Zonampanel

Cat. No.: HY-15072

CAS No.: 210245-80-0

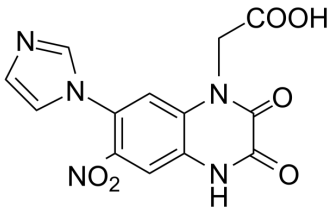
Molecular Formula: $C_{13}H_9N_5O_6$

Molecular Weight: 331.24

Target: iGluR

Pathway: Membrane Transporter/Ion Channel; Neuronal Signaling

Storage: 4°C, sealed storage, away from moisture and light
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (150.95 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	3.0190 mL	15.0948 mL	30.1896 mL
	5 mM	0.6038 mL	3.0190 mL	6.0379 mL
	10 mM	0.3019 mL	1.5095 mL	3.0190 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 (7.55 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (7.55 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Zonampanel (YM 872) is a selective antagonist of the glutamate receptor subtype, α-amino-3-hydroxy-5-methylisoxazole-4-propionic acid (AMPA) receptor.

In Vitro

Zonampanel inhibits the human MRP4-mediated transport of [^{3}H]oestradiol 17-D-glucuronide in a concentration-dependent manner. In contrast, Zonampanel (up to 1000 mM) does not inhibit the human MRP2- or BCRP-mediated transport of [^{3}H]oestradiol 17-D-glucuronide or [^{3}H]methotrexate[1]. Zonampanel inhibits the uptake of typical substrates by Oat1, Oat2, and Oat3 with inhibition constant (K_i) values of 7.02 to 10.4 μM. A time- and saturable concentration-dependent increase in [^{14}C]Zonampanel uptake is observed in these cells [K_m values: 13.4 to 53.6 μM][2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

In in vivo experiments, probenecid and cimetidine decrease intrinsic clearance for both the renal secretion and biliary

excretion of Zonampanel[2].

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PROTOCOL

Animal Administration [2]

Seven-week-old male Sprague-Dawley rats are used at 8 weeks after acclimatization for at least 1 week. During acclimatization, the rats are kept in an air-conditioned room with temperature and humidity controlled at 22.9 to 23.3°C and 50 to 78%; the room is lit for 12 h 30 min from 7:30 AM to 8:00 PM. Rats are given free access to solid food and water until just before drug administration. YM 872 (15 mg/kg) is administered at a single bolus dose into the rat tail vein with or without probenecid (50 mg/kg) or cimetidine (40 mg/kg). At 5, 15, and 30 min and 1, 2, 3, 4, and 6 h after dosing, blood is sampled under ether anesthesia via the inferior vena cava using a heparinized syringe and immediately stored on ice using four rats each per sampling time point per administration group (total of 128 rats for 8 sampling time points and 4 administration groups). Plasma is obtained by centrifugation at 4°C, 1870 g for 15 min and kept frozen at -20°C. Rats for plasma sampling at 3 and 6 h after administration are housed in metabolic cages after administration, spontaneously excreted urine is collected, and the cages are washed using water. Regarding specific gravity as 1, urine volume (including the cage-wash water) is calculated according to differences in the weight of the sampling tube before and after sampling. Urine samples are kept frozen at -20°C until assay as described below. All plasma and urine samples are protected from light throughout the sampling, storage, and assay procedures.

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REFERENCES

[1]. Minematsu T, et al. Characterization of renal tubular apical efflux of zonampanel, an alpha-amino-3-hydroxy-5-methylisoxazole-4-propionate receptor antagonist, in humans. Xenobiotica. 2008 Sep;38(9):1191-202.

[2]. Minematsu T, et al. Role of organic anion transporters in the pharmacokinetics of zonampanel, an alpha-amino-3-hydroxy-5-methylisoxazole-4-propionate receptor antagonist, in rats. Drug Metab Dispos. 2008 Aug;36(8):1496-504.

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