

Product Data Sheet

Product Name: (+)-Bicuculline

Cat. No.: GN10745

Chemical Properties

Cas. No. 485-49-4

Chemical Name (6R)-6-[(5S)-6-methyl-7,8-dihydro-5H-[1,3]dioxolo[4,5-g]isoquinolin-5-yl]-6H-furo[3,4-g][1,3]benzodioxol-8-one

SMILES CN1CCC2=CC3=C(C=C2C1C4C5=C(C6=C(C=C5)OCO6)C(=O)O4)OCO3

Formula $C_{20}H_{17}NO_6$

M.Wt 367.11

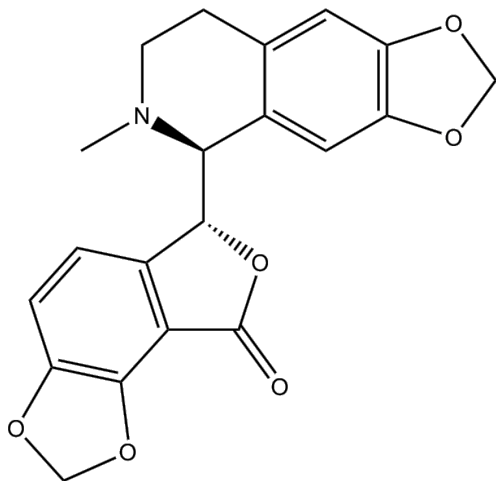
Solubility $\geq 13.1\text{mg/mL}$ in DMSO

Storage Store at -20°C , protect from light

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C 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



Protocol

Cell experiment [1]:

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Cell lines	Primary cortical neurons
Preparation method	Primary cortical neurons were isolated from rat E18 embryos. Cells were plated on poly-D-lysine-coated plates (1×10^6 cells/well) in Neurobasal Media supplemented with 2% B27 and grown for 14–18 days. Neurons were treated with (+)-Bicuculline (10 μ M for 15–60min), picrotoxin (50 μ M for 15–60 min), or D-serine (100 μ M for 30–120 min).
Reaction Conditions	10 μ M ; 15–60min
Applications	(+)-Bicuculline treatment could potentiate synaptic NMDAR signaling in the primary cortical neurons. (+)-Bicuculline led to a rapid decrease in STEP61 expression and a concomitant increase in the tyrosine phosphorylation of STEP substrates including GluN2B, Pyk2, and ERK1/2.
Animal experiment [2]:	
Animal models	13-month old Fischer-344 virgin female rats

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Preparation method	rats ovaries and the tips of uterine horns were ligatured and removed. Beginning two days after surgery all drugs were administered via two daily subcutaneous injections in the scruff of the neck. For the first injection, animals received either a control vehicle solution or progesterone. For the second injection, animals received either a control vehicle solution or (+)-Bicuculline (3.5 mg/kg; dissolved in sesame oil + 10% DMSO).
Dosage form	3.5 mg/kg; s.c.
Applications	The GABA _A antagonist (+)-Bicuculline attenuated progesterone-induced memory impairments in middle-aged ovariectomized rats.
References: [1]Xu J1, Kurup P1, et al. Synaptic NMDA Receptor Activation Induces Ubiquitination and Degradation of STEP61 [J]. Mol Neurobiol. 2017. [2]Blair B B , Kingston M L , Koenig E N ,et al. The GABA_A antagonist bicuculline attenuates progesterone-induced memory impairments in middle-aged ovariectomized rats[J].Frontiers in Aging Neuroscience, 2015.	

Background

(+)-Bicuculline ((+)-Bicuculline)) is a competitive GABA_A receptor antagonist with an IC_{50} of 2 μ M [1]. (+)-Bicuculline also inhibits Ca²⁺-activated potassium channels [2]. (+)-Bicuculline reduces the effects of GABA without affecting the effects of glycine [3].

In vitro, (+)-Bicuculline (10 μ M) treated primary cortical neuronal cells of rat E18 embryos for 15–60 min, enhanced neuronal synaptic NMDAR signaling, down-regulated STEP 61 expression, and

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accompanied the STEP substrate GluN 2B , increased tyrosine phosphorylation of Pyk 2 and ERK 1/2 [4]. (+)-Bicuculline (10μM) treatment of rat hippocampal neuron cells can cause calcium oscillations [5].

In vivo, (+)-Bicuculline (3.5mg/kg) treated Ovx rats via daily subcutaneous injection significantly reversed progesterone-induced cognitive decline and alleviated working memory impairment [6]. (+)-Bicuculline (1, 2, 4 mg/kg) affects the auditory steady-state response (ASSR) of SD rats through subcutaneous injection, dose-dependently reduces the ASSR signal, and significantly decreases within 10-30 minutes after administration Spectral Perturbation (ERSP) [7].

References:

[1]Collins M , Duke R , Huang S ,et al. Bilobalide, a sesquiterpene trilactone from Ginkgo biloba, is an antagonist at recombinant alpha1beta2gamma2L GABA(A) receptors.[J].European Journal of Pharmacology, 2003, 464(1):1-8.

[2]Khawaled R , Bruening-Wright A , Adelman J P ,et al.Bicuculline block of small-conductance calcium-activated potassium channels[J].Pflügers Archiv, 1999, 438(3):314-321.

[3]Johnston G A. Advantages of an antagonist: bicuculline and other GABA antagonists[J].British Journal of Pharmacology, 2013.

[4]Xu J1, Kurup P1, et al. Synaptic NMDA Receptor Activation Induces Ubiquitination and Degradation of STEP61 [J]. Mol Neurobiol. 2017.

[5]Maiorov S A, Kairat B K, Gaidin S G, et al. Activation of the Cannabinoid Receptors Suppresses Hyperexcitation of Rat Hippocampal Neuronal Networks In Vitro[J]. Biochemistry (Moscow), Supplement Series A: Membrane and Cell Biology, 2023, 17(2): 169-175.

[6]Blair B B , Kingston M L , Koenig E N ,et al. The GABA _A antagonist bicuculline attenuates progesterone-induced memory impairments in middle-aged ovariectomized rats[J].Frontiers in Aging Neuroscience, 2015.

[7]Yamazaki M, Honda S, Tamaki K, et al. Effects of (+)-bicuculline, a GABA_A receptor antagonist, on

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auditory steady state response in free-moving rats[J]. PLoS One, 2020, 15(7): e0236363.

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