Advances in Research on Sunscreen Peptides

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Abstract: Prolonged or excessive exposure to ultraviolet (UV) radiation, particularly UVA and UVB, can cause significant skin damage, including sunburn, photoaging, immune suppression, and even skin cancer. Although conventional sunscreens are effective, they raise concerns regarding safety and environmental impact. As a result, the development of novel, safe, and eco-friendly sunscreen ingredients has become a key research focus. Sunscreen peptides-emerging UV protectants based on bioactive peptides-are gaining attention. This review systematically outlines the definition, classification, and mechanisms of action of sunscreen peptides, highlights current research progress and preclinical as well as clinical evidence for several major types, and thoroughly discusses the challenges facing their development. It also provides insights into future directions. Sunscreen peptides represent a highly promising strategy in photoprotection, potentially paving the way for the next generation of sunscreen products.

Keywords: Sunscreen Peptides; UV Protection; Cosmetics

1. Introduction

Ultraviolet radiation is the primary external factor responsible for skin damage. Based on wavelength, UV radiation is categorized into UVA, UVB, and UVC. UVA penetrates deep into the dermis, leading to photoaging and hyperpigmentation, while UVB primarily affects the epidermis, causing sunburn and DNA damage—key contributors to the development of skin cancer. To protect against UV exposure, various sunscreens have been developed, mainly classified as physical and chemical agents. Physical sunscreens work by reflecting and scattering UV rays but often feel heavy on the skin and may leave a whitish cast. Chemical sunscreens, on the other hand, absorb UV energy and convert it into heat for release, yet they carry potential risks such as skin irritation, photosensitivity, and environmental accumulation[1]. Thus, there is an urgent need to develop novel sun protection technologies that feature innovative mechanisms, excellent biocompatibility, and environmental sustainability. In this context, sun-protective peptides have emerged as a "bio-inspired" strategy. Rather than directly absorbing or reflecting UV radiation, these peptides modulate the skin's biological responses, enhancing its intrinsic defense and repair capabilities from within—offering a smart, inside-out approach to photoprotection. This review aims to systematically summarize recent advances in sunscreen peptides, providing a comprehensive overview of their mechanisms of action, major types, current challenges, and future development directions.

2. Main Types and Mechanisms of Action of Sunscreen Peptides

Based on their mechanisms of action, sun protection peptides are primarily categorized into two types: one that stimulates melanin production—the skin’s natural pigment—known as pigmentation-activating peptides; the other involved in or promoting the repair of photo-induced DNA damage, referred to as reparative peptides. Through distinct signaling pathways and molecular targets, these peptides collectively build an endogenous photoprotective shield within the skin.

2.1 Melanin-Stimulating Sunscreen Peptides

These peptides function primarily by mimicking endogenous α-melanocyte-stimulating hormone (α-MSH), activating the melanocortin-1 receptor (MC1R) on melanocytes. This triggers the downstream cAMP signaling pathway, ultimately enhancing the expression and activity of tyrosinase, thereby promoting melanin synthesis and distribution. Melanin provides broad-spectrum photoprotection by effectively absorbing and scattering ultraviolet radiation and neutralizing free radicals. The most well-known representative of this class is Afamelanotide, a

linear analog of α-MSH with high affinity and stability for MC1R. Langendonk et al. evaluated the efficacy and safety of Afamelanotide in patients with erythropoietic protoporphyria through a two-part trial conducted in the European Union and the United States. The study involved implanting the drug every 60 days, with observation periods of 180 and 270 days. Results showed that patients receiving Afamelanotide could tolerate significantly longer sun exposure without pain compared to those in the placebo group, and experienced fewer phototoxic reactions. Quality-of-life assessments further indicated substantial improvements in patients' daily living following treatment[2]. Ye et al. found that Acetyl Hexapeptide-1, a analog of Afamelanotide, effectively improves the appearance of photoaged skin in the Chinese population by enhancing skin texture, elasticity, firmness, pore size, radiance, and stratum corneum hydration, with good tolerability, offering a valuable skincare solution for addressing photoaging in this demographic[3].

2.2 DNA Repair-Targeted Sunscreen Peptides

These peptides operate through a more direct mechanism, either mimicking or constituting key fragments of DNA repair enzymes. Capable of penetrating the stratum corneum and entering epidermal cells, they actively participate in and accelerate the repair of UV-induced DNA damage. T4 endonuclease V, derived from marine cyanobacteria, is an enzyme specifically targeting cyclobutane pyrimidine dimers (CPDs). Peptides based on this enzyme enhance cellular clearance of CPDs, thereby reducing the risks of UV-induced mutations and immune suppression. Photolyase is another enzyme that uses blue light as an energy source to directly reverse CPD lesions. Research into its active site has inspired the development of small peptide molecules with photolyase-like activity. Such photolyase-derived peptides help alleviate UV-induced skin damage. Additionally, a dipeptide mimic of thymine dimer repair enzyme, known as "Dipeptide-76," accelerates DNA repair, reduces the formation of sunburn cells, and improves the survival rate of UV-exposed fibroblasts, demonstrating clinical efficacy in diminishing signs of photodamage[4].

2.3 Sunscreen Peptides Derived from Frogs

Sunscreen peptides derived from frog skin secretions demonstrate unique research value and application potential. These frog-derived sunscreen peptides exhibit strong antioxidant activity, effectively scavenging free radicals, maintaining redox balance in the skin, reducing intracellular malondialdehyde levels, and enhancing the activity of antioxidant enzymes such as catalase and superoxide dismutase. By doing so, they help protect skin cells from UV-induced damage. The peptide OA-GI13, a mature 13-amino acid peptide with a molecular weight of 1.42 kDa, displays free radical-scavenging capacity comparable to vitamin C at a concentration as low as 1 nM, particularly against $ABTS^{+}$ and DPPH radicals. This peptide is non-cytotoxic, does not induce hemolysis, and can reduce oxidative stress in H_2O_2-stimulated cells and UVB-irradiated mouse skin by inhibiting the phosphorylation of p38 protein. At concentrations of 1 nM and 10 nM, it helps maintain the viability of HaCaT cells under H_2O_2 stress, lowers cellular oxidative stress, boosts antioxidant levels, and reduces markers of oxidative damage such as lipid peroxides and malondialdehyde. Furthermore, OA-GI13 alleviates UVB-induced erythema and edema on the backs of mice, with optimal repair effects observed at 10 nM. It also reduces sunburned cells in the mouse epidermis and improves the organization of collagen fibers in the dermis[5]. OM-GL15 is a 15-amino acid peptide with a molecular weight of 1.48 kDa, known for its ability to scavenge free radicals, reduce Fe^{3+}, and protect against acute photodamage in the skin. In models of acute UV-induced skin damage, OM-GL15 effectively alleviates erythema, minimizes loss of skin elasticity and moisture, maintains epidermal integrity, and reduces sunburn cell formation. Furthermore, it decreases the number of apoptotic cells and lowers levels of 8-OHdG, a marker of DNA damage. OM-GL15 also suppresses the expression of key proteins involved in the mitochondrial apoptosis pathway, including p53, caspase-3, caspase-9, and Bcl-2-associated proteins, indicating its role in inhibiting keratinocyte apoptosis through mitochondrial regulation[6]. Nigrocin-OA27 is a 27-amino acid mature peptide with a molecular weight of 2.3 kDa, exhibiting both skin-whitening and sun-protective properties. It shows no cytotoxicity within the concentration range of 0–100 μM and demonstrates dose-dependent antioxidant activity, including

free radical scavenging and ferric ion reducing capacity. Topical application of Nigrocin-OA27 on the ears of C57 mice effectively prevents UVB-induced hyperpigmentation and abnormal epidermal thickening. Furthermore, it also exerts a depigmenting effect on existing UVB-triggered skin darkening. The peptide possesses transdermal penetration ability, reaching the entire dermal layer within approximately 1 to 2 hours. With an IC50 value of 229.2 μM, Nigrocin-OA27 outperforms arbutin in inhibiting tyrosinase activity at the same concentration[7]. Cathelicidin-NV, derived from the spotted frog, effectively alleviates UVB-induced skin photoaging. It protects HaCaT cells from photodamage by suppressing cytotoxicity, DNA strand breaks, and apoptosis, as well as downregulating the expression of specific proteins. Additionally, this peptide scavenges intracellular reactive oxygen species, thereby mitigating skin aging. This finding broadens our understanding of the antioxidant capabilities within the defensin family and offers a promising therapeutic candidate for the prevention and treatment of ultraviolet-induced skin photoaging[8].

3. Challenges in the Development of Sunscreen Peptides

Despite the promising potential of sunscreen peptides, their transition from laboratory to market faces significant challenges. These peptides are prone to chemical degradation and hydrolysis in solution, on the skin surface, and during storage. Additionally, they can be easily broken down and inactivated by proteases present on the skin. Enhancing their stability through structural modifications, cyclization, or advanced formulation techniques is essential to ensure product efficacy. Moreover, peptide synthesis—especially for long-chain or heavily modified sequences—remains costly, potentially leading to high end-product prices and limiting widespread market adoption. Developing more cost-effective and efficient synthesis or bioproduction methods is a critical hurdle that must be overcome for large-scale commercialization.

4. Future Development Direction

Future research on sun-protective peptides will focus on the development of novel peptides, optimization of delivery systems, and multi-target synergistic strategies. The discovery and rational design of new peptides involve leveraging technologies such as computer-aided drug design and phage display libraries to screen and engineer peptides with enhanced activity, improved stability, and reduced immunogenicity. Exploring naturally occurring peptides with inherent photoprotective properties will also remain a key avenue. Moreover, future efforts will increasingly center on intelligent, stimuli-responsive nanocarriers—such as pH-, enzyme-, or UV-responsive nanoparticles—that enable precise, on-demand release of peptides within specific skin layers, thereby maximizing their bioavailability. Additionally, combining peptides with distinct mechanisms—such as melanogenesis-stimulating peptides and DNA repair peptides—or integrating them with conventional sunscreens and potent antioxidants like vitamins C and E, can generate synergistic effects, establishing a multi-layered, comprehensive defense system against ultraviolet radiation[9].

5. Conclusion

As an emerging class of "bio-inspired" sunscreen ingredients, photoprotective peptides represent the evolving trend toward personalized, intelligent, and environmentally friendly sun protection products. By activating or enhancing the skin’s intrinsic defense and repair mechanisms against light-induced damage, they introduce a new paradigm in photoprotection—shifting from traditional "physical/chemical barrier" approaches to "biological regulation." Although challenges remain in areas such as stability and cost control, ongoing advances in peptide chemistry, formulation technologies, and skin biology are steadily overcoming these limitations. In the future, through interdisciplinary innovation, photoprotective peptides are expected to play an increasingly significant role in high-end cosmetics, preventive dermatology, and even adjunctive therapies, making substantial contributions to safer, more effective, and precisely targeted skin photoprotection.

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