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Menthosomes: A Comprehensive Review

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ABSTRACT

Menthosomes represent an innovative class of nanocarriers that combine menthol with lipid based vesicles, typically phospholipids, to improve the delivery of therapeutic agents. The inclusion of menthol enhances the permeability of the skin and mucous membranes, making these carriers highly effective for transdermal and mucosal drug delivery. This review provides an in-depth examination of menthosomes, discussing their composition, preparation methods, and the mechanisms by which they enhance drug absorption and stability. Furthermore, it highlights the role of menthol in improving the bioavailability, solubility, and controlled release of encapsulated compounds. The review also explores the broad potential applications of menthosomes in pharmaceutical and cosmetic industries, while identifying current challenges and suggesting future avenues for their development and optimization in drug delivery systems.

Keywords: Menthosomes, Menthol, Controlled release, Targeted drug delivery, Nanocarriers.

INTRODUCTION

In recent years, there has been a surge in the development of advanced drug delivery systems aimed at overcoming the limitations of conventional routes of administration. One of the most significant challenges in drug delivery is the poor bioavailability of active pharmaceutical ingredients (APIs), which is often attributed to barriers such as the skin's stratum corneum or the gastrointestinal tract's enzymatic environment[1]. To address these challenges, researchers have focused on creating more efficient, targeted, and controlled release systems. Among the promising innovations in this area are menthosomes, a novel class of vesicular drug delivery systems that incorporate menthol into their structure to enhance the delivery of therapeutic agents. Menthosomes are lipid-based vesicles that derive from liposomes or ethosomes, but they stand apart due to the incorporation of menthol, a compound extracted from peppermint oil[2]. Menthol is well-known for its cooling, soothing, and permeation-enhancing properties, which make it an ideal candidate for improving drug absorption through biological membranes, especially the skin. When integrated into vesicular systems, menthol not only facilitates the enhanced penetration of drugs but also improves the overall stability, fluidity, and encapsulation efficiency of the vesicles. These

features are particularly useful for drug delivery applications that require increased bioavailability, sustained release, and efficient permeation through the skin or mucosal surfaces[3].

Composition

Menthosomes are a type of nano-carrier system designed for enhancing the delivery of therapeutic agents or active compounds, particularly in the field of drug delivery. These nanocarriers typically consist of liposomes, which are lipid-based structures, but with added functionalization to increase their effectiveness. Here's a breakdown of the composition of menthosomes in detail[4].

Phospholipids

The core structure of a menthosome is composed of phospholipids, which are the primary building blocks of the lipid bilayer. Phospholipids are amphiphilic molecules, meaning they have both hydrophilic (water-attracting) and hydrophobic (water-repellent) regions. This amphipathic nature allows phospholipids to form bilayers in aqueous environments, which is essential for the formation of liposomes or menthosomes. Commonly used phospholipids include:

- Lecithin (phosphatidylcholine)
- Phosphatidylethanolamine
- Phosphatidyl serine[5].

Menthol

The defining feature of menthosomes is the inclusion of menthol, a natural compound often derived from peppermint oil. Menthol has been found to enhance the permeability of the lipid bilayer and improve the delivery of active compounds by interacting with the skin or mucosal surfaces. The menthol molecules can be incorporated into the liposomal structure or used to modify the surface properties of the carrier. Menthol can also enhance the transdermal delivery of drugs due to its cooling and soothing properties[6].

Cholesterol

Cholesterol is often added to the formulation of menthosomes to provide additional stability to the lipid bilayer. It reduces the permeability of the liposomes and increases the rigidity of the membrane, which helps protect the encapsulated drug from degradation. Cholesterol also aids in the maintenance of liposomal fluidity, allowing for better fusion with cell membranes and facilitating the release of the encapsulated agent[7].

Surfactants

Surfactants are commonly included in menthosomes to improve the dispersion and solubility of the formulation. Non-ionic surfactants such as Polysorbate 80 (Tween 80) or Span 60 are frequently used to reduce surface tension, improve drug encapsulation efficiency, and ensure better stability of the menthosome system. These surfactants can help in forming a stable and homogeneous dispersion of the liposomal nanoparticles[8].

