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Simultaneous Determination of Fexofenadine and Montelukast sodium by Zero-crossing First Derivative Spectrophotometry in Pharmaceutical Preparations

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Abstract : A first-derivative spectrophotometric method is described for simultaneous determination of fexofenadine (FEX) and Montelukast sodium (MON). All measurements are made at the zero-crossing wavelengths at 215.0 nm for FEX and 262.0 nm for MON. Calibration graphs were linear over the range 12.0-60.0 mg/l of FEX and 1.0-5.0 mg/l of MON. The relative standard deviation achieved were 3.4% for 20 mg/l of FEX and 4.2% for 3.0 mg/l of MON. The proposed methods were suitably applied to assay of pharmaceutical preparations.

Keywords: Derivative spectrophotometry, Fexofenadine, Montelukast sodium.

1. Introdution

Montelukast sodium and Fexofenadine hydrochloride were used in asthma, allergic reactions, allergies, allergen, allergic sinusitis, allergic cough. This is a real world study of montelukast Sodium, fexofenadine Hydrochloride drug interactions for a 26 year old female patient who has Asthma, Allergy to Animal Dander. Montelukast Sodium (MON) (Molecular Formula C35 35 l 3 leukotriene receptor antagonist (LTRA) H C NNaO S) is a used for the maintenance treatment of asthma and to relieve symptoms of seasonal allergies[1].

It is usually administered orally. Montelukast is a CysLT1 antagonist; that is it blocks the action of leukotriene D4 on the cysteinyl leukotriene receptor CysLT1 in the lungs and bronchial tubes by binding to it. Fexofenadine is indicated for the relief from physical symptoms associated with seasonal allergic rhinitis and treatment of chronic urticaria[2]. One such combination contains 10 mg of Montelukast Sodium and 120 mg of Fexofenadine hydrochloride.

Several methods were reported for quantitative determination of FEX and MON by various method such as voltametric[3], capillary electrophoresis[4], spectrophotometry[5,6] and HPLC method using various detectors[7]. The voltametric, capillary electrophoresis and spectrophotometry is very complicated and lengthy.

Derivative spectrophotometry opens up possibilities for increasing selectivity of the analytical methods without the need for prior separation and masking agents procedure[8]. It consists of calculating and plotting one of the

mathematical derivatives of a spectral curve. Most of the spectrophotometers are equipped with suitable software. On the other hand, the high solubilization capacity of surfactants and micellar systems permits modification or development of analytical procedures and improves the sensitivity and selectivity of the analytical methods[9]. In the proposed method, a simple, rapid, sensitive and selective method has been developed for simultaneous determination of fexofenadine and Montelukast sodium in mixtures by first derivative spectrophotometry using a zero-crossing technique.

2. Experimental

2.1. Reagents

All chemical and solvents were of analytical reagent grade and were used without further purification. A standard stock solution of FEX (1000.0 mg/l) was prepared by dissolving 0.1g of fexofenadine (Merck) in water and diluting with distilled water to 100.0 ml in volumetric flask. A standard stock solution of MON (1000.0 mg/l) was prepared by dissolving 0.1g of Montelukast (Merck) in water and diluting with distilled water to 100.0 ml in volumetric flask.

Titrazol buffers (Merck) were used at different pHs for this study.

2.2. Pharmaceutical Products

A commercial tablet product (fexofenadine ® tablet, Deva Pharm.Ind., Turkey, Batch no. 432-1775) is containing 180 mg FEX tablet, was studied .

The other commercial product that was studied (Montelukast capsule, Brown & Burk Ind., UK, Batch no. MON34E3) is containing 10 mg Montelukast per capsule.

2.3. Apparatus

All spectral measurements and treatment of data were carried out in 1cm quartz cells using a Perkin-Elmer Lambada 25 double beam spectrophotometer. Measurements of pH were made using a Jenway Model 3510 pH-meter equipped with a glass-saturated calomel combined electrode.

2.4. Procedure

Different volumes of stock solutions of FEX and MON (1000.0 mg/l) were used simultaneously and placed in a 10 ml calibrated flask and diluted with distilled water to gave final different concentration of FEX and MON.

