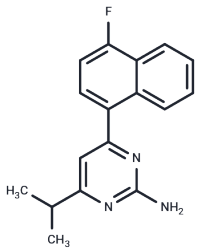
Data Sheet (Cat.No.T6973)

TargetMol

RS-127445

Chemical Properties



CAS No. : 199864-87-4

Formula: C17H16FN3

Molecular Weight: 281.33

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	RS-127445 (MT500) is a selective 5-HT2B receptor antagonist with pKi of 9.5 and pIC50 of 10.4, exhibits >1000-fold selectivity against other 5-HT receptors.
Targets(IC50)	5-HT Receptor
In vitro	RS-127445 is a novel high affinity, selective 5-HT2B receptor antagonist devoid of detectable intrinsic activity. RS-127445 is found to have nM affinity and 1000 fold selectivity for the 5-HT2B receptor. RS-127445 is thus among the highest affinity, most selective 5- HT2B receptor ligands. RS-127445 potently blocks the 5-HT evoked increase in inositol phosphate formation and blocks the 5-HT evoked increases in intracellular calcium concentrations with a potency 1000 times greater than that of yohimbine. [1]
In vivo	RS-127445 is readily absorbed with no obvious dose or route-dependent limitations and rapidly absorbed following both oral and intraperitoneal administration with peak plasma concentrations being achieved within 15 min of dosing. RS-127445 concentration in the plasma are proportional to the administered dose. RS-127445 administrated at dose of 5 mg/kg with approximately 60% of an intraperitoneal dose and 14% of the oral dose is bioavailable. RS-127445 concentration in the plasma is predicted to fully saturate accessible 5-HT2B receptors can be readily achieved and maintained in the rat. RS-127445 administered at 1 to 10 mg/kg with oral significantly inhibits visceral hypersensitivity up to 35 to 74% provoked by restraint stress. Oral RS-127445 produces a significant suppression of TNBS-induced visceral hypersensitivity (15 to 62% inhibition at 3 to 30 mg/ kg), although RS-127445 has no significant effect on the visceral nociceptive threshold of native rats. RS-127445 administrated orally with 1 to 30 mg/kg also dose -dependently reduce the restraint stress-induced defecation in native and TNBS-treated rats. [2]. RS-127445 inhibits colonic motility and defecation. [3]
Kinase Assay	Radioligand binding: The selectivity of RS-127445 for 5-HT2B receptors is examined by testing the compound for affinity at over 100 additional ion channel or receptor binding sites. CHO-K1 cells expressing human 5-HT2A, 5-HT2B or 5-HT2C receptors are harvested using 2 mM EDTA in phosphate buffered saline. Cell membranes are prepared by four cycles of homogenization and centrifugation (48,000×g for 15 min). Each assay is established so as to achieve steady state conditions and to optimize specific binding. For the 5-HT2A receptor, membranes from 1×106 cells are incubated with 0.2 nM [3 H]-ketanserin at 32 °C for 60 min. Nonspecific binding is determined using 10 μM methysergide. For the 5-HT2B receptor, membranes from 1.5×106 cells are incubated

Kinase Assay	with 0.2 nM [3 H]-5-HT at 48 °C for 120 min. Nonspecific binding is determined using 10 μM 5-HT. For the 5-HT2Creceptor, membranes from 3×10 5 cells are incubated with 0.5 nM [3 H]-mesuler -gine at 32 °C for 60 min. Nonspecific binding is determined using 10 μM methysergide. Assays are terminated by vacuum filtration through glass fibre filters (GF/B) which has been pretreated with 0.1% polyethyleneimine. Total and bound radioactivity is determined by liquid scintillation counting. Greater than 90% specific binding is achieved in each of these assays.
Cell Research	RS-127445, vehicle or other antagonists are pre-incubated with 240 μl of HEK-293 cells expressing the human 5-HT2B receptor suspension at 37 °C for 20 min. HEK-293 cells are incubated with[3H]-myoinositol (1.67 μCi/ml) in 162 cm2 flasks overnight at 37 °C in an inositol free Ham's F12 medium containing 10% dialyzed foetal bovine serum. The cells are harvested, washed five times with phosphate bufffered saline and resuspended in inositol free Ham's F12 media at density of approximately 3×103 cells/ml. The reactions are initiated by addition of 5-HT. Sixty minutes later, the reactions are terminated by adding 50 μl of ice-cold 20% perchloric acid, chilled in an ice-water bath for 10 min and then neutralized with 160μl of 1 N KOH. Each sample is diluted with 2 ml of 50 mM Tris-HCl, pH 7.4 at room temperature. The aqueous portion (2.2 ml) is transferred onto Dowex AG1X8 columns (1 ml, 1 : 1, w/v) which has been washed with 5 ml of distilled water. The columns are then washed with 18 ml of distilled water and the inositol phosphates are eluted with 3 ml of 1 N HCl. The eluted radioactivity is determined by liquid scintillation spectroscopy using a Packard 1900CA analyzer. [1] (Only for Reference)

Solubility Information

Solubility	Ethanol: 8 mg/mL (28.44 mM),Sonication is recommended. DMSO: 52 mg/mL (184.84 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 1 mg/mL (3.55 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	3.5545 mL	17.7727 mL	35.5454 mL
5 mM	0.7109 mL	3.5545 mL	7.1091 mL
10 mM	0.3555 mL	1.7773 mL	3.5545 mL
50 mM	0.0711 mL	0.3555 mL	0.7109 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Douglas W Bonhaus, et al. Br J Pharmacol, 1999, 127(5), 1075-1082.
Ohashi-Doi K, et al. Neurogastroenterol Motil, 2010, 22(2),e69-e76.
Bassil AK, et al. Br J Pharmacol, 2009, 158(1), 252-258.

Tel:781-999-4286 E_mail:info@targetmol.com Address:34 Washington Street,Wellesley Hills,MA 02481