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NOTE

Spectrophotometric Determination of Famciclovir in Bulk and in Pharmaceutical Dosge Forms

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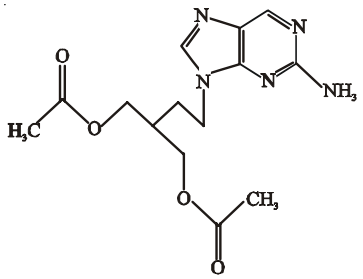
Two new, selective and sensitive visible spectrophotometric methods (method A and B) have been developed for the estimation of famciclovir in bulk and in pharmaceutical preparations Famciclovir was subjected to acid hydrolysis and this acid hydrolyzed drug was used for the estimation. Method A is based on the reaction with 3-methyl-2-benzothiazolinone hydrazone in the presence of ferric chloride, to form a colored species with a λ_{max} at 565 nm. Method B is based on the reaction with Folin-Ciocalteu Phenol's reagent under alkaline conditions with a λ_{max} at 760 nm. Beer's law is obeyed in the concentration range of 50-250 μg/mL for method A and 40-200 μg/mL for method B, respectively. These methods were extended to pharmaceutical formulations and there was no interference from any common pharmaceutical excepients and diluents.

Key Words: Spectrophotometric determination, 3-Methyl-2-benzothiazolinone hydrazone, Folin-ciocalteu Phenol's reagent, Famciclovir.

Famciclovir (FCV) is an antiviral drug and chemically known as 1,3-propanediol, 2-[2-(2-amino-9H-purin-9yl)ethyl]diacetate (ester). Literature survey reveals that no visible methods are reported, however, an UV[1] spectrophotometric and few HPLC[2,3] methods in pure and dosage forms were reported for famciclovir.



Structure of famciclovir

The present investigation has been undertaken to develop, two simple visible spectrophotometric methods in which, the colored species obtained in Method A, can be considered to be the oxidative coupling product between the acid hydrolyzed drug and 3-methyl-2-benzothiazolinone

hydrazone (MBTH) in the presence of $FeCl_3$ as an oxidant, with a λ_{max} at 565 nm. Method B is based on the formation of blue colored chromogen (λ_{max} : 760 nm), when it reacts with filin-ciocalteu phenol´s (FCP) reagent under alkaline conditions.

All the measurements were made using Systronics visible spectrophotometer moel 167 with 10 mm matched quartz cells. All the chemicals used were of analytical grade.

3-Methyl-2-benzothiazolinonehydrazone (0.2%): 200 mg of MBTH dissolved in 100 mL of distiller water.

Folin-Ciocalteu phenol's reagent (1 N): 1:1 dilution of FCP reagent with distilled water.

Ferric chloride (0.2 %): Freshly prepaerd by disolving 200 mg of ferric chloride in 100 mL of distilled water.

Sodium carbonate (5 N): 26.5 g of sodium carbonate dissolved in 100 mL of distilled water.

Preparaton of standard solution: Accurately weighed 100 mg of FCV was dissolved in 50 mL of distilled water, add 9.01 mL of conc. HCl, reflux for 2 h and the solution was diluted to 100 mL with distilled water to obtain 1 mg/mL stock solution. This stock solution was further diluted with distilled water to obtain the working standard of 1000 μg/mL for method A and 800 μg/mL for method B.

Preparation of sample solution: Accurately weighed tablet powder equivalent to 100 mg of drug was disolved in 50 mL of distilled water, add 9.01 mL of conc. HCl, reflux for 2 h and the solution was diluted to 100 mL with distilled water to obtain 1 mg/mL solution. This hydrolyzed drug solution was further diluted with distilled water to obtain a concentration of 1000 μg/mL for method A and 800 μg/mL for Method B.

Assay Procedure

Method A: Aliquots of standard drug solution ranging from 0.5-2.5 mL (1000 μg/mL) were transferred to a series of 10 mL volumetric flasks. To each, 2.0 mL of MBTH, 2.0 mL of ferric chloride were added and the volume was made upto mark with distilled water and the absorbance was measured at 565 nm against a reagent blank. The colored species was stable for 0.5 h and the amount of the drug in the sample was computed from its calibration curve.

Method B: Aliquots of standard drug solution ranging from 0.5-2.5 mL (800 μg/mL) were transferred to a series of 10 mL volumetric flasks. To each, 1.0 mL of FCP reagent, 2 mL of sodium carbonate were added and the volume was made upto mark with distilled water and the absorbance was measured at 760 nm against a reagent blank. The coloured species was stable for 0.75 h and the amount of the drug in the sample was computed from its calibration curve.

The optical characteristics such as Beer's law limits, Sandell's sensitivity, molar extinction coefficient, percent relative standard deviation, (calculated from the eight measurements containing 3/4th of the amount of the upper Beer's law limits) were calculated and the results are summarized in Table-1. Regression characteristics like slope, intercept, correlation coefficients and % range of error (0.05 and 0.01 confidence limits) were calculated and are shown in Table-1.

TABLE-1
OPTICAL CHARACTERISTICS AND PRECISION OF THE PROPOSED METHOD A AND B

Parameter		Method A	Method B
λ_{max} (nm)		565	760
Beer's law limits (μg mL^{-1})		50-250	40-200
Sandell's sensitivity (μg cm^{-2}/0.001 absorbance unit)		0.333	0.280
Molar absorptivity (L mol^{-1} cm^{-1})		0.963×10^3	1.144×10^3
Regression equation (Y = a + bC)	Slope (b)	0.00305	0.00362
	Intercept (a)	-0.0006	-0.0006
Correlation coefficient (r)		0.9999	0.9999
Relative standard deviation (%)*		0.8834	0.9455
% Range of error (Confidence limits)*	0.05 level	0.7386	0.7905
	0.01 level	1.0928	1.1696

*Average of eight determinations

Commercial formulation of famciclovir tablet was successfully analyzed by the proposed and reference methods. The values obtained by the proposed and reference methods[5] are presented Table-2. To evaluate validity and reproducibility of the method, a fixed amount of pure drug were added to the pre-analyzed formulations. These results are summarized in Table 2. There is no interference in the proposed analytical methods. In conclusion the proposed spectrophotometric method for the estimation of FCV is simple, sensitive, accurate and can be used for the routine quality control of the drug in bulk as well as in pharmaceutical formulations.

TABLE-2
ASSAY AND RECOVERY OF FAMCICLOVIR IN PHARMACEUTICAL FORMULATIONS

S. No.	Labelled amount (mg)	Content of drug found			% Recovery by proposed methods**	
		Proposed method (mg)		Reported method[5] (mg)		
		A	B		A	B
Tablet I	250	249.0	248.9	249.3	99.6	99.5
Tablet II	250	248.3	248.6	249.2	99.3	99.4

* Reference was UV method[5]
** Recovery amount was the average of five determinations.

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