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Atorvastatin: A Review on Analytical Methods for Determination in Pharmaceutical Formulations and Biological Matrix

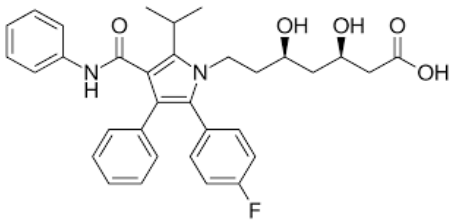
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Abstract: Among HMG-CoA reductase inhibitors, Atorvastatin is the most efficacious in lowering cholesterol levels, preventing atherosclerosis and stroke and reducing cardiovascular risk. In addition to quality control pharmacokinetic and pharmacodynamic studies, an analytical framework is required to conduct stability studies of Atorvastatin by using effective clinical and pharmaceutical procedures. In order to determine whether a given drug is a single drug or used with an integration of other similar bulk drugs, formulations and biological fluids. We have evaluated the studies in various analytical and pharmaceutical chemistry journals, as well as the instrumental analytical methods that have been developed and applied. Numerous analytical methods are discussed in this review including spectroscopic techniques, chromatographic techniques like liquid chromatography, HPTLC, mass spectroscopy, HPLC and RP-HPLC

Introduction

A statins class drug commonly named as "Atorvastatin". Chemically, Atorvastatin is "(3R, 5R)-7-[2-(4-Fluoropheny)-3-phenyl-4-(phenyl carbamoyl)-5-propan-2-ylpyrrol-1-yl]-3,5-dihydroxyheptaaoic acid". Atorvastatin which is a competitive inhibitor of "3-hydroxy-3-methylglutaryl coenzyme A" (HMG-CoA) reductase enzyme. HMG-CoA reductase enzyme acts by converting HMG-CoA to mevolonate, which is a rate-determining step in cholesterol biosynthesis. It is used to reduce cholesterol levels. Atorvastatin works by decreasing the cholesterol that is deposited on the walls of the arteries that leads to blocking of flow of blood and supply of oxygen in the brain, heart and various parts of the body. Statins prescribe as first-line treatment for prevention of cardiovascular disease. In cardiac risk conditions, atorvastatin is mainly used as an antilipidemic agent to reduce the cholesterol level. Generally, this medication is recommended to administer in bed time because at night time the production of cholesterol is high. This medication should be administered every day at the same time and once a day[1234].

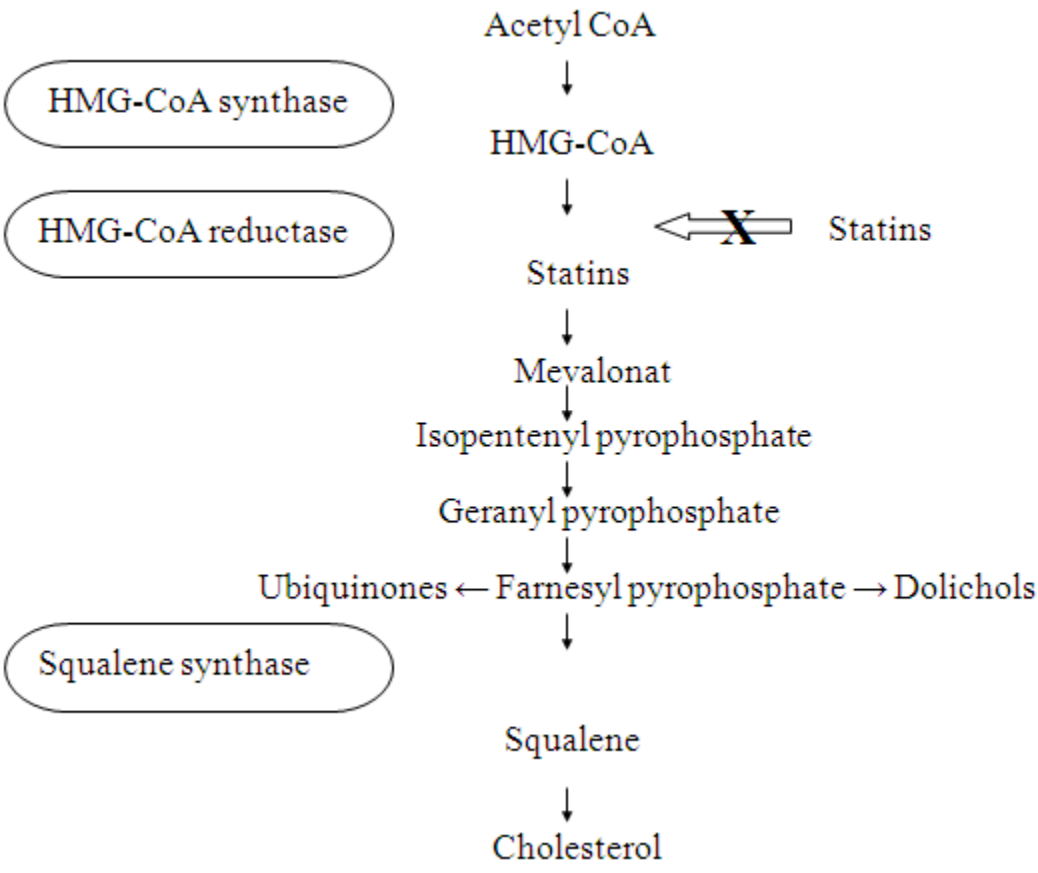
Structure:



