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Review Article

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

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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.

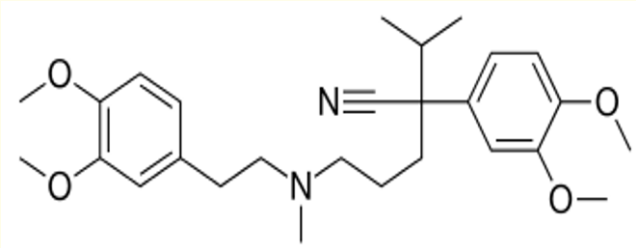

Figure 1: Chemical structure of verapamil.

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 [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 (µg/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 (µg/ml)	Comment	Ref
Acetonitrile: 0.025 M KH_2PO_4 buffer (pH 2.5) Diltiazem (Internal standard)	C18 Lichrospher 60	0.01–0.5	HPLC Human plasma	[8]
Metanol: Water: Tri ethyl amine (70: 30: 0.2)	Hypersil ODS	-	HPLC Residues	[9]
Mobile phase A: 50mM Ammonium phosphate (pH 4.5) Mobile phase B: 50mM Ammonium phosphate: Acetonitrile (70:30) Propranolol (Internal standard)	Capcell Pak C18	0.01-2.5	HPLC Rat plasma (Fluorescence detection)	[10]
Acetonitrile: Water (pH 2.7) (55: 45)	RP-CLCODS	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) Ondansetron (Internal standard)	Purosphere C18	1 - 496	LC-ESI-MS/MS (Human plasma)	[14]
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) Mobile phase B: Acetonitrile: Formic acid (100 : 0.1)	Discovery C18	0.001-0.1	LC-MS/MS (Gradient mode) (Caco-2 cell monolayers)	[16]
5 mM Ammonium acetate: Acetonitrile (Gradient mode)	LUNA C8	-	LC-MS (Plasma and Intestinal 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.

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