

EMULSOMES: PIONEERING THE FUTURE OF DRUG DELIVERY -A REVIEW**Revathi S, Allimalarkodi S*, Vignesh R, Vanitha S, Raja mani C****Department of Pharmaceutics, The Erode College of Pharmacy, Erode – 638112***Corresponding Author's E mail: allimalarkodi1968@gmail.com

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ABSTRACT

Oral administration of medications is the most significant, convenient, and economical method. Thus, researchers faced the challenge of developing more effective dosage forms, particularly for long-term use. Various drug problems have prompted the development of targeted medication delivery systems. The acidic stomach environment can break down medications and reduce their bioavailability; these systems try to shield them from that. Many other types of vesicular drug delivery systems have received considerable attention. These include ethosomes, nanoparticles, niosomes, proniosomes, solid lipid nanoparticles, liposomes, emulsions, pharmacosomes, and many more. But emulsomes, a new system of lipid vesicles, have an acceleration mechanism that gets rid of most of the problems with the old systems. For medications that are not very soluble, this method works wonders. Because emulsomes enclose the drug, it remains in the bloodstream for far longer than it would otherwise. Antisense oligonucleotides and gene therapy plasmids are two kinds of emulsome-based genetic treatments that appear to have potential systemic benefits but are becoming more accessible. This review primarily focuses on development, assessment, advantages, biopharmaceutical characteristics, stability, and many aspects pertaining to drugs. It also discusses emulsome delivery systems and emphasizes their effectiveness in distributing small molecules.

Keywords: Drug delivery, Phospholipid bilayer, Lipid core, Surfactants, Cholesterol, Emulsomes.

INTRODUCTION

Nanotechnology offers an additional strategy for reducing the side effects of systemic distribution by increasing the bioavailability of drugs and improving their transport to their destinations¹. The emulsome (EML) is a vesicular system that integrates the advantages of nanoemulsions and lipid bivalve vesicles. Emulsomes consist of a solid lipid core and a phospholipid coating, enhancing the vesicle's stability². It combines the advantages of nanoemulsions with liposomes. The PL sheath makes pharmaceuticals that don't dissolve easily more bioavailable and soluble than liposomal vesicular frameworks. Emulsomes' intrinsic lipid core is a strong or fluid crystalline form, not fluid oil. In order to accomplish certain goals, including enabling medication targeting, researchers must think of ways to alter the emulsomal surface³. A notable feature of emulsomes is that their inner core is a

solid lipid rather than an oil-liquid phase that remains solid at 25°C and has a solid-liquid phase transition temperature close to physiological levels. Inside the lipid core are spaces for hydrophobic drugs, whereas the aqueous compartments of the phospholipid layers on the exterior are ideal for water-soluble pharmaceuticals. The goal is to maximize drug penetration by covering emulsomes with trimethyl chitosan, a mucosal adhesive polymer, so they attach better to the nasal mucosa and stay there longer⁴. Emulsomes regulated drug release, biocompatibility, biodegradability, and efficient drug encapsulation have made it a consistent drug delivery technology known for dependability. The lipophilicity of EMLs raises their cellular permeability, therefore improving the solubility, availability, and efficacy of undissolved drugs^{5,6}. Unlike liquid oil, EML has as its main feature a lipid nucleus in a solid or liquid, crystalline form. It is interesting, that this helps EML to record more lipid-soluble medicines with a delayed release pattern. The external structure of EML, a bilayer of phospholipids, precludes the necessity for surfactant stabilization. This property guarantees a high level of biocompatibility and stability with minimal toxicity. Furthermore, the Nanosize of the Formulation can substantially enhance the drug's response to emulsion dispersions. As a result, the surface of emulsomes is PEGylated to enhance steric stabilization and facilitate long-term circulation^{7,8}.

Drug release from the solid matrix of Emulsions is by Dissolution and hence slower than diffusion-based Release from Emulsions, such as (solid) polymeric Nanoparticles. This guarantees an ongoing medication release over an extended length of time. Both safe and non-toxic is this dosing form. In several respects, S-layer-Technology can help emulsomes: I) enhanced anti-adhesion properties, which are especially relevant in biological environments; II) the ability to reveal functional regions in an orderly manner; and iii) the capacity to self-assemble more than one S-layer (fusion) protein in emulsomes for the synthesis of multifunctional DDS⁹. Furthermore, taken into consideration also a benefit in cancer treatment is the site-specificity coming from emulsomenanosize, which rises drug targeting¹⁰. Solvent- and surfactant-free Emulsion-Approaches have shown increased drug delivery and enhanced preclinical oral efficacy as well as great Encapsulation-Capacity for water-insoluble antifungal and anticancer medicines¹¹.

Soy lecithin and cholesterol are the stabilizers applied in the emulsion formulation. The vesicular drug delivery system (VDDS) is one of the latest drug delivery techniques used to increase drug solubility. It also facilitates the development of a controlled-release drug delivery system. Water-soluble compounds with rate-regulating effects encircle the medications in the core of VDDS¹². In addition, charge-inducing chemicals are included in emulsomes to produce monodisperse vesicles, stabilizing

the formulation and preventing agglomeration of similarly charged vesicles¹³. Emulsomes may be cheaper than commercial lipid formulations for fungal and viral infections. Emulsomes ensure drug release is controlled and constant and also have a self-release window of up to twenty-four hours, while liposomes have a window of six hours. Emulsomes are tiny compared to niosomes, pharmacosomes, and ethosomes, which are also vesicular, transport systems¹⁴.

Evidenced of emulsion instability during storage:

- Creaming
- Flocculation
- Coalescence

Advantages

- Emulsomes consist of a lipid core. Lipids are used to develop a controlled oral drug. Widespread adoption of lipid-based strategies to enhance drug discovery is limited.
- Emulsomes are an economical alternative to current commercial lipid formulations because they reduce the frequency of drug dosing.
- The emulsion-based system demonstrated excellent targeting capabilities.
- Emulsomes improve the therapeutic rate and efficacy of drugs¹⁵.
- It improves the bioavailability and solubility of poorly soluble drugs.
- Emulsomes prevent drugs from breaking down in the harsh stomach environment because the drug is enclosed in the lipid core of triglycerides. And this encapsulation also protects the drug from the external environment.
- Emulsomes with high systemic absorption, targeting and increased delivery of drugs to affected tissues.
- Emulsomes are economical compared to other conventional lipid preparations.
- Emulsomes change the pharmacokinetic activity of drugs.
- It works against the development of multidrug resistance.
- Emulsomes are completely biodegradable, non-toxic and immunogenic.
- It has a safe cytotoxicity profile.

Disadvantages

- The medicate stacking capacity of emulsomes is constrained.
- A safeguard needs to be taken for parenteral organization because it causes numerous side impacts.
- In case medicate epitome past 1% is required at that point expansive sum of oil stage is required to break down the drug.
- Due to emulsomes are tall in oil substance, to preserve the solidness expansion of surfactants and co-solvents are vital.
- On the off chance that the emulsome is implied for parenteral organization, the utilize of surfactants is limited, as the cleanser properties of the surfactants.
- In case of organisms zone containing sodium de oxy cholate harmful response may happens.
- Possibility of dumping due to defective organization.
- Bunch to group variety may happen¹⁶.

Structure of Emulsomes

Emulsomes are lipoid vesicles containing a solid lipid (SL) core surrounded by a phospholipid (PL) multilayer envelope. It combines the advantages of both nanoemulsions and liposomes

An important feature of emulsomes is their inner core, which consists of a lipid in the solid state instead of an oil-liquid phase, which remains solid at 250 C and has a solid.-phase transition temperature close to physiological temperature^{17,18}

The phospholipid envelope also gives the possibility of encapsulating hydrophilic molecules in the aqueous parts of the surrounding phospholipid layers and/or loading lipophilic molecules into their inner core.

Emulsions are heterogeneous in which one lipid is dispersed in another lipid in the form of droplets typically larger than 1 micrometer in diameter. Emulsomes contain a microscopic lipid with a lipid core that holds water-insoluble drugs^{19,20}.

