Available online <u>www.jocpr.com</u>

Journal of Chemical and Pharmaceutical Research, 2016, 8(5):906-914



Review Article

ISSN : 0975-7384 CODEN(USA) : JCPRC5

The current role of nanomaterials in cosmetics

Kurapati Srinivas

Associate Professor in Physics, Gitam School of Technology, Gitam University, Bengaluru-562163, India

ABSTRACT

Nanotechnology entered the field of cosmetics and consumer health products nearly 40 years ago with moisturizing creams that used liposome, a vesicle of phospholipid layers with an aqueous core. Nanomaterials in cosmetics include nanoemulsions, nanosomes and nanopigments commonly used in sunscreens, barrier skin creams and oral hygiene products. Nanotechnologically manufactured materials (so-called biocomposites) in toothpaste promote the natural tooth repair mechanism of saliva. In healthcare products, nanocapsules protect and transport active ingredients and enhance their effect. Nanoemulsions in cosmetics can increase the nutritious oil content of products such as high performance moisturisers, which may employ tiny pocket-like structures called nanosomes to help protect fragile ingredients from degrading. These nanoemulsions and nanosomes are soluble and break down upon application to the skin. However, nanotoxicological research expressed concern about the impact of manufacturing and use of nanomaterials on human health and environment with silver nanoparticles used in socks to reduce foot odour are being released in the wash water causes destruction of natural ecosystem. Therefore, nanomaterials require a health risk assessment, which should be performed on a case-by-case basis, using pertinent information. Europe has already passed new laws that will require most nano-ingredients in sunscreens, cosmetics to face new safety testing and mandatory labeling.

Key words: anticoagulant, bacteriostatic, biocomposites, nanotubes, nanoemulsions, nanosomes, nanomaterials.

INTRODUCTION

Over 4000 years ago, prehistoric Egyptians, Greeks and Roman researchers were making use of nanotechnology in hair dye preparations. [1] From 1959 onwards, the concept of nanotechnology came into existence in different fields of sciences like biology, physics, chemistry, and engineering. [2] Also it has been entered in the field of cosmetics for instance; dermal preparations and other health products with moisturising creams prepared by using liposomes nearly existed 40 years ago. The prefix "Nano" from nanotechnology is a Greek word: "Nanos" – which means "little old man or dwarf". Nanotechnology is a powerful new technology in which a material is reconstructed or engineered at an atomic and molecular level. One nanometer (nm) is one billionth, or 10⁻⁹ of a meter. According to the definition of National Nanotechnology Initiative in the US, the scale range of nanomaterial is 1 to 100 nm.[3]. As nanoparticles are smaller in size, so, they exhibit different physiochemical properties[4]. Several types of cosmetics, sunscreens and personal care products which contain engineered nanomaterials are commercially available right now [5] in the global market. Many cosmetic formulations incorporate special nanoparticles that may be coated or may not be coated, provides sunscreen, tactile, light scattering and matte effects for the weare[6]. Compared to their respective bulk materials, the nanomaterials may produce better self-cleaning or selfadhesive properties on a surface, increase the toughness of a particular material, improve resistance to friction & improve the quality of textiles, etc. There are also increased concerns about the impact of these nanomaterials in the environment

and their possible impact on human health. The question of what is meant by nanotechnologies and nanomaterials [7] especially in food and cosmetics, remains one of the key issues in the debate between public authorities, industry, scientists, consumers, environmental groups and the media. The debate about what constitutes a nanomaterial has major implications for the entire risk governance cycle, including problem-framing, the assessment of risks and concerns, risk-benefit management options. As the design, development and production levels of self engineered nanomaterials will no doubt increase and intensify over the coming years, the question of their possible effects on health is of immediate concern.

