DOI 10.47176/sjfst.5.4.1

Review Article

SRPH

SJFST, 2023; 5(4): 1-14

Gold Nanoparticles in Anti-Aging Interventions: A Comprehensive Exploration of Skin Health and Cosmeceuticals

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Received: 11 September, 2023
Accepted: 05 December, 2023
Published: 25 December, 2023

ABSTRACT

The aging population presents a significant challenge in modern society, with an increase in age-related diseases due to a longer life expectancy not matched by a similar extension in healthy lifespan. This situation demands focused medical research and healthcare advancements in treating aging-associated conditions. An integrated approach is recommended, encompassing lifestyle changes, diet, and mental and emotional health, to mitigate aging and its related diseases. In skin health, innovative nanoparticle-based formulations are being explored to enhance the anti-aging properties of active ingredients. Skin aging is influenced by intrinsic factors like metabolic slowdown, disease, mitochondrial DNA damage, hormonal changes, and extrinsic factors such as UV radiation, smoking, pollutants, and lifestyle choices. These factors lead to skin issues like dryness, uneven texture, and visible pores. UVB radiation and high blood sugar levels accelerate aging by increasing oxidative stress and collagen damage. Antioxidants are crucial in defending against reactive oxygen species (ROS). Nanoparticles, with sizes under 100 nm, include various types like carbon-based, inorganic, organic, and composite nanomaterials. They are used in skincare due to their enhanced skin penetration properties. These nanoparticles, both organic and inorganic, show promise as anti-aging agents, working at different stages of the skin aging process. Understanding the delivery mechanisms of anti-aging agents through the skin is key to creating effective anti-aging products. Nanotechnology in cosmeceuticals integrates biologically active ingredients with therapeutic benefits into cosmetics. This technology addresses the limitations of traditional products by reducing particle size and improving ingredient efficacy. Nanocosmeceuticals are being developed for anti-aging, sun protection, skin lightening, and hair growth.

Overall, the article highlights the potential of gold nanotechnology in developing effective and safe anti-aging strategies. Further research is warranted to explore the long-term safety and efficacy of nanoparticle-based formulations for skin rejuvenation and to optimize their delivery for enhanced therapeutic outcomes.

Keywords: Gold Nanoparticles, Anti-Aging, Skin Health, Cosmetic

Introduction

The aging of the population poses a growing societal and economic challenge in contemporary times. The prolonged human life expectancy is not paralleled by a similar extension of a healthy lifespan, leading to an escalating prevalence of age-related ailments in most developed nations over recent decades [1]. Consequently, there is an urgent need for medical research and the healthcare industry to prioritize the development of treatment approaches specifically addressing the pathways associated with aging [2-4].

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Researchers emphasize a comprehensive approach to mitigating aging and age-related diseases involving lifestyle modifications, dietary habits, mental well-being, and emotional health. The demand for innovative techniques in skin health has led to research exploring nanoparticle-based formulations to enhance the anti-aging properties of active ingredients [5]. The aging process of the skin is attributed to intrinsic and extrinsic factors. Intrinsic factors include metabolic slowdown, disease states, mitochondrial DNA damage, and hormonal activity. Extrinsic factors encompass UV radiation, smoking, pollutants, and lifestyle choices, leading to issues like dryness, uneven skin texture, and increased visibility of pores. UVB radiation and high serum glucose levels contribute to skin aging by increasing oxidative stress and inducing collagen fragmentation. Antioxidants play a crucial role in defending against ROS through various mechanisms [6, 7].

Nanoparticles, characterized by dimensions smaller than 100 nm and diverse shapes [8], are classified into categories such as carbon nanomaterials, inorganic, organic, and composite-based nanomaterials. Notable examples include nanotubes, fullerenes, quantum dots, metals (silver, gold), metal oxides (titanium dioxide, zinc oxide), and lipophilic NPs [9], which leverage their advantageous properties for enhanced skin penetration [10]. The efficacy of certain nanoparticles as potent anti-aging agents is noted, and ongoing studies focus on their skin-protective properties. Both organic and inorganic nanoparticles are extensively utilized for their anti-aging and skin-protective attributes, operating at various levels of the aging process. Understanding the kinetics and mechanisms of delivering anti-aging agents through the skin is crucial for designing effective formulations for anti-aging applications [11].

