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Review Article

NANOCREAM: A REVIEW NANOTECHNOLOGICAL ASPECT

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ABSTRACT

Nanoparticles are defined as particles with size in the range of 1 to 100 nm at least in one of the three dimensions. Because of this very small size scale, they possess an immense surface area per unit volume, a high proportion of atom in the surface and near surface layers, and the ability to exhibit quantum effect. Nanotechnology represents one of the most capable technologies of the 21st century. Solid lipid nanoparticles introduced in 1991 represent an alternative carrier system to traditional colloidal carriers such as emulsion, liposomes and polymeric micro and nanoparticles. Nanotechnology is widely used in various cosmetic and dermatological products like lipsticks, soap, antiwrinkle cream, perfumes, toothpaste etc. Nanoparticles serve as the fundamental building block for various nanotechnology applications. Nanotechnology is one of the most capable techniques which are safe and effective for targeted drug delivery system. Nanoparticulate delivery system have been developed for good therapeutic effect with low toxicity. Nanotechnology is concerned with development and utilization of structures and devices with development and utilization of structures and devices with organizational features at the intermediate scale between individual molecules and about 100 nm where nanoparticles occur as compared to bulk materials. The overall objective is to disseminate knowledge of the physical, chemical and biological phenomenon and processes in structures that have at least one length scale ranging from molecular to approximately 100nm (or submicron in some situations) and exhibit novel properties because of size. Use of carrier system in nanotechnology has added advantage of improved skin penetration, depot effect with sustained release drug action. As compared to conventional drug delivery system is more prominent and exhaustive. Nanotechnology has completely novel characteristic and application over others. Nanotechnology is a key technology leading to product innovation. Nanotechnologies use materials on an incredibly small scale so that they take on new properties compared to their larger form. The technology has the potential to transform many of the everyday consumer products that we use and wide range of product are already on the market. The focus of the article is on the specific properties, phenomenon and processes that are realized because of the nano size. Experimental and theoretical tool of investigation at nanoscale as well as synthesis, processing and utilization of particles and related nanostructure are integral part of this publication.

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INTRODUCTION

Creams

Creams are viscous semisolid emulsion system with opaque appearance as contrasted with translucent ointments. Consistency and rheological character depends on whether the cream is w/o or o/w.

- Properly designed O/W creams are elegant drug delivery system, pleasing in both appearance and feel post application.
- O/W creams are non-greasy and are rinsable.
- They are good for most topical purpose and are considered particularly suited for application to oozing wounds.

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Factors Affecting Skin Penetration

The factors that influence skin penetration are essentially the same as those for gastro intestinal absorption, with the rate of diffusion depending primarily on the physicochemical property of drug and only secondarily on the vehicle, pH, and concentration (Anonymous, 2008).

The principle physicochemical factor in skin penetration is the hydration state of stratum corneum, which affects the rate of passage of all substances that penetrate the skin. The clinical importance of hydration can be found in the use of occlusive plastic film in steroid therapy. Here, the prevention of water loss from the stratum corneum and the subsequent increased water concentration in this skin layer apparently enhances the penetration of the steroid. The temperature of skin and the concentration of the drug play significant roles, but they are secondary to that of hydration. The solubility of a drug determines the concentration presented to the absorption site, the water or lipid partition coefficient influences the rate of transport. An inverse relationship appears to exist between the absorption rate and the molecular weight. Small molecules penetrate more rapidly than large molecules, but within a narrow range of molecular size, there is little correlation between the size and the penetration rate. The transdermal delivery depend on

1. Release of the medicament from the vehicle.
2. Penetration through the skin barrier.
3. Activation of the pharmacological response (Chopda, 2006).¹

