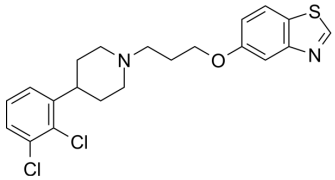
UNC9994

Cat. No.:	HY-117829
CAS No.:	1354030-51-5
Molecular Formula:	$C_{21}H_{22}Cl_2N_2OS$
Molecular Weight:	421.38
Target:	Dopamine Receptor; 5-HT Receptor; Histamine Receptor; Arrestin
Pathway:	GPCR/G Protein; Neuronal Signaling; Immunology/Inflammation
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

UNC9994, an analog of Aripiprazole, is a functionally selective β-arrestin-biased dopamine D2 receptor (D2R) agonist with EC_{50} <10 nM for β-arrestin-2 recruitment to D2 receptors. UNC9994 is simultaneously partial agonists of β-arrestin-2 translocation and antagonists of G_i-regulated cAMP production. Antipsychotic Activity[1].

IC_{50} & Target

D_2 Receptor 79 nM (Ki)	D_3 Receptor 17 nM (Ki)	D_4 Receptor 138 nM (Ki)	5-HT_{2A} Receptor 140 nM (Ki)
5-HT_{2B} Receptor 25 nM (Ki)	5-HT_{2C} Receptor 512 nM (Ki)	5-HT_{1F} Receptor 26 nM (Ki)	H_1 Receptor 2.1 nM (Ki)

In Vitro

UNC9994 displays a lower binding affinity (K_i=79 nM) to D2R than UNC9975, UNC0006, and aripiprazole. At serotonin (as known as 5-HT) receptors, UNC9994 displays moderate to high binding affinities (K_i=25-512 nM) for $5HT_{2A}$, $5HT_{2B}$, $5HT_{2C}$, and $5HT_{1A}$, but is significantly less potent in functional assays (Ca^{2+} mobilization FLIPR or cAMP biosensor). UNC9994 is an antagonist at $5HT_{2A}$ and $5HT_{2B}$ and agonists at $5HT_{2C}$ and $5HT_{1A}$. UNC9994 has relatively high affinities to H_1-histamine receptor (K_i=2.4 nM) but is less potent antagonists in H_1 functional assays[1].

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

In Vivo

The antipsychotic-like activity displayed by UNC9994 (2 mg/kg; i.p.) in wild-type mice is completely abolished in β-arrestin-2 knockout mice[1].

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

Animal Model:	C57BL/6J wild-type and β-arrestin-2 knockout mice (phencyclidine-induced hyperlocomotion)[1]
Dosage:	2 mg/kg
Administration:	I.p. followed 30 min later with 6 mg/kg phencyclidine
Result:	Markedly inhibited PCP-induced hyperlocomotion in wild-type mice. This significant antipsychotic-like activity of UNC9994 was completely abolished in β-arrestin-2 knockout mice.

REFERENCES

[1]. Allen JA, et al. Discovery of β-arrestin-biased dopamine D2 ligands for probing signal transduction pathways essential for antipsychotic efficacy. Proc Natl Acad Sci U S A. 2011;108(45):18488-18493.

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