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Review Article

Emulsome: A Revolutionary Advancement in Pharmaceutical Delivery

Rajput Amrapali V., Dr. Shaikh Nasheer S.*, Anantwal Akshat B., Joshi Maharudra R., Limaye Akhilesh S.

Department of Pharmaceutics, Channabasweshwar Pharmacy College, Latur.

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ABSTRACT

Emulsome are emerging as a promising lipid-based nanocarriers system designed to address the challenges of delivering hydrophobic drugs. By combining the structural advantages of liposomes and emulsions, emulsome feature a solid lipid core enveloped by a phospholipid bilayer. This unique architecture enhances drug solubility, protects bioactive compounds from degradation, and enables controlled and targeted drug release. This review provides a comprehensive analysis of emulsome composition, preparation techniques, and physicochemical properties. It also explores their versatile applications in drug delivery, particularly for improving the bioavailability and therapeutic performance of poorly water-soluble drugs. Finally, key challenges and recent advancements are highlighted, offering insights into the future potential of emulsome in revolutionizing drug development.

INTRODUCTION

Emulsome are an emerging class of lipid-based nanoparticle system that have gained significant attention in drug delivery and biomedical applications[(1)]. These vesicular systems are characterized by a solid lipid core surrounded by phospholipid bilayer, combining features of both liposomes and solid lipid nanoparticle[(2)].The unique structural properties of emulsome enable them to encapsulate hydrophobic drugs within their solid core, while also supporting hydrophilic or amphiphilic drugs within the bilayer. This versatility makes emulsome especially promising for improving the bioavailability, stability, and targeted delivery of a wide range of therapeutic compounds [(3)]. Developed initially to overcome the limitations of conventional liposome, such as limited drug loading capacity and low stability, emulsome offer enhanced stability in biological environments, prolonged drug release profiles, and the ability to bypass hepatic metabolism when appropriately modified. Recent advancements have seen emulsome used in diverse therapeutic

***Corresponding Author:** Dr. Shaikh Nasheer S.
Address: Department of Pharmaceutics, Channabasweshwar Pharmacy College, Latur.
Email ✉: nasheershaikh@gmail.com
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areas, including cancer therapy, anti-inflammatory treatments, and antimicrobial applications, as well as in diagnostic imaging and vaccine delivery. This versatility has led to growing interest in emulsome as a multifunctional platform for complex drug delivery needs[4]. This review aims to summarize the current state of emulsome research, with a focus on their structure, preparation method, drug loading techniques, and the physicochemical properties that contribute to their performance in drug delivery. We also explore recent in vitro and in vivo studies, highlighting the potential and limitations of emulsome in clinical applications. By examining these developments, we hope to provide a comprehensive understanding of emulsome and outline key areas for future research that could enable their translation from laboratory research to clinical settings.

Emulsome

Emulsome are nanocarriers composed of a solid lipid core surrounded by one or more layers of phospholipids, combining features of liposomes and emulsions. They are designed to enhance the delivery of both lipophilic and hydrophilic drugs by improving stability, solubility, and bioavailability.

