Available online at www.ijpcr.com
International Journal of Pharmaceutical and Clinical Research 2018; 10(7): 186-195

ISSN- 0975 1556

Review Article

Valsartan - A Review of Analytical Methods

S Alexandar*, M Kumar

Department of pharmaceutical Chemistry, Vinayaka missions College of pharmacy, Vinayaka Missions Research Foundation (Deemed to be University) Salem -636008, Tamilnadu, India.

Available Online: 25th July, 2018

ABSTRACT

This review focuses on the recent developments in analytical techniques for estimation of Valsartan alone or in combinations with other drugs in various biological media like human plasma and urine. This review will critically examine the analytical methods UV Spectroscopy, high performance liquid chromatography (HPLC), ultra performance liquid chromatography (UPLC), high performance thin layer chromatography (HPTLC), liquid chromatography coupled to tandem mass spectrometry (LC-MS).

Keywords: Analytical Techniques, Valsartan, Solid phase extraction, HPLC, Spectrophotometry.

INTRODUCTION

Valsartan is a new potent, highly selective and orally active antihypertensive drug belonging to the family of Angiotensin II type I receptor antagonists. Angiotensin II receptor type I antagonists have been widely used in the treatment of hypertension, heart failure, myocardial infraction and diabetic nephropathy. It is a lipophilic drug and it was first developed by Novartis and has a wide market in the developed and developing countries. It is available as single and in combination with other antihypertensive drugs. Valsartan is rapidly absorbed after oral administration. Volume of distribution at steady state has been estimated 17L and mean absolute Bioavailability is 23%. Food decreases the exposure of Valsartan by about 40% and peak plasma concentration by about 50%. 94%-97% of drug bound to serum protein mainly albumin. This review focuses on the recent developments in analytical techniques for estimation of Valsartan alone or in combinations with other drugs in various biological media like human plasma and urine, Various analytical techniques are discussed, from simple colorimetric methods of intermediate selectivity and sensitivity to sophisticated highly selective and sensitive, chromatographic methods applied in a modern analytical laboratory. This review will critically examine the (a) sample pretreatment method such as solid phase extraction (SPE), (b) separation methods such as thin layer chromatography (TLC), high performance liquid chromatography (HPLC), ultra performance liquid chromatography (UPLC), high performance thin layer chromatography (HPTLC), liquid chromatography coupled to tandem mass spectrometry (LC-MS) and capillary electrophoresis (CE), other methods such as spectrophotometry, diffuse reflectance near infrared spectroscopy and electrochemical methods.

Physicochemical Properties

Valsartan is N-(1-oxopentyl)-N-[[2-(1H-tetrazol-5- yl) [1, 1-biphenyl]-4-yl] methyl]-l-valine[14]. It is a white powder with empirical formula $C_{24}H_{29}N_5O_3$ and molecular weight 435.52g/mol. It is synthesized from L-valine methyl ester hydrochloride. Key step involves palladium catalysed Suzuki coupling. Melting range of 105-110 °C and specific rotation [α]D/20 in methanol is 68° and partition coefficient of Valsartan is 0.033 (logP=1.499) indicating that the compound has a rather hydrophilic characteristic at physiological pH. Due to its fine particle size, Valsartan absorbs water reversibly from ambient atmosphere. The compound is stable when stored under dry conditions[2]. For ionizable molecules, pH plays a crucial role. The charge state that a molecule exhibit at particular pH is characterized by ionization constant pKa of the molecules. Buffer affects pH gradients weakly acidic and weakly basic drug exhibit pH dependent solubility. Valsartan is a tetrazole derivative that contains two weakly acidic function groups (acid and carboxylic acid) with pKa value of 4.7 and 3.9. These groups making compound stable in the neutral pH range[3].

DETERMINATION METHODS

Many analytical methods have been developed for the determination of Valsartan in pharmaceutical formulations and in biological fluids. Such as UV spectroscopy[13,19-23], HPLC[24-31], RP-HPLC[12,32-50], HPTLC[51-53], TLC[54], absorption ratio method[55,56] voltammetry[57] has been developed. Methods such as HPLC, Capillary electrophoresis and simultaneous UV spectroscopic methods of Valsartan are reported for estimation of Valsartan alone or in combination with other drugs. The advantages of UV- spectroscopic methods over HPLC is significantly shortening analysis time, low cost of analysis, widespread access to the apparatus, while the HPLC procedure is time consuming, require too many solvents and expensive apparatus.

Author for Correspondence:

UV spectroscopic method:

Title	Method	Wavelength	Linearity and r^2	Recovery	Ref
Spectrophotometric method for the determination of Valsartan in bulk and pharmaceutical preparations	UV	720 nm	0.999	99.6-100.8	4
Spectroscopic method for the estimation of valsartan in pure and pharmaceutical dosage form	UV	250nm	0.9968	98.64%	5
Spectrofluorimetric method for the drug combination of Amlodipine with Valsartan	Conventional and Synchronous fluorescence spectroscopy	460nm and 385 nm 390nm and 227nm	0.9999 and 0.9998 0.9997 and 0.9997	100.16 and 99.95 % 99.5 and 99.7 %	6
Determination of valsartan and hydrochlorothiazide in tablets by UV Spectroscopy	absorption ratio method	270.5 nm and 231.5 nm	0.9997 and 0.9993	97.42-102.23%	7
Spectrophotometric method for the simultaneous estimation of Valsartan and Nifedipine	First derivative method	248.43 nm and 216.52 nm	0.9994 and 0.9963	99.50-100.50%	8
UV-spectrophotometric methods for simultaneous estimation of valsartan and hydrochlorothiazide	Simultaneous equations and absorbance ratio method	249.4 nm and 272.6 nm 258.4nm and 272.6nm	0.9998 and 0.9999	97.96% - 100.20%	9
simultaneous spcetroptometric determination of valsartan and Amlodipine	Wavelet transform (CWT) Method	258.5 and 263.3 265.7 and 270 nm	0.9999 and 0.9998	99.40% - 101.20%	10
Simultaneous UV spectrophotometric method for the estimation of amlodipine besylate, valsartan and hydrochlorothiazide	simultaneous equation, Q-analysis and area under curve method	359 nm, 317 nm and 250 nm	0.9999, 0.9999 and 0.9998	99.32–102.2%	11
Spectrophotometric method for simultaneous determination of Amlodipine and valsartan	zero order UV spectrophotometry Method	360.5 nm and 290 nm	0.9996 and 0.9997	99.15 – 100.90 %	12
Simultaneous estimation of Nebivolol hydrochloride valsartan and hydrochlorothiazide	simultaneous equation and Q-analysis method	270.4 nm, 280.2nm and 270 nm	0.9998, 0.9999 and 0.9998	99.0 – 101.2 %	`13
Spectrophotometric method for the simultaneous estimation of Valsartan and Ramipril	Second order derivative spectroscopy method	289.36 and 226.89 nm	0.9973 and 0.9987	98.10 – 99.25 %	14
Estimation of valsartan in pure and pharmaceutical formulation	UV-Method	250.80nm	0.9996	99.26% - 100.7%	15
Spectrophotometric method for estimation of Valsartan	UV-Method	250nm	0.9998	99.18- 99.77 %	16
Simultaneous determination of valsartan and hydrochlorothiazide	H-point standard additions method and partial least squares	216 and 228 nm	0.9981 and 0.9978	92.6 - 109.1 %	17

