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Spectrophotometric determination of Valacyclovir HCl through oxidative coupling reaction in bulk and its pharmaceutical preparations

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Abstract: Two simple, sensitive, highly accurate UV-Visible spectrophotometric methods have been developed for the determination of valacyclovir HCl in bulk and tablet dosage form with MBTH as an oxidative coupling reagent. Method A and B are based on the oxidative coupling reaction of drug with MBTH in presence of ferric chloride Fe(III) and sodium periodate ($NaIO_4$) to form colored chromogens exhibiting λ_{max} at 630 and 624 nm respectively. Beer's law was obeyed in the concentration range of 5-25 µg ml^{-1} and 2-10 µg ml^{-1} with molar absorptivity values of $8.17x10^3$ l mol^{-1} cm^{-1} & $2.83x10^4$ l mol^{-1} cm^{-1}, the slope, intercept, correlation coefficient were also calculated. The results of analysis for the two methods have been validated statistically and by recovery studies. The results are compared with those obtained using UV spectrophotometric method in alcohol at 255 nm.
Keywords: Valacyclovir HCl, Visible spectrophotometery, MBTH, and recovery studies.

INTRODUCTION

Valacyclovir [VCH] L-valine-2-[(2-amino-1, 6-dihydro-6-oxo-9-hipurin-9-yl) methoxy] ethyl ester is the L-valyl ester prodrug of the antiviral drug acyclovir that exhibits activity against herpes siplex virus types,1(HSV–1) and 2(HSV–2) and vericellazoster virus[1]. The mechanism of action of acyclovir involves the highly selective inhibition of virus DNA replication, via enhanced uptake in herpes virus-infected cells and phosphorylation by viral thymidine kinase. The substrate specificity of acyclovir triphosphate for viral, rather than cellular, DNA polymerase contributes to the specificity of the drug[2,3]. Valacyclovir is rapidly converted to acyclovir and further phospharilated to acyclovir triphosphate. The incorporation of acyclovir tri phosphate into the growing chain of viral DNA results in chain termination[4-10].Literature survey revealed the dissolution studies[11,12] ,pharmacological data [13,14],and few methods are reported in literature for the estimation of Valacyclovir in pharmaceutical dosage forms which includes spectrophotometry [15-18], HPLC[19] and RPHPLC methods[20].The objectives of the work are to develop new spectrophotometric method for its estimation in bulk and tablet dosage form with good accuracy, simplicity, precision and economy. Hence the present work deals with the spectrophotometric estimation of Valacyclovir using MBTH with ferric chloride Fe(III) and MBTH with sodium periodate ($NaIO_4$).

EXPERIMENTAL:

Materials and Methods

UV-Visible spectrophotometer: An ELICO SL-207 model, 2nm high resolution, double beam and 1cm length quartz coated optics, wavelength 190-1100nm, high stability, linearity; precision instrument was used for all the spectral measurements.

Reagents: All the chemicals and reagents were of analytical grade and the freshly prepared solutions were always used in the present investigation.
MBTH(3-methyl-2-benzothialinone hydrazone hydro - chloride) **solution:** Prepared by dissolving 200 mg of MBTH in 100 ml distilled water.
Fe(III) solution: Prepared by dissolving 1.0 mg of anhydrous ferric chloride in 100 ml distilled water.
($NaIO_4$) solution: Prepared by dissolving 200 mg of sodium periodate in 100 ml distilled water.
Preparation of standard solution of Valacyclovir HCl (VCH): Valacyclovir Hcl (100mg) was accurately weighed and dissolved in 20ml of distilled water, transferred to a standard 100ml volumetric flask. The final volume was made up to the mark with distilled water. The final concentration was brought to 100µg/mL with distilled water.

