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A REVIEW ON ANALYTICAL METHOD FOR DETERMINATION OF CALCIUM CHANNEL BLOCKER IN DIFFERENT DOSAGE FORMS

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ABSTRACT

Calcium channel blockers (CCBs) or Calcium antagonists are among the most widely used drugs in cardiovascular medicine with roles not only in hypertension but also in angina. CCBs promote vasodilator activity by reducing calcium influx into vascular smooth muscle cells by interfering with voltage-operated calcium channels in the cell membrane. Interference with intracellular calcium influx is also important in cardiac muscle, cardiac conduction tissue and gastrointestinal smooth muscle. It includes drugs like Amlodipine Diltiazem, Felodipine, Isradipine, Lacidipine, Lercanidipine, Nicardipine, Nifedipine, Nisoldipine and Verapamil. . This Review enlists different method developed for determination of Calcium channel blocker like U.V. Spectrophotometric, HPLC, RP-HPLC, LC-MS/MS.

Key Words: Calcium channel blocker, Hypertension, Spectrophotometric

INTRODUCTION [1]:

Calcium channel blockers (CCBs) are another class of first line antihypertensive in. All 3 subgroups of CCBs dihydropyridine (Nifedipine), phenylak=lkylamine and benzothiazepine are equally efficacious antihypertensive. They lower BP by decresing peripheral resistance without compromising c.o. despite vasodilatation, fluid retention is insignificant. The onset of antihypertensive action is quick. With the availability of long acting preparations, most agents can be administered once a day. Mono therapy with CCBs is effective in~50% hypertensive, their action is independent of patient's rennin status, and they may improve arterial compliance. Other advantages of CCBs are:

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1. Do not compromise haemodynamic: No impairment of physical work capacity.
2. No sedation or other CNS effect; cerebral perfusion is maintained: compatible with intense mental activity.
3. No contraindicated in asthma, angina (specially variant) and PVD patients: may benefit these conditions. Do not impair renal perfusion.
4. Do not affect male sexual function. No deleterious effect on plasma lipid profile, uric acid level and electrolyte balance.
5. Shown to have no\minimal effect on quality of life. No adverse foetal effects noted: Can be used during pregnancy (but can weaken uterine contractions during labour).

CCBs promote vasodilator activity by reducing calcium influx into vascular smooth muscle cells by interfering with voltage-operated calcium channels in the cell

membrane. Interference with intracellular calcium influx is also important in cardiac muscle, cardiac conduction tissue and gastrointestinal smooth muscle. In cardiac tissues, CCBs have potential for negative inotropic, chronotropic and dromotropic activity while the gastrointestinal effects predispose to constipation. These effects vary with different agents according to ability to penetrate cardiac and other tissues, relative affinity for calcium channels in different tissues and the influence of reflux cardiac stimulation secondary to peripheral vasodilation. There are 3 types of calcium channels.

(a) Voltage sensitive channel: Activated when membrane potential drop to around -40 mV or lower.

(b) Receptor operated channel: Activated by Adr and other agonists-independent of membrane depolarization.

(c) Leak channel: small amounts of Ca^{2+} leak into the resting cell and are pumped out by Ca^{2+} ATP ase.

Reported methods are categorized depending on the following considerations:

1. Single component Calcium channel blocker analyzed by UV-Spectroscopy methods and Chromatographic method.

2. Analysis of Calcium channel blocker with combination with other class drugs by UV-Spectroscopy methods and Chromatographic method

Table 1: Analysis of single component of Calcium channel blocker by UV-Spectroscopy methods

Sr. no.	Drug	Method	Description	Ref
1	Estimation of Amlodipine besylate in tablets	UV spectroscopic Method	**Detection wavelength:** 366 nm **Linearity range:** 5-25 µg/ml. **Co-relation co-efficient**: 0.999. **LOD:** 0.136 **LOQ:** 0.400	2
2	Validation of Cilnidipine	UV spectroscopic Method	**Detection wavelength:** 240 nm **Linearity range:** 3-18µg/ml **Co-relation co-efficient**: 0.9994 **% Recovery range:** 98.0%-102.0%	3
3	Isradipine Loaded into Solid Lipid Nanoparticles	UV Spectroscopic Method	**Detection wavelength:** 327 nm **Linearity range:** 5-30µg/ml **Co-relation co-efficient**: 0.999 **% Recovery range:** 100.08% **LOD:** 0.1115 µg/ml **LOQ:** 0.3378 µg/ml	4
4	Nicardipine hydrochloride in bulk and formulation	UV Spectroscopic Method	**Detection wavelength:** 235 nm **Linearity range:** 5-25µg/ml **Co-relation co-efficient**: 0.999 **% Recovery range:** 98.8-101.5% **LOD:** 0.1032 µg/ml **LOQ:** 0.3130 µg/ml	5
5	Nimodipine in Bulk and Tablet Formulation	UV Spectroscopic Method	**Detection wavelength:** 238.5 nm **Linearity range:** 5-30µg/ml **Co-relation co-efficient**: 0.9981 **% Recovery range:** 100.001% **LOD:** 0.7469 µg/ml **LOQ:** 2.26 µg/ml	6

Table 2: Analysis of Calcium channel blocker with combination with other drugs by UV spectroscopy

Sr.no	Drug	Method	Description	Ref.
6.	Amlodipine and Losartan in bulk drug and tablet dosage formulation	Simultaneous Estimation of UV-Spectroscopic Method	**Detection wavelength:** **Amlodipine besylate:** 237 nm **Losartan potassium:** 202 nm **Linearity range:** **Amlodipine besylate:** 1.257.5µg/ml **Losartan potassium:** 12.5-75µg/ml **Co-relation co-efficient**: **Amlodipine besylate:** 0.998 **Losartan potassium:** 0.999 **% Recovery range:** 97.3-102.3% **LOD:** **Amlodipine besylate:** 0.02µg/ml **Losartan potassium:** 0.03µg/ml **LOQ:** **Amlodipine besylate:** 0.03µg/ml **Losartan potassium:** 0.05µg/ml	7
7.	Amlodipine Besylate and Bisoprolol Fumarate in Pharmaceutical Preparations	UV Spectrophotometric Method	**Detection wavelength:** **Amlodipine besylate:** 222 nm **Bisoprolol fumarate:** 365 nm **Linearity range:** **Amlodipine besylate:** 5-100 µg/ml **Bisoprolol fumarate:** 5-100 µg/ml **Co-relation co-efficient**: 0.999 **% Recovery range:** **Amlodipine besylate:** 99.33-99.61% **Bisoprolol fumarate:** 100.28-100.80% **LOD:** **Amlodipine besylate:** 4.31 µg/ml **Bisoprolol Fumarate:** 13.07 µg/ml **LOQ:** **Amlodipine besylate:** 1.45µg/ml **Bisoprolol Fumarate:** 4.42µg/ml	8
8	Cilnidipine and Telmisartan in tablet dosage form	UV Spectrophotometric Method for the Simultaneous Estimation and Absorbance Ratio Method	**Simultaneous Equation Method** **Detection wavelength:** **Cilnidipine:** 240 nm **Telmisartan:** 297nm **Linearity range:** **Cilnidipine:** 4-10µg/ml **Telmisartan:** 6-18µg/ml **Co-relation co-efficient**: **Cilnidipine:** 0.9998 **Telmisartan:** 0.9992 **Q-Absorbance Ratio Method** **Detection wavelength:** 270 nm **Linearity range:** **Cilnidipine:** 4-10µg/ml **Telmisartan:** 6-18µg/ml **Co-relation co-efficient**: **Cilnidipine:** 0.9998 **Telmisartan:** 0.9990	9
9	Estimation of Nebivolol and Cilnidipine in Pharmaceutical Formulation	First Order Derivative UV Spectrophotometric Method	**Detection wavelength:** **Nebivolol:** 221.6 nm **Cilnidipine:** 249 nm **Linearity range:**	10

