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Review Article

Advancements In Nano emulgel Formulations for Cosmeceutical Applications: A Comprehensive Review

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ABSTRACT

This comprehensive review explores the recent advancements in nanoemulgel formulations for cosmeceutical applications. Nanoemulgels, which combine the benefits of nanotechnology and emulgel systems, offer enhanced stability, bioavailability, and targeted delivery of active ingredients in skincare products. The review highlights the key components of nanoemulgels, including the choice of surfactants, oils, and gelling agents, and their impact on the formulation's properties. Advances in preparation techniques, characterization methods, and the incorporation of novel active ingredients are discussed. The review also addresses the potential challenges and future prospects of nanoemulgels in the cosmeceutical industry, emphasizing their role in improving the efficacy and consumer appeal of skincare products. Through this review, researchers and industry professionals can gain a deeper understanding of the technological innovations driving the development of next-generation cosmeceuticals..

INTRODUCTION

Cosmetics are any substances that are applied topically to the body in order to maintain dental hygiene, clean, perfume, protect, alter the appearance, or reduce body odour. As per the US FFDCA (Federal Food, Drug and Cosmetic Act) 1938, a cosmetic is any substance used to improve or alter one's outward look. Typically, they are combinations of chemical substances obtained from natural or synthetic sources. The global cosmetics market is predicted to expand considerably by 2026. Cosmetics include skin care, body hair removal, antiperspirants, shaving cream, foundation, perfumes, sunscreen, hair and scalp products, and many others.

Cosmeceuticals are defined as those cosmetic products that elicit pharmaceutical therapeutic benefits, but not biological therapeutic benefits. It indicates those skincare products with active ingredients beneficial for improving the

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appearance of the skin as well as nourishment of the skin. Localized drug delivery in any region of the via different topical routs such as rectal, ophthalmic, vaginal, and skin is considered as topical drug administration. The main route for topical drug administration is skin because of its ease of accessibility and availability. Topical delivery system is more advantageous due to avoidance of first pass metabolism. Topical drug delivery system is the dosage form which is administered delivery get on the skin and other routes of drug failed or for skin disorders. The topical drug delivery system has the advantage of negotiating the first pass metabolism. It also helps to avoid the risk and inconvenience of intravenous route therapy.[1]

8Since the mid-1980s, emulsion gels have been picking up significance in pharmaceutical topical semisolid dosage forms. Their wide usage as pharmaceutical dosage form originates from the wide use of emulsion systems, especially for dermatological formulae. Mostly cosmetic products are formulated as emulsion. Advantages of emulsions include a certain degree of elegance, easily wash off, high ability of skin penetration and controllable viscosity, appearance, and degree of greasiness. Both types of emulsions, that is, w/o and o/w can be formulated and used to deliver active pharmaceutical ingredients and other therapeutic properties. w/o emulsions are mostly formulated for emollient applications and treatment of skin dryness, while o/w emulsions are employed for water washable drug bases and for general cosmetic purposes.[2]

Gels are new and more acceptable among all topical formulations. They have better drug release properties, but they cannot be used for hydrophobic drugs. For hydrophobic drug delivery in the form of gel, a new formulation is introduced, which is combination of emulsion and gel, called emulgel.[3]

Topical formulations are prepared in different consistency such as solid, semisolid, and liquid. The topical delivery system is failed in the administration of hydrophobic drug. In each formulation with the active ingredients many excipients are used. Sometimes more than one formulation can be combined to enhance the drug delivery; emulgel is such type of combination. It is the combination of emulsion and gel.[4]

Emulgel are emulsions, either of the water-in-oil or oil-in-water type, which are gelled by mixing with a gelling agent. The emulsion also acts as controlled release drug delivery system in which drug particles entrapped in internal phase go through the external phase to the skin and slowly get absorbed. The drug reaches the external phase of the skin in a controlled manner through the internal phases which act as a reservoir of the drug. Gel captures small drug particles and provides its release in a controlled manner because of a cross linked network. It prolongs the contact period of medication over the skin because of its mucoadhesive property. Since Emulgel possesses the property of both gel and emulsions it acts as dual control release system. Water-in-oil emulsions are employed more extensively for emollient actions and for the treatment of dry skin and emollient applications while oil-in-water emulsions are most useful in general cosmetic acts as a water washable drug bases.[5]

The emulgel have many advantages like thixotropic, greaseless, easily spreadable, easily removable, emollient, non-staining, bio-friendly, pleasing appearance, transparent and cosmetically acceptable, which also have a good skin penetration and long shelf- life.

Two types of topical delivery products are available. They are external and internal products. As their name indicates, the external products are applied by spreading or spraying, and the internal products are applied orally, vaginally or rectally.[6]

Types Of Emulgel Based On Emulsions:

1. Macroemulgel
2. Microemulgel
3. Nanoemulgel

Formulation Of Emulgel:

For the preparation of emulgel some constituents are used including drug, which are:

• Vehicle

Vehicle should follow the ideal characters given in the Pharmacopeias.

