



A Systematic Review on the Analytical Techniques for the Quantification of Valacyclovir

Chodimella Sahitya Bharathi and Mukthinuthalapati Mathrusri Annapurna*

GITAM Institute of Pharmacy, GITAM (Deemed to be University), Visakhapatnam, India

*Corresponding Author: Mukthinuthalapati Mathrusri Annapurna, GITAM Institute of Pharmacy, GITAM (Deemed to be University), Visakhapatnam, India.

Received: April 07, 2021

Published: April 30, 2021

© All rights are reserved by Chodimella Sahitya Bharathi and Mukthinuthalapati Mathrusri Annapurna.

Abstract

Valacyclovir is used for the treatment of viral infections caused by Herpes simplex viruses which include shingles, chickenpox and genital herpes. Valacyclovir converts rapidly into acyclovir after its oral administration and there by inhibits the viral DNA replication. In the present paper the authors have reviewed the analytical methods already published till now in the literature for the estimation of Valacyclovir in pharmaceutical formulations and in biological samples.

Keywords: Valacyclovir; Drug; DNA

Introduction

Lines 16-22: Valacyclovir is an anti-viral drug. Valacyclovir is chemically defined as 2-amino-3-methyl butanoate derivative of acyclovir [1,2]. Valacyclovir (Figure 1) has a molecular formula $C_{13}H_{20}N_6O_4$ and molecular weight 360.8 g/mole and it is soluble in water. The pKa values of Valacyclovir are found to be 1.90, 9.43 and 7.47 respectively. Valacyclovir is converted into Acyclovir triphosphate which competitively inhibits viral DNA synthesis by incorporating into the DNA polymerase of virus and finally inactivates and terminates the DNA polymerase chain [3,4].

Valacyclovir is available as tablets with brand names VALTOVAL (Sun Pharmaceutical Industries Ltd., India) and VALCIVIR (Cipla Ltd, India) etc. with a labelled claim of 500 mg for each of the brand product. Valacyclovir is also available as tablets in combination with Cefotaxime, Ritonavir etc. in marketed formulations. This article summarises the analytical techniques proposed by differ-

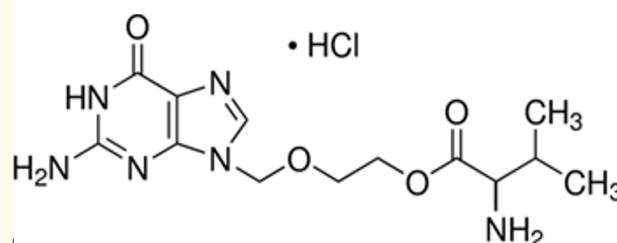


Figure 1: Chemical structure of valacyclovir.

ent authors for the quantification of Valacyclovir. Such analytical techniques include spectrophotometry [5-9] (Table 1), liquid-mass spectrometry [LC-MS] [10], LC-MS/MS [11,12], ultraperformance liquid chromatography [UPLC] [13], high performance liquid chromatography [HPLC] [14-19]. Reverse phase high performance

Reagent	Linearity ($\mu\text{g/ml}$)	λ_{max} (nm)	Comment	Reference
0.1N HCl	5-25	255	UV region	[5]
Vanillin	20-100	428	Visible region	[6]
PDAB	100-500	388	UV region	
Distilled water	4-24	252	UV region	[7]
Phenyl hydrazine HCl/ $\text{Fe}^{3+}/\text{H}^+$	2 - 10	520	Visible region	[8]
$\text{Fe}^{3+}/1,10\text{-phenanthroline}$	5 - 25			
Sodium acetate (pH 4.0)		251	UV region	[9]
Phosphate buffer (pH 5.0)	1 - 80	251		
Phosphate buffer (pH 7.0)		252		
Borate buffer (pH 9.0)		253		
0.1N NaOH		265		

Table 1: Review of spectrophotometric methods.

Mobile phase (v/v)	Column	Linearity ($\mu\text{g/ml}$)	Comment	Ref
Liquid chromatography- Mass spectrometry methods				
Acetonitrile: 0.05% Aq. diethyl amine (50:50)	Porous graphitized carbon (PGC)	0.02 - 0.80	LC-ESI/MS Ganciclovir (Internal standard) Human plasma	[10]
Mobile phase A: 2 mM Ammonium acetate: 0.2% Formic acid: Mobile phase B: Acetonitrile: 0.2% Formic acid	Waters Atlantis T3 C18	-	LC-MS/MS (Gradient mode) Mouse & human plasma	[11]
0.1% Formic acid: Methanol (30:70)	Gemini C18	-	LC-ESI-MS/MS Human plasma and its metabolite (Isocratic mode)	[12]
Ultra performance Liquid chromatography				
0.1% o-phosphoric acid: Acetonitrile (70: 30)	-	12.5 - 75	UPLC	[13]
High performance Liquid chromatography				
Mobile phase A: Acetic acid: Water (1:1000) Mobile phase B: Methanol (70: 30)	ODS C ₁₈	-	HPLC	[14]
0.1% Formic acid: Acetonitrile (90: 10)	C18 (Develosil)	10 - 50	HPLC	[15]

