DC60782 | Lipid A4B4-S3

Instructions for Use

A4B4-S3 is a novel biodegradable ionizable lipid that has been meticulously designed through modular platforms and optimized specifically for mRNA delivery. It serves as a critical component of lipid nanoparticles (LNPs) and enhances mRNA delivery efficiency by facilitating endosomal escape. The structural design of A4B4-S3 leverages the Passerini reaction, a highly efficient and modular chemical method that enables the rapid generation of diverse lipid libraries. The design focuses on optimizing the methylene units between lipid headgroups and linkages to strengthen hydrogen bonding interactions with mRNA ribophosphate complexes. This enhanced hydrogen bonding allows for more effective release of mRNA from endosomes, thereby boosting delivery efficiency. Concurrently, the structural optimization improves biodegradability, reducing potential long-term toxicity risks.
In experimental studies, A4B4-S3 has demonstrated superior gene editing efficacy in mouse liver compared to SM-102, a clinically prevalent lipid used in Moderna's COVID-19 vaccine. It also shows potential for repeat-dose protein replacement therapies, suggesting enhanced stability and safety for long-term treatment regimens. Technologically, A4B4-S3 not only provides a more efficient LNP formulation but also deepens the understanding of the relationship between structure and delivery efficiency. This offers new directions for the development of future mRNA therapeutics. In summary, A4B4-S3 represents a next-generation delivery carrier achieved through rational design and high-throughput screening strategies. Its performance enhancements and biodegradable properties position it as a promising candidate for gene therapies and vaccine applications.

Product information

CAS No.	Not available
Chemical Name	Lipid A4B4-S3
Formula	C47H90N2O5
M.Wt	762.68
Purity	ELSD-HPLC>95%
Storage	Original product: up to 1 year under the storage conditions stated on the vial, kept tightly sealed. Stock solutions: aliquots at -20°C, generally up to one month.
Shipping condition	Ships from Shanghai. Pure lipid is stable during ice-pack transport.

Formulation & study context

Literature values apply to the cited study only. Administration routes describe research, not clinical instructions.

A complete product-specific formulation has not been verified. No standard ratio is substituted.

N/P ratio	Not reported in the verified record
Cargo	Not available in the verified record
Administration route	Not available in the verified record

Animal model	Not available in the verified record
Formulation process	Not available in the verified record

N/P is a nitrogen-to-phosphate molar ratio. Lipid:cargo mass ratio is a different quantity and must not be used as N/P.

Stock-solution preparation table

Calculated using product-page MW: 762.68 g/mol. Volumes are final solution volumes.

Mass	1 mM	5 mM	10 mM
10 mg	13.112 mL	2.622 mL	1.311 mL
25 mg	32.779 mL	6.556 mL	3.278 mL
50 mg	65.558 mL	13.112 mL	6.556 mL
100 mg	131.117 mL	26.223 mL	13.112 mL
250 mg	327.791 mL	65.558 mL	32.779 mL

Volume (mL) = mass (mg) × 1000 / [MW (g/mol) × concentration (mM)]. Mathematical conversions only; not measured solubility. Confirm solvent compatibility and the exact material before preparation.

Handling & storage

Provided that storage conditions are as stated on the product vial and the vial is kept tightly sealed, the product can be stored for up to 1 year.

Wherever possible, prepare and use solutions on the same day. If stock solutions must be prepared in advance, store them as aliquots in tightly sealed vials at -20°C. Generally, these will be usable for up to one month.

Before use, and prior to opening the vial, allow the product to equilibrate to room temperature for at least 1 hour.

References

Rational design and modular synthesis of biodegradable ionizable lipids via the Passerini reaction for mRNA delivery-Yue Xu # 1, Fanglin Gong # 2, Alex Golubovic # 1, Amy Strilchuk 1, Jingan Chen 2, Muye Zhou 1, Songtao Dong 1, Breanna Seto 3, Bowen LiProc Natl Acad Sci U S A . 2025 Feb 4;122(5):e2409572122. doi: 10.1073/pnas.2409572122. Epub 2025 Jan 30.