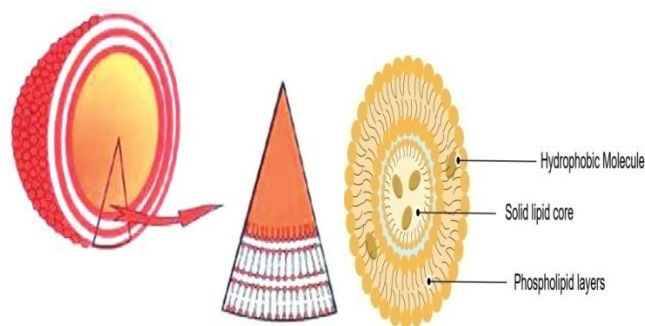


Fig -1: Structure of Emulsomes

Mechanism of Emulsomes Absorption

Structural similarities between emulsomes and chylomicrons, the body's natural lipoprotein, lead one to believe them to behave similarly. Often driven by an endogenous lipid absorption process, these small, lipid-like particles pass through enterocytes of the GIT tract. Through a complicated mechanism that coordinates the synthesis of apolipoproteins and lipids before assembling them intracellularly into mature lipid-containing particles, the intestine absorbs long-chain triglycerides from enterocytes. Triglycerides are mostly related with the stomach through monoglycerides and free greasy acids. The endoplasmic reticulum (ER), which converts complex lipids into triglycerides, absorbs them by detached diffusion into enterocytes. The ER and Golgi devices generate prechylomicrons, which are precursors to chylomicrons. Lipoproteins are produced in the ER and subsequently transported to the Golgi. At that point, the ER secretes triglyceride-rich lipoproteins into the intercellular space, whereas chylomicrons migrate to the horizontal film of enterocytes and are exocytosed. Lipid-based excipients can impact verbal assimilation by a variety of physiological effects, including reduced gastric emptying, increased bile stream and pancreatic liquid emission, and a specific influence on enterocyte-based drug transport and distribution²¹.

Formulation of Emulsomes

- ✓ Lipid core
- ✓ Antioxidant
- ✓ Negatively charged particle
- ✓ Phosphatidyl choline
- ✓ Cholesterol
- ✓ Surfactants

LIPID CORE

An imperative component of emulsomes is the internal hydrophobic center or the lipid center contains a lipid with a strong or lipid crystalline stage or a blended strong and fluid crystalline stage at room temperature (25 °C). An expansive number of lipids or lipid-like excipients are commercially accessible. All of these are collectively called lipids within the restorative field. Lipids are by and large insoluble in water and are frequently recognized by their greasy corrosive composition, dissolving point, and hydrophilic-lipophilic adjust (HLB). Lipids with moo HLB and tall dissolving point are appropriate for maintained discharge. Semi-solid and tall HLB excipients act as quick discharge and bioavailability upgrading excipients. Triglycerides, which are strong at 25°C, have been found to be an appropriate centre since they decrease o/ w worthy rack life. w emulsion. Triglycerides are utilized to create emulsomes, which comprise of straight greasy acids with a chain length of C₁₀ to C₁₈.

ANTIOXIDANTS

The lipid core of the emulsome particles according to the invention can optionally contain one or more antioxidants. A preferred antioxidant is α -tocopherol or a derivative thereof, which belongs to the vitamin E family. Other antioxidants include butylhydroxytoluene (BHT). Antioxidants reduce the generation of oxidative breakdown products of unsaturated lipids, such as peroxides. The need for an antioxidant can be protected by making a lipid core from a saturated fatty acid²².

NEGATIVELY CHARGED PARTICLES

To increase the zeta potential of the compound that stabilizes the particles, negatively charged lipid particles such as oleic acid or negatively charged phospholipids such as phosphatidic acid, phosphatidylinositol and phosphatidylsterol can be added to the emulsomes. Moreover, the addition of these negatively charged lipid compounds into emulsomes leads to the formation of oppositely charged

phospholipid bilayers. Thus, the water fraction formed by the phospholipid bilayers surrounding the lipid core increases. This effect is due to the fact that the water space between the bilayers causes an electrostatic repulsion between them. The negative charge reduces particle aggregation, which minimizes coalescence, flocculation or fusion²³.

PHOSPHATIDYL CHOLINE

Phosphatidylcholine is an important component of lecithin. Phosphatidylcholine has a 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 generally classified as amphipathic. They are essential components of biological membranes and can be easily obtained from several readily available sources such as egg yolk or soybeans. Depending on the source, they are called egg lecithin and soy lecithin. The addition of lecithin further increased the percentage of drug entrapment to 96.1% and resulted in smaller vesicles due to increased hydrophobicity, resulting in reduced vesicle size²⁴.