Mechanism of action

In statin medication, atorvastatin decreases cholesterol production within the liver by impeding "HMG-CoA reductase", which convert into to mevalonate and it causes decrease in cholesterol level in hepatic cells and increase the LDL receptors in liver that results in hepatic uptake of LDL and reduce the LDL levels in the circulations. It also decreases the triglycerides level and increases HDL cholesterol level. Atorvastatin that lowers the LDL cholesterol, triglycerides,apolipoprotein B (apo-B) and it raises the HDL cholesterol levels. Atherosclerosisand cardiovascular diseases are mainly caused due to high LDL level triglycerides levels and low HDL levels in the circulation.Cardiovascular risks can be reduced by increase in the levels of HDL cholesterol. In patients having "homozygous familial hypercholesterolemia" atorvastatin helps to decrease the plasma LDL levels. The shape of the atorvastatin is complementary to the active site of HMG-CoA reductase and within the active site it forms specific hydrogen bonds. Statins used as primary and secondary coronary heart disease prevention by lowering lipid levels[5678910].

Mechanism of Action:



COMBINATIONS OF ATORVASTATIN:

1. Amlodipine + Atorvastatin
2. Fenofibrate + Atorvastatin
3. Ezetimibe + Atorvastatin
4. Methylcobalamine + Atorvastatin
5. Clopidogrel + Atorvastatin
6. Nicotinic acid + Atorvastatin
7. Aspirin + Atorvastatin
8. Aspirin + Clopidogrel + Atorvastatin
9. Telmisartan + Atorvastatin
10. Pioglitazone + Atorvastatin

Table 1: Summary of Chromatographic Method of Atorvastatin[11-45]

Drug and its combination	Method	Conditions	Wave length	Linearity	Detectors	Ref
Atorvastatin	HPLC	Lichrospher ODS , Lichrosorb ODS, Spherisorb ODS & Hypersil OS column, Water:Acetonitrile (48:52 v/v) pH 2.0 as M.P and flow rate 1.5ml/min	245nm	_	UV - visible detector model SPO –6 AV	11
Atorvastatin calcium	RP-HPLC	LichroCART® 250*4mm, HPLC Cartridge, lichrospher 100, RP-18 (5mm) Merck-column, 0.1% Acetic acid:Acetonitrile (45:55v/v) as M.P and flow rate 0.8ml/min	246nm	Atorvastatin: 8.13-23.77µg/ml	UV-visible detector Hewlett Packard detector (model 1050)	12
Atorvastatin calcium	HPLC	C18- column, Acetonitrile:Dichloromethane: Acetic acid (68.6:30.6:0.8v/v) as M.P and flow rate 1.0 ml/min	246nm	Atorvastatin: 15-300 µg/ml	WDM 3000 photodiode array UV-visible detector	13
Atorvastatin and Amlodipine	RP-HPLC	RP-C18 column, Acetonitrile:0.03M Phosphate	240nm(AT)	Atorvastatin: 0.2-20µg/ml	Waters 2487 UV- dual	14

