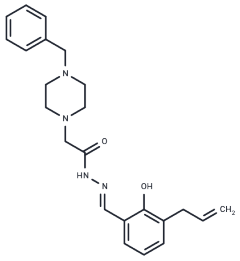
Data Sheet (Cat.No.T2503)

TargetMol

PAC-1

Chemical Properties



CAS No. : 315183-21-2

Formula: C23H28N4O2

Molecular Weight: 392.49

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	PAC-1 (Procaspase activating compound 1) has been used in trials studying the treatment of Lymphoma, Melanoma, Solid Tumors, Breast Cancer, and Thoracic Cancers, among others.
Targets(IC50)	Apoptosis,Caspase,Autophagy
In vitro	PAC-1 was able to induce cell death in a delayed manner in Bax/Bak double knockout cells and Bcl-2 and Bcl-xL overexpressing cells with the same efficacy as its wild-type counterpart.PAC-1 induced the release of cytochrome c in a caspase-3 nondependent manner, which subsequently triggered the downstream activation of caspase-3 and cell death.PAC-1 did not induce cell death in Apaf-1 knockout cells. Apaf-1 knockout cells induced cell death and cystatinase-3 activation, suggesting that apoptosome formation is required for cystatinase-3 activation via PAC-1-mediated cell death.PAC-1 induced apoptosis in primary carcinoma cells with IC50 values ranging from 3 nM to 1.41 μM, and was more potent than that in neighboring noncancerous cells with IC50 values ranging from 5.02 μM to 9.98 μM, which is also consistent with procaspase-1-induced apoptosis in primary cancer cells with IC50 values ranging from 3 nM to 1.41 μM. This was also directly related to the concentration of procaspase-3. PAC-1 activated procaspase-3, producing caspase-3 with an EC50 of 0.22 μM, and activated procaspase-7 with an EC50 of 4.5 μM. Increased levels of caspase 3 in the cancer cell lines caused PAC-1 to selectively induce apoptosis according to the ratio of the concentration of procaspase-3 to the concentration of procaspase-3. PAC-1 selectively induces apoptosis in a manner proportional to procaspase-3 concentration, with an IC50 of 0.35 μM in NCI-H226 cells and approximately 3.5 μM in UACC-62 cells.PAC-1 activates cystatinase-3 by chelating zinc ions, which attenuates zinc-mediated inhibition and permits the self-activation of cystatinogen-3 to cystatinase-3.PAC-1 is also known to activate cystatinogen-3 by chelating zinc ions, which is a zinc-mediated inhibition.
In vivo	PAC-1 was able to induce cell death in a delayed manner in Bax/Bak double knockout cells and Bcl-2 and Bcl-xL overexpressing cells with the same efficacy as its wild-type counterpart.PAC-1 induced the release of cytochrome c in a caspase-3 nondependent manner, which subsequently triggered the downstream activation of caspase-3 and cell death.PAC-1 did not induce cell death in Apaf-1 knockout cells. Apaf-1 knockout cells induced cell death and cystatinase-3 activation, suggesting that apoptosome formation is required for cystatinase-3 activation via PAC-1-mediated cell death.PAC-1 induced apoptosis in primary carcinoma cells with IC50 values ranging from 3 nM to 1.41 μM, and

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Kinase Assay	In vitro procaspase-3 activation: Procaspase-3 is expressed and purified in Escherichia coli. Various concentrations of PAC-1 are added to 90 μL of a 50 ng/mL of procaspase-3 in caspase assay buffer in a 96-well plate, The plate is incubated for 12 hours at 37 °C. A 10 μL volume of a 2 mM solution of caspase-3 peptidic substrate acetyl Asp-Glu-Val-Asp-p-nitroanilide (Ac-DEVD-pNa) in caspase assay buffer is then added to each well. The plate is read every 2 minutes at 405 nm for 2 hours in a Spectra Max Plus 384 well plate reader. The slope of the linear portion for each well is determined, and the relative increase in activation from untreated control wells is calculated.
Cell Research	Cells are exposed to various concentrations of PAC-1 for 72 hours. Cell death is quantified by the addition of MTS/PMS CellTiter 96 Cell Proliferation Assay reagent. The plates are incubated at 37 °C for approximately 1 hour (until the colored product formed), and the absorbance is measured at 490 n(Only for Reference)

Solubility Information

Solubility	DMSO: 250 mg/mL (636.96 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (5.1 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.5478 mL	12.7392 mL	25.4784 mL
5 mM	0.5096 mL	2.5478 mL	5.0957 mL
10 mM	0.2548 mL	1.2739 mL	2.5478 mL
50 mM	0.051 mL	0.2548 mL	0.5096 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Putt KS, et al. Nat Chem Biol, 2006, 2(10), 543-550.
Peterson QP, et al. J Mol Biol, 2009, 388(1), 144-158.
Seervi M, et al. Cell Death Dis, 2011, 2, e207.