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Review Article

Glycerosomes: Novel Vesicles Revolutionizing Topical Drug Delivery.

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ABSTRACT

Topical drug delivery is a preferred approach for treating common skin infections because it targets the site directly and minimizes systemic side effects. However, the skin's outer layer, called the stratum corneum, often blocks drugs from reaching deeper where they're needed. Glycerosomes overcome this by blending phospholipids, cholesterol, water, and high levels of glycerol, which acts as a safe penetration enhancer and edge activator. This makes the vesicles more fluid, stable, and able to carry both water-loving and fat-loving drugs deeper into the skin, improving entrapment (often >80%), release, and efficacy compared to creams or basic liposomes. Studies show they boost permeation flux, reduce minimum inhibitory concentrations, and enhance zones of inhibition, making them ideal for conditions like otomycosis or cutaneous candidiasis, while offering improved safety profiles with reduced systemic toxicity.

INTRODUCTION

Topical drug delivery system:

Topical drug delivery is one of the most convenient route of drug administration. Topical drug administration is a localized drug delivery system anywhere in the body through ophthalmic, rectal, vaginal and skin as topical routes. Topical medication delivery methods allow to minimize the entry of medicine to the systemic circulation. New drugs are being developed utilizing the transdermal approach in addition to the existing formulations due to the inherent benefits of delivery via this route. Although low skin permeability limits its applicability, it does provide a non-invasive route of medication administration[1]. Topical drugs are formulated by vehicle, or base which can be optimized for a particular site of the body or type of skin condition[2]. Topical drug delivery includes the better bioavailability, maintenance of plasma levels, longer duration of action so the dosing frequency can be reduced, reduction of side effects and enhanced and more consistent therapy by sustaining plasma levels through the entire dosing interval, unlike conventional oral dosage forms[3]. The main advantage of topical administration is

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that it bypasses first-pass metabolism, avoids gastrointestinal incompatibilities, and improves patient compliance. Another benefit is that topical formulation avoids the risks and drawbacks of intravenous therapy. Topical application may or may not require intracutaneous injection[4].

The main limitations of the topical delivery are predominantly associated with the skin's barrier function. The skin is a multi-laminate tissue; the outermost layer comprises the major barrier to drug permeation. A unique hierarchical structure of lipid-rich matrix with embedded corneocytes in the upper strata (15 μm) of skin, the stratum corneum (SC), is responsible for this barrier and severely constrains the absolute amount of a drug that is absorbed across a reasonable area of the skin during a dosing period.

The minimum requirements for a drug to penetrate the skin are as follows:

a. High potency (dose < 10 mg/day),

b. Small molar mass (molar mass < 500 g/mol),

c. Partition coefficient (moderate 1–5), and

d. Melting point (<250 °C).

Drugs administrated trough topical route is mainly for local actions like anti-septic, anti-inflammatory, anti-fungal, also as skin emollients for protection[5].

Innovative research using penetration-enhancing technologies such as iontophoresis (electric current-driven delivery), electroporation (temporary membrane pores via pulses), microneedles (painless skin disruption for deeper access), sonophoresis (ultrasound waves to loosen tight junctions), and chemical permeation enhancers like alcohols or terpenes. These technologies promise broader clinical adoption of consumer-friendly transdermal dosage forms, from smart patches with biosensors to personalized microneedle arrays[6].

As such Novel Drug Delivery Systems (NDDS) have transformed dermatological therapy by overcoming the limitations of traditional creams and ointments through sophisticated internal and external architectures[7,8.] And by utilizing phospholipids, the amphiphilic molecules that organize into supra-structures, these systems can be tailored in specific size, shape, and surface charge to meet specific clinical needs. Beyond foundational carriers like liposomes[9,10], transferosomes, and niosomes[11,12], the field has expanded to include high-stability options such as solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs) and nanoemulsions. Specialized vesicles like ethosomes (high ethanol content for deep penetration), liposomes, nanoparticles, invasomes (containing terpenes), and glycerosomes (utilizing glycerol to enhance stability and skin permeation) offer targeted action, while advanced platforms like dendrimers, emulsomes, bilosomes, and carbon nanotubes further broaden the scope of non-covalent drug entrapment for localized or systemic effects[13]. These are novel vesicular drug delivery systems and these have emerged to achieve targeted and controlled drug delivery.

