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Determination of Febuxostat by Complexation with Mercury (Hg II) Ions Using Spectrophotometry

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A B S T R A C T

A simple, sensitive and accurate Colorimetric method was described for the determination of Febuxostat (FBX) an antigout drug. The method is based on yellow coloured chelate formation between [FBX and Mercury (HgII)] in alkaline medium. The complex showed an absorption maximum at 510nm with apparent molar absorpitivity of 4.62×10^4 $L\text{-}M^{-1}Cm^{-1}$.The solution of the complex obeyed beer's law in the concentration range of 5-30 µg/ml . The limit of detection and Limit of quantification were calculated and RSD were calculated. The chelate composition between [FBX and Hg (II)] ion was found to be 2:1 ratio determined by Job's continuous method and by Molar ratio method. The proposed method was applied for the determination of FBX in tablets without interference from common excipients. The results obtained by the application of this procedure showed percentage recoveries were 99.8±0.15.

Keywords: Febuxostat, Chelate, Alkaline media, Colorimetric

A R T I C L E I N F O

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1. Introduction

Febuxostat is chemically 2-(3-cyano-4-isobutoxyphenyl)-4 methyl-1, 3-thiazole-5-carboxylic acid. The molecular mass of Febuxostat (C16H16N203S) is 316.374gm/mol. Febuxostat is a urate lowering drug, a non-purine selective inhibitor of xanthine oxidase that is indicated for use in the treatment of hyperuricemia and chronic gout .It works by

non-competitively blocking the molybdenum pterin centre which is the active site on xanthine oxidase. Febuxostat is not official in Indian pharmacopeia, the literature studies of Febuxostst was determined and approved certain analytical methods of RP-HPLC development and validation, UV visible spectrophotometric methods of simultaneous result of optimizing the parameters of accurate, precision, simple, linearity in both bulk drug formulations and combined dosage forms. Assay of drug has also been performed and have been reported.

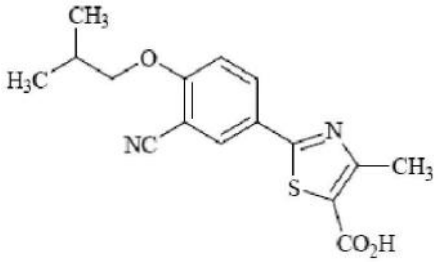

Figure 1: Structure of Febuxostat

2. Experimental

Apparatus: All absorption Spectra were made using ELICO U.V-VIS Spectrophotometer equipped with 10mm matched Quartz cells.

Materials and reagents:

0.271 gm of Mercuric Chloride (AR, Merck Ltd) was dissolved by adding double distilled water and diluted by using double distilled water in 100ml standard flask and standardized.

Standard stock solution was prepared by dissolving 317 mg of Febuxostatin dimethyl sulphoxide. The volume was made upto 100 ml with DMSO to get a concentration of $1X10^{-3}$M. 0.1 N Sodium Hydroxide**:** 4gm of sodium hydroxide is dissolved in 1000ml of distilled water

Determination of absorption maxima for drug metal chelate: Aliquots of standard drug solution of Febuxostat 1ml were taken and transferred into 10ml of volumetric flasks to each flask 2 ml of 0.1N sodium hydroxide and 1-3ml of metal ion solution were added. The flasks were shaken for 10 minutes. The absorbance of the yellow colored chromogen was measured against reagent blank .The absorption maxima of the drug metal chelate was found to be 510nm.(Figure No:1)

Procedure for dosage form: An accurately weighed amount of finely powdered tablet equivalent to 317mg of drug was dissolved in about 10ml of dimethyl sulphoxide and transferred in to 100ml of calibrated volumetric flask after 15minutes of mechanical shaking was filtered into a 100ml of calibrated volumetric flask through Whatmann no: 41 filter paper, diluted to 100ml with DMSO and the same procedure was followed as described above.

Optimum conditions

Effect of pH: To arrive the optimum pH required for achieving the maximum and constant absorbance, the effect of pH on the absorbance of the mercury (II)-CP complex was studied by employing in a set of 10-ml standard flasks, 2 ml of acid, base, buffer of pH 7.4 solution, constant amount of drug and metal ion (usually 20- 30 fold molar excess to drug) solution were taken, made up to the mark with distilled water. The absorbance of each solution (metal complex) was measured at a selected wavelength (λ_{max}) against corresponding reagent blank prepared accordingly. A plot was made between absorbance and pH from which the working pH was selected. The complex shows high absorbance values in alkaline medium and all the absorbance values were found to be constant in alkaline medium.

