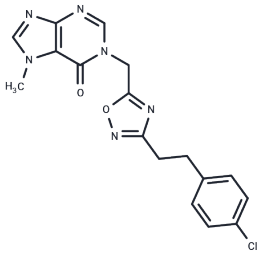
Data Sheet (Cat.No.T7430)

TargetMol

AM-0902

Chemical Properties



CAS No. : 1883711-97-4

Formula: C17H15ClN6O2

Molecular Weight: 370.79

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	AM-0902 is a potent and specific TRPA1 antagonist (IC50s: 71/131 nM for rTRPA1 and hTRPA1).
Targets(IC50)	TRP/TRPV Channel
In vitro	AM-0902 is highly permeable (average Papp=44.5 μcm/s in MDCK cells), an unlikely substrate for P-gp (efflux ratio=1.3 in P-gp overexpressing MDCK cells), and demonstrates good solubility (PBS pH 7.4: 226 μM, SIF: 248 μM). AM-0902 shows good selectivity over other TRP channels, as no activity is observed against human TRPV1 or TRPV4, or rat TRPV1, TRPV3, or TRPM8, at concentrations up to 10 μM. AM-0902 inhibits 45Ca2+ flux upon activation of rat TRPA1 with methylglyoxal (IC50: 0.019 μM).
In vivo	AM-0902 has moderate terminal elimination half-life (t1/2=0.6 h and 2.8 h for rat (0.5 mg/kg, iv), rat (30 mg/kg, oral)). A dose-dependent reduction of allyl isothiocyanate (AITC)-induced flinching is observed for AM-0902, with a significant reduction in flinching, observed postdosing of 10 and 30 mg/kg. The unbound plasma concentrations (Cu) at 1 h for the 1, 3, 10, and 30 mg/kg doses are 0.051±0.024, 0.19±0.11, 0.58±0.35, and 2.2±0.40 μM, covering the in vitro rat TRPA1 45Ca2+ IC50 at 0.72, 2.7, 8.2, and 30.3 fold, respectively. A good exposure-response relationship is observed in this target coverage model. An unbound in vivo IC50 of 0.35 μM, which is in good agreement with the in vitro rat TRPA1 45Ca2+ IC50, and unbound in vivo IC90 of 1.7 μM are determined. It is noteworthy that at a dose of 30 mg/kg, AM-0902 engages TRPA1 at concentrations that exceed the in vivo IC90, making it a useful tool for the exploration of in vivo models of acute pain.
Cell Research	On the day of assay, culture media is removed and MDCK cells are incubated for 10 min at room temperature (RT) with 50 μL of AM-0902 in AM-0902 dilution buffer [HBSS containing 1 mM HEPES+0.1 mg/mL BSA] at final concentrations (2.0 nM to 40 μM, 1:3 ratio), followed by another 3 min incubation at RT. The reaction mixture is aspirated, and cells are washed three times with PBS containing 0.1 mg/mL BSA. Radioactivity is measured using a TopCount microplate scintillation counter. The activation of TRPA1 is measured by the cellular uptake of radioactive calcium.
Animal Research	Rats are dosed orally with either vehicle (2% HPMC/1% Tween-80) or AM-0902 at 1, 3, 10, or 30 mg/kg. After 1 h, one left ventral hind paw is injected with the TRPA1 agonist AITC (0.1%). AM-0902 is also given by an intravenous (IV) injection to rats (0.5 mg/kg).

Solubility Information

Solubility	DMSO: 145 mg/mL (391.06 mM),Sonication and heating are recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 4 mg/mL (10.79 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.6969 mL	13.4847 mL	26.9694 mL
5 mM	0.5394 mL	2.6969 mL	5.3939 mL
10 mM	0.2697 mL	1.3485 mL	2.6969 mL
50 mM	0.0539 mL	0.2697 mL	0.5394 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Schenkel LB, et al. Optimization of a Novel Quinazolinone-Based Series of Transient Receptor Potential A1 (TRPA1) Antagonists Demonstrating Potent in Vivo Activity. J Med Chem. 2016 Mar 24;59(6):2794-809.