**World Journal of Pharmaceutical Sciences**
ISSN (Print): 2321-3310; ISSN (Online): 2321-3086
Available online at: http://www.wjpsonline.org/
**Review Article**

# Vesicular Structured Drug Delivery Systems: An Innovative Slant towards Drug Targeting

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***Received: 25-04-2019 / Revised Accepted: 20-06-2019 / Published: 30-06-2019***

## ABSTRACT

Targeted drug delivery is an approach of transporting the therapeutic agent to the tissues of interest and reduces the relative concentration of therapeutic agent in remaining tissues which improves the therapeutic efficacy and condenses the side effects. The vesicular systems are very well organised assemblies of one or some concentric lipid bilayer formed, when certain amphiphilic building blocks are confronting with water. A number of novel vesicular drug delivery systems have been emerged encompassing various routes of administration, to achieve targeted and controlled drug delivery numbers of carriers were utilized to deliver the drug at target site; these include immunoglobulins, serum proteins, synthetic polymers, microspheres, liposomes, niosomes, erythrocytes etc. The present review focus more on the recent approaches and advancement in Vesicular Structured drug delivery systems.

**Keywords**: Vesicular system, Liposomes, Niosomes, Erythrocytes

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**How to Cite this Article:** Sagar Trivedi, Kamlesh Wadher, Milind Umekar. Vesicular Structured Drug Delivery Systems: An Innovative Slant towards Drug Targeting. World J Pharm Sci 2019; 7(7): 20-30.

## INTRODUCTION

In the modern era there has been a tremendous growth in the arena of new drug delivery system. The novel drug delivery system found to be the most suitable and appropriate in designing the delivery system which improves the therapeutic efficacy of drugs and provides controllable drug delivery to the specific site. [1] Targeted drug delivery is an approach of transporting the therapeutic agent to the tissues of interest and reduces the relative concentration in remaining tissues which improves the therapeutic efficacy and reduces the side effects [2]. Drug targeting means the delivery of drugs to receptor, organs or any other specific part of body to which one wishes to deliver the entire drug Development of vesicular delivery system can be utilized to targeting, modulating the release of the drug and reduce the toxicity. Vesicular Structured drug delivery systems aim to deliver the drug at a rate directed by indispensable need of body thought the treatment and localize the active entity to the site of action. [3]The vesicular systems are highly ordered assemblies of one or several concentric lipid bilayers. Vesicles can be formed from a diverse range of amphiphillic building blocks. Vesicles as a carrier system have become the vehicle of choice for drug delivery due to improved efficiency, cost effectiveness and incorporation of hydrophillic and hydrophobic drugs, improved bioavailability.

Different types of pharmaceutical carriers can be classified as, particulate, polymeric, macromolecular, and cellular carrier. In this article, an attempt has been made to review types, preparation and advancements in various lipoidal vesicular systems such as liposomes, emulsomes, ethosomes, sphingosomes transfersomes, pharmacosomes and non-lipoidal system such as aquasomes, niosomesen listed in table no 1.

| VESICULAR SYSTEM | DESCRIPTION | APPLICATION |
|---|---|---|
| **Liposomes** | Liposomes are simple microscopic lipid vesicles ranging from 20 nanometers to several micrometers in size | Drug targeting to various organs. Enhance the skin permeation of drugs. Useful for RES targeting; rapid and saturable uptake by RES, short circulation half life. |
| **Niosomes** | An aqueous solution is enclosed in a highly ordered bilayer made up of non- ionic surfactant, with or without cholesterol | Specific targeting, molecular shielding. |
| **Aquasomes** | Three-layered self-assembly composition with ceramics carbon nanocrystalline particular core coated with glassy cellobiose | Specific targeting, molecular shielding. |
| **Cryptosomes** | Lipid vesicles with a surface coat composed of PC and of suitable polyoxyethylene derivative of phosphatidyl ethanolamine | Ligand mediated drug targeting. |
| **Discomes** | Niosomes solubilized with non ionic surfactant solutions (polyoxyethylenecetyl ether class) | Ligand mediated drug targeting. |
| **Emulsomes** | Nanosize lipid particles consist of microscopic lipid assembly with apolar core. Emulsomes have the characteristics of both liposomes and emulsions. | Parenteral delivery of poorly water-soluble drugs. |
| **Enzymosomes** | Liposomes engineered to provide a mini bio-environment where enzymes are covalently immobilized or coupled to the surface of liposomes. | Targeted delivery to tumour cells |
| **Ethosomes** | Ethosomes are soft lipid vesicles containing phospholipids, alcohol (ethanol) in relatively high concentration and water. | Targeted delivery to deep skin layer cells |
| **Genosomes** | Artificial macromolecular complexes for functional gene transfer. Cationic lipids are most suitable because they posess high biodegradability and stability in the blood stream. | Cell specific gene transfer |
| **Photosomes** | Photolysase encapsulated in liposomes, which release the content photo-trigged charges in membrane permeability characteristics. | Photodynamic therapy |
| **Virosomes** | Liposomes spiked with virus glycoprotein, | Immunological adjuvants |