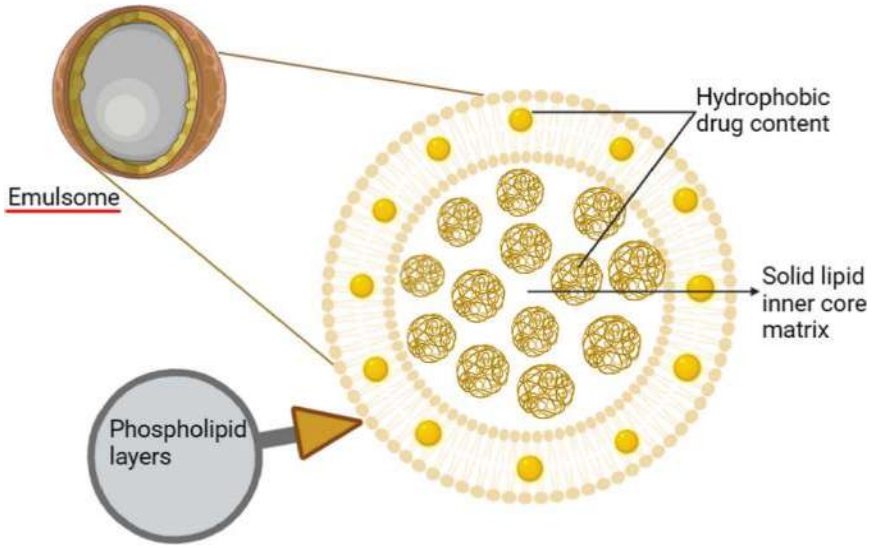

Fig 1: Structure of Emulsome

Emulsome: Principles and Preparation

Emulsome are complex lipid-based nanocarriers that combine the features of both emulsions and liposomes. They are typically composed of an internal aqueous core surrounded by a lipid bilayer, similar to liposomes, but with an additional oil phase dispersed within the lipid layer [5] .This unique structure allows for the encapsulation of both hydrophilic and hydrophobic drug molecules, making emulsome a versatile platform for drug delivery [6].

The preparation of emulsome involves a multistep process that includes the formation of an emulsion, followed by the assembly of the lipid bilayer around the emulsion droplets. (Rajpoot et al., 2011)(Elzayat et al., 2021) The emulsion is typically formed by the high-energy emulsification of an oil phase and an aqueous phase, stabilized by the addition of surfactants. The lipid bilayer is then assembled around the emulsion droplets, typically through the use of a phospholipid and/or cholesterol.

Materials and methods

Material

Lipid core

The interior lipid core or hydrophobic core is made up of lipid is crucial part of emulsome(6). At normal temperature (25˚c), the internal hydrophobic core or lipid core of emulsome is made up of lipid, which has a solid or lipid crystal phase or mixed solid and liquid crystal phase. Lipids and lipid-like excipients may be found in abundance on the market. Instant release and bioavailability enhancement excipients have a high HLB and a semi-solid form, while sustained-release lipids have a low HLB and a high melting point. Because o/w emulsions have a limited storage life, solid triglycerides at 25°C have been proven to be an appropriate core material. Emulsome, which are made up of unbranched fatty acids with chain lengths ranging from C-10 to C-18, are formed using triglycerides[4]. Triglycerides such as tristearin, tripalmitin, tricaprin and trilaurin that solidify at 25°C are thought to be good core materials since they reduce the amount of time that o/w emulsion may be stored in an acceptable manner[6].

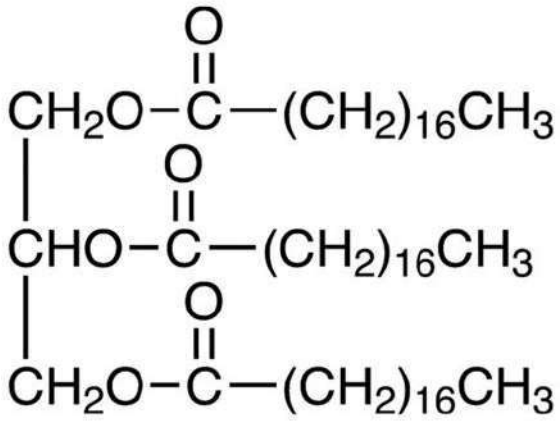

Fig 2: Chemical Structure of Tristearin

Antioxidant

The lipid core of the emulsome particle in this invention may include one or more antioxidants. The antioxidants of choice are alphatocopherol or its derivatives, which are members of the vitamin E family. An additional antioxidant is butylated hydroxytoluene (BHT). Unsaturated lipids are prevented from forming oxidative breakdown products such as peroxides by antioxidants[4].

