

## ADVANCES IN DELIVERY SYSTEMS FOR HAIRCARE: A REVIEW

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### ABSTRACT

Over the last 10-15 years, hair problems such as hair loss, slow hair growth, and reduced follicular function have been among the most common issues faced by younger generations, which in turn drives the need to seek out conventional cosmetic products dominating in the forms like liquids, lotions, oils, and creams, although these formulations have encountered efficiency issues such as inadequate penetration of the active in the stratum corneum, rapid wash-off of the formulation, poor follicular retention, and potential instability of the active components. Consequently, to address these challenges and enhance the bioavailability, stability, and therapeutic effectiveness of these hair growth agents, numerous advanced delivery systems such as liposomes, niosomes, nano-emulsions, solid lipid nanoparticles (SLN), nanostructured lipid carriers

(NLC), cyclodextrins, and various innovative carriers are effectively utilised. This article mainly highlights the function and mechanism of these novel delivery systems and examines their application in currently marketed products, while simultaneously emphasising the future direction of the field. To conclude, these delivery systems demonstrate significant promise in the haircare industry, providing improved outcomes and a scope for the creation of more efficient, scientifically supported cosmetic products.

**KEYWORDS:** Haircare delivery systems, Nanotechnology in haircare, Liposomes, Niosomes, Solid lipid nanoparticles, Follicular drug delivery.

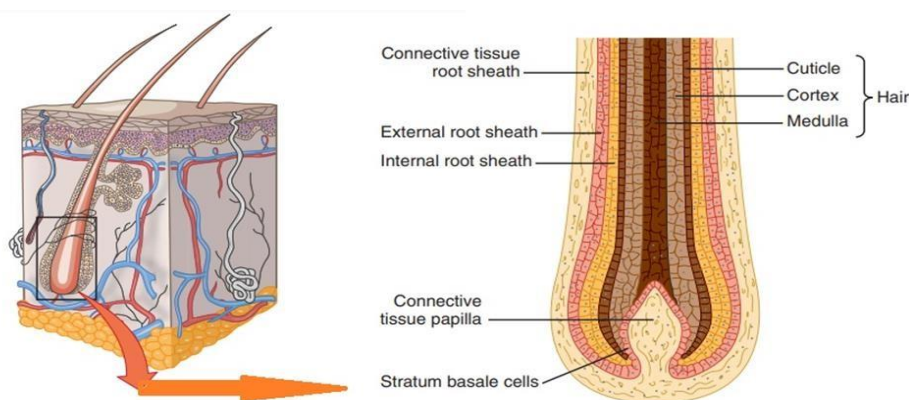
### INTRODUCTION

The hair follicle is a complex mini-organ of the skin that consists of multiple segmented

regions, including the infundibulum, isthmus, and bulb, which are associated with sebaceous glands and arrector pili muscles. Together, they contribute to the overall function and structure of the system.<sup>[1]</sup>

The follicle is one of the few skin appendages that spans multiple skin layers, extending deep into the dermis and in some areas to the subcutaneous tissue.<sup>[2]</sup> The hair follicle itself consists of structurally and functionally distinct components that form concentric epithelial and dermal sheaths around the keratinizing terminal strand at the medulla, including the inner root sheath, outer root sheath, and dermal papillae; these concentric compartments regulate their respective roles in hair shaft formation and cycling.<sup>[3]</sup>

Beyond its function as a hair-producing organ, the follicle is also an important immunological, sensory, and reservoir structure in the skin. Hair follicle is therefore a target site for therapeutics, cosmeceuticals, and cosmetics in stimulating hair growth, as well as in treating disorders of hair follicles.<sup>[4]</sup>



**Figure 01: Hair follicle Image courtesy: - pharmacy180.com.**

### PENETRATION PATHWAY

The interfollicular epidermis is the part of the epidermis that lies between hair follicles. In other words, it is the “normal skin surface” of the scalp that is not part of the hair follicle opening.<sup>[5]</sup> Now, as a result, traditional formulations often rely on diffusion through this barrier, which is inherently inefficient for delivering molecules to deeper targets such as hair follicles, mainly because of the presence of a Dense corneocyte lipid matrix showcasing highly selective permeability, which is designed to prevent chemical entry.<sup>[6,7]</sup> For instance, when caffeine was applied through a typical shampoo, it showed minimal absorption into the hair follicles, indicating both inadequate penetration and brief retention.<sup>[8]</sup> On the contrary,

