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QUANTIFICATION OF RIFAXIMIN IN BULK AND PHARMACEUTICAL DOSAGE FORM BY VALIDATED VISIBLE SPECTROPHOTOMETRIC METHODS

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ABSTRACT

Two simple sensitive and precise colorimetric methods A and B were developed for the estimation of Rifaximin in bulk drug as well as in pharmaceutical dosage form. Method A is based on the formation of yellow colored chromogen by condensation reaction of Rifaximin with Isoniazid which has absorption maximum at 456nm. Method B is based on the formation of an orange colored complex by oxidation reaction of Rifaximin with 1,10-phenanthroline in the presence of ferric chloride which has absorption maximum at 510nm. The proposed methods are statistically validated and found to be useful for the routine determination of Rifaximin in tablets.

KEYWORDS: Rifaximin, Colorimetry, Tablets, Validation.

INTRODUCTION

Rifaximin (RFX) is an oral antibiotic with broad spectrum of action that acts locally in the gastrointestinal tract with minimal systemic adverse effects. It is practically not absorbed and reaches high concentrations in the human intestine, where it is active against many enteropathogens. Chemically Rifaximin is 2S,16Z,18E,20S,21S,22R, 23R,24R,25S,26S,27S,28E-5,6,21,23,25 pentahydroxy27- methoxy-2,4,11,16,20,22,24,26 octa- methyl -2,7-epoxypentadeca-[1,11,13] trienimino) benzofuro [4,5-e] pyrido [1,2 benzimidazole 1,15(2H)-dione,25-acetate.[1] The empirical formula is $C_{43}H_{51}N_3O_{11}$ and its molecular weight is 785.9. It acts by binding to the β −subunit of bacterial DNA dependent RNA polymerase resulting in inhibition of bacterial RNA synthesis and bacterial growth.[2] Rifaximin is used as an antibiotic for the treatment of traveler's diarrhea and irritable bowel

syndrome.[3] Rifaximin does not have spectrophotometric method in the ultraviolet region described in official compendiums. In the literature, an article which describes a spectrophotometric method in the ultraviolet region has been found[4] and also chromatographic methods like HPLC,[5] HPLC-TMS[6] and determination of rifaximin by LC-ESI-MS in human plasma.[7] In the present work, Method A involves the condensation of RFX with Isoniazid to form a yellow chromogen, which absorbs intensively at 456nm. In method B, RFX forms an orange colored complex with 1,10-phenanthroline and ferric chloride which exhibited λ_{max} at 510nm. The method is alternative and comparable in specificity and accuracy to chromatography methods, which although highly specific and accurate, are more time consuming, performed in several steps and are rather expensive. The proposed analytical methods were validated as per ICH guidelines.[8]

MATERIALS AND METHODS

Instrumentation: All spectral and absorbance measurements were made on UV-Visible spectrophotometer model-LMSP-UV 1900s.

Reagents

Isoniazid-2%w/v

Ferric chloride-1% w/v

1,10-phenanthroline-2%w/v

Preparation of standard solution

A 1 mg/ml stock solution of RFX was prepared by dissolving 100 mg of drug in 100 ml of ethanol.

Sample preparation

Twenty tablets were weighed and powdered. A quantity equivalent to 25 mg of RFX was weighed accurately, transferred to a beaker, dissolved in ethanol, filtered through whatmann filter paper No. 1 into a 50 ml volumetric flask and made up to volume with ethanol to get a concentration of 1mg/ml.

Assay

Method A

Appropriate aliquots of RFX were pipetted out into a series of 10 ml volumetric flasks. To each flask 2 ml of Isoniazid was added, mixed thoroughly and made up to volume with ethanol. The λ_{max} of the yellow coloured chromogen was found to be 456nm (Figure-1). The

absorbance of the yellow coloured chromogen was measured at 456 nm against the reagent blank. The calibration curve was constructed by plotting concentration versus absorbance.

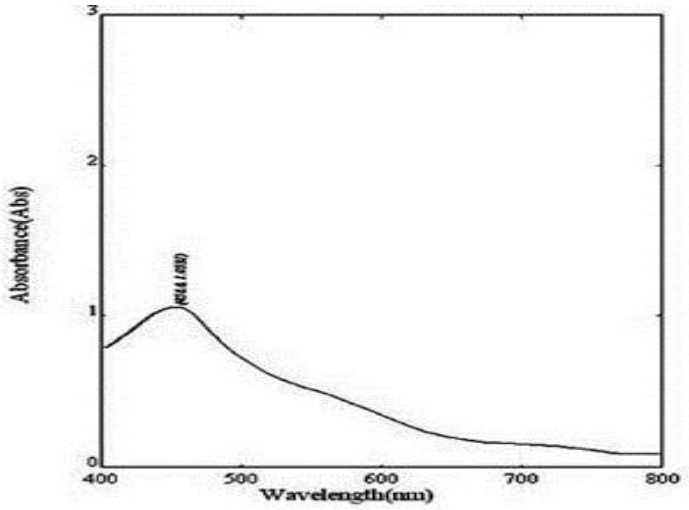

Figure 1: λ_{max} of RFX by Method – A.

