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Review Article

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

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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 tri phosphate 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].

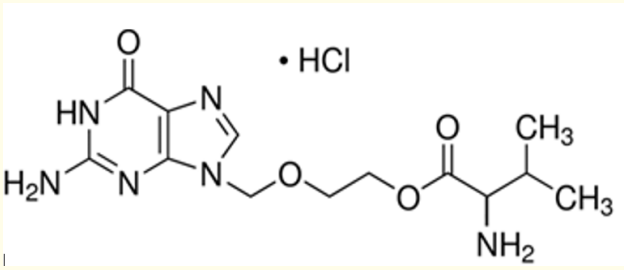

Figure 1: Chemical structure of valacyclovir.

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 different 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 (µg/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/Fe^{3+}/H^{+}	2 - 10	520	Visible region	[8]
Fe^{3+}/1,10-phenanthroline	5 - 25			
Sodium acetate (pH 4.0)	1 - 80	251	UV region	[9]
Phosphate buffer (pH 5.0)		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 (µg/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_2PO_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 phosphate 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_2PO_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_2PO_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.

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