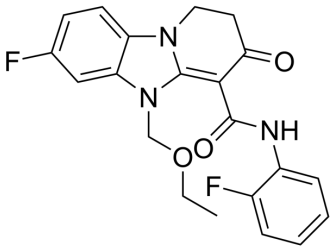
RWJ-51204

Cat. No.:	HY-19308
CAS No.:	205701-85-5
Molecular Formula:	$C_{21}H_{19}F_2N_3O_3$
Molecular Weight:	399.39
Target:	GABA Receptor
Pathway:	Membrane Transporter/Ion Channel; Neuronal Signaling
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	RWJ-51204 is a partial agonist of GABA(A) receptor, with K_i of 0.2-2 nM to the benzodiazepine site on GABA(A) receptors.
IC_{50} & Target	Ki: 0.2-2 nM (GABA(A))[1]
In Vitro	RWJ-51204 binds to receptors in the cerebral cortex, cerebellum, or medulla-spinal cord with K_i ranging from 0.2 to 0.6 nM. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	RWJ-51204 is orally active in anxiolytic efficacy tests. WJ 51204 dose-relatedly antagonizes PTZ-induced clonic convulsions when administered orally (ED_{50} = 0.04 mg/kg). RWJ-51204 is effective in the conflict test in monkeys (ED_{50} of approximately 0.5 mg/kg p.o.). RWJ-51204 potently impairs rotarod performance in rats (ED_{50} = 0.12 mg/kg), and all rats given RWJ-51204 orally at 30 mg/kg exhibit sedation, reduced skeletal muscle tone, and impairment of rotarod performance. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	For each sample, a portion of the membrane fraction containing 0.1 to 0.2 mg of protein is incubated in 2 mL of a 3 mM phosphate-buffered solution containing 0.1 M NaCl and 0.01 to 0.03 μCi of a ^{3}H-labeled ligand [^{3}H]Ro15-4513, [^{3}H]flumazenil. The receptor-ligand binding reaction is allowed to reach equilibrium at an ambient temperature of 21-23°C (30 min) and then the reaction is terminated by vacuum filtration to separate the incubation medium from the biological membranes. The membrane samples are washed to remove unbound ligand. The^{3}H bound to each membrane sample is quantified using liquid scintillation spectrometry. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Adult rats are deprived of water for 48 h and are deprived of food for at least 16 h before testing. After the first 24 h of water deprivation, they are placed in a sound-attenuating chamber for a training period, in which they are allowed 200 licks from a bottle containing tap water. The experiment is performed the next day. Vehicle or compounds are administered orally by gavage, and at specified times after dosing, rats are placed in the chamber and allowed access to tap water. The first lick at the stainless steel sipper tube of a water bottle initiates a 3-min test session in which every 20th lick is punished by a 0.2 s, 0.5 mA shock (root mean square, measured across the electrodes) delivered via the sipper tube. If rats fail to drink within 5 min, the experiment is terminated, and they are evaluated for signs of CNS depression. Rats are not reused in this experiment. The anxiolytic effectiveness of a compound in this assay is determined from the number of rats, at each dose,

	that receive a number of shocks that is equal to or greater than the calculated 90th percentile of the number of shocks received by approximately 600 vehicle-treated rats. This criterion is eight shocks when rats are tested 1 h after administration and 10 shocks when rats are tested 4 h after administration. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Dubinsky B, et al. 5-ethoxymethyl-7-fluoro-3-oxo-1,2,3,5-tetrahydrobenzo[4,5]imidazo[1,2a]pyridine-4-N-(2-fluorophenyl)carboxamide (RWJ-51204), a new nonbenzodiazepine anxiolytic. J Pharmacol Exp Ther. 2002 Nov;303(2):777-90.

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