

7ACC1

Chemical Properties

CAS No. :	50995-74-9
Formula:	C ₁₄ H ₁₅ NO ₄
Molecular Weight:	261.273
Storage:	Keep away from direct sunlight Powder: -20°C for 3 years In solvent: -80°C for 1 year <small>Actual storage temperature shall be subject to the COA.</small>

Biological Description

Description	7ACC1 (D 142) selectively affects a single part of the MCT symporter translocation cycle, leading to strict inhibition of lactate influx. This singular activity is associated with antitumor effects less prone to resistance and side effects.
Targets(IC50)	Monocarboxylate transporter
In vitro	7-(Diethylamino)coumarin-3-carboxylic acid compounds on lactate influx using oxidative cancer cells known to maintain in vitro their capacity to take up lactate as an energetic fuel, and the lack of effects on lactate efflux using highly glycolytic cells. Accordingly, in oxidative human cancer cervix cells, SiHa and Hela, which express both MCT1 and MCT4 isoforms, a potent inhibition of both lactate influx and cell proliferation was obtained with 7-(Diethylamino)coumarin-3-carboxylic acid, whereas the bona fide MCT1/MCT2 inhibitor AR-C155858 failed to do so. The effects of 7-(Diethylamino)coumarin-3-carboxylic acid were confirmed in MCT1/4-expressing pharynx squamous FaDu tumor cells. These observations strongly suggest that 7-(Diethylamino)coumarin-3-carboxylic acid compounds are inhibitors of lactate entry through both MCT1 and MCT4 preventing any compensatory effects when MCT1, the main path for lactate uptake, is inhibited.
In vivo	7-(Diethylamino)coumarin-3-carboxylic acid developed to selectively interfere with lactate fluxes in the lactate-rich tumor microenvironment. The pharmacologic properties of two compounds of this family, including their effects on lactate influx and efflux and antitumor activity, were investigated using human cancer cell lines and mouse xenograft models. Contrary to the reference MCT1 inhibitor AR-C155858, 7-(Diethylamino)coumarin-3-carboxylic acid unexpectedly inhibited lactate influx but not efflux in tumor cells expressing MCT1 and MCT4 transporters. 7-(Diethylamino)coumarin-3-carboxylic acid delayed the growth of cervix SiHa tumors, colorectal HCT116 tumors, and orthotopic MCF-7 breast tumors. MCT target engagement was confirmed by the lack of activity of 7-(Diethylamino)coumarin-3-carboxylic acid on bladder UM-UC-3 carcinoma that does not express functional MCT. 7-(Diethylamino)coumarin-3-carboxylic acid also inhibited SiHa tumor relapse after treatment with cisplatin. Finally, we found that contrary to AR-C155858, 7-(Diethylamino)coumarin-3-carboxylic acid did not prevent the cell entry of the substrate-mimetic drug 3-bromopyruvate (3BP) through MCT1, and contributed to the inhibition of tumor relapse after 3BP treatment.