NEED OF NANOMETERIALS IN COSMETICS

The increased usage of nanomaterials in cosmetic products is indicative of the huge potential nanotechnology represents for the cosmetics industry and its consumers because of their advantages(as shown in Fig.1). A number of nanomaterial types are already in use, including nanoemulsions, and nanoparticles of minerals present in our natural environment, such as titanium dioxide (TiO₂), zinc oxide (ZnO), alumina, silver, silicon dioxide, calcium fluoride and copper. The rationale for the use of nanomaterials in cosmetic products is, of course, that they offer added value in terms of product performance. The unique properties and behaviour of nanomaterials mean that nanotechnologies could profoundly transform industry and everyday life. In formulation of cosmetics, Titanium dioxide (TiO₂) and Zinc Oxide (ZnO) nanopigments are the main compounds used as highly efficient UV-filters, able to reflect and scatter the visible part of solar radiation while absorbing UV light. Given these properties, they are extensively used in sunscreens. Other examples of nanocosmetic products on the market include body firming lotion, bronzer, exfoliant scrub, eye liner, and styling gel, to name but a few.



Fig.1 various advantages linked with nanocosmetics

The nanomaterials found its next use as encapsulated carrier for topical delivery of photolabile and skin sensitizing compounds. Liposomes and Niosomes are used in the cosmetic industry as delivery vehicles to improve;

- Direct interaction of sensitive agents with skin.
- The delayed release of sensitizing agents.
- Reduction in the amount of agents and additives.
- · Increased lifespan and hence greater product acceptability

Nanocrystals, microemulsions, nanoemulsions, Fullerenes and dendrimers are also being explored in modern cosmetic and beauty care applications. Nanopigments are custom built to stay on the surface of the skin and are a major component of some sunscreens. Nanoemulsions are oil and water droplets often protecting fragile active ingredients (like vitamins). Unstable Vitamins can be suspended in nanoemulsions. The industry calls them nanocapsules, liposomes, lyphazones, etc. and nanoemulsions release the entrapped load upon contact with the skin

on application. The next class of cosmetics includes fullerenes or fullersomes that are used as cages for active ingredients. Some fullerenes, specifically carbon based, might be hazardous when inhaled and they may oxidize some cells.[8-10]

DIFFERENT TYPES NANOMATERIALS USED IN COSMETICS

In this section we have discussed various types nanomaterials that used in cosmetics. Figure 2. Shows various structures available in nanoscale.

1.Liposomes:

Liposomes are vesicular structures with an aqueous core surrounded by a hydrophobic lipid bilayer, created by the extrusion of phospholipids. They are most widely known cosmetic delivery systems. Liposomes can vary in size, from 15 nm up to several μ m and can have either a single layer (unilamellar) or multilayer (multilamellar) structure. The first liposomal cosmetic product to appear on the market was the anti-ageing cream 'Capture' launched by Dior in 1986. Phosphatidylcholine, one of the main ingredients of liposomes, has been widely used in skin care products and shampoos due to its softening and conditioning properties [11].



Figure 2. Shows various structures available in nanoscale.

Liposomes have been formed that facilitate the continuous supply of agents into the cells over a sustained period of time, making them an ideal candidate for the delivery of vitamins and other molecules to regenerate the epidermis. They have also been used in the treatment of hair loss. Minoxidil, a vasodilator, is in the active ingredient in products like Regaine that claim to prevent or slow hair loss. The skin care preparations with empty or moisture loaded liposome reduce the transdermal water loss and are suitable for the treatment of dry skin. They also enhance the supply of lipids and water to stratum corneum [12, 13]. Table 1- Some of the liposomal cosmetic formulations currently available in the market [14, 15, 16, 17, 18, 19]

2.Nanoemulsions:

