REVIEW

Spectrophotometric, chromatographic and bioanalysis of selected recently approved drugs from 2015–2020 to treat cardiovascular diseases: an analytical review

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Abstract

Background Heart Study has been operating for more than 40 years, and throughout that time it has found a number of risk variables that interact negatively to have an overall negative effect on cardiovascular disease (CVD) with an estimated 17.9 million deaths per year, CVD is the world's leading cause of death.

Main body In the current study, we present spectrophotometric, chromatographic analysis and bioanalysis methods for qualitative and quantitative evaluation of 15 drugs, including small and large molecules, that the U.S. FDA approved between 2015 and June 2020 to treat CVD's and in the current review work, they were presented.

Short conclusion The review's conclusion is that spectroscopic, chromatographic and bioanalysis methods play important role in quality control and standardization of recently approved drugs from 2015 to 2020 for treating CVD's in its bulk, pharmaceutical dosage form, synthetic mixture or human/rat plasma.

Keywords Cardiovascular disease, Spectrophotometric, Pharmaceutical dosage form, Chromatographic, U.S. FDA

Background

Heart Study has been operating for more than 40 years, and throughout that time it has found a number of risk variables that interact negatively to have an overall negative effect on cardiovascular disease (CVD) (Nabel 2003). Experience has revealed that the best method for preventing coronary heart disease is probably a

multifactorial one, one that considers all the risk factors (CHD) (Anderson et al. 1991). According to estimates, 17.9 million annual deaths from CVD each year. The collection of heart and blood vessel disorders known as CVDs includes conditions like coronary heart disease, cerebrovascular disease, rheumatic heart disease, and other illnesses. More than four out of every five CVD deaths result from heart attacks and strokes, and one-third of these deaths occur before the age of 70 (WHO report n.d.).

Premature deaths were significantly more common than premature CVD deaths globally (34%) and in Asia (35%) as well as in Europe (22%) and the USA (23%). Ischemic heart disease (IHD) (47%) and stroke (87%) accounted for the majority of CVD deaths (40%). The number of CVD deaths in Asia increased from 5.6 million to 10.8 million during 1990 and 2019, and the proportion of CVD deaths in all deaths increased from 23 to

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35%. Furthermore, crude CVD mortality rates increased steadily for both men and women during 1990 and 2019 (Burden and of Disease Collaborative Network. Global Burden of Disease 2019; Zhao 2021).

Drug discovery is a multidisciplinary method that is complex and it still presents a wide range of difficulties for the pharmaceutical industry and related sectors (Drews 2000). There were mainly 201 novel molecules authorized for the treatment of CVDs between 1937 and 2013. (Patridge et al. 2016) The US FDA's Centre for Drug Evaluation and Research (CDER) has approved 15 therapeutic medicines for cardiovascular diseases over the past five years, nine of which are small molecules, with the initial three are macromolecules (Table 1 and Fig. 1). The following is a description of the medications approved under this category (Bhutani et al. 2021).

The major goal of developing and validating analytical methods is to demonstrate that they are accurate, specific, precise, and robust for the particular drug (Doltade and Saudagar 2019; Kagawad et al. 2021).

Literature survey reveals that various analytical method have been developed to estimate recently approved drugs from 2015 to 2020 for treating cardiovascular diseases in bulk, tablet dosage form, synthetic mixture and in biological sample. The method consists of UV Spectrophotometric Analysis, Stability indicating RP-HPLC Method, LC/MS/MS, HPTLC, Spectrofluorimetry. Numerous researchers have worked on various spectrophotometric, chromatographic, and bioanalytical analyses, and they have published their findings in a number of journals and scientific databases. A survey of the literature indicated that, as of this writing, no reports on its detailed review about spectrophotometric and chromatographic analysis and bioanalysis of selected recently approved drugs from 2015 to 2020 for treating cardiovascular diseases. Hence, we attempted to complete the current review work since there is a clear need for collective information regarding spectrophotometric, chromatographic, and bioanalytical analysis that will be useful to other researchers and readers. The need to examine and compare the available analytical and bioanalytical tests used to determine these drugs, either alone or in combination, is essential.

