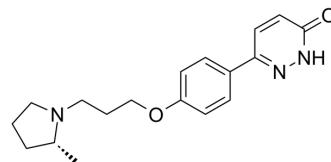


Irdabisant

Cat. No.:	HY-109968
CAS No.:	1005402-19-6
Molecular Formula:	C ₁₈ H ₂₃ N ₃ O ₂
Molecular Weight:	313.39
Target:	Histamine Receptor
Pathway:	GPCR/G Protein; Immunology/Inflammation; Neuronal Signaling
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Irdabisant (CEP-26401) is a selective, orally active and blood-brain barrier (BBB) penetrant histamine H ₃ receptor (H ₃ R) inverse agonist/inverse agonist with K _i values of 7.2 nM and 2.0 nM for rat H ₃ R and human H ₃ R, respectively. Irdabisant has relatively low inhibitory activity against hERG current with an IC ₅₀ of 13.8 μM. Irdabisant has cognition-enhancing and wake-promoting activities in the rat social recognition model. Irdabisant can be used to research schizophrenia or cognitive impairment ^{[1][2]} .										
IC₅₀ & Target	rat H ₃ receptor 7.2 nM (K _i)	human H ₃ receptor 2 nM (K _i)									
In Vitro	<p>Irdabisant (CEP-26401, compound 8a) shows antagonist activity with K_{b, app} values of 1.0 nM and 0.4 nM for rat H₃R and human H₃R, respectively; shows inverse agonist activity with EC₅₀ values of 2.0 nM and 1.1 nM for rat H₃R and human H₃R, respectively^[1].</p> <p>Irdabisant has moderate activity at Muscarinic M₂ (K_i = 3.7 ± 0.0 μM) and Adrenergic α_{1A} (K_i = 9.8 ± 0.3 μM) receptors, Dopamine transporters (K_i = 11 ± 2 μM), Norepinephrine transporters (K_i = 10 ± 1 μM), and phosphodiesterase PDE3 (IC₅₀ = 15 ± 1 μM)^[1].</p> <p>Irdabisant inhibits the cytochrome P450 enzymes CYP1A2, 2C9, 2C19, 2D6, and 3A4 with IC₅₀ values of greater than 30 μM, indicating less potential for drug-drug interactions^[1].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>										
In Vivo	<p>CEP-26401 (0.01-0.3 mg/kg; p.o.; single dosage) dose-dependently inhibits H₃R agonist RAMH-induced dipsogenia^[1].</p> <p>CEP-26401 (0.0001-0.1 mg/kg; i.v. or p.o.; single dosage) improves performance in the rat social recognition model of short-term memory^[1].</p> <p>CEP-26401 (3-30 mg/kg; p.o.; single dosage) exhibits wake-promoting activity in rat^[2].</p> <p>CEP-26401 (3-30 mg/kg; i.p.) increases prepulse inhibition (PPI) in DBA/2NCrI mice^[2].</p> <p>CEP-26401 (1 mg/kg for i.v. and 3 mg/kg for p.o.; single dosage) is rapidly absorbed with high oral bioavailability in rat and monkey, and shows a moderate clearance in monkey and dog compared to the rat^[1].</p> <p>Pharmacokinetic Parameters of Irdabisant (compound 8a) in rats, dogs and monkeys^[1].</p> <table border="1" data-bbox="345 1787 1508 1942"> <thead> <tr> <th></th> <th>Rat</th> <th>Dog</th> <th>Monkey</th> </tr> </thead> <tbody> <tr> <td>i.v. t_{1/2} (h)</td> <td>2.6</td> <td>2.9</td> <td>5.4</td> </tr> </tbody> </table>				Rat	Dog	Monkey	i.v. t _{1/2} (h)	2.6	2.9	5.4
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i.v. V _d (L/kg)	9.4	3.5 ± 1.1	3.8 ± 0.9
i.v. CL (mL/min/kg)	42	13.2 ± 1.5	7.7 ± 1.8
p.o. t _{1/2} (L/kg)	2.9	2.7	5.0
p.o. AUC (ng·h/mL)	984	1190 ± 180	1919 ± 611
p.o. C _{max} (ng/mL)	270	230 ± 70	760 ± 74
p.o. F (%)	83	22 ± 2	83 ± 18
Brain to plasma ratio	2.6 ± 0.2	2.4 ± 0.4	/

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

Animal Model:	Male Sprague-Dawley rats (i.p. 10 mg/kg RAMH-induced dipsogenia model) ^[1]
Dosage:	0.01-0.3 mg/kg
Administration:	p.o.; single dosage
Result:	Dose-dependently inhibited H3R agonist RAMH (HY-100999)-induced dipsogenia (which manifests as water drinking) with an EC ₅₀ value of 0.06 mg/kg.
Animal Model:	Male Sprague-Dawley rats (adult rats were briefly exposed to a juvenile rat for build social recognition model) ^[2]
Dosage:	0.0001, 0.001, 0.01 and 0.1 mg/kg for i.p.; 0.01 and 0.1 mg/kg for p.o.
Administration:	i.v. or p.o.; single dosage
Result:	Effectively reduced the ratio of investigation duration (RID) at doses over the range from 0.001 to 0.1 mg/kg i.p. and at 0.01 and 0.1 mg/kg p.o., demonstrating potent enhancement of short-term sensory memory in this model.
Animal Model:	Male Sprague-Dawley rats ^[2]
Dosage:	3, 10 and 30 mg/kg
Administration:	p.o.; single dosage
Result:	Exhibited robust wake promotion with the treated animals awake 90% of the time up to 3 h postdosing at 30 mg/kg.
Animal Model:	Male DBA/2NCRl mice (19-27 g; 7-9 weeks) ^[2]
Dosage:	3, 10 and 30 mg/kg
Administration:	i.p.; single dosage

Result:	Increased prepulse inhibition (PPI) in DBA/2NCrl mice, whereas the antipsychotic Risperidone (HY-11018) is effective at 0.3 and 1 mg/kg i.p..
Animal Model:	Male Sprague-Dawley rats, male beagle dogs and male cynomolgus monkeys ^[1]
Dosage:	1 mg/kg for i.v. and 3 mg/kg for p.o.
Administration:	i.v. and p.o.
Result:	Exhibited rapid absorption with high oral bioavailability in rat and monkey, and showed a moderate clearance in monkey and dog compared to the rat.

REFERENCES

- [1]. Hudkins RL, et al. Discovery and characterization of 6-{4-[3-(R)-2-methylpyrrolidin-1-yl]propoxy}phenyl)-2H-pyridazin-3-one (CEP-26401, irdabisant): a potent, selective histamine H₃ receptor inverse agonist. *J Med Chem.* 2011 Jul 14;54(13):4781-92.
- [2]. Raddatz R, et al. CEP-26401 (irdabisant), a potent and selective histamine H₃ receptor antagonist/inverse agonist with cognition-enhancing and wake-promoting activities. *J Pharmacol Exp Ther.* 2012 Jan;340(1):124-33.

Caution: Product has not been fully validated for medical applications. For research use only.

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