Product Data Sheet

Product Name: NNC 05-2090 hydrochloride
Cat. No.: GC11821

Chemical Properties

Cas. No.	184845-18-9		
Chemical Name	1-(3-(9H-carbazol-9-yl)propyl)-4-(2-methoxyphenyl)piperidin-4-ol hydrochloride		
SMILES	COC1=CC=CC=C1C(CC2)(O)CCN2CCCN3C4=CC=CC=C4C5=CC=CC=C53.Cl		
Formula	$C_{27}H_{30}N_2O_2$.HCl	M.Wt	451.01
Solubility	<5.64mg/ml in ethanol; <45.1mg/ml in DMSO	Storage	Desiccate at RT
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	NNC 05-2090 hydrochloride		

Protocol

Cell experiment [1]:

Cell lines	Rat astrocytes (DI TNC1) and HepG2 cells (human liver hepatocellular carcinoma cell line)
Preparation Method	Cells were cultured and then pre-incubated with hypertonic media overnight. Cells were then treated with different concentrations of the BGT1 inhibitor NNC 05-2090 (50–150μM) for 1 hour, followed by the addition of betaine (100μM).

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Reaction Conditions	50–150μM; 1h.
Applications	NNC 05-2090 hydrochloride significantly inhibited betaine transport through BGT1 in a concentration-dependent manner, showing the highest activity against BGT1. NNC 05-2090 hydrochloride also reversed the osmoprotective effect of betaine, abrogating betaine-mediated reduction in cell shrinkage under hypertonic conditions.

Animal experiment [2]:

Animal models	DBA/2 mice, NMRI mice, Amygdala-kindled rats
Preparation Method	Animals received intraperitoneal (i.p.) administration of NNC 05-2090 hydrochloride (0-242μmol/kg). Seizure tests (sound-induced seizures or maximal electroshock) were conducted at specified times (1 hour) after drug injection.
Dosage form	19-242μmol/kg; i.p.; single injection.
Applications	NNC 05-2090 hydrochloride dose-dependently antagonized sound-induced tonic and clonic convulsions in DBA/2 mice and tonic hindlimb extension in the maximal electroshock (MES) test in mice. In amygdala-kindled rats, NNC 05-2090 hydrochloride significantly reduced generalized seizure severity at the highest tested doses.

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References:
[1] Pukale DD, Farrag M, Gudneppanavar R, et al. Osmoregulatory Role of Betaine and Betaine/γ-Aminobutyric Acid Transporter 1 in Post-Traumatic Syringomyelia. ACS Chem Neurosci. 2021 Oct 6;12(19):3567-3578.
[2] Dalby NO, Thomsen C, Fink-Jensen A, et al. Anticonvulsant properties of two GABA uptake inhibitors NNC 05-2045 and NNC 05-2090, not acting preferentially on GAT-1. Epilepsy Res. 1997 Jul;28(1):51-61.

Background

NNC 05-2090 hydrochloride is a GABA uptake inhibitor selective for the BGT-1 (mGAT-2) transporter[1]. NNC 05-2090 hydrochloride can be used for research related to epilepsy and neurological diseases[2-3].

In vitro, NNC 05-2090 hydrochloride (1.25–20μM) treated primary hepatocytes for 15 minutes, followed by stimulation with TNF-α (20ng/ml)/ActD (200ng/ml) for 24 hours. NNC 05-2090 hydrochloride inhibited TNF-α-mediated hepatocyte apoptosis and upregulated the expression of the anti-apoptotic gene c-Met[4]. NNC 05-2090 hydrochloride (50–150μM) treated rat astrocytes and HepG2 cells for 1 hour. NNC 05-2090 hydrochloride inhibited betaine transport through BGT1 and reversed the osmoprotective effect of betaine against cell shrinkage under hypertonic conditions[5].

In vivo, NNC 05-2090 hydrochloride (8mg/kg) was administered intraperitoneally to mice 1 hour after intracerebroventricular injection of Aβ25-35. NNC 05-2090 hydrochloride significantly attenuated the preventive effect of betaine on Aβ25-35-induced cognitive

impairment but did not affect betaine's inhibition of brain oxidative stress[6]. NNC 05-2090 hydrochloride (0–242μmol/kg) was administered intraperitoneally to DBA/2 mice 1 hour before acoustic stimulation. NNC 05-2090 hydrochloride dose-dependently antagonized sound-induced tonic and clonic convulsions[7].

References:

[1] Jinzenji A, Sogawa C, Miyawaki T, et al. Antiallodynic action of 1-(3-(9H-Carbazol-9-yl)-1-propyl)-4-(2-methyoxyphenyl)-4-piperidinol (NNC05-2090), a betaine/GABA transporter inhibitor. J Pharmacol Sci. 2014;125(2):217-26.
[2] Thomsen C, Sørensen PO, Egebjerg J. 1-(3-(9H-carbazol-9-yl)-1-propyl)-4-(2-methoxyphenyl)-4-piperidinol, a novel subtype selective inhibitor of the mouse type II GABA-transporter. Br J Pharmacol. 1997 Mar;120(6):983-5.
[3] Kunisawa K, Kido K, Nakashima N, et al. Betaine attenuates memory impairment after water-immersion restraint stress and is regulated by the GABAergic neuronal system in the hippocampus. Eur J Pharmacol. 2017 Feb 5;796:122-130.
[4] Liu Z, Li Q, Shen R, Ci L, et al. Betaine/GABA transporter-1 (BGT-1) deficiency in mouse prevents acute liver failure in vivo and hepatocytes apoptosis in vitro. Biochim Biophys Acta Mol Basis Dis. 2020 Mar 1;1866(3):165634.
[5] Pukale DD, Farrag M, Gudneppanavar R, et al. Osmoregulatory Role of Betaine and Betaine/γ-Aminobutyric Acid Transporter 1 in Post-Traumatic Syringomyelia. ACS Chem Neurosci. 2021 Oct 6;12(19):3567-3578.
[6] Ibi D, Tsuchihashi A, Nomura T, et al. Involvement of GAT2/BGT-1 in the preventive effects of betaine on cognitive impairment and brain oxidative stress in amyloid β peptide-injected mice. Eur J Pharmacol. 2019 Jan 5;842:57-63.
[7] Dalby NO, Thomsen C, Fink-Jensen A, et al. Anticonvulsant properties of two GABA uptake inhibitors NNC 05-2045 and NNC 05-2090, not acting preferentially on GAT-1. Epilepsy Res. 1997 Jul;28(1):51-61.

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