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Review

Lipid Nanoparticles Based Cosmetics with Potential Application in Alleviating Skin Disorders

Javed Ahmad

Department of Pharmaceutics, College of Pharmacy, Najran University, Najran 11001, Saudi Arabia; jahmad18@gmail.com or jaahmed@nu.edu.sa

Abstract: The lipids mainly oils, fats, waxes and phospholipids are of substantial importance in the development and functioning of cosmetic products. The lipid nanoparticles-based cosmetic product is highly capable of protecting the skin against harmful radiations and is utilized for anti-aging therapy. Naturally derived antioxidants such as carotenoids, retinoids and tocopherols could be employed for their antioxidant properties as therapeutics and skincare active moieties in cosmetic products. Such a lipid nanoparticles-based cosmetic formulation consisting of antioxidants are very effective against irritated and inflamed skin and very promising for treating skin disorders such as atopic dermatitis and psoriasis. Therefore, the present review provides an insight into lipid nanoparticles based cosmetics and the mechanistic of their percutaneous absorption. The manuscript discussion highlights the role of lipid nanoparticles-based cosmetics/cosmeceuticals employing active ingredients of synthetic and natural origin in alleviating dermatological disorders and enhancing skin health and appeal. Furthermore, the manuscript also updates about contemporary research studies carried on the concept of lipid nanoparticles based formulation design of cosmetic preparation and significant outcome to alleviate skin disorders.

Keywords: lipid nanoparticles; cosmetics; cosmeceuticals; percutaneous absorption; antioxidants; skin disorders

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1. Introduction

The application of cosmetic products has been vital since a long time. However, currently, the significance of cosmetic products has repositioned itself towards therapeutic as well as nutritional products that extend to skin health and further the cure of dermatological disorders. Cosmetic products with the potential of disease prevention play a vital role in augmenting the annual growth for cosmetic products in the market. Nutritionists, pharmacists and physicians have made monumental efforts in fabrication of cosmetic products which have potential therapeutic or nutritional value in order to gratify the demands and requirements of the consumer [1–3].

The novel cosmetic products are launched at a very fast pace in a highly dynamic cosmetic market which can be attributed to the introduction of a novel lipid-based nanoparticulate system. Lipid nanoparticles encapsulated active ingredient-based cosmetics offer mounting advantages of enhanced skin penetration into the deeper strata of skin layers, sustain and targeted release of active ingredient to cellular and subcellular regions, and improved overall functionality of the final product with potential cosmetic cum therapeutic effect [4,5]. The delivery of active ingredients loaded lipid nanoparticles based cosmetics gives a new meaning to cosmetics which is way more than just beauty enhancing products. Cosmetic products that are effective in treating dermatological disorders along with providing glow to the skin are in great demand right now [4,5]. The definition of cosmetic products have been revolutionized with the focus now being shifted to influx of therapeutically efficacious cosmetics which is considered as "cosmotherapy".

The term "cosmeceutical", coined by Kligman, is the amalgamation of cosmetics and pharmaceuticals which is defined as the product constituting ingredients intended for

either personal and/or therapeutic use [6]. The cosmeceuticals encompasses a number of products which include creams, lotions, ointments and ingestible beauty products which can be in the form of liquids, pills and functional foods. These cosmeceutical products particularly contain ingredients or nutrients having the ability to promote healthy skin, hair and nails and may include vitamins, minerals, plant extracts and antioxidants [7–9]. However, in the present manuscript, the cosmetic preparations which are specifically applied to the skin to treat skin disorders and help in maintaining good skin health are discussed in detail. This cosmo-therapeutic approach is different from cosmeceuticals as it does not cover ingestible beauty products and the products containing nutrients. The focus is mainly on prevention and cure of dermatological diseases such as acne, dermatitis, psoriasis along with keeping the beauty of skin intact. The present manuscript encourages the use of natural ingredients in treating dermatological disorders however, it also includes the cosmotherapy with pharmaceutical drugs.

Nano-based technology has further added to the enhanced efficacy of cosmetics products. For instance, nanosized sunscreens containing ZnO or TiO_2 nanoparticles offer significantly better performance than micron-sized ones [10]. The present review provides an insight into lipid nanoparticles based cosmetics and the mechanistic of their percutaneous absorption. The review highlights the role of lipid nanoparticle-based cosmetic preparations in alleviating dermatological disorders. Furthermore, the manuscript also updates about contemporary research studies carried on the concept of cosmo-therapeutic approach in order to design lipid nanoparticles based cosmetic preparations.

2. Lipid Nanoparticles Utilized in Formulation Design of Nanocosmetics

The essential fatty acids and triglycerides containing unsaturated fatty acids are the cornerstones of cosmetic product's composition and development [11,12]. The oils having linoleic and α-linolenic acid in high content are vital in preventing eczemas or atopic dermatitis. Such essential fatty acids integrate within the cell membranes and restore the damaged lipid barrier of the epidermis and prevent water loss. The unsaturated fatty acids contribute substantially to the healing of the inflamed skin and are often used as an integral component of cosmetic preparation [11,12]. The lipid nanoparticles-based cosmetic products possess tremendous chemical stability, remarkable skin compatibility and significantly protect skin against radiation and aging [11].

Lipid nanoparticle based cosmetics have garnered substantial attention in the past few decades owing to their biocompatibility, safety and enhanced functionality. The lipidic nanocargos contribute significantly to cosmetic preparations targeted for dermal disease prevention because of their higher loading and modulated active ingredient release properties. Their small particle size ranged 1–100 nm and high specific surface area by volume which is greater than 60 m^2/cm^3 make them ideal carrier candidates for constituting active ingredients in cosmetic products [13–15]. An active ingredient-loaded lipid nanoparticle based cosmetic/cosmeceutical results in specialized function in healing dermatological disorders attributed to enhanced penetration, modulated drug release, local targeting and minimal toxicity. The role of lipid nanoparticles-based cosmetics/cosmeceuticals in treating dermatological disorders is discussed in detail in the upcoming sections. The small size, high loading and capabilities to prolong the release of the active ingredient, distinctive internalization routes, selectivity, local targeting, biocompatibility and safety are the distinct attributes of lipid nanoparticles based cosmetics which has made them stand tall in the plethora of other nanoparticulate formulations that can be utilized in cosmetic preparations [15].

There are different classes of lipid-based nanoparticulate systems that are utilized in cosmetic products such as solid lipid nanoparticles (SLN), nanostructured lipid carriers (NLC), liposomes and nanoemulsions. Nanoemulsions which are colloidal dispersion of nanoscale droplets of one fluid within another fluid are being widely used in skincare products, deodorants, sunscreens and hair care products. Their notable characteristic

feature of rapid penetration, assimilating textures and hydration capability allows their inclusive utility in skin delivery of cosmetics [16–18].

In the early 90s, Muller and Gasco introduced a lipid-based nanoparticulate system which is continuously modifying with a more advanced and smart generation of lipid nanoparticles [19]. From the perspective of cosmetic utility, lipid-based nano delivery systems can be broadly classified as liposomes and smart generation lipid nanoparticles (including particularly SLN and NLC) [20]. Liposomes can be defined as spherically shaped microscopic vesicles that consist of an aqueous core surrounded by one or more phospholipid bilayer membranes. The most commonly used phospholipids are phosphatidylcholine and phosphatidylethanolamine. Liposomes are among the core lipid-based nano delivery systems that are used in cosmotherapy to deliver therapeutic agents [21,22]. The first commercially launched cosmetic product based on liposomes as nanocosmetics was an anti-aging cream known as 'Capture' (by Dior in 1986) [21,22]. The key ingredient of liposomes is phosphatidylcholine which has skin-softening attributes and thus, has invincible utility in dermatological and skincare products [21]. The liposome can be efficaciously used to encapsulate both hydrophilic and lipophilic active ingredients intended for therapeutic or cosmetic purposes. Furthermore, the major attraction of liposomal mediated delivery in cosmotherapy is their biocompatibility, biodegradability, low toxicity and site-specific active ingredient delivery. Nonetheless, liposomes do suffer a setback due to their low solubility and short half-life [22–24].

The next category of lipid-based nano delivery system consists of advanced and smarter generation lipidic nanocargos namely SLN and NLC as depicted in Figure 1. SLN and NLC are peculiar categories of lipid nanoparticles owing to their unique matrix composition. SLN is chiefly constituted of solid lipids particularly fatty acids, waxes, glycerides and triglycerides whereas the NLC matrix is an imperfect hybrid of solid lipids and liquid lipids [13,14,20,25,26]. Both SLN and NLC are currently being explicitly explored in the field of cosmotherapy. These novel formulations specifically offer advantages of skin adhesion, enhanced hydration, substantial penetration, improvised and controlled release of the active ingredient, avoidance of systemic uptake and improved percutaneous absorption [25–27]. The imperfections in the NLC matrix structure results in higher active ingredient loading capacity and mitigated expulsion during storage in contrast to SLN [13,26]. The comparable structures of SLN and epidermal lipid in the skin make SLN an ideal nanoparticle for transdermal delivery of active ingredients in cosmotherapy. However, due to the presence of solid lipid in SLN, the lipid particles tend to form crystals resulting in recrystallization. This is one of the major drawbacks with SLN leading to the reduced loading capacity of active ingredients [14,25,26].

The liposomes, SLN and NLC have outstanding adhesion properties when they come in contact with the skin surface [26]. It has been established by various studies that lipid nanoparticles of 200 nm size range can efficiently form hydrophobic monolayers when applied in fixed concentration on the skin [21,25,26]. These hydrophobic monolayers prevent loss of water by forming moisture cover over the skin surface. This property of the lipid nanoparticles system is explicitly utilized to address occlusion and hydration concerns in cosmetic products.

The next-generation lipid nanoparticles—SLN and NLC have found enormous potential application in delivering active ingredients and treating dermatological disorders along with remarkable skincare attributes. These formulations are being intricately worked upon by researchers worldwide to come up with excellent cosmetic products having tremendous healing potential of skin disorders with concomitant skin-beautifying attributes. The list of commercially available lipid nanoparticles-based cosmetic products is presented in Table 1.

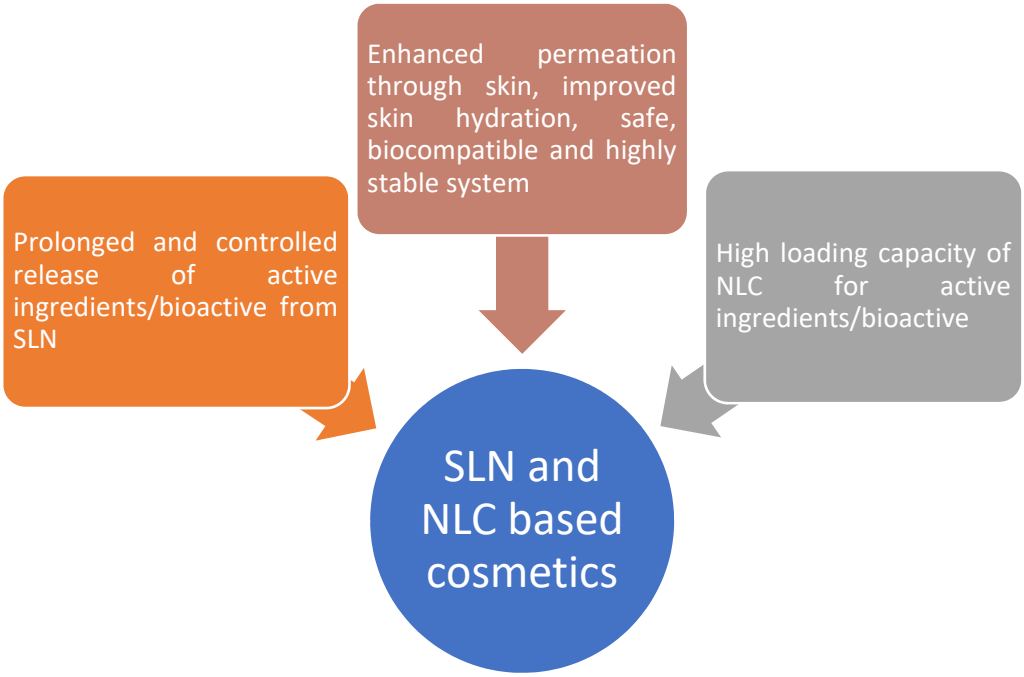

Figure 1. Advantages of solid lipid nanoparticles (SLN) and nanostructured lipid carrier (NLC) based cosmetic products.

Table 1. Lipid nanoparticles-based cosmetics products in the market.

