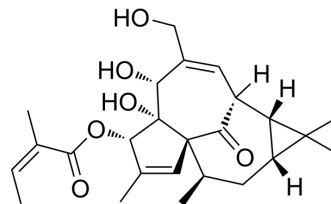


Ingenol Mebutate

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 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (232.27 mM)
 * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	Mass		
		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

- 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
- 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
- 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.

IC₅₀ & Target

PKC-β 0.105 nM (K _i)	PKC-γ 0.162 nM (K _i)	PKC-ε 0.171 nM (K _i)	PKC-α 0.3 nM (K _i)
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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_{i} s 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- β I), 10.5 ± 2.2 nM (PKC- β II), 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- β I), 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- β I), 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 PKC δ and inhibits PKC α . Colo205-R cells (IC_{50} : >10 μ M) 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 μ M-20 μ M) 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 μ M Ingenol Mebutate. At 72 hours, 20 μ L MTT substrate at 5 mg/mL is added and plates are incubated at 37°C. After 3 hours, 150 μ L media is removed and replaced with 200 μ L 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.

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

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