

A COMPREHENSIVE REVIEW ON NANO CREAM**Vaishali Kaushik* and Kapil Kumar**

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Corresponding Author*Vaishali Kaushik**Global Institute of
Pharmaceutical Education
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Uttarakhand, India.**ABSTRACT**

Nanoformulations have a definite place in the delivery of the active compounds to and through the skin for a range of therapeutic purposes. These are elegant, relatively simple and inexpensive to make and offer significant delivery advantages over coarse emulsions. Nanotechnology is an important technology paving the way for innovative products. Nanotechnologies make use of materials on a minute scale to impart new properties to them differently than their original larger form. Moreover, this technology is capable of modifying a wide variety of consumer products used in daily life that are currently on the market. One such interesting field is Nano-cosmetics owing to the fact that nanomaterials can be used to develop

novel products. However, the production of UV filters used in sunscreens in a nano form could be more harmful due to their different behaviour than larger forms. Over the past few decades, there has been extensive research demonstrating the effectiveness of these delivery technologies. Also, the development of new excipients with potential utility in nanoformulations continues to offer new opportunities for formulations with high delivery capacity coupled with low irritancy and toxicity. Droplet size, electrical conductivity, drug content, pH and rheological parameters are the parameters that have been studied under different temperatures to evaluate the stability of nano-cream preparation. Thus, the industry, as well as human life, can be drastically modified with exceptional behaviour and properties of nanomaterials. It is probable that we will witness the new Nanoemulsions products for topical and transdermal delivery into the future.

KEYWORDS: Nanocream, Laser ablation, Chemical vapour deposition.

1. INTRODUCTION

Recent years have drawn increasing attention to the use of topical vehicle systems to help in drug permeation through the skin. Drugs of choice are usually those that are problematic when taken orally, such as piroxicam, a highly effective anti-inflammatory, antipyretic, and analgesic. Nano-cream/semi-solid emulsion falls under the category of topical preparations that are applied on the outer surface.^[1-2] Nanocream can be prepared by high-energy techniques like ultrasound generators, high-pressure homogenizers or high shear stirring.^[3] As a result, they are very useful in composing cosmetics and personal care products due to the small droplets having a particle size in the range of nanoparticle (100–600 nm) thereby permitting uniform and smooth deposition of the cream onto the skin surface. This increases the effective release of active drug ingredients on the skin surface contained in the cream in a semisolid base for the purpose of healing several diseases. Moreover, the semisolid base can be of either nature namely hydrophilic or hydrophobic.^[4]

Nanotechnology is nothing but the fundamental study about how materials or particles react or work at the nanoscale (be it at the atomic, molecular or subatomic level) in the development and use of structures, devices, and systems having unique characteristics and purposes.^[5] Nanotechnology entered in the field of cosmetics and health products nearly 40 years ago with liposome moisturizing creams. Rising usage of the technology substantiates the enormous future it has for both the industry as well as the consumers. In fact, there are currently a variety of nanomaterials in practice such as nanoemulsions and nanoparticles of naturally occurring minerals namely copper, silver, titanium dioxide, silicon dioxide, alumina, zinc oxide, and calcium fluoride.^[6] It is well known that when the drug molecules are transported through the skin, they undergo two processes, starting with the drug penetration through the stratum corneum followed by the drug diffusion method into the deeper tissues. However, various factors such as size, log P, ionic strength, the ability of hydrogen bonding, and physicochemical characteristics of the vehicle govern the rate as well as the degree of the transport of drug through the stratum corneum.^[7] Nanomaterials have secured extensive use in the composition hair repairing shampoos, serums and conditioners, creams to heal wrinkles, moisturizing and skin whitening creams.^[8]

Microemulsions and nanoemulsions have many advantages owing to their potential to act as delivery systems for topical drugs. Out of all perceived benefits, the fact that a huge amount of drug can be incorporated into the composition is the most significant advantage of these

dosage forms owing to their high potential to solubilize leading to increased thermodynamic activity into the skin. Moreover, the rate at which the drug penetrates could be improved by using micro/nanoemulsion on account of the synergistic effect of different substances to increase drug delivery across the skin. Furthermore, the main ingredients, i.e., oil, water, and surfactant mixtures, or surfactant- cosurfactant mixtures, can be combined with synergistically to enhance drug flux.^[9] Consisting of water or volatile substances to a proportion of more than 20% and hydrocarbons, polyols, or waxes as mediums, these dosage forms are termed as creams.^[10] Moreover, such forms can comprise of drug substances in an appropriate base.

