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Two Wavelength Method for Estimation of Drotaverine Hydrochloride and Mefenamic Acid in their Combined Tablet Dosage Form

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Abstract: A new, simple, accurate and sensitive UV-spectrophotometric Two wavelength method has been developed for simultaneous determination of Drotaverine HCL and Mefenamic Acid in combined pharmaceutical dosage form. Two wavelength i.e. 240 nm and 277 nm were selected for estimation of Drotaverine HCL where as wavelength 233 nm and 253 nm was selected for estimation of Mefenamic Acid using Methanol solution as solvent . Drotaverine HCl and Mefenamic Acid shows linearity in the concentration range of 0-30 µg/ml and 0-30 µg/ml respectively. The method was validated statistically.
Keywords: Drotaverine HCl, Mefenamic Acid, Two wavelength method.

INTRODUCTION:

Drotaverine,1-(3,4-diethoxybenzylidene)-6,7-diethoxy-1,2,3,4-tetrahydroisoquinoline, is an antispasmodic drug, structurally related to papaverine. It is a selective inhibitor of phosphodiesterose 4 and has no anticholinergic effect. It is used in treating renal colic and has also been used to accelerate labor[1-4]

Few methods have been reported for the determination of Drotaverine in dosage forms and in biological fluids including, high performance liquid chromatography (HPLC)[5–8] thin layer densitometric[9] spectrophotometric[9–12] differential spectrophotometric[13,14] computer-aided spectro - photometric[15] and potentiometric[16–19] methods. Also Fulop[20] proposed a polarographic method for determination of Drotaverine in 1M H_2SO_4 at −420 mV in the range 4–80 µg and recently Ziyatdinova[21] proposed voltammetric method for determination of the drug by oxidation at a graphite electrode in 0.1 M H_2SO_4 at 1.05 and 1.28 V, but up to now nothing has been published concerning the adsorptive cathodic stripping voltammetric determination of this drug using HMDE.

Mefenamic acid (MF), *N*-(2,3-Xylyl) anthranilic acid, is a non-steroidal drug. It has analgesic and antipyretic properties. Mefenamic acid is used in musculoskeletal and joint disorders such as osteoarthritis and rheumatoid arthritis[22] the compound is almost insoluble in water but is readily soluble in organic solvents such as dioxane, alcohols and dimethyl formamide.[23]

MEF is official in BP and USP NF [24],[25]. Literature survey revealed that HPLC [26] methods have been reported for the estimation of Drotaverine HCl and Mefenamic Acid individually and with other drugs in pharmaceutical dosage forms. Literature review revealed that two spectrophotometric methods is yet reported for the simultaneous estimation of the DRO and MEF in combined tablet dosage form namely derivative and multicomponant spectrophotometric method. [27] Therefore, it was thought worthwhile to develop simple, precise, accurate Absorbance ratio method for simultaneous estimation of DRO and MEF in combined tablet dosage form.

MATERIAL AND METHOD:

Pharmaceutical grade DRO and MEF were supplied as a gift sample by Alkem Laboratory, Mumbai, (Maharashtra), India. The tablet dosage form (Drofem, Batch No. MAC 9094, Mfg. Dt. 09/09 and Exp. Dt. 08/2011) was procured from the local market (Label claim: 80 mg DRO and 250 mg MEF) marketed by FDC Limited, Aurangabad. All chemicals used were of HPLC grade and were purchased from Samar Chemicals, Nagpur, India.

PREPARATION OF STANDARD SOLUTION

Drotaverine Hydrochloride standard stock solution:

An accurately weighed quantity of DRO 2.5 mg was transferred to the 25 ml volumetric flask and dissolved in methanol and sonicate for 5 min. The volume was made up to the mark with methanol (100 µg/ml).

Mefenamic Acid standard solution

An accurately weighed quantity of MEF 2.5 mg was transferred to the 25 ml volumetric flask and dissolved in methanol and sonicate for 5 min . The volume was made up to the mark with the methanol (100 µg/ml).

Study of spectra and selection of wavelength:

The aliquot portions of stock standard solutions of DRO and MEF were diluted appropriately with solvent to obtain concentration 10 µg/mL of each drug. The solutions were scanned in the range of 400 – 200 nm in 1 cm cell against blank. The overlain UV absorbance spectrum of DRO and MEF is shown Fig no.1.

From the overlain spectrum shown in Fig.1, the wavelength selected for estimation of DRO was 240 nm and 277 nm, where as for MEF was 233 and 253 nm. The DRO and MEF obey Beer's law in the concentration range of 0 to 30 µg/ml and 0 to 30 µg/ml.