Water and Aqueous Phase

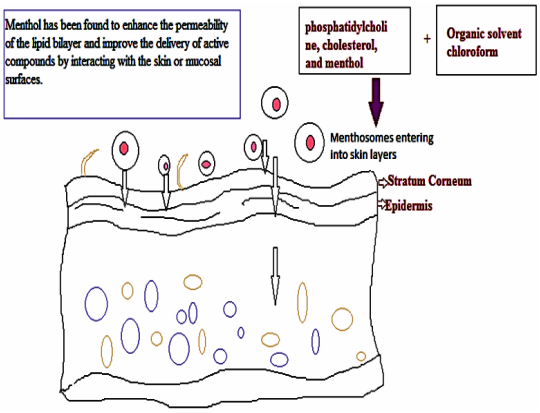
The aqueous phase inside the liposomes or menthosomes holds the hydrophilic compounds. The bilayer formed by the phospholipids encapsulates the aqueous core, and in the case of menthosomes, this system might also allow the encapsulation of menthol, which can aid in the enhanced permeability of certain drugs[9].

Structure of Menthosomes

Menthosomes are liposomal structures that contain menthol as an integral part of their lipid bilayer or as a co-solvent in the aqueous phase. The structure of menthosomes can be outlined as follows:

- **Lipid Bilayer:** The outer membrane of menthosomes consists of a lipid bilayer, which can be made from various lipid materials such as phospholipids (e.g., lecithin, cholesterol). This bilayer is similar to the structure of natural cell membranes, providing stability and flexibility to the vesicle[10].
- **Menthol Incorporation:** Menthol, a volatile compound, can be embedded within the lipid bilayer or solubilized in the aqueous core of the vesicle. The inclusion of menthol in the structure enhances the vesicle's ability to penetrate skin layers, improve the solubility of lipophilic drugs, and provide a cooling effect, which is beneficial in dermatological applications[11].

Encapsulation of Active Ingredients: Active pharmaceutical ingredients (APIs) can be encapsulated within the menthosome structure, which helps protect these sensitive compounds from degradation and enables controlled release[12].



Size and Charge: Menthosomes typically range in size from 50 nm to several micrometers. They may also carry a surface charge depending on the lipid composition used in their formulation, which influences their interaction with biological membranes[13].

Mechanism of Action of Menthosomes

The mechanism of action of menthosomes is largely related to their ability to enhance the delivery and absorption of encapsulated drugs, especially in topical applications. This mechanism can be explained through the following points:

1. **Enhanced Skin Penetration:** Menthol, when incorporated into the menthosome structure, facilitates the penetration of the vesicle through the skin barrier. Menthol acts as a skin permeation enhancer by disrupting the lipid layers in the stratum corneum, the outermost layer of the skin. This disruption increases the permeability of the skin and allows for the deeper penetration of the vesicle, carrying the encapsulated drugs[14].
2. **Cooling and Sensory Effects:** Menthol is known for its cooling effect, which provides a sensory experience when applied topically. This cooling sensation occurs due to menthol's ability to activate cold-sensitive receptors (TRPM8) in the skin. The presence of menthol in menthosomes can enhance the therapeutic effect by providing both a physical cooling effect and a psychological soothing effect for the patient[15].
3. **Controlled Release:** Menthosomes offer controlled release of their encapsulated drug payloads. The liposomal structure allows for the slow and sustained release of the active ingredient over time, reducing the frequency of administration and enhancing therapeutic efficacy. This controlled release is influenced by factors such as the lipid composition, size, and surface charge of the menthosome[16].
4. **Stabilization of Active Ingredients:** The encapsulation of drugs in menthosomes protects sensitive active ingredients from degradation due to environmental factors such as light, heat, and oxidation. This stabilization allows for a longer shelf-life and ensures the stability of the encapsulated compounds when applied to the skin or other biological surfaces[17].
5. **Targeted Delivery:** In some cases, menthosomes may be designed for targeted delivery to specific tissues or skin layers. The lipid bilayer can be modified with surface-active agents or functionalized to enhance targeting ability, ensuring that the menthosome delivers its payload to the desired site of action[18].