The article also touches upon the field of nanotechnology in cosmeceuticals, where biologically active ingredients with therapeutic benefits are incorporated into cosmetic products. Nanotechnology addresses challenges associated with conventional products, such as particle size and stability, by reducing particle size and enhancing ingredient efficiency. Various nano cosmeceuticals, including solid lipid nanoparticles, nanostructured lipid carriers, and gold and silver nanoparticles, are explored for their anti-aging purposes [12, 13]. NPs serve various functions, such as antioxidants and anti-reflective agents. For instance, titanium dioxide NPs are used for their wp) hite pigment properties in creams, silver NPs are included in shampoos and toothpaste formulations [14], and gold nanoparticles as potential antioxidant agents with low cytotoxicity and good cell permeability. These antioxidant AuNPs, mostly derived from plant extracts, are explored for their efficacy in counteracting the aging process [15, 16].

In vascular aging and related disorders, age stands out as the primary risk factor. Aging-induced changes in vascular structure, functions, and phenotypes play a central role in the onset and progression of various vascular aging-related diseases, including cardiovascular, cerebrovascular, and kidney diseases [17, 18]. Pathological alterations associated with aging are closely linked to vascular disorders involving molecular and cellular events, such as cell proliferation, migration, inflammation, apoptosis, angiogenesis, and thrombosis, all contributing to vascular cell senescence [19, 20]. Nanoparticles designed for diagnostics and therapeutics play a pivotal role in augmenting both diagnostic and therapeutic efficiencies, thereby mitigating the occurrences and magnitudes of side effects. This is achieved through heightened drug accumulation at pathological sites and concurrent reduction of drug accumulation in healthy tissues [21, 22].

Despite their potential benefits, the use of NPs raises concerns about toxicity. Research indicates that exposure to NPs can lead to the production of reactive oxygen species (ROS) and result in cytotoxic and genotoxic effects. Various factors, including chemistry, dosage, particle size, shape, and surface characteristics, influence the cytotoxic impact of the NPs [23]. Despite these concerns, the advantages of NP use outweigh the potential drawbacks, as emphasized in recent literature [24].

This article underscores the versatile applications of gold nanoparticles in anti-aging skin care, cosmetics, anti-aging formulations, and cosmeceuticals. Ongoing review focuses on gold nanoparticle characteristics and understanding their mechanisms for effective anti-aging interventions.

Gold Nanoparticles: A Scientific Exploration, Diverse Structures

Among all nanoparticles utilized in experimental studies, Gold Nanoparticles (GNPs) stand out as the most efficient due to their low systemic toxicity. GNPs have been extensively researched for their use in cancer therapy. They have various therapeutic applications in the medical field, including photothermal therapy, radiotherapy sensitization, imaging properties, and targeted drug delivery. What makes them suitable for these applications are their optical properties. Gold represents a system with an equal number of positive ions (stationary) and conducting electrons (free and mobile) [25]. Thus, when an electromagnetic wave impinges upon the metal surface, the oscillating electric fields of the wave interact with the free electrons, causing surface electrons to oscillate in resonance with the visible light frequency. The free electrons are driven by the electric field to oscillate coherently. These collective oscillations of free electrons are referred to as 'plasmons,' and the oscillations of surface electrons as 'surface plasmons.' Surface plasmons interact with visible light, resulting in a phenomenon known as

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'Surface Plasmon Resonance' (SPR). The SPR phenomenon leads to the formation of strong electromagnetic fields on the surface and enhances GNP properties such as absorption, scattering, and light-to-heat conversion.

For medical imaging purposes, larger GNPs are preferred due to their better light-scattering properties. At the same time, smaller nanoparticles are used more in photothermal therapy due to their higher efficiency in converting light to heat [26]. Furthermore, the intracellular distribution of GNPs in various cellular compartments and their toxicity is determined by their size, morphology, and surface properties. GNPs can be engineered into shapes like spherical, semi-spherical, star-shaped, rod-like, branched, etc. [27]. GNPs can be produced in large quantities, with specific shapes and sizes. They can also be synthesized directly by reducing gold salts using physical, chemical, and green methods. The size of GNPs plays a crucial role in how the nanoparticles are internalized by cells and in their cytotoxic effects on cells.

