Nanoemulsions for Topical Skin Delivery: Recent Advances

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***Abstract*—The stratum corneum provides an immense physiological impediment to the delivery of pharmaceuticals and cosmeceuticals to the skin and often reduces the effectiveness of conventional topical delivery formulations through insolubility, low skin permeability, and active chemical instability. The excellent nanocarrier capacity to bypass barrier impairments arises with nanoemulsions - isotropic, thermodynamically stable colloidal dispersions containing droplet dispersions within the nanometer range (10-200 nm). The aim herein is to have a cumulative understanding of new progress in the formulation and design of topical nanoemulsions. Principles that make nanoemulsions and microemulsions different especially selection of core excipients, strategies in preparation and physical-chemical characterization methods coupled with the penetration mechanisms are highlighted, followed by the diverse applications in skin disorders (psoriasis, acne, wound healing, oncology) with anti-inflammatory effect, as well as in cosmeceutical product for depigmentation of skin pigment targeting melanogenesis route by stabilized actives, such as kojic dipalmitate, arbutin, bakuchiol and multi-targeted system. Developments on hybrid nanoemulgels, pickering nanoemulsions, ionic liquid-based nanoemulsions together with considerations of intoxication, scale-up, and regulatory affairs, are additionally described.**

***Index Terms*—Nanoemulsions, Topical skin delivery, Nanoemulgel, Cosmeceuticals, Dermal therapeutics**

I. Introduction

The skin barrier is the primary physiological protection from external sources of damage and provides a major barrier to the effective use of topical and transdermal formulations. Barrier function is mainly located in the stratum corneum, which is the outer skin layer that has the particular morphology described as “brick-and-mortar.” In the brick-and-mortar construction, corneocytes (“bricks”) loaded with proteins are placed in a continuous lipid matrix (“mortar”), which is made of ceramides, cholesterol, and free fatty acids arranged as densely packed lamellar structures [1,2]. The passive permeation of active pharmaceutical substances (APIs) and cosmeceuticals is significantly impaired by some physicochemical limitations, when the suitable compounds should have the following properties: low molecular weight (≤500 Da), moderate lipophilicity (log P between 1 and 3), and good solubility. Therefore, traditional topical drugs such as ointments, macroemulsions, and creams are ineffective due to poor active solubility [3].
Nanotechnology-based delivery systems have revolutionized dermal therapies, overcoming the above structural barriers. The ultimate colloidal nanocarrier among other topical carriers employed so far for dermal delivery is the nanoemulsion (NE). It can be designated as an isotropic, thermodynamically unstable but kinetically stable macro- or microfluid dispersion consisting of thermodynamically immiscible oils and water, stabilized by amphiphilic surface films at the oil-water interface [2]. Nanoemulsions are clear dispersions consisting of spherical, monodisperse droplets with an average droplet size ranging from 10–200 nm. This small size provides a large surface-area-to-volume ratio, leading to an excellent affinity and increased interaction of these nanocarriers at the interface with the stratum corneum of the skin, enhancing the thermodynamic driving force to permeate drugs more effectively, thus promoting excellent stability against breakdown [4]. It has also been revealed that nanoemulsions act as a vehicle for delivering

hydrophilic/hydrophobic/essential oils/phytoconstituents and drugs, such as lipophilic depigmenting drugs that are unstable, safely down to cutaneous layers without triggering localized irritation and systemic toxicity [5]. In this review, an overall perspective on the basics of nanoemulsions, their mechanism of formation/ dynamics and high energy/low energy modes of preparation, characterization, application for clinical dermatologic indications and in cosmetic skin-brightening formulations has been studied in detail.

