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Progress in Research on Photoaging and Barrier Function Damage

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Abstract: Research on photoaging and barrier dysfunction holds significant implications for cutaneous health. Ultraviolet radiation stands as the principal pathogenic factor in photoaging, inducing oxidative stress, DNA damage, and extracellular matrix degradation. Environmental aggressors, inappropriate skincare practices, and underlying systemic pathologies compromise epidermal barrier integrity. Emerging evidence elucidates autophagy's regulatory role in photoaging pathogenesis. Current therapeutic innovations demonstrate promising potential, with novel modalities including nanotechnology-driven delivery systems, stem cell therapies, and exosome-based interventions showing efficacy in combating photoaging and barrier restoration. Conventional approaches such as retinoid derivatives, laser photothermolysis, and radiofrequency technologies remain clinically validated for photoaged skin rehabilitation. These multimodal strategies offer promising alternatives for clinical management. Future investigations should prioritize elucidating the complex interplay among multiple pathogenic determinants and their synergistic effects on cutaneous aging processes.

Keywords: Photoaging; Skin Barrier Function; Ultraviolet Damage.

1. Background

Research on photoaging and epidermal barrier dysfunction holds critical significance for cutaneous health. As the largest organ, the skin serves not only as the primary defense against environmental insults but also maintains epidermal barrier homeostasis - a pivotal determinant of cutaneous integrity. Chronic ultraviolet (UV) radiation-induced photoaging has emerged as a central etiological factor in barrier impairment, potentially predisposing to cutaneous malignancies. Distinct clinical manifestations of photoaging in Asian populations encompass pigmentary disorders (ephelides, melasma, and solar lentigines) and accentuated rhytides in frontal, perioral, and crow's feet regions [1], with wrinkle formation demonstrating correlation with molecular dysregulation of barrier mechanisms. Recent advances in cutaneous biology have illuminated the pathophysiological interplay between photoaging and barrier compromise, while novel therapeutic strategies targeting this axis continue to evolve. These scientific breakthroughs provide a theoretical foundation for developing preventive and therapeutic interventions against photoaging-related dermatoses.

2. Current Status of Research

2.1. The Molecular Damage Mechanism of Photoaging to the Skin Barrier

TheUltraviolet radiation (particularly UVB and UVA) induces excessive generation of reactive oxygen species (ROS), thereby disrupting stratum corneum lipid architecture and tight junction proteins, ultimately leading to elevated transepidermal water loss (TEWL) and compromised cornified layer integrity [2]. Mechanistic studies have demonstrated that UVB irradiation significantly downregulates filaggrin expression - a critical precursor of natural moisturizing factors (NMFs) - whose depletion directly impairs cutaneous hydration capacity and exacerbates barrier dysfunction [3]. Furthermore, through activation of matrix metalloproteinases (MMPs), particularly MMP-1 and MMP-9, UV radiation initiates proteolytic degradation of collagen and elastic fibers within the extracellular matrix (ECM) [4]. This cascade of events disrupts dermo-epidermal junction (DEJ) architecture, manifesting as multilaminar disorganization or frank disruption of the basement membrane zone, thereby undermining the structural foundation essential for optimal barrier function.

2.2. The Role of Autophagy in Photoaging

Autophagy, a cellular process induced under various stress conditions, facilitates cellular survival through regulation of macromolecular homeostasis. Three principal subtypes exist: macroautophagy, chaperone-mediated autophagy, and microautophagy, with macroautophagy demonstrating predominant protective effects against cutaneous photoaging [5]. This lysosomal degradation pathway maintains cellular equilibrium by eliminating damaged mitochondria and misfolded proteins, thereby suppressing ROS generation and mitigating oxidative injury. Ultraviolet A (UVA) radiation indirectly induces DNA damage via ROS-mediated formation of cyclobutane pyrimidine dimers (CPDs), whereas UVB is directly absorbed by epidermal DNA to generate CPDs and other photoproducts. Autophagy activation enhances nucleotide excision repair through upregulation of XPC, a DNA damage sensor protein, thereby promoting CPD clearance [6]. Furthermore, coordinated regulation of cellular proliferation and apoptosis through multiple molecular mechanisms contributes to its photo-protective properties [7].

2.3. Research Progress in the Treatment of Photoaging

2.3.1. Medication Therapy

UseRetinoids, FDA-approved therapeutic agents for cutaneous photoaging, demonstrate efficacy in structural rejuvenation but may induce irritant reactions including erythema and desquamation [8,9]. These compounds mediate

biological effects through retinoic acid receptors (RARs), forming heterodimers with retinoid X receptors (RXRs) to regulate genomic transcriptional activity. Their therapeutic mechanisms in photoaged skin encompass: 1) Stimulation of collagen synthesis through activation of procollagen gene expression; 2) Initiation of epidermal renewal via keratinocyte proliferation and differentiation modulation; 3) Suppression of UV-induced matrix metalloproteinase (MMP) production, thereby preserving extracellular matrix integrity [10].

Adjuvant antioxidant therapies incorporating ascorbic acid, hyaluronic acid, and collagen derivatives have been extensively investigated for photoaging mitigation [11]. These compounds neutralize reactive oxygen species (ROS) generated by UV irradiation, attenuating oxidative damage to cellular components while maintaining normal metabolic functions. Botanical extracts containing saponins, flavonoids, polyphenols, and polysaccharides demonstrate comparable photoprotective effects through dual mechanisms: enhancement of endogenous antioxidant enzyme systems and inhibition of inflammatory mediators [12].

2.3.2. Physical Therapy

Among physical therapeutic modalities, laser intervention constitutes a principal approach in photoaging management. Non-ablative fractional lasers (e.g., 2910nm erbium-doped glass fiber systems) stimulate neocollagenesis through controlled thermal stimulation of dermal fibroblasts, thereby improving cutaneous texture and viscoelasticity while reducing rhytid formation [13]. In contrast, ablative laser modalities such as carbon dioxide fractional devices achieve more profound tissue remodeling by precisely vaporizing damaged epidermal architecture [14]. This modality facilitates coordinated epidermal regeneration and dermal remodeling through controlled microthermal zones, demonstrating particular efficacy in addressing deep wrinkles and actinic keratosis.

Intense pulsed light (IPL) technology has gained prominence in photo-rejuvenation protocols through its multiwavelength photothermal effects. This broadband light system selectively targets chromophores (melanin and oxyhemoglobin) to ameliorate dyschromia and telangiectasia, while concurrently activating fibroblast-mediated collagen production via subablative thermal stimulation [15]. The cumulative therapeutic outcomes manifest as enhanced skin homogeneity, restored dermal density, and improved luminosity.

2.3.3. Novel Therapy

Emerging therapeutic modalities including stem cell-based interventions, extracellular vesicle technology, and nanoliposomal delivery systems demonstrate novel potential in photoaging management. The topical application of human umbilical cord mesenchymal stem cell-derived exosomes (hUC-MSC-Exos) combined with sponge spicules enhances cutaneous bioavailability through optimized transdermal penetration [16]. These stem cell derivatives exhibit multipotent differentiation capacity and self-renewal properties, enabling cellular replenishment of photoaged epidermal and dermal compartments. Mechanistically, hUC-MSC-Exos promote dermal thickening and dermo-epidermal junction (DEJ) reconfiguration through genomic upregulation of collagen and elastin biosynthesis, thereby facilitating comprehensive tissue regeneration.

MCZT nanoparticles demonstrate remarkable anti-photoaging efficacy in both in vitro and in vivo models. Through surface modification with anti-TRPV1 monoclonal antibodies, these engineered nanoparticles achieve active targeting of senescent dermal fibroblasts, enhancing photosensitization resistance and prolonging therapeutic duration under UVA irradiation [17]. While these innovative approaches address limitations of conventional therapies through enhanced specificity and regenerative capacity, challenges persist regarding formulation stability optimization and cost-effectiveness in clinical translation.

3. Conclusion

The therapeutic landscape for photoaging and barrier restoration continues to evolve through technological innovation, with distinct modalities exhibiting complementary advantages and clinical indications. Future advancements are anticipated to focus on synergistic combination therapies and refinement of emerging technologies, potentially enabling personalized treatment paradigms for cutaneous barrier dysfunction and photoaging sequelae. Importantly, interventions targeting photoaging-associated barrier impairment extend beyond cosmetic applications, demonstrating prophylactic and therapeutic relevance for barrier-related dermatoses including atopic dermatitis and psoriasis [16]. Current research challenges necessitate multidisciplinary approaches integrating multi-omics technologies to elucidate the molecular networks underlying barrier pathology. Concurrent development of targeted delivery systems promises enhanced therapeutic precision and efficacy, particularly for recalcitrant cases of photoaging [17]. Future investigations should prioritize translational studies addressing formulation optimization and clinical validation of these innovative strategies.

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