Virome: A vector in vaccine delivery

ABSTRACT: Virome can bind to and “infect” host cells and deliver the vaccine antigens directly into the host cell's cytoplasm. Virome is essentially an artificial virus that can carry the vaccine antigens to the host cell without undergoing the process of replication. Virome has a broad field of various macromolecules to vaccinations. Novel virome are transported to cells, tissue, and organs targeted cell, tissue, and intracellular pathways. The capacity of today's vaccinations to stimulate the host's immune system even after infection helps the patient build a strong defence against similar microorganisms. In order to find additional methods to improve vaccines and carrier systems are expected to be commercialized. The development of virome, specifically virosomes, can allow the vaccine antigens to be directly delivered to the host cell, where they can then be presented to the immune system, inducing a strong immune response. Virosomes are essentially a lipophilic protective immune responses is consequently a crucial research emphasis.

Keywords: Virome, virosome, unilamellar liposomes.

1 Introduction

Virome are essentially a lipophilic protective immune responses is consequently a crucial research emphasis. Virome are reconstructed viral envelopes that serve as both vaccinations and delivery systems for the vaccine antigens. These days vaccines are considered the best economical and effective technique for preventing and handling bacterial infections, such as human papillomavirus (HPV) or meningitis, allergies, autoimmune Relevant Disorders, Microbial Infections, and many more viral diseases. Annually millions of lives are saved from death of these diseases with the help of proper immunization with the help of vaccines. But still, many diseases are not yet preventable by vaccines and there is a chance of reoccurrence. One of these is a compound known as a virosome, which is produced when pure antigens are extracted from the outer membrane of a virus and then chemically modified with lipids to form a liposome.

A virome can bind to and “infect” host cells and deliver the vaccine antigens directly into the host cell's cytoplasm. Virome has a broad field of various macromolecules to vaccinations. Novel virome are transported to cells, tissue, and organs targeted cell, tissue, and intracellular pathways. The capacity of today's vaccinations to stimulate the host's immune system even after infection helps the patient build a strong defence against similar microorganisms. In order to find additional methods to improve vaccines and carrier systems are expected to be commercialized. The development of a virome, specifically virosomes, can allow the vaccine antigens to be directly delivered to the host cell, where they can then be presented to the immune system, inducing a strong immune response. Virosomes are essentially a lipophilic protective immune responses is consequently a crucial research emphasis.
2 History of different carrier systems

The leading type of carrier is a liposome, which is mostly utilised as a nanocarrier for medicinal molecules. So many modifications are done in liposomes with time to make better and upgrade the physicochemical and natural features, stimulants responsive liposomes, performing in long-circulating and ligand-targeted among others. In this research on carrier systems, different nomenclatures were reported in various articles and literature. In many cases, the new names suggested becoming known as new nanocarriers, which caused confusion these vesicle systems are new vesicles or consider modified liposomes. So above we prepared Table 1 which gives a general introduction to the vehicles with the suffix "somes" which can be used in the delivery of drugs as well as other therapeutically active materials with different proportions of the lipids as well as others hydrophilic or lipophilic composites.

Table 1. Different vehicle systems with the suffix "somes"

<table>
<thead>
<tr>
<th>Year</th>
<th>Name</th>
<th>Chief components</th>
<th>Therapeutic application</th>
<th>Size</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1965</td>
<td>Liposome</td>
<td>Phospholipids (natural or synthetic)</td>
<td>Mostly in drug, vaccine, and gene delivery</td>
<td>50–1000 nm</td>
<td>[14]</td>
</tr>
<tr>
<td>1979</td>
<td>Niosome</td>
<td>Non-ionic surface active agent, Cholesterol</td>
<td>Mostly in gene and drug molecule delivery system</td>
<td>100 nm - 1000 nm</td>
<td>[15]</td>
</tr>
<tr>
<td>1997</td>
<td>Ethosome</td>
<td>Phospholipids, Propylene glycol, Cholesterol, Ethanol</td>
<td>Mostly in drug molecule delivery system</td>
<td>50–500 nm</td>
<td>[16]</td>
</tr>
<tr>
<td>1996</td>
<td>Enzymosome</td>
<td>Phospholipids, ethanol (edge activator), Cholesterol, Stearylamine</td>
<td>Mostly in enzymes delivery</td>
<td>100–800 nm</td>
<td>[17]</td>
</tr>
<tr>
<td>1995</td>
<td>Transferosome</td>
<td>Non-ionic or single chain surface active agent, edge activator, Phospholipids, Cholesterol</td>
<td>Mostly in drug molecule delivery system</td>
<td>60–200 nm</td>
<td>[18]</td>
</tr>
<tr>
<td>1989</td>
<td>Phytosome</td>
<td>Phytoconstituents, Phospholipids</td>
<td>Mostly in phytochemicals delivery</td>
<td>60–20 μm</td>
<td>[19]</td>
</tr>
<tr>
<td>1986</td>
<td>Pharmacosome</td>
<td>Phosphatide (natural or synthetic)-drug conjugate</td>
<td>Mostly in pro-drugs</td>
<td>70 nm - 150 μm</td>
<td>[20]</td>
</tr>
<tr>
<td>1973</td>
<td>Virosome</td>
<td>Haemagglutinin (HA) and neuraminidase (NA) derived from virus and lipids.</td>
<td>Vaccine</td>
<td>&gt;200 nm</td>
<td>[21]</td>
</tr>
</tbody>
</table>

Virosomes were first generated by, when the virus that causes influenza contains haemagglutinin as well as neuraminidase projections on the surface were relocated from the envelope of the virus to the outermost layer of unilamellar liposomes & purified, the virosome structure was created. In the 1970s, virosomes were first implicated as a vaccine is proposed. This resulting structure was examined with the help of an electron microscope, and it looked like an original virus, so the "virosome" name is proposed for this new entity.
3 Comparison of virosomes with liposomes

As there are so many carrier systems available for targeting biomolecule delivery for the delivery to living organisms both in vivo as well as in vitro but they sometimes fail to give good results for delivering the encapsulated molecules in the cytosol of the host cell. This is because of its potential to connect with the host cell. As we know Virosome contain the active glycoproteins of the origin of viruses, they have the property of receptor-mediated binding as well as membrane fusion which gives the optimum delivery of that specific molecule inside the cell of the host's cytosol.

Some comparative studies are done on virosomes with liposomes in earlier periods one of them is that HVJ (Hemagglutinating virus of Japan) virosome intracellularly deliver oligonucleotides and they have three times higher potential contrasted with cationic liposomes. In virosomes, HA (one of the important components present in the influenza virosomal membrane and homogeneity, fusion, and binding properties as well as stability in the structure of the virosome. pH inside the host cell’s endosome is low which boosts the cell fusion which is HA-mediated are packed inside the membrane of virosome are released from the microenvironment of the endosome into the host cell’s Cytosol, by improving cytosolic delivery.

The problem associated with liposomal systems such as minimum protection for therapeutic biomolecules from external microenvironments, for instance, acidic and alkaline PH inside the organelles can be overcome by using virosomal technology. Virosomes with their immunogenic properties can stimulate the immune system of the host which results with the advantage of as adjuvant and carrier to introduce the antigens. In addition as in liposomes, the clearance by the body’s mononuclear phagocyte system is rapid as compared to virosomes.

