

## Novel Topical Nanoformulations: An Overview

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### Review Article

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**Abstract:** Novel drug delivery system (NDDS) refers to the approaches, formulation, technologies and systems for transporting a pharmaceutical compound in the body as needed to safely achieve its desired therapeutic effects. Novel drug delivery systems have got several advantages like delivering drug at optimum dose, reduction in the production cost, better therapy. Nanomiemgel is one of the NDDS, which utilizes the “multi absorption mechanism” concept. It consists of two matrices namely, Nano emulsion and Nano micelle. There are several methods for the preparation of these two matrices. These novel drug delivery systems have broad applicability in the field of pharmaceutics.

**Keywords:** NDDS, Nanomiemgel, Nano emulsion, Nano micelle.

### INTRODUCTION

Nanotechnology is the field that contains the studies related to Nano sized and nanostructured materials, their functions and performers with respect to medicinal and life science systems. The role of nanotechnology in the field of pharmaceutics has incredible changes in the way of understanding about the Nano drugs and the uses of nanoparticles as carriers of drug have become the basic criteria for the production and design of a drug. Nowadays most of the pharmaceutical companies are approaching to designing new pharmaceutical dosage forms of existing drugs rather than discovering a new drug product. Utilization of the existing resources of marketed and patented drug substances with known therapeutic effects, and modifying their pharmacotherapeutic characterisation by incorporating a suitable drug delivery system has been the goal of recent pharmaceutical development [1].

Topical drug administration is the favoured route for local delivery of therapeutic agents due to its convenience and affordability [2]. Topical drug delivery is one of the attractive choices for the treatment of cutaneous infections due to its advantages such as targeting of drugs to the site of infection and reduces the risk of systemic side effects [3]. One of the most promising drug delivery systems in nanotechnology for enhancing skin permeation of the drugs is the micro emulsion and Nano emulsion system [4]. Nano emulsions are emulsions with thermodynamically stable transparent dispersion of oil in water stabilized by an interfacial film of surfactant and co-surfactant

molecules with droplet size less than 1000nm. Nanomiemgel is a novel drug delivery system which utilizes the Multi Absorption Mechanism (MAM) concept and broad applicability. Nanomiemgel consists of two types of matrices A and B. Matrix A comprises the Nano emulsion and Matrix B comprises Nano micelles [5].

### NOVEL DRUG DELIVERY SYSTEMS

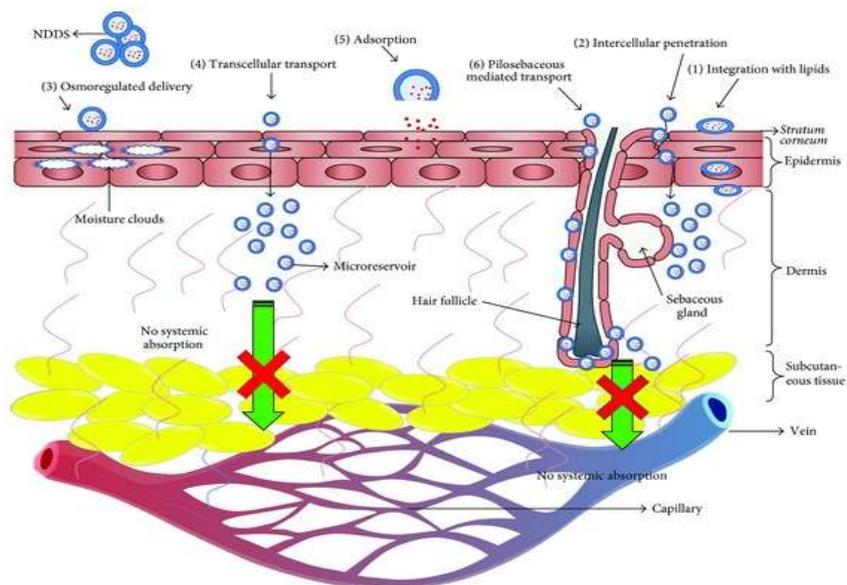
Novel drug delivery system (NDDS) refers to the approaches, formulations, technologies, and systems for transporting a pharmaceutical compound in the body as needed to safely achieve its therapeutic effects [6].

**Table-1: Advantages of NDDS [7]**

- |   |
|---|
| a) Availability of Versatile carriers         |
| b) Protection to drug molecules               |
| c) Biocompatible                              |
| d) Interaction with skin components           |
| e) Loading of variety of drugs                |
| f) Modification in physicochemical properties |
| g) Intact penetration                         |
| h) Passive targeting                          |

The conception of the concept of NDDS can be linked to the drug molecule as “Magic bullet” which

can hit the particular site, only to exhibit the effect.



