International Journal of Research in Pharmacy and Pharmaceutical Sciences
ISSN: 2455-698X
Impact Factor: RJIF 5.22
www.pharmacyjournal.in
Volume 3; Issue 1; January 2018; Page No. 109-118

A review on chromatographic and spectrophotometric method for estimation of Aliskiren and losartan potassium in bulk and in different dosage forms

[1] Rimpalben Patel, *[2] Dr. Jignesh Shah, [3] Dr. Dilip G Maheshwari
[1] M.Pharm, Department of Quality Assurance, L.J. Institute of Pharmacy, Ahmedabad, India
[2] Associate Professor, Department of Quality Assurance, L.J. Institute of Pharmacy, Ahmedabad, India
[3] Associate Professor (HOD), Department of Quality Assurance, L.J. Institute of Pharmacy, Ahmedabad, India

Abstract
Aliskiren is direct renin inhibitor and used in treatment of hypertension. Losartan potassium is angiotensin receptor blocker and used in treatment of hypertension. Under clinical trial it's proved that the combination of Aliskiren with angiotensin receptor blocker Losartan Potassium provides greater reduction in aldosterone which leads to reduction in LVH (left ventricular hypotrophy) than losartan alone.

Keywords: aliskiren, losartan potassium, UV- spectroscopy, HPLC (high performance liquid chromatography), HPTLC (high performance thin layer chromatography), LC (liquid chromatography)

Introduction [1-4]

Aliskiren((2S,4S,5S,7S)-5-amino-N-(2-carbamoyl-2,2-dimethylethyl)-4-hydroxy-7-{[4-methoxy-3-(3-methoxypropoxy)phenyl]methyl}-8-methyl-2-(propan-2-yl)nonanamide)is direct renin inhibitor and used in treatment of hypertension. Renin is secreted by the kidney which cleaves angiotensinogen to form the inactive decapeptide angiotensin I (Ang I). Ang I is converted to the active octapeptide angiotensin II (Ang II) by ACE and non- ACE pathways. Ang II inhibits renin release, thus providing a negative feedback to the system. Aliskiren is soluble in water and methanol and available as white to bright to yellowish crystalline powder. Losartan potassium(Potassium; [2-butyl-5-chloro-3-[[4-[2-(1,2,3-triaza-4-azanidacyclopenta-2,5-dien-5-yl)phenyl]phenyl]methyl]imidazol-4-yl]methanol)is angiotensin receptor blocker and used in treatment of hypertension. Losartan potassium competitively inhibits the binding of angiotensin II to AT1 in many tissues including vascular smooth muscle and the adrenal glands. Inhibition of angiotensin II binding to AT1 inhibits its AT1-mediated vasoconstrictive and aldosterone-secreting effects and results in decreased vascular resistance and blood pressure. Losartan Potassium is soluble in water and methanol and available as white to off white crystalline powder.

Official and Reported methods are categorized depending on the following considerations:

1. Single component analyzed by UV-spectroscopy methods and chromatographic method.
2. Analysis of Aliskiren and Losartan Potassium in combination with other drugs by UV-spectroscopy methods and chromatographic method.

Table 1: Reported Analytical Method of Aliskiren: [5-21]

Sr No	Drug	Method	Description	Ref No
1	Aliskiren in pharmaceutical dosage form	UV spectrophotometric method	Detection wavelength: 279 nm Linearity range: 4-24 µg/ml	5
2	Aliskiren in bulk and pharmaceutical dosage form	RP-HPLC Method	Detection wavelength: 234 nm Mobile phase: acetonitrile: phosphate buffer 0.02M 60:40(v/v) with pH 3.5 Stationary phase: symmetry C18(150×4.6 mm packed with 5µ) Flow rate: 1.0 ml min^1 Retention time: 2.28 min Linearity range: 50-175 µg/ml	6
3	Aliskiren in bulk and pharmaceutical dosage form	Stability indicating RP-HPLC Method	Detection wavelength: 280nm Mobile phase: acetonitrile and 0.05M KH_2PO_4 buffer (45:55 v/v) and pH adjusted to 2.5 with 10% ortho- phosphoric acid Stationary phase: hyperchrom-ODS 5µ C18 column (250×4.6 mm) Flow rate: 1.0 ml/ min Linearity range: 10-60 µg/ml	7