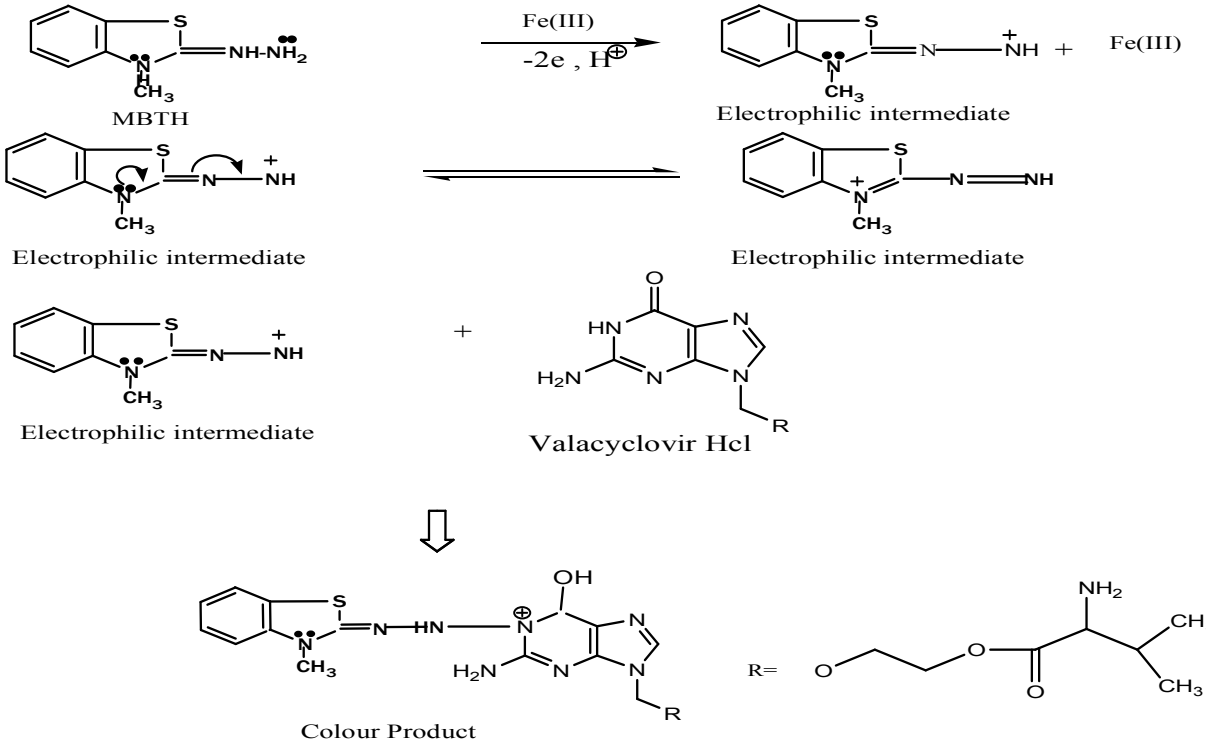
Recommended procedures:

Method-A: MBTH+ Fe(III)
Into a series of 25 ml calibrated tubes containing aliquots of standard VCH solution (0.5 – 2.5 ml), 0.5 ml of 0.2% MBTH solution was added and kept aside for 5 min. After that, 2.0 ml of Fe(III) solution was added and again kept aside for 10 min. The volume was made upto the mark with distilled water. The absorbance was measured at 630 nm against a similar reagent blank. The amount of VCH was deduced from its calibration curve.

