YM348

Cat. No.: HY-100330

CAS No.: 372163-84-3

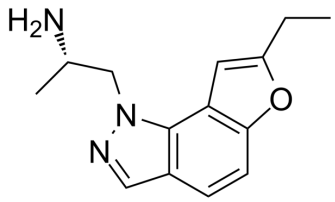
Molecular Formula: $C_{14}H_{17}N_3O$

Molecular Weight: 243.3

Target: 5-HT Receptor

Pathway: GPCR/G Protein; Neuronal Signaling

Storage: 4°C, sealed storage, away from moisture and light
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (411.02 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	4.1102 mL	20.5508 mL	41.1015 mL
	5 mM	0.8220 mL	4.1102 mL	8.2203 mL
	10 mM	0.4110 mL	2.0551 mL	4.1102 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: ≥ 2.5 mg/mL (10.28 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (10.28 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

YM348 is a potent and orally active 5-HT_{2C} receptor agonist, which shows a high affinity for cloned human 5-HT_{2C} receptor (K_i: 0.89 nM).

IC_{50} & Target

5-HT_{2C} Receptor 0.89 nM (Ki)	5-HT_{2B} Receptor 2.5 nM (Ki)	5-HT_{2A} Receptor 13 nM (Ki)	5-HT_{2C} Receptor 1 nM (EC50)
5-HT_{2B} Receptor 3.2 nM (EC50)	5-HT_{2A} Receptor 93 nM (EC50)		

In Vitro

YM348 has high affinity for cloned human 5-HT_{2C} receptors with a K_i value of 0.89 nM and lower affinities for human-cloned 5-HT_{2B} (K_i: 2.5 nM) and 5-HT_{2A} receptors (K_i: 13 nM). To assess the binding specificity of YM348, a broad evaluation of an

	additional 46 binding sites including several other 5-HT receptor subtypes (1A, 1B, 1D, 3, 4, 5A, 6, 7) is performed. IC_{50} values of YM348 are found to be >1 μM for all of the binding sites except for the human 5-HT_{1A} receptors (K_i: 130 nM), bovine 5-HT_{1D} receptors (K_i: 481 nM), human 5-HT_7 receptors (K_i: 177 nM), and human α_{2A} receptors (K_i: 126 nM).YM348 exhibits a full-agonistic activity on human 5-HT_{2A} and 5-HT_{2B} receptors. The EC_{50} values of YM348 for 5-HT_{2C}, 5-HT_{2A}, and 5-HT_{2B} receptors are 1.0, 93 and 3.2 nM, respectively[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Oral administration of YM348 induces penile erections and hypolocomotion in rats, being completely inhibited by a selective 5-HT_{2C} receptor antagonist, SB242084. YM348 inhibits spontaneous activity in a dose-dependent manner with a minimum effective dose of 0.203 mg/kg[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Experiments are performed with membranes obtained from Chinese Hamster Ovary (CHO) cells expressing human 5-HT_{2C} or 5-HT_{2A} receptors and Human Embryonic Kidney 293-Epstein-Barr virus nuclear antigen (HEK293-EBNA) cells expressing human 5-HT_{2B} receptors. Binding assays with [^{3}H] 5-HT are carried out. The reaction medium (50 mM Tris-HCl buffer (pH 7.4) containing 4 mM $CaCl_2$, 10 M pargyline and 0.1 mg/ml L-(+)-ascorbic acid) containing [^{3}H] 5-HT, membrane preparation and test compounds are incubated at 37°C for 30 min. Nonspecific binding is determined in the presence of 10 M 5-HT, and specific binding is calculated as the total binding minus the nonspecific binding. After incubation, 4 mL of 50 mM Tris-HCl buffer (pH 7.4) containing 4 mM $CaCl_2$ is added, and the medium is filtrated under decompression through a Whatman GF/B glass filter pretreated with 0.1% polyethyleneimine. The filter is washed with the same buffer solution (4 mL×3). The glass filter is immersed in 6 mL of liquid scintillator (Packard, Aquasol-2), and the radioactivity is measured with a liquid scintillation counter. The amount of protein is measured. The dissociation constants (K_d values) are obtained by Scatchard analysis using SAS (ver. 6.11). The concentrations of compounds showing 50% inhibition of receptor binding, IC_{50} values, are obtained by nonlinear analysis using SAS (ver. 6.11). The Ki values indicating affinity for receptors are calculated[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Rats[1] Male Wistar rats (215-350 g) are used. Rats are administered YM348 (0.0677, 0.203, 0.677, and 2.03 mg/kg) orally and moved again to their home cages. After 20 min, thereafter, the rats are individually placed in transparent acrylic plastic cages (35×30×18 cm), and their motor activity is measured for 40 min. The measurements are carried out using a SUPER-MEX sensor. SB242084 (0.1-3 mg/kg i.p.) is administered 30 min before YM348 treatment. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Kimura Y, et al. Pharmacological profile of YM348, a novel, potent and orally active 5-HT_{2C} receptor agonist. Eur J Pharmacol. 2004 Jan 1;483(1):37-43.

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