4	Aliskiren in tablet dosage form	Stability indicating RP-LC Method	Detection wavelength: 229 nm using photodiode array detector Mobile phase: acetonitrile: water (95:5v/v)/phosphoric acid (25 mm, pH 3.0) (40:60, v/v) Stationary phase: Waters XBridge C18 column (150 ×4.6 mm i.d.), maintained at 25°C. Flow rate: 1.0 ml/ min Retention time: 3.68 min Linearity range: 10-300 µg/ml	8
5	Simultaneous estimation of aliskiren and hydrochlorothiazide in tablet formulation	UV spectroscopic Method	Simultaneous equation method Detection wavelength: Aliskiren :271 nm Hydrochlorothiazide:280 nm Linearity range: Aliskiren :6-300 µg/ml Hydrochlorothiazide: 0.5-25µg/ml Absorbance ratio method Detection wavelength: Aliskiren: 255 nm Hydrochlorothiazide: 271 nm Linearity range: Aliskiren :6-300 µg/ml Hydrochlorothiazide: 0.5-25µg/ml First derivative spectroscopic methods Detection wavelength: Aliskiren: 241nm Hydrochlorothiazide: 280.2 nm Linearity range: Aliskiren :6-300 µg/ml Hydrochlorothiazide: 0.5-25µg/ml	9
6	Aliskiren and valsartan in their fixed dosage form	UV Spectrophotometric Method	Ratio spectra derivative spectrophotometric method Detection wavelength: Aliskiren: 289 nm Valsartan: 245 nm Linearity range: Aliskiren: 50-200 µg/ml Valsartan: 5-24 µg/ml	10
7	Aliskiren and amlodipine in combined dosage form	UV spectrophotometric method	Absorbance correction method Detection wavelength: Aliskiren: 256.0 nm Amlodipine: 354.5 nm Linearity range: Aliskiren: 20-120 µg/ml Amlodipine: 10-60 µg/ml	11
8	Aliskiren and valsartan their bulk drug	RP-HPLC Method	Detection wavelength: 220 nm. Mobile phase: Acetonitrile and Phosphate buffer and Methanol was used as mobile phase in the composition of 45:40:15, phosphate buffer (0.02Mm) adjusted the pH to 4 with Orthophosphoric acid within a short runtime of 8 min. Stationary phase: C8 Column (4.6 x 250 mm, 5 µm) Flow rate: 1 ml/min Retention time: Aliskiren: 3.407 min Valsartan: 4.268 min Linearity range: Aliskiren: 15-45 ppm Valsartan: 16-48 ppm	12
9	Aliskiren and hydrochlorothiazide in combined tablet formulation	RP-HPLC Method (Quantitative determination)	Detection wavelength: 280nm Using PDA detector Mobile phase: 0.2 %v/v triethylamine in water (pH 6 was adjusted with orthophosphoric acid): methanol (10:90 %v/v) Stationary phase: Enable C_{18} column (250×4.6 mm, 5 µm) Flow rate: 1 ml/min Retention time: Aliskiren: 5.315 min Hydrochlorothiazide: 2.824 min Linearity range:	13

			Aliskiren: 1.2-240 µg/ml Hydrochlorothiazide: 0.1-20 µg/ml	
10	Aliskiren and amlodipine in tablet dosage form	RP-HPLC Method	Detection wavelength: 237 nm using photodiode array (PDA) detector Mobile phase: Phosphate buffer: Acetonitrile (60: 40) Stationary phase: Kromasil, ODS 3V (250 x 4.6mm, 5µm) C18 column with 5µm particle size. Flow rate: 1 ml/min Retention time: Aliskiren: 3.9 min Amlodipine: 5 min Linearity range: Aliskiren: 25-150 µg/ml Amlodipine: 2.5-15µg/ml	14
11	Aliskiren and enalapril in bulk and synthetic mixture	RP-HPLC Method	Detection wavelength:210 nm Mobile phase: acetonitrile and water in ratio of 80:20 and adjusting pH 4.0 with ortho phosphoric acid (10%) Stationary phase: Phenomenex-luna C18 (250 × 4.6 mm, 5µm) column Flow rate: 1 ml/min Retention time: Aliskiren: 2.63 min Enalapril: 7.25 min Linearity range: Aliskiren: 2-10 µg/ml Enalapril: 15-75 µg/ml	15
12	Aliskiren, hydrochlorothiazide and amlodipine besylate in pharmaceutical formulation	RP-HPLC Method	Detection wavelength: 239nm Mobile phase: ACN: Methanol: pH 3.0 buffer (20:50:30 (v/v) Stationary phase: Hiber@ Lichrosphere, (C18 4.6×250mm 5.0µm) Flow rate: 1 ml/min Retention time: Aliskiren: 6.4 min Hydrochlorothiazide: 2.6 min Amlodipine besylate: 5.8 min Linearity range: Aliskiren: 75-450 µg/ ml Hydrochlorothiazide: 12.5 -75 µg/ ml Amlodipine besylate: 5 –30 µg/ ml	16
13	Aliskiren and valsartan in bulk and pharmaceutical dosage form	Stability indicating RP-HPLC Method	Detection wavelength: 225nm Mobile phase: methanol: potassium dihydrogen ortho phosphate buffer (adjusted pH with 3 with orthophosphoric acid) Stationary phase: nucleocil C18(250mm×4.6mm 5µ) Flow rate: 1 ml/min Retention time: Aliskiren: 3.84 min Valsartan: 5.96min Linearity range: Aliskiren: 5.50 mcg/ml Valsartan:5-30 mcg/ml	17
14	Aliskiren, amlodipine and hydrochlorothiazide in tablet dosage form.	Stability indicating RP-HPLC Method	Detection wavelength: 228nm Mobile phase: Acetonitrile:1ml TEA in 1000 potassium phosphate buffer 0.01M (40:60% v/v) Stationary phase: Hypersil BDS, 250 x 4.6 mm, 5µ column Flow rate: 1 ml/min Retention time: Aliskiren: 5.9 min Amlodipine: 8.0 min Hydrochlorothiazide: 3.3 min Linearity range: Aliskiren: 75-450µg/ml Amlodipine: 2.5-15µg/ml Hydrochlorothiazide: 6.25-37.5µg/mL	18
15	Aliskiren in human plasma	HPLC Method (assay)	Detection wavelength:230 nm Mobile phase: acetonitrile: water: phosphoric acid (45:55:0.01, v/v/v, pH 3.2)	19