Formulation approaches of Menthosomes

Menthosomes are specialized vesicular carriers that are used to enhance the transdermal delivery of active ingredients. They are essentially liposomes modified with menthol, which acts as a penetration enhancer. The formulation of menthosomes involves the careful selection of ingredients and techniques to achieve effective drug delivery through the skin. Here are some key formulation approaches used to develop menthosomes[19].

Liposome-Based Formulation

- Menthosomes are typically made by modifying conventional liposomes with menthol. The process of formulating menthosomes usually involves the preparation of a phospholipid bilayer using lipids such as phosphatidylcholine, which encapsulates the active substance. Menthol is incorporated into the lipid phase or used as a co-solvent in the formulation to enhance skin permeability[19].
- **Method:** The liposome preparation can be done through methods like thin-film hydration, solvent evaporation, or reverse-phase evaporation. During this, menthol is introduced either by direct inclusion in the lipid matrix or as part of the hydration medium[20].

Hydration Method

- This is the most commonly used approach for the preparation of menthosomes. The lipid components (like phosphatidylcholine, cholesterol, and menthol) are dissolved in an organic solvent such as chloroform, followed by the evaporation of the solvent under reduced pressure. After solvent removal, the lipid film is hydrated with an aqueous phase containing the active ingredient. The hydration process results in the formation of vesicles[21].
- **Menthol Role:** Menthol can be incorporated into the lipid phase during the hydration step. It is believed to increase the fluidity of the lipid bilayer, improving the release rate and stability of the drug encapsulated in the vesicles[22].

Reverse Phase Evaporation Method

- In this method, a water-in-oil emulsion is first prepared using an aqueous solution containing the active ingredient and an organic solvent containing the lipids. This is followed by solvent evaporation, leading to the formation of a bilayer structure. The reverse-phase evaporation method is particularly useful for encapsulating hydrophilic and hydrophobic drugs within menthosomes, providing a versatile approach for a range of drug delivery applications[23].

Solvent Injection Method

- In this method, lipids are dissolved in an organic solvent and then injected into an aqueous phase under controlled conditions. The solvent rapidly evaporates, leading to the formation of menthosomes. The use of menthol in the solvent phase facilitates its incorporation into the lipid structure, aiding in drug penetration.

Challenges in formulating Menthosomes

Formulating menthosomes involves several challenges due to their unique structure and properties. Menthosomes are liposomal systems that encapsulate menthol, aiming for controlled release or enhanced skin penetration. Some of the key difficulties in their formulation include[24]:

Incorporation of menthol

- **Solubility Challenges:** Since menthol has low solubility in water, integrating it into water-based formulations can be tricky. Proper techniques must be used to ensure menthol is adequately dissolved and incorporated into the liposome structure.
- **Retention of Menthol:** Ensuring that menthol stays encapsulated within the liposomes without leaking prematurely is a significant hurdle during formulation[25].

Liposome Formulation

- **Selection of Lipid Materials:** The choice of lipids, such as phospholipids or cholesterol, plays a critical role in achieving efficient encapsulation and maintaining liposomal stability. The lipid composition needs to be optimized for the best balance between stability and menthol retention.
- **Size and Uniformity:** Achieving a uniform size distribution and preventing aggregation of liposomes is essential for formulation consistency. Techniques like sonication or high-pressure homogenization need to be carefully controlled to ensure proper vesicle formation[26].

Release dynamics

Controlled Release: A key objective of menthosomes is to provide a controlled, sustained release of menthol.Balancing the release of menthol over time while preserving its effectiveness requires careful formulation adjustments.

Skin or Mucosal Tissue Interaction

- **Skin Penetration:** Effective delivery of menthol to deeper layers of the skin or mucosal tissues is a challenge, as the formulation must be designed for optimal penetration without causing irritation.
- **Sensory Effects:** Menthol is known for its cooling sensation, and controlling this effect is crucial. Rapid or excessive menthol release could lead to discomfort or an unpleasant sensory experience[27].

Regulatory and safety concern

- **Safety Concerns:** The safety of menthosomes must be thoroughly assessed, particularly with regard to skin irritation and potential toxicity. Both the menthol and liposomal ingredients need to meet safety standards.

- **Regulatory Compliance:** Depending on the region, there are strict guidelines regarding the use of menthol in products, which must be adhered to during formulation and testing to obtain regulatory approval[28].