II. Nanoemulsions: Basic Concepts and Components

2.1 Thermodynamic vs Kinetic Stability

Understanding the differences between nanoemulsions, microemulsions, and common macroemulsions is important for developing meaningful formulations. Macroemulsions are systems in which there is kinetic instability and larger droplet sizes of 1 μm, where the effects of gravitational separation, creaming, sedimentation, flocculation, and coalescence can be seen with the flow of time. At the same time, microemulsions are thermodynamically stable systems that are spontaneously formed by mixing certain amounts of oil, water, and high amounts of surfactants/co-surfactants (usually higher than 20% w/w). When formulating microemulsions, the need of high amounts of surfactants leads to skin irritation, localised cytotoxicity, and poor formulation stability after dilution [6] .

Nanoemulsions occupy a different physical territory: they are thermodynamically metastable systems that are very stable from the kinetic point of view. Owing to the impressive Brownian motion of nano-drops (with a size of 10–200 nm), the ice kinetic energy is greater than the force of gravity, that eliminated the effect of creaming and sedimentation[7]. In addition, the created barrier (either electrostatic or steric) set by the surfactant layer creates a high level of kinetic barrier that prevents the coalescence process. As a result, nanoemulsions can be formulated using significantly lower surfactant concentrations (typically 5–10% w/w), making them far better tolerated on cutaneous tissue [8].

Table 1: Differences in sub-micron droplet scale, kinetic versus thermodynamic stability, required surfactant concentration, visual appearance, energy requirements for fabrication, and primary physical destabilization pathways

System Property	Macroemulsion	Microemulsion	Nanoemulsion
Droplet Size Range	$> 1000\,nm$ ($> 1\,\mu m$)	$10 - 100\,nm$	$10 - 200\,nm$
Thermodynamic Stability	Unstable	Thermodynamically Stable	Thermodynamically Metastable
Kinetic Stability	Unstable (quick s	High	Exceptionally High (long shelf-life)
Surfactant Concentration	Low ($1 - 5\%\,w/w$)	High ($> 20\%\,w/w$)	Moderate ($5 - 10\%\,w/w$)
Appearance	Opaque / Milky White	Transparent / Translucent	Transparent to Monodisperse Translucent

Preparation Energy	Low to Moderate	Low (Spontaneous)	High Energy or Specific Low Energy
Primary Breakdown Mode	Creaming, Coalescence	Phase Separation upon dilution	Ostwald Ripening

2.2 Core Formulation Components

The properties of a topical nanoemulsion, including its safety and stability, as well as its ability to encapsulate drugs, depend entirely on the types of its main components.

- The oil phase is responsible for dissolving lipophilic drugs and bioactive substances. This means that the oil phase is important because it determines the capacity of the preparation for active drug delivery to human skin. In general, oil phases are presented by either artificial medium chain triglycerides (MCTs), natural oils obtained from plants (such as olive, canola, and rose hip oils), or natural essential oils (like garlic, ginger, oregano, or tea tree). The use of essential oils in this context is twofold since they not only take over the function of oils but also represent powerful therapeutic agents [9].
- Surfactants are special types of molecules that appear at the oil-water interface and reduce the interfacial tension in no time. Nonionic surfactants are most commonly used in topical formulations because they do not irritate the skin and are completely safe for humans [10]. Nowadays, biodegradable glycolipid surfactants and lecithin are used instead of surfactants.
- Co-surfactants and co-solvents, such as alcohols (both short- and medium-chain) and polyethene glycol (PEG), are used [11].
- Aqueous phase and additives, such as purified water, act as the continuous phase of O/W nanoemulsion. Buffers such as phosphate buffers were used to set the pH to a value near the physiological pH of the skin (skin surface pH4.5-6.0). Antioxidants and chelating agents are used for chemical stability [12].

III. Preparation Methods of Nanoemulsions

Creating nanoemulsions necessitates breaking down large macro-droplets into smaller sub-micron droplets. The choice of manufacturing technique depends on the thermal sensitivity of the added substances, viscosity requirements, overall energy efficiency, and potential for industrial scaling. Two main approaches for emulsification processing can be identified: high-energy mechanical processes and low-energy chemical methods.