			Stationary phase: C18 column Flow rate: 1 ml/min Linearity range: 50-400 ng/ml	
16	Aliskiren, amlodipine, and hydrochlorothiazide in spiked human plasma and urine	HPLC Method	Detection wavelength:271nmby PDA detector Mobile phase:10 mm orthophosphoric acid containing 0.1% tri-ethylamine (pH 2.5, v/v) and acetonitrile Stationary phase: RP-C18 column (4.6 mm × 250 mm, 5 µm, Phenomenex) Flow rate: 1 ml/min Linearity range: (in plasma & urine) Aliskiren: 0.01-10 µg/ml Amlodipine: 0.05-10 µg/ml Hydrochlorothiazide: 0.0125-2.5 µg/ml	20
17	Aliskiren and hydrochlorothiazide in pharmaceutical preparation and spiked human plasma	HPTLC Method (d(densitometric analysis)	Detection wavelength:225 nm Mobile phase: methanol: chloroform (6:4 v/v) Stationary phase: silica gel 60 GF_{254} plates R_f value: Aliskiren: 0.26 Hydrochlorothiazide: 0.71 Linearity range: Aliskiren: 1-10µg/ band^{-1} Hydrochlorothiazide: 0.10-1 µg/ band^{-1}	21

Table 2: Official Analytical Method of Losartan Potassium: [22-23]

Sr No	Drug	Method	Description	Ref no.
1	Losartan potassium (IP 2014)	Liquid chromatography	Detection wavelength:254nm Mobile phase:(A)0.1% w/v solution od orthophosphoric acid in water (B)acetonitrile (75:25) Stationary phase: a stainless-steel column 25cmx4.0mm packed with octadecylsilane bounded with porous silica(5µ) Flow rate: 1.0 ml/min	22
2	Losartan in tablet dosage form (IP 2014)	Liquid chromatography	Detection wavelength:237nm Mobile phase: A mixture of 65 volumes of 0.005M ammonium acetate, 30 volumes of acetonitrile, 5 volumes of methanol and 0.2 volumes of triethylamine, adjust pH to 6.6 with glacial acetic acid Stationary phase: A stainless steel column 25cm x4.0mm packed withoctadecylsilane bounded with porous silica(5µ) (such as Lichrosphere RP8) Flow rate: 1.0 ml/min	22
3	Losartan potassium (USP 29-NF 24)	Liquid chromatography	Detection wavelength:254nm Mobile phase:(A) 0.1%phospheric acid in water (B) acetonitrile (3:2) Stationary phase: 4.0mm x25cm column Flow rate: 1.0 ml/min	23

Table 3: Reported Analytical Method of Losartan Potassium: [24-48]

Sr No	Drug	Method	Description	Ref No
1	Losartan bulk and pharmaceutical dosage form	UV spectrophotometric method	Detection wavelength: 237nm Linearity range: 6-20µg/ml Co-relation Coefficient: 0.990	24
2	Quantitative determination of Losartan in pharmaceutical dosage form	Second derivative UV spectrophotometric method	Detection wavelength: 234nm Linearity range: 8-22 µg/ml Co-relation Coefficient: 0.9989	25
3	Losartan potassium in capsules	UV spectrophotometric method	Direct UV spectrophotometry Detection wavelength: 205nm Linearity range: 3.0-7.0 mg L^{-1} First derivative UV spectrophotometry Detection wavelength: 234nm Linearity range: 6.0-14.0 mg L^{-1}	26
4	Losartan potassium in tablet	RP-HPLC Method	Detection wavelength: 254nm Mobile phase: buffer and acetonitrile (65:35) Stationary phase: Spherisorh C18, 250 X 4.6 mm, 5µ	27