Acetonitrile: Phosphate buffer (pH- 3.6) (50:50)	Hypersil ODS C18	0.5 - 200	HPLC	[16]
Acetonitrile: Phosphate buffer (pH- 3.6) (50:50)	Hypersil, ODS C18	0.5 - 200	HPLC	[17]
Mobile phase A: NaH ₂ PO ₄ buffer (pH 3.5 adjusted with dilute ortho phosphoric acid) Mobile phase B: Acetonitrile: Methanol (60:40)	Hypersil BDS C18	15 - 225	HPLC	[18]
Acetonitrile: Phosphate buffer (pH- 3.6) (50:50)	Hypersil ODS C-18	0.5 - 200	HPLC	[19]
n-Hexane: Ethanol: Diethyl amine (30:70:0.1)	Chiralpak AD	0.9 - 6	Enantio selective	[20]
Acetonitrile: 0.025 M mono ammonium phos- phate buffer (pH 4.0; adjusted with 10% diluted phosphoric acid) (2:98) 1-methylguanosine (Internal standard)	Symmetry Shield RP-8	0.5 - 20	Biological fluids (Serum Dialysis liquid & Urine) Run time 12 min	[21]
Acetonitrile: Methanol: 0.067 M KH ₂ PO ₄ (27:20:53)	Waters Spherisorb C18	0.005 - 20	Human serum	[22]
Mobile phase A: Buffer (pH 3): Acetonitrile (95: 5) Mobile phase B: Acetonitrile: Methanol (90:10) Diluent: Buffer: Acetonitrile (50: 50)	ODS 3V	50 - 150	Box-Behnken design Impurity Profiling and Related Products Run time 40 min (Gradient mode)	[23]
0.1% aqueous Phosphoric acid (85%): Methanol (90:10)	Daicel Chiral Phase Crown pack CR (+)	0.3 - 6	Related substances	[24]
0.015 M Acetic acid: Methanol (95: 5)	ODS	6 - 90	Related substances	[25]
Mobile phase A: Phosphate buffer (KH ₂ PO ₄): Methanol (90:10) Mobile phase B: Buffer: Methanol: Acetonitrile (50: 30:20) (pH 6.7 adjusted with Tri ethyl amine)	Inertsil ZODS 3V	-	Related substances Run time 65 min (Gradient mode)	[26]

Table 2: Review of liquid chromatographic methods.

liquid chromatography [RP-HPLC] methods have been used to determine the drug following enantiometric separation [20], in biological fluids [21,22], impurity profiling using Box-Behnken design [23] and related substances [24-26]. Table 2 presents some of the significant chromatographic conditions and parameters.

Conclusion

The present review has presented some of the analytical techniques employed in the determination of Valacyclovir in various sample matrices. Of all the techniques, high performance liquid chromatographic techniques seem to be the techniques of interest.

