Ingenol Mebutate

Cat. No.: HY-B0719

CAS No.: 75567-37-2

Molecular Formula: $C_{25}H_{34}O_6$

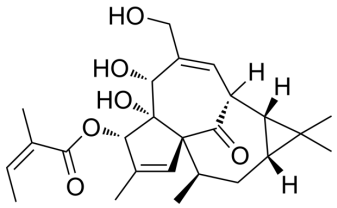
Molecular Weight: 430.53

Target: PKC

Pathway: Epigenetics; TGF-beta/Smad

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (232.27 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3227 mL	11.6136 mL	23.2272 mL
5 mM	0.4645 mL	2.3227 mL	4.6454 mL
10 mM	0.2323 mL	1.1614 mL	2.3227 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: ≥ 2.5 mg/mL (5.81 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.81 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.81 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Ingenol Mebutate is an active ingredient in Euphorbia peplus, acts as a potent PKC modulator, with K_is of 0.3, 0.105, 0.162, 0.376, and 0.171 nM for PKC-α, PKC-β, PKC-γ, PKC-δ, and PKC-ε, respectively, and has antiinflammatory and antitumor activity.

IC_{50} & Target

PKC-β	PKC-γ	PKC-ε	PKC-α
0.105 nM (Ki)	0.162 nM (Ki)	0.171 nM (Ki)	0.3 nM (Ki)

	PKC-δ 0.376 nM (Ki)
In Vitro	Ingenol Mebutate (Ingenol 3-angelate) is an active ingredient in Euphorbia peplus, acting as a potent PKC activator, with K_is of 0.3, 0.105, 0.162, 0.376, and 0.171 nM for PKC-α, PKC-β, PKC-γ, PKC-δ, and PKC-ε, respectively. Ingenol Mebutate also EC_{50} s of 13 ± 2.4 nM (PKC-α), 4.37 ± 0.4 nM (PKC-βI), 10.5 ± 2.2 nM (PKC-βII), 38.6 ± 2.9 nM (PKC-δ), 1.08 ± 0.01 nM (PKC-ε), 0.9 ± 0.13 nM (PKC-μ) in WEHI-231 cells, 198 ± 12.5 nM (PKC-α), 69.1 ± 8.2 nM (PKC-βI), 4.6 ± 0.4 nM (PKC-ε) and 1 nM (PKC-μ) in HOP-92 cells, 635 ± 245 nM (PKC-α), 146 ± 35 nM (PKC-βI), 4.7 ± 0.7 nM (PKC-δ), 1.1 ± 0.5 nM (PKC-ε), and 30 nM (PKC-μ) in Colo-205 cells. Ingenol Mebutate sensitizes WEHI-231 cells, HOP-92 and Colo-205 cells, with IC_{50}s of 1.41 ± 0.255 nM, 3.24 ± 2.01 nM, and 11.9 ± 1.307 nM, respectively[1]. Ingenol Mebutate (PEP005; 20 nM) actions are PKC-δ dependent, induces apoptosis in primary AML marrow blasts but not in normal myeloblasts[2]. Ingenol Mebutate (PEP005) activates PKCδ and inhibits PKCα. Colo205-R cells (IC_{50}: >10 μM) are >300-fold more resistant to Ingenol Mebutate than parental Colo205-S cells [3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	KG1a cells are transiently transfected with EGFP-tagged mouse PKC-δ subcloned into pEGFP-N1 plasmid using an Amaxa nucleofection apparatus. Cells are treated with Ingenol Mebutate (0.2 μM-20 μM) 24 hours after transfection. Cell viability in EGFP-positive cells is assessed and loss of viability confirmed in the total cell culture by MTT assay after 3 days. Briefly, 24 hours after transfection, 2×10^4 cells are plated in 5 wells in 96-well plates and exposed to 0, 0.2, 2, and 20 μM Ingenol Mebutate. At 72 hours, 20 μL MTT substrate at 5 mg/mL is added and plates are incubated at 37°C. After 3 hours, 150 μL media is removed and replaced with 200 μL dimethyl sulfoxide (DMSO). Absorbance at an optical density (OD) of 550 nm is read on a plate reader and corrected for absorbance obtained from blank media controls[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- bioRxiv. 2023 Apr 9.

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REFERENCES

[1]. Kedei N, et al. Characterization of the interaction of ingenol 3-angelate with protein kinase C. Cancer Res. 2004 May 1;64(9):3243-55.

[2]. Hampson P, et al. PEP005, a selective small-molecule activator of protein kinase C, has potent antileukemic activity mediated via the delta isoform of PKC. Blood. 2005 Aug 15;106(4):1362-8.

[3]. Ghoul A, et al. Epithelial-to-mesenchymal transition and resistance to ingenol 3-angelate, a novel protein kinase C modulator, in colon cancer cells. Cancer Res. 2009 May 15;69(10):4260-9.

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