The most toxic GNPs are those with smaller sizes (1 to 2 nanometers), exhibiting toxicity to both malignant and healthy human cells. Larger GNPs (4.8 to 12 nanometers) possess significant toxicity to cancer cells but have less toxicity to healthy cells, while GNPs larger than 15 nanometers are considered non-toxic [27]. In some cases, GNPs attract specific proteins, leading to their instability, but this is usually prevented by coating them with a layer of dendrimer, polylysine, PEI, or biocompatible hydrophilic polyethylene glycol. Another issue is that upon entering an organism, they might be sequestered by macrophages and other cells of the reticuloendothelial system (RES). Since foreign particles are absorbed by the RES, to prevent GNPs from being sequestered inside the body by RES cells, the nanoparticles should not be allowed to remain within the organism for an extended period, with the size of the nanoparticles playing a significant role in this regard. It has been observed that smaller particles, compared to larger nanoparticles, have a significantly longer lifespan in the bloodstream [27]. The most common sites of GNP impact are the nucleus, mitochondria, and endoplasmic reticulum. At the nuclear level, GNPs work with drug toxicity, modulation of gene expression, or direct toxicity.

In contrast, at the mitochondrial level, GNPs cause changes in membrane potential, ROS production, and activation of autophagy [28]. In 1857, Michael Faraday made a pioneering discovery in nanotechnology when he uncovered the light-scattering properties of suspended gold nanoparticles, a phenomenon now recognized as the Faraday-Tyndall effect [29]. Approximately fifty years later, Hirsch et al. identified the unique ability of gold nanoparticles (GNPs) irradiated at an electromagnetic wavelength of 820 nm to elevate surrounding temperatures, a property with significant implications for the solid tumor therapy [30]. In a landmark approval in July 2019, the United States Food and Drug Administration (FDA) endorsed an oral drug based on CNM-Au8 (developed by Clene Nanomedicine, Inc.) for treating Amyotrophic Lateral Sclerosis (ALS) [31]. Consequently, GNPs have emerged as a reliable and potent tool in therapeutic interventions. Over the past two decades, extensive research has been conducted on GNPs in various forms, including nano-clusters [32], nano-rods [33], nano-sheets [34], nano-shells [35], nano-cages [36], and nano-stars [37]. Their roles in combating different diseases have been a particular focus.

Gold Nanoparticles Anti-Aging Skin Care: Drug delivery, skin penetration, and Antibacterial properties

The epidermis, being the body's most expansive organ and directly exposed to environmental elements, undergoes aging influenced by both internal and external factors [38]. This aging process manifests through skin dehydration, diminished elasticity, and wrinkle formation [39]. The increasing societal emphasis on aesthetic standards has heightened the focus on skin aging, especially as populations worldwide are aging, thus amplifying the psychosocial impacts and underscoring the need for efficacious treatments [40]. In this scenario, there has been a notable rise in the employment of nutraceuticals as dietary enhancements [41].

Collagen, which constitutes 80% of the skin's dry weight, is a primary structural protein in various connective tissues [42]. Its unique triple helical structure, comprising a glycine repeat every third residue and interspersed with proline and hydroxyproline, is a defining feature [43]. As a major component of the extracellular matrix, collagen not only provides structural support but also guides tissue development [44].

With aging, there is a notable decrease in the enzymes responsible for collagen's post-translational processing, leading to reduced collagen synthesis by fibroblasts and diminished vascular supply to the skin [45]. The age-related deterioration in skin quality is marked by decreased collagen production and lower skin vascularity, culminating in reduced elasticity and wrinkle formation [46]. These alterations are attributable to the reduced activity of fibroblasts and a lesser number of blood vessels in the skin [47]. Consequently, the skin experiences regressive alterations, including dehydration, reduced epidermal thickness, and loss of elasticity [48]. To combat these changes, various nutritional and supplementary strategies have been adopted to enhance preserve a youthful appearance and skin health [49]. These methods encompass collagen supplements, topical creams, and injectable fillers. While topical creams incorporate collagen for improved skin hydration and firmness, their limited skin penetration may diminish their efficacy [50]. Injectable fillers like

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hyaluronic acid stimulate collagen production and offer immediate skin-plumping effects, but they are costly and carry risks like bruising and infection [50]. Alternatively, collagen supplements, especially those containing hydrolyzed collagen peptides, are recognized for their safety, cost-effectiveness, and ease of oral intake [51].