			Flow rate: 1.5 ml/min Retention time:7.496 min	
5	Losartan potassium in bulk drug and dosage form formulation	Stability indicating RP-HPLC Method	Detection wavelength: 250nm Mobile phase: (40:60) Acetonitrile: Buffer consist of 10.5mM of disodium hydrogen phosphate and 10mM potassium dihydrogen phosphate, pH 3.5 adjusted by 10 % Orthophosphoric acid Stationary phase: C 18 column (Kromasil 100-5C18 (250mm x4.6mm)E82860 i.d., 5µm particle) Flow rate: 1.0 ml/min Retention time: 9.98 min Linearity range: 6.4-9.6µg/ml	28
6	Atenolol and losartan potassium in combined dosage form	UV spectrophotometric method(Q-analysis method) Absorption ratio method	Detection wavelength: Atenolol: 275nm Losartan potassium: 282nm Linearity range: 5-30 µg/ml	29
7	Losartan potassium and hydrochlorothiazide in bulk and tablet dosage form	UV spectrophotometric method	Simultaneous Equation Method Detection wavelength: Losartan potassium: 235nm Hydrochlorothiazide: 271nm Linearity range: 5-30 µg/ml Absorptivities: Losartan potassium(235nm): 0.0094 Hydrochlorothiazide(271nm): 0.0271 Dual Wavelength Method Detection wavelength: Losartan potassium: 229 and 242nm Hydrochlorothiazide: 265 and 282nm Linearity range: 5-30 µg/ml Area under Curve Method Detection wavelength: Losartan potassium: 229-242nm(λ1-λ2) Hydrochlorothiazide: 265-282nm(λ3-λ4) Linearity range: 5-30 µg/ml	30
8	Perindopril and losartan in solid dosage form	UV spectrophotometric method	First order derivative spectrophotometric method Detection wavelength: Perindopril: 219nm Losartan: 214nm Linearity range: Perindopril: 10-30 mcg/ml Losartan: 1-5 mcg/ml	31
9	Losartan potassium and Ramipril in tablet	UV spectrophotometric method	First order derivative spectrophotometric method Detection wavelength: Losartan potassium: 234nm Ramipril: 271nm Linearity range: Losartan potassium: 10-90 g/ml Ramipril: 2-18 g/ml	32
10	Losartan potassium and chlorthalidone in combined dosage form	UV spectrophotometric method	Ratio spectra derivative method Detection wavelength: Losartan potassium: 249nm Chlorthalidone: 244.4nm Linearity range: Losartan potassium: 16-32 µg/ml Chlorthalidone: 4-8 µg/ml	33
11	Amlodipine and losartan in bulk and tablet dosage formulation	UV spectrophotometric method	Detection wavelength: Amlodipine: 237nm Losartan: 202nm Linearity range: Amlodipine: 1.25-7.5µg/ml Losartan: 12.5-75µg/ml	34
12	Amlodipine and losartan in binary mixture	RP-HPLC Method	Detection wavelength: 237nm Mobile phase: Phase-A: 70% v/v of buffer pH-3.7 and 30%v/v of acetonitrile phase–B :70% v/v of acetonitrile and 30% v/v of buffer pH-3.7. Stationary phase: Inertsil ODS 3V C18 (150 X 4.6 mm, 5µm)	35

			Flow rate: 1.0 ml/min Retention time: Amlodipine: 5.13 min Losartan: 11.11 min Linearity range: Amlodipine: 1.25-7.5 µg/mL Losartan: 12.5-75 µg/mL	
13	Losartan potassium and amlodipine besylate in tablet formulation	RP-HPLC Method	Detection wavelength:226nm Mobile phase: Triethylamine in water: acetonitrile (60:40), pH adjusted to 2.5 with O- phosphoric acid Stationary phase: RP C-18 Column (Microsorb-MV 100-5, 250 x 4.6 mm) Flow rate: 1.0 ml/min Retention time: Losartan potassium: 2.32min amlodipine besylate: 10.10min Linearity range: Losartan potassium: 50-500µg/ml amlodipine besylate: 5-50 µg/ml	36
14	Hydrochlorothiazide and losartan potassium in pharmaceutical formulation	RP-HPLC Method	Detection wavelength: 226nm Mobile phase: Acetonitrile: Phosphate Buffer (50:50) pH 3.1 in proportion of 50:50(v/v); the pH of phosphate buffer adjusted to (3.1) using orthophosphoric acid Stationary phase: GRACE C18 [4.6 x 250 mm] column Flow rate: 1.0 ml/min Retention time: Hydrochlorothiazide: 4.250 min losartan potassium: 8.30min Linearity range: Hydrochlorothiazide: 2-10 µg/ml losartan potassium: 8-40 µg/ml	37
15	Losartan potassium and perindopril erbumine in its tablet form	RP-HPLC Method	Detection wavelength: 210nm Mobile phase: ACN: water in proportion of 50:50 v/v, pH adjusted to 3.2 ± 0.1 with 1 % o-phosphoric acid Stationary phase: HiQSil-C-18W ODS, (250 mm × 4.5 mm i.d.) Flow rate: 1.0 ml/min Retention time: Losartan potassium: 6.5min perindopril erbumine: 4.7min Linearity range: 2-18 µgmL-1	38
16	Losartan and chlorthalidone in pharmaceutical dosage form	RP-HPLC Method	Detection wavelength: 284nm Mobile phase: acetonitrile: water(80:20 v/v) Stationary phase: phenomenex C18 column Flow rate: 1.0 ml/min Retention time: Losartan: 1.72 min Chlorthalidone: 2.64min Linearity range: 20-100 µg/ml	39
17	Losartan potassium and metolazone in bulk drug and formulation	RP-HPLC Method	Detection wavelength: 237nm Mobile phase: acetonitrile: water (60:40) Stationary phase: ThermoHypersil BDS–C18 (250 mm × 4.6 mm, 5.0 µm) Flow rate: 0.8 ml/min Retention time: Losartan potassium: 2.57 min Metolazone: 4.81 min Linearity range: Losartan potassium: 2-12 µg/ml Metolazone: 0.2-1.2 µg/ml	40
18	Losartan potassium and Ramipril in combined dosage form	RP-HPLC Method	Detection wavelength: 210nm Mobile phase: acetonitrile: methanol:10 mm tetra butyl ammonium hydrogen sulphate in water in the ratio of 30:30:40% v/v/v Stationary phase: hypersil ODS C18, 4.6×250 mm, 5 µm column Flow rate: 1.0ml/min Retention time:	41

