Spectrophotometric and Chromatographic Methods for Determination of Calcium Channel Blockers: A Review

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ABSTRACT

Several analytical techniques are advantageous in pharmaceutical field to estimate the quality of active pharmaceutical ingredients, amount of drug in biological fluids and in formulations. The intention of this review article is to provide paramount current analytical methods for analysis of calcium channel blockers like felodipine, isradipine, amlodipine, and nifedipine in pure form and its related formulations including novel formulations. Calcium Channel blockers is a major chemical class of drugs used in the treatment of hypertension and various coronary artery diseases. The present review includes the current analytical methods available for above active pharmaceutical ingredients and its related formulations with extensive method conditions which can be used in analysis of calcium channel blockers drugs outlined from official pharmacopoeias and other relevant research articles. From the review, it can be inferred that a vast array of chromatographic techniques have been created, with HPLC-UV techniques often employed for calcium channel blocker detection and estimation.

Keywords: Felodipine, Isradipine, Amlodipine, Nifedipine, Chromatographic methods and Spectrophotometric methods.

INTRODUCTION

The calcium-channel blockers signify a group of organic chemical structures that share the ability to inhibit Ca2+ entry into excitable cells. In coronary and peripheral arterial smooth muscle and the heart, inhibition of Ca2+ entry blunts the ability of Ca2+ to serve as an intracellular messenger. Thus, calcium-channel blockers are smooth-muscle dilators and have a negative inotropic effect on the working myocardial cells of the atria and ventricles. Calcium-channel blockers also have effects on impulse formation and conduction in some regions of the heart. A fast, Na+-dependent ionic current is responsible for the upstroke of the action potential in the working cells of the atria and ventricles and in the rapidly conducting cells of the His-Purkinje system, so that the calcium-channel blockers do not inhibit conduction in these cells. In the sinoatrial and atrioventricular nodes, where depolarization is due primarily to a Ca2+-dependent slow inward current, the calcium-channel blockers slow the sinus pacemaker and inhibit atrioventricular conduction. The actions of different calcium-channel blockers are not always similar; for example, nifedipine is much more potent as an inhibitor of calcium channels in smooth muscle than in the heart, whereas verapamil and diltiazem are approximately equipotent in heart and vascular smooth muscle. It is likely that the calcium-channel blockers reach their specific binding sites in membranes by first dissolving in the phospholipid bilayer, after which they may interact with hydrophobic regions of proteins that make up, or regulate, these channels. Further knowledge of these molecular properties should facilitate the development of new calcium-channel blockers with improved specificity. [1]

Calcium-channel blockers target L-type calcium channels and binds to them. These L-type calcium channels are located on the smooth muscle of vessels, cardiac myocytes, and nodal tissues in heart. These channels regulate the entry of calcium into muscle cells, which stimulates smooth muscle and cardiac myocyte to contract.Vasodilation occurs when calcium entry is blocked this way into cells. Hence there will be decrease in myocardial force generation (negative inotropy), decrease in heart rate (negative chronotropic), and decrease in conduction velocity within the heart (negative dromotropic) [2]

Calcium channel blockerseffectively lower blood pressure, especially in combination with other drugs, and some formulations of agents of this class are approved for treating angina or cardiac dysrhythmias. They reduce blood pressure across all patient groups, regardless of sex, race/ethnicity, age, and dietary sodium intake. Non-dihydropyridine calcium channel blockers are more negatively chronotropic and inotropic than the dihydropyridine subclass, which is important for patients with cardiac dysrhythmias or who need β-blockers. Extensive

experience in comparative randomized trials indicates that an initial calcium antagonist can prevent all major types of cardiovascular disease, except heart failure (for which a diuretic is superior). Initial dihydropyridine calcium channel blockers have not reduced the rate of progression of renal disease as well as inhibitors of the renin-angiotensin system, although members of the non-dihydropyridine subclass can reduce albuminuria. [3]

Significant research has been done on a variety of analytical approaches that could be helpful in estimating calcium channel blockers in biological matrices and formulations. For the estimation of calcium channel blocker alone or in combination with other medications, analytical techniques such as ultraviolet (UV) spectrophotometry, HPLC, High Performance Thin Layer Chromatography have been reported. This thorough study includes the majority of the spectrophotometric and chromatographic techniques that have been reported for determining pure forms of isradipine, felodipine, amlodipine, and nifedipine in various pharmaceutical dosage forms and biological fluids up to this point.