Glycerosomes-

A new vesicular system with improved entrapment and penetration designed using lipids and glycerol, are glycerosomes. Glycerosomes are mainly used in topical preparation. Glycerosomes represent an innovative class of bilayer vesicles pioneered by Manca et al. specifically for enhanced dermal and transdermal delivery of diclofenac to the skin[14]. Unlike conventional liposomes, glycerosomes incorporate phospholipids combined with high concentrations of glycerol (typically 10-30% v/v),

which imparts greater bilayer fluidity and distinguishes them fundamentally in structure and performance. Glycerosomes demonstrate superior stability and elevated fluidity compared to traditional liposomes, making them particularly suitable for topical drug delivery applications[15].

The inclusion of glycerol plays a pivotal role by improving the deformability index of the liposomal bilayers, which in turn facilitates deeper skin penetration. Composed of phospholipids, water, and elevated levels of glycerol, these novel vesicular structures benefit from glycerol's inherently harmless, non-toxic, and non-irritating properties, ensuring safety for topical use. Glycerol enhances both the fluidity and overall stability of the vesicles, allowing glycerosomes to penetrate the skin surface more effectively than standard liposomes[14].

Depending on the excipients and preparation technique, glycerosomes can yield unilamellar vesicles or multilamellar vesicles (MLVs). These nanostructures are surging in global interest due to their straightforward preparation, benign composition, and advantageous properties such as improved stability, fluidity, and penetration over conventional vesicular systems[16].

Glycerosomes serve as versatile delivery systems capable of encapsulating both hydrophilic and hydrophobic therapeutic agents. In these formulations, poorly water-soluble (hydrophobic) drugs are typically embedded within the lipid bilayers composed of phospholipids and cholesterol, while hydrophilic compounds are sequestered within the aqueous core of the vesicles. Although thin-film hydration is a standard technique for loading water-soluble drugs, it often presents a trade-off, potentially reducing the overall encapsulation efficiency despite facilitating the initial entrapment. Ultimately, these vesicular networks are designed to protect the chemical entity from degradation, ensuring targeted delivery to the intended site of action[17].

Structure of glycerosomes

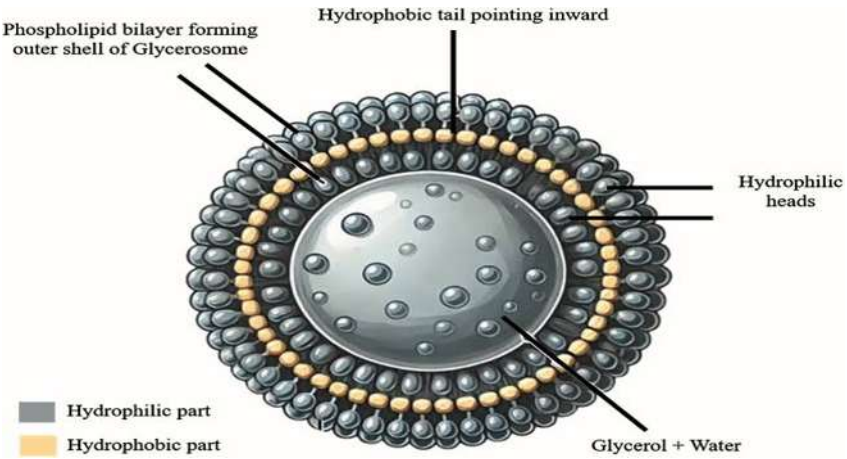

Fig no:1 structure of glycerosome[2]

Composition of glycerosomes:

Glycerosomes are new vesicular systems composed of phospholipids, glycerol, water and cholesterol. Glycerosomes are analogous to conventional lipid-based vesicular system[18]. These contains the concentration of about 10,20,30,40, and 50% of water and glycerol. It is completely harmless and non-toxic method of drug delivery[2].

a. Glycerol

b. phospholipids

c. cholesterol

a. Glycerol - Glycerol is a viscous liquid and an alcohol. It consists of three hydroxyl group which renders hydrophilic properties. It is used in pharmaceutical preparations as a lubricant, humectants, edge activator and emulsifier. And in glycerosomes it mainly acts as penetration enhancer[19].

b. Phospholipids- Phospholipids are a class of amphipathic lipids that act as the primary structural component of cell membranes, forming a stable phospholipid bilayer. They consist of a hydrophilic phosphate head, a glycerol backbone, and two hydrophobic fatty acid tails. This structure allows them to regulate cellular transport and maintain membrane integrity[20].