Main text
UV Spectroscopy (Verma and Mishra 2018)
Ultraviolet (UV) spectroscopy is an optical spectroscopy technique based on the Beer–Lambert equation, the concentration of the absorbing species in a solution and the path length directly affect the solution's absorbance. It makes use of near-infrared, ultraviolet, and visible light. As a result, it can be used to measure the concentration of the absorber in a solution for a particular path length. Since UV–VIS spectroscopy has been in widespread use

for the past 37 years, it has evolved into the most important analytical tool in the modern laboratory. It is important to understand how quickly the absorbance varies with concentration. Other methods could be used in many applications, but none compared to UV–VIS spectroscopy's ease of use, flexibility, precision, speed, and cost-effectiveness. (Table 2).

HPLC methods (LC, RP-HPLC, UPLC) (Saibaba et al. 2016a)
In the pharmaceutical sector, reversed-phase liquid chromatography is the analytical technique that is most frequently utilized liquid chromatographic techniques are used to assess the quality of the drug substance (active pharmaceutical ingredient) and drug product during the drug development process (Table 3).

TLC and HPTLC method (Fenimore and Davis 1981 Feb 1)
Enhanced and improved separation effectiveness and detection limit than thin-layer chromatography (TLC), high-performance thin-layer chromatography (HPTLC) is a sophisticated and automated version of TLC. It is also referred to as flatbed chromatography, planar chromatography, and high-pressure thin-layer chromatography. It is a potent analytical technique that works for both qualitative and quantitative tasks. Depending on the type of solvent solution and adsorbent employed on development plates, separation may be caused through partition, absorption, or both. (Table 4).

LC-MS/MS, LC- MS method (Saibaba et al. 2016b)
Liquid chromatography/Mass Spectrometry (LC/MS) is quickly replacing traditional liquid chromatography as the main method of analysis. It is a powerful analytical technique that combines the liquid chromatography resolving strength and the mass spectrometric detection specificity. Liquid chromatography (LC) is used to separate the components of the sample, and the mass spectrometer is then used to analyze the separated components (MS). The molecular weight, structure, identity, and quantity of particular sample components can be determined using the LC/MS data; charged ions are produced and found by the MS. (Table 5).

Conclusions
Since drug design, bioavailability and safety studies have been greatly influenced by the improvement in quality of life, extremely sensitive and precise analytical techniques are required to meet these objectives. The presented work is focused on the use of various analytical methods such as HPLC (High-Performance Liquid Chromatography), HPTLC (High-Performance Thin-Layer Chromatography), TLC (Thin-Layer Chromatography), UPLC (Ultra Performance Liquid

Table 1 Compilation of illustrations of U.S. FDA-approved drugs from the year 2015 until June 2020 for drugs for treating cardiovascular diseases and their signs, approval year, sponsor, target, chemical class, major drug metabolizing enzyme(s) and route of administration/elimination

