Nanotechnology in cosmetics pros and cons

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Abstract

The field of nanotechnology is being greatly explored by cosmetic industries in order to improve the efficacy of cosmetic products. The increased use of nanomaterials in the field of cosmetics can have two sides as health-related benefits and detrimental effects. This review mainly seeks the pros and cons of the use of nanomaterials in cosmetics along with some examples of nanomaterials that are widely used in cosmetic industries along with different types of nanotechnology-based cosmetic products. The benefits of nanomaterials in cosmetic formulations are huge. Moreover, the study regarding the toxic effects on the health also equally matters. This review gives a brief outline of the advantages as well as disadvantages of nanotechnology in cosmetics.

1. Introduction

Nanotechnology has wide applications in various fields such as agriculture, food, paints, medicine, textiles. The cosmetic industry has extensive use of nanomaterials for various benefits. The extensive surge in the customers’ demands has led to the development of formulations in cosmetics with better performance, retentions, attractive appearance, and more importantly safety [1, 2]. The major benefits of the use of nanoparticles in cosmetics include everlasting stability, proper penetration of formulation at the site of application. The integration of nanoparticles in cosmetics is gaining demand because of their high surface-to-volume ratio which helps in better penetration through the skin [3–7]. The property of UV filters of nanoparticles has made the nanoparticles which can be used in the Sunscreens. In 1986, for the first time, Christian Dior launched the anti-aging cream named CaptureTM in which liposomes were used [8]. Later on, various cosmetic industries started the use of nanoparticles in the formulations of cosmetics. The very well-known cosmetic manufacturers; L’Oréal S.A. registered about seven patents for the use of nanoparticles in cosmetic preparations [9]. TiO2, ZnO, silica, carbon black nanoparticles are used in some of their cosmetic products as shown in figure 1 [10, 11].

The concerns regarding the usage of nanoparticles in cosmetics have been raised by various organizations such as World Health Organization (WHO), government as well as non-government organizations. The guidance regarding the use of nanoparticles has been proposed by European Commission (EC) and Food and Drug Administration (FDA) by their own guidance for the utilization of nanoparticles in cosmetics. The European Union Observatory for Nanomaterials (EUON) has set forth the REACH registration compliant (REACH is a Registration, Evaluation, Authorization, and Restriction of Chemicals). The usage of nanoparticles should fall under the limits of REACH and the main aim of it is to provide information regarding the safe usage of nanoparticles. The review presents the benefits and the harmful effects of nanoparticles in cosmetics along with a brief insight into the type of nanoparticles majorly used in the cosmetic industry [5, 12–14]. Firstly the review gives a brief outline of the types of nanomaterials used in cosmetic formulations along with their potential benefits followed by different types of nanotechnology-based cosmetics. Later the second section highlights the pros of nanomaterials in cosmetics. The latter part deals with the different facets of the effects of nanomaterials on the health and environment. Finally, different views are expressed along with few suggestions in order to reduce the adverse impacts of nanomaterials, which can be useful for further research in the above-stated subject.
2. Nanotechnology in cosmetics

2.1. Nanoparticles used in the cosmetic industry

The cosmetic industry is attaining the benefits of nanotechnology by developing nanoparticles for the enhanced performance and bioavailability of active components in cosmetics, sunscreens, anti-aging creams, moisturizers, and perfumes [15]. There are various nano-delivering systems used in cosmetic preparations to enclose vital elements. This is beneficial for the efficient delivery of active components via skin. The nano-based products are helpful in the efficient absorption and penetration through the skin. The active ingredients are adsorbed on the surface of nanoparticles which act as a vehicle for the delivery. The cosmetics may contain nanoparticles of different morphologies and chemical compositions to harness the advantages of shape and size-dependent activities of nanoparticles to exaggerate the activities of cosmetic products. The cosmetics are formulated by using different types of metal and metal oxide nanoparticles such as silver nanoparticles (AgNPs), gold nanoparticles (AuNPs) and titanium dioxide nanoparticles (TiO$_2$ NPs), zinc oxide nanoparticles, (ZnO NPs), iron oxide nanoparticles, (Fe$_3$O$_4$ NPs) and carbon-based NPs [16–18]. The nanoparticles such as titanium dioxide (TiO$_2$), zinc oxide (ZnO) are substantially used, since these nanoparticles are non-oily, easily absorbed. TiO$_2$ is essentially a UV filter (UVA and UVB filter) hence widely used in sunscreens and moisturizers as well. The well-known cosmetic companies Boots, Avon, The Body Shop, L’Oreal, Nivea, and Unilever are implementing nanoparticles in the formulations of cosmetics. Along with sunscreens TiO$_2$ is used in lip balms, foundations, day creams as UV filters so as to protect the skin from the carcinogenic effects of UV radiations. Besides TiO$_2$, ZnO, zirconium oxide (ZrO$_2$), Cerium oxide (CeO$_2$) nanoparticles are used in cosmetics as UV filters as the particles are able to scatter and reflect the UV radiations. CeO$_2$ is able to hinder the UV radiation but not able to produce the Reactive Oxygen Species (ROS) like TiO$_2$ nanoparticles. Cerium phosphate nanoparticles with low photocatalytic activity showed effectiveness in UV absorption. The better feel and distribution of the cosmetics can be achieved through the use of zinc oxide and titanium oxide nanoparticles. The usual shaped TiO$_2$ and ZnO nanoparticles execute very useful applications in the cosmetic industry. The most important features for the use of these nanoparticles include their defined size and surface area. This ultimately determines the efficacy of UV filtration in sunscreens [19]. The only distinction between TiO$_2$ and ZnO is TiO$_2$ can be used for the UV B diminution while ZnO is a UV A safeguard to protect against aging caused owing to ultraviolet rays. As compared to ZnO, TiO$_2$ acts as an effective measure to protect against UV B, and hence when sun protection factor (SPF) is concerned TiO$_2$ is more effective in terms of SPF at a given concentration [20, 21].

Titanium dioxide is esteemed for its high refractive index and white coloration, making it advantageous as the most commonly used white pigment. It absorbs UVR because of its semiconductive property. UV absorption is one of the natural features of TiO$_2$ that can be explained by solid band theory. Both zinc oxide and titanium dioxide nanoparticles are common ingredients of sunscreen. The size can also influence the efficacy of...
nanoparticles used in cosmetics. As per the study, TiO$_2$ nanoparticles are effective in UV B and ZnO nanoparticles are efficient in UV A. These microsized particles are effective as sun protection factors. The size reduction in the particles of TiO$_2$ and ZnO enhances the UV absorption at the expense of UVA1 as a result UV protection becomes unbalanced. This can be overcome through a combination of diverse ZnO microsized particles (∼200 nm or minor to preserve transparency) and nanosized TiO$_2$. Further studies reveal that the combinations of two different grades of zinc oxide nanoparticles are used for cosmetic formulations. Studies in this area reveal that further optimization results in the combination of two grades of ZnO particles (dispersed in Cyclopentasiloxane or isononyl isononanoate) with slightly whitened 35 nm TiO$_2$ NPs offering better UVB protection. The balanced UVA and UVB protection can be achieved through the ZnO dispersions of small nanosized and large microsized particles. This research explains that aggregated ZnO particles of dimension 130 nm rather than the 20 nm primary particles influence UVA-1 protection [22, 23]. The fabrications of polycyronitrile (PAN) nanofibers which are associated with the UV protection property are possible with various concentrations of multi-walled carbon nanotubes (MWCNT) and TiO$_2$ nanoparticles. The hybrid of MWCNT and TiO$_2$ nanoparticles resulted in excellent activity in the UV blockage [24].

The presence of non-cytotoxicity, biocompatibility, and stability of gold nanoparticles make gold nanoparticles significantly useful in cosmetic formulations [25, 26]. Presently there is a lot of debate about AuNPs cytotoxicity, as it depends on the variety of parameters such as size, shapes, cell lines used in toxicity assays, concentrations and coatings of nanoparticles, incubation time, synthesis method, surface functionalization [27–29]. It is found that AuNPs in concentration between 1 and 67 μM/L are not cytotoxic to Hep3B (hepatocellular carcinoma) and Panc-1 (pancreatic epithelioid carcinoma) cells [27]. In another study, it was revealed that 10 and 50 nm citrate-coated AuNPs did not show toxicity towards embryonic fibroblast cells [28]. Besides these characteristics, the antifungal and antibacterial nature of gold nanoparticles is also beneficial. Gold nanoparticles have been employed in various cosmetic products such as skin wound disinfection, anti-inflammatory creams and lotions, face packs, and anti-aging creams. Gold nanoparticles in cosmetic products offer numerous benefits such as antiseptic and anti-inflammatory properties, enhanced blood flow, acts as anti-aging, making the skin more elastic and firm, and energizing skin metabolism. As the skin gets exposed to various factors such as pollution, smoke, harmful sunlight rays it results in the formation of ROS. Excessively produced ROS are able to damage healthy cells and tissues. This may affect the different macromolecules of cells such as DNA and RNA [11]. Therefore, antioxidants present in cosmetics can protect the skin. The green synthesis of gold nanoparticles by using Hubertia ambavilla plant exhibited that gold nanoparticles are biocompatible in nature as these nanoparticles are non-toxic to human dermal fibroblasts, ability to scavenge free radicals and impart UVA protection to fibroblast and dermal cells [30]. The safety of gold nanoparticles in the cosmetics was determined through various tests such as acute toxicity test, skin sensitization potential of AuNPs, irritation of the skin and eyes. Genotoxicity of AuNPs was reported as nonphototoxic, nongenotoxic, non-irritant and non-sensitizing according to OECD guidelines. These results suggest that green AuNP is a promising ingredient for cosmetic applications.

The eco-friendly synthesis of gold nanoparticles is achieved through the Punica granatum juice which is valuable in cosmetic preparations [31]. The pomegranate juice contains different alkaloids and polyphenols. The ellagic acid present in the pomegranate juice, which has the ability to protect the cells from free radical damage. Along with this, anthocyanidins also have a vital role in free radical scavenging. Therefore, these antioxidants play a very important role in cosmetic formulations. Punicalagins of pomegranate revealed the presence of free radical scavenging capacity. These components are water-soluble and high bioavailability.

The nanoparticles present in cosmetic products can behave as active ingredients, carriers, consistency-enhancing components, improving the efficacy of cosmetic products. Besides, the silver nanoparticles are also utilized in cosmetic formulations because of the broad antimicrobial activities of silver nanoparticles as well as the property of acting as a preservative. The creams containing silver nanoparticles have antimicrobial activity and hence they can be used as a skin and wound disinfectant [32]. There has been the utilization of silver nanoparticles in toothpaste and shampoos as preservatives. This benefits the treatment of dandruff, itchy and oily scalp [33]. AgNPs have also been popular in dental materials because of the unique properties of nanoparticles [34]. The use of silver nanoparticles in peel-off face mask formulation was also possible. The bacterial synthesized (Bacillus nakamura) silver nanoparticles possess antibacterial activity and used in the formation of antibacterial peel-off face mask [35]. Silica nanoparticles are being predominantly used in cosmetics because of their hydrophilic surfaces and economical synthesis. The silica nanoparticles are able to augment the efficacy, evenness and shelf life of cosmetic products. The cosmetic products are also improved for their absorbency. The use of silica nanoparticles in various colouring cosmetics is also useful such as lipsticks. The even distribution of pigments of lipsticks can be made possible by means of silica nanoparticles. The other cosmetics of skin, nails, hair and face utilize silica nanoparticles in order to achieve efficiency of products. The results regarding the safety of silica nanoparticles are contentious, so deeper studies regarding the use of nanoparticles in cosmetics need to be conducted [36].
On that note, there are some types of nanoparticles that are used to study the penetration of nanoparticles through the skin by optical imaging, which is fluorescent in nature. The upconversion nanoparticles are nontoxic, photostable offer high-contrast optical imaging, photoluminescence properties and allows the nanoparticles potentially applicable in biological systems. The coating of upconversion nanoparticles with polymers improves the penetration in the skin as shown in figure 2.