HPLC-MS/MS[58] and LCMS/ MS[59] methods have been developed for analysis of ACE inhibitors in plasma.

UV spectroscopic method

Absorbance ratio method, First order derivative spectrophotometric, Simultaneous equations method, continuous wavelet transform (CWT), Q-value analysis method, H-point standard additions method (HPSAM) and partial least squares (PLS) calibration methods were described for simultaneous determination of Valsartan.

Chromatographic Methods

HPLC methods were widely used chromatographic methods in the analysis of valsartan in Formulation. LC-MS/MS, LC-MS and UPLC use for estimation of valsartan in Plasma. HPTLC method also developed for determination of valsartan in pharmaceutical dosage form and plasma.

CONCLUSION

In conclusion, a broad range of techniques are available for the analysis of valsartan in biological samples and

pharmaceutical formulations. The analysis of the published data revealed that the HPLC methods were extensively used for the determination of valsartan in various matrices like plasma, serum and urine. For determination of valsartan in biological samples, were commend the HPLC–MS/MS method, since this method combines the HPLC separation ability with MS sensitivity and selectivity, allowing the unambiguous identification of valsartan and its metabolites. For

Chromatographic Methods

Title	Method	Mobile phase	Stationary phase	Wavelength	Ref
Development and validation of HPLC method to determine valsartan in nanoparticles	HPLC	Ammonium formate and Acetonitrile (57:43v/v)	Phenomenex C18 , 250 mm × 4.6 mm id, 5 µ	250 nm	`18
Determination of Valsartan for stability indicating studies	HPLC	Methanol and Phosphate buffer pH 3 (65:35v/v)	Microbondapak,C18, 25cm 4.6mm i.d, 5µm	210 nm	19
Simultaneous determination of Valsartan and Hydrochlorothiazide in Pharmaceutical Formulation	HPLC	Acetonitrile: Methanol: Phosphate buffer pH 3 (65:35v/v)	Phenomenex Luna C18, 150 mm × 4.6 mm i.d., 5 µ	250 nm	20
Comparative study on the degradation behavior of Valsartan and Losartan	HPLC	Acetonitrile: Phosphate buffer, pH 3.5, (60: 40 v/v)	ACEC18, 250 mm × 4.6 mm i.d, 5µ	225 nm	21
Simultaneous estimation of atenolol, hydrochlorothiazide, losartan and valsartan	HPLC	Phosphate buffer: Acetonitrile, pH 3.0, (50: 50 v/v)	Nucleodur100C18, 250 × 4.6 mm i.d., 5 µ	210 nm	22
Method Development for Quantification of Valsartan in Tablet Dosage Form	HPLC	Acetonitrile: Phosphate buffer, pH 3.5, (50: 50 v/v)	KromasilC-18, 250 × 4.6 mm i.d., 5µ	250 nm	23
Analysis of Valsartan in Pharmaceutical Dosage Forms	HPLC	Phosphate buffer: Acetonitrile, pH 3.0, (50: 50 v/v)	Xterra C18 100×4.6 mm i.d., 5 µ	210 nm	24
Determination of Valsartan in Tablet Dosage Form	HPLC	Water: Acetonitrile: glacial acetic acid (500:500:01).	Thermo-hypersil ODS 150 mm×4.6 mm i.d., 5 µ	273 nm	25
Analytical Method Development and Validation of Valsartan	HPLC	Methanol and phosphate buffer pH 2.5, (75:25 v/v)	Phenomenex C18 250×4.6 mm, 5µ	250 nm	26
Simultaneous Determination of Amlodipine, Valsartan, Telmisartan, Hydrochlorothiazide and Chlorthalidone	HPLC	0.05 M sodium dihydrogen phosphate buffer and Acetonitrile, Gradient mode	Cosmosil PAQ 150 mm × 4.6 mm i.d., 5 µ	220 nm	27
Estimation of Valsartan in Pure and Tablet Dosage Form	HPLC	Phosphate buffer and Acetonitrile (55:45 v/v)	Kromasil C18 , 250 × 4.6 mm i.d., 5 µ	233 nm	28
Estimation of Valsartan in Bulk Drug	HPLC	Phosphate buffer: Acetonitrile, pH 3.0, (50: 50 v/v)	Acquity HSS Y- 3, 2.1× 100 mm i.d., 1.8 µ	205 nm	29
Determination of Hypertensive Drug Products	HPLC	Ammonium acetate buffer and Acetonitrile , Gradient mode	XTerra C18 150 × 4.6 mm i.d., 5 µ	230 nm	30
Estimation and Separation of Valsartan, Losartan and Irbesartan in Bulk and Pharmaceutical formulation	HPLC	Acetonitrile and Phosphate buffer (40:60 v/v)	Eurospher, C8 250 × 4.6 mm i.d., 5 µ	254 nm	31
Estimation of Valsartan in Solid Oral Dosage Forms	HPLC	Acetate buffer : Acetonitrile : methanol (38:24:38 %, v/v)	ODS C8 250 × 4.6 mm i.d., 5 µ	248 nm	32
Determination of valsartan in human volunteers and its application in bioequivalence	HPLC	Phosphate buffer: Acetonitrile, pH 3.0, (50: 50 v/v)	Zorbax Extend-C18 150 × 4.6 mm i.d., 5 µ	230and 370 nm	33

