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Method Development and Validation of Spectrophotometric Method for the Estimation of Febuxostat in Pure and Tablet Dosage Form

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Spandana R*, Pushpa Latha E, Jenny susmitha

Department of Pharmaceutical Analysis & Quality Assurance,
Creative Educational Society's College of Pharmacy,
Chinnatekur, Kurnool - 518218,
Andhra Pradesh - 518218, India.

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ABSTRACT

The present research work discusses the development of UV Spectroscopic method for the estimation of Febuxostat. Simple, specific, accurate and cost effective spectroscopic method has been developed for the estimation of Febuxostat in bulk as well as formulation. The optimum conditions for the analysis of the drug were established. The maximum wavelength (λ_{max}) was found to be 314nm. The validation was performed as per ICH guidelines for linearity, accuracy, precision, LOD and LOQ. The method shows high sensitivity with linearity in the range of 1-6 µg/ml and a linear relationship between the absorbance and concentration with coefficient of correlation 0.999. The regression of curve was Y = 0.06233x + 0.01631. The precision of method was found to be good. The percentage recovery was found to be 99.25 ± 0.0684. The optimization showed good reproducibility and recovery with RSD <2%. The proposed method will be suitable for analysis of Febuxostat in bulk as well as pharmaceutical formulations in quality control purpose. It is thus concluded that the proposed method is new, simple, cost effective, safe, accurate, precise and environment friendly.

INTRODUCTION

Febuxostat is used as xanthine oxidase inhibitor which works by blocking an enzyme in the body (xanthine oxidase), which lowers levels of uric acid in the blood. This helps to prevent gout flare-ups [1]. Chemically it is 2-(3-Cyano-4-isobutoxyphenyl)-4-methyl-1,3-thiazole-5-carboxylic acid [2]. It is available as white crystalline powder which is freely soluble in di methyl formamide, soluble in dimethyl sulfoxide, sparingly soluble in ethanol, slightly soluble in methanol & acetonitrile, practically insoluble in water [3]. Several methods have been reported for the quantitative determination of Febuxostat which includes UV [4-6], HPLC [7-12], Stability indicating LC method [13-15], related substances LC method [16, 17], bioanalytical method using LC [18], LC-MS [19-22], HPTLC [23]. Several methods have been reported in literature for the determination of Febuxostat in the presence of other drugs which includes UV [24-29], HPLC [30, 31], bioanalytical method using LC [32]. The aim of present work was to develop simple, sensitive, specific spectrophotometric method for detection of Febuxostat in bulk as well as pharmaceutical formulation.

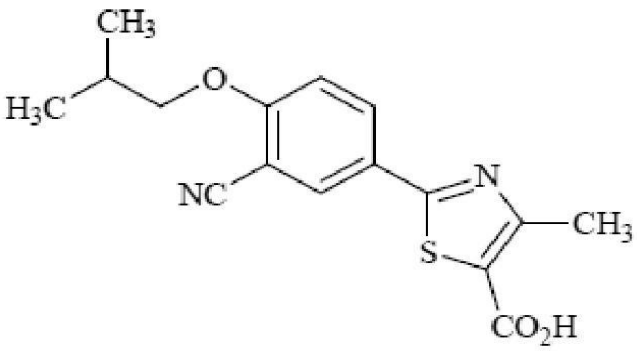

Figure 1: Structure of Febuxostat

MATERIALS AND METHODS

Equipment and reagents

A Labindia model 3000+ double beam UV-Visible Spectrophotometer with two matched cuvette cells of one cm light path were used for the measurement of absorbance. The Febuxostat bulk drug was kindly gifted by Chiral Biosciences Ltd., Hyderabad. The pharmaceutical dosage form was procured from market. 0.1N NaOH was used for the study.

Preparation of standard stock solution

Accurately weighed 10mg of Febuxostat was transferred into 10ml volumetric flask volume was made up to 10ml with 0.1N NaOH to get a concentration of 1000µg/ml and filtered through the Whatman filter paper no. 41.

Determination of λ_{max}

From the stock solutions, 1.0ml of Febuxostat was transferred to 100ml volumetric flask and the volume was adjusted to the mark with distilled water to obtain strength of 10µg/ml. The solution was scanned in the UV range 200-400 nm**. (Figure 2).**

Construction of calibration curve

Calibration curve was plotted against concentration and absorbance, regression equation was computed. The results tabulated in the Table 1.

