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Novel spectrophotometric methods for the determination of Famciclovir in pharmaceutical formulations

K. Ratna Kumari[1*], C. Bala Sekaran[2]

[1]*Department of Biochemistry, Montessori Mahila Kalasala, Vijayawada, Andhra Pradesh*
[2]*Department of Biotechnology, J. K. C. College, Guntur, Andhra Pradesh*

Abstract

Two simple and sensitive spectrophotometric methods (method **A** and **B**) were developed for the determination of Famciclovir (FCV) either in raw material or in pharmaceutical formulations. Method A is based on the formation of orange yellow colored chromogen due to the diazotization reaction of FCV with nitrous acid. The orange yellow colored chromogen complex absorbs at λ_{max} 460 nm. Method B is based on reaction of FCV with paradimethylaminocinnamaldehyde (PDAC) resulting in the formation of yellow colored species having absorption maxima at 390 nm. Beer's law is obeyed in the concentration range of 4 – 20 µg/ml for both method **A** and **B**. The proposed methods were successfully applied to the assay of FCV in pharmaceutical preparations with recoveries varying from 99.91 to 100.26% (method **A**) and 99.31 to 100.84% (method **B**), with relative standard deviation of 1.604% and 0.90% for method **A** and **B** respectively. No significant interference was observed from the excipients commonly used as pharmaceutical aids with the assay procedure.

Key Words: Famciclovir, Sandell's sensitivity, Beer's law, Spectrophometry.

Introduction

Famciclovir [1]chemically known as 2–[2–(2–Amino–9H Purine–9–yl) ethyl]–1,3–propane diol diacetate (ester) [2,3]. FCV recently introduced drug, is a synthetic guanine derivative[4]which is metabolized to the potent antiviral compound penciclovir. Penciclovir is active against Herpes Simplex virus type 1 and type2, Varicella zoster virus, Epstein Barr virus and Hepatitis B [5].

A very few physicochemical methods appeared in the literature for the determination of FCV in bulk and pharmaceutical dosage formulations. The literature suggested and reported only a few HPLC [6-9], spectrophotometric [10-17] and electrophoretic [18,19] techniques. The analytical

important functional groups of FCV were not fully exploited. Hence, the authors made some attempts in this direction and succeeded in developing two visible spectrophotometric methods (A and B) for the determination of FCV in bulk and in pharmaceutical formulations. In the present work, the reactions of Famciclovir (FCV) and nitrous acid is a diazotization reaction which results in the formation of orange yellow colored chromogen (Method A) and formation of Schiff's base when FCV reacts with PDAC resulting in the formation of yellow colored chromogen (Method B) were used for its estimation.

Materials and Methods

Experimental

Instrumentation

Systronics UV -Visible double beam Spectrophotometer model 2201 with 1 cm match Quartz cells were used for absorbance measurements.

Materials and Reagents

All the chemicals used were of analytical grade. All the solutions were freshly prepared in distilled water.

- 0.1% w/v Sodium nitrite was prepared by dissolving 1 mg of sodium nitrite in 100 ml of distilled water (method A).
- 5N HCl (method A)
- 0.1% w/v paradimethylaminocinnamaldehyde was prepared by dissolving 1 mg of PDAC in 100 ml of methanol (method B).

Drug sample: The pharmaceutical grade FCV sample was gifted from the local pharmaceutical company. The formulations of CPZ samples were procured from the local pharmacy.

Preparation of standard and sample solution:

Accurately weighed 100 mg of drug was dissolved in 100 ml of water to give a concentration of 1 mg/ml. The final concentration was brought to 100 µg/ml for Methods A and B.

Assay Procedure

Method A

Aliquots of standard drug solutions of FCV ranging from 0.2–1.0 ml (100 µg/ml) were taken into a series of 10 ml volumetric flasks and solution of 5 N HCl (1ml) and 0.1% sodium nitrite (1ml) were added and kept aside for five min. The contents in each volumetric flask were finally made up 10 ml with distilled water and the absorbance of the orange yellow colored chromogen was measured at 460 nm against the corresponding reagent blank. The amount of FCV was computed from the Beer – Lambert's plot.

Method B

To a series of volumetric flasks, FCV solution ranging from 0.2–1 ml (100 µg/ml) and aqueous solutions of 0.1% PDAC (1.5 ml) was added and the solution was kept aside for 5 min. The solution was finally made up to the mark with methanol. The absorbance of the yellow colored

chromogen was measured at 390 nm against the corresponding reagent blank. The amount of FCV was computed from the corresponding Beer – Lambert's plot.

Assay of pharmaceutical tablets

Twenty tablets were weighed and ground to a fine powder using a pestle and a mortar. The average weight of a tablet was calculated. An accurately weighed portion of the powder, equivalent to 100 mg of FCV, was transferred into a 100 ml volumetric flask. The volume was made up to the mark with water, shaken well, and filtered through an ordinary filter paper. The concentration of the resulting solution was found to be 1 mg/ml. This solution was considered as the stock. Convenient aliquots from this solution were taken for the determination of FCV.

Results and Discussion

The results obtained method A wes based on the diazotization of the FCV under acidic conditions with sodium nitrite to form a orange yellow colored chromogen having absorption maxima at 460 nm against the corresponding reagent blank.

The results obtained in method B was based on the formation of the schiff's base between the primary amino group present in the FCV and aldehyde group present in the PDAC to produce a yellow colored complex having maximum absorption at 390 nm against the corresponding reagent blank.

