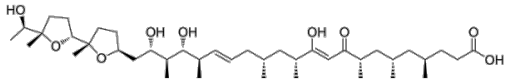
Product Data Sheet

Product Name: Ionomycin free acid
Cat. No.: GC15446

Chemical Properties

Cas. No.	56092-81-0		
Chemical Name	(4R,6R,8R,10E,12S,14S,16E,18S,19S,20R,21S)-11,19,21-trihydroxy-22-((2R,2'R,5R,5'R)-5'-((R)-1-hydroxyethyl)-2,5'-dimethyloctahydro-[2,2'-bifuran]-5-yl)-4,6,8,12,14,18,20-heptamethyl-9-oxodocosa-10,16-dienoic acid		
SMILES	O[C@H](C)[C@]1(C)O[C@H](CC1)[C@]2(C)O[C@@H](C[C@@H]([C@@H](C)[C@H]([C@H](/C=C/C[C@H](C)C[C@H](C)/C(O)=C\C([C@H](C)C[C@H](C)C[C@H](C)CCC(O)=O)=O)C)O)O)CC2		
Formula	$C_{41}H_{72}O_9$	M.Wt	709.01
Solubility	1.4mg/mL in DMSO, 2.5mg/mL in DMF	Storage	Desiccate at -20°C
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

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Cell experiment [1]:	
Cell lines	L6 cells (rat skeletal muscle myoblast cell line)
Preparation Method	L6 cells were maintained in DMEM supplemented with 10% FBS and 5% penicillin/streptomycin at 37°C, 5% CO_2. Detached L6 cells were treated with 1μM Ionomycin free acid in PBS with 1.5mM Ca^{2+} for 10min at room temperature, then rinsed with Ca^{2+}-free PBS and resuspended in 8.5% sucrose and 0.3% dextrose solution.
Reaction Conditions	1μM; 10min
Applications	Ionomycin free acid significantly increased cytoplasmic conductivity and decreased cytoplasmic permittivity
Animal experiment [2]:	
Animal models	Female athymic nude mice (BALB/c nu/nu, 6-8 weeks old)
Preparation Method	Mice were subcutaneously inoculated with 5×10^6 HT1376 human bladder cancer cells in the flank. Starting 5 days after implantation, mice received intratumoral injection of 100μg Ionomycin free acid in 100μL PBS 3 times per week for 4 weeks. Tumor size (length×width) was measured with caliper at least twice weekly. In a separate combination arm, mice additionally received intraperitoneal injection of 50μg cisplatin in 100μL PBS 3 times per week for 4 weeks. Tumors were resected at 2 and 4 weeks for Northern blot analysis of Bcl-2 and Bax mRNA.

Caution: Product has not been fully validated for medical applications. For research use only.
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Dosage form	100μg per mouse; intratumoral; 3 times/week for 4 weeks
Applications	Ionomycin free acid reduced subcutaneous HT1376 tumor size in nude mice. Ionomycin free acid downregulated Bcl-2 mRNA and upregulated Bax mRNA in HT1376 tumor tissues. Combined intratumoral Ionomycin free acid plus intraperitoneal cisplatin further suppressed HT1376 tumor growth compared with either agent alone.

References:

[1] Ferguson CA, Santangelo C, Marramiero L, et al. Broadband electrical spectroscopy to distinguish single-cell Ca^{2+} changes due to ionomycin treatment in a skeletal muscle cell line. Sensors. 2023 Apr 28;23(9):4358.

[2] Miyake H, Hara I, Yamanaka K, et al. Calcium ionophore, ionomycin inhibits growth of human bladder cancer cells both in vitro and in vivo with alteration of Bcl-2 and Bax expression levels. J Urol. 1999 Sep;162(3):916-21.

Background

Ionomycin free acid is a highly selective calcium ionophore produced by *Streptomyces conglobatus*. Ionomycin free acid binds Ca^{2+} and facilitates transport across biological membranes. Ionomycin free acid elevates cytosolic Ca^{2+} levels to activate calcium-dependent signaling pathways, induce apoptosis and autophagy. Ionomycin free acid is often used together with PMA to activate T cells and promote the production of cytokines such as IL-2. Ionomycin free acid can be used for research related to calcium signal transduction, apoptosis, immune activation and cytokine production[1-4].

