Highly fusogenic multicomponent lipid nanoparticles for nucleic acid delivery and process for the preparation thereof.

KEYWORDS

- ❑ VACCINES
- ❑ LIPID NANOPARTICLES
- ❑ MICROFLUIDICS
- ❑ NUCLEIC ACIDS
- ❑ RARE GENETIC DISEASES

AREA

- ✓ PHARMACEUTICAL

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Patent Type
Patent for invention

Co-Ownership
Sapienza University of Rome 55%, UNICAM-University of Camerino 40%, Scuola Normale Superiore Pisa 5%.

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Industrial & Commercial Reference
The present invention refers to the pharmaceutical/biomedical field, principally interested in the development of lipid formulations for DNA vaccination.

Time to Market
Current state of development is TRL4 and thanks to the collaboration with industrial organizations interested in we estimate to reach TRL5 before the end of 2022..

Availability
Cession, Licensing, Research, Development, Experimentation, Collaboration, Start-up and Spin-off.

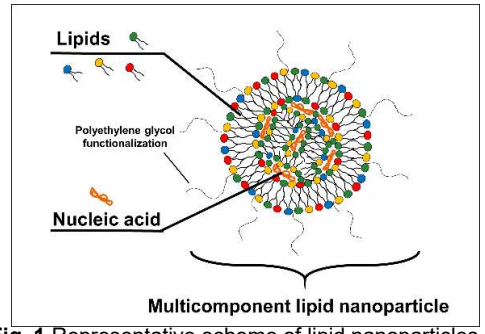

Fig. 1 Representative scheme of lipid nanoparticles.

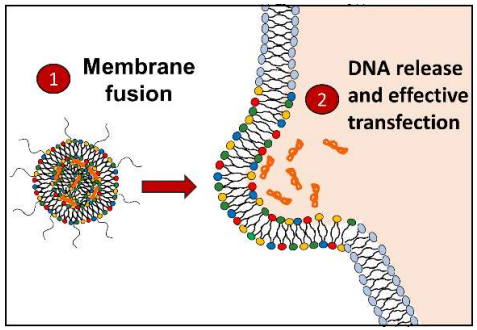

Fig. 2 Interaction of lipid nanoparticles with the cell membrane and subsequent release of their molecular cargo.

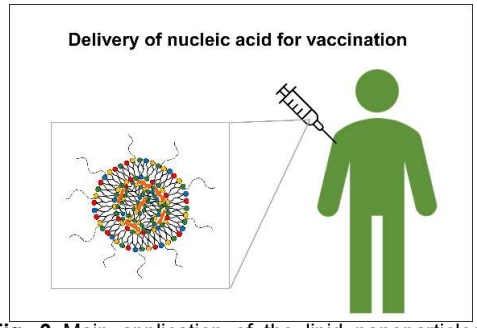

Fig. 3 Main application of the lipid nanoparticles: vaccination.

Abstract

The present innovation falls into the pharmaceutical/biomedical field, in particular, in the area of the development of lipid formulations for DNA vaccination. The invention is related to the preparation of highly fusogenic multicomponent lipid nanoparticles obtained by combining cationic and ionizable lipids in a specific ratio for nucleic acid delivery with vaccination purposes. The invention includes the lipid nanoparticles obtained through the procedure. The lipid nanoparticles are prepared using an automatized microfluidic device which ensures reproducibility for large-scale production.

Publications

- ❖ Cui, Lishan, et al. "Efficient Delivery of DNA Using Lipid Nanoparticles." Pharmaceutics 14.8 (2022): 1698.
- ❖ Quagliarini, Erica, et al. "Microfluidic Formulation of DNA-Loaded Multicomponent Lipid Nanoparticles for Gene Delivery." Pharmaceutics 13.8 (2021): 1292.
- ❖ Pozzi, Daniela, et al. "Programmed packaging of multicomponent envelope-type nanoparticle system for gene delivery." Applied Physics Letters 96.18 (2010): 183702.
- ❖ Caracciolo, Giulio, et al. "Factors determining the superior performance of lipid/DNA/protammine nanoparticles over lipoplexes." Journal of medicinal chemistry 54.12 (2011): 4160-4171.

