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A Review on Liposomes as a Vaccine Delivery System

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A B S T R A C T

Vaccines are formulations administered to patients in order to stimulate immune responses that result in the creation of humoral antibodies or cell-mediated responses that will fight infectious pathogens as well as non-infectious diseases like cancer. A number of compelling factors, including the concerning safety profile of live vaccines, the weak immunogenicity of subunit vaccines and immunization, and the inability of immunization due to inadequate patient adherence to booster doses that should potentiate prime doses, made the development of a new generation of preventive and therapeutic vaccines necessary to support effective immunization. Efforts are underway to administer vaccinations via carriers, which regulate the timing and location of antigen presentation to the immune system, resulting in their targeted and sustained release. Therefore, it is possible to efficiently trigger immune responses with smaller doses of weak immunogens, obviating the necessity for prime and booster doses as part of the traditional vaccination schedule. The interest in liposome-based vaccines has grown significantly, and liposomes and liposome-derived nanovesicles like virosomes and archaeosomes have emerged as significant carrier systems in vaccine research. This study presents liposomal vaccine drug delivery system.

Keywords: Vaccines, liposomes, immunity, immunization, adjuvants.

Introduction

The best way to reduce the morbidity and death associated with infectious diseases is through vaccination. According to estimates from the World Health Organisation (WHO), vaccinations save the lives of approximately 2.5 million children globally annually. A biological preparation known as a vaccination works to increase immunity to a certain illness. Vaccines including protein subunits, polysaccharide antigens or conjugates, inactivated toxins (Toxoid), dead or live-attenuated microbes, and other conventional vaccine forms have all been employed in clinical settings to date. Numerous novel vaccines, including DNA and recombinant vector vaccines are being developed. These substances mimic disease-causing germs and encourage the immune system to identify the substance as foreign, eliminate it, and "remember" it, making it easier for the immune system to fight these pathogens in the future. (1)

A successful vaccination depends on the administration and distribution of vaccines in an appropriate manner. Subcutaneous (SC) or intramuscular (IM) administration are the usual methods used to give vaccinations. In addition to requiring highly skilled individuals for administration, hypodermic injections are linked to discomfort and anguish that may result in poor patient compliance. Because there is a chance of needle stick injuries or reusing infected needles, they come with a risk of disease transmission. When mass immunization is required, inadequate vaccine supplies or restrictions on vaccine manufacture may potentially provide issues. (2, 3)

To effectively elicit a protective response, these vaccinations need to be enhanced with substances known as "adjuvants." It is thought that adjuvants work by combining with the substance that has to be administered to produce complexes from which immunogens are gradually released.

Vaccine delivery systems: Liposomes, emulsions, microparticles, immune-stimulating complexes ISCOMs, etc.

Adjuvants that boost immunity: Preserved molecular patterns of pathogens activate immunity because they are recognised by pattern recognition receptors such as "Toll" receptors, which are mostly found on B-cells and mammalian dendritic cells (e.g., DNA containing unmethylated CpG).

Adjuvants are non-immunogenic, harmless, and biodegradable on their own; nonetheless, they enhance the immunostimulatory effect of the antigen.

Liposomal delivery system

The hollow, spherical structures known as liposomes and their derivatives, "lipoplexes" (liposome/DNA complexes), are made of phospholipid bilayers that may entrap hydrophilic molecules in the aqueous compartment and hydrophobic molecules in the lipid bilayers, with cholesterol giving the bilayer stiffness. Because of their many advantages, including high loading capacity, targeted delivery, dependable agent protection, good biocompatibility, flexible membrane flexibility, and adjustable characteristics like size, surface charge, and agent loading mode, liposomes are frequently used as carriers to increase the therapeutic efficacy of agents. (4) Nevertheless, because DNA's negative charge neutralises the positive charge on liposomes, lipoplexes

have a tendency to cluster while being stored. The formulation of liposomes/protamine/DNA (LPD) overcomes this limitation. A peptide high in arginine is called protamine. It gives stability to the preparation by condensing with DNA before DNA may bind with positive lipids.