| | | |
|---|---|---|
| | incorporated into the liposomal bilayers based on retro viruses derived lipids. | |
| **Vesosomes** | Nested bilayer compartment in vitro via the interdigital bilayer phase formed by adding ethanol to a variety of saturated phospholipids | Multiple compartment of the Vesosomes give better protection to the interior contents in serum |
| **Proteosomes** | High molecular weight multi-submit enzyme complexes with catalytic activity, which is specifically due to the assembly pattern of enzymes | Better catalytic activity turnover than non-associated enzymes. |
| **Transfersomes** | Transfersomes are deformable lipid supramolecular aggregates | They are used as a carrier for protein, peptides and hormones. |
| **Sphingosomes** | These Contains sphingolipids instead of phospholipids present in liposomes | They provide selective passive targeting to tumour tissues |
| **Pharmacosomes** | Pharmacosomes are amphiphilic lipoidal colloidal dispersions of drugs, covalently bound to lipids | Targeted delivery to liver and tumour cells |

**LIPOSOMES**

Liposomes are spherical vesicles with concentric phospholipid bilayers that are formed spontaneously in aqueous solution.[4]Lipid bilayered membrane encloses an aqueous core and hydrophilic drugs may get entrapped in the central aqueous core of the vesicles while lipophilic drugs are entrapped within the bilayered membrane as shown in figure 1.[5]When phospholipids are placed in water and sufficient energy is provided from sonication, heating, homogenization and, results in the arrangement of the lipids and formation of bilayer vesicles. [6]

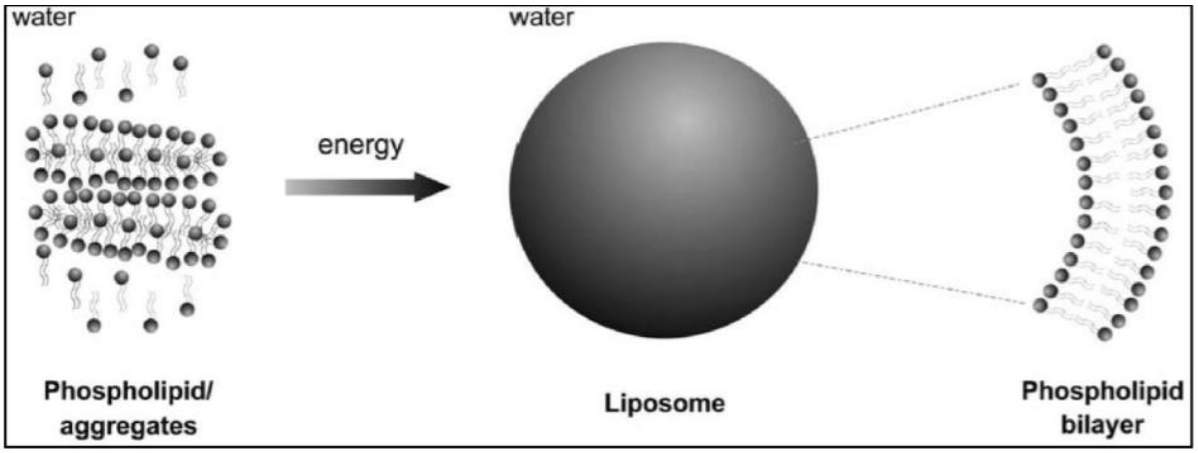


**Figure 1 : Liposomes**

**Classification of liposome based on the method of preparation**

- VET - Vesicles prepared by Extraction Technique
- REV - Reverse Phase Evaporation method SUVs, MLVs & OLVs are made by reverse phase evaporation (REV) Method
- DR V - Dehydration- Rehydration method
- FATMLV - Frozen and thawed multi lamellar vesicle
- FPCV- French Pressure Cell method
- FTMV- Frozen and thawed Multilayered Vesicles:

**Classification of liposome based on their composition and application**

- Fusogenic liposome - RSVE Reconstituted Sendai virus envelops.
- Long circulatory liposome LCL Neutral high temp, cholesterol, and 5- 10% PEG, DSP.
- pH sensitive liposomes - Phospholipids such as PER or DOPE with either CHEMS or OA.
- Conventional liposome CL Neutral or negatively charge phospholipids and cholesterol.
- Cationic liposome - Cationic lipid with DOPE.