3D tissue engineering constructs (3D TECs) were used to test the cytotoxicity of upconversion nanoparticles having a coating of polymers [37]. Figure 3 gives an idea about the confocal laser scanning microscopy (CLSM) images of interactions of polymer-coated upconversion nanoparticles with the culture of HaCaT monolayer cell lines. The cell lines were exposed to these nanoparticles for 24 h to understand the interaction and uptake of nanoparticles by cells. Polyethyleneimine coated upconversion nanoparticles are taken up by cells within 4hrs as compared to others.

The comparative study of the uptake of upconversion nanoparticles coated with polymers with 3D epidermal TEC was carried out as shown in figure 4 [37]. These TEC cells were treated with the same concentrations of nanoparticles as used in HaCaT cell lines. The internalization of upconversion nanoparticles coated with polymers was found to be lowered as compared to uptake by HaCaT cell lines as shown in figure 4.

When the comparison of results of the 3-(4, 5-Dimethylthiazolyl)-2, 5-diphenyl-2H-tetrazolium bromide (MTT) assay of upconversion nanoparticles cytotoxicity in the 3D tissue engineering constructs and monolayer cell cultures of HaCaT cells was done it was found that the viability of cells lines due to PAA and PEG-coated upconversion nanoparticles reduced to 85%, while in case of PEI coated nanoparticles it was decreased upto 65% [37]. Therefore, the PEI-coated upconversion nanoparticles were found to be toxic to the cells. On the contrary, in the case of TEC cells the viability of cells due to PEI coated upconversion nanoparticles; it was increased to 115%. Therefore, these PEI-coated nanoparticles were found to be non-toxic along with PEG and PAA-coated upconversion nanoparticles. Toxicity studies of polymer-coated upconversion nanoparticles were thoroughly studied in 3D tissue engineering constructs. Thus, these upconversion nanoparticles being nontoxic, compatible in nature upconversion nanoparticles can be used as carriers. These nanoparticles enable new methods for cosmetic industries in designing and testing with no animal testing which also becomes cost-effective [37].

2.2. Nanomaterials used in cosmetics
The synthesis of nanomaterials is possible with the help of nanotechnology [38]. These nanomaterials can be used in cosmetics to impart new characteristics to the cosmetics. The varied types of nanomaterials with various characteristics and may create different benefits. The types of nanomaterials that are used include nanocapsules,
dendrimers, nanoemulsions, nanoliposomes, nano-hydroxyapatite materials, which have been used in cosmetics for various purposes such as oral care, protective carriers and delivering ingredients through the skin. The brief outline of their methods of synthesis has been summarised in Table 1.

2.2.1. Liposomes

These are spherical double phospholipid membrane-bound molecules. These liposomes can behave as vehicles for the delivery of enclosed desired molecules into or through the skin. These nanomaterials act as a storehouse of desired actives. The uses of liposomes in cosmetics derive various benefits such as non-toxic, biodegradable, flexibility. These liposomes can be used to encapsulate active components for easy and safe delivery.

![Figure 3. CLSM images of uptake of upconversion nanoparticles coated with polymers with uptake by HaCaT cell lines. HaCaT cell lines treated with upconversion nanoparticles coated with polyethyleneimine (PEI), polyacrylic acid (PAA) polyethylene glycol-amine (PEG) in the concentration of 250 μg per ml for 24 h. Upconversion nanoparticles and nuclei are pseudo-colored in green and blue, respectively. Scale bar, 10 μm. Reprinted with permission from [37]. Copyright (2019) from Elsevier.](image)

![Figure 4. Cellular uptake of CLSM images of uptake of upconversion nanoparticles coated with polymers with uptake by TEC cells. Cells treated with upconversion nanoparticles coated with polyethyleneimine (PEI), polyacrylic acid (PAA) polyethylene glycol-amine (PEG) in the concentration of 125 μg per ml for 24 h. The internalization of nanoparticles is represented by arrows. Reprinted with permission from [37]. Copyright (2019) from Elsevier.](image)
| Type of Nanomaterials | Synthesis Method | Procedure | Size of Nanomaterials | References |
|----------------------|------------------|-----------|----------------------|------------|
| Liposomes            | Sonication       | Phospholipid components + cholesterol in chloroform (2:1 v/v) filtration, the addition of Glass beads with 550 μm diameter to the flask + lipids + distilled water or buffer; vortex mix for 6 min to form liposomes. Micro-fluidization Components of the liposomes + distilled water or buffer (Dispersion), Place in the tank of the microfluidizer + air regulator to maintain operating pressure + collect, put the product at above phase transition temp, under inert conditions using N₂ or Ar for 1 h. | 100 to 200 nm | [39] |
| Noisome              | Ether injection method | Dissolution of surfactant in diethyl ether followed by injection of solution through a 14-gauge needle into an aqueous solution of drug maintained at 60°C. After vaporization of ether single layer vesicles are formed. | 50 to 1000 nm | [40, 41] |
| Thin-film hydration technique | Surfactant + cholesterol in a volatile organic solvent, evaporation thin layer deposited on the wall of the flask, hydrated with the desired drug. | 200 to 1000 nm | |
| Reverse-phase evaporation technique | The drug in aqueous phase + surfactant and cholesterol in ether or chloroform (1:1), sonication, the addition of phosphate buffer saline, sonication, remove ether or chloroform, suspension heated at 60°C for 10 min. to form niosomes. | 3460 to 3610 nm | |
| Dendrimers           | Divergent method | Synthesis gets initiated from the core part of the dendrimer’s building blocks at the exterior. | 1 nm up to 10 nm | [42–44] |
| Convergent method    | The synthesis starts from the exterior part to the core part to form the final dendrimers. | | |
| Nano-emulsions       | Microfluidization | The solution was passed through an air-driven microfluidizer, 500 ml sample passed through the microfluidizer at the set pressure for 1 cycle. Then one-third part of the microfluidized sample was taken away for size analysis and the remaining volume was again passed through it for the 2nd and same for the third cycle. | 20–200 nm | [45] |
| High Pressure Homogenization | 3 wt% lipid phase + 95 wt% aqueous phase 10 mM sodium phosphate buffer premix blending the lipid and aqueous phases together for 2 min at RT coarse emulsions passed through an air-driven microfluidizer at various homogenization pressures | | [46] |
| Solid lipid nanoparticles (SLN) and Nanostructured lipid carriers (NLCs) | Solvent emulsification-evaporation technique | Drug + core material + coat material + chloroform evaporated in rotary evaporator + 10 ml PBS + sonication to form lipid nanoparticles Microemulsion technique | 50nm-1000 nm | [47] |
|                       | Water + co-surfactant(s) + surfactant heated to the same temperature as the lipids mild stirring to the lipid melt, mixed in the correct ratios for microemulsion formation. | | |
| Type of Nanomaterials | Synthesis Method | Procedure | Size of Nanomaterials | References |
|----------------------|------------------|-----------|----------------------|------------|
| Fullerenes           | Vapourization of carbon source | Carbon source followed by carbon soot followed by separation of fullerene mix and purification. | C$_{60}$ fullerenes 60 carbon atoms, 20 hexagons and 12 pentagons, forming a sphere of outer diameter 7.1 Å and an interior cavity diameter of 3.7 Å | [48] |
|                      | Synthesis by laser irradiation of polycyclic hydrocarbons | Polycyclic hydrocarbons are 'rolled up' to form fullerenes under flash vacuum pyrolysis (FVP) conditions to form fullerene C60 when it is laser irradiated at 337 nm wavelength. | | [49] |
| Nano-Hydroxyapatite  | Wet chemical Precipitation Technique | H$_2$PO$_4$ + Ca(OH)$_2$ at a rate of 1.5 ml/min, stirring for 24 h 1000 r/min, the temperature of 20°C + NH$_4$OH was added to the HA slurry after 24 h ripening period HA is formed | 20–80 nm long and 2–5 nm thick. | [50] |
|                      | Ultrasound Assisted technique | 40 ml 0.32 M Ca(NO$_3$)$_2$ + 2.5 ml NH$_4$OH, ultrasound, 60 ml 0.19 M KH$_2$PO$_4$, white precipitate, filtered and heat treated | | [51] |
| Nanocapsules         | Miniemulsion polymerization | Monomer + hydrophobe was mixed with the initiator + surfactant in water stirring for 1 h. mini emulsification was achieved by ultra sonicating for 120 s | 10 nm-1000 nm | [52] |
|                      | Chemical Vapour Condensation method | Cobalt carbonyl (CO$_2$(CO)$_8$) used as a precursor and carbon monoxide (CO) as a carrier gas in the furnace with temperatures ranging from 400 to 1000°C, nanoparticles formed to form core-shell nanocapsules. | | [53] |
| Nanotubes            | Chemical vapour deposition | A mixture of xylene and ferrocene, decomposition of the ferrocene-xylene mixtures in the temperature range 625-775 °C at atmospheric pressure, begin to deposit carbon as well-aligned pure MWNT arrays on the quartz surfaces. | 1.4 nm | [54] |
|                      | Electrochemical Anodization | The electrolyte was 1 M (NH$_4$)$_2$SO$_4$ with small amounts of NH$_4$F (0.5–5 wt.%). The electrochemical treatment consisted of a potential ramp from the open-circuit potential (OCP) to 20 V with a different sweep rate followed by holding the applied potential at 20 V for different times. The samples were rinsed with deionized water & dried with an N$_2$ stream. | | [55] |
| Nanospheres          | Solvo-thermal routes | Charging of metallic copper powder and CCl$_4$ into a Teflon-lined cylindrical stainless steel autoclave sealed, heated up to 200°C within 30 min, and maintained at 200°C for 2 h in an oven, cooled, the product collected and treated with HNO$_3$ for 20 h under ambient conditions stirring. The product recovered by filtration, washed with deionized water dried at 60°C for 10 h. | 100–1000 nm | [56] |
hydrophilic and hydrophobic molecules can be delivered through the liposomes. The phospholipids present in the liposomes are able to maintain the softness and smoothness of the skin. The lipids present in the liposomes protect the active ingredients from UV rays and in turn, helps in the enhancement of the shelf life of products [57]. Nanoliposomes and liposomes can be synthesized through the methods of sonication and microfluidization. The very first method of synthesis of liposomes was extrusion. In that process liposomes depending on the pore size of the filters employed and structurally modified to large unilamellar vesicles (LUV) or nanoliposomes [39, 58, 59]. The hair and skin also get protected from the UV rays because of liposomes. The release of the active ingredients at the site can be possible with the help of liposomes. The different types of components such as vitamins, antioxidants and other lipid molecules can be delivered with the help of liposomes. ‘Capture’ was the first liposomal anti-aging cream launched by Dior in 1986 [60]. Cosmetic products such as creams, shampoos, conditioners implement these liposomes. The phosphatidylcholine type of phospholipid present in liposomes can soften and condition due to which these can be used in various shampoos and conditioners. The oxidation of liposomes may cause quality deterioration of liposomes.

2.2.2. Noisome
These are nano-vesicles made of self-assembly of essentially non-ionic surfactants [61], with or without the incorporation of cholesterol or lipids. These vesicles can be unilamellar (0.025–0.05 μm) or multilamellar (more than > 0.05 μm) containing aqueous solutions of solutes and the membrane formed by the arrangement of surfactant molecules to form bilayer [40, 62]. The different components of noisome such as cholesterol and non-ionic surfactants are widely used [61]. Niosomes are formed by non-ionic surfactants which were first established by Handjani-Vila et al. The widely used methods for the synthesis of niosomes are ether injection method, film method, sonication method of Handjani–Vila, reverse-phase evaporation and heating method [40, 63]. The scientists from L’Oréal (Clichy, France) were applied noisome in cosmetic formulations in the 1970s and 1980s. Along with the cosmetic applications, these were utilized in various other sectors such as pharmaceuticals, and food [64]. The bioavailability of actives can be higher with the help of noisome. Therefore, these can be considered as drug delivery vehicles [65, 66]. The various parameters such as structure, type of surfactants, nature of encapsulated drug and temperature can affect the synthesis of noisome [67]. Along with noisome, proniosomes are used in order to get improved drug delivery vehicles [68]. The moisturizers and skin whitening creams, anti-wrinkle creams, shampoos and conditioners have also been formulated through noisome [41, 69, 70].

