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REVIEW ON NANOPARTICLES USED IN COSMETICS AND DERMAL PRODUCTS

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ABSTRACT

Nanotechnology is widely used in various cosmetic and dermatological products like lipstick, soap, anti-wrinkle cream, perfumes, toothpaste etc. In this century, Nanotechnology is one of the most capable techniques which are safe and effective for targeted drug delivery system. The present review focus on the recent applications of nanoparticles in cosmetics and dermal product. Nanoparticulate delivery systems have been developed for good therapeutic effect with low toxicity. As compared to conventional drug delivery system Nanoparticulate delivery system is more prominent and exhaustive. Nanotechnology has completely novel characteristic and application over others. It also summarizes methods of preparation of nanoparticles, characterization of nanoparticles and application of nanoparticles in current drug delivery. The review according to industrial point of view shows that nanoparticles have wide application as alternative carrier for cosmetic and dermal products.

KEY WORDS: Nanotechnology, Solid lipid Nanoparticles, Cosmetics, Ultrasonication.

INTRODUCTION

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 size [1]. Solid lipid nanoparticles (SLNs) are introduced as a carrier system for poorly water soluble drug and cosmetic active drug [2]. The prefix 'Nano' from nanotechnology it is a Greek word, in which 'Nano' means Small or little [3]. It has come to focus in recent year that there is an increase in need to study on nannomaterial 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 nanoparticle [4]. Cosmetic product is any substance or mixture intended to be placed in contact with the external parts of the human body i.e. epidermis, hair, nails, lips and external genital organs or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance, protecting them and keeping them in good condition [5]. Solid lipid Nanoparticle (SLN) represents an alternative carrier system to traditional colloidal carriers, likewise liposomes, emulsions and polymeric micro and nanoparticles [6]. Nanoparticles have a specific physical, chemical and biological property. These properties make nanoparticle as potent molecules for diagnostics and therapeutics in modern medicine. Nanoparticles are widely used because of its desirable properties in industrial, medical and cosmetic fields. Nanoparticles have wide variety of application like it improves protection against sun exposure and deeper skin access [3].

Advantages Of Nanoparticles

1 Large scale production is possible.
2 Long-term stability [2].
3 Controlled and sustained release of active drug can be achieved.
4 Organic solvents can be avoided
5 It can be lyophilized [7].
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 compound [8].

Disadvantages Of Nanoparticles

1 Poor drug loading capacity.
2 High water content of dispersion.
3 The low capacity to load hydrophilic drugs [7].

Method Of Preparation Of Nanoparticle

1. High pressure homogenization

1.1 Hot homogenization

1.2 Cold Homogenization

2. Microemulsion technique

3.Ultrasonication or high speed homogenization

4. Double emulsion method

5. Spray drying method

1. 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 nannodispersions [9]. 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

1.1 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 temperature [10]. 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 800bar [11]. Because of high kinetic energy of particles, particle size is increased due to particle coalescence [2].

1.2 Cold homogenization

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

aqueous phase during homogenization [10]. 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 microparticles [12]. This suspension is passed through a high pressure homogenizer at room temperature or below it, applying typically 5-10 cycles at 1500 bar [11]. As compared to hot homogenization in this technique broader particle size distribution and larger particle sizes are typical of cold homogenized sample [13].

2. Microemulsion Techniques

This method is based on the dilution of microemulsions. As micro-emulsions are two-phase systems composed of an inner and outer phase. Microemulsions are clear, thermodynamically stable system composed of a lipophilic phase, water, surfactant and co-surfactant [14]. Microemulsions 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°C [10]. 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 microemulsion determines the dilution process [15]. 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 [4]. 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 characteristics [4].

3. Ultrasonication or high speed homogenization

SLN were also developed by high speed stirring or sonication. The most advantage of this method is that, the Equipments that are used here are very common in every lab [7]. 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 ºC).In order to prevent recrystalization during the process, the production temperature kept at least 5 ºC 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 ºC. To increase the stability of the formulation, it was lyophilized by a lyophilizer to obtain freeze-dried powder and sometime mannitol (5%) was added into SLNs as cryoprotector [11]. 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 contamination [16].

