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Review Article

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

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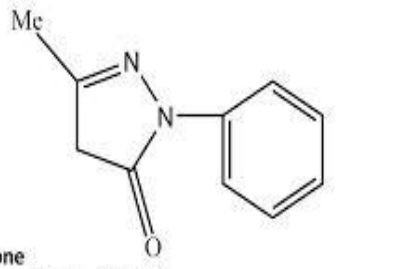
ABSTRACT

Edaravone is a potent free radical scavenger (antioxidant) mainly use 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 represent 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

INTROCUTION[1-2]

Edaravone is 5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one is apyrazole 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.



Edaravone
Alternative Name: MCI-186
Chemical Name: 3-Methyl-1-phenyl-2-pyrazolin-5-one
M.Wt: 174.2
Formula: $C_{10}H_{10}N_2O$

Figure:1 Structure of edaravone

MECHANISM OF ACTION [3]

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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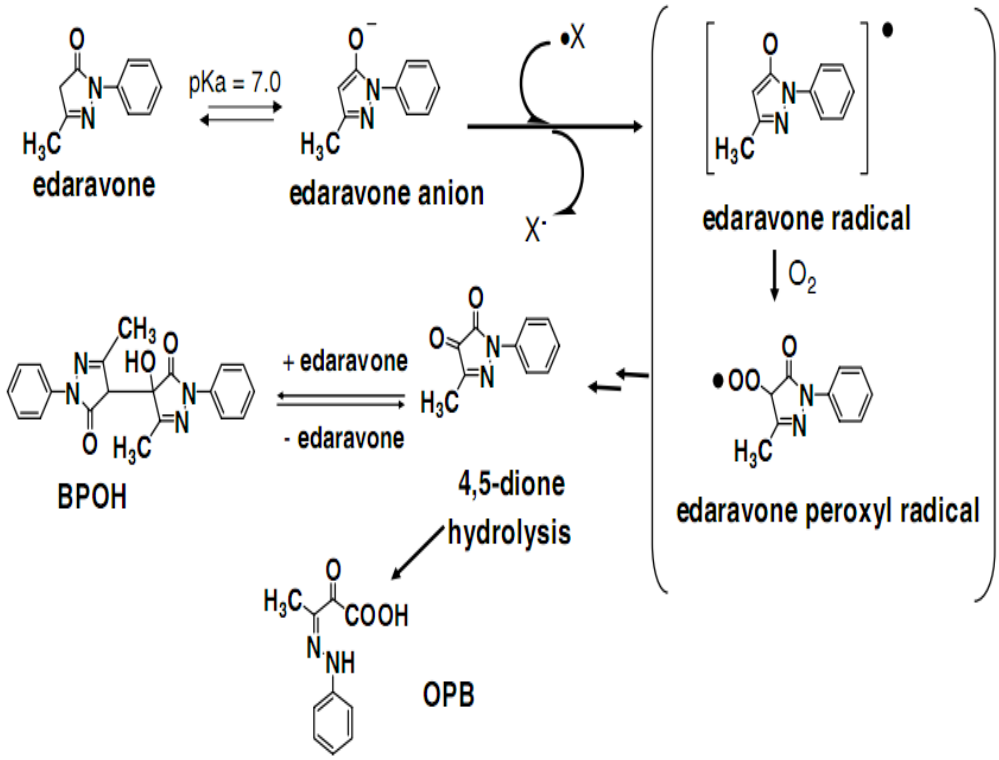

Figure :2 Mechanism of Edaravone

Edaravone is excreted as unmetabolized drug (~1%) or metabolized by sulfation (5–13%) or glucuronidation (68–83%) and excreted in urine within 24hours 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:
I. Fluorescent Method: A Novel Fluorescent Assay for Edaravone with Aqueous Functional Cdse Quantum Dots.

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Table No.1: Summary of Fluorescent methodfor edaravone [14]

Drug	Method	Quantum Dots	Calibration range
Edaravone	Fluorescent Assay	Aqueous Functional Cdse	1.45–17.42 µg/mL

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

Title	Method	Mobile phase	Stationary phase	Wave Length	Reference
Invitro estimation of Edaravonein Human Plasma	RP-HPTLC	-	Pre coated RP-18 GF $_{254}$-aluminum sheet	-	15
Determination of phenyl hydrazine Residue in edaravone	HPLC	0.05mol/L ammonium acetate - acetonitrile (80:20)	Diamonsil C_{18} column	233nm	16
Determination of edaravone and its related substance	HPLC	1%acetic acid :methanol (40:60)	Hypersil - ODC_{18} column	243 nm	17
Estimate Conc. of edaravone in human serum	RP HPLC	H_3PO_4 :Methanol (50:50)	Hypersil C_{18} column	240 nm	18

