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Validated Spectrophotometric Estimation of Famciclovir in Tablet Dosage Form

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ABSTRACT: Two simple and sensitive spectrophotometric methods have been developed for the estimation of Famciclovir in bulk and tablet dosage form. Methods A and B are based on the condensation reaction of Famciclovir with carbonyl reagents such as p-dimethylaminobenzaldehyde (PDAB) and vanillin in acidic condition to form orange yellow colored chromogen with absorption maxima at 480 nm and 470 nm respectively. Beer's law is valid in the concentration range of 2-10 mcg/ml for both the methods. The developed methods were validated for precision, accuracy, ruggedness and robustness. Statistical analysis proves that the methods are reproducible and selective for the routine analysis of said drug.
Key words: Famciclovir, spectrophotometer, p-dimethylaminobenzaldehyde, vanillin, validation.

INTRODUCTION AND EXPERIMENTAL

Famciclovir is an orally administered prodrug of the antiviral agent[1] penciclovir. Chemically, famciclovir is known as 2-[2-(2-amino-9H-purin-9-yl) ethyl] - 1, 3-propanediol diacetate[2] (Fig. 1). Its molecular weight is 321.3. It is a synthetic acyclic guanine derivative. Famciclovir is a white to pale yellow solid. It is freely soluble in acetone and methanol and sparingly soluble in ethanol and isopropanol. Famciclovir is marketed as a white, film-coated tablet. The 125-mg and 250-mg tablets are round; the 500-mg tablets are oval. Inactive ingredients consist of hydroxypropyl cellulose, hydroxypropyl methylcellulose, lactose, magnesium stearate, polyethylene glycols, sodium starch glycolate and titanium dioxide[3, 4]. Extensive literature survey revealed that the determination of the drug in pure and tablet dosage form is not official in any pharmacopoeia and therefore, require much more investigation. Few analytical methods have been reported for the estimation of Famciclovir in biological fluids or pharmaceutical formulations include liquid chromatography[5, 6] and UV-visible spectrophotometry[7-10]. The objective of the work is to develop new spectrophotometric methods for its estimation in bulk and tablet dosage form with good accuracy, simplicity, precision and economy. The proposed method is based on the formation of yellow colored Schiff's bases with PDAB and vanillin respectively[11].

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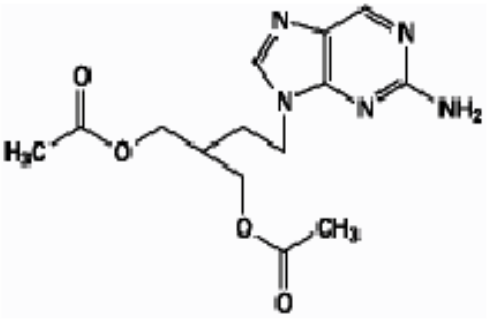

Fig. 1: Chemical Structure of Famciclovir.

A Schimadzu UV/VIS spectrophotometer (model 1201, schimadzu, japan) was employed for all the spectral measurements. All the chemicals used in the investigation were of analytical grade. The ethanolic solution of PDAB was prepared by dissolving 1 gm in 30 ml of 95 % ethanol, 180 ml of butanol and 30 ml of concentrated hydrochloric acid and made up to volume with water in a 250 ml volumetric flask. Ethanolic vanillin of 0.5 % and 5 N nitric acid were prepared. 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). The method was extended for determination of famciclovir in tablet dosage form. The tablet containing 250 and 500 mg strength were taken. Twenty 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 mg/ml with methanol and used for the analysis. In method A, aliquots of famciclovir ranging from 0.2-1.0 ml of standard solution were transferred into a series of 10 ml volumetric flasks. To each flask 1 ml of ethanolic PDAB and 2 ml of 5 N nitric acid were added, the solution was heated on a boiling water bath for 25 min., cooled to room temperature and made up to 10 ml with distilled water. The absorbance were measured at 480 nm against the reagent blank prepared simultaneously. The amount of the drug in a sample was calculated from the calibration graph. In method B, aliquots of famciclovir ranging from 0.2-1.0 ml were transferred into a series of 10 ml volumetric flasks. To each 1.5 ml of ethanolic vanillin and 1 ml of 5 N nitric acid were added, the solution was heated on a boiling water bath for 25 min., cooled to room temperature and made up to 10 ml with distilled water. The absorbance of the yellow colored chromogen was measured at 470 nm against the reagent blank. The amount of famciclovir present in the sample was computed from the calibration curve.