Brand name (Active ingredient/route of administration)	Types of molecule	Signs	Year of approval/sponsor/review classification	Chemical class	Major drug metabolizing enzyme(s)	Target	ROE
Uptravi (Selexipag/PO)	Small molecules	PAH	2015/Actelion/S, O	Organonitrogen compounds	Carboxylesterases, CYP2C8, CYP3A4	Prostacyclin receptor agonist	93% in feces and only 12% in urine
Entresto (Selexipag/PO)	Small molecules	Heart failure	2015/Novartis/P	Benzene and substituted derivatives	Esterase	Neprilysin inhibitor	Urine (50–70%)
Entresto (Valsartan/PO)				Carboxylic acids and derivatives	Minimal metabolism	Angiotensin II receptor blocker	Feces (86%)
Kengreal (Cangrelor/IV)	Small molecules	Avoid blood clots	2015/Medicines company/S	Purine nucleotide	Dephosphorylation	P2Y12 platelet inhibitor	58% via urine, 35% feces
Corlanor (Ivabradine/PO)	Small molecule	Heart failure	2015/Amgen/P	Benzazepines	CYP3A4	HCN-channels inhibitor	Feces (50%) and Urine (50%)
Savaysa (Edoxaban/PO)	Small molecule	Systemic embolism	2015/Daiichi/Sankyo/S	Carboxylic acids and derivatives	Carboxylesterase I	Factor Xa inhibitor	Feces (50%) and urine (50%)
Praxbind (Idarucizumab/IV)	Antibody fragment	Reverse Pradaxa's blood thinning effects	2015/BoehringerIngelheim/P, O, A, B	Fab derived from an IgG2	Hydrolytic Enzymes	Binds to dabigatran	Similar to endogenous IgG
Repathan (Evolocumab/SC)	Monoclonal antibody	High cholesterol	2015/Amgen/S, O	Humanized IgG2	Hydrolytic Enzymes	PCSK9 inhibitor	Similar to endogenous IgG
Praluent (Alirocumab/SC)	Monoclonal antibody	High cholesterol	2015/Sanofi/P	Humanized IgG1	Hydrolytic Enzymes	PCSK9 inhibitor	Similar to endogenous IgG
Defitelio (Defibrotide sodium/IV)	Oligonucleotide	Hepatic venooclusive disease	2016/Gentium/P, O	Single-stranded oligo-deoxyribonucleotides	Nucleases	Increase levels of Prostaglandin I2, E2 and prostacyclin	NA
Bevyxxa (Betrixaban/PO)	Small molecule	Venous thromboembolism	2017/Portola pharma/P	Anilids	Predominantly remain unchanged	Factor Xa inhibitor	85% feces and 11% urine
Hemlibra (Emicizumab/SC)	Monoclonal antibody	Hemophilia A	2017/Roche/Genetech/P, O, B	Humanized IgG4	Hydrolytic Enzymes	Factor Ixa and X inhibitor	Similar to endogenous IgG
Giapreza (Angiotensin II/IV)	Small molecule	Septic or other shocks	2017/La Jolla pharma/P	Amino acids, peptides and analogues	Aminopeptidase A and ACE2 to angiotensin	Angiotensin II agonist	NA
Vyndaqel (Tafamidis meglumine/PO)	Small molecule	Cardiomyopathy	2019/Pfizer/Foldrx/P, O, B	Benzoxazole derivatives	Glucuronidation	Transthyretin stabilizers	59% feces and 22% urine
Cablivi (Caplacizumab-yhdp/IV or SC)	Antibody fragment	Acquired thrombotic thrombocytopenic purpura	2019/Sanofi/Ablynx/P, O	Vwf-directed Fab	Hydrolytic Enzymes	A1-domain of vWF	Similar to endogenous IgG
Nexletol (Bempedoic acid/PO)	Small molecule	Familial hypercholesterolemia	2020/Esperion/S	Fatty acids and conjugates	Glucuronidation	Adenosine triphosphate citrate lyase inhibitor	NA

