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Development and Validation of Spectrophotometric method for the determination of Famciclovir in its dosage forms

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Abstract: Two simple, sensitive, accurate and rapid methods were developed for the estimation of Famciclovir in bulk and tablet dosage forms. Method A is based on the extraction (Redox followed by complex formation) product with Potassium ferricynide – Fe(III) reagent to form bluish green colored chromogen exhibiting absorption maximum at 500 nm with apparent molar absorptivity of $3.69x10^4$ L mol^{-1} cm^{-1} and obeyed Beer's law in the concentration range 3-10µg/ml. Method B is based on the oxidation followed by complex formation product with 2,2- Bipyridyl –Fe(III) to form orange colored chromogen exhibiting absorption maximum at 485 nm with apparent molar absorptivity of $4.28x10^4$ L mol^{-1} cm^{-1} and obeyed Beer's law in the concentration range 2-10 µg/ml. The developed methods were validated for precision and accuracy. Statistical analysis proves that the methods are reproducible and selective for the routine analysis of said drug. The results obtained by the proposed methods are in good agreement with the labeled amount.

Keywords: Spectrophotometry,Famciclovir,2,2-Bipyridyl, Potassium ferricyanide, Orthophos phoric acid, Ferric Chloride, Chloroform.

Introduction

Famciclovir (FCV) is an anti viral drug[1] and is chemically known as 2-(-(2-amino -9H- purin -9-yl) ethyl)-1, 3 – prpopanediol diacetate[2] (Fig.I). Famciclovir is an orally available nucleoside analog with potent in vitro activity against HIV, is being investigated for treatment of chronic hepatitis B. It is highly efficient in treatment of acute uncomplicated herpes Zoster. It was reported that FCV dosed at 250 mg 3 times daily for 7 days was effective as 800 mg acyclovir dosed 5 times daily for 7 days in the treatment of the acute signs and symptoms of herpes zoster[3]. This drug is also used for the treatment of the ophthalmic zoster Famciclovir is a synthetic guanine derivative, which is metabolized to penciclovir having the potent antiviral activity as another 9- substituted guanine derivative like acyclovir. Penciclovir is active against herpes simplex virus type 2, vricella zoster virus I,Epstein – Barrvirus and hepatitis B[5]. Famciclovir induced rapid, dose dependent suppression of viral replication and reduction in alanine aminotransferase with greatest efficiency in 500 mg tid tretment group. Since Famciclovir is widely used in the antiviral therapy, it is important to develop and validate analytical methods for its determination in pharmaceutical dosage forms. Extensive literature

survey revealed that the determination of the drug in pure and tablet dosage form is not official in any pharmacopoeia and there fore, require much more investigation. The literature suggested and reported a few analytical methods have been reported for its quantitative estimation in plasma and urine by HPLC[6-8], spectrophotometric[9-16], electrophoretic [17-18] techniques and liquid chromatography in biological fluids and pharmaceutical formulations [19-20]. The present work is to develop new spectrophotometric methods for its estimation in bulk and tablet dosage forms with good accuracy, simplicity, precision and economy.

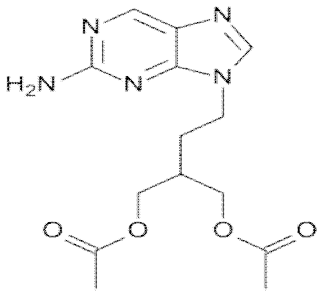

Fig.1: Structure of Famciclov

Experimental

Instrumentation

Shimadzu UV- Visible double beam spectrophotometer (model 2450) with 1 cm matched quartz cells was used for all the spectral measurements. All chemicals used were of AR grade.

Chemicals and Reagents

Methanol, Potassium ferricynide, Ferric Chloride, Orthophosphoric acid and Chloroform All chemicals used were of analytical grade and solutions were prepared with double distilled water.

Preparation of sample solution

The Famciclovir tablet containing 250 mg and 500 mg strength were taken. 20 tablets are weighed and powdered. The tablet powder equivalent to 100 mg of Famciclovir was transferred in to 100 ml volumetric flasks containing 50 ml of methanol and flasks were 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 41, to get concentration of 1 mg/ml. From the above solution 10 ml was pipette out in to 100 ml volumetric flask and the volume was made upto the mark with methanol. The final concentration of Famciclovir was brought to 100 µg/ml with ethanol and used for the analysis. Working standard solutions were prepared by appropriate dilution of standard stock solution with methanol for method A and B.