• Aqueous material

This forms aqueous phase of the emulsion. Generally, water and alcohol is used.

• Oil

Oils are used for preparation of emulsion. Mineral oils and paraffin are used either alone or in combination Pharmacopeias.

They are responsible for the oily phase of the emulsion. The oil phase has great importance in the formulation of emulsion /microemulsion/nano emulsion as physicochemical properties of oil (e.g., molecular volume, polarity, and viscosity) significantly govern the spontaneity of the emulsification /micro- emulsification / nano emulsification process, the droplet size of the respective emulsion, drug solubility. Usually, the oil, which has the maximum solubilizing potential for the selected drug candidate, is preferred as an oily phase for the formulation of emulsion/microemulsion/nano emulsion. This helps to attain the maximal drug loading.

• Emulsifiers

Emulsifiers used for preparation of emulsion. Some examples are span 80, tween 80, stearic acid, sodium stearate.

• Gelling agents

Gelling agents are used for prepare gels, which enhance consistency of preparation.

• Penetration enhancers

Penetration enhancers help to absorb drug to the skin.

• pH adjusting agent [7]

Ideal Properties Of Additives:

- They should be nontoxic.
- They should be easily available.
- They should be cheap.
- They do not be contraindicated.
- They should chemically and physically be stable.[8]

Preparation Of Emlgel:

Emulgel are prepared by incorporating gel and emulsion.

The emulsion and gel are prepared separately and mixed together.

For preparing emulsion, aqueous phase and oil phase are taken separately and mixed together. Then the gel is prepared by using gelling agent. After preparing gel and emulsion, they are mixed with gentle stirring. The chemicals are used as oil phase are castor oil, clove oil, liquid paraffin, etc. Water and alcohol are used as aqueous phase. The aqueous phase is prepared by mixing tween 80 and water and also the oil phase prepared by mixing paraben and propylene glycol. The drug is dissolved in ethanol and the two phases are mixed with continuous stirring. Then the polymers are dissolved in water with the pH of 6.0-6.5. After preparing emulsion and gel separately, they are mixed together to get emulgel.[9]

Nano emulgel:

A nanoemulgel is a semisolid preparation consisting of nanoemulsion and gel. It is one of the most famous routes for topical drug administration. This formulation was the subject of extensive research, which included the emulgel from a variety of perspectives, including pharmaceutical inspection of emulgel, methods of emulgel preparation, and the advantages of emulgel over emulsion and gel due to its unique set-in pharmaceutical sciences. Then emulgel enhances the penetration of the oil through the skin due to the fact that the oily droplets stay intact on the skin due to the gel matrix and go into its layers. Then the oily droplets reach their targets in the

body. Many natural compounds with antimicrobial activity that can be used in conjunction with pharmaceutical drugs to treat some bacterial infections have been widely used for this purpose due to their high concentration of active compounds.[10]

NEs are clear, kinetically stable, isotropic colloidal systems composed of oil, water and surfactant/co-surfactant combination. The appearance and stability of NEs depend on their globule size. NEs generally appear to be clear or transparent with a mean droplet diameter of less than 200 nm while some appear milky with the droplet size up to 500 nm. Currently, NEs are the area of focus for cosmetics and drug delivery applications attributable to their small size and large surface area. Nevertheless, their application for topical drug delivery is limited due to their low viscosity that leads to poor retention on the skin. Incorporation of NEs to a gelling system has been evolved as a strategy to overcome these problems thereby enhancing their viscosity and related clinical applications.

NEG is a combined preparation of stable NEs and a hydrogel matrix for therapeutic and application related improvements. NEGs possess gel characteristic with improved NE properties for drug delivery. The hydrogel in the formulation will enable close proximity of the formulation with the skin facilitating cutaneous absorption of the active moiety. This will lead to accumulation of the active moiety in the skin and prevent leaching into systemic circulation.

Regardless of the advancement made in the drug delivery systems and countless techniques applied for better therapeutic enhancement, there are a number of newly approved drugs which are being barred from the development of pipeline because of their low bioavailability. This low bioavailability can be seen as a result of low solubility, low permeability or both. So, to enhance the therapeutic efficacy it will be the prime necessity to improve the various pharmacokinetic parameters of the drug moiety such as solubility, permeability and hence bioavailability.[11]

Materials Required For Nanoemulgel Fabrication:

Fabrication of nanoemulgel for the purpose of drug delivery through topical route requires a variety of materials suitable and compatible with the skin along with consideration of some important factors such as the amount of drug to be loaded, amount of water to be used and route of permeation of the drug through the skin.

Aqueous Phase

For the formulation of nanoemulgel, most commonly distilled water or ultra-purified water is used as the aqueous phase and this phase is responsible for the conversion of emulsion form into the emulgel in the presence of a gelling agent.

Oils and lipids

In nanoemulgel formulation, selection of oils and lipids is the most crucial parameter and responsible for the selection of the other components such as surfactants and co-surfactants. In the oil which has maximum solubilizing potential for a selected drug candidate is selected as an oily phase for the formulation of nanoemulgel. This helps to achieve maximum drug loading in the Nanoemulges.