1.1. Advantages

1. The use of nano cream is aimed to make fragrances last longer, sunscreens more effective and anti-ageing creams.
2. To optimize manufacturing conditions for skincare formulation, a multi-component system.
3. It keeps skin thriving with the help of different constituents that are rich in anti-oxidants.
4. The cream lightens the skin and helps get rid of marks that are a result of unequal arrangement and spread of melanin such as sunspots, age spots, and freckles.
5. It averts the occurrence of grey hair and also plays an important role in medical care given in the case of loss of hair. Additionally, it acts as a preservative to keep lightness and transparency of ingredients namely anti-oxidants as well as vitamins.
6. Another major advantage is that it protects from the harmful effects of the UV radiation in conjunction with other substances called organic sunscreens such as 2- hydroxy-4-methoxy benzophenone. The purpose of organic sunscreens is to facilitate a decrease in the absorption of UV radiation.
7. The most skin brighteners also have anti-ageing effects. Such substances help to beautify the skin. This keeps the skin looking young and beautiful.
8. Nanomaterials used as UV filters in sunscreen products.^[11]

1.2. Disadvantages

People's undesirable experiences are based on the skin type and the ingredients found in a specific nano cream. Such undesirable effects could be anything ranging from mild to very serious.

1. Smaller particles have a higher reactivity, are more chemically reactive and produce more significant numbers of reactive oxygen species.
2. Nanoparticles of TiO_2 that were photo-activated were found harmful to skin fibroblasts and nucleic acids and human colon carcinoma cells.
3. It may cause oxidative stress, inflammation, and subsequent harm to proteins, membranes, and DNA.
4. However, certain ingredients such as hydroquinone, ammoniated mercury and alcohol can be the cause of danger and result in severe and far-reaching health effects on the body.
5. Besides, ultrafine particles such as dust, coal, silicate, asbestos, etc. if inhaled can cause pulmonary inflammation. Such happenings can result in pulmonary fibrosis, cytotoxicity, and even malignancy.^[11,12]

2. Methods of Preparation of Nanocreams

Nanocream/Nanoemulsions can be prepared by using high and low energy methods. In high energy methods, mechanical devices deliver the requisite high disruptive forces. On the contrary, in low energy methods, there is no requirement for external power. Production of nano cream is achieved by using the intrinsic physiological properties of the system. In this nano cream preparation method, the stored energy of the system is utilized by alteration of parameters such as temperature, the composition of the system.^[13] At the initial studies of nano cream, the high energy methods were the only choice for researches. Thus, high energy stirring and ultrasonic emulsification were the most widely used method for the preparation of nanocream.^[14] Nowadays, the low-energy methods have drawn considerable attention since they are 'soft', nondestructive and cause no damage to encapsulated molecules.^[15]

1.) High – Energy Emulsification Method:

Nanocream or nanoemulsions are those non-equilibrium systems that cannot be formed rapidly. For this cause, mechanical or chemical energy input is essential to make them. Nanocream are generally prepared by using high energy methods in which mechanical energy input is applied by high-pressure homogenizers, high shear stirring, and ultrasound generators.^[16] The mechanical devices provide strong forces that disrupt oil and water phases to form cream. In high energy methods, input energy density is about 108 -1010 W kg⁻¹. The Required energy is supplied in the shortest time to the system to obtain homogeneous small-sized particles. High-pressure homogenizers have the potential to do this and therefore they are hence extensively for preparation of nanocream.^[17]

2.) High-Pressure Homogenization

This is the most popular method used for the production of nano cream. This method offers benefits from the high-pressure homogenizer or the piston homogenizer to manufacture that particle sizes are up to 1 nm. During this method, the macroemulsion is forced to pass through in a small orifice at an operating pressure between 500 to 5000 psi.^[18] This process can be again carried out until the final product reaches the required size of the droplet and polydispersity index (PDI). Also, the uniformity of the size of the droplet in such formulations is specified by PDI.^[19] Higher PDI indicates a lower uniformity of droplet size as observed in the case of such cream formulations. Monodisperse tests have PDI lower than 0.08, PDI somewhere in the range of 0.08 and 0.3 states a limited size circulation, though PDI more noteworthy than 0.3 shows wide size appropriation.^[20]

This quantity of energy and rise in temperatures during the high-pressure homogenization process might cause deterioration of the components. Thermolabile compounds such as proteins, enzymes, and nucleic acids may be damaged.^[21]