4. Double emulsion method

For the preparation of hydrophilic loaded SLNs, a novel method based on solvent Emulsification-evaporation has been used [3]. In double emulsion technique hydrophilic drugs was dissolved in aqueous solution, and then was emulsified in melted lipid [12]. 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 emulsion [13]. Stabilized primary emulsion was dispersed in aqueous phase which contains hydrophilic emulsifier after that the double emulsion was stirred and was isolated by filtration.

5. 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 lyophillization [12]. 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 thermolabile [17]. 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) [3]. Due to high temperature and shear force it may cause aggregation of particle.

Table 1 Advantages and drawbacks of various techniques

Sr.No.	Techniques	Drugs	Advantages	Drawbacks	Ref
1.	High pressure homogenization	Olanzapine	Well developed tech., Scalable, Commercially demonstrated.	Energy intensive process, damage to biomolecule.	13
2.	Hot homogenization	Diazepam	Applicable to insoluble and lipophillic drugs, at high temperature exposure time is short.	For hydrophilic drug there is low entrapment efficiency.	15
3.	Cold omogenization	Vinorelbin-bitartrate	Applicable for hydrophilic, thermolabile and thermosensitive drugs.	Exposure to heat can't be completely avoided.	13
4.	Microemulsion ech.	Paclitaxel	Low mechanical energy input.	Sensitive to change, low concentration of Nanoparticle.	15
5.	Ultrasonication	Insulin	Effective at laboratory scale, reduced shear stress.	Energy intensive process, high metal contamination potential.	15
6.	Double emulsion method	5-Fluorouracil	Enhancing the encapsulation efficiency and loading capacity.	Formation of high percentage of microparticles.	13

Characterization Of Nanoparticles

After preparation of nanoparticles, it is essential to ensure that the particles obtained have the desired properties and are suitable for administration. Various parameters include in the characterization of SLN like Particle size analysis, zeta potential, scanning electron microscopy, differential scanning colorimetry and drug release and drug stability.

A) Particle size analysis and zeta potential

Many techniques are available for particle size analysis and zeta potential like scanning electron microscopy (SEM), atomic force microscopy (AFM), scanning tunneling microscopy (STM) and photon correlation spectroscopy [6]. Maximally, photon correlation and laser diffraction are used. But there is one drawback of photon correlation spectroscopy, it can't detect large microparticle. To overcome this problem, additional techniques are use that is light microscopy which gives fast indication in the presence and character of microparticle [7]. Solvent removal may cause modification which may impact on particle shape [2]. In both methods one thing is clear that both methods are not measuring the particle size; they only detect light scattering effect which is used to calculate the particle size. Zeta potential is an important characteristic of SLN; its high value may lead to break the particles

in the absence of other complicating factor likewise static stabilizers. Zeta potential is generally measured by zetameter [10].

B) Scanning electron microscopy

Scanning electron microscopy (SEM) and Transmission electron microscopy (TEM) provides information on nanoparticles and physical characterization of nanoparticles [2]. Electron microscopy provides information on morphology and crystallography. Scanning electron microscopy is better for morphological information. It has high resolution [4]. Transmission electron microscopy has a small limit of detection. Transition electron microscopy and light microscopy both are based on same principle but one difference is that in light microscopy light is used instead of electron [16].

C) Differential Scanning Colorimetry

Differential scanning colorimetry (DSC) and powder X-ray diffractometry is carried out for the determining the degree of crystallinity in the dispersion of particle. In DSC samples were heated from 25-85 ˚C and cooled at 85-20 ˚C under liquid nitrogen [34]. DSC also used for determining the nature and speciation of crystallinity within nanoparticles through the measurement of glass and melting point temperature [2].

D) Acoustic method

This method used to measure the attenuation of sound waves for determining the size through the physically relevant equation [11]. The oscillating electric field is generated by the movement of charged particle under the effect of acoustic energy, which provides information on surface charge [13].

E) Infra red spectroscopy

IR spectroscopy (IR) can be used to identify the ligand of nanoparticles. The order and disorder of transition in nanoparticles is detected with the help of IR & NMR. FTIR shows as the temperature increases gauche defect increases. Nuclear magnetic resonance (NMR) detects the size and nature of nanoparticles [8]. The Hydroxyapatite was also pure (noncarbonated) which was confirmed by Fourier transform infrared (FTIR) and x-ray diffraction (XRD) analysis [18].

Application Of Nanoparticle In Cosmetics And Dermal

The use of nannomaterial in cosmetics is not new. Since thousand years of ago in ancient Egypt it is used. But in today's century recent development in nanotechnology, engineered nannomaterial have been embrassed by the cosmetics industry for several reasons.

1. Penetration into deeper skin access than any other cosmetic.
2. Some nanoparticles have antioxidant property.
3. Due to their small size and specific optical properties.

1. Sunscreen cream

In the field of cosmetics, nanoparticles are wide range of application in sunscreen. Some inorganic components in sunscreen cream like TiO_2, ZnO which act as UV filters and have been shown to photogeneric free radicals. It has been shown that the addition of these inorganic compounds into sunscreens which effectively reduce the absorption of UVA and UVB radiation and give protection against UV radiation harmful effects [19]. Nanoparticles are very beneficial for UV protection due to its small size [8]. TiO_2 is most widely use due to its brightness and high refractive index [20]. They have a significant increase in their effectiveness of blocking UV light compared to natural material due to their large surface area to volume ratio. Titanium dioxide and zinc oxide are the main inorganic component of sunscreen; TiO_2 and ZnO are used to applied in sensitive skin, baby products and in daily wear skin lotion [21]. TiO_2 Nanoparticle can be coated with silica to increase UV absorption. For increasing the absorption of Zinc oxide (ZnO) it is prepared in particles that have an optimal size of 20-30 nm. ZnO is also usually coated with silicon oils, SiO_2, or Al_2O_3 in sunscreen formulations additionally, ZnO is considered a better sunscreen ingredient than TiO_2 because it is more transparent for a given concentration and is more protective against UV light [4]. SLNs are advantageous because they approach a zero-order release profile, which means that they release less of the sunscreen formulation over time than o/w emulsions. Thus, the sunscreen remains on the surface of the skin longer and provides better protection against UV [19].

2. Antioxidant

Antioxidants are used in the cosmetic industry for prevention of the new wrinkles and reduce skin aging which is caused by UV light. These antioxidants, such as vitamin C, vitamin E and pycnogenol, have been shown to have a synergistic effect when combined for photoprotection; Photostabilizers have also been shown to exhibit antioxidant properties,

diethylhexyl syringylidene malonate (DESM) can be used as a photostabilizer for avobenzone as well as an effective antioxidant [22].

3. Hair disorder

Nanotechnology drug delivery systems rather than aqueous alcohol solutions are gaining importance in the treatment of hair disorders like alopecia androgenetica and *alopecia areata*. By using nanoemulsion to encapsulate active ingredients and carry them deeper into hair. They do so by increasing drug penetration into the hair follicle openings and can act as a depot for a sustained drug release within the hair follicle [3]. RBC Life Science's Nanoceuticals Citrus Mint Shampoo and conditioner are made with nanocluster which is used to nourish scalp and for shining the hair. Due to lack of other therapeutic options, gene therapy of hair and the novel particle based drug delivery systems for a promising active follicular targeting of disease-related cell populations in the hair follicle are getting importance [8].

