Spectrophotometric Estimation of Famciclovir in Bulk and Tablet Dosage Form

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Two, simple, accurate, rapid and sensitive methods have been developed for the estimation of famciclovir in tablet dosage forms. Method A is based on the nucleophillic substitution product with Folin's reagent to form colored chromogen exhibiting absorption maximum at 454 nm with apparent molar absorptivity of 3.99×10^4 l/mol.cm and obeyed Beer's law in the concentration range of 2-10 µg/ml. Method B is based on diazotisation and coupling reaction with resorcinol to form colored chromogen exhibiting absorbance maximum at 386 nm with apparent molar absorptivity of 3.15×10^4 l/mol.cm and obeyed Beer's law in the concentration range of 7-21 µg/ml.

Famciclovir chemically 2-[2-(2-Amino-9H-purin-9-yl)ethyl]trimethylene diacetate[1,2] is an acyclic guanine nucleoside analog, 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 simple colorimetric methods for the estimation of famciclovir in pharmaceutical dosage forms. Method A involves nucleophillic substitution product with Folin's reagent to form colored chromogen exhibiting absorption maximum at 454 nm against reagent blank. Method B is based on diazotisation and coupling reaction with resorcinol to form colored chromogen exhibiting absorbance maximum at 386 nm against reagent blank.

A Shimadzu UV/Vis double beam spectrophotometer (model 1601) with 1 cm matched quartz cells was used for all spectral measurements. Solution of Folin's reagent [sodium (1,2-naphthaoquinone-4-sulphonate] (1% w/v), NaOH (5% w/v), HCl (1M), $NaNO_2$ (1% w/v), resorcinol (0.2% w/v) and NaOH (1M) were freshly prepared in distilled water. All chemicals used were of AR grade from S. D. Fine Chemicals, Mumbai.

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 tablets. Famtrex, Cipla Ltd. 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 upto 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 and used for the analysis.

In method A aliquots of famciclovir ranging from 0.2-1.2 ml portion of standard solution were transferred into a series of 10 ml volumetric flasks. To each flask 0.2 ml of sodium 1,2-naphthaoquinone-4-sulphonate (1% w/v) and 2 ml of NaOH (5% w/v) solutions were added to each flask and kept for 20 min at lab temperature. The solutions were made upto the mark with distilled water. The absorbances were measured at 454 nm against a 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 0.7–2.1 ml were transferred into a series of 10 ml volumetric flasks. To each 1 ml of HCl (1M) and 0.5 ml of $NaNO_2$ (1%w/v) were added at room temperature. After 5 min, 1.5 ml of resorcinol (0.2% w/v) and 0.5 ml of NaOH (1M) were added. The volumes were made up to the mark with distilled water. The absorbance of the yellow colored chromogen was measured at 386 nm against reagent blank. The amount of famciclovir present in the sample was computed form calibration curve.

For method A, the use of Folin's reagent >0.2 ml resulted in decrease the absorbance and <0.7 ml resulted in cloudiness and use 5% NaOH, >4 ml and <2.5 ml was found to disturbs the Beer's law. For method B, 1 ml of 1M HCl and 1% $NaNO_2$ was necessary for completion of reaction. 0.5 ml of 1M NaOH gives the good linearity and 1.5 ml of 0.2% resorcinol gives good result, addition of more than 2 ml resulted in non-linear color production.

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TABLE 1: ANALYSIS DATA OF FAMCICLOVIR IN TABLET FORMULATION

Tablets	Labeled amount (mg)	Reference method	Amount obtained* (mg) Proposed method		% Recovery**±SD	
			A	B	A	B
Brand 1	250	249.6±0.03	251.32±0.03	248.12±0.03	100.53±0.03	99.25±0.02
Brand 1	500	500.8±0.02	501.2±0.04	499.32±0.02	100.24±0.02	99.86±0.04

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

TABLE 2: OPTICAL CHARACTERISTICS AND PRECISION OF THE METHODS

Parameters	Method A	Method B
λ_{max} (nm)	454	386
Beer's law limits (µg/ml)(C)	2-10	7-21
Molar extinction coefficient (l/mol.cm)	3.9903×10^4	1.1568×10^4
Sandell's sensitivity (µg/ cm^2/0.001 A.U.)	0.0082	0.028
Regression equation (Y*)		
Slope (b)	0.1231	0.0357
Intercept (a)	0.0019	0.0003
Correlation co-efficient (r)	0.9999	0.9994
Percentage RSD	0.1142	0.21
Range of errors**		
Confidence Limits with 0.05 level	0.00071	0.0009
Confidence limits with 0.01 level	0.00105	0.0014

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

To test the accuracy and reproducibility of the proposed method, adding known amounts of the drug to the preanalysed formulation and reanalyzing the mixture by proposed method carried out recovery experiments. The results are shown in Table 1. Stability study of the chromogen was carried out by measuring the absorbance values at time intervals of 10 min-4 h and it was found to be stable for 30 min 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 replicates readings are incorporated in Table 2. The molar absorptivity and Sandell's sensitivity values show 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 (0.1142 for method A and 0.21 for method B). The percentage recovery value obtained (100.24-100.53 for method A and 99.25-99.86 for method B) indicates no interference from excipients used in the formulation. Thus the developed methods are simple, sensitive, accurate, and precise and can be successfully applied for the routine estimation of famciclovir in pharmaceutical dosage forms.

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