A Review on Analytical Methods for Ranolazine determination in synthetic mixture

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ABSTRACT
Ranolazine is a piperazine derivative is a new anti-ischemic drug for the treatment of angina. Ranolazine is to inhibit late INa thus preventing sodium overload of the cell. As a consequence, ranolazine prevents reverse mode sodium-calcium exchange and thus diastolic accumulation of calcium possibly resulting in improved diastolic tone and improved coronary blood flow.
This review article represent the various analytical methods which has been reported for estimation of Ranolazine in synthetic mixture. The spectrophotometric techniques like fluorescent assay and area under curve spectroscopy; Chromatographic methods like HPLC, HPTLC and RP HPLC, GC, LC-MS, LC-MS/MS were reported.

Keywords: Ranolazine, anti-ischemic, Angina

INTRODUCTION
Ranolazine is -(2,6-dimethylphenyl)-2-[4-[2-hydroxy-3-[2-methoxyphenoxo]propyl piprazine-1-yl]-acetyl amide is piprazine derivative appears as white to off white crystalline powder. The drug is freely soluble in Methanol. Ranolazine is a strong base with pKa values of 13.6, Six-membered Piprazine Ring. Ranolazine melts at 122-124 °C.

Chemical formula: C_{24}H_{33}N_{5}O_{4}
Molecular weight: 427.54 g/mol

MECHANISM OF ACTION
It is act via selective inhibition of the late inward sodium current (I_{Na}) in cardiac muscle cells. This reduces intracellular sodium accumulation and calcium overload, and consequently improves myocardial relaxation and decreases left ventricular diastolic stiffness.

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Ranolazine is administered orally and metabolize by CYP3A and excreted in intestine (5%) and in urine.

Analytical Method
A. Compendial Method:
Ranolazine is not official in Pharmacopoeia.

B. Reported Method:
I. Chromatographic Methods
The high-pressure liquid chromatography (HPLC) for Ranolazine estimation. GC method for residual solvent determination in Ranolazine. HPTLC method are widely used chromatographic methods in the analysis of Ranolazine in Formulation. LC-MS/MS, LC-MS and UHPLC use for estimation of Ranolazine in Plasma. RP HPLC method also developed for determination of concentration of Ranolazine in human serum and also for simultaneous determination of Ranolazine and Dronederone.

<table>
<thead>
<tr>
<th>Title</th>
<th>Method</th>
<th>Mobile phase</th>
<th>Stationary phase</th>
<th>Wave Length</th>
<th>REF.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ranolazine in bulk &amp; marketed formulation</td>
<td>HPLC &amp; UV</td>
<td>Methanol : 0.5% tri ethyl amine pH 6 with orthophosphoric acid (75:25)</td>
<td>-</td>
<td>271</td>
<td>3</td>
</tr>
<tr>
<td>Estimation of Ranolazine HCL in Tablet Dosage Form</td>
<td>RP-HPLC</td>
<td>Buffer : Acetonitrile(60:40),pH adjust with triethylamine</td>
<td>Inertsil ODS C18</td>
<td>224 nm</td>
<td>4</td>
</tr>
<tr>
<td>Determination of Ranolazine HCL in bulk and dosage form</td>
<td>LC</td>
<td>Methanol : water (99:1 %, V/V)</td>
<td>HiQ Sil C18 HS</td>
<td>273 nm</td>
<td>5</td>
</tr>
<tr>
<td>Quantitation of Ranolazine in rat plasma</td>
<td>LC</td>
<td>Acetonitrile : water : formic acid : 10% n-butylamine (70:30:0.5:0.08, v/v/v/v)</td>
<td>Nova-Pak C18 column</td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>Determination of Ranolazine in human plasma</td>
<td>HPLC</td>
<td>Acetonitrile: 0.1% formic acid(90:10)</td>
<td>Agilent-ZORBAX C18 column</td>
<td></td>
<td>7</td>
</tr>
<tr>
<td>Estimation of Ranolazine in Human Plasma</td>
<td>LC</td>
<td>methanol-10mM ammonium acetate (60:40 v/v, pH 4.0)</td>
<td>Zorbax extend C18 column</td>
<td></td>
<td>8</td>
</tr>
<tr>
<td>Ranolazine HCL in bulk and tablet dosage form</td>
<td>HPTLC</td>
<td>Chloroform: methanol : toluene (5 : 1 : 1 v/v/v/v)</td>
<td>silica gel aluminium plate 60 F - 254</td>
<td>273 nm</td>
<td>9</td>
</tr>
<tr>
<td>Determination of residual solvents in Ranolazine</td>
<td>GC</td>
<td>-</td>
<td>HP-INNOWAX column</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

II. UV spectroscopic method
First order derivative spectroscopy and Area Under curve spectroscopic technique was developed for simultaneous determination of Ranolazine was developed.

<table>
<thead>
<tr>
<th>Title</th>
<th>Method</th>
<th>Wavelength</th>
<th>Linearity and $R^2$</th>
<th>Recovery</th>
<th>REF.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimation of Ranolazine in bulk drug and pharmaceutical formulation</td>
<td>UV method</td>
<td>272 nm</td>
<td>10-100 µg/ml</td>
<td>99.77-100.33 %</td>
<td>11</td>
</tr>
</tbody>
</table>
Estimation of Ranolazine in bulk and pharmaceutical dosage form

First order derivative spectroscopic method

263 nm and 282 nm

10-35 µg/ml and 0.9992

-

Estimation of Ranolazine in API and tablet formulation

Area under curve method

261nm and 281 nm

75-200 µg/ml and 0.998

99.42-99.97 %

<table>
<thead>
<tr>
<th>Title</th>
<th>Method</th>
<th>Mobile phase</th>
<th>Stationary phase</th>
<th>Wave length</th>
<th>REF.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simultaneous estimation of Ranolazine and Dronodereone in bulk and pharmaceutical dosage forms.</td>
<td>HPLC</td>
<td>0.02N NH2PO4 buffer (pH 4) : Acetonitrile (50 :50 V/V)</td>
<td>ODS column</td>
<td>282 nm</td>
<td>14</td>
</tr>
</tbody>
</table>

Table No.3: HPLC Method for simultaneous estimation of Ranolazine and Dronedereone

DISCUSSION

Presented systematic review covers the current analytical methods for the determination of Ranolazine and its combination in pharmaceutical and biological samples like serum and plasma. HPLC method were found to be most widely use for Ranolazine. Various chromatographic conditions are presented in table.

CONCLUSION

The sensitivity, specificity, and better separation efficiency enable HPLC to be used frequently for simultaneous qualitative and quantitative determination of Ranolazine. The presented information is useful for the future study for researcher involved in formulation development and quality control of Ranolazine.

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