Effect of metal ion concentration:

To 1ml of $1x10^{-3}$ M FBX stock solution, aliquots of 1.0 to 5ml of $1x10^{-2}$M metal ion solution was added into 10 ml Volumetric flask and make up to the volume to 10ml with distilled water and the absorbance values at 510nm were noted. Investigation of metal ion concentration revealed that only thirty-fold molar excess of reagent was sufficient for optimum and maximum colour intensity of the chelate of FBX using 31.7µg/ml concentration.

Effect of time:

The absorbance of [FBX-Hg (II)] complex was measured at different time intervals to ascertain the time stability of the complex. The full colour development of the complex remains constant for twenty four hours. Then the absorbance of [FBX-Hg (II)] complex was measured at 510 nm.

Determination of chelate stability and composition

The composition of the chelate [20-25] of [FBX with Hg(II)] ion used was studied by Job's continuous method and Molar ratio method .The chelate of 1:1 ratio was obtained between FBX and Hg(II). (Fig3-4)

Linearity range and quantification procedure

Beer's law was found to be obeyed in the concentration range of 2.0to 20µg/ml. A (1%, 1Cm) was calculated .The results were tabulated in Table no: . (Fig 2).

Assay of dosage form [16-17]

An accurately weighed amount of finely powdered tablet equivalent to 317mg of drug was dissolved in about 10ml of dimethyl sulphoxide and transferred in to 100ml of calibrated volumetric flask, after 15minutes of mechanical shaking was filtered into a 100ml of calibrated volumetric flask through Whatmann no: 41 filter paper and was diluted to 100ml with DMSO and the same procedure was followed as described above.

3. Results and Discussion

The method was based on the chelation of the drug with Hg (II) which gave a orange- yellow colour complex showing maximum absorbance at 510nm. The linearity range of FBX-Hg(II) chelate covered over a range of 2.0-10 μg /ml of drug with A(1%,1cm) equals to $4.62x10^4$ L $Mole^{-1}cm^{-1}$. The drug chelate absorbance were plotted against the corresponding concentrations . Data were fitted to the equation Y=a+bx, where Y is the absorbance at relevant maximum is the Drug concentration in mcg/ml; b is the slope and a is the intercept of the calibration curve. The correlation coefficient is 0.999 indicating exact linearities. The Accuracy of the proposed procedure were 99.9%. Repeatability and reproducibility were evaluated. The limit of detection does not exceed 3.2 μg /ml where as limit of quantification was 10.2μg /ml. Proposed procedure for FBX

is a stability indicating one which can be used for the determination without interference with the excipients. The drug being soluble in DMSO and considered more selective drug to chelate with Hg (II) ion in alkaline medium.

Table 1: Optimum conditions and results of the proposed method for the determination of [FBX-Hg(II)]

$^{a}_{max}$ (nm)	**510**
Beer's law limits	5-30 µg /ml
Regression Equation* (Y) Slope (m) Intercept (c)	y = 0.002x - 0.23 0.001 0.23
Correlation Coefficient(r)	**0.997**

*Y=mx+c, where X is the concentration in micrograms/ml and Y is absorbance unit.

Table 2: Beer's Plot – Verification of [FBX-HgII] at 510nm

S.No	Concentration (µg/ml)	Absorbance
1	5	0.031
2	10	0.068
3	15	0.112
4	20	0.362
5	25	0.712
6	30	0.964

Table 3: Accuracy of [FBX-Hg (II)] at 510nm by proposed method

Drug	Amount added (µg)	Amount recovered* (µg)	% recovery*	Average recovery (%)	% RSD
Febuxostat 40 mg	20	19.89	99.45	99.76	0.318
	40	40.12	100.3		
	60	59.72	99.53		

Table 4: Precision of [FBX-Hg(II)] at 510nm by proposed method

Drug	Amount taken (mcg/ml)	Inter-day		Intra-day	
		Amount found* (mcg/ml)	%RSD	Amount found* (mcg/ml)	%RSD
Febuxostat	20	19.73	0.535	19.87	0.473
	40	40.23	0.238	40.13	0.198
	60	59.89	0.183	59.88	0.157