Nanoemulsions can be defined as "ultrafine emulsions" because of the formation of droplets in the submicron range. The average droplet size of nanoemulsions has been ranging from 50 to 1000 nm. They have attracted considerable attention in recent years for application in personal care products as potential vehicles for the controlled delivery of cosmetics. Nanoemulsions are transparent due to the droplets tiny size and they also remain stable for a longer period of time [20]. They are mostly used in deodorants, sunscreens, shampoos, and skin and hair care products. The nanoemulsions are easilyvalued in skin care because of their good sensorial properties i.e. rapid penetration, merging textures and their biophysical properties especially, hydrating power. A significant improvement in dry hair aspect (after several shampoos) is obtained with a prolonged effect after a cationic nanoemulsion use. Hair becomes more fluid and shiny, less brittle and non-greasy [21, 22].

| Product | Manufacturer | Liposomes and key ingredients |
|--------------------------|---------------------------|---|
| Capture effect du Soleil | Cristian Diar L'Or'eal | Liposomes in gel Training agents in Liposomes |
| Formulae Liposome Gel | Payot(Fredinand Muehlens) | Thymoxin, hyaluronic acid |
| Future Perfect Skin Gel | Estee Lauder | TMF. Vitamin E, A palamitate cerebrosideceramide phospholipid |
| Symphatic 2000 | Biopharm Gmbh | Thymus extract, vitamin a palamitate |
| Natipide II | Nattermann PL | Liposomal gel for do it-yourself cosmetics |
| Flawless finish | Elizebath Arden | Liquid make-up |
| Inovota | Pharm/Apotheke | Thymus extract, hyaluronic acid, Vitamin E |
| Eye Perfector | Avon | Soothing cream to reduce eye irritation |

 Table 1- Some of the liposomal cosmetic formulations currently available in the market

 [14, 15, 16, 17, 18, 19]

3. Microemulsions:

Hoar and Schulman introduced the term microemulsion in 1943. Microemulsion is currently defined as nano – sized emulsion of water oil and amphiphile, an optically isotropic and thermodynamically stable liquid, containing particles with diameters of 100nm and less. In many cosmetic applications such as skin care products, hair products etc., emulsions are widely used with water as the continuous phase [23]. Cosmetic microemulsions of silicone oils, produced by emulsion polymerization are not thermodynamically stable products because of low solubility of silicone oil in the surfactants. Eli Lilly and Company had been assigned a patent for their stable w/o microemulsion i.e., non-irritating moisturizing composition which when applied to skin promoted the penetration of moisturizers into the skin and leave little residue on the surface of the skin [24].

4.Nanocapsules:

Nanocapsules are submicroscopic particles that are made of a polymeric capsule surrounding an aqueous or oily core. It has been found that the use of nanocapsules decreases the penetration of UV filter octyl methoxycinnamate in pig skin when compared with conventional emulsions [25].

5.Solid lipid nanoparticles:

They are oily droplets of lipids which are solid at body temperature and stabilized by surfactants. They can protect the encapsulated ingredients from degradation, used for the controlled delivery of cosmetic agents over a prolonged period of time and have been found to improve the penetration of active compounds into the stratum corneum. In vivo studies have shown that an SLNcontaining formulation is more efficient in skin hydration than a placebo. They have also been found to show UVresistant properties, which were enhanced when a molecular sunscreen was incorporated and tested. Enhanced UV blocking by 3, 4, 5-trimethoxybenzoylchitin (a good UV absorber) was seen when incorporated into SLNs [25, 26].

6.Nanocrystals:

Nanocrystals are crystals having size less than 1 μ m. They are aggregates comprising several hundred to tens of thousands of atoms that combine into a "cluster". Typical sizes of these aggregates are between 10-400 nm [27]. Nanocrystals of poorly soluble drugs can also be incorporated in cosmetic products where they provide high penetration power through dermal application. The first cosmetic products appeared on the market recently; Juvena in 2007 (rutin) and La Prairie in 2008 (hesperidin). Rutin and hesperidin are two, poorly soluble, plant glycoside antioxidants that could not previously be used dermally. Once formulated as nanocrystals, they became dermally available as measured by antioxidant effect. The nanocrystals can be added to any cosmetic topical formulation, e. g. creams, lotions and liposomal dispersions [28].