Methods to overcome challenges

Stability Issues

- **Use of Stabilizing Agents:** To prevent physical instability like aggregation or fusion, stabilizing agents such as polyethyleneglycol (PEG) or other surfactants can be incorporated into the formulation. These agents help to stabilize the liposomes and reduce their tendency to aggregate.
- **Encapsulation Optimization:** The lipid composition, including the use of cholesterol or other rigid lipids, can be adjusted to increase the stability of the liposomal bilayer. This helps prevent the premature leakage of menthol and improves the overall shelf life of the menthosomes.
- **Antioxidants:** Including antioxidants (e.g., vitamin E or ascorbic acid) can help prevent the chemical degradation of menthol and other components within the liposomes, especially when exposed to oxygen and light[29].

Incorporation of menthol

- **Solubilization Techniques:** To overcome the poor solubility of menthol in water, techniques like co-solvent systems, use of surfactants, or the formation of menthol complexes with other substances (such as cyclodextrins) can be employed. These methods enhance menthol's solubility and improve its incorporation into the liposomes.
- **Encapsulation Efficiency Enhancement:** To improve the retention of menthol, factors like optimizing the lipid-to-water ratio, using higher concentrations of phospholipids, or employing methods like reverse-phase evaporation or ethanol injection can improve menthol encapsulation and minimize leakage[30].

Liposome formulation

- **Optimization of Lipid Composition:** Careful selection of lipids is critical. The inclusion of lipids like phosphatidylcholine, phosphatidylethanolamine, or sphingolipids, along with cholesterol, can create more stable liposomal membranes that are less prone to leakage and rupture.
- **Size Reduction Techniques:** The size and uniformity of liposomes can be controlled by applying techniques like high-pressure homogenization, extrusion through membranes with defined pore sizes, or sonication. These methods allow precise control over the size distribution and prevent aggregation.
- **Cryoprotection and Lyophilization:** To improve long-term storage stability, menthosomes can be lyophilized (freeze-dried) after encapsulating menthol. Cryoprotectants like sucrose or trehalose can be added to preserve the liposome structure during the drying process[31].

Release kinetics

- **Controlled Release Systems:** To ensure controlled release of menthol, formulations can incorporate slow-releasing lipids or crosslinking agents to modulate the release rate. Polymer-lipid hybrid systems or the inclusion of biodegradable polymers can help achieve a more gradual release profile.
- **Multilamellar Vesicles (MLVs):** Using MLVs, which have multiple lipid layers, can extend the release of menthol over a longer duration, reducing the burst release and providing sustained action[32].

Skin or mucosal tissue interactions

- **Penetration Enhancers:** To ensure menthol reaches deeper layers of the skin, chemical penetration enhancers like ethanol, oleic acid, or other lipid-based substances can be added to the formulation. These enhance the permeability of the stratum corneum, allowing better menthol absorption.
- **pH Adjustments:** Formulating menthosomes with an optimal pH (around 5.5-6.0) can ensure that the menthol is effectively released while minimizing irritation or discomfort upon application to the skin or mucosa[33].

Regulatory and safety concerns

- **In-depth Safety Testing:** Comprehensive safety evaluations, including skin irritation tests, toxicity assessments, and allergenicity screening, should be conducted to ensure the product is safe for its intended use.

- **Regulatory Compliance:** Ensuring that the ingredients, formulation processes, and final product meet local and international regulatory standards (e.g., FDA, EMA) is crucial. Detailed documentation, including safety and efficacy data, must be provided to regulatory agencies for approval.
- **Natural and Non-toxic Ingredients:** Using biocompatible and non-toxic ingredients in the formulation, such as naturally derived lipids, can help meet safety standards and appeal to consumers looking for eco-friendly or skin-safe products[34].

Characterization of Menthosomes

Menthosomes are specialized lipid-based vesicular structures that are designed to encapsulate and deliver active ingredients efficiently, particularly for pharmaceutical or cosmetic applications. They are primarily composed of phospholipids and menthol, which enhance their permeability.

Particle Size and Distribution

- The particle size is a critical parameter as it determines the release rate and bioavailability of the encapsulated substance. Typically, dynamic light scattering (DLS) is used to measure the particle size and the polydispersity index (PDI), which reflects the uniformity of the vesicles[35].

