

Product Data Sheet

Product Name: PACMA 31

Cat. No.: GC50102

Chemical Properties

Cas. No. 1401089-31-3

SMILES O=C(C#C)N(C(C2=CC=CS2)C(NCC(OCC)=O)=O)C1=CC=C(OC)C=C1OC

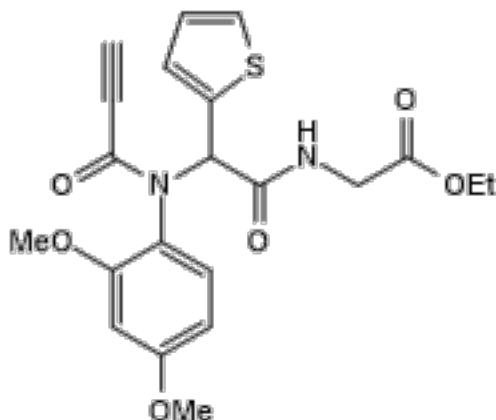
Formula $C_{21}H_{22}N_2O_6S$ M.Wt 430.47

Solubility DMSO: 100 mM Storage Store at RT

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

Cell experiment [1]:

Cell lines	MDA-MB-231 cells (human triple-negative breast cancer cell line)
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Caution: Product has not been fully validated for medical applications. For research use only.

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Preparation Method	MDA-MB-231 cells were maintained in DMEM with 10% fetal bovine serum at 37°C, 5% CO ₂ , treated with 2.5µM PACMA 31 for 24h, then assessed by Western blotting, immunofluorescence, EdU assay, 2D scratch wound assay, cell polarisation assay and 5µm pore space-restrictive migration assay.
Reaction Conditions	2.5µM; 24h
Applications	PACMA 31 reduced SUN1, SUN2, Lamin A, Lamin B1, Vimentin, Keratin 8 and Keratin 18 protein levels, displaced Nesprin-2 from the nuclear envelope, increased perinuclear F-actin structures, reduced cell proliferation, delayed 2D wound closure and Golgi polarisation, and increased migration of MDA-MB-231 cells through 5µm restrictive pores.
Animal experiment [2]:	
Animal models	5 week old female BALB/c nude mice with subcutaneous Hep3B xenografts
Preparation Method	When average tumor volume reached 200mm ³ , mice were treated with PACMA 31 (20mg/kg) by intraperitoneal injection alone or with oral sorafenib (30mg/kg) once daily for 4 weeks, and tumor volume was measured every 2 to 3 days.
Dosage form	20mg/kg; i.p.; once daily for 4 weeks
Applications	PACMA 31 alone produced no significant reduction of Hep3B xenograft tumor volume, while PACMA 31 with sorafenib reduced Hep3B xenograft tumor volume and suppressed tumor growth.

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References:[1] Young N, Gui Z, Mustafa S, et al. Inhibition of PDIs Downregulates Core LINC Complex Proteins, Promoting the Invasiveness of MDA-MB-231 Breast Cancer Cells in Confined Spaces In Vitro. Cells. 2024 May;13(11):906.[2] Won JK, Yu SJ, Hwang CY, et al. Protein disulfide isomerase inhibition synergistically enhances the efficacy of sorafenib for hepatocellular carcinoma. Hepatology. 2017;66(5):1569-1585.

Background

PACMA 31 is a novel, orally active, irreversible inhibitor of Protein Disulfide Isomerase (PDI; $IC_{50}=10\mu M$). PACMA 31 disrupts endoplasmic reticulum protein folding and induces tumor cell apoptosis. It inhibits thioredoxin reductase (TrxR) and promotes reactive oxygen species accumulation. PACMA 31 is used for studying ovarian cancer, chemotherapy-resistant tumors, and endoplasmic reticulum stress-related cancers^[1-4].

In vitro, OVCAR-8 cells were treated with 0-10 μM PACMA 31 for 24h. PACMA 31 inhibited cell viability and colony formation in a concentration-dependent manner^[5]. U87MG cells were treated with 0.1-1 μM PACMA 31 for 24h. PACMA 31 downregulated transcription of DNA repair and DNA damage response related genes and reduced E2F target gene expression^[6]. MDA-MB-231 cells were treated with 2.5 μM PACMA 31 for 24h. PACMA 31 upregulated HO-1 and downregulated SUN1, SUN2, Lamin A, and Lamin B1 expression. PACMA 31 reduced cell viability and proliferation^[7].

In vivo, C57BL/6J mice received a single unilateral intraplantar injection of 10 μL Complete Freund's Adjuvant (CFA). Twenty-four hours later, the mice received a single intraperitoneal injection of 20mg/kg PACMA 31. PACMA 31 alleviated CFA-induced mechanical allodynia^[8]. Nude mice with subcutaneous SNU-484 cell xenografts were intraperitoneally injected with 10mg/kg PACMA 31 every 3 days for 28 days. PACMA 31 inhibited tumor growth^[9]. BALB/c nude mice with subcutaneous Hep3B cell xenografts were orally administered 30mg/kg sorafenib and intraperitoneally injected with 20mg/kg PACMA 31 once daily for 4 weeks. PACMA 31 and sorafenib inhibited Hep3B xenograft tumor growth^[10].

References:

[1] Xu Q, Zhang J, Zhao Z, et al. Revealing PACMA 31 as a new chemical type TrxR inhibitor to promote cancer cell apoptosis. Biochim Biophys Acta Mol Cell Res. 2022 Oct;1869(10):119323.

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- [3] Young HS, McGowan LM, Jepson KA, et al. Impairment of cell adhesion and migration by inhibition of protein disulphide isomerases in three breast cancer cell lines. *Biosci Rep.* 2020 Oct 30;40(10):BSR20193271.
- [4] Krajewski D, Polukort SH, Gelzinis J, et al. Protein Disulfide Isomerases Regulate IgE-Mediated Mast Cell Responses and Their Inhibition Confers Protective Effects During Food Allergy. *Front Immunol.* 2020 Dec 22;11:606837.
- [5] Xu S, Butkevich A, Yamada R, et al. Discovery of an orally active small-molecule irreversible inhibitor of protein disulfide isomerase for ovarian cancer treatment. *Proc Natl Acad Sci U S A.* 2012 Oct 2;109(40):16348-53.
- [6] Xu S, Liu Y, Yang K, et al. Inhibition of protein disulfide isomerase in glioblastoma causes marked downregulation of DNA repair and DNA damage response genes. *Theranostics.* 2019;9(8):2282-2298.
- [7] Young N, Gui Z, Mustafa S, et al. Inhibition of PDIs Downregulates Core LINC Complex Proteins, Promoting the Invasiveness of MDA-MB-231 Breast Cancer Cells in Confined Spaces In Vitro. *Cells.* 2024;13(11):906.
- [8] Rouwette T, Sondermann J, Avenali L, et al. Standardized Profiling of The Membrane-Enriched Proteome of Mouse Dorsal Root Ganglia (DRG) Provides Novel Insights Into Chronic Pain. *Mol Cell Proteomics.* 2016;15(10):2152-2168.
- [9] Oh M, Jang S, Lee J, et al. The lipoprotein-associated phospholipase A2 inhibitor Darapladib sensitises cancer cells to ferroptosis by remodelling lipid metabolism. *Nat Commun.* 2023 Sep 15;14:5728.
- [10] Won JK, Yu SJ, Hwang CY, et al. Protein disulfide isomerase inhibition synergistically enhances the efficacy of sorafenib for hepatocellular carcinoma. *Hepatology.* 2017;66(5):1569-1585.

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