2.2.3. Dendrimers
These are monodispersed, unimolecular and nanostructures with the dimensions of 20 nm. The presence of a total number of series of branches determines the generation of dendrimers [71]. The 1st generation dendrimer has one series of branches; in the case of 2nd generation dendrimers, there are two series of branches. These are used as vehicles for the slow, controlled delivery of active ingredients at the desired site. The particles are symmetrical in nature with various functional groups at the circumference of particles. These functional groups act as the site of attachment for the various chemical components. The surface of dendrimers can act as carriers for the various external functional groups. In 1985, the Newkome dendrimers were one of the first artificially synthesized dendrimers. The synthesis of dendrimers is possible with two mechanisms as a divergent method or a convergent method. The divergent method of synthesis gets initiated from the core part of the dendrimers followed by the addition of building blocks at the exterior. While latter includes vice versa as that of the divergent method in which the synthesis starts from the exterior part that ultimately becomes the outermost arm of the final dendrimer [42–44]. There are several cosmetic companies that patented the usage of dendrimers in various products of skin, hair, nail [72]. Because of such characteristics of the dendrimers, both hydrophilic and hydrophobic molecules are enclosed into dendrimers [73]. These nanostructures have been used in different cosmetic products such as sunscreens, shampoos, anti-acne creams, and hair-styling materials. The cosmetic companies such as Dow Chemical Company, L’Oréal, Revlon, and Unilever, have registered patents on dendrimer-dependent cosmetic preparations for various applications for skin, nail, and hair care products.

2.2.4. Nanoemulsions
Nanoemulsions comprising nanoparticles in the range of 50 to 1000 nm and it is also a mixture of oil and water. These nanoemulsions are used in various hair sunscreens, shampoos, skin and deodorants. Korres’ Red Vine Hair sunscreen cosmetic company uses nanoemulsions [74, 75]. The nanoemulsions impart various properties to the cosmetics such as improvement in the shelf life of products and texture. These nanoemulsions act as carriers for various lipid compounds like liposomes. The nanoemulsions are able to reduce the delicacy and oily nature of hair making the hair shiny. They are considered safe. These are basically used in the sprayable form. The presence of characteristic properties such as high surface area, minimal viscosity, stability, solubility makes the increased usage of nanoemulsions. Nanoemulsion synthesis involves a two-step process where a
Solid lipid nanoparticles (SLN) and Nanostructured lipid carriers (NLCs)

The solid lipid nanoparticles (SLN) are of sub-micrometer in dimensions. These nanoparticles are made of a unique outer shell in which oily or lipid materials are present as a core. These are of polymeric in nature contain different types of fatty acids such as stearic acid or a mixture of fatty acids [78–81]. When the structure of the skin is considered, it is composed of the outer epidermis which covers the layer of the dermis which confines blood and lymph vessels. The use of SLN for the skin becomes appropriate as the nanoparticles contain lipid particles which allow the easy absorption of these nanoparticles through topical applications. The SLN being hydrophobic in nature, the particles are able to protect the skin from dehydration and to maintain the moisture of the skin. Therefore, these nanoparticles have better skin penetration, non-toxicity and effective carrier. These nanoparticles are able to liberate the active components instead of deeper penetration through the skin. SLN and NLC (Nanostructured Lipid Carrier) are widely used as carriers for sunscreens, anti-acne and anti-aging components [82–84]. These lipid nanoparticles are promising carrier systems as compared to conventionally used carriers such as nanoemulsions, liposomes. SLN and NLCs show many beneficial features such as the controlled release of actives, occlusion, and increased skin hydration effect for cosmetic applications. These are considered as a ‘nanosafe’ carrier system that has negligible cytotoxicity and remarkable tolerance as these are made of biodegradable and physiological lipids. Different methods for the synthesis of lipid nanoparticles are reported such as using a high-pressure homogenization process. Ultrasound is another method for preparing lipid nanoparticles using high energy. Techniques based on microemulsions, double emulsion formation, phase inversion induced by temperature, membrane contactor and cold homogenization are a few of the most studied in this regard. Solvent emulsification–evaporation technique, solvent emulsification diffusion technique, high shear homogenization and/or ultrasonication technique are also widely used methods for their synthesis [47, 85, 86].

The presence of high absorbance, stability makes the NLCs greater than SLNs in cosmetic products. These lipid nanoparticles are able to penetrate the skin more efficiently. The colourless lipid particles improve the appearance of cosmetic products. Nanorepair cream was the first cosmetic product containing these lipid particles in 2005. The skin lotion of Dr. Rimpler GmbH, Germany, improved skin penetration using NLCs [87, 88].

2.2.6. Fullerene

These fullerences contain carbon rings of odd numbers of three-dimensional spherical nanostructures [89, 90]. These are like cage structures. The discovery of fullerences won a Nobel Prize and from which the nanotechnology field launched. Synthesis of fullerences by vaporization of a carbon source, laser vaporization of carbon in an inert atmosphere, electric arc heating of graphite, laser irradiation of polycyclic hydrocarbons (PAHs) and resistive arc heating of graphite are reported [48, 49].

Carbon fullerences are able to forage the free radicals and also able to rejuvenate the skin. These are mainly hydrophobic in nature and difficult to get solubilized but when they are attached with other molecules like surfactants these can be solubilized and can be applied in various cosmetic formulations. The carboxy- fullerences are able to protect the keratinocytes from UVB-induced damages. The fullerences are able to scavenge the free radicals and protect the cells from apoptosis. Because of such antioxidant nature of fullerences, they are highly useful in anti-aging cosmetic products, for example, fullerene-C60 (Lipo-Fullerene) is used as a potential ingredient because of the anti-wrinkle property of fullerences [91–93].

2.2.7. Nano-hydroxyapatite

Nano-hydroxyapatite is mainly used in oral care products as well as cosmetic products. In dental care, hydroxyapatite is used for remineralization and in case of hypersensitivity. Various oral care products have included these nanohydroxyapatite nanomaterials in dentifrices and mouthwashes, and because of remineralization and desensitization nature, nano-hydroxyapatite can be a substitute for fluoride toothpaste [94–96]. Microwave-assisted preparation of nano-hydroxyapatite for bone substitutes, wet chemical
precipitation technique, ultrasound-assisted method, surfactant-assisted synthesis, and sol-gel technique is employed for the synthesis of nano-hydroxyapatite [97, 50, 51, 98, 99].

2.2.8. Nanocapsules
These are used in cosmetics in order to protect vital actives as these are confined by an oily or water state. The polymeric forms of nanocapsules in the form of suspensions can be used on the skin and these are used to encapsulate the different components. The modifications of nanocapsules can also be achieved through the type of polymer and surfactants used. The stable forms of nanocapsules of dimensions 115 nm can be achieved through the use of poly-l-lactic acid by nanoprecipitation. These nanocapsules have entrapped with fragrant molecules that make the continuous release of perfume. Thus, these nanocapsules are biocompatible in nature and are used in various deodorants. The entrapment of jasmine essence in the γ-polyl glutamic acid/quotosans could release the fragrance in a sustained manner [100]. Various methods such as surfactant-assisted, mini-emulsion polymerization techniques, chemical vapour condensation process have been employed for the synthesis of nanocapsules [52, 53]. For the first time, L’Ore’al named cosmetic company in 1995 initiated the use of nanocapsules dependent cosmetic products [101]. These nanocapsules can be used for the entrapment of both hydrophobic and hydrophilic types of carriers. The surfaces of nanocapsules can be attached with proteins, polymers and biomolecules. These nanocapsules are stable in an aqueous medium, biodegradable and biocompatible in nature [102–107]. The polymers attached with nanocapsules affect the dimensions of particles. These particles are biocompatible in nature and get degraded into CO2 and water. These products can be excreted from the body. The nanocapsules are used as a carrier for the antioxidant components which are helpful in anti-aging cosmetic formulations [108].

2.2.9. Nanotubes
The graphene-based nanomaterials have been implemented in various hair colouring agents. The attachments of different polymers with the nanomaterials produce coloured products. This combination of polymers and nanomaterials resulted in the formation of highly resistant hair colours, thus cannot be washed easily with shampoos. Carbon nanotubes (CNTs) are the rolled graphene, hollow, cylindrical fibers and are made of graphene walls, cylindrical hollow fibers, and composed of graphene walls. CNTs are highly light in weight and with dimensions of 0.7 to 50 nm in diameter, with lengths of approximately 10 s of microns [109]. There are different types of CNTs like single-walled, double-walled, and multi-walled CNTs. Single-walled CNTs contain a single sheet of graphene, the double-walled CNTs have two concentric single-walled CNTs. The multiple layers of graphene tubes lead to form multi-walled CNTs [110]. Carbon nanoparticles, CNTs, and peptide-based CNTs are used in cosmetics preparations [108, 109]. Chemically modified CNTs are applied for coloring hair, eyelashes, or eyebrows [110]. Peptide-based CNTs synthesized by integrating a hair-binding peptide on the surface of the nanotube, increase the affinity to hair by covalent bonding. Halloysite clay nanotubes, nickel vanadate nanotubes, and boron-nitride nanotubes are also utilized in hair care formulations. Chemical vapor deposition (CVD), electrochemical anodization processes have also been widely used methods for the fabrication of carbon nanotubes [54, 55]. It is due to the high abundance in nature, minimal toxicity and economic nanoclay nanotubes have high demand in hair care products [111–113].

2.2.10. Nanospheres
The nanospheres are bounded by a polymeric matrix with the spherical nature of the matrix of 10 to 200 nm. These are amorphous and crystalline in nature. There can be both biodegradable and non-biodegradable nanospheres. Albumin, pristine-based nanospheres along with modified starch or gelatine-based nanospheres are mainly biodegradable in nature while polyactic acid (PLA) presents the non-biodegradable type of nanospheres. The deep delivery of active ingredients present in cosmetics can be achieved through nanospheres. This system makes an efficient and precise delivery of actives present in cosmetics. The anti-acne, anti-wrinkle, and moisturizing creams are included with the nanospheres [114–116]. Ubiquinone (UQ) containing poly(lactide-co-glycolic acid) (PLGA) nanospheres are being stable, efficient and have the ability to control the release of actives present in the cosmetics. The nanospheres can also be synthesized by catalytically assisted chemical vapour deposition (CCVD), hydrothermal routes and reduction mechanism [56, 117, 118].

3. Types of nanotechnology-based cosmetics
Various nanomaterials have been reportedly used in the production of different formulations, aiding packaging as well as technology for manufacturing units in the field of cosmetics by virtue of their multi-faceted properties. Nanomaterials-based approaches have been widely used in cosmetics by virtue of their diversified interactions with different tissues like skin, hair, teeth, etc [8]. Nanotechnology-based formulations have been immensely
used in different beauty products, skincare products as well as sunscreens, hair care products, deodorants and perfumes in addition to dental products as a result of associated advantages like enhanced performance and high bio-availability [119].