The optimum conditions for each method were established by varying one parameter at a time and keeping the others fixed and observing the effect produced on the absorbance of colored species and incorporated in the procedure. The optical characteristics such as absorption maxima, Beer's law limits, Molar absorptivity and Sandell's sensitivity for these methods are presented in Table-1. The regression analysis using the method of least squares was made for the slope (a) and intercept (b) obtained from different concentrations are summarized in Table-1. The precision and accuracy were found by analyzing six replicate samples containing known amounts of the drug and the results are summarized in Table-1.

The accuracy of the method was ascertained by comparing the result 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 analyzed dosage forms and percent recovery values obtained were listed in Table 2. Recovery indicated the absence of interferences from the commonly encountered pharmaceutical additives and excipients.

Table 1: Optical characteristics, accuracy and precision of the proposed methods

Parameter	Method A	Method B
λ_{max}(nm)	460	390
Beer's law limits (µg/ml)	4 – 10	4 – 10
Sandell's sensitivity (µg/cm^2/0.001 Absorbance Unit)	0.00779	0.0045
Molar absorptivity (Liter/mole^{-1}cm^{-1})	2.684 X 10^4	3.3 X 10^4
Correlation Coefficient (r)	0.9998	0.9997
Regression Equation (Y)*		
Slope (b)	0.00107	0.0008
Intercept(a)	0.468	1.25
%RSD**	1.604	0.90
% Range of Error		
0.05 Significance Level	±1.3414	±0.7523
0.01 Significance Level	±1.9845	±1.1137

*Y = a + bX, where X is the concentration of FCV in µg/ml and Y is the absorbance at the respective $\lambda_{max.;}$ ** For six replicate samples

Table 2: Estimation of Famciclovir in pharmaceutical formulations

Formulation (Injection)*	Labelled amount (mg)	Amount found by proposed methods** (mg)		Reference Method[2] (mg)	% Recovery***	
		Method A (mg)	Method B (mg)		Method A	Method B
1	250	249.64	249.12	250.64	100.26	100.84
2	250	250.41	250.41	249.41	99.31	99.31
3	250	250.21	249.18	250.48	99.91	100.64

*Three types of formulations of FCV from three pharmaceutical companies; ** Average ± standard deviation of six determinations; *** Recovery of 10 mg added to the pharmaceutical formulations (average of three determinations)

Conclusion

The proposed methods were found to be simple, economical, selective and sensitive. The statistical parameters and recovery study data clearly indicate the reproducibility and accuracy of the methods. Analysis of the authentic samples containing FCV showed no interference from the common excipients. Hence, these methods could be considered for the determination of FCV in the quality control laboratories.

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References

[1] The Merck Index, Merck and co.Inc., Rahway, USA, 11th Edn., 1996, **1945**.
[2] R. Saltzman, R. Jurewicz and R. Boon, *J.Antimicrobe Agents Chemother.,* **1994**, 38, 2454.
[3] S. C. Sweetman, In; Martindale, The Complete Drug References, Pharmaceutical Press, London(U.K), **2002**, 33rd Edn., 602.
[4] M. R. Rashidi., J. A. Smith, S. E. Clarke and C. Beedham., *J. Drug Metabolism and Disposition*, **1997**, 25, 805.
[5] Maryadele J.O'Neil. Eds., In;Merck Index; An Encyclopedia of Chemicals Drugs and Biologicals, Merck, and Co., INC., Whitehouse Station, NJ., **2001**, 13th Edn., 3960.
[6] S. C. Boike, M. Pue, P. R. Audet, M. I. Freed, A. Fairless, B. E. Ilson, N. Zariffa and D. K. Jorkasky, *The Journal Of Clinical Pharmacology*, **1994**, 34, 1197.
[7] P. T. Petrov, T. V. Trukhacheva, D. V. Moiseev and A. I. Zhebentyaev, *J. Pharmaceutical Chemistry*, **2004**, 38, 391.
[8] Arianna Loregian., Rosalba Gaatti., Giorgio Palu and Elio F. De Palo, *Journal of Chromatography B: biomedical Sciences and Applicatons*, **2001**, 764, 289.
[9] S. C. Boike, M. Pue, P. R. Audet, M. I. Freed, A. Fairless, B. E. Ilson, N. Zariffa and D. K. *J. Clin. Pharmacol. Ther.,* **1994**, 55 , 418.
[10] S. Nizamuddin, D. Goli, Y. N. Manohara and M. C. Ravi, *Asian Journal of Chemistry*, **2007**, 19, 3617.
[11] K. V. Subramanyam, P. Mohanraj, V. S. Saravanan and N. Gopal, *Asian Journal of Chemistry*, **2007**, 19, 4911.
[12] G. S. Babu, I. S. Babu, N. K. Kumar, N. M. Yugandhar and C. A. I. Raju, *Asian Journal of Chemistry*, **2007**, 19, 1636.
[13] D. G. Sankar, N. Sujatha, B. A. Kumar and P. V. M. Latha, *Asian Journal of Chemistry*, **2007**, 19, 16027.
[14] J. Zhang, *West China Journal Of Pharmaceutical Sciences*, **2006**, 21, 302.
[15] D. G. Sankar, A. K. M. Pawar, S. K. Sumanth and P. V. M. Latha, *Asian Journal of Chemistry.,* **2005**, 17, 2043.
[16] Ayman A. Gouda, Zeineb EI Shafey, Nagda Hossny and Rham EI-Azzazy, *J. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy.,* **2007**.

[17] S. Nizamuddin, B. M. Gurupadayya, M. C. Ravi, Y. N. Manohara and R. S Appala, *Indian Journal of Pharmaceutical Sciences,* **2007**, 69, 451.
[18] Jin O Huang and Z. Y, *Chinese Journal of Biochemical Pharmaceutics*, **2001**, 22, 1891.
[19] H. Zongyu and J. Ou, *Chinese Journal of Biochemical Pharmaceutics*, **2000**, 20, 111.