NA:No interaction reported, PCSK9: proprotein convertase subtilisin kexin type 9, PAH: pulmonary arterial hypertension, HCN: hyperpolarization-activated cyclic nucleotide-gated, FXa: factor Xa, Fab: monoclonal antibody fragment, vWF: von Willebrand factor, PO: peroral; IV: intravenous; SC: subcutaneous, CYP: cytochrome P450, IgG: immunoglobulin G; UGT: UDP- glucuronosyltransferase, P-gp: p-glycoprotein, A-accelerated, B-breakthrough, O-orphan, P-priority, S-standard, ROE: Route of Elimination.
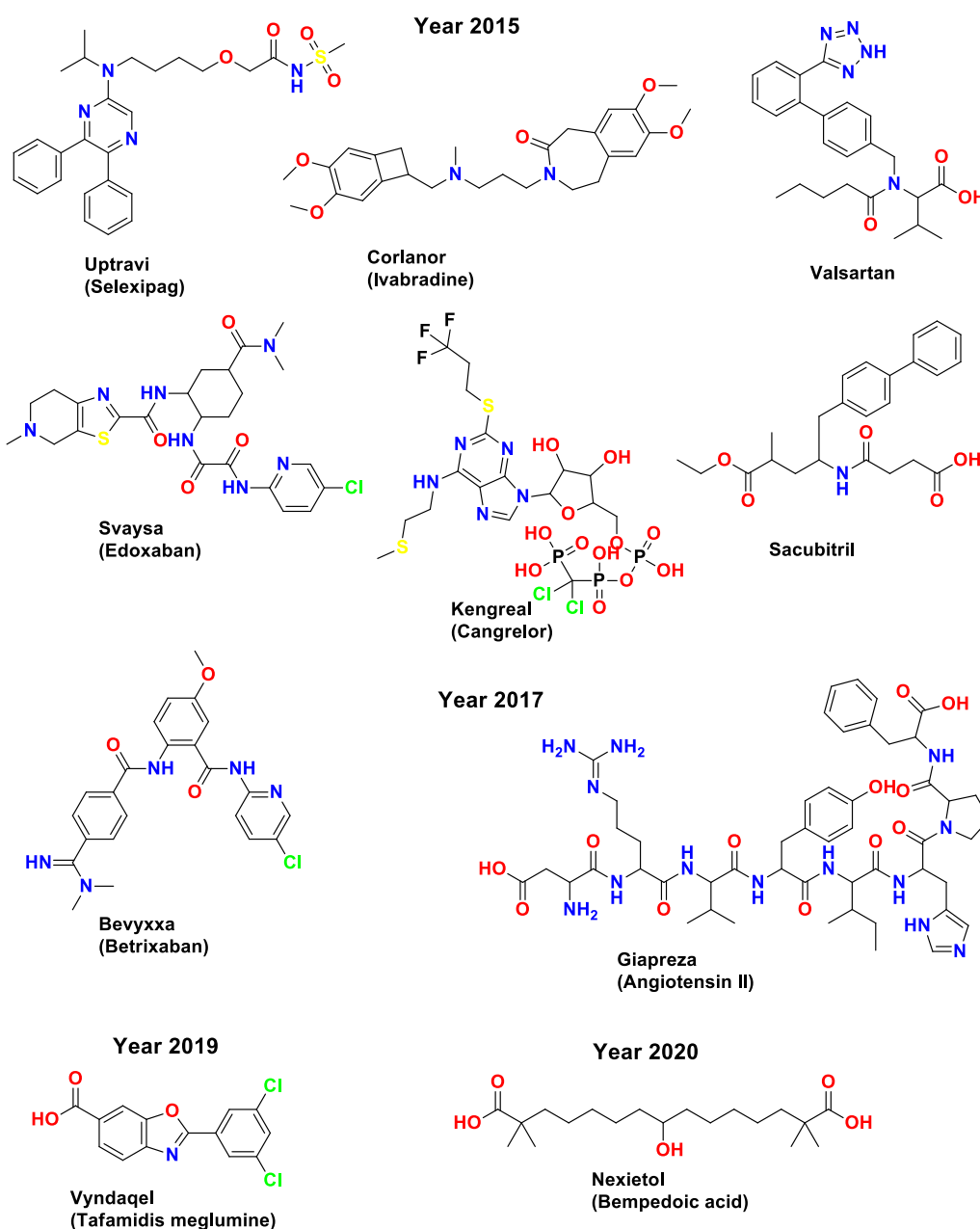
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Fig.1 Chemical structures of small compounds approved by the FDA for use in treating various cardiovascular diseases between 2015 and June 2020

Chromatography), and LC/MS/MS. For the purpose of determining the effectiveness of a medicinal compound in a certain matrix, a critical analytical method should be established for recently approved drugs from 2015 to 2020 for treating cardiovascular disease drug analytes in formulation as well as in API. Various analytical methods detection is appropriate for the examination of recently approved medications from 2015 to 2020 for treating cardiovascular illnesses since it yields precise results at a lower cost than more sophisticated detection methods. This paper provides a summary of the most advanced analytical techniques to estimate the recently approved cardiovascular medications. Analytical chemists would benefit from knowing the essential solvents and their combinations for the tools they have access in the laboratories.

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Table 2 Spectrophotometric methods for analysis of FDA-approved treatments for several cardiovascular illnesses from 2015 to June 2020