			Nebivolol: 4-20 **Cilnidipine:** 5-25 **Co-relation co-efficient**: **Nebivolol:** 0.999 **Cilnidipine:** 0.998	
10	Atorvastatin Calcium and Felodipine from Tablet Dosage Form	Dual Wavelength Spectrophotometric Method for Simultaneous Estimation	**Detection wavelength:** **Atorvastatin Calcium:** 245 nm **Felodipine:** 268 nm **Mobile Phase:** Acetonitrile: Double Distilled Water (70:30) **Linearity range:** **Atorvastatin Calcium:** 20-100 µg/ml **Felodipine:** 2-12 µg/ml	11
11.	Metoprolol and Amlodipine in bulk and Their formulation	UV-spectrophotometric method for simultaneous Estimation	**Detection wavelength:** **Metformin:** 223 nm **Amlodipine:** 240 nm **Linearity range:** **Metformin:** 10-90 µg/ml **Amlodipine:** 1-60 µg/ml **Co-relation co-efficient**: 0.999 **% Recovery range:** **Metformin:** 99.78% **Amlodipine:** 99.82%	12
12	Atenolol and Lercanidipine Hydrochloride in combined dosage form	Ratio Derivative and Dual Wavelength Method	**Ratio Derivative (Method A)** **Detection wavelength:** **Atenolol:** 266.98 nm **Lercanidipine Hydrochloride:** 386.97 nm **Linearity range:** **Atenolol:** 25-125 µg/ml **Lercanidipine Hydrochloride:** 5-25 µg/ml **Co-relation co-efficient**: **Atenolol:** 0.99985 **Lercanidipine Hydrochloride:** 0.99971 **Dual Wavelength (Method B)** **Detection wavelength:** **Atenolol:** 234.01 nm and238.66nm **Lercanidipine Hydrochloride:** 253.33 nm and286.07nm **Linearity range:** **Atenolol:** 50-90 µg/ml **Lercanidipine Hydrochloride:** 10-18 µg/ml **Co-relation co-efficient**: **Atenolol:** 0.99983 **Lercanidipine Hydrochloride:** 0.99979	13
13	Nifedipine and Atenolol in Combine Dosage Forms	Simultaneous Estimation of UV-Spectroscopic Method	**Detection wavelength:** **Nifedipine:** 341.2 nm **Atenolol:** 273.8 nm **Linearity range:** **Nifedipine:** 2-10 µg/ml **Atenolol:** 5-25 µg/ml **LOD:** **Nifedipine:** 0.273 µg/ml **Atenolol:** 0.159 µg/ml **LOQ:** **Nifedipine:** 0.824 µg/ml**, Atenolol:** 0.483	14

14	Nifedipine and Metoprolol Succinate in Their Synthetic Mixture	Simultaneous Estimation of UV-Spectroscopic Method	**Detection wavelength:** **Nifedipine:** 313 nm **Metoprolol Succinate:** 275.40 nm **Linearity range:** **Nifedipine:** 5-25 µg/ml **Metoprolol Succinate:** 25-125 µg/ml **% Drug Recovery:** **Nifedipine:** 100.68 **Metoprolol Succinate:** 100.33	15
15	Nifedipine and Metoprolol Succinate in Their Synthetic Mixture	Spectrophotometry	**Detection wavelength:** **Nifedipine:** 313 nm **Metoprolol Succinate:** 275.40 nm **Linearity range:** **Nifedipine:** 5-25 µg/ml **Metoprolol Succinate:** 25-125 µg/ml **% Drug Recovery:** **Nifedipine:** 100.68 **Metoprolol Succinate:** 100.33	16
16	Nifedipine and Candesartan Cilexetil in Synthetic Mixture	Simultaneous Estimation of UV-Spectroscopic Method	**Detection wavelength:** **Nifedipine:** 235nm **Candesartan Cilexetil:** 255nm **Linearity range:** **Nifedipine:** 6-21µg/ml **CandesartanCilexetil:**3.2-11.2µg/ml **Co-relation co-efficient**: **Nifedipine:** 0.999 **CandesartanCilexetil:** 0.998 **% Recovery range:** **Nifedipine:** 98-102%. **Candesartan Cilexetil:** 98-102%	17

Table 3: Analysis of single component Calcium channel blocker by chromatographic method

Sr.no.	Drug	Method	Description	Ref
17	Cilnidipine, a new calcium antagonist, in human plasma	high performance liquid chromatography with tandem mass spectrometric detection	**Internal standard:** Nimodipine **Column**: C_{18} column **Mobile phase:** CH_3OH : NH4Ac (96:4 v/v). **Linearity range:** 0.1–10 ng mL−1 **Co-relation co-efficient**:0.9994 **Run time:** 3 min	18
18	Felodipine in bulk and pharmaceutical dosage form	RP-HPLC Method	**Detection wavelength:** 238 nm **Stationary phase:** C_{18} (150 x 4.6 mm i.d. of 5) coupled with guard column **Mobile phase:** Acetonitrile: Water 70:30 **Run time:** 10 min **Retention time:** 8.29 min **% RSD:** <2%	19
19	Felodipine In Rat Plasma	RP-HPLC Method	**Detection wavelength:** 260 nm **Stationary phase:** Spherisorb ODS column(250mm x 4.6mm, 5 µm) **Mobile phase:** Methanol:Water 80:20 %v/v **Linearity:** 50 ng - 150 ng/ml **LOD:** 25 ng/ml	20

