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A COMPREHENSIVE STUDY ON THE REVIEW OF VIROSOMES AS A NOVEL DRUG DELIVERY SYSTEM

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Abstract

Virosomes can be used as vaccines and vehicles for the cellular transport of various macromolecular molecules. The potential for drug delivery and targeting systems to be implemented using virosomes represents an exciting area of research. Virosomes are biocompatible, biodegradable, nontoxic, and nonimmunogenic, so efforts have been made to utilize them as anti-inflammatory or adjuvant agents, as well as drug and organic delivery frameworks for therapeutic applications. The success of virosomal drug delivery depends on the strategy used to assemble and fuse typeable bioactive materials into virosomes. Potential innovations of virosomes could be used to transport peptides and nucleic acids or qualities and drugs such as antitoxins, anticancer agents, and steroids.

Keywords: Virosome, Non-immunogenic, Glycoproteins, Haem Agglutinin.

Introduction

Viruses, drugs, and even genetic material can be transported to specific cells through the use of virosomes, which are specialized vehicles designed to target these substances through receptor-mediated, specific exocytosis (endocytosis)[1]. Virosomes, like liposomes, are composed of functional Viral Envelope Glycoproteins (VEGs) that are contained in a lipid-like bilayer membrane (Phospholipid). Clinically, they are used as delivery systems for vaccines [2].

For example

Inflex v® is a vaccine for the flu, made up of small, spherical vesicles that contain a mixture of synthetic and naturally synthesized proteins and surface proteins of the flu virus. These vesicles are not replicated. Hence, they are called pure fusion action vesicles. Virosomal carriers help to protect medicines from the process of protein degradation and the pH of the endosomes. That is one of the main benefits of using virosomes [3,4].

Definition

Virosomes are semisynthetic complexes derived from nucleic-acid-free viral particles. They are essentially viral coats in which the infective nucleocapsids are replaced by a synthetic compound of choice. The nucleocapsids retain their mucogenic activity, which allows them to deliver the incorporated compound (antigen, drug, gene) into the target cell.[5]

Structure of Virosome

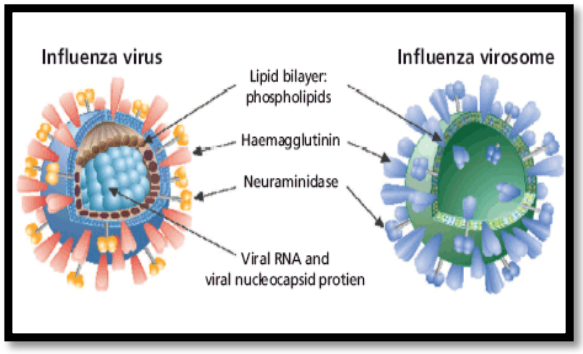

Figure No: - 01 Virus and Virosome

The Virosome is composed of naturally occurring Phosphatidyl Choline (PC) and Phospholipid (PL) which form about 70% of its structure. The remaining 30% of the membrane components contain enveloped phospholipids originating from the flu virus to facilitate the delivery of Haem Agglutinin (HA) and Neuraminidase (NA)

glycoproteins. A variety of ligands such as peptides, cytokines, and monoclonal antibodies can be incorporated into the virosome and are also visible on the vesicle surface [6, 7]. Virosomes can be optimized for maximum inclusion of the drug. They can even be used to generate carriers of antisense-oligonucleotides or other oxidative genetic molecules, depending on whether positive or negatively loaded-phospholipids are included in the vesicle membrane. Mutations of Tumour-Specific Monoclonal Antibodies (MABs) can be linked to the virosomes and directed to selected tumour cells [8].

Types of Virosomes [9]

Sl. No	Virosomes	Parent virus	Family	Viral glycoprotein
1	Influenza	Influenza	Orthomyxoviridae	HA, NA
2	Sendai	Sendai	Paramyxoviridae	HN, F
3	HBV	HBV	Orthohepadnaviridae	S, M, L
4	HIV	HIV	Retroviridae	gp120, gp41, p17
5	NDV	NDV	Paramyxoviridae	HN, F

Method of Preparation of Virosomes

1. Selection of viruses:

Virosomes are prepared from viral envelopes of different viruses. The majority of the viruses used to create virosomes are influenza virus envelopes. However, virosomes can be made from other viruses such as Sendai virus, Sindhi's virus, Epstein-Burr virus, Murine leukaemia virus, and Herpes simplex virus [10, 11].