4 Patents regarding preparation and composition of influenza virosomes

Table 2. Preparations and compositions of influenza virosomes

<table>
<thead>
<tr>
<th>Filing date</th>
<th>Publication number</th>
<th>Title</th>
<th>Content</th>
<th>Owner</th>
</tr>
</thead>
<tbody>
<tr>
<td>08 May 1992</td>
<td>WO92/19267</td>
<td>Immunostimulant and immunopotentiating reconstituted influenza virosomes and vaccines containing them</td>
<td>An IMMUNOSTIMULATING RECONSTITUTED INFLUENZA VIROSOME (IRIV) comprising a mixture of Phospholipids; essentially reconstitute functional virus envelops; an influenza HA protein that is capable of inducing the fusion of said IRIV with cellular membranes and an antigen</td>
<td>Swiss Serum and Vaccine Institute (Crucell Switzerland AG)</td>
</tr>
<tr>
<td>11 February 2004</td>
<td>WO2004/071492</td>
<td>Virosomes-like particles</td>
<td>A technique for producing virus-like particles that involves dissolving encapsulated viruses in short-chain phospholipids and forming a functionally reconstituted viral envelope once the short-chain phospholipids have been removed.</td>
<td>By Bestewil (mymeticsInC.)</td>
</tr>
<tr>
<td>18 June 2004</td>
<td>WO2004/110486</td>
<td>Functionally reconstitute viral membranes containing adjuvant</td>
<td>Reconstituted viral membrane lipid bilayer vesicle that is fusion compatible and comprises an influenza virus membrane protein and an amphiphilic adjuvant</td>
<td>By Bestewil (mymeticsInC)</td>
</tr>
<tr>
<td>26 May 2005</td>
<td>WO2004/110486</td>
<td>A vaccine composition comprising virosomes and a saponin adjuvant</td>
<td>It contains IMMUNOSTIMULATING RECONSTITUTED INFLUENZA VIROSOME (IRIV and Q521 and additionally an exogenous sterol such as cholesterol)</td>
<td>By GlaxoSmithKline (GSK)</td>
</tr>
</tbody>
</table>
Virosome particles comprising antigens from the influenza virus and hepatitis B virus

Envelop proteins from the influenza virus and antigens from the hepatitis B virus make up viral chromosomes (HBV and HBC)

By Crucell Switzerland AG

Lyophilization of virosomes

A composition of IMMUNOSTIMULATING RECONSTITUTED INFLUENZA VIROSOME (IRIV) with cationic cholesterol, which enables lyophilization and functional reconstitution of virosomes

By Pevion Biotech AG

An adjuvant system comprising virosomes and liposomes

A mixture that contains an empty INFLUENZA VIROSOME RECONSTITUTIONAL IMMUNOSTIMULATOR and a liposome with at least one antigen trapped inside of it or attached to its membrane by a lipophilic anchor, with the pH of the mixture kept at a healthy level.

By Pevion Biotech AG, MymeticsIn C. INSERM

Virosomes - like vesicles comprising gp41-derived antigens

The gp41 P1-terminus is covalently attached to a lipid molecule in virosomes for localization on their exterior surfaces.

By Pevion Biotech AG, MymeticsIn C. INSERM

Intranasal influenza vaccine based on virosomes

INFLUENZA VIROSOME RECONSTITUTIONAL IMMUNOSTIMULATOR with no additional adjuvant or lipid from an external source for stimulation of systemic or local immune response against influenza virus in humans by single intranasal or inhalation administration

By Solvay Pharmaceuticals

Virosomes, methods of preparation and immunogenic compositions

Virosomes with at least one adjuvant molecule and on the virosome surface, there is a single surface glycoprotein produced from a distinct encapsulated virus.

By Emory University

Nonspecific immunostimulant agents

Influenza virosomes for stimulation of a nonspecific immune response against neoplastic, viral, or bacterial disease or disorder

By Pevion Biotech AG

Intradermal influenza vaccine

Virosomes comprising influenza virus HA but no additional adjuvant for intradermal application as influenza vaccine in humans

By Crucell Switzerland AG

Virosomes comprising HA derived from an influenza virus produced in a cell line, compositions, methods of manufacturing

Virosomes containing HA derived from the influenza virus produced in an avian cell line, featuring increased fusion activity and immunogenicity

By Pevion Biotech AG
5 Composition of different reconstituted virosomes

By Franvax SRL, Italy.