Among these supplements, hydrolyzed collagen (HC) stands out as the most favored and effective anti-aging nutraceutical for the skin [52]. Studies have revealed the presence of serine–hydroxyproline–glycine and alanine–hydroxyproline–glycine in human blood within an hour of HC ingestion [53, 54], indicating deposition in the skin [55]. Recent research confirms HC's beneficial effects on skin elasticity and hydration [52]. However, not all HC sources are equally efficacious, with variations in effectiveness observed even at identical dosages and treatment durations [56]. This highlights the need for further research to identify optimal HC sources and treatment durations for combating skin aging.

Gold Nanoparticles as Drug Delivery Systems

The human skin, as the largest organ, serves not only as a critical protective barrier but also as a vital medium for drug administration, facilitating both topical and systemic therapeutic effects. However, the inherent barrier function of the skin poses a significant challenge, limiting the penetration of many drugs, especially those with high hydrophilicity or substantial molecular weight, at therapeutic levels [57-59]. In response to this impediment, the advancement of nanocarrier-mediated delivery systems has emerged, revolutionizing the landscape of dermatological drug delivery [60, 61]. These systems encompass a diverse array of technologies, including lipid-based colloidal nano-systems, polymeric nanoparticles/micelles, metallic nanocarriers, carbon-based nanomaterials, and nano-gels, each offering unique benefits [59].

Among these, metallic nanocarriers, particularly gold nanoparticles (GNPs), have garnered extensive attention due to their inherent advantages, such as robust stability, consistent particle size distribution, adjustable morphology, and facile surface functionalization capabilities, making them highly suitable for a range of medical applications [62]. GNPs have been extensively researched for their potential as drug-delivery agents, diagnostic tools, and therapeutic agents [63]. Their compatibility with biological systems and minimal toxicity, coupled with a large surface area amenable to functionalization with biomolecules through physical adsorption or with reactive groups (like amine, thiol, and carboxyl groups) through ionic or covalent bonding for ligand or antibody modification, further enhance their applicability [64, 65]. Additionally, GNPs can be engineered into various shapes and sizes (ranging from 1 to 100 nm), which is advantageous for circumventing biological barriers [66].

GNPs are distinguished by their unique optical properties, primarily due to localized surface plasmon resonances (LSPR) - a phenomenon involving the collective oscillation of surface-free electrons at resonant frequencies, enabling interaction with light. These properties are leveraged in applications such as imaging, sensing, and photothermal transition, setting them apart from other nanomaterials [67]. Given the skin's accessibility, GNPs present a promising avenue for developing multifunctional systems in skin drug delivery.

Skin penetration

The exploration of material penetration through human skin holds paramount importance, particularly for the advancement of transdermal drug delivery systems. In these systems, drugs bypass the gastrointestinal tract and liver, entering directly into systemic circulation via the skin. This route offers distinct advantages, including circumvention of first-pass metabolism, enhanced pharmacokinetics, and improved patient compliance [68]. Despite a surge in demand for transdermal patches over the past two decades, the number of drugs effectively utilized in these systems remains limited, primarily due to the skin's inherent barrier function, which impedes the penetration of most compounds [69]. The skin, primarily through its outermost layer, the stratum corneum (SC), acts as a formidable barrier, effectively restricting the penetration of small molecules [70]. Unlike systemic drug delivery, topical applications target conditions affecting the skin without requiring drug entry into the systemic circulation [71]. However, for conditions affecting deeper skin structures like sebaceous glands and hair follicles — pertinent in disorders like alopecia, acne, and rosacea — deep skin layer penetration is crucial [72].

Skin permeation can occur via intracellular, extracellular, or trans-follicular routes, the first two being constrained to lipophilic drugs with certain molecular characteristics [73, 74]. Trans-follicular delivery, utilizing the unique anatomy of hair follicles as conduits to deeper layers, has spurred the development of novel transdermal methods [75, 76]. Nanoparticles have revolutionized drug delivery, enhancing stability, efficacy, and selectivity. Their fabrication utilizes various materials tailored for specific pharmaceutical roles [77]. For instance, PEG-coated liposomes are employed for prolonging the half-life of antibacterial drugs [78], while biodegradable polymers are utilized in chemotherapy, optimizing drug targeting and reducing nonspecific cellular uptake [79]. Nanoparticles have shown superior follicular penetration compared to their free small-molecule counterparts, promoting the development of follicle-targeting nanocarriers for efficient systemic drug release [80-82]. This approach is potentially advantageous for both topical and systemic therapies, including targeting specific cells like melanocytes and epithelial stem cells involved in pigmentation and regeneration [83]. Particle size plays a pivotal role in follicular penetration, with specific submicron sizes showing enhanced accumulation [84]. Physical properties, including particle