First derivative spectrums of sample solutions were recorded against its blank in the wavelength rang of 200-300 nm with interval ($\Delta\lambda$=2nm) using scan speed of 960 nm/min and spectral slit width 2 nm. The first derivative analytical signals were at zero-crossing wavelength of 215 nm and 262 nm respectively, for FEX and MOn determination.

2.5. Analysis of Pharmaceutical Formulations

For preparation of sample, 20 tablets were accurately weighed and powdered in a mortar. A mass corresponding to a tablet was dissolved in 0.1 M HCl in 100 ml calibrated flask. After 30 min of mechanically shaking, the solution was filtrated in a 100 ml calibrated flask through Whatman no: 40 filter paper. The residue was washed three times with 10 ml solvent then the volume was completed to 100 ml with 0.1 M HCl and then was diluted 1:500 with water.

3. Results And Discussion

3.1 Spectrophotometric Measurements

In Fig.1 the zero-order spectra of 30.0 mg/l FEX , 4.0 mg/l of MON in the wavelength range of 200-400 nm are shown. FEX exhibits an absorbance maximum at 220 nm and for MON at 344 nm. As can be seen, there is a

clear overlapping of two spectra, which prevents the simultaneous determination of the two compounds by direct UV-Vis absorbance measurement. The pH of the solutions of FEX and MON varied. The results were obtained showed that the λ_{max} and sensitivity is not dependent on the pH range between 1.0 to 10.0.

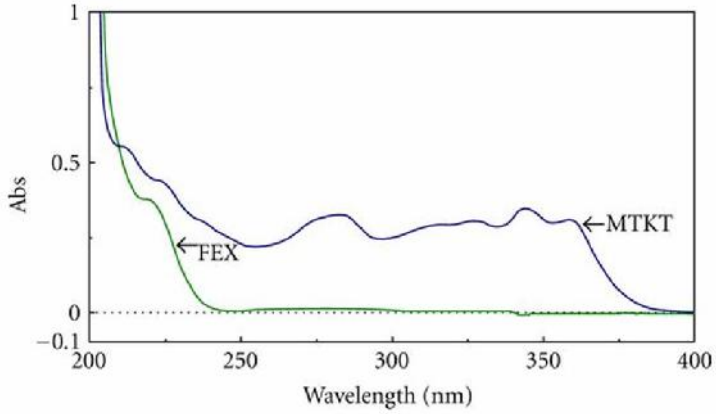

Fig.1: Absorption (zero-order) spectra of (A) 30.0 mg/l of FEX; (B) 4.0 mg/l of MON

A suitable technique for overcoming the problem is derivative spectrophotometry with the zero-crossing method being the most common procedure for preparation of analytical calibration graphs. In the zero-crossing derivative method, the measurements selected are those which exhibit the best linear response, give a zero or near zero intercept on the ordinate of the calibration graphs and it is necessary that zero-crossing wavelength do not change by varying concentration of related species. Zero-crossing method can not be used for determination of species which their spectra are shifted with change of concentration.

3.2. The Linear Plot (Calibration Curve)

First-order spectra of solutions containing fixed concentration of FEX (5.0 mg/l) and different concentration of MON (1.0-4.0 mg/l) are shown in Fig 2 and first-order spectra of solutions containing fixed concentration of MON (1.0 mg/l) and different concentration of FEX (10.0-20.0 mg/l) are shown in Fig 3.

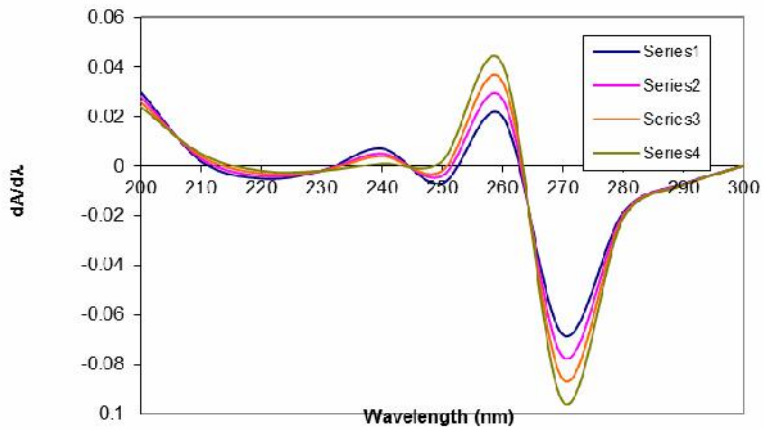

Fig 2: First derivative spectra of solution containing fixed 5.0 mg/l FEX and MOn concentrations (1)1.0 mg/l (2) 2.0 mg/l (3) 3.0mg/l (4) 4.0mg/.

