Chem Sci Trans., 2013, **2(1),** 61-64
DOI:10.7598/cst2013.284

Chemical Science Transactions
ISSN/E-ISSN: 2278-3458/2278-3318

RESEARCH ARTICLE

Spectrophotometric Determination of Valacyclovir in Pharmaceutical Formulations

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Received 2 July 2012 / Accepted 28 July 2012

Abstract: A simple spectrophotometric method has been developed for the estimation of valacyclovir in pharmaceutical preparations. The method is based on the reaction of the valacyclovir with methanolic solution of *para* dimethyl amino benzaldehyde (PDAB) in acidic condition producing Schiff base having absorption maximum at 400 nm. Beer's law is obeyed in the concentration of 50-250 μg/mL of valacyclovir. Statistical analysis proves that the proposed method is reproducible and selective for the estimation of valacyclovir in bulk drug and in its tablet dosage form.

Keywords: Spctrophotometry, Valacyclovir, *para* dimethyl amino benzaldehyde, Formulations

Introduction

Valacyclovir chemically, *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 simplex virus types, 1 (HSV-1) and 2 (HSV-2) and vericellazoster virus. The mechanism of action of acyclovir involves the highly selective inhibition of herpes virus DN areplication, 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. Valacyclovir is available as tablet dosage form in the market. Few spectrophotometrc methods[1-4], HPLC methods[5-11], RP-HPLC method[12], are reported in the literature for the determination of valacyclovir in pharmaceutical formulations.

This paper describes a simple rapid, simple, sensitive and economical spectrophotometeric method for the determination of valacyclovir in commercial formulations. In the proposed method the valacyclovir is reacted with methanolic solution of *para* dimethyl amino benzaldehyde in acidic condition producing Schiff's base. Hence we have made an attempt to develop simple and sensitive spectrophotometric methods for the estimation of valacyclovir in bulk drugs and in pharmaceutical formulations.

Experimental

All absorbance measurements were made on a Spectronic 1001 plus spectrophotometer (Milton Roy Company, USA) with 1 cm matched quartz cells. All the solutions were freshly prepared. All solvents and other chemicals used through this study were of analytical grade. Double distilled water was used throughout the investigation. 0.1 N sulphuric acid was prepared and standardized with standard procedure. 1% w/v of *para* dimethyl amino benzaldehyde in methanol was prepared.

Preparation of standard solution

A standard stock solution containing 1 mg/mL was prepared by dissolving 50 mg of valacyclovir in 50 mL of methanol. From this, a working standard solution containing 100 µg/mL was prepared.

Assay procedure

Aliquots of valacyclovir ranging from 0.5-2.5 mL were transferred into a series of 10 mL volumetric flask. To each of the flask 1.0 mL of methanolic *para* dimethyl amino benzaldehyde and 1.0 mL of 0.1 N H SO_4 were added and warmed on a water bath for 2 min and kept aside for 15 min. at room temperature, the color development was developed. The volume was made up to mark with methanol. The absorbance of the dark green chromogen was measured at 400 nm against reagent blank. The amount of valacyclovir present in the sample was computed from calibration curve (Figure 1).

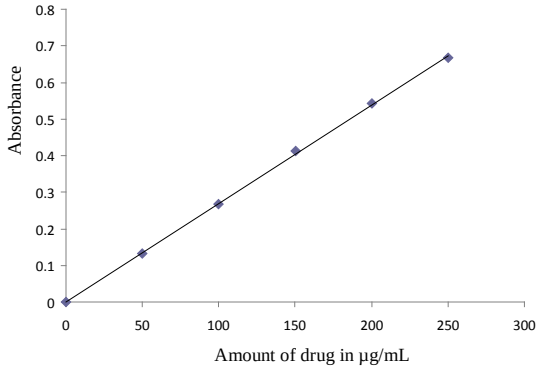

Figure 1. Calibration curve of valacyclovir

Pharmaceutical formulations

Twenty tablets containing valacyclovir were weighed and finely powdered. An accurately weighed portion of the powder equivalent to 50 mg of valacyclovir was dissolved in a 25 mL of methanol and mixed for about 5 minutes and then filtered. Then the volume was diluted to 50 mL with methanol and analyzed as given under the assay procedure for bulk samples. The results are represented in Table 2.