4. Anti-inflammatory

The non-steroidal anti-inflammatory drugs like celecoxib and valecoxib are act by selective inhibition of COX-2 have been investigated for dermal application using NLC based delivery systems. Celecoxib is widely used for the treatment of rheumatoid arthritis, acute pain, familial adenomatous polyposis and primary dysmenorrheal. Furthermore, topical formulations of COX-2 inhibitors have been developed for the treatment of COX-2 mediated skin diseases like inflammation, pain, injury and wounds. Chitosan-alginate nanoparticles also have anti-inflammatory activities as they inhibited propioni bacterium acnes-induced inflammatory cytokine production in human monocytes and keratinocytes. Furthermore, benzoyl peroxide (BP), a commonly used anti-acne drug, was effectively encapsulated in the Chitosan-alginate NPs and then it show superior antimicrobial activity against propionibacterium acnes compared with Benzoyl peroide alone while demonstrating less toxicity to eukaryotic cells. From, this it is conclude that the potential utility of topical delivery of chitosan-alginate nanoparticles encapsulated drug therapy for the treatment of dermatologic conditions with infectious and inflammatory components [4].

5. Toothpaste

By using a nanotechnology in toothpaste, it is very helpful for preventing damage to tooth enamel. Hydroxyapatite is a key component of tooth enamel as nanocrystals. Hydroxyapatite with the chemical formula $Ca(PO_4)_6(OH)_2$, is the main component of bone and teeth. Nano

hydroxyapatite is used in toothpaste, it forms protective film around tooth enamel, and even restores the surface in damaged areas and it also reduces the pain. This is world's first 'remineralizing' toothpaste. Ace Silver plus Nano silver toothpaste is manufactured and available in Korea [8].

6. Antiandrogen

The oral application of cyproterone acetate can be used to reduce sebum secretion rate and acne lesions. In female patients, combination of cyproterone acetate and ethinyl estradiol is given to exclude teratogenic effects of cyproternoe acetate. In male patient's loss of libido, gynecomastia, and loss of bone mineral density can be observed as cyproterone acetate side effects, which is acceptable when used for metastatic prostate cancer but not acceptable for acne treatment. Application of cyproterone acetate-loaded solid lipid nanoparticles increased the skin penetration at least four times compared to cream and emulsion, whereas the drug amount found in the dermis was low for all preparations. Cyproterone acetate loaded solid lipid nanoparticles enhanced skin absorption resulting in therapeutic drug levels within the target tissue and reduces the systemic side effects compared to the oral administration [4].

7. Fullerenes

It is new type of material which is produced by using nanotechnology like carbon fullerenes. Fullerenes are also known as "buckyballs" are spherical molecules of carbon atoms measuring about 1 nm in diameter. They are not biodegradable [29]. One of the main causes of skin problems are reactive radical species. On exposure to ultra-violet radiation it may produce flecks, skin irritation and wrinkle formation. For curing these problem antioxidants such as vitamin C and vitamin E are used. But Fullerenes are super powerful antioxidant activity at least two order of magnitude over Vitamins. Fullerene is also having brightening effect. It shows its brightening effect by eliminating UV-induced free radicals and by preventing excessive melanin production. Fullerene derivatives have also been shown to have anti-inflammatory capabilities through their ability to stabilize Mast Cells (MC) preventing inflammatory mediator release [23]. .

Stability Of Nanoparticles

Solid lipid nanoparticles stability considered from two aspects, particle size distribution and crystalline state. In which crystalline state generally related with release rates, drug loading and geometry of particles. Particle size is also important factor which affect on

reticuloendothelial system and biodistribution. The degree of polydispersibility affects on growth of particle size by Ostwald ripening and can smash the drug release kinetics [16].

Dermal Toxicity Of Nanoparticles

Nanoparticles of titanium dioxide and zinc oxide commonly used in sunscreens cream and in cosmetics which may produce free radicals, damage to DNA and may cause cell toxicity, especially when exposed to UV light. Nanoparticles used in sunscreens and cosmetics could actually result in serious skin damage [3]. While carrying out work with ultrafine nanoparticles without sufficient protection may increase risk of skin exposure. Small size particles produce toxic effect on lungs which are deposited deeper and may cause greater damage. Toxicity is also related to dimensions, one dimensional structure shows greater toxicity. Nanoparticles have not only adverse effect like cytotoxicity but also it may also affect on immunological response of cell [24]. There is a general relationship between particle size and toxicity. The small size, greater surface area and greater chemical reactivity of nanoparticles results in an increased production of reactive oxygen species (ROS) and it also includes free radicals [27].