hair follicles prove to be a shunt pathway which can not only increase the efficacy of the actives by targeted penetration but can also store those actives temporarily in the follicular reservoirs.<sup>[9,10]</sup> The hair follicles, together with the interfollicular epidermis, play a crucial role in the scalp's overall barrier function.<sup>[6,10]</sup> suggesting that both epidermal and follicular elements affect topical absorption. Although hair follicles present a promising method for precise delivery and temporary storage of active substances, conventional topical products such as oils, serums, lotions, shampoos, etc. often have difficulty taking full advantage of this method. As a result, in recent decades, nanotechnology has been widely utilised in creating innovative cosmetic products for hair and scalp care. This trend is supported by the evidence that roughly 19% of all nanocosmetics listed in the StatNano database focus on hair and scalp care.

Formulations utilising nanotechnology, such as nanoparticles, cyclodextrins, liposomes, and nanoemulsions, have surfaced as innovative methods owing to their chemical stability and regulated release. In hair care formulations, nanocarriers can focus on the hair shaft, hair follicle, and scalp. Consequently, they have been utilised to address various hair issues, such as dandruff and other hair-damaging ailments.<sup>[11,12]</sup>

## **FACTORS AFFECTING DELIVERY TO THE SCALP AND HAIR FOLLICLES**

Delivery of active compounds to the scalp and hair follicles is influenced by multiple physiological and physicochemical factors, such as:

**The barrier nature of stratum corneum:** The stratum corneum (outermost skin layer), made up of corneocytes and a dense lipid barrier, limits passive penetration of topically applied actives into the deeper layers.<sup>[6,7]</sup>

- 1. Role of interfollicular epidermis:** Furthermore, the interfollicular epidermis, being thick and tightly packed, has a hand in restricting penetration between follicular systems.<sup>[6,10,13]</sup>
- 2. Follicular structure and sebum-flow pattern:** Structurally, Hair Follicles have a sinus-like, narrow infundibulum (neck), which makes it difficult for larger-sized molecules to pass through<sup>[9]</sup> Only particles of specific sizes and vehicles with suitable characteristics can penetrate deeper regions of the follicular canal.<sup>[14]</sup> Furthermore, Ongoing sebum production and the external flow of follicular materials may decrease the duration for which applied actives remain at the targeted site, restricting their effective absorption.<sup>[9]</sup>

3. **The physicochemical properties of molecules:** Moreover, factors like the size, charge, and lipophilicity of the molecules critically influence their ability to permeate skin barriers. Small, moderately lipophilic compounds pass more effectively through the stratum corneum, while large or highly hydrophilic compounds face difficulty.<sup>[15,16]</sup> Smaller carrier systems (<100 nm) have demonstrated better penetration through the stratum corneum than larger systems, suggesting that size is a crucial physicochemical factor influencing topical delivery efficacy.<sup>[17]</sup>
4. **Contact duration of the topical application:** Additionally, short contact duration of wash-off formulations like shampoos further limits follicular retention (8)Wherein we can enhance the follicular accumulation and its reservoir effects by opting for modern nanocarrier designs as delivery systems.

## TRADITIONAL DELIVERY SYSTEMS

Traditional haircare products like solutions, emulsions, gels, oils, and lotions are commonly used for the scalp because they are easy to formulate and well-known to consumers. However, these systems largely act as passive carriers as they often fail to deliver sufficient concentrations of active compounds to the targeted sites involved in hair growth regulation.

### 1. Solutions and lotions

For example, solutions and low viscosity lotions generally evaporate quickly and are washed away by daily activities, thus also reducing the duration that actives on the surface of skin can remain in place and so penetrate further into layers of skin.<sup>[15]</sup>

### 2. Emulsions and gels

While emulsions and gels tend to retain actives at the surface only, which are delivered for topical application by these formulations, due to barrier properties presented primarily from the stratum corneum and interfollicular epidermis layers.<sup>[6,10,13]</sup> So larger or barely permeable molecules will have limited ability to move through such barriers.