Zeta Potential

- Zeta potential indicates the surface charge of the menthosomes, which influences their stability. A higher absolute value of zeta potential generally correlates with improved stability due to electrostatic repulsion between the particles. It is measured using electrophoretic light scattering.

Morphology and Structure

- The shape and surface characteristics of menthosomes can be analyzed using techniques like Transmission Electron Microscopy (TEM) or Scanning Electron Microscopy (SEM). These techniques provide high-resolution images of the vesicular structure and surface smoothness, crucial for determining their suitability in drug or cosmetic delivery[21].

Characteristics of menthosomes

Property	Menthosomes
Vesicle Size	~100–200 nm (nanometric range)
Surface Charge	Slightly negative (Zeta potential)
Entrapment Efficiency	High for lipophilic and moderately hydrophilic drugs
Skin Permeation	Superior due to menthol+deformability
Drug Release	Sustained over several hours

Encapsulation Efficiency:

- Encapsulation efficiency is calculated to determine how effectively the active ingredient is incorporated within the vesicle. It is determined by separating the free drug from the encapsulated one using methods like ultracentrifugation or dialysis, and then quantifying the amount of active ingredient using spectrophotometry or HPLC (HighPerformance Liquid Chromatography).

Thermal Analysis

- Differential Scanning Calorimetry or Thermogravimetric Analysis can be used to study the thermal properties of menthosomes. These analyses help in understanding the phase transition temperature, stability under different temperatures, and the interaction of components like menthol with lipids36.

In vitro Release Studies

- To assess the release profile of the encapsulated substance, in vitro release studies are conducted. This typically involves using diffusion cell apparatus to simulate skin or mucosal environments, tracking the release of the active ingredient over time.

Stability Studies

- Stability of menthosomes is vital for their practical use. Physical stability (e.g., aggregation or sedimentation) and chemical stability (e.g., degradation of the encapsulated compound) are assessed under various conditions such as temperature, pH, and light exposure.

Skin Permeability and Penetration

- Since menthosomes are often designed for topical applications, the ability of the vesicles to penetrate the skin is crucial. In vitro skin permeation studies, using models like Franz

diffusion cells, can evaluate how well the menthosomes deliver their active ingredients across different skin layers[37].

Applications of menthosomes

Menthosomes are a specialized type of nano-sized vesicles made of menthol (or menthol derivatives) and phospholipids. They have garnered interest in recent years for their unique properties, particularly in drug delivery systems. Here's a detailed overview of their applications across various fields.

Drug Delivery Systems

- **Transdermal drug delivery:** Menthol, a key component in menthosomes, has a wellknown ability to improve skin permeability by temporarily opening pores and increasing drug absorption. This property is leveraged in menthosomes to deliver active pharmaceutical ingredients (APIs) through the skin more effectively.
- **Targeted drug delivery:** The incorporation of menthol helps in targeting drugs to specific tissues or organs, improving the therapeutic efficacy and reducing side effects. The menthosomal structure can encapsulate both hydrophilic and lipophilic drugs, offering versatility in drug delivery[38].

Cosmetic formulations

- **Anti-aging treatments:** Menthosomes enhance the skin penetration of anti-aging agents, such as retinoids and peptides, improving their effectiveness.
- **Skin hydration and nourishment:** Incorporating menthosomes in moisturizers allows the gradual release of hydrating ingredients, which can reach deeper layers of the skin.
- **Sun protection:** In sunscreen formulations, menthosomes can encapsulate sunscreen agents, improving their stability and ensuring a prolonged release on the skin's surface.

Wound healing and Dermatology

- **Promote skin regeneration:** By facilitating the delivery of growth factors, antibiotics, and other healing agents directly to the wound site, menthosomes accelerate the healing process.
- **Anti-inflammatory effects:** The menthol in menthosomes has mild analgesic and antiinflammatory properties, which can help reduce pain and inflammation at the wound site, contributing to faster recovery[39].

Cancer Therapy

- **Targeted drug delivery to tumor cells:** Menthosomes can be designed to target cancer cells by incorporating ligands that bind to cancer cell-specific receptors. This helps to concentrate the drug in the tumor site while minimizing systemic side effects.
- Increased bioavailability of drugs: Since menthosomes can improve the solubility of poorly soluble drugs, they offer a way to enhance the bioavailability of cancer drugs, making them more effective at lower doses[40].