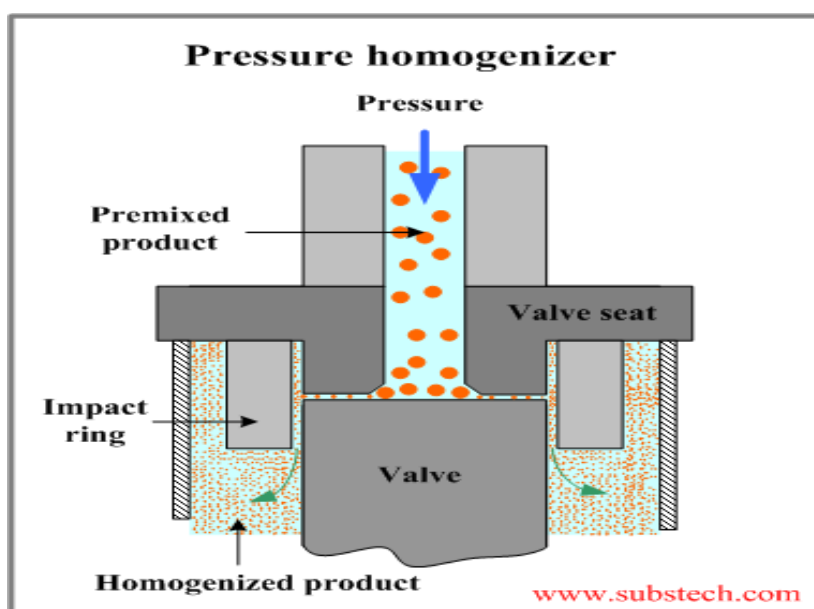


Figure 1: Schematic representation of high-pressure valve homogenizer.

3.) High – Shear Stirring

Right now, vitality blenders and rotor-stator frameworks are utilized for the arrangement of nanocream. Bead sizes of the inward stage can be fundamentally diminished by expanding the blending force of these gadgets. Be that as it may, acquiring emulsions with the normal bead size under 200-300 nm is somewhat troublesome.^[22]

4.) Ultrasonic Emulsification

There are two mechanisms that occur in the process of ultrasonic emulsification. Firstly, the acoustic field makes interfacial waves that make the oil stage to scatter in the nonstop stage as beads. Furthermore, ultrasound incites acoustic cavitation which gives development and breakdown of microbubbles individually because of weight changes of a solitary sound wave. In this way, levels of highly localized turbulence are generated, and this causes micro implosions which disrupt large droplets into sub-micron size.^[23] In this method, the premixed blend is disturbed by vibrating strong surface at 29 kHz or bigger frequencies. High-power ultrasonic gadgets, for example, centering horns and pointed tips cause outrageous shear and cavitation that bring about separating of beads. The advancement of these parameters is important to get ready definitions having fine beads. Be that as it may, there are a few worries about sonication techniques since they can incite protein denaturation, polysaccharide depolymerization and lipid oxidation.^[24,25]

5.) Microfluidization

It is the most widely used method in the pharmaceutical industry to acquire fine particles. In this technique, a device named microfluidizer is utilised thereby offering high pressures. During this process, a high-pressure force applied to the particle interaction chamber and thus small sizes with submicron ranged particles can be produced. Uniform nano cream or nanoemulsion production can be achieved by repeating the process many times and varying the operating pressure to get the desired particle size.^[26] There is an impact between rough emulsion planes from two inverse diverts in the spout of microfluidizer which is additionally called the collaboration chamber. The portability of unrefined emulsion is given by a pneumatically fueled siphon that has the ability to pack air up to pressures between 150 to 650 MPa. This high weight powers the unrefined emulsion stream to experience microchannel and after the impact of two inverse channels, colossal degree of shearing power is gotten.