### 3. Oil-based formulations

On the other hand, Conventional oils may provide occlusion and skin hydration but are limited by inadequate follicular penetration and the absence of targeted delivery. These formulations are likely dependent on passive trans-epidermal diffusion, which is restricted by the stratum corneum barrier, whereas incorporating drug delivery carriers into traditional

formulations appears to augment the penetration and local deposition of actives by targeting the pilosebaceous unit via trans-follicular routes.<sup>[6,18]</sup>

## LIMITATIONS

Although popular and economical to the consumers, Conventional haircare formulations have their own set of limitations, which include

- 1. Poor penetration:** As discussed earlier, the nature and structure of the stratum corneum add up to its dominant barrier-like characteristics,<sup>[6]</sup> leading to poor passive penetration of actives upon topical application.<sup>[7,19]</sup>
- 2. Fast evaporation and Wash-off:** In vitro human skin research done to assess the absorption of an aromatic compound, Linalool, and the effects of vehicle composition, on evaporation, and penetration, clearly indicates that the vehicle composition largely determines the in vitro skin absorption and distribution of active compounds.<sup>[20]</sup> While its rapid evaporation from some vehicles decreases the amount of active available for partitioning on or in the skin, this might explain why “simple” formulations are often retained only temporarily (a few hours) before losing much of their actives to volatilisation.<sup>[8]</sup>
- 3. Low stability:** Oxidative as well as lipid peroxidation in emulsion systems results in decreased formulation stability, which may lead to undesirable changes in texture and efficacy of the product.<sup>[21,22]</sup>
- 4. High irritations at effective concentrations:** Conventional delivery systems generally need to use higher active concentrations for efficacy<sup>(18)</sup> as they do not penetrate well due to passive diffusion and are not retained in these formulations. i.e., they will be washed off too quickly, leading to locally elevated exposure on the skin surface, and thus increasing the chances of irritation.<sup>[17]</sup> whereas delivery systems enhance targeted, controlled operations, which ultimately lead to better follicular targeting, resulting in a reduced effective dose with less risk of irritation.<sup>[19]</sup>

We can get a better grip on this concept with the following analogy

- Firstly, Inefficient delivery → will require a higher dose
- Higher dose → higher surface concentration and interaction
- Higher surface concentration → barrier damage/irritation

- Whereas Advanced carriers → better localization + controlled release
- Better localization → lower dose needed
- Lower dose → improved tolerability

Lastly, to overcome these shortcomings, higher concentrations of actives are usually demanded, as In conventional topical systems, penetration depends upon the concentration gradient between the skin and formulation, which often means higher applied concentrations must be used to improve delivery. Premised on passive diffusion, skin permeation of a topically administered molecule occurs largely through free energy driving forces, with transport across an effective barrier following Fick's law as it is driven by the concentration gradient between formulation and skin.<sup>[15]</sup> which in turn causes greater risk of sensitisation and scalp irritation. These inevitable limitations reveal the demand for innovative delivery technologies to improve the penetration, retention, and controlled release of hair growth-promoting actives.

## NOVEL DRUG DELIVERY SYSTEMS

### 1. LIPOSOMES

The significance of liposomes as a delivery system for cosmetics has been well established over the years. It is important to understand their structure as well as mode of action, particularly concerning their role in the haircare industry.<sup>[24]</sup> Liposomes are spherical vesicles composed of one or more phospholipid bilayers surrounding an aqueous nucleus. Liposomes find extensive applications in cosmetic and pharmaceutical preparations, mainly due to their high biocompatibility, durability, and high drug-loading efficiency.<sup>[25]</sup> These are versatile lipid-derived systems for delivering drugs. It is an approach that replicates the lipid bilayer structure of the organ to enhance drug absorption across epidermal layers. They are biocompatible, minimally immunogenic, non-harmful, and easily decomposed by enzymes.<sup>[26]</sup> These can efficiently encapsulate medications/actives and transport them to the target tissues or cells, enabling targeted treatment. They are utilised in cosmetics to improve the infiltration of active components into the skin, enhancing their effectiveness.<sup>[25]</sup>

