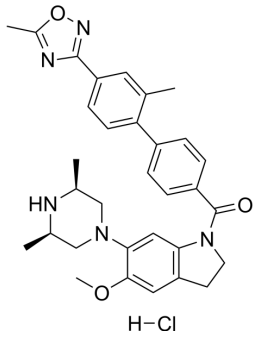
SB-616234-A

Cat. No.:	HY-19477
CAS No.:	908601-49-0
Molecular Formula:	$C_{32}H_{36}ClN_5O_3$
Molecular Weight:	574.11
Target:	5-HT Receptor
Pathway:	GPCR/G Protein; 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 : 10 mg/mL (17.42 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7418 mL	8.7091 mL	17.4183 mL
	5 mM	0.3484 mL	1.7418 mL	3.4837 mL
	10 mM	0.1742 mL	0.8709 mL	1.7418 mL

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

BIOLOGICAL ACTIVITY

Description

SB-616234-A is a selective and orally bioavailable 5-HT1B receptor antagonist, with anxiolytic and antidepressant activity.

IC_{50} & Target

$5\text{-}HT_{1B}$ Receptor

In Vitro

SB-616234-A possesses high affinity for human 5-HT1B receptors stably expressed in Chinese hamster ovary (CHO) cells (pK_i 8.3 ± 0.2), and is over 100-fold selective for a range of molecular targets except h5-HT1D receptors (pK_i 6.6 ± 0.1). Similarly, affinity (pK_i) for rat and guinea pig striatal 5-HT1B receptors is 9.2 ± 0.1. In [^{35}S]-GTPγS binding studies in the human recombinant cell line, SB-616234-A acts as a high affinity antagonist with a pA_2 value of 8.6 ± 0.2 whilst providing no evidence of agonist activity in this system. In [^{35}S]-GTPγS binding studies in rat striatal membranes, SB-616234-A acts as a high affinity antagonist with an apparent pK_B of 8.4 ± 0.5, again whilst providing no evidence of agonist activity in this system. SB-616234-A (1 μM) potentiates electrically stimulated [^{3}H]-5-HT release from guinea pig and rat cortical slices (S2/S1 ratios of 1.8 and 1.6, respectively)[2].

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

In Vivo

SB-616234-A reverses the 5-HT1/7 receptor agonist, SKF-99101H-induced hypothermia in guinea pigs in a dose related manner with an ED_{50} of 2.4 mg/kg p.o. SB-616234-A produces dose-related anxiolytic effects in both rat and guinea pig maternal separation-induced vocalisation models with an ED_{50} of 1.0 and 3.3 mg/kg i.p., respectively[1]. SB-616234-A (0.3-30

mg/kg p.o.) causes a dose-dependent inhibition of ex vivo [^{3}H]-GR125743 binding to rat striatal 5-HT1B receptors with an ED_{50} of 2.83 ± 0.39 mg/kg p.o[1].

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PROTOCOL

Animal Administration [1]

Seven days post surgery animals are placed in microdialysis cages for overnight habituation prior to microdialysis experimentation. The following morning microdialysis probes (2 mm cuprophane membrane) are implanted, via the guide cannulae, into the frontal cortex and/or dentate gyrus. Probes are perfused with artificial cerebrospinal fluid (aCSF) containing NaCl 145 mM, KCl 2.7 mM, $MgCl_2$ 1.0 mM, $CaCl_2$ 1.2 mM, Na_2HPO_4 2.0 mM (pH 7.4) at a flow rate of 1 μL/min. A 30 min sampling regime is used throughout the microdialysis procedure. Following a 2 h equilibration period, 3 microdialysis samples are collected to establish basal extracellular levels of 5-HT. Guinea pigs are then dosed with vehicle (1% methyl cellulose, 1 mg/kg p.o.), paroxetine (3 mg/kg p.o.) or SB-616234-A (3, 10 or 30 mg/kg p.o.). Microdialysis samples are collected for a further 5 h following drug administration. 5-HT content of microdialysate samples is measured using high performance liquid chromatography (HPLC) with electrochemical detection (ECD). At the end of the experiment probes are removed and animals return to their home cage. Animals are re-used in a randomised cross-over design with 7 days between uses and a maximum of 4 uses per subject.

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

REFERENCES

[1]. Lee A.Dawson, et al. Characterisation of the selective 5-HT1B receptor antagonist SB-616234-A (1-[6-(cis-3,5-dimethylpiperazin-1-yl)-2,3-dihydro-5-methoxyindol-1-yl]-1-[2′-methyl-4′-(5-methyl-1,2,4-oxadiazol-3-yl)biphenyl-4-yl]methanone hydrochloride): In vivo neurochemical and behavioural evidence of anxiolytic/antidepressant activity. Neuropharmacology Volume 50, Issue 8, June 2006, Pages 975-983

[2]. Scott C, et al. SB-616234-A (1-[6-(cis-3,5-dimethylpiperazin-1-yl)-2,3-dihydro-5-methoxyindol-1-yl]-1-[2'methyl-4'-(5-methyl-1,2,3-oxadiazol-3-yl)biphenyl-4-yl]methanone hydrochloride): a novel, potent and selective 5-HT1B receptor antagonist. Neuropharmacology. 2006 Jun;50(8):984-90. Epub 2006 Mar 20.

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