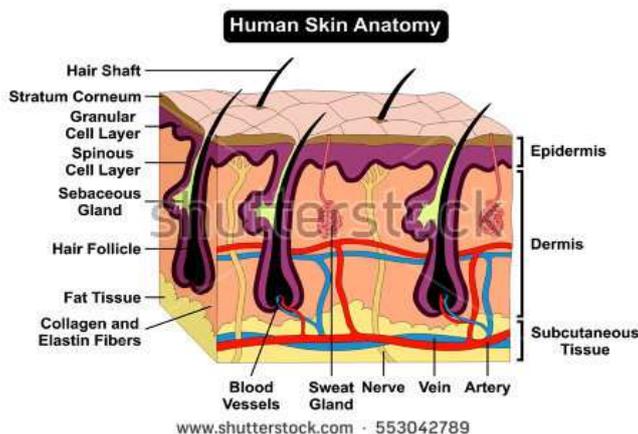
**Fig-1: Various mechanism of penetration of drug loaded NDDS across skin**

As shown in (Figure-1), these carriers interact with skin components and effectively deliver the loaded drug depending on their compositional attributes to the various layer of the skin by one or many processes [8].

#### TOPICAL DELIVERY THROUGH SKIN

Human skin is a well-organized membrane and it has main three layers, which are called as epidermis,

dermis and hypodermis. (Figure-2) shows the anatomy of human skin, Stratum corneum, the outermost layer of skin, is an effective barrier for penetration of drugs in to the deeper layer of the skin [9]. Topical delivery is an attractive choice for the treatment of fungal infection due to its advantageous such as targeting of drugs to the site of infection and reduces the systemic side effects.



**Fig-2: Human skin Anatomy**

Skin disorders afflict millions of people daily. These can be categorized as bacterial, fungal, viral and autoimmune. Topical delivery to the skin surface is continually being explored for the local treatment of these diseases [10]. However resistance to permeability for most of the exogenous substances (drug /active moiety) represents a major challenge in designing the topical drug delivery system. Alteration in skin permeability and its barrier properties with the disease

condition make it hard to fabricate an efficient topical drug delivery [11].

#### METHOD OF PREPARATION

Nanomiemgel mainly utilizes the Multi Absorption Mechanism concept and has high broad applicability .Nanomiemgel consist of two types of matrixes A and B. Matrix A comprises the Nano emulsion and matrix B comprises the Nano micelle.

### **Preparation methods of Nano emulsion**

Various methods for their preparation including the high energy and low energy emulsification and the combined methods are reviewed.

### **HIGH PRESSURE HOMOGENIZER**

In a high pressure homogenizer, the dispersion of two liquids (oily phase and aqueous phase) is achieved by forcing their mixture through a small inlet orifice at very high pressure (500 to 5000 psi), which subjects the product to intense turbulence and hydraulic shear resulting in extremely fine particles of emulsion. Advantage: produce Nano emulsion of extremely low particle size (up to 1nm). Disadvantage: high energy consumption and increase in temperature of emulsion during processing.

### **MICROFLUIDIZATION**

Micro fluidization technology makes use of a device called "micro fluidizer". This device uses a high pressure positive displacement pump (500 to 20000 psi), which forces the product through the interaction chamber, which consists of small channels called micro channels. The products flow through the micro channels on to an impingement area resulting in very fine particles of sub-micron range.

### **PHASE INVERSION METHOD**

Fine dispersion obtained by chemical energy resulting of phase transition occur through emulsification method. The adequate phase transition is produced by changing the composition of constant temperature or by changing the temperature at the constant composition.

### **SONICATION METHOD**

In this method the droplet size of the conventional emulsion are reduced with the help of sonication mechanism. Only small batches of Nano emulsion can be prepared by this method [12].

### **PREPARATION METHODS OF NANO-MICELLE**

Generally micelles are prepared by various methods which are divided in to major groups including simple dissolution method, dialysis method, oil in water emulsion, solvent evaporation method and lyophilisation or freeze drying method.

### **DIRECT DISSOLUTION METHOD**

It is a frequently employed method for the micelle preparation from copolymers with relatively high water solubility. This method involves dissolving the drug and blocks the copolymers directly in the aqueous media. This method is generally employed for moderately hydrophobic polymers such as poloxamers and formulates polyion complex micelles.

### **DIALYSIS METHOD**

This method employed for the micelle preparation from amphiphilic copolymers with low

water solubility. The drug loading procedure is also useful for copolymers which require a common organic solvents to solubilize. In the case of water miscible organic solvents, the copolymers mixture can be dialyzed against aqueous medium (water) to produce micelles due of the organic solvents [13].

