

Product Data Sheet

Product Name: GF 109203X (Bisindolylmaleimide I)

Cat. No.: GC15431

Chemical Properties

Cas. No. 133052-90-1

Chemical Name 3-[1-[3-(dimethylamino)propyl]indol-3-yl]-4-(1H-indol-3-yl)pyrrole-2,5-dione

SMILES CN(C)CCCN1C=C(C2=CC=CC=C21)C3=C(C(=O)NC3=O)C4=CNC5=CC=CC=C54

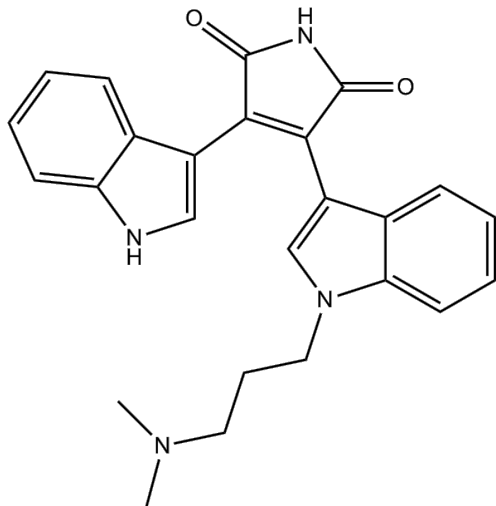
Formula $C_{25}H_{24}N_4O_2$ M.Wt 412.49

Solubility $\geq 20.6\text{mg/mL}$ in DMSO Storage 4°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]:

Cell lines N2a cells

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Preparation Method

Cells treated with and without GF 109203X (1μM; 1h) were collected and homogenized in 10mM Tris, 150mM NaCl, 2mM EGTA, 2mM dithiothreitol (DTT), 0.1mM Na₂VO₄ and protease inhibitors. The cell homogenates were centrifuged at 18000g for 15min at 4°C and protein concentration in the supernatants was determined. GSK-3 activity was measured using phospho-GS peptide 2. 7.5μg protein was incubated in 25μl buffer containing 30mM Tris, 10mM MgCl, 10mM NaF, 1mM Na₂VO₄, 2mM EGTA, 10mM B-mercaptoethanol, 200μM γ-[³²P]ATP (1500cm/pmol ATP) and 20μM phospho-GS peptide 2 with pH 7.4 at 30°C for 30min. The reaction was stopped with 25μl 300mM phosphoric acid. After washing out the free ³²P with PBS three times, half of the incubation mixture was used for liquid scintillation counting analysis. Enzyme activities were calculated as pmoles of phosphate incorporated per milligram of protein per minute at 30°C and expressed as activity relative to control.

Reaction Conditions

1μM; 1h

Applications

inhibition of PKC by GF 109203X (1μM; 1h) activates GSK-3, whereas activation of PKC by phorbol-12,13-butyrate inhibits GSK-3

Animal experiment [2]:

Animal models

Male Wistar rats

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Each rat was first anesthetized by chloral hydrate [30mg/kg, intraperitoneally (i.p.)] and placed on a stereotactic instrument with the incisor bar set 2mm below the ear bars (i.e. flat skull). A 50-IL syringe was stereotactically placed into the left ventricle at the co-ordinates for bregma and dura of AP-0.8, L-1.5 and V-4 (in mm) after the scalp was incised and retracted. Different concentrations of Preparation Method wortmannin or GF 109203X or LiCl, separately or in combination, in a total volume of 10µL were injected into each rat using artificial cerebrospinal fluid (aCSF) containing 140mM NaCl, 3.0mM KCl, 2.5mM CaCl₂, 1.0mM MgCl₂, 1.2mM Na₂HPO₄, pH7.4, as vehicle . All surgical procedures were completed under sterile conditions and penicillin [200000U, intramuscularly (i.m.)] was injected to prevent infection.