study					
Estimation of Valsartan in Pharmaceutical Dosage Forms	HPLC	Methanol: water: THF 60:35:05 (v/v/v).	Inertsil ODS C-18 250 × 4.6 mm i.d., 5 µ	269 nm	34
Stability Indicating Method for Simultaneous Estimation of Nebivolol HCL and Valsartan	HPLC	Acetonitrile, methanol and phosphate buffer (pH 4.0) (50:20:30 v/v)	Inertsil ODS C-18 150 × 4.6 mm i.d., 5 µ	210 nm	35
Simultaneous estimation of Aliskiren and Valsartan in Tablet Dosage Form	HPLC	Methanol, Phosphate buffer (pH 3.0) Acetonitrile, (50:20:30 v/v)	Lichrosphere C-18 150 × 4.6 mm i.d., 5 µ	271 nm	36
Stability-Indicating Method for the Simultaneous Determination of Valsartan and Ezetimibe	HPLC	Phosphate buffer: Acetonitrile, pH 3.15, (58: 42 v/v)	Symmetry C18 , 250 × 4.6 mm i.d., 5 µ	230 nm	37
Stability Indicating Method for Quantification of Valsartan and hydrochlorothiazide	HPLC	Ammonium acetate buffer pH 5.6, and Acetonitrile , Gradient mode	XTerra C18 250 × 4.6 mm i.d., 5 µ	265 nm	58
Determination of triple drug combination of valsartan, Amlodipine and hydrochlorothiazide in plasma	HPLC	Acetonitrile and ammonium formate, pH 3.5, Gradient mode	Gemini C18 250 × 4.6 mm i.d., 5 µ	254 nm	39
Simultaneous estimation of Nebivolol and Valsartan in Tablet Dosage Form	HPLC	Acetonitrile and Phosphate buffer (60:40 v/v)	Inertsil ODS C-18 250 × 4.6 mm i.d., 5 µ	278 nm	40
Stability-Indicating Method for the Determination of Aliskiren Hemifumarate and Valsartan	HPLC	Phosphate buffer and Methanol pH 3.0, (70 : 30 v/v)	Nucleosil ODS C-18 250 × 4.6 mm i.d., 5 µ	225 nm	41
Stability Indicating Method for Quantification of Impurities in Amlodipine and Valsartan	HPLC	Water, Acetonitrile and Methanol (70:20:10 v/v)	Zorbax SB C8 150 × 4.6 mm i.d., 3.5 µ	240 nm	42
Simultaneous Determination of Amlodipine, Valsartan, Hydrochlorothiazide in Dosage Form and Spiked Human Plasma	HPLC	Acetonitrile and Phosphate buffer pH 2.8 (40:60 v/v)	Phenomenex Kinetex 150 × 4.6 mm i.d., 5 µ	227 nm	43
Stability indicating Simultaneous Determination of Valsartan and Ramipril in binary combination	HPLC	Acetonitrile and Water (55:45 v/v)	Hypersil C-18 250 × 4.6 mm i.d., 5 µ	215 nm	44
Determination and validation of ketoprofen, pantoprazole and valsartan in human plasma	HPLC	Phosphate buffer and Acetonitrile pH 3.15, (58 : 42 v/v)	Kromasil C18 250 × 4.6 mm i.d., 5 µ	225 and 272nm.	45
Stability indicating method for the estimation of Valsartan	HPLC	Methanol and Phosphate buffer pH 3.0 (65:35 v/v)	Phenomenex C18 250 × 4.6 mm i.d., 5 µ	210 nm	46
Estimation of valsartan in bulk and tablet dosage forms	HPLC	Water, Acetonitrile and Glacial acetic acid (55:45:1 v/v)	XTerra C18 250 × 4.6 mm i.d., 5 µ	240 nm	47
Estimation of Valsartan in bulk formulation and human serum	HPLC	Acetonitrile and Phosphate buffer pH 3.0, (40 : 60 v/v)	Eurospher, C 18 250 × 4.6 mm i.d., 5 µ	254 nm	48
Inherent Stability of Valsartan by Stress Degradation and Its Validation	HPLC	Water and Acetonitrile (60:40 v/v)	Kromasil C18 , 250 × 4.6 mm i.d., 5 µ	265 nm	49
Quantitative Determination of three Angiotensin-II-receptor Antagonists in Presence of Hydrochlorothiazide	HPLC	Phosphate buffer and Acetonitrile pH 6.0, (65 : 35 v/v)	Hypersil C-18 250 × 4.6 mm i.d., 5 µ	220 nm	50

