugs ware scanned in the range of 200-400 nm. For Area Under Curve method, the sampling

wavelength ranges selected for estimation of MEF and ETH are 337-344 nm (λ_1-λ_2) and 300-306 nm (λ_3-λ_4). Mixed standard were prepared and their Area Under the Curve were measured at the selected wavelength ranges [8,9]. These were used to construct following equations which were used to calculate the concentration of two drugs in mixed standard and the sample solution.

$A_1 = 1800C_{MEF} + 1007.4\ C_{ETH}$……...(1) at 337-344 nm.
$A_2 = 1000C_{MEF} + 1999.13\ C_{ETH}$…….. .(2) at 300-306 nm.

Where,
1800 and 1007.4 are absorptivity values of MEF at (λ_1-λ_2) and (λ_3-λ_4) respectively.
1000 and 1999.13 are absorptivity values of ETH at (λ_1-λ_2) and (λ_3-λ_4) respectively.
A_1 and A_2 are absorbances of mixed standard at (λ_1-λ_2) and (λ_3-λ_4) respectively.
C_{MEF} and C_{ETH} are the concentrations in g/L.

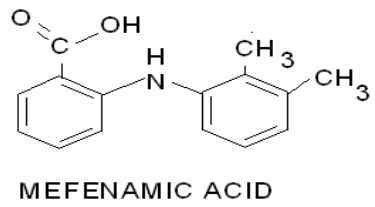
Recovery Studies
The accuracy of the proposed method was checked by recovery studies, by addition of standard drug solution to preanalysed sample solution at three different concentration levels (50 %, 100 % and 150 %) within the range of linearity for both the drugs. The basic concentration level of sample solution selected for spiking of the drugs standard solution was 6 µg /mL of both the drugs.

Solution stability: The solutions were found to be stable in methanol up to 12 hrs. Hence it does not showed any stability problems in methanol. Thus their %RSD were found to be <1.4

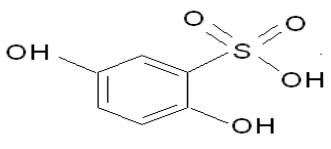
RESULTS AND DISCUSSION

Analytical features
Simple, precise and accurate Area under curve and dual wavelength methods were developed for the simultaneous estimation of MEF and ETH in combined dosage form.

For This Method Beer's law obeyed in the concentration range 5-25 µg/mL of both the drugs, respectively. Results of recovery studies are shown in Table 2. For MEF, the recovery study results ranged from 99.01% to 101.46 % with % RSD values ranging from 0.36% to 0.94 %. For ETH, the recovery results ranged from 98.51 % to 100.25 %, with % RSD values ranging from 1.05 % to 1.79 %. The accuracy and reproducibility is evident from the data as results are close to 100 % and standard deviation is low.



MEFENAMIC ACID



ETHAMSYLATE

Fig.I The chemical structures of Mefenamic acid and Ethamsylate

Spectral Behaviour:

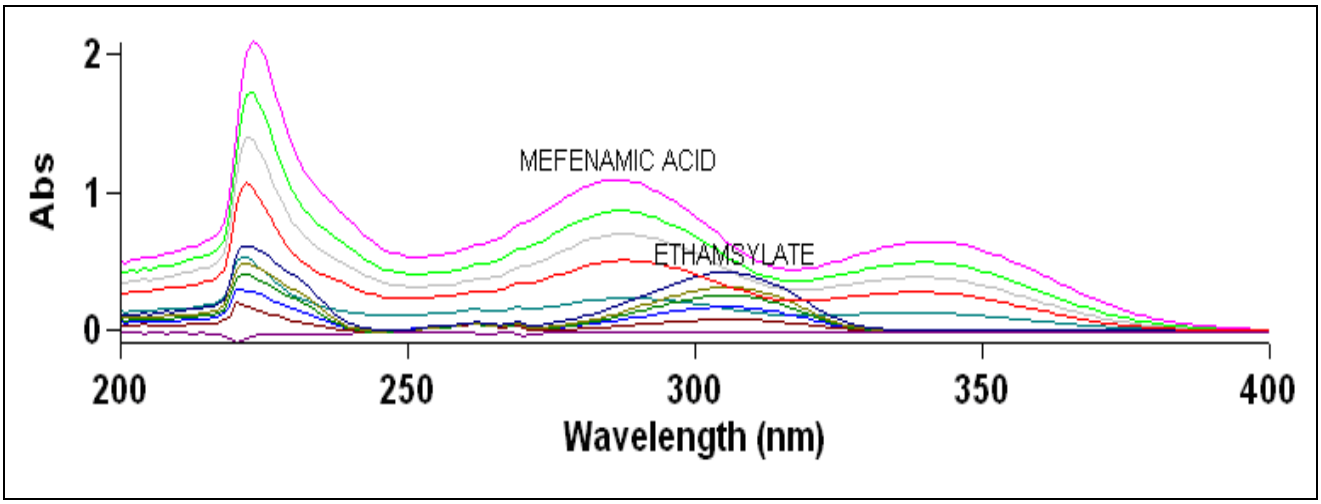


Fig II. Overlain spectra of Mefenamic Acid and Ethamsylate in the concentration range 5-25 µg/ml each in methanol.

Table I: Optical characteristics of the proposed method

Parameter			**Method A (AUC)**			
			Mefenamic acid	**Ethamsylate**		
λ (nm)			337 - 344	300 - 306		
Beer's law limit (µg/mL)			5 - 25	5 - 25		
RegressionEquation (y = mx + c)		Intercept (c)	-	-		
		Slope (m)	-	-		
Correlation Coefficient			-	-		
Accuracy (%Recovery) n=6			101.53	98.564		
Precision(n = 6)		Repeatability	0.46	0.56		
		Interday	0.35	1.02		
		Intraday	0.12	0.88		
		Analyst	0.68	0.92		
Result of recovery Study (Accuracy)	Level	Recovery of	Amount (µg mL^{-1})		% Mean Recovery (n=3)	% R.S.D.
			Spiked	Recovered		
	50 %	MEF	3.06	3.08	100.39	0.38
		ETH	3.04	2.98	98.75	1.05
	100 %	MEF	6.12	6.09	98.90	0.92
		ETH	6.08	6.06	99.90	1.72
	150 %	MEF	9.18	9.20	100.05	0.74
		ETH	9.12	9.11	99.93	0.93

Table II. Results of commercial formulation analysis

Formulation	Drug	Label Claim (mg/tablet)	% of Label Claim Estimated	% R.S.D. (n=6)
I (Sylate-M)	MEF	500	101.5	0.35
	ETHM	500	98.64	1.02
II(E-sylate M)	MEF	500	100.5	0.39
	ETHM	500	99.64	1.07

CONCLUSION

The validated spectrophotometric method employed here proved to be simple, economical, precise and accurate. Thus, this method can be used as IPQC test and for routine simultaneous determination of MEF and ETH in tablet dosage form.

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