- Immuno liposome IL with attached monoclonal antibody or recognition sequences.

**Methods of preparation**

**Thin film method**: In this method, liposomes are prepared by hydrating the thin lipid film in an organic solvent and then organic solvent is removed under vacuum. After completely removing the solvent, the solid lipid mixture is hydrated by aqueous buffer. The lipids spontaneously swell and hydrate to form liposome. This method has low encapsulation efficiency.[7]

**Reverse Phase Evaporation**: In this method, the lipid mixture is added to a round bottom flask and the organic solvent (diethyl ether and isopropyl ether) is removed under reduced pressure by a rotary evaporator. The liposomes are formed when residual solvent is removed by continued rotary evaporation under reduced pressure.[1]

**Freeze-thaw method**: In FT method, liposomes formed by the film method are vortexed with the solute to be entrapped until the entire film is suspended. Then liposomes are frozen in dry ice-ethanol (-80 ˚C) or in liquid nitrogen and are thawed and then vortexed again. The freeze and thawing cycles are repeated. This method is used widely for encapsulation of protein

**Ultrasonic Method**: The method is used for the preparation of SUV liposomes. Ultrasonication of an aqueous dispersion of phospholipids is done by two types of sonicators; probe sonicators or bath sonicators for the small volumes and large volumes, respectively.[7]

**Calcium induced fusion method**: The method is used for preparation of LUV liposomes from acidic phospholipids. Calcium is added to SUV liposomes that induce fusion and cause formation of multilamellar vesicle. The addition of EDTA to the preparations results in the formation of LUV liposomes .[8]

**Applications [9]:**

- Drug delivery to tumours such as breast, colon, pancreatic, lungs and ovarian cancers
- Targeted delivery of antimicrobial agent to macrophages
- Gene delivery
- Specific targeting of antibodies to brain
- Site specific delivery of drugs for the treatment of solid tumours

**AQUASOMES**

Aquasomes are like “bodies of water" and their water like properties protect and preserve fragile biological molecules, and this property of maintaining conformational integrity as well as high degree of surface exposure. Aquasomes are spherical in shape with 60–300 nm particles size. Aquasomes are three layered structures (core, coating and drug) that are self-assembled through non covalent bonds, ionic bonds and vanderwaals forces. The solid core provides the structural stability, while the carbohydrate coating protects against dehydration and stabilizes the biochemically active molecules.[10] Aquasomes are one of the most recently developed delivery system for bioactive molecules like peptide, protein, hormones, antigens and genes to specific sites. [11]

**Principle of self-assembly**[12]

**I- Interaction between charged groups**the interaction of charged groups, such as amino, carboxyl, sulphate, phosphate groups facilitate long range approach of self-assembly sub units

**II- Hydrogen bonding and dehydration** effect Hydrogen bond helps in base pair matching and stabilization of secondary protein structure such as alpha helices and beta sheets. Molecules forming hydrogen bonds are hydrophilic and this confers a significant degree of organization to surrounding water molecules.

**III- Structural stability** Molecules that carry less charge than formally charged groups exhibit a dipole moment. The forces associated with dipoles are known as van der waals forces. Structural stability of protein in biological environment determined by interaction between charged group and hydrogen bonds largely external to molecule and by van der waals forces largely internal to molecule.

**Composition of aquasomes**[11]

- **Core material** Ceramic and polymers are most widely used core materials. Polymers such as albumin, gelatin or acrylate are used. Ceramic such as diamond particles, brushite (calcium phosphate) and tin oxide are used.
- **Coating material** Coating materials commonly used are cellobiose, pyridoxal 5 phosphate, sucrose, trehalose, chitosan, citrate etc. Carbohydrate plays important role act as natural stabilizer; its stabilization efficiency has been reported. Beginning with preformed carbon ceramic nanoparticle and self-assembled calcium phosphate dihydrate particles (colloidal precipitation) to which glassy carbohydrate are then allowed to adsorb as a nanometres thick surface coating a molecular carrier is formed.
- **Bioactive** they have the property of interacting with film via non-covalent and ionic interactions

**Method of preparation of Aquasomes**

The method of preparation of aquasomes involves three steps.