3.1 High-Energy Emulsification Procedures

High-energy procedures utilize particular engineering devices producing considerable shearing stresses, turbulence, and fragile cavitation forces to rupture the oil-water interface into nano sizes.
High-Pressure Homogenization (HPH): A macro-emulsion pre-blend is forced through a small homogenizer valve at great pressure (500-2000 bar). A sudden fall in the fluid pressure causes heavy hydraulic shear, impact, and cavitation forces, reducing large oil droplets to nanosized emulsions (30-150nm). HPH is a repeatable and scalable process but requires using heat exchangers to cool the heat induced during operations [13] .

Microfluidization is another emulsification method characterised by ultra-high-pressure pumps up to 20,000 psi to pump fluids through micro-engineered reaction micro-channels. Two opposed fluid streams collide at great speed in the mixing chamber, leading to the generation of high shear and impact forces[14] .

Ultrasonic Homogenization technology makes use of high-frequency waves (≥20 kHz) emitted from an ultrasonic probe to generate controlled cavitation in the liquid mix. The fast growth and collapse of microscopic cavitation bubbles results in the emergence of shear forces leading to the breaking up of droplets to 20-200nm. Although this method is suitable for laboratory formulation tests, there are issues related to possible probe erosion and problems with scale[15] .

3.2 Low-energy Emulsification Methods

Low-energy techniques rely on the inherent physical and chemical properties of surfactants and the phase changes occurring due to variations of the nature of the environment or the mixture composition.
Phase Inversion Temperature (PIT): This is used in the case of non-ionic polyoxyethylene surfactants, where the degree of hydration depends systematically on temperature. At ambient temperatures, the hydration layer of the surfactant generates O/W generation. As the temperature reaches the PIT value, the polyoxyethylene chains lose moisture and become hydrophobic, which produces the reversal of the phase into a W/O type of nanoemulsion with practically zero interfacial tension. As the temperature drops below the PIT value, the system is caught in the process of formation of nanoemulsion of O/W type [16].

Phase Inversion Composition (PIC)/Emulsion Phase Inversion (EIP): At constant temperature, progressive dilution of the oil-surfactant phase with the addition of water occurs. Continuous water input changes the spontaneous curvature of the surfactant monolayer, which results in a phase shift first passing through a bicontinuous or liquid crystalline phase and finally leading to the formation of tiny droplets [17].

Solvent Diffusion Method: Injection of water-miscible organic co-solvent (containing dissolved drug and oil) into continuous aqueous phase with surfactant. High diffusion of the organic solvent from oil to the continuous water phase results in strong interfacial turbulance, the spontaneous formation of nanodroplets. Further evaporation of organic solvent affords the resultant aqueous nanoemulsion [18].

Table 2: Summary of high-energy mechanical processes

Method	Mechanism	Range	Advantages	Limitations
High-Pressure Homogenization	Hydraulic hear, impact, cavitation via high-pressure valve	$30 - 150\ nm$	Scalable, highly reproducible, flexible	High energy input, thermal heating of heat-sensitive APIs
Microfluidization	Hyper-velocity micro-stream collision in micro-channels	$20 - 100\ nm$	Extremely narrow PDI, ultra-fine droplet control	High capital equipment cost, potential micro-channel clogging
Ultrasonic Homogenization	Acoustic cavitation bubble collapse	$20 - 200\ nm$	High lab-scale efficiency, simple operation	Titanium probe erosion, metal shedding, difficult scale-up

Phase Inversion Temperature (PIT)	Thermal hydration shift in non-ionic surfactants	$20 - 100\ nm$	Low energy, no high-shear machinery, gentle processing	Requires specific non-ionic ethoxylated surfactants
Phase Inversion Composition (PIC)	Compositional dilution changing surfactant monolayer curvature	$30 - 150\ nm$	Low energy, ambient processing conditions	Sensitive to dilution rate, complex phase diagram mapping