Pharmaceutically approved long-chain triglycerides (LCTs), medium-chain triglycerides (MCTs) and shortchain triglycerides are mainly used for nanoemulgel formulation. As most of the recently approved active pharmaceutical ingredients have solubility and permeability limitation, MCTs are more attractive than LCTs for the emulsification purpose because of their more solubilizing capacity as compared to LCTs.

Vegetable Oils

Plants are the source of these oils that are found in the form of fatty acid glycerides. Many plant derivative oils are approved for the topical

delivery of drugs such as soybean oil, olive oil, coconut oil, almond oil and castor oil through various drug delivery systems. Many of these oils like sesame oil and soybean oil are also used for the preparation of nanoemulgel. These oils are fixed in nature and comparatively less preferred in many nanolipoidal formulations due to the low solubility of drugs.

Fatty Acids and Alcohols

Many fatty acids are widely distributed in plant oils. Fatty acids are mainly carboxylic acids along with a long aliphatic chain which are either saturated or unsaturated in nature. for topical drug delivery, US FDA has approved many oils belonging to the category of fatty acids and alcohols such as Oleic acid, Undecylenic acid, acetyl alcohol Stearyl alcohol and Oleyl alcohol etc.

Fatty Acid Ester and Glycerol

These categories of lipids are the most commonly used oil phase for the preparation of nanoemulgel and microemulsions. In case of topical preparation also, these oils are most preferred because of their comparatively better solubility in recently approved APIs. These oils exhibit some of the properties of the surfactants. This category of lipids can be re-categorized as monoglycerides, diglycerides and triglycerides and are mainly medium-chain triglyceride.[12]

Surfactant and Co-Surfactant:

Surfactants are used both to give emulsification at the time of formulation and control day to day stability during shelf life of prepared Nanoemulgel. General selection of surfactant depends on the type of emulsion. (O/W or W/O) E.g. Span 80 (Sorbitanmonooleate), Acrysol K 140, Polyethyleneglycol-40-stearate, Acrysol, Labrasol, Stearic acid, PlurolOleique, Tween 80 (Polyoxyethylene- sorbitanmonooleate), Labrafil, Sodium stearate, Where agents like, Transcutol ,Captex, Cammul, Migyol, etc. can be use as cosurfactant or co-solvents.

Gelling Agents

Polymers essential to give the structural network for the preparation of gels are known as gelling agents. The gelling agent is one of the major components of nanoemulgel and it gives texture to the formulation. These are actually cross-linking agents. - Agar, Tragacanth, Guar gum, Xanthan Gum, Semisynthetic and Synthetic Carbapol, Poloxamer, HPMC etc. are some of the gelling agents used in nanoemulgel preparation.

Preservatives

These are the chemical agents used to protect the formulation by the microbial attack and hence increase the shelf life. Phenoxyethanol, Benzalkonium chloride, Benzoic acid, Methyl paraben and Propyl paraben are generally used preservatives in the formulation of nanoemulgel.[13]

Permeation Enhancers:

They interact with different skin constituents to produce a reversible temporary increase in permeability. They can act by one or more mechanisms like

i. Disrupting the highly compact structure of SC.

ii. Improving partition of drug or solvent or co-enhancer into the SC.

iii. Interacting intercellular protein. Causing conformational changes in protein or solvent swelling is the key for alternating polar path. Some enhancers improve the fluidity of protein in SC, where some act on both pathways by disrupting multilaminate pathway. They can increase the diffusion of drug through skin proteins. Type of enhancer has a significant impact product designing E.g. Eucalyptus oil, Linoleic acid, Lecithin, Oleic acid, Chenopodium oil, Isopropyl myristate, Urea.

Antioxidants

These are the chemical agents used in the formulation to protect the various components from oxidation. Butylated hydroxyl toluene, Ascorbylpalmitate, and Butylated hydroxyl

anisole are most preferred antioxidants in topical nanolipoidal preparation.[14]

Method Of Preparation For Nanoemulgel:

1. **High-pressure homogenization method:**

This method involves the use of a high-pressure homogenizer to break down the oil phase into nanosized droplets that can be easily dispersed in a hydrophilic gel matrix. The homogenization process generates high shear forces that help to reduce the droplet size and create a stable Nanoemulgel.

2. **Ultrasonication method:**

In this method, ultrasonic waves are used to create Nanoemulgel. The oil phase and the hydrophilic matrix are mixed together, and the mixture is subjected to high-frequency ultrasound waves. The ultrasonic energy breaks down the oil phase into nanosized droplets, which are dispersed uniformly in the gel matrix.

3. **Solvent evaporation method:**

This method involves the use of a water-miscible solvent to dissolve the oil phase and the hydrophilic matrix. The solvent is then evaporated under reduced pressure, leaving behind a Nanoemulgel with nanosized droplets of oil dispersed throughout the gel matrix.

4. **Microfluidization method:**

In this method, the oil phase and the hydrophilic matrix are passed through a microfluidizer to create Nanoemulgel. The microfluidizer generates high shear forces that break down the oil phase into nanosized droplets, which are dispersed in the gel matrix.

5. **Self-emulsifying gel method:**

This method involves the use of a self-emulsifying drug delivery system (SEDDS)that can create Nanoemulgel in situ. The SEDDS is a mixture of oil, surfactants, and co-solvents that can spontaneously emulsify when in contact with water. When the SEDDS is mixed with a hydrophilic gel matrix, a nanoemulgel is formed.

6. **High-energy emulsification method**:

This method involves the use of high-energy input to create small droplets of the dispersed phase (oil) in the continuous phase (water). This can be achieved through various methods such as sonication, high-pressure homogenization, or micro fluidization. The resulting emulsion can then be transformed into a gel by adding a gelling agent such as a polymer or a surfactant.

7. **Phase inversion temperature (PIT) method:**

This method involves the use of a thermosensitive surfactant that undergoes a phase transition from a water-soluble to a water-insoluble state at a certain temperature. By adjusting the temperature of the system, the surfactant can be induced to form a gel-like structure that entraps the dispersed phase.

8. **Sol-gel transition method:**

This method involves the use of a sol-gel transition system, where a gel is formed by the aggregation of a network of particles or polymers in a solvent. This can be achieved by adding a crosslinking agent or a thermosensitive polymer to the emulsion, which triggers the formation of a gel-like structure at a certain temperature or under certain conditions.

9. **Electrostatic complexation method:**

This method involves the use of oppositely charged polymers or surfactants to create a stable emulsion, which can then be transformed into a gel by adding a crosslinking agent or a gelling agent.

10. **Coacervation method:**

This method involves the use of two or more polymers that undergo phase separation in the presence of an electrolyte or a pH change, resulting in the formation of a gel-like structure. The dispersed phase can then be incorporated into the gel by high-energy emulsification or other methods.[15]

Method Of Formulation Of Nanoemulgel:

a. Screening of components
b. Preparation of Nanoemulsion
c. Preparation of Nano emulgel

d. Preparation of Gelling Agent
e. Incorporation of Gelling Agent

a. Screening of compound: Drug solubility was determined in different oils by adding more than drugs in different ingredients, then stirring continuously for 72 h to reach equilibrium. Then, samples were centrifuged and the supernatant was collected and the solubility was determined using appropriate analytical methods. Thereafter, excipients from each class with the highest drug solubility were selected for additional studies.

b. Preparation of Nanoemulsion: The drug is then solubilized in oil and oil is added to Nmix, this mixture is diluted with water to form of Nanoemulsion of the given drug.

c. Preparation of Nanoemulgel: Gel base is ready mistreatment 1g of the Carbopol in a very needed amount of water. When the Carbopol solution has fully swelled and dispersed over a twenty-four-hour period, the ready nanoemulsion is progressively added to the mixture while stirring continues. The addition of Triethanolamine offers homogenized gel dispersion. Finally needed remaining half is adjusted with H2O.[16]

d. Preparation of Gelling Agent: In fabrication of a nanoemulgel, the purpose of using a gelling agent is to change the physical form from liquid to semi-solid which has many advantages in terms of patient compliances. Various categories of the gel base for the purpose of gelling can be prepared by adding the polymer in purified water and stirred continuously with a glass rod or any other suitable mechanical device until desired texture achieved and then pH should be adjusted. In various experimental works, the preparation of the gelling agent is carried out by adding the polymer in purified water by a cold method. In cold method, the components are added in purified water at 20o C followed by the addition of gelling polymer and cooling the water up to 4o C.

e. Incorporation of Gelling Agent: After the preparation of nanoemulsion as well as the gelling agent, both are mixed and a nanoemulgel is prepared. Here a liquefied form of water in oil (w/o) or oil in water (o/w) nanoemulsion is converted into a thick and semisolid nanoemulgel with the help of various polymeric gelling agents. This gel form can change again into a solution form after applying a mechanical force such as rubbing. This property of the material is known as thixotropy where gel to sol and sol to gel transformation occurs on the application of shear stress and reversal of the same respectively without a change in volume. Innumerable polymers have been used as gelling agents such as Carbomer 940, Carbopol 943, Chitosan, Carbopol 934, Carbopol 940, Poloxamer 407, Methyl cellulose etc. for the preparation of nanoemulgel of desired characteristics for various applications.[17]

Characterization Of Nanoemulgel

Appearance:

The prepared nanoemulgel formulations were inspected visually for their color, homogeneity, consistency and pH. The pH values of 1% aqueous solutions of the prepared gellified emulsion are measured by a pH meter (Digital pH meter DPH 115 pm).

Spreadability Testing:

Desirable spreadability is one of the important criteria for the selection of a topical delivery system. In nanoemulgel dosage form, spreadability can be determined by some special apparatus made up of a wooden block or glass having a pulley on the opposite end. With the help of this apparatus, spreadability is measured which comes under ‘Slip’ and ‘Drag’ method.