3.1. Beauty products

Different nanoparticles have been reportedly used in various beauty products such as fairness creams, concealers, foundations, makeup bases, lipsticks, etc by virtue of their physico-chemical, electronic as well as optical properties [4]. For example, gold and silver nanoparticles have been exploited in different cosmetic compositions on the basis of their optical properties. Gold nanoparticles have been used for red or blue coloration; silver nanoparticles for yellowish coloration as well as gold-silver nanocomposites have been used for orange coloration [120]. In addition to this, nanoparticles have been successfully used in the modulation of skin colour. This approach makes use of blending techniques using formulations having nanoparticles that establish the original skin colour initially followed by the desired skin colour. For example, silver nanoparticles resulting in blue coloration are used to set the initial skin colour followed by complimenting silver nanoparticles with gold nanoparticles which give green colour collectively contributing to a brighter shade. Depending upon the skin type and colour, nanoparticles used have been selected [121]. Solid lipid nanoparticles have been used in skin whitening formulations for topical delivery of active ingredients like 6-methyl-3-phenethyl-3,4-dihydro-1H-quinazoline-2-thione (JSH18) which is effective in skin lightening due to its property of tyrosinase inhibition crucial for melanin production. Application of JSH18 containing SLN formulations has shown effective recovery of skin coloration in hairless rats within 4 days post-exposure to UV irradiation for a time period of 7 days thus suggesting its potential applicability in skin whitening [122]. Both forms of arbutin, i.e., α-arbutin and β-arbutin, have been immensely used in beauty products because of their hyperpigmentation and antioxidant properties. Chitosan nanoparticles have been used for entrapping α-arbutin and β-arbutin. These chitosan NPs entrapped α and β-arbutin have been observed to show higher stability and greater bioavailability as compared to their free forms thus proving chitosan NPs a promising carrier for topical delivery in skin whitening formulations [123, 124].

Apart from skincare products, nanoparticles have also been used in lip care as well as nail care products. Different nanoparticles have been incorporated in lip balms, lip gloss and lipstick in order to trap the moisture within the lips thereby retaining its softness. For example, silver and gold nanoparticles have been used in different ratios depending on the desired colour for long-lasting colour retention [125]. Silica nanoparticles have also been used in lip care products to ensure high coverage as well as even distribution [126]. Moreover, nail care products containing nanoparticles impart benefits like enhanced toughness as well as resistance to blemishes in comparison with traditional counterparts [127]. The nail colour incorporated with nanoparticles developed by Nano Labs Corp. has been associated with different advantages like easy drying, shock resistance, elimination of cracks and scratches as well as easy application. The future beholds the use of nail care products with nanoparticles having antimicrobial properties to be used in treating microbial infections thereby serving aesthetic as well as therapeutic purposes [128].

3.2. Hair products

Nanotechnology-based technology has been extensively used in various hair care products such as hair shampoos, hair conditioners, hair colour, hair serums, hair sprays as well as other hair styling products. The use of nanoparticles has been employed in order to facilitate the prevention of hair loss, treatment of hair-related issues, enhancement of hair growth, enrichment of hair quality, etc. Out of different nanoparticles used, nanospheres, nanoliposomes as well as nanoemulsions have shown promising results in hair care as compared to conventional hair care products [129]. In another study, sericin nanoparticles which have been prepared using sericin protein extracted from the cocoons of silkworm Bombyx mori have been used in hair care products after functionalization using quaternary ammonium salts thus forming sericin cationic nanoparticles. These nanoparticles which have been intended to be used in the repair of damaged coloured hair have shown promising results by promoting hair shine, softness, tangibility thereby restoring hair health in addition to maintenance of hair colour [130]. Polymeric nanoparticles have been reported to be used for follicular drug delivery which can be used to treated hair problems. Roxithromycin (ROX) loaded pluronic lecithin organogel (PLO) have been used against hair loss problem because of its hair restoration property. Efficient penetration of ROX-loaded PLO into the hair follicles has been confirmed by fluorescence tracking which in turn increases the effectiveness of these nanoparticles-based hair formulations in treating hair loss [131].

Different metal nanoparticles, metal oxide nanoparticles, carbon-based nanoparticles as well as quantum dots have been used in hair colour in order to improve the retention of hair colour along with its manageability. Metallic nanoparticles such as silver, gold, copper, palladium, platinum, selenium, cadmium, etc along with their alloys have been used in hair colouring products. These metallic nanoparticles with a coated layers of
organosulfur compounds have been observed to improve hair quality, help in hair-dressing, enhance hair conditioning as well as impart protection against heat and solar radiations [132]. Carbon nanotubes with chemical and physical modifications have also been used in hair coloring. The use of carbon nanotubes has been observed to impart black color to human hair without damaging it. These CNTs-based hair colour forms a thin layer upon human hair by virtue of its small size thus imparting smooth texture as well as volumizing them. The high surface area to volume ratio increases retention of CNT-based hair colour as compared to conventional hair dyes [133, 134].

3.3. Skin products
Different skincare products like sunscreens, moisturizers, skin cleansers, anti-aging formulations, etc make use of biomolecules such as antioxidants, proteins and vitamins by virtue of their anti-aging properties. The use of nanoparticles, nanoemulsions as well as solid lipid nanoparticles provides a greater advantage over conventional skincare products by increasing the bioavailability of the active ingredients in addition to enhancement of other cosmetic benefits. Metal-based nanoparticles have been exploited for their antioxidant properties thereby nullifying the effect of free radicals contributing to anti-aging. For example, cerium oxide nanoparticles loaded liposomes have been used in anti-aging creams in order to minimize the adverse effects caused for the generation of free radicals thereby promoting tissue longevity [135]. Solid lipid nanoparticles (SLNs), as well as nanostructured lipid carriers (NLCs), have been widely used in transdermal drug delivery. SLNs loaded with different antioxidants like resveratrol, vitamin E (VE), and epigallocatechin Gallate (EGCG) have been observed to provide excellent skin protection. SLNs ensured a controlled release profile in case of resveratrol up to 70% in a time period of 24 hrs thereby increasing its bioavailability. Moreover, resveratrol encapsulated SLNs showed more efficient penetration into stratum corneum thus suggesting to be a promising alternative to be used in skincare products due to its lasting antioxidant properties [136].

Nanoemulsions have been used in cosmetic applications aiding delivery of active ingredients with issues in storage, solubility, stability, loss of activity, etc. Nanoemulsions have been reported to be synthesized using the phase inversion emulsification method using rice bran oil along with sorbitan oleate and castor oil mixture thereby providing a moisturizer with high stability and low irritability. These nanoemulsions provide excellent antioxidant properties due to the presence of tocopherols and gamma-oryzanol in addition to superior hydration properties in comparison with conventional moisturizers [137]. Sunscreens make use of metal oxide nanoparticles like zinc oxide and titanium dioxide with intrinsic properties to absorb UV irradiation. These nanoparticles scatter UV light thereby preventing its harmful effect on the skin. In addition to this, these nanoparticles show inherent biocompatibility upon interaction with dermal tissues due to which they have been widely used in sunscreens with excellent efficiency [138].

3.4. Oral products
Nanotechnology-based approaches have been used in various oral care products like toothpaste, toothbrushes, mouthwashes, dental floss, etc so as to improve the efficacy of the product as compared to its traditional counterparts. Different types of nanocarriers such as nanoparticles, liposomes, quantum dots, polymers, hydrogels as well as dendrimers have been used for this purpose. Toothpaste containing nanomaterials helps in improving tooth healing and rebuilding of enamel by facilitating remineralization, fixing tooth sensitivity as well as help to fight dental problems against bacterial infections. Different nanoparticles such as silver, gold, zinc oxide, titania, calcium carbonate, hydroxyapatite, etc have been known to be exploited in oral care [139]. Use of bioactive non-stoichiometric hydroxyapatite nanoparticles substituted using carbonates in dental formulations has been reported. These nanoparticles are 20-200 nm long, 5-30 nm wide in addition to crystalline nature less than 40% with an aspect ratio within the range of 2 to 40. The dental formulations containing hydroxyapatite nanoparticles facilitate efficient tooth desensitization as well as remineralization in a time frame that can be devoted to routine oral care. The use of hydroxyapatite nanoparticles also increases the shelf life up to 2–3 months due to its stable nature [140]. Zinc nanoparticles in non-aggregated form have been reported to be used in oral composition with anti-plaque as well as anti-malodor benefits. The use of zinc ions in the form of its nanoparticles further reduces the total amount of zinc present in the composition thereby enhancing its negative organoleptic characteristics as well as improving the clarity of the oral formulation [141].

The most commonly occurring oral diseases like dental caries as well as periodontal diseases are attributed to a remarkable increase in microbial load [142]. These problems can be managed preliminarily by using oral care products containing nanoparticles with antimicrobial properties. Silver nanoparticles have been reported to show excellent antimicrobial activity against multiple aerobic and anaerobic oral pathogens like Escherichia coli, Aggregatibacter actinomycetemcomitans, Fusobacterium nuceatum, Streptococcus mitis, Streptococcus mutans as well as Streptococcus sanguinis in a size-dependent manner. Thus, the use of silver nanoparticles in dental formulations can aid in controlling microbial infections selectively by virtue of its high antimicrobial activity as
well as biocompatibility against human cells [143]. Gutta-percha (GP) which has been used as a dental filler during root canal therapy gives rise to problems like leakage, dental reinfection as well as sub-standard mechanical properties. These shortcomings can be overcome by using GP embedded nanodiamonds which show excellent mechanical properties as well as high biocompatibility thereby making them suitable for dental applications. Moreover, functionalization of these GP embedded nanodiamonds with traditional antibiotics specific for oral infections such as amoxicillin further enhances its applicability in dental treatments with excellent results [144].

4. Pros of use of nanomaterials in cosmetics

The various types of nanoparticles titanium dioxide (TiO$_2$), zinc oxide (ZnO), silver, silicon dioxide, gold nanoparticles have been utilized in cosmetics [145–150]. The main purpose of the use of nanoparticles in cosmetics is that the nanoparticles affect the efficiency of the products, shelf life of products. The use of zinc oxide and titanium oxide as UV blockers is more beneficial than that of Avobenzone, a compound present in sunscreens. The compound is found to be very greasy and noticeable when applied. However, the ZnO and TiO$_2$ nanoparticles are non-oily, odourless and colourless nanoparticles which are better UV blockers and do not form any kind of white residue upon application on the skin. This is the main reason for the extensive use of zinc oxide and titanium dioxide nanoparticles in sunscreens. The evenness to the cosmetics creams can be offered by the incorporated nanoparticles along with full and even coverage of the skin.

There is a wide usage of nanoparticles in anti-aging products because of their carrier nature [151, 152]. The delivery of antioxidants to the skin could be possible with the help of these carriers. The topical administration of retinoids, antioxidants, for rejuvenation of the skin can be achieved through the field of nanotechnology as most of the components cannot pass through the skin.

Some of the benefits of the use of nanoparticles in cosmetics are listed as follows

- They act on the top of the skin
- They are used in tiny measures
- They improve the texture of cosmetic products
- They enhance the rate of absorption
- They enhance the solubility of products
- They increase the surface area of products
- They infuse enhanced shelf life in the cosmetics

5. Cons of use of nanomaterials in the cosmetic products

The presence of high reactivity of nanomaterials because of the high surface to volume ratio gives rise to toxicity. These various properties of nanoparticles can be acquired through the reduction of dimensions of particles. These nanoparticles are able to catalyze various reactions and cause toxic effects. This leads to the increased penetration of nanoparticles through the skin and affects the cells of the human body. Therefore, the use of nanomaterials is a double-edged sword as the nanoparticles are useful for medical purposes, but result in far penetration of nanoparticles that exert an adverse health effect. Regardless of the various benefits of nanoparticles in cosmetics, there are strong apprehensions with respect to the safety of nanoparticles in cosmetic products. This jeopardy is not only related to the consumers but also to the workers which are in daily contact with these nanoparticles [153–157].

As every coin has two sides, the use of nanoparticles in cosmetics also has both advantages and disadvantages. As the nanoparticles possess different characteristics as compared to bulk materials, they might be able to alter the biological properties. Therefore, a study related to the toxicity of nanoparticles is warranted. The evaluation of the influence of size, morphology, charge, interactions of particles with the biological cells and correlations with toxicity and safety issues afford no consensus to date. Because of the presence of unique features of nanoparticles, they are exploited in various applications. Conversely, these characteristics are hypothesized to be the basis for nanoparticles induced toxicity which arises due to the complex interplay between nanoparticle uniqueness (e.g. size, shape, surface chemistry and charge), administered dosage and host immunity. Changes in these attributes may influence interactions of nanoparticles with biomolecules, proteins, cell lines, and tissues. It is imperative to assess the intracellular activity and function of nanoparticles, for the development of effective and safe nanoparticles to be used in cosmetics [158–165].
The presence of nanoparticles is found to be more reactive which results in the production of huge numbers of ROSs. The nanosized particles can cross different barriers of the human body and affect different systems of the human body including blood, respiratory system, skin. These ROS affects the macromolecules present in the cells such as proteins, DNA even the cell membranes. The nanoparticles could be toxic to human cells and tissues because of which cell death can take place [166–168]. The widely used TiO\(_2\) nanoparticles have effects on the DNA of cells as the particles tend to produce ROS which increases the oxidative stress of the cells of fibroblast. The skin fibroblast cells, as well as nucleic acids, get affected due to photo-activated TiO\(_2\) nanoparticles [169].

Titanium dioxide and zinc oxide nanoparticles are able to absorb UV radiations and produce free radicals which affect the skin. This may lead to cell damage and skin cancer. Along with the size of nanoparticles, the chemical nature of nanoparticles also affects the human system. When the rats were administered with nanoparticles by instillation the lungs of rats revealed some inflammatory signs and consequently, the tumours were observed in the lungs. The risk of nanoparticles can depend upon the hazard and the exposure [170]. When pregnant mice were exposed to TiO\(_2\) nanoparticles male offspring caused brain damage. In the long term, the traces of TiO\(_2\) affect the brain [171]. When the cosmetics are taken into consideration, the way of exposure, by the topical application cannot cause this kind of exposure (inhalation) necessary to cause such kinds of damages. It was observed when the mode of application gets changed to aerosols. Crossing the skin barrier and entering into the bloodstream is the main concern in the case of cosmetics. The nanoparticles are able to deliver actives present in cosmetics into the deeper layers of skin. These chemicals may cause irritation. Along with beneficial effects, the adverse effects of nanomaterials on the cells have been studied. The aluminium oxide and iron oxide were investigated for their \textit{in vitro} toxic effects. The free radicals generated from aluminium oxide nanoparticles were investigated for their induced concentration-dependent stem cell toxicity and produced inflammation that may lead to diseases such as atherosclerosis disrupted the blood–brain barrier and directly toxic to brain blood vessel cells [172–174].

The benefits of the use of nanoparticles are usually depicted. However, the risks, health and environmental hazards are caused due to exposure to nanoparticles which are not fully understood [175]. When the nanoparticles are absorbed through the skin, skin, pulmonary tract, brain, and other organs (via blood) damage can result. Some of the nanoparticles affect the brain and raise some perilous effects. The present knowledge regarding the safety of nanoparticles is insufficient. There is a need for research that focuses on the synthesis methods, characteristics, safety assessments in both \textit{in vitro} and \textit{in vivo} models, dosage determinations likewise.

The components of cosmetic products should be safe to use and the products need to be mentioned as safe for usage. FDA plays the role of approval of specific products into the market. The cosmetic products used should be in pure and active forms without any adulterations. In this regard, FDA has separate safety guidelines as ‘Guidance for Industry: Safety of Nanomaterials in Cosmetic Products’ for the usage of nanomaterials in cosmetics [176]. This document gives an idea about the safety concerns of nanomaterials in cosmetics and proposes to support interested companies in the recognition of significant safety measures and their evaluation ways.

6. Toxicity issues

6.1. Human safety issues

The extensive use of nanomaterials in cosmetic products has been attributed to its multi-faceted nature. The use of lipid and polymeric nanoparticles as delivery systems has been preferred because its biocompatible nature as well as their ease of biodegradation. However, there do exist toxicity factors upon interaction with the human body which should be taken into consideration while using nanomaterials so abundantly in the cosmetic industry [177, 178]. For example, implications of the use of metal-based nanoparticles in cosmetic products on human health have been reported. Traces of different metal nanoparticles such as copper, iron, cobalt, nickel, chromium, cadmium, lead, arsenic, mercury, etc have been detected in cosmetics which pose a severe threat to human health. It is due to their small size, these nanoparticles can easily penetrate through the dermal tissue thereby entering blood via which it can reach almost every vital organ leading to a much severe response after its accumulation [179]. In another study, the effect of polyvinylpyrrolidone-functionalized silver nanoparticles of size 15 nm on human keratinocytes has been evaluated. It is observed that exposure to silver nanoparticles remarkably decreases cell viability, metabolic rate as well as severely impairs its migration and proliferation. Furthermore, prolonged exposure of silver nanoparticles results in caspase 3/7 activation and DNA damage thereby triggering genotoxicity as well as cytotoxicity [180].

Metal oxide nanoparticles such as zinc oxide and titanium dioxide nanoparticles have been extensively used in cosmetics, especially in skincare products owing to their UV blocking properties. Effect of TiO\(_2\) nanoparticles on penetration and cytotoxicity upon interaction with skin cells have been studied Evaluation of skin penetration of TiO\(_2\) nanoparticles using \textit{in vivo} studies shows penetration through a dermal layer which further
invades tissue causing pathological lesions in various organs thus causing a systemic response [181]. Toxicity associated with exposure to ZnO nanoparticles has also been extensively studied. Prolonged exposure of human keratinocytes to ZnO nanoparticles has been associated with reduced mitochondrial function, changes in cellular morphology, free radical production as well as alterations in cell cycle profiles which collectively contribute to decreasing in cell viability. Thus, it is critical to consider toxicity effects upon exposure to the human body while using nanotechnology-based cosmetics [182]. However, there do exist several ways using which toxicity of nanoparticles can be dramatically reduced. For example, TiO2 nanoparticles coated with fatty acids like palmitoleic acid, oleic acid, palmitic acid, stearic acid, etc show a dramatic decrease in cytotoxicity as well as cell penetration in humans fibroblast skin cells as well as adenocarcinoma lung cells in comparison with bare TiO2 nanoparticles [183]. Thus, the presence of fatty acids does protect human cells from nanoparticle cytotoxicity which can in turn be exploited while using nanoparticles in the cosmetic industry. Moreover, further research focusing on newer ways to reduce nanoparticle toxicity should be undertaken which in turn would increase its applicability in the cosmetic industry.

6.2. Environmental safety issues

The environmental impact of the use of nanomaterials in the cosmetic industry is tremendous as it would contribute significantly to the generation of global nanowastes which is followed by disposal-related problems as well as the risks it poses to the environment considering their long term management. The discarded nanowastes can contaminate groundwater by penetration through wastewater treatment plants and landfills severely affecting the process [21]. For example, silver nanoparticles have been reported to show excellent antibacterial activities against Staphylococcus aureus and Escherichia coli. Silver nanoparticles have been observed to physically interact with bacteria resulting in pit formation thereby causing increased membrane permeability which further causes leakage of vital components ultimately resulting in cell death [184]. Such bactericidal properties of nanoparticles would severely hamper wastewater management, especially the ones employing microbial communities for the removal of organic wastes.

ZnO and TiO2 nanoparticles which are extensively used in skincare products as UV blockers are also known for ROS generation after photoexcitation. The presence of ROS in the environment has been observed to be harmful to phytoplanktons thereby causing serious damage to the aquatic ecosystem. Exposure to TiO2 nanoparticles for a prolonged period of 21 days has been observed to decrease the proportion of viable embryos in zebrafish thereby affecting its reproduction severely [185]. Similarly, anatase and rutile forms of TiO2 nanoparticles have shown reduced cell viability as well as a decrease in chlorophyll content in freshwater microalgae Chlorella sp. following exposure to UV irradiation. Damaged nucleus and cell membranes were observed post interaction with anatase TiO2 whereas rutile TiO2 caused damage to chloroplasts as well as other cell organelles [186]. ZnO nanoparticles are also known to cause toxic effects in freshwater white suckerfish, Catostomus commersonii by causing damage to its gill epithelium by affecting cardiovascular regulation due to impaired acetylcholine signaling followed by problems in oxygen uptake attributed to ROS generation [187]. Assessment of toxicity of silver and TiO2 nanoparticles against planktonic crustacean, Daphnia magna via behavioural and biochemical studies post-exposure. It has been observed that there were remarkable effects on behavioural patterns upon exposure to ASTM-dispersed silver nanoparticles. Also, silver nanoparticles present in the wastewater were found to show higher toxicity in comparison with TiO2 nanoparticles from the wastewater as well [188]. Thus, there is a need to study the impact of environmental hazards in detail before commercialization of their use in the cosmetic industry.

7. Future perspectives

The cosmetic industry makes wide usages of nanomaterials for various purposes such as UV filters, preservatives. The characteristic properties of nanomaterials can impose some undesired effects on the consumers. In this regard, the standard safety measures should be designed and the necessary experiments of nanomaterials should be carried out. The various characteristics of nanomaterials such as physical, chemical, aggregation, porosity, morphology, size, solubility, and purity should be evaluated as per FDA guidelines. The studies regarding in vitro testing of non-cytotoxic concentrations of nanoparticles are reported for example, for AgNPs synthesized by using fenugreek leaves revealed the least cytotoxic effect against HaCaT cells at a concentration of 250 μg ml⁻¹ [189]. AgNPs synthesized by using Albizia lebbeck flowers showed biocompatibility against the cell lines A549 revealed as the nanoparticles did not affect the viability of cell lines at a concentration range of 2 μg per ml to 50 μg per ml [190]. Iron oxide nanoparticles in the concentration of 0.1–10 μg per ml did not affect the cell lines (normal cell lines, glial cell lines and breast cancer cell lines) revealing the biocompatible nature of nanoparticles [191]. A thorough study regarding safe doses of nanoparticles should be carried out so that the toxic effect of nanoparticles on the cells can be circumvented. The
in vitro and in vivo toxicological studies of nanomaterials should be studied along with dermal penetration and potential inhalation, genotoxicity studies, and possible skin and eye irritation studies.

The route of exposure of nanomaterials is one of the vital facets to consider. The prime route of exposure to nanomaterials is skin specifically the stratum corneum. There are still some ambiguities with respect to the exposure of nanomaterials and penetration through the first layer of skin and this may lead the toxic effects. The nanomaterials which are used in cosmetic products should be subjected the further tests. The cosmetics which are in the form of sprays or aerosols should be taken more care of as these particles may enter through inhalation. The nanomaterials may show some changes in storage and handling. It can be more difficult to foretell the reactivities and risks associated with the products. The newly developed cosmetics should be tested for safety, efficiency, stability and aesthetics [192].

Due to the presence of significant properties of nanomaterials, the nanotechnology field has been growing to a greater extent as a large number of publications on this field can provide the evidence. However, research on nanoparticle toxicity needs to be considered. The risks associated with the use of nanomaterials need to be defined in different aspects. Strict implementations of different safety regulations are needed. Toxicity studies, the effect on human health and the environment of various nanomaterials used in the industry should be studied thoroughly.

8. Conclusions

Nanotechnology is a versatile field in which controlled synthesis of nanomaterials and their varied applications in different fields for different purposes can be achieved. In a current scenario, the main focus is upon the applications of nanomaterials for various purposes but the side effects or long-term effects of these nanomaterials on health should be taken into consideration. The toxic effects such as skin inflammation, skin cancer and genotoxicity may arise and they need to be thoroughly studied. The interactions between the nanomaterials and the skin have been derived through the experiments. Various types of nanoparticles have been used in cosmetic formulations. Nonetheless, further studies are needed to understand the toxic effects of nanomaterials as the side-effect-free character of cosmetic products is a significant aspect.

Data availability statement

All data that support the findings of this study are included within the article (and any supplementary files).