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shape and surface texture, are also hypothesized to influence follicular penetration, although systematic data is required [85]. While the therapeutic benefits of nanoparticle skin penetration are evident, potential adverse effects raise safety concerns. Certain nanoparticles, like those containing Fe3O4 and ZnO, may harm the skin barrier, while Ag nanoparticles could affect collagen synthesis and cellular viability [86]. The safety implications of nanoparticle use, particularly on impaired skin, are increasingly scrutinized by both the scientific community and regulatory bodies like the U.S. Food and Drug Administration [87]. The interactions between nanoparticles and skin, including the risks of transdermal flux into the bloodstream, are areas of ongoing investigation [88]. The impact of nanoparticle shape on skin penetration, in particular, requires further research to inform safer product design in medicine and cosmetics [89].

In recent research, investigators delved into the influence of nanoparticles' physical characteristics, specifically size and shape, on skin penetration via hair follicles. Using gold nanoparticles (GNPs) as a model due to their controllable size and shape, they investigated various morphologies without altering their composition [90, 91]. The researcher's fabrication technique, based on the seed and grow chemical reaction, yielded GNPs in a size range of 10-250 nm, with a focus on 100-200 nm particles due to the heterogeneity in larger sizes [92-94]. To evaluate nanoparticle skin penetration, researchers developed the Follicular Transversal Segmentation (FTS) method, a novel assay providing quantitative data on follicular transport. Using transverse histological sectioning, FTS offers a precise assessment of follicular penetration depth. Their findings indicated that GNPs within the 100-200 nm range demonstrated optimal follicular penetration. The method confirmed that particles with increased anisotropy and complex surfaces accumulated more effectively in sebaceous glands and hair follicles, as demonstrated with variously structured labeled GNPs [95].

Antibacterial properties

Bacterial infections, prevalent in various degrees of severity among humans, have historically been combated using antibiotics. These pharmaceutical agents have saved innumerable lives [96-98], but their effectiveness is increasingly compromised due to the rise of drug-resistant strains [99, 100]. This growing resistance is a significant public health concern, prompting the need for innovative therapies that differ from conventional antibiotics [101, 102].

The human skin, a protective barrier for internal tissues and organs, is susceptible to bacterial invasions. Skin-related bacterial infections are particularly problematic in wound healing, especially in burn victims and individuals with chronic diseases like diabetes [103-107]. Predominant bacteria in skin and soft tissue infections (SSTIs) include Staphylococcus aureus and Escherichia coli, with a worrying trend of resistance to common antibiotics observed in these pathogens [108]. For instance, a study identified ampicillin resistance as the most common in 102 E. coli strains isolated from SSTI patients, followed by resistance to tetracycline and fluoroquinolones [109].

Antimicrobial peptides (AMPs) are known for their high efficiency and broad-spectrum activity against bacteria, surpassing traditional antibiotics in some aspects. However, they face challenges such as low stability, brief serum half-life, and poor permeability through biological barriers, limiting their use in antibacterial treatments [110, 111]. Nanomaterials, employed as carriers for AMPs, can address these limitations and facilitate multi-mechanistic antibacterial approaches [112, 113]. For example, Piras and colleagues demonstrated prolonged antibacterial activity against Staphylococcus epidermidis in vitro using AMPs loaded onto chitosan nanoparticles [114]. Gold nanoparticles (AuNPs) are particularly noteworthy among various nanoplatforms for their biocompatibility and significant antibacterial properties [102, 115, 116]. Small-molecule-capped AuNPs, as reported by Jiang et al., have shown potent antibacterial effects against Gram-negative bacteria [117].

Role of Nanostructured in Cosmetics

Beyond their traditional roles in enhancing beauty through products like perfumes and nail and hair care, cosmetics have evolved to encompass skin protection, lightening, moisturizing, acne treatment, and anti-aging properties [118]. This evolution has led to the integration of active pharmaceutical ingredients (APIs) into cosmetic products, giving rise to the concept of "cosmeceuticals" [119]. A 2022 MDPI report indicates that cosmetics prescriptions now constitute 40% of all global dermatology prescriptions, highlighting a growing consumer preference for multifunctional personal care products [120].