Glycerophospholipids and sphingomyelins are widely used in the glycerosomes preparation. These phospholipids are capable of including pharmaceutical ingredients in them and these are harmless. Phospholipids give rise to vesicles that are compatible with other excipients of the formulation.

c. Cholesterol- It is a vital lipid in animal cell membrane and synthetic vesicular systems like glycerosomes which acts as permeability barrier, structural regulator, retention efficiency and preventing the vesicle from collapsing.

Mechanism of action of Glycerosomes: In dermal and transdermal drug delivery, glycerosomes significantly enhance drug penetration through the skin. Glycerol, a key component, acts as a humectant, increasing the hydration of the stratum corneum. This hydration softens the skin and reduces its barrier function, facilitating drug penetration[21]. Additionally, the incorporation of glycerol into the lipid bilayer of glycerosomes increases membrane fluidity. This fluidization promotes the fusion of glycerosomes with the lipid matrix of the stratum corneum, allowing deeper drug penetration. Furthermore, glycerosomes can fuse with the lipid layers of the skin, releasing the drug directly into the deeper layers of the epidermis and dermis[22]. And these combination of phospholipids, glycerol, and cholesterol enhances permeability, solubility, entrapment efficiency and controlled release[23].

Advantages of glycerosomes:

- **Enhanced Drug Solubility:** By incorporating glycerol as a co-solvent, glycerosomes significantly increase the solubility of weakly water-soluble drugs.
- **Controlled Drug Release:** These vesicles facilitate a sustained and prolonged release of their cargo, which enhances therapeutic efficacy and reduces the required frequency of administration[25].
- **Potential for Targeted Delivery:** Like other vesicular systems, glycerosomes can be engineered with surface ligands or modifications to enable site-specific drug delivery[26].
- **Enhanced Skin Penetration:** Glycerol acts as a humectant, increasing skin moisture and softening the stratum corneum. This allows glycerosomes to deliver bioactive compounds more effectively into and through the skin.
- **Improved Skin Permeability:** The hydration of the stratum corneum provided by glycerol enhances drug permeation, making these systems highly efficacious for topical and transdermal administration.

- **Thermal and Osmotic Protection:** Glycerosomes exhibit superior resistance to temperature fluctuations and osmotic stress relative to traditional liposomes, ensuring stability during storage and transport under varying conditions[27].

- **Reduced Dehydration Risk:** The presence of glycerol inhibits the dehydration of the vesicles, preserving their structural integrity and effectiveness over long durations, even in adverse environments.

- **Biocompatibility:** Glycerol is a naturally occurring, non-toxic, and biocompatible substance. Consequently, glycerosomes are safe for medical and cosmetic use and are well-tolerated by tissues, minimizing the risk of irritation.

- **Versatility:** These systems can encapsulate both hydrophilic and hydrophobic drugs, offering high flexibility. They are suitable for various delivery routes, including:

  - **Topical:** For localized treatments and hydration.

  - **Transdermal:** For systemic delivery via the skin.

  - **Ocular:** For treating eye-related conditions.

  - **Oral:** For improving absorption in the gastrointestinal tract[27].

- **Improved Patient Compliance:** By enhancing stability, enabling controlled release, and increasing permeability, glycerosomes simplify drug administration, particularly in chronic pain management and transdermal systems.

- **Stability Improvement:** The addition of glycerol reinforces the lipid bilayer structure, which enhances the overall physical and chemical stability of the delivery system.

- **Enhanced Drug Loading Capacity:** Glycerol reduces the rigidity of the bilayer membrane, which can significantly improve the encapsulation efficiency and loading capacity for specific drugs[27].

Disadvantages of glycerosomes:

- High glycerol concentrations can enlarge vesicles and slow down drug release rates.

- While high viscosity enhances vesicle stability, it may simultaneously impede the migration speed of the vesicles to the skin surface[21]

Methods of preparation of Glycerosomes-

The various methods of preparations are used according to the vesicle lamellarity. The most commonly used method is thin film hydration method.