Improvement of oral Bio availability

Menthosomes can also be used in oral drug delivery systems to enhance the absorption of drugs that are poorly bioavailable. The menthol helps in increasing the permeability of the gastrointestinal tract, facilitating the absorption of drugs. This is particularly useful for drugs that have limited solubility or absorption issues when administered orally[41].

Antibacterial and Antifungal activity :

- **Antibacterial delivery:** By encapsulating antibiotics or antimicrobial peptides within menthosomes, their effectiveness can be enhanced, and the release can be controlled, ensuring sustained antimicrobial action.
- **Fungal infections:** Menthol's natural antifungal properties, when combined with the vesicular structure, can help deliver antifungal agents more efficiently to affected areas, leading to improved treatment outcomes[42].

Vaccine and Immune therapy

- **Improved vaccine efficacy:** The vesicular nature of menthosomes can be used to encapsulate and protect antigens, improving the stability and immune response to vaccines.
- **Adjuvant properties:** Menthol has immune-modulating effects, and when incorporated into menthosomes, it could enhance the body's immune response to vaccines, making them more effective.

NeuropharmacologicalApplications

Menthosomes may have applications in

neuropharmacology by enhancing the delivery of drugs to the brain. The menthol in the system can help increase the permeability of the blood-brain barrier, making it easier to deliver therapeutic agents for neurological conditions such as Alzheimer's disease, Parkinson's disease, and other central nervous system disorders[43].

Advantages of Menthosomes

Menthosomes are a specialized type of liposomal carrier system that incorporate menthol, a naturally occurring compound, into lipid-based vesicles. These vesicles are designed to encapsulate active pharmaceutical ingredients (APIs) or cosmetic agents and improve their delivery to target sites, often through the skin. The unique properties of menthosomes due to the combination of menthol and phospholipids offer a variety of advantages, especially in drug delivery and skincare applications. Below is a detailed explanation of these advantages[44].

Enhanced skin penetration

Menthol plays a key role in improving the permeability of the skin, which is a major barrier to the effective delivery of many active ingredients. Skin is a relatively impermeable barrier, particularly to large or hydrophilic molecules, which can limit the efficacy of topical treatments. Menthol, being a known penetration enhancer, can disrupt the lipid bilayer of the stratum corneum (the outermost layer of skin), allowing the active ingredients in menthosomes to penetrate deeper into the skin.

- **How it works:** Menthol interacts with the skin's lipid matrix, reducing the barrier effect of the skin and allowing the menthosomes to pass through more efficiently. The lipid membrane of the menthosome also mimics the skin's own lipid layers, which enhances its ability to fuse with the skin layers and release the encapsulated ingredients[45].

Targeted delivery

Menthosomes, as vesicular carriers, can encapsulate a wide range of active agents, including drugs, vitamins, and cosmetic ingredients, and deliver them to specific target sites. The liposomal structure allows the ingredients to be protected from degradation before reaching their target area.

- **How it works:** The vesicles can be designed to release their contents at specific locations. For instance, when menthosomes are applied topically, they can target localized skin issues like acne, eczema, or pain sites. This targeted delivery enhances the therapeutic effects while reducing unwanted systemic absorption, which leads to side effects[46].

Controlled Release

Menthosomes offer controlled release of encapsulated substances over an extended period. This feature is crucial for improving the overall efficacy of the treatment and minimizing the need for frequent reapplication.

- **How it works:** The phospholipid membrane of the menthosome is designed to release the encapsulated ingredients in a controlled manner as it interacts with the skin or other biological membranes. This controlled release ensures a steady and prolonged therapeutic effect, which is particularly useful for chronic conditions or when the active ingredient needs to be delivered over several hours or days[47].

Improved stability

The encapsulation of active ingredients within the liposomal structure of menthosomes offers enhanced stability, particularly for sensitive compounds that might degrade in the presence of light, heat, or oxygen[48].