			LOQ: 5Ong/ml **Correlation coefficient:** 0.9943 **Run time:** 0.9 ml/min **Retention time:** 9.94 min	
20	Amlodipine in human plasma	Liquid Chromatography Tandem Mass Spectrometry Method (LC-MS/MS)	**Internal standard:** Imipramine **Column**: Hypersil BDS C_{18} column **Linearity range:** 0.1–10.0 ng/mL **Recovery:** 63.67% **Run time:** 3.2 min	21
21	Estimation of Felodipine in human plasma .	LC-MS Method and Stability studies of freeze thaw analyte	**Internal standard :** Pantaprazole **Stationary phase:** Princeton SPHER C_{18} (150 x 4.6 mm i.d. of 5) **Mobile phase**: Acetonitrile : 2mM ammonium acetate Elution mode : Isocratic A: B= 80:20% v/v **Flow rate:** 0.8 ml/min **Linearity range:** 0.8-13.0ng/ml **Retention factor :** 2.97 **Felodipine:** **LOD:** 0.10 ng/ml **LOQ:** 0.50 ng/ml **Pantaprazole:** **LOD:** 0.06 ng/ml **LOQ:** 0.21 ng/ml	22

Table 4: Analysis of Calcium channel blocker with combination with other drugs by Chromatographic methods

Sr.no.	Drug	Method	Description	Ref
22	Amlodipine besylate and Olmesartan medoxomil from tablet	RP-HPLC Method	**Detection Wavelength:** 248 nm **Mobile phase**: Acetonitrile: water 60:40 **Flow rate**: 1.0 ml/min **Retention time:** 3.69 & 4.90 min for Metformin Hydrochloride and Sitagliptin Phosphate respectively. **Linearity range**: 5-35 µg ml-1 **Mean percent recovery:** **Olmesartan medoxomil:** 99.75 % to 100.62 % **Amlodipine besylate:** 98.91 % to 102.05 %	23
23	Valsartan and Amlodipine in Capsule Formulation.	Stability Indicating RP-HPLC Method	**Detection wavelength**: 234 nm **Stationary phase:** RP C_{18} Column (Kromasil, 250 x 4.6 mm) **Mobile phase:** Acetonitrile: Phosphate buffer (0.02M, pH 3.0), (56:44 v/v) **Flow rate:** 1.0 ml/min **Retention time:** **Amlodipine:** 3.07 min **Valsartan:** 6.20 min	24
24	Amlodipine and Benazepril hydrochloride from	Stability indicating RP-HPLC Method	**Detection wavelength**: 240 nm **Stationary phase:** Zorbax SB C_{18}, 5 µm, 250 mm × 4.6 mm	25

	their combination drug product		**Mobile phase:** Phosphate buffer: Acetonitrile 65:35 (v/v) **Linearity:** **Amlodipine:** 6–14 µg/ml **Benazepril hydrochloride:** 12–28 µg/ml **Mean percent recovery:** **Amlodipine:** 99.91 **Benazepril hydrochloride:** 100.53%	
25	Chlorthalidone and Cilnidipine in bulk and combined tablet dosage form	RP-HPLC Method	**Detection wavelength:** 240 nm **Stationary phase**: Inertsil ODS 3V (250 × 4.6 mm, i.d., 5 µm) **Mobile Phase**: 0.025 M Potassium dihydrogen orthophosphate buffer whose pH was adjusted to 2.5 using dilute orthophosphoric acid (solvent A) and Acetonitrile (solvent B) **Linearity range**: **Chlorthalidone:** 200-600 µg/ml **Cilnidipine:** 160-480 µg/ml **Regression coefficient(r2):** 0.999 **LOD:** **Chlorthalidone:** 0.50 µg/ml **Cilnidipine:** 0.40 µg/ml **LOQ**: **Chlorthalidone:**1.50µg/ml **Cilnidipine:** 1.20 µg/ml **Retention time:** **Chlorthalidone:** 3.872 minutes **Cilnidipine:** 7.668 minutes **Flow rate:** 1 ml/min	26
26	Cilnidipine and Olmesartan medoxomil in their combined tablet dosage form	RP-HPLC METHOD	**Detection wave;ength:** 265 nm **Stationary phase**: C18 (250 x 4.6mm,5 µm in particle size) **Mobile Phase**: Acetonitrile:Buffer (75:25 %v/v) pH 6.5 adjusted by 1 % Triethylamine **Linearity range**: **Cilnidipine:** 10-90 µg/ml **Olmesartan medoxomil:** 20-180 µg/ml for **LOD:** **Cilnidipine:** 0.130 **Olmesartan medoxomil:** 0.790 **LOQ**: **Cilnidipine:** 0.395 **Olmesartan medoxomil:** 2.397 **Correlation coefficient:** **Cilnidipine:** 0.9982 **Olmesartan medoxomil:** 0.9951 **Retention time:** **Cilnidipine:** 2.655 min **Olmesartan medoxomil:** 4.720 min **Flow rate:** 1 ml/min	27
27	Cilnidipine and Telmisartan in combined tablet dosage form	RP-HPLC Method	**Detection wavelength:** 245 nm **Stationary phase**: HiQ sil C18 HS column (250 × 4.6 mm i.d.) **Mobile Phase**: Methanol: 40 mM	28

