Olesoxime

Cat. No.: HY-14796

CAS No.: 22033-87-0

Molecular Formula: $C_{27}H_{45}NO$

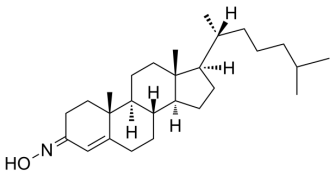
Molecular Weight: 399.65

Target: Mitochondrial Metabolism

Pathway: Metabolic Enzyme/Protease

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (125.11 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.5022 mL	12.5109 mL	25.0219 mL
5 mM	0.5004 mL	2.5022 mL	5.0044 mL
10 mM	0.2502 mL	1.2511 mL	2.5022 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.26 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.26 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.26 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Olesoxime (TRO 19622) is a mitochondrial-targeted neuroprotective compound with mean EC_{50} value for increasing cell survival is 3.2±0.2 μM.

IC_{50} & Target

Mitochondrial[1]

In Vitro

Exposure to Olesoxime (TRO 19622) (ranging from 0.1 to 10 μM) at 1 h after plating significantly protects primary embryonic rat spinal MNs (that had been cultured for 3 days without brain-derived, ciliary and glia-derived neurotrophic factors) from

	cell death. At a concentration of 10 μM, Olesoxime (TRO 19622) maintains survival of 74±10% of the neurons supported by a combination of neurotrophic factors (brain-derived, ciliary and glia-derived neurotrophic factors). The mean EC_{50} in this assay is 3.2±0.2 μM. In addition to preserving MN cell bodies, Olesoxime (TRO 19622) also promotes the outgrowth of neurites. At a concentration of 1 μM, which increases cell survival by only 38%, Olesoxime (TRO 19622) increases overall neurite outgrowth per cell by 54%[1]. Olesoxime (TRO 19622) belongs to a new family of cholesterol-oximes identified for its survival-promoting activity on purified motor neurons deprived of neurotrophic factors. Olesoxime (TRO 19622) targets proteins of the outer mitochondrial membrane, concentrates at the mitochondria and prevents permeability transition pore opening mediated by, among other things, oxidative stress[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Daily administration of Olesoxime (TRO 19622) (3 or 30 mg/kg sc) to adult mice for more than 2 months is well tolerated without toxicity or adverse effects[1]. When animals are treated orally for 5 days following the lesion, Olesoxime (TRO 19622) increases motor neuron cell body survival in a dose-dependent manner with significant rescue at the highest dose of 100 mg/kg. At this dose, motor neuron survival is 29 ±2% (n=18) corresponding to a 42% increase in survival compared with vehicle-treated animals[3]. Paclitaxel-treated rats that receive prophylactic treatment with 3 mg/kg/d or 30 mg/kg/d Olesoxime (TRO 19622) have 239±17.6 and 247±14.4 IENFs per cm, respectively. For both doses, the decreases are significantly less than the 46% decrease seen in the Paclitaxel-treated rats administered vehicle. However, both doses produce decreases (25% and 22%) that are significantly different relative to the naïve control group[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [3][4]	Mice[3] Eight-week-old C57bl/6 RJ mice are anesthetized using 60 mg/kg i.p. ketamine chlorohydrate. To reduce the risk of gender-related differences in response to Olesoxime (TRO 19622), only female mice are used. The right sciatic nerve is surgically exposed at mid-thigh level, and it is crushed 5 mm proximal to the trifurcation of the sciatic nerve. The nerve is crushed twice for 30 s with hemostatic forceps (width, 1.5 mm) with a 90° rotation between each crush. Sciatic nerve degeneration/regeneration is assessed over 6 weeks by measurement of the compound muscular action potential (CMAP) and histological studies of the damaged area of the sciatic nerve. Olesoxime (TRO 19622) is given subcutaneously at 0.3, 3, and 30 mg/kg. Treatments started the day of the crush injury, and they continued daily for 6 weeks. In total, 15 animals per group are used in the study. Electromyography is performed once a week for 6 weeks using a Neuromatic 2000M electromyograph. Mice are anesthetized using 100 mg/kg i.p. ketamine chlorohydrate. CMAP is measured in the gastrocnemius muscle after a single 0.2-ms stimulation of the sciatic nerve at supramaximal intensity (12.8 mA). The amplitude (millivolts) and the latency (milliseconds) of the action potential are measured. Rats[4] Adult male Sprague-Dawley rats (200-300 g) are used. Olesoxime (TRO 19622) or the vehicle is administered via oral gavage in a volume of 5 mL/kg. The TRO19622doses used here (3-100 mg/kg) are chosen based on prior reports of neuroprotective and analgesic activity. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Martin LJ, et al. Olesoxime, a cholesterol-like neuroprotectant for the potential treatment of amyotrophic lateral sclerosis. IDrugs. 2010 Aug;13(8):568-80.

[2]. Bordet T, et al. Olesoxime (TRO19622): A Novel Mitochondrial-Targeted Neuroprotective Compound. Pharmaceuticals (Basel). 2010 Jan 28;3(2):345-368

[3]. Bordet T, et al. Identification and characterization of cholest-4-en-3-one, oxime (TRO19622), a novel drug candidate for amyotrophic lateral sclerosis. J Pharmacol Exp Ther. 2007 Aug;322(2):709-20.

[4]. Xiao WH, et al. Olesoxime (cholest-4-en-3-one, oxime): analgesic and neuroprotective effects in a rat model of painful peripheral neuropathy produced by the chemotherapeutic agent, paclitaxel. Pain. 2009 Dec 15;147(1-3):202-9

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

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