

## Cold Atmospheric Plasma (CAP): A Non-Invasive and Painless Treatment for Skin Diseases

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### Abstract

Cold Atmospheric Plasma (CAP) has emerged as a groundbreaking technology, attracting substantial interest for its versatile applications across medicine, food processing, agriculture, and industry. This comprehensive review systematically evaluates CAP's therapeutic potential in treating a wide range of skin diseases, including acne, atopic dermatitis, rosacea, vitiligo, psoriasis, and autoimmune skin disorders. The efficacy of CAP is attributed to its unique characteristics, including the generation of reactive species, cost-effectiveness, environmental sustainability, and device portability, facilitated by techniques such as dielectric barrier discharge, corona discharge, and floating electrode methods, utilizing gases like nitrogen, argon, or helium. Through an exhaustive analysis of peer-reviewed studies spanning 2013 to 2025, this research underscores CAP's role as a highly effective and adaptable tool in dermatological applications. The findings highlight CAP's capacity to neutralize pathogens, modulate inflammatory and autoimmune responses, establishing it as a promising modality in clinical dermatology. This rigorous and comprehensive review emphasizes the critical need for future research to optimize CAP treatment protocols, enhance delivery systems, and fully explore its therapeutic potential across expanding biomedical and interdisciplinary fields.

### Keywords

Cold Atmospheric Plasma (CAP),  
Skin disease,  
Acne,  
Atopic dermatitis,  
Psoriasis,  
Rosacea,  
Vitiligo

## Soğuk Atmosferik Plazma (CAP): Cilt Hastalıkları İçin Non-invaziv ve Ağrısız Bir Tedavi Yöntemi

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### Özet

Soğuk Atmosferik Plazma (CAP), tıp, gıda işleme, tarım ve endüstri gibi geniş bir yelpazede çok yönlü uygulamalarıyla dikkat çeken çığır açıcı bir teknoloji olarak ortaya çıkmıştır. Bu kapsamlı inceleme, CAP'nin akne, atopik dermatit, rozasea, vitiligo, sedef hastalığı ve otoimmün cilt bozuklukları gibi geniş bir cilt hastalığı yelpazesini tedavi etmedeki terapötik potansiyelini sistematik olarak değerlendirmektedir. CAP'nin etkinliği, reaktif türlerin üretimi, maliyet etkinliği, çevresel sürdürülebilirlik ve cihaz taşınabilirliği gibi benzersiz özelliklerine bağlanmaktadır; bu özellikler, nitrojen, argon veya helyum gibi gazlar kullanılarak dielektrik bariyer deşarjı, korona deşarjı ve yüzer elektrot yöntemleri gibi tekniklerle desteklenmektedir. 2013'ten 2025'e kadar olan hakemli çalışmaları kapsayan kapsamlı bir analiz aracılığıyla, bu araştırma, CAP'nin dermatolojik uygulamalarda son derece etkili ve uyarlanabilir bir araç olduğunu vurgulamaktadır. Bulgular, CAP'nin patojenleri nötralize etme, inflamatuvar ve otoimmün yanıtları modüle etme kapasitesini öne çıkararak, onu klinik dermatolojide umut verici bir yöntem olarak konumlandırmaktadır. Bu titiz ve kapsamlı derleme, CAP tedavi protokollerinin optimize edilmesi, uygulama sistemlerinin geliştirilmesi ve genişleyen biyomedikal ile disiplinlerarası alanlarda terapötik potansiyelinin tam anlamıyla araştırılması için gelecekteki çalışmalara duyulan kritik ihtiyacı vurgulamaktadır.

### Anahtar kelimeler

Soğuk Atmosferik Plazma (CAP), Cilt hastalığı, Akne, Atopik dermatit, Sedef hastalığı, Rozasea (gül hastalığı), Vitiligo

## 1. INTRODUCTION

The human skin, encompassing an approximate surface area of 2 square meters, constitutes a critical interface between the internal and external environments and represents nearly 20% of the total body mass. Human skin is a multi-talented organ, acting as a shield against harm, a sensory portal to the world, a pathway for nutrients and waste, a thermostat for body temperature, and a vigilant defender against infection. Skin consists of three layers: the epidermis (outer skin), dermis (skin proper), and hypodermis (subcutaneous tissue) from superficial to deep. The skin, as the largest organ of the human body, serves as a primary barrier against physical, chemical, and microbial insults while also playing essential roles in preventing trans epidermal water loss, regulating body temperature, modulating sweat and sebum production, providing structural support, and transmitting sensory information [1-4].