			Losartan potassium: 4.7min Ramipril: 3.3min Linearity range: Losartan potassium: 0.04-100 µg/ml Ramipril: 0.2-300 µg/ml	
19	Enalapril maleate and losartan potassium in bulk and pharmaceutical dosage form	RP-HPLC Method	Detection wavelength: 235nm Mobile phase: Buffer-Acetonitrile(60:40 v/v) pH4.5 adjusted With o-Phosphoric Acid Stationary phase: Hyperchrom phase C-18 BDS Hypersil column (250mm × 4.6 mm id 5µm) Flow rate: 1.0ml/min Retention time: Enalapril maleate: 3.150 min losartan potassium: 5.420 min Linearity range: Enalapril maleate: 5-15 µg/ml losartan potassium: 25-75 µg/ml	42
20	Perindopril and losartan Potassium in their combined marketed dosage form	Stability Indicating RP-HPLC	Detection wavelength: 230nm Mobile phase: Buffer (Potassium Dihydrogen Phosphate): Methanol (80:20v/v) Stationary phase: C18 (25cm x 0.46 cm) Hypersil BDS analytical column Flow rate: 1.0ml/min Retention time: Perindopril: 3.867min losartan potassium: 5.287min Linearity range: Perindopril: 2-6 µg/ml losartan potassium: 50-150 µg/ml	43
21	Amlodipine and losartan in bulk drug and tablet dosage formulation	Stability Indicating RP-HPLC	Detection wavelength: 230nm using PDA detector. Mobile phase:0.05M potassium dihydrogen phosphate: acetonitrile(pH 3.0)(50:50v/v) Stationary phase: enable C18 G(250mm×4.6mm 5µ) Flow rate: 1.0ml/min Retention time: Amlodipine: 4.3min Losartan: 6.7min Linearity range: Amlodipine: 0.125-0.75µg/ml Losartan: 1.25-7.5µg/ml	44
22	Losartan potassium and Ramipril in tablets	Stability Indicating RP-HPLC	Detection wavelength: 210nm Mobile phase: acetonitrile and (0.2% v/v, pH 2.5) aqueous trifluoroacetic acid (45:55, v/v) Stationary phase: C_{18} reverse phase endcapped column (250×4.6 mm, 5 µm, 100 Å) Flow rate: 1.0ml/min Retention time: Losartan potassium: 10.59min Ramipril: 22.2min Linearity range: Losartan potassium: 62.5-5000 ng/ml Ramipril: 125-10,000 ng/ml	45
23	Atenolol, Hydrochlorothiazide and losartan in bulk and pharmaceutical dosage form	Stability Indicating RP-HPLC	Detection wavelength: 224nm Mobile phase: acetonitrile and 0.5% ortho phosphoric acid(30:70v/v) Stationary phase: SHESHADO C18,250mm×4.6mm5µ Flow rate: 1.0ml/min Retention time: Atenolol: 2.242min Hydrochlorothiazide: 3.963min Losartan: 6.733min Linearity range: Atenolol: 4-12 µg/ml Hydrochlorothiazide: 4-12 µg/ml Losartan: 1-3 µg/ml	46