7.Nanosilver and Nanogold:

Cosmetic manufacturers are harnessing the enhanced antibacterial properties of nanosilver in a range of applications. Some manufacturers are already producing underarm deodorants with claims that the silver in the product will provide up to 24-hour antibacterial protection. Nano-sized gold, like nanosilver, is claimed to be highly effective in disinfecting the bacteria in the mouth and has also been added to toothpaste [29, 30].

8.Dendrimers:

Dendrimers are unimolecular, monodisperse, micellar nanostructures, around 20 nm in size, with a well-defined, regularly branched symmetrical structure and a high density of functional end groups at their periphery. A dendrimer is typically symmetric around the core, and often adopts a spherical three-dimensional morphology. One of the very first dendrimers, the new kome dendrimer, was synthesized in 1985 [31]. Dendrimers have also been considered for

use in the cosmetic industry. Several patents have been filed for the application of dendrimers in hair care, skin care and nail care products. Dendrimers have been reported to provide controlled release from the inner core. However, drugs are incorporated both in the interior as well as attached on the surface. Due to their versatility, both hydrophilic and hydrophobic drugs can be incorporated into dendrimers [32].

9.Cubosomes:

Cubosomes are discrete, sub-micron, nanostructured particles of bi-continuous cubic liquid crystalline phase. It is formed by the self assembly of liquid crystalline particles of certain surfactants when mixed with water and a microstructure at a certain ratio [33]. Cubosomes offer a large surface area, low viscosity and can exist at almost any dilution level. They have high heat stability and are capable of carrying hydrophilic and hydrophobic molecules. Combined with the low cost of the raw materials and the potential for controlled release through functionalization, they are an attractive choice for cosmetic applications as well as for drug delivery [34].

10.Hydrogels:

They are 3D hydrophilic polymer networks that swell in water or biological fluids without dissolving as a result of chemical or physical cross-links. They can predict future changes and change their property accordingly to prevent the damage [35].

11.Buckyballs:

Buckminster fullerene, C60, is perhaps the most iconic nanomaterial and is approximately 1 nm in diameter [36]. It has found its way into some very expensive face creams. The motivation is to capitalize on its capacity to behave as a potent scavenger of free radicals [37].

12.Niosomes:

Niosomes are vesicles composed of nonionic surfactants. The niosomes have been mainly studied because of their advantages compared with the liposomes: higher chemically stability of surfactant than phospholipid, require no special conditions for preparation and storage, they have no purity problems and the manufacturing costs are low [38]. The advantages of using niosomes in cosmetic and skin care applications include their ability to increase the stability of entrapped drugs, improved bioavailability of poorly absorbed ingredients and enhanced skin penetration [39].

13.Transfersomes:

In the 1990s, transfersomes, i.e., lipid vesicles containing large fractions of fatty acids, were introduced by Cevc and coworkers. Transfersomes are vesicles composed of phospholipids as their main ingredient with 10-25 percent surfactant and 3-10 percent ethanol. In consequence, their bilayers are much more elastic than those of liposomes and thus well suited for the skin penetration. Transfersomes consist of phospholipids, cholesterol and additional surfactant molecules such as sodium cholate. The inventors claim that transfersomes are ultradeformable and squeeze through pores less than one-tenth of their diameter. Therefore 200 to 300nmsized transfersomes are claimed to penetrate intact skin [40-42].

14.Lipid Nanoparticle:

The first generation of solid lipid nanoparticles (SLN) was developed at the beginning of the nineties as an alternative carrier system to emulsions, liposomes and polymeric nanoparticles. Solid lipid nanoparticles (SLNs) are nanometre sized particles with a solid lipid matrix. They are oily droplets of lipids which are solid at body temperature and stabilized by surfactants [43]. In the second generation technology of the nanostructured lipid carriers (NLC), the particles are produced by using a blend of a solid lipid with a liquid lipid, this blend also being solid at body temperature. SLNs have occlusive properties making them ideal for potential use in day creams. NLC were developed to overcome some potential limitations associated with SLN. Compared to SLN, NLC show a higher loading capacity for a number of active compounds, a lower water content of the particle suspension and minimize potential expulsion of active compounds during storage. Solid lipid nanoparticles (SLNs) and nano-structured lipid carriers (NLC) are novel colloidal delivery systems with many cosmetic and dermatological features; such as skin adhesive properties when applied to the skin resulting in occlusion, enhanced skin hydration, whitening effects, protection against degradation, absorption increasing effects, active penetration enhancement, and controlled release properties [44, 45].

PRESENT STATUS & FUTURE PROSPECTS

Nanotechnology is the fastest developing area of research involved in resolving science based solutions for innovative therapeutics and cosmetics. In future, it is going to become a big prospect for cosmetics and consumer care product manufacturers. As this area of technology is still relatively new, researchers have to look into solubility and bio-persistence of the nanometerials very carefully. The most commonly used nanopigments in cosmetics are titanium dioxide, zinc oxide and aluminium oxide. Nano-aluminium oxide is used in concealers and mineral foundations because it diffuses light, giving a 'soft focus' effect that disguises wrinkles. Nano-titanium dioxide is used to give protection from UV rays of sun. As a larger particle, titanium dioxide is white and opaque. But in nano size, titanium dioxide becomes transparent. Nanoparticles of iron oxide are used as pigments. Nanosized TiO_2 particles stay on the outer surface or stratum corneum of the skin and do not penetrate through the living skin. Production of free radicals by nanoparticles used in sunscreens and cosmetics is greater when exposed to UV light. Nano-sized titanium dioxide sometimes penetrates the skin and therefore be of prime concern for people with healthy skin. Fullerenes have been also used as nanomaterials in anti-aging cosmetic products but uncertain about their potential toxicity as well as scepticism about their anti-aging claims. Some cosmetics developers create an idea about silver nanoparticles, they want to use this type of nanoparticles in toothpaste. Nowadays, Gold nanoparticles are included in facial masks, being used in beauty clinics and saloons. It is believed to work by improving the blood circulation, skin elasticity, and reducing the formation of wrinkles & they do not produce toxicity in human skin [47-49].

The most common product in cosmetics that uses nanotechnology is sunscreens. The particles used in sunscreens are zinc oxide and titanium dioxide. The use of these nanoparticles makes the sunscreen transparent and less greasy. There are other cosmetics such as skin moisturizers, anti-wrinkle products, skin cleansers, and hair products that benefits from nanotechnology[46](as shown in Fig.3).



Figure 3.Cosmetics such as skin moisturizers, anti-wrinkle products, skin cleansers, and hair products from nanotechnology. (a) http://tinaounds2016.blogspot.in, and (b)https://www.nanotechia.org

RISK ASSESSMENT TECHNIQUES

Making of nanomaterials attractive to the cosmetics and personal care industries have to alter color, transparency, solubility and chemical reactivity [49] Currently there are few social issues about the impact of nanoparticles used extensively in sunscreens like Titanium dioxide, Zinc oxide, on environment, health and safety. Nanomaterials used in sunscreens, an assessment of phototoxicology is necessary to determine if nanoparticles/nanomaterials have the capacity to generate free radicals in the presence of sunlight and if the addition of antioxidants in the formulation could eliminate any free-radical damage. Recent sunscreens contain insoluble nanoparticles (colourless) of titanium dioxide (TiO₂) or zinc oxide (ZnO), which reflect / disperse ultraviolet more effectively than bigger particles. The nano-sized particles are used in sunscreens as a substitute to existing chemical UV absorbers, such as p-aminobenzoic acid and benzophenones, which can cause sensitivity reactions individuals. The National Institute for Occupational Safety and Health (NIOSH) has published a report in 2005 with conclusion that little concentrations of inhaled TiO₂ were an unlikely cause of cancer in humans. Although other nanoparticles like carbon nanotubes, fullerene derivatives and quantum dots may have properties that require safety assessment on case to case basis prior to human use.[50-51] Fullerenes in cosmetics will enhance human exposure through product utilization, and like other chemicals found in personal care products, can potentially be released into the environment after being rinsed "down the drain". [52] Such evaluations must use validated analytical techniques like high-performance

liquid chromatography (HPLC) for fullerene detection in complex matrices like cosmetics. Satisfactory assessment of the environmental and human health impacts of nanoparticles (e.g., C60) in consumer products would be valuable information for decision- making, and could therefore help prevent public distrust. [53]

OPPORTUNITIES IN THE COSMETIC INDUSTRY

• TiO2 and ZnO are widely used in cosmetic formulations. However, there is a need for an in-depth toxicity study these materials as the studies so far have brought mixed results.

• Liposomes and nanoemulsions do not disturb the integrity of the skin lipid bilayers and are not washed out while cleansing the skin. So, these formulations are believed to have a great future in the cosmetic science.

• Acceptability of microemulsions, however, would be governed by the use of safer surfactants, which do not appreciably change the permeability of membrane over repeated use.

• Encapsulation techniques and trigger-release mechanisms have been developed for the active delivery of cosmetic molecules. However, there is a need for reliable, cost effective triggers for controlled release.

• Improvements in the drug loading efficiency of lipid based nanoparticles (SLNs and NLCs) and nanocapsules are required.

• Better understanding of how lipid nanoparticles modify drug penetration into the skin, how they affect the drug penetration and how they interact with lipids of the stratum corneum is required.

• Fundamental conditions for the formation of SLNs and NLCs and the effect of surfactants used for modifications need to be studied further.

• Further in vivo studies on the effect of cosmetics that contain nanomaterials.

CONCLUSION

Growth of cosmeceutical industry is increasing day by day as the cosmeceuticals market is highly diversified, with products coming from major and small manufacturers and local

companies around the world. Nanotechnology represents the key technologies of the twenty-first century, offering excellent opportunities for both research and business. The rapid spread and commercialization of nanotechnology in cosmeceuticals have given rise to great technical and economic aspirations but also question about the emerging risks to health and safety of consumers. Thus, cosmeceutical products based on nanotechnology should be designed and sold in a way that fully respects the health of consumers and the environment.

Acknowledgements

I would like to acknowledge Prof. Vijaya Bhaskara Raju, Director of GITAM Institute of Technology, GITAM University Bengaluru Campus, India and Prof. R. Venkatanadh, Research Coordinator, GITAM University, Bengaluru for their constant encouragement to finish this work.

REFERENCES

[1]Dureja H, Kaushik D, Gupta M, Kumar K, Lather V. Indian J Pharmacol. 2005; 37(3):155-159.

[2]Bangale MS, Mitkare SS, Gattani SG, Sakarkar Dm; Int J Pharm Sci, 2012; Vol 4, Issue 2, 88-97.

[3]Article 2(k) of provisional text for EU Cosmetics Regulation, **2009**http://www.europarl.europa.eu/sides/getdoc.do?tye=TA&language=EN&reference=P6-TA-2009-0158.

[4]U.S. Food and Drug Administration, "Cosmetics Q&A: FDA's Authority," http://www.fda.gov/Cosmetics/ResourcesForYou/ Consumers/CosmeticsQA/ucm135709.htm

[5] M. H. Fulekar, *Nanotechnology: Importance and Application*, **2010**IK International Publishing House, New Delhi, India,.

[6] S. Mukta and F. Adam, *Journal of Drugs in Dermatology*, **2010**vol. 9, no. 5, pp. s62– s66,. [7] Risk Governance of Nanotechnology Applications in Food and Cosmetics, A report prepared for IRGC by Antje Grobe, Ortwin Renn and Alexander Jaeger Dialogik GmbH.