A shorter interval indicates better Spreadability. Spreadability is calculated by using the formula:

$S = M.L/T$

Where,

S = spreadability,

M = Weight tied to upper slide,

L = Length of glass slides

T = Time taken to separate the slides from each.

Globule size and Its distribution in nanoemulgel

Globule size and distribution was determined by Malvern zetasizer. A 1.0 gm sample was dissolved in purified water and agitated to get homogeneous dispersion. Sample was injected to photocell of zetasizer. Mean globule diameter and distribution was obtained.

Drug released study:

To analyze the mechanism of drug release from the topical nanoemulgel, the release date is fitted to the following equations:

Zero-order equation:

$Q=K0t$

Where Q is the amount of drug released at time t, and K0 is the zero-order release rate.

First-order equation:

$In\ (100-Q) = In\ 100 - K1t$

Where Q is the percentage of drug release at time t, and K1 is the first-order release rate constant.

Higuchi's equation**:**

$Q=K2\sqrt{t}$

Where Q is the percentage of drug release at time t, and K2 is the diffusion rate constant.

Accelerated stability studies of gellified nanoemulgel:

Stability studies were performed according to ICH guidelines. The formulations were stored in a hot air oven at 37±2°, 45±2° and 60±2° for 3 months [19]. The samples are analyzed for drug content every two weeks by UV-Visible spectrophotometer. A stability study was carried out by measuring the change in pH of the formulation at a regular interval of time.[18]

Skin irritation test:

0.25 gm Nanoemulgel is applied to each different site (two sites/rabbit). After 24 hr. of application rabbit skin site are wiped and cleaned, change in color of skin or undesirable change in morphology is noted and checked.

In-vitro Diffusion studies

Franz diffusion cell is used to perform diffusion study of prepared nanomeulgel. A cellophane membrane is used for study and 0.5g of sample applied on membrane and diffusion is carried out for 8 hr at 37±1°C using phosphate buffer (pH 7.4). At time interval of 1 hr, 1 ml sample is collected and replaced with new buffer solution. Collected samples are analyzed by using suitable analytical method.

Rheological Characterizations

It has been discussed that a nanoemulgel contains oil, surfactants and a gelling agent as fabricating components. A minute change in the physicochemical properties of formulation components can greatly affect the rheological properties of a dosage form such as viscosity and flowability. The change in viscosity can further affect the stability factors as well as drug release and other biological functions. Taking these factors into consideration, it is very essential to understand the rheological properties of nanoemulgel. Viscosity measurement can be carried out with different kinds of viscometers.

Measurement of Bioadhesive strength:

On each arm of the apparatus, one glass slide was separated from two additional glassed plates. A single plate is used to add weight. Between slides containing rate skin fragments, 1 gram of nanoemulgel is inserted precisely. By putting weight on a single glass slide, you can detach the sandwich of two slides. The extra weight is added at a rate of 200 mg/min until the skin surface detaches. It is calculated by using the following equation: Bioadhesive Strength = W / A Where W denotes the desired weight (in gm) and A denotes the area (cm2).[19]

Swelling Index:

1 gm of prepared topical nanoemulgel is taken on porous aluminum foil which is then placed on 10ml of 0.1 N NaOH solutions. The sample is removed from time to time and weight is noted till

no further change in weight: Swelling Index (SW) % = [[Wt-Wo]/Wo]*100 Where, (SW) % = Percentage swelling, Wo = Original weight of nanoemulgelWt = Weight of swollen nanoemulgel at time.

Skin irritation test

0.25 gm Nanoemulgel is applied to each different site (two sites/rabbit). After 24 hr of application rabbit skin site are wiped and cleaned, change in colour of skin or undesirable change in morphology is noted and checked.

In- vitro release study

Franz diffusion cell (with effective diffusion area 3.14 cm2 and 15.5 ml cell volume) was used for the drug release studies. Nanoemulgel (200 mg) was applied onto the surface of egg membrane evenly. The egg membrane was clamped between the donor and the receptor chamber of diffusion cell. The receptor chamber was filled with freshly prepared PBS (pH 5.5) solution to solubilize the drug. The receptor chamber was stirred by magnetic stirrer. The samples (1.0 ml aliquots) were collected at suitable time interval. Samples were analysed for drug content by UV visible spectrophotometer at 226 nm after appropriate dilutions. Cumulative corrections were made to obtain the total amount of drug release at each time interval. The cumulative amount of drug released across the egg membrane was determined as a function of time.

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Advantages Of Nanoemulgel:

a. Stability of Nanoemulsion is enhanced due to distribution of oil droplets in Gel base; where affinity of the drug toward oil determines stability.

b. Also good adhesion on the skin with high solubilising power leads to high concentration gradient that increase penetration of drug as it moves down.

c. Moreover, these types of formulation give support to delivery of lipophilic and poorly water-soluble drugs and also improve patient compliance.

d. Nanoemulgel also helps in controlled release of drugs having the shorter half-life.

e. Provide higher Spread-ability of the formulation than creams.

f. Nanoemulgel are Non-toxic and non-irritant.

g. Better loading of drug compare to other formulation.

h. Increase skin permeability and drug deposition.

Disadvantages:

1.Bubbles formed during emulgel formulation.

2.For utilization in pharmaceutical application, surfactant used ought to be non-poisonous.

3.Possibility of allergenic reactions.

4.Skin irritation on contact dermatitis.

Characterization Of Nano Emulgel:

- Viscosity.
- pH.
- Spread ability.
- Skin irritation test.
- Drug Content.
- In vitro Permeation Study.
- Study of drug release kinetics.
- Comparison of nanoemulgel with marketed products.
- Stability Study.[21]

Regulatory Challlenges In Cosmeceutical Industry:

Cosmetic Regulation in India:

The cosmetic products in India are regulated under the Drugs and Cosmetics Act 1940 and Rules 1945 and Labelling Declarations by the Bureau of Indian Standards (BIS). BIS sets the standards for cosmetics for the product listed under schedule 'S' of the Drugs and cosmetics standards for cosmetics for the products listed under Schedule 'S' of the Drugs and cosmetics

Rules 1945. BIS has also provided the specification for Skin Creams and Lipstick in the Indian Standards (IS) 6608:2004 and 9875:1990 respectively.

According to IS 6608:2004, all the raw materials requiring test for heavy metals have been so tested and comply with the requirements, then the manufacturer may not test the finished cosmetic for heavy metals and arsenic. The Rule 134 of Drugs and Cosmetics Rules has laid down restrictions on use of cosmetics containing dyes, colours and pigments other than those specified by the Bureau of Indian Standards (IS: 4707 Part 1 as amended) and Schedule Q. The Rule 145 of the Drugs and Cosmetics Rules prohibits use of lead and arsenic compounds in cosmetics for the purpose of colouring. Rule 135 prohibits import of cosmetics in which a lead or arsenic compound has been used for the colouring purpose. Rule 145 D and 135 A prohibits manufacture and import respectively of cosmetics containing mercury compounds.

Registration of Import of Cosmetics:

All cosmetic products that are imported for sale in India now need to be registered with the Central Drugs Standard Control Organisation (CDSCO) which has been appointed as the licensing authority for the purpose of these rules. This new 'registration' requirement is primarily to regulate indiscriminate import of beauty and personal care products by traders with no accountability for contents and no mechanism to fix responsibility in case a consumer is not satisfied with the quality. The new regulation is an attempt to check the sale of sub-standard cosmetic products and also to harmonise import requirements with products manufactured in India.

What is the timeline for processing of application?

Within 90 days from the date of submission of the application form and submission of the required documents (especially details required with schedule D III), the registration certificate will be issued.

What is the validity of the registration certificate?

Registration certificate for import of cosmetics is valid for a period of three years from the date of its issuance. With a view to implementing the provisions of the aforesaid notification and facilitate the registration process for import of cosmetics, there are various guidelines/clarifications and requirements for the grant of Registration Certificate.

Manufacturing of Cosmetics:

The procedure to be followed in order to manufacture cosmetics in India has been laid down under the Drugs and Cosmetics Rules, 1945. A license has to be obtained from a Licensing Authority appointed by the State Government to manufacture any of the cosmetics classified under Schedule M-II. The application has to be submitted in Form 31 along with a license fee and an inspection fee. The manufacturer has to ensure that the production is done in the presence of a competent and qualified technical staff. The Licensing Authority is required to order an inspection of the whole premises where the operations are to be carried out, before granting or refusing the license. The inspectors are appointed under the Act are required to submit a detailed report to the Licensing Authority which can then decide whether to grant the or not.[22]

key challenges facing cosmetic companies:

Cosmetic companies worldwide are facing multiple, simultaneous challenges to fast, sustainable growth:

1. Accelerating time to market
2. Managing product claims
3. Ensuring global quality and compliance
4. Attracting and retaining top talent.

Challenge 1: Accelerating Time To Market:

You don't have to attend Beautycon to realize that the cosmetics industry has changed dramatically from just a decade ago. Today, the industry can change on a dime — which means that teams across global cosmetics brands are feeling the pressure to accelerate time to market.

Why is the industry evolving so quickly? For one, social media influencers now have an outsized hand in shaping consumer demand, and can cause regional stock-outs simply by making a single post on Facebook or Instagram.2 For another, the industry is saturated with new, innovative brands that can rapidly respond to the latest trends.3 But established global brands are held back.

Challenge 2: Managing Product Claims:

Cosmetics companies can also run into hot water if they can't back up their claims about what their products do with hard data or if those claims are proven wrong. That's why 49% of companies surveyed by Cosmetics Compliance named claims substantiation as one of their top compliance challenges.

Managing product claims is complex enough on its own. But many cosmetics companies also do not keep important product information in a centralized location, meaning that it can become a logistical nightmare for teams to track down the most up-to-date claims from the relevant departments. This can hold up the process of taking a product to market, not to mention even cause avoidable misrepresentations in public-facing content.

The solution is clear: Companies can streamline the process of managing their product claims by keeping critical information in a centralized location that can be updated in real time.