Table 5: Assay of Marketed formulation of Febuxostat by proposed method

Drug	Label claim (mg/tablet)	Amount estimated* (mg/tablet)	% Amount estimated*	% RSD
Febulal	40	40.84	100.12	1.74

*Mean of five determinations

RSD – Relative Standard Deviation

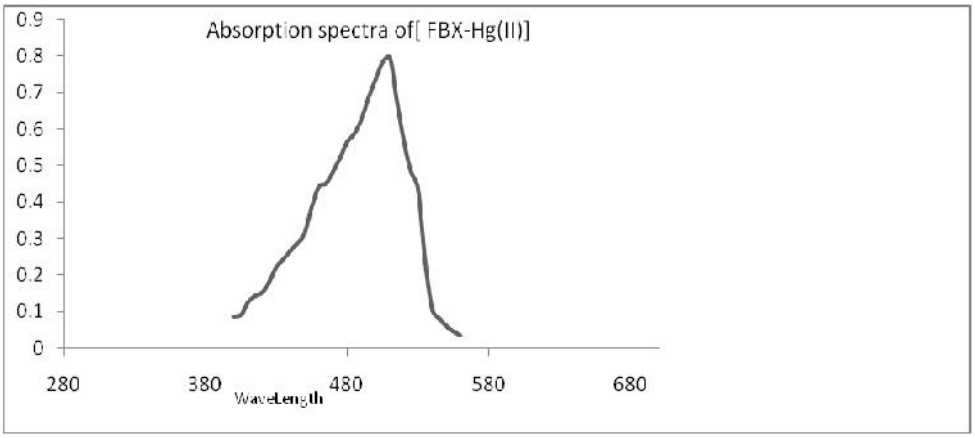

Figure 1: Absorption Maxima of [FBX-Hg (II)] at 510 nm

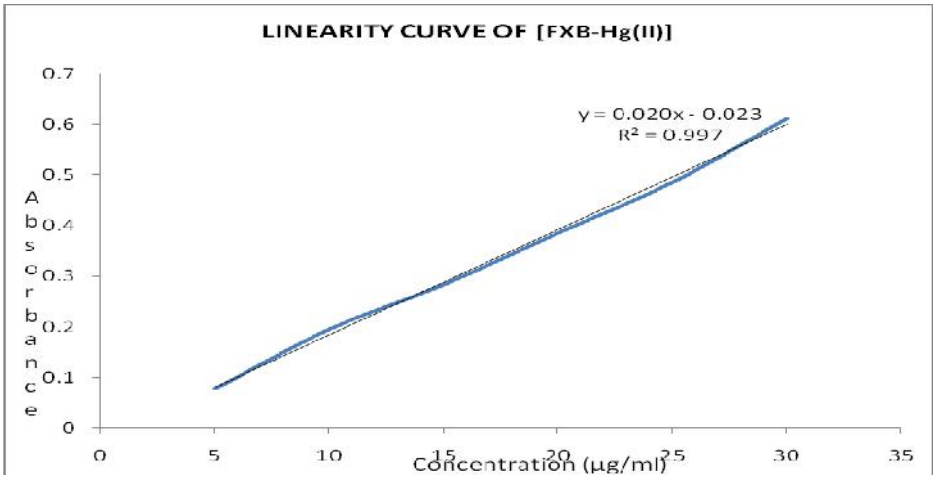

Figure 2: Beer's Plot of [FBX-Hg (II)] at 510 nm

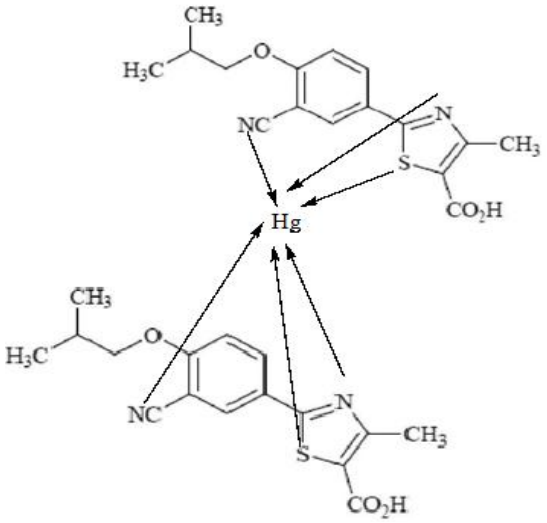

Figure 3: Drug –Metal Complex (2:1)

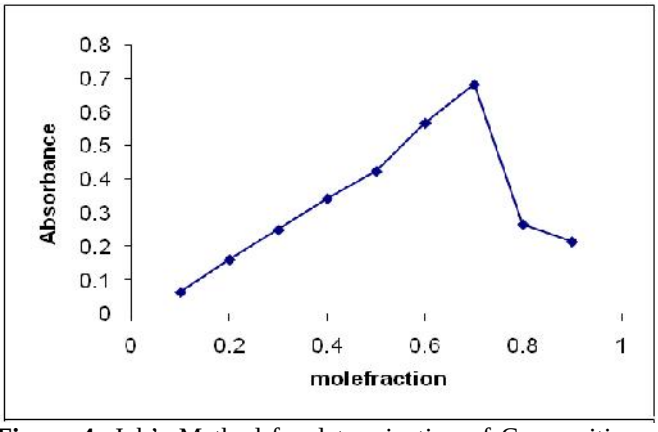

Figure 4: Job's Method for determination of Composition of Drug-Metal complex of [FBX-HgII]

4. References

[1] J.A. Barman Balfour, L.R. *Wiseman*, *Drugs*, **1999**, *57*, 363.

[2] Babu Rao Chandu, Kanchanamala Kanala, Nagiat T Hwisa, Prakash Katakam and Mukkanti Khagga Bioequivalance and pharmacokinetic study of febuxostat in human plasma by using LC-MS/MS with liquid liquid extraction method. *Springerplus*, 2013, 2, 194.

[3] BL, Barrons R, Veverka A, Snider KM. Urate-lowering therapy for gout: focus on febuxostat. *Pharmacotherapy*. 2010, 30(6): 594-608.

[4] Lukram O, Parmar S and Hande A (2013). Determination of febuxostat in human plasma using ultra-performance liquid chromatography tandem mass spectrometry. *Drug Testing and Analysis* 5(6) 492-9.

[5] Mathrusri Annapurna Mukthinuthalapati1, Sai Pavan Kumar Bandaru, Venkatesh Bukkapatnam and Chitaranjan Mohapatro (2012). Development and Validation of a Stability-Indicating RP-HPLC Method for the Determination of Febuxostat (a Xanthine Oxidase Inhibitor). *Journal of Chromatographic Science* 1–8.

[6] Muvvala Subrahmanya Sudhir, Pavuluri Madan Mohan and Ratnakaram Venkata Nadh (2013). Simple and validated UV spectroscopic method for the estimation of Febuxostat in bulk and pharmaceutical dosage forms. *Oriental Journal of Chemistry* 235-240.

[7] Andrija Ciric, R.Jelic,L.Joksovic, M.Jelikic, Stankov, P. Djurdjevic, *Canadian journal of analytical sciences* and *spectroscopy*,,**2007**, *52(6*), 343-350.

[8] Sanjay K Motwani, Roop KK, Ahmad FJ, Shruthi C. Spectrochimica Acta part A; *Molecular and Biomolecular spectroscopy*, **2007**, *68(2)*, 250.

[9] Al-Ghannam SM, Spectrochimica Acta Part A: *Molecular and Biomolecular Spectroscopy*, 2008, *69(4)*, 1188-1194.

[10] R.B. Cole, John Wiley and sons *Inc., Chichester, 1997***.**

[11] L. Messori, F.Kratz and E. Alessio, *metal based drugs* **1996,** 3(1), 1-9.

[12] Marczenko, Z., "*spectrophotometric determination of elements*", Wiley and sons Inc., New York, 1st Edn **1976**.

[13] Foster R, Organic charge transfer complexes, *Academic press*, London, **1969**, pp 51, 387.

[14] P. Job *Anal. Chim* **1936,** *16*, 97. Melby L R, in: Patai S. *The chemistry of the cyano group Ed., Interscience*, NewYork. **1970** 639-670.

[15] *IUPAC Compendium of Analytical Nomenclature*, Definitive Rules,ed. by Irving H. M. N. H., Freiser H., West T. S., Pergamon Press, Ox-ford,**1981**.

[16] Miller J. C., Miller J. N., Significance tests "*Statistics in Analytical Chemistry*," Chapt. 3, **3rd ed**., Ellis Horwood , Chichester, **1993**.