		buffer of pH 2.9 (55:45v/v) as M.P & flow rate 1ml/min	362nm(AML)	Amlodipine: 0.1-20µg/ml	λ absorbance detectors	
Atorvastatin and Amlodipine	HPLC	Hitachi L-7420, Lichrospher -100, C18 column, Acetonitrile:50mM Potassium dihydrogen phosphate buffer (60:40v/v) as M.P and flow rate 1.0ml/min	254nm	Atorvastatin: 1-90µg/ml Amlodipine : 1-80µg/ml	UV-visible detector	15
Atorvastatin and Nicotinic acid	RP-HPLC	Agilent, ZORBAX SB C18 column, Acetonitrile:Distilled water(85:15) pH 4.5 as M.P and flow rate 1ml/min	261nm	Atorvastatin: 2-12µg/ml Nicotinic acid: 10-80µg/ml	UV-2075 plus detector	16
Atorvastatin calcium and Amlodipine Besylate	RP-HPLC	Eurosphere100, C18 column, Methanol:Water (55:45v/v) as M.P and flow rate 1.0ml/min	207nm	Atorvastatin: 5-25µg/ml Amlodipine: 2.5-12.5µg/ml	UV-visible detectors	17
Atorvastatin calcium and Amlodipine Besylate	RP-HPLC	Grace smart, RP C18 (250*4.6) column, Phosphate buffer:Acetonitrile:Methanol (53:43:4v/v) as M.P and flow rate 1ml/min	246nm	Atorvastatin: 40-60µg/ml Amlodipine: 80-120µg/ml	UV-visible detectors	18
Atorvastatin calcium and Aspirin	RP-HPLC	0.02M Potassium dihydrogen phosphate:Methanol (20:80v/v) as M.P and flow rate 1ml/min	240nm	Atorvastatin: 0.5-4µg/ml Aspirin: 5-25µg/ml	Variable wavelength UV-visible detector SPD - 10 AVP	19
Atorvastatin and Ezetimibe	HPLC	Phosphate buffer:Methanol:Acetonitrile (40:10:50 v/v) as M.P and flow rate 1.2ml/min	233nm	Atorvastatin: 5-25µg/ml Ezetimibe: 5-25µg/ml	UV or Photodiode array detector	20
Atorvastatin +Fenofibrate +Ezetimibe	RP-HPLC	Reverse-phase C18 column, Methanol:Acetonitrile:Water (80:10:10v/v) as M.P	256nm	Atorvastatin: 3-7µg/ml Fenofibrate: 48-112µg/ml Ezetimibe: 3-7µg/ml	PDA-detector	21
Atorvastatin calcium and Amlodipine Besylate	RP-HPLC	RP stainless steel column ODS C18, 0.03 M Potassium buffer:Acetonitrile (30:70v/v) as M.P and flow rate 1.0ml/min	—	Atorvastatin: 80-120µg/ml Amlodipine: 80-120µg/ml	—	22
Atorvastatin calcium and Amlodipine Besylate	RP-LC	Hypersil silica BDS column, 0.05M Ammonium acetate buffer:Acetonitrile (40:60v/v) as M.P and flow rate 1.0ml/min	240 nm	Atorvastatin: 60-140µg/ml Amlodipine: besylate: 30-70µg/ml	SPD-10 AVP UV-VIS detector	2