Method	Solvent system	Linearity (μg/ml)	λ max	Applications
Direct UV	Methanol: Water: phosphate buffer (pH 9)	10–60	298	Estimation of selexipag in tablets (Prathyusha et al. 2020)
Direct UV	Methanol: Water	5–30	600	Estimation of selexipag in tablets (Gorumutchu and Ratnakaram VN. 2018)
Direct UV	P-nitroanaline:1 N HCl: Distilled water	2–12	510	Determination of diazo coupling for selexipag in tablets (Ratnakaram 2018)
Direct UV	Methanol	2.5–25	226	Estimation of sacubitril in tablets (Naazneen and Sridevi 2017)
Direct UV	Methanol	4–12	226	Estimation of sacubitril in tablets (Kajal and Archana 2022)
Direct UV	Methanol: Water (25:75)	2–12	242	Determination of sacubitril in synthetic mixture (Leela Madhuri et al. 2019)
Direct UV	Methanol	2–14	230	Determination of sacubitril in combined dosage forms (Banu et al. 2021)
Direct UV	Methanol	4.9–24.5	242	Determination of sacubitril in bulk and dosage forms (Murugan and Vetrichelvan 2019)
Hybrid Spectrofluorimetry	Methanol	20–200	204	Determination of sacubitril in LCZ696 (Youssef et al. 2021)
Emission Spectroscopy	Methanol	0.04–0.8	314	Determination of sacubitril in LCZ696 (Ragab et al. 2017 Dec)
Direct UV	Water	10–30	276	Estimation of ivabradine in bulk and dosage forms (Thete and Saudagar 2018)
Q-absorbance ratio	Methanol	2–10	286	Estimation of ivabradine in bulk and dosage forms (Patil et al. 2016)
Direct UV	Methanol	2–10	291.2	Determination of edoxaban in dosage forms (Ravisankar et al. 2018)
Direct UV	Methanol	4–24	290	Determination of edoxaban in tablets (Dhiware et al. 2019)
Direct UV	Methanol	5–25	289	Estimation of edoxaban in synthetic mixture (Kalyankar et al. 2018)
Direct UV	Methanol	1–20	229.4	Determination of betrixaban in greenness assessment (El-Masry et al. 2022)
Direct UV	Phosphate buffer 6.8	5–30	220	Estimation of valsartan in bulk and tablet dosage form (Rao et al. 2013)
Direct UV	Methanol	5–30	250.80	Determination of valsartan in pure and in formulation (Tarkase et al. 2010)

Table 3 HPLC methods for analysis of FDA-approved treatments for several cardiovascular illnesses from 2015 to June 2020

Stationary phase	Mobile Phase (v/v)	Detection (nm)	Applications
X-bridge phenyl column	0.1% formic acid: Acetonitrile (50:50)	300	Characterization of process related impurities including degradation products of selexipag (Amara Babu et al. 2021)
C-18 column	Acetonitrile: Water (95:5)	254	Determination of sacubitril in bulk and dosage forms (Moussa et al. 2018)
C-18 column	Acetonitrile: Triethylamine buffer (50:50)	239	Determination of sacubitril in tablets (Mishra et al. 2020)
C-18 column	OPA (0.1%): Acetonitrile (60:40)	254	Estimation of sacubitril in bulk and pharmaceutical dosage forms (Tohidi et al. 2019)
C-18 column	Water: Methanol (30:70)	254	Determination of sacubitril in tablets (Phalguna et al. 2018)

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Table 3 (continued)

