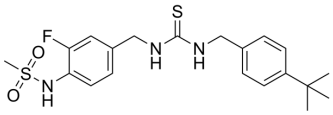
JYL 1421

Cat. No.:	HY-100668
CAS No.:	401907-26-4
Molecular Formula:	$C_{20}H_{26}FN_3O_2S_2$
Molecular Weight:	423.57
Target:	TRP Channel
Pathway:	Membrane Transporter/Ion Channel; Neuronal Signaling
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (236.09 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3609 mL	11.8044 mL	23.6088 mL
	5 mM	0.4722 mL	2.3609 mL	4.7218 mL
	10 mM	0.2361 mL	1.1804 mL	2.3609 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 (5.90 mM); Suspended solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.90 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.90 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

JYL 1421 is a TRPV1 receptor antagonist, with an IC_{50} of 8 nM.

IC_{50} & Target

IC50: 8 nM (TRPV1 receptor)[1].

In Vitro

Incubation with JYL 1421 for 5 min concentration-dependently inhibits the capsaicin (330 nM)-evoked Ca^{2+} accumulation. The inhibitory effect of the lowest concentration (5 nM) of JYL 1421 reaches the level of significance and 1 μM almost abolishes the response, only 3.1±0.65% of the first capsaicin-induced Ca^{2+} influx could be observed. The IC_{50} value is 8 nM for JYL 1421. Meanwhile, the effect of capsazepine is markedly smaller, it induces 41.7% inhibition in 1 μM concentration,

	but this inhibitory effect does not increase further in 10 μM and does not reach 50%[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Instillation of 50 μL capsaicin solution (10 μg/mL) into the left eye of the rat evokes 12.9±1.3 wiping movements within 3 min. Pretreating the rats with 0.4 or 1 mg/kg i.p. JYL 1421 does not influence significantly the wiping behavior, but 2-5 mg/kg dose-dependently reduces the number of wiping movements. The ID_{50} value is 4.6 mg/kg. The mean arterial pressure of untreated rats is 109.9±4.2 Hgmm (n=6). One and 2 μg/kg capsaicin i.v. injection evokes a transient drop of blood pressure by 47.4±4.7 and 59.6±4.2 Hgmm (n=6), respectively. Both applied doses of JYL 1421 (0.4 and 1.6 mg/kg) fail to evoke hypotension. JYL 1421 dose-dependently inhibits the capsaicin-induced fall in blood pressure as shown by the need for higher capsaicin doses to elicit the reflex hypotension after JYL 1421 administration than before treatment. Capsazepine fails to induce a significant inhibition of the capsaicin-evoked hypotension up to a dose of 2 mg/kg[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Rats[1] Pretreatment with JYL 1421 (0.4, 1, 2, or 5 mg/kg) is performed i.p. 20 min before capsaicin administration. In control rats the solvent is injected in the same volume, in the reference group capsazepine (2 or 5 mg/kg) is administered i.p. The number of wiping movements in response to 50 μL capsaicin solution (10 μg/mL) drops into the left eye of male Wistar rats (180-220 g) is determined during 60 s after instillation. The body temperature is maintained at 37°C by a heating lamp. Drugs are administered through a cannula inserted into the right jugular vein. The pulmonary chemoreflex is evoked by rapid injections of capsaicin (1 and 2 μg/kg i.v.) separated by a 5 min interval. Thereafter JYL 1421 (0.4 and 1.6 mg/kg i.v.) is administered and 5 min later capsaicin injections are repeated at increasing doses until the magnitude of the control responses could be achieved. For quantitative analysis the area under the curve (AUC) of the capsaicin-induced hypotension is determined[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Jakab B, et al. Pharmacological characterization of the TRPV1 receptor antagonist JYL1421 (SC0030) in vitro and in vivo in the rat. Eur J Pharmacol. 2005 Jul 4;517(1-2):35-44.

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