Phosphatidylcholine

Lecithin contains a lot of Phosphatidylcholine. Water does not readily dissolve Phosphatidylcholine. Depending on temperature and hydration level, the phospholipid in this solution can form lamellar, micelle, or bilayer sheets. They are readily available from a range of conveniently accessible sources, like egg yolk or soy beans, and they are an important part of biological membranes. Lecithin incorporation increased the percentage of drug entrapment to 96.1% and caused the size of the vesicles (smaller vesicles) to be reduced as a result of an increase in hydrophobicity [4,6]

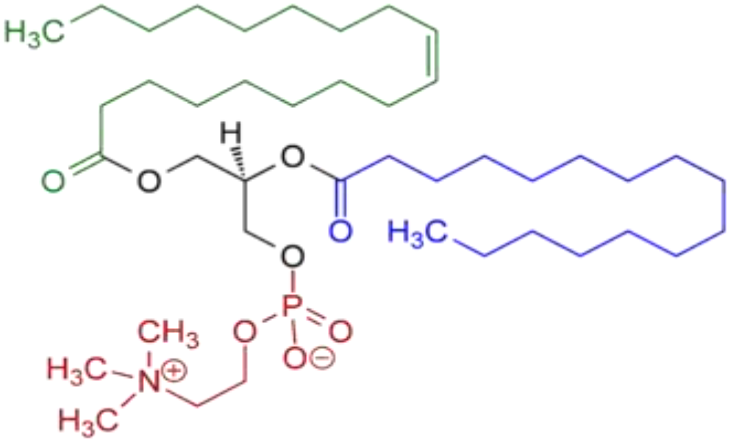

Fig 3. Chemical Structure of Phosphatidylcholine

Cholesterol

In emulsome, cholesterol is essential for the production of vesicles. Cholesterol was added to all formulation as a stabilizing agent since it can cause the creation of the liquid crystal phase by changing the fundamental packing structure. Additionally, it has the ability to stabilize the outer phospholipid layers, which increases drug entrapment effectiveness and decreases drug leakage. Cholesterol also plays a crucial role in increasing the entrapment efficiency of emulsome. A very high cholesterol content was found to have a negative impact on drug entrapment in the vesicles[6].cholesterol has an influence on vesicle stability. The amount of cholesterol in the blood influences drug trapping in vesicles. When cholesterol levels were very high, drug trapping in the vesicle was shown to be decreased. This may be because too much cholesterol disrupts the bilayer structure, making it easier for the drug to leak out [4].

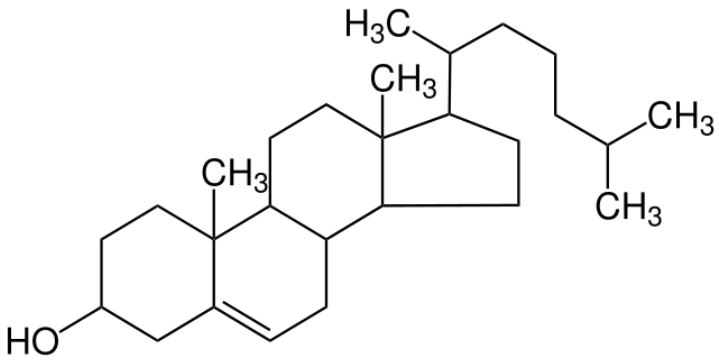

Fig 4. Chemical Structure of Cholesterol

Surfactant

To choose a surfactant, the hydrophilic lipophilic balance (HLB) value should be employed. HLB levels between 4 and 8 were found to be compatible with vesicle generation since HLB is stronger indicator of a surfactant's potential to create vesicles. The spans with the highest phase transition temperature have the most entrapment for the drug, and vice versa. Drug leakage from the vesicles is low because they have a high phase transition temperature and low permeability. Span 40 and 60, which have high HLB values, help form larger vesicles with more surface area, making them more stable by lowering surface energy. Phosphatidylcholine also plays a key role in

forming and stabilizing these vesicles [4]. A layer of surface-active phospholipids forms around the lipid core, with the polar head groups facing outward. This creates a bilayer that can hold water-based drugs. Emulsome can carry both water- and fat-soluble drugs because of their multiple bilayer structure. The ability to trap drugs also depends on the surfactants' phase transition temperature the lower the temperature, the better the drug is trapped, and vice versa [6].

