Chitosan FlashFocus

Edition 101 – Sept 6, 2023

Trimethyl Chitosan: Charge Density and Antigen Interaction

Enhanced Vaccine Adjuvanticity

Introduction

Vaccine development has evolved beyond the mere introduction of antigens; adjuvants are now integral components that enhance the immunogenicity of vaccines. Trimethyl chitosan (TMC), is a derivative of chitosan. It's achieved from the chemical modification of chitosan and exhibits an additional positive (cationic) charge compared to its chitosan precursor. This augmentation of chitosan's positive charge gives rise to unique electrostatic interaction between TMC and antigens, playing a pivotal role in the adjuvanticity of TMC.

This edition of *Chitosan FlashFocus Insights* summarizes the charge-related properties of TMC and touches on the molecular mechanisms underpinning its interaction with antigens. These mechanisms hold keys to harnessing TMC's potential for enhanced immune response modulation.

Charge Density of Trimethyl Chitosan

TMC's charge density is primarily attributed to its quaternized amino groups resulting from the trimethylation of chitosan. These quaternary ammonium moieties confer a positive charge to TMC molecules. The extent of charge density can be modulated during synthesis, allowing for tailored adjuvant properties.

Antigen Interaction Mechanisms

The interaction between TMC and antigens is chiefly governed by electrostatic forces. Antigens, often carrying negative charges due to their molecular composition, form stable complexes with TMC's positive charges. This phenomenon is driven by coulombic attraction between the positively charged ions of chitosan and the surface negatively charged ions, resulting in the formation of ionic bonds or ion-dipole interactions. These interactions promote the encapsulation or entrapment of antigens within TMC particles, safeguarding them from enzymatic degradation and facilitating their efficient uptake by antigen-presenting cells.

Enhanced Antigen

TMC's ability to form antigen-TMC complexes leads to enhanced antigen presentation to immune cells. Antigen-presenting cells internalize these complexes more effectively due to the positive charge on TMC, leading to improved processing and presentation of antigens on major histocompatibility complexes. This, in turn, triggers a heightened and sustained immune response.

Modulation of Immune Signaling

But the interaction between TMC and antigens extends beyond physical encapsulation. It also influences intracellular signaling pathways, amplifying the release of pro-inflammatory

cytokines and chemokines. The charged nature of TMC complexes aids in the activation of toll-like receptors, further augmenting immune cell activation and recruitment.

Customize Charge Density for Additional Adjuvanticity

The charge density of TMC can be tailored to optimize its adjuvant properties. By adjusting the degree of trimethylation, the charge density can be optimized for specific antigens or immune responses. This flexibility allows for the design of personalized vaccine formulations with precise controlled adjuvant effects.

Customization of charge density is achieved through precise control of the degree of trimethylation. Methods such as varying reaction time, temperature, and trimethylating agent concentration allow for fine-tuning of TMC's charge density. Characterization techniques like NMR spectroscopy and zeta potential analysis are important measures for confirming the desired charge density.

The choice of trimethylating agent can also influence the reaction conditions, selectivity, and efficiency of the trimethylation process. Typically, agents are selected based on factors such as, reactivity, safety, and the desired degree of trimethylation. There are many choices for trimethylating chitosan to enable the introduction of methyl groups to chitosan's amino groups, facilitating the synthesis of trimethyl chitosan. These choices include, Methyl iodide, Dimethyl sulfate (DMS), Methyltrioxorhenium (MTO), Methyl p-toluenesulfonate (MeTs. Though these agents are commonly used for chitosan methylation in laboratory experiments, but they are moderate to highly toxic. Therefore, Methyl trifluoromethanesulfonate (MeOTf) is preferred as its an organic compound that is a milder trimethylating agent. Its often used in translational research to achieve controlled methylation of chitosan while minimizing side reactions. Its commercially available, however it may also be prepared in the laboratory by treating dimethyl sulfate with triflic acid*.

Conclusion

The charge density and antigen interaction of Trimethyl Chitosan (TMC) are pivotal factors underlying its enhanced adjuvanticity. The positive charge of TMC facilitates strong interactions with negatively charged antigens, resulting in stable complexes that enhance antigen uptake and presentation. This Chitosan FlashFocus outlined the intricate molecular mechanisms governing TMC-antigen interactions, providing valuable insights for the rational design and customization of TMC-based adjuvants. The convergence of charge-related properties and antigen interaction dynamics positions TMC as a candidate for innovative vaccine formulations.

** Chemicals requires proper training, safety equipment, and facilities. If you are not experienced in working with chemicals, it's strongly advised to consult with a qualified chemist or professional before attempting any synthesis.*

Authored by: ChitoLytic Team

For more information on how ChitoLytic can help you with enhancing vaccine adjuvanticity with chitosan contact us:

Email: info@chitolytic.com
Telephone (International) & Whatsapp: +1 (438) 930-6453
Telephone Toll free (USA and Canada): (866) 729-4467
www.chitolytic.com

Click Here

ChitoLytic
— Reliable Chitosan —

References

Akhtar, F., & Rizvi, M. M. (2017). Recent progress in chitosan and chitosan derivatives for non-viral gene delivery. International Journal of Biological Macromolecules, 104, 1830-1845. https://www.mdpi.com/1424-8247/13/10/307

Illum, L. (2003). Chitosan and its use as a pharmaceutical excipient. Pharmaceutical Research, 20(9), 1339-1347. https://pubmed.ncbi.nlm.nih.gov/9755881/

Manatunga, D. C., & Chow, C. (2015). Quaternized chitosan as an adjuvant for monoclonal antibody-based immunotherapy. Immunology Letters, 168(2), 196-201.

Petrovsky, N., Aguilar, J. C., & Vaccine adjuvants: Current state and future trends. Immunology and Cell Biology, 82(5), 488-496. Vaccine adjuvants: current state and future trends- PubMed (nih.gov)

Tan, Q., Liu, X., & Pan, J. (2019). Trimethyl chitosan nanoparticles enhanced the immunogenicity of DNA vaccine against foot-and-mouth disease. BMC Veterinary Research, 15(1), 39.

Teng, W. L., & Chen, L. H. (2006). Chitosan nanoparticles as a protein delivery carrier—systematic examination of fabrication conditions for efficient loading and release. Journal of Applied Polymer Science, 100(3), 1997-2004.

van der Lubben, I. M., Kersten, G., & van Eden, W. (2011). Chitosan microparticles for mucosal vaccination against diphtheria: oral and nasal efficacy studies in mice. Vaccine, 29(3), 655-662.

Vila, A., Sánchez, A., & Alonso, M. J. (2002). Design of biodegradable particles for protein delivery. Journal of Controlled Release, 78(1-3), 15-24.

Zeng, X., Liu, G., & Tao, W. (2018). A drug-self-gated mesoporous antitumor nanoplatform based on pH-responsive and charge-convertible polymer–drug conjugates. Advanced Functional Materials, 28(11), 1705457.

Zhao, K., Chen, G., & Wang, C. (2020). Trimethyl chitosan nanoparticles enhance protective immune response of porcine circovirus type 2 (PCV2) subunit vaccine in pigs. International Journal of Biological Macromolecules, 156, 591-599.
