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The application of nanotechnology in preventing photoaging and photodamage

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Abstract. Skin is the first protecting us barrier from the external environment. Overexposure to sunlight, containing harmful ultraviolet radiation (UVR), may lead to photoaging. Prolonged exposure to UVR produces a notable volume of reactive oxygen species (ROS) that can exacerbate the degradation of the skin's essential structural proteins, including collagen and elastin. This interference may result in conditions like dermal solar elastosis and extracellular matrix (ECM) remodelling. UVR can cause different types of skin damage, including direct and indirect DNA damage, oxidative stress, and immune suppression. These effects can have severe consequences and lead to various skin problems, such as melanoma, squamous cell carcinoma (SCC), and basal cell carcinoma (BCC) skin cancers. In this review, we will examine how nanotechnology can be used in the prevention and treatment of skin aging and damage resulting from UVR exposure. Nanotechnology offers potential solutions for safeguarding the skin against UVR's harmful effects and repairing resulting damage.

Keywords: Nanotechnology, Photoaging, Photodamage.

1. Introduction

The skin is a vital organ that maintains homeostasis and ensures our well-being by shielding us from environmental damage, making it susceptible to damage from external factors. Overexposure to harmful environmental factors can result in several skin issues including skin aging and damage. Of these environmental factors, light exposure is a primary contributor.

The skin is highly susceptible to environmental photo-oxidative stress. A growing body of research indicates that ROS that modify the structural and functional properties of components related to the skin is achieved through exposure to UVR. The long-term implications of this process for photoaging are significant. The skin's ability to defend against the cumulative effects of photooxidative stress may impact photoaging. According to the theory of free radicals, photoaging, which differs from chronological aging both qualitatively and quantitatively, may result from insufficient protection against free radical damage caused by chronic and recurrent exposure to UVR [1]. Therefore, protecting the skin from environmental damage and neutralizing free radicals requires appropriate cosmetic treatment.

DNA photodamage is the harm caused to DNA molecules by exposure to UVR [2]. This damage is an important concern since it can result in mutations and genetic instability, thereby elevating the risk of skin cancer. DNA absorbs UVR from sunlight, which induces mutagenic lesions like pyrimidine dimers. These lesions distort the DNA helix and, if they remain unrepaired, can lead to mutations during DNA replication. Endogenous photosensitizers play a major role in mediating the genotoxic effects of

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solar UVA, leading to the creation of a local oxidative stress. Exogenous substances, such as medications like psoralens or fluoroquinolones, may in some cases intensify the negative effects of UVR. These substances could potentially interact with the DNA, resulting in additional types of damage upon exposure to UVR. Moreover, DNA photodamage is also associated with a variety of skin-specific responses to UVR. For instance, DNA photolesions can impact processes such as skin redness (erythema), reduced immune response (immunosuppression), and production of pigment (melanogenesis).

Advancements in science and technology have uncovered various methods to mitigate or eliminate the problem of skin aging. In recent years, nanomaterial-based products have gained popularity across an array of industries, such as dermatology, pharmaceutics, and cosmetics. Nanoparticles, with their high surface-to-volume ratio allowing deeper skin penetration, continued stability, and UV-filtering properties, among other advantages, have seen increasing use in cosmetic products [3].

2. Photoaging and photodamage caused by UVR

2.1. UVR

UVR stands for "Ultraviolet Radiation". It refers to the portion of electromagnetic radiation emitted by the sun with wavelengths longer than X-rays, yet shorter than visible light. UVR consists of three wavelength-based categories: UVC (200–290 nm), UVB (290–320 nm), and UVA (320–400 nm), each with different wavelengths that determine the depth to which they penetrate skin.

UVA rays primarily penetrate deeper layers of the skin and may lead to premature aging, wrinkling and contribute to skin cancer. On the contrary, UVB rays are responsible for sunburn and can penetrate only superficial skin layers. UVC rays pose a significant risk to living organisms. Nonetheless, the majority of UVC rays are absorbed by the ozone layer surrounding the Earth, which makes it difficult for them to reach the surface unless they penetrate an ozone hole. Artificial UVC is used in germicidal lamps and is effective at killing microorganisms like bacteria and viruses.

Solar radiation is the primary source of UVR in the environment around us., it consists of approximately 95% UVA and roughly 5% UVB [4]. Therefore, UVA and UVB are the primary forms of UVR under discussion.