Preparation method

Various methods for preparing emulsome:[4,6][7]

1) High-Pressure Homogenization

Preparation of lipid and mixture:

The lipid (often a solid lipid) and the drug are dissolved in an organic solvent or melted together if they are solid at room temperature. This lipid-drug mixture is then dispersed in an aqueous phase containing a surfactant or emulsifier.

Homogenization:

The mixture is subjected to high pressure (typically in the range of 500 to 1500 bar) in a high-pressure homogenizer. The high pressure forces the mixture through a narrow gap in the homogenizer, creating a high shear environment. This process results in the formation of fine emulsome particles due to the breakdown of larger droplets.

Cooling and Solidification:

As the emulsion exits the homogenizer, it is rapidly cooled. The lipid solidifies, forming stable emulsome encapsulating the drug.

Multiple Passes:

To achieve a uniform and small particle size, the mixture may be passed through the homogenizer multiple times. Each pass through the homogenizer further reduces the size and polydispersity of the emulsome.

Recovery and Purification:

The emulsome suspension is collected and may be subjected to purification processes to remove unencapsulated drug or residual

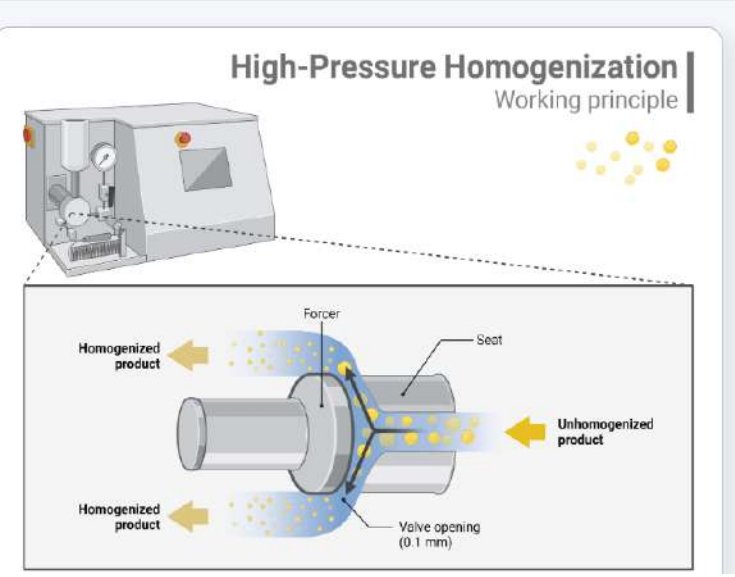

Fig 5. High Pressure Homogenization

2) Solvent evaporation method:

Preparation of lipid and drug solution

Dissolve the lipid and drug in a volatile organic solvent

Emulsification

Emulsify the organic phase into an aqueous phase containing an emulsifier under stirring to form an oil-in-water emulsion

Solvent evaporation

The emulsion is then subjected to evaporation to remove organic solvent, by usually heating or using a rotatory evaporator

Solidification and formation of emulsome

As solvent evaporates, the lipid solidifies, forming stable emulsome with the drug encapsulated.

Purification

The resultant emulsome suspension purified to remove any unencapsulated drug or residual solvent.

Fig 6: Solvent Evaporation Method

3) Ultra sonication:

Preparation of lipid and drug mixture

Dissolve the lipid and drug in an appropriate solvent

Emulsification

The lipid phase is mixed with the aqueous phase , this can be done by magnetic stirring or high shear mixing at 50-70˚c to ensure uniform dispersion

Ultra sonication

The coarse emulsion is subjected to ultrasonic waves using either, Probe sonication: high frequency probe directly placed into the emulsion Bath sonication: a water bath with ultrasonic energy to break large lipid droplet

Cooling and solidification

Cooling solidifies the lipid core forming stable emulsome.

