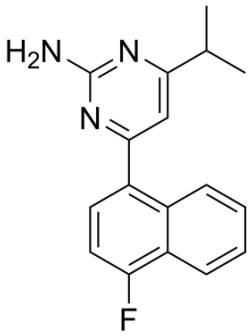
RS-127445

Cat. No.:	HY-15419A
CAS No.:	199864-87-4
Molecular Formula:	$C_{17}H_{16}FN_3$
Molecular Weight:	281.33
Target:	5-HT Receptor
Pathway:	GPCR/G Protein; Neuronal Signaling
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	RS-127445 is a selective, high affinity, orally bioavailable 5-HT_{2B} receptor antagonist with a pK_i of 9.5. RS-127445 shows 1000 fold selectivity for this receptor as compared to numerous other receptor and ion channel binding sites[1].
IC_{50} & Target	5-HT_{2B} Receptor 9.5 nM (pKi)
In Vitro	RS-127445 is found to has nanomolar affinity for the 5-HT_{2B} receptor (pK_i=9.5±0.1) and 1,000 fold selectivity for this receptor as compared to numerous other receptor and ion channel binding sites. RS-127445 potently displaces [^{3}H]-5-HT from human recombinant 5-HT_{2B} receptors expressed in CHO-K1 cells. The affinity (pK_i value) of RS-127445 for the 5-HT_{2B} receptor is 9.5±0.1 (n=9). RS-127445 is selective for the 5-HT_{2B} receptor, having approximately 1000 fold lower affinity for the human recombinant 5-HT_{2A}, 5-HT_{2C}, 5-HT_5, 5-HT_6 and 5-HT_7 receptors, a 5-HT_{1A} receptor in rat brain membranes, a 5-$HT_{1B/D}$ receptor in bovine caudate, and a monoamine uptake site in rabbit platelets. RS-127445 potently blocks the 5-HT (10 nM) evoked increases in intracellular calcium concentrations in the HEK-293 cells expressing the 5-HT_{2B} receptor (pIC_{50} of 10.4±0.1). In cells expressing human recombinant 5-HT_{2B} receptors, RS-127445 potently antagonizes 5-HT-evoked formation of inositol phosphates (pK_B=9.5±0.1) and 5-HT-evoked increases in intracellular calcium (pIC_{10}=10.4±0.1). RS-127445 also blocks 5-HT-evoked contraction of rat isolated stomach fundus (pA_{2B}=9.5±1.1) and (±)α-methyl-5-HT-mediated relaxation of the rat jugular vein (pA_2=9.9±0.3)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	In rats, the fraction of RS-127445 that is bioavailable via the oral or intraperitoneal routes is 14 and 60% respectively. Intraperitoneal administration of RS-127445 (5 mg/kg) produced plasma concentrations predicted to fully saturate accessible 5-HT_{2B} receptors for at least 4 h.RS-127445 (5 mg/kg) is administered to rats by oral, intraperitoneal and intravenous routes. Peak plasma concentrations are 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 is 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 is approximately 14 and 62% of that obtained by intravenous administration. Approximately 60% of an intraperitoneal dose and 14% of the oral dose of RS-127445 (5 mg/kg) is bioavailable[1]. RS-127445 (1-30 mg/kg), dose-dependently reduces faecal output, reaching significance at 10 and 30 mg/kg (n=6-11). In blood and brain, >98% of RS-127445 is protein-bound[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Bonhaus DW, et al. RS-127445: a selective, high affinity, orally bioavailable 5-HT2B receptor antagonist. Br J Pharmacol. 1999 Jul;127(5):1075-82.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA