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Review Article Nanoemulgel- A revolutionary approach for local gel oriented formulation

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ARTICLE INFO	A B S T R A C T
Article history: Received 22-09-2020 Accepted 13-04-2021 Available online 11-05-2021	In previous years, incredible efforts have been made for different techniques of drug discovery, a variety of drug molecules available today have contributed to the resolution of the numerous health care system challenges. Unfortunately because of their restricted clinical use, more than half of such drugs have either been classified in BSC (biopharmaceutical classification system) class II / IV, or both are excluded from the development process. A nanotechnological theory acknowledges great anticipation and it is observed
<i>Keywords:</i> Nanolipoidal delivery Nanoemulgel Lipophilic drug Human skin etc	that lipoid processing is appropriate for the development of these drugs. From numerous nanolipoidal formulations Nanoemulsion based gel i.e. Nanoemulgel, has been considered to be an appropriate strategy for effective drug delivery across topical route. Nanoemulgel exists in two systems in which nanoemulsion containing drug is integrated in a gel base. Lipophilic drugs can be instantly integrated, and because of the finely dispersed oil droplets in the gel form, the skin absorption co-efficient of the incorporated drugs can be increased in numerous stages. At the same time, it can be more precisely targeted to the site of action and can prevent first pass metabolism and alleviate the patient from gastric/ systemic incompatibilities. The nanoemulgel drug delivery mechanism is a formulation-related technology designed to enhance drug absorption and lipophilic drug therapeutic profile. A significant growth in nanoemulgel has been noted in recent years owing to the high toleration of the formulation to the patients, due to their non-greasy, convenient spreadability, easy applicability, strong therapeutic and safety feature. Even after having few drawbacks, the formulation of nanoemulgel may in future be recognized as key and effective targets for the topical delivery of lipophilic drugs.
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1. Introduction

Skin is considered as readily approachable and convenient part of the human body for topical application. The average surface area of the adult human skin is 1.8m[?] containing almost 200-300 sweat ducts and 40-70 hair follicles. The pH of skin ranges from 4 to 5.6, which relies on the exudation from the sweat glands. Molecules enter the skin mainly by three routes- undamaged stratum corneum, sweat ducts and sebaceous glands.[?] The stratum corneum is the upper part of epidermis and made up of dead cells. It serves as a strong barrier to water and safeguards the deep internal components and blood vesicles that are scattered under the skin. The lipid matrix, present in the stratum corneum, is a multilayer structure made up of various fatty acids cholesterol, ceramides, cholesteryl ester, and cholesteryl sulphate.[?] This unconventional combination establishes a skin barrier. The drug needs to overcome these obstacles in order to deliver the desired concentration of drugs at the targeted site and also to enter the systemic circulation¹. To this prerequisite, a nanoemulgel will be an optimal strategy.

2. Introduction of Nanoemulgel

Nanolipoidal delivery system belongs to the category of Novel drug delivery system, which is used mostly for different stabilization activities and for enhancing bioavailability.² To the following different nanolipoidal delivery system such as- such as solid lipid nanoparticles

* Corresponding author. E-mail address: vihanverma656@gmail.com (V. Verma). (SLNs), liposomes, microemulsions, nanostructured lipid carriers (NLCs), etc., nanoemulsion is the most effective delivery system for drugs with low bioavailability and lipophilic nature that are administered through different routes along with the topical route. In the case of transdermal delivery, a pharmaceutically modified type of nanoemulsion with the addition of an effective gelling agent may be a safer option for BCS class II or IV drugs.? Formulation comprising nanoemulsion in the gel base is called Nanoemulgel. It is the insertion of the embedded nanoemulsion system into the gel core which promotes a stronger skin permeability of the skin.[?] This nanoemulgel composition serves as drug repositories, controlling the release of drugs from the internal phase to the external phase, and beyond.? Nanoemulgel, without affecting the skin releases oil droplets from the gel and these oil droplets permeate the subcutaneous layer of the skin and transmit the drug to the desired site.? Nanoemulsion-gel seems to have a strong adherence potential and higher solubilization of the drug in the oily phase results in higher concentration gradient towards the skin which ultimately increases the skin permeability of drug. Patient adherence has been significantly enhanced due to increased succor capacity compared with creams and ointments, with minimal stickiness.?

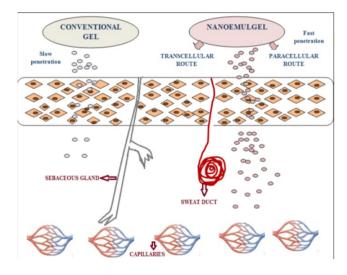


Fig. 1: Graphical representation of nanoemulgel path of action showing penetration of nanoemulgel through both Paracellular and Transcellular route.