Determination and validation of valsartan and its degradation products	HPLC	Methanol and Water pH 7.2 (60:40 v/v)	HIQ sil C18 ODS 250 × 4.6 mm i.d., 5 µ	250 nm	51
Simultaneous determination of Propranolol and valsartan in bulk drug and gel formulation	HPLC	Acetonitrile, Methanol and Phosphate buffer pH 3.5 (50 : 35 : 15 v/v)	Hypersil C-18 ODS 250 × 4.6 mm i.d., 5 µ	250 nm	52
Analysis of Some Antihypertensive Agents in their Pharmaceutical Dosage Forms	HPLC	0.2 % v/v Triethylamine buffer (pH 3.0) and Acetonitrile. Gradient mode	Purosphere Star 250 × 4.6 mm i.d., 5 µ	215 nm	53
Specific Stability Indicating method for Valsartan	HPLC	Phosphate buffer : Acetonitrile pH 2.5, (58 : 42 v/v)	Symmetry C18 , 250 × 4.6 mm i.d., 5 µ	250 nm	54
Stability-Indicating Determination of Valsartan and Hydrochlorothiazide Using Quality by Design	HPLC	Water, Methanol and Acetonitrile (50:38:12 v/v)	Hypersil C-18 ODS 250 × 4.6 mm i.d., 5 µ	271 nm	55
Simultaneous Estimation of Nebivolol HCL and Valsartan in bulk and pharmaceutical dosage form	HPLC	Phosphate buffer and Acetonitrile pH 6.0, (52 : 48 v/v)	Altima C18 , 150 × 4.6 mm i.d., 5 µ	282 nm	56
Simultaneous estimation of ramipril and valsartan in combined dosage form	HPLC	Phosphate buffer and Acetonitrile pH 3.2, (40 : 60 v/v)	Hypersil C18 250 × 4.6 mm i.d., 5 µ	25 nm	57
Simultaneous Estimation of Antihypertensive and Antidiabetic Drugs	HPLC	Acetic acid and Acetonitrile (60 : 40 v/v)	Phenomenex C18 250 × 4.6 mm i.d., 5 µ	240 nm	58
Improved analytical validation and pharmacokinetics of valsartan	HPLC	Acetonitrile and Phosphate buffer pH 2.0, (42 : 58 v/v)	Phenomenex C18 250 × 4.6 mm i.d., 5 µ	220 nm	59
Method Development of Aliskiren Hemifumarate and Valsartan in bulk drug	HPLC	Acetonitrile, Phosphate buffer and Methanol pH 4.0 (45 : 40 : 15 v/v)	Waters C18 , 250 × 4.6 mm i.d., 5 µ	220 nm	60
Rapid determination of valsartan in human plasma by protein precipitation	HPLC	Acetonitrile and Phosphate buffer pH 2.0, (45 : 55 v/v)	Nucleosil C-18 120 × 4.6 mm i.d., 5 µ	234 nm	61
Determination of irbesartan and valsartan in human urine	HPLC	0.3 % Formic acid and Methanol (30:70 v/v)	C-18 120 × 4.6 mm i.d., 5 µ	236 nm	62
Determination of losartan, Telmisartan, and valsartan by direct injection of human urine	HPLC	Phosphate buffer, Acetonitrile and Methanol pH 3.8 (65 : 20 : 15 v/v)	LiChrocart 250 × 4.6 mm i.d., 5 µ	259 and 399nm	63
Determination of Amlodipine, Hydrochlorothiazide and Valsartan	HPLC	Phosphate buffer pH 5.5 and methanol (38 : 62 v/v)	Waters C18 , 250 × 4.6 mm i.d., 5 µ	234 nm	64
Monitoring of Impurity Level of Valsartan and Hydrochlorothiazide	HPLC	Acetonitrile and Water pH 2.5 Gradient mode	Hypersil – ODS 250 × 4.6 mm i.d., 5 µ	256 nm	65
Simultaneous determination of valsartan and hydrochlorothiazide	LC	Phosphate buffer, Acetonitrile pH 3.2 (55 : 45 v/v)	Symmetry C18 , 250 × 4.6 mm i.d., 5 µ	225 nm	66
Quantitative Estimation of Valsartan in Bulk and Dosage Forms	HPLC	Phosphate buffer, Acetonitrile (20 : 80 v/v)	Venusil XBP C-18 250 × 4.6 mm i.d., 5 µ	273 nm	67

Stability Indicating Method for Determination of Valsartan in Pure and Pharmaceutical Formulation	HPLC	Phosphate buffer and Methanol pH 3.5 (50 : 50 v/v)	Phenomenex Gemini C18 250 × 4.6 mm i.d., 5 µ	210 nm	68
Concurrent Estimation of Amlodipine Besylate, Hydrochlorothiazide and Valsartan	HPLC	Acetonitrile and Water (50 : 50 v/v)	Kromasil KR-5 C18 250 × 4.6mm i.d., 5 µ	232 nm	69
Determination of Valsartan, Amlodipine Besylate, and Hydrochlorothiazide	UPLC	Methanol : Phosphate buffer pH 3.0 (70:30 v/v)	Acquity RP18 100 mm × 2.1 mm i.d.,1.7 µ	239 nm	70
Simultaneous Determination of Valsartan & Hydrochlorothiazide in Drug Products	UPLC	Triethylamine buffer : Methanol (75:25 v/v)	Kromasil eternity C-18 50 mm×2.1 mm i.d.,3.5 µ	225 nm	71
Determination of Valsartan and their degradation products in pharmaceutical dosage forms	UPLC	Acetic acid : Acetonitrile Gradient mode	Waters Acquity C18 100mm×2.1mm i.d.,1.7 µ	225 nm	72
Quantitative Analysis Of Valsartan And hydrochlorothiazide	HPTLC	Chloroform, ethyl acetate and acetic acid, 5:5:0.2 (v/v)	Aluminium plates precoated silica gel 60F254	248 nm	73
Concurrent Estimation of Amlodipine Besylate, Hydrochlorothiazide and Valsartan	HPTLC	Ethyl acetate, Methanol, Toluene and ammonia (7.5:3:2:0.8, v/v/v/v)	Aluminium plates precoated silica gel 60F254	242 nm	69
Simultaneous Estimation Of Cilnidipine And Valsartan In Bulk And Tablet Dosage Form	HPTLC	Toluene: Methanol: Ethyl acetate: Glacial Acetic acid in the ratio 8:1:1:0.1 (v/v/v/v)	Aluminium plates precoated silica gel 60F254	240 nm	74
Simultaneous Estimation of Ramipril and Valsartan	HPTLC	Chloroform: ethyl acetate: methanol: glacial acetic acid (5.0:5.0:1.0:02 v/v/v/v).	Aluminium plates precoated silica gel 60 F254	210 nm	75
Simultaneous Estimation of Ramipril & Valsartan in Tablets by	HPTLC	Ethyl acetate: chloroform: glacial acetic acid, (8:2:0.2, v/v)	Aluminium plates precoated silica gel 60 F254	220 nm	76
Analysis of angiotensin II receptor antagonist and protein markers	LC-MS-MS	Acetonitrile : Formic acid (45 : 55 v/v)	RP C18 nano-flow column 150 µ inner diameter 375 µ outer diameter 3 µ	-	77
Simultaneous Estimation of Amlodipine and Valsartan in Human Plasma	LC-MS-MS	Acetonitrile : Ammonium formate (80 : 20 v/v)	Luna C18 100A 150 x 4.6 mm, 5 µ	--	78
Simultaneous quantification of valsartan and hydrochlorothiazide in human plasma	LC-MS-MS	Acetonitrile : Ammonium Acetate pH 4.5 (60 : 40 v/v)	Zorbax SB-Aq C18 150 x 4.6 mm, 5 µ	--	79
Bio- analytical method development of Valsartan by precipitation method	HPLC-MS/MS	0.1% formic acid and Methanol (25:75, v/v)	Hypurity C18 150 × 4.6 mm i.d., 5 µ	-	80
Optimization and validation of bioanalytical method for estimation of Valsartan in rat plasma	HPLC-ESI-MS-MS	0.1 % Formic acid and Methanol (25:75 v/v)	Ascentis Express C-18 50 × 4.6 mm i.d., 2.7 µ	-	81