Acne (pimples), eczema (atopic dermatitis), psoriasis, dermatitis, vitiligo, rosacea, are among the most common skin diseases worldwide. The main factors that cause skin diseases include genetic predisposition, environmental factors, infections, allergies, hormonal changes, ageing, the consumption of highly processed foods, and autoimmune diseases [5]. Genetic predisposition is associated with genetic changes or variations that increase the likelihood of developing a particular skin disease. These genetic variations can lead to skin problems by affecting the normal function of certain skin cells or proteins. Most skin diseases are caused by the combined effects of multiple genes. Therefore, genetic predisposition often has a polygenic (under the influence of multiple genes) structure [6]. In addition to genetic predisposition, environmental factors (such as sun exposure, stress, excessive smoking and alcohol consumption, poor dietary habits, and exposure to chemicals) can also play a role in the development of various skin diseases [7]. Bacterial, fungal, viral, or parasitic infections are skin conditions that occur when the immune system is weakened, or the skin barrier is disrupted. They are characterized by symptoms such as redness, swelling, pain, itching, rash, and discoloration. During puberty, pregnancy, and menopause, the body undergoes significant hormonal changes. Uncontrolled increases and decreases in the levels of the hormones progesterone and estrogen can lead to changes in the skin (such as dryness, thinning, loss of elasticity, excessive hair growth (hirsutism), and acne) [8-10]. Autoimmune diseases are caused by the immune system mistakenly identifying the body's cells as a foreign threat, leading to an immune system attack on the body's tissues. These diseases of the skin, such as scleroderma, dermatomyositis, pemphigus, pemphigoid, and vitiligo, can cause a variety of skin symptoms, including skin hardening, bruising, redness, rash, and pigment loss [11, 12].

Skin diseases are typically treated with systemic medications, antibiotics, topical creams, surgical procedures, and different phototherapies (UV rays) depending on the type and severity of the disease. But, due

to the potential side effects of these treatments (such as itching, burning, swelling, stomach upset, and headaches), the high likelihood of recurrence of the disease, and the effect on routine daily functioning, there is a need for alternative treatment methods [13, 14]. In the last ten years, plasma medicine has gained increasing attention as a potential therapeutic modality, especially within the field of dermatology, due to its broad range of biomedical applications. Plasma is generally described as an ionized state of matter generated either by the dissociation of polyatomic gas molecules or by the ionization of monoatomic gases through the removal of electrons from their atomic orbitals [15, 16]. While ionized gases contain charged particles, not all qualify as plasma. In a plasma system, macro-molecules are neutral (semi-neutral), and the net electric charge that arises without external factors is zero. Therefore, plasma contains (nearly) equal densities of positive and negative charged particles. A defining characteristic of plasma is "Debye shielding," a phenomenon where the influence of a single charged particle's electric field is effectively neutralized by the surrounding charged particles within a specific distance (Debye length) [16, 17].

Plasma, often referred to as the fourth and most abundant state of matter in the universe, is an electrically conductive ionized gas composed of a dynamic mixture of charged and neutral particles, including atoms and molecules in both ground and excited states, free electrons, reactive oxygen and nitrogen species (ROS and RNS), ozone, and ultraviolet (UV) radiation [18, 19]. Plasma can be categorized as either thermal or non-thermal, depending on its temperature profile and thermodynamic behavior. High-temperature plasma, often called thermal plasma, boasts a state of thermal equilibrium where electrons and heavier particles share a uniform temperature. In contrast, non-thermal plasma features a non-equilibrium state. Here, electrons reach significantly higher temperatures compared to the heavier particles (ions and neutrals). This plasma is called "Cold plasma" [17, 20]. Since producing plasma at pressures below atmospheric pressure is quite costly, the development of atmospheric pressure cold plasma technologies has accelerated [21].

Cold Atmospheric Plasma (CAP) is a cutting-edge technology making waves in dermatology. This non-invasive approach offers a safe and promising way to treat a variety of skin conditions. CAP's unique properties endow it with the power to combat microbial infections, promote wound healing, and reduce inflammation, making it valuable for managing a range of skin ailments [7, 10, 22, 23]. Since the skin is the outermost organ of the human body and the most easily accessible organ, CAP therapy is seen as easy to apply and promising [24].

CAP comprises a complex mixture of biologically active components, including Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS) (e.g.,  $\text{OH}^\cdot$ ,  $\text{H}_2\text{O}_2$ ,  $\text{O}_2^-$ ,  $\text{NO}$ ,  $\text{ONOO}^-$ ), charged particles (ions), electrons, UV radiation, visible light, and high electric fields. These components exert diverse, synergistic biological effects on treated tissues [25]. The specific composition and

concentration of reactive species depend on the working gas and plasma source used [26]. This inherent versatility combined with demonstrated efficacy across multiple disease models positions CAP as a compelling therapeutic modality, particularly for readily accessible skin conditions [27].

The therapeutic effects of CAP stem from the synergistic interplay of its components: RONS modulate redox signaling and induce controlled oxidative stress in microbial and mammalian cells, while charged particles and electric fields alter membrane permeability and cellular signaling pathways. Together, these interactions drive CAP's antimicrobial, anti-inflammatory, and tissue-regenerative properties [28, 29].