The general procedure consists of Formation of an inorganic core, followed by Coating of the core with polyhydroxy oligomer, and finally loading of the drug of choice to this assembly.[13]

**I- Formation of an inorganic core** It involves the fabrication of a ceramic core, and the procedure depends upon the materials selected. The two most commonly used ceramic cores are calcium phosphate and diamond.

**a) Synthesis of nanocrystalline** tin oxide core ceramic It can be synthesized by direct current reactive magnetron sputtering. Here, a 3 inches diameter target of high purity tin the ultrafine particles formed in the gas phase are then collected on copper tubes cooled to 77 0K with flowing nitrogen.

**b) Self assembled nanocrystalline** brushite (calcium phosphate dihydrate) These can be prepared by colloidal precipitation and sonication by reacting solution of disodium hydrogen phosphate and calcium chloride.

**c) Nanocrystalline carbon ceramic, diamond particles** These can also be used for the core synthesis after ultra-cleansing and sonication. The common feature of various cores is that they are crystalline and that when they are introduced into the synthetic processes, they measure between 50-150 nm and exhibit extremely clean and therefore reactive species. Ceramic materials, being structurally highly regular, are most widely used for core fabrication

II- **Coating of the core with polyhydroxyoligomer:** In the second step, ceramic cores are coated with carbohydrate (polyhydroxyl oligomer). The coating is carried out by addition of carbohydrate into an aqueous dispersion of the cores under sonication. These are then subjected to lyophilization to promote an irreversible adsorption of carbohydrate onto the ceramic surface.

**III-Loading of the drug of choice** to this assembly The final stage involves the loading of drug to the coated particles by adsorption. For that, a solution of known concentration of drug is prepared in suitable pH buffer, and coated particles are dispersed into it. The dispersion is then either kept overnight at low temperature for drug loading or lyophilized after some time so as to obtain the drug-loaded formulation (i.e., aquasomes). The preparation thus obtained is then characterized using various techniques.[14]

**Applications of aquasomes[15]**

- Insulin delivery
- Oral delivery of acid labile enzyme
- As oxygen carrier
- Antigen delivery
- Delivery of drug
- For delivery of gene

**EMULSOMES**

Emulsomes is a lipoidal vesicular system where the internal lipid core (fats and triglycerides) are stabilized in form of o/w emulsion by addition of high concentration of lecithin. The drug is loaded followed by sonication to produce emulsomes of small size.[16]In emulsomes, Emulsomes have the characteristics of both liposomes and emulsions. Emulsome represents lipid-based drug delivery systems with broad variety of therapeutic applications particularly for drugs that are poor aqueous soluble. Emulsomes consist of microscopic lipid assembly with a polar core, which contains water insoluble drugs in the solution form without requiring any surface-active agent or co-solvent. when compare with other vesicular formulations, emulsomes are much stabilized and nano range vesicles.[17]

**Emulsomal formulation**

- **Lipid core** An essential component of emulsomes is an internal hydrophobic core or lipid core comprises lipid, which exhibits solid or lipid crystal phase or mixed solid and liquid crystal phase at room temperature (25°C).[18] The lipid used may be single or mixture of lipids.[19] Triglycerides which are solid at 25°C are found to be appropriate core material because these lessen the acceptable storage life of o/w emulsion. The triglycerides are used for preparation of emulsome composed of un-branched fatty acid with chain length in the c-10 to c-18 range.[20]
- **Antioxidant** The lipid core of emulsome particles of this invention optionally may contain one or more antioxidant. The preferred antioxidant is a-tocopherol or its derivative, which are members of vitamin E family. Other antioxidants include butylated hydroxytouline (BHT). Antioxidants lessen the formation of oxidative degradation products of unsaturated lipids such as peroxides. The need of antioxidant may be protected by preparing the lipid core form saturated fatty acid.
- **Surfactants** Selection of surfactant should be done on the basis of Hydrophilic Lipophilic Balance (HLB) value. As HLB is a good indicator of the vesicle forming ability of any surfactant, HLB number in between 4 and 8 was found to be compatible with vesicle formation.[21]
- **Phosphatidyl choline** Phosphatidyl choline is such a major component of lecithin. Phosphatidyl choline has low solubility in water. In aqueous solution its phospholipids

can form bilayer sheets, micelles, or lamellar structures, depending on hydration and temperature. This results in a type of surfactant that is usually classified as amphipathic.[22]

- **Cholesterol** Cholesterol is essential component of emulsomes as vesicles. Incorporation of cholesterol influences vesicles stability. [40,41] Concentration of cholesterol plays an important role in entrapment of drug in vesicles.[22] There are reports that entrapment efficiency increases with increasing cholesterol content.[23]

**Application of Emulsomes**

- Drug targeting
- Anti-neoplastic treatment
- Leishmaniasis
- Used in biotechnology

**PHYTOSOMES**

Phytosomes is a complex connecting natural product and natural phospholipids, like soya phospholipids. Such a complex is obtained by reaction of stoichiometric amounts of phospholipids with the substrate in an appropriate solvent. According to the spectroscopic data the main phospholipids-substrate interaction is due to the formation of hydrogen bonds between the polar head of phospholipids (i.e. Ammonium and phosphate groups) and the polar functionalities of the substrate.[24]

Phytosomes on treatment with water assumes a micellar shape forming liposomal-like structures. In liposomes the active constituent is dissolved in the internal pocket or is floating in the layer membrane, while in phytosomes the active principle is anchored to the polar head of phospholipids, becoming an integral part of the membrane.[25]

**Preparation Methods**

- Phospholipid Dissolved in organic solvent containing drug/extract
- Solution of phospholipids in organic solvent with drug/extract
- Drying Formation of thin film Hydration
- Formation of phytosomal suspension

Phytosomes are prepared by complexation of polyphenolic phytoconstituents in 1:2 or 1:1 ratio with natural or synthetic phospholipid like phosphatidylcholine, phosphatidylethanolamine or phosphatidylserine, either alone or in an aprotic solvent, such as dioxane or acetone. The complex that is formed is isolated by precipitation with an aliphatic hydrocarbon or 17 sprays drying or lyophilization. Some liposomal drug complexes are effective in the presence of water or buffer solution where the phytosomes interact with a solvent which has a reduced dielectric constant. The conditions for the preparation are: lecithin to PVP and solvent-tetrahydrofuran ratio - 2:5, temperature - 40°C and reaction time-3 hrs.[26]

**NIOSOMES**

Niosomes are multilamellar vesicular structure of non-ionic surfactants, similar to liposomes and are composed of non-ionic surfactant instead of phospholipids which are the components of liposomes So, niosome or non-ionic surfactant vesicles are now widely studied as an alternative tool to liposome.[27]

Various types of surfactants have been reported to form vesicles and have the capacity to entrap and retain the hydrophilic and hydrophobic solute particles. Niosomes mainly contain two types of components i.e., non-ionic surfactant and the additives. The non-ionic surfactants form the vesicular layer and the additives used in niosome preparation are cholesterol and the charged molecules the presence of the steroidal system (cholesterol) improves the rigidity of the bilayer and is important component of the cell membrane and their presence in membrane affects bilayer fluidity and permeability. This carrier system protects the drug molecules from the premature degradation and inactivation due to unwanted immunological and pharmacological effects.[28]

**Components of Niosomes**

Niosomes mainly contains following types of components:

- **Non-ionic Surfactants[16]**

The non-ionic surfactantsorient themselves in bilayer lattices where the polar or hydrophobic heads align facing aqueousbulk (media) while thehydrophobic head or hydrocarbon segments align in such away that the interaction with the aqueous media would beminimized. To attain thermodynamic stability, every bilayer fold over itself as continuous membrane i.e. forms vesiclesso that hydrocarbon/water interface remains no more ex-posedMainly following types of non-ionic surfactants are usedfor the formation of niosomes:

1) Surfactant-I (molecular weight (MW 473)) is Cmonoalkyl glycerol ether with average of three glycerol units.

2) Surfactant-II (MW 972) is diglycerol ether with average of the seven glycerol units.

3) Surfactant III (MW 393) is ester linked surfactant.

- **Cholesterol**

It is a steroid derivative, which is mainly used for the formulation of niosomes. incorporation of cholesterol affects properties of niosomes like

membrane permeability, rigidity, encapsulation efficiency, ease of rehydration of freeze dried niosomes and their toxicity. It prevents the vesicle aggregation by the inclusion of molecules that stabilize the system against the formation of aggregates by repulsive steric or electrostatic forces that leads to the transition from the gel to the liquid phase in niosome systems. As a result of this, the niosome becomes less leaky in nature.[19]

- **Charged Molecule**

They are added to niosomes to increase stability of niosomes by electrostatic repulsion which prevents coalescence. The negatively charged molecules used are diacetyl phosphate (DCP) and phosphotidic acid. Similarly, stearylamine (STR) and stearylpyridinium chloride are the well-known positively charged molecules used in niosomal preparations. These charged molecules are used mainly to prevent aggregation ofniosome.[30]