2.1. Properties of nanoemulgel

Because of number of globules in nanoscale size, nanoemulsions are known for following specific characteristics-

1. Optimized stability, increased capacity for solubility, improvisatory formulation and high tolerance for the loading of hydrophobic and hydrophilic substances.²

- 2. Nanoemulsions are visually transparent or translucent identical structures consisting of different lipid, surfactant and co-surfactant components.²
- 3. Nanoemulsions are of two types: water-in-oil (W/O) and oil-in-water (O/W) and globules are present within the range of 5-500nm.⁹

2.2. Components necessary for Design and manufacture of Nanoemulgel

A gel based nanoemulsion preparation for topical application comprises of specialized components apart from lipids and surfactants such as gelling agents, permeation enhancers, preservatives and antioxidants.²

2.2.1. Aqueous phase

In this impendence of gelling agent, this element is responsible for transforming the emulsion into an emulgel. For the composition of nanoemulgel generally ultra-purified water or the distilled water is used.[?]

2.2.2. Oily phase

When oil or other lipid components are selected, it must be assured that the oily phase is genuine and protected from undesirable constituents such as peroxides, free radicals and other fatty acids such as sterols and polymers.[?] The majority of hydrocarbon chains are one of the main considerations behind the selection of lipids for the development of nanoemulgels and the logic behind this is that essence of emulsification and its consistency.[?] Oils which are commonly used in nanoemulsion- Mineral oil as a vehicle for drugs, cottonseed oil, maize oil, arachisoil, olive oil, coconut oil, eucalyptus oil, rose oil, clove oil, etc.[?]

2.2.3. Surfactants and Co-surfactants

In the manufacturing of nanoemulgel, surfactants are used in order to provide stability and emulsification to the final formulation. Because of the low toxic nature non-ionic surfactants are used in the formation of nanoemulgel.[?] Some of the commonly used non-ionic surfactants are: Sorbitan fatty acids esters, Polyoxyethylene fatty acids esters.[?] Co-surfactants are usually used to minimize surfactant concentration, and also to enhance the thermodynamic stability of the end product.[?] Examples of some of the co-surfactants are- Transcutol HP, PEGs, Glycerine, PGs, and ethyl alcohol.[?]

2.2.4. Penetration enhancers

Using penetration enhancers has been one of the best ways to increase transportation efficiency through the skin and associated layers.[?] Penetration enhancers are one of the key elements of the conventional drug delivery system and are generally used in topical nanoemulgel.[?] These permeation enhancers normally work by interfering with the components of skin and cause a short term and cumulative increase in the permeability of skin.[?]

2.2.5. Gelling agent

The gelling agent has been one of nanoemulgel main element, which gives the formulation a perfect structure.[?] Rationally these are cross-linking agents. Some of the gelling agents used are- Tragacanth, HPMC, Carbopol, etc.[?]

2.2.6. Preservatives

Preservatives are the chemical agents used to preserve the substance from microbial attack and thus improve the shelf life of a product. Commonly used preservatives arephenoxyethanol, benzalkonium chloride, methyl paraben, propyl paraben, etc[?].

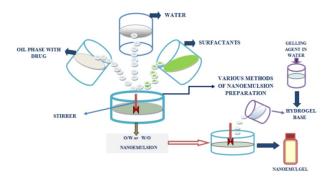
2.2.7. Antioxidants

Antioxidants are chemical agents that are utilized in the composition to avoid oxidation of the different elements. Ex. Butylated hydroxyl toluene, Ascorbyl palmitate, etc.[?]

2.3. Manufacturing of Nanoemulgel

Nanoemulgel is basically a multistage mechanism in which a formulated nanoemulsion is mixed with an appropriate gel base^{?.M}anufacturing of nanoemulgel can be done by following three essential steps:

- 1. Screening of components.
- 2. Preparation of nanoemulsion.
- 3. Preparation of nanoemulgel.



Schematic diagram of nanoemulgel preparation.[26]

2.4. Optimization of Nanoemulgel:

- 1. 1pH Measurement :
- 2. Globules size
- 3. % of drug content
- 4. Swelling index
- 5. Bioadhesive strength measurement
- 6. Accelerated stability studies

- 7. Spreadability test
- 8. Interpretation of skin permeation.

2.5. Application of Nanoemulgel

- 1. Used as an anti-inflammatory agent
- 2. As anti-psoriatic
- 3. As an anti-fungal agent
- 4. Used in alopecia

3. Conclusion

Scientifically proven facts suggests that formation of nanoemulgel may be considered as an alternate to transitional drug delivery system for BCS class II and IV drugs of various pharmacological categories. It was also found that methods of processing and implicating different elements are significant considerations in the consistency of the dosage form and therapeutic behavior. The future prospects of formulations based on nanoemulgel will provide a progressively better and dependable solution for the hydrophobic drug delivery. While there are several obstacles, nanoemulgel having the potential of primary responsibility in future for the topical transport of lipophilic drugs.

4. Conflicts of Interest

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Author biography

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