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 methods 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), phenylalkylamine 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:

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.
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

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<th>Sr. no.</th>
<th>Drug Description</th>
<th>Method</th>
<th>Description</th>
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<td>Estimation of Amlodipine besylate in tablets</td>
<td>UV spectroscopic Method</td>
<td>Detection wavelength: 366 nm Linearity range: 5-25 μg/ml Co-relation co-efficient: 0.999. LOD: 0.136 LOQ: 0.400</td>
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<td>UV Spectroscopic Method</td>
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<td>Nicardipine hydrochloride in bulk and formulation</td>
<td>UV Spectroscopic Method</td>
<td>Detection wavelength: 235 nm Linearity range: 5-25 μg/ml Co-relation co-efficient: 0.999 % Recovery range: 98.8-101.5% LOD: 0.1032 μg/ml LOQ: 0.3130 μg/ml</td>
</tr>
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<td>5</td>
<td>Nimodipine in Bulk and Tablet Formulation</td>
<td>UV Spectroscopic Method</td>
<td>Detection wavelength: 238.5 nm Linearity range: 5-30 μg/ml Co-relation co-efficient: 0.9981 % Recovery range: 100.001% LOD: 0.7469 μg/ml LOQ: 2.26 μg/ml</td>
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Table 2: Analysis of Calcium channel blocker with combination with other drugs by UV spectroscopy

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| 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: 1.257.5 μg/ml  
Losartan potassium: 12.5-75 μg/ml  
Co-relation co-efficient:  
Amlodipine besylate: 0.998  
Losartan potassium: 0.999  
% Recovery range: 97.3-102.3%  
LOD:  
Amlodipine besylate: 0.02 μg/ml  
Losartan potassium: 0.03 μg/ml  
LOQ:  
Amlodipine besylate: 0.03 μg/ml  
Losartan potassium: 0.05 μg/ml | 7 |
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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: 1.45 μg/ml  
Bisoprolol Fumarate: 4.42 μg/ml | 8 |
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Detection wavelength:  
Cilnidipine: 240 nm  
Telmisartan: 297 nm  
Linearity range:  
Cilnidipine: 4-10 μg/ml  
Telmisartan: 6-18 μg/ml  
Co-relation co-efficient:  
Cilnidipine: 0.9998  
Telmisartan: 0.9992  
Q-Absorbance Ratio Method  
Detection wavelength: 270 nm  
Linearity range:  
Cilnidipine: 4-10 μg/ml  
Telmisartan: 6-18 μg/ml  
Co-relation co-efficient:  
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Cilnidipine: 249 nm  
Linearity range: | 10 |
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<td>Acetonitrile: Double Distilled Water (70:30)</td>
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<td>Co-relation co-efficient: Nebivolol: 0.999 Cilnidipine: 0.998</td>
<td>Linearity range: Atorvastatin Calcium: 20-100 μg/ml Felodipine: 2-12 μg/ml</td>
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<td>Linearity range: Metformin: 10-90 μg/ml Amlodipine: 1-60 μg/ml</td>
<td>Co-relation co-efficient: 0.999 % Recovery range: Metformin: 99.78% Amlodipine: 99.82%</td>
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<td>Ratio Derivative and Dual Wavelength Method</td>
<td>Linearity range: Atenolol: 25-125 μg/ml Lercanidipine Hydrochloride: 5-25 μg/ml</td>
<td>Co-relation co-efficient: Atenolol: 0.99985 Lercanidipine Hydrochloride: 0.99971</td>
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<td>Dual Wavelength (Method B) Detection wavelength: Atenolol: 234.01 nm and238.66nm</td>
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<td>Lercanidipine Hydrochloride: 253.33 nm and286.07nm</td>
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<td></td>
<td></td>
<td>Linearity range: Atenolol: 50-90 μg/ml Lercanidipine Hydrochloride: 10-18 μg/ml</td>
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<td></td>
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<td>Linearity range: Nifedipine: 2-10 μg/ml Atenolol: 5-25 μg/ml</td>
<td>LOD: Nifedipine: 0.273 μg/ml Atenolol: 0.159 μg/ml</td>
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<td>LOQ: Nifedipine: 0.824 μg/ml Atenolol: 0.483</td>
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</tbody>
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Table 3: Analysis of single component Calcium channel blocker by chromatographic method

