REVIEW ARTICLE

RECORDS OF PHARMACEUTICAL AND BIOMEDICAL SCIENCES

A Brief Review on Analytical Techniques for Quantitative Determination of Rosuvastatin and Losartan in Different Matrices

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1. Introduction

1.1. Cardiovascular diseases

Cardiovascular diseases, including coronary heart disease (CHD), heart failure, and hypertension, represent major global contributors to death and illness.

1.1.a. Coronary heart disease (CHD) Primarily targeting the coronary arteries, this condition can be exacerbated by thrombotic events, potentially culminating in acute myocardial infarction. Individuals who survive such incidents face an increased risk of developing heart failure or experiencing sudden cardiac death due to ventricular arrhythmias. Additionally, persistent hypertension serves as a significant risk factor, potentially leading to coronary heart disease, heart failure, and cerebrovascular accidents such as strokes. Consequently, many patients present with multiple coexisting cardiovascular disorders, necessitating comprehensive and concurrent therapeutic interventions. (Whalen 2018).

1.1.b. Heart failure (HF) is a multifaceted and progressive syndrome characterized by the heart's inability to pump sufficient blood to meet the body's metabolic demands. Clinical manifestations typically include dyspnea, fatigue, and fluid retention, resulting from impaired cardiac filling or ejection. HF can arise due to various underlying pathophysiological mechanisms, with common etiological factors including atherosclerosis, myocardial infarction, hypertension, valvular heart disease, dilated cardiomyopathy, and congenital cardiac anomalies. (Richir et al. 2008).

1.1.c. Systemic arterial hypertension is a major predisposing factor for the development of ischemic heart disease, stroke, renal failure, and heart failure. Despite its clinical significance, hypertension often remains inadequately managed. Essential hypertension, characterized by persistently elevated blood pressure without an identifiable secondary cause, represents the most prevalent form observed in patients with chronic hypertension. (Whalen 2018).

The formation of neointima within arterial walls represents a critical pathophysiological process in the progression of various angiogenic disorders, including the development of atherosclerotic plaques. This pathological remodeling involves endothelial dysfunction, smooth muscle cell proliferation, and extracellular matrix deposition, contributing to vascular lumen narrowing and impaired blood flow (Horiuchi et al. 2003). Interestingly, these characteristic arterial responses to vascular injury can be mitigated through the administration of various angiotensin II receptor blockers (ARBs), such as the class prototype, losartan (LOS). Additionally, other pharmacological classes, particularly statins, have demonstrated comparable cardioprotective effects that extend beyond their primary mechanism of action on cholesterol metabolism. These lipid-lowering agents have been shown to exert a beneficial inhibitory effect on neointimal proliferation, a phenomenon that has been well-documented with several statins, including rosuvastatin (ROS) (Moon et al. 2004). Building on this evidence, the co-administration of angiotensin II receptor blockers (ARBs) and statins has been recognized for its synergistic vascular protective effects. This therapeutic combination has gained widespread clinical acceptance for managing cardiovascular complications, as it offers complementary benefits in reducing vascular inflammation, inhibiting neointimal proliferation, and improving overall cardiovascular outcomes (Lee et al. 2019). One such combination therapy involves Losartan (LOS) and Rosuvastatin (ROS), representing a clinically relevant strategy for preventing large blood vessel restenosis and mitigating atherosclerosis, particularly in hypertensive patients. This dual approach leverages the complementary mechanisms of ARBs and statins, enhancing vascular protection and improving long-term cardiovascular outcomes (Yi et al. 2010).

ROS, a prominent member of the statin class, is chemically designated as; (*E*)-(3*R*,5*S*)-2-[methyl (methylsulfonyl) amino]-7-[4-(*p*-fluorophenyl)-6-propan-2-yl pyrimidin-5-yl]-3,5-dihydroxy hept-6-ene carboxylate (**Fig. 1**). ROS is classified as a lipid-lowering agent that exerts its therapeutic effects by inhibiting hepatic hydroxymethylglutaryl coenzyme-A (HMG-CoA) reductase, the key enzyme responsible for cholesterol biosynthesis. Following oral administration, ROS undergoes partial absorption in the gastrointestinal tract, attaining peak plasma concentration (C_{max}) within approximately 3 to 5 hours. The drug exhibits a prolonged elimination half-life of nearly 19 hours. However, its absolute bioavailability is estimated to be around 20%, primarily due to its extensive volume of distribution (134 L/kg) and high plasma protein binding (~90%), predominantly to albumin (Martin, Mitchell, and Schneck 2002). Regarding its metabolism, Rosuvastatin (ROS) undergoes minimal biotransformation despite hepatic first-pass extraction via organic anion-transporting polypeptides (OATPs). Notably, CYP2C9 serves as the primary cytochrome P450 enzyme responsible for the metabolic conversion of ROS into its less active major metabolite, N-desmethylrosuvastatin. The primary route of elimination for both ROS and its metabolite is fecal excretion, accounting for approximately 90% of an orally administered dose (AstraZeneca Pharmaceuticals 2003).