Purification

For purification of emulsome centrifugation method is used

4) Micro fluidization:

Micro fluidization involves passing a coarse emulsion through a micro fluidizer, which forces the sample through small channels at very high pressures (typically 5000–30,000 psi), producing nano sized particles due to shear, cavitation, and impact forces. This is ideal for forming uniform, stable emulsome.

Pre-emulsion Preparation

Dissolve lipids and drug in a suitable organic solvent. Remove the solvent under reduced pressure (via rotary evaporation) to form a thin lipid film. Hydrate the film with the aqueous phase to obtain a coarse emulsion or multilamellar vesicles (MLVs)

Micro fluidization

Pass the coarse emulsion through a micro fluidizer. Use multiple cycles (3–10 passes) at high pressure (e.g., 10,000–20,000 psi). Maintain temperature (lipid phase transition temp) using a cooling system.

Collection & Characterization

Collect the emulsome. Characterize for: Particle size, PDI, Zeta potential, Entrapment efficiency, Morphology (TEM/SEM), Stability

5) Double Emulsion Method:

Double emulsions, particularly water-in-oil-in-water (W/O/W) types, are used to encapsulate hydrophilic compounds within a lipid-based system. This method creates a system where an internal aqueous phase is enclosed in oil droplets, which are further dispersed in an external aqueous phase. This is particularly useful for: Hydrophilic drug delivery, Controlled release formulations, improving stability of sensitive compounds

Primary Emulsion (W/O)

Dissolve the hydrophilic drug in water (internal aqueous phase). Prepare the lipid phase by dissolving phospholipids and cholesterol in organic solvent or melted oil. Emulsify the aqueous phase into the oil phase using probe sonication **or** high-speed homogenizer to get the W/O emulsion.

Secondary Emulsion (W/O/W)

Disperse the primary W/O emulsion into a larger volume of external aqueous phase containing a hydrophilic surfactant (e.g., Tween 80). Emulsify again using homogenization or sonication to form a W/O/W multiple emulsion.

Solvent Removal or Hardening

Evaporate the organic solvent under reduced pressure (rotary evaporator or stirring) to allow lipid vesicles to form around internal droplets. This results in formation of emulsome-like structures with an inner aqueous core and lipid bilayer.

6) Solvent Injection Method:

In this method, the lipids and drug are dissolved in a water-miscible organic solvent (like ethanol or acetone), and this solution is injected slowly into an aqueous phase under constant stirring. The lipids spontaneously form emulsome due to self-assembly upon contact with water.

Prepare Organic Phase

Dissolve lipids and drug in a minimum amount of ethanol (or other water-miscible solvent). Heat gently (~45–60°C) if necessary to ensure full dissolution.

Injection

Inject the organic phase slowly (drop wise or through a syringe) into the pre-warmed aqueous phase (same temperature) under constant stirring (magnetic or overhead). Stirring should be vigorous (800–1500 rpm) to ensure fine dispersion.

Formation of Emulsome

On contact, the lipids self-assemble into emulsome due to the polarity difference. Continue stirring for 30–60 minutes to evaporate residual solvent.

Size Reduction

If smaller or more uniform emulsome are needed, apply probe sonication or pass through a micro fluidizer**.**

Applications of Emulsome

Oral Drug Delivery

Emulsome have shown great promise in the field of oral drug delivery, particularly for the delivery of hydrophobic drugs. The lipid-based structure of emulsome can improve the solubility and bioavailability of poorly soluble drugs, while the emulsion core can provide protection against enzymatic degradation and hydrolysis. Emulsome have been explored for the oral delivery of a wide range of drugs, including antifungal agents, antibiotics, and anticancer drugs.

Parenteral Drug Delivery

In addition to oral administration, emulsome have also been investigated for parenteral drug delivery. The ability of emulsome to solubilize large amounts of hydrophobic drugs and protect them from enzymatic degradation makes them an attractive option for intravascular administration. Emulsome have been explored for the delivery of drugs such as anticancer agents, antimicrobials, and anti-inflammatory drugs through the parenteral route.

