



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

Bangaru Divya 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 09, 2021

Published: April 30, 2021

© All rights are reserved by **Bangaru Divya and Mukthinuthalapati Mathrusri Annapurna.**

Abstract

Verapamil is a calcium channel blocker. Verapamil is used for the treatment of high blood pressure and for the control of angina. In the present paper the authors have reviewed the analytical methods published in the literature for the estimation of Verapamil in pharmaceutical formulations and in biological samples.

Keywords: Verapamil; Calcium Channel Blocker; Analytical Techniques

Introduction

Verapamil is a calcium channel blocker with anti-anginal, anti-hypertensive and anti-arrhythmic activities. Verapamil belongs to non-dihydro pyridine class of calcium channel blockers and it is administered as racemic mixture. The S-enantiomer of Verapamil is approximately 20 folds more potent than R-enantiomer [1,2]. Verapamil (Figure 1) has a molecular formula $C_{27}H_{38}N_2O_4$ and molecular weight 454.602 g/mole and is soluble in methanol, ethanol and water. The pKa value of Verapamil is 8.92.

Verapamil HCl is available as sustainable release caplets with brand names Calan SR (Labelled claim 180 mg.), extended release capsules (Labelled claim 300 mg.) and as injection (Labelled claim 5 mg, 10 mg; 2.5 mg/ml). Verapamil HCl is also available as tablets with label claim 40, 80 and 120 mg (Nicholas Piramal India Ltd). This article summarises the analytical techniques proposed by different authors for the quantification of Verapamil such as spectrophotometry [3-6] (Table 1), HPLC [8-12], UPLC [13], LC-MS/MS

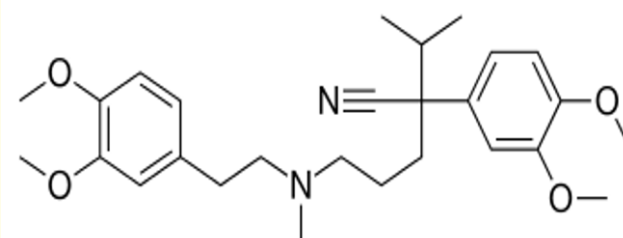


Figure 1: Chemical structure of verapamil.

[14-16] and LC-MS [17] and table 2 represents some of the significant parameters observed in liquid chromatographic methods. The State Pharmacopoeia of Ukraine [18] has a monograph on the substance of verapamil hydrochloride and on verapamil hydrochloride tablets. To identify the substance of verapamil hydrochloride, State Pharmacopoeia of Ukraine offers UV-spectrophotometry, absorption spectrophotometry in the infrared region, TLC (mobile

Reagent	Linearity ($\mu\text{g/ml}$)	λ_{max} (nm)	Ref
N-bromosuccinimide in perchloric acid	10-200	415	[3]
bromokresol green in an acetone medium	1.9648-4.4208	409	[4]
Bromothymol Blue and pH adjusted to 4 with NaOH and HCl	0.08-0.8	420	[5]
0.1N HCl and 0.1N NaOH (Differential spectroscopy)	5-25	278	[6]
Chloramine-T in HCl medium	0-340	425	[7]

Table 1: Review of spectrophotometric methods.

Mobile phase (v/v)	Column	Linearity ($\mu\text{g/ml}$)	Comment	Ref
Acetonitrile: 0.025 M KH_2PO_4 buffer (pH 2.5)	C18	0.01-0.5	HPLC	[8]
Diltiazem (Internal standard)	Lichrospher 60		Human plasma	
Metanol: Water: Tri ethyl amine (70: 30: 0.2)	Hypersil ODS	-	HPLC Residues	[9]
Mobile phase A: 50mM Ammonium phosphate (pH 4.5)	Capcell Pak C18	0.01-2.5	HPLC	[10]
Mobile phase B: 50mM Ammonium phosphate: Acetonitrile (70:30)			Rat plasma (Fluorescence detection)	
Propranolol (Internal standard)				
Acetonitrile: Water (pH 2.7) (55: 45)	RP-CLCDS	2.5-25	HPLC Verapamil and NSAIDs Human serum	[11]
Methanol: Water (pH 7.4) (70:30)	A HIQ sil ODS C-18	10-60	HPLC Synthesized metabolite (Impurity) Norverapamil	[12]
Ammonium formate: ortho phosphoric acid: Acetonitrile	Shimpak XR ODS	-	UPLC Related substances	[13]
Ammonium acetate: Methanol (20:80)	Purosphere C18	1 - 496	LC-ESI-MS/MS (Human plasma)	[14]
Ondansetron (Internal standard)				
0.1% Ammonium formate: Acetonitrile (35:65)	Thermo Hypurity C 18	0.0004575-0.2342	LC-MS/MS Human plasma	[15]
Mobile phase A: Acetonitrile: Water: Formic acid (5 : 95 : 0.1)	Discovery C18	0.001-0.1	LC-MS/MS (Gradient mode)	[16]
Mobile phase B: Acetonitrile: Formic acid (100 : 0.1)			(Caco-2 cell monolayers)	
5 mM Ammonium acetate: Acetonitrile (Gradient mode)	LUNA C8	-	LC-MS (Plasma and Intes- tinal fluid)	[17]