Product Name	Active Ingredient	Manufacturer
NanoLipid Repair CLR	Black currant seed oil and manuka oil	Chemisches Laboratorium Dr. Kurt Richter, CLR—Berlin, Germany
Cutanova Cream Nano Repair Q10	Coenzyme Q10, polypeptide, hibiscus extract, ginger extract, ketosugar	Dr. Rimpler GmbH, Wedemark, Germany
Intensive Serum NanoRepair Q10	Coenzyme Q10, polypeptide, mafane extract	Dr. Rimpler GmbH, Wedemark, Germany
Cutanova Cream NanoVital Q10	Coenzyme Q10, TiO_2, polypeptide, ursolic acid, oleanolic acid, sunflower seed extract	Dr. Rimpler GmbH, Wedemark, Germany
NLC deep effect repair cream	Q10, TiO_2, highly active oligo saccharides	Beate Johnen GmbH, Aschheim, Germany
Extra moist softener	Coenzyme Q10, -3 und -6 unsaturated fatty acids	Amorepacific Corp. Seoul, South Korea
Regenerations creme intensive	*M. ternifolia* seed oil, avocado, urea, black currant seed scholl oil	Scholl, Mannheim, Germany
SURMER Crème	kukuinut oil, Monoi Tiare Tahiti®, pseudopeptide, hydrolyzed wheat protein	Lancray International S.A. Paris, France
Olivenol Augenpflegebalsam	Senegal, Tocopheryl Acetate *Olea Europaea* Oil, *Prunus Amygdalus Dulcis* Oil, Hydrolized Milk Protein, Tocopheryl Acetate, *Rhodiola rosea*, Root Extract, Caffeine	Dr. Theiss Naturwaren GmbH, Homburg, Germany
Swiss Cellular White Illuminating Eye Essence	Glycoprotiens, *Panax ginseng* root extract, *Equisetum Arvense* extract	Laboratoires La Prairie SA, Volketswil, Zurich, Switzerland

3. Mechanism of Percutaneous Absorption and Release of Active Ingredient from Lipid Nanoparticles Based Cosmetics

The three major layers of the skin are classified as the dermis, viable epidermis and stratum corneum. The existence of blood vessels, sweat glands and hair follicles account for the complex structure of the skin. The foremost layer, i.e., stratum corneum (SC), constitutes the key skin barrier, is also called the horny layer. The stratum corneum is made up of tightly crammed keratinized cells. The intercellular places present in SC are filled with non-polar lipids and heterogeneous bilayers [27].

Routes for penetration into the skin can be broadly classified into three main categories as depicted in Figure 2: (a) corneocytes and superseding lipids which constitut the most preferred way for lipophilic compounds (b) sequential hydrophilic areas in lipid bilayers make up for the main route for the transport of active ingredients (c) skin appendageal transport is the prime route for infiltration of particulate systems and iontophoretic passage of charged molecules [28,29].

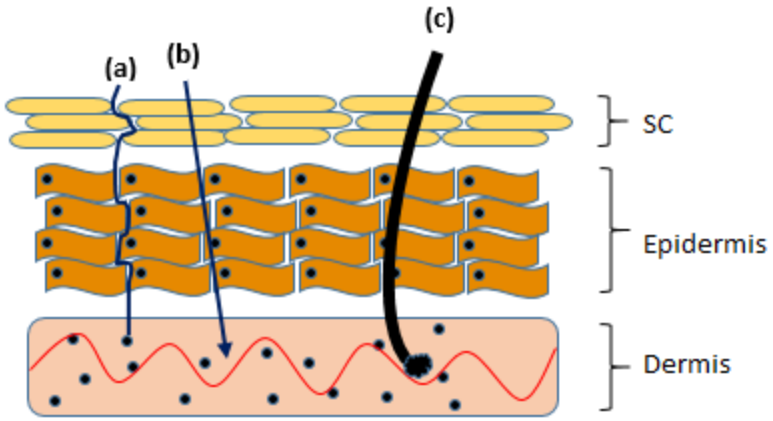

Figure 2. The figure depicts probable permeation routes (**a**–**c**) for lipid nanoparticles loaded with active ingredients/bioactive in a cosmetic product upon skin application. The uppermost layer of skin is the stratum corneum (SC) consisting of corneocytes and lipids. The second layer is the epidermis subsequent to the dermis. The lipid nanoparticles travel through either of these routes (**a**) intercellular through lipid bilayers, (**b**) transcellular through corneocytes and (**c**) shunt through hair follicles and sweat glands.

Skin acts as the first line of defense for any external stimuli, and is also the largest sense organ in the human body. Therefore, dermal absorption is of the utmost importance and requires special attention. Permeation of lipid nanoparticles through the skin depends upon their properties such as surface morphology, charge and particle size (Figure 3). Usually negative surface charge or zeta potential and smaller particle size favor transdermal penetration. The microenvironment around lipid nanoparticles has substantial influence in affecting the release of active ingredients for instance. presence of moisture or lipids would aid hydration/dissolution and thus permeation of lipid nanoparticles. Importantly, the route of penetration largely governs the release of active ingredients from lipid nanoparticles. Furthermore, the hydrophilic-lipophilic balance (HLB) of incorporated surfactant in lipid nanoparticles could be used as a penetration enhancement strategy for improving the release of active ingredient-loaded lipid nanoparticles. Intercellular, transcellular/trans appendageal routes are cited as possible pathways for dermal drug delivery through nanoparticles as per available literature which may follow passing over the epidermal layer and dermis and then to the blood vessels [21].

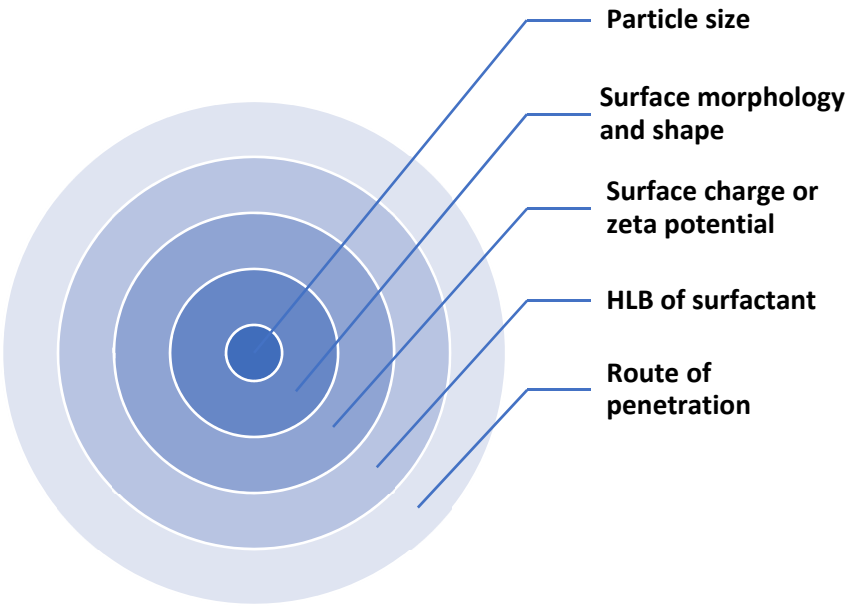

Figure 3. Major factors affecting percutaneous permeation and release kinetics of lipid nanoparticles loaded with active ingredients/bioactive. HLB = hydrophilic-lipophilic balance.

3.1. Release of Active Ingredients/Bioactive from Lipid Nanoparticles Based Cosmetic Product

Novel lipid nanoparticles-based drug delivery is an effort to achieve prolonged drug release with minimal adverse effects. Controlled release, adjacent to the target organ to a specific cell type via these systems, can also be achieved by localizing active substances through the use of carriers [30].

Comparative study of different models of drug release through a carrier needs to be carried out to understand their drug release profile. Multiple factors exert their effects on the active ingredient's pattern of release from lipid nanoparticles such as concentration of the active ingredient in a lipid matrix, particles size, type of surfactant, lipid matrix and nature of active moiety. There should be an in vitro in vivo correlation between drug release and the environment of the release site. The composition of nanoparticles and their enzymatic degradation are also relatable to some extent [31].

Liposomes can provide continuous and prolonged release of the active ingredient to target skin sites to ensure optimum efficacy of the cosmo-therapy [32]. Three models define drug release from SLN's viz. lipid core with active component supplemented shell, lipid shell with active component supplemented core and homogenous matrix [33]. Some factors that affect drug release from NLC's include manufacturing temperature, the proportion of oil in the matrix of lipid and surfactant composition [34]. For active ingredient release, there are two types of behaviors expected by NLC's viz, burst release from the outer part of the nanoparticles shell impregnated with active moiety and continuous release of the active substance from the augmented cores. Prolonged-release of active ingredients from NLC's can be attributed to the partitioning of the active moiety between water and the lipophilic matrix and the role of the interfacial membrane which acts as a barricade for passage of the active ingredient [35,36].

3.2. Mechanism of Absorption of Lipid Nanoparticles Based Cosmetic Products across Skin Layers

The uppermost layer of skin SC plays vital functions in maintaining sound skin health and functioning that specifically include prevention of excessive water loss and averting penetration of xenobiotics across the dermal layers. Corneocytes and intercellular lipids, which are enclosed in a covering of highly crosslinked proteins (loricrin, filaggrin), are the chief components of SC. Corneocytes and lipids are accountable for retaining optimal water gradients that keep SC adequately hydrated [37]. The lipids present in cosmetic products such as phosphatidylcholine contribute largely to enhancing skin humidity and emollient

properties. Certainly, phosphatidyl lecithins present in creams, lotions and shampoos play a crucial role in imparting skin softening properties. Moreover, the surfactants and polar lipids present in lipid nanoparticles-based cosmetics are also among the crucial components in maintaining skin functionality and health and more importantly guarding the skin from various diseases [38].

