

Product Data Sheet

Product Name: ALC-0315

Cat. No.: GC19792

Chemical Properties

Cas. No. 2036272-55-4

SMILES OCCCCN(CCCCCCOC(C(CCCCCC)CCCCCCCC)=O)CCCCCOC(C(CCCCCC)CCCCCCCC)=O

Formula $C_{48}H_{95}NO_5$ M.Wt 766.27

Solubility DMSO : 100 mg/mL (130.50 mM) Storage 4°C, protect from light
Ethanol : 100 mg/mL (130.50 mM)

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

siRNA-LNP Formulation and Analysis [1]:

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Preparation Method siRNAs were dissolved in sodium acetate (pH 4) and combined with a lipid solution at an amine-to-phosphate (N/P) ratio of 3. The lipid formulations consisted of DSPC, cholesterol, and PEG-DMG at a 10:38.5:1.5% molar ratio, with either 50% DLin-MC3-DMA or ALC-0315. The LNPs were dialyzed against phosphate-buffered saline (PBS) at pH 7.4 in 500-fold excess. For quality control, cholesterol content was measured using the Cholesterol E Assay Kit. To determine siRNA concentration and entrapment, a RiboGreen assay was used. Encapsulation efficiency was measured by comparing Ribogreen signal in LNP samples with or without Triton X-100 detergent. Particle size was measured using a Malvern-Zetasizer Nano.

Animal experiment [2]:

Animal models C57BL/6J mice

Preparation Method 2'-O-Methylated siRNA targeting murine FVII (siFVII), ADAMTS13 (siADAMTS13) and a negative control siRNA targeting luciferase (siLuc) were used. The resulting LNPs were diluted to a final concentration of 0.1 mg/mL siRNA in PBS prior to intravenous (IV) injection. Injected mice with 1 mg siRNA per kg body weight (mg/kg) for knockdown studies and 5 mg/kg dose for toxicity studies.

Dosage form 1, 5 mg/kg

Applications Mice treated with siADAMTS13-ALC-0315 at the same dose had greater ADAMTS13mRNA and protein knockdown, compared to mice treated with siADAMTS13-MC3.

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

References:

[1] : Ferraresso F, Strilchuk A W, Juang L J, et al. Comparison of DLin-MC3-DMA and ALC-0315 for siRNA Delivery to Hepatocytes and Hepatic Stellate Cells[J]. Molecular Pharmaceutics, 2022.

Background

ALC-0315 is a key component of the COVID-19 mRNA vaccine and a highly sought-after lipid for nucleic acid therapeutics research [1]. Ionizable cationic lipids are essential for efficient in vivo delivery of RNA by lipid nanoparticles (LNPs). DLin-MC3-DMA (MC3), ALC-0315, and SM-102 are the only ionizable cationic lipids currently clinically approved for RNA therapies. ALC-0315 and SM-102 are structurally similar lipids used in SARS-CoV-2 mRNA vaccines [2].

Cationic lipids (CLs) and ionizable lipids (ILs) initiate the first step of self-assembly via electrostatic interactions. because of toxicity issues and lack of in vivo efficacy, CLs have been replaced by pH-sensitive ILs. The overall architecture of CLs and ILs can be broken down into three parts: (1) the headgroup, (2) the linker, and (3) the tails. The headgroups of ALC-0315 contain a terminal hydroxyl group which could decrease the hydration of the headgroup and improve hydrogen-bonding interactions with the nucleic acid, potentially leading to improved transfection ability. The linker typically connects the headgroup with the tails, although the linkers may also be buried within the tails. DLin-MC3-DMA, ALC-0315, and SM-102 all have ester linkers. DLin-MC3-DMA has two linoleyl tails, while ALC-0315 and SM-102 contain two branched saturated tails that are postulated to endow a cone-shaped geometry, facilitating destabilization of the endosomal membrane and cytosolic release of the nucleic acid [3].

References:

- [1]. Saadati F, Cammarone S, Ciufolini M A. A Route to Lipid ALC-0315: a Key Component of a COVID-19 mRNA Vaccine[J]. Chemistry—A European Journal, 2022, 28(48): e202200906.
- [2]. Ferraresso F, Strilchuk A W, Juang L J, et al. Comparison of DLin-MC3-DMA and ALC-0315 for siRNA Delivery to Hepatocytes and Hepatic Stellate Cells[J]. Molecular Pharmaceutics, 2022.
- [3]. Eygeris Y, Gupta M, Kim J, et al. Chemistry of lipid nanoparticles for RNA delivery[J]. Accounts of Chemical Research, 2021, 55(1): 2-12.

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA