Edaravone: A Review on Analytical Method and its Determination in Biological Matrix and Synthetic Mixture

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ABSTRACT
Edaravone is a potent free radical scavenger (antioxidant) mainly used in the form of injection. It is used in the treatment of various cardiovascular diseases like acute ischemic stroke as well as in gastrointestinal injuries. This review article represents the various analytical methods which has been reported for estimation of edaravone in biological matrix as well as in synthetic mixture. The spectrophotometric techniques like fluorescent assay and ratio derivative spectroscopy; Chromatographic methods like HPLC, HPTLC and RP HPLC were reported.

Keywords: Edaravone, analytical methods, Compendial Method, UV spectroscopic method

INTRODUCTION

Edaravone is 5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one is a pyrazole derivative appears as white to off white crystalline powder. The drug is freely soluble in Distilled Water. solubility in water is 3 g/1 L. Edaravone is a weak base with pKa values of 7.3, Five-membered Pyrazole Ring, Edaravone melts at 127-131 °C. Boils at 287° C.

MECHANISM OF ACTION

Edaravone has been reported to exert antioxidant effects because it can quench hydroxyl radicals and hydroxyl radical-dependent lipid peroxidation. Edaravone reduces elevated levels of hydroxyl radicals and superoxide radicals in several models of ischemia. In early studies of antioxidant activity of edaravone, its pKa was found to be 7.0, and the rate of oxidation for edaravone was positively correlated with pH. The putative mechanism underlying the antioxidant action of edaravone is electron transfer from an edaravone anion to peroxyl radical, and this reaction breaks the chain oxidation of lipids.

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Edaravone is excreted as unmetabolized drug (~1%) or metabolized by sulfation (5–13%) or glucuronidation (68–83%) and excreted in urine within 24 hours of administration.

**Edaravone** is a neuroprotective agent used for aiding neurological recovery following acute brain ischemia and subsequent cerebral infarction.\(^4\) It acts as a potent antioxidant and strongly scavenges free radicals, protecting against oxidative stress and neuronal apoptosis.\(^5-7\) Edaravone has been shown to attenuate methamphetamine- and 6-OHDA-induced dopaminergic neurotoxicity in the striatum and substantia nigra, and does not affect methamphetamine-induced dopamine release or hyperthermia.\(^8,9\) It has also been demonstrated to protect against MPTP-mediated dopaminergic neurotoxicity to the substantia nigra, though notably not to the striatum.\(^10-12\)

### Combination of edaravone\(^{13}\)
- Edaravone + ozagrel
- Edaravone + alteplase (tPA)
- Edaravone + citicholine sodium

### Marketed formulation of edaravone\(^{13}\)
- Radicut®, Radicut bag

**1. Analytical Method**
A. Compendial Method:
Edaravone is not official in Pharmacopoeia.

B. Reported Method:
Table No.1: Summary of Fluorescent method for edaravone

<table>
<thead>
<tr>
<th>Drug</th>
<th>Method</th>
<th>Quantum Dots</th>
<th>Calibration range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edaravone</td>
<td>Fluorescent Assay</td>
<td>Aqueous Functional Cdse</td>
<td>1.45–17.42 μg/mL</td>
</tr>
</tbody>
</table>

II. Chromatographic Methods:
The high-pressure liquid chromatography (HPLC) for residue determination. HPTLC methods are widely used chromatographic methods in the analysis of Edaravone in plasma. RP HPLC method also developed for determination of concentration of edaravone in human serum and also for simultaneous determination of edaravone and citicoline sodium.

Table No.2: Summary of Chromatographic Method of Edaravone

<table>
<thead>
<tr>
<th>Title</th>
<th>Method</th>
<th>Mobile phase</th>
<th>Stationary phase</th>
<th>Wave Length</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Determination of phenyl hydrazine residue in edaravone</td>
<td>HPLC</td>
<td>0.05mol/L ammonium acetate - acetonitrile (80:20)</td>
<td>Diamonsil C18 column</td>
<td>233nm</td>
<td>16</td>
</tr>
<tr>
<td>Determination of edaravone and its related substance</td>
<td>HPLC</td>
<td>1%acetic acid :methanol (40:60)</td>
<td>Hypersil ODC18 column</td>
<td>243 nm</td>
<td>17</td>
</tr>
<tr>
<td>Estimate Conc. of edaravone in human serum</td>
<td>RP HPLC</td>
<td>H3PO4 : Methanol (50:50)</td>
<td>Hypersil C18 column</td>
<td>240 nm</td>
<td>18</td>
</tr>
</tbody>
</table>

III. UV spectroscopic method
First order derivative spectroscopy and Ratio derivative spectroscopic technique was developed for simultaneous determination of edaravone and citicoline sodium.
The ratio derivative spectroscopy method is based on dividing the spectrum for a mixture in to standard spectra for each of analysis and to obtain a spectrum that is independent of analyte concentration used as devisor.

Table No.3: Summary of UV spectroscopic method

<table>
<thead>
<tr>
<th>Title</th>
<th>Method</th>
<th>Zero crossing point for edaravone</th>
<th>Zero crossing point for citicoline sodium</th>
<th>$R^2$</th>
<th>REF.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simultaneous estimation of Edaravone and citicoline sodium in synthetic mixture</td>
<td>Ratio derivative spectroscopic method</td>
<td>258.40</td>
<td>267 nm</td>
<td>0.999</td>
<td>19</td>
</tr>
</tbody>
</table>
Simultaneous estimation of Edaravone and citicoline sodium in synthetic mixture | First order derivative spectroscopic method | 245.60 nm | 271.20 nm | 0.9996 | 0.9996 | 19

Table No.4: RP HPLC Method for simultaneous estimation of edaravone and citicoline sodium

<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 edaravone and citicoline sodium in synthetic mixture</td>
<td>RP HPLC</td>
<td>Acetonitrile and water (70:30)</td>
<td>Phenomenexluna®</td>
<td>244 nm</td>
<td>20</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Presented systematic review covers the current analytical methods for the determination of Edaravone and its combination in pharmaceutical and biological samples like serum and plasma. HPLC method were found to be most widely use for edaravone. 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 edaravone. The presented information is useful for the future study for researcher involved in formulation development and quality control of edaravone.

**REFERENCES**

9. Kawasaki T. et al. Protective effect of the radical scavenger edaravone against methamphetamine-
17. Fu Gui-Ying, WEN Ming-Ling, JIA Li-Hua,ZUOXiu-Ping, Determination of content and related substance of edaravone injection by HPLC.; Pharmaceutical Journal Of Chinese people’s Liberation Army.2009-02.101-14
18. WEI Min, XIAO Yi (Guangxi Liuzhou Municipal People’s Hospital, China), Determination of concentration of edaravone in human serum by RP HPLC; Clinical pharmacy 2007-08.142-143