24	Losartan potassium, Ramipril and hydrochlorothiazide in bulk and pharmaceutical dosage form	Stability Indicating RP-HPLC	Detection wavelength: 233nm Mobile phase: (Methanol: phosphate buffer-pH 4.0) in the ratio of 70:30% v/v Stationary phase: reverse phase Kromasil 100-5 C18 column (250mm x 4.6mm) Flow rate: 0.8ml/min Retention time: Losartan potassium: 2.851 min Ramipril: 5.019 min Hydrochlorothiazide: 6.921 min Linearity range: Losartan potassium: 100-500 µg/ml Ramipril: 10-50 µg/ml Hydrochlorothiazide: 20-100µg/ml	47
25	Losartan potassium formulation	HPTLC Method	Detection wavelength: 270nm Mobile phase: acetonitrile: methanol:0.1%acetic acid (3.5:2.6:3.9v/v) Stationary phase: aluminium backed silica gel 60F254 HPTLC plate(10cm×10cm) Linearity range: 5-30 ng/spot	48
26	Losartan potassium and chlorthalidone in combined dosage form	HPTLC Method	Detection wavelength: 254 nm Mobile phase: Chloroform: Methanol: Ammonia (9: 2: 0.2, v/v) Stationary phase: aluminium plates precoated with silica gel 60 G F254 Linearity range: Losartan potassium: 1.4 - 2µg/spot Chlorthalidone: 0.5 – 1.1µg/spot	49
27	Atenolol and losartan in bulk and in pharmaceutical dosage form	HPTLC Method	Detection wavelength:226nm Mobile phase: Methanol: Ethyl acetate: Toluene: Triethylamine (4:3.9: 2: 0.1 v/v) Stationary phase: precoated Silica Gel 60 F254 plates Linearity range: 400-1400 ng/spot	50
28	Losartan in human plasma	HPLC Method (using monolithic column)	Detection wavelength:254 nm Mobile phase: 0.01 mol/L disodium hydrogen phosphate buffer-acetonitrile (60:40 v/v) adjusted to pH 3.5 Stationary phase: Chromolith Performance (RP-18, 100 x 4.6 mm) column Linearity range: 50-300 ng/ml^{-1}	51
29	Hydrochlorothiazide, Ramipril, Losartan in human plasma	Stability indicating RP-HPLC (bioanalytical method)	Detection wavelength:210 nm Mobile phase: potassium dihydrogen phosphate (KH_2PO_4) and acetonitrile [HPLC Grade] in the ratio of 68:32 (% v/v) Stationary phase: Symmetry C18 column (4.6 x 150mm, 5µ, Make: Hypersil) in an isocratic mode Linearity range: Hydrochlorothiazide: 12.5-32.5 µg/ml Ramipril:1.25-3.25 µg/ml Losartan:50-130 µg/ml	52

Conclusion

According to this review it was concluded that for Aliskiren and Losartan PotassiumDifferent Spectroscopic and Chromatographic methods are available for single and combination with other drugs. The mobile phase containing Acetonitrile, Water, Methanol, and Phosphate buffer were common for most of the chromatographic method to provide good resolution. For chromatographic method flow rate is observed in the range 0.8-1 ml/min to get good resolution time. For most of the Spectroscopic methods common solvent is Methanol and water. Hence this all methods found to be simple, accurate, economic, precise and reproducible in nature. Most of Methods were of RP-HPLC and UV absorbance detection because these methods provided with best available reliability, repeatability, analysis time and sensitivity.

Acknowledgement

The authors are thankful to Dr. K. Pundarikakshudu, Director of L. J. Institute of Pharmacy, Ahmedabad, India for providing all the facilities and encouragement to carry out the work.

References

1. Aliskiren in combination with losartan compared to losartan on regression of left ventricular hypertrophy in overweight patients with essential hypertension ALLAY, https://clinicaltrials.gov/ct2/show/NC T00219141.
2. Pouler AC, Uno H, Prescott MF, Appelabaum E. Suppression of aldosterone mediates regression of left ventricular hypertrophy in patients with hypertension. https://www.ncbi.nlm.nih.gov/pubmed/21746765?dopt=Abstract.

