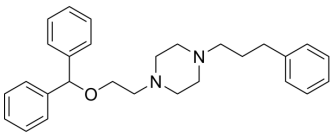
GBR 12935

Cat. No.:	HY-12242A
CAS No.:	76778-22-8
Molecular Formula:	$C_{28}H_{34}N_2O$
Molecular Weight:	414.58
Target:	Dopamine Transporter
Pathway:	Neuronal Signaling
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

GBR 12935 is a potent, and selective dopamine reuptake inhibitor, with the binding constant (K_d) of 1.08 nM in COS-7 cells. GBR 12935 stimulates the locomotion activity in different mice strains but fails to induce stereotypy. Thus, GBR 12935 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 (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 (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 (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 with either 100 μM Sulpiride (HY-B1019) or Raclopride (HY-103414) produces a significant reduction in the GBR 12935 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 (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].

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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 in mice pretreated with seven dally injections of either 32 mg/kg cocaine or saline.

REFERENCES

[1]. Darmani NA. Cocaine and selective monoamine uptake blockers (sertraline, nisoxetine, and GBR 12935) prevent the d-fenfluramine-induced head-twitch response in mice. Pharmacol Biochem Behav. 1998 May;60(1):83-90.

[2]. 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.

[3]. 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.

[4]. 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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