2. Selection of Antigens

Antigens are used according to our needs. Examples of antigens are bacterium parasite antigens, carcinogenic cell antigens,or whole cell antigens. Other cell components include RNA, DNA, plasmid, etc [12].

3. Reconstituted virosome

The virosome is reconstituted by solubilizing it with a detergent, such as Octal glucosides or Nonideal-40. Subsequently, the genetic material and the internal viral protein will be sedimented, and the detergent is removed through various methods, such as hydrophobic resin and dialysis from the supernatant. Following this, the virus matrix protein and the nuclei capsid are removed. The antigen has been coupled to lipid anchors (Lipid-linked proteins) mixed with a surfactant or polymer solution. This solution is then used to facilitate the process of the mover of antigen-bound virosomes [13, 14].

Route of Administration

Virosomes should be given in a variety of ways like IV, subcutaneously, orally, transdermally, topically, intra-artery, and inhaled. Plus, they come in implantable devices for long-term release [15].

Pharmacokinetics of Virosomes

Pharmacokinetic studies can provide pharmacological information on the free and encapsulated drugs that can be used to guide dose design. Additionally, pharmacokinetic studies provide information on the time of absorption, distribution and degradation, as well as in vivo dispersal and breakdown of virosomal transport. The following pharmacokinetic effects were demonstrated on virosomes [16, 17].

- Greater therapeutic index.
- Greater concentration at targeted sites.
- Protection of drug in plasma.
- Decrease in toxicity & nonspecific reaction.
- Reduction in nonspecific localization.

Mechanism of Action of Virosomes

Virosomes play both a carrier and an adjuvant function during the induction of the immune response in our body. The carrier function involves the positive effect of the incorporation of the antigen into the higher structure, that is, the virosome. The adjuvant function relates to the immune-stimulating properties of the virosome, without causing any non-specific inflammation. Thus, antigen-specific helper immunogenicity is induced there by both the humoral and the cellular immune system [18, 19, 20, 21].

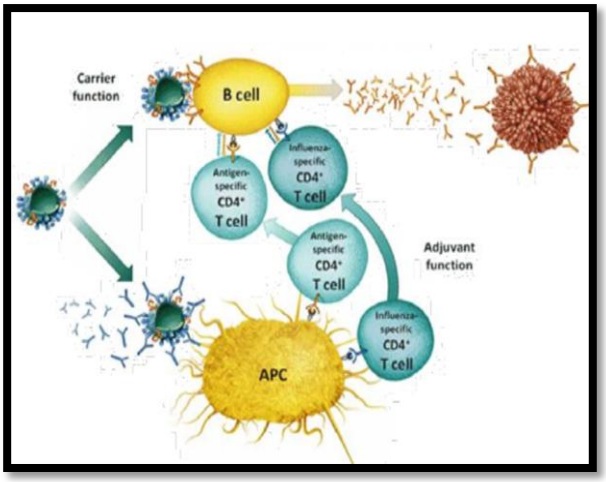

Figure no: 02 Mode of action of virosomes

ADVANTAGES [22, 23, 24]

- Virosomes are biodegradable, biocompatible, and non-toxic.
- There is no risk of disease transmission.
- No auto immunogenicity or anaphylaxis.
- It is broadly applicable to almost all-important drugs (Anti-cancer, proteins, peptides, nucleic acids, antibiotics, fungicides, etc.)
- It enables the drug delivery into the cytoplasm of the target.
- Non-infectious adjuvant (For immune system activation).
- No replicative nature in the host.

DISADVANTAGES [25, 26, 27]

- Since they have viral glycoprotein on the surface may induce an immune response.
- Quick disintegration in the blood compartment.
- Low shelf life.
- Problems during manufacturing.
- Very poor raw material quality.
- Unavailability of data about chronic use of virosome.
- The payload is very slow.

Other Applications

Cancer

Virosomes are utilized to transport peptides associated with tumours, such as those found in parathyroid and hormone-related proteins or recombinant proteins. Sendai Virosomes play an essential role in cancer research [28].

Gene delivery

The membrane fusion protein present on the surface of Influenza virus HA is capable of initiating a low pH-dependent fusion reaction between the virus envelope and the membrane of the endosomal cell compartment, followed by cellular uptake of the virus particle through receptor-mediated endocytosis [29, 30].

RNA/DNA Delivery:

Small interfering RNA molecules (i.e., RNA encapsulated) can interfere with the synthesis of newly produced and constitutive proteins by overcoming the absence of appropriate delivery pathways for these molecules [31].