Dosage form 10µM and 100µM; once; i.p

Applications ventricular co-injection of wortmannin and GF 109203X (WT/GFX) can induce tau hyperphosphorylation and memory impairment of rats through activation of GSK-3

References:

[1] Wang, Ze-Fen et al. "Effects of endogenous beta-amyloid overproduction on tau phosphorylation in cell culture." Journal of neurochemistry vol. 98,4 (2006): 1167-75. doi:10.1111/j.1471-4159.2006.03956.x

[2] Liu, Shi Jie et al. "Overactivation of glycogen synthase kinase-3 by inhibition of phosphoinositol-3 kinase and protein kinase C leads to hyperphosphorylation of tau and impairment of spatial memory." Journal of neurochemistry vol. 87,6 (2003): 1333-44. doi:10.1046/j.1471-4159.2003.02070.x

Background

GF 109203X is a selective inhibitor of protein kinase C, selective for the α and β 1 isoforms with IC₅₀ values of 0.0084, 0.0180, 0.210, 0.132, and 5.8µM for α , β 1, δ , ϵ and ζ isoforms of protein kinase C respectively^[1]. GF 109203X selectively inhibits over MLCK, PKG, and PKA (IC₅₀ values are 0.6, 4.6,

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and 33 μ M respectively). GF 109203X is also an antagonist at the 5-HT₃ receptor with a K_i of 29.5nM^[2]. GF 109203X shows an anti-inflammatory effect targeting human neutrophils *in vivo*^[3].

In vitro, inhibition of PKC by GF 109203X (1 μ M; 1h) activates GSK-3, whereas activation of PKC by phorbol-12,13-butyrate inhibits GSK-3^[4]. Inhibition of protein kinase C with GF 109203X (3 μ M; 6h) resulted in concentration-dependent but partial inhibition of [(35)S] sulfate incorporation accompanied by a reduction in the particle size of biglycan and decorin^[5]. PKC inhibitor GF 109203X (1 μ M; 5min) did not inhibit KCl-induced tonic force and myosin light chain (MLC) phosphorylation in rabbit artery^[6].

In vivo, ventricular co-injection of wortmannin and GF 109203X (WT/GFX) (10 μ M and 100 μ M; once; i.p) can induce tau hyperphosphorylation and memory impairment of rats through activation of GSK-3^[7]. GF 109203X (0.3pg/site; once; local injection) impaired memory reconsolidation in the presence of spermidine (200pmol/site)^[8].

References:

- [1] Toullec, D et al. "The bisindolylmaleimide GF 109203X is a potent and selective inhibitor of protein kinase C." *The Journal of biological chemistry** vol. 266,24 (1991): 15771-81.
- [2] Coultrap, S J et al. "Competitive antagonism of the mouse 5-hydroxytryptamine₃ receptor by bisindolylmaleimide I, a "selective" protein kinase C inhibitor." *The Journal of pharmacology and experimental therapeutics** vol. 290,1 (1999): 76-82.
- [3] Cabanis, A et al. "Effect of the protein kinase C inhibitor GF 109 203X on elastase release and respiratory burst of human neutrophils." *General pharmacology** vol. 27,8 (1996): 1409-14.
doi:10.1016/s0306-3623(96)00053-5
- [4] Wang, Ze-Fen et al. "Effects of endogenous beta-amyloid overproduction on tau phosphorylation in cell culture." *Journal of neurochemistry** vol. 98,4 (2006): 1167-75. doi:10.1111/j.1471-4159.2006.03956.x
- [5] Ivey, Melanie E, and Peter J Little. "Thrombin regulates vascular smooth muscle cell proteoglycan synthesis via PAR-1 and multiple downstream signalling pathways." *Thrombosis research** vol. 123,2 (2008): 288-97. doi:10.1016/j.thromres.2008.04.019
- [6] Urban, Nicole H et al. "K⁺ depolarization induces RhoA kinase translocation to caveolae and Ca²⁺ sensitization of arterial muscle." *American journal of physiology. Cell physiology** vol. 285,6 (2003): C1377-85. doi:10.1152/ajpcell.00501.2002

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- [7] Liu, Shi Jie et al. "Overactivation of glycogen synthase kinase-3 by inhibition of phosphoinositol-3 kinase and protein kinase C leads to hyperphosphorylation of tau and impairment of spatial memory." *Journal of neurochemistry* vol. 87,6 (2003): 1333-44. doi:10.1046/j.1471-4159.2003.02070.x
- [8] Girardi, Bruna Amanda et al. "Spermidine-induced improvement of reconsolidation of memory involves calcium-dependent protein kinase in rats." *Learning & memory (Cold Spring Harbor, N.Y.)* vol. 23,1 21-8. 15 Dec. 2015, doi:10.1101/lm.039396.115

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