<table>
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<th>Method</th>
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<td>Cilnidipine, a new calcium antagonist, in human plasma</td>
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<td>Internal standard: Nimodipine Column: C_{18} column Mobile phase: CH_{3}OH : NH4Ac (96:4 v/v). Linearity range: 0.1–10 ng mL⁻¹ Co-relation co-efficient: 0.9994 Run time: 3 min</td>
<td>18</td>
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<td>Felodipine in bulk and pharmaceutical dosage form</td>
<td>RP-HPLC Method</td>
<td>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: &lt;2%</td>
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<td>Felodipine In Rat Plasma</td>
<td>RP-HPLC Method</td>
<td>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</td>
<td>20</td>
</tr>
<tr>
<td>Sr.no</td>
<td>Drug</td>
<td>Method</td>
<td>Description</td>
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| 20   | Amlodipine in human plasma | Liquid Chromatography Tandem Mass Spectrometry Method (LC-MS/MS) | LOQ: 50ng/ml  
Correlation coefficient: 0.9943  
Run time: 0.9 ml/min  
Retention time: 9.94 min | 21 |
| 21   | Estimation of Felodipine in human plasma | LC-MS Method and Stability studies of freeze thaw analyte | Internal standard: Imipramine  
Column: Hypersil BDS C<sub>18</sub> column  
Linearity range: 0.1–10.0 ng/mL  
Recovery: 63.67%  
Run time: 3.2 min | 22 |

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

<table>
<thead>
<tr>
<th>Sr.no</th>
<th>Drug</th>
<th>Method</th>
<th>Description</th>
<th>Ref</th>
</tr>
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</table>
| 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<sup>-1</sup>  
Mean percent recovery: Olmesartan medoxomil: 99.75 % to 100.62 %  
Amlodipine besylate: 98.91 % to 102.05 % | 23 |
Stationary phase: RP C<sub>18</sub> 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: Valsartan: 6.20 min  
Amlodipine: 3.07 min | 24 |
| 24   | Amlodipine and Benazepril hydrochloride from | Stability indicating RP-HPLC Method | Detection wavelength: 240 nm  
Stationary phase: Zorbax SB C<sub>18</sub>, 5 μm, 250 mm × 4.6 mm | 25 |
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<tr>
<th>Page</th>
<th>Method</th>
<th>Detection wavelength</th>
<th>Stationary phase</th>
<th>Mobile Phase</th>
<th>LOD</th>
<th>LOQ</th>
<th>Correlation coefficient</th>
<th>Retention time</th>
<th>Flow rate</th>
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<tr>
<td>25</td>
<td>Chlorthalidone and Cilnidipine in bulk and combined tablet dosage form</td>
<td>RP-HPLC Method</td>
<td>240 nm</td>
<td>Inertsil ODS 3V (250 × 4.6 mm, i.d., 5 μm)</td>
<td>Chlorthalidone: 0.50 μg/ml</td>
<td>Cilnidipine: 0.40 μg/ml</td>
<td>0.999</td>
<td>3.872 minutes</td>
<td>1 ml/min</td>
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<td>26</td>
<td>Cilnidipine and Olmesartan medoxomil in their combined tablet dosage form</td>
<td>RP-HPLC METHOD</td>
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<td>C18 (250 x 4.6mm,5 μm in particle size)</td>
<td>Chlorthalidone: 0.130</td>
<td>Olmesartan medoxomil: 0.790</td>
<td>0.9982</td>
<td>2.655 minutes</td>
<td>1 ml/min</td>
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<td>Cilnidipine and Telmisartan in combined tablet dosage form</td>
<td>RP-HPLC Method</td>
<td>245 nm</td>
<td>HiQ sil C18 HS column (250 × 4.6 mm i.d.)</td>
<td>Methanol: 40 mM</td>
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</tbody>
</table>
| 28 | Atenolol and Nitrendipine in Tablet Dosage Form | RP-HPLC Method | 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 |
|---|---|---|---|
| 29 | Atenolol and Nifedipine in pharmaceutical dosage forms | 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: 30-70 μg/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 |
| 30 | Nifedipine and dehydro-nifedipine in human plasma | Liquid chromatography tandem mass spectrometry | Detection wavelength: 235nm  
**Mobile Phase:**  
Methanol: Acetonitrile: Water (60:20:20)  
**Stationary Phase:**  
ODS C₁₈ column  
**Linearity:**  
Nifedipine: 2-10 μg/ml  
Atenolol: 5-25 μg/ml  
**Flow rate:** 1.0 ml/min |
| 31 | | | 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 |
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<sub>18</sub> 250×4.6 mm
Retention time:
Atenolol : 1.8 min
Nifedipine : 7.7 min

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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REFERENCES:


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