Composition of different reconstituted virosomes

FIGURE 2. Virosome structure under electron microscope carrying two hepatitis A virion particles. The influenza glycoproteins (on the top of the image haemagglutinin (HA) and neuraminidase (NA) form thorn-like structures that protrude from the virosome membrane.

FIGURE 3. Architectural structure of the virosomal adjuvanted influenza vaccine on electron microscopy (Electron Microscopy Unit of the Department of Health Sciences University of Genoa).
After numerous efforts were made to develop and subsequently commercialise various vaccine adjuvants based on the virosome formulation, such as Inflexal® V for influenza, Epaxal® for hepatitis A, HIV, HPV, Cancer, and SARS-CoV-2 (some vaccine projects are ongoing), the virosome-based viral nano vaccines are now available.

Virosomal vaccine against Influenza

The population is protected by conventional influenza vaccination platforms against some highly pathogenic strains, but reliable information shows that these products are insufficient against the impending epidemic. Therefore, the development of new vaccination technologies is crucial to ensuring community impunity.

The trivalent influenza virosome vaccine known as Inflexal® V has an expression with two inactivated strains of the virus and one strain of the B virus, both of which have the HA and NA subunits that are specific to the influenza virus.

The optimal quantity of cleansers has solubilized influenza contagions and removed their nucleocapsid in the manufacture of influenza virosomes, like other virosomes pharmaceutical methods. Accordingly, INFLUENZA VIROSOME RECONSTITUTIONAL IMMUNOSTIMULATOR spontaneously created when viral lipids and glycoproteins are present. In reconstitutions of virosomes, phospholipids (PL), particularly phosphatidylcholines (PC), are present. To produce the NA and HA glycoproteins, envelope phospholipids from the influenza contagion were responsible for 30 of the contagious lipid content, which was assigned to PC.

The schematic representation of an influenza virosome reconstituted is shown in the upper picture.

Protection of people against some highly infective strains of influenza virus by the traditional vaccine, although appropriate report clarifies that these vaccines do not have enough protection against the prospective pandemic. Hence the development of novel vaccine technology has become necessary to provide public immunity.

Crucell, Berna Biotech has created a trivalent influenza virus virosome vaccine that consists of two inactivated strains of viruses and one B virus strain containing influenza virus antigens for the HA and NA subunits.

The preparation of other virosome is comparable to the preparation of influenza virosome. It includes that the influenza virus is solubilized in the optimal number of detergents, therefore its nucleocapsid was removed. In reconstitutions of virosomes, phospholipids (PL), particularly phosphatidylcholines (PC), are attained. The influenza virus’s envelope phospholipids contributed 30% of the virus’s 70% lipid content, which in turn produced 30% of the NA and HA glycoproteins.

NA function has a significant impact on viral pathogenicity and improves virosome functionality. N-acetylneuraminic acid (sialic acid) reduces the viscosity of the host’s secretions, and also makes it simpler for developing viruses to spread their offspring.

The virus-endosomal fusion required the HA1 and HA2 subunit bearing HA epitopes, which also caused cellular response. Additionally, only virosome-virosome fusion results in the inclusion of HA into the virosome membrane.

From 1997, Inflexal® V has been produced by the Swiss Serum & Vaccine Institute in Berne, Switzerland. It is currently offered in more than 20 nations under a variety of trade names, such as Viroflu® in the United Kingdom and Isiflu® V in Italy. Up to this point, more than 2500 healthy volunteers have gotten involved in 18 scientific investigations that have proven the security and efficiency of Inflexal® V.

More than 10 million doses of the vaccine...
investigations on the responses. Immunisation with the stable HIV adjuvants, promotes the release of TNF, IFN, and IL12 cytokines, which in turn encourages dendritic cells to develop type 2, both of which types were engineered by the addition of 3 mLecithin, cephalin, as well as phospholipids which have been reconstituted with gp41 virosome type 1 and p1 virosome stiffness of the virosome membrane.