Mechanism of action

Calcium channel antagonists block the inward movement of calcium by binding to the L-type “long-acting” voltage-gated calcium channels in the heart, vascular smooth muscle, and pancreas. There are two major categories of calcium channel antagonists based on their primary physiologic effects. The non-dihydropyridines have inhibitory effects on the sinoatrial (SA), and atrioventricular (AV) nodes are resulting in a slowing of cardiac conduction and contractility. This allows for the treatment of hypertension, reduces oxygen demand, and helps to control the rate in tachydysrhythmias. The dihydropyridines, in therapeutic dosing, have a little direct effect on the myocardium, and instead, are more often peripheral vasodilators, which is why they are useful for hypertension, post-intracranial haemorrhage associated vasospasm, and migraines. [4-5].

Pharmacokinetics

The calcium channel blockers have the same anti-hypertensive actions, they have a vast difference in their pharmacological actions, pharmacokinetic profile. Calcium channel antagonists are absorbed well orally, however many have low bioavailability due to hepatic first-pass metabolism, primarily by CYP3A4. Calcium channel antagonists are highly protein-bound, and many have high volumes of distribution. In repeated doses, or overdose, the hepatic enzymes responsible for metabolism become saturated and reduce first-pass effects, which therefore increases absorption of the active drug. Modified release formulations and saturation of metabolism of these drugs increase the half-life of various calcium channel antagonists. Calcium channel antagonists are primarily excreted renally after metabolism [6]. Summary of

different routes of administration, bioavailability, metabolism, plasma protein binding and excretion between the individual compounds is depicted in Table 1. The different physicochemical properties of calcium channel blockers are represented in Table 2.Chemical structures, nomenclatures and molecular weights of these drugs are shown in Table 3.

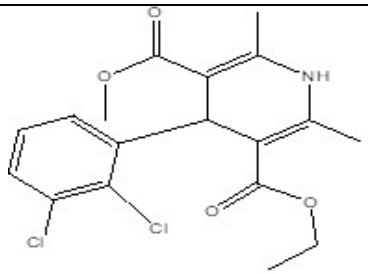
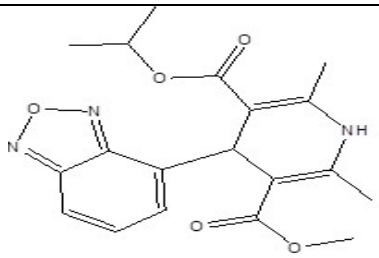
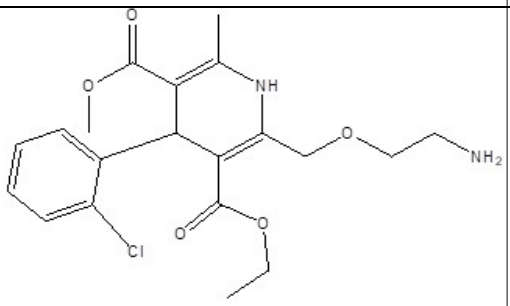
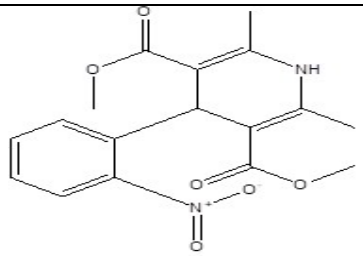
Table 1: Pharmacokinetic properties of calcium channel blockers

