

Product Data Sheet

Product Name: α -Hydroxylinoleic acid (ABTL-0812)

Cat. No.: GC30761

Chemical Properties

Cas. No. 57818-44-7

SMILES CCCCC/C=C\C/C=C\CCCCCCC(O)C(O)=O

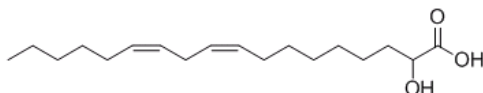
Formula $C_{18}H_{32}O_3$ M.Wt 296.44

Solubility DMSO: 5 mg/mL (16.87 mM) Storage Store 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

Cell experiment [1]:

Cell lines Neuroblastoma cell lines (SK-N-AS, SH-SY5Y, IMR-32, CHLA-90, SK-N-BE(2), LA1-5s)

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Preparation Method Neuroblastoma cell lines were cultured and maintained in Iscove's modified Dulbecco's medium supplemented with 10% heat-inactivated fetal bovine serum, 1% insulin-transferrin-selenium supplement, 100U/mL penicillin, 100µg/mL streptomycin and 5µg/mL plasmocin at 37°C in 5% CO₂. Cells were treated with α-Hydroxylinoleic acid diluted in culture medium supplemented with 0.5% FBS.

Reaction Conditions 30–60µM; 24–72hours

Applications α-Hydroxylinoleic acid significantly impaired cell viability, induced endoplasmic reticulum stress (ER stress), activated the unfolded protein response (UPR), triggered autophagy and apoptosis, and potentiated the antitumour activity of irinotecan and 13-cis-retinoic acid.

Animal experiment [2]:

Animal models Immunodeficient female athymic nude mice (for HEC-1A subcutaneous xenografts)

Preparation Method For xenografts, mice were subcutaneously injected with HEC-1A cells (1.5×10^6) and tumors were allowed to grow for 15 days before treatment. α-Hydroxylinoleic acid was administered daily by oral gavage at doses of 60mg/Kg or 120mg/Kg (for HEC-1A xenografts, treatment lasted 25 or 46 days).

Dosage form 60mg/kg or 120mg/kg; 25 or 46 days

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Applications α -Hydroxylinoleic acid treatment significantly reduced tumor growth in HEC-1A xenografts in a dose-dependent manner, increased TRIB3 expression and LC3-II conversion.

References:

- [1] París-Coderch L, Soriano A, Jiménez C, et al. The antitumour drug ABTL0812 impairs neuroblastoma growth through endoplasmic reticulum stress-mediated autophagy and apoptosis. *Cell Death Dis.* 2020 Sep 17;11(9):773.
- [2] Felip I, Moiola CP, Megino-Luque C, et al. Therapeutic potential of the new TRIB3-mediated cell autophagy anticancer drug ABTL0812 in endometrial cancer. *Gynecol Oncol.* 2019 May;153(2):425-435.

Background

α -Hydroxylinoleic acid (ABTL-0812) is an orally active anticancer compound. α -Hydroxylinoleic acid induces endoplasmic reticulum stress by activating PPAR α/γ nuclear receptors, while simultaneously inhibiting the Akt/mTOR pathway through the induction of TRIB3 overexpression, thereby triggering autophagy-mediated cancer cell death. α -Hydroxylinoleic acid can be used in research related to various cancers such as lung cancer, endometrial cancer, and pancreatic cancer^[1-4].

In vitro, α -Hydroxylinoleic acid (30–60 μ M) was used to treat neuroblastoma cell lines (including SK-N-AS, SH-SY5Y, IMR-32, CHLA-90, SK-N-BE(2), and LA1-5s) for 24–72 hours. α -Hydroxylinoleic acid significantly impaired cell viability, induced endoplasmic reticulum stress (ER stress), unfolded protein response (UPR), autophagy, and apoptosis^[5]. α -Hydroxylinoleic acid (10–100 μ M) was used to treat human cancer cell lines (including lung adenocarcinoma A549, pancreatic cancer MiaPaca2, endometrial cancer Ishikawa, squamous non-small cell lung cancer H157, etc.) for 48 hours. α -Hydroxylinoleic acid significantly increased intracellular long-chain dihydroceramide levels and induced apoptosis^[6].

In vivo, α -Hydroxylinoleic acid (120mg/kg and 240mg/kg; once daily; 5 days per week) was administered orally to CD1-nu/nu mice bearing U87MG or T98G tumors for 5 weeks. α -Hydroxylinoleic acid significantly impaired tumor growth and increased disease-free survival and

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overall survival of mice^[7]. α -Hydroxylinoleic acid (60mg/kg or 120mg/kg; once daily) was administered orally to immunodeficient female athymic nude mice bearing HEC-1A tumors for 25 or 46 days. α -Hydroxylinoleic acid significantly reduced tumor growth^[8].

References:

- [1] Vidal L, Victoria I, Gaba L, et al. A first-in-human phase I/Ib dose-escalation clinical trial of the autophagy inducer ABTL0812 in patients with advanced solid tumours. *Eur J Cancer*. 2021 Mar;146:87-94.
- [2] Erazo T, Lorente M, López-Plana A, et al. The New Antitumor Drug ABTL0812 Inhibits the Akt/mTORC1 Axis by Upregulating Tribbles-3 Pseudokinase. *Clin Cancer Res*. 2016 May 15;22(10):2508-19.
- [3] Noguera-Castells A, Mancino M, Morán T, et al. The novel proautophagy anticancer drug ABTL0812 potentiates chemotherapy in adenocarcinoma and squamous nonsmall cell lung cancer. *Int J Cancer*. 2020 Aug 15;147(4):1163-1179.
- [4] Leary A, Estévez-García P, Sabatier R, et al. ENDOLUNG trial. A phase 1/2 study of the Akt/mTOR inhibitor and autophagy inducer Ibrilatazar (ABTL0812) in combination with paclitaxel/carboplatin in patients with advanced/recurrent endometrial cancer. *BMC Cancer*. 2024 Jul 22;24(1):876.
- [5] París-Coderch L, Soriano A, Jiménez C, et al. The antitumour drug ABTL0812 impairs neuroblastoma growth through endoplasmic reticulum stress-mediated autophagy and apoptosis. *Cell Death Dis*. 2020 Sep 17;11(9):773.
- [6] Muñoz-Guardiola P, Casas J, Megías-Roda E, et al. The anti-cancer drug ABTL0812 induces ER stress-mediated cytotoxic autophagy by increasing dihydroceramide levels in cancer cells. *Autophagy*. 2021 Jun;17(6):1349-1366.
- [7] Mancini A, Colapietro A, Cristiano L, et al. Anticancer effects of ABTL0812, a clinical stage drug inducer of autophagy-mediated cancer cell death, in glioblastoma models. *Front Oncol*. 2022 Nov 2;12:943064.
- [8] Felip I, Moiola CP, Megino-Luque C, et al. Therapeutic potential of the new TRIB3-mediated cell autophagy anticancer drug ABTL0812 in endometrial cancer. *Gynecol Oncol*. 2019 May;153(2):425-435.

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