3. Pub chem. national chemistry database September 2017, https://pubchem.ncbi.nlm.nih.gov/compound/Aliskiren.
4. Pub chem. national chemistry database September 2017, https://pubchem.ncbi.nlm.nih.gov/compound/losartan_potassium
5. Kumara SG, Kumar JMR, Sheshagirirao JVLN, Vinay DK, Ratna CM, Eswara VNVK *et al*. Validated Spectrophotometric Determination of Aliskiren in Pharmaceutical Dosage Form JPR, 2011; 4:2574-2575.
6. Saroj KR, Ravi BVVK, Ajaya KP, Negireddy NR. A RP-HPLC method development and validation for the estimation of aliskiren hemifumarate in bulk and pharmaceutical dosage forms JCPR. 2012; 4(11):4810-4815.
7. Krishna RG, Kiren NK. Development and validation of stability of stability indicating RP-HPLC method for determination of aliskiren in bulk and pharmaceutical dosage form IJCPA. 2015; 2(5):1-15.
8. Sangoi MW, Sangoi MS, Oliveira, Secretti LT, Rolim CMB. Determination of Aliskiren in Tablet Dosage Forms by a Validated Stability-indicating RP- LC Method Journal of chromatographic science, 2011; 49:170-175.
9. Ashim KS, Dhanya BS, Rajesh AM, Ramchandran B, Avinash KS. Simultaneous estimation of Aliskiren hemifumarate and Hydrochlorothiazide in combined Tablet Formulation by Simultaneous equation, Absorbance ratio and First Derivative Spectroscopic Methods JAPS. 2016; 6(7):164-170.
10. Kokila P, Jignesh S. Simultaneous Estimation of Aliskiren and Valsartan by Ratio Spectra Derivative Spectrophotometry Method in their Fixed Dosage Forms Int. J Chemtech Res. 2014; 6(2):1268-1279.
11. Samixa PR, Chhaganbhai PN. Development and validation of zero absorbance method for simultaneous estimation of aliskiren and amlodipine in combined dosage form AJPRHC, 5(2):43-51.
12. Somsubhra G, Anusha B, Santhoshi, David B, Chaithanya YK, Raghavendra P *et al*. Method Development and Validation of Aliskiren Hemifumarate and Valsartan in bulk drug by RP-HPLC method AJRC. 2013; 6(1):19-2.
13. Ashim KS, Dhanya BS, Rajesh.AM, Balaraman R, Seth AK. Quantitative simultaneous determination of aliskiren hemifumarate and hydrochlorothiazide in combined tablet formulation by RP-HPLC Int. J Pharm Pharm. Sci. 2015; 7(8):142-145.
14. Divya P, Aleti P, Venisetty RK. Development and validation of RP-HPLC method for the simultaneous estimation of aliskiren and amlodipine in tablet dosage form Int. J Pharm Bio Sci. 2013; 3(4):241-246.
15. Ishan RS, Jignesh SS, Dilip GM. Method development and validation for simultaneous estimation of aliskiren and enalapril in bulk and synthetic mixture by reversed phase high performance liquid chromatographic method Pharmacophore. 2014; 5(2):239-245.
16. Kumara GS, Rajendra JMK, Seshagirirao JVLN. Validated RP-HPLC Method for the Simultaneous Determination of Aliskiren, Hydrochlorothiazide and Amlodipine besylate in Pharmaceutical Formulations Int. J Chemtech Res. 2012; 4(4):1666-1673.
17. Riswan SH, Girija SV. Development and validation of stability indicating RP-HPLC method for simultaneous estimation of aliskiren hemifumarate and valsartan in bulk and pharmaceutical dosage form Asian. J pharm clin. Res. 2015; 8(6):223-227.
18. Vijay KR, Vinay UR. Stability indicating RP-HPLC method development and validation for simultaneous estimation of aliskiren, amlodipine and hydrochlorothiazide in tablet dosage form Int. J Pharm Pharm Sci. 2014; 6(1):724-730.
19. Belal F, Walash M, El-Enany N, Zayed S. Highly sensitive HPLC method for assay of aliskiren in human plasma through derivatization with 1-naphthyl isocyanate using UV detection J Chromatogr B Analyst Technol Biomed Life Sci., 2013.
20. Zeynep A. simultaneous determination of aliskiren, amlodipine and hydrochlorothiazide in Human plasma and Urine by high performance liquid chromatography Journal of Analytical Chemistry. 2015; 70(4):502-509.
21. Juhi JP, Nejal MB, Vijay DC, Primal S, Malika S, Pranav SS *et al*. simultaneous estimation of aliskiren and hydrochlorothiazide in pharmaceutical preparation and spiked human plasma by HPTLC Journal of Taibah University for Science, 2017; 11:667-676.
22. Indian Pharmacopoeia. Government of India Ministry of Health and Family Welfare Published by Indian Pharmacopoeia Commission, Ghaziabad, 2014; 2:2123-2124.
23. United States pharmacopoeia. USP29-NF24 pharmacopeial forum, 30, 1280. http://www.pharmacopeia.cn/v29240/usp29nf24s0_m45933.html
24. Pranshu T, Prem S, Lakhmanya, Syantan M, Shaffi T. Development and validation of spectrophotometric method for estimation for losartan bulk drug and pharmaceutical formulation IRJP. 2012; 3(5):391-393.
25. Rao PLKM, Venugopal V, Anil KG, Rajesh B, Prasad G, Ravindergoud D. Quantitative estimation of losartan potassium in pharmaceutical dosage form by UV spectrophotometry IJPRC. 2011; 1(3):295-302.
26. Rudy B, Livia BF, Ghislaine RP, Roberta CPA, Magali BA. Comparative study of analytical methods by direct and first derivative UV spectrophotometry for evaluation of losartan potassium in capsules BJPS. 2010; 46(1):147-155.
27. Kathiresan K, Gothandaraman S, Swamivel M, Manickam S, Mathan K, Manavalan R. Analytical method development and validation of losartan potassium tablet by RP-HPLC RJC. 2008; 1(3):521-525.
28. Elsadig HR, Amna BW, Hussien EM, Ahmed E, Saeed M. Method development and validation of stability indicating RP-HPLC method for analysis of losartan potassium in bulk drug and dosage form formulation IJPSR. 2016; 7(4):1413-1421.
29. Lalitha KV, Kirenjyothi R, Padma B. UV spectrophotometric method development and validation for the determination of atenolol and losartan by Q-analysis International Bulletin of Drug Reserch. 2013; 3(4):54-62.
30. Chaitali T, Jyoti D, Pawar PY. Simultaneous estimation and validation of losartan potassium and