Cosmetic formulations are increasingly designed to be not only aesthetically appealing but also functionally effective [121]. For example, the use of fragrances and essential oils in cosmetics has surged, particularly in response to the psychological stress associated with the COVID-19 pandemic, boosting demand for such products [122]. Advanced nanotechnology has been extensively employed to enhance the efficacy and safety of drug delivery, particularly in terms of skin distribution and the development of insoluble medications [123]. The cosmetics industry has been at the forefront of incorporating nanotechnology principles into product development [124, 125]. This innovation has led to over 500 registered products that improve drug delivery while maintaining skin integrity [126]. However, concerns have been raised about the potential risks associated with nanomaterials in cosmetics, such as skin irritation, sensitivity, and systemic exposure issues [127, 128]. Addressing these challenges may involve the use of straightforward and efficient nanoparticles.

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Nanoparticles have garnered significant interest and application across various fields, including medicine, environmental science, and cosmetics, owing to their unique properties [129-131]. The European Commission has defined nanomaterials as particulate substances, whether naturally occurring, incidental, or manufactured, where 50% or more of the particles in the number size distribution have at least one external dimension within the 1–100 nm range [131].

In the realm of nanoparticle synthesis, two distinct methods have been documented [132]. One involves using the hydrosoluble crude extract of medicinal plants, leading to the formation of nanoflower-shaped particles. The other method utilizes the total of flavonoids, resulting in smaller, monodispersed spherical nanoparticles. The type and proportion of phytochemical fractions play a crucial role in nanoparticle formation. Specifically, Hubertia ambavilla, a plant rich in flavonoids, tannins, proanthocyanidins, and carbohydrate complexes, has been noted for its potential anti-inflammatory and healing properties, along with other therapeutic benefits for conditions like renal infections, asthma, and diabetes [133-135].

Gold nanoparticles, in particular, have found applications in the cosmetic industry. They are used in products such as skin wound disinfectants and creams for anti-inflammation and anti-aging purposes. The skin is constantly exposed to various damaging factors like pollution, ultraviolet (UV) rays from the sun, and cigarette smoke, all of which contribute to the production of reactive oxygen species (ROS). An overabundance of ROS can induce oxidative stress, causing damage to cells, DNA, and proteins. This oxidative stress accelerates skin aging by increasing the expression of matrix metalloproteinases (MMPs), which degrade collagen and elastin [136]. Therefore, providing the skin with additional antioxidants is essential for enhancing its natural protective mechanisms against oxidative stress [137].

Characterizing Nanoparticles in Cosmetics

Nanoparticles (NPs) in cosmetics are categorized into two groups based on their physicochemical characteristics: 'soluble/biodegradable' and 'insoluble/non-biodegradable' NPs. The former includes nanoemulsions, solid lipid nanoparticles, nanostructured lipid carriers, and liposomes [128, 138, 139]. The latter encompasses carbon black, metals, quantum dots, metal oxides, and fullerenes [128, 138, 139], defined by EU regulation (N°1223/2009) as intentionally manufactured materials with dimensions in the 1–100 nm range [140]. These insoluble, stable nanoparticles are recognized as nanoproducts with potential safety concerns for consumers, as they can enter the body through skin, inhalation, and ingestion [128, 140, 141]. Particular attention is given to the inhalation risks from spray cosmetics and the incidental ingestion of lip and oral care products containing NPs [140, 142]. Only a few NPs, like zinc oxide, titanium dioxide, and carbon black, are approved by EC regulations as UV filters in cosmetics due to their inert toxicity and stability [140].

Moreover, the environmental impact of these NPs, particularly those used as UV filters like TiO2, is a growing concern. These NPs can accumulate in aquatic environments, leading to detectable and potentially toxic concentrations [140, 143-145]. The need for further research on their environmental fate and biological effects is critical for developing appropriate regulations. Current analytical methods for monitoring NPs in the environment are diverse and still improving [146], and their lifecycle effects must be considered [143-145].

The chemical characterization of NPs in cosmetics is crucial for the industry, not only for product performance but also for understanding their toxicity and environmental impact. The ISO/TC 229 technical committee recommends characterizing various parameters like size, distribution, concentration, composition, and more [140]. Analytical techniques vary, and the complexity of cosmetic matrices poses challenges in sample preparation, requiring a balance between reducing complexity and maintaining representativeness [147].

