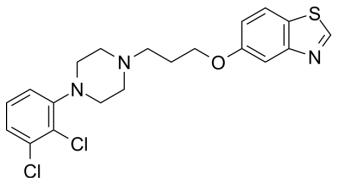
UNC9995

Cat. No.:	HY-120920
CAS No.:	1354030-52-6
Molecular Formula:	$C_{20}H_{21}Cl_2N_3OS$
Molecular Weight:	422.37
Target:	Dopamine 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 : 50 mg/mL (118.38 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3676 mL	11.8380 mL	23.6759 mL
	5 mM	0.4735 mL	2.3676 mL	4.7352 mL
	10 mM	0.2368 mL	1.1838 mL	2.3676 mL

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: ≥ 1.25 mg/mL (2.96 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

UNC9995 is a β-arrestin2-biased agonist of dopamine receptor Drd2. UNC9995 inhibits NLRP3 inflammasome activation by enhancing β-arrestin2-NLRP3 interaction, thus prevents neuronal degeneration. Futhermore, UNC9995 activates the Drd2/β-arrestin2 signaling to prevent inflammation-related genes transcription-induced by JAK/STAT3. UNC9995 improves depressive behavior in mouse model, and improves astrocytes dysfunctions[1].

IC_{50} & Target

D_2 Receptor

In Vitro

UNC9995 (10 μM; 1 h) promotes the combination of STAT3 and β-arrestin2, induced by IL-6 (300 ng/mL; 24 h) in primary astrocytes. And it also inhibits activation of STING, TBK1, JAK[1].

UNC9995 (1, 5, 10, and 20 μM; 1 h) abolishes the apoptosis and inflammation of both WT and $Arrb2^{-/-}$ astrocytes stimulated with IL-6 (300 ng/mL) for 24 h[1].

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

Western Blot Analysis[1]

Cell Line:	Primary astrocytes
Concentration:	10 μM
Incubation Time:	1 h for pre-incubation; with 300 ng/mL IL-6
Result:	Enhanced the interaction between STAT3 and β-arrestin2. Abolished the activation of cGAS-STING and JAK/STAT3 pathway stimulated by IL-6, decreased the level of p-STING, p-TBK1, p-JAK.

In Vivo

UNC9995 (2 mg/kg/day, i.p, 2 weeks) ameliorates depressive-like behavioral phenotype and improves the loss of astrocytes in the hippocampus in both Chronic social defeated stress (CSDS) model and Chronic unpredictable mild stress (CUMS) model in mouse[1].

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

Animal Model:	Chronic unpredictable mild stress (CUMS) mouse model[1]
Dosage:	2 mg/kg/d
Administration:	IP; 2 weeks
Result:	Improved depressive-like symptoms of CUMS mouse model in WT mice but not Arrb2$^{-/-}$ mice.

REFERENCES

[1]. Liu Y, et al. β-Arrestin2-biased Drd2 agonist UNC9995 alleviates astrocyte inflammatory injury via interaction between β-arrestin2 and STAT3 in mouse model of depression. J Neuroinflammation. 2022 Oct 1;19(1):240.

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