Moving forward towards the orally active, non-peptide ARB therapeutic agent, LOS is chemically identified as; 4-chloro-2-*n*-butyl-5-(hydroxy methyl)-1-[(*o*-(1*H*-tetrazol-5-yl)bisphenyl-4'-yl) methyl] imidazole (**Fig. 1**). Such blood pressure-lowering agent blocks the angiotensin-II mediated vasoconstriction through competitive yet selective inhibition of AT1 receptors within the blood vessels and adrenal glands(Xu et al. n.d.). Following oral administration, Losartan (LOS) is efficiently absorbed in the gastrointestinal tract, demonstrating an absolute bioavailability of approximately 32.6% when administered as a 50 mg tablet. Hepatic first-pass metabolism, primarily mediated by CYP2C9 and CYP3A4, converts LOS into its more pharmacologically active carboxylated metabolite, EXP3174. This metabolite exhibits 10- to 40-fold greater potency than the parent compound and is responsible for the majority of LOS's antihypertensive effects.

The peak plasma concentration (Cmax) of LOS is typically achieved within one hour, whereas EXP3174 reaches its Cmax within 3 to 4 hours. Both LOS and its active metabolite display extensive plasma protein binding, with affinities of 98.8% and 99.7%, respectively. Regarding elimination, approximately 4% of a single oral dose is excreted unchanged in the urine, while nearly 6% is eliminated as the active metabolite. Additionally, both LOS and EXP3174 undergo biliary excretion, further contributing to their elimination from the body (Sica, Gehr, and Ghosh 2005).

2. Analytical methods

2.1. Official analytical methods for the analysis of ROS and LOS.

The official methods for the quantification of Rosuvastatin (ROS) and Losartan (LOS) as per the British Pharmacopoeia (BP) and European Pharmacopoeia (EP) involve liquid chromatography techniques for both drugs. These standardized analytical methods ensure the accuracy, precision, and reliability of ROS and LOS determination in pharmaceutical formulations. A comprehensive summary of these chromatographic methodologies is provided in **Table 1**.

2.2 Reported analytical methods for the analysis of ROS and LOS.

Several analytical techniques have been documented for the quantitative determination of Rosuvastatin (ROS) and Losartan (LOS), whether in their pure forms, pharmaceutical formulations, or in combination with other pharmaceutical agents. These methods encompass a range of chromatographic, spectrophotometric, and representative approaches, each designed to ensure accuracy, specificity, and reproducibility in drug analysis.

2.2.1. Chromatographic methods

2.2.1.a. Chromatographic methods depend on UV detection of ROS and LOS.

Chromatographic methods utilizing UV detection for the quantification of Rosuvastatin (ROS) and Losartan (LOS) are systematically compiled in Table 2 and Table 3, respectively. These methods provide sensitive and selective analytical approaches for determining ROS and LOS in various pharmaceutical and biological matrices.

2.2..1.b. Chromatographic methods depend on Mass detection of ROS and LOS.

Analytical methods based on liquid chromatography–mass spectrometry (LC-MS) for the determination of Rosuvastatin (ROS) and Losartan (LOS), either individually or in combination with other pharmaceutical agents in biological samples, are comprehensively summarized in **Table 4** and **Table 5**, respectively.

These LC-MS techniques offer high sensitivity, selectivity, and accuracy, making them valuable for pharmacokinetic and bioanalytical studies.

2.2.2. Spectrophotometric methods:

Spectrophotometric methods employed for the analysis of Rosuvastatin (ROS) and Losartan (LOS), whether individually or in combined dosage formulations, are systematically These LC-MS techniques offer high sensitivity, selectivity, and accuracy, making them valuable for pharmacokinetic and bioanalytical studies.