I. Mechanical methods

- Lipid thin film hydration
- Ultrasonic method

II. Organic solvent replacement methods

- Reverse phase evaporation
- solvent dispersion

III. Size transformation method

- Freeze thaw extrusion method
- the dehydration-rehydration method

All these methods follow basic four stages: Drying, hydrating, purifying and analysing[29].

I. Mechanical methods

a) **Lipid thin film hydration:** The formulation of glycerosomes is a streamlined process that begins with dissolving phospholipids in an organic solvent to create a thin lipid film upon evaporation. This film is then hydrated using an aqueous phase consisting of a water and glycerol solution, followed by high-intensity ultrasonication to achieve a stable dispersion. This specific approach is preferred for its ability to produce vesicles with superior physical attributes namely a uniform spherical shape and smooth texture while yielding higher encapsulation efficiency than other techniques[30]. To ensure optimal drug loading, hydrophilic medications are incorporated via the aqueous hydration buffer, whereas lipophilic drugs are integrated directly into the initial lipid film[30].

b) **Ultrasonic Methods:** The ultrasonic method is primarily utilized to produce small unilamellar vesicles, typically ranging from 15 to 25 nm in diameter. This process involves the ultrasonication of a glycerol-lipid dispersion through one of two distinct techniques:

i. **Probe Sonication:** In this high-energy approach, the sonicator tip is immersed directly into the dispersion, delivering intense energy to facilitate lipid breakdown. Because this process generates significant localized heat at the tip, the formulation must be kept in an ice/water bath to prevent thermal degradation. A notable drawback of this method is the potential for titanium particles to shed from the probe, contaminating the solution and necessitating a subsequent centrifugation step for purification[31].

ii. **Bath Sonication:** This method involves placing the container holding the glycerosomal dispersion into a sonication bath. The process is typically conducted for five to ten minutes at temperatures exceeding the lipid's critical solution temperature (T_c). Unlike the probe method, bath sonication allows for easier temperature regulation and avoids the risk of metal contamination[31].

II. Organic solvent replacement method:

This method lipid materials are co-solvated in organic solution which is then dispersed in glycerol solution containing drug that to be entrapped within the vesicles

i. **Reverse phase evaporation:** In the reverse-phase evaporation method, lipid materials are first co-solvated in an organic solution before being dispersed into a glycerol phase containing the substances targeted for entrapment. This process begins with the formation of a water-in-oil emulsion, created by sonicating a two-phase system of phospholipids and cholesterol in organic solvents such as ethanol, isopropyl ether, or a chloroform-ether mixture alongside an aqueous glycerol solution. As the organic solvent is removed under reduced pressure of 200rpm and 20-25^{0}C, the mixture transforms into a viscous gel; subsequent rotary evaporation then eliminates any residual solvent to yield the final glycerosomes. A primary advantage of this technique is its ability to produce both large unilamellar and multilamellar vesicles, which are particularly effective for encapsulating large macromolecules. However, the method is limited by the potential for material

degradation, as the entrapped substances are subjected to both organic solvent exposure and mechanical stress during sonication[32].

ii. **Solvent dispersion method:** It is divided into two categories on the type of solvent used

a) **Ether injection method:** The ether injection method involves the gradual introduction of a lipid solution dissolved in diethyl ether or an ether-methanol blend into an aqueous or buffered glycerol phase containing the substances to be encapsulated. This procedure is typically executed at temperatures between 55°C and 65°C or under reduced pressure to facilitate solvent evaporation. While functional, the technique often yields a non-uniform glycerosome population, with vesicle sizes ranging widely from 70 to 190 nm. Furthermore, a significant limitation of this approach is the potential degradation of sensitive compounds due to their direct exposure to both organic solvents and elevated processing temperatures[27].

b) **Ethanol injection method:** The ethanol injection method involves dissolving lipids in ethanol and rapidly forcing the solution through a small aperture, such as a syringe needle, into an excess of aqueous medium. Immediate and thorough mixing is critical to ensure that phospholipids disperse effectively as the ethanol is diluted into the hydration phase. A primary advantage of this technique is its ability to generate small, uniform liposomes typically under 100 nm without the need for secondary processes like sonication or extrusion. However, the method is constrained by the solubility of lipids in ethanol, which limits the total lipid concentration that can be incorporated. Additionally, while residual ethanol can be removed via dialysis, its presence during the initial formation remains a potential limitation for sensitive formulations[30].

