

Utilization of Polyunsaturated Fatty Acids in Amphiphilic Dendrimers for Lipid Nanoparticle Vaccine Delivery

Abstract

This project explores the potential of amphiphilic dendrimers as targeted delivery vehicles for therapeutics. We focused on Arachidonoyl Ethanolamide (AEA). In order to build efficient carriers for vaccines contained within lipid nanoparticles, we purified AEA and we are exploring its utility by coupling it with dendrimers. In addition to modifying AEA, we will also be making second generation dendrimers for the AEA to attach to.

Dendrimers are unique molecules with a tree-like structure that possess both hydrophilic and hydrophobic properties, making them versatile delivery systems. Dendrimers can mimic the behavior of lipids, aiding in the fusion of lipid nanoparticles with cell membranes for efficient drug delivery.

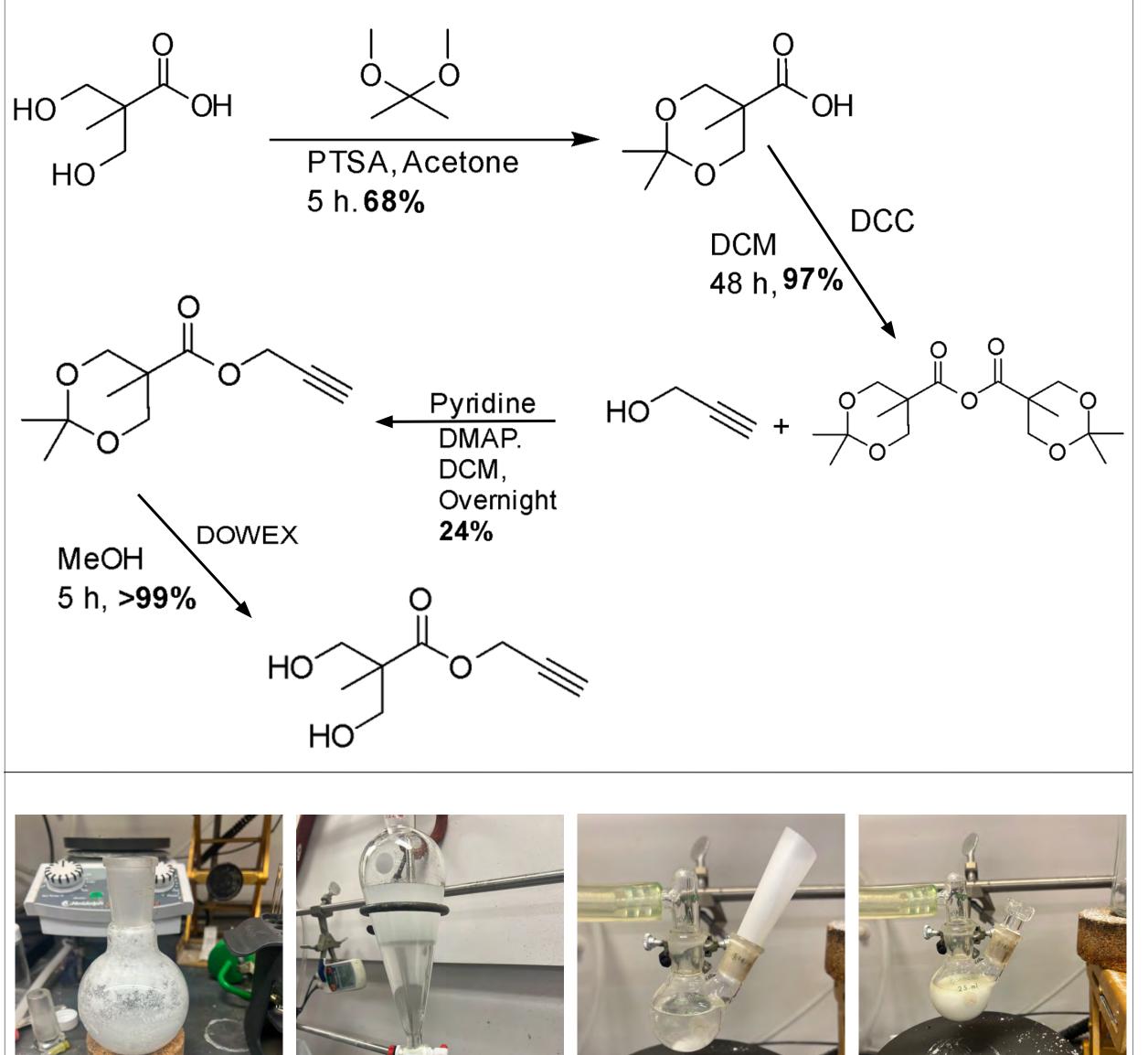
After facing challenges in the initial purification attempts using esterification and amination techniques, we are now exploring a different strategy. Our focus is on protecting the hydroxyl group of AEA to reduce its polarity, allowing for a smoother separation using a silica column.