### **SOLVENT EVAPORATION METHOD**

In this method both the copolymers and active agent are dissolved in a common solvents or the mixture of the miscible solvents. The drug copolymers film is formed upon stirring and drying the mixture. Micelle is spontaneously formed when the film is reconstituted with warm water or buffer. The samples may be sonicated or passed through a high pressure extruder to prevent multimodal size distribution.

### **LYOPHILIZATION METHOD**

This method is to formulating micelles by the dissolution of both the copolymers and the drug in a mixture of aqueous and organic solvent. Dimethylacetamide and tert-butanol have generally employed as a copolymers because of their high vapour pressure which offers by the rapid sublimation followed by lyophilisation. The micelles also demonstrate adequate shelf- life along with high water dispersibility [14].

### **NOVEL NANOMIEMGEL IN DRUG DELIVERY**

Nanomiemgel is a novel drug delivery system through a novel formulation strategy, which utilizes the multi absorption mechanism concepts and has high broad applicability. Nanomiemgel is prepared by using two types of matrixes. The two types of matrixes comprise Nano emulsion and Nano micelles. The Nano emulsion is prepared by high pressure homogenization method and Nano micelle was prepared by solvent evaporation method [15].

### **PHARMACEUTICAL APPLICATIONS**

In the novel drug delivery system, there are various novel carriers which have advantages over the conventional dosage forms. Conventional dosage forms show high dose and low availability, instability, first pass effect, plasma drug level fluctuations and rapid release of the drug. It minimize problem by enhancing efficacy, safety, patient compliance and product shelf life.

### **NANOEMULSION**

Nano emulsion is more advantages for the iv administration. Both o/w and w/o Nano emulsion system can be used. The Nano emulsions are cleared more slowly than coarse particle emulsion and therefore have a longer residence time in body. Parenteral Nano emulsion formulations such as carbamazepine, diazepam, dexamethasone etc are documented [16]. Nanoemulsion is mainly used as a vehicle system for brain targeted drug delivery. It can be loaded with drugs like risperidone, rizatriptan etc, are very useful in the

treatment of CNS disorders like Parkinson's, migraine, meningitis [17]. Nanoemulsion is also increase the contact time of the drug in the eye. Its offers high ability of drug penetration in to deeper layers of the ocular structure and aqueous humor. Nano emulsion loaded with dorzolamide Hcl shows high therapeutical efficacy and prolonged effects [18]. Nano emulsion is mainly act as vehicle for targeted drug delivery of various aqueous insoluble anti-cancer drugs, photosensitizers and diagnostic agents for cancer therapy. Magnetic Nano emulsion is an innovative approach for cancer therapy. They can deliver photosensitizes like Foscan to the deep layers across the skin thereby reducing hyperthermia [19]. Nano emulsion was developed to increase oral bioavailability of hydrophobic drugs .High concentration of paclitaxel was observed in the systemic circulation when it is formulated in Nano emulsion forms [20]. Nano sized emulsion are able to easily penetrate the pores of the skin and reach the systemic circulation.it able to controlled the locally applied drug redistribution through cutaneous blood and lymph vessel system. W/o emulsion of caffeine, indomethacin, aceclofenac etc. have developed for transdermal drug delivery [21].

#### NANOMICELLE

Nanomicellar approach can be used for topical delivery of different small molecules as well as several genes to the anterior segment of the eye. Its mechanism is that Polymeric and surfactant micelle improves penetration of topically applied drugs through the cornea and hence enhancing ocular bioavailability. Nano micelle entrapped with Dexamethasone is suggested as a potential colloidal drug carrier for ocular drug delivery [22]. Nanomicellar was developed to increase oral bioavailability of poorly water soluble beta blockers. carvedilol (CAR) is a poorly water soluble beta blockers. If it is encapsulated with Nano micelles could improve drug solubility, allowing the development of a paediatric liquid CAR formulation with commercially available polymers [23]. Nano micelle enhanced the anti-cancer effect of pure drug arenobufagin (ABG).Cellular uptake of ABG control specific clathrin-mediated endocytosis, it improve the drug pharmacokinetics with an increased area under the curve and decreased elimination clearance [24].

#### CONCLUSION

Conventional topical formulations are not able to provide prolonged drug release and also associated with many side effect like gastric irritation, nausea, vomiting, bleeding etc. the Nanomiemgel comprising Nano emulsion and Nano micelle enhanced the skin permeation by trans locating the nanoparticles across the deeper skin layers by improving the skin contact time and it forms a thin layer on the skin surface. It remains adhered to the effected part for a longer period without getting rubbing and it's provide sustained drug release and improve the patient compliance.

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