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SPECTROPHOTOMETRIC ESTIMATION OF RIFAXIMIN IN PURE AND TABLET DOSAGE FORM.

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ABSTRACT

Rifaximin is a newer antibiotic, used for the treatment of patients (more than 12 years of age) with travellers diarrhoea caused by noninvasive strains of Escherichia coli. In this study spectrophotometric methods have been developed for the determination of rifaximin in its tablet dosage forms. Two methods were developed, method A involving a visible spectroscopic method in double distilled water and method B involving a first derivative visible method in methanol. Analysis was performed at 437 nm and 474 nm for method A and B, respectively. Linearity ranges were found as 1 - 200 μg ml^{-1} for method A and 2 - 100 μg ml^{-1} for method B. Developed methods were validated and showed good precision and accuracy. The proposed methods were successfully applied to the assay of rifaximin in pure and tablet dosage form. No interference was found from tablet excipients at the selected wavelengths and assay conditions.

Keywords: Rifaximin, Visible Spectrophotometry, First Derivative Visible Spectrophotometry, Tablet Dosage Form.

INTRODUCTION

Rifaximin (RFX) is a benzimdazole derivative and chemically it is 2S, 16Z,18E, 20S, 21S,22R, 23R,24R, 25S, 26S, 27S, 28E-5,6,21,23,25-pentahydroxy- 27-methoxy-2,4,11, 16, 20,22, 24, 26, - octamethyl-2,.7-

(epoxypentadeca- [1,11,13] trienimino) benzofuro [4,5-e] pyrido[1,2-a]- benzimidazole-1,15(2H)- dione,25acetate. Rifaximin (Figure 1) is a newer antibiotic, used for the treatment of patients (more than 12 years of age) with travellers diarrhoea caused by noninvasive strains of Escherichia coli. RFX is a product of synthesis of Rifamycin, an antibiotic with low gastrointestinal absorption and good antibacterial activity. It acts on the beta–subunit of the deoxyribonucleic acid (DNA) dependent ribonucleic acid (RNA) polymerase enzyme of micro organisms to inhibit RNS synthesis.[1-2]

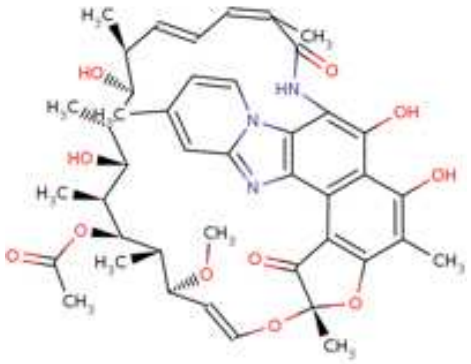

Figure 1 Chemical structure of Rifaximin

Methods for the determination of RFX in pharmaceutical formulations and biological materials which have been reported previously include LC-UV[3-4], LC-MS-MS[5], LC-ECD[6], 2D-LC-ESI/MS/MS[7] and two spectrophotometric determinations[8].

The main purpose of the present study was to establish a relatively simple, sensitive, validated and inexpensive spectrophotometric method for the determination of RFX in pure form and in pharmaceutical dosage form, since most of the previous methods have been found to be relatively complicated and expensive.

Two methods have been described for determination of Rifaximin in its pure and tablet dosage form. Method A is a simple visible spectrophotometric method using water (λ_{max}at 437 nm) and Method B is a first derivative spectrophotometric method using methanol (dA/dλ minima at 474 nm).

MATERIALS AND METHODS

A Shimadzu UV/VIS spectrophotometer 1800 was employed for all the spectral measurements. Double distilled water and methanol (AR grade- Merck Ltd.) were used as the solvent for the two methods, respectively. Gift sample of Rifaximin was obtained from Torrent Pharmaceuticals Limited, India. RCIFAX (Lupin) and TORFIX (Torrent) each containing 200 mg of RFX per tablet were purchased from local market.

METHODOLOGY

According to the solubility characteristics of drug, the drug was initially dissolved in methanol and further dilutions were made with double distilled water (Method A) and methanol (Method B). Standard stock solution (1000µg/ml) of RFX was prepared in methanol.

The method was extended for determination of RFX in tablet dosage forms. Twenty tablets were weighed and powdered. The tablet powder equivalent to 100 mg of RFX was transferred into 100 ml volumetric flask containing 50 ml of methanol and flask was kept for ultrasonication for 5 min, then it was diluted up to the mark with distilled water and the solution was filtered through Whatman filter paper No. 41. From the above solution 10 ml was pipette out into a 100 ml volumetric flask and the volume was made up to the mark with double distilled water for method A and methanol for method B and used for the analysis.

METHOD A

Aliquots of RFX (1 – 200 µg/ml) were prepared taking 0.01 – 2.0 ml from the stock solution of RFX in 10 ml volumetric flasks and making up the volume with double distilled water. Two of the dilutions, i.e. of 10µg/ml and 20µg/ml were scanned over the entire visible range against the reagent blank (Figure 2) and the detection wavelength was fixed at the λ_{max}, i.e. 437 nm. Calibration curve was prepared by plotting concentration versus absorbance at 437 nm. Similarly, absorbance of sample solutions of the formulations were measured at 437 nm and the amount of RFX was determined from the regression equation of the standard calibration curve.

METHOD B

Aliquots of RFX (2 – 100 µg/ml) were prepared taking 0.02 – 1 ml of the stock solution in 10 ml volumetric flasks and making up the volume with methanol. Two of the dilutions, 10 and 20 µg/ml were scanned over the wavelength region 400 – 600 nm. The spectrum obtained was transformed to first order derivative spectrum (Figure 3). The maxima, minima and the zero crossing point were found out to be at 417, 474 and 450 nm respectively. The minima values (at 474 nm) were used for the estimation. Calibration curve was prepared by plotting concentration versus dA/dλ at 474 nm and was found to be linear in the range 2 - 100 µg/ml. Similarly, the amount of RFX in the sample solution of formulation was determined from the regression equation of the standard calibration curve.

