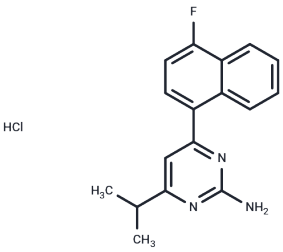
Data Sheet (Cat.No.T7519)

TargetMol

RS-127445 hydrochloride

Chemical Properties



CAS No. : 199864-86-3

Formula: C17H17ClFN3

Molecular Weight: 317.79

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 hydrochloride (MT 500) is a selective, high affinity, orally bioavailable 5-HT2B receptor antagonist(pKi : 9.5).
Targets(IC50)	5-HT Receptor
In vitro	RS 127445 potently displaced [3H]-5-HT from human recombinant 5-HT2B receptors expressed in CHO-K1 cells.?The affinity (pKi value) of RS-127445 for the 5-HT2B receptor was 9.5±0.1 (n=9).?RS-127445 was selective for the 5-HT2B receptor, having approximately 1000 fold lower affinity for the human?recombinant 5-HT2A, 5-HT2C, 5-HT5, 5-HT6 and 5-HT7 receptors, a 5-HT1A receptor in rat brain membranes, a 5-HT1B/D receptor in bovine caudate, and a monoamine uptake site in rabbit platelets[1]
In vivo	RS 127445 (5 mg kg^?1) was administered to rats by oral, intraperitoneal and intravenous routes.?Peak plasma concentrations were rapidly achieved with the highest concentrations being found at the first time-point measured following intravenous and intraperitonael administration (0.08 h) and by 0.25 h following dosing by the oral route of administration.?RS-127445 was cleared from plasma with an estimated terminal elimination half-life of approximately 1.7 h. The bioavailability of RS-127445, when administered by the oral and intraperitoneal routes was approximately 14 and 62% of that obtained by intravenous administration .?To test?whether plasma levels were proportional to the dose administered, RS-127445 was given by the intraperitoneal route at doses of 1, 3 and 10 mg kg^?1.?Increasing the dose of RS-127445 resulted in proportional increases in its concentration in the plasma[1]
Animal Research	Rats were euthanized.?Right and left external jugular veins were dissected, cleaned of connective tissues and cut into ring segments approximately 5 mm long.?Tungsten hooks (0.125 mm diameter) were inserted through the lumen of the vein and connected to tension transducers.?Tissues were kept in 10 ml organ baths containing Kreb's solution supplemented with cocaine (30 μm), corticosterone (30 μm), ketanserin (0.3 μm) and indomethacin (3 μm) at 37°C at a resting tension of 0.5 g.?Prior to the initiation of any studies, monamine oxidases were inactivated by a 30 min pre exposure of the tissue to pargyline (0.1 mm).?The veins were then exposed to 0.1 μm U46619 (9,11-dideoxy-9 α, 11 aα-methano-epoxy-PGF2α;?a thromboxane A2 mimetic) until a stable contraction was attained.?Acetylcholine (0.1 μm) was used to verify the integrity of the endothelium and to determine the maximum amount of nitric?oxide-dependent relaxation that was achievable.?After washout of the acetylcholine and recontraction

Animal Research	with U46619, cumulative concentration-response curves to (±)-α-methyl-5-HT were constructed.?When maximum relaxation was reached, the baths were rinsed, and the tissues were maintained undisturbed for 2 h. Antagonists (RS 127445)were then added to the bath and allowed to equilibrate with the tissue for at least 1 h before a second concentration-response curve to (±)-α-methyl-5-HT was generated[1].

Solubility Information

Solubility	DMSO: 31 mg/mL (97.55 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (6.29 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	3.1467 mL	15.7337 mL	31.4673 mL
5 mM	0.6293 mL	3.1467 mL	6.2935 mL
10 mM	0.3147 mL	1.5734 mL	3.1467 mL
50 mM	0.0629 mL	0.3147 mL	0.6293 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

Bonhaus D W , Flippin L A , Greenhouse R J , et al. RS-127445: a selective, high affinity, orally bioavailable 5-HT2B receptor antagonist[J]. 1999, 127(5):1075-1082.

Devroye, Céline, Haddjeri N , Cathala A , et al. Opposite control of mesocortical and mesoaccumbal dopamine pathways by serotonin 2B, receptor blockade: Involvement of medial prefrontal cortex serotonin 1A, receptors[J]. Neuropharmacology, 2017, 119:91-99.