Pharmacokinetic Parameter	Felodipine	Isradipine	Amlodipine	Nifedipine
Administration Route	Oral	Oral	Oral	Oral
Bioavailability (%)	20	15-24	60-65	56 -77
Metabolism	CYP3A4	CYP3A4	CYP3A4	CYP3A
Elimination Half-Life (hr)	25	8	35-45	1.7
Plasma Protein Binding (%)	More Than 99	95	95	98
Excretion	Urine	Urine	Urine	Urine

Table 2: Physicochemical properties of studied calcium channel blockers

Drug	Pk_a	Solubility	λmax, nm
Felodipine	5.07	Soluble in organic solvents such as ethanol, DMSO, DMF and sparingly soluble in aqueous buffers	237
Isradipine	2.56	Practically insoluble in water, soluble in ethanol and freely soluble in acetone, chloroform and methylene chloride	332
Amlodipine	8.6	Slightly Soluble in water, freely soluble in methanol	365
Nifedipine	3.93	Soluble in methanol, ethyl acetate, acetone	546

Table 3: Chemical structures of studied calcium channel blockers

Drug	Chemical Structure	Chemical Name	Mol. Wt.
Felodipine		5-*O*-Ethyl 3-*O*-Methyl (4*s*)-4-(2,3-Dichlorophenyl)-2,6-Dimethyl-1,4-Dihydropyridine-3,5-Dicarboxylate	384.2
Isradipine		3-Methyl 5-Propan-2-Yl 4-(2,1,3-Benzoxadiazol-4-Yl)-2,6-Dimethyl-1,4-Dihydropyridine-3,5-Dicarboxylate	371.38
Amlodipine		3-*O*-Ethyl 5-*O*-Methyl 2-(2-Aminoethoxymethyl)-4-(2-Chlorophenyl)-6-Methyl-1,4-Dihydropyridine-3,5-Dicarboxylate	408.87
Nifedipine		Nifedipine (3,5-Dimethyl 2,6-Dimethyl-4-(2-Nitrophenyl)-1,4-Dihydropyridine-3,5-Dicarboxylate)	346.33

Reported Analytical Methods

Ultraviolet spectrophotometry

Ultraviolet spectrophotometric methods such as Vierodt's, absorption ratio, area under curve method and Dualwavelengthmethodshavebeenreported for the determination of different calcium channel blockers in bulk and pharmaceutical dosage forms. Ultraviolet spectrophotometric methods for estimation of Felodipine as bulk drug and in tablet dosage form has been reported [7-9]. Ultraviolet spectrophotometric methods for simultaneous determination of felodipine with atorvastatin calcium are reported [10, 11]. Ultraviolet

spectrophotometric methods for estimation of Isradipine in single and in combination with butylated hydroxyanisole were also reported [12, 13]. Spectrophotometric methods for determination of amlodipine as single drug [14-16] and in combination with Celecoxib [17], Atorvastatin [18, 19], Hydrochlorothiazide [20], Telmisartan [21], Aliskiren [22], Valsartan [23], Atenolol [24] were also found in the literature.UVspectrophotometric method for simultaneous estimation of Nifedipine in combination with Atenolol [25] and Telmisartan [26] are also reported. The summary of reported spectrophotometric methods for estimation of calcium channel blockers is given in Table 4.

Table 4: UV methods for determination of calcium channel blockers

Sr No.	Drug	Method	λmax (nm)	Solvent	Ref. No.
1	Felodipine	Calibration curve	362.4	Methanol	7
2	Felodipine	Absorbance maxima	363.5	Ethanol	8
3	Felodipine	Absorbance maxima	237	Methanol	9
4	Felodipine	Absorbance maxima	366.5	Methanol: 0.1N HCl(1: 9, v/v)	10
5	Felodipine	Simultaneous equation	268	Acetonitrile: water (70: 30, v/v)	11
6	Isradipine	Absorbance maxima	372	Methanol: chloroform (7:3, v/v)	12
7	Isradipine	Absorbance maxima	326	Methanol	13
8	Amlodipine	Calibration curve	365	Sodium acetate	14
9	Amlodipine	Calibration curve	237, 360	Methanol	15
10	Amlodipine	Absorbance maxima	238	Water	16
11	Amlodipine with Celecoxib	Calibration curve	364.3	Ethanol	17
12	Amlodipine with Atorvastatin	Simultaneous equation	245, 363	Methanol	18
13	Amlodipine with Atorvastatin	Simultaneous equation	240, 369	Phosphate buffer	19