A virosome confronting the HIV infection because of the predilection for the mucosal pathway. Moreover, the P1 peptide improved the mobility and functionality of protein epitopes. CD4 receptor on immune component cell physical stability, antigen integrity, and robustness that HIV has evolved. Infections because of the predilection for the mucosal pathway. The robust immunological response induced by the mucosal dose form of the HIV virosome vaccine is has been injected intramuscularly, intradermally, or subcutaneously and is expected to be quickly available on the market. The robust immunological response induced by the mucosal dose form of the HIV virosome vaccine is has been injected intramuscularly, intradermally, or subcutaneously and is expected to be quickly available on the market. The robust immunological response induced by the mucosal dose form of the HIV virosome vaccine is has been injected intramuscularly, intradermally, or subcutaneously and is expected to be quickly available on the market. The robust immunological response induced by the mucosal dose form of the HIV virosome vaccine is has been injected intramuscularly, intradermally, or subcutaneously and is expected to be quickly available on the market.

Virosomal vaccine against Hepatitis A

Virosomal vaccine against HIV

Virosomal vaccine against HPV
Viral virome vaccines against cancer

Corona viridae. The SARS-CoV-2 virus started in Wuhan, China, and spread in December 2019, despite numerous studies warning of the first illness symptom in February 2019. Since the most recent pandemic that resulted in the SARS-CoV-2 virus to be infectious in the cytoplasm, a low pH is needed for the virus to evade immune detection. Notably, a variant strain of SARS-CoV2 was isolated. Virosome particles are surrounded by a double membrane, employed to synthesise the viral RNA in the cytoplasm, where coronaviruses spread at the end of the virosomes contained the PEG derivatized lipids. Notably, influenza virosomes showed favourable traits for virosome-based vaccines for SARSCoV-2. The potential of virosomes in the treatment of cancer has been examined in numerous research. Reconstituted influenza virus envelopes (virosomes) have been thoroughly investigated in preclinical studies and clinical trials, including with OVCAR, a potential delivery system for the SARSCoV2 vaccination. The European MI Matrix Company is working on the Transvac 2 project, a virosomal delivery system. This novel strategy showed promise for effective tumour growth inhibition combined with virosomes that were extensively coated in HA spikes to provide a unique and selective drug molecule that the virus exists in over 40 different variations. Geographic localisation of clinical symptoms has also been seen. These issues still exist, making the creation of a potent COVID-19 vaccine difficult and complex. Furthermore, the basic residue of amino acids that makes up the virus' persistence within host cells, have been studied in relation to HPV. Additionally, E6 and E7 have been thoroughly investigated in preclinical studies and clinical trials, including with OVCAR vectors, in the context of treating malignancies such ovarian carcinoma. PEG derivatized lipids may also be found in others, might be delivered by virosome (TAA). It is recommended to recognize that cancer vaccines provide a unique and selective drug molecule that the virus exists in over 40 different variations. Geographic localisation of clinical symptoms has also been seen. These issues still exist, making the creation of a potent COVID-19 vaccine difficult and complex. Additionally, E6 and E7 have been thoroughly investigated in preclinical studies and clinical trials, including with OVCAR vectors, in the context of treating malignancies such ovarian carcinoma. PEG derivatized lipids may also be found in others, might be delivered by virosome (TAA). It is recommended to recognize that cancer vaccines provide a unique and selective drug molecule that the virus exists in over 40 different variations. Geographic localisation of clinical symptoms has also been seen. These issues still exist, making the creation of a potent COVID-19 vaccine difficult and complex. Additionally, E6 and E7 have been thoroughly investigated in preclinical studies and clinical trials, including with OVCAR vectors, in the context of treating malignancies such ovarian carcinoma. PEG derivatized lipids may also be found in others, might be delivered by virosome (TAA). It is recommended to recognize that cancer vaccines provide a unique and selective drug molecule.
medications in a targeted manner. The basic mechanism underlying the operation of virosomes is their continued capacity to merge. This fusion capability makes it easier to transport crosslinked or encapsulated antigens into antigen-presenting cells via receptor-mediated endocytosis. Virosomes are also efficient in the antigen-presenting pathways of MHC class I (CD8+) and class II (CD4+), allowing for thorough immune responses. However, the reason behind antigen delivery vesicle cum adjuvant excellency is that it can start or initiate cytotoxic cells as well as helper T cells against as compared to vaccines.

