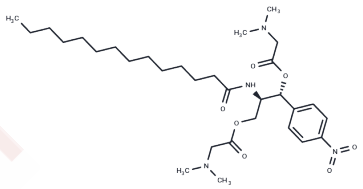
Data Sheet (Cat.No.T11835)

TargetMol

LCL521

Chemical Properties



CAS No. : 1226851-11-1

Formula: C31H52N4O7

Molecular Weight: 592.77

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	LCL521 inhibits lysosomal acid sphingomyelinase (ASMase).LCL521 is an acid ceramidase (ACDase) inhibitor.
Targets(IC50)	Phospholipase
In vitro	LCL521 (1μM) effectively inhibited ACDase in MCF7 cells, but the effects were transient. LCL521 (10μM) caused a profound decrease of sphingosine and an increase of ceramide, but additionally affected the processing and regeneration of the ACDase protein, with biphasic and reversible effects on the expression of ACDase, which paralleled the long-term changes of cellular sphingosine and ceramide. The higher concentrations of LCL521 also inhibited Dihydroceramide desaturase (DES-1). In summary, LCL521 exhibits significant effects on ACDase in a dose and time-dependent manner.[2]
In vivo	When PDT-treated SCCVII cells are used to vaccinate SCCVII tumor-bearing mice, adjuvant LCL521 treatment (75 mg/kg; i.p.) resulted in marked retardation of tumor growth. This effect can be attributed to the capacity of LCL521 to effectively restrict the activity of two main immunoregulatory cell populations (Tregs and myeloid-derived suppressor cells, MDSCs) that are known to hinder the efficacy of PDT vaccines. The interaction of LCL521 with PDT-based antitumor mechanisms is dominated by immune system contribution that includes overriding the effects of immunoregulatory cells but could also include a tacit contribution from boosting direct tumor cell kill.[3]

Solubility Information

Solubility	DMSO: 148.5 mg/mL (250.52 mM),Sonication is recommended. Ethanol: 90 mg/mL (151.83 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween-80+45% Saline: 3.3 mg/mL (5.57 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.687 mL	8.435 mL	16.8699 mL
5 mM	0.3374 mL	1.687 mL	3.374 mL
10 mM	0.1687 mL	0.8435 mL	1.687 mL
50 mM	0.0337 mL	0.1687 mL	0.3374 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

Bai A, et al. Targeting (cellular) lysosomal acid ceramidase by B13: design, synthesis and evaluation of novel DMG-B13 ester prodrugs. Bioorg Med Chem. 2014 Dec 15;22(24):6933-44.
Bai A, et al. Dose dependent actions of LCL521 on acid ceramidase and key sphingolipid metabolites. Bioorg Med Chem. 2018;26(23-24):6067-6075.
Korbelik M, et al. Interaction of acid ceramidase inhibitor LCL521 with tumor response to photodynamic therapy and photodynamic therapy-generated vaccine. Int J Cancer. 2016;139(6):1372-1378.
Liu F, et al. Ceramide activates lysosomal cathepsin B and cathepsin D to attenuate autophagy and induces ER stress to suppress myeloid-derived suppressor cells. Oncotarget. 2016;7(51):83907-83925.
White-Gilbertson S, et al. Polyploid giant cancer cells are dependent on cholesterol for progeny formation through amitotic division. Sci Rep. 2022;12(1):8971.
Korbelik M, et al. Mechanistic insights into ceramidase inhibitor LCL521-enhanced tumor cell killing by photodynamic and thermal ablation therapies. Photochem Photobiol Sci. 2020;19(9):1145-1151.