Table 2: Review of liquid chromatographic methods.

phase-diethylamine P-cyclohexane (15: 85), qualitative reaction to chlorides, quantitative determination-alkalimetry, potentiometric titration [18]. For identification of verapamil hydrochloride in tablets, the State Pharmacopoeia of Ukraine proposes UV-spectrophotometry, HPLC/ UV etc.

Conclusion

The present review helps the readers to do research in a new field apart from the presenting existing analytical techniques for the anti-anginal agent Verapamil.

Bibliography

- Basile J. "The role of existing and newer calcium channel blockers in the treatment of hypertension". *Journal of Clinical Hypertension (Greenwich)* 6.11 (2004): 621-629.
- Nafisur Rahman and Syed Najmul Hejaz Azmi. "Spectrophotometric method for the determination of Verapamil hydrochloride in pharmaceutical formulations using N-brmosuccinimide as oxidant". *Farmaco* 59.7 (2004): 529-536.
- Marta Sulyma. "Spectrophotometric determination of Verapamil hydrochloride using Bromokresol Green". *Der Pharma Chemica* 10.5 (2018): 143-147.
- Salh DM. "Spectrophotometric determination of Isoptin (Verapamil hydrochloride) in Pharmaceutical Preparations". *Haitham Journal for Pure and Applied Science* 2.3 (2017): 106-115.
- Leena Trivedi and Roshan Telrandhe "Differential spectrophotometric method for estimation and validation of Verapamil in Tablet dosage form". *International Journal of Pharmaceutics and Drug Analysis* 5.11(2017): 419-422.
- Rahman N and Nasrul Hoda MD. "Spectrophotometric determination of Verapamil hydrochloride in drug formulations with chloramine-T as oxidant". *Analytical and Bioanalytical Chemistry* 374.3 (2002): 484-489.
- Ivanova V., et al. "HPLC method for determination of Verapamil in human plasma after solid-phase extraction". *Journal of Biochemical and Biophysical Methods* 70.6 (2008): 1297-1303.
- Milenović DM., et al. "Development and validation of an HPLC method for the determination of Verapamil residues in supports of cleaning procedure". *Journal of Analytical Chemistry* 68 (2013): 545-551.
- Jhee OH., et al. "Direct determination of Verapamil in rat plasma by coupled column microbore-HPLC method". *Journal of Pharmaceutical and Biomedical Analysis* 37.2 (2005): 405-410.
- Sultan N., et al. "Method development of Verapamil in presence of NSAIDs using RP-HPLC technique". *Bulletin- Korean Chemical Society* 32.7 (2011):2274 -2278.
- Pathade., et al. "Synthesis, characterization, and determination of metabolite of Verapamil hydrochloride by reversed-phase high performance liquid chromatography". *Chronicles of Young Scientists* 4.2 (2013): 164-169.
- Vijayabaskara S., et al. "Analytical method development and validation for the analysis of Verapamil hydrochloride and its related substances by using ultra performance liquid chromatography". *Journal of Pharmaceutical and Biomedical Analysis* 137.15 (2017):189-195.
- Dheeraj B., et al. "Determination of Verapamil in human plasma by tandem mass spectrometry". *Asian Journal of Chemistry* 21.9 (2009): 6785-6791.
- Chen Y., et al. "LC-MS/MS determination of Verapamil in human plasma and its application in bioequivalence evaluation". *Journal of Chinese Pharmaceutical Sciences* 47.7 (2012): 546-550.
- Logoyda L., et al. "HPLC MS/MS method development for the quantitative determination of verapamil hydrochloride from Caco-2 cell monolayers". *Pharmacia* 67.2 (2020): 63-69.
- Oliver von Richter., et al. "Rapid and highly sensitive method for the determination of Verapamil, [2H7] Verapamil and metabolites in biological fluids by liquid chromatography-mass spectrometry". *Journal of Chromatography B: Biomedical Sciences and Applications* 738.1 (2000): 137-147.

17. The State Pharmacopeia of Ukraine. State Enterprise "Ukrainian Scientific Expert Pharmacopoeial Center of the Quality of Medicines" (2nd issue). Kharkiv: State Enterprise "Ukrainian scientific and experimental pharmacopoeial center for the quality of medicinal products 3 (2015): 1128.
18. The European Pharmacopoeia (2016).

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