F-15599

Cat. No.: HY-19863

CAS No.: 635323-95-4

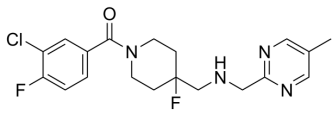
Molecular Formula: $C_{19}H_{21}ClF_2N_4O$

Molecular Weight: 394.85

Target: 5-HT Receptor

Pathway: GPCR/G Protein; Neuronal Signaling

Storage: 4°C, protect from light
* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (633.15 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5326 mL	12.6630 mL	25.3261 mL
	5 mM	0.5065 mL	2.5326 mL	5.0652 mL
	10 mM	0.2533 mL	1.2663 mL	2.5326 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.17 mg/mL (5.50 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.17 mg/mL (5.50 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.17 mg/mL (5.50 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

F-15599 is a highly selective G-protein biased 5-HT1A receptor agonist, with K_i of 3.4 nM.

IC_{50} & Target

$5\text{-}HT_{1A}$ Receptor
3.4 nM (Ki)

In Vivo

F15599 (0.06 or 0.12 mg/kg) significantly reduces l-DOPA-induced dyskinesia (LID), without affecting motor performance of rats. Rats treated with F15599 manifest less LID and mild 5-HT syndrome with the high dose of 30 μg/μL[1]. F15599 (0.0625, 0.125, 0.25, 0.5 and 1.0 mg/kg, i,p,) results in a significant and dose-dependent (MED = 0.125 mg/kg) delay in the latency to attack, and a potent reduction (ID_{50} = 0.095 mg/kg) in the amount of aggressive behaviour directed towards the intruder rat.

Starting from the 0.25 mg/kg dose, F15599 induces clear signs of the so-called serotonin syndrome characterized by flat body posture, head-waving, lower lip retraction and hindlimb abduction, leading to increased behavioural inactivity scores and social disengagement[2]. F15599 increases the discharge rate of pyramidal neurones in medial prefrontal cortex (mPFC) from 0.2 μg/kg i.v and reduces that of dorsal raphe 5-hydroxytryptaminergic neurones at doses >10-fold higher (minimal effective dose 8.2 μg/kg i.v.). F15599 increases dopamine output in mPFC (an effect dependent on the activation of postsynaptic 5-HT1A receptors) with an ED_{50} of 30 μg/kg i.p., whereas it reduces hippocampal 5-HT release (an effect dependent exclusively on 5-HT1A autoreceptor activation) with an ED_{50} of 240 μg/kg i.p[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [2]

Briefly, in this paradigm, male rats are housed individually in large observation cages (80 × 55 × 50 cm) with an oviduct-ligated female to avoid social isolation and allow sexual behaviour, thereby facilitating territorial behaviour. After 1 week, the baseline level of offensive aggressive behaviour is tested on 3 consecutive days during maximally a 10-min confrontation with an unfamiliar male conspecific (WTG rats). The female partner of the experimental rat is removed from the home observation cage approximately 60 min prior to the start of this social provocation test. Naive male WTG rats, socially housed in groups of 3 in transparent makrolon type IV cages, are used as conspecific intruder animals (average weight 372 ± 9.5 g and 3.5-4 months old). During the first 3 tests, the intruder is removed immediately after the first full attack from the resident and the attack latency time (ALT) is noted. Experimental groups are balanced on the basis of the ALT and the level of offensive behaviour performed during the fourth baseline test (day 4), during which the full range of behaviours is recorded and analysed. Only animals that attacked (i.e. ALT <600 s) are included in the experimental groups. Non-attacking individuals (11 out of 144) are excluded from this study. On the next day (day 5), vehicle (sterile Ultra Pure water, n = 19 and n = 20) or either F15599 (0.0625, 0.125, 0.25, 0.5 and 1.0 mg/kg, IP, experiment 1, n = 45) or F13714 (0.003, 0.006, 0.012, 0.025, 0.062, 0.125, 0.250, IP, experiment 2, n = 50) is administered 30 min before the 10 min confrontation with a drug-free unfamiliar intruder conspecific and their behaviour is recorded again. In addition, in experiment 3, animals are tested 30 min after treatment with either vehicle/vehicle (UP), vehicle/F15599 (0.1 mg/kg) or F13714, WAY-100635 (0.3 mg/kg)/vehicle or WAY100635 (0.3 mg/kg)/ F15599 (0.1 mg/kg) or F13714. Each treatment group consists of 6-8 subjects (n = 41 animals total).

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CUSTOMER VALIDATION

- Pharmacol Biochem Behav. 2024 Mar 8:173749.
- Mol Pharmacol. 2023 Nov;104(5):230-238.

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REFERENCES

[1]. Meadows SM, et al. Characterizing the differential roles of striatal 5-HT1A auto- and hetero-receptors in the reduction of l-DOPA-induced dyskinesia. Exp Neurol. 2017 Jun;292:168-178.

[2]. de Boer SF, et al. Anti-aggressive effects of the selective high-efficacy 'biased' 5-HT?A receptor agonists F15599 and F13714 in male WTG rats. Psychopharmacology (Berl). 2016 Mar;233(6):937-47.

[3]. Lladó-Pelfort L, et al. Preferential in vivo action of F15599, a novel 5-HT(1A) receptor agonist, at postsynaptic 5-HT(1A) receptors. Br J Pharmacol. 2010 Aug;160(8):1929-40.

Caution: Product has not been fully validated for medical applications. For research use only.

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