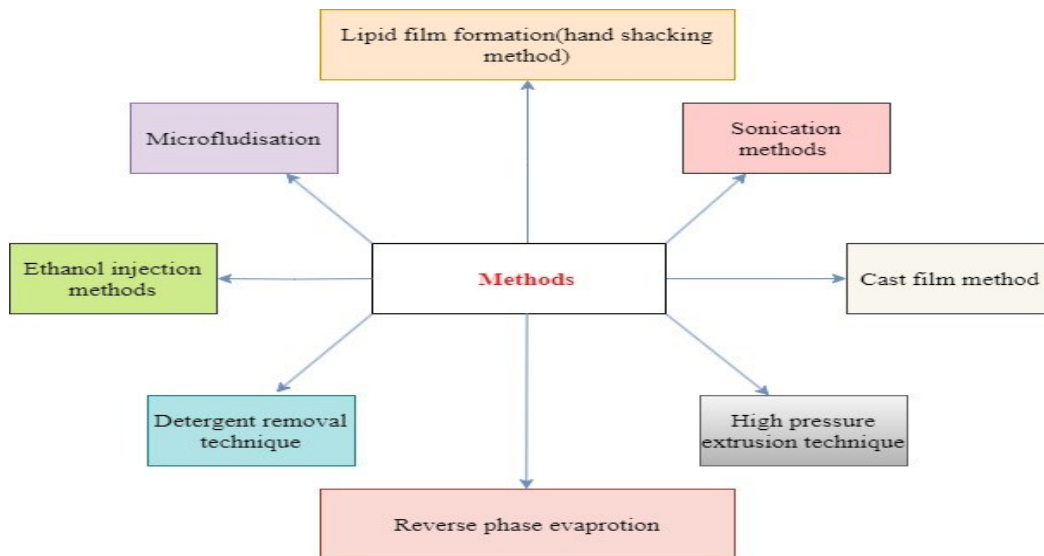
CHOLESTEROL

Cholesterol is an important component of emulsomes in the form of vesicles. Cholesterol binding affects vesicle persistence. Cholesterol concentration plays an important role in drug retention in vesicles. It has been reported that the entrapment efficiency improves with increasing cholesterol concentration. Very high cholesterol concentrations have been found to reduce drug adhesion to vesicles. This may be because cholesterol above a certain level begins to disrupt the normal bilayer structure, leading to a loss of drug retention.

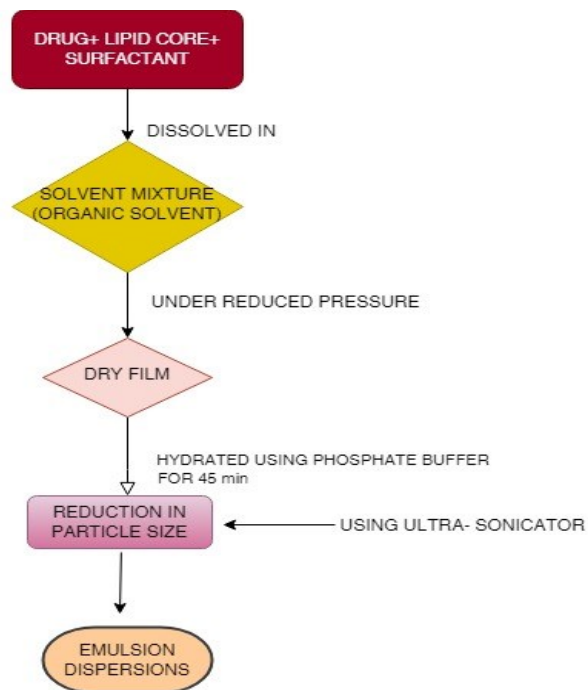
SURFACTANTS

The choice of surfactant should be based on the hydrophilic lipophilic balance (HLB) value. Since HLB is a good indicator of the bubble-forming ability of any surfactant, an HLB number between 4 and 8 has been found to be suitable for bubble formation. The transition temperature of surfactants also affects drug adhesion to vesicles. Regions with the highest phase change temperatures give the highest drug retention and vice versa. Drug leaching from bubbles is reduced due to high phase change temperature and low permeability. The high HLB value of Span 40 and 60 reduces the surface free energy, allowing the formation of larger bubbles and thus a large surface area exposed to the solvent^{21,25-30}.

