

## Product Data Sheet

Product Name: EUK 134

Cat. No.: GC10089

### Chemical Properties

Cas. No. 81065-76-1

Chemical Name manganese(2+);2-methoxy-6-[2-[(3-methoxy-2-oxidophenyl)methylideneamino]ethyliminomethyl]phenolate;chloride

SMILES COC1=CC=CC(=C1[O-])C=NCCN=CC2=C(C(=CC=C2)OC)[O-].[Cl-].[Mn+2]

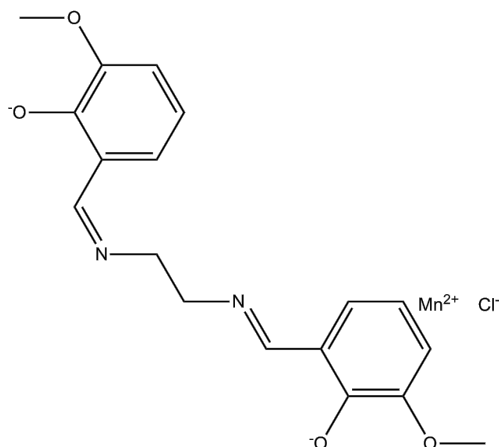
Formula  $C_{18}H_{18}ClMnN_2O_4$  M.Wt 416.74

Solubility  $\geq 20.85\text{mg/mL}$  in DMSO Storage Store at  $-20^{\circ}\text{C}$

General tips For obtaining a higher solubility, please warm the tube at  $37^{\circ}\text{C}$  and shake it in the ultrasonic bath for a while. Stock solution can be stored below  $-20^{\circ}\text{C}$  for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure



### Protocol

#### Cell experiment [1]:

Cell lines Human dermal fibroblasts

**Caution: Product has not been fully validated for medical applications. For research use only.**

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|                               |                                                                                                                                                                                                                                                                                                                                                                                                        |
|-------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Preparation method            | The solubility of this compound in DMSO is >20.9mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37°C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.                                                                                                                                 |
| Reacting condition            | 0, 20, 40, 60 and 80 $\mu$ M, 18h                                                                                                                                                                                                                                                                                                                                                                      |
| Applications                  | In human dermal fibroblasts, EUK-134 had significantly greater cytoprotective activity than did EUK-8. EUK-134 (80 $\mu$ M) was equally as protective as 290 units/ml of bovine liver catalase.                                                                                                                                                                                                        |
| <b>Animal experiment [1]:</b> |                                                                                                                                                                                                                                                                                                                                                                                                        |
| Animal models                 | male Sprague-Dawley rats with middle cerebral artery occlusion (MCA-o)                                                                                                                                                                                                                                                                                                                                 |
| Dosage form                   | 0.25 and 2.5 mg/kg, diluted in 0.9% saline, single intravenous bolus injection at 3 hr after MCA-o, killed at 21 hr or 72 hr.                                                                                                                                                                                                                                                                          |
| Application                   | In male Sprague-Dawley rats with middle cerebral artery occlusion (MCA-o), EUK-134 significantly lowered infarct volumes compared with those of vehicle-injected rats. EUK-134 at 2.5 mg/kg reduced the infarct volume by ~90%. After 72 hr, the EUK-134-treated group still exhibited a substantial degree of protection and the mean infarct volume did not differ significantly from that at 21 hr. |
| Other notes                   | Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.                                                                                                                                                                                                         |

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### References:

[1]. Baker K, Marcus C B, Huffman K, et al. Synthetic combined superoxide dismutase/catalase mimetics are protective as a delayed treatment in a rat stroke model: a key role for reactive oxygen species in ischemic brain injury[J]. Journal of Pharmacology and Experimental Therapeutics, 1998, 284(1): 215-221.

### Background

EUK 134, a synthetic superoxide dismutase (SOD)/catalase mimetic, has exhibited potent antioxidant activities and inhibited the formation of  $\beta$ -amyloid and related amyloid fibril.

In vitro:EUK-134, a salen-manganese complex, showed potent catalase and cytoprotective activities and SOD activity. After middle cerebral artery occlusion, EUK-134 administration at 3 hr significantly reduced brain infarct size, with the highest dose apparently preventing further infarct growth[1]. Administration of EUK 134 (20  $\mu$ M) prevented A $\beta$ -induced microglial proliferation in vitro[2]. In human neuroblastoma cell line SK-N-MC, pre-treatments with EUK134 protected cells against H<sub>2</sub>O<sub>2</sub>-induced oxidative stress through inhibition of MAPK pathway in a dose-dependent manner.EUK134 also decreased the expression of pro-apoptotic genes p53 and Bax and enhanced expression of anti-apoptotic Bcl-2 gene [3]. Incubation of human amylin with EUK-134 significantly inhibited amyloid formation at two molar ratios of 1:1 and 5:1 (drugs to protein)[4].

In vivo:Compared to the vehicle-injected rats, the EUK-134-treated group at doses of 0.5 and 5.0  $\mu$ mol/kg (0.25 and 2.5 mg/kg, respectively) exhibited infarct volumes that were significantly lower than those of vehicle-injected rats. At 5.0  $\mu$ mol/kg, EUK-134 reduced the infarct volume by 90% when compared with that of the vehicle controls [1].EUK-134 protected most of the vulnerable neurons from excitotoxic cell death.EUK-134 significantly reduced ( $P < 0.05$ ) KA-induced neuronal damage in CA1 (22% of total neurons), an almost complete protection in CA3 (7%) and piriform cortex (14%), indicating that EUK-134 prevented most but not all neuronal damage resulting from KA-induced seizure activity [5].

### References:

[1]. Baker K, Marcus C B, Huffman K, et al. Synthetic combined superoxide dismutase/catalase mimetics are protective as a delayed treatment in a rat stroke model: a key role for reactive oxygen species in ischemic brain injury[J]. Journal of Pharmacology and Experimental Therapeutics, 1998,

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284(1): 215-221.

[2]. Jekabsone A, Mander P K, Tickler A, et al. Fibrillar beta-amyloid peptide A $\beta$  1–40 activates microglial proliferation via stimulating TNF- $\alpha$  release and H<sub>2</sub>O<sub>2</sub> derived from NADPH oxidase: a cell culture study[J]. Journal of neuroinflammation, 2006, 3(1): 1.

[3]. Mohammadi M, Yazdanparast R. Modulation of H<sub>2</sub>O<sub>2</sub>-Induced Mitogen-Activated Protein Kinases Activation and Cell Death in SK-N-MC Cells by EUK134, a SalenDerivative[J]. Basic & clinical pharmacology & toxicology, 2011, 108(6): 378-384.

[4]. Bahramikia S, Yazdanparast R. Inhibition of human islet amyloid polypeptide or amylin aggregation by two manganese-salenderivatives[J]. European journal of pharmacology, 2013, 707(1): 17-25.

[5]. Rong Y, Doctrow S R, Tocco G, et al. EUK-134, a synthetic superoxide dismutase and catalase mimetic, prevents oxidative stress and attenuates kainate-induced neuropathology[J]. Proceedings of the National Academy of Sciences, 1999, 96(17): 9897-9902.

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