Method A: In method A, fresh aliquots of standard drug solution of Famciclovir ranging from 0.3 -1.0 ml (3- 10 µg/ml) were transferred into a series of 10 ml of volumetric flasks. To each flask 1 ml of 0.5 % $FeCl_3$ and 1 ml of 0.5 % Potassium ferricynide was kept on water bath for 15 min for complete color development and cooled. Then transferred the colored solution in 125 ml separating funnel. The mixture was extracted twice with 10 ml Chloroform by shaking for 2 min, and then allowed to stand for clear separation of the two phases. The absorbance of the separated Chloroform layer i.e bluish green colored complex was measured against their reagent blank at 500 nm. The colored species was stable for more than 14 hrs. The amount of Famciclovir present in the sample was computed from the calibration curve.

Method B: To a series of 10 ml graduated tubes, Famciclovir solution ranging from 0.2 -1.0 ml (2-10 µg/ml). To each tube 1 ml of 0.2 % 2, 2-Bipyridyl was added followed by 1 ml of 0.2 % $FeCl_3$ solution and the resulting solution was heated for 15 min at 100^0C and finally 2 ml of 0.1 N Orthophoric acid was added. The volume was made upto 10 ml with distilled water and the absorbance of the orange colored chromogen was measured at 485 nm against the corresponding reagent blank. The procedure was repeated for other analyte aliquots and calibration plots were drawn to calculate the amount of drug in unknown analyte sample.

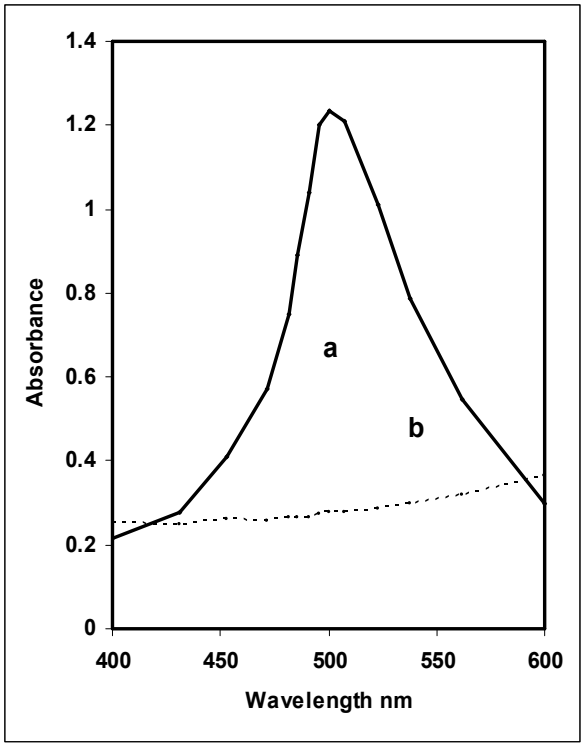

Fig: 2. Absorption spectrum of a)Famciclovir with potassium Ferricynide + Ferric Chloride b)Potassiun ferricynide and Chloroform (Method A)

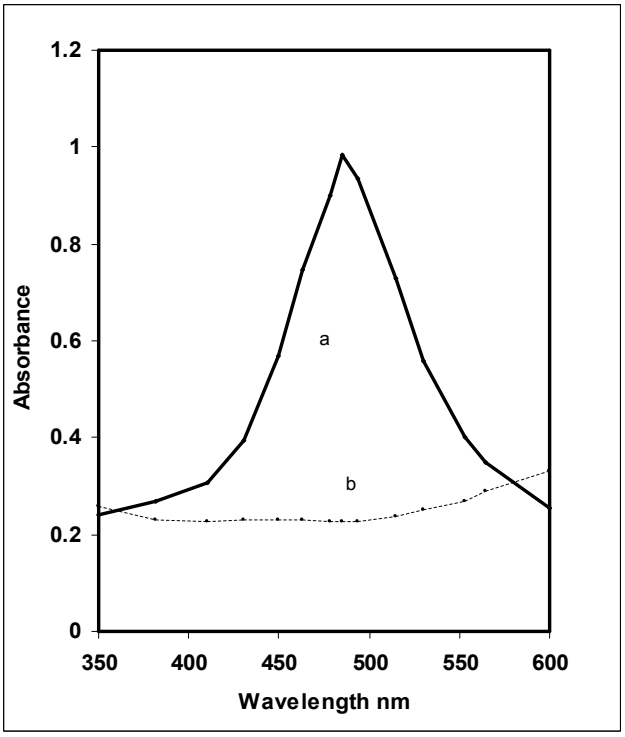

Fig: 4. Absorption spectrum of a) Famciclovir with 2,2-bipyridyl + Ferric chloride b) 2, 2-bipyridyl and ferric chloride Method B

