Emixustat

Cat. No.: HY-19720

CAS No.: 1141777-14-1

Molecular Formula: $C_{16}H_{25}NO_2$

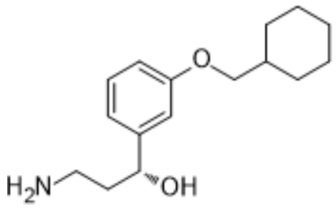
Molecular Weight: 263.38

Target: Others

Pathway: Others

Storage:

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



SOLVENT & SOLUBILITY

In Vitro

Ethanol : 100 mg/mL (379.68 mM; Need ultrasonic)

DMSO : ≥ 43 mg/mL (163.26 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.7968 mL	18.9840 mL	37.9680 mL
5 mM	0.7594 mL	3.7968 mL	7.5936 mL
10 mM	0.3797 mL	1.8984 mL	3.7968 mL

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

In Vivo

1. Add each solvent one by one: 10% EtOH >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 3 mg/mL (11.39 mM); Clear solution
2. Add each solvent one by one: 10% EtOH >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 3 mg/mL (11.39 mM); Clear solution
3. Add each solvent one by one: 10% EtOH >> 90% corn oil
   Solubility: ≥ 3 mg/mL (11.39 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Emixustat is an orally active RPE65 inhibitor with an IC_{50} value of 4.4 nM. Emixustat is also a visual cycle modulator, capable of regulating visual cycle activity by inhibiting retinol isomerization, and holds potential for studying vision disorders such as age-related macular degeneration (AMD)[1][2][3][4].

IC_{50} & Target

IC50: 4.4 nM (Retinal Pigment Epithelium 65-kDa protein (RPE65))[4]

In Vitro

Emixustat (0.1 nM - 10 μM, 1 h) concentration-dependently reduces the production of 11-cis-retinol, thereby inhibiting RPE65 activity[4].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Emixustat (1-10 mg/kg, oral administration, single dose, or twice daily for 6 days; 1 mg/kg, i.p., measurement after 30-60 minutes) reduced cation influx and oxygen consumption in the retinas of brown Norway rats under dark adaptation conditions[3].

Emixustat (0.03-3.0 mg/kg, intravenous injection, once daily for 5 days) inhibits neovascularization and protects the retina in the oxygen-induced retinopathy mouse model[4].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Brown norway rats (200-300 g, 3 months old)[3]
Dosage:	1, 5 or 10 mg/kg
Administration:	Oral gavage (p.o.), single dose (1, 10 mg/kg), 2 hours followed by 4 hours of dark adaptation, or twice a day for 6 days (5 mg/kg)
Result:	Reduced the conductance of the retinal cation channels after dark adaptation.

Animal Model:	Brown norway rats (200-300 g, 3 months old)[3]
Dosage:	1 mg/kg
Administration:	Intravenous injection (i.v.), retinal PO_2 was measured 30-60 min later
Result:	Reduced the oxygen consumption during dark adaptation.

Animal Model:	Oxygen-induced retinopathy (OIR) mice model (BALB/c and 129/Sv / C57BL/6 mixed background)
Dosage:	0.03, 0.1, 0.3, 1.0, 3.0 mg/kg
Administration:	Intravenous injection (i.v.), once daily for 5 days
Result:	Dose-dependently reduced retinal neovascularization.

REFERENCES

[1]. Kubota R, et al. Emixustat Reduces Metabolic Demand of Dark Activity in the Retina. Invest Ophthalmol Vis Sci. 2019 Nov 1;60(14):4924-4930.

[2]. Bavik C, et al. Visual Cycle Modulation as an Approach toward Preservation of Retinal Integrity. PLoS One. 2015 May 13;10(5):e0124940.

[3]. Bavik C, et al. Visual Cycle Modulation as an Approach toward Preservation of Retinal Integrity. PLoS One. 2015 May 13;10(5):e0124940.

[4]. Kiser PD, et al. Catalytic mechanism of a retinoid isomerase essential for vertebrate vision. Nat Chem Biol. 2015 Jun;11(6):409-15.

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