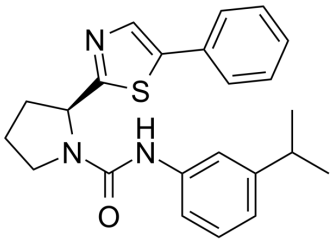
TRPV1 antagonist 3

Cat. No.:	HY-144372
CAS No.:	2765294-54-8
Molecular Formula:	$C_{23}H_{25}N_3OS$
Molecular Weight:	391.53
Target:	TRP Channel
Pathway:	Membrane Transporter/Ion Channel; Neuronal Signaling
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (255.41 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5541 mL	12.7704 mL	25.5408 mL
	5 mM	0.5108 mL	2.5541 mL	5.1082 mL
	10 mM	0.2554 mL	1.2770 mL	2.5541 mL

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

BIOLOGICAL ACTIVITY

Description

TRPV1 antagonist 3 (Compound 7q) is a potent TRPV1 antagonist with an IC_{50} of 2.66 nM against capsaicin. TRPV1 antagonist 3 is mode-selective, oral bioavailable (F = 60%) and CNS-penetrant[1].

IC_{50} & Target

hTRPV1	TRPM8
2.66 nM (IC_{50})	7.45 μM (IC_{50})

In Vitro

TRPV1 antagonist 3 (Compound 7q) is highly selective for the TRPV1 receptor relative to other TRP channels[1].

TRPV1 antagonist 3 shows acceptable aqueous solubility (solubility at pH 7.4 = 26 μg/mL) [1].

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

In Vivo

TRPV1 antagonist 3 (Compound 7q) (0-30 mg/kg; i.p.; 30 min) shows anti-nociceptive effect mainly mediated by blocking CAP-activated channel[1].

TRPV1 antagonist 3 (0-100 mg/kg; i.g.) had no obvious thermal effect in rats[1].

TRPV1 antagonist 3 (10 mg/kg; i.v.) shows a good concentration in the brain at 0.5 h, with value of 2311 ng/g, and has good

CNS penetration, with a brain/plasma ratio of 1.66[1].

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

Animal Model:	KM male mice (18-22 g), capsaicin, acetic acid, and thermal induced pain model[1]
Dosage:	3, 10, and 30 mg/kg. 20 μL of solution of capsaicin (16 mg/20 mL) was injected s.c. under the skin of the dorsal surface of the right hind paw, or injected with 0.6% acetic acid (0.1 mL/10 g/mouse i.p.).
Administration:	Intraperitoneally administration; 30 min
Result:	In capsaicin-induced nociception, licking time decreased significantly in a dose-dependent manner. In acid-induced nociception, no significant anti-nociceptive activities were found compared with the control (SB-705498 and BCTC) at all dosage. In thermal-induced nociception, the latency time of nociceptive responses was increased at the doses of 10 and 30 mg/kg.

Animal Model:	Spragur-Dawley male rats (220-250 g)[1]
Dosage:	10 mg/kg or 20 mg/kg
Administration:	Intravenous injection of 10 mg/kg or oral dose of 20 mg/kg (Pharmacokinetic Analysis)
Result:	In vivo pharmacokinetic parameters of TRPV1 antagonist 3 in rats (n=3)[1]

Parameters	IV	PO
$t_{1/2}$ (h)	0.106 ± 0.076	
$t_{1/2}$, ka (h)		0.462 ± 0.096
$t_{1/2}$, k_{10} (h)		0.527 ± 0.106
k_a (1/h)		1.65 ± 0.364
k_{10} (1/h)	12.076 ± 2.337	1.133 ± 0.358
V (L/kg)	0.003 ± 0.001	0.016 ± 0.006
CL (L/h/kg)	0.024 ± 0.013	0.022 ± 0.01
T_{max} (h)		0.711 ± 0.144
C_{max} (ng/mL)		311.377 ± 108.017
AUC $_{0\text{-inf}}$ (ng/mL*h)	495.955 ± 214.634	598.873 ± 212.319

REFERENCES

[1]. Yue Qiao, et al. Discovery of (S)-N-(3-isopropylphenyl)-2-(5-phenylthiazol-2-yl)pyrrolidine-1-carboxamide as potent and brain-penetrant TRPV1 antagonist. Eur J Med Chem. 2022 Apr 5;233:114191.

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