Atorvastatin calcium & Amlodipine Besylate	HPTLC	Aluminium plates , Chloroform:Methanol:Acetic acid (85:10:5v/v) as M P and flow rate	247nm	—	—	2
Atorvastatin calcium & Ezetimibe	RP-HPLC	Luna C18 column, Methanol:Acetate buffer (70:30v/v) as M.P and flow rate 1.0ml/min	248nm	Atorvastatin calcium : 0-20µg/ml Ezetimibe : 0-20µg/ml	—	2
Atorvastatin calcium and Ramipril	RP-HPLC	HIQ SII C18 column, Acetonitrile:0.02M Potassium dihydrogen phosphate (80:20v/v) as M.P and flow rate 1ml/min	217nm	Atorvastatin calcium :0.4-25.6µg/ml Ramipril: 0.8-51.2µg/ml	UV detector	2
Atorvastatin and Ramipril	RP-HPLC	C18 column, Acetonitrile:Water:Methanol (55:40:05v/v/v) as M.P and flow rate 1.0ml/min	237nm	Atorvastatin: 5-26µg/ml Ramipril: 2.5-12.5µg/ml	Duel wavelength UV-VIS detector	2
Atorvastatin and Fenofibrate	RP-HPLC	Thermohypersile BDS C18 column, Water:Methanol (60:40v/v) as M.P and flow rate 1ml/min	274nm	Atorvastatin: 0.01-0.03µg/ml Fenofibrate: 0.16-0.48µg/ml	PDA detector	2
Atorvastatin calcium and Losartan potassium	HPTLC	Precoated aluminum sheets of silica gel 60 F254, Toulene:Methonol (8:2v/v) as M.P	260nm	Atorvastatin: 200-1200ng/band Losartan: 500-3000ng/band	CAMAG TLC visualize	2
Atorvastatin calcium and Clopidogrel bisulphate	RP-HPLC	Eurospher 100-5 C18 column, Acetonitrile:Potassium dihydrogen phosphate 0.01M (75:25v/v) as M.P and flow rate 1.0ml/min	240nm	Atorvastatin: 60-140µg/ml Clopidogrel: 294-686µg/ml	SPD- 20A UVdetector	3
Atorvastatin calcium and Aspirin	RP-HPLC	SS Grace –C18 column, Acetonitrile:Ammonium acetate 0.02M (68:32v/v) as M.P and flow rate 0.8ml/min	245nm	Atorvastatin: 2-10µg/ml Aspirin: 15-75µg/ml	UV detector	3
Atorvastatin and Atenolol	RP-HPLC	Phenomenes ODS C18 column, Acetonitrile:Phosphate buffer (72:28v/v) as M.P and flow rate 1.0ml/min	238nm	Atorvastatin: 4-20µg/ml Atenolol: 20-100µg/ml	SPD- 10A UV-VIS detector	3
Atorvastatin and Fenobirate	RP-HPLC	Thermohypersil BDS C18 column, Water:Methonol (60:40v/v) as M.P and flow rate 1ml/min	274nm	Atorvastatin: 0.01-0.03µg/ml Fenofibrate: 0.16-0.48µg/ml	PDA detector	3
Atorvastatin calcium and Olmesartan medoxomil, Candesarta, Hydrochlorothiazide and Chlorthalidone	RP-HPLC	Cosmosil PAQ analytical column, Acetonitrile: 0.05M Sodium dihydrogen phosphate buffer in gradient ratio as M.P and flow rate 1.0ml/min	220nm	Atorvastatin calcium:10-150µg/ml Olmesartan medoxomile:10-150µg/ml Candesartan:10-150µg/ml Hydrochlorotiazide: 10-150µg/ml	Photodiode array detector	3