			Potassium dihydrogen ortho phosphate buffer (pH 3) (90:10, v/v)) **Linearity range**: **Cilnidipine: 1-10 µg mL^{-1}** **Telmisartan: 5-30 µg mL^{-1}** **LOD:** **Cilnidipine: 0.60** µg mL^{-1} **Telmisartan: 0.28** µg mL^{-1} **LOQ**: **Cilnidipine: 1.81** µg mL^{-1} **Telmisartan: 0.86** µg mL^{-1} **Correlation coefficient:** **Cilnidipine:** 0.996 **Telmisartan:** 0.999 **% Recovery:** **Cilnidipine:** 99.60-99.83 **Telmisartan:** 99.40-100.39	
28	Atenolol and Nitrendipine in Tablet Dosage Form	RP-HPLC Method	**Detection wavelength:** 235 nm **Stationary phase**: Phenomenox C-18 column having dimensions of 4.6×250 mm and particle size of 5 µm. **Mobile Phase**: Methanol: Acetonitrile: Water (40:40:20 v/v) **Linearity range**: **Atenolol:** 30-70µg/ml **Nitrendipine:** 6-14 µg/ml **LOD:** **Atenolol:** 1.96 µg/ml **Nitrendipine:** 0.34 µg/ml **LOQ**: **Atenolol:** 5.95 µg/ml **Nitrendipine:** 1.03 µg/ml **Retention time:** **Atenolol:** 2.61 min **Nitrendipine:** 6.11 min **% Recovery:** **Atenolol:** 99.05-100.51% **Nitrendipine:** 99.14-101.60% **Flow rate:** 1.5 ml/min	29
29	Atenolol and Nifedipine in pharmaceutical dosage forms	RP-HPLC Method	**Detection wavelength:** 235nm **Mobile Phase:** Methanol: Acetonitrile: Water (60:20:20) **Stationary Phase:** ODS C_{18} column **Linearity:** Nifedipine : 2-10µg/ml Atenolol:5-25 µg/ml **Flow rate:** 1.0ml/min	30
30	Nifedipine and dehydro-nifedipine in human plasma	Liquid chromatography tandem mass spectrometry	**Mobile Phase:** Methanol : 50 mM ammonium acetate solution (50:50, v/v). **Stationary Phase:** RP-18 (4 µm) **Linearity range:** 0.5–100 ng/ml	31

31	Nifedipine and Atenolol in capsule formulation	RP-HPLC Method	**Detection wavelength:** 237 nm **Mobile Phase:** 0.01M phosphate buffer solution: Methanol (50:50 v/v, pH 4.0) **Stationary Phase:** ODS metaphase C_{18}-250×4.6 mm **Retention time:** Atenolol : 1.8 min Nifedipine : 7.7 min	37

CONCLUSION:

This Review represents the Reported Spectrophotometric and Chromatographic Methods Developed and Validated for determination of Calcium channel blocker in different Dosage Forms. Here Calcium channel blocker shows the simple, accurate, precise method development of the different drug formulations. The blocker, HPLC, RP-HPLC, and LC-MS/MS.

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