RESULTS AND DISCUSSION

The absorption spectral analysis shows the λ max of Famciclovir was found to be 480 nm for method A and 470 nm for method B. The calibration curve was obtained for a series of concentration in the range of 2-10 mcg/ml for both the methods (Fig. 2 and Fig. 3). They were found to be linear and hence, suitable for the estimation of the drug. The slope, intercept, correlation coefficient and optical characteristics are summarized in Table 1. Regression analysis of Beer's law plot revealed a good correlation. The effects of various excipients generally present in the tablet dosage form of Famciclovir were investigated. The results indicated that they did not interfere in the assay in amounts far in excess of their normal occurrence in it. The proposed methods were validated as per the ICH guidelines[12 -14]. The precision was measured in terms of repeatability, which was determined by sufficient number of aliquots of a homogenous sample. The % RSD was found and lying with in the range of ± 2.0. This showed that the precision of the methods are satisfactory. The recovery technique was performed to study the accuracy and reproducibility of the proposed methods. For this, known quantities of the Famciclovir solution were mixed with definite amounts of pre-analyzed formulations and the mixtures were analyzed. The total amount of Famciclovir was determined by using the proposed methods and the amount of added drug was calculated by the difference. The % RSD was less than ± 2.0. This showed that the recoveries of Famciclovir by the proposed methods are satisfactory and the results are shown in Table 2. Ruggedness and Robustness were determined and the % RSD values were calculated from precision study was less than ± 2.0. Limit of detection (LOD) and Limit of quantitation (LOQ) were determined by the proposed methods. Thus it can be concluded that the methods developed in the present investigation are simple, sensitive, accurate, rapid and precise. Hence, the above said methods can be successfully applied for the estimation of Famciclovir in tablet dosage form.

Table 1: Regression analysis of the calibration curve for the proposed method

Parameters	Values	
	Method A	Method B
Absorbance maximum (nm)	480	470
Linearity range (mcg/ml)	2-10	2-10
Correlation coefficient (r^2)	0.9994	0.9991
Regression equation	Y= 0.0128 X + 0.0239	Y=0.015 X + 0.02
Slope	0.0128	0.015
Intercept	0.0239	0.02
Limit of detection (mcg/ml)	0.61	0.63
Limit of quantitation (mcg/ml)	1.79	1.88

Table 2: summary of validation parameters

Parameters	Method A		Method B	
Label claim (tablet- mg)	250	500	250	500
Amount found ± SEM[a]	250.1±0.24	500.2±0.23	250.3±0.22	500.4±0.21
Precision (RSD, %)	0.906	0.853	0.793	0.374
% Recovery ± SEM[a]	100.4±0.74	100.5±0.63	100.7±0.50	99.6±0.84
Recovery (% RSD)	0.98	0.92	0.96	0.79

[a]*Mean of six determinations, SEM indicates standard error mean, RSD indicates relative standard deviation*

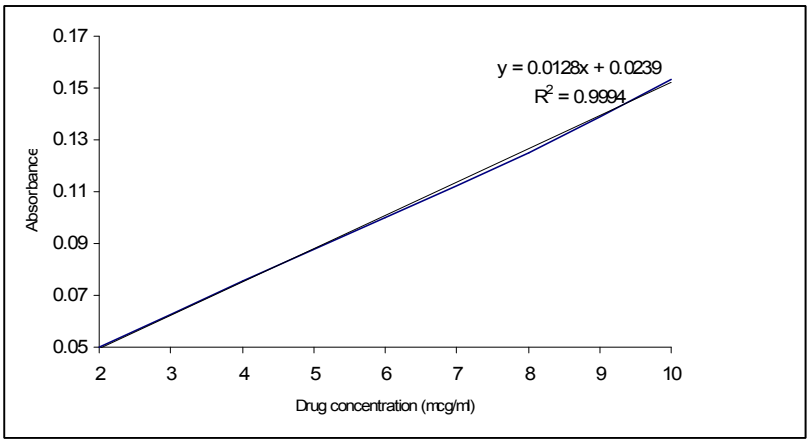

Fig. 2: Calibration curve of Famciclovir by method A.

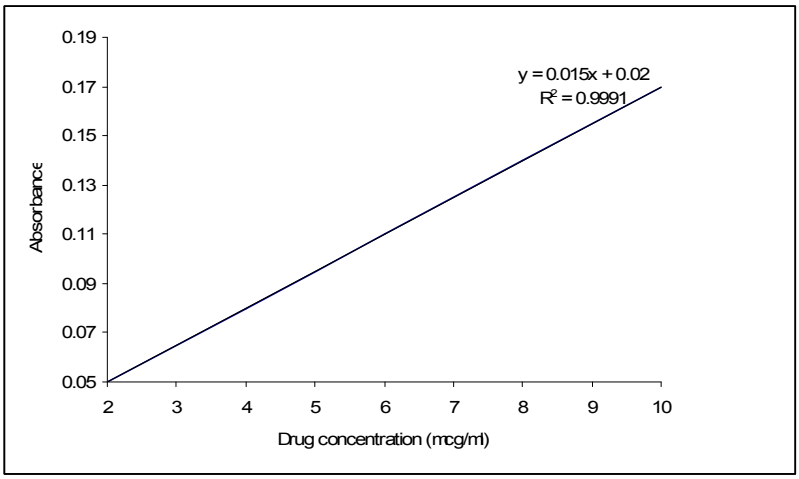

Fig. 3: Calibration curve of Famciclovir by method B.

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