As shown in Fig 2 and 3 has been seen that zero-crossing wavelengths do not change by varying concentration of the related species.

Two calibration graphs were constructed at the zero-crossing wavelengths (215 nm for FEX and 262 nm for MON) for the simultaneous determination of FEX and MON. In table 1 figures of merit of first derivative zero-crossing method for simultaneous determination of FEX and MON were shown.

The linear range of FEX and MON are 12.0-60.0 and 1.0-5.0 mg/l, respectively and detection limit were obtained 1.5 and 0.15 mg/l for FEX and MON, respectively. The relative standard deviation achieved were 3.4% for 20 mg/l of FEX and 4.2% for 3.0 mg/l of MON.

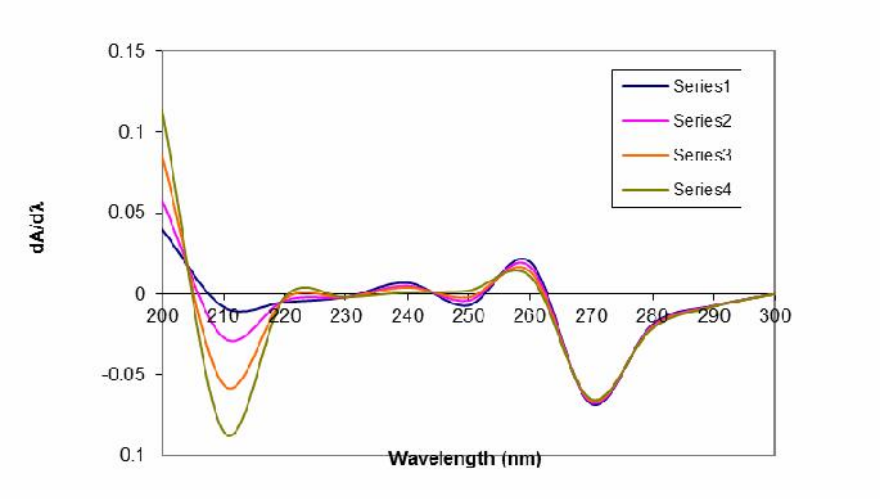

Fig 3: First derivative of solution containing fixed 1.0 mg/l FEX and MON concentrations of (1)10.0mg/l (2) 20.0mg/l (3) 30.0 mg/l (4) 40.0mg/l.

Table.1. calibration data for the determination of fexofenadine and montelukast sodium

Sample	Regression equation	λ (nm)	r	linear range (mg/l)	DL[a] (mg/l)	RSD
FEX	$dA/d\lambda=0.0023C_{FEX}-0.0066$	215	0.9987	12.0-60.0	1.5	3.4[b]
MON	$dA/d\lambda=0.0038C_{MON}-0.0064$	262	0.9972	1.0-5.0	0.15	4.2[c]

[a] detection limit (DL)=3sb/m
[b] concentartion of FEX=20.0 mg/L
[c] concentartion of MON=3.0 mg/L

3.3. Application

In order to confirm the usefulness of the proposed derivative spectrophotometric methods, it has been applied to the simultaneous determination of fexofenadine and montelukast sodium in different samples commercial pharmaceutical where excellent agreement between reported and obtained results was achieved (Table 2).

Table 2: Simultaneous determination of Paracetamol and Caffeine in real samples

sample	Reported		Obtained [a,d]		RSD%	
	FEX	MON	FEX	MON	FEX	MON
fexofenadine ® tablet	180.0	0.0	184.0±1.50	-	3.0	-
Montelukast capsule	0.0	10.0	-	11.5±0.14	-	3.5

[a] Mean ± standard deviation (mg) for four determination
[b] After dilution and determination by the proposed method

3.4. Conclusions

The proposed second-derivative method is suitable for simultaneous determination of FEX and MON without requiring a separation procedure. It is a simple, accurate and precise method which can be used, for rapid and reliable study of FEX and MON simultaneously in pharmaceuticals Products and can be used in the routine analysis of these compounds.

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