2.2. Mechanism of photoaging

Overexposure to UV radiation is the primary cause of photoaging, which is characterized by a decrease in the expression of dermal fibres. This overexposure triggers the generation of ROS, which endangers collagen and elastin, the skin's main structural proteins. Notably, ROS production is contributed to by UVR, including UVA and UVB. While UVA indirectly generates ROS, leading to DNA strand breaks, UVB causes direct DNA damage. This damage includes the formation of cyclobutane dimers and photoproducts [4].

ROS formation in the skin happens via two distinctive pathways [4]. The first pathway generates ROS entities, like superoxide anion, peroxide, and singlet oxygen, upon exposure to UVR. These levels of ROS become normal when UVR stops. On the other hand, the second pathway produces ROS hydrogen peroxide when nicotinamide adenine dinucleotide phosphate is activated. This process activates a catalyst reaction between molecular oxygen and superoxide anion, resulting in a multifaceted skin response to UVR that includes ROS generation and subsequent damage to collagen and elastin.

Solar elastosis, a dystrophic elastic substance in the dermis that results from a series of processes leading to the degradation of elastic fibres, is a notable characteristic of photoaging. Following the aforementioned process, the formation of the extracellular matrix (ECM) occurs, leading to its reconnection into a structure that differs from its initial state [5]. The structural modification to the skin is a result of prolonged exposure to UVR and subsequent ROS generation.

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2.3. Photodamage

UVR can cause various skin issues, known collectively as UV-induced skin damage or photodamage. Skin cell DNA can sustain damage from UVR through direct and indirect mechanisms [6]. Direct damage to DNA may occur in the form of lesions, CPDs, and (6–4) photoproducts when UVB light penetrates the DNA molecule. UVR also causes indirect damage to DNA. UVR exposure induces a significant amount of ROS in skin cells, leading to oxidative stress. This stress can result in additional DNA damage, as well as harm to proteins and lipids in the skin cells [7,8]. Moreover, exposure to UVR can weaken the immune system, potentially increasing the risk of cancer and reactivating viruses like cold sores [6].

Skin cancers, including melanoma, SCC (which is a malignancy that generally spreads less than melanoma and is less likely to cause death), and BCC (which is a slowly developing skin cancer that affects mainly older adults), can arise under extreme conditions due to the accrual of DNA damage and mutations, particularly in genes like P53 [6,8].

3. Nanotechnology in preventing skin problems caused by UVR

3.1. Definition of nanomaterials in cosmetics

Determining the concept of nanomaterials used in cosmetic products poses challenges due to the evolving definition of what constitutes a nanomaterial and varying definitions across different countries. The term "nano" may not be used by regulatory authorities in the same way as it is used in cosmetic advertising and labelling [9]. Generally, nanomaterials used in cosmetics are typically defined as materials with one or more external dimensions in the range of nanoscale, which is roughly between 1 nanometer (nm) and 100 nanometers. Compared to bulk materials, their size is smaller and the surface area is much larger, as a result, these materials exhibit distinct characteristics and behaviors. In the context of cosmetics, nanomaterials are often incorporated into cosmetic products to enhance their performance, appearance, or stability.

3.2. SPF

Sun Protection Factor (SPF) is a critical term in the field of skincare and sun safety. It acts as a significant indicator of how well sunscreen or sunblock products can protect the skin from the harmful impacts of UVB. While examining different sunscreen options, you will come across SPF values that are prominently showcased on the labels, giving you essential insight into the level of protection a particular product provides against the sun's harmful rays. The SPF rating increases in value from 10 to 50 and beyond. But what exactly does this numerical value signify? As an illustration, let's consider SPF30. The number 30 denotes that merely 1/30th of the UVB that strike the skin's surface are absorbed by it after using sunscreen products. Thus, assuming that a person does not protect his skin, after 15 minutes of exposure to the sun at noon, his skin will show light red spots because of the absorption of UVB. With the application of SPF 30 sunscreen products, it would take 450 (15 x 30) minutes of skin exposure for reddening to occur. However, in reality, SPF30 sunscreen products may not effectively protect the skin for seven and a half hours without experiencing reddening due to factors like skin sweating that can reduce the actual sunscreen effect [10]. As the SPF number increases, the incremental difference in protection becomes less significant.

3.3. The impact of aggregate size on UV-blocking effectiveness

Nanosized TiO_2 and ZnO exist in three distinct forms: primary particles, aggregates, and agglomerates [11]. The production of TiO_2 and ZnO nanoparticles begins with primary particles, which measure between 5 and 20 nm in size. As a result of strong attraction forces, these primary particles bind tightly together to form aggregates. The aggregates in a final sunscreen formulation typically have sizes ranging between 30 and 150 nm, making them the smallest units. However, the manufacturing process causes the formation of loosely bound agglomerates due to drying and heat treatment processes, which have particle sizes larger than 1 μm. However, the efficiency of these sizable agglomerates in providing the

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desired UV attenuation is inadequate, thus requiring their fragmentation into aggregates. The SPF of sunscreens containing TiO_2 and ZnO relies heavily on the aggregate size of these metal oxides. In fact, the SPF may fluctuate significantly when sunscreen compositions contain the same amount of inorganic particles but vary in particle size within the formulation. In contrast, the concentration of the filters is closely related to the UV absorption profiles of organic UV filters.

TiO_2 particles of different sizes offer varying levels of protection against UVA and UVB rays. Particles with an average aggregate size of 100 nm are effective in protecting against both types of rays and cause less whitening than older TiO_2 grades. Particles of around 50 nm size provide higher UVB protection, are more transparent but offer lower UVA protection, necessitating blending with other UVA filters for comprehensive protection. However, 20 nm particles provide significantly less protection against both UVA and UVB rays compared to 50 nm and 100 nm particles. In the final sunscreen formulation, it's crucial to maintain the particle size. To prevent agglomerate reformation and preserve the fine aggregate size, nanosized TiO_2 and ZnO are usually stabilized with dispersing agents. The difference in UV protection offered by these two sunscreen products can be attributed to the presence of polymers and agglomerates in the same TiO_2 matrix. Formulation A incorporates agglomerated TiO_2 powder into the oil phase of the sunscreen. In contrast, Formulation B uses the same agglomerated TiO_2 as Formulation A, but the powder is pre-dispersed with a dispersing agent in C12-C15 alkyl benzoate to create stable aggregates before being added to the oil phase. In vitro measurements show that Formulation B, which uses pre-dispersed agglomerated TiO_2, has an SPF value five times higher than Formulation A [11-13].

3.4. Other nanomaterials in preventing UVR

Arora et al.'s research indicates that silver nanoparticles (AgNPs) can prevent DNA damage and apoptosis caused by UVB [14]. According to the study, pretreatment with AgNPs can prevent UVB-induced apoptosis in human immortalized keratinocytes (HaCaT) and considerably lessen the development of cyclobutane pyrimidine dimers (CPDs) in HaCaT following UVB irradiation. In addition, pretreatment with AgNPs can effectively induce cell cycle in the phase of G1 in HaCaT following UVB exposure, which allows for ample time for the repair of cyclobutane pyrimidine dimers. Additionally, HaCaT treated with AgNPs exhibited enhanced internalization and localization of AgNPs to both cytoplasmic and nuclear sites following UVB exposure. Additionally, after UVB exposure, pretreatment with AgNPs changed the expression of several genes in HaCaT, including the genes linked to the cell cycle, apoptosis, and nucleotide excision repair steps. This discovery clearly demonstrates the potential application of AgNPs as a novel chemopreventive agent for inhibiting skin carcinogenesis and skin aging caused by UVB radiation.

The study done by Zhu et al. demonstrates that quercetin-loaded nanoparticles made of PLGA-TPGS can enhance the anti-UVB effect by overcoming quercetin's low hydrophilicity [15]. These nanoparticles have the capacity to significantly impede COX-2 up-expression and NF-kB activation caused by UVB radiation in Hacat cells. As a practical consequence, this research suggests that quercetin-loaded PLGA-TPGS nanoparticles offer potential as a safeguarding agent against skin damage resulting from UVB exposure. This approach could have significant implications for preventing and treating skin conditions triggered by UVB exposure, such as skin cancer.