METHOD OF PREPARATION



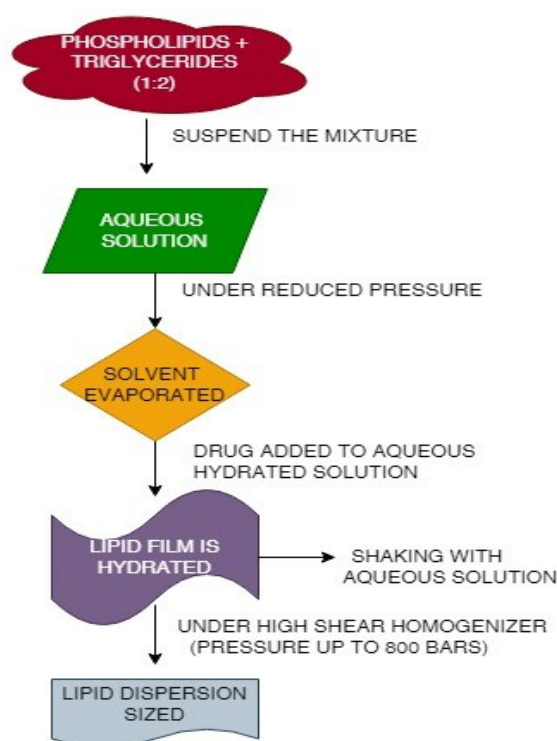
Thin-Film Hydration Technique



Reverse phase evaporation

This procedure, the so-called "reverse-phase dissipation" or REV strategy, comprises of two steps. Plan a water-in-oil emulsion of the phospholipids and weaken the natural stage in abundance. Evacuate the natural stage beneath diminished weight. These two stages (phospholipids and water) are as a rule emulsified by mechanical strategies or sonication. Evacuation of the natural dissolvable beneath vacuum causes the phospholipid-coated water beads to coalesce to create a gel-like lattice. Expulsion of the natural dissolvable beneath advance decreased pressure causes the gel-like network to create into a uniform glue. This glue could be a suspension of LUV. Utilizing this strategy, up to 60-65% drug capture effectiveness can be accomplished. This strategy was utilized to typify both little and expansive particles. The most drawback of this strategy is the contact of the medicate to be typified with natural solvents and mechanical blending. In this strategy, phospholipids are broken up in natural solvents such as chloroform, isopropyl ether or freon. To guarantee great emulsification conditions, it may now and then be essential to blend the two natural solvents to alter the thickness to solidarity, which is closer to that of the fluid stage. Naturally dynamic particles such as chemicals, protein drugs, and RNA-like particles can experience conformational changes, protein denaturation, or DNA strand breaks beneath the cruel conditions of natural dissolvable presentation and mechanical tumult.