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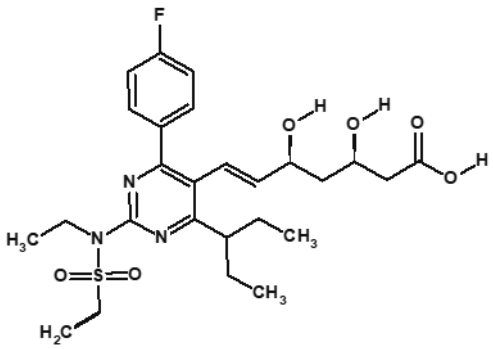
A:



B:

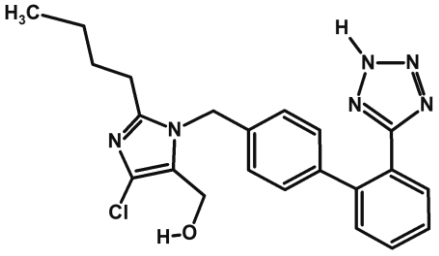


Figure 1. Chemical structure of (A) ROS, (B) LOS

Table 1: Official methods for analysis of Rosuvastatin and Losartan.

Method	Conditions	Application	Reference	
Liquid chromatography	Mobile phase—Acetonitrile: 1% trifluoroacetic acid: Water (37:1:62) on 3.2-mm × 25-cm; 5-µm packing L1. Flow rate 0.75 mL/min. Detection at 242 nm. Injection volume about 10 µL.	Rosuvastatin Tablets	(Anon 2018)	USP
Liquid chromatography	A: 1% solution of trifluoroacetic acid: Acetonitrile: water (1:29:70, v/v/v), B: 1% solution of trifluoroacetic acid:water: Acetonitrile (1:24:75, v/v/v), gradient elution on C18 column Flow rate 0.75 mL/min. Detection at 242 nm. Injection volume about 10 µL.	Rosuvastatin	(Beludari, Prakash, and Mohan 2013)	Eur.P.
liquid chromatography	Mobile phase—Solution A— Prepare a 0.1% solution of phosphoric acid in water. Solution B— Use acetonitrile with flow rate is about 1.0 mL per minute and a 4.0-mm * 25-cm column containing packing L1. Detection at 254-nm.	**Losartan Potassium Tablets**	(Bulletin 2011)	USP
liquid chromatography	Mobile phase— mobile phase A: dilute 1.0 mL of phosphoric acid to 1000 mL with water; — mobile phase B: acetonitrile; — stationary phase: end-capped octadecylsilyl silica gel for chromatography R (5 µm); Flow rate 1.3 mL/min. Detection Spectrophotometer at 220 nm.	**Losartan Potassium Tablets**	(Bulletin 2011)	Eur.P.

Table 2: Reported HPLC methods for Rosuvastatin analysis using UV detector

Stationary phase	mobile phase	Wave length	Application	Reference
X-terra C18 100 × 4.6 mm, 3.5 µ	KH_2PO_4 buffer (mobile phase A) and acetonitrile (mobile phase B)	230 nm	Rosuvastatin in Combination Drug Products	(Palacharla and Krishna Mohan 2019)
BDS Hypersil C18	methanol: acetonitrile:buffer (0.05 M sodium acetate, pH adjusted to 4.0 using acetic acid) (60:35:5; v/v/v)	231 nm	Rosuvastatin and Propranolol in Pharmaceutical Dosage Form	(El-Abasawi et al. 2018)
BISCOF HPLC C18	water at pH 2.51 with 0.1 % (v/v) orthophosphoric acid (OPA): acetonitrile in the ratio 50:50	237 nm	Determination of aspirin, rosuvastatin and clopidogrel	(Pisal et al. 2018)
Lichrosphere C18 column	Acetonitrile:MeOH:0.1 M formic acid (65:5:35 v/v)	242 nm	Rosuvastatin Calcium	(Dudhipala and Veerabrahma 2017)
Perkin Elmer Brownlee C18	MeOH:water (68:32 v/v)	241	Pharmacokinetics of Rosuvastatin	(Nazir, Iqbal, and Nasir 2016)