Preparation of sample solution

Twenty tablets were weighed, average weight determined and crushed into fine powder. An accurately weighed quantity of powder equivalent to 10mg of Febuxostat was transferred into 10ml volumetric flask containing 3ml 0.1N NaOH, shaken manually for 10min., volume was adjusted to mark with same solvent and filtered through Whatmann filter paper no. 45. An appropriate aliquot was transferred to 10ml volumetric flask, volume was adjusted to the mark and absorbance was recorded at 314nm.

METHOD VALIDATION

The proposed method was validated as per the ICH Q2 (R1) guidelines for linearity, accuracy, precision, LOD and LOQ.

Accuracy

Accuracy was carried out at 80%, 100% and 120% of target concentration. From the amount found, percentage recovery was calculated.

Precision

Precision of the method was studied by carrying out intraday, interday analysis and expressed as percentage Relative Standard Deviation. For this purpose 2µg/ml (LQC), 4µg/ml (MQC) and 6µg/ml (HQC) solutions were prepared and the absorbances of the solutions were measured for six times within the same day and in different days at 314nm against blank.

Limit of Detection (LOD) and Limit of Quantization (LOQ)

LOD and LOQ of the drug were calculated using the following equations according to International Conference on Harmonization (ICH) guidelines:

$$LOD = 3.3 \times \sigma/S$$

$$LOQ = 10 \times \sigma/S$$

Where σ = the standard deviation of the response and

S = the slope of the regression equation.

RESULTS AND DISCUSSION

The proposed method for determination of Febuxostat in marketed formulation (tablet) showed Sandell's sensitivity of 0.0133µg/cm^2/0.001 absorbance units. Linear regression of absorbance on concentration gave the equation y = 0.0623x + 0.0163 with a regression co-efficient (R^2) of 0.999 and the linearity range was 1- 6µg/ml. The higher percentage recovery value (95-105%) indicates that there is no interference of the excipients present in the formulation. Thus the method is useful for the determination of Febuxostat in bulk and pharmaceutical formulations.

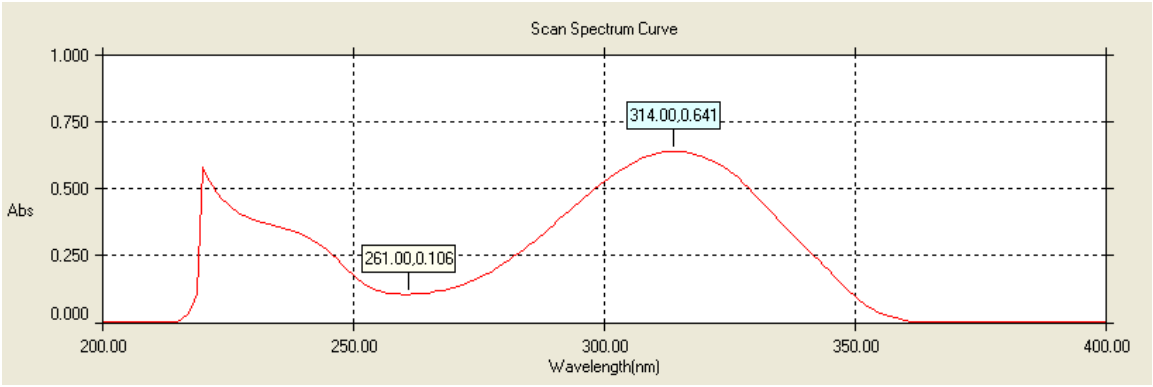

Figure 2: UV Spectrum of Febuxostat

Table 1: Calibration of Proposed Method

S.NO.	Conc. (mcg / ml)	Absorbance at 314 nm
1	1	0.075
2	2	0.143
3	3	0.205
4	4	0.265
5	5	0.333
6	6	0.385