hydrochlorothiazide in bulk and tablet dosage form by using different spectrophotometric method Der. Pharma. Chemica. 2014; 6(2):24-30.
31. Vijayalakshmi R, Archana S, Dhanaraju MD. A Simultaneous Estimation of Perindopril and Losartan in Solid Dosage Forms by UV Spectrophotometry AJRC. 2010; 3(3):571-573.
32. Neela MB, Rituraj BD, Swapnil DJ. Simultaneous estimation of losartan potassium and ramipril from tablets by first order derivative spectroscopy ACAIJ. 2013; 12(6):211-213.
33. Suryanarayan M, Jignesh G, Rasmita M, Dharmistha C, Rajesh KS. ratio spectra derivative method development and validation for the drug combination of losartan potassium and chlorthalidone PHARMAGENE. 2014; 194:40-46.
34. Ramya G, Puranik SB, Kumar GVS, Sridhar KA. Simultaneous estimation of amlodipine and losartan by UV-method in bulk drug and tablet dosage formulation Arch. Appl. Sci. Res. 2012; 4(5):2206-2212.
35. Krishna KC, Gowari SD, Samsol ID. RP-HPLC method development and validation of amlodipine and losartan in binary mixture JGTPS, 2013; 4(3):1144-1152.
36. Priyanka RP, Sachin U, Rakesh, Dhabale PN, Burade KB. RP- HPLC Method for Simultaneous Estimation of Losartan potassium and Amlodipine besylate in Tablet Formulation Int. J ChemTech Res. 2009; 1(3):464-469.
37. Gadewar CK, Jadhao RG, Shelke PG, Chandewar AV. validated RP-HPLC method for simultaneous determination of hydrochlorothiazide and losartan potassium in pharmaceutical formulation IJAPA, 2013; 3(4):85-89.
38. Oza CK, Prajapati JP, Vyas AJ, Mehta P. RP-HPLC method for the determination of losartan potassium and perindopril erbumine in combined tablet dosage form IJPBS. 2011; 2(1):705-715.
39. Aneesh TP, Renju R, Arvind PM, Anuja S, Manisha C. RP-HPLC method for simultaneous determination of losartan and chlorthalidone in pharmaceutical dosage form Int. Res. J Pharm. 2015; 6(7):453-457.
40. Ramkumar D, Vidhya KB, Sunil RD. Validated RP-HPLC Method for Simultaneous Quantitation of Losartan Potassium and Metolazone in Bulk Drug and Formulation Sci. Pharm. 2011; 79:545-554.
41. Srinivasha KR, Srinivas K. RP-HPLC Method for the Determination of Losartan Potassium and Ramipril in Combined Dosage Form Indian J Pharm. Sci. 2010; 72(1):108-111.
42. Bhaumik CP. Method Development and Validation for Simultaneous Estimation of Enalapril Maleate and Losartan Potassium in Bulk and Pharmaceutical Dosage Form IAJPR. 2013; 3(5):3767-3790.
43. Gurjeet K, Nikhil P, Mandev BP, Bhumika S. Development and Validation of Stability Indicating Analytical Method for Simultaneous Estimation of Perindopril and Losartan Potassium in Their Combined Marketed Dosage Form J Pharm Sci. Bioscientific Res. 2016; 6(4):542-546.
44. Ramya G, Puranik SB, Kumar GVS, Sridhar KA. Development and validation of stability indicating RP-HPLC method for simultaneous estimation of amlodipine and losartan in bulk drug and formulation IJRP. 2012; 3(11):92-95.
45. Kolipara S, Bende G, Bansal Y, SahaR. Stability-indicating Reversed-phase Liquid Chromatographic Method for Simultaneous Determination of Losartan Potassium and Ramipril in Tablets Indian J Pharm. Sci. 2012; 74(3):201-210.
46. Meesala SN, Bonathu MG, Raju VB, Srinivas KS, Srinivas K, Pasala M *et al*. Development and validation of stability indicating reverse phase high performance liquid chromatography method for simultaneous estimation of atenolol, hydrochlorothiazide, and losartan in bulk and pharmaceutical dosage form Asian J Pharm. clinical. res, 2016; 9:118-124.
47. Venkateshwara BRS, Vidyadhara S, Sasidhar RLC, Ganesh TNVK, Rokiya MD. A Novel Stability Indicating RP-HPLC Method Development and Validation for The Simultaneous Estimation of Losartan Potassium, Ramipril and Hydrochlorothiazide in Bulk and Pharmaceutical Dosage Form Eurasian. J Anal Chem. 2016; 11(5):255-265.
48. Muralidharan S, Subramaniya N, Meyyanathan. Sensitive and accurate estimation of losartan potassium formulation by high-performance thin-layer chromatography pharmaceutical methods, 2011; 2:95-98.
49. Soniya AT, Mary M. Validated HPTLC method for the simultaneous estimation of losartan potassium and chlorthalidone in combines dosage form IJPBS, 2015; 5(2):314-322.
50. Nikita DP, Ananadkumar DC, Kreny EP. Development and validation of HPTLC method for simultaneous determination of atenolol and losartan potassium in bulk and in pharmaceutical dosage form Int. J Pharm & Pharm. Sci. 2013; 5(2):325-331.
51. Zarghi A, Foroutan SM, shafaaatiA, KhoddamA. A rapid HPLC method for determination of losartan in human plasma using monolithic column NCBI, 2005; 55:569-72.
52. Ashutosh KS, Manidipa D, Seshagiri R, Gowri S. New Validated Stability Indicating Rp-Hplc Bioanalytical Method Development and Validation for Simultaneous Estimation of Hydrochlorothiazide, Ramipril and Losartan in Human Plasma by Using PDA Detector pharm anal acta, 2015, 6.