In vitro, 1μM Ionomycin free acid treatment for 16 hours reduced degranulation and cytotoxic activity of NK cells against K562, Jurkat, Molt4 and 721.221 target cells. Ionomycin free aciddecreased IFN-γ production and impaired the ability of NK cells to form stable conjugates with target cells[5]. 1μM Ionomycin free acid treatment for 10 minutes in phosphate-buffered saline containing 1.5mM Ca^{2+}

elevated cytosolic Ca^{2+} concentration in L6 cells. Ionomycin free acid significantly increased cytoplasmic conductivity and decreased cytoplasmic permittivity[6]. 5-10μM Ionomycin free acid treatment for 2-10 minutes rapidly and persistently elevated cytosolic free Ca^{2+} concentration in rat kidney cortical epithelial cells. Ionomycin free aciddissipated mitochondrial membrane potential and caused loss of cell viability[7].

In vivo, a single injection of 6μL 25μM Ionomycin free acid into the peroneal and tibial fascicles of the left sciatic nerve of Sprague-Dawley rats induced vesicular demyelination originating at paranodes and Schmidt-Lanterman incisures and extending along compact internodal myelin[8]. A single injection of 0.5μL 2-50μM Ionomycin free acid at depths of 400μm and 700μm at the T10-T11 intervertebral space of Sprague-Dawley rats induced focal primary vesicular demyelinating lesions in the dorsal column, accompanied by oligodendrocyte damage, astrocyte edema and axonal degeneration[9]. Intratumoral injection of 100μg Ionomycin free acid 3 times per week for 4 weeks in BALB/c nu/nu mice subcutaneously inoculated with 5×10^6 HT1376 cells reduced subcutaneous HT1376 tumor size. Ionomycin free acid downregulated intratumoral Bcl-2 mRNA expression and upregulated Bax mRNA expression[10].

References:

[1] Phillippe M, Chien EM, Freij M, et al. Ionomycin-stimulated phasic myometrial contractions. Am J Physiol. 1995 Oct;269(4 Pt 1):E779-85.

[2] Chen C, Sun T, Yin M,et al. Ionomycin-induced mouse oocyte activation can disrupt preimplantation embryo development through increased reactive oxygen species reaction and DNA damage. Mol Hum Reprod. 2020 Oct 1;26(10):773-783.

[3] Aiken EJ, Kilberg BG, Yu S, et al. Ionomycin-Induced Changes in Membrane Potential Alter Electroporation Outcomes in HL-60 Cells. Biophys J. 2018 Jun 19;114(12):2875-2886.

[4] Hunt JM, Silinsky EM. Ionomycin-induced acetylcholine release and its inhibition by adenosine at frog motor nerve endings. Br J Pharmacol. 1993 Oct;110(2):828-32.

[5] Romera-Cardenas G, Thomas LM, Lopez-Cobo S, et al. Ionomycin treatment renders NK cells hyporesponsive. PLoS ONE. 2016 Mar 23;11(3):e0150998.

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[6] Ferguson CA, Santangelo C, Marramiero L, et al. Broadband electrical spectroscopy to distinguish single-cell Ca2+ changes due to ionomycin treatment in a skeletal muscle cell line. Sensors. 2023 Apr 28;23(9):4358.

[7] Jiang T, Grant RL, Acosta D. A digitized fluorescence imaging study of intracellular free calcium, mitochondrial integrity and cytotoxicity in rat renal cells exposed to ionomycin, a calcium ionophore. Toxicology. 1993;85(1):41-65.

[8] Smith KJ, Hall SM. Peripheral demyelination and remyelination initiated by the calcium-selective ionophore ionomycin: in vivo observations. J Neurol Sci. 1988 Jun;83(1):37-53.

[9] Smith KJ, Hall SM. Central demyelination induced in vivo by the calcium ionophore ionomycin. Brain. 1994;117(6):1351-6.

[10] Miyake H, Hara I, Yamanaka K, et al. Calcium ionophore, ionomycin inhibits growth of human bladder cancer cells both in vitro and in vivo with alteration of Bcl-2 and Bax expression levels. J Urol. 1999 Sep;162(3):916-21.

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