- **How it works:** The lipid bilayer of the menthosome protects the enclosed substances from environmental factors, thus prolonging their shelf life[49]. In the case of pharmaceutical compounds, this means better preservation of the drug's potency, while for cosmetic ingredients, it may help maintain the effectiveness of ingredients like vitamins or antioxidants that can easily break down when exposed to the environment[50].

Reduced Irritation

Menthol itself has a soothing and cooling effect on the skin, which makes menthosomes an ideal formulation for treating skin conditions that cause irritation or inflammation. For example, menthol is often used in creams or gels designed to relieve itching, redness, or irritation caused by conditions such as insect bites, sunburn, or mild burns.

- **How it works:** When menthol is included in the menthosome formulation, it provides a dual effect: it helps cool and soothe the skin while also enhancing the skin's absorption of active ingredients. This can reduce the risk of skin irritation associated with certain topical treatments, making menthosomes a good option for sensitive skin[51].

Non invasive drug delivery

Menthosomes offer a non-invasive alternative to traditional drug delivery systems, such as injections or oral medications. Topical administration via menthosomes is an attractive option for many patients, particularly those with needle phobia, difficulties swallowing pills, or those in need of long-term, consistent medication.

- **How it works:** The liposomal structure of menthosomes enables them to deliver therapeutic compounds directly through the skin, avoiding the need for injections or oral ingestion. This non-invasive method can also be less stressful for patients and reduce the risk of complications associated with other drug delivery routes.

Improved Bioavailability

The bioavailability of a drug or active ingredient refers to the proportion of the compound that reaches its target site and becomes biologically active. Menthosomes can enhance bioavailability by improving the solubility and absorption of drugs through the skin or mucous membranes.

- **How it works:** The lipid bilayer of menthosomes helps to solvate hydrophobic drugs, improving their stability and absorption through biological membranes. Furthermore, the addition of menthol can act as a penetration enhancer, making it easier for the active ingredients to pass through skin layers and reach deeper tissues or systemic circulation if needed[52].

Dual effects (cooling effect and therapeutic effect)

Menthosomes provide the unique advantage of offering both therapeutic effects from the active ingredients and a cooling sensation from the menthol. This makes menthosomes an excellent choice for formulations aimed at soothing discomfort, such as those used in pain relief, muscle relaxation, or headache treatments.

- **How it works:** Menthol causes a cooling effect through the activation of cold-sensitive receptors in the skin. When included in menthosomes, this cooling effect can enhance the comfort of the user while also providing relief from conditions like muscle soreness, headaches, or minor skin irritation. This dual-action approach is particularly beneficial for products like topical pain relievers, anti-inflammatory creams, or anti-itch lotion[53].

Versatile Applications

Menthosomes are highly versatile and can be used in a wide range of applications, including pharmaceuticals, cosmetics, and food products.

- **Pharmaceuticals:** Menthosomes can be used for transdermal drug delivery, particularly for pain relief medications (e.g., analgesics), anti-inflammatory drugs, and even hormones for hormone replacement therapy[54].
- **Cosmetics:** They are commonly used in anti-aging products, moisturizers, and sunscreens, as they help in delivering active ingredients like vitamins (A, C, E), antioxidants, or peptides more effectively to the skin[55].

Drug/Agent	Therapeutic Area	Outcome
Meloxicam	Anti-inflammatory	Increased skin penetration
Ibuprofen	Pain/arthritis	Reduced edema in animal studies
Ketoconazole	Antifungal	Faster onset, deeper delivery
Vitamin C+E	Cosmeceutical	Antioxidant+brightening effec
Luteolin	Antidepressant	Co-delivery in microneedles

CONCLUSION

Menthosomes represent a promising advancement in the field of drug delivery systems. Their unique structure, which combines menthol with liposomal technology, enhances the permeation of drugs through biological membranes, thereby improving the bioavailability of various therapeutic agents. This innovative approach can potentially

revolutionize the treatment of various diseases, including those requiring enhanced transdermal delivery. The versatility and effectiveness of menthosomes in improving the stability, release profiles, and targeted delivery of drugs make them an exciting area of research in pharmaceutical sciences. Future studies and clinical trials will be essential to fully understand their potential, optimize formulations, and establish their safety and efficacy across diverse medical applications.

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Conflict of interest

The author declare that we have no conflict of interest.

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