Hemagglutinin (HA)-mediated attachment of virosomes to cell membrane receptors made of glycoproteins or glycolipids with terminal sialic acid starts the release process. Virosomes then enter cells by receptor-mediated endocytosis.

FIGURE 5. Preparation and mode of action of virosome, 0102 (2024)
FIGURE 6. General Mechanism of action of virosome

Virosomes get stuck inside endosomes, where the internal environment causes the virosomes and the endosomal membrane to fuse together.

Hemagglutinin, a viral membrane glycoprotein, promotes fusion activity (HA).

The endosome’s subsequent membrane fusion action frees the virosome from its lipid sheath and provides access for the medications that are encapsulated to reach the cells’ cytoplasm.

7 Method of preparation

Preparation at the laboratory level

Preparation at the laboratory level may be created from viruses in vitro using a procedure called membrane solubilization and reconstitution, which involves four basic steps. First, a sufficient viral count is attained by cultivating the target virus. The virus is then purified, rendered inactive, and dispersed in detergent. Third, the nucleic acids and other viral proteins are isolated from the envelope fraction, which is composed of the membrane-associated virion proteins and lipids. Fourth, removing detergents from envelope fractions causes membrane lipids and related proteins to reassemble into vesicles.

Since the viral lipophilic envelop layer and viral outer membrane proteins of virus’s majority of the virosomal framework, it is ideal to create a similar virosome by replacing the virus envelopes and proteins with synthetic materials. Liposomes have been utilized extensively in the past to transport a variety of medicinal compounds into cells. In the literature, methods for making liposomes with synthesized lipids have been described.
To prepare influenza virosomes, the influenza virus must be transformed into pellets using the ultracentrifugation process. Additionally, the particles are isolated and left overnight in 100mM C12E8. This will make it possible to completely dissolve the viral membrane. After homogenizing and ultracentrifuging prepared solutions, viral nucleocapsids are made from pellets. With the aid of detergent, BioBeads are employed for separation. Virosome suspension is purified using a discontinuous sucrose gradient to get rid of unencapsulated material. The surface of the sucrose layer is where the virosomes may be found. Additionally, the layer is eliminated using dialysis over the buffer, and the ready virosomes are filtered to sterilize them.

Production of the Virosomal Influenza vaccine at Industrial level

Schematic representation of manufacturing of influenza virosomes in a commercial setting. Consists of four phases, the first of which is the separation of the components of the influenza envelope with solubilization the inactivated influenza virus (step 1), adding the necessary excipients such as carbohydrates and lipids made in a lab (step 2). The virosome components are put together by controlled elimination of the detergent to produce the intermediate product (step 3). The atypical product incorporates the antigen of interest (API) in two different ways. The following antigen is attached to the virosomal membrane by lipid in the first-generation B-cell vaccines. Before the assembly of the particles, the anchor is added (A). The heterologous HAV antigen is adsorbed to the surface of the intermediate product in the first-generation HAV vaccine Epaxal® (B). The intermediate product is then sterile filtered and diluted to the final antigen dosage (step 4). The finished product might either be liquid or stable freeze-dried (only with second-generation influenza virosomes). On the intermediate and finished products, chemical, biological, and biophysical analysis (QC) is carried out [61].
Characterization of virosomes