**VIROSOMES**

Virosomal technology presents a novel sophisticated delivery system to meet these challenges. Virosomes are reconstituted viral envelopes, including membrane lipids and viral spike glycoprotein, but devoid of viral genetic material. The external surface of the virosome resembles that of a virus particle, with spike proteins protruding from the membrane, but their interior compartment is empty. Semi-synthetic complex derived from nucleic-acid free viral particles .[31]

They are essentially reconstituted viral coats, where the infectious nucleocapsid is replaced by a compound of choice. Virosomes retain their Fusogenic activity and thus deliver the incorporated compound (antigens, drugs, genes) inside the target cell. They can be used for vaccines (VACCINES, VIROSOME), drug delivery, or gene transfer. Virosomes are spherical unilamellar vesicles with a mean diameter of around 150 nm. Influenza virus is most commonly used for virosome production.[32]

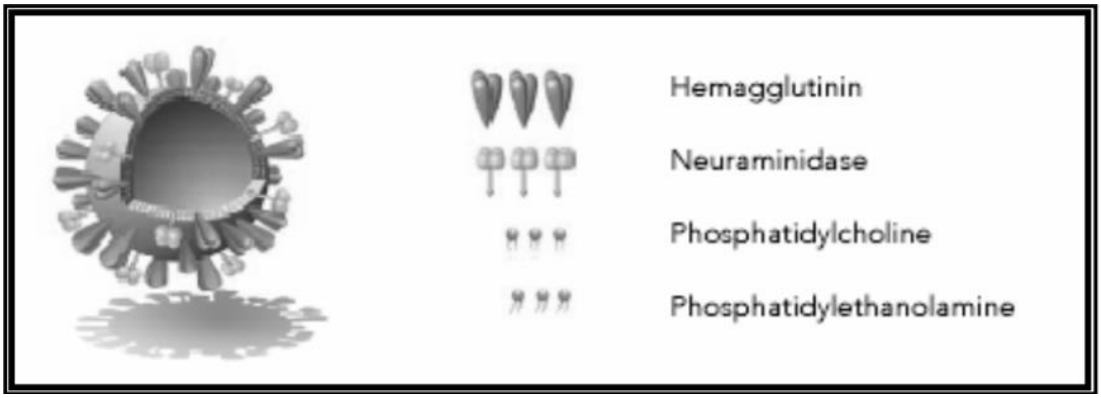


FIG NO :2

Virosomes cannot replicate but are pure fusion-active vesicles. In contrast to liposomes, virosomes contain functional viral envelope glycoproteins: influenza virus hemagglutinin (HA) and neuraminidase (NA) are intercalated within the phospholipids bilayers membrane. Further characteristics of virosomes depend on the choice of bilayer components. Virosomes can be optimized for maximal incorporation of the drug or for the best physiological effect by modifying the content or type of membrane lipids used .[33]

**Method of preparation**[34]

- **Selection of virosomes** Virosome are reconstituted viral envelope that can be derived from different virosome. Influenza virus envelope is the most commonly used to produce virosome but virosomes can be made from Sendai virus, Epstein burr- virus, HIV, Sindbis, Semlikiforest, virus Friend murine leukaemia virus, herpes simplex virus.
- **Selection of antigen** Antigen is selected as per requirement. Antigen such a parasite, carcinogenic cell, bacterium or whole cell is used. As antigen such as cell component DNA, RNA or plasmid can also used as antigen. This antigen is coupled to lipid anchor so antigen will ready to load on virosomes
- **Reconstituted of virosome** Virosome solubilised with detergent (octaglucoside, triton x-100, nonidert p-40) Due to solubilization with detergent internal viral protein and genetic material will sediment then detergent is removed by different method such as dialysis and hydrobhobic resins from supernatant. Then using ultracentrifugation process viral matrix protein and nucleicapsid is removed. Viral phospholipid (82%) and viral protein is recovered. Now antigen which is already coupled to lipid anchor is mixed with polymer or surfactant solution and this solution is processed with virosome carrier so that antigen bound virosome is obtained.

**Mechanism of action of virosome** Virosome act both as a carrier and as an adjuvant with multiple functions during the induction of an immune

response. The carrier function comprises the positive effects of embedding the antigen into a higher structure, the virosome particle. The adjuvant function relates to immune stimulating properties of virosome and their components on immune system most importantly virosome succeed in stimulating specific immunity without causing non- specific inflammation.