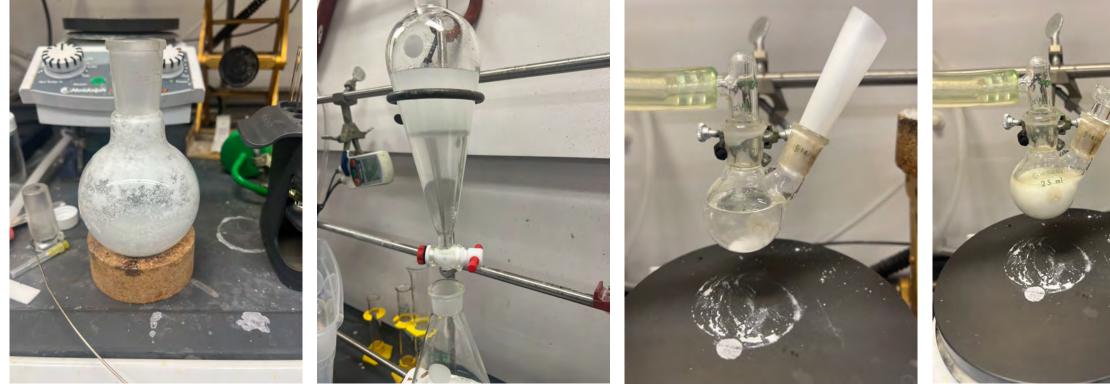
Through this study, we aspire to overcome the hurdles of AEA purification and establish a strong foundation for developing advanced drug delivery systems. The successful coupling of AEA with dendrimers for lipid nanoparticle vaccine delivery holds significant promise in revolutionizing targeted therapies and enhancing vaccine effectiveness.

Objectives

- The objective of this project is to modify Arachidonoyl Ethanolamide so it can be coupled with dendrimers, enabling effective lipid nanoparticle vaccine delivery.
- We have employed chemical modification techniques such as esterification and amination to obtain pure AEA material.
- Due to unsuccessful purification attempts, we decided to protect the OH group of AEA to reduce its polarity.
- Finally, we are developing second generation dendrimers to facilitate the efficient attachment of the modified AEA

Developing the Dendrimers





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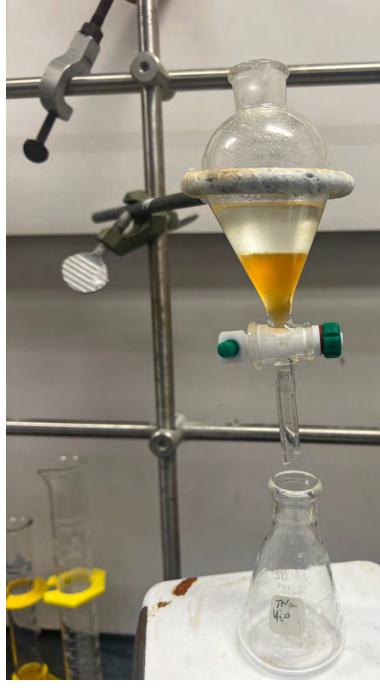
Protecting the Hydroxyl Group Imidazole. **TBDMS-CL** DMAP, DCM 0°C to RT