				Chlorrthalidone:10-150µg/ml		
Atorvastatin calcium, Ramipril and Aspirin	HPTLC	Precoated silica gel 60 F254 HPTLC plates, Benzene:Ethyl acetate:Toluene:Methanol:Glacial acetic acid (4.0:4.5:1.0:0.5:0.1v/v/v/v/v)	220nm	Atorvastatin: 0.5-2.5µg/spot Ramipril: 0.5-2.5µg/spot Aspirin: 0.75-3.75µg/sport	—	3
Atorvastatin Amlodipine and Ezetimibe	RP-HPLC	Phenomenex C18 analytical column, Acetonitrile: Methanol: Dipotassium hydrogen phosphate (36.74:20:43.26 v/v/v) as M.P and flow rate 1.20ml/min	231nm	Atorvastatin: 0.5-5.0µg/mlAmlodipine: 0.25-2.5µg/mlEzetimibe: 0.5-5.0µg/ml	SPD 10A UV-Visible detector	3
Atorvastatin, Metformin, Glimepiride and Pioglitazone	HPLC	Phenomenex C18 column, Methanol: Phosphate buffer (75:25v/v) as M.P and flow rate 1.0ml/min	230nm	Metformin: 500-5000µg/mlGlimepiride: 5.0-60.0µg/ml Pioglitazone: 50.0-170.0µg/ml	—	3
Atorvastatin, Metformine hydrochloride and Glimepiride	HPTLC	Water:Methanol:Ammonium sulphate (1:1:4v/v/v) as M.P	237nm	Atorvastatin: 150µg Metformine hydrochloride:50 µgGlimepiride: 150µg	—	3
Enalapril maleate, Hydrochlorothiazide, Aspirin and Atorvastatin	RP-HPLC	C18 Column, Acetonitrile: Methanol:Triethylammonium phosphate buffer(pH 2.5) (50:25:25v/v/v) as M.P and flow rate 0.6ml/min	225nm	Einalapril maleate: 12.5-250µg/mlHydrochlorothiazide: 12.5-250µg/mlAspirin: 25-500µg/mlAtorvastatin: 500-1000µg/ml	UV-detector	3
Pravastain, Atorvastatin	HPLC	C18 reversed-phase column, Methanol:0.1% Orthophosphoric	238nm	Pravastain: 120-240µg/ml Atorvastatin: 120-	UV-detector	4

and Simvastatin		acid in water as M.P and flow rate 1.0ml/min		240µg/mlSimvastatin: 20-140µg/ml		
Atorvastatin, Ezetimibe and Fenofibrate	HPLC - PDA	C18 Guard Column, Methanol with water andAcetonitrile with water as M.P and flow rate 0.7ml/min	240nm	Atorvastatin: 0.50-32µg/mlEzetimibe: 0.50-32µg/mlFenofibrate: 8-512µg/ml	PDA – detector	4
Atorvastatin calcium, Aspirin, Clopidogrel Bisulphate	RP-HPLC	RP-Inertsil® ODS analytical column, Acetonitrile:Phosphate buffer (pH 3.0) (50:50v/v) as M.P and flow rate 1.2ml/min	235nm	Atorvastatin calcium: 5-30µg/ml Aspirin: 30-105µg/mlClopidogrel Bisulphate: 30-105µg/ml	UV - detector	4
Atorvastatinand Amlodipine	RP-HPLC	Lichrospher® 100 C18column, Acetonitrile: Phosphate buffer (pH3±0.1) (60:40v/v) as M.P & flow rate 1.0ml/min	254nm	Atorvastatin : 1-90µg/mlAmlodipine : 1-80µg/ml	Hitachi L-7420 UV visible detector	4
Atorvastatin calcium, Pioglitazone	RP-HPLC	Reverse – phase Qualisil -100 C8 column, Acetonitrile : Water (45:55 v/v) (pH 6.2) as M.P & flow rate 1.0ml/min	232nm	Atorvastatin calcium: 10-80µg/mlPioglitazone: 10-80µg/ml	UV – PDA detector	4
Atorvastatin , Ezetimibe	Liquid chromatography	Hypersil phenyl – 2 column, M-Ammonium acetate (pH 6.5):Acetonitrate (28:72v/v) as M.P & flow rate 0.5ml/min	242nm	Atorvastatin: 12-52µg/mlEzetimibe: 12-52µg/ml	UV – detector	4

Table 2: Summary of UV-Spectroscopic Method of Atorvastatin[46-76]

Drug Name	Method	Solvent	Wavelength of Atorvastatin	Wavelength for other drugs	Linearity	Ref

Atorvastatin Calcium:	UV Spectroscopy	Anhydrous methanol	291nm	-	Atorvastatin: 5 - 35 µg/ml	46
Atorvastatin:	UV Spectroscopy	Methanol	247nm	-	Atorvastatin: 5 - 20 µg/ml	47
Atorvastatin andAmlodipine:	UV Spectroscopy	50% v/v aqueous methanol	245nm	363 nm	Atorvastatin: 14 - 26 µg/mlAmlodipine: 7 -13 µg/ml	48
Atorvastatin and Amlodipine:	UV Spectroscopy	Phosphate buffer(pH 6.8)	240nm	369 nm	Atorvastatin: 5 - 26 µg/mlAmlodipine: 10-50 µg/ml	49
Atorvastatin calcium:	UV-Visible Spectroscopy	Methanol, Acetonitrile, Iodine	246nm	_	Atorvastatin: 0.5586 – 11.173 µg/ml	50
Atorvastatin calcium and Amlodipine Besylate	UV-spectroscopy	Methanol	246nm	361nm	Atorvastatin calcium: 0.5-30µg/mlAmlodipine: 0.5-30µg/ml	51
Atorvastatin and Amlodipine	Orthogonal function ratio spectrometry	Methanol	243nm	364 and 238nm	Atorvastatin: 10-50µgAmlodipine: 5-25µg/ml	52
Atorvastatin and Amlodipine	UV spectroscopy	Methanol	257.6nm	360nm	Atorvastatin: 5-30µg/mlAmlodipine: 10-60µg/ml	53
Atorvastatin calcium and Aspirin	UV-spectroscopy	Methanol	246nm	225.5nm	Atorvastatin calcium: 4-30µg/mlAspirin: 4-32µg/ml	54
Atorvastatin and Ezetimibe	UV-spectroscopy	Methanol	246.5nm	232.5nm	___	55
Atorvastatin and Ezetimibe	UV-spectroscopy	Methanol	235nm	258.2nm	Atorvastatin: 5-30µg/mlEzetimibe: 5-30µg/ml	56

Atorvastatin and Aspirin	UV-spectroscopy	Methanol	242nm	222nm	Atorvastatin: 5-40µg/mlAspirin: 5-30µg/ml	57
Atorvastatin and Aspirin	UV-Spectroscopy	Methanol: water (50:50v/v)	246nm	276nm	Atorvastatin: 6-14µg/ml Aspirin: 20-100µg/ml	58
Atorvastatin and Pioglitazone	Derivative Spectroscopy	Water	226nm	278nm	Atorvastatin: 2-16µg/mlPioglitazone: 2-16µg/ml	59
Atorvastatin and Pioglitazone	Simultaneous estimation	Ethanol	210nm	225nm	----------	60
Atorvastatin and Losartan	Simultaneous estimation	Methanol	207nm	246nm	----------	61
Atorvastatin and Glimepiride	Spectrometric method	0.1 NaoH	241nm	231nm	----------	62
Atorvastatin and Fenofibrate	Spectrometric method	Methanol	246nm	286nm	Atorvastatin: 1-10µg/mlFinofibrate: 2-20µg/ml	63
Atorvastatin and Fenofibrate	Simultaneous estimation	Methanol	238nm 256nm	259nm 298nm	Atorvastatin: 5-30µg/mlFinofibrate: 5-30µg/ml	64
Atorvastatin and Fenofibrate	Simultaneous equation	Methanol	245nm	285nm	----------	65
Atorvastatin and Ramipril	Derivative Spectroscopy	Water:Methanol (40:60)	294nm	229nm	----------	66
Atorvastatin and Nicotinic acid	Simultaneous estimation	Methanol	248nm	261.5nm	Atorvastatin: 2-12µg/mlNicotinic acid: 10-60µg/ml	67
Atorvastatin and Telmisartan	Simultaneous estimation	Water	297nm	241.8nm	Atorvastatin: 5-30µg/mlTelmisartan: 5-30µg/ml	68
Atorvastatin and Telmisartan	Simultaneous estimation	Methanol	247nm	296nm	Atorvastatin: 5-30µg/mlTelmisartan: 5-30µg/m1	69