Water's C18 column	Acetonitrile:water:0.02 M phosphate buffer pH 8 (40:10:50 v/v/v)	230	estimation of rosuvastatin and ezetimibe	(Beludari et al. 2013)
Waters Sun Fire C18	Acetonitrile:MeOH:0.1 M formic acid (60:10:30)	240	rosuvastatin calcium	(Balakumar et al. 2013)
Kromasil KR 100-5 C18	0.05 M formic acid: Acetonitrile (55:45 v/v)	240	rosuvastatin rat plasma	(Kumar et al. 2006)
Symmetry C18	Acetonitrile:MeOH:buffer 0.01 M sodium dihydrogen phosphate (30:20:50 v/v), pH adjusted to 3.0 using orthophosphoric acid	263	estimation of rosuvastatin calcium and ezetimibe	(Raul, Aravelli, and Jhansi 2015)
Acquity UPLC BEH C18	0.1% trifluoroacetic acid:MeOH, gradient elution	240	rosuvastatin and related substances	(Trivedi and Patel 2012)
RP-C18 column	0.02 M phosphate buffer pH 6.8: Acetonitrile (60:40 v/v)	242	estimation of rosuvastatin	(Lakshmi, Krishna, and Jayaveera 2015)
Nucleodour RP-8	EtOH:MeOH:ethyl acetate (6:3:1 v/v)	254	analysis of rosuvastatin	(Haq et al. 2018)
C18 analytical column	Water: Acetonitrile:MeOH (40:40:20 v/v/v)	245	Determination of Rosuvastatin Calcium	(Mostafa et al. 2014)
Agilent Eclipse XDB- C8	Sodium dihydrogenphosphate buffer: Acetonitrile (50:50 v/v)	245	Determination of Rosuvastatin Calcium	(Mohamed Hassouna 2017)

Table 3: Reported HPLC methods for Losartan analysis using UV detector

Stationary phase	mobile phase	Wave length	Application	Reference
Zorbax C-18	Mixture of water: acetonitrile: triethyl amine: ortho phosphoric acid (60:40:0.1:0.1, v/v).	225 nm	Determination of losartan potassium, atenolol and hydrochlorothiazide in pharmaceutical preparations	(Durga Rao et al. 2009)
Microsorb-MV C18	phosphate buffer solution 10 mM pH 3.0 (channel A) and acetonitrile (channel B) in a linear gradient from A to B (65:35, v/v)	237 nm	Determination of losartan potassium and amlodipine besilate in pharmaceutical preparations	(Pedroso et al. 2009)
octylsilane column	potassium phosphate buffer (pH 6.2; 58 mmol L-1)–acetonitrile (65:35, v/v)	254 nm	determination of losartan potassium in capsules	(Bonfilio et al. 2009)
LC 118 Beckman-Coulter liquid chromatography system	acetonitrile and 20 mM disodium hydrogen phosphate buffer (34:66, v/v)	250 nm	determination of losartan urinary metabolic ratio	(Dorado et al. 2012)
Luna CN analytical column	A mixture of phosphate buffer (pH 1.9) and acetonitrile (315:195)	250 nm	Determination of Losartan and Its Metabolite E3174 in Rat Urine	(Pronina et al. 2012)

spherical monomeric C18 column	0.01 M ammonium acetate buffer (pH 5.5): acetonitrile	240 nm	Determination of Amlodipine Besylate, Losartan Potassium, Valsartan and Atorvastatin Calcium	(Abdelaziz LM 2014)
phenomenex C18 column	acetonitrile and water in the ratio 80:20 percentage v/v	284 nm	Determination of losartan and chlorthalidone	(T P et al. 2015)
C18 (250 mm × 4.6 mm, 5 μm) column	Acetonitrile: Water (50: 50, v/v)	220 nm	Determination of Chlorthalidone and Losartan Potassium	(Hinge, Bhanusali, and Mahida 2016)
Intersil® ODS-3" column	45% Acetonitrile and 55% 50 mM KH2PO4 (pH 4.5)	210 nm	hydrochlorothiazide, losartan, irbesartan and valsartan	(Hashem, Ibrahim, and Elhenawee 2016)
Chromolith® RP-18 column	acetonitrile and acetate buffer (pH 3.8; 10 mM)	220 nm	losartan and valsartan in human plasma	(Babarahimi et al. 2018)
Eurospher 100-5 C18	Acetonitrile / MeOH/phosphate buffer (25 mM) (43.5:20:36.5)	240 nm	determination of losartan, carvedilol, and amlodipine besylate	(Heidari and Limouei-Khosrowshahi 2019)
Kromasil C18 column	0.1% ortho-phosphoric acid in acetonitrile and 0.1% ortho-phosphoric acid in water (28:72, v/v)	235 nm	metolazone with losartan potassium or spironolactone	(Zaazaa et al. 2020)