analysis of valsartan in pharmaceuticals, HPLC with UV detection is applicable because this method provides accurate results and low cost compared to more advanced detection techniques. This review carried out an overview of the current state-of-art analytical methods for the determination of valsartan.

The review would help analytical chemists in knowing the key solvents and their combinations for their available

set of instruments in the analytical laboratory. The effective combination of parameters should minimize the cost of the analysis and reduce the time required for producing are liable analytical method. The methods are also useful for determining parameters for in-process evaluation during the manufacturing of API.

ACKNOWLEDGMENTS

The authors thankful to Principal and Staff of Vinayaka mission's College of Pharmacy,Vinayka missions university for providing the necessary facilities for this work.

REFERENCES

1. Julio TA et al, Compatibility and stability of Valsartan in a solid pharmaceutical formulation, Brazil J Pharm Sci, 2013; 49(1):645-651.
2. Saydam M, Takka S, Bioavailability file: Valsartan, Fabad J pharm.sci 2007;32:185-196
3. Avdeef A, Physicochemical profiling (solubility, permeability and charge state), Curr Top Med Chem 2001;1(4): 277-351.
4. Sandhya Rani, Raghu Babu and Srividhya. A Novel Method for Estimation of Valsartan in Bulk and pharmaceutical preparations by visible spectrophotometry. *International journal pharmaceutical and research*; 2015 5 (1), 55-61.
5. Nataraj, Ramakrishnama Charya, Swathi Goud, and Ramanjineyulu. Simple quantitative method development and validation of valsartan in pure form and pharmaceutical dosage forms by UV – Spectroscopy. *International Journal of Pharmacy and Biological Sciences*; 2011 1(2), 67-73.
6. Taghreed Abd-El-Fattah Mohammed. Native and synchronous spetroflurimetric methods for imultaneous determination of Amlodipine/valsartan combination in tablets. *Asian Journal of Science and Technology;* 2015 6 (8), 1690-1698.
7. Ankit B. Chaudhary, Rakesh K. Patel, Sunita A. Chaudhary, Krupa V. Gadhvi. Estimation of valsartan and hydrochlorothiazide in pharmaceutical dosage forms by absorption ratio method. *International Journal of Applied Biology and Pharmaceutical Technology*; 2010 1 (2), 455-464.
8. Pankti M. Shah, Jignesh S. Shah and Dilip G. Maheswari. Development and validation of first order derivative spectrophotometric method for the simultaneous estimation of Valsartan and nifedipine in bulk and synthetic mixture. *International Journal Of Pharmacy & Technology*; 2015 7 (2), 9161-9169.
9. Monika L. Jadhav, Manoj V. Girase, Shripad K. Tidme, and Manish S. Junagade. Development and Validation of Spectrophotometric Methods for Simultaneous Estimation of Valsartan and Hydrochlorothiazide in Tablet Dosage Form. *International Journal of Spectroscopy;* 2014 1-6.
10. Erdal dinci, Dumitru baleanu. Continuous Wavelet Transform Applied to the Simultaneous Spectrophotometric Determination of Valsartan and Amlodipine in Tablets. *Rev. Chem;* 2010 61, (3)290-294.
11. Varsha R. Galande, Baheti, Indraksha and Dehghan. Estimation of Amlodipine Besylate, Valsartan and Hydrochlorothiazide in Bulk Mixture and Tablet by UV Spectrophotometry *Indian Journal of Pharmaceutical Sciences*; 2012 1, 18-23.
12. Nashwah Gadallah Mohamed. Simultaneous Determination of Amlodipine and Valsartan *Analytical Chemistry Insights*; 2011 6, 53–59.
13. Meyyanathan, Arunadevi S., Birajdar and Bhojraj Suresh. Simultaneous Estimation of Nebivolol Hydrochloride and Valsartan and Nebivolol Hydrochloride and Hydrochlorothiazide in Pharmaceutical Formulations by UV Spectrophotometric Methods *Indian J.Pharm. Educ. Res*; 2010 44 (2), 156-159.
14. Rajesh, Sai Praveen, Ramesh, Jagathi and Devalarao. Simultaneous Spectrophotometric estimation of Valsartan and Ramipril by derivative method. *Int.J.Pharm.& Health Sci*; 2010 1(2) 132-135.
15. Sivasankara Rao, S Venkat Raoa, SVM Vardhanb and D Ramachandrana. Development and validation of new UV-spectrophotometric assay method for valsartan in pure and in formulations. *Journal of Chemical and Pharmaceutical Research; 2013* 5 (7) 229-232.
16. Tarkase Kailash N., Tajane Sachin, Jadhav Manisha. Development and Validation of UV-Spectrophotometric methods for estimation of Valsartan in bulk and tablet dosage form *Journal of Pharmacy Research*; 2012 5 (4), 2344-2346.
17. Karunanidhi santhana lakshmi and Sivasubramanian lakshmi. Simultaneous spectrophotometric determination of valsartan and hydrochlorothiazide by H-point standard addition method and partial least squares regression. *Acta Pharm;* 2011 61 37–50.
18. Lalit kumar,M.sreenivasa reddy, Renuka S. Managuli, Girish pai K. Full factorial design for optimization development and validation of HPLC method to determine valsartan in nanoparticles. *Saudi pharmaceutical journal;* 2015,23, 549-555.
19. Arabinda patnaik, Malikarjuna shetty, Subash sahool, diptish kumar nayak. A new RP-HPLC method for the determination of valsartan in bulk and its pharmaceutical formulations with its stability Indicate studies. *An international journal of pharmaceutical science*; 2011 2 (3), 43-53.
20. Jothieswari.D, Priya.D, Brito raj.S , Mohanambal.E , Wasim raja.S. Design and RP-HPLC method for the simultaneous determination of valsartan and hydrochlorothiazide in bulk and in pharmaceutical formulation. *International journal of novel trends in pharmaceutical science*; 2011 1, 18-22.
21. Magda M.Ibrahim, Maha A.Hegazy and Mohamad A, Abdei-Ghanil. Application of a RP-HPLC method for comparative study on the degradation behavior of two angiotension II receptor antagonists, valsartan and losartan potassium. *IJPCBS;* 2015 5 (2), 417- 426.