3.3. Permeation of Lipid Nanoparticles through Follicular Routes

Hair follicles as can be seen in Figure 2c represent an alternative and potential penetration route for lipid nanoparticles particularly SLN and NLC. Hair follicle predominantly constitutes of sebum milieu which is composed of lipid, waxes and squalene. The comparability of lipids in sebum and SLN and NLC facilitates the deeper and remarkable penetration of these lipid nanoparticles across the skin. The subsequent release of active ingredients is attributed to the erosion or dissolution of the lipid matrix in sebum. Therefore, hair follicles exemplify a substantial penetration route for deeper penetration of lipid nanoparticles in comparison to SC. In SC layers the lipid nanoparticles are mostly accumulated on the surface whereas, through the follicular route, a preferential interaction between the lipid matrix of SLN and NLC dispersion and sebum expedites deeper percutaneous absorption [39].

4. Significance of Lipid Nanoparticles Based Cosmetics Utilized in Targeting Cutaneous Inflammations

The lipid nanoparticles such as liposomes, SLNs and NLCs are often employed as carriers of chemically labile agents such as vitamin E in order to prevent the chemical degradation of incorporated components [40]. Furthermore, lipid nanoparticles are also very useful in the delivery of different forms of active ingredients efficiently for treating skin disorders. The ability of lipid nanoparticles to get incorporated into aqueous dispersions keeping their physical stability intact and subsequent mixing with dermal formulations such as cream to form an adhesive film with potential occlusive effect is of extreme significance. Such occlusive influence accelerates the penetration of cosmetic formulation into the skin resulting in enhanced therapeutic effect [37,38]. In this section, the potential of lipid nanoparticles-based cosmetics/cosmeceuticals in alleviating dermatological disorders is highlighted.

4.1. Lipid Nanoparticles Based Cosmetics/Cosmeceuticals and Acne

Acne is among the most widespread dermatological disorders in adolescence. There is an ample number of cosmetic preparation available in the market that claims to treat acne. However, their associated side-effect overshadows their beneficial and therapeutic effects. The introduction of lipid nanoparticles in cosmetics successfully overcome the toxicity concerns associated with anti-acne cosmetic products by significantly improving the dermal localization of anti-acne agents [41]. In a study by Munster and associates, SLN were used as carriers of nonsteroidal antiandrogen prodrug RU 58841 myristate (RUM) intended for follicular targeting [42]. The study findings demonstrated that RUM-loaded SLN were efficiently taken up by follicles and then prepared formulation was localized and confined in the upper layers of skin. The study outcomes confirmed the significantly improved acne therapy as a result of SLN facilitated local depot formation that mediates sustain release of the antiaging agent in addition to impeding its systemic absorption.

4.2. Lipid Nanoparticles Based Cosmetics/Cosmeceuticals and Skin Mycoses

The fungal infections of the skin are very prevalent and afflicting skin diseases. To treat such superficial infections, cosmetic products having antifungal agents are applied topically [43]. The advanced generation lipid nanoparticles SLN and NLC have been investigated by different researchers worldwide to validate their potential in enhancing the antifungal efficacy of cosmetic products. Antifungal agents, particularly clotrimazole and ketoconazole, are most frequently used in treating skin mycoses. These antifungal drugs were encapsulated in SLN and NLC based cosmetic preparation to investigate their

therapeutic efficacy. Souto and coworkers developed clotrimazole-encapsulated lipid nanoparticles (both SLN and NLC) and observed delayed and sustained antifungal effects with SLN whereas immediate and fast therapeutic effects with NLC. The difference in the therapeutic effect is certainly attributed to prolonged release of clotrimazole from solid lipid integrated SLN in contrast to fast release rate from hybrid lipid matrix from NLC. The prolonged therapeutic effect as observed with SLN is desirable in enhancing the therapeutic efficacy of cosmetic preparations to treat skin disorders such as mycoses [44,45].

In a study, Sanna and associates formulated econazole nitrate-loaded SLN and found out the rigorously controlled release and multifold enhanced diffusion of an antifungal agent in comparison to a standard product. They concluded the enhanced and controlled permeation of antifungal agents through SLN is mainly attributed to lipid content and particle size [46,47]. Moreover, Bhalekar and associates investigated miconazole nitrate-loaded SLN formulation for its influence on the permeation profile of the drug through the skin [48]. The study outcomes revealed significantly increased permeation of miconazole through SLN in comparison to marketed gel. Nonetheless in a study by Jain and coworkers, miconazole nitrate-loaded SLN exhibited long-lasting drug release for over 24-h with concomitant 10-folds greater retention in comparison with reference products [49].

4.3. Lipid Nanoparticles Based Cosmetics/Cosmeceuticals and Psoriasis

Some skin disorders immensely threaten the quality of life of suffering patients. One such disorder is psoriasis which is a chronic inflammatory skin disorder characterized by redness, itchy scaly patches, most commonly on the knees, elbows, trunk and scalp. Even though there are plenty of creams, ointments and gels available on the market to treat symptoms of psoriasis, certain drawbacks mainly toxic side effects drastically limit their use in therapy. However, lipid nanoparticles such as SLN and NLC have the potential to substantially improve the efficacy and safety of topical products. In a study by Lin and associates, the combination of calcipotriol and methotrexate was loaded in NLC to study its efficiency in treating psoriasis [50]. The permeation profile of each drug alone or in the association was examined by employing hyperproliferative skin as a permeation barrier. The study outcomes demonstrated that the permeation of calcipotriol from NLC was slightly increased in comparison to the hydro-alcoholic gel used as reference formulation, whereas the amount of methotrexate permeated across skin was significantly higher as compared to control formulation.

4.4. Lipid Nanoparticles Based Cosmetics/Cosmeceuticals and Atopic Dermatitis

Another intriguing skin disorder that is long-lasting and difficult to treat is atopic dermatitis which is a chronic relapsing form of eczema characterized by inflamed skin [51]. For treating atopic dermatitis, tacrolimus is the immunosuppressive drug of choice. Nonetheless localized delivery of tacrolimus to the infected site with minimum possible side effects is challenging. Encapsulating tacrolimus in lipid nanoparticles could prove promising in treating such an order with much reduced toxic effect. In a study by Pople and coworkers tacrolimus-loaded lipid nanoparticles was developed and investigated for targeted and localized delivery of drug in different skin layers [52]. The results of in vitro studies demonstrated significantly increased drug release, skin penetration and skin accumulation as compared with a marketed product. The study was evidence of the reach of tacrolimus to deeper skin layer where specific cells, accountable for the immunopathogenesis of atopic dermatitis, mainly reside through lipid nanoparticles.

4.5. Other Specialized Applications of Lipid Nanoparticles Based Cosmetics/Cosmeceuticals

At present, treatment of hair loss has grabbed huge attention and has provided a landscape of research area for scientists to work upon. Lipid nanoparticles have been tried by various researchers to come up with promising results. It is well established that minoxidil, which is an antihypertensive exhibits an interesting side effect of hair growth. However, the major limitation with minoxidil is the redness or irritation at the treated area.

Moreover, alcohol content present in topical preparations results in drying of the scalp and dandruff. To address this issue Silva and coworkers developed minoxidil-encapsulated NLC to subside conventional topical alcoholic solutions [53]. The developed formulation proved to be a safe and effective alternative to topical alcoholic solutions. More recently Padois and associates developed minoxidil-encapsulated SLN and concluded that the developed SLN suspension was having enhanced penetration and was non-corrosive in contrast to marketed products [54].

5. Contemporary Research Signify the Role of Lipid Nanoparticles Based Cosmetic/Cosmeceutical Product Development

The conventional approach for treating skin disorders such as acne, psoriasis, atopic dermatitis is founded on antibiotics or steroids loaded as a therapeutic agent in cosmetic products. Certainly, the synthetic drugs in cosmetic products are accompanied by severe side effects and restrict patient compliance. These days special attention is being given to the use of a naturally derived therapeutic agent in lipid nanoparticles-based cosmetic products [55]. The approach of treating skin disorders and enhancing skin health and appeal using herbal or naturally derived active ingredients in lipid nanoparticles-based cosmetic products can be called bio-cosmo-therapy. Arduous efforts are being made by researchers worldwide to develop cosmetic products in accordance with bio-cosmo-therapy.

Very recently Arsenie and co-workers developed an NLC formulation with efficient loading of three bio-actives, azelaic acid, white willow bark extract and panthenol to enhance skin hydration and antioxidant action. The developed NLC formulation improved the reconstruction of epidermal cells and significantly reduced hemolysis. The incorporation of developed NLC into a Carbopol gel stemmed from a sophisticated cosmetic formulation with a substantially high hydration effect. The research work came up with novel bio-cosmo-therapy based NLC cosmetic formulations for dual application in acne and atopic dermatitis [55].

In acne treatment retinol and retinoids play significant roles, however, keeping their photostability intact in cosmetic preparation is challenging. In a study, Tretinoin-loaded SLN-based gels were developed by Mandawgade and co-workers using purified grade stearine acquired from fruit kernel fats [56]. They developed a formulation that exhibited reduced skin irritation, good skin compatibility, enhanced occlusive effect and sustained release of active ingredients and thus proved better cosmetic preparation for treating acne in comparison to marketed product [57]. Furthermore, all-trans retinoic acid (ATRA)-loaded SLN developed by Castro and associates using glyceryl behenate as solid lipid demonstrated a marked comedolytic effect comparable to that of commercially available products. However, the important finding of the study was that the developed formulation was able to significantly reduce ATRA-induced skin irritation which is the major setback of commercially available products.

Psoralen is a naturally occurring furocoumarin in the seeds of Psoralea corylifolia and is most frequently used to treat Psoriasis. In a study, Fang and associates investigated the percutaneous absorption of psoralen derivatives from SLN and NLC by employing mice skin as permeation membrane [58]. The study findings confirmed enhanced permeation and controlled release of psoralen delivery from NLC. Furthermore, acitretin is another widely used herbal ingredient in the treatment of severe forms of psoriasis. Agrawal and coworkers prepared acitretin-loaded NLC which is further incorporated in gel base [59]. The study outcomes demonstrated significantly high deposition of acitretin in human cadaver skin from the acitretin-NLC gel in comparison to reference gel. The clinical study confirmed remarkable enhancement in therapeutic response along with the concomitant reduction in toxic effects through acitretin-NLC-gel.

In an interesting study by Lacatusu and associates, NLC based hydrogel was developed which is constituted of phytochemicals- carrot extract and marigold extract having substantial health benefits [60]. The study outcome established significantly improved therapeutic response attributed to cumulative antioxidant, anti-inflammatory and anti-acne effects, along with the absence of any adverse reaction. Additionally, the degree of skin

hydration and elasticity were substantially enhanced by the application of developed phytochemical-loaded NLC hydrogel.

In a recent study by Masiero and associates, it has been demonstrated that lipid nanoparticles containing vegetable oils vehave superior efficacy compared to commercial therapy, which highlights their promising use in cosmetic products intended for treating skin disorders with a safer and more effective approach [61].

Such investigations strongly encourage the cosmetic industry to design novel lipid nanoparticles based bio-cosmo therapeutic products that are bestowed with tremendous health benefits along with concomitant therapeutic (antioxidant, anti-inflammatory and anti-acne actions) and skin appeal enhancing (hydration and elasticity) prospects. The most important aspect of such products would be achieving improved therapeutic efficacy and skin appeal based on completely assured safety grounds.

6. Opportunities and Challenges of Lipid Nanoparticles Based Cosmetic Products

The cosmetic market calls for novel discoveries that ensure the safety and efficacy of the developed products. The lipid nanoparticles constituted cosmetic products vehad substantial accountability for safety and enhanced functionality. The foremost benefits associated with lipid nanoparticles are the capability to boost the penetration of active ingredients into the skin augmenting treatment efficiency. Lipid nanoparticles chiefly target the epidermis and deeper layers of skin by restricting reduce the systemic absorption and consequently minimize the untoward effects of active ingredients or therapeutics. The complete biodegradation of lipid nanoparticles has garnered their special place and credibility in the plethora of other nanoparticulate systems of metallic or inorganic origin. Further, the potential of lipid nanoparticles to carry and release active ingredients across deeper layers of skin has led to promising prospects of cosmetic/cosmeceutical products beyond simply adorning the skin.

The future challenge of lipid nanoparticles constituted cosmetics could be to improve the wellness of the skin by tackling important functional issues to meet the demands of the consumers. Novel herbal raw materials and excipients are needed to be explored to meet growing market needs. There is a great need to explore the possibility of using novel lipid matrices and surfactants that can be better tolerated. A broader choice of lipid raw materials could strengthen industrial research in this area. The setting up of important industrial processes should be facilitated such as spray drying which is not utilized until today and needs to be explored for its untapped potential [20,21].

7. Conclusions

The current scenario calls for safe cosmetic products, consisting of naturally derived active ingredients and excipients, and possessing therapeutic cum beautifying application. SLN, NLC and liposomes are potential lipid-based nanocarriers, or we can say tools, that play a significant role in enhancing the activity of such bioactive and embellishing appeal of cosmetic products. Moreover, utilizing bioactive ingredients or therapeutics of natural origin in cosmetic preparation multiplies the commercial and clinical value of cosmetic products. The role of lipid nanoparticles-based cosmetics/cosmeceuticals for skin application employing bioactive ingredients and the active moiety of synthetic/herbal origin for alleviating skin disorders could be of significant importance for the researchers working in this area. Such comprehensive insights into the potential of lipid nanoparticles-based cosmetics/cosmeceuticals deserve to be taken from small-scale research laboratories to large-scale industrial stage after further clinical investigation for its safety and efficacy.

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