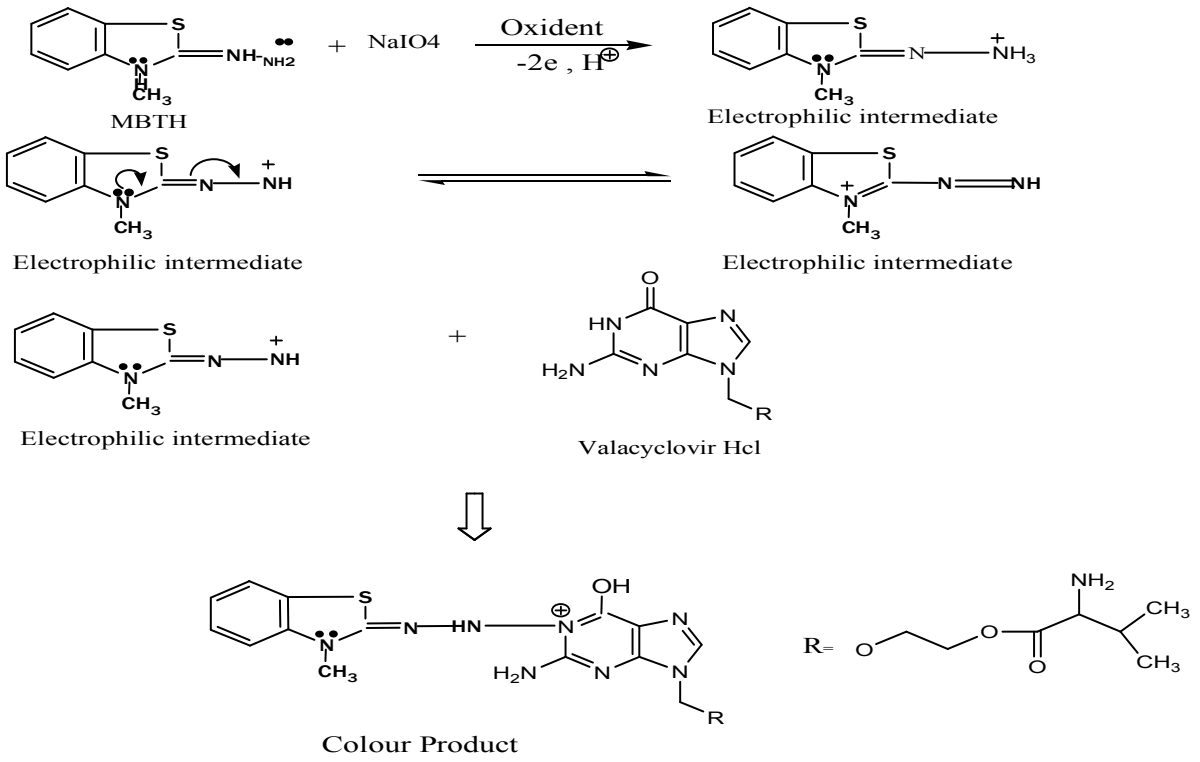
Method B: MBTH+ $NaIO_4$
Aliquots of standard VCH solution (0.5 – 2.5 ml,) were transferred into a series of 10 ml calibrated tubes. To each of the above aliquots 1.0 ml of water and MBTH solution were added and mixed thoroughly and then the reaction kept aside for 15 min. After that 2.0 ml of sodium periodate was added, then the total solution was diluted with distilled water, shaken well and the absorbance of each colored species was measured after 10 minutes at 624 nm against a similar reagent blank. The amount of VCH was computed from its calibration graph.

Procedure for the assay of Valacyclovir HCl in pharmaceutical dosage forms: Twenty tablets were weighed accurately and reduced to fine powder, drug equivalent to 100 mg of Valacyclovir HCl taken in a 100 ml volumetric flask, sonicated for about 30 min, and the volume was made upto the mark with distilled water, filtered by using Whattmann-42 filter paper. The filtrate was quantitatively diluted with methanol to yield concentrations in the linear range of the assay of Valacyclovir HCl.