IV. Nanoemulsions for Topical Skin Delivery

4.1 Skin Architecture and Permeation Routes

Cutaneous drug delivery must overcome three primary anatomical barriers: the stratum corneum (10–20 m thick), the viable epidermis (50–100 m), and the dermis (inner layer). To accomplish this, drug delivery can occur via three routes:

- Intercellular Route: The intercellular route is the major route used by most drugs delivered through topical applications. The drugs diffuse through continuous lipid medium surrounding the corneocytes.
- Transcellular Route: The transcellular route means the drugs must cross from corneocytes to lipid layers repeatedly, requiring drugs to partition between highly hydrophilic keratin-rich layers and oily lipid layers.
- Transappendageal Route: The transappendageal route means drugs penetrate organs directly through hair follicles, sebaceous glands, and sweat glands. Although appendages occupy a small skin surface area, the pathway allows drugs to reach direct access to deep follicular reservoirs and highly branched capillary networks [19,20].

4.2 Mechanisms of Permeation Enhancement by Nanoemulsions

Nanoemulsions promote transdermal delivery via synergistic physical and biochemical mechanisms:

- The Lipid Fluidization of the Stratum Corneum: The surfactants and co-surfactants in nanoemulsions can be termed as chemical penetration enhancers. With application on the skin, these amphiphilic chemicals are inserted into the tightly packed ceramide-cholesterol bilayer of the stratum corneum, causing disruption of lipid packing, lowering of temperature of phase transition, and enhancement of lipid fluidity [18].
- Formation of High Thermodynamic Activity and Contact Surface area: The nano-size droplets (<200 nm) make sure that the area of contact of the container with the skin surface is much increased. The rapid evaporation or absorption of the volatile components of the container at the skin surface elevates the concentration of the drug and establishes the high thermodynamic activity needed for drug diffusion [21] .
- Occlusion with Hydration: Nanoemulsion produces a thin and uniform layer of lipid film that limits transepidermal water loss (TEWL). The increase in water content causes swelling of corneocytes and loosening of the lipid packing, giving rise to the presence of large capillary channels for diffusion[22].

- Follicular Targeting with Deep Tissue Deposition: Nanodroplets effectively penetrate into the hair follicles and sebaceous glands. Tracking by Confocal Laser Scanning Microscopy (CLSM) confirms the deep-penetrating effects that nanoemulsions and deformable nanovesicles are able to go as deep as 179µm into dermal skin layers, while traditional solutions are no better than 84µm. Hence, it is effective for in-depth delivery targeting the dermal layers but without systemic toxicity [23,24].

V. Formulation and Evaluation

5.1 Physicochemical Characterization

A careful characterization process is crucial to ensuring consistency between batches, structural soundness, and the stability of the physical features of the product.

- Droplet size and polydispersity index (PDI) through either Dynamic Light Scattering (DLS) or Photon Correlation Spectroscopy (PCS). In order to be classified as nanoemulsions, the Z-average diameter should ideally range from 10 to 200 nm. PDI readings below 0.25 suggest that the product is monodispersed, which implies an even distribution of droplets and resistance to the phenomenon of Ostwald ripening. [25]
- Zeta Potential, which is an indicator of the electrokinetic potential at the droplet hydrodynamic shear plane, is measured by means of electrophoretic light scattering. Zeta Potential values that are more positive than +30mV or more negative than _30mV also indicate that the colloids are stable enough [25].
- Morphology of the droplets should be verified through Transmission Electron Microscopy (TEM) or Cryo-TEM. Through these techniques, one can confirm the presence of spherical shapes, independent nanodroplets, as well as no aggregation [26] .
- Rheological behavior: Rotational rheometers in cone-and-plate geometry were used.

Spreadability, time on skin and consumer acceptance are dependent on rheology. The non-Newtonian shear-thinning (pseudoplastic) behavior of most nanoemulsions means that the viscosity decreases as shear rate increases, ensuring effortless spreadability on the skin [26].

