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NANOSTRUCTURED LIPID CARRIERS IN COSMECEUTICALS

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Abstract: Nanostructured lipid carriers (NLCs) are a novel kind of lipid-based nanoparticle that have gained a lot of attention in the cosmetics industry because to their superior qualities like high drug loading capacity, improved stability, and increased skin penetration. NLCs are made up of a solid lipid matrix mixed with a liquid lipid, resulting in a distinct structure that allows for better drug entrapment and release characteristics .NLCs have been employed as carriers in cosmetics to improve the transport and performance of active compounds including as antioxidants, vitamins, and sunscreens. The small size of NLCs allows for deeper penetration into the skin, resulting in improved absorption and targeted distribution of active substances.

This review article will provide an overview of the present use of NLCs in cosmetics, including formulation strategies, characterization methodologies, and prospective skin care benefits. Furthermore, the obstacles and future prospects of using NLCs in cosmetics will be highlighted, emphasising the importance of continued research and development in this promising subject.

Index Terms **- Nano lipid, NLCs, Antioxidants.**

I. INTRODUCTION

Nanotechnology has essentially had an impact on all technical areas over the past 20 years, including pharmaceuticals. The industry estimates that about 40% of lipophilic drug candidates fail because of solubility and formulation stability problems, despite the fact that these problems have been addressed by a variety of cutting-edge and innovative lipophilic drug delivery systems. (How targeted medications are now delivered using nanostructured lipid carriers) Pharmaceutical nanotechnology is a modern biological field. Modifying structures at the nanometric scale is particularly exciting because it offers distinctive qualities not present nano at higher scales, such as improved bioavailability and better interfacial area contact with biological tissues. The utilization of these nanoengineered systems is rapidly expanding as fewer medications are needed as a result of their features.

Nanostructured lipid carriers are reliable. (Nanostructured lipid carriers and their current application in targeted medication administration) Solid lipid nanoparticles (SLN) are believed to be the most effective lipid-based colloidal carriers. One of the most popular techniques for improving the oral bioavailability of drugs is this one. After oral administration, SLNs are absorbed by the lymphatic pathway due to the stimulation of chylomicron formation. The payload for the majority of medications is too low, pharmaceuticals expel during storage, and the nano lipid dispersions have a high water content. The drug-loading capacity is projected to increase because to the uneven crystal lattice, drug ejection during storage will be decreased by NLCs, and the drug release profile can simply be adjusted by altering the content of the lipid. NLCs' matrix contains a range of spatially different lipid molecules, often a mixture of solid and liquid lipid, to compensate for the deficiency of SLNs. Even though the NLC matrix contains liquid lipids, it is solid at body or room temperature. [1]

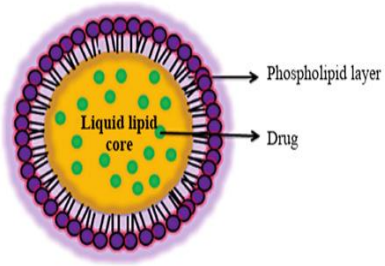

Figure 1 nanostructured lipid carrier

NLCs combine liquid and solid lipids and control the concentration of the liquid lipid to maintain their solid state. Because of the solid matrix, NLCs, as opposed to emulsions, can more efficiently immobilize drugs and prevent the particle from coalescing. NLC advantages include lower toxicity, biodegradability, drug protection, and delayed release. (The current use of nanostructured lipid carriers in the delivery of targeted drugs).[2]

TYPES OF NLC

Several varieties of NLCs are produced depending on the different production methods and the composition of the lipid blends. The main idea is to give the lipid matrix a specific nanostructure in order to improve the pay-load for active chemicals and decrease compound ejection during storage.

1. *Imperfect type NLC (imperfectly structured solid matrix***)**

In order to achieve the maximum incompatibility leads to the highest drug payload, small volumes of liquid lipids (oils) that are chemically significantly different from each other are mixed with solid lipids.