Stationary phase	Mobile Phase (v/v)	Detection (nm)	Applications
C-18 column	Methanol	254	Determination of sacubitril in bulk dosage forms (Trefi et al. 2019)
OJ-H Column	n-hexane 0.1%: TFA (80:20)	254	Determination of stereoisomers of sacubitril in bulk dosage forms (Zhou et al. 2018)
C-18 column	Methanol: Water (60:40)	245	Determination of sacubitril in tablets (Kumar et al. 2021)
C-18 column	Acidified water (pH 3, adjusted with Acetic acid: Acetonitrile (55:45)	254	Determination of sacubitril in rat plasma (Moussa et al. 2018)
C-18 column	Methanol:Ethanol:Water (40:30:30)	254	Estimation of sacubitril in human plasma and in tablets (Alamein and AM. 2018)
C-18 column (LC)	Methanol: Water (80:20)	241	Estimation of sacubitril in bulk and pharmaceutical dosage forms (Vaka and Parthiban 2017)
C-18 column	Acetonitrile:Methanol:Potassium dihydrogen phosphate (30:50:20)	263	Forced degradation study of sacubitril in tablets (Naazneen and Sridevi 2017)
C-18 column	Acetonitrile:Potassium hydrogen phosphate (30:70)	371	Determination of sacubitril in rat plasma (Anjaney-ulu et al. 2018)
C-8 column (UHPLC)	THF:Water:Acetonitrile (5:15:80) as ingredient mode	240	Determination of sacubitril in tablets (Prajapati et al. 2020)
C-18 column (LC-UV)	0.2% Formic acid	285	Characterization of Cangrelor IV (Guvvala et al. 2019)
ODS-3 V Column	0.5% Formic acid: Acetonitrile (65:35)	286	Determination of ivabradine HCl in tablets (Mahesh-wari et al. 2010)
C-18 column	Phosphate buffer (pH 7.4): Methanol (35:65)	286	Determination of ivabradine HCl in formulation (Patra and Panda 2014)
C-8 column	Acetonitrile:20 mmol ammonium acetate (40:60)	207 and 286	Determination of dual wavelength in ivabradine tablets (Nowakowska et al. 2017)
C-18 column	Methanol: Acetonitrile (80:20)	286	Estimation of ivabradine HCl in bulk and dosage forms (Thete and Saudagar 2019)
C-18 column	Methanol: Acetonitrile: Phosphate buffer (pH 3) (50:40:10)	230	Determination of ivabradine HCl in tablets (Mostafa et al. 2016)
C-18 column	Methanol: Acetonitrile (85:15)	291.2	Determination of edoxaban HCl in bulk and dosage forms (Sankar et al. 2021)
C-18 column	0.1% Formic acid water: Acetonitrile (80:20)	291.2	Determination of edoxaban HCl in powder inhaler formulation (Rashid et al. 2021)
C-18 column	Methanol: Acetonitrile (85:15)	291	Rapid assay therapeutic drug monitoring of edoxaban (Rashid et al. 2022 Apr 17)
C-18 column	Acetonitrile: Water (90:10)	249	Determination of edoxaban HCl in human plasma (Gouveia et al. 2020)
C-8 column	Methanol: Phosphate buffer (pH 4)	290	Determination of edoxaban HCl in human plasma (Younis et al. 2020)
C-18 column	0.1 M K_2HPO_4: Methanol (65:35)	245	Determination of edoxaban HCl in bulk and dosage forms (Reddy et al. 2016)
C-18 column	Potassium dihydrogen phosphate:Acetonitrile (30:70)	230	Determination of edoxaban HCl in bulk and dosage forms (Banda 2022)
C-18 column	0.01 m sodium acetate (pH 4): Acetonitrile (70:30)	290	Determination of edoxaban HCl in bulk and dosage forms (Todkar et al. 2020)
C-18 column	Acetonitrile:Methanol:Water (35:35:30)	240	Determination of betrixaban in pharmaceuticals and biological matrixes (El-Masry et al. 2021)
RP-18	0.1% trifluoroacetic acid with water:Acetonitrile (42:58)	280	Determination of tafamidis in plasma concentration in patients (Smerikarova et al. 2021)
C-18 column	KH_2PO_4: Acetonitrile (55:45)	246	Determination of bempedoic acid in bulk and dosage forms (Maheshwari and Rani 2022)
C-18 column (RP-UPLC)	Methanol:Acetonitrile:Water (50:30:20)	260	Stability indicating estimation of bempedoic acid in bulk and dosage forms (Yarra and Gummadi 2021)

Table 3 (continued)