Bibliography

1. Budawari S. "The Merck index". 13th Edition, Merck and Co. Inc., U.S.A. (2001).
2. Williams DA and Lemke TL. "Foye's Principles of Medicinal Chemistry". 5th Edition, Lippincott Williams and Wilkins, Wolters Kluwer Health Pvt. Ltd., New Delhi (2006).
3. HP Range., *et al.* "Pharmacology". 5th Edition, Churchill Livingstone (2003).
4. Katzung. "Basic and Clinical Pharmacology". 9th Edition, Mcraw Hill (2004).
5. Ganesh M., *et al.* "UV Spectrophotometric method for the estimation of Valacyclovir HCl in tablet dosage form". *E-Journal of Chemistry* 6.3 (2009): 814-818.
6. Prasad Reddy DV., *et al.* "Spectrophotometric determination of Valacyclovir hydrochloride in bulk and pharmaceutical formulations". *Asian Journal of Chemistry* 19.4 (2007): 2797-2800.
7. Sugumaran M and Jothieswari D. "Development and validation of spectroscopic method for estimation of Valacyclovir in tablet dosage form". *Oriental Journal of Chemistry* 26.1(2010): 163-165.
8. Siva Ramakrishna V., *et al.* "Development and determination of Valacyclovir HCl in pharmaceutical dosage forms by visible spectrophotometry". *International Journal of Pharm Tech Research* 4.3 (2012): 1009-1014.
9. Reddy Narendra., *et al.* "Development and validation of new analytical methods for the estimation of Valacyclovir hydrochloride in pharmaceutical dosage form". *Scholars Research Library Der Pharmacia Lettre* 8.1(2016): 296-303.
10. Maria Kasiari., *et al.* "Selective and rapid liquid chromatography/negative-ion electrospray ionization mass spectrometry method for the quantification of Valacyclovir and its metabolite in human plasma". *Journal of Chromatography B* 864.1-2 (2008): 78-86.
11. Shi J., *et al.* "A sensitive liquid chromatography-tandem mass spectrometry method for the quantification of valacyclovir and its metabolite acyclovir in mouse and human plasma". *Journal of Chromatography B* 1092 (2018): 447-452.
12. Yadav M., *et al.* "Stability evaluation and sensitive determination of antiviral drug, valacyclovir and its metabolite acyclovir in human plasma by a rapid liquid chromatography-tandem mass spectrometry method". *Journal of Chromatography B* 877.8-9 (2009): 680-688.
13. Sunkara Namratha and Vijayalakshmi A. "Analytical method development and validation of Valacyclovirin dosage forms by UPLC technique". *Journal of Global Trends in Pharmaceutical Sciences* 11.2 (2020): 7590-7594.
14. Palacios ML., *et al.* "Validation of an HPLC Method for the determination of Valacyclovir in pharmaceutical dosage". *Journal of Liquid Chromatography and Related Technologies* 28.5 (2005): 751-762.
15. Rasool SK., *et al.* "RP-HPLC method for the estimation of Valacyclovir in bulk and pharmaceutical formulations". *International Journal of Pharmacy and Pharmaceutical Sciences* 4.1 (2012): 214-218.
16. Srinivasa Rao K and Sunil. "Stability-indicating liquid chromatographic method for Valacyclovir". *International Journal of ChemTech Research* 1.3 (2009): 702-708.
17. Dillip Kumar Sahoo and Prafulla Kumar Sahu. "Stability-indicating RP-HPLC method for the determination of Valacyclovir hydrochloride in bulk and pharmaceutical dosage forms". *Chemical Science Transactions* 3.2 (2014): 510-517.
18. Jahnvi Bandla and Ashok Gorja. "Method development and validation of Valacyclovir hydrochloride assay by RP-HPLC in pharmaceutical dosage form". *International Journal of Advanced Research in Pharmaceutical and Bio Sciences* 3.1 (2013): 33-41.
19. Juluri Krishna Dutta Tejaswi. "Stability indicating determination of Valacyclovir by RP-HPLC method". *International Journal of Advance Research and Innovative Ideas in Education* 6.3 (2020): 526-532.
20. Jadhav AS., *et al.* "Development and validation of enantioselective high performance liquid chromatographic method for Valacyclovir, an antiviral drug in drug substance". *Journal of Pharmaceutical and Biomedical Analysis* 43.4 (2007): 1568-1572.

21. Pham-Huy C., *et al.* "Rapid determination of Valacyclovir and acyclovir in human biological fluids by high-performance liquid chromatography using isocratic elution". *Journal of Chromatography B* 732.1 (1999): 47-53.
22. Ayhan Savaşer., *et al.* "Development and validation of an RP-HPLC method for the determination of Valacyclovir in tablets and human serum and its application to drug dissolution studies". *Journal of Liquid Chromatography and Related Technologies* 26 (2003): 1755-1767.
23. Katakam P., *et al.* "An Experimental Design Approach for Impurity Profiling of Valacyclovir-Related Products by RP-HPLC". *Scientia Pharmaceutica* 82.3 (2014): 617-619.
24. Girija BB., *et al.* "Development and validation of RP-HPLC method for the determination of Valacyclovir hydrochloride and its related substances in tablet formulation". *International Journal of Pharmaceutical Sciences Review and Research* 25.1 (2014): 53-58.
25. Mani Ganesh., *et al.* "Development and validation of RP-HPLC method for the determination of Valacyclovir hydrochloride and its related substances in tablet formulation". *Asian Journal of Chemistry* 23.3 (2011): 1317-1320.
26. Tholkappiyam B., *et al.* "Analysis of related substances by high performance liquid chromatography [HPLC] method for Valacyclovir hydrochloride". *The Bioscan* 5.1 (2010): 117-121.

Assets from publication with us

- Prompt Acknowledgement after receiving the article
- Thorough Double blinded peer review
- Rapid Publication
- Issue of Publication Certificate
- High visibility of your Published work

Website: www.actascientific.com/

Submit Article: www.actascientific.com/submission.php

Email us: editor@actascientific.com

Contact us: +91 9182824667