Nanotechnology is the fastest growing area for the maintenance of skin health as well as for the diagnosis and management of cutaneous disease. It encircles the study of particles smaller than 100 nm in size² Solid lipid nanoparticles (SLNs) are introduced as a carrier system for poorly water-soluble drug and cosmetic active drug³. The prefix 'Nano' from nanotechnology it is a Greek word, in which 'Nano' means Small or little⁴. It has come to focus in recent year that there is an increase in need to study on nanomaterial at systemic and in cellular level not only for its therapeutic application but also to minimize the side effect. In the beginning of 1990s, there were only the research group of Muller, Gasco and Western working on nanoparticles, but now in world there are more than 20 research groups are working on lipid nanoparticles. In India Institute of chemical technology, Mumbai which is one of the most leading institute of India is vigorously working on lipid nanoparticle⁵

Nanocream or semisolid emulsion is one of the pharmaceutical topical formulations that are applied externally^{[1],[6]}. The nanocream can be prepared by using high-energy methods such as high shear stirring, high-pressure homogenizers or ultrasound generators⁷. Generally, a nanocream is very useful in personal care and cosmetics because the small size of the droplets which are in the nano range of 100-600 nm⁸ allow them to deposit uniformly onto the skin and enhances the efficient delivery of active ingredients through the skin^{9,10}. Basically, the cream contains various drugs for different remedial properties in an appropriate semi solid base either hydrophobic or hydrophilic in character¹¹.

Advantages of Nanoparticles

1. Large scale production is possible.
2. Long-term stability³
3. Controlled and sustained release of active drug can be achieved.
4. Organic solvents can be avoided
5. It can be lyophilized¹²
6. It can be freeze dried to form powder formulation.
7. By autoclaving and gamma radiation Sterilization is possible.
8. It improves skin protection with organic compound¹³

Disadvantages of Nanoparticles

1. Poor drug loading capacity.
2. High water content of dispersion.
3. The low capacity to load hydrophilic drugs¹²

Method of Preparation of Nanoparticles

1. High pressure homogenization
 - a. Hot homogenization
 - b. Cold Homogenization
2. Microemulsion technique
3. Ultrasonication or high speed homogenization
4. Double emulsion method
5. Spray drying method

High Pressure Homogenization

In high pressure, homogenization liquid is pushed at high-pressure 100-2000 bar through a narrow gap. The fluid accelerates at very high velocity (1000 km/h). In this typical lipid contents in the range of 5-10% which represents no problem to the homogenizer. Higher lipid concentrations up to 40% have been also homogenized to lipid nannodispersions¹⁴. It is widely used than any other method, because it is advantageous than other method. Following are some of the advantages of this method-

1. Easy scale up
2. Powerful technique
3. Short production time
4. Feasibility is more

Hot homogenization

This method is similar to homogenization of an emulsion, because this is also carried out at temperature above the melting point of lipid. In this active compound is dissolved in solid lipid which is melted for Solid lipid Nanoparticle. Due to lowered viscosity of liquid phase smaller particle size is obtained at high temperature¹⁵. In which lipid melt containing active compound is disperse in hot surfactant solution at the temperature 5-10°C by continuous high stirring, after that we got pre-emulsion which is then passed through high pressure homogenizer and maintain same temperature (5-10°C) as above and three cycle at 500 bar or 2 cycles at 800bar¹⁶. Because of high kinetic energy of particles, particle size is increased due to particle coalescence³.

Cold homogenization

This technique is developed to overcome the problems, which are associated with homogenization like temperature induced drug degradation and drug distribution into the aqueous phase

during homogenization¹⁵. In this active compound is dissolved or dispersed in melted solid lipid then cool down it. After solidification of mass then crush it and ground to obtain lipid microparticle. Dispersing the powder in a cold aqueous surfactant solution which yields a cold presuspension of micronized lipid microparticle¹⁷. This suspension is passed through a high pressure homogenizer at room temperature or below it, applying typically 5-10 cycles at 1500 bar¹⁶. As compared to hot homogenization in this technique broader particle size distribution and larger particle sizes are typical of cold homogenized sample¹⁸.