<p>Cell Research</p>	<p>Usage:</p> <p>I. Solution preparation</p> <ol style="list-style-type: none"> 1. Stock solution: Dissolve 7ACC1 in an appropriate organic solvent (such as DMSO), usually prepared as a 1-10 mM stock solution. 2. Working solution: Dilute the stock solution to the required working concentration, usually 0-50 µM, using an experimental buffer (such as PBS, pH 7.4) according to experimental needs. <p>II. Application steps</p> <p>Cell culture experiment</p> <ol style="list-style-type: none"> (1) Cell type: 7ACC1 is mainly used in the study of renal cancer cells, breast cancer cells and other cancer cell lines. (2) Treatment method: Add 7ACC1 to the cell culture medium, culture the cells for 24-96 hours, and adjust the concentration as needed. (3) Cell function detection: <ol style="list-style-type: none"> a. Proliferation detection: MTT or CCK-8 method can be used to detect cell proliferation. b. Migration and invasion detection: The migration and invasion ability of cells can be evaluated by scratch test or Transwell test. c. MCT-1/MCT-4 expression detection: Western blot or qPCR method was used to detect the protein or mRNA expression level of MCT-1/MCT-4. d. Lactate concentration detection: Lactate determination kit was used to detect the lactate content in cell culture medium. <p>Animal experiment</p> <ol style="list-style-type: none"> (1) Treatment method: 7ACC1 was injected or administered to experimental mice by intraperitoneal injection or oral administration. The dose was usually 10-50 mg/kg according to the experimental design. (2) Tumor inhibition experiment: The inhibitory effect of 7ACC1 on tumor growth was evaluated by measuring tumor size. (3) Immunohistochemical analysis: Immunohistochemical analysis was performed on tumor tissue to detect the expression level of MCT-1/MCT-4 and lactate accumulation. <p>3. Calibration and control</p> <ol style="list-style-type: none"> (1) Control group: An untreated cell or animal group was set as a control to verify the effect of 7ACC1. (2) Standard curve: In the lactate concentration detection experiment, a standard curve is established to calibrate the relationship between lactate concentration and fluorescence signal. <p>Notes</p> <ol style="list-style-type: none"> (1) Solubility: 7ACC1 has good solubility in DMSO. When using, avoid leaving undissolved solids in the solution. (2) Storage conditions: 7ACC1 should be stored at -20°C in a dark environment and avoid repeated freezing and thawing. (3) Cytotoxicity: Although 7ACC1 has an inhibitory effect on cancer cells, it may be toxic to normal cells at high concentrations. The concentration should be adjusted according to experimental requirements. (4) Photosensitivity: 7ACC1 may be sensitive to light. Avoid direct light during the experiment. <p>The above information is based on published literature. Experimental procedures should be appropriately modified to meet specific research demands.</p>
<p>Animal Research</p>	<p>Eight-week-old NMRI female nude mice (Elevage Janvier) were injected subcutaneously with 2×10^6 SiHa cells, 2×10^6 HCT-116 cells, or 5×10^6 UM-UC-3 cells. An orthotopic breast cancer model was also used with MCF-7 tumor cells injected into the mammary fat pad of mice; a 17β-estradiol pellet had first been subcutaneously implanted in these</p>

Animal Research	<p>mice as previously described . When tumors reached a mean diameter of 5 mm, 7-(Diethylamino)coumarin-3-carboxylic acid compounds (3 mg/kg) or AR-C155858 (3 mg/kg) were daily injected intraperitoneally; in some experiments, 7-(Diethylamino) coumarin-3-carboxylic acid treatment was combined with cisplatin (5 mg/kg) injected intraperitoneally at days 0 and 7 (7-(Diethylamino)coumarin-3-carboxylic acid administered daily except at days 0 and 7) or 3BP(3 mg/kg) injected i.p. from day 0 to 4 and day 7 to 11 (7-(Diethylamino)coumarin-3-carboxylic acid administered together with 3BP). Cisplatin and 3BP were also administered alone and control mice were injected with vehicle (dimethyl sulfoxide). Tumor sizes were tracked with an electronic calliper and determined using the formula: $(\text{length} \times \text{width}^2 \times \pi)/6$.</p> <p>The above information is based on published literature. Experimental procedures should be appropriately modified to meet specific research demands.</p>
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Solubility Information

Solubility	DMSO: 32.00 mg/mL (122.48 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
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Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	3.8275 mL	19.1373 mL	38.2746 mL
5 mM	0.7655 mL	3.8275 mL	7.6549 mL
10 mM	0.3827 mL	1.9137 mL	3.8275 mL
50 mM	0.0765 mL	0.3827 mL	0.7655 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

Liu Y, et al. Limosilactobacillus reuteri and caffeoylquinic acid synergistically promote adipose browning and ameliorate obesity-associated disorders. *Microbiome*. 2022 Dec 15;10(1):226. doi: 10.1186/s40168-022-01430-9.

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Hodges WT, et al. Mitochondrial pyruvate carrier inhibitors improve metabolic parameters in diet-induced obese mice. *J Biol Chem*. 2022 Feb;298(2):101554.

Guo C, et al. Monocarboxylate transporter 1 and monocarboxylate transporter 4 in cancer-endothelial co-culturing microenvironments promote proliferation, migration, and invasion of renal cancer cells. *Cancer Cell Int*. 2019 Jun 28;19:170.

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