14	Amlodipine with Hydrochlorothiazide	Simultaneous equation	238, 271	Sodium hydroxide	20
15	Amlodipine besylate with Telmisartan	Absorbance correction	365.2, 291.2	0.1 N Hcl	21
16	Amlodipinewith Aliskiren	Absorbance correction	279, 361	Methanol	22
17	Amlodipine with Valsartan	Simultaneous Equation Absorption Correction	250, 238	Methanol	23
18	Amlodipine besylate with Atenolol	Calibration Curve	278.5, 286	Methanol	24
19	Nifedipine with Atenolol	Simultaneous equation	328, 276	Methanol	25
20	Nifedipine with Telmisartan	Simultaneous equation	292.2, 235.5	Methanol	26

Chromatographic methods

High performance thin layer chromatography

Validated HPTLC methods for estimation of Felodipine in bulk and pharmaceutical dosage form has been developed and reported [27, 28].TLC-densitometric methods for simultaneous determination of Felodipine in combination with metoprolol and ramipril in fixed dose combinations tablets have been developed and validated [29, 30]. HPTLC method for estimation of Isradipine in bulk drug and butylated hydroxyanisole in selected food stuffs is also reported [31]. Validated HPTLC methods for simultaneous estimation of amlodipine with Metoprolol Succinate [32, 33], Benazepril [34] Nebivolol Hydrochloride [35] Hydrochlorothiazide and Telmisartan [36] Celecoxib [37] Olmesartan medoxomil and Hydrochlorothiazide [38] Hydrochlorothiazide and Valsartan [39] Telmisartan [40] AzilsartanMedoxomil [41] atenolol [42]Aliskiren and Hydrochlorothiazide [43] Hydrochlorothiazide and Olmesartan Medoxomil [44] Losartan potassium and Hydrochlorothiazide [45, 46] in pharmaceutical formulations has been developed and validated. High performance thin layer chromatographic determination of Nifedipine as bulk drug and in pharmaceuticals and human serum is also reported [47, 48]. ThesummaryofreportedHPTLC-densitometricmethodsforseparationandestimation of calcium channel blockers inhibitors in bulk and pharmaceutical dosage forms is listed in Table 5.

Table 5: HPTLC methods for determination of calcium channel blockers

Sr No.	Drug	Mobile Phase	λmax (nm)	Ref. No.
1	Felodipine	n-Hexane: ethyl acetate (6: 4, v/v)	366	27
2	Felodipine	Acetonitrile: water: glacial acetic acid (8: 2: 1, v/v/v)	237	28
3	Felodipine with Metoprolol, Ramipril	Toluene: ethyl acetate: methanol: ammonia (20: 8: 6: 0.6, v/v/v/v)	223	29
4	Felodipine with Metoprolol	Chloroform: toluene: methanol: glacial acetic acid (6: 3: 1: 0.04, v/v/v/v)	238	30
5	Isradipine	Toluene: methanol: glacial acetic acid (9: 1: 0.05, v/v/v)	331	31
6	Amlodipine	Chloroform: methanol: acetic acid (15 :2.5: 0.4, v/v/v)	365	32
7	Amlodipine with Metoprolol	Toluene: ethyl acetate: methanol: triethylamine (4: 1: 1: 0.4, v/v/v/v)	254	33
8	Amlodipine with Benazepril	Ethyl acetate: methanol: ammonia (8.5: 2: 1, v/v/v)	254	34
9	Amlodipine with Nebivolol	Methylene chloride: methanol: ammonia (8.5: 1: 0.5, v/v/v)	285	35
10	Amlodipine with Hydrochlorothiazide, Telmisartan	Chloroform: butanol: ammonia (6: 4: 0.1, v/v/v)	254	36
11	Amlodipine with Celecoxib	Toluene: methanol: acetonitrile (6.6: 1.5: 2, v/v/v/v)	240	37
12	Amlodipine with Olmesartan Medoxomil, Hydrochlorothiazide	Toluene: chloroform: methanol: acetonitrile: formic acid (2: 7: 1.8: 0.8: 0.2, v/v/v/v/v)	232	38
13	Amlodipine with Hydrochlorothiazide, Valsartan	Ethyl acetate: methanol: toluene: ammonia (7.5: 3: 2: 0.8, v/v/v/v)	232	39