Challenge 3: Ensuring Global Quality And Compliance:

As many cosmetics companies have learned the hard way, consistently producing a high-quality product is no easy feat. On top of being effective, these products also need to be compliant with numerous levels of regulations before entering each unique market.

Compliance is an especially challenging task because regulatory bodies are constantly introducing new regulations and refining existing ones. Ensuring regulatory compliance is a complex, resource-intensive step in the product journey. Global brands often have to release dozens of products, packaging, and claim variations in order to meet different regulatory requirements. Tracking all of this information is challenging and can complicate a team's efforts to quickly launch a product in multiple markets. As Bing reflected, "There's no true global harmonization. You'll never have that one box.

The issues caused by using outdated compliance processes and document management tools can be resolved by switching to unified cloud-based software we'll discuss that further in the following sections.

Challenge 4: Attracting And Retaining Top Talent:

Did the unexpected FDA audit describe at the start of this paper trigger traumatic memories of past audits? If so, you're not alone.

Most cosmetics companies are managing their business processes and content the same way they did 20 years ago: with on-site solutions like spreadsheets, emails, and paper files. If you're lucky, maybe your company has upgraded to using Share point or Google Drive.[23]

India Legislation

Labeling requirement is governed by Rule 148 of Drugs and Cosmetic act, covers;

- Name of the cosmetic
- Name of the manufacturer and complete address of the premises of the manufacturer where the cosmetic has been manufactured.
- Use before (month and year)
- Declaration of the net contents
- Adequate direction for safe use
- Any warning, caution or special direction required to be observed by the consumer
- A statement of the names and quantities of the ingredients that are hazardous or poisonous
- Batch number
- Manufacturing license number
- INCI in descending order of weight or volume at the time they are added, followed by those in concentration of less than or equal to one percent, in any order, and preceded by the words "INGREDIENTS'.
- Import Registration No. (in case of Imports) Addition to D&C Act requirement, the following information should be a part of labeling as per Legal Metrology Act [5]
- Manufacturing date - Consumer care & registered office details
- Importer name and address details (if import)
- Month and year of import (if import)
- MRP (Inclusive of all taxes)
- Package containing soap, Shampoos, toothpaste and other Cosmetics and Toiletries shall bear the Red or brown dot for products of non-vegetarian origin and green dot for products of Vegetarian origin
- Font compliance (Area, Size and Letter)
- As per Rule 7 to 9 of LM Act *other statutory declarations which are common in D&C and LM are captured under D&C in India) is following EU REACH compliance, any update in EU legislation is followed by India.[24]

Table 1: Marketed Nano emulgel

Sr. No	Product Name	Active Ingredient	Manufracturer
1.	Ultra sun Transparent Sports Sunscreen Spray SPF 50 | 150 ML	Grapeseed oil+Vitamine C	Ultra sun
2.	Nosology (moisturizer)	10%glycerine+Hydroxy steric acid	-
3.	Eye Refining Matrix	Vitamin c + Hyaluronic Acid	FCL (Fix derma Cosmetic Laboratories)
4.	Dermdoc (Lotion)	Ceramides, Squalane and Vitamin	Honest Science
5.	AHA BHA Exfoliating Serum	Salicylic Acid, Glycolic Acid, Niacinamide	fox tale

REFERENCE

1. Panwar AS, Gandhi S, Sharma A, Upadhyay N, Bairagi M, Gujar S, Darwhekar GN, Jain DK. EMULGEL: A REVIEW. Asian J Pharm Life Sci. 2011;1(3):333. Available from: http://www.ajpls.com
2. Gandhi S. Teva Pharmaceuticals, Harlow, CM20 2FB, UK.
3. Sharma A. College of Pharmacy and Health Science Center, St. John's University, Queens, 11439, New York, USA
4. Ashara KC, Soniwala M, Shah K. Emulgel: A novel drug delivery system. J Pak Assoc Dermatol. 2016;26(3):244-249.
5. Raj ELPS, Balakrishnan S. Short review - emulgel. J Compr Phar. 2016;3(1):34-37.
6. Tasneem R, Khan HMS, Zaka HS, Khan P. Development and cosmeceutical evaluation of

topical emulgel containing Albizialebbeck bark extract. J CosmetDermatol. 2021;XX(X):XX-XX. doi:10.1111/jocd.14244

