PAC-1

Cat. No.: HY-13523

CAS No.: 315183-21-2

Molecular Formula: $C_{23}H_{28}N_4O_2$

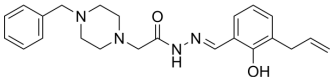
Molecular Weight: 392.49

Target: Caspase; Autophagy; Apoptosis

Pathway: Apoptosis; Autophagy

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 : 50 mg/mL (127.39 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
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

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 (6.37 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (6.37 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.37 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PAC-1 is a procaspase-3 activator that induces apoptosis in cancer cells with an EC_{50} of 2.08 μM.

IC_{50} & Target

Procaspase-3
2.08 μM (EC50)

In Vitro

PAC-1 activates procaspase-3 with an EC_{50} of 2.08 μM. PAC-1 exhibits an enhanced zinc chelating ability (EC_{50}= 7.08 μM).

	PAC-1 induces leukemia cell death with IC_{50} of 4.03 μM, which is consistent with the values reported by other investigators. PAC-1 treatment also results in death of other malignant cells in a concentration-dependent manner with IC_{50}s ranging from 4.03 to 53.44μM. The overall mean IC_{50} in the fifteen malignant cell lines is 0.88 mM for WF-210 and 19.40 μM for PAC-1. In contrast, the sensitivity of the normal human cells (PBL, L-02, HUVEC and MCF 10A) to WF-210 is 2.6-fold lower (mean IC_{50} =412.34 μM) than PAC-1 (mean IC_{50}=158.29 μM)[1]. Procaspase-activating compound-1 (PAC-1) is the first direct caspase-activating compound discovered. PAC-1 treatment upregulates Ero1α in multiple cell lines, whereas silencing of Ero1α significantly inhibits calcium release from ER and cell death[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	To evaluate the in vivo effect of WF-210 on the growth of malignant tumors, we examined the ability of WF-210 to suppress tumor growth in mouse Hep3B and MDA-MB-435 xenograft models. These two cell lines express procaspase-3 at relatively high levels. Tumors induced by xenografts of the liver cancer cell Hep3B are allowed to develop and grow to a size of 100 mm^3, after which WF-210 (2.5 mg/kg) or PAC-1 (5.0 mg/kg) is given daily for two weeks by intravenous (i.v.) administration. As shown in both PAC-1 and WF-210 significantly inhibits the growth of Hep3B tumor xenografts[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Various concentrations of WF-210 or PAC-1 are added to procaspase-3 in buffer containing 50 mM HEPES, 0.1% CHAPS, 10% glycerol, 100 mM NaCl, 0.1 mM EDTA, 10 mM DTT pH 7.4,and incubated for 12 h at 37°C. The final volume is 10 mL and the final concentration of procaspase-3 is 1 mM. Then 40 mL of the substrate Ac-DEVD-pNA (final concentration 0.4 mM) in buffer containing 50 mM HEPES pH 7.4, 100 mM NaCl, 10 mM DTT, 0.1 mM EDTA disodium salt, 0.10% CHAPS, 10% glycerol is added and the absorbance of the plate is read at 405 nm for a total of 1 h. The slope of the linear portion for each well is determined as the enzyme activity[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	Cell viability is measured using the MTT method or the Cell Titer-Glo luminescent assay. For the MTT assay, the cells ($1×10^5$ cells/mL) are seeded into 96- well culture plates. After overnight incubation, cells are treated with various concentrations of agents (PAC-1, WF-210 or other agents) for 24 or 72 h. Then 10 mL MTT solution (2.5 mg/mL in PBS) is added to each well, and the plates are incubated for an additional 4 h at 37°C. After centrifugation (2500 rpm, 10min), the medium containing MTT is aspirated, and100mL DMSO is added. The optical density of each well is measured at 570 nm with a Biotek Synergy HT Reader. The Cell Titer-Glo kit is used to determine the relative levels of intracellular ATP as a biomarker for live cells[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] To determine the in vivo anti-tumor activity of WF-210, viable human gallbladder cancer GBC-SD cells ($5×10^6$/100 mL PBS per mouse), human breast cancer MDA-MB-435 cells ($1×10^7$/100 mL PBS per mouse), human liver cancer Hep3B cells ($5×10^6$ /100 mL PBS per mouse) and human breast cancer MCF-7 cells ($1×10^7$/100 mL PBS per mouse) are subcutaneously (s.c.) injected into the right flank of 7- to 8-week old male SCID mice or Balb/c nude mice. Cell numbers are confirmed by trypan blue staining prior to injection. Specially, MCF-7 xenograft mice are also administered with the hormone 17-beta-estradiol (3 mg/kg) on alternate days. When the average s.c. tumor volume reached 100 mm^3, mice are randomly divided into various treatment and control groups (eight mice per group). Tumor size is measured once every two days with a caliper (calculated volume=shortest $diameter^2$×longest diameter/2). Body weight, diet consumption and tumor size are recorded once every two days. After two or four weeks, mice are sacrificed and tumors are excised and stored at -80°C until further analysis. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Mol Cancer Ther. 2020 Aug;19(8):1751-1760.

- Cancers (Basel). 2023 Apr 23, 15(9), 2427.
- Vet Microbiol. 2021, 109177.
- Poult Sci. 2019 Dec 1;98(12):6367-6377.
- Oncotarget. 2017 Feb 14;8(7):12311-12322.

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REFERENCES

[1]. Wang F, et al. A novel small-molecule activator of procaspase-3 induces apoptosis in cancer cells and reduces tumor growth in human breast, liver and gallbladder cancer xenografts. Mol Oncol. 2014 Dec;8(8):1640-52.

[2]. Seervi M, et al. ERO1α-dependent endoplasmic reticulum-mitochondrial calcium flux contributes to ER stress and mitochondrial permeabilization by procaspase-activating compound-1 (PAC-1). Cell Death Dis. 2013 Dec 19;4:e968.

[3]. Putt KS, et al. Small-molecule activation of procaspase-3 to caspase-3 as a personalized anticancer strategy. Nat Chem Biol. 2006 Oct;2(10):543-50.

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