While being non-immunogenic, cytotoxic, and biodegradable on their own, carbohydrates, viruses, nucleic acids, proteins, glycoproteins, and lipids can be captured and targeted at the cellular and subcellular level to elicit immunological responses of the antigen.

Table 1: Current research in liposomes as vaccine delivery systems (5-8)

Antigen	Result
BSA as a model antigen	Increased IgG and SlgA after nasal administration of liposomes in mice
Diphtheria, tetanus, HAV, HBV and influenza	Shows good immunogenicity and tolerance in humans
Hepatitis A virus, formalin inactivated	Protective antibody levels in clinical trials; currently marketed in Europe
HIV-1, subunit from gp-120	Induces humoral and cellular immunity after both oral and IM administration
P. falciparum circumsporozoite protein	Cytotoxic T-cell lymphocytes and an antibody response inhibited sporozoite invasion of hepatoma cells in vitro
Vibrio cholerae cell free lysate	Liposome vaccines were effective orally and parenterally

These systems function as adjuvants for vaccines because they are particulate and may bind to lipid receptors on the cell surface, including CD1a, following complement activation. This can have immunomodulatory effects. Because the phospholipid bilayer bonds with the cell wall, it tends to quickly integrate into the reticuloendothelial system (RES) components. Mucosal vaccination may benefit from the creation of polymerized liposomes that have demonstrated greater stability in the gastrointestinal tract. Targeting molecules, such as antibodies, antibody fragments, antigens, and chemicals, can attach to certain cell surface receptors present in mucosal tissues through polymerized liposome coating. Because PEG coats liposomes, forming a covalent bond with the polyethylene present in the lipid bilayer, stealth liposomes, also known as sterically stabilised liposomes, have hydrophilic surfaces. This decreases opsonization by serum proteins and lengthens circulation half lives.

Along with adjuvants such as aluminium phosphate, aluminium hydroxide, calcium phosphate, calcium hydroxide, QS21, Quil A, zinc hydroxide, a glycolipid analogue, an octadecyl ester of an amino acid, a muramyl dipeptide, and a lipoprotein, the nucleic acid molecules encoding a basal body rod protein of a strain of Campylobacter, specifically Campylobacter jejuni, were purified and isolated.

It has been shown that proteins produced by nucleic acids are immunogenic against the Campylobacter infection and may be employed as diagnostic tools for the infection as well as to produce immunological reagents. Monoclonal antibodies or antisera produced against these peptides can be utilised in passive immunisation to prevent and cure Campylobacter-related disorders, as well as for the specific identification of Campylobacter in in vitro and in vivo experiments. (9)

Research was done on the effectiveness of oral liposomes encased with recombinant H. pylori heat shock protein 60 (rHsp60) (10) against H. pylori infection in mice. Results involving rHsp60 plus Cholera Toxin, liposome-encapsulated rHsp60, and liposome-encapsulated rHsp60 plus Cholera Toxin demonstrated immune responses against H. pylori infection of 73.3%, 66.7%, and 86.7%, respectively. In Europe, liposomal vaccines against influenza and. hepatitis A have been licenced as products. These vaccines are based on viral membrane proteins (virosomes). (11)