**Properties of virosomes** Virosome are biodegradable, biocompatible non- toxic, an antigen can be incorporated into virosome, adsorbed to virosome surface and integrated into to the lipid membrane either hydrophobic domain or lipid moieties cross- linked to antigen. They are also being considered for HIV –I vaccine research. They were used as a drug carrier mechanism for experimental cancer therapies.

**Applications of virosome**

- Cancer treatment.
- Gene delivery
- RNA\DNA
- Malaria therapy

**ENZYMOSOMES**

Enzymosomes is an innovative currently emerging targeted vesicular drug delivery system. Enzymosomes fundamentally uses enzymes, which are having a targeted catalytic function for a substrate, which are incorporated within cell-like structures having high lipid background. They yield newly designed liposomes, in which the enzymes are coupled covalently to the surface of lipid molecules. The liposomes so devised to provide proper microsurrounding for the enzymes to be incapacitated within them. Liposomes are micro-sized vesicles consisting of a lipid bilayer enclosing with an aqueous environment. The hydrophilic drugs can be solubilised within the internal aqueous compartment and the lipophilic drugs are incorporated intothe lipid bilayer membrane consisting of phospholipid-cholesterol Enzymosomes is an innovative currently emerging targeted vesicular drug delivery system. Enzymosomes fundamentally uses enzymes, which are having a targeted catalytic function for a substrate, which are incorporated within cell-like structures having high lipid background. They yield newly designed liposomes, in which the enzymes are coupled covalently to the surface of lipid molecules. The liposomes so devised to provide proper micro surrounding for the enzymes to be incapacitated within them. Liposomes are micro-sized vesicles consisting of a lipid bilayer enclosing with an aqueous environment. The hydrophilic drugs can be solubilised within the internal aqueous compartment and the lipophilic drugs are incorporated into the lipid bilayer membrane consisting of phospholipid-cholesterol.

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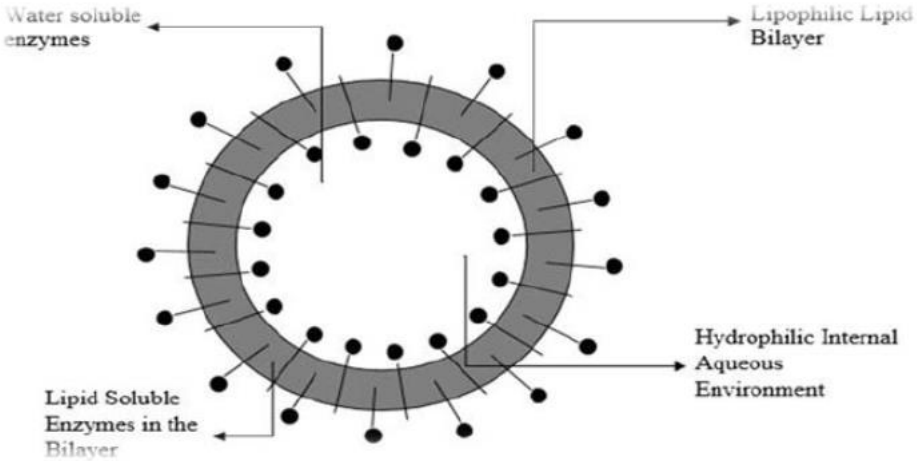
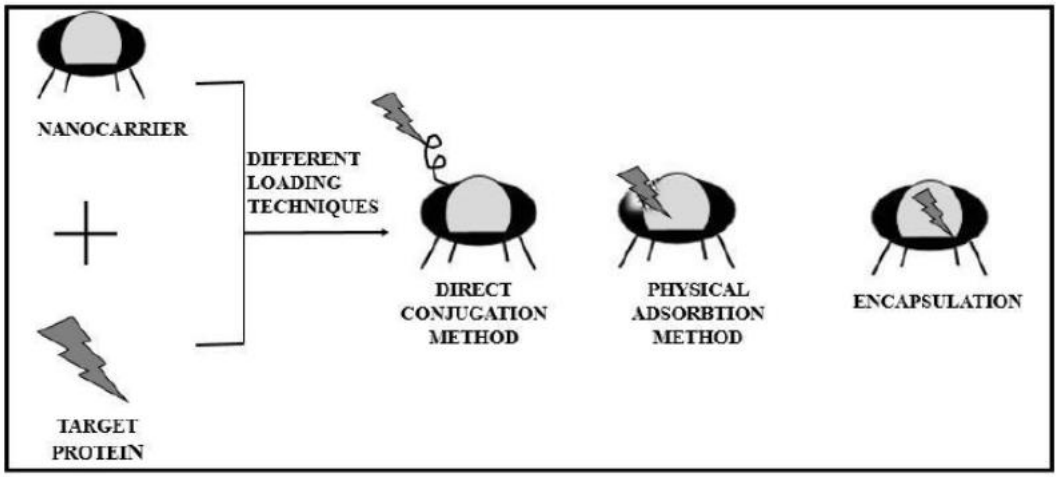