Table 4: Reported analytical liquid chromatography–mass spectrometry methods for the analysis of Rosuvastatin alone or in combination with other drugs in biological samples.

Stationary phase	mobile phase	Detection	Application	Reference
Agilent Eclipse-Plus® ODS	0.1 formic : Acetonitrile (70:30 vv)	ESI+ MRM 482>258	Rosuvastatin and Losartan	(Wadie et al. 2020)
Phenomenex Luna C18 column	2% formic acid: methanol (20:80 v/v)	ESI+ MRM 482>258	Rosuvastatin	(Lan et al. 2007)
Zorbax XDB-C18 column	methanol: water (75:25 v/v) adjusted to pH 6 by aqueous ammonia	ESI- MRM 480>418	Rosuvastatin	(Qiao et al. 2009)
Atlantis C18 column	0.2% formic acid: MeOH (30:70 v/v)	ESI+ MRM 482>258	Rosuvastatin	(Xu et al. 2008)
Inertsil ODS-3 column	0.05 mol/L formic acid: Acetonitrile (20:80 v/v)	ESI+ MRM 482>258.3	Rosuvastatin	(Kallem et al. 2007)
Diamonsil C18 column	Acetonitrile:methanoic acid (0.1%) (60:40 v/v)	ESI+ MRM 482.1>258.1	Rosuvastatin	(Zhang et al. 2010)
Luna C18 column	MeOH:0.2% formic acid in water (70:30 v/v)	ESI+ MRM 482.2>258.2	Rosuvastatin	(Hull et al. 2002)
Microbore columns	MeOH:water (7:3 v/v) with 0.2% (v/v) formic acid	ESI+ MRM 482.2>258.2	Rosuvastatin	(Oudhoff et al. 2006)
Symmetry Shield RP18 column	A: Water:MeOH (35:65 v/v); ammonium formate 5 mM; B: 100% MeOH, gradient elution	ESI+ MRM 482.2>258.2	Rosuvastatin	(Hussain, Patel, and Tan 2009)

C18 column	Acetonitrile:10 mM ammonium acetate pH 3.1 (55:45 v/v)	ESI+ MRM 478.2>237.2	Rosuvastatin	(Siddartha 2014)
YMC J' Sphere ODS H-80 column	0.2% formic acid in water: Acetonitrile (40:60 v/v)	ESI+ MRM 482>258	Rosuvastatin	(Singh et al. 2005)
Zorbax SB C18 column	0.1% formic acid in 5 mM ammonium acetate:MeOH: Acetonitrile (20:20:60 v/v/v)	ESI+ MRM 482.1>258.3	Rosuvastatin and amlodipine	(Narapusetti et al. 2015)
Xterra MS C18 column	0.05 M formic acid: Acetonitrile (45:55 v/v)	ESI+ MRM 482.3>258.2	Rosuvastatin and fenofibric acid	(Trivedi et al. 2005)
Luna C18 column	0.1% (v/v) formic acid:MeOH (20:80 v/v)	ESI- MRM 482.1>258.3	Rosuvastatin and ezetimibe	(Varghese and Ravi 2013)
Thermo Hypurity C18 column	0.1% formic acid in water: Acetonitrile (30:70 v/v)	ESIC MRM 482.1>258.1	Rosuvastatin and metformin	(Shaikh et al. 2020)