Scheme-A:



Scheme-B:



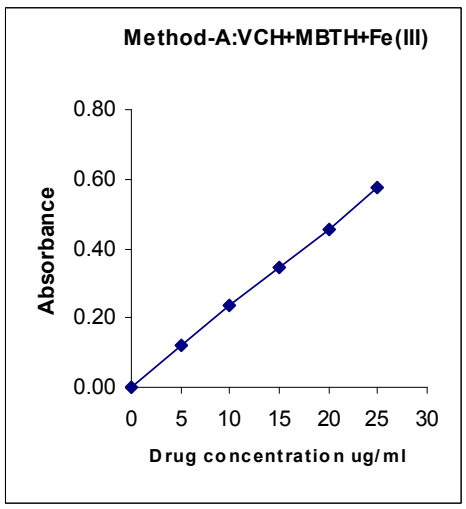


Fig: 1 Beer's law plot of valacyclovir HCl with MBTH+Fe (III)

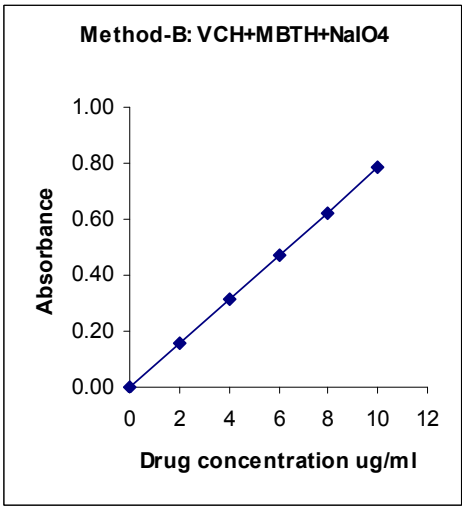


Fig: 2 Beer's law plot of valacyclovir HCl with MBTH+ $NaIO_4$

Table-1: Optical Characteristics, Precision, Accuracy of the methods proposed for the determination of Valacyclovir.

S.No.	Optical Characteristics	Method A	Method B
1.	λmax (nm)	630	624
2.	Beer's Law Limits (µg/ml)	5-25	2-10
3.	Molar absorptivity (1 $mol^{-1}cm^{-1}$)	8.17×10^3	2.83×10^4
4.	Correlation coefficient (r)	0.9999	0.9999
5.	Sandell's sensitivity (µg/cm^2/0.001 absorbance unit)	0.042	0.013
6.	Regression Equation (y = a+bC) : (i) Slope (b)	2.26×10^{-2}	7.83×10^{-2}
	(ii) Standard deviation on slope (S_b)	1.31×10^{-4}	4.50×10^{-4}
	(iii) Intercept (a)	5.80×10^{-3}	1.50×10^{-3}
	(iv) Standard deviation on intercept (S_a)	2.16×10^{-3}	2.98×10^{-3}
	(v) Standard Error of Estimation (S_e)	2.06×10^{-3}	2.85×10^{-3}
7.	Optimum Photometric range (µg/ml)		
8.	Standard Deviation	8.98×10^{-2}	3.58×10^{-2}
9.	Relative Standard Deviation *	1.781	1.428
10.	% of range error (confidence limit) (i) 0.05 level	0.223	0.088
	(ii) 0.01 level	0.370	0.147

* Average of six determinations considered.

Table -2:Determination of VCH in Pharmaceutial Formulations.

Sample	Labelled amount (mg)	Amount found by proposed methods*		Ref. Method[21]	% Recovery by proposed methods*	
		Method A	Method B		Method A	Method B
Tablet	500	488.2 ±0.17 F = 0.49 t = 0.59	487.6 ± 0.14 F = 0.73 t = 0.27	499.8 ± 0.12	97.68 ±0.03	97.56±0.19

*Average ± standard deviation of six determinations, the t-and F-test values refer to comparison of the proposed method with the reference method. Theoretical values at 95% confidence limit, F = 5.05, t = 2.228

** Recovery of 10 mg added to the preanalysed pharmaceutical formulations (average of three determinations).

RESULTS AND DISCUSSION:

