Product Data Sheet

Product Name: RS 127445
Cat. No.: GC11729

Chemical Properties

Cas. No.	199864-87-4		
Chemical Name	4-(4-fluoronaphthalen-1-yl)-6-isopropylpyrimidin-2-amine		
SMILES	FC1=CC=C(C2=CC(C(C)C)=NC(N)=N2)C3=CC=CC=C31		
Formula	$C_{17}H_{16}FN_3$	M.Wt	281.33
Solubility	≥ 15.89mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	RS 127445		

Protocol

Animal experiment [1]:

Animal models	Adult male C57BL/6J mice

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Preparation Method	Animals were given the test compound (RS 127445 1, 3, 10 or 30mg/kg) or vehicle (10% ethanol, 40% polyethylene glycol, 50% distilled H_2O) intraperitoneally in a final dose volume of 3mL/kg. Following drug administration, animals were returned to the home cage. Three hours following treatment, the faecal output was collected and weighed; pellets were collected onto paper tray liners, to minimize contamination from urine or water. Because of a high variability in the numbers and sizes of faecal pellets excreted by individual rats, the results are expressed as the mean wet weight SEM of pellets excreted.
Dosage form	1, 3, 10 or 30mg/kg; i.p.
Applications	RS 127445 (1-30 mg/kg), dose-dependently reduced faecal output, reaching significance at 10 and 30mg/kg.

References:
[1]Bassil A K, Taylor C M, Bolton V J N, et al. Inhibition of colonic motility and defecation by RS-127445 suggests an involvement of the 5-HT2B receptor in rodent large bowel physiology[J]. British journal of pharmacology, 2009, 158(1): 252-258.

Background

RS 127445 is an orally active, highly selective 5-HT_{2B} receptor antagonist with a pK_i of 9.5 and a selectivity for 5-HT_{2B} that is more than 1000 times greater than that for other

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related receptors such as 5-HT_{2A} and 5-HT_{2C}[1, 2]. 5-HT_{2B} receptors play important roles in the central and peripheral nervous systems, participating in the regulation of various physiological functions, such as cardiovascular effects and neuronal sensitization[3]. RS 127445 can inhibit dopamine neurotransmission in the nucleus accumbens[4].

In vivo, intraperitoneal injection of RS 127445 (1-30mg/kg) in mice significantly inhibited intestinal peristalsis and reduced fecal output in a dose-dependent manner[5]. RS 127445 (10mg/kg) significantly inhibited visceral hypersensitivity induced by restraint stress in experimental visceral hypersensitivity rats when administered orally, with an inhibition rate of 74%, and also reduced defecation[6].

References:
[1] Bonhaus D W, Flippin L A, Greenhouse R J, et al. RS-127445: a selective, high affinity, orally bioavailable 5-HT2B receptor antagonist[J]. British journal of pharmacology, 1999, 127(5): 1075-1082.
[2] Maroteaux L. Gene structure, expression, and 5-HT2B receptor signaling[M]//5-HT2B Receptors: From Molecular Biology to Clinical Applications. Cham: Springer International Publishing, 2021: 1-32.
[3] Monassier L. 5-HT2B Receptor, the Heart and Blood Vessels[M]//5-HT2B Receptors: From Molecular Biology to Clinical Applications. Cham: Springer International Publishing, 2021: 153-163.
[4] Cathala A, Devroye C, Robert É, et al. Serotonin2B receptor blockade in the rat dorsal raphe nucleus suppresses cocaine-induced hyperlocomotion through an opposite control of mesocortical and mesoaccumbens dopamine pathways[J]. Neuropharmacology, 2020, 180: 108309.
[5] Bassil A K, Taylor C M, Bolton V J N, et al. Inhibition of colonic motility and defecation by RS-127445 suggests an involvement of the 5-HT2B receptor in rodent large bowel physiology[J]. British journal of pharmacology, 2009, 158(1): 252-258.
[6] Ohashi-Doi K, Himaki D, Nagao K, et al. A selective, high affinity 5-HT2B receptor antagonist inhibits visceral hypersensitivity in rats[J]. Neurogastroenterology & Motility, 2010, 22(2): e69-e76.