Trans-2-ethylhexyl-p-methoxycinnamate (trans-EHMC) was encapsulated into nanoparticles composed of poly-d, l-lactide-co-glycolide (PLGA), a polymer which is biodegradable and biocompatible [16]. This process entails dispersing EHMC in a PLGA solution, which subsequently leads to the formation of nanoparticles through mechanisms like emulsion or nanoprecipitation. The encapsulated EHMC exhibited considerably less photodegradation than the free EHMC. The nanoparticle shell most likely acts as a barrier against direct exposure of EHMC to UV radiation, thus securing the encapsulated EHMC. Additionally, the concentration of EHMC in the nanoparticles did not notably affect the photostability of the encapsulated EHMC, indicating that the shielding effect of the nanoparticle encapsulation is non-dependent on how much EHMC is inside the nanoparticles. Nanoparticle encapsulation has the potential to enhance the photostability of sunscreen agents, such as

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EHMC. This could result in sunscreens that remain effective for longer periods of time, reducing the frequency of reapplication. Furthermore, it may improve the protection against UV radiation provided by sunscreens, potentially reducing the risk of skin cancer and other forms of skin damage. However, additional research is necessary to fully comprehend the implications of this technology. For instance, studies must ascertain the long-term safety of nanoparticle-encapsulated sunscreens and their efficacy in removing them from the skin. Furthermore, environmental impact assessments are required to assess the potential consequences of these nanoparticles if they were to enter natural water systems.

Avobenzone and octyl methoxycinnamate are organic UV filters with low photostability that can transform into photoallergenic or phototoxic substances under UVR exposure [17]. The utilization of nano-TiO_2 composites, combined with these organic UV filters, can aid in decreasing their photodegradation [18]. It enhances UV protection effectiveness and reduces potential skin irritations by preventing direct contact with the skin. This application of microencapsulation brings dual benefits to UV filter performance. The use of microencapsulation technology makes the UV filters in cosmetics much more efficient and safer. The incorporation of nano-TiO_2 composites into organic UV filters, such as avobenzone and octyl methoxycinnamate, can greatly enhance their photostability and safety. This improvement makes the filters more appropriate for sun protection products.

4. Conclusion

So far, this review has discussed the application of nanotechnology in the prevention and treatment of UVR-induced skin aging and damage. This paper assessed the mechanisms behind photoaging and photodamage resulting from UVR, which entail the generation of ROS, DNA harm, and immune system deficiency. The paper identified various nanomaterials, such as silver, TiO_2, ZnO, quercetin, and trans-2-ethylhexyl-p-methoxycinnamate, that can be employed to protect the skin from harmful UVR. The paper also explained how the use of these nanomaterials has the potential to enhance the stability, safety, and effectiveness of sunscreen agents, and some of them may even be able to prevent or repair DNA damage and apoptosis in skin cells.

UVR induces photoaging and photodamage by producing ROS, resulting in DNA damage and immune system impairment. The development of diverse nanomaterials permits the protection of skin against UVR. These include nanoparticles composed of silver, TiO_2, ZnO, quercetin, and trans-2-ethylhexyl-p-methoxycinnamate, each with unique characteristics suitable for use in skincare products.

AgNPs have the potential of preventing DNA damage and apoptosis by regulating HaCaT. TiO_2 and ZnO nanoparticles serve as physical sunscreens by reflecting and scattering UVR, preventing it from penetrating the skin. It is essential to note that their use is effective and safe for protecting the skin against harmful UVR. Quercetin functions as a potent antioxidant that is able to neutralize ROS produced by UVR. The use of quercetin-loaded nanoparticles composed of PLGA-TPGS renders improved resistance against damage caused by UVB. EHMC encapsulated into PLGA nanoparticles shows less photodegradation than free EHMC, potentially improving UV protection and reducing sunscreen reapplication frequency. Further research is needed for long-term safety and environmental impact. The use of nano-TiO_2 composites with organic UV filters like avobenzone and octyl methoxycinnamate can decrease their photodegradation, enhance UV protection, and reduce skin irritations. This makes UV filters in cosmetics more efficient and safer.

Furthermore, certain nanomaterials exhibit potential for preventing or repairing DNA damage caused by UVR. This is achieved either by neutralizing ROS prior to DNA damage or by increasing the skin's inherent DNA repair mechanisms.

In conclusion, nanotechnology holds significant potential for advancing skincare products. It provides inventive solutions to safeguard our skin against the harmful impacts of UVR. As research advances, researchers can anticipate the development of more sophisticated nanomaterial-based skincare products that offer superior protection against skin aging and damage induced by UVR.

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