Bisindolylmaleimide I

Cat. No.: HY-13867

CAS No.: 133052-90-1

Molecular Formula: $C_{25}H_{24}N_4O_2$

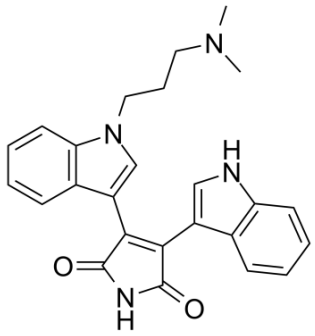
Molecular Weight: 412.48

Target: PKC

Pathway: Epigenetics; TGF-beta/Smad

Storage: 4°C, protect from light

* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 32 mg/mL (77.58 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.4244 mL	12.1218 mL	24.2436 mL
5 mM	0.4849 mL	2.4244 mL	4.8487 mL
10 mM	0.2424 mL	1.2122 mL	2.4244 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1 mg/mL (2.42 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Bisindolylmaleimide I (GF109203X) is a highly selective, cell-permeable, and reversible protein kinase C (PKC) inhibitor with a K_i of 14 nM.

IC_{50} & Target

Bovine brain PKC 10 nM (IC_{50})	PKCβII 16 nM (IC_{50})	PKCβI 17 nM (IC_{50})	PKCα 20 nM (IC_{50})
PKCγ 20 nM (IC_{50})	FDGFR 65 μM (IC_{50})		

In Vitro

Bisindolylmaleimide I is a competitive inhibitor with respect to ATP (K_i=14 nM) and displays high selectivity for PKC as compared to five different protein kinases. GF 109203X efficiently prevents PKC-mediated phosphorylations of an M_r=47,000 protein in platelets and of an M_r=80,000 protein in Swiss 3T3 cells. GF 109203X inhibits collagen- and a-thrombin-induced platelet aggregation as well as collagen-triggered ATP secretion. However, ADP-dependent reversible aggregation is not

	modified. In Swiss 3T3 fibroblasts, GF 109203X reverses the inhibition of epidermal growth factor binding induced by phorbol 12,13-dibutyrate and prevents [^{3}H] thymidine incorporation into DNA, only when this is elicited by growth promoting agents which activate PKC[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Pial arteriole diameter changes are monitored using a closed cranial window in vivo microscopy technique. The pial arteriole dilatory response associated with SNS is decreased by 45%, when comparing DM vs either ND or TR rats. Also, pial arteriolar dilations to topical KCl and NS1619 are largely attenuated in DM rats, but not in ND or TR animals. These responses are completely restored by the acute application of Bisindolylmaleimide I to the brain surface. The PKC inhibitor has no effect on vascular responses in normoglycemic and TR animals. In conclusion, DM-associated chronic impairment of neurovascular coupling may be readily reversed by a PKC-α/β/γ inhibitor or prevented via pancreatic islet transplantation. Specific PCK isoforms (α/β/γ) are believed to be mechanistically linked to the neurovascular uncoupling seen with hyperglycemia[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Assay of PKC is arrayed by measuring ^{32}Pi transferred from [γ-^{32}Pi] ATP to lysine-rich histone type Ill-s. The reaction mixture (80 μL) contains 50 mM Tris-HCI, pH 7.4. 100 μM $CaCl_2$, 10 mM $MgCl_2$, 37.5 μg/mL histone type Ill-s, l0 μM [γ-^{32}Pi] ATP (1250cpm/pmol), 31 μM bovine brain phosphatidylserine and 0.5 μM 1,2 sn-dioleylglycerol. 15 μL of purified PKC (final concentration in assay 0.38 μg/mL) is added to the incubation mixture. After 10 minutes, the reaction is stopped by addition of at 30 μL of casein 30 mg/mL and 0.9 mL of 12% trichlomacetic acid[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Three sets of Lewis rats is used for this study: 1) euglycemic 4–6 month old non-diabetic controls (ND group, n=11); 2) streptozotocin (STZ)-treated diabetic rats (6 month old, 4 months post-STZ) (DM group, n=6); and 3) STZ-treated diabetic animals, subjected to pancreatic islet transplantation soon after the establishment of the diabetic model, studied 100–110 days after the transplant (TR group, n=7)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Elife. 2021 Mar 3;10:e60889.
- J Nutr Biochem. 2020 Nov 26;108555.
- Food Chem Toxicol. 2020 Dec 28;148:111925.
- Food Chem Toxicol. 2019 Mar;125:46-54.
- Cells. 2020 Jun 15;9(6):1467.

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REFERENCES

[1]. Toullec D, et al. The bisindolylmaleimide GF 109203X is a potent and selective inhibitor of protein kinase C. J Biol Chem. 1991 Aug 25;266(24):15771-81.

[2]. Vetri F, et al. Impairment of neurovascular coupling in Type 1 Diabetes Mellitus in rats is prevented by pancreatic islet transplantation and reversed by a semi-selective PKC inhibitor. Brain Res. 2017 Jan 15;1655:48-54.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA