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Visible Spectrophotometric Determination of Famciclovir in Bulk and Pharmaceutical Dosage Formulations

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Two simple colorimetric methods for the estimation of famciclovir in pharmaceutical dosage forms. In method **A** famciclovir undergoes complexation with SNP and to form coloured chromogen exhibiting absorption maximum at 428 nm and obeyed Beer's law in the concentration range of 2-12 μg/mL. In the method **B** based on the formation of an ion pair with bromocresol green in acidic medium and the subsequent extraction of the ion pair in chloroform. The yellow coloured ion pair showed an absorption maximum at 421 nm with apparent molar absorptivity. The proposed methods gave reproducible results for the estimation of famciclovir from its pharmaceutical formulation.

Key Words: Spectrophotometric analysis, Famciclovir.

INTRODUCTION

Famciclovir is chemically 2-[2-(2-amino-9H-purin-9-yl)ethyl] trimethylene diacetate[1,2] is an acyclic guanine nucleoside analogue. It is a new generation antiviral drug which is active *in vitro* and *in vivo* against herpes simplex virus types 1 and 2 and against varicella-zoster virus[3-6]. It is not official in any Pharmacopoeia. A few analytical methods have been reported for its quantitative estimation in pharmaceutical formulations that include estimation in plasma and urine by HPLC[7] and UV[8] spectrophotometric estimation in methanol. The present work describes two spectrophotometric methods for the estimation of famciclovir in its formulations.

EXPERIMENTAL

All spectral and absorbance measurements were made on a Shimadzu UV/Vis double beam spectrophotometer (model 1601) with 1 cm matched quartz cells. All the reagents were freshly prepared, all chemicals used were of A.R. grade from S.D. Fine Chemicals Ltd., Mumbai, India.

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Accurately weighed 50 mg of bromocresol green was transferred to a 100 mL of standard volumetric flask. To this 0.72 mL of 0.1 M NaOH and 20 mL of (95 %) ethanol was added. The above solution was then diluted to 100 mL with distilled water.

Accurately weighed 40.85 g of potassium hydrogen phthalate was dissolved in 1000 mL of distilled water. To this sufficient dilute hydrochloric acid was added to prepare buffer solutions of pH 3.

Preparation of standard solution: Standard solution of famciclovir was prepared by dissolving 100 mg in 100 mL and diluting 10 mL of this solution to 100 mL with methanol (100 µg/mL). For the analysis of famciclovir in tablets, one commercial brand of 250 and 500 mg strength (Cipla) were taken. 20 Tablets were weighed and powdered. The tablet powder equivalent to 100 mg of famciclovir was transferred into 100 mL volumetric flask containing 50 mL of methanol and flask was kept for ultrasonication for 5 min, then it was diluted up to the mark with methanol and the solution was filtered through Whatman filter paper No.41. From the above solution 10 mL was pipetted out into a 100 mL volumetric flask and the volume was made up to the mark with methanol. The final concentration of famciclovir was brought to 100 µg/mL with methanol is used for the analysis.

Assay procedure

Method A: Aliquots of famciclovir ranging from 0.2-1.2 mL (10 µg/mL) were transferred into a series of 10 mL volumetric flasks. To each flask 1mL of SNP (5 % w/v) and 2 mL of hydroxylamine (5 % w/v) solutions were successively added to each test tube and shaken for 2 min. Then 1 mL of sodium carbonate (10 % w/v) solution was added and warm on water bath for 10 min. The contents were diluted to 10 mL with water and the absorbance measured after 10 min at 428 nm against reagent blank. The amount of famciclovir present in the sample was computed from calibration curve.

Method B: In to a series of 125 mL separating funnels, aliquots of standard drug solution (0.4-2 mL) were pipetted out. To each separating funnel 2 mL of 0.2 M potassium hydrogen phthalate solution and 2 mL of bromocresol green dye solution were added. The aqueous phase was made up to 10 mL with distilled water. To each separating funnel, 10 mL of chloroform was added to extract the ion pair complex. The contents were shaken for 2 min and allowed to stand for clear separation of two layers and the absorbance of the chloroform layer was measured against reagent blank at 421 nm. The amount of famciclovir present in the sample was computed form calibration curve.

RESULTS AND DISCUSSION

To test the accuracy and reproducibility of the proposed methods, recovery experiments were carried out by adding known amounts of the drug to the preanalyzed formulation and reanalyzing the mixture by proposed methods. The results are summarized in Table-1. Stability study of the chromogen was carried out by measuring the absorbance values at time intervals of 10-40 min and it was found to be stable for 0.5 h for both methods. The optical characteristics such as absorption maxima, Beer's law limits, correlation coefficient (r), slope (m), y-intercept (c), molar absorptivity and Sandell's sensitivity calculated from 8 replicate reading are incorporated in Table-2.

TABLE-1
ANALYSIS DATA OF TABLET FORMULATION

Tablets	Labelled amount (mg)	Reference method	Amount obtained* (mg) Proposed method		Percentage Recovery**	
			A	**B**	**A**	**B**
T1	250	249.6±0.03	246.45±0.03	250.8±0.04	98.58±0.02	100.32±0.02
T2	500	500.8±0.02	496.32±0.04	500.31±0.02	99.26±0.07	100.06±0.01

*Average of eight determinations.
**Mean and Standard deviation of eight determinations.

TABLE-2
OPTICAL CHARACTERISTICS AND PRECISION

Observation	**Method A**	**Method B**
λ_{max} (nm)	428	421
Beer's Law Limits (μg/mL) (C)	2-12	4-20
Molar absorptivity (L mol^{-1} cm^{-1})	2.8324×10^4	1.4488×10^4
Sandell's Sensitivity (μg/cm^{-2} 0.001 abs unit)	0.0020	0.0222
Regression equation (Y*)		
Slope (b)	0.0866	0.0461
Intercept (a)	0.0051	0.0043
Correlation co-efficient (r)	0.9995	0.9997
Percentage RSD	0.2146	0.1711
Range of errors**		
Confidence limits with 0.05 level	0.001263	0.000770
Confidence limits with 0.01 level	0.001869	0.001145

*Y = bC + a where C is the concentration of famciclovir in μg/mL and Y is the absorbance at the respective λ_{max}.
**For eight measurements.

The molar absorptivity and Sandell's sensitivity values shows the sensitivity of both the methods. The analysis results of marketed formulations are in good agreement with the official methods. The reproducibility,

repeatability and accuracy of these methods were found to be good, which is evident by low standard deviation values (0.2146 for method **A** and 0.1711 for method **B**). The percentage recovery obtained (98.58-99.26 for method **A** and 100.06-100.32 for method **B**) indicates non-interference from excipients used in the formulation. Thus the developed methods are simple, sensitive, accurate, precise and can be successfully applied for the routine estimation of famciclovir in pharmaceutical dosage forms.

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