RESULTS AND DISCUSSION

The calibration curve was obtained for a series of concentration in the range of 1 -200 µg/ml for method A and in the range of 2 - 100 µg/ml. It was found to be linear and hence, suitable for the estimation of the drug. The optical characteristics were summarized in Table 1. Regression analysis of Beer's law plot revealed a good correlation. The effects of various excipients generally present in the tablet dosage forms of RFX were investigated. The recovery from the formulation (Table 2) was found to be 98.48 - 99.28 for method A and 99.59 – 100.40 for method B. The proposed methods were validated as per the ICH guidelines[9-11]. The precision was measured in terms of repeatability, which was determined at three levels (10, 50 and 100 µg/ml)\and the % RSD were found to be less than 2.0 (0.6 – 1.51%) showing that the method is more precise. The accuracy study was conducted by adding known quantities of the standard RFX solution (80%, 100% and 120%) to a particular concentration of pre-analyzed formulations and the mixtures were analyzed and the % recovery values were found to be within the range of 98.27 – 100.83 % (% RSD = 0.76 – 0.93 %). This showed that the recovery of RFX by the proposed method is satisfactory. Ruggedness and Robustness were determined and the % RSD values were found to be less than 2.0. Thus it can be concluded that the methods developed in the present investigation are simple, sensitive, accurate,

rapid and precise. Hence, the proposed methods can be successfully applied for the estimation of Rifaximin in tablet dosage forms.

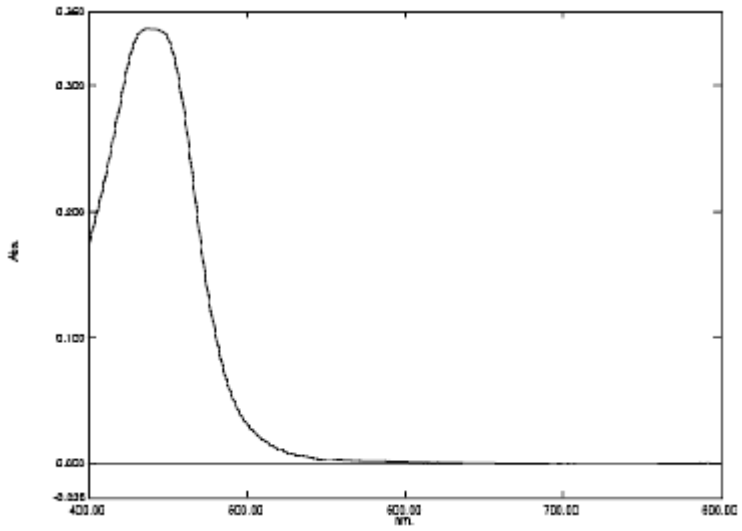

Figure 2. Visible Absorption Spectrum of Rifaximin (20 µg/ml) in water (λ_{max} 437nm) [Method A]

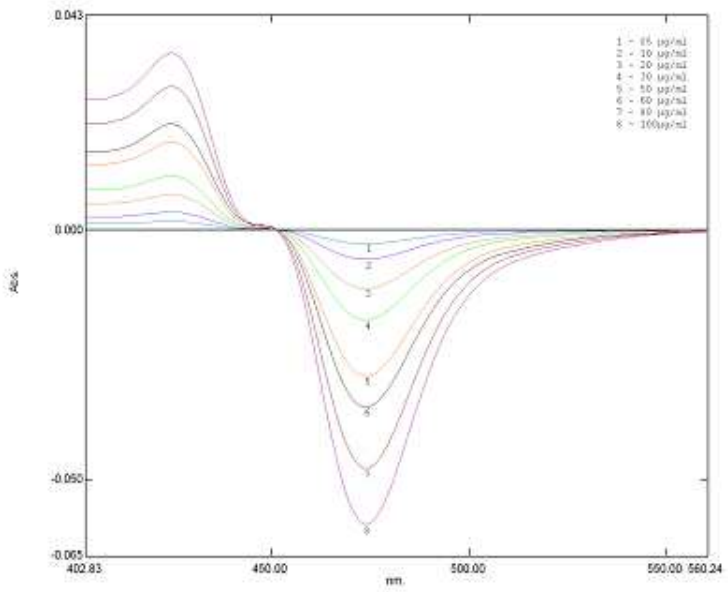

Figure 3. First Derivative overlain spectra of Rifaximin in Methanol (Minima at 474nm) [Method B]

Table-1: Optical Characteristics.

Parameters	Method A	Method B
λ_{max} (nm)	437	474
Linearity range (µg ml^{-1})	1 – 200	2 – 100
Sandell's sensitivity (µg/cm^2/0.001 absorbance unit)	6.02 x 10^{-2}	5.2 x 10^{-2}
Molar extinction coefficient (litre $mole^{-1}$ cm^{-1})	1.304561 x 10^4	1.499 x 10^4
Regression equation	y = 0.0165x + 0.0027	y = 0.00059x + 0.00008
Slope	0.0165	0.00059
Intercept	0.0027	0.00008
Correlation coefficient (r^2)	0.9995	0.9998

Table-2: Recovery Studies.

Brand Name	Labeled amount (mg)	Amount found(mg)		% Recovery	
		Method A	Method B	Method A	Method B
RCIFAX	200	198.56	199.18	99.28	99.59
TORFIX	200	196.96	200.08	98.48	100.04

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