22. Havalder freddy H, and Vairal dharmendra. Simultaneous estimation of atenolol, hydrochlorothiazide, losartan and valsartan in the pharmaceutical dosage form. *International journal of pharmacy and life science;* 2010 1(5), 282-289.
23. Meghraj D. kendre. Surabh K. Banerjee. Precise and accurate RP-HPLC method development for quantification of valsartan in tablet dosage form. *International journal of pharmaceutical science and drug research*; 2012 4 (2), 137-139.
24. Bhaskara raju and Lakshmana rao. Reversed phase HPLC analysis of valsarten in pharmaceutical dosage forms. *International journal of chemical cnbironmental and pharmaceutical research*; 2011 2 (1), 56-60.
25. Vinzuda D.V, Sailor G.U, Sheth N.R. RP-HPLC Method for determination of valsartan in tablet dosage form. *International journal of chem. tech research*; 2010 2(3), 1461-1467.
26. Ajita makula, Naga praveena, Rajani kumari kondepudi, Radhika tanga palli. Analytical method development and validation of Valsartan in bulk by RP-HPLC method. *International journal of pharmaceutical science review and research*; 2012 1 (6), 88-90.
27. Mhaske R.A, Garole D.J, Mhake A.A and Sahasrabudhe S. RP-HPLC Method for simulataneous determination of amlodipine besylate,valsartan,telmisarten, hydrochlorothiazide and chlorthalidone: Application to commercially available drug product. *International journal of pharmaceutical science and research*; 2012 3 (1), 141-149.
28. Santosh kumar P.V, Manoranjan sahu K, Durga prasad and Chandra shaker M.) Development and Validation of Analytical method for the estimation of valsartan in pure and tablet dosage form by RP-HPLC Method. *International journal of research in pharmaceutical chemistry*; 2011 1 (4), 945-949.
29. Anita shindu, Suman Malik, Asati amit asati. Analytical development and validation of reverse phase liquid chromatography for estimation of valsartan in bulk drug. *Indo American journal of pharmaceutical research*; 2014 4, (2) 931-938.
30. Phani.R.S.C.H,K.R.S Prasad, and useni reddy mallu. High resolution RP-HPLC Method for the determination of hypertensive drug products. *International journal of bioscience*; 2013 4 (1), 440-454.
31. Reem yousef, Adnan hbash, Ahmad Hassan. Development and validation of RP-HPLC Method for the estimation and separation of valsartan, losartan and irbesartan in bulk and pharmaceutical formulations. *International journal of pharmaceutical review and research*; 2014 24 (2), 311-314.
32. Subhajit Ghanty,Rudranil das, Sabyasachi maitikalyan kumarsen. RP-HPLC Method for the estimation of valsarten in solid oral dosage forms. J*ournal of Pharma science tech*; 2014 3 (2), 88-91.
33. Ola M. Abdullah, and Khalid abuzeid. HPLC Fluoresence determination of valsarten in human volunteers and its application in bioequivalance study of two valsarten tablets. *Life science journal;* 2013 10 (2), 583-590.
34. Manoranjani M., and bhagyakumar T. RP-HPLC Method for the estimation of valsartan in pharmaceutical dosage forms *international journal of Pharma science innovations and discoveries;* 2011 1(2), 101-108.
35. Kalpana nekalaV. Shanmuka kumar J. D.Ramachandran,Ganji ramanaiah and Ganta srinivas Method development and validation of stability indicating RP-HPLC method for simultaneous estimation of nebvolol HCL and valsarten in bulk and its pharmaceutical formulations. *American journal of advanced drug delivery;* 2014 2 (5), 624-637.
36. Kumaraswamy G1, kumar JMR 1, Sheshagiri Rao JVLN2, Lakshmi Surekha.M1 validated RP-HPLC method for simultaneous estimation of alikiren and valsartan in tablet dosage form. *Journal of Drug Delivery & Therapeutics*; 2012 2 (5), 162-166.
37. Sridevi Ramachandran1, Badal Kumar Mandal and Sameer Navalgund. Stability-Indicating HPLC Method for the Simultaneous Determination of Valsartan and Ezetimibe in Pharmaceuticals. *Tropical Journal of Pharmaceutical Research*; 2014 13 (5).
38. Maher knaroaf, Numen malkish, mured abulhasan, Raqi shubitah, nindal jaradat, abdel naser zaid. Tablet formulations and development of a validated stability indicating HPLC method for quantification of Valsartan and hydrochlorothiazide combination. *International journal of pharmaceutical sciences*; 2012 4 (2), 683-687.
39. Ritesh N. Sharma and Shyam sunder pancholi. Simple RP-HPLC method for determination of triple drug combination of valsartan, amlodipine and hydrochlorothiazide in human plasma. *Acta Pharm;* 2012 62, 45–58.
40. Madhavi, Siddartha, Parthiban. Simultaneous estimation and validation of nebivolol and valsarten in tablet dosage form by RP-HPLC *International journal of pharmacy and pharmaceutical sciences*; 2014 6 (1) 278-282.
41. Rizwan SH, Girija sastry. Development and validation of stability indicating RP-HPLC Method for the simultaneous estimation of aliskiran hemifumarate and valsartan in bulk and pharmaceutical dosage form. *Asian journal of phamaceutical and clinical research*; 2015 8 (6) 223-227.
42. Rama joga venkata eranki, Gopi chand, venkata subramaniyan jayaraman, sudhakar rao vidiyalaya, and Sree ramula. New stability indicating method for quantification of impurities in amlodipine and valsartan tablets by validated by HPLC. *ISRN medicinal chemistry*; 2013 1-9.
43. Samya M.E, Gizway, Osma.H, Abdelmageed, mahmoud A, Omar sayed M. Deryea. Development and validation of HPLC Method for simultaneous

determination of amlodipine valsartan hydrochlorothiazide an dosage form and spiked human plasma. *American journal of analytical chemistry;* 2012 3,422-430.
44. Lakshmi. K.S and Lakshmi sivasubramanian. Stability indicating HPLC method for the simultaneous determination of Valsartan and ramipril in binary combination. *J. Chil. Chem. Soc*; 2010 3, 223-226.
45. Kocyig itKaymakc, Nsalan, S. Rollas. Determination and validation of ketoprofen, pantoprazole and valsartan together in human plasma by high performance liquid chromatography. *Pharmazie*; 2006 61,(7) 586-589.
46. Akiful Haque M, Hasan Amrohi A, Prashanth Kumar.K, Nivedita.G, Pradeep Kumar.T, and Prakash.V. Diwan. Stability indicating RP-HPLC method for the estimation of Valsartan in pharmaceutical dosage form. *IOSR Journal of Pharmacy;* 2012 2(4),12-18.
47. Srinath Nissankararao, Anil Kumar. A, Sravanthi. S. L. and Naga Silpa. J. Method development and validation for the estimation of valsartan in bulk and tablet dosage forms by RP-HPLC. *Scholars Research Library*; 2013 5 (2), 206-211.
48. Reem Youssef and Ahmad Hassan Development and validation of chromatographic method for the estimation of valsartan in bulk pharmaceutical formulation and human serum. *International Journal of Current Research in Chemistry and Pharmaceutical Sciences*; 2014 1 (4), 44-49.
49. Vivek Agrahari, Vibhuti Kabra, Sandeep Gupta, Rajesh Kumar Nema, Mayank Nagar, Chandrabose Karthikeyan, Piyush Trivedi. Determination of Inherent Stability of Valsartan by Stress Degradation and Its Validation by HPLC. *International Journal of Pharmaceutical and Clinical Research;* 2009 1 (2) 77-81.
50. Hany Mohammed Hafez, Abdullah Ahmed Elshanawane, Lobna Mohammed Abdelaziz and Magda Mohammed Kamal. Quantitative Determination of three Angiotensin-II-receptor Antagonists in Presence of Hydrochlorothiazide by RP-HPLC in their Tablet Preparations *Journal of Pharmaceutical Research* ; 2013 12 (4), 635-643.
51. Bhatia M. Sudesh and Kokil S. Uttamrao . Determination and validation of valsartan and its degradation products by isocratic HPLC. *Journal of chemical metrology;* 2009 3 (1) 1-12.
52. Syed Sarim Imam, Abdul Ahad1, Mohammed Aqil, Yasmin Sultana, Asgar Ali A validated RP - HPLC method for simultaneous determination of propranolol and valsartan in bulk drug and gel formulation. *Journal of Pharmacy and BioAllied Sciences Sciences* ; 2013 5 (1), 61-65.
53. Shalini pachauria, Sarvesh paliwalb, Kona. Srinivasa, Yogendra Singha and Varun Jaina. Development & Validation of HPLC Method for Analysis of Some Antihypertensive Agents in their Pharmaceutical Dosage Forms. *Journal of pharmaceutical science and research;* 2010 2 (8),459-464.
54. Rao KS, Jena N, Rao MEB 2010 Development and Validation of a Specific Stability Indicating High Performance Liquid Chromatographic Method for Valsartan. *J Young Pharm*; 2010 2 (2), 183-189.
55. Ashok K. SHakya. Development and Validation of a Stability-Indicating Liquid Chromatographic Method for Determination of Valsartan and Hydrochlorothiazide Using Quality by Design Oriental Journal of chemistry; 2016 32 (2), 777-788.
56. Siddartha, Sudheer Babu, Ravichandra Gupta and Parthiban. Analytical method development and validation for simultaneous estimation of Nebivolol and valsartan in bulk and pharmaceutical dosage forms by RP-HPLC method. *International journal of pharmacy*; 2014 4 (1), 340-346.
57. Nitin Dubey, Nidhi Dubey , Mayank Mandhanya , Upendra Bhadoriya , Praveen Sharma. Simultaneous estimation of ramipril and valsartan by RP-HPLC method in combined dosage form. *Asian Journal of Pharmacy and Medical Science*; 2012 2 (1), 23-28.
58. Mohammad Farhadur Rahman, Md. Zakir Sultan, Asma Rahman, Md. Anisur Rahman and Md Abdus Salam. Simultaneous Estimation of Antihypertensive and Antidiabetic Drugs by HPLC. *Journal of Pharmaceutical Quality Assurance*; 2015 1 (1), 25-29.
59. Zong-Zhu Piao, Zong-Zhu Piao, Eung-Seok Lee and Beom-Jin Lee. Improved analytical validation and pharmacokinetics of valsartan using HPLC with UV detection. *Archives of Pharmacal Research;* 2008 31,(8) 1055-1059.
60. Somsubhra Ghosh B. Anusha , Santhoshi , David Banji , Y. Chaithanya Kumar , P. Raghavendra and Subhadip Roy. Method Development and Validation of Aliskiren Hemifumarate and Valsartan in bulk drug by RP-HPLC method. *Asian Journal of Research in Chemistry*; 2013 6(1), 19-23.
61. Macek J. Macek, J. Klíma, and P. Ptacek. Rapid determination of valsartan in human plasma by protein precipitation and high-performance liquid chromatography. *Journal of Chromatography B;* 2006 832 (1), 169–172.
62. Zhiling Li, Fan Chen and Xuedong Wang. Ionic liquids dispersive liquid–liquid microextraction and high-performance liquid chromatographic determination of irbesartan and valsartan in human urine. *Biomedical Chromatography. 2013* 27(2) , 254–258.
63. María del Rosario Brunetto , Yaritza Contreras, Sabrina Clavijo and Dina Torres Martin. Determination of losartan, telmisartan, and valsartan by direct injection of human urine into a column-switching liquid chromatographic system with fluorescence detection. *Journal of Pharmaceutical and Biomedical Analysis;* 2009 50 (2), 194–199.
64. Silvana E. Vignaduzzo, Patricia M. Castellano and Teodoro S. Kaufman. Development and validation of an HPLC method for the simultaneous determination of amlodopine, hydrochlorothiazide and valsartan in tablets of their novel triple combination and binary pharmaceutical associations. *Journal of Liquid*