Quantitative estimation of these drugs was carried out by using following formulae's.

$$C_{DROTA} = \frac{A_{240} - A_{277}}{a_{240} - a_{277}} \quad \text{------ (1)}$$

$$C_{MEF} = \frac{A_{233} - A_{253}}{a_{233} - a_{253}} \quad \text{- ------- (2)}$$

A_{240} = Abs. of test solution at 240 nm ---- (1)
A_{277} = Abs. of test solution at 277 nm. ----(2)
A_{233} = Abs. of test solution at 233 nm ---- (3)
A_{253} = Abs. of test solution at 253 nm ----(4)
a_{240} = Absorptivity of DRO at 240 nm ----(5)
a_{277} = Absorptivity of DRO at 277 nm ----(6)
a_{233} = Absorptivity of MEF at 233 nm ----(7)
a_{253} = Absorptivity of MEF at 253 nm---- (8)

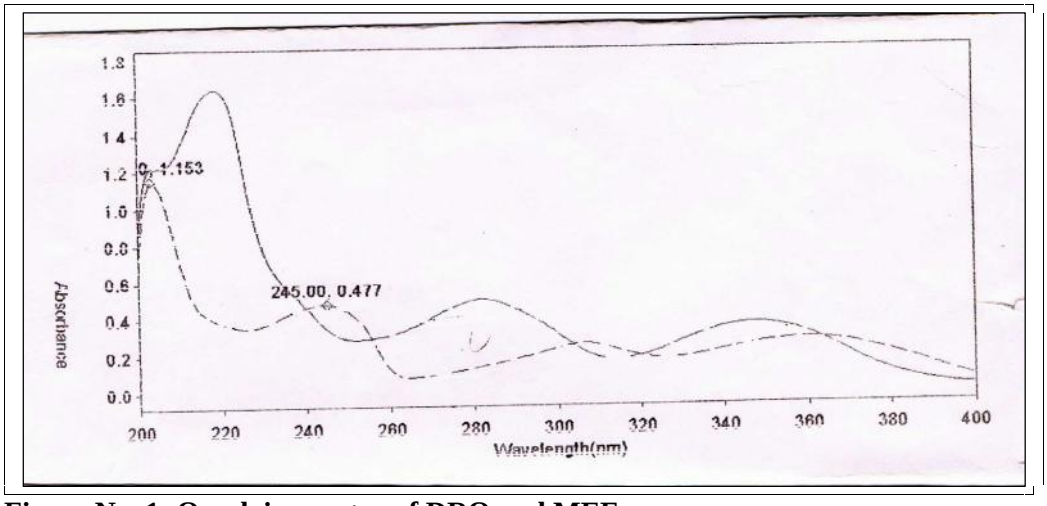

Figure No. 1: Overlain spectra of DRO and MEF

ESTIMATION OF DRUGS IN COMMERCIAL TABLET FORMULATION

Twenty tablets were accurately weighed. Average weight of tablet was calculated. The tablets were reduced to fine powder and mixed thoroughly. A quantity of tablet powder equivalent to weight of one tablet was transferred to 100 mL volumetric flask and dissolved in 25 ml of solvent Methanol and sonicate for 5 min. and volume was made to 100 mL with the same solvent to get final concentration of about 8 g/mL DRO and 25 g/mL MEF. The solution was filtered through Whatman filter paper no. 41.The absorbance of sample solution was measured at 233 nm, 240 nm ,253 nm and 277nm in 1 cm cell against blank.

VALIDATION

The proposed method was validated on the basis of parameters namely accuracy, precision, ruggedness and linearity and range. The accuracy of the proposed method was ascertained by carrying out recovery studies using standard addition method. The recovery study was performed to determine if there was any positive or negative interference from excipients present in the formulation. Precision of an analytical method is expressed as SD or RSD of a series of measurements. It was ascertained by replicate estimation of drug by the proposed method. Test for ruggedness was carried out by repeating the procedure under different conditions, i.e., on different days, at different time and by different analysts. Linearity and range study was done by preparing concentration in the range of 80 -120 % of test concentration and absorbance values were recorded at 233 nm, 240 nm , 253 nm and 277 nm The plot of linearity and range is shown in Fig. 2 & 3.

Table No.1: Result of estimation of DRO in tablet formulation
Brand name: DROFEM

Sr. No.	Wt. of tablet powder (mg)	Absorbance		% Label claim
		240 nm	277 nm	
1	58.32	0.869	0.659	99.7
2	58.70	0.872	0.657	99.5
3	58.20	0.868	0.655	100.1
			Mean	99.76
			± S.D.	0.3056
			C.V.	0.3063

Table No.2: Result of estimation of MEF in tablet formulation
Brand name: DROFEM

Sr. No.	Wt. of tablet powder (mg)	Absorbance at nm		% Label claim
		233	253	
1	58.32	0.825	0.616	99.7
2	58.70	0.829	0.619	99.4
3	58.20	0.825	0.619	99.8
			Mean	99.63
			± S.D.	0.2082
			C.V.	0.20898

Table NO. 3: Results of recovery studies of DRO

Sr. No	Weight of tablet powder (mg)	Amount Added In µg.	Absorbance		Amount Recovered in µg.	% Recovery
			240 nm	277 nm		DRO
1	58.62	0.8	0.957	0.723	0.79	99.4
2		0.8	0.957	0.724	0.79	99.5
3		1.6	1.043	0.789	1.58	99.2
4		1.6	1.045	0.797	1.59	99.7
5		2.4	1.129	0.851	2.37	99.1
6		2.4	1.131	0.854	2.39	99.6
					Mean	99.41
					± S.D.	0.231
					C.V.	0.233

