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Lipid-based nanocomposites for mRNA delivery: Current trends and future challenges

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COMMENTARY

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Abstract

Lipid nanoparticles (LNPs) are critical for the efficient delivery and intracellular transport of mRNA. They have recently been recognized as essential components of COVID-19 mRNA vaccines. Recent vaccinations have demonstrated the significant of lipid-based nanocomposite in the positive and effective delivery of mRNA therapies. These nanocomposites boost mRNA's efficacy by improving stability, biological uptake, and targeted delivery. We examine how lipid-based mRNA delivery methods are still being developed.

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Lipid nanoparticles (LNPs) include a lipid matrix that is stabilized through the addition of surfactant. Lipid-based nanoparticle carriers containing therapeutically active substances usually contain solid lipids, surfactants, and, if required, cosurfactants [1]. LNPs have been the most studied platform to date with examples of using ionizable lipids that serve as the core of the mRNA material, whilst aiding in membrane fusion, phospholipids that stabilize the structure of the nanoparticle, "cholesterol" that assists to compact the core lipid, and PEGylated lipids, which offer extended circulation time and reduction of immune recognition [2, 3].

Lipid-based nanocomposites are extensively utilized systems for vaccine delivery, employing liposomes and lipid nanoparticles. A special and adaptable release of the components is provided by the liposomes, which are composed of spherical vesicles with lipid bilayers containing hydrophobic and hydrophilic antigens [4, 5]. Therefore, they are made to particularly target cancer cells. After entering the cancer cell, the nanocomposite transports the therapeutic cargo to the cytoplasm by evading the endosome. Lipids that disrupt membranes or are pH-sensitive are used to accomplish this. Therapeutic cargo is released from the malignant cell by diffusion or enzymatic breakdown of the lipid bilayer (miR34a)[4].

Novel systems have incorporated lipid-polymer hybrid nanoparticle, which may also offer tissue-sensitive and selective delivery and therefore provide a targeting element in the delivery of mRNA therapeutics [6]. There has also been a trend toward hybrid nanoparticles developed from lipid- and polymer-based components to improve stability and targeting methodologies. Targeted delivery approaches, like ligand conjugation, create organ-specific mRNA delivery, which increases the accuracy of therapeutics while decreasing off-target effects [7]. The rapid clinical success of lipid nanoparticle (LNP)-based COVID-19 vaccines has led to further interest to broaden the applications of LNPs for instance in cancer immunotherapy, protein replacement and gene editing [8, 9].

Despite the advances in delivery systems, there will remain challenges for mRNA therapeutics in regard to improving endosomal escape, targeting specificity, reducing immunogenicity, establishing longer-term safety, while balancing cost-effective manufacture and storage [10]. Addressing these challenges will be required before the k5 of lipid-based nanomaterials can put mRNA discovery findings into practice beyond vaccination, including cancer immunotherapy and gene editing [11]. Continued investigation and innovation will help to develop safer, more effective , and more broadly available mRNA based therapeutics [12]. However, there continue to be challenges: The inefficient endosomal escape is still the limiting step for intracellularly releasing mRNA into the cell; issues with achieving cell or tissue specific targeting needs further refinement [13]; the necessity of developing strategies to deal with immune responses against nanoparticle components including PEG that may decrease efficacy and safety; the stability of the materials affects, storage and distribution [14]. Manufacturing and quality control practices that are scalable and reproducible initial constructions, because of clinical demands should be ramped more [15]. Overall, the emerging research on lipid–based nanocomposites indicates that the drug delivery community was quite enthusiastic about these nanocarriers. We are certain that these diverse drug delivery methods could have a significant clinical impact with additional

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research investments at the manufacturing level and pre-clinical evaluation in suitable animal models.

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Matin Sorkhabi: Conceptualization, Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare no conflict of interest.

Data availability

No data is available.

REFERENCES

[1] E. Musielak, A. Feliczak-Guzik, I. Nowak, Synthesis and Potential Applications of Lipid Nanoparticles in Medicine, Materials, 2022.
[2] Y. Eygeris, M. Gupta, J. Kim, G. Sahay, Chemistry of lipid nanoparticles for RNA delivery, Accounts of chemical research 55(1) (2021) 2-12.
[3] X. Hou, T. Zaks, R. Langer, Y. Dong, Lipid nanoparticles for mRNA delivery, Nature Reviews Materials 6(12) (2021) 1078-1094.
[4] H. Nsairat, D. Khater, U. Sayed, F. Odeh, A. Al Bawab, W. Alshaer, Liposomes: structure, composition, types, and clinical applications, Heliyon 8(5) (2022) e09394.
[5] A.H. Saleh, D. Kumar, I. Sirakov, P. Shafiee, M. Arefian, Application of nano compounds for the prevention, diagnosis, and treatment of SARS-coronavirus: A review, Journal of Composites and Compounds 3(9) (2021) 230-246.
[6] L. Khalili, G. Dehghan, N. Sheibani, A. Khataee, Smart active-targeting of lipid-polymer hybrid nanoparticles for therapeutic applications: Recent advances and challenges, International Journal of Biological Macromolecules 213 (2022) 166-194.
[7] L. Lin, K. Su, Q. Cheng, S. Liu, Targeting materials and strategies for RNA delivery, Theranostics 13(13) (2023) 4667.
[8] T.T.H. Thi, E.J. Suys, J.S. Lee, D.H. Nguyen, K.D. Park, N.P. Truong, Lipid-based nanoparticles in the clinic and clinical trials: from cancer nanomedicine to COVID-19 vaccines, Vaccines 9(4) (2021) 359.
[9] R. Singh, Z. Rabiei Dolatabadi, N. Tripathi, S. Mukhtar, D. Sultan Sheriff, F.G. Morais, P. Shafiee, Recent progress on filtration technologies for the fabrication of effective COVID masks: A review, Journal of Composites and Compounds 3(9) (2021) 218-229.
[10] C. Zhang, Y. Ma, J. Zhang, J.C.-T. Kuo, Z. Zhang, H. Xie, J. Zhu, T. Liu, Modification of lipid-based nanoparticles: an efficient delivery system for nucleic acid-based immunotherapy, Molecules 27(6) (2022) 1943.
[11] D.f. Li, Q.s. Liu, M.f. Yang, H.m. Xu, M.z. Zhu, Y. Zhang, J. Xu, C.m. Tian, J. Yao, L.s. Wang, Nanomaterials for mRNA-based therapeutics: Challenges and opportunities, Bioengineering & Translational Medicine 8(3) (2023) e10492.
[12] S. Qin, X. Tang, Y. Chen, K. Chen, N. Fan, W. Xiao, Q. Zheng, G. Li, Y. Teng, M. Wu, mRNA-based therapeutics: powerful and versatile tools to combat diseases, Signal transduction and targeted therapy 7(1) (2022) 166.
[13] A. Chan, A. Tsourkas, Intracellular protein delivery: approaches, challenges, and clinical applications, BME frontiers 5 (2024) 0035.
[14] M.L. Guevara, F. Persano, S. Persano, Advances in lipid nanoparticles for mRNA-based cancer immunotherapy, Frontiers in chemistry 8 (2020) 589959.
[15] J. Whitley, C. Zwolinski, C. Denis, M. Maughan, L. Hayles, D. Clarke, M. Snare, H. Liao, S. Chiou, T. Marmura, Development of mRNA manufacturing for vaccines and therapeutics: mRNA platform requirements and development of a scalable production process to support early phase clinical trials, Translational Research 242 (2022) 38-55.