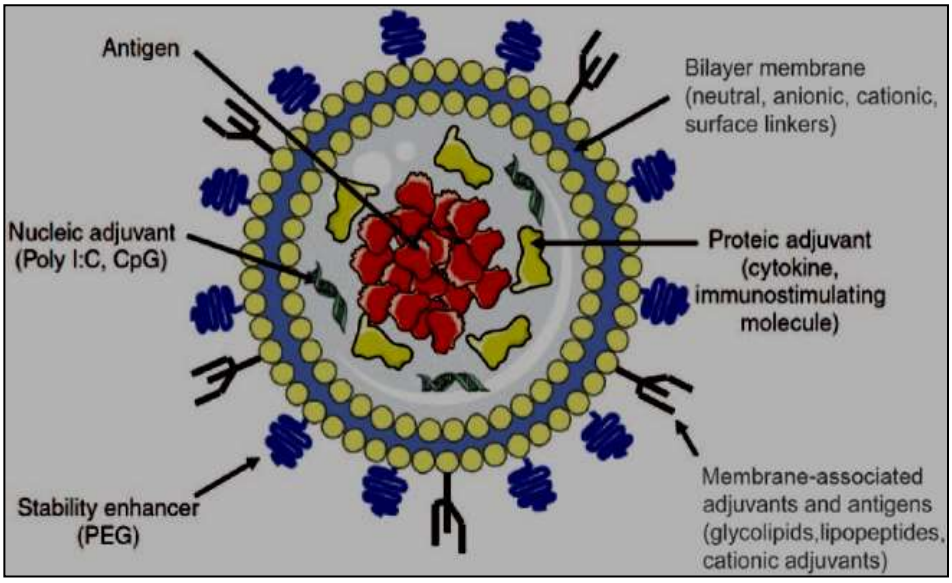

Fig 1: Diagrammatic illustration of a tiny unilamellar liposome demonstrating the variety of chemical inclusion via lipid bilayer membrane surface attachment, bilayer integration, or containment in the aqueous internal space. PEG stands for poly(ethyleneglycol); CpG stands for cytosine–phosphorothioate–guanine oligodeoxynucleotide.(12, 13)

Liposomes as a ideal carrier and adjuvant

Gregoriadis and Allison were the first to report on the capacity of liposomes to elicit immunological responses to integrated or linked antigens. (14) Since then, there has been a noticeable a rise in interest in liposome-based vaccines, and liposomes and liposome-derived nanovesicles, such as virosomes and archaeosomes, have become significant carrier systems.

Liposomes, as well as archaeosomes, virosomes and liposome-based delivery methods, have the benefit of being highly versatile and malleable. To get desired properties such lipid composition, charge, size, size distribution, entrapment, and adjuvant placement, one may select the synthesis and composition of liposomes. Water-soluble substances, such as carbohydrates, nucleic acids, proteins, peptides, and haptens, are trapped in the aqueous inner space of the liposome, while lipophilic substances, such as lipopeptides, antigens, adjuvants, and linker molecules, intercalate into the lipid bilayer. Antigens can adhere to the liposome surface through stable chemical linking or adsorption (15). Liposomal vaccinations can be customized for specific uses by combining coformulations with various antigens and adjuvants.

Adjuvants

The capability of certain chemicals to boost the immune response to vaccinations was initially shown when aluminium salts, sometimes known as "adjuvants," were added to viruses that had been killed or attenuated. Their roles involved creating a depot that allowed APCs to be exposed to antigens for longer periods of time. Effective adjuvants, however, also activate the immune system by direct contact with APCs. Immune adjuvants come in a wide variety of forms. Adjuvants can be further classified as delivery methods or immunostimulants. While delivery methods, depending on their unique properties, boost the immune response through a variety of ways, immunostimulants work with specialised receptors, such as TLRs and others. Therefore, adjuvants including pathogen-derived subcellular components, recombinant proteins, peptides, and nucleic acid sequences are included in current vaccinations. Potent therapeutic cancer vaccines are being produced as a result of advancements in formulation technology and an increased understanding of the immune system. Present-day obstacles in vaccine production are associated with intricate pathogens (like malaria, TB, and HIV) and antigens that can be mutated genetically (like influenza), as well as individuals with impaired or non-functioning immune systems.

Adjuvant action is produced by nanoparticulate carriers by either improving antigen transport or stimulating innate immune responses. A number of variables, including particle size, chemical composition, and uniformity charge, the kind and placement of adjuvants and/or antigens inside the carrier, and, last but not least, the delivery site, affect the immunostimulation processes and strength of nanocarrier vaccines. (16-18)

Conclusion

These days, vaccine medication delivery systems are becoming more and more popular because of their advantages. It's becoming clear that vaccine medication delivery systems are patient-friendly since they don't require booster doses and offer a long-term treatment in tiny doses. The area of liposomes and vaccines based on liposomes is quite broad. In addition to the potent immune response elicited by co formulated adjuvants, liposome-based vaccinations offer qualities essential to the creation of contemporary vaccine formulations. It is expected that these delivery methods will be successfully used more often in the near future, which will result in significant advancements in the creation of vaccines.

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Conflict of interest statement

The author declares that there is no conflict of interest.

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