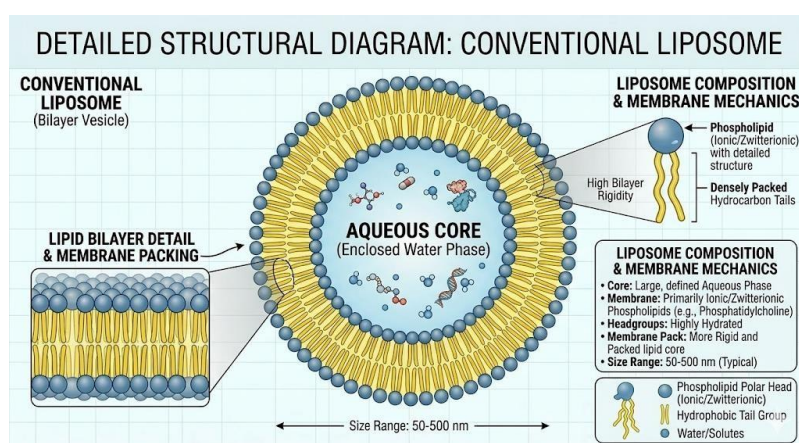
Liposome structures are categorised into four types based on size and bilayer count:

- Small unilamellar vesicles (SUV),
- Large unilamellar vesicles (LUV),
- Multilamellar vesicles (MLV),

- Multivesicular vesicles (MVV).<sup>[27]</sup>

Liposomes have a single phospholipid bilayer in a unilamellar form, while they exhibit an onion-like configuration in a multilamellar form. MVV create a multilayered structure with layered phospholipid spheres, whereas multiple unilamellar vesicles are formed inside larger liposomes.<sup>[27,28]</sup>

The encapsulation efficiency of liposomes rises with the size of the liposomes and falls with an increase in the number of bilayers, though this is applicable only for hydrophilic compounds.<sup>[27,29]</sup>



**Figure 02: Liposome structure.**

Image courtesy: Google Gemini

Androgenic alopecia (AGA) is among the most common types of hair loss. Liposomes (LPSs) serve as a localized dermal drug reservoir with sustained release capabilities, effectively extending and improving drug retention in the skin.<sup>[30]</sup>

The localized administration of transgenes to hair follicles holds promise for addressing skin and hair disorders. One such study demonstrates that applying liposome-DNA mixtures (lipoplex) to human skin xenografts led to effective *in vivo* transfection of hair follicle cells. Transfection relied on liposome formulation and transpired solely at the beginning of a new growth phase of the hair cycle. These results establish a basis for future topical lipoplex applications to modify hair follicle phenotype and address conditions of the hair and skin.<sup>[31]</sup>

Therefore, Liposomes have successfully established a novel application in cosmetic preparations like Hair growth serum, anti-dandruff preparations, herbal extracts, etc.

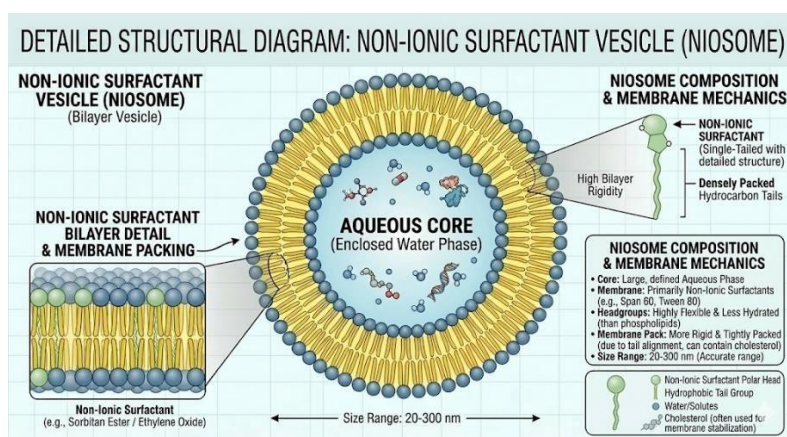
## 2. NIOSOMES

Niosomes are Nonionic surfactant-based vesicles, which are uni/multilamellar in structure, enclosing lipophilic components in an aqueous solution of solutes. These vesicles are produced by the self-assembly of hydrated surfactant monomers.<sup>[32,33]</sup> Compared to liposomes, niosomes overcome problems related to large-scale production, sterilization, and stability, including oxidation, high cost, and purity that influences size and shape.<sup>[33–35]</sup>

Furthermore, the raw materials for niosomes are generally less expensive and more easily accessible than the phospholipids required for liposomes. Niosomes can be prepared as either unilamellar or multilamellar vesicles using techniques similar to those used for liposomes.<sup>[34,36–38]</sup>

Niosomes are categorized into three types based on particle size:

large unilamellar vesicles (LUVs), Small unilamellar vesicles (SUVs), Multilamellar vesicles (MLVs)<sup>[32,34]</sup>



**Figure 02: Niosome structure.**

Image courtesy: Google Gemini

Vesicles of niosomes are formed by various techniques (depending upon the scale of preparation, small/Large scale), such as thin film hydration, Reverse phase evaporation, sonication, microfluidization, etc.<sup>[33]</sup>

Niosomes have gained much interest in topical drug delivery and haircare-related topical applications. Their bilayer structure can encapsulate both hydrophilic and lipophilic compounds, thus enhancing active ingredient stability and bioavailability. Niosomes have

been proven to be helpful for various hair-related therapies.

An example is the use of pumpkin seed oil-loaded niosomes, which possess more significant skin permeation and greater deposition in hair follicles while having notable anti-hair-loss activity by inhibition of 5- $\alpha$  reductase and anti-inflammatory effect.<sup>[39]</sup> Niosomal formulations of minoxidil have also been shown to improve skin penetration and retention qualitatively compared with similar vehicles used for conventional topical administration.<sup>[40]</sup> These results suggest that niosomes can overcome the delivery issue of therapeutic molecules into hair follicles effectively, thus serving as an innovative class of nanosystems.

### 3. LIPID NANOCARRIERS: NLCS AND SLNS

As advanced delivery systems, lipid-based nanocarriers such as Nanostructured lipid carriers (NLCs) and Solid lipid nanocarriers (SLNs) have gained significant attention in both dermatological and cosmetic formulations.

#### a. Solid lipid carriers (SLNs)

SLNs are colloidal carriers that were created in the past ten years as a substitute for the conventional carriers that are now in use (emulsions, liposomes, and polymeric nanoparticles). Sized about 50 nm to 500 nm.<sup>(41)</sup> They are a new class of submicron-sized lipid emulsions in which a solid lipid has been used in place of the liquid lipid (oil).<sup>[42]</sup>

These are produced by adding cationic lipids to liposomes, which then surround negatively charged oligonucleotides through electrostatic interactions.<sup>[43]</sup> SLNs are known for their potential to enhance cosmeceutical efficacy because of their special qualities, which include tiny size, vast surface area, high drug loading, and phase interaction at the interfaces.<sup>[42]</sup>

These are prepared by various methods depending upon their size and therapeutic benefits, such as

1. Homogenization Method
2. Single and Double Emulsions Solvent Evaporation Method
3. Solvent Injection Method
4. Solvent Diffusion, etc.<sup>[43]</sup>

These carriers have exhibited considerable promise in haircare applications owing to their ability to facilitate follicular drug targeting and increase retention of active compounds within the scalp.<sup>[42]</sup>

A classical paper has shown that flutamide-loaded SLNs have much higher skin deposition, and it was also observed that the number of hair follicles associated with a drug was enhanced to a significant extent, and the redistribution of the drug in the follicles was observed to be better than a traditional formulation.<sup>[44]</sup> Likewise, SLNs carrying finasteride exhibited improved skin retention and noticeable hair restoration in experimental studies of androgenetic alopecia.<sup>[45]</sup>

SLNs still encounter specific difficulties, such as inadequate drug loading capacity, erratic gelation propensity, polymorphic transitions, and drug leakage during storage.<sup>[46,47]</sup>

#### **b. Nanostructured lipid carriers**

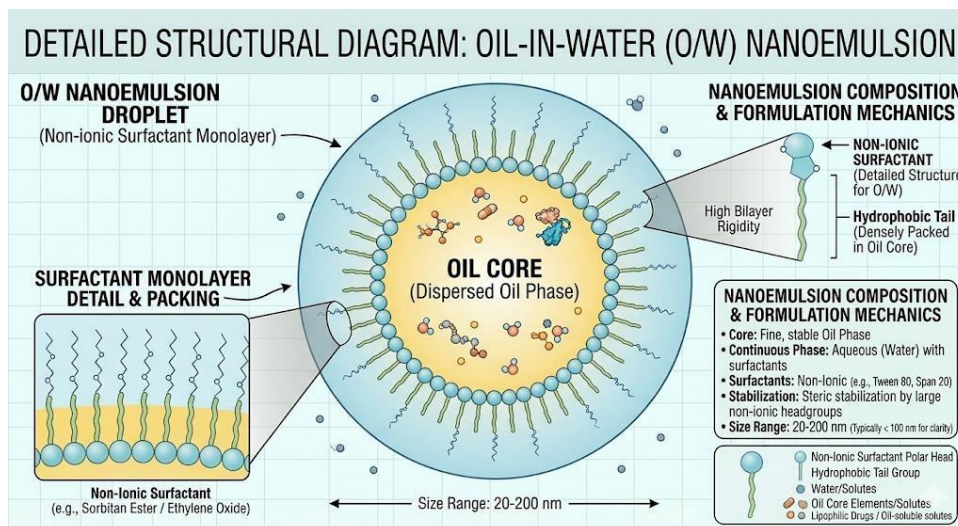
Nanostructured lipid carriers (NLCs) emerge as the second generation of lipid nanoparticles to address the limitations of the first generation, namely SLNs. In recent years, NLCs have attracted the interest of researchers as an alternative to SLNs, polymeric nanoparticles, emulsions, microparticles, and liposomes, etc.<sup>[46]</sup>

In NLC, a portion of the solid lipid is replaced with oil, yielding an irregularly organised lipid matrix that increases drug loading and prevents drug leakage during storage.<sup>[48]</sup> Similarly, NLCs provide greater stability by preventing solid lipids from recrystallising, maintaining a practically constant size throughout storage.<sup>[49,50]</sup>

### **4. NANOEMULSIONS**

Nanoemulsions are minute dispersed oil-in-water or water-in-oil systems with droplet dimensions usually varying from 20 to 200 nanometers that can favour follicular drug penetration.<sup>[51,52]</sup> These submicron emulsions exhibit thermodynamic instability yet possess kinetic stability, allowing them to endure phase separation and coalescence over time due to the application of surfactants and co-surfactants.<sup>[51,53]</sup>

Different methods for creating nanoemulsions include high-energy and low-energy techniques, such as High-pressure homogenization, Microfluidization, Jet dispersion, and Phase inversion processes. The characteristics of a formulation can be affected by factors such as droplet composition, concentration, size, and charge, which can subsequently influence the manufacturing technique.<sup>[51]</sup>



**Figure 02: Nanoemulsion structure.**

Image courtesy: Google Gemini

Several studies have already demonstrated the role and effect of nanoemulsions in enhancing the follicular delivery of actives. The Nanoemulsion formulations of minoxidil or dutasteride demonstrate better targeting at the hair follicle level, improved drug penetration through the skin barrier, and sustained or controlled release of drugs that may lead to enhanced therapeutic effect in treating alopecia.<sup>[52,54]</sup> Moreover, compared with conventional topical formulations, cedrol nanoemulsions have been shown to considerably stimulate hair growth and improve bioavailability.<sup>[55]</sup>

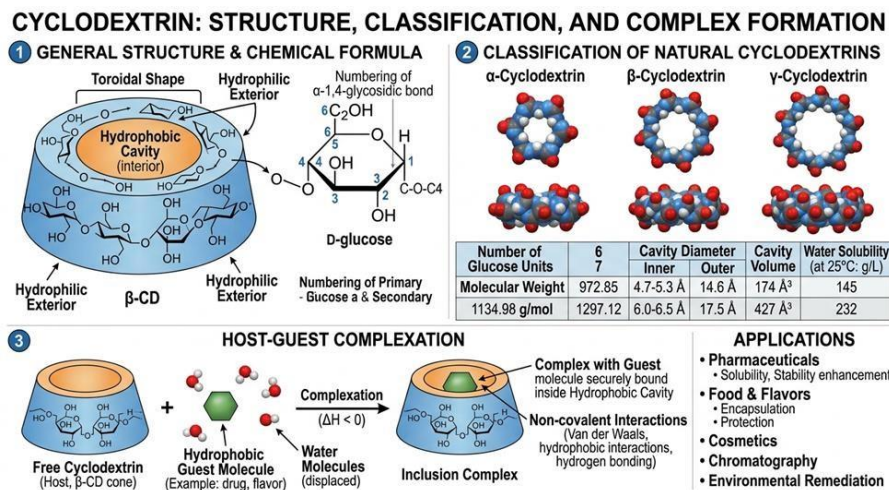
These results suggest that nanoemulsions could represent new generation delivery systems with potential in haircare and growth applications.