Immune Stimulation

Virosomes boost both the humoral and cellular immune response. Virosomes possess a pathogen-associated molecular pattern (PAM) that provides stimulation signals to antigen-presenting cells (APCs) [32, 33].

Malarial Therapy

The formulation of Virosomes containing Malarial Vaccine is based on Antimalarial Peptides, which have been demonstrated to provide excellent tolerability and enhanced immune response. The effectors of the Virosomes are Apical Membranous Antigen-1 (AMA-1), and Circumspect Protein (CSP) [34, 35].

General Applications [36, 37, 38]

- Pharmaceutical pigments or dyes.
- Biological response modifiers.
- Radiopharmaceutical and radio diagnosis carriers.
- Drug/protein drug delivery vehicles.
- Drug solubilisation enhancers.
- In cosmetics and dermatology.
- Drug overdose treatment.
- Separation and extraction technique
- Enzyme immobilization.
- In the fabrication of micro capsulated dosage form.
- Antifungal, antimicrobial, and antiviral therapy.

Virosomes as immune potentiating agents

A virosome is a molecule that can be used to deliver specific antigens or drugs to a particular type of cell. The primary function of a virosome is to interact between the antigenic proteins of the virus and the cell receptors [39, 40]. Identification, uptake, and representation of the antigen in the vesicle by the antigen-presenting cells helps to activate the immune system. Effective regulatory and effector immunological responses are elicited. Vesicles trigger both cell-mediated and immune system alarm signals. Additionally, vesicle-derived antigen elicits both cytotoxic as well as helper T-cell immune responses [41, 42]. In addition to being a means of delivering the immunogen into the body, virosomes can also be used as adjuvant to direct the immune system's response to a specific antigen. Because they are particulate, virosomes readily attract dendritic cells and other antigen-presenting cells for immunological benefit [43]. The structure of the virosome guarantees that the antigen – whether it is intercalated into a lipid bilayer or conjugated into surface proteins or in a central cavity – is continually delivered to the immune system. This delayed release of the antigen can help direct the immune response to the specific antigen to achieve a depot-like response. Additionally, the combined delivery of antigen and adjuvant helps in achieving exaggerated immune protection against a variety of diseases. In murine models, virosome-based products elicited a humoral response that was up to four times better than that seen with the delivery of nascent antigen. [44, 45, 46]

Difference between virosomes and liposomes

Viral envelop glycoproteins have receptor-official and layer combination properties thatenable the phone liposomes to focus on and transport organically dynamic atoms in vitro and in vivo to living cells. Liposomes may combine with cells and generally neglect to clearly transfer epitomized atoms into the cell's cytoplasm.Virosomes contains practical conveyance [49, 50].

EVALUATION OF VIROSOMES [51-60]

a) The surface morphology and the shape of the vesicles can be determined by transmission electron microscopy.
b) The size dispersion and the size of the vesicle can be determined by dynamic light scrambling, transmission electron microscope, zeta sizer, photon connection spectrometry, laser light diffusing, gel saturation, and gel avoidance.
c) The surface charge can be determined by free stream electrometry.
d) The surface pH and the electrical surface potential can be determined by zeta potential estimates and pH touch-sensitive tests.
e) The lamellarity can be determined by small edge x-beams dissipating, freeze break electron microscope, and 13p-nMR.
f) The phase conduct can be determined by freeze crack electron microscope and differential checking colorimeters.
g) The percentage of free medication can be determined by mini-section centrifugation, gel avoidance and ion trade chromatography, protamine accumulation, radiolabelling, and drug discharge.

h) Pyrogenicity can be determined by a rabbit fever reaction test or a limulus lysate test. The chemical examination of the surface can be determined by the static auxiliary particulate mass spectrometer.

Conclusion

Virosomes are revolutionizing the waydrugsare delivered and targeted to biological systems. They can be used in a variety of ways to deliver antigens, molecules, and even drugs to cells, without any side effects. They can also be used to target specific cells with antibodies that are specifically designed to bind to them. Plus, there are other types of virosomes, like the Sendai virosome and the Epstein Burr virosome, that can be used in different fields of science. Cancer is a complex disease and virosomes could be a great way to treat it. In the clinical setting, however,planning for cancer treatment using a range of therapeutic approaches is essential.

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No Conflict of Interest

Inform Consent and Ethical Considerations

Not Applicable

Author Contribution

All authors are contributed equally.

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