Atorvastatin and Niacin	Simultaneous estimation	Methanol	246nm	262nm		70
Atorvastatin and Olmesartan	Ratio derivative spectroscopy	Methanol	313nm	223nm	Atorvastatin: 4-16µg/mlOlmesartan: 8-32µg/ml	71
Atorvastatin and Olmesartan	Simultaneous equation First order derivative	Methanol	247nm 310nm	256.5nm 247nm		72
Atorvastatin and Atenolol	Simultaneous estimation	Methanol	241nm	225nm	Atorvastatin: 2-12µg/mlAtenolol: 5-30µg/ml	73
Atorvastatin, Glimepiride, Metformin	Multicomponent simultaneous estimation	Methanol	255nm	G 225nm M 285nm	----------	74
Atorvastatin, Ezetimibe, Fenofibrate	Simultaneous estimation	Methanol	247nm	E 233nm F 287nm	Atorvastatin: 5-30µg/ml Ezetimibe: 5-30µg/ml Fenofibrate: 5-30µg/ml	75
Atorvastatin, Ramipril, Acetylsalicylic acid	Simultaneous estimation	Methanol	246nm	R 206nm A 226nm	Atorvastatin: 2-10µg/mlRamipril: 1-5µg/mlAcetylsalicylic acid: 10-50µg/ml	76

Table 3:Other method for Determination of Atorvastatin[77-98]

Drug	Title	Method	Ref
Atorvastatin and Ezetimibe	Simultaneous estimation of Atorvastatin and Ezetimibe in bulk and their combined Dosage form by Dual wavelength UV-Spectroscopic method	Dual wavelength UV - Spectroscopic method	77
Atorvastatin and Ezetimibe	Simultaneous estimation of Ezetimibe and Atorvastatin Calcium using Spectrophotometric and TLC-densitometric methods	Spectrphotometroic and TLC- densitometric method	78

Atorvastatin	Determination of Atorvastatin by Liquid Chromatography in bulk drugs, tablets and human plasma	Liquid Chromatography	79
Atorvastatin and Ezetimibe	Micellar electro kinetic capillary chromatography for Simultaneous estimation of atorvastatin and Ezetimibe from combined pharmaceutical dosage forms	Micellar electro kinetic capillary chromatography	80
Atorvastatin, Metformin and Glimepiride	LC-MS/MS method for Simultaneous estimationof Atorvastatin, Metformin and Glimepiride in human plasma and its application to a human pharmacokinetic study	LC- MS	81
Atorvastatin	Determination of atorvastatin in pharmaceutical products by Validated Spectrofluorimetric method	Spectrofluorimetric method	82
Atorvastatin and Ezetimibe	Simultaneous estimation of Atorvastatin and Ezetimibe in human plasma by LC-MS-MS method	LC-MS-MS	83
Atorvastatin	Estimation of Atorvastatin Calcium by Development and Validation of RP-HPTLC Densitometric method in Bulk Drug and Tablets	RP- HPTLC Densitometric method	84
Atorvastatin and Ramipril	RP-HPLC and Spectroscopy methods for Simultaneous determination of Ramipril and Atorvastatin	RP- HPLC and spectroscopy	85
Atorvastatin	Simultaneous determination of Atorvastatin and its active metabolites in human plasma by Development and validation of a simple, sensitive and rapid method using LC-ESI-MS/MS	LC-ESI-MS/MS	86
Atorvastatin Calcium and Ezetimibe	Simultaneous determination of Atorvastatin calcium and Ezetimibe in combined dosage form using Development and Validation of analytical method	Simultaneous estimation, HPLC, HPTLC method	87
Atorvastatin calcium and Ezetimibe	Simultaneous determination of atorvastatin calcium and Ezetimibe in pharmaceutical dosage form by Application of UV-Spectrophotometry and RP-HPLC methods	UV-Spectrophotometry and RP-HPLC	88
Atorvastatin calcium and	Formulation, optimization and simultaneous estimation of Losartan potassium and Atorvastatin Calcium in pure and bilayer tablets	UPLC and HPTLC	