III. UV spectroscopic method

First order derivative spectroscopy and Ratio derivative spectroscopic technique was developed for simultaneous determination of edaravone and citicolin 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

Title	Method	Zero crossing point for edaravone	Zero crossing point for citicoline sodium	R^2	REF.
Simultaneous estimation of Edaravone and citicoline sodium in synthetic mixture	Ratio derivative spectroscopic method	258.40	267 nm	0.999 0.999	19

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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

Title	Method	Mobile phase	Stationary phase	Wave length	Ref.
Simultaneous estimation of edaravone and citicoline sodium in synthetic mixture	RP HPLC	Acetonitrile and water (70:30)	Phenomenexluna®	244 nm	20

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

1. Edaravone Drug Info.(database available on internet):Chemical Book. Available from: chemicalbook.com/ProductMSDSDetailCB1287462_EN.htm
2. Edaravone Drug Info.(database available on internet):Lookchem. Available from: lookchem.com/Edaravone/
3. Toshiaki W, Munenori T, Satoru T. The Novel Antioxidant Edaravone: From Bench to Bedside. Cardiovascular Therapeutics; 20098,26:101–114.
4. Doherty AM. Annual Reports in Medicinal Chemistry. Boston: Academic Press; 2002, 37.
5. Watanabe T. et al. Research and development of the free radical scavenger edaravone as a neuroprotectant. Yakugaku Zasshi (in Japanese); 2004, 124(3):99–111.
6. Higashi Y, Jitsuiki D, Chayama K, Yoshizumi M. Edaravone (3-methyl-1-phenyl-2-pyrazolin-5-one), a novel free radical scavenger, for treatment of cardiovascular diseases. Recent Patents on Cardiovascular Drug Discovery; 2006, 1(1):85–93.
7. Yoshida H. et al.Neuroprotective effects of edaravone: a novel free radical scavenger in cerebrovascular injury. CNS Drug Reviews; 2006, 12(1):9–20.
8. Yuan WJ. et al. Neuroprotective effects of edaravone-administration on 6-OHDA-treated dopaminergic neurons. BMC Neuroscience; 2008, 9:75.
9. Kawasaki T. et al. Protective effect of the radical scavenger edaravone against methamphetamine-

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PHARMACY INFOPEDIA
ISSN: 2347-7881

induced dopaminergic neurotoxicity in mouse striatum. European Journal of Pharmacology; 2006, 542(1-3):92–99.
10. Kawasaki T. et al. Edaravone (3-methyl-1-phenyl-2-pyrazolin-5-one), a radical scavenger, prevents 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine induced neurotoxicity in the substantia nigra but not the striatum. The Journal of Pharmacology and Experimental Therapeutics; 2007, 322(1):274–281.
11. Yokoyama H. et al. Role of reactive nitrogen and reactive oxygen species against MPTP neurotoxicity in mice. Journal of Neural Transmission; 2008, 115(6):831–842.
12. Yokoyama H. et al. Comparative pharmacological study of free radical scavenger, nitric oxide synthase inhibitor, nitric oxide synthase activator and cyclooxygenase inhibitor against MPTP neurotoxicity in mice. Metabolic Brain Disease; 2008, 23(3):335–349.,
13. Paul A., Lapchak, PhD, FAHA, A Critical Assessment Of Edaravone in Acute Ischemic stroke Efficacy trials, Expert Opinion On Pharmacotherapy, July2010-11(10):1753-1763.
14. Ping Liao, Zheng-Yu Yan, Zhi-JiXu, Xiao Sun. A novel fluorescent assay for edaravone with aqueous functional CdSe quantum dots. SpectrochimicaActa Part A: Molecular and Biomolecular Spectroscopy; 2009, 72(5):75
15. Gandhimathi M, Kumar MS, Baghla R and Ravi TK. RP-HPTLC Method for the In Vitro Estimation of Edaravone in Human Plasma. Indian Journal of Pharmaceutical Science; 2010,72(2):276-282.
16. Li jin-linet al. Determination of Phenylhydrazine Residues in Edaravone by HPLC. Institute of Medical Information; CAMS, 2009.
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
19. Bhumi K.Patel, Hasumati A.Raj, Vineet C.Jain, Simultaneous Estimation of Edaravone and Citicoline sodium by Ratio derivative spectroscopic method in synthetic mixture,; Pharmascience Monitor, An International Journal Of Pharmaceutical Science, 5(2)sup-1 Apr-June 2014,:118-128.
20. Bhumi K Patel, Hasumati A Raj, Vineet C Jain, Vishnu Sutariya, Mihir Bhatt, Kaushik Patel, method development and validation of RP HPLC for simultaneous estimation of edaravone and citicoline sodium in synthetic mixture, inventi rapid: pharm analysis & quality assurance publication date: 2014/5/6.