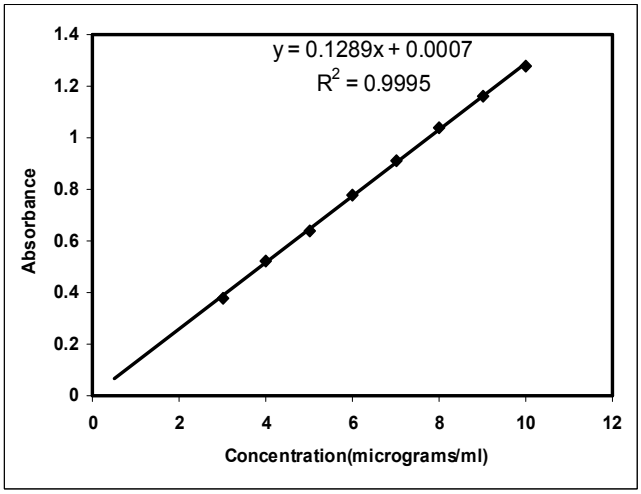

Fig: 3. Calibration curve of Famciclovir Method A

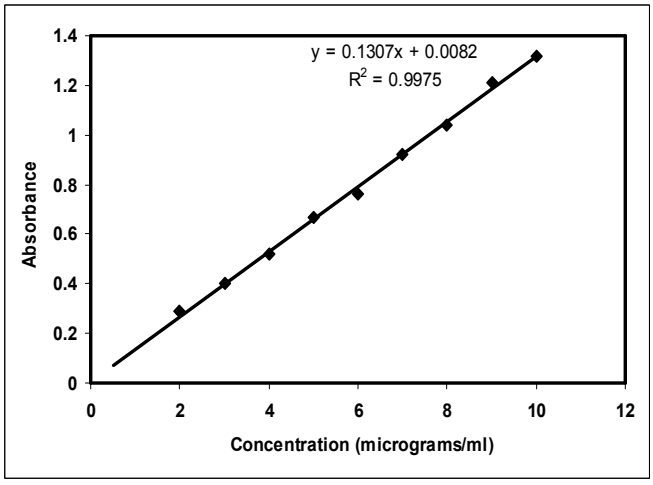

Fig: 5. Calibration curve of Famciclovir Method B

Table.1: Optical Characteristics of proposed methods

Parameters	Method A	Method B
λmax nm	500	485
Beer's Law limit (µg ml^{-1})	3-10	2-10
Molar absorptivity (L. mol^{-1} cm^{-1})	$3.69x10^4$	$4.28x10^4$
Specific absorptivity	0.115	0.133
Sandell's sensitivity (µg.cm^{-2}/0.001 A.U)	0.0086	0.0075
Correlation coefficient (r^2)	0.9995	.9975
Regression equation (Y = mX + C)		
Slope (m)	0.1289	0.1307
Intercept (C)	0.0007	0.0082
% Relative Standard deviation	0.1.0564	0.6241
Colour	Bluish green	Orange

Table.2: Determination Famciclovir in its dosage forms

Method	Amount added (µg/ml)	Amount found (µg/ml)	% Found ± SD*	RSD %
A	Inter-day			
	10	9.889	99.89 ± 0.027	0.284
	20	19.866	99.33 ± 0.035	0.176
	Intra-day			
	10	9.858	99.58 ± 0.014	0.150
	20	19.834	99.17 ± 0.141	0.212
B	Inter-day			
	10	9.844	98.44 ± 0.041	0.422
	20	19.814	99.07 ± 0.056	0.284
	Intra-day			
	10	9.822	98.22 ± 0.045	0.463
	20	19.836	99.18 ± 0.064	0.323

*Average of five determinations

Table 3: Assay of Famciclovir in tablet dosage forms

Sample	Labelled amount (mg)	Amount found (mg)		%Found ± SD		%RSD	
		A	B	A	B	A	B
Famtrex	250	249.71	249.83	99.8±0.13	99.93±0.11	0.052	0.045

Results and Discussion

The absorption spectral analysis shows λmax of Famciclovir was found to be 500 nm for method A and 485 nm for Method B. The calibration curve were obtained for the series of concentrations in the range of 3- 10 µg/ml for method A and 2- 10 µg/ml for method B. 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 accuracy of the method was ascertained by comparing the results obtained with proposed and reported methods, in case of each dosage form and experiments were performed by adding known amount of pure drug to pre analysed dosage forms and percent recovery values obtained were listed in Table 2 and 3. Recovery indicated the absence of interferences from the commonly encountered pharmaceutical additives and excipients.

Conclusions

Thus it can be concluded that the methods developed in the present investigation are simple, sensitive, accurate rapid and precise. The statistical parameters and recovery study data clearly indicate the reproducibility and accuracy of the methods. Analysis of the authentic samples containing Famciclovir showed no interference from the common excipients .Hence, these methods could be considered for the determination of Famciclovir in the quality control laboratories.

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