Topical and Transdermal Drug Delivery

Emulsome have also demonstrated their potential in topical and transdermal drug delivery. Their unique structure and composition allow for the encapsulation of both hydrophilic and lipophilic drugs, making them suitable for the delivery of a wide range of therapeutic agents through the skin. emulsome have been investigated for the topical and transdermal delivery of drugs such as antifungals, anti-inflammatory agents, and skin-lightening compounds.(4)

Gene and protein delivery

Emulsome can deliver genetic materials (DNA, RNA) or proteins for gene therapy or vaccination purposes.

They protect sensitive biomolecules from degradation and enhance cellular uptake.

Vaccination and immunotherapy

Acts as adjuvants in vaccines to boost immune responses. Enables the delivery of antigens to specific immune cells for effective immunotherapy.

Cosmetics and dermatology

Skin care products: used for delivering active ingredients like vitamins and antioxidants to the skin. Anti-aging: enhance the stability and penetration of bioactive compounds in anti-aging

formulations. Sun protection: improves the delivery of UV filters in sunscreens.

Nutraceuticals

Emulsome are used for delivering dietary supplements and functional foods, especially hydrophobic nutrients like vitamins (A, D, E, and K) and omega-3 fatty acids.

Diagnostic applications

Imaging agents: used to encapsulate contrast agents for imaging techniques like MRI and CT scans. Biomarker delivery: aid in the targeted delivery of biomarkers for diagnostic purposes.

Antioxidant delivery

Protects and delivers antioxidants like curcumin or resveratrol to prevent oxidative stress and associated diseases.[8]

Therapeutic application

Inflammatory diseases: Encapsulation of anti-inflammatory drugs for better targeting and reduced side effects.[4]

Ophthalmic delivery

Conjunctivitis and bacterial keratitis, both external infections of the eye. By combining it into a novel Emulsome in situ gelling technology, which increases patient compliance, it may solve the problems of existing ophthalmic formulations, such as short residence time, drug drainage, and frequent instillation.[4]

Future aspects

The future of emulsome is highly promising, driven by advancements in nanotechnology, biomedicine, and material sciences. They are expected to play a pivotal role in personalized medicine, delivering drugs tailored to individual needs and enabling targeted and controlled release of therapeutic agents, including poorly water-soluble drugs. Innovations may lead to multifunctional emulsome capable of co-delivering drugs and diagnostic agents, paving the way for theranostics and real-time treatment monitoring. In gene delivery of mRNA, siRNA, or CRISPR/ cas9 system, while in vaccine development, they could improve the stability and efficacy of DNA or mRNA vaccines. With enhanced biocompatibility and scalability, emulsome are likely to find application in neurological disorders, regenerative medicine, and stem cell therapy. Beyond medicine, their potential extends to sustainable agriculture, eco-friendly formulations, and advanced skincare products. Integration with AI, 3D printing, and nanorobotics may further revolutionize their design and applications, making emulsome a cornerstone of innovation across multiple industries.

CONCLUSION

Emulsome represent a promising and versatile drug delivery system heir unique structure, combining the attributes of both emulsions and liposomes, allows for the encapsulation and delivery of a wide range of therapeutic agents. emulsome have demonstrated promising results in enhancing the solubility, stability, and targeted delivery of drugs, leading to improved therapeutic outcomes[5,9]. As research in this field continues to advance, it is expected that emulsome will play an increasingly important role in the development of novel and effective treatments for a variety of diseases[9–13]. Micro emulsions have demonstrated utility across diverse sectors, including pharmaceuticals, cosmetics, electronics, and the petroleum industry. They help deliver drugs, serve

as reaction media, and extract substances, all thanks to their special ability to mix oil and water. The versatility and applicability of emulsome highlight their potential to address unmet needs in drug delivery and contribute to the advancement of personalized medicine[2,4,6,8]. Further research and development efforts focused on optimizing emulsome formulations, enhancing their targeting capabilities, and evaluating their clinical efficacy will pave the way for the successful translation of this technology into clinical practice [4,8,10,14,15].

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