Navacaprant

Cat. No.: HY-124754

CAS No.: 2244614-14-8

Molecular Formula: $C_{25}H_{32}FN_5O_2$

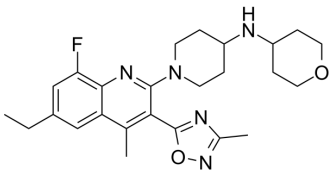
Molecular Weight: 453.55

Target: Opioid Receptor

Pathway: GPCR/G Protein; 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 : 3.85 mg/mL (8.49 mM; ultrasonic and warming and adjust pH to 4 with HCl and heat to 60°C)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2048 mL	11.0241 mL	22.0483 mL
	5 mM	0.4410 mL	2.2048 mL	4.4097 mL
	10 mM	---	---	---

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.67 mg/mL (3.68 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1 mg/mL (2.20 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1 mg/mL (2.20 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Navacaprant (BTRX-335140) is a selective and orally active κ opioid receptor (KOR) antagonist, has antagonist activity for κ OR, μOR and δOR with IC_{50} values of 0.8 nM, 110 nM, and 6500 nM, respectively.Navacaprant endows with favorable in vitro ADMET and in vivo pharmacokinetic profiles and medication-like duration of action in rats. Navacaprant distributes well into the CNS and can be used for the research of neuropathy[1].

IC_{50} & Target	κ Opioid Receptor/KOR	μ Opioid Receptor/MOR	δ Opioid Receptor/DOR
	0.8 nM (IC_{50})	110 nM (IC_{50})	6500 nM (IC_{50})

In Vitro

Navacaprant (BTRX-335140) (0-10 μM; 4 h) shows selective antagonist activity towards Kappa Opioid Receptor[1].

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

Cell Viability Assay[1]

Cell Line:	OPRK1-BLA U2OS cells
Concentration:	0-10 μM
Incubation Time:	4 hours
Result:	Exibited antagonist activity to KOR, DOR and MOR with IC_{50} values of 0.8, 110 and 6500 nM respectively, and showed selective antagonist activity to KOR.

In Vivo

Navacaprant (BTRX-335140) (0.01-3 mg/kg; p.o. once) reduces U69,593- stimulated plasma prolactin secretion to levels of without U69,593 treatment[1].

Navacaprant (BTRX-335140) (1 mg/kg; i.p. once) blocks U-50488-induced antinociception from hot water[1].

Pharmacokinetic Parameters of BTRX-335140 in rodents[1].

	Rats IV 1 mg/kg	Mice IV 3 mg/kg	Rats PO 5 mg/kg	Mice PO 10 mg/kg
CL (mL/min/kg)	105	66.5		
$t_{1/2}$ (h)	1.81	1.91	6.19	2.57
AUC_{0-t} (h•ng/mL)	153	725	265	232
V_{ss} (L/kg)	13.8	7.72		
F (%)			30.2	12

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

Animal Model:	Rat PRL model[1]
Dosage:	0.01, 0.03, 0.1, 0.3, 1 and 3 mg/kg
Administration:	Oral gavage; 0.01-3 mg/kg once
Result:	Effectively decreased the high level prolactin caused by U69,593 even at a dosage of 0.1 mg/kg.

Animal Model:	Adult male ICR mice with tail dipped into 50°C hot water[1]
Dosage:	1 mg/kg
Administration:	Intraperitoneal injection; 1 mg/kg once
Result:	Blocked the U-50488-induced antinociception at 1 h but not at 24 h pretreatment time and showed a medication-like duration of action in blocking the KOR.

REFERENCES

[1]. Guerrero M, et al. Design and Synthesis of a Novel and Selective Kappa Opioid Receptor (KOR) Antagonist (BTRX-335140). J Med Chem. 2019 Feb 28;62(4):1761-1780.

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