14	Amlodipine with Telmisartan	Chloroform: methanol: formic acid (8: 2.5: 0.5, v/v/v)	251	40
15	Amlodipine with AzilsartanMedoxomil	Chloroform: methanol: glacial acetic acid (7: 1.5: 0.5, v/v/v)	243	41
16	Amlodipine with Atenolol	Methylene chloride: methanol: ammonia (8.8: 1.3: 0.1, v/v/v)	230	42
17	Amlodipine with Aliskiren, Hydrochlorothiazide	Ethyl acetate: methanol: ammonia (7.5: 2.8: 0.2, v/v/v)	229	43
18	Amlodipine with Hydrochlorothiazide, Olmesartan Medoxomil	Chloroform: ethyl acetate: toluene: methanol: glacial acetic acid (19.5: 19.5: 38.5: 19.5: 3, v/v/v/v/v)	230	44
19	Amlodipine with Losartan Potassium, Hydrochlorothiazide	Chloroform: ethyl acetate: methanol: ammonia (4: 4: 2: 0.2, v/v/v/v)	232	45
20	Amlodipine with Losartan Potassium, Hydrochlorothiazide	Chloroform: methanol: acetone: formic acid (7.5 : 1.3 : 0.5 : 0.03, v/v/v/v)	254	46
21	Nifedipine	Chloroform: ethyl acetate: cyclohexane (19: 2: 2, v/v/v)	236	47
22	Nifedipine	Chloroform: ethyl acetate: cyclohexane (19: 2: 2, v/v/v)	236	48

High Performance Liquid Chromatography

High performance liquid chromatography has been widely used for determination of studied calcium channel blockers. Also, HPLC come out to be a method frequently regularly used in all fields of calcium channel blockers. The various reported HPLC methods [49-109] based on use of different stationary phases (silica C8, C18, cyanopropyl), mobile phases and using UV, fluorescence or tandem mass spectrometry for detection and quantitative determination of calcium channel blockers either as single or in combination with other drugs in pure, pharmaceutical dosage forms and biological fluids are shown in Table 6.