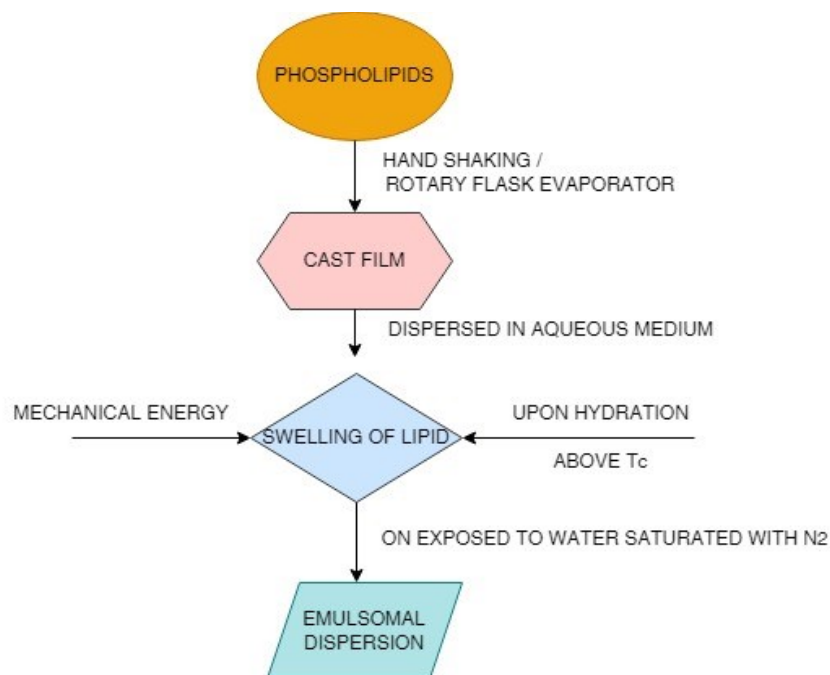
Cast Film Method³¹



Ethanol injection method

This strategy has been portrayed as one way to plan little unilamellar vesicles (SUVs). In this strategy, an ethanol arrangement of surfactant is quickly infused through a fine needle into an abundance of saline or other watery medium. The vanishing of ethanol causes the arrangement of bubbles. Within the ethanol infusion strategy, a contract dissemination of little liposomes (underneath 100 nm) can be gotten basically by infusing a lipid arrangement containing ethanol into water, i.e. in one step, without expulsion or sonication. The ethanol spray strategy may be an appropriate strategy to invigorate the unconstrained arrangement of emulsomes with a little normal span. On the other hand, the lipid or blend of lipids is broken down in a liquor dissolvable and a 200, 500 or 600 ml aliquot is quickly infused at room temperature into a 1 ml syringe containing water or saline dissemination arrangement and assist weakened to 9.8 ml. 1:50, 9.5 ml weakened to 1:20 or 9.8 ml to 1:17. The arrangement was at that point shaken energetically by hand for 20-30 seconds. After that, the ethanol arrangement is quickly infused into the 5% glucose solution. Vesicles had a normal breadth of approximately 60 nm and may be steady for at slightest one week.

Lipid film formation (Hand shaking method)



High-pressure extrusion technique

It was illustrated by a few analysts that when MLV are over and over passed through exceptionally little pore polycarbonate films (0.8 to 1.0 μm) beneath tall weight the normal breadth of the vesicles gotten to be dynamically littler coming to a least of 60-80 nm after 5-10 passes. As the normal estimate is diminished the vesicles tend ended up unilamellar. When MLV were passed through a

Microfluidizer. Microfluidizer is an instrument that powers the bolster fabric beneath tall weight through a limit hole. It shows up that when MLV are constrained through the little hole, layers of bilayers are expelled from the vesicular structure, as on the off chance that the layers of onion skin are isolated when it is peeled. It was moreover recommended that the instrument of layer partition is as it were appropriate to vesicles made with emphatically charged phospholipids and the vesicles that are more noteworthy than 70 pm in measure.

Sonication method

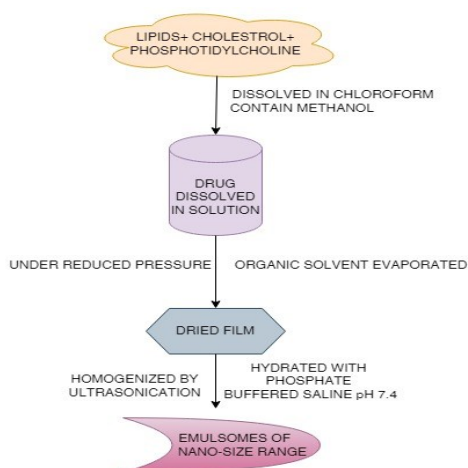


Fig-6

Detergent Removal Technique

In this method, phospholipids and detergent are mixed into micellar mixtures. Detergent then leaves the product, while the micelles are gradually enriched in their phospholipid content and then the lipids come together to form unilamellar vesicles. Methods such as dialysis, column chromatography or adsorption on biobeads can be used to remove the detergent from the formulation. Dialysis technology was first reported to recover biological membranes dissolved by detergents. This method is also suitable for making emulsions. Detergents with a high critical micelle concentration (CMC) are usually used for this purpose. Materials such as sodium cholate, sodium deoxycholate and octylglucoside and other detergents with a high CMC (on the order of 10-20 mM) are suitable detergents for this work. Technically, the detergent was removed from the phospholipid detergent mixture by flow through a dialysis chamber. This method was reported to yield a homogeneous population of monolayer emulsomes with an average diameter of 50–100 nm²¹.

