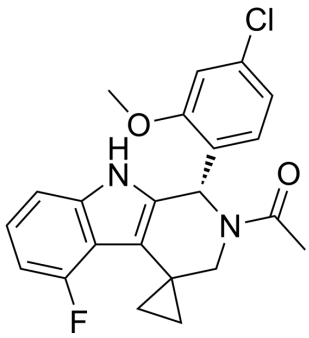
ONO-2952

Cat. No.:	HY-111191
CAS No.:	895169-20-7
Molecular Formula:	$C_{22}H_{20}ClFN_2O_2$
Molecular Weight:	398.86
Target:	Adrenergic 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 : 180 mg/mL (451.29 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5071 mL	12.5357 mL	25.0715 mL
	5 mM	0.5014 mL	2.5071 mL	5.0143 mL
	10 mM	0.2507 mL	1.2536 mL	2.5071 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: 4.5 mg/mL (11.28 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 4.5 mg/mL (11.28 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ONO-2952 is a potent, selective and orally active translocator protein 18 kDa (TSPO) antagonist with K_i of 0.33-9.30 nM for rat and human TSPO. ONO-2952 is more selective for TSPO than other receptors, transporters, ion channels and enzymes. ONO-2952 exerts its anti-stress effects through inhibition of excessive activation of noradrenergic system in the brain without the amnesic effect. ONO-2952 has the potential for irritable bowel syndrome treatment[1][2].

IC_{50} & Target

Ki: 0.33-9.30 nM (Rat and human TSPO)[1]

In Vitro

As for its selectivity for TSPO, ONO-2952 at a concentration of 10 μM showed good selectivity for TSPO against 98 off-targets (<50% inhibition). Determination of ONO-2952 K_i or IC_{50} values for the remaining 35 targets (50% inhibition at 10 μM) reveal K_i values of less than 1 μM only for 3 receptors, i.e. melatonin 2, progesterone B, and adrenergic α2C. The affinity of ONO-

	2952 for these receptors is at least 59 times lower than that for TSPO. ONO-2952 K_i value for the $GABA_A$ receptor is more than 600 times higher than that for TSPO[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	ONO-2952 (0.03-3 mg/kg; oral administration; male Sprague Dawley rats) treatment dose-dependently suppresses restraint stress-induced defecation in rats with brain TSPO occupancy of more than 50%. ONO-2952 also suppresses conditioned fear stress-induced freezing behavior in rats[1]. ONO-2952 inhibits both neurosteroid accumulation and noradrenaline release in the brain of rats exposed to acute stress[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male Sprague Dawley rats (8 weeks old) under conditioned fear stress test[1]
Dosage:	0.03 mg/kg, 0.1 mg/kg, 0.3 mg/kg, 1 mg/kg, 3 mg/kg
Administration:	Oral administration
Result:	Dose-dependently suppressed restraint stress-induced defecation in rats. And suppressed conditioned fear stress-induced freezing behavior in rats.

REFERENCES

[1]. Mitsui K, et al. Anti-stress effects of ONO-2952, a novel translocator protein 18 kDa antagonist, in rats. Neuropharmacology. 2015 Dec;99:51-66.

[2]. Whitehead WE, et al. Randomised clinical trial: exploratory phase 2 study of ONO-2952 in diarrhoea-predominant irritable bowel syndrome. Aliment Pharmacol Ther. 2017 Jan;45(1):14-26.

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