Microemulsion Techniques

This method is based on the dilution of micro emulsions. As micro-emulsions are two-phase systems composed of an inner and outer phase. Micro emulsions are clear, thermodynamically stable system composed of a lipophilic phase, water, surfactant and co-surfactant¹⁹. Micro emulsions are produced at a temperature above the melting point of the lipids, so the lipid should have melting point above room temperature. At first lipids are melt at the temperature 65-70°C¹⁵. The lipid (fatty acids and/or glycerides) are melted, a mixture of water, co-surfactant(s) and the surfactant is heated to the same temperature as the lipid and added under mild stirring to the lipid melt. A transparent, thermodynamically stable system is formed when the compounds are mixed in the correct ratio for microemulsion formation. This microemulsion is then dispersed in a cold aqueous medium (2±38°C) under mild mechanical mixing, which ensure that small particle size due to precipitation. The ratio of microemulsion to cold water ranges from 1:10 to 1:50 using a specially developed thermostated syringe with gentle stirring the composition of micro emulsion determines the dilution process²⁰. Surfactants and co-surfactants include lecithin, biliar salts, but also alcohols such as butanol. Excipients such as butanol are less favourable with respect to regulatory aspects The SLN preparations were washed three times with distilled water and filtered using a membrane; the excess water was removed either by ultra-filtration or by lyophilisation in order to increase the particle concentration. The microemulsion is prepared in a large, temperature-controlled tank and then pumped from this tank into a cold-water tank for the precipitation step. Important process parameters during the scaling up are the temperatures of the microemulsion and the water, but also temperature flows in the water medium and the hydrodynamics of mixing which should change as little as possible during scaling up to maintain the same product characteristics²¹

Ultrasonication or High Speed Homogenization

High-speed stirring or sonication also developed SLN. The most advantage of this method is that, the Equipments that are used here are very common in every lab²². First step of this process is the drug was added to previously melt solid lipid. Then in second step, the heated aqueous phase was added to the melted lipid and emulsified by using high speed stirrer or aqueous phase added to lipid phase drop by drop followed by magnetic stirring. The obtained pre-emulsion was ultrasonicated by using probe sonicator with water bath (at 0°C). In order to prevent recrystallization during the process, the production temperature kept at least 5 °C above the lipid melting point. The obtained nanoemulsion (o/w) was filtered

through a 0.45 µm membrane in order to remove impurities, which are carrying out during ultrasonication. Then obtained SLN is stored at 4 °C. To increase the stability of the formulation, a lyophilizer to obtain freeze-dried powder lyophilized it and sometime mannitol (5%) was added into SLNs as cryoprotector¹⁶. The problem of this method is broader particle size distribution ranging into micrometer range. It also produces physical instability like growth of particle upon storage, and also causes potential metal contamination²³.

Double Emulsion Method

For the preparation of hydrophilic loaded SLNs, a novel method based on solvent Emulsification-evaporation has been used⁴. In double emulsion technique hydrophilic drugs was dissolved in aqueous solution, and then was emulsified in melted lipid¹⁷. In this method the drug is encapsulated with a stabilizer to prevent drug partitioning to external water phase during solvent evaporation in the external water phase of w/o/w double emulsion¹³. Stabilized primary emulsion was dispersed in aqueous phase which contains hydrophilic emulsifier after that the double emulsion was stirred and was isolated by filtration¹⁸.

Spray Drying Method

It is an alternative procedure to lyophilization in order to transform an aqueous SLN dispersion into a drug product. This method is cheaper than lyophilization¹⁷. This method cause particle aggregation due to high temperature, shear forces and partial melting of the particle. In this method short drying time and consequently fast stabilization of feed material at moderate temperatures make spray drying method suitable for producing nanoparticles of drugs that are thermolabile²⁴. The best result was obtained with SLN concentration of 1% in a solution of trehalose in water or 20% trehalose in ethanol-water mixtures (10/90 v/v)⁴. Due to high temperature and shear force it may cause aggregation of particle.

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