# Review on Cubosomes Drug Delivery for the Management of Hanging-nail

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## ABSTRACT

A hanging nail, medically termed as a paronychia or nail spicule, is a small, torn piece of skin next to a fingernail or toenail. It may appear harmless initially but can cause significant discomfort, pain, inflammation, and potential infection if left untreated. While it is most seen in individuals with dry skin or those frequently exposed to water or irritants, it is also a common occurrence due to mechanical trauma such as nail biting or improper nail trimming.[1]

Though a seemingly minor condition, a hanging nail can have a considerable impact on the quality of life. It often results in localized pain and, in more severe cases, can lead to bacterial or fungal infections that may necessitate systemic therapy or surgical removal. In professional settings, particularly healthcare or hospitality industries, it poses a risk of cross-infection and cosmetic concerns [2]. Thus, effective management of hanging nail is important not just from a symptomatic relief perspective but also from a preventive healthcare standpoint.

Conventional treatment strategies for hanging nails include topical antiseptics, antibiotics, antifungal agents, moisturizers, and minor surgical interventions in extreme cases. However, these treatments suffer from limitations such as poor drug penetration, frequent dosing, local irritation, and a lack of targeted delivery [3]. The nail structure acts as a formidable barrier due to its dense keratinized matrix, making drug delivery particularly challenging [4]. Moreover, patient non-compliance is common due to slow onset of action and recurring symptoms.

To address the limitations of current therapies, advanced drug delivery systems are gaining attention. Among these, nanotechnology-based carriers such as Cubosomes offer promising potential. Cubosomes are nanostructured lipid carriers with unique cubic-phase architecture that enables efficient drug encapsulation and sustained release. Their bio adhesive nature, biocompatibility, and ability to enhance penetration make them suitable candidates for the treatment of localized conditions like hanging nails [5]. The concept of using Cubosomes for nail disorders is relatively novel but aligns well with the pharmaceutical trend of employing nanotechnology to overcome biological barriers.

## INTRODUCTION

Cubosomes are nanostructured liquid crystalline particles formed by certain amphiphilic lipids in the presence of water and stabilizers. They possess a unique internal structure resembling a honeycomb or cubic lattice, hence the name “Cubosomes” [6]. First reported in the late 1980s, Cubosomes were identified as a novel class of lipid-based nanoparticles that self-assemble into thermodynamically stable cubic phases. Their ability to mimic biological membranes makes them ideal candidates for various drug delivery applications.[7]

**Structural and Physicochemical Characteristics of Cubosomes**

Structurally, Cubosomes consist of two continuous but non-intersecting hydrophilic regions separated by a lipid bilayer folded in three dimensions, creating a bicontinuous cubic phase. This allows them to encapsulate both hydrophilic and lipophilic drugs simultaneously [8]. Their size typically ranges between 100–300 nm, depending on formulation parameters, and they possess high surface area, which aids in enhanced drug loading. The cubic phase provides a slow and sustained drug release profile, which is particularly advantageous for chronic conditions like paronychia or recurring hanging nails [9].

**Formulation of Cubosomes**

The main components used in Cubosomes formulation include:

- **Lipids**: The most commonly used lipid is **Glyceryl monooleate (GMO)**, a biocompatible and biodegradable lipid that forms a cubic phase in the presence of water.
- **Stabilizers**: Typically, surfactants like **Poloxamer 407** are used to prevent aggregation and maintain colloidal stability [10].
- **Aqueous Phase**: Water or buffer solutions aid in the self-assembly of the cubic structure during dispersion.

The choice and ratio of these components play a critical role in determining the final morphology, stability, and drug release characteristics of Cubosomes.

Cubosomes offer a sophisticated internal structure for drug encapsulation. Hydrophobic drugs partition within the lipid bilayer, while hydrophilic drugs are trapped within the aqueous channels of the cubic phase. Amphiphilic molecules may localize at the interface. The drug release mechanism is largely governed by diffusion through the tortuous aqueous channels and the degradation of lipid matrices over time [11]. This slow and controlled release pattern makes Cubosomes especially beneficial for localized and sustained drug action, such as in treating hanging nail inflammation and infection

**Comparison with Other Nanocarriers like Liposome and Noisome**

Cubosomes have been increasingly explored in the treatment of skin diseases such as psoriasis, eczema, and fungal infections. Their **bioadhesive nature** allows them to stick to the skin and nail surfaces, ensuring prolonged residence time and deeper penetration. Cubosomes have been increasingly explored in the treatment of skin diseases such as psoriasis, eczema, and fungal infections. Their **bioadhesive nature** allows them to stick to the skin and nail surfaces, ensuring prolonged residence time and deeper penetration.

