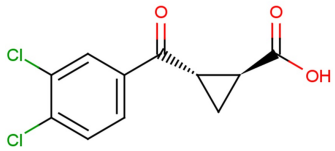
Data Sheet (Cat.No.T13258L)

TargetMol
A DRUG SCREENING EXPERT

UPF-648

Chemical Properties



CAS No.:	213400-34-1
Formula:	C11H8Cl2O3
Molecular Weight:	259.09
Appearance:	N/A
Storage:	0-4℃ for short term (days to weeks), or -20℃ for long term (months).

Biological Description

Description	UPF-648 is a potent kynurenine 3-monooxygenase inhibitor. It also shows highly active at 1 uM (81 ± 10% KMO inhibition).
Targets(IC_{50})	Others: None
In vitro	UPF 648 totally blocked KMO at 0.1 and 0.01 mM and was still highly active at 0.001 mM (81 ± 10 % inhibition), but the compound was essentially ineffective at blocking KAT activity. UPF 648 binds close to the FAD cofactor and perturbs the local active-site structure, preventing productive binding of the substrate l-kynurenine. Functional assays and targeted mutagenesis reveal that the active-site architecture and UPF 648 binding are essentially identical in human KMO, validating the yeast KMO-UPF 648 structure as a template for structure-based drug design [1][3].
In vivo	Applying an identical experimental design, separate rats were used to study the effect of KMO inhibition on the de novo synthesis of KP metabolites in the lesioned striatum. These animals were bilaterally injected with 0.1 mM UPF 648 and 3H-kynurenine in PBS. 0.1 mM UPF 648 significantly reduced the biosynthesis of 3-HK and QUIN in the lesioned striatum (by 77 % and 66%, respectively) and moderately (27%) but significantly increased the de novo formation of KYNA. Administered to pregnant rats or mice on the last day of gestation, UPF 648 (50 mg/kg, i.p.) produced qualitatively similar changes (i.e., large increases in kynurenine and KYNA and reductions in 3-HK and QUIN) in the brain and liver of the offspring. Rat pups delivered by UPF 648-treated mothers and immediately exposed to neonatal asphyxia showed further enhanced brain KYNA levels. UPF 648, has an IC50 of 20 nM and provides protection against intrastriatal QUIN injections in kynurenine aminotransferase (KAT II) deficient mice. UPF 648 treatment also shifts KP metabolism towards enhanced neuroprotective KYNA formation [1][2][3].

Solubility Information

Solubility	Ethanol: 50 mg/mL (192.98 mM) (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	3.86 mL	19.298 mL	38.597 mL
5 mM	0.772 mL	3.86 mL	7.719 mL
10 mM	0.386 mL	1.93 mL	3.86 mL
50 mM	0.077 mL	0.386 mL	0.772 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. The storage conditions and period of the stock solution: - 80 ℃ for 6 months; - 20 ℃ for 1 month. Please use it as soon as possible.

Reference

1. Amori L, et al. On the relationship between the two branches of the kynurenine pathway in the rat brain in vivo. J Neurochem. 2009 Apr;109(2):316-25.
2. Ceresoli-Borroni G, et al. Perinatal kynurenine 3-hydroxylase inhibition in rodents: pathophysiological implications. J Neurosci Res. 2007 Mar;85(4):845-54.
3. Amaral M, et al. Structural basis of kynurenine 3-monooxygenase inhibition. Nature. 2013 Apr 18;496(7445):382-5.

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