GBR 12935 dihydrochloride

Cat. No.: HY-12242

CAS No.: 67469-81-2

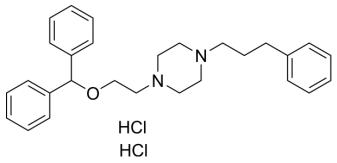
Molecular Formula: $C_{28}H_{36}Cl_2N_2O$

Molecular Weight: 487.5

Target: Dopamine Transporter

Pathway: Neuronal Signaling

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (51.28 mM; Need ultrasonic)
H_2O : 7.14 mg/mL (14.65 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0513 mL	10.2564 mL	20.5128 mL
5 mM	0.4103 mL	2.0513 mL	4.1026 mL
10 mM	0.2051 mL	1.0256 mL	2.0513 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: ≥ 2.5 mg/mL (5.13 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.13 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.13 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GBR 12935 dihydrochloride is a potent, and selective dopamine reuptake inhibitor, with the binding constant (K_d) of 1.08 nM in COS-7 cells. GBR 12935 dihydrochloride stimulates the locomotion activity in different mice strains but fails to induce stereotypy. Thus, GBR 12935 dihydrochloride also prevents the d-Fenfluramine-induced head-twitch response in mice[1][2][3][4].

In Vitro

GBR 12909 (10-100 nM) also shows a high affinity for CYP2D6 with the K_d value of 42.2 nM, lower than the affinity for dopamine transporter. The binding effect can be reduced by Quinidine (HY-B1751) and Quinine (HY-D0143), which are the specific and potent inhibitors of CYPZD enzymatic activities[1].

GBR 12935 dihydrochloride (10 nM; 2 min) increases the extracellular levels of dopamine to approximately 400% of basal during the application in the nucleus accumbens[2].
GBR 12935 dihydrochloride (100 μM; 60 min) increases extracellular levels of dopamine compared with levels for artificial cerebrospinal fluid (ACSF) by local perfusion for 60 min[2].
GBR 12935 dihydrochloride (1-9 nM) dose-dependently inhibits active uptake of [^{3}H]dopamine in homogenates of the nucleus accumbens[2].
Co-perfusion of 100 μM GBR 12935 dihydrochloride with either 100 μM Sulpiride (HY-B1019) or Raclopride (HY-103414) produces a significant reduction in the GBR 12935 dihydrochloride induced increase in the extracellular levels of dopamine to basal levels[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

GBR 12935 dihydrochloride (1-32 mg/kg; repeat injection; 7 d) elevates locomotion activity to a greater extent in C57BL/6J mice than DBA/2J mice, and (10 mg/kg; injection; 7 d) results few mice sensitized to cocaine-induced stereotypy with repeated injections[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Adult male DBA/2J and C57BL/6J mice (22-30 g)[3]
Dosage:	1.0, 3.2, 10, 32 mg/kg
Administration:	Repeat injection; for 7 days
Result:	Elevated locomotion activity to a greater extent in C57BL/6J mice than DBA/2J mice. No stereotypy was induced by an eighth day challenge of 10 mg/kg GBR 12935 dihydrochloride in mice pretreated with seven dally injections of either 32 mg/kg cocaine or saline.

REFERENCES

[1]. Hiroi T, et al. Specific binding of 1-[2-(diphenylmethoxy)ethyl]-4-(3-phenyl propyl) piperazine (GBR-12935), an inhibitor of the dopamine transporter, to human CYP2D6. Biochem Pharmacol. 1997 Jun 15;53(12):1937-9.

[2]. Rahman S, et al. Negative interaction of dopamine D2 receptor antagonists and GBR 12909 and GBR 12935 dopamine uptake inhibitors in the nucleus accumbens. Eur J Pharmacol. 2001 Feb 23;414(1):37-44.

[3]. Tolliver BK, et al. Comparison of cocaine and GBR 12935: effects on locomotor activity and stereotypy in two inbred mouse strains. Pharmacol Biochem Behav. 1994 Jul;48(3):733-9.

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