Table 5: Reported HPLC methods for Losartan analysis using tandem mass spectrometry

column	Mobile phase	Detection	application	Reference
Agilent Eclipse-Plus® ODS	0.1 formic : Acetonitrile (70:30 vv)	ESI+ MRM 482>258	Losartan and Rosuvastatin	(Wadie et al. 2020)
Agilent Zorbax Eclipse® C8	acetonitrile – 0.05% acetic acid (70:30, v/v)	ESI- MRM 434.2 > 179.1	Losartan and Hydrochlorothiazide	(Salvadori et al. 2009)
Zorbax SB C-18	methanol/ Acetonitrile (75:25 v/v)	ESI- MRM 421.0 > 127.0	losartan and losartan acid	(Shah et al. 2009)
Waters XTerra® RP18	40% acetonitrile and 60% aqueous ammonium acetate (10 mM)	ESI- MRM 421.0 > 127.0	losartan and its active metabolite	(Rao et al. 2012)
C18 column	85:15, v/v mixture of methanol and 0.1% v/v formic acid	ESI+ MRM 423.1 to 207.2	losartan, losartan acid and amlodipine	(Karra et al. 2012)
Agilent Poroshell 120, EC-C18	Acidified methanol/water mixture	ESI+ MRM 423.2 to 207.0	Metolazone, Losartan and Losartan Carboxylic Acid	(Dubey et al. 2015)
Acquity UPLC®BEH C18	(0.1% formic acid) (A) and acetonitrile (0.1% formic acid) (B)	ESI+ MRM 423.19 to 207	Losartan	(Alam et al. 2019)

Table 6: Spectrophotometric methods for the analysis of Rosuvastatin alone or in combined dosage formulations.

Analyte(s)	Wavelength (nm)	Solvent or reagent	Linear range for ROS	Reference
Rosuvastatin	243	MeOH	1–60 µg/mL	(Uyar, Celebier, and Altinoz 2007)
Rosuvastatin	244	MeOH	2–18 µg/mL	(Gupta, Mishra, and Shah 2009)
Rosuvastatin	530 (A) or 655 (B)	Safranin O in water (A); methylene blue in alkaline buffer of pH 9.8 (B)	6.0–23.0 µg/mL	(Kumar, Manohara, and Hedge 2009)
Rosuvastatin	291; 360	Iodine/ Acetonitrile	2.408–48.154 µg /mL	(Ramadan, Mandil, and Alshelhawi 2014)
Rosuvastatin	579	MeOH/Quinalizarin	6–15 µg/L	(Lima, Cassella, and Pacheco 2017)
Rosuvastatin	λ(exc) 227; λ(em) 370	Acidic medium pH 2	0.38–5 µg/L	(Braga et al. 2013)
Rosuvastatin	416	Chloroform/Bromocresol green	0.482–24.077 µg/mL	(Ramadan, Mandil, and Alsayed-Ali 2015)
Rosuvastatin	518	Chloroform/Safranin	5–25 mg/m	(Nemade et al. 2014)
Rosuvastatin	242	MeOH	4–16 mg/mL	(Ângelo n.d.)
Rosuvastatin and fenofibrate	244 ROS; 286.7 FEN	MeOH	1–10 mg/mL	(Kondawar et al. 2011)
Rosuvastatin and ezetimibe	λ (exc) 315; λ(em) 362	MeOH	0.5–10 mg/mL	(El-Bagary, Elkady, and Kadry 2012)
Rosuvastatin and fenofibrate	243 ROS; 224 FEN	MeOH	4–12 mg/mL	(Suresh Kumar and Rajendraprasad 2010)
Rosuvastatin and aspirin	259 ROS; 238 ASP	MeOH:water (1:1)	0.5–2 mg/mL	(Ambole, Shirote, and Kondawar 2012)
Rosuvastatin and fenofibrate	243 ROS; 287 FEN	MeOH	1–7 mg/mL	(Karunakaran et al. 2011)
Rosuvastatin and fenofibrate	244 ROS; 286.7 FEN	MeOH	1–10 mg/m	(Karunakaran et al. 2011)
Rosuvastatin and glimepiride	241 ROS; 231 GLI	0.1 M NaOH	10–22 mg/mL	(Ansari et al. 2005)
Rosuvastatin and fenofibrate	224 FEN; 243, 258 ROS	MeOH	4–12 mg/mL	(Bedair, Korany, and Issa 1988)

Table 7: spectrophotometric methods for the analysis of Losartan alone or in combined dosage formulations.