Method B

Appropriate aliquots of RFX were pipetted out into a series of 10 ml volumetric flasks. To each flask 1 ml of ferric chloride and 2ml of phenanthroline were added, heated on a boiling water bath for 15 minutes, cooled and then made up to volume with ethanol. The λ_{max} of the orange colored chromogen was found to be 510nm (Figure-2). The absorbance of the orange colored chromogen was measured at 510 nm against the reagent blank. The amount of RFX was computed from the calibration curve obtained by plotting concentration versus absorbance.

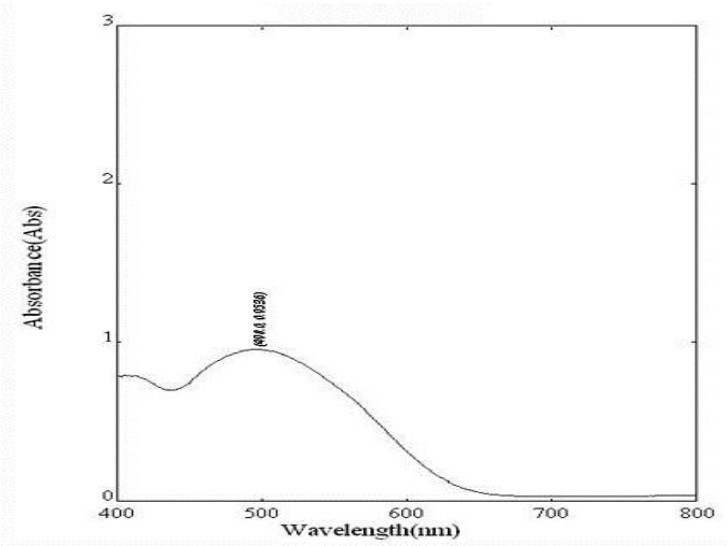

Figure 2: λ_{max} of RFX by Method – B.

Sample Analysis

Pharmaceutical formulation of RFX was successfully analyzed by the proposed methods. Appropriate aliquots were subjected to the above methods and the amount of the RFX was estimated. The results of sample analysis are furnished in table- 2.

RESULTS AND DISCUSSION

The optical characteristics such as absorption maxima, Beer's law limits, Molar absorptivity and Sandell's sensitivity are furnished in table-1. The regression characteristics like slope (b), intercept(a), correlation coefficient(r), percent relative standard deviation(%RSD) and standard error (SE) obtained from different concentrations were calculated and the results are summarized in table-1.

To study the accuracy and reproducibility of the proposed methods, recovery experiments were carried out by adding a known amount of drug to pre-analyzed sample and the percentage recovery was calculated. The results are furnished in table-2. The results indicate that there is no interference of other ingredients present in the formulation. Thus, the proposed methods are simple, sensitive, precise, accurate and reproducible and useful for the routine determination of RFX in bulk drug and its pharmaceutical dosage form.

Table 1: Optical Characteristics, Precision and Accuracy of the proposed methods.

Parameter	Method A	Method B
λ_{max} (nm)	456nm	510nm
Beer's law limit(µg/ml)	50 – 150	5-30
Molar absorptivity ($Lmol^{-1}cm^{-1}$)	$2.104* 10^3$	$2.788*10^3$
Sandell's sensitivity (µg/cm²/0.001 absorbance unit)	0.0023	0.03715
Regression equation(*y)		
Slope(b)	0.012718	0.002666
Intercept(a)	0.038792	0.002286
Correlation co-efficient (r)	0.999628	0.999988
% RSD	0.038	0.021
Standard error(SE)	0.0612	0.0345

*y = a+bc where c is the concentration of RFX in µg/ml.

Table 2: Assay and Recovery of RFX in dosage form (Tablets).

Method	Labelled amount (mg)	Amount obtained (mg)*	Percentage recovery**
A	400mg	399.38mg	99.98
B	400mg	398.8mg	98.99
**Average of six determinations*		*** Average of three determinations*	

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