Three features are often assessed to characterize virosomes:

a. Protein Detection

b. Size and Organization

c. The Fusion Process

No matter how the virosome was created or what type it was, the result should have a constant protein-to-lipid ratio. Utilizing electrophoretic methods, the HA protein in the virosomal complex can be evaluated quantitatively (SDS-PAGE being the most used). Negative stain electron microscopy can be used to see the ultrastructure and size of virosome particles. The staining solutions should be neutral in pH to prevent acid from changing the conformational configurations of HA. Virosomes also display pH-dependent film combination mobility, which is like the natural influenza virus's local flu infection features. The excimer assay (made by combining virosome with organic or fake target film) is used to visualize virosomal fusion with biological and artificial target membranes in vitro. Lipids are used in this experiment. Here, the drop in PPC label surface density following membrane fusion corresponds to a decrease in excimer fluorescence.

Analysing haemolytic activity, which has a pH dependence similar to that of the fusion process, is another way to assess fusion activity [62].

The numerous methods used to characterize virosomes are listed below:

Bradford's assay

By incorporating Coomassie dye into the sample when it is acidic, the Bradford Protein Assay calculates the protein content. The sample turns blue when proteins bind to the Coomassie dye, turning it from brown to blue. A spectrophotometer may then be used to quantify the amount of blue to calculate the amount of protein in the sample [63].

Dynamic light scattering (DLS)

It is a monitoring method for the quick variations in laser light intensity caused by dispersed molecules or particles in solution, one may calculate size and size distribution. For many biologics, including peptide, proteins, viruses, and VLPs, DLS provides a fast and also not involving damage or destruction technique to determine size [60].

Electron scanning microscopy (SEM)
Transmission electron microscopy (TEM)

Visualizing virus particles, their sizes, morphologies, and locations using a beam of electrons travelling at energy level to concentrate and examine samples, the scanning electron microscope (SEM) is a type of electron microscope that scans the surface areas of microbes. The transmission electron microscope (TEM) is applied for visualizations of virus particles, their sizes, morphologies, and locations.

9 Regulations for virosome-based nano vaccines

Regulations for virosome-based vaccines are established based on regulatory organisations like, FDA, EMA, ICH, and a different legitimate regulatory body. The main objective of the Production Procedure for Cold Chain Independent Virosome (MACIVIVA) project is to develop virosome vaccine formulations that are sustainable for an extended period of time at room temperature as well. One of the features of virosome-based vaccines is Quality by Design (QbD), which requires being efficient, and repeatable. The interplay between the CQAs and the quality goal product profile.

10 Commercial virosome-based vaccines

Commercial virosome-based vaccines have received human use authorization and are now on the market. For instance, virosome-based nasal flu vaccine dosage forms does not require sterilization, and the management of microbiological labelling. Vaccine components should be used to precisely adjust vaccine storage conditions. For instance, freezing renders aluminum salt in vaccinations useless. Packages for vaccines should have IATA time, shipping regulations, and adequate packaging.

Table 3: Some Virosomal vaccines with composition, Status for marketing, and Dosage form

<table>
<thead>
<tr>
<th>Target vaccine</th>
<th>Composition</th>
<th>Status</th>
<th>Dosage form</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza virosome</td>
<td>HA, NA</td>
<td>Marketed</td>
<td>IM</td>
<td>[74]</td>
</tr>
<tr>
<td>Hepatitis A virosome</td>
<td>HA, NA, HAV2</td>
<td>Marketed</td>
<td>IM</td>
<td>[41]</td>
</tr>
<tr>
<td>HIV (RSV) virosome</td>
<td>HA, NA, RSV fusion</td>
<td>Under GMP</td>
<td>IM</td>
<td>[73]</td>
</tr>
<tr>
<td>Respiratory syncytial virus</td>
<td></td>
<td>Under GMP</td>
<td>IM</td>
<td>[72]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Under GMP</td>
<td>IM</td>
<td>[71]</td>
</tr>
</tbody>
</table>
Table 4. Few virosomal vaccines with a type of antigen