III. **Size transformation method:**

The following techniques utilize thermal and hydration cycles to manipulate vesicle size and structure:

i. **Freeze-Thaw Extrusion Method:** This technique relies on rapid cycles of freezing and thawing to transform small unilamellar vesicles (SUVs) into large unilamellar vesicles (LUVs). Primarily applicable to crude or charged phospholipids, the process causes the SUV bilayers to fuse during the thermal cycles, followed by sonication to stabilize the resulting LUVs. However, the efficiency of this method decreases with higher ionic strength or liposome concentrations. A notable limitation is its incompatibility with certain sensitive biological components, as the prolonged, temperature-sensitive nature of the process can lead to the loss or degradation of these materials[28].

ii. **Dehydration-Rehydration Method:** In this approach, pre-formed empty SUVs are mixed with an aqueous solution containing the target material and then dried. This drying process creates a finely subdivided lipid dispersion. Upon rehydration with the aqueous phase, the lipids reform into vesicles, typically yielding oligo-lamellar glycerosomes. This method is particularly useful for achieving a high degree of dispersion in the final formulation[32].

IV. **Double emulsion evaporation:** In this method $W_1/O/W_2$ is prepared it consists of inner and outer aqueous phase. Outer phase consists of dispersed individual oil globules

and inner aqueous phase as small droplets in each oil globules of outer aqueous phase. This process is of double emulsion in which aqueous phase consisting of drug is dissolved in water and added to organic solvent contains lipids, this forms water in oil emulsion which is then homogenised to form primary emulsion and then combined with outer aqueous phase containing stabilizer gets converted into double emulsion.

V. **Calcium-induced fusion method**: In this method LUV's (larger unilamellar vesicles) are formed in addition calcium to SUV's (smaller unilamellar vesicles) and results in fusion, then give rise to large planar lamellae which transforms to cochleate cylinders. Then mixed with EDTA which re-establishes the negative charge and maintains the fluidity of the membrane and these further transforms to generate LUV's[27].

Characterization of glycerosomes:

The characterization of glycerosomes involves several critical analytical parameters to ensure their efficacy and stability as delivery vehicles. The following points detail the methodologies used for their evaluation:

a) Vesicle Size and Size Distribution

For parenteral administration, the particle size and distribution of glycerosomes are vital factors. Various techniques are employed for this assessment, including light microscopy, laser light scattering, photon correlation spectroscopy, gel permeation, and gel exclusion. However, transmission electron microscopy (TEM) is considered the most definitive method, as it facilitates the direct observation of individual vesicles to provide precise data on size distribution[34].

b) Vesicle Shape and Lamellarity

The morphology and internal structure (lamellarity) of the vesicles are typically evaluated via advanced electron microscopy. Specifically, freeze-fracture electron microscopy and 31P nuclear magnetic resonance (NMR) studies are used to assess lamellarity, while freeze-etch techniques allow for the detailed analysis of surface morphology and overall shape[35].

c) Percentage Encapsulation Efficiency

The quantity of drug successfully sequestered within the vesicles is often measured using the dialysis method.

The dialysis method purifies glycerosomes by removing unentrapped drug, excess glycerol, and free lipids using a cellulose-based semi-permeable membrane (MWCO ~12–14 kDa). After soaking the membrane, the crude glycerosomal dispersion is sealed in the dialysis bag and immersed in a large volume of release medium (e.g., buffer with 1% Tween 20) at 37 ± 0.5°C with stirring. Small molecules diffuse out through the membrane while glycerosome vesicles (with 20–40% glycerol) are retained, and the dialysate is refreshed periodically over 2–24 hours until free drug is negligible. The cleaned vesicles are used for further characterization and *in vitro* release studies, and encapsulation efficiency (%EE) is calculated from the drug obtained after dialysis relative to the initial drug content[25,30].

%EE= (Total drug added – Free drug in dialysate/Total drug added) ×100

d) Drug Release Profile

The release kinetics of the encapsulated drug can be investigated using a calibrated Franz diffusion cell. These *in vitro* tests are essential for understanding the absorption characteristics and

functional performance of the glycerosomal formulation prior to conducting *in vivo* (animal or human) studies.