Evaluation test for Emulsomes

Vesicle size and Size distribution

Maintaining a constant size and size distribution over a long period of time indicates the stability of the emulsion. Electron microscopy is widely used to assess the surface morphology, size and size distribution of emulsomes. In addition to conventional laboratory techniques such as gel chromatography, etc., techniques based on light scattering and electron microscopy are required for statistically significant analysis of carrier size and size distribution. Average bubble size and size distribution were determined by photon correlation spectroscopy using a zetasizer (Nanoplus 5.01, Particle System). The dispersion sample was diluted 1:9 with deionized water. The bubble size distribution curve is shown by average bubble size (diameter) and polydispersity index.

Zeta potential

The zeta potential of a particle is the total charge that a particle acquires in a certain environment. Knowing the zeta potential can help predict the fate of a formulation in vivo and assess the stability of colloidal systems. Zeta potential of the emulsion formulations was determined by photon correlation spectroscopy using a Zetasizer Nanoser (Nanoplus 5.01, particle system) using a flow cell.

Shape and surface morphology

Emulsome shape and surface morphology were determined using a transmission electron microscope (TEM) technique. The sample (10 µl) was placed on grids and allowed to stand at room temperature for 90 seconds. Excess liquid was removed by touching the edge filter paper. All samples were examined with a transmission electron microscope at an accelerating voltage of 100 kV and photomicrographs were taken at 1400X. The 3D view of the prepared emulsomes was photographed using scanning electron microscopy (SEM, NOVA NanoSEM 450)³².

Determination of Entrapment Efficiency

Sephadex G-50 column preparation: Sephadex G-50 was expanded in 10 mL of 0.9% sodium chloride solution for 5 h at room temperature with occasional shaking. The gel thus formed was stored at 4 °C. A 2 ml disposable syringe was taken and the lower part of the syringe was blocked with filter paper and cotton. The Sephadex gel was poured into a syringe and the gel-filled syringe was further used as a filter.

Determination of drug entrapment efficiency: The emulsion dispersion was filtered dropwise through a Sephadex G-50 column. The filtrate was treated with a few drops of Triton X-100. Triton X100 breaks the phospholipid bilayer of the emulsome vesicles and the entrapped drug comes out of the solution, which was analyzed by HPLC to determine the area under the curve to estimate the entrapped drug. The entrapped efficiency (EE) was calculated using the following formula³³.

$$\text{Amount of drug entrapped} = \frac{\text{Amount of drug entrapped}}{\text{Amount of drug used}} \times 100$$

Biopharmaceutical Aspects

Emulsomes help to increase the inefficient luminal solubility of the drug. The presence of lipids in the gastrointestinal tract stimulates the secretion of bile salts and endogenous bile lipids, including phospholipid and cholesterol, which causes the formation of mixed micelles of bile salt/phospholipid/cholesterol in the intestine and increases the solvency of the gastrointestinal tract. However, exogenous lipids into these bile salt structures, either directly or secondary to digestion, cause swelling of the micellar structures and a further increase in solubility. Therefore, by stimulating intestinal lymphatic transport, lipids can increase the extent of lymphatic transport and directly or indirectly increase bioavailability through a reduction in first-pass metabolism.

Emulsomes can improve bioavailability by altering the biochemical barrier of the gastrointestinal tract. It is clear that the lipids and triglycerides in the emulsome formula can reduce the activity of intestinal efflux transporters, as indicated by the p-glycoprotein efflux pump, and also reduce the extent of enterocyte-based metabolism. Emulsomes can alter the physical barrier function of the gastrointestinal tract. Various combinations of lipids and triglycerides have been shown to have permeability-enhancing properties. However, passive intestinal permeability is not likely to be a major barrier to the bioavailability of most poorly water-soluble and lipophilic drugs.