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Technical Description

The lipid nanoparticles (LNPs) related to the invention are obtained by combining cationic lipids and ionizable lipids at a specific ratio to be administered both subcutaneously (intradermally or intramuscularly) and systemically with less side effects than the known lipid nanoparticles. These are obtained using an automated microfluidic platform that ensures the reproducibility of the preparation technique and the standardization of chemical and physical features, essential for large-scale production. Indeed, LNPs have been obtained by properly tuning the fluid-dynamic parameters that are involved in the microfluidic mixing process, to optimize the delivery efficiency of their nucleic cargo.

Technologies & Advantages

DNA vaccines have numerous advantages over current pathogen-based (i.e. attenuated and inactivated viral vaccines) or protein-based vaccines, such as simple and rapid manufacturing processes or easy handling, through DNA engineering. Furthermore, the thermo-stability of DNA vaccines solves the complications related to the maintenance of the cold chain, essential to avoid the inactivation during the supply of less stable vaccines (e.g., mRNA vaccines). In general, compared to other vaccination strategies, the use of DNA vaccines can be considered advantageous, for the following aspects:

Applications

The main application of the invention concerns the use of multicomponent lipid nanoparticles that encapsulate nucleic acids (i.e., DNA and RNA) for the delivery of DNA vaccines (with anticancer activity or against infectious diseases). The global vaccine market is growing rapidly, firstly because of emerging infectious diseases but also as a result of the growing attention to immunization which has encouraged company and national initiatives to improve research on vaccines and their development. However, the absence of innovative technological solutions is a factor that can slow the growth of this business. Therefore, nano-vectors for DNA vaccination, such as those objects of the present invention, can attract the interest of pharmaceutical companies that dominate the market.

Fig. 4 Representative scheme of the preparation process for the lipid nanoparticles.

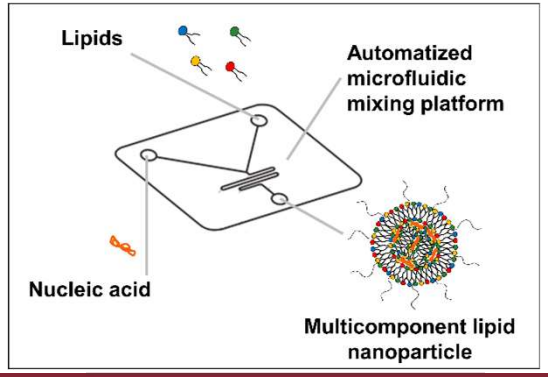


Fig. 5 Main advantages of the lipid nanoparticles.

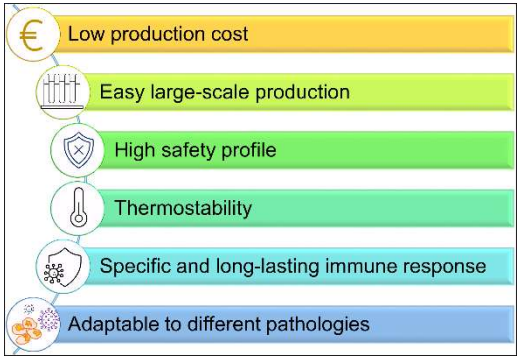
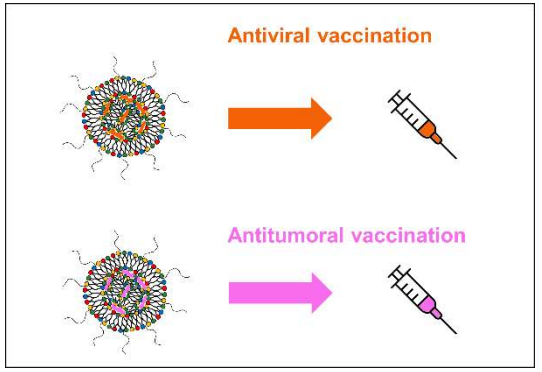


Fig. 6 Adaptability of lipid nanoparticles to different types of vaccinations.



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