Protecting the OH group



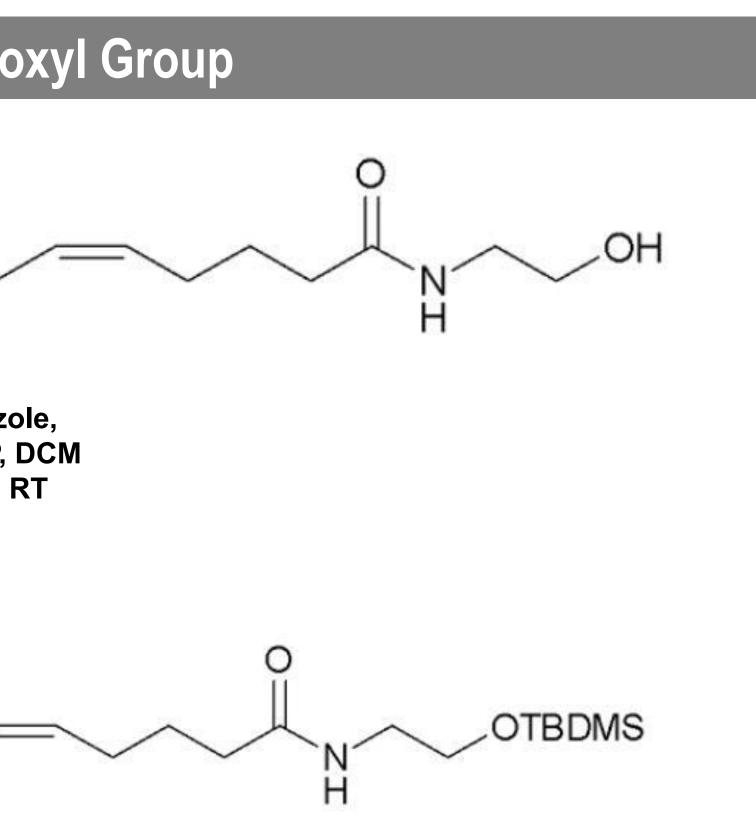
Experimental Procedures

Separation of organic and aqueous material

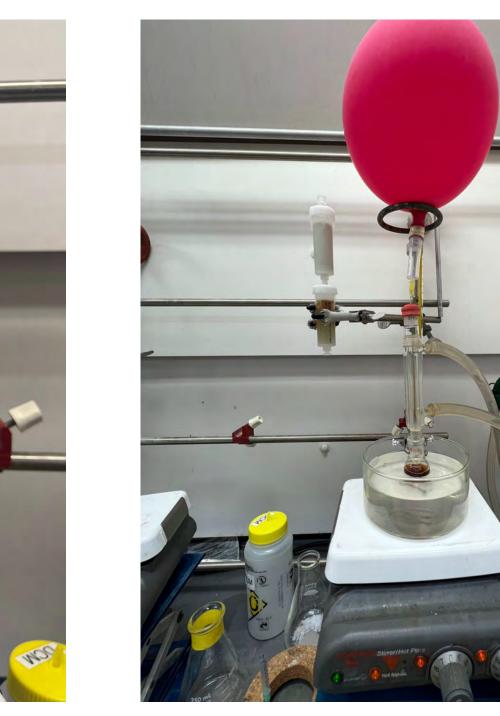


TLC Plate of attempted protection of AEA

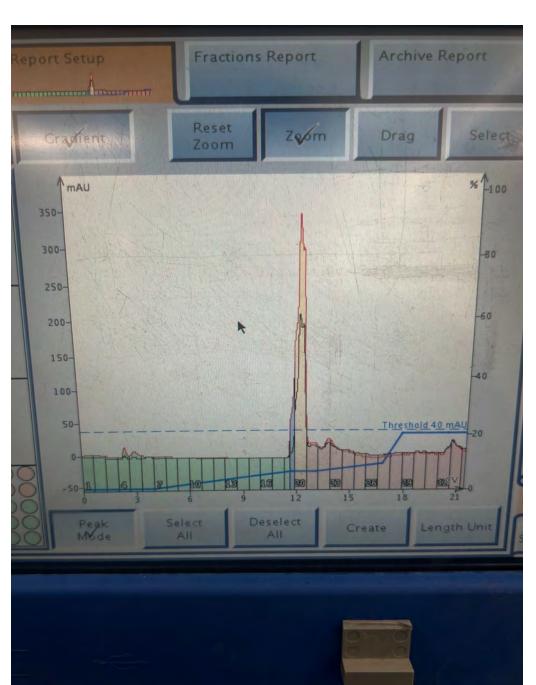




Refluxing of attempted hydrolysis



Autocolumn results of attempted protection of AEA



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In the initial purification attempts using esterification and amination, our desired results were not obtained on the TLC plate or the silica column. As a response to these challenges, the project shifted focus to a new strategy-protecting the OH group of AEA. This will reduce the polarity, potentially enabling easier separation when using a silica column. Currently, the experiment to protect the OH group is ongoing, and the results are yet to be determined. The project also involved the development of second-generation dendrimers. However, we are currently facing difficulties with a particular step in this process. In conclusion, we will continue experimentation to overcome purification challenges and optimize the development of advanced drug delivery systems.

Thank you to Dr. Valery Fokin for giving me the opportunity to work in his lab. I would also like to thank my mentor, Joshua lbs, for his invaluable guidance and support throughout my research project. Lastly, I would like to thank the rest of my colleagues for all their advice and help throughout the summer.

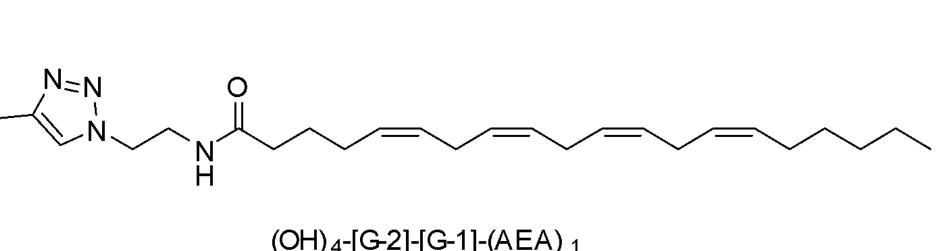
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Final Structure



Summary

Acknowledgements