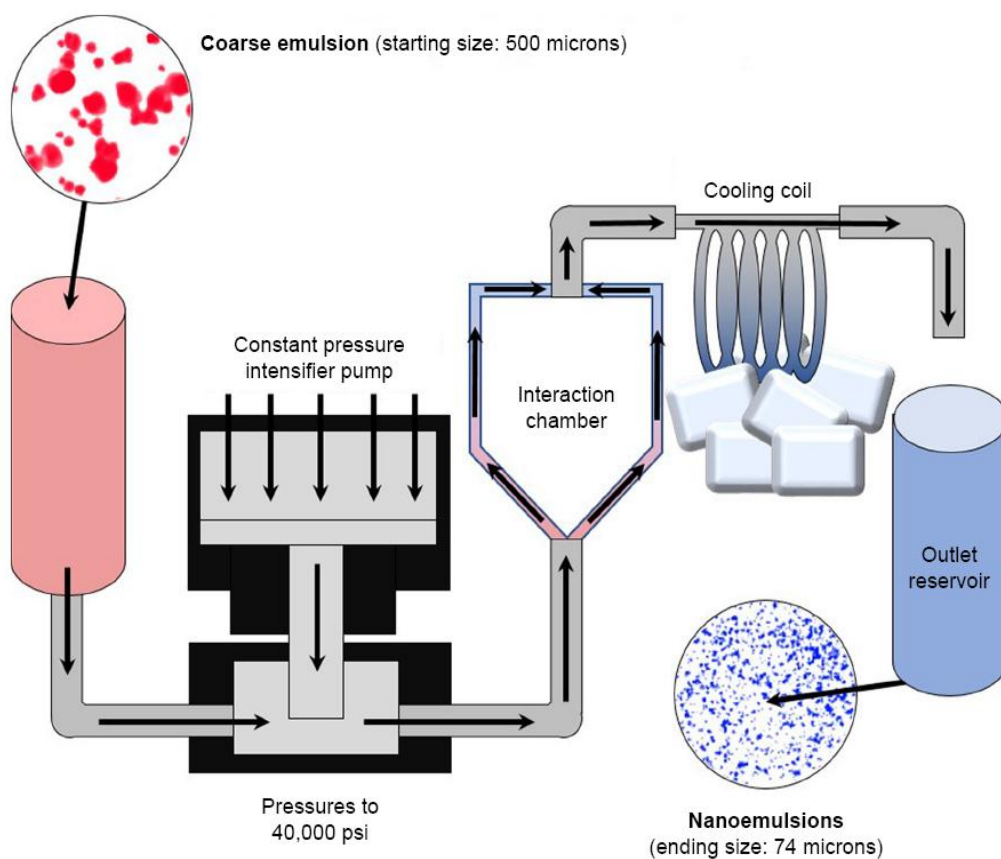


Figure 1 Microfluidization process for the preparation of nanodelivery systems.

Figure 2: Schematic representation of microfluidization.

6.) Phase Inversion Temperature

In this method, the temperature is changed at constant composition. Non-ionic surfactants which have temperature-dependent solubility like polyethoxylated surfactants play an essential role. Emulsification is achieved by modifying the affinities of surfactants for water and oil as a function of temperature.^[27] During the heating of polyethoxylated surfactants, they become lipophilic because of the dehydration of polyoxyethylene groups. within the PIT method, the droplet sizes and also the interfacial tensions reach their minimum value. it's been reported that stable and fine particles droplets will be produced by the rapid cooling of the emulsion near the temperature of PIT.^[28]

7.) Phase Inversion Composition

In this method, the composition is changed at a constant temperature. It is more appropriate for massive production on a bigger scale than the PIT method as the incorporation of an additional substance to an emulsion is simpler than adjusting change in temperature. By adding water to the system, the volume of water increases thereby resulting to reach a transition composition.

3. General Parameters for Evaluation of Nanocream

1.) Formulation Properties

The formulation properties of the cream were studied by visual appearance and characteristics.

2.) Presence of foreign particles/grittiness

A small amount of cream was taken and spread on a glass slide free from grease and was observed against diffused light to check for the presence of foreign particles.

3.) pH of the cream

The pH of assorted formulations makes up my mind by employing a digital pH meter. About 1 g of the cream was weighed and dissolved in 100 ml of water and stored for 2 hours. The measurement of the pH of each formulation was done in triplicate, and average values were calculated.

4.) Viscosity

The viscosity of the formulation was determined by Brookfield Viscometer II + model using spindle no S – 64 at 20 RPM at a temperature of 25° C and the determinations were carried out in triplicate, and the average of three readings was recorded.

5.) Rheological behavioural of the cream

The rheological property was firm to grasp the flow behaviour of the formulation. The viscosity at different RPMs was measured using Brookfield viscometer. The rheological behaviour of the formulation was studied by taking 100 g of the cream within the beaker. the speed of shear was increased gradually from minimum to maximum, and corresponding dial reading was noted; then, the speed of shear was progressively decreased to an all-time low value, and also the dial reading was recorded.