5.2 Physical Stability Protocols

Accelerated stability testing protocols distinguish between nanoemulsions that are kinetically stable and formulations that are liable to phase separation.

The centrifugation stress test was conducted at 3000 to 5000 rpm for 30 minutes. The products that did not present any signs of creaming or phase separation after centrifugation tests were submitted to thermal cycling.

The samples underwent heating and cooling for 6 cycles between 4°C- °C with 48 hours at each temperature.

The formulation was then subjected to freeze-thaw cycling of 3 to 6 cycles between -20°C and +25°C.

Real-time and accelerated shelf-life studies involved storage under specific ICH conditions for (5C, 25C/60% RH, and 40C/75% RH) over 3 to 6 months and control of such parameters as droplet size, PDI, pH, zeta potential and API content [27,28].

5.3 In Vitro and Ex Vivo Skin Permeation Studies

The evaluation of in vitro percutaneous absorption is conducted using the Franz Diffusion Cell apparatus, which quantitatively determines the kinetics of topical absorption. The apparatus consists of a donor compartment filled with a formulation and separated from the receptor compartment using human ex vivo skin, full thickness porcine skin or synthetic cellulose acetate membranes.

- Experimental settings: The receptor chamber contains physiological buffer solution (e.g. PBS at pH 7.4) at 32±1C with continuous stirring.
- Sink conditions: The drug concentration in the receptor chamber should be less than 10 - 20% of its maximum solubility limit in order to mimic the systemic clearance.

- Permeation Metrics: Aliquots withdrawn at specified intervals are analyzed via HPLC. Key parameters include:

Cumulative Permeated Amount (Qn, g/cm2).
Steady-State Flux (Jss, g/cm2/h): Determined from the linear slope of Qn versus time.
Permeability Coefficient (Kp, cm/h): Calculated as Kp=JssC0, where C0 is the initial active concentration in the donor phase [29].

Table 3: Comprehensive physicochemical evaluation framework for topical and transdermal nanoemulsions.

Parameter	**Technique**	**Standard Values**	**Significance**
Droplet Size	Dynamic Light Scattering	$10 - 200\,nm$	Dictates skin permeation pathway and kinetic stability
Polydispersity Index	Photon Correlation Spectroscopy	< 0.25	Prevents Ostwald ripening and droplet growth
Zeta Potential	Electrophoretic Mobility	$>+ 30\,mV$ or $<- 30\,mV$	Ensures electrostatic repulsion against aggregation
Viscosity & Rheology	Rotational Cone-Plate Rheometer	Pseudoplastic	Ensures retention, spreadability, and user compliance
Physical Stability	Stress testing	Zero phase separation or precipitation	Guarantees extended product shelf-life
Permeation Flux (J_{ss})	Franz Diffusion Cell with HPLC	Significant multi-fold increase over control	Quantifies drug bioavailability across skin layers

VI. Applications in Skin Care and Skin Brightening

6.1 Applications in Clinical Dermatology

Nanoemulsions applied topically exhibit significant efficacy as therapeutics in various dermatological diseases:

- **Psoriasis:** An autoimmune, inflammatory condition marked by excessive proliferation of the epidermis and infiltration of immune cells. Nanoemulsion-based delivery of immunosuppressive and anti-inflammatory agents like Methotrexate, Clobetasol propionate, Tacrolimus, Quercetin, and Tannic acid increases their cutaneous penetration, gets accumulated in affected areas, reduces PASI scores (Psoriasis Area and Severity Index), and decreases side effects due to reduced systemic exposure [30].