7. Mohamed MI. Optimization of chlorphenesinemulgel formulation. AAPS J. 2004;6(3):Article 26. Available from: http://www.aapsj.org
8. Ajazuddin, Alexander A, Khichariya A, Gupta S, Patel RJ, Giri TK, Tripathi DK. Recent expansions in an emergent novel drug delivery technology: Emulgel. J Control Release. 2013;171:122-132.
9. Kumar D, Singh J, Antil M, Kumar V. Emulgel-novel topical drug delivery system - a comprehensive review. Int J Pharm Sci Res. 2016;7(12):4733-4742.
10. Sreevidya VS. An overview on emulgel. Int J Pharm Phytopharmacol Res. 2019;9(1):92-97.
11. Vats S, Saxena C, Easwari TS, Shukla VK. Emulsion Based Gel Technique: Novel Approach for Enhancing Topical Drug Delivery of Hydrophobic Drugs. International Journal for Pharmaceutical Research Scholars (IJPRS). 2014;3(2):V-3. ISSN No: 2277-7873.
12. Sindi AM, Rizg WY, Khan MK, Alkhalidi HM, Alharbi WS, Sabei FY, Alfayez E, Alkharobi H, Korayem M, Majrashi M, Alharbi M, Alissa M, Safhi AY, Jali AM, Hosny KM. Tailoring and optimization of a honey-based nanoemulgel loaded with an itraconazole–thyme oil nanoemulsion for oral candidiasis. Drug Delivery. 2023;30(1):2173337. DOI: 10.1080/10717544.2023.2173337.
13. Sharma RB, Kumar G, Thakur H, Tomar S. Nanoemulgel: A Novel Approach for Topical Delivery System: Updated Review. Int J Drug Dev Res. ISSN: 0975-9344.
14. Anand K, Ray S, Rahman M, Shaharyar MA, Bhowmik R, Bera R, Karmaka S. Nano-emulgel: Emerging as a Smarter Topical Lipidic Emulsion-based Nanocarrier for Skin Healthcare Applications. Bentham Science Publishers. 2019; 19:1574-891X.
15. Donthi MR, Munnangi SR, Krishna KVK, Saha RN, Singhvi G, Dubey SK, et al. Nanoemulgel: A Novel Nano Carrier as a Tool for Topical Drug Delivery. Pharmaceutics. 2023 Jan;15(1):164. doi: 10.3390/pharmaceutics15010164. PMCID: PMC9863395 PMID: 36678794.
16. Harshitha V, Swamy MV, Kumar DP, Rani KS, Trinath A. Nanoemulgel: A Process Promising in Drug Delivery System. Vishnu Institute of Pharmaceutical Education and Research, Vishnupur, Narsapur, Medak District– 502313, Telangana, India. *Corresponding Author E-mail: mvenkataswamyviper@gmail.com.
17. Lodha D, Kardile A, Raut V, Mahadik M, Lad S. A REVIEW ON NANOEMULGEL. Department of Pharmaceutical Science, SAJVPM's, College of Pharmaceutical Sciences and research centre, Kada, Ashti, Beed MH-414202. IJCRT. 2023;11(5):May. ISSN: 2320-288.
18. Vispute S et al. Review on: Nano-Emulgel. Human Journals. September 2021;22(2).
19. Sultana N, Akhtar J, Badruddeen, Khan MI, Ahmad U, Arif M, Ahmad M, Upadhyay T. Nanoemulgel: For Promising Topical and Systemic Delivery. Published: 11 April 2022. DOI: 10.5772/intechopen.103878.
20. Harshitha V, Swamy MV, Kumar DP, Rani KS, Trinath A. Nanoemulgel: A Process Promising in Drug Delivery System. Research Journal of Pharmaceutical Dosage Forms and Technology. 2020;12(2):April-June. ISSN: 0975-234X (Print), 0975-4377 (Online). Available online at www.anvpublication.org. Home page www.rjpdft.com.

21. Jivani MN, Patel CP, Prajapati BG. Innovative Approach for Topical Gel Based Formulation. Research and Reviews on Healthcare: Open Access Journal. UPINE PUBLISHERS. 2018 Feb 15. Department of Pharmaceutical Technology, India. Received: February 5, 2018. *Corresponding author: Bhupendra G Prajapati, Associate Professor, Shree S. K. Patel College of Pharmaceutical Education and Research, Ganpat University, Ganpat Vidyanagar, Mehsana, Gujarat, India.
22. Mishra K, Panda P, Singh B, Chaudhary B. Development of Standard Formula for Ketoconazole Nanoemulgel and Its Assessment. World Journal of Pharmacy and Pharmaceutical Sciences. 2023;12(7):1148-1159. ISSN 2278-4357. Institute of Technology and Management, Gida, Gorakhpur, UP, India.
23. Kale SN, Deore SL. Emulsion Micro Emulsion and Nano Emulsion: A Review. Sys Rev Pharm. 2017;8(1):39-47. Department of Pharmaceutical Sciences, Shri Jagdish Prasad Jhabarmal Tibrewala University, Rajasthan, INDIA. Department of Pharmacognosy, Govt College of Pharmacy, Amravati, INDIA.
24. Beg MR. Cosmetic regulations, research & marketing challenges, and global compliance: An overview. *Institute of Chemical Technology, Mumbai*. M. Pharm.
25. Veeva- 4 Quality & Regulatory Challenges Facing the Cosmetics Industry and How to Avoid Them.
26. Singh BM, Jain A, Mishra A. Cosmetic regulations in India vs. globally and challenges in harmonization. *Int J Pharm Sci Drug Res.* [Year of Publication]; 10(3):150-157. Available from: www.ijpsdr.com. ISSN: 0975-248X. CODEN (USA): IJPSPP

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