Stability Aspects of Emulsomes

Emulsomes have properties of both liposomes and emulsions; offer advantages related to the large number of hydrophobic bioactive compounds in the inner solid lipid core and the ability to encapsulate water-soluble drugs or antigens in the aqueous parts of the surrounding phospholipid bilayers. Pharmaceutically stable emulsomes can be prepared without ionic or non-ionic non-natural surfactants or surfactants such as polyoxamers, deoxycholate, polysorbates, etc. They are stabilized by a

combination of relatively high lecithin content and the use of solid lipid formulations as a core. . The particle size distribution of the emulsions is based on a different mass percentage in the range of 10-250 nm, which makes them suitable for parenteral administration with the addition of water for injection. Oral blister formulations are generally unstable, mainly due to leakage and possible destruction by gastric fluids. Emulsomes are a dry, free-flowing powder when in contact with water. Stability problems associated with conventional liposomes or other vesicular delivery systems include aggregation, susceptibility to hydrolysis, and oxidation. These problems can be avoided by the use of emulsomes. Because emulsomes are dry powder and hydrated, they are more suitable for the development of sustained-release formulations for oral administration.

An important factor related to stability is the zeta potential; The measurement of the zeta potential in electrostatically stabilized vesicles is a key factor in understanding the implementation of diffusion and aggregation processes, and it is certainly an important criterion in studying the storage stability of these vesicles. Lipid modification type, increased the absolute value of the zeta potential, while the fats used in emulsomes give a large negative zeta potential value. Therefore, the decrease in particle size and zeta potential due to the high input energy while sonication ensures stable and well-packed emulsomes²¹.

APPLICATION OF EMULSOMES

Uses

Nanoparticle formulations for transdermal delivery prefer to be preloaded into an available topical formulation such as a cream, gel, cream, or lotion.

Drug Targeting

One of the most useful aspects of emulsomes is their ability to target drugs. Emulsomes can be used to deliver drugs to the reticuloendothelial system. Emulsomes are mainly taken up by the reticuloendothelial system. The assimilation of emulsomal vesicles is regulated by circulating serum factors called opsonins. These opsonins mark vesicles for clearance. Such a drug site is used to treat tumors in animals known to metastasize to the liver and spleen. This localization of drugs can also be used to treat parasitic infections of the liver. Emulsomes can also be used to deliver drugs to organs other than the reticuloendothelial system. A delivery system (such as antibodies) can be attached to the vesicles to target specific organs.

Anti-Neoplastic Treatment

Most anticancer drugs cause serious side effects. Emulsomes can alter metabolism; prolongs the blood circulation and half-life of the drug, which reduces the side effects of the drugs. Emulsomal entrapment of methotrexate has shown beneficial effects compared to unentrapped drugs, such as reduced tumor proliferations and higher plasma concentrations with slower elimination.

Leishmaniasis

Leishmaniasis is a disease whose genus is a parasite. Leishmania invades liver and spleen cells. Commonly prescribed drugs are antimony derivatives (antimonies), which in higher concentrations can cause heart, liver and kidney damage. The use of emulsome in the conducted tests showed that it was possible to administer the drug in larger quantities without side effects, which allowed greater efficiency in the treatment.

Used in biotechnology

Emulsomes are used to study the immune response due to their immunological selectivity, low toxicity and better stability. They are used to study the nature of the immune reaction caused by antigens. The *in vitro* penetration of estradiol from vesicular preparations through the human cerebral cortex was studied. The bubbles were composed of nonionic n-alkyl polyoxyethylene ether surfactants. Two mechanisms are expected to play an important role in blister-skin interactions, i.e., the permeability-enhancing effect of surfactant molecules and the effect of blister structures resulting from their adsorption at the crust-suspension interface³⁴.

Future aspects

Emulsomes are a promising approach for the preparation of drug compounds with poor aqueous solubility and variable oral bioavailability. Oral delivery of hydrophobic drugs is possible using emulsomes, which have been shown to significantly improve oral bioavailability. The rebirth of the use of emulsomes in recent decades is attracting more and more attention. Recent trends focus on the development of modified emulsome solid or semi-solid formulations as an alternative to the conventional liquid system. However, the development of emulsomes is still largely empirical, and there are no *in vitro* models that predict improved oral bioavailability. There is a need for *in vitro* methods to predict dynamic drug changes in the gut to monitor drug dissolution status *in vivo*. One must also pay attention to the interactions between lipid systems and the pharmacological agent. There is also a need to understand the properties of different lipid formulations in order to develop guidelines

for early identification of suitable candidate formulations. Future studies should include human bioavailability as well as basic studies on the mechanisms of action of this exciting and versatile group of formulations.

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