**Preparation of Enzymosomes**

Surface exposed superoxide dismutase (sod) Binding of enzymes directly to the lipids of liposomes is a demanding work, yet they are used presently as a persuasive mechanism in the treatment of immune-mediated diseases or antibody. A model of such direct conjugated therapeutic enzyme includes SOD (Super Oxide Dismutase). The enzyme Cu, Zn-superoxide dismutase (SOD) was delineated as an innate

defence mechanism which decreases the teratogenicity produced by toxic free radicals. It sets off dismutation of the toxic superoxide radical anion O 22_to O2and H2O2. Through physical adsorption method, spontaneous binding is achieved by utilizing the driving electrostatic force. Nanoparticles can be congregated from a variety of materials to covetable geometries and configurations and thus to acquire useful functionalities and properties. Conventional chemotherapy treatments bear various adverse reactions along with the in ability to access the core of the disease. Thus nano-sized polymeric carriers prove to be selectively and specifically cell-targeted drug delivery. disorganising the array of biochemical inflammatory processes induced by the free radical. SOD appears to be a promising substitute for conventional anti-inflammatory therapies, by the use of non-steroidal anti-inflammatory drugs avoiding their side effects. The enzyme was not clinically acceptable due to its finite characteristics, short half-life time in the bloodstream and poor penetration into cells. Many studies were done for modifying the substrate on which the enzyme was loaded with enhanced half-life and liposomal incorporation efficiency along with clinical trials in specific risk groups like obesity, Type 2 DM, etc. To date, the most frequently used application for intracellular SOD delivery is targeting protein to cell penetrating peptides (CPPs) or protein transduction domains (PTDs). Regardless of the practical advantages of the enzyme transduction technology, the main interest of this plan is the inefficient escape from the endosome to cytosol thus leading to CPP-tagged cargoes secluded in intracellular vesicles. Proteins are of importance to biological needs and thus for controlling delivery of these peptides, modern techniques of encapsulation paved way for its adorable use in the treatment of various diseases.




**Applications of enzymosomes**

Enzymosomes coming underclass of lipid nanoparticulate drug delivery system, prepared primarily from phospholipids, which are arranged to a bilayer form, incorporates any substance within them, independent of solubility, electric charge, molecular weight and thus improve GIT absorption and oral bioavailability. The enzymosomes can be loaded over lipid-based nanocarriers like liposomes, solid-lipid nanoparticles, inorganic nanocarriers like gold nanoparticle and magnetic nanoparticles, polymeric nanocarriers like nanogels and micelles, protein-mediated nanocarriers like super positively charged proteins etc. One assuring a current set of drugs without DNA interaction resides within ether and alkylphospholipids since cell membrane was used as the target for therapeutic intervention. In studies, these were especially effective against the clinical treatment of metastases, breast cancer, anti-inflammatory action etc.[37]

**Conclusion**

Site specific targeting of drugs has lots of advantages; vesicular drug delivery system is gaining popularity in present scenario. Drugs can be directly targeted to their site of action to prevent toxic and undesired effects to other sites, further these can be used for bioavailability enhancement of the drugs, having poor bioavailability, to reduce the dose of drug administered and to enhance pharmacological action of drug. Vesicular system is valuable for drugs having narrow therapeutic index because targeting of drug to their site of action improves the overall pharmacokinetic and pharmacodynamic profile of drug and hence improvement in the overall therapy of the disease. Drugs can be successfully delivered using lipoidalbiocarriers such as liposomes, enzymosomes, ethosomes, transferosomes, pharmacosomes, sphingosomes, virosomes,

emulsomes and non lipoidalbiocarriers such as niosomes, bilosomes and aquasomes as per the convenience of therapy. All these biocarriers have been reported for their successfully sitespecific targeting. More stress should be given on control of the membrane assembly through physico-chemical pathways such as entropic parameters, interactions, incorporation of additional reactants and environmental parameters (temperature, ph...), and lipid gel phase structures which may play a role on the domain morphologies of vesicles it is also important to remember that the membrane curvature can greatly influence the membrane structure. Micro-structures that are very useful in drug delivery and templating agents, or for the development of compartmentalized chemistry and biochemistry and as fundamental systems to understand complex biological behaviors in cells.

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