2. *Amorphous type (structure less solid amorphous matrix)*

This type of NLC can be produced by combining solid lipids with specific lipids, such as medium chain triglycerides as Miglyol® 812, isopropyl myristate, or hydroxy octa cosanylhydroxystearate. As NLC are solids in an amorphous but non-crystalline state, the unique structure of the lipid matrix prevents drug ejection caused by the crystallization process to develop during storage.

3. *Multiple types (multiple oil in fat in water (O/F/W) carrier)*

During the cooling process following homogenization and the crystallization process during storage, the drug's solubility in the lipophilic phase reduces. Particularly when the drug concentration in the formulation is too high, continuously decreasing drug solubility results in drug expulsion from the lipid nanoparticles. Several medications are more soluble in liquid lipids than in solid lipids. Addition of more liquid lipid to the lipophilic phase demonstrates the benefits of the solid matrix that prevented drug leakage while the liquid regions (oily nano compartments) show relatively high solubility for lipophilic medicines when lipids lack the necessary drug solubilities. [3]

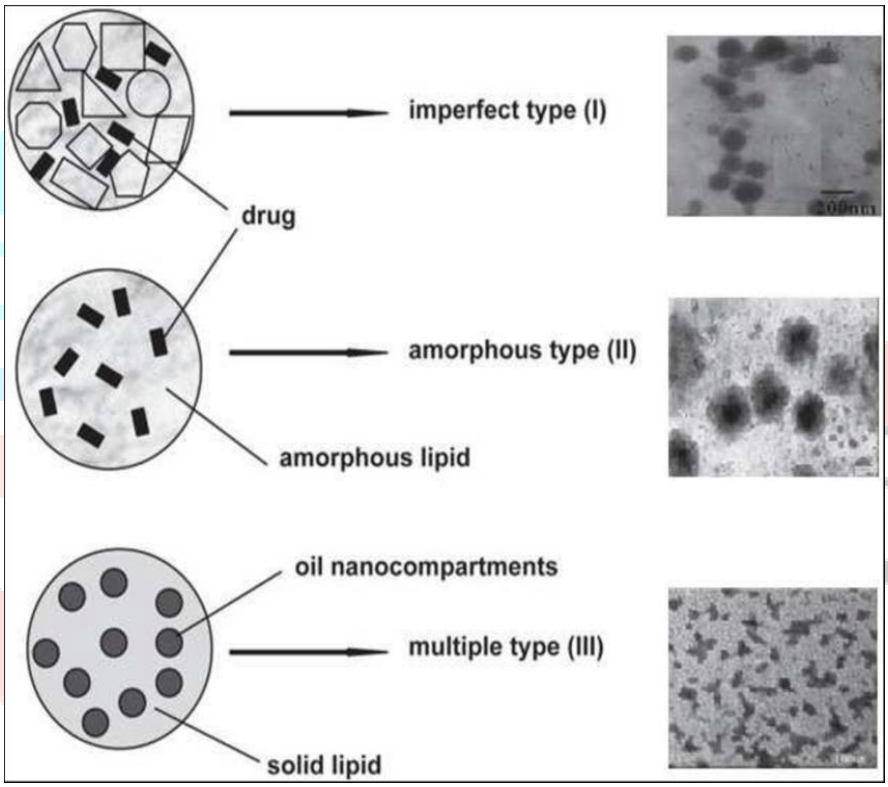

Figure 2 type of nlc

Preparation of lipid Nanoparticle[-]

1. *HIGH PRESSURE HOMONIZATION*

HPH technology has developed as a reliable and effective method for producing lipid nanoparticles. This method for the mass manufacture of LNs is an alternative to previous methods. Both hot and cold techniques for homogenization were developed. In both methods, the medicinal ingredient is dissolved or disseminated in the melted lipid prior to the HPH. The fluid is moved by high pressure (100–2000 bar) via the homogenizer small gap. The typical particle size is in the sub-micron range. Homogenization has a number of benefits, such as mass production, the absence of organic solvents, enhanced product stability, and improved drug loading, but its use is problematic due to special high pressure and temperature conditions.[4,5] In this procedure, homogenization takes place at temperatures over the lipid melting point. Pre-emulsions are created when drug-loaded lipid melt is mixed with hot, isothermal aqueous surfactants using a mixing device (Ultra-Turrax)[6] Particle size primarily decreases at high temperatures due to the reduced viscosity. There are three main issues with hot homogenization. The first is the drug temperature-dependent breakdown; the second is drug penetration into the aqueous phase during homogenization; and the third is the nano emulsion complicated crystallization stage, which can result in multiple modifications and/or supercooled melts,[7]

2. *COLD HOMOGINIZATION*

The drug is dissolved in the lipid melt, much like the hot homogenization process, and then quickly cooled by liquid nitrogen or dry ice. The result of milling is the generation of 50–100 nm nanoparticles that can be dispersed in a cold surfactant phase to form a pre–suspension. Process is carried out at room temperature, which causes the nanoparticles

to break down into SLNs. To address the issues with the hot homogenization approach, the cold homogenization technique has been improved [8]

3. *SOLVENT EMULSIFICATION/EVAPOURATION*

In this procedure, the lipid is dissolved in an organic solvent that is immiscible with water. The formation of an emulsion in an aqueous phase that contains surfactant follows. The solvent is removed from the emulsion via evaporation under reduced pressure. The aqueous phase dispersion of nanoparticles is caused by evaporation (using lipid precipitation process in the aqueous phase). Unlike cold homogenization, this process does not involve any heat stress; however, the organic solvent utilized in this method is a disadvantage. According to the solid lipid and surfactant, particle size can change. [9]

4. *SUPERCRITICAL FLUID EXTRACTION OF EMULSION[SFEE]*

SFEE is a comparatively new method of SLN preparation. Solvent extraction from o/w emulsions is accomplished with this technique using a supercritical fluid, such as carbon dioxide. It should be mentioned that while carbon dioxide is an excellent alternative, many of the medications cannot be dissolved by it. Hence, supercritical antisolvent precipitation (SAS) can be used instead of SFEE. [9]

5. *SPRAY DRYING*

The lyophilization process, which produces pharmaceutical products from aqueous SLN dispersion, is replaced by this technology. Although spray drying is a more affordable approach than lyophilization, it is not frequently employed for the synthesis of lipids. Due of the particle aggregation caused by the high temperatures and shear pressures used in this method. Lipids with a melting point higher than 70 °C are appropriate for spray drying, according to earlier investigations. [10]

6. ULTRASONICATION/HIGH SHEAR HOMOGENIZATION

High-shear homogenization, often known as ultra sonification, is one technique for making LNPs. In this phase, the lipid phase and the surfactant-rich aqueous phase are distributed. The high concentration of surfactant will be viewed negatively. This approach also has the drawback of not producing a narrow particle size distribution, which causes instability during storage. Unlike hot and cold homogenization, this method makes use of straightforward equipment that is accessible in every laboratory.[11]

Nanocarriers and Skin Interaction

Lipid nanoparticles may penetrate anatomical barriers and release their contents, making them ideal for regulated medication delivery due to their unique size and composition. [12] Bionanotechnological products must be small, yet this alone is insufficient. Such goods should also achieve and sustain acceptable qualities over a reasonable time frame. They should also be able to respond to changes in boundary circumstances, making them 'smart'. A great nanotechnological device should be able to quickly and accurately react to environmental changes. Developing a viable nanotechnological product for cutaneous delivery of cosmetic actives is challenging because to the skin barrier's complicated structure. [13]

The challenge is proportional to the potential opportunity. Fig.3 shows how the skin's layers and structures form an effective biological barrier. Skin anatomy refers to the structure of the skin, which is divided into two parts: the epidermis, which is thinner on the outside, and the dermis, which is thicker inside. Anatomically, the skin is divided into four layers: the stratum corneum (nonviable epidermis), viable epidermis, dermis, and subcutaneous tissue. In addition to these structures, there are several associated appendages, including hair follicles, sweat glands, apocrine glands, and nails. Because of its content and structure, the stratum corneum is thought to constitute the primary barrier to material exchange between the body and the environment. Therefore it became the real challenge on active agent delivery into and through the skin.

Solid lipid nanoparticles and nanostructured lipid carriers effectively adhere to the stratum corneum, increasing active agent penetration into the skin. Lipid particles ranging in size from 200 to 400 nm have been shown to occlude artificial membranes.[14] Reducing trans-epidermal water loss has been shown to improve penetration of occlusion-sensitive actives into skin layers.[14,15]

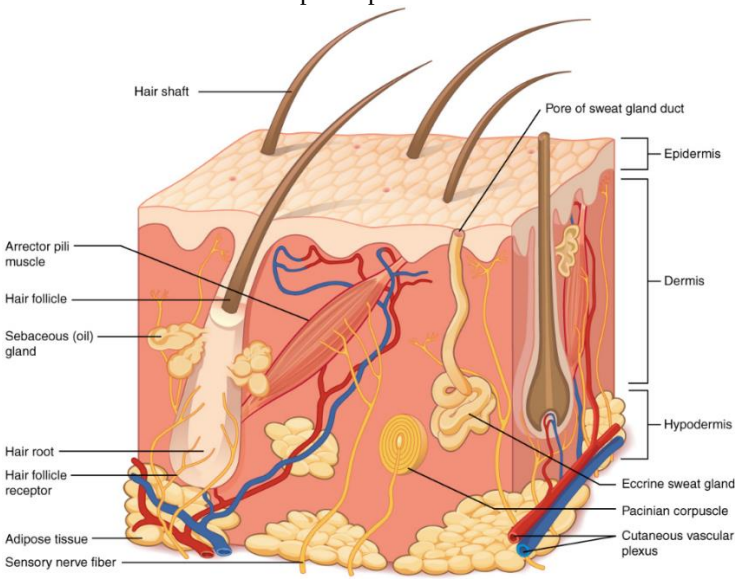

Figure 2- anatomy of skin

1. *Formulations and Products*
NLC and SLN are advantageous for dermal applications, making them a promising technology for commercial cosmetic product development. Topical products (e.g. creams and lotions) can be formulated using both technologies. Novel products can be created by adding lipid nanoparticles to existing products, adding viscosity enhancers to the aqueous phase of SLN/NLC to create a gel, or directly combining the two.[16]

2. *Encapsulation as a Protective Tool*
Lipid nanoparticles can improve the chemical stability of molecules that are sensitive to light, oxidation, and hydrolysis. Many cosmetic actives, including as coenzyme Q10 [17, 18], tocopherol (vitamin E) [17], and retinol (vitamin A), have been shown to improve their chemical stability following inclusion into lipid nanocarriers [19–22]. Directly incorporating active substances into the SLN and NLC matrix protects them from chemical degradation. Coenzyme Q10 and extremely sensitive retinol were both observed to have improved stability. Retinol-containing cosmetic products require costly safety measures such as light exposure and inert gas protection. Stabilising retinol in SLN and NLC reduces production costs and improves the preservation of the active ingredient, extending product shelf life. It may also offer various advantages in controlled release applications. SLN and NLC dispersions have already been shown to release both bursts and steady amounts. When applying cosmetic active agents to the skin, both profiles are important. The former improves penetration through concentration gradients, while the latter prevents high concentrations of irritating compounds from coming into contact with the skin quickly.