Table 6: RP-HPLC methods for determination of calcium channel blockers

S. No.	Drug (S)	Column	Mobile Phase	λmax (nm)	Ref. No.
1	Felodipine	C18	Methanol: acetonitrile: water (50:15: 35, v/v/v)	238	49
2	Felodipine with Ramipril	Adsorbosil C8	Methanol: acetonitrile: water (50:30:20, v/v/v)	250	50
3	Felodipine	Luna C18	Methanol: 0.055 M phosphate buffer (83:17, v/v)	275	51
4	Felodipine in plasma	Capcell pak C8	5 Mm Phosphate Buffer (pH 4.8): acetonitrile (25: 75, v/v)	360	52
5	Felodipine	Inertsil ODS C18	Buffer: acetonitrile: methanol (2:2: 1, v/v/v)	238	53
6	Felodipine	HiQ Sil C 18 HS	Methanol : 0.055M phosphate buffer (pH 3) (83: 17, v/v)	232	54
7	Felodipine	C18	Diethyl ether: hexane (80:20, v/v)	237	55
8	Felodipine	Eclipse XDB C18	Acetonitrile: 0.1 % formic acid (75:25, v/v)	238	56
9	Felodipine	C18	Tetra butyl ammonium hydrogen sulphate: acetonitrile (18: 82, v/v)	237	57
10	Felodipine	Thermo BDS Hypersil C18	Phosphate buffer (pH 3): acetonitrile (50:50, v/v)	238	58
11	Felodipine	C18	Acetonitrile: water (80:20, v/v)	243	59
12	Felodipine with Ramipril	Hyperchom C18	Potassium dihydrogen phosphate (pH 3.5): methanol: acetonitrile (15:15:70, v/v/v)	210	60
13	Felodipine with Metoprolol	Phenomenex C8	Water (pH 3.5):acetonitrile : methanol (30:60: 10, v/v/v)	225	61
14	Felodipine with Ramipril	Hypersil BDS C18	Phosphate buffer (pH 5.5): acetonitrile (40:60, v/v)	243	62

15	Felodipine withEnalpril	Phenomenex Luna C18	Phosphate buffer (pH 3): acetonitrile (25:75, v/v)	237	63
16	Felodipine with Enalapril	Lichrosorb RP 8	Acetonitrile 0.001 M KH_2PO_4 (pH 2) (35:65, v/v)	215	64
17	Felodipine with Pioglitazone	InertsilC18	Acetonitrile: 50 Mm ammonium acetate buffer(67:33, v/v)	240	65
18	Felodipine with Aliskiren	Hypersil BDS C8	Water (pH 3.0): acetonitrile : methanol (20:30:50, v/v/v)	254	66
19	Felodipine with Atorvastatin	HIQ Sil C18 HS	Acetonitrile: water (70:30, v/v)	238	67
20	Isradipine	Agilent Zorbax C8	Methanol: acetonitrile: 0.1% OPA (55:35:10, v/v/v)	264	68
21	Isradipine	Kromasil C18	Water: methanol:THF (50:40:10, v/v/v)	330	69
22	Isradipine	C18	Methanol: acetonitrile: acetate buffer (pH 2.8)(60:30: 10, v/v/v)	290	70
23	Isradipine	C18	Methanol: water (70: 30, v/v)	290	71
24	Isradipine	Chiralpak AD	Hexane: 2-propanol: ethanol (94:4:2, v/v/v)	325	72
25	Isradipine	C8	Water: acetonitrile (50: 50,v/v)	290	73
26	Isradipine	C18	Methanol: water (60:40, v/v)	325	74
27	Isradipine	Kromasil C18	Water: methanol: THF	326	75
28	Amlodipine	Waters C18	Acetonitrile: 70mm KH_2PO_4 buffer: methanol(15:30:55, v/v/v)	240	76
29	Amlodipine	Nucleosil C8	0.01 M Sodium dihydrogen phosphate buffer: acetonitrile (63:37, v/v)	239	77
30	Amlodipine with Hydrochlorothiazide, Telmisartan	Thermosil C18	Potassium dihydrogen orthophosphate buffer: methanol (40:60, v/v)	248	78