Safety and Environmental Impact of Insoluble Nanoparticles in Cosmetic Products

Various insoluble nanomaterials (NMs) are commonly utilized as key components in cosmetic and personal care products. These include carbon black, metallic nanoparticles (NPs) like silver and metal oxides, and gold such as titanium dioxide, silica, and zinc oxide [128, 138, 139]. Carbon black nanoparticles, with an average size range of 10-100 nm, are primarily used for coloring in eye makeup products, with concentrations up to 10% [140]. These nanoparticles are considered safe for use in the European Union (EU) when they are 20 nm or larger and do not exceed a 10% concentration [141, 148]. Silver nanoparticles are known for their antibacterial qualities and are utilized in various cosmetic products, although their use is restricted in certain applications by EC/1223/2009 cosmetic regulations [149-151]. Gold nanoparticles are employed in cosmetics for their antioxidant properties and targeting skin aging and wounds [152-154].

Among metal oxide nanoparticles, titanium dioxide (TiO2), silica (SiO2), and zinc oxide (ZnO) are the most prevalent in cosmetics. Silica nanoparticles are used for their hydrophilic nature and ability to enhance the effectiveness of toothpastes, while their safety is still under scrutiny [154-157]. Titanium dioxide nanoparticles are effective as UV filters in sunscreens and other personal care products, but EU regulations restrict their use as colorants in cosmetics. Zinc oxide nanoparticles, recognized as safe by the EU SCCS and the FDA-USA, are used for their UV filtering capabilities [140].

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However, concerns regarding the safety of TiO2 and ZnO nanoparticles have been raised, particularly in relation to their photoreactivity and potential to produce reactive oxygen species (ROS) [158]. These issues have been mitigated by coating the nanoparticles with materials like Al2O3 or SiO2. Studies suggest that these nanoparticles largely remain on the skin's surface after application and do not penetrate deeper skin layers [140]. The environmental impact of these nanoparticles, especially TiO2, is also a significant concern. Their release into water bodies can affect aquatic ecosystems, and various physicochemical factors influence their behavior in these environments. The surface properties of these nanoparticles can change under different environmental conditions, potentially leading to ecological risks [159].

Conclusion

The battle against aging has captivated humanity for millennia, and with scientific advancements, innovative weapons are emerging in this timeless fight. Nanotechnology, the manipulation of matter at the atomic and molecular level, promises a revolution in anti-aging strategies, offering targeted solutions for both intrinsic and extrinsic causes of skin aging. While wrinkles, dryness, and sun damage may paint the visible tapestry of aging, the underlying canvas comprises complex cellular processes. Intrinsic factors like metabolism, DNA damage, and hormonal changes orchestrate the internal symphony of decline. Extrinsic factors, from sun exposure to pollutants and even bad habits, add their discordant notes to the score. Nanoparticles, miniscule actors on this cellular stage, hold the potential to rewrite the aging narrative. Their small size grants them unique access, bypassing skin barriers to deliver potent anti-aging agents directly to their targets. Imagine antioxidants mopping up free radicals like miniature janitors, or collagen-boosting peptides weaving their magic at the source of wrinkle formation. Nanoparticles can encapsulate these active ingredients, enhancing their stability and effectiveness while minimizing side effects.

The arsenal of these microscopic warriors is diverse. Green synthesis of gold nanoparticles derived from natural materials offers biocompatibility and targeted delivery, while inorganic nanoparticles like chemical gold and silver lend their inherent anti-inflammatory and antimicrobial properties. Combined, they offer a synergistic orchestra of rejuvenation, targeting different aspects of the aging process. Nanotechnology also revolutionizes cosmeceuticals, infusing conventional creams and serums with nano-empowered ingredients. The result? Products with improved penetration, enhanced stability, and targeted action, minimizing waste and maximizing results. From sun protection to skin lightening, hair growth, and even wound healing, the scope of applications is vast. However, this journey to the fountain of youth with nanotechnology requires cautious navigation. Long-term safety and efficacy studies ensure these microscopic allies remain true to their benevolent purpose. Understanding the intricacies of nanoparticle behavior and optimizing their delivery mechanisms will further unlock their potential.

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[DOI: 10.47176/sjfst.5.4.1]

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Citation: Saleshi Sichani A, Gharooni S, Fard F, Nejad A, Kordlashkenari A, Farokhimanesh S. Gold Nanoparticles in Anti-Aging Interventions: A Comprehensive Exploration of Skin Health and Cosmeceuticals. SJFST, 2023; 5(4): 1-14.

https://doi.org/10.47176/sjfst..5.4.1

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