3. *The Occlusion Effect and film formation*
The stratum corneum contains between 10 and 20% water. If the skin's water content falls below a certain level (due to increased evaporation), the protective layer becomes damaged and chapped. Occlusive topicals can rejuvenate the stratum corneum and heal the skin's surface. Occlusion reduces water evaporation from the skin, causing water retention within the skin. Swelling in the stratum corneum enhances medication absorption. However, several topicals with good occlusive characteristics, such as petrolatum, lipids, and fatty acids, have unappealing cosmetic or aesthetic look. Various w/o and o/w emulsions have been created. These products strike a balance between occlusive function and skin attractiveness. SLN's occlusive properties stem from the creation of a film on the skin, which reduces water evaporation. [23, 24] According to Souto et al. [24],SLN has a stronger occlusive factor than NLC with comparable lipid content. Increasing oil concentration reduces the occlusive property, according to NLC comparisons. According to [22], utilising low-temperature melting lipids with highly crystalline and tiny particles results in the best occlusion efficiency. Nanoparticles have been shown to be 15 times more occlusive than microparticles [25]. The most effective particles are those smaller than 400 nm that include at least 35% high crystallinity lipids. Souto et al. [24] found that SLN had a larger occlusive factor than NLC with comparable lipid content. They attributed this to the degree of order caused by re-crystallization. The study found that increasing oil content reduces the occlusive factor as compared to NLC. Lipid nanoparticle occlusion factor depends on lipid concentration, crystallinity, and particle size. The connections shown in the sequence assume that two of the three stated parameters are set equal for comparative purposes. Reducing particle size typically increases particle number, creating a denser coating with a larger occlusion factor. The same mechanism is validated by increasing the lipid concentration.

4. *Loading Capacity*
SLN has a low loading capacity of around 10% of the lipid, resulting in only 1% of the ultimate dispersion to maintain system stability. This is owing to the solid lipid matrix's unique properties, particularly for APIs with moderate lipophilicity. Therefore, both the physicochemical properties of the active drug and the lipid must be considered. Mehnert's analysis [26,27] highlights issues such as limited drug payload and ejection during storage (Figure 2). NLC was created to address the disadvantages of SLN. They are considered the second generation of lipid nanoparticles. NLC has a larger loading capacity for active compounds than SLN because to its less ordered solid lipid matrix. This is done by blending a liquid lipid with a solid lipid, resulting in higher particle drug loading. NLC has a higher drug loading capacity than SLN and reduces the risk of drug expulsion during storage. [28, 29]

5. *Skin Hydration and Elasticity*
Occlusion reduces trans epidermal water loss (TEWL), resulting in increased skin hydration after applying SLN, NLC, or their formulations. An in-vivo investigation found that SLN-containing o/w cream significantly enhanced skin hydration compared to standard o/w creams. This study compared the skin hydration effects of an o/w cream with SLN to a standard o/w cream over 28 days. Müller et al. [30] showed that an NLC-containing cream increased skin moisture significantly more than a regular cream.

6. *UV blocking effect*
UV Blocking Effect Wissing et al. [22] found that SLN can both act as a physical UV blocker and enhance UV protection when combined with organic sunscreens like 2-hydroxy-4-methoxy benzophenone. This allows for a lower concentration of the UV absorber. Lipid nanoparticle-containing formulations can reduce organic sunscreen use by 50% while providing the same level of protection as conventional emulsions [31]. Encapsulating inorganic sunscreens like titanium dioxide in NLC has been shown to significantly improve SPF by up to 50 [32].

CONCLUSION

In conclusion, nano lipid carriers have shown great potential in the field of cosmetics due to their ability to improve the stability, bioavailability, and efficacy of active ingredients. These carriers are able to efficiently penetrate the skin barrier and deliver the active ingredients to the target site, resulting in enhanced performance of cosmetic products. The use of nano lipid carriers can help to address various skin concerns such as aging, hyperpigmentation, and dehydration, making them a valuable tool for formulators and cosmetic companies. Further research and development in this area are warranted to explore the full potential of nano lipid carriers in cosmetic formulations. SLN and NLC are very well-tolerated carrier systems that are not specifically developed for, but are exceptionally effective at, assessing controlled release of cosmetic and medicinal cutaneous goods. Taking advantage of nanotechnology's benefits, these carrier systems overcome the fact that the skin is refractive to most molecules, particularly hydrophilic ones, despite the presence of trans-barrier pathways. The first lipid nanoparticle-based cosmetic product was released to the market in 2005, showing that the mentioned technology is still in its early stages in terms of future potential. This revolutionary technology has demonstrated its appropriateness, as evidenced by the availability of many goods on the market after only five years, as well as the acquisition of multiple patent rights by various companies within that time frame.

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