[8] F. S. Brandt, A. Cazzaniga, and M. Hann, "Cosmeceuticals: current trends and market analysis," *Seminars in CutaneousMedicine and Surgery*, **2011** vol. 30, no. 3, pp. 141–143.

[9] L. Mu and R. L. Sprando, *Pharmaceutical Research*, 2010, vol. 27, no. 8, pp. 1746–1749,.

[10] I. P. Kaur and R. Agrawal, Recent Patents on Drug Delivery & Formulation, 2007, vol. 1, no. 2, pp. 171–182...

[11] Souto EB, Müller RH. Challenging Cosmetics-Solid Lipid Nanoparticles (SLN) and Nanostructured Lipid Carriers (NLC) In: Wiechers JW, editor. Science and Application of Skin Delivery Systems. Allured Publ. Co; IL, USA, Coral Stream: **2008**. pp. 227–250.

[12] Morganti P. Meccanismo d'azione dei prodotti cosmetici: miti e realta'. Presented at Giornata di studio: Prodotti Cosmetici. Approfondimenti e proposte su regolamentazione, sicurezza e mercato. Milano. 2009. 29-Gennaio.

[13] Hides L, Trotter G. A new paradigm in mineral UVA and UVB protection. Presented at PCHI Shanghai meeting; **2008**, March 17–19.

[14] Nasu A, Otsubo Y. J Cabloid Interfacial Sci. 2006; 296:558–564.

[15] Pflücker F, Bunger J, Hitzel S, Vitte J, et al. SÖFW Journal. 2005; 131(7):20–30.

[16] Vinetsky Y, Magdassi S. Microcapsules in cosmetics. In: Magdassi S, Touitou E, editors. Novel Cosmetic Delivery Systems. New York: Marcel Dekker Inc; 1999. pp. 295–313.
[17] Royal Society and Royal Academy of Englneering nanoscience and nanotechnologies, opportunities and uncertainties. 2004. URLwww.royalsoc.uk/policy/.2004.

[18]Dreyler K. The future of nanotechnology: molecular manufacturing. **2003**. URLwww.eurekartet.org/context.p4p2. context=nano&slow=essays.

[19] SCCP Scientific Committee on Consumer Products Preliminary opinion on safety of nanomaterials in cosmetic products. **2007**.

[20] Ball P. Nanotechnology in the firing line. **2003**. URLhttp://nanotechweb.org/cws/article/indepht/18804. [21] Dreher K. Health risk assessment of manufactured nanomaterials: more than just size. Nanotechnology for Remediation Technical Workshop, National Health and Environmental Effects Laboratory, US Environmental Protection Agency; Washington, USA. **2005**.

[22] Oberdoester G, Oberdoester E, Oberdoester J. Environ Health Perspect. 2005; 113(7):823-839.

[23] Colvin V. Physical properties of nanomaterials. Towards predictive assessments of risk, international nanomaterial environmental health and safety research needs assessmentWorkshop 1: **2007**US national institute of health; USA.. URLhttp://cohesion.rice.edu/CentersAndlnst//CON/emplibrary/C olvinRNADJan2007.pdf. [24] European Parliament resolution of 24 April **2009** on regulatory aspect of nanomaterials. Available from: URLhttp://www.europarl.europa.eu/sides/getDoc.do?pubRef=-

//EP//TEXT+TA+P6-TA-2009-0328+0+DOC+XML+V0//EN.

[25] Nohynek GJ, Lademann J, Ribaud C, et al. Crit Rev Toxicol. 2007; 37(3):251–277.

[26] Dussert AS, Gooris E. Int J Cosmet Sci. 1997; 19:119–129.

[27] Lademann J, Weigmann HJ, Rickmeier CH, et al. *Skin Pharmacol Appl Skin Physiol.* 1999; 2:247–256.
[28] SCCNFP Brussels, Belgium: European Commission; 2000. Opinion of the Scientific Committee on Cosmetic Products and Non-Food Products Intended for Consumers Concerning Titanium Dioxide. URLhttp://ec.europa.eu/health/ph_risk/ committees/04_scp/04_sccp_en.htm.