The Franz diffusion method evaluates in vitro release and permeation of glycerosomes by applying the suspension to a membrane (e.g., cellophane or synthetic skin) placed between donor and receptor compartments. The receptor, filled with phosphate buffer (pH 6.8–7.4) to maintain sink conditions, is kept at 37 ± 0.5°C with magnetic stirring. Samples are withdrawn at set intervals, replaced with fresh buffer, and analyzed by UV or HPLC to quantify drug release and build cumulative release profiles[38,39]. Glycerosomes typically show biphasic or sustained release with high entrapment efficiency and enhanced permeability versus conventional liposomes, indicating controlled kinetics favorable for deeper topical absorption[40].

e) Stability Studies

To determine the stability of glycerosomes over time, various dimensional analysis at regular intervals are performed. This involves measuring the Zeta potential, Dynamic Laser Light Scattering, and the polydispersity index (PDI) via Photon Correlation Spectroscopy to ensure the physical and chemical integrity of the system[35].

f) Deformation Index Analysis

The flexibility or "deformability" of the vesicles is assessed by calculating the deformation index. This is determined by forcing the glycerosomal preparation through an extruder with a pore size significantly smaller than the vesicles' mean diameter, measuring their ability to adapt and pass through confined spaces without losing integrity[32].

$$DI= J\times(d_0/p)\times(d_0/d_0-d_1)$$

where,

DI= Deformability index of glycerosome vesicle

J= The fraction of vesicle suspension recovered after extrusion

d_0= The mean hydrodynamic diameter of the vesicles before extrusion.

d_1= The mean hydrodynamic diameter of the vesicles after extrusion.

p= The nominal pore diameter of the polycarbonate membrane filter used[30].

Therapeutic Applications of glycerosomes:

- Recent research highlights the significant potential of glycerosomes in both cosmetic and dermatological applications due to their superior performance. Studies focusing on triptolide-loaded vesicles have demonstrated that glycerosomes, optimized through precise experimental designs, offer enhanced stability, biocompatibility, and transdermal permeability, making them ideal for deep dermal delivery. Furthermore, investigations into treating conditions like rosacea have compared various specialized systems including hexosomes, glycerosomes, and ethosomes utilizing ingredients such as soy phospholipids, tretinoin, and glycerol. While all these systems show promise, glycerosomes were particularly noted for their ability to boost skin penetration, suggesting that these advanced vesicular formulations could significantly improve the effectiveness of topical treatments for inflammatory skin disorders[37].

- **Aerosolized glycerosomal transport:** Glycerosomes are emerging as highly effective vehicles for pulmonary drug delivery, offering advantages like sustained release, improved stability, and reduced irritation compared to

standard aerosols. Research into the delivery of rifampicin and curcumin shows that these vesicles, particularly when reinforced with polymers like sodium hyaluronate or trimethyl chitosan, significantly increase drug accumulation in the lungs while avoiding hepatic first-pass metabolism. These polymer glycerosomes form a unique hydrophilic mesh that stabilizes the unilamellar vesicles (typically 65–112 nm), enhancing their biocompatibility and ability to be efficiently aerosolized for deep lung penetration. By boosting the anti-inflammatory and antioxidant effects of the encapsulated drugs and ensuring high deposition rates, these advanced formulations represent a promising strategy for treating respiratory illnesses and improving patient adherence[33].

- **Peroral delivery:** These advanced delivery systems are specifically designed to treat diseases of the oral cavity by ensuring the effective dispersion and sustained release of therapeutic agents into the oral mucosa**.** Glycerosomes and penetration-enhancing vesicles significantly boost the biological performance of Citrus Lemon Extract, supporting keratinocyte viability in the oral epithelium when facing oxidative stress. Furthermore, these formulations provide robust antibacterial activity and potent antioxidant protection, making them highly effective tools for managing oral infections and promoting tissue repair within the mouth[31].

- **Targeted Relief for Rheumatoid Arthritis:** Managing rheumatoid arthritis effectively is often a struggle because traditional treatments like corticosteroids and NSAIDs fail to reach the synovial cavity in high enough concentrations. Glycerosomes solve this by acting as specialized carriers that can penetrate deep into the joint space. For example, when the immune-regulating drug papeiflorin is encapsulated in these vesicles, it accumulates much more effectively within the synovial cavity, overcoming its usual limitations and improving clinical outcomes[41].