<table>
<thead>
<tr>
<th>Sr.No.</th>
<th>Name of the vaccines</th>
<th>Type of Antigens</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Invivac®</td>
<td>Influenza virus surface antigens (haemagglutinin and neuraminidase)</td>
<td>[77]</td>
</tr>
<tr>
<td>2.</td>
<td>Inflexal® V</td>
<td>Subunit virosomal influenza vaccine</td>
<td>[2]</td>
</tr>
<tr>
<td>3.</td>
<td>NasalFlu®</td>
<td>Flu virus antigen</td>
<td>[78]</td>
</tr>
<tr>
<td>4.</td>
<td>Recombivaxengerix-B</td>
<td>Recombinant hepatitis B virus (HBV)</td>
<td>[79]</td>
</tr>
<tr>
<td>5.</td>
<td>Gardasil®</td>
<td>Self-assembled particles of human papillomavirus (HPV)</td>
<td>[80]</td>
</tr>
<tr>
<td>6.</td>
<td>Epaxal™</td>
<td>Hepatitis A virus vaccine</td>
<td>[81]</td>
</tr>
</tbody>
</table>

10 1 Epaxal®

Epaxal® is a virosomal vaccine for hepatitis A. It consists of isolated and formalin-inactivated RG-SB strain hepatitis A viruses grown in MRC-5 human diploid cell culture. These viruses have been attached to influenza virosome surfaces. Lecithin and cephalin are two of the lipids that make up the membranes of Epaxal. Patrick A. Bovier's thorough analysis of the study on Epaxal provides a complex and in-depth list of findings. [6]

10 2 Inflexal® V

Inflexal® V is a combination of three monovalent virosome pools, each created with the unique HA and NA glycoproteins of a different influenza strain. The influenza strains are chosen in accordance with the WHO and European Medicines Agency's yearly guidelines. All age ranges can get the influenza vaccination Inflexal® V without a problem. [83,84] InfectoVac®, Isiflu® V, and Viroflu® are additional trade names for Inflexal® V that are used in Germany, Italy, as well as the United Kingdom, respectively [85-87].

11 Conclusion

- Because of their adaptability, influenza virosomes can be a fantastic instrument for transporting antigens and biomolecules of many kinds, such as proteins, peptides, plasmids, oligonucleotides, and even medications, to cells.
- The delivery system is a crucial component in the protection of illnesses. It has been demonstrated that APCs, particularly DCs, can process influenza virosome-delivered antigens. DCs guarantee that the antigen is presented via MHC class I or II, which triggers a humoral and cell-mediated immune system response.
- Depending on the goal of the immunization, virosomes can be used to deliver an antigen in the host by various routes, including intranasal, transdermal, or Intramuscular injections, without causing any adverse effects, as has already been demonstrated in clinical testing with available commercially virosomal-based vaccines.
- Virosomes have an adjuvant effect that can be used to boost the immune response in people without risk.
- Virosomes might be used as delivery systems for immunomodulating particles and targeted medicines, both of which are finding new uses every day, notably in the treatment of cancer. Due to all of these characteristics, influenza virosomes are thought to be a promising prototype for the delivery of antigens and/or unrelated molecules, which may enter cells in liposome frequently used to transport therapeutic chemicals to target cells. This is because when therapeutic drugs are internalised by cells in liposome encapsulated forms, they are unable to fully escape from endosomal/lysosomal confinement processes of virosome activity.

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- Targeted virosomes might be used following surgical removal of tumours to deliver therapeutic agents directly to the site of the tumour. This could be particularly useful in situations where persistent viral infections necessitate an active cytotoxic immune system response.

- There has also been a greater interest in the formulation procedures, such as emulsification, DNA complexation, and novel sustained release drug delivery system. The ability to direct virosomes to specific cells by employing Fab' segments of monoclonal antibodies designed for antigen binding is a desirable property of virosomes. The virosome concept for influenza vaccines.

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