STORAGE STABILITY OF NANOPARTICLEs

The physical properties of loaded solid lipid nanoparticles during prolonged storage can be determined by change in particle size, zeta potential, viscosity and appearance. For the physically stability of nanoparticle, it should be remain higher than -60mv for a dispersion [9]. 4˚C Most favorable storage temperature. 20˚C- Long term storage not results in SLN aggregation or loss of drug. 50˚C- A rapid growth of particle size was observed [25].

Parameters Which Directly Impact On Stability

1. Degree of crystallinity
2. Particle size and zeta potential
3. Coexistence of colloidal structure [26].

Future Novel Plan For Uv Protection

In future UV protection is achieved by optimizing the photostability of the sunscreen while protecting against the broadest possible spectrum of UV light. Few novel ideas for UV protection.

In textiles as UV-absorbers

A new idea in UV protection is to incorporate UV protectant nanoparticles into fabric used for clothing. Zinc Oxide (ZnO) nanoparticles have been incorporated into the surface of cotton and wool fabrics. The addition of ZnO increases the mechanical strength of both fabrics and results in an UV absorbing fabric [19].

Table 2 Polymeric Nanoparticulate System with their Particle Size Distribution (nm)

Sr. No.	Polymeric system	Paricle size distribution (nm)	Ref
1	Nanoparticles	50-500	32
2	Nanocapsules	100-300	32
3	Nanogels	200-800	33
4	Solid lipid nanoparticles	50-400	33
5	Fullerene	1-10	33

BRANDS AVAILABLE IN THE MARKET

Table 3 Marketed formulation of Nanoparticles as a cosmetic

Sr. No.	Brand Name	Composition	Company Name	Indication	Ref
1	Emend	Nanocrystalline aprepitant	Elan, Merck	Antiemetic	28
2	Tricor	Nanocrystalline fenofibrate	Elan, Abbott	Antihyperlipidemic	28
3	DepoDur	Liposomal morphine	SkyePharma, Endo	Postsurgical analgesia	30
4	Abelect	Liposomal Amphotericin B	Enzon	Fungal Infections	31
5	Ambisome	Liposomal Amphotericin B	Giled (Foster City, a,Usa)	Fungal Infections	30
6	Macugen	Pegylated anti-EGFaptamer	OSI Pharmaceuticals	Age-relatedmacular degeneration	31
7	Abraxane	Paclitaxel protein bound nanoparticles	Abraxis BioScience	In Cancer therapy	33
8	Myocet	Liposomal doxorubicin	Zeneus Pharma	Breast Cancer	30
9	Acticoat	Silver Nanoparticle	Nucryst (USA)	Antimicrobial wound care	30
10	Rapamune	Nanocrystalline sirolimus	Elan, Wyeth	Immunosuppressant	33

11. CONCLUSION

This review summarizes that nanotechnology is considered as new industrial revolution for pharmaceutical field. Nanoparticles have broad application in field of cosmetics, now it is good opportunities zfor cosmetuceutical industries to improve medical therapeutics by using nanoparticulate techniques. SLN is well tolerated carrier system for cosmetics and dermal product, TiO_2 is successfully applied in cosmetics due to its stability and low toxicity concerns. A novel concept in future that is use of nanoparticle fabrics in cotton which play role as UV absorber. To improve better therapeutics application and less toxicity of nanoparticle more research study is required. Today so many marketed formulations are in

the markets which have good therapeutic application over other. Global market for nanoparticles in Biotechnology and Pharmaceuticals in 2012 it is nearly about $9.4 billion and in future i.e. in 2017. It may grow up to nearly $20.5billion. Solid lipid nanoparticle also enhances the drug discovery process through speed and reliability of assays. It is also important to create awareness in society about this new technology, which is very safe and effective drug delivery system.

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