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References

[1] Wu X and Guy R H 2009 Applications of nanoparticles in topical drug delivery and in cosmetics J. Drug Deliv. Sci. Technol. 19 371–84
[2] Bowman D M, Van Calster G and Friedrichs S 2010 Nanomaterials and regulation of cosmetics Nat. Nanotechnol. 5 92
[3] Santos A C, Panchal A, Rahman N, Pereira-Silva M, Pereira I, Veiga F and Ivov Y 2019 Evolution of hair treatment and care: prospects of nanotube-based formulations Nanomaterials 9 903
[4] Mihryanian A, Ferraz N and Stromme M 2012 Current status and future prospects of nanotechnology in cosmetics Prog. Mater. Sci. 57 875–910
[5] Pastrana H, Avila A and Tsai C S 2018 Nanomaterials in cosmetic products: The challenges with regard to current legal frameworks and consumer exposure Nano Ethics. 12 123–37
[6] Carrouel F, Viennot S, Ottolenghi L, Gaillard C and Bourgeois D 2020 Nanoparticles as anti-microbial, anti-inflammatory, and remineralizing agents in oral care cosmetics: a review of the current situation. Nanomaterials. 10 140
[7] Revia R A, Wagner B A and Zhang M 2019 A portable electrospinning for nanofiber synthesis and its application for cosmetic treatment of alopecia Nanomaterials 9 1317
[8] Raj S, Jose S, Sumod U S and Sabitha M 2012 Nanotechnology in cosmetics: Opportunities and challenges J. Pharm. Bioall. Sci. 4 186
[9] Rigano I and Lionetti N 2016 Nanobiomaterials in galenic formulations and cosmetics Nanomaterials in Galenic Formulations and Cosmetics 1 121–48
[10] Fytianos G, Rahdar A and Kyzas G Z 2020 Nanomaterials in Cosmetics: Recent Updates Nanomaterials 10 979–95
[11] Shiseido What Is Nano Particles? https://our-products-policy.shiseido.com/en/ingredients/nano-particles
[12] Singh P and Nanda A 2012 Nanotechnology in cosmetics: a boon or bane? Toxicol. Environ. Chem. 94 1467–79
[13] Bernauer U et al 2019 SCCS. Guidance on the Safety Assessment of Nanomaterials in Cosmetics SCCS/161/I/19/Scientific Committee on Consumer Safety (https://ec.europa.eu/health/sites/health/files/scientific_committees/consumer_safety/docs/scss_o_233.pdf)
[14] Food and Drug Administration (FDA) 2014 Guidance for Industry: Safety of Nanomaterials in Cosmetic Products. Center for Food Safety and Applied Nutrition (Rockville, MD: US Department of Health and Human Services) (http://www.fda.gov/downloads/ Cosmetics/GuidanceRegulation/GuidanceDocuments/UCM309932.pdf)
[15] Kaul S, Gulati N, Verma D, Mukherjee S and Nagaich U 2018 Role of nanotechnology in cosmeceuticals: a review of recent advances J. Pharma. 2018 Article ID 3420204
16. Boxall A B, Tieke K and Chaudhry Q 2007 Engineered nanomaterials in soils and water: how do they behave and could they pose a risk to human health? Nano Scale 2 919–27
17. 2007 Report by the Central Science Laboratory (CSL) York for the Department of the Environment and Rural Affairs (DEFRA), United Kingdom (https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/250291/0568.pdf)
18. Sioutas C, Delfino R J and Singh M 2005 Exposure assessment for atmospheric ultrafine particles (UFPs) and implications in epidemiologic research. Environ. Health Perspect. 113 947–55
19. Egamberam O P, Kesavan Pillai S and Ray S S 2020 Materials science challenges in skin UV protection: a review Photochem. Photobiol. Sci. 96 779–97
20. Wiechers J W and Musee N 2010 Engineered inorganic nanoparticles and cosmetics: Facts, issues, knowledge gaps and challenges J. Biomed. Nanotech. 6 408–31
21. Smijs T G and Pavl S 2011 Titanium dioxide and zinc oxide nanoparticles in sunscreens: focus on their safety and effectiveness Nanotechnol. Sci. Appl. 4 95
22. Schulz J, Hohenberg H, Pfüller F, Göttler E, Will T, Pfeiffer S, Wepf R, Wendel V, Gers-Barlag H and Wittem K P 2002 Distribution of sunscreens on skin Adv. Drug Deliv. 54 S157–65
23. Popov A P, Kirill M Y, Priezhev A V, Lademann J, Hast J and Myllyr A 2005 Optical sensing of titanium dioxide nanoparticles within horny layer of human skin and their protecting effect against solar UV radiation SPIE 5702 113–22
24. Koozekonan A G, Esmaeilpour M R M, Kalantary S, Karimi A, Azam K, Moshiran V A and Golbabaei F 2020 Fabrication and characterization of PAN/CNT, PAN/TiO2, and PAN/CNT/TiO2 nanofibers for UV protection properties J. Text. Inst. 1–9
25. Penders J, Stolzoff M, Hickey D J, Andersson M and Webster T J 2017 Shape-dependent antibacterial effects of non-cytotoxic gold nanoparticles Int. J. Nanomed. 12 2457
26. Jeyarani S, Vinita N M, Puja P, Senthimalis elvi S, Devan U, Velangani A J, Birumanta M, Pugazhendhi A and Kumar P 2020 Biomimetic gold nanoparticles for its cytotoxicity and biocompatibility evidenced by fluorescence-based assays in cancer (MDA-MB-231) and non-cancerous (HEK-293) cells J. Photoch. Photobio. 202 111717
27. Gannon C J, Patra C R, Bhattacharya R, Mukherjee P and Curley S A 2008 Intracuticular gold nanoparticles enhance non-invasive radiotherapy fractional depth of human gastrointestinal cancer cells J. Nanobiotechnology. 6 2
28. Qu Y and Liu X 2009 Aqueous synthesis of gold nanoparticles and their cytotoxicity in human dermal fibroblasts-fetal Biomater. Mater. 4 2–7
29. Ankamwar B and Yadwade R 2021 A review: Non-Antibacterial, non-antifungal and non-anticancer properties of nanoparticles the forgotten paradigm Nano Exp 201203
30. Haddada M B, Gerometta E, Chawech R, Sorres J, Bialecki A, Pesnel S, Spadavecchia J and Morel A L 2020 Assessment of antioxidant and dermoprotective activities of gold nanoparticles as safe cosmetic ingredient Colloid Surf. B 189 110855
31. Gubitosi E et al 2018 One pot environmental friendly synthesis of gold nanoparticles using Punica Granatum Juice: A novel antioxidant agent for future dermatological and cosmetic applications J. Collid Interf Sci 521 50–61
32. You C, Han C, Wang X, Zheng Y, Li Q, Hu X and Sun H 2012 The application of silver nanoparticles in the antibacterial mechanism, clinical application and cytotoxicity Mol. Biol. Rep. 39 9193–201
33. Agnihotri S, Mukherji S and Mukherji S 2012 Antimicrobial chitosan–PVA hydrogel as a nanoreactor and immobilizing matrix for silver nanoparticles Appl. Nanosci. 2 179–88
34. Noronha V T, Paula A J, Duran G, Galembeck A, Cogo-Mueller K, Franz-Montan M and Duran N 2017 Silver nanoparticles in dentistry Dent. Mater. 33 1110–26
35. Badnore A U, Sorde K I, Datir K A, Ananthanarayan L, Pratap A P and Pandit A B 2019 Preparation of antibacterial peel-off facial mask formulation incorporating biosynthesized silver nanoparticles. Appl. Nanosci. 9 279–87
36. Beck R et al (ed) 2011 Nanocosmetics and Nanomedicines: New Approaches for Skin Care (New York City, NY: Springer Science & Business Media) (https://dx.doi.org/10.1007/978-3-642-19792-5)
37. Khabir Z, Guller AE, Rozova V S, Liang L, Lai Y J, Goldys E M, Hu H, Vickery K and Zvyagin A V 2019 Tracing upconversion nanoparticle penetration in human skin Colloid Surf. B 184 110480
38. Puliti-Proicjak J, Chwastowski J, Siudek M and Banach M 2018 Incorporation of metallic nanoparticles into cosmetic preparations and assessment of their physicochemical and utility properties J. Surf. Funct. Det. 23 575–91
39. Panahi Y, Farshbaf M, Mohammadhosseinmi T, Mirhamidi M, Khallol R, Saghifi S and Akbarzadeh A 2017 Recent advances on liposomal nanoparticles: synthesis, characterization and biomedical applications Artif. Cells Nanomed. Biotechnol. 45 788–99
40. Yeo P L, Lim C L, Chye S M, Ling A P K and Koh R Y 2018 Niosomes: a review of their structure, properties, methods of preparation, and medical applications Asian Biomed. 11 301–14
41. Ge X, Wei M, He S and Yuan W E 2019 Advances of non-ionic surfactant vesicles (niosomes) and their application in drug delivery Pharmaceutics 11 55
42. Abbasi E, Aval S F, Akbarzadeh A, Milani M, Nasrabad H T, Ioo S W, Hanifehpour Y, Nejati-Koshki K and Pashaei-Asl R 2014 Dendrimers: synthesis, applications, and properties NZJ 9 1–10
43. Myers V S, Weir M G, Carino E V, Yancey D F, Pande S and Crooks R M 2011 Dendrimer-encapsulated nanoparticles: new synthetic and characterization methods and catalytic applications Chem. Sci. 2 1632–46
44. Copidas K R, Whitesell J K and Chaudhry Q 2007 Engineered nanomaterials in soils and water: how do they behave and could they pose a risk to human health? Nano Scale 2 919–27
45. Jafari S M, He Y and Bhandari B 2007 Optimization of nano-emulsions production by microfluidization Eur. Food Res. Technol. 225 733–41
46. Qian C and McClements D J 2011 Formation of nanoemulsions stabilized by model food-grade emulsifiers using high-pressure homogenization: factors affecting particle size Food Hydrocol. 25 1000–8
47. Jaiswal P, Gidwani B and Vyas A 2016 Nanostructured lipid carriers and their current application in targeted drug delivery Artif. Cells Nanomed. Biotechnol. 44 27–40
48. Mozica A, Alonzo J A and Méndez F 2013 Synthesis of fullerenes J. Phys. Org. Chem. 26 S26–39
49. Nirmobha A, Newton E A, Cyprain A Y and Donbeke W 2018 Fullerene: synthesis and applications J. Mater. Sci. 22 33
50. Abid SSA and Murtaza Q 2014 Synthesis and characterization of nano-hydroxyapatite powder using wet chemical precipitation reaction J. Mater. Sci. Technol. 30 307–10
51. Poimert G E, Bhindavanaz R K, Mondinos N and Jiang Z T 2009 Synthesis and characterisation of nanohydroxyapatite using an ultrasound assisted method Ultrason. Sonochem. 16 469–74
Anis M, AlTaher G, Sarhan W and Elsemary M 2017 Cosmetic applications

Müller R H, Petersen R D, Hommoss A and Pardeike J 2007 Nanostructured lipid carriers

Müller R H, Alexiev U, Sinambela P and Keck C M 2016 Nanostructured lipid carriers

Lens M 2009 Use of fullerenes in cosmetics Recent Pat. Biotechnol. 3 118–23

Yapar E A 2012 Nanomaterials and cosmetics J. Pharm. Inst. Univ. 42 43–70 (https://ergipark.org.tr/ing/10.2174/1879201261104101450102)

Dingler A and Gohla S 2002 Production of solid lipid nanoparticles (SLN): Scaling up feasibilities J. Microencapsul. 19 11–6

Joo H H, Lee H Y and Kim J C 2009 Stability, release property and skin penetration of stearic acid nanoparticles Mol. Cryst. Liq. Cryst. 508 137–49

Müller R H, Alexiev U, Sinambela P and Keck C M 2016 Nanostructured lipid carriers (NLC): The second generation of solid lipid nanoparticles Percutaneous Penetration Enhancers: Chemical Methods in Penetration Enhancement ed N Dragicevic and H Maibach (Berlin, Heidelberg: Springer) (https://doi.org/10.1007-3-662-47862-2_11)

Müller R H, Petersen R D, Hommoss A and Pardeike J 2007 Nanostructured lipid carriers (NLC) in cosmetic dermal products Adv. Drug Deliv. Rev. 59 522–30

Wissing S A and Müller R H 2002 Solid lipid nanoparticles as carrier for sunscreens: In vitro release and in vivo skin penetration J. Control. Rel. 85 225–35

Anis M, AlTaher G, Sarhan W and Elsemary M 2017 Cosmetic applications Nanove (Cham: Springer) 243–60