While liposomes and noisome have been widely used as drug carriers, Cubosomes offer several distinctive advantages:

| **Feature** | **Cubosomes** | **Liposomes** | **Noisome** |
|---|---|---|---|
| Internal structure | Bicontinuous cubic | Bilayer vesicle | Bilayer vesicle |
| Drug loading | High (both hydrophilic & lipophilic) | Moderate | Moderate |
| Stability | High | Low to moderate | Moderate |
| Release profile | Sustained | Often burst release | Variable |
| Adhesiveness | Strong | Weak | Moderate |

Cubosomes, owing to their **viscous gel-like internal structure**, provide slower and more sustained release compared to the burst-type release seen in liposomes. Moreover, Cubosomes are more **physically and thermodynamically stable**, making them suitable for topical and transungual delivery systems [12].

**Advantages of Cubosomes in Drug Delivery**

Cubosomes have emerged as one of the most promising carriers in the field of nanotechnology-based drug delivery, especially for localized applications like dermatological and nail disorders. Their **BIcontinuous cubic phase** structure allows the encapsulation of both hydrophilic and lipophilic drugs, as well as amphiphilic molecules. Some of the key advantages include:

- **High drug loading capacity**
- **Controlled and sustained release profiles**
- **Bio adhesiveness**, especially to mucosal and keratinized tissues
- **Non-toxicity and biocompatibility**
- **Physical stability over long periods**

These features make Cubosomes highly suitable for applications where prolonged local therapy is beneficial, such as in the treatment of inflamed and infected nail folds in hanging nail conditions.

**Drug incorporated with Cubosomes**

Several types of drugs can be effectively encapsulated within Cubosomes for the treatment of hanging nails. These include:

- **Antibiotics**: Antibiotics such as **mupirocin** or **clindamycin** can be encapsulated to treat bacterial infections of the periungual region, common in hanging nails [13].
- **Antifungals**: **Terbinafine** or **ketoconazole** are effective for fungal infections that can complicate hanging nails, especially in immunocompromised individuals [14].
- **Anti-inflammatory agents**: **Hydrocortisone** or **diclofenac** can reduce inflammation and relieve pain associated with hanging nails.
- **Moisturizers**: Emollients like **urea** or **glycerine** can be encapsulated to hydrate and protect the skin around the nail, preventing further irritation and dryness.

The **biocompatibility** of Cubosomes ensures that these drugs can be delivered without causing toxicity to the surrounding tissues, making them ideal for topical applications.

**Mechanism of absorption of Cubosomes**

One of the key challenges in treating hanging nails is ensuring that drugs penetrate the tough, keratinized nail plate and reach the underlying nail matrix and periungual skin. Cubosomes enhance drug penetration due to their **small size** and **biomimetic lipid structure**, which facilitates the movement of drugs through the nail plate and into the surrounding tissue [15].

Studies have shown that Cubosomes can effectively penetrate the **stratum corneum** (the outermost layer of the skin) and **nail plate**, allowing for deeper drug delivery compared to conventional formulations. The **bio adhesive properties** of Cubosomes further enhance retention at the application site, leading to prolonged therapeutic activity and reducing the need for frequent reapplication.

## CONCLUSION

The use of Cubosomes for hanging nail management presents a promising avenue for **novel therapeutic strategies** in dermatology. While several challenges remain, including formulation optimization and regulatory hurdles, the continued research and development in **nanotechnology** and **drug delivery systems** hold great promise for revolutionizing the treatment of nail disorders. With the potential for improved drug efficacy, reduced side effects, and enhanced patient outcomes, Cubosomes could become a cornerstone in the management of hanging nails and other related dermatological conditions in the near future.

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