Analyte(s)	Wavelength (nm)	Solvent or reagent	Linear range for LOS	Reference
Losartan	234 nm	distilled water	4:6.00 mg/l	(Lastra et al. 2003)
Losartan	232.5 nm	distilled water	2:50 µg/ml	(AlKhalidi et al. 2008)
Losartan	603 nm	alkaline potassium permanganate	7.5-60 µg/ml	(Rahman, Rahman, and Azmi 2005)
Enalapril and Losartan	250 nm	distilled water	1–50 µg/ml	(Thomas et al. 2009)
Losartan and amlodipine	230 nm	distilled water	8–40 µg/ml	(Nagavalli et al. 2010)
Losartan	248 nm	Methanol	0.025-0.5 µg/ml	(Demirkaya-Miloglu, Yaman, and Kadioglu 2015)
Losartan	400 nm	deionized water	0.1–5 µg/ml	(Taher, Asadollahzadeh, and Fazelirad 2015)
metolazone and losartan	335 nm	acidic methanolic solution	0.2–2.0 µg/mL	(Fathy, El-Awady, and Belal 2019)

Table 8: Representative methods for the analysis of Rosuvastatin.

Method	Condition	Detection	Ref. No
Electrode	Vertically aligned carbon nanotubes and graphene oxide; phosphate buffer pH 2.0	1.26 V vs. Ag/AgCl (3.0 mol/L KCl)	(Silva et al. 2015)
HPTLC	Silica gel F254; Ethyl acetate:toluene:glacial acetic acid (6:3:1 v/v/v)	240 nm UV	(Purkar et al. 2014)
Capillary zone electrophoresis	Fused-silica capillary (50 mM, total length of 48.5 cm and effective length of 40.0 cm); 50 mM borate buffer at pH 9.5	243 nm UV	(Porrà, Quaglia, and Fanali 1995)
TLC	Silica gel 60F254 HPTLC plates; toluene:MeOH:ethylacetate -formic acid (6C1C3C0.1)	265 nm UV	(Sane et al. 2005)
Micellar electrokinetic chormatography	Fused silica of 63.0 cm total length with an effective length of 45.0 cm having 50.0 mm internal diameter; borate buffer (25.0 mM, pH 9.5), 10.0% organic modifier (5.0% MeOH C 5.0%Acetonitrile)	215 nm UV	(El-Kommos et al. 2014)
Charge-transfer complex	Various π-acceptors	Various λ	(Alzoman et al. 2013)
Charge-transfer complex	2,3-dichloro-5,6-dicyano-1,4-benzoquinone	460 nm visible	(Wani et al. 2011)

Table 9: Representative methods for the analysis of Losartan.

Method	Condition	Detection	Ref. No
binary complex formation with eosin	non-ionic surfactant (methylcellulose)	540 nm	(Abd El-Hay, El-Mammli, and Shalaby 2016)
conductometry	protonation of losartan producing a white precipitate and resulting in a slow increase in conductivity	sharp increase in conductivity	(De Oliveira Rossini, Felix, and Angnes 2012)
TLC	silica gel G60 F 254, mobile phase: 7.5:1.5:5:5:0.01:0.03 = $CHCl_3$–CH_3OH–acetone– toluene–CH3COOH	254 nm	(Tsvetkova and Obreshkova 2012)
voltammetric determination	boron-doped diamond electrode	separation of 0.23 V	(Santos et al. 2013)
potentiometric determination	molecularly imprinted polymer-based potentiometric nano-graphene/ionic liquid/carbon paste electrode	59.64 ± 0.20 mV	(Bagheri, Shirzadmehr, and Rezaei 2015)
fluorimetry techniques	imidazolium ionic liquid (Imz)-modified nanoparticles was utilized as an adsorbent	325 nm	(Farnoudian-Habibi et al. 2015)
light scattering	reaction of Los-K with Cu (II) ions	LED based photometer	(Lima and Reis 2017)
differential pulse voltammetry	iron metal–organic framework/mesoporous carbon nanocomposite-modified glassy carbon electrode	signals at 50 mV	(Rajpurohit, Bora, and Srivastava 2018)

Conclusion

This review provides a clear and comprehensive summary of the various analytical methods utilized for the determination of Losartan (LOS) and Rosuvastatin (ROS), either individually or in combination. Among these techniques, high-performance liquid chromatography (HPLC) emerged as the most advanced and widely employed method due to its superior sensitivity, selectivity, and precision. Spectroscopic techniques also demonstrated significant utility, offering simpler and cost-effective alternatives for routine analysis.

Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could influence this study.

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