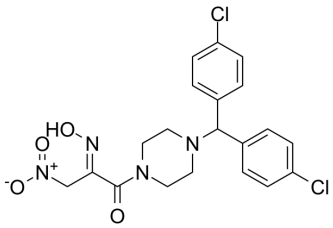
JKE-1674

Cat. No.:	HY-138153
CAS No.:	2421119-60-8
Molecular Formula:	$C_{20}H_{20}Cl_2N_4O_4$
Molecular Weight:	451.3
Target:	Ferroptosis; Glutathione Peroxidase
Pathway:	Apoptosis; Metabolic Enzyme/Protease
Storage:	4°C, protect from light * In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (221.58 mM; Need ultrasonic)
Ethanol : ≥ 50 mg/mL (110.79 mM)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2158 mL	11.0791 mL	22.1582 mL
	5 mM	0.4432 mL	2.2158 mL	4.4316 mL
	10 mM	0.2216 mL	1.1079 mL	2.2158 mL

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

In Vivo

1. Add each solvent one by one: 10% EtOH >> 90% PEG400
   Solubility: 5 mg/mL (11.08 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.54 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.54 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

JKE-1674 is an orally active glutathione peroxidase 4 (GPX4) inhibitor and an active metabolite of GPX4 inhibitor ML-210. JKE-1674, an analog of ML-210 in which the nitroisoxazole ring is replaced with an α-nitroketoxime. JKE-1674 can convert into a nitrile oxide JKE-1777. JKE-1674 kills LOX-IMVI cells in a manner that is equipotent to ML-210 and is completely rescued by ferroptosis inhibitors[1][2][3].

IC_{50} & Target

GPX4[1]

In Vitro	JKE-1674 exhibits activity indistinguishable from that of ML210 in cellular target engagement assays including yielding the same +434Da GPX4 adduct in cells. JKE-1674 kills LOX-IMVI cells in a manner that is equipotent to ML210 and is completely rescued by ferroptosis inhibitors. JKE-1674 forms a nitrile-oxide electrophile in cells. JKE-1674 dehydration yields a nitrile-oxide electrophile that binds GPX4. JKE-1674 exhibits far greater stability than chloroacetamide inhibitors[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	JKE-1674 (50 mg/kg; p.o.) can be detected in the serum of mice dosed orally with the compound[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	SCID mice[1]
Dosage:	50 mg/kg (Pharmacokinetic Analysis)
Administration:	P.o.
Result:	Could be detected in the serum of mice dosed orally with the compound.

REFERENCES

[1]. Eaton JK, et al. Selective covalent targeting of GPX4 using masked nitrile-oxide electrophiles. Nat Chem Biol. 2020;16(5):497-506.

[2]. Kathman SG, et al. A masked zinger to block GPX4. Nat Chem Biol. 2020;16(5):482-483.

[3]. Viswanathan VS, et al. Unraveling Masked GPX4 Inhibitors. Nat. Chem. Biol. 2020, 16, 497–506.

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