Stationary phase	Mobile Phase (v/v)	Detection (nm)	Applications
C-18 column (RP-UPLC)	0.1% TFA in water:Acetonitrile (60:40)	236	Stability indicating estimation of bempedoic acid in bulk and dosage forms (Dandamudi and Rangapuram 2021)
C-18 column (HPLC–PDA)	0.1% TFA in water: Acetonitrile (40:60)	236	Determination of bempedoic acid in rat plasma (Karla et al. 2022)
C-18 column (UPLC)	0.1% OPA:Acetonitrile (50:50)	230	Determination of degradation products of bempedoic acid (Vejendla et al. 2021)
C-18 column	Ammonium formate:acetonitrile (57:43)	250	Determination of valsartan in nanoparticles (Alexander and Kumar 2018)
C-18 column	Acetate buffer (pH 4.6): acetonitrile: methanol (38:24:38)	248	Estimation of valsartan in solid oral dosage form (Tarkase et al. 2020)
C-18 column	Acetonitrile:Phosphate buffer (52:48)	255	Valsartan quantification in human plasma (Tammam and Talib 2019)
C-18 column	Acetonitrile:Water:Glacial acetic acid (40:59:1)	264	Determination of valsartan in biological fluid (Ghayas et al. 2017)
C-18 column	Acetonitrile: Phosphate buffer (adjusted to pH 2.7 ± 0.1 with phosphoric acid) (45:55)	265	Determination of valsartan in human plasma (Pérez et al. 2017)
RP-C18 column	Acetonitrile: Phosphate buffer (0.05 M) with pH 2.8 (40/60)	227	Estimation of Valsartan in Dosage Form and Spiked Human Plasma (EL-Gizawy SM, Abdelmageeb OH, Omar MA, Deryea SM, Abdel-Megieb AM 2012)
RP-18 column	0.01 M disodium hydrogen phosphate buffer: acetonitrile (60:40)	230	Estimation of Valsartan in Human Plasma (Zarghi et al. 2008)
C-18 column (RP-UPLC)	The solvent A:1.0% acetic acid buffer, Acetonitrile (90:10): Solvent B1.0% acetic acid buffer and acetonitrile (10:90)	225	Valsartan and its degradation products' estimation in active medicinal ingredients and dose forms (Krishnaiah et al. 2010)
C-18 column	Ammonium dihydrogen phosphate: methanol (33.5:66.5)	265	Stability indicating estimation of valsartan in tablet dosage form (Parambi et al. 2011)
C-18 column	0.02 mM sodium dihydrogen orthophosphate acetonitrile (58:42)	250	Stability indicating estimation of valsartan in tablet dosage form (Rao et al. 2010)
C-18 column (Isocratic)	Methanol: Water (60:40)	250	Estimation of valsartan and its degradation products (Bhatia and Kokil 2009)
C-18 column	Water: Acetonitrile (60:40)	265	Inherent stability estimation of valsartan by stress degradation (Agrahari et al. 2009)

Table 4 TLC and HPTLC methods for analysis of FDA-approved treatments for several cardiovascular illnesses from 2015 to June 2020

Stationary phase	Mobile phase (v/v)	Detection (nm)	Applications
Silica gel 60GF254	Glacial acetic acid: Ethyl acetate: Methanol: (0.1:9:1)	260	Estimation of sacubitril and valsartan in pharmaceutical dosage forms (Alamein 2018)
Silica gel 60F254 (TLC)	Toulene:Ethylacetate:Methanol(4:4:2)	260	Determination of sacubitril and valsartan by densitometry (Khalid et al. 2018)
Silica gel 60GF254	Ethylacetate:0.389 m ammonium acetate in methanol (1:5)	287	Determination of ivabradine in bulk and marketed formulation (Motisariya et al. 2013)
Silica gel 60GF254	Methanol:Chlorofrom:Water (8:1:1)	286	Stability indicating chromatographic method of ivabradine (Damle and Bagwe 2015)
Silica gel 60GF254	Toulene:Methanol:Triethylamine(7.5:1:0.2)	230	Determination of edoxaban in bulk and marketed formulation (Dhiware et al. 2019)

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Table 5 LC-MS/MS, LC-MS methods for analysis of FDA-approved treatments for several cardiovascular illnesses from 2015 to June 2020

Stationary phase	Mobile phase (v/v)	Applications
C-18 column (LC–MS/MS)	5 mm ammonium formate in water:Acetonitrile (95:5)	Determination of betrixaban in tablets (Jasemizad and Padhye 2019)
C-18 column	Acetonitrile:10 mm ammonium formate (80:20)	Determination of selexipag in human plasma (Bhadru et al. 2019)
C-18 column	Mathanol:5 mm ammonium formate (75:25)	Determination of selexipag in human plasma (Satheshkumar and Muruganantham 2021)
C-18 column	1% formic acid: Acetonitrile	Determination of selexipag and its impurities in rat plasma (Rao et al. 2021)
C-18 column	0.1% formic acid in mili Q water, 0.1% formic acid in acetonitrile	Simultaneous estimation of sacubitril and valsartan in rat plasma (Chunduri and Dannana 2016)
C-18 column	Methanol: 0.1% formic acid (80:20)	Estimation of Valsartan in Human Plasma (Chinthala et al. 2017)

Declarations

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