Recovery studies

To ensure the accuracy and reproducibility of the results obtained, known amounts of pure drug was added to the previously analyzed formulated samples and these samples were reanalyzed by the proposed methods and also performed recovery experiments. The percentage recoveries thus obtained were given in Table 2.

Results and Discussion

In the proposed method the valacyclovir is reacted with methanolic solution of *para* dimethyl amino benzaldehyde in acidic condition producing Schiff base. The absorption of Schiff base was measured at 400 nm against reagent blank prepared similar manner omitting drug solution. The absorption spectra of dark green Schiff base were shown in Figure 2.

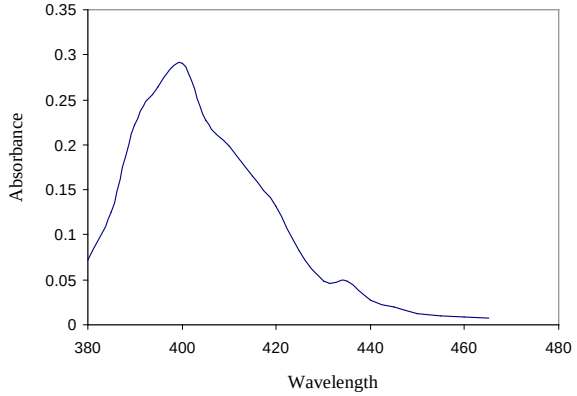

Figure 2. Absorption spectrum of valacyclovir condensed with PDAB at 440 nm

The optimum conditions were established by varying one parameter at a time and keeping the others fixed and observing the effect on absorbance of chromogen for the proposed method**.** Statistical analysis was carried out and the results were found to be satisfactory. Recovery studies were close to 100% that indicates indicating good accuracy of the methods. The optical characteristics such as absorption maxima, Beer´s law limits, molar absorptivity and Sandell´s sensitivity are presented in Table 1. The regression analysis using method of least squares was made for the slope (b), intercept (a) and correlation (r) obtained from different concentrations and results are summarized. The high molar absorptivities of the resulting colored complex indicate the high sensitivity of the method. The percent relative standard deviation, standard deviation and student's 't' test values calculated from the five measurements of valacyclovir are presented in Table 2.

Table 1. Optical characteristics of proposed method

Parameters	Proposed method
λ_{max}, nm	400
Beer's law limit, µg/mL	50-250
Molar absorptivity (l mole^{-1} cm^{-1})	$3.6x10^3$
Sandell's sensitivity (µg cm-2 / 0.001 absorbance unit)	0.361
Regression equation (Y = a + bC)	Y=0.0028x+0.003
Slope (b)	0.0028
Intercept (a)	0.003
Correlation coefficient (r)	0.9995

Table 2. Assay of valacyclovir in tablets

Sample	Labeled amount, mg	*Amount found ±S.D*	% Recovery	**t_{cal}	%RSD
Tablet 1	500	500.06±0.34	99.9	0.3878	0.0691
Tablet 2	500	500.12±0.65	100.02	0.4067	0.1319

Relative standard deviation values and standard deviation were low that indicates the reproducibility of the proposed methods. In the student's 't' tests, no significant differences were found between the calculated and theoretical values of the proposed method at 95% confidence level. This indicated similar precision and accuracy in the analysis of valacyclovir in its tablets. The commonly used additives such as starch, lactose, titanium dioxide, and magnesium stearate do not interfere with the assay procedures.

Conclusion

The proposed method was found to be simple, rapid, sensitive, accurate, precise and economical and can be used for the routine quality control analysis of valacyclovir in industry, research laboratories and hospitals.

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