- **Acne Vulgaris and Infections Caused By Microbes:** Pathogenesis entails hyper-colonisation of Cutibacterium acnes, follicular hyperkeratinization, and over-production of sebum. Nanoemulsions delivering both antibacterial bioactives (oregano essential oil, garlic/ginger oils, tea tree oil) along with common antibiotics (Neomycin) possess excellent activity against bacterial biofilms that are resistant to treatment, penetrate deep within acidic sebaceous follicles, and facilitate tissue regeneration [31].
- **Wound Healing and Tissue Regeneration:** Herbal nanoemulsions enriched with active lipids, geraniol, curcumin, and neem extracts increase cell migration, eliminate ROS, produce more collagen, and promote faster wound healing than conventional creams [31].
- **Cutaneous Oncology:** Delivery of chemotherapeutic agents and photodynamic therapy drugs into deeper layers of epidermis and dermis induces necrosis of tumor cells and spares nearby healthy tissue [32] .

6.2 Applications in Cosmeceuticals and Skin Brightening

Melanogenesis refers to the physiological process that occurs in melanocyte melanosomes. The copper-dependent enzyme tyrosinase catalyzes the hydroxylation of L-tyrosine to L-DOPA followed by its oxidation into dopaquinone. Further reactions through enzymatic activities mediated by Tyrosinase-Related Protein-1 (TRP-1) and TRP-2 result in the formation of eumelanin (dark/brown) and pheomelanin (red/yellow). Melanogenesis, when dysregulated leads to hyperpigmentation conditions such as melasma, post-inflammatory hyperpigmentation (PIH), and solar lentigines[33] .

Conventional depigmenting therapies pose tough formulation problems:

- Hydroquinone: A very potent tyrosinase inhibitor that is banned in cosmetic formulations in various jurisdictions because of the dangers of exogenous ochronosis, irreversible melanocyte cytotoxicity, and even carcinogenesis[34].
- Kojic acid (KA): It is a fungal metabolite which acts on tyrosinase by chelating the copper ions in the active site. However, KA is hydrophilic, exhibits low stratum corneum permeability, and rapidly degrades under light, heat, and air exposure [35].
- To overcome these problems, following methodologies are adopted in derivative chemistry and nanoemulsion technology:
- Kojic Dipalmitate (KDP) Nanoemulsions: Upon the formation of esters, Kojic Acid transforms into Kojic Dipalmitate (KDP) which is stable, non-irritant lipophilic compound that doesn't degrade under thermal and photolytic conditions. Nanoemulsions with KDP (O/W type; using rosehip or canola oil phase stabilized by Polysorbate 80/Span 80 surfactants mixture) have droplets size smaller than 130 nm with high incorporation efficiencies more than 95%. Cutaneous esterases convert KDP to active Kojic Acid near melanocytes. During Franz permeability studies, Kojic Acid ester nanoemulsions enhanced skin penetration from 4.94% at 1 hour to 59.64% at 8 hours, yielding a steady-state flux (Jss) of 4659.50 µg/cm2/h and permeability coefficient (Kp) of 0.48 cm/h [36].
- Arbutin & Combination Therapy: Arbutin is hydroquinone-based glycoside which inhibits tyrosinase competitively. Nanoemulsions protect arbutin from premature enzymatic degradation, enhance its delivery and minimize skin irritation [37].
- Synergistic Multi-Active Nanoemulsions: Co-delivery of complementary actives via one nanocarrier system gives better effect of depigmenting. Nanoemulsions co-delivering 4-Butylresorcinol (powerful tyrosinase and TRP-1 inhibitor) and Undecylenoyl Phenylalanine (an -MSH receptor antagonist) demonstrate synergistic suppression of cellular melanogenesis. Similarly, nanoemulsions carrying Oxyresveratrol / Dihydrooxyresveratrol (DHO), Bakuchiol (a natural retinoid mimic non-inferior to 0.5% retinol in reducing hyperpigmentation without skin irritation), and Azelaic acid provide multi-targeted skin brightening [38].

