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# Cold Atmospheric Plasma in Skin Regeneration and Collagen Stimulation: Molecular Mechanisms and Clinical Insights

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## ABSTRACT

**Introduction:** Cold atmospheric plasma (CAP) is an emerging therapeutic modality that is gaining attention for its applications in skin regeneration and cosmetics. It enables efficient, rapid, and painless tissue repair without toxic or allergic effects. Since cytokines, growth factors, and fibroblast activity are central to wound healing, this review aimed to assess whether CAP can modulate cellular functions that are essential for collagen synthesis and skin rejuvenation.

**Materials and Methods:** This review surveyed articles from various databases and credible scientific websites, including ScienceDirect, PubMed, and Scopus. The keywords used for the search included "Cold atmospheric plasma", "Dermatology", "Regenerative medicine", "Wound healing", "Fibroblasts", and "Skin rejuvenation", covering studies from 2010 to 2025.

**Results and Discussion:** In vitro studies showed that CAP upregulates pro-fibrotic mediators, including TGF- $\beta$ 1 and TGF- $\beta$ 2, increasing type I collagen synthesis and enhancing fibroblast proliferation and migration. Preclinical in vivo models confirm that CAP accelerated the initiation and resolution of inflammation, improved wound closure, and organized collagen deposition without causing necrosis or excessive inflammation. Additionally, low-intensity CAP used in cosmetic applications improves skin elasticity and texture, likely through increased fibroblast activity and extracellular matrix remodeling. Mechanistic studies have indicated that CAP-generated ROS act as secondary messengers, activating NF- $\kappa$ B and NOX2 pathways, promoting fibroblast activation and collagen production.

**Conclusion:** CAP effectively stimulates fibroblasts, accelerates early inflammatory responses, and enhances collagen synthesis, demonstrating strong potential as a tool for regenerative and aesthetic dermatology. Although clinical use is evolving, accumulating evidence supports CAP as a promising adjunct for skin rejuvenation and wound repair. Broader clinical studies and optimized treatment parameters are needed to clarify its therapeutic value and expand its applications in dermatology.



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**Keywords:** Cold atmospheric plasma, Dermatology, Fibroblasts, Regenerative medicine, Wound healing

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