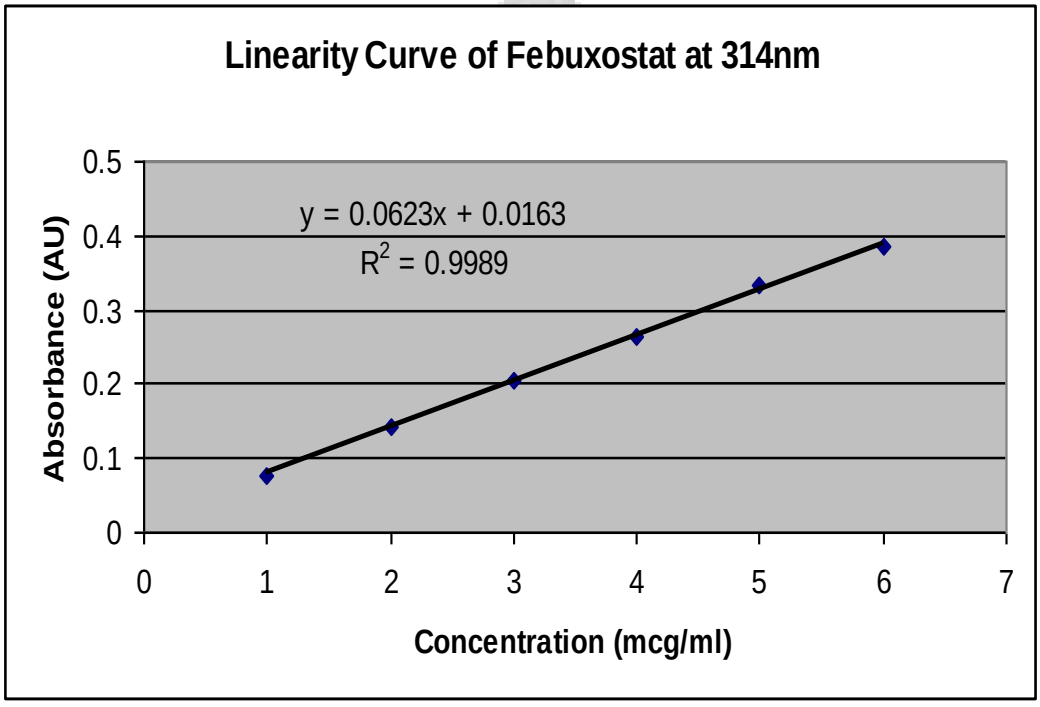

Figure 3. Calibration Curve of Febuxostat at 314nm

Table 2. Optimum Conditions, Optical Characteristics and Statistical Data of the Regression Equation in UV Method

Parameter	UV method
λ_{max} (nm)	314
Beer's law limits (mcg / ml)	1-6
Sandell's sensitivity (mcg / cm^2-0.001 absorbance units)	0.0133
Regression equation (Y*)	y =0.0623x+0.0163
Slope (b)	0.0623
Intercept (a)	0.0163
Correlation coefficient(r^2)	0.999
% RSD**	< 2%
Limit of detection (mcg / ml)	0.176
Limit of quantitation (mcg / ml)	0.534

*Y=bX + a where X is the concentration of Febuxostat in mcg/ml and Y is the absorbance at the respective $\lambda_{max.}$

**Average of six determinations

Table 3. Assay of Febuxostat formulation

S.No	Formulation	Label claim (mg/tab)	Amount found (mg) (n=3) Mean ± SD	Assay	%RSD
1	**Febula**	40mg	40.35± 0.0346	100.88	0.085

Table 4. Determination of Accuracy Results for Febuxostat

Brand name	Amount of sample (mcg / ml)	% of Spiked sample	Amount of drug added (mcg / ml)	Amount Recovered	% Recovery ± SD
Febula	2	80	1.6	3.54	98.33 ± 0.0843
Febula	2	100	2	3.95	98.75 ± 0.0672
Febula	2	120	2.4	4.43	100.68 ± 0.0537

Table 5. Determination of Precision Results for Febuxostat

Conc. mcg / ml	Inter-day Absorbance Mean ± SD**	% RSD	Intra-day Absorbance Mean ± SD**	% RSD
LQC (2mcg/ml)	0.145± 0.000577	0.397	0.143 ±0.000389	0.272
MQC (4mcg/ml)	0.263± 0.000488	0.186	0.264±0.000931	0.352
HQC (6mcg/ml)	0.384±0.000872	0.227	0.385±0.000749	0.194

**Average of six determinations.

CONCLUSION

A simple, sensitive, accurate and precise UV spectrophotometric method has been developed for quantitative determination of Febuxostat in bulk and Pharmaceutical dosage form (tablet). The UV spectrum was scanned between 200 to 400nm and 314nm was selected as maximum wavelength for absorption. Beer's law was obeyed in the concentration range of 1–6µg/ml. % Recovery was calculated, was found to be 98.33 – 100.68 and the method was successfully applied to the pharmaceutical dosage form containing the Febuxostat drug without any interference by the excipients. The method was fast and economical and it was also selective and

sensitive for the desirable range. Results of the analysis were validated as per ICH guidelines and by recovery studies.

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