Wissing S A and Müller R H 2003 Cosmetic applications for solid lipid nanoparticles (SLN) Int. J. Pharm. 254 65–8

Salvi V R and Pawar P 2019 Nanostructured lipid carriers (NLC) system: A novel drug targeting carrier J. Drug Deliv. Sci. Technol. 51 255–67

Gordillo–Galeano A and Mora–Huertas CE 2018 Solid lipid nanoparticles and nanostructured lipid carriers: a review emphasizing on particle structure and drug release Eur. J. Pharm. Biopharm. 133 285–308

Pardeike J, Hommoss A and Müller R H 2009 Lipid nanoparticles (SLN, NLC) in cosmetic and pharmaceutical dermal products Int. J. Pharm. 366 170–94

Müller R H, Radlde M and Wissing S A 2002 Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) in cosmetic and dermato logical preparations Adv. Drug Deliv. Rev. 54 513–55

Sinitsa A S, Lebedeva I V, Polynskaya Y G, Popov A M and Knizhnik A A 2020 Molecular dynamics study of sp–Defect migration in odd fullerene: possible role in synthesis of abundant isomers of fullerene J. Phys. Chem. 124 11652–61

Hirsch A 1993 The chemistry of the fullerenes: an overview Angew. Chem. Int. Ed 32 1138–41

Lens M 2009 Use of fullerenes in cosmetics Recent Pat. Biotechnol. 3 118–23

Yapar E A 2012 Nanomaterials and cosmetics J. Pharm. Inst. Univ. 42 43–70 (https://dergipark.org.tr/en/pub/ijsf/issue/381/5843/article_cite)

Kato S, Taira H, Aishima H, Saito H and Miwa N 2010 Clinical evaluation of fullerene–C60 dissolved in squalane for anti-wrinkle cosmetics J. Nanosci. Nanotechnol. 10 6769–74

[52] Tiarks F, Landefester K and Antonietti M 2001 Preparation of polymeric nanocapsules by miniemulsion polymerization Langmair 17 908–18

[53] Wang Z H, Choi C J, Kim B K, Kim J C and Zhang Z D 2003 Characterization and magnetic properties of carbon-coated cobalt nanocapsules synthesized by the chemical vapor–condensation process Carbon 41 1751–8

[54] Andrews R, Jacques D, Qian D and Rantell T 2002 Multwall carbon nanotubes: synthesis and application Acc. Chem. Res. 35 1008–17

[55] Macák J M, Tsuchiya H and Schumppi P 2003 High-aspect-ratio TiO2 nanotubes by anodization of titanium Angew. Chem. Int. Ed 42 2100–2103

[56] Sawant S Y, Somani R S, Newvalkar B L, Choudary N V and Bajaj H C 2009 Synthesis of submicron size hollow carbon spheres by a chemical reduction—solvolithographic method using carbon tetrachloride as carbon source Mater. Lett. 63 2339–42

[57] Saraswat A, Agarwal R, Kataré O P, Kaur I and Kumar B 2007 A randomized, double blind, vehicle controlled study of a novel lipidosomal dithranol formulation in psoriasis J. Dermatol. Treat. 18 40–5
[94] Coelho C C, Grehno L, Gomes P S, Quadros P A and Fernandes M H 2019 Nano-hydroxyapatite in oral care cosmetics: characterization and cytotoxicity assessment Sci. Rep. 91–10

[95] Bernauer U 2018 Opinion of the scientific committee on consumer safety (SCCS)—revision of the opinion on hydroxyapatite (nano) in cosmetic products Regul. Toxicol. Pharmacol. 98 274–5

[96] Ramis J M, Coelho C C, Córdoba A, Quadros P A and Monjo M 2018 Safety assessment of nano-hydroxyapatite as an oral care ingredient according to the EU cosmetics regulation Cosmetics 5 33

[97] Hassam M N, Mahmoud M M, Abd El-Fattah A and Kandil S 2016 Microwave-assisted preparation of Nano-hydroxyapatite for bone substitutes Ceram. Int. 42 3725–44

[98] Wang Y, Chen J, Wei K, Zhang S and Wang X 2006 Surfactant-assisted synthesis of hydroxyapatite particles Mater. Lett. 60 3227–31

[99] Vijayalakshmi U and Rajeswari S 2012 Influence of process parameters on the sol–gel synthesis of hydroxyapatite using various phosphorous precursors J. Solgel Sci. Technol. 63 45–55

[100] Chiari-Andrèo B G, de Almeida-Cincotto M G, Oshiro J A Jr, Taniguchi C Y, Chiavacci I A and Isaac V L 2019 Nanoparticles for cosmetic use and its application Nanopharmaceutics in Pharmacotherapy (William Andrew Publishing) 113–46

[101] Poletto F S, Beck R C, Gutteres S S and Pohlmann A R 2011 Polymeric nanocapsules: Concepts and applications Nanocapsitics and Nanomedicines (Berlin, Heidelberg: Springer) 49–68

[102] Nieto-Márquez A, Romero R, Romero A and Valverde J L 2011 Carbon nanospheres: synthesis, physicochemical properties and applications J. Mater. Chem. 21 1664–72

[103] Kaur I P, Kapila M and Agrawal R 2007 Role of novel delivery systems in developing topical antioxidants as therapeutics to combat photosaging Ageing Res. Rev. 6 271–88

[104] Santos A C, Morais F, Simões A, Pereira I, Sequeira J A, Pereira-Silva M, Viega F and Ribeiro A 2019 Nanotechnology for the development of new cosmetic formulations Expert Opin. Drug Deliv 16 313–30

[105] Chung B H, Ha T H, Jeong J Y, Jung B H, Kim J K and Lim Y T 2007 Cosmetic pigment composition comprising carbon nanotubes US Patent 7260888B2

[106] Huang X, Kobos R and Xu G 2007 Hair coloring and cosmetic compositions comprising carbon nanotubes US Patent 7260888B2

[107] Ha T H, Jeong J Y, Jung B H, Kim J K and Lim Y T 2007 Peptide-based carbon nanotube hair colorants and their use in hair colorant and cosmetic compositions US Patent 20050229335A1

[108] Poletto F S, Beck R C, Guterres S S and Pohlmann A R 2011 Polymeric nanocapsules: Concepts and applications Colloids Surf. Physicochem. Eng. Asp 410 38–44

[109] Panchal A, Fakhrrullin G, Fakhrrullin R and Lvov Y 2018 Self-assembly of clay nanotubes on hair surface for medical and cosmetic nanofluids Colloids Surf. Physiochem. Eng. Apt 10 802–10

[110] Liu M, Fakhrrullin R, Novikov A, Panchal A and Lvov Y 2019 Tubule nanoclay–organic heterostructures for biomedical applications Macromol. Biosci. 19 1800419

[111] Gutteres S S, Alves M P and Pohlmann A R 2007 Polymeric nanoparticles nanospheres and nanocapsules for cutaneous applications Drug Target Insights 2 147–55

[112] Deen I, Pang X and Zhitomirsky I 2012 Electrophoretic deposition of composite chitosan–halloysite nanocapsule–hydroxyapatite films Colloids Surf. Physiochem. Eng. A 490 38–44

[113] Sun X and Li Y 2005 Hollow carbon nanotube capsules from glucose solution J. Colloid Interface Sci 291 7–12

[114] Nieto-Márquez A, Romero R, Romero A and Valverde J L 2011 Carbon nanospheres: synthesis, physicochemical properties and applications J. Mater. Chem. 21 1664–72

[115] de Almeida-Cincotto M G, Oshiro J A Jr, Taniguchi C Y, Chiavacci I A and Isaac V L 2019 Nanoparticles for cosmetic use and its application NAnopharmaceutics in Pharmacotherapy (William Andrew Publishing) 113–46

[116] Santos A C, Morais F, Simões A, Pereira I, Sequeira J A, Pereira-Silva M, Viega F and Ribeiro A 2019 Nanotechnology for the development of new cosmetic formulations Expert Opin. Drug Deliv 16 313–30

[117] Chung B H, Ha T H, Jeong J Y, Jung B H, Kim J K and Lim Y T 2007 Cosmetic pigment composition comprising gold or silver nanoparticles WO 2007011103

[118] Alfano R R, Ni X and Zevallas M 2007 Changing skin-color perception using quantum and optical principles in cosmetic preparations US Patent 709274938

[119] So J W, Kim S, Park I S, Kim B H, Jung S H, Shin S C and Cho C W 2010 Preparation and evaluation of solid lipid nanoparticles with JSH18 for skin-whitening efficacy Pharm. Dev. Technol. 15 415–20

[120] Megas P and Krause-Baranowska M 2015 The significance of arbutin and its derivatives in therapy and cosmetics Phytocem. Lett. 13 35–40

[121] Ayumi N S, Sahudin S, Hussain Z, Hussain M and Samah N H A 2019 Polymeric nanoparticles for topical delivery of alpha and beta arbutin: preparation and characterisation Drug Deliv. Transl. Res. 9 482–96

[122] Ha T H, Jeong J Y, Jung B Y T H, Kim J K and Lim Y T 2008 Cosmetic pigment composition containing gold or silver nano-particles EP 0997454A1

[123] Viladot P J L, Delgado G R and Fernandez B A 2013 Lipid nanoparticle capsules EP 2549977A2

[124] Amato S W, Farer A, Hoyte W M, Pavlovsky M, Smith R and Valdiviezo G 2010 Coatings for mammalian nails that include nanosized particles EP 1986594A2

[125] Lohani A, Verma A, Joshi H, Yadav N and Karki N 2014 Nanotechnology-based cosmeceuticals Int. Sch. Res. Notices 2014 483687

[126] Hu Z, Liao M, Chen Y, Cai Y, Meng L, Liu Y, Lv N, Liu Z and Yuan W 2012 A novel preparation method for silicone oil nanoemulsions and its application for coating hair with silicone Int. J. Nanomedicine 7 5719–24

[127] Pereda M D C V, Polezel M A, de Campos Dieamant G, Nogueira C, Marcelino A G, Rossan M R and Santana M H A 2014 Serumic cationic nanoparticles for application in products for hair and dyed hair WO 2010146415A1

[128] Główka W, Wosicka-Pręgowski H, Hyla K, Stefanowicz J, Jastrzębska K, Klapiszewski L, Jesionowski T and Cal K 2014 Polymeric nanoparticles–embedded organogel for roxithromycin delivery to hair follicles Eur. J. Pharm. Biopharm. 88 75–84
[133] Giroud F, Livoreil A and Vic G 2003 Use of organomodified metallic particles for the treatment of human keratinic fibres FR 2838052R (https://patents.google.com/patent/EP1352634A1/en)  
[134] Huang X, Kobos R K and Xu G 2005 Hair coloring and cosmetic compositions comprising carbon nanotubes US 20050229934  
(https://patents.google.com/patent/US7276088B2)  
[135] Chen J, McGinnis J F, Patil S, Seal S, Sezate S and Wong L 2007 Inhibition of reactive oxygen species and protection of mammalian cells US 20070202193 (https://patents.google.com/patent/US7347987B2/en)  
[136] Chen J, Wei N, Lopez-Garcia M, Ambrose D, Lee J, Annelm C and Peterson T 2017 Development and evaluation of resveratrol, vitamin E, and epigallocatechin gallate loaded lipid nanoparticles for skin care applications Eur. J. Pharm. Biopharm. 117 286–91  
[137] Bernardi D S, Pereira T A, Maciel N R, Bortolotto J, Viara G S, Oliveira G C and Rocha-Filho P A 2011 Formation and stability of oil-in-water nanoemulsions containing rice bran oil: in vitro and in vivo assessments J. Nanobiotechnol. 9 44  
[138] Nohyne G J, Lademann J, Riedl C and Roberts M S 2007 Grey goo on the skin? Nanotechnology, cosmetic and sunscreen safety Crit. Rev. Toxicol. 37 251–77  
[139] Nanda A, Nanda S, Nguyen T A, Slimani Y and Rajendran S 2020 Nanocosmetics: Fundamentals Applications and Toxicity (Amsterdam: Elsevier) ISBN 978–0–12–822286–7  
[140] Gazzaniga G, Roveri N, Rimondini L, Palazzo B, Iafisco M and Gualandi P 2007 Biologically active nanoparticles of a carbon-based substituted hydroxyapatite, process for their preparation and compositions incorporating the same WO 2007317666 (https://patents.google.com/patent/US8367043B2)  
[141] Arvanitidou E, Boyd T J, Fruge L, Gaffar A, Visco D and Xu G 2007 Oral composition containing non-aggregated zinc nanoparticles US 20070020201 (https://patents.google.com/patent/US9242125B2)  
[142] Asikainen S and Alaluusua S 1993 Bacteriology of dental infections Eur. Heart J. 14 43–50  
[143] Lu Z, Kong K, Li J, Yang H and Chen R 2013 Size-dependent antibacterial activities of silver nanoparticles against oral anaerobic pathogenic bacteria J. Mater. Sci. Mater. Med. 24 1465–71  
[144] Lee D K et al 2015 Nanodiamond–gutta percha composite biomaterials for root canal therapy ACS Nano 9 11490–501  
[145] Lu P, Huang S C, Chen Y P, Chiu L C and Shih D Y C 2015 Analysis of titanium dioxide and zinc oxide nanoparticles in cosmetics J. Food Drug Anal. 23 587–94  
[146] Mogrant P 2010 Use and potential of nanotechnology in cosmetic dermatology Clin. Cosmet. Investig. Dermatol. 3 5–15  
[147] Pulit–Prociak J, Grabowska A, Chwastowski J, Majka T M and Banach M 2019 Safety of the application of nanosilver and nanogold in topical cosmetic preparations Colloids Surf. B Biointerfaces 183 110416  
[148] Kalantary S, Jahan A and Jahan R 2020 MLR and ANN approaches for prediction of synthetic/ natural nanofibers diameter in the environmental and medical applications Sci. Rep. 10 1–10  
[149] Kalantary S, Golkubaci F, Latifi M, Shokrgozar M A and Yaseri M 2020 Assessment of electrospinning antioxidant nanofibers in skin exposure to oxidative stress J. Macandranur Uni. Med. Sci. 30 68–79 (https://journals.mazandaran.ac.ir/article-1-13844-en.html)  
[150] Kalantary S, Jahan A, Pourbakhsh R and Beigzadeh Z 2019 Application of ANN modeling techniques in the prediction of the diameter of PCL/gelatin nanoparticles in environmental and medical studies RSC Adv. 9 24858–74  
[151] Khezi K, Saeedi M and Dizaji S M 2018 Application of nanoparticles in percutaneous delivery of active ingredients in cosmetic preparations Biomed. Pharmacother. 106 1499–505  
[152] Costa R and Santos L 2017 Delivery systems for cosmetics- From manufacturing to the skin of natural antioxidants Powder Technol 322 402–16  
[153] Bakand S, Hayes A and Dechakulthorn F 2012 Nanoparticles: a review of particle toxicology following inhalation exposure Inhal. Toxicol. 24 125–35  
[154] Ladics G S, Chapin R E, Hastings K L, Holsapple M P, Makris S L, Sheets L P, Woolhiser M R and Burns-Naas L A 2005 Developmental toxicity evaluations—issues with including neurotoxicity and immunotoxicity assessments in reproductive toxicology studies Toxicol. Sci. 88 24–9  
[155] Gurr J R, Wang A S, Chen C H and Jan K Y 2005 Ultrafine titanium dioxide particles in the absence of photoactivation can induce oxidative damage to human bronchial epithelial cells Toxicology. 213 66–73  
[156] Chen T H, Lin C Y and Tseng T C 2011 Behavioral effects of titanium dioxide nanoparticles on larval zebrafish (Danio rerio) Mar. Pollut. Bull. 63 303–8  
[157] Faunce T, Murray K, Nasu H and Bowman D 2008 Sunscreen safety: The precautionary principle, the Australian therapeutic goods administration and nanoparticles in sunscreens Nano Ethics 2 331–40  
[158] Eifler A C and Thaxton C S 2011 Nanoparticle therapeutics: FDA approval, clinical trials, regulatory pathways, and case study Biomedical Nanotechnology Volume 726 ed S Hurst (Totowa, New Jersey, United States: Humana Press) 325–38  
[159] Hofmann–Amtenbrink M, Grainger D W and Hofmann H 2015 Nanoparticles in medicine: Current challenges facing inorganic nanoparticle toxicity assessments and standardizations Nanomedicine: NBM 11 1689–94  
[160] Sajid M, Ilyas M, Basheer C, Tarig M, Daud M, Baig N and Shehzad F 2015 Impact of nanoparticles on human and environment: review of toxicity factors, exposures, control strategies, and future Prospects Environ. Sci. Pollut. R 22 4122–43  
[161] Doktorovova S, Kovačević A B, Garcia M L and Souto E B 2016 Preclinical safety of solid lipid nanoparticles and nanostructured lipid carriers: current evidence from in vivo and in vitro evaluation Eur. J. Pharm. Biopharm. 108 235–52  
[162] Patel P and Shah J 2017 Safety and toxicological considerations of nanomedicines: the future directions Curr. Clin. Pharmacol. 12 73–82  
[163] Robertson T A, Sanchez W Y and Roberts M S 2010 Are commercially available nanoparticles safe when applied to the skin? J. Biomed. Nanotech. 6 652–68  
[164] Ma X, Zhao Y and Liang X J 2011 Theranostic nanoparticles engineered for clinic and pharmacetics Acc. Chem. Res. 44 1114–22  
[165] Ankanwar B 2012 Size and shape effect on biomedical applications of nanomaterials Biomedical Engineering-Technical Applications in Medicine ed Radiosn Huda et al (Croatia: InTech Publishers) pp 93–114  
[166] Pucarini M, Qian Y, Fu W, Schweger-Berry D, Ding M, Castranova V and Guo N L 2012 Cell permeability, migration, and reactive oxygen species induced by multivalent carbon nanotubes in human microvascular endothelial cells J. Toxicol. Environ. 75 112–28  
[167] Braydich-Stolle L, Hussain S, Schlager J and Hofmann M C 2005 In vitro cytotoxicity of nanoparticles in mammalian germline stem cells Toxicol. Sci. 88 412–9  
[168] Oesterling E, Chopra N, Gavalas V, Arzua A, Lim E J, Sultana R, Butterfield D A, Bachas I. and Hennig B 2008 Alumina nanoparticles induce expression of endothelial cell adhesion molecules Toxicol. Lett. 178 160–6  
[169] Grieger K D, Fjordbøge A, Hartmann N B, Eriksson B, Bjerg P L and Baum A 2010 Environmental benefits and risks of zero-valent iron nanoparticles (nZVI) for in situ remediation: risk mitigation or trade-off? J. Contam. Hydrol. 118 165–83
[170] Jatana S, Callahan L M, Pentland A P and DeLouise L A 2016 Impact of cosmetic lotions on nanoparticle penetration through ex vivo C57BL/6 hairless mouse and human skin: a comparison study Cosmetics 3 6
[171] Jia X, Wang S, Zhou L and Sun L 2017 The potential liver, brain, and embryo toxicity of titanium dioxide nanoparticles on mice Nanoscale Res. Lett. 12 478
[172] Patrick L 2006 Lead toxicity part II: the role of free radical damage and the use of antioxidants in the pathology and treatment of lead toxicity Altern. Med. Rev. 11 114–21
[173] Guitx M, Carbonell C, Comenge J, Garcia-Fernández L, Alarçon A and Casals E 2008 Nanoparticles for cosmetics: how safe is safe? Centr. Sci 4 213–7
[174] Chaudhari U, Nemade H, Sureshkumar P, Vinken M, Ates G, Rogiers V, Heschler J, Hengstler J G and Sachinidis A 2018 Functional cardiotoxicity assessment of cosmetic compounds using human-induced pluripotent stem cell-derived cardiomyocytes Arch. Toxicol. 92 371–81
[175] Crosera M, Bovenzi M, Maina G, Adami G, Zanette C, Florio C and Larese F F 2009 Nanoparticle dermal absorption and toxicity: a review of the literature Int. Arch. Occup. Environ. Health 82 1043–55
[176] Food and Administration D 2014 Guidance for Industry Safety of Nanomaterials in Cosmetic Products; Center for Food Safety and Applied Nutrition (Rockville, MD, United States of America: US Department of Health and Human Services) Available online: (http://www.fda.gov/downloads/Cosmetics/GuidanceRegulation/GuidanceDocuments/UCM3)(accessed on 7 April 2020)
[177] Katz L M, Dewan K and Bronbaugh R L 2015 Nanotechnology in cosmetics Food Chem. Toxicol. 85 127–37
[178] Muller H R, Shegokar R and Keck M C 2011 20 years of lipid nanoparticles (SLN & NLC): Present state of development & industrial applications Curr. Drug Discov. Technol. 8 207–27
[179] Borowska S and Brzozka M M 2015 Metals in cosmetics: implications for human health J. Appl. Toxicol. 35 551–72
[180] Szymd R et al 2013 Effect of silver nanoparticles on human primary keratinocytes Biol. Chem. 394 113–23
[181] Wu J, Liu W, Xue C, Zhou S, Lan F, Bi L, Xu H, Yang X and Zeng F D 2009 Toxicity and penetration of TiO2 nanoparticles in hairless mice and porcine skin after subchronic dermal exposure Toxicol. Lett. 191 1–6
[182] Kocbek P, Teskac K, Kreft M E and Kristl J 2010 Toxicological aspects of long-term treatment of keratinocytes with ZnO and TiO2 nanoparticles Small 6 1908–17
[183] Chang J, Lee C W, Alsuilimani H H, Choi I E, Lee J K, Kim A, Park B H, Kim J and Lee H 2016 Role of fatty acid composites in the toxicity of titanium dioxide nanoparticles used in cosmetic products J. Toxicol. Sci. 41 533–42
[184] Shahverdi A R, Fakhimi A, Shahverdi H R and Minaian S 2007 Synthesis and effect of silver nanoparticles on the antibacterial activity of different antibiotics against Staphylococcus aureus and Escherichia coli Nanomedicine: Nanotechnol. Biol. Med 3 168–71
[185] Ramsden C S, Henry T B and Handy R D 2013 Sub-lethal effects of titanium dioxide nanoparticles on the physiology and reproduction of zebrafish Aquat. Toxicol. 126 404–13
[186] Iwarya V et al 2015 Combined toxicity of two crystalline phases (anatase and rutile) of Titania nanoparticles towards freshwater microalgae: Chlorella sp Aquat. Toxicol. 161 154–69
[187] Callaghan N I, Allen G J P, Robart T E, Dieni C A and MacCormack T J 2016 Zinc oxide nanoparticles trigger cardiorespiratory stress and reduce aerobic scope in the white sucker Catostomus commersonii Nano Impact 2 29–37
[188] Galhano V et al 2020 Impact of wastewater–borne nanoparticles of silver and titanium dioxide on the swimming behaviour and biochemical markers of Daphnia magna: an integrated approach Aquat. Toxicol. 220 105404
[189] Senthil B, Devasena T, Prakash B and Rajasekar A 2017 Non-cytotoxic effect of green synthesized silver nanoparticles and its antibacterial activity J. Photoch. Photobio. B 177 1–7
[190] Gharpure S, Kirtiwat S, Palwe S, Akash A and Ankamwar B 2019 Non–antibacterial as well as non-anticancer activity of flower extract and its biogenous silver nanoparticles Nanotechnology 30 195701
[191] Ankamwar B, Lai T C, Huang J H, Liu R S, Hsiao M, Chen C H and Hwu Y K 2010 Biocompatibility of Fe3O4 nanoparticles evaluated by in vitro cytotoxicity assays using normal, glia and breast cancer cells Nanotechnology 21 075102
[192] Ajazzuddin M, Jeswani G and Kumar Jha A 2015 Nanocosmetics: Past, present and future trends Recent Pat. Nanomed. 5 3–11