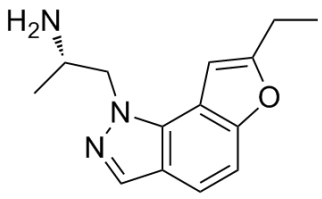
YM348

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:	Please store the product under the recommended conditions in the COA.



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].
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].

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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