[29] Pluecker F, Wendel V, Hohenberg H, et al. Skin Pharmacol Appl Skin Physiol. 2001;14(Suppl 1):92–97.

[30] Schulz J, Hohenberg F, Pluecker F, et al. Adv Drug Deliv Rev. 2002; 54(Suppl 1):S157–S163.

[31] Butz T. SÖFW Journal. 2009; 135(4):8–10.

[32] Menzel F, Reinet T, Vogt J, Butz T. Nucl Instrum Methods Phys Res B. 2004:219-220.

[33]Cross SE, Innes B, Roberts MS, Tsuzuki T, Robertson TA, McCormick P. Skin Pharmacol Physiol. 2007; 20:148–154.

[34]Gamer A, Leibold E, van Ravenzwaay B. Toxicol In Vitro. 2006; 20(3):301–307.

[35]Mavon A, Miquel C, Lejune O, Payre B, Moretto P. Skin Pharmacol Physiol. 2007; 20:10–20.

[36]Commission of the European Communities Commission Recommendation on a Code of Conduct for responsible nanosciences and nanotechnologies research. Brussels. 07/02/2008 C, **2008**, 424 final. [37]EMEA Reflection paper on nanotechnology-based products for human use. 2006. EMEA/CHMP/79769/2006. Asian J. Pharm. Res. **2014**; Vol. 4: Issue 1, Pg 16-23 [AJPRes.] 23

[38]Starzyk E, Frydrych A, Solyga A. SÖFW Journal. 2008; 134(6):42-52.

[39] Morganti P, Muzzarelli RAA, Muzzarelli C. J Appl Cosmetol. 2006; 24:105–114.

[40] Morganti P, Morganti G. Clin Dermatol. 2008; 26:334–340.

[41] Muzzarelli RAA. Carbohydr Polym. 1993; 3:53–75.

[42] Percot A, Viton C, Domard A. *Biomacromolecules*. 2003; 4:8–18.

[43] Muzzarelli RAA, Mattioli-Belmonte M, Pugnaloni A, et al. Biochemistry, histology and clinical uses of chitins and chitosans in wound healing. In: Jollés P, Muzzarelli RAA, editors. Chitin and Chitinases. Basel, Swizterland: Birkhaüser Verlag; **1999**. pp. 251–264.

[44] Muzzarelli RAA, Muzzarelli C. Chitin nanofibrils. In: Dutta PK, editor. Chitin and Chitosan: Research Opportunities and Challenges. Contai, India: SSM International Publication; 2005.pp. 129–146.
[45] Morganti P, Fabrizi G, Bruno C. *Skinmed*. 2004; 3(6):310–316.

[46]Cosmetics such as skin moisturizers, anti-wrinkle products, skin cleansers, and hair products from nanotechnology. (a) http://tinaounds **2016**.blogspot.in, and (b) https://www.nanotechia.org

[47] Sonavane G, Tomoda K, Sano A, Ohshima H, Terada H, Makino K. *Colloids Surf Biointerfaces* 2008; 65:1–10.
[48] Menon GK, Brandsma JL, Schwartz PM. *Skin Pharmacol Physio.* 2007; 20:141–7.

[49] Mulholland WJ, Arbuthnott EAH, Bellhouse BJ, Cornhill JF, Austyn JM, Kendall MAF, et al. J Invest Dermatol 2006; 126:1541–8.

- [50] Dean HJ, Haynes J, Schmaljohn C. Adv Drug Deliv Rev 2005; 57:1315–42.
- [51] Oberdorster E. Environ Health Perspect.2004; 112:1058-1062.
- [52] Johannes F. Jacobs, Ibo van de Poel, Patricia Osseweijer. Nanoethics 2010; 4:103-113.
- [53] Thomas Faunce & Katherine Murray & Hitoshi Nasu & Diana Bowman, Nanoethics 2008; 2:231–240.