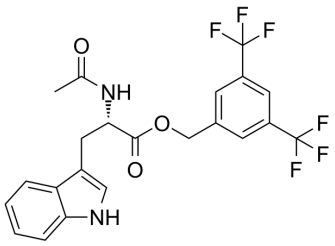
L-732138

Cat. No.:	HY-101249
CAS No.:	148451-96-1
Molecular Formula:	$C_{22}H_{18}F_6N_2O_3$
Molecular Weight:	472.38
Target:	Neurokinin Receptor
Pathway:	GPCR/G Protein; Neuronal Signaling
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (529.23 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1169 mL	10.5847 mL	21.1694 mL
5 mM	0.4234 mL	2.1169 mL	4.2339 mL
10 mM	0.2117 mL	1.0585 mL	2.1169 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: ≥ 6.25 mg/mL (13.23 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 6.25 mg/mL (13.23 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

L-732138 is a selective, potent and competitive neurokinin-1 (NK-1) receptor antagonist with an IC_{50} of 2.3 nM. L-732138 has 200-fold more potent in cloned human NK-1 receptors than cloned rat NK-1 receptors, and has > 1000-fold more potent than human NK-2 and NK-3 receptors. L-732138 can reduce hyperalgesia and has antitumor action[1][2].

IC_{50} & Target

NK1
2.3 nM (IC_{50})

In Vitro

L-732138 (0 -100 μM; first doubling time; COLO 858, MEL HO and COLO 679 cells) treatment results in a concentration-dependent cytotoxicity. L-732138 inhibits cell growth with IC_{50} of 44.6 μM for COLO 858 cells, 76.3 μM for MEL HO cells and 64.2 μM for COLO 679 cells. L-732138 blocks substance P (SP) mitogen stimulation[1].

L-732,138 treatment results in a large number of apoptotic cells were found in COLO 858, MEL HO and COLO 679 melanoma cell lines. In DAPI-stained cultures, at IC_{50} concentration of 43.6% apoptotic cells for the three melanoma cell lines, whereas at IC_{100} concentration of 51.4 % apoptotic cells[1].

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

Cell Proliferation Assay[1]

Cell Line:	COLO 858, MEL HO and COLO 679 cells
Concentration:	0 μM, 20 μM, 40 μM, 60 μM, 80 μM, 100 μM
Incubation Time:	First doubling time
Result:	Resulted in a concentration-dependent cytotoxicity.

In Vivo

L-732138 (10^{-4}-10^{-2} mol/kg; intravenous injection; for 15 minutes; male Dunkin-Hartley guinea-pigs) treatment abolishes vagally-induced plasma exudation and significantly inhibits the enhancement by LPS. The LPS-enhanced vagally-induced plasma exudation is not completely inhibited by either L-732138 or SOD pretreatment alone, but is blocked by the combination of both pretreatments[3].

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

Animal Model:	Male Dunkin-Hartley guinea-pigs (350-500 g) injected with lipopolysaccharide (LPS)[3]
Dosage:	10^{-4} mol/kg , 10^{-3} mol/kg and 10^{-2} mol/kg
Administration:	Intravenous injection; for 15 minutes
Result:	Abolished the vagally-induced plasma leakage in tracheobronchial tissues, and dose-dependently inhibited the LPS enhanced vagally-induced plasma exudation in traceobronchial tissues.

REFERENCES

[1]. Muñoz M, et al. The NK-1 Receptor Antagonist L-732,138 Induces Apoptosis and Counteracts Substance P-Related Mitogenesis in Human Melanoma Cell Lines. Cancers (Basel). 2010 Apr 20;2(2):611-23.

[2]. Cascieri MA, et al. Characterization of the interaction of N-acyl-L-tryptophan benzyl ester neurokinin antagonists with the human neurokinin-1 receptor. J Biol Chem. 1994 Mar 4;269(9):6587-91.

[3]. Kuo HP, et al. Lipopolysaccharide enhances neurogenic plasma exudation in guinea-pig airways. Br J Pharmacol. 1998 Oct;125(4):711-6.

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