Losartan potassium			89
Atorvastatin calcium and Ezetimibe	Ratio Spectra derivative Spectrophotometry and Reverse phase- high performance liquid chromatography methods for Simultaneous estimation of Ezetimibe and Atorvastatin Calcium	Spectrophotometry and RP-HPLC	90
Atorvastatin calcium and Amlodipine Besylate	UV-Spectrphotometric method for Simultaneous determination of Amlodipine besylate and Atorvastatin calcium by using hydrotropic solubalization	Hydrotropic solubalization	91
Atorvastatin and Amlodipine	Spectrofluorimetry and HPLC coupled with Fluorescence Detection for Simultaneous estimation of Atorvastatin Calcium and Amlodipine besylate in Binary mixture	Spectrofluorometric, spectrophotometric and HPLC methods	92
Atorvastatin and Amlodipine	Simultaneous determination of Amlodipine and Atorvastatin in Pharmaceutical Products using Development and validation of RP-HPLC and Spectrophotometric methods	UV-Spectrophotometry and RP-HPLC	93
Atorvastatin calcium and Aspirin	LC-MS/MS method for Simultaneous estimation of Aspirin and Atorvastatin in Human Plasma and Its Pharmacokinetic Application	Liquid Chromatography-Tandem Mass Spectrometry	94
Atorvastatin Calcium and Amlodipine Besylate	HPLC method Implementing Design of Experiment and Spectrophotometric method with Multivariate Calibration method for Simultaneous estimation of Atorvastatin Calcium and Amlodipine besylate	UV-Spectrophotometry and HPLC	95
Atorvastatin Calcium and Aspirin	Determination of Atorvastatin Calcium and Aspirin in Combined Dosage Forms by using RP-HPLC method	Spectrphotometric and RP-HPLC methods	96
Atorvastatin and Amlodipine	Simultaneous estimation of Atorvastatin and Amlodipine and in Combined formulations using Derivative-Ratio Spectrophotometric, Chemometric and HPLC validated methods	Derivative-Ratio Spectrophotometric, Chemometric and HPLC	97
Atorvastatin and Glimepride	LC-MS/MS method for Simultaneous Estimation of Glimepride and Atorvastatin in Human Plasma and Their Application to a Pharmacokinetic Study	Liquid-Chromatography-Tandem Mass Spectrometry	98

REPORTED METHOD:

1.Chromatographic methods:

The HPLC was developed for determination and validation for simultaneous determination of single and combination drug. Plasma and pharmaceutical dosage forms of Atorvastatin are commonly analyzed using HPTLC methods. Atorvastatin concentrations in human serum can also be determined by RP-HPLC, as well as simultaneously in synthetic mixtures, combination formulations like Losartan, Amlodipine, etc. (Table 1).

2.UV spectroscopic Method:

A simultaneous estimation of Atorvastatin and their combination with other anti-hyperlipidemic drugs and anti-hypertensive drugs was undertaken using first order derivative spectroscopy, standard addition method, ratio derivative spectroscopy techniques and Q analysis method. (Table 2).

3.Other simultaneous combination analytical method for Atorvastatin and its combination:

Shown in Table 3.

CONCLUSION:

This systemic review summarizes the current methods for analyzing serum and plasma samples for the presence of Atorvastatin and its combination drugs. The mostly widely used method for Atorvastatin determination is HPLC method. In addition to being sensitive, specific and with better separation efficiency, HPLC can also be used to determine Atorvastatin quantitatively and qualitatively simultaneously. For the determination of Atorvastatin in blood, serum, pharmaceutical dosage form and synthetic mixture other analytical were used like RP-HPLC, HPTLC, UV-Spectroscopy and LC/MS/MS methods. The reported information is useful for further research studies includes formulation development comparing and quality control of Atorvastatin.

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