Valacyclovir HCl (VCH) possesses different functional moieties such as primary amine, secondary amine, and keto group of varied reactivity. The methods (A&B) are based on the oxidative coupling reaction with MBTH in presence of Fe (III) & in the presence of $NaIO_4$ by concerning the reagents used for color development by exploiting appropriate functional groups in VCH and portable scheme of reactions is shown in Scheme-A and Scheme-B .The optical characteristics such as Beer's law limits, Sandell's sensitivity, molar extinction coefficient, percent relative standard deviation and percent range of error were calculated (Figures 1&2) for the methods(A&B) and the results are summarized in Table 1. The accuracy of the methods was ascertained by comparing the results of the proposed methods with that of reported method (Table 2). In order to justify the reliability and suitability of proposed methods, known amounts of pure drug was added to its various pre analyzed dosage forms and were analyzed by the proposed method, which indicates that the proposed method can be successfully applied for the analysis of Valacyclovir in dosage forms. The additives and excipients usually present in pharmaceutical preparations did not interfere. Thus the proposed methods were simple, sensitive, accurate, and reproducible and can be used for the routine analysis of Valacyclovir in bulk and in pharmaceutical dosage forms.

REFERENCES

1. Ormrod D, Scott L J and Perry C M, Drugs, 2000, 59(4), 839.
2. O'Brien J J and Campoli-Richards D M, Drugs, 1989, 37, 233.
3. Landowski C P, Sun D, Foster D R, Menon S, Barnett J L, Welage L S, Ramachandran C and Amidon G L,J Pharmacol Exp Ther.,2003, 306, 778.
4. Beutner Karl R: Antiviral Research 1995; 28: 281-290.
5. Bengi Uslu, Sibel A O zkana: Analytical Chemical Acta 2006; 555: 341–347.
6. Maria Kasiari, Evagelos Gikas, Sofia Georgakakou, Michael Kazanis, Irene Panderi: Journal of Chromatography 2008; 864: 78 –86.
7. Ravi K, Ramadass R. J. R. Aravinda Raj, Parloop A., Chromatographia 2009;70: 407-414.
8. Gerda Marie Friedrichsen, Weiqing Chen, Mikael Begtrup, Chao-Pin Lee, Philip L.Smith: European Journal of Pharmaceutical Sciences 2002;16: 1–13.
9. Patil1 G.D, Yeole P.G, Manisha Puranik, Wadher S.J.,International Journal of ChemTech Research 2009; 1: 16-26.
10. Jadhav A.S, Pathare D.B, Shingare M.S.,Journal of Pharmaceutical and Biomedical Analysis 2007; 43: 1568–1572.
11. Hardman J.G, LimbirdL.E, Eds. Goodman and Gilman's, The Pharmacological Basis of Therapeutics, 9th ed,; The MC Graw Hill Co.; 1996.
12. Banakar, U.V.Pharmaceutical dissolution testing, 1st Ed.; Marcel Dekker inc.; New York, 1992.
13. AndreiG, and Eur, J Clin Microbiol Infect Dis 1992,11,143.
14. AndreiG, Eur J Clin Microbiol Infect Dis 1995, 4,318.
15. Ganesh.M, et al. E-J Chem, 2009, 6(3), 814-818.
16. Anil KumarT,. Gurupadayya B.M, Rahul Reddy M.B and Prudhvi Raju M.V, Journal of Pharmacy Research. 2011, 4(1), 24-27.
17. Aswani Kumar C.H., Anil Kumar T,Gurupadayya B.M, Navya Sloka S and Rahul Reddy M.B, Archives of Applied Science Research. 2010**,** 2(4), 278-287.
18. Venkata Reddy P and Sudha Rani B, E-Journal of Chemistry Vol. 3, No.12, pp. 154-158, July 2006.
19. Pharmhuy C. et al. J.Chromatogr. B, 1999; 732:47-53.
20. Ayhan Savaser Cansel Ozkan Yalıcn K, Ozkan Bengi Uslu Sibel and Ozkan A, Journal of Liquid Chromatography & Related Technologies. 2003**,** 26(11), 1755- 1767.
21. Ganesh M, Narasimha RaoC.V, Saravana Kumar, A, Kamalakannan K, Vinoba M, Mahajan H.S and Siva Kumar T., E-Journal of Chemistry, 2009, 6(3**),** 814-818.

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