Chromatography & Related Technologies; 2011 34 (19), 2383-2395.

65. Darko Ivanovic, Anđelija Malenovic, Biljana Jancic, and Marija Maskovic. Monitoring of Impurity Level of Valsartan and Hydrochlorothiazide Employing an RP–HPLC Gradient Mode. *Journal of Liquid Chromatography & Related Technologies*; 2007 30 (19), 2879-2890.
66. Eda Şatana, Şadi Altınay, Nilgün Günden Goger Sibel A. ozkan and Zuhre Şenturk. Simultaneous determination of valsartan and hydrochlorothiazide in tablets by first-derivative ultraviolet spectrophotometry and LC. *Journal of Pharmaceutical and Biomedical Analysis* ; 2001 25 (5), 1009–1013.
67. Thanusha , Jose Gnana Babu and Channa Basavaraj. Validated RP- HPLC Method for the Quantitative Estimation of Valsartan in Bulk and Pharmaceutical Dosage Forms. *International Journal of ChemTech Research*; 2010 2 (2), 1194-1198.
68. Patro, S. K., Kanungo, S. K. and Choudhury, N. S. K. Stability indicating RP-HPLC method for determination of Valsartan in pure and pharmaceutical formulation. *E-Journal of Chemistry*; 2010 7(1), 246-252.
69. Manish Sharma, Charmy Kothari, Omkar Sherikar and Priti Mehta Concurrent Estimation of Amlodipine Besylate, Hydrochlorothiazide and Valsartan by RP-HPLC, HPTLC and UV–Spectrophotometry. *Journal of Chromatographic Science*; 2014 (52), 27–35.
70. Lahsini and Moner. Development of New UPLC Method For Simultaneous Determination of Valsartan, Amlodipine Besylate, and Hydrochlorothiazide Pharmaceutical Products. *Acta Chromatographica*; 2015 2 (73) 449–460.
71. Antil P, Kaushik D, Jain G, Srinivas K and Indu Thakur. UPLC Method for Simultaneous Determination of Valsartan & Hydrochlorothiazide in Drug Products. *J Chroma. Separation Technique*; 2013 4 (5), 7064.
72. Ch. Krishnaiah , Raghupathi Reddy, Ramesh Kumar and Mukkanti. Stability-indicating UPLC method for determination of Valsartan and their degradation products in active pharmaceutical ingredient and pharmaceutical dosage forms. *Journal of Pharmaceutical and Biomedical Analysis*; 2010 53 (3), 483–489.
73. Kadam and Bari. B. Quantitative analysis of valsartan and hydrochlorothiazide in tablets by HPTLC with ultra violet absorption densitometry. *Acta chromatographia*. 2007 18, 260-269.
74. Ritesh P. Bhole.Vinayak C. Pawara, Sohan S. Chitlange, Sager B. Wankhede Development and validation of HPTLC method for simultaneous estimation of clinidipine and valsartan in bulk and tablet dosage form. *International Journal of Pharmaceutical Chemistry and Analysis*; 2015 2 (1) 102-107.
75. Shirish P. Lokhande, Surya Prakash Gupta, Sureshkumar, Dharuman, Gopal Garg and Neeraj Upmanyu. Development and Validation of a HPTLC Method for the Simultaneous Estimation of Ramipril and Valsartan. *International Journal of Pharmacy Teaching & Practices;* 2012 3 (1), 225-227.
76. Gaikwad A, Rajurkar V, Shivakumar T, Dama G and Tare H. Simultaneous Estimation of Ramipril & Valsartan in Tablets by HPTLC. *Indo-Global Journal of Pharmaceutical Sciences;* 2011 1(1), 99-112.
77. Chi-Yu Lua, Yung-Ming Changd,Wei-Lung Tsengb, Chia-Hsien Fenge, Chin-Yuan Luf Analysis of angiotensin II receptor antagonist and protein markers at microliter level plasma by LC-MS/MS. *Journal of Pharmaceutical and Biomedical Analysis*; 2009 49,123-128.
78. Hemanth Jangala, Poonam, Arshad and Tausif. Development and Validation of a LC-MS/MS Method for the Simultaneous Estimation of Amlodipine and Valsartan in Human Plasma: Application to Bioequivalence Study. *Scientia Pharmaceutica*; 2014 82, 585–600.
79. Hao Li., Yingwu Wang., Yao Jiang., Yunbiao Tang., Jiang Wang. and Limei Zhao. A liquid chromatography/tandem mass spectrometry method for the simultaneous quantification of valsartan and hydrochlorothiazide in human plasma. *Journal of Chromatography B*; 2007 852, 436–442.
80. Venkata Suresh. P, Rama Rao Nadendla and B. R. Challa. Bio- analytical method development and validation of Valsartan by precipitation method with HPLC-MS/MS: Application to a pharmacokinetic study *J. Chem. Pharm. Res;* 2013 5(7) 7-20.
81. Praveen Kumar, Srinivasa Rao. Optimization and validation of bioanalytical method for quantitative determination of Valsartan in rat plasma samples using HPLC-ESI-MS/MS *Journal of Chemical and Pharmaceutical Sciences*; 2015 8 (4), 636-642.