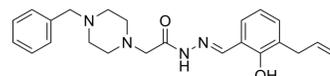


PAC-1

Cat. No.:	HY-13523		
CAS No.:	315183-21-2		
Molecular Formula:	C ₂₃ H ₂₈ N ₄ O 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)
 H₂O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Solvent Concentration	Mass		
		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

- 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
- 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
- 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 EC₅₀ of 2.08 μM.

IC₅₀ & Target

Procaspase-3
 2.08 μM (EC₅₀)

In Vitro

PAC-1 activates procaspase-3 with an EC₅₀ of 2.08 μM. PAC-1 exhibits an enhanced zinc chelating ability (EC₅₀= 7.08 μM).

PAC-1 induces leukemia cell death with IC₅₀ 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 IC₅₀s ranging from 4.03 to 53.44 μM. The overall mean IC₅₀ 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 IC₅₀ = 412.34 μM) than PAC-1 (mean IC₅₀ = 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 mm³, 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 μL 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, 0.1% 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 (1×10⁵ 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 μL 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, 10 min), the medium containing MTT is aspirated, and 100 μL 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 (5×10⁶/100 mL PBS per mouse), human breast cancer MDA-MB-435 cells (1×10⁷/100 mL PBS per mouse), human liver cancer Hep3B cells (5×10⁶/100 mL PBS per mouse) and human breast cancer MCF-7 cells (1×10⁷/100 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 mm³, 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 diameter² × 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.

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- 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. ERO1 α -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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Caution: Product has not been fully validated for medical applications. For research use only.

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