VII. Recent Advances, Challenges and Future Perspectives

7.1 Hybrid Nanoemulgel Systems

The major limitation of liquid nanoemulsions lies in their low viscosity, which results in inadequate cutaneous residence, dripping, and non-localised application of the formulation. In order to solve this problem, contemporary research is concentrated on nanoemulgels, which are hybrid drug delivery systems prepared through mixing of liquid nanoemulsions and hydrogel matrices made from the following polymers such as Carbopol, Xanthan gum, Sodium carboxymethyl cellulose, and Hyaluronic acid [39]. The nanoemulgels inherit properties of both the systems, including high API solubilization, lipid matrix fluidization, and permeation increase of nanoemulsion system, as well as viscoelasticity, pseudoplasticity, high spreadability, bioadhesion, and controlled active release from hydrogel system [40].

7.2 Emerging Nanocarrier Concepts

- **Pickering Nanoemulsions:** Using solid colloidal nanoparticles (for example, starch nanoparticles, silica, and cellulose nanocrystals) rather than artificial surfactants. Irreversible adsorption of solid particles at the interface of the oil and water results in very high stability against coalescence while removing skin irritation from the surfactants [41].
- **Stimuli-Responsive Nanoemulsions:** Developed to change their physical form or release mechanisms in response to the specific stimuli of the skin environment, such as increased temperature or local changes in pH levels in case of acne and specific enzyme activity [42].
- **Ionic Liquid-Based Nanoemulsions:** Use of task-specific ionic liquids in the interfacial layer or core to dissolve poorly soluble APIs and offer antimicrobial activity [42].

7.3 Toxicological and Regulatory Barriers

Although the preclinical data are encouraging some of the existing limitations will need to be overcome:

- **Surfactant Irritancy & Nanotoxicity:** Continuous contact with large concentration of synthetic surfactant can disorder lipid arrangement of intact stratum corneum causing localized contact dermatitis and local erythema & compromising the barrier properties of the stratum corneum. This will lead to formulation with naturally derived biosurfactant, use of food grade formulation ingredients etc is in focus [43].
- **Industrial Scale-up & Process Consistency:** High energy processing techniques such as high-pressure homogenisation entail high capital & operating costs associated with the equipment as well as substantial energy and cooling requirements due to heat-sensitive biomolecules being formulated [44].
- **Regulatory Classification & Safety validation:** The regulatory lacunae at the global level, about nanocosmeceuticals, result in marketing ambiguity and the required intensive characterisation, a comprehensive nanotoxicology assessment and a thorough analysis regarding irritancy and stability of the delivery platform under varying temperature and humidity conditions will only enable regulators such as USFDA and European EMA to permit the product in the market [45].

VIII. Conclusion

Nanoemulsions-an advanced nanocarrier- offer unique and efficient application platforms in topical skin delivery and the realm of cosmeceuticals. The special physicochemical features that make nanoemulsions an excellent skin delivery system are their very small sub-micron droplet size of 10-200 nm, massive interfacial surface area, and remarkable kinetic stability that facilitates skin stratum corneum permeability. Nanoemulsions help fluidize intercellular lipid domains, boost follicular accumulation, and augment the thermodynamic activity of drugs, thereby leading to effective bioavailability and skin residence of difficult therapeutically/cosmeceutically active compounds, in addition to enhancing their photolytic stability. In dermatology, nanoemulsions offer great scope for targeted delivery of antipsoriatic drugs,

antimicrobial phytoconstituents, wound healing agents, and antineoplastics to the diseased site by minimising systemic adverse reactions.

The application in skin brighteneing and cosmeceuticals has achieved successful management over the serious chemical instability, high tendency for oxidation and poorer skin-permeability problems of classical tyrosinase inhibitors like Kojic acid, HQ derivative and plant derived phytoconstituents respectively. The developing hybrid nanoemulsions have further attempted to overcome the poor viscosity problem associated with liquid nanoemulsions while providing great rheological behaviour and good bioadhesion along with extended sustained release characteristics. Moving into green formulation methods (using Pickering stabilization, biosurfactants) and standardization of scale-up procedures, setting regulatory safety standards for easier clinical translation of newer nanoemulsion-based topical products remains the key point in future studies.

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