Table NO. 4: Results of recovery studies of MEF

Sr. No	Weight of tablet powder	Amount Added in µg	Absorbance		Amount Recovered in µg	% Recovery
			233nm	253nm		
1	58.62	2.5	0.661	0.889	2.496	99.85
2		2.5	0.661	0.887	2.494	99.76
3		5	0.744	0.994	4.99	99.92
4		5	0.745	0.994	4.99	99.91
5		7.5	0.801	1.068	7.41	98.9
6		7.5	0.802	1.070	7.43	99.1
					Mean	99.573
					ïS.D.	0.4521
					C.V.	0.4541

Table NO. 5: Summary of result of Ruggedness studies

Parameter	Statistical data	Two wavelength method	
		MEF	DRO
Interday	Mean	99.60	99.76
	ïS.D.	0.3000	0.3512
	C.V.	0.3012	0.3521
Intraday	Mean	99.36	99.33
	ïS.D.	0.3512	0.4725
	C.V.	0.3535	0.4757
Different analyst	Mean	99.66	99.5
	ïS.D.	0.4022	0.5291
	C.V.	0.4056	0.5318

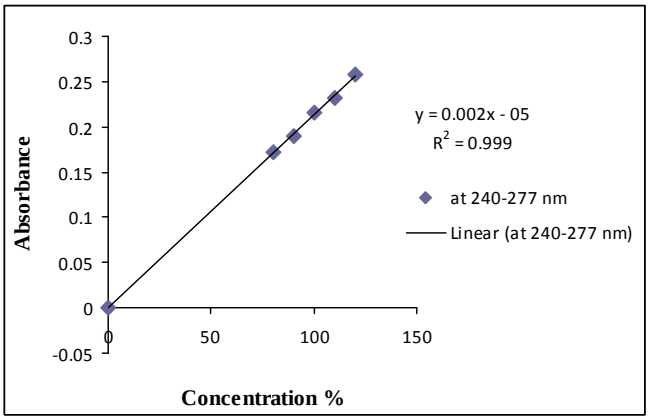

Figure No. 2: Plot of linearity and range for DRO

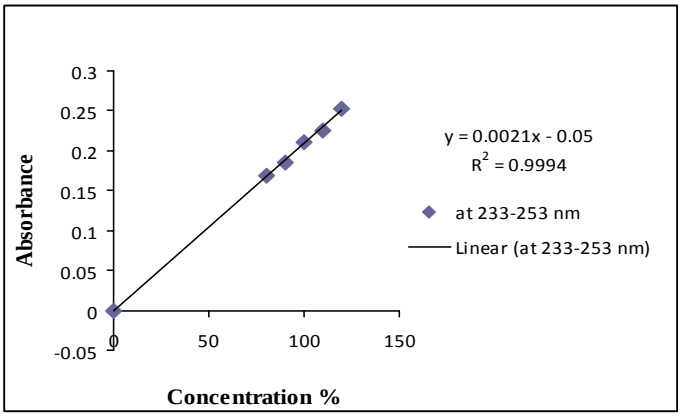

Figure No. 3: Plot of linearity and range for MEF

RESULTS AND DISCUSSION:

An attempt has been made to develop a simple, fast, sensitive, precise, reproducible and economical analytical method for simultaneous estimation of RIS and THP in their combined dosage form. In this method DRO and MEF obey Beer's law in the concentration range of 0 to 30 µg/ml and 0 to 30 µg/ml. It was observed that both the drugs showed additivity of absorbance at selected wavelengths indicating that both the drugs do not interact with each other in the solvent system used. The result of percentage estimation of drugs is shown in Table No.1& 2. The method was validated as per the ICH and USP guidelines. The results of recovery study were found to be within the prescribed limit of 98 - 102 %, proving the accuracy and showing that the method is free from interference from excipients. The results are shown in Table No. 3 & 4. For precision, replicate estimation of both DRO and MEF in the same batch of tablets was done by proposed method, which yielded quite concurrent results, indicating reliability of the method. The values of SD or RSD are within the prescribed limit of 2 %, showing high precision of the method, as shown in Table No.1 & 2. For ruggedness the proposed method was repeated under different conditions like different time, on different day and by different analyst. The results shown in Table No. 5, prove that the method is reproducible. During the linearity study it was observed that absorbance values of DRO and MEF in the marketed formulation were linear in the range of 80 % to 120 % of the test concentration with R^2 close to one for this method of analysis. From the study of validation parameters namely accuracy, precision (SD and RSD), ruggedness (interday, intraday and different analyst), linearity and range, it was observed that the method is specific, accurate, precise, reproducible and rugged. Hence, this method can be employed for routine analysis of tablet dosage form.

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