## 5. CYCLODEXTRINS

Cyclodextrins are a group of non-toxic and biocompatible cyclic oligosaccharides composed of  $\alpha$ -1,4-linked glucopyranose units characterised by a hydrophilic outer surface and a hydrophobic inner cavity.<sup>[56]</sup>

These features allow the formation of inclusion complexes with numerous organic compounds (host-guest interactions),<sup>[57]</sup> which in turn greatly improves the water solubility, chemical stability and bioavailability of poorly water-soluble cosmetic actives with additional protective means, protecting them from degradation by light, oxidation and/or volatilization.<sup>[56,58]</sup> CDs are categorized based on the number of glucopyranose units present

in their structure. Commonly used natural CDs include  $\alpha$ -cyclodextrin ( $\alpha$ -CD) 6-glucose units,  $\beta$ -cyclodextrin ( $\beta$ -CD) 7-glucose units, and  $\gamma$ -cyclodextrin ( $\gamma$ -CD) 8-glucose units<sup>[56]</sup> Additionally, synthetic derivatives like hydroxypropyl- $\beta$ -cyclodextrin are widely accepted in the cosmetic industry, considering they offer improved aqueous solubility and stability in the system.<sup>[59]</sup>



**Figure 03: Cyclodextrin structure.**

Image courtesy: Google Gemini

Cyclodextrins play a dual role of acting as versatile functional excipients which can be integrated into formulations of hair care products by enabling the inclusion of hydrophobic ingredients such as essential oils, vitamins and fragrance compounds into aqueous systems, including shampoos, conditioners and serums.<sup>[58,60]</sup> In shampoo, CDs are incorporated to increase the contact time of actives with the scalp. Several cosmetic businesses sell dry shampoo with free  $\beta$ -CDs to fight oily hair by keeping dirt and oil in their cavities and lengthening the intervals between washes.<sup>[56,61]</sup>

## FUTURE ASPECTS

The advent of sophisticated delivery systems in hair care has revolutionized the approach to the management of hair loss, scalp disorders and impaired follicular activity. Better performance than traditional formulations has been reported for novel carrier systems, including liposomes, niosomes, nanoemulsions, solid lipid nanoparticles (SLN), nanostructured lipid carriers (NLC), cyclodextrins, and polymeric nanoparticles, in terms of follicular targeting, active stability, scalp retention, and controlled release.<sup>[14,63]</sup> Future research will focus on multifunctional and personalised delivery systems with enhanced

efficacy, while also considering consumer safety and sustainability. Site-specific and stimulus-triggered delivery directly into the hair follicle using smart nanocarriers responsive to pH, temperature, enzymes or sebum composition may be possible. In addition, biotechnologies and nanotechnologies, such as stem cell-derived growth factors, peptides, exosomes, and gene-based therapeutics in advanced carriers, could provide new avenues for the more efficient management of alopecia and follicular dysfunction.<sup>[44,64,65]</sup> Furthermore, follicular penetration research, in vivo bioavailability investigations, and scalp imaging can improve formulation optimization and focused product development.<sup>[66]</sup> Commercial innovation in this area is probably going to pick up speed because to the increasing customer desire for scientifically sophisticated, evidence-based, and minimally irritating haircare products.<sup>[67,68]</sup>

Another promising avenue is the use of biodegradable, eco-friendly and naturally-derived carriers to mitigate long-term nanomaterial safety and environmental impact concerns.<sup>[69,70]</sup> For safe commercialization of these technologies in cosmeceutical and dermatological markets, regulatory standardization and detailed toxicological studies will be needed.<sup>[71-73]</sup>

## CONCLUSION

In conclusion, by overcoming significant drawbacks like poor penetration, quick wash-off, low stability, and insufficient follicular targeting, Novel delivery systems have become incredibly effective substitutes for traditional haircare formulations. Through improved trans follicular targeting and controlled release, novel carriers such as liposomes, niosomes, nanoemulsions, SLNs, NLCs, cyclodextrins, and other nanotechnological systems greatly improve the delivery, retention, bioavailability, and therapeutic performance of haircare actives. These developments not only increase effectiveness but also lessen the possibility of irritation and aid in the creation of more cutting-edge, consumer-friendly products. The future of haircare formulations is also anticipated to be shaped by continuous developments in biodegradable carriers, safety evaluations, and customized delivery methods. All things considered, cutting-edge delivery technologies offer a potential and revolutionary method for creating next-generation hair care and scalp treatment products.

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