- **Reliable Sustained Drug Release:** One of the standout benefits of using glycerosomes is their ability to maintain steady drug levels in the body over a set period. By providing a continuous release of medication, they minimize the effect of drug peaks and valleys, which also reduces the risk of side effects. This approach has been successfully used for medications like betamethasone and rifampicin, ensuring optimal therapeutic rates and better long-term stability *in vivo*[33].

- **Precision Delivery to Hair Follicles:** For skin and scalp conditions such as hair loss, getting the medication exactly where it's needed like the sebaceous glands or hair follicles is crucial. Advanced glycerosomal formulations make it possible for substances that are normally hard to absorb, such as minoxidil, to be applied topically for localized action. This intrafollicular delivery ensures the treatment stays focused on the target area, boosting the effectiveness of hair restoration therapies[16].

- **Boosting Anti-Inflammatory Power:** While anti-inflammatory drugs are essential for many treatments, they often come with a laundry list of side effects. Encapsulating ingredients like diclofenac, celecoxib, or cupferron in glycerosomes significantly increases their therapeutic efficacy while maintaining high biocompatibility with human cells. This means the medicine works better where it's needed most without causing excessive irritation or damage to healthy keratinocytes[42].

- **Stronger and Safer Antimicrobial Action:** Glycerosomes improve antimicrobial therapy in two vital ways: they act as a protective shield against enzymatic breakdown and their lipid-based structure helps the medication slip into microbial cells more easily. By loading agents like resveratrol, gallic acid, and citrus lemon extract into these vesicles, researchers have seen a major boost in antibacterial performance against species like Streptococcus and Lactobacillus, all while lowering overall toxicity for the patient[32].

- **Advancing Ocular Care:** While primarily known for skin applications, glycerosomes are now making waves in eye care. Recent developments include eye drops formulated with the antifungal drug natamycin. These glycerosomal drops enhance the drug's entrapment and significantly improve its ability to penetrate ocular tissues, providing a more effective way to treat stubborn eye infections compared to traditional methods[33].

- **Neurological disorders:** Glycerosomes helps in delivery of drug to specific site of the brain by crossing blood-brain barrier, so makes possible to treat Alzheimer's, Parkinson's, and brain cancer. these are administered as neuroprotector drug or small interfering (RNA)[31].

Example of Marketed Glycerosome:

Glycerosomal Technology is currently most prominent in the marketed dermo cosmetic sector rather than as a primary platform for mass-marketed prescription drugs.

The primary commercial application is found in the high-end skincare line Gen-Hyal, developed by the pharmaceutical company Prigen.

Marketed Products using Glycerosomes

Gen-Hyal Extreme: A high-performance serum designed with soothing and repairing active ingredients, utilizing glycerosomes to boost effectiveness by 3 to 5 times.

Gen-Hyal Urban Serum: A detoxifying and anti-aging serum that uses glycerosomes for deeper skin penetration of purifying active ingredients.

Gen-Hyal Eyes: An eye contour serum that uses the technology to deliver moisturizing and anti-aging agents more efficiently.

Gen-Hyal Plus / Premium / Elargan: Other facial care formulations within the Prigen line that leverage this patented delivery system for anti-aging results[43].

CONCLUSION:

Glycerosomes represent an advanced vesicular drug delivery system that outperforms traditional liposomes in stability, flexibility, and penetration. They incorporate high glycerol concentrations (10-50% v/v) with phospholipids, enhancing bilayer fluidity for better drug entrapment and release control. Glycerosomes provide superior entrapment efficiency (up to 92%), smaller vesicle sizes (around 190 nm), and negative zeta potentials for stability. They enable controlled biphasic drug release, extended stability (up to 3 months at 2-8°C), and spherical morphology, making them ideal for topical, transdermal, and multi-route applications. Overall, they address limitations of conventional drug delivery by improving deformability, skin permeation via stratum corneum moisturization, and protection from harsh environments like the GI tract. Emerging Trends Recent 2025 advancements focus on hybrid variants like STO-glycerosomes (with essential oils), HY-glycerosomes (sodium hyaluronate),

TMC-glycerosomes (trimethyl chitosan), glycethosomes, and glycerospanlastics for boosted stability and efficacy.

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