31	Amlodipine withValsartan, Hydrochlorothiazide	Phenomenex KinetexC18	Acetonitrile: 0.05 M phosphate buffer (40: 60, v/v)	227	79
32	Amlodipine with Atorvastatin	Grace Smart RP C18	Phosphate Buffer: acetonitrile: methanol (53:43:4, v/v/v)	246	80
33	Amlodipine with Valsartan, Hydrochlorothiazide	Hypersil C18	Acetonitrile: phosphate buffer (pH 6.8) (55:45, v/v)	237	81
34	Amlodipine with Telmisartan	Phenomenex Luna C18	Phosphate buffer (pH 4): acetonitrile (42:58, v/v)	236	82
35	Amlodipine with Telmisartan	Prontosil C18	Methanol: potassium dihydrogen phosphate buffer (75:25, v/v)	240	83
36	Amlodipine Besylate with perindopril erbumine	Eclipse Xdb C8	Buffer (pH 2.6): acetonitrile (65:35, v/v)	210	84
37	Amlodipine with Losartan, Hydrochlorthiazide	RP C18	Phosphate buffer (pH 7): methanol: acetonitrile(60: 20: 20, v/v/v)	238	85
38	Amlodipine with Valsartan	C18 Column ODS	Phosphate buffer (pH 3.6): acetonitrile: methanol (46:44:10, v/v/v)	240	86
39	Amlodipine with Metoprolol	KromasilC18	0.02 M Phosphate buffer (pH 3) : acetonitrile (70: 30, v/v)	221	87
40	Nifedipine in human plasma	C18	KH2PO4 (pH 4.8) : acetonitrile (42:58, v/v)	240	88
41	Nifedipine	Novopak C18	Methanol: water(48:52, v/v)	235	89
42	Nifedipine	C18	Phosphate buffer: acetonitrile (60:40, v/v)	242	90
43	Nifedipine	Octadecyl Silane	Acetonitrile: TEA(78:22, v/v)	326	91
44	Nifedipine with Lignocaine Hcl	Hypersil BDS C18	Buffer (0.05 KH_2PO_4 pH 3.0):Methanol(50:50, v/v)	234	92

45	Nifedipine	RP C18	Methanol: water(70:30,v/v)	262	93
46	Nifedipine	C18	Acetonitrile: methanol: water (25:25:50,v/v/v)	235	94
47	Nifedipine with Atenolol	C8	Phosphate buffer: methanol (75:25, v/v)	237	95
48	Nifedipine	C18	Methanol: water(40:60, v/v)	237	96
49	Nifedipine with Atenolol	RP C18	Acetonitrile:50 mM sodium perchlorate (50:50, v/v)	230	97
50	Nifedipine	Shim-Pack CLC ODS C18	Methanol: water(70:30, v/v)	238	98
51	Nifedipine with Triamterene	ODS C18	Methanol: water(80:20, v/v)	238	99
52	Nifedipine with Atenolol	Phenomenex Kinetex C18	Methanol: orthophosphoric acid (75:25, v/v)	237	100
53	Nifedipine	Primesil C8	Acetonitrile: methanol: water (9:36:55, v/v/v)	235	101
54	Nifedipine with Atenolol	ODS C18	Methanol: acetonitrile: phosphate buffer(60:20:20, v/v/v)	235	102
55	Nifedipine	C18	Methanol:0.1% trifluoroacetic acid(55:45, v/v)	265	103
56	Nifedipine with Nateglinide, Lovastatin	C18	Acetonitrile:10 mm phosphate buffer(60:40, v/v)	208	104
57	Nifedipine in plasma	Nova Pak C18	Acetonitrile: water (48:52, v/v)	240	105
58	Nifedipine in plasma	C18	Acetonitrile: 5mm ammonium acetate (60:40, v/v)	240	106

59	Nifedipine with Atenolol	YMC Pack C18	Acetonitrile:phosphate buffer (62.5:37:5, v/v)	230	107
60	Nifedipine	C18	Methanol: triethylamine (68: 32, v/v)	235	108
61	Nifedipine with Atenolol	C18	Methanol: orthophosphoric acid (70:30, v/v)	233	109

CONCLUSION

This review focuses on different spectrophotometric and chromatographic methods which are reported for the determination of four calcium channel blockers viz. felodipine, isradipine, amlodipine, and nifedipine in bulk, different pharmaceutical dosage forms and biological matrices. The studied data revealed that HPLC was comprehensively used for the quantitative determination of calcium channel blockers as it offers excellent specificity and adequate precision. This review will assist in appropriate selection of analytical technique, solvent, mobile phase, and column, detector based on available analytical instruments and chemicals, by referring tabulated extensive method conditions. It can be implemented in quality control and quality assurance department for quality assessment of diverse pharmaceutical formulations.

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