6.) Partition coefficient of cream

The partition coefficient of the drug between phosphate buffer solution (pH 7.4) and n-hexane was determined at (37.0 C \pm 0.20 C). An excess amount, i.e., 50 mg of cream was taken in a separating funnel containing 1:1 ratio of buffer 7.4 and hexane. It was placed on a water bath for 24 h. The solution was shaken occasionally. Then, both of them were separated and filtered through a 2 μ filter and the amount solubilized in each phase was determined by measuring the absorbance using a UV spectrophotometer. Hexane has polarity zero. Hence it is chosen for the study of the partition coefficient.

4. Nanocream Product

- 1.) Chantecaille Nano Gold Energizing Cream claims that “nanoparticles of 24-karat gold are bound to moisturising, antioxidant and anti-inflammatory silk microfiber.
- 2.) Moisturisers/anti-wrinkle creams: Lancôme Hydra Zen Cream with “nanoencapsulated Triceramides renew skin’s healthy look”; L’Oreal Revitalift Double Lifting anti-wrinkle cream is their “first double-action cream that instantly retautens the skin and reduces the looks of wrinkles”, and contains Nanosomes of Pro-Retinol A.
- 3.) Breast cream: St Herb Nano Breast Cream claims it is a blend of "nanotechnology and the immortal Thai herb, Pueraria Mirifica" and that nanosomes "extends the cell substructure and advancement of the lobules and alveoli of the bosoms", with expanded size from one to three cups.^[29-31]
- 4.) The new CBD Nano Cream—it will quickly penetrate your skin's outer oil layer, so the CBD can get to work more precisely and with less wait time. This means less waste for you and a better topical CBD experience.



- 5.) The Nano Breast Cream is a wonderful mix of science and nature, i.e. of nanotechnology and Pueraria Mirifica.



5. Pharmaceuticals applications of Nanocream

- 1.) Topical applications of drugs are applied with a variety of desired effects, including the targeting of local tissues for a dermatological impact.
- 2.) The commonly used drug in the management of a wide variety of conditions ranging from dermatitis and psoriasis to skin infections to acne.
- 3.) Nanocream also provides a means of sustained delivery and thus minimises the frequency of drug administration.^[32]

Table 1: Nanocream formulation currently available in the market.

Company	Ingredient	Brand	Product	Nano size
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Acne Treatment

Celazome New Zealand limited	Celazome	Target Acne Spot Treatment	Lyphazomes Nanosphers
Wilma Schumann	Wilma Schumann	Acne kit	Vitamin E Nanoparticles
DS Laboratories, Inc	DS laboratories	Anti- Acne gel	Arnica Nanosomes

After-sun product

L'oreal	Lancome	Cooling sun spirtz	Vitamin Nanocapsule
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Anti aging^[33]

Sircuit Skin cosmeceuticals Inc.	Sircuit Skin	Anti- Oxidant serum	Fullerenes
Cosmetic Dermatology, Inc.	Dr. Brandt	Dr. Brandt laser tight	Nanocapsulated Ingredient
Procyte Corporation	Neova	Dual-action lotion	Nanoencapsulated Retinol
DS Laboratories, Inc	DS Laboratories	Cream for wrinkles and expression lines	Nanosomes of Vitamin A
DS Laboratories, Inc	DS Laboratories	Viterol A (Viatrazene gel 16%)	Nanosomes of Vitamin A
L' Oreal	Lancome	Lancome Soleil soft-touch anti-wrinkles suncream	Vitamin Nanocapsules

Around Eye cream^[34]

Perfect RX	Perfect RX	Eye perfect serum	Nanodelivery System
Ciba Vision Corporation	Eye	Eye treat with lyphazome technology	Lyphazomes Nanospheres

Facial moisturizer/treatment^[35]

Ferndale Laboratories, Inc.	Ferndale Nouriva	Nouriva Repair Moisturizing Cream	Nanoparticle
Ferndale Laboratories, Inc	Ferndale Nouriva	Ferndale Nouriva – Nouriva Repair Moisturizing Cream	Nanoparticle

6. CONCLUSION

There is a lot of semisolid based pharmaceutical dosages available which are mostly used in the field of dermatology. There is a lot of creams based semisolid dosages available to protect our skin such as moisture cream, sun lotions, baby lotions, anti-ageing cream, etc. Over the last decade, nanotechnology is extensively being employed in the field of dermatology, cosmetics, and biomedical applications for its perceived benefits as discussed. Additionally, there have been inventions of the latest technologies as well as novel delivery systems that are presently in practice for the development of cosmeceuticals products. Nanoproducts should be formulated in a manner such that the value and health of the customers are improved. Besides, nanotechnology has an immense potential to transform the industry.

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