CAP can be applied in two primary modes direct and indirect each defined by the nature of the plasma-tissue interface. These modes differ in RONS delivery, penetration depth, exposure homogeneity, and safety profile. In direct mode, the plasma discharge or jet interacts directly with the target surface using systems such as Dielectric Barrier Discharge (DBD) or plasma jets. RONS, ions, and electric fields act simultaneously, generating high local reactivity. This approach is highly effective for localized disinfection and wound decontamination. However, penetration is limited (<1 mm), and uniformity varies with surface irregularities. Precise control of treatment parameters, voltage, current, and duration is critical to prevent adverse electrical or thermal effects [30, 31]. In indirect mode, plasma does not contact tissue directly. Instead, plasma-activated liquids or gases such as Plasma-Activated Water (PAW) is generated and applied via irrigation, soaking, or injection. These media retain stable, long-lived RONS that deliver therapeutic effects with greater homogeneity and safety. This mode is ideal for larger treatment areas, sensitive tissues, or internal applications. However, reactive species concentrations are lower than in direct CAP, requiring optimized preparation and storage to maintain bioactivity [32].

The capacity of CAP to be directly applied to cells and tissues for therapeutic purposes without causing tissue damage is significantly broadening the scope of research [25, 27, 33]. Numerous studies have explored the application of CAP in dermatology, particularly in areas such as skin disorders, acne, eczema, psoriasis, scar treatment, and ichthyosis/epidermal barrier dysfunctions [24, 25, 27]. However, the translation of these biomedical applications into routine clinical practice remains hindered by several technical limitations.

Despite the broad application potential of CAP technology, various technical challenges such as energy efficiency, process repeatability, and plasma stability limit its scalability and clinical integration [34]. To overcome these issues, the use of artificial intelligence (AI)-based control algorithms and real-time plasma sensors offers the potential to dynamically optimize systems, thereby enhancing the energy efficiency, precision, and reliability of CAP processes. Furthermore, CAP platforms integrated with robotic systems are

shaping the future of personalized medicine through automated process control and targeted application capabilities. This integration provides innovative solutions particularly in tumor treatment, prevention of viral infections, precision surgical procedures, diagnostics, and risk management.

Plasma robots developed at macro or micro scales enable more stable, directed, and effective CAP applications through interdisciplinary collaboration between engineering and biomedical sciences [35, 36]. Such intelligent system-based approaches will overcome existing technical limitations, making the clinical and industrial use of CAP technology safer, more sustainable, and better controlled. Additionally, the development of low-cost and portable plasma devices is of critical importance, especially for food safety and field applications. These innovations will accelerate the transition of cold plasma technology from laboratory scale to industrial scale, paving the way for more sustainable, economical, and reliable applications in fields such as biotechnology, food safety, and medicine.

This review evaluates studies published between 2013 and 2025 that investigated the use of cold atmospheric plasma (CAP) in the treatment of various dermatological conditions, including inflammatory skin disorders, and autoimmune diseases. CAP therapy emerges as a promising alternative to conventional treatments for skin conditions driven by genetic or physical etiologies, offering innovative therapeutic potential. This work provides a comprehensive analysis of CAP's efficacy in managing conditions such as acne, atopic dermatitis, psoriasis, rosacea, and vitiligo. Although a limited number of studies have investigated comprehensively the therapeutic effects of CAP on specific skin diseases, this review is the first to systematically and examine its applications across. It fills an important gap in the literature and provides a foundational framework for future research and clinical use.

## 2. SKIN DISEASES AND CAP

Skin diseases represent one of the most prevalent categories of health disorders worldwide. Each skin disease has different causes and symptoms. CAP demonstrates its versatility in dermatology by tackling a wide spectrum of skin diseases. This includes promoting wound healing, calming inflammatory disorders, combating infections and parasites, and even offering the potential to treat skin cancers, genetic conditions, and hair loss [2]. CAP consists of a mixture of charged particles, light, and electric fields. Upon interacting with air, it generates reactive molecules that enhance blood flow, activate immune cells, and stimulate skin repair. These reactive species induce changes at both cellular and tissue levels, making CAP a promising approach for various skin conditions [37–40]. Despite these promising effects, the full potential of CAP remains unrealized due to gaps in understanding its precise mechanisms of action.

*In vitro* studies have shown that CAP modulates cellular and inflammatory pathways relevant to skin repair.

Specifically, it balances cytokine expression by suppressing IL-6 and TNF- $\alpha$  while enhancing IL-10, and promotes fibroblast proliferation via VEGF and TGF- $\beta$  signaling. CAP also exhibits broad antimicrobial activity against pathogens such as *Staphylococcus aureus*, *Cutibacterium acnes*, and *Candida albicans* through oxidative mechanisms [41, 42]. These molecular and antimicrobial effects are supported by *in vivo* and early clinical studies, which report accelerated wound healing, improved epithelialization, and reduced bacterial load, with minimal side effects in chronic wounds and inflammatory skin disorders [43, 44].

### 2.1. Acne

Acne vulgaris is a prevalent dermatological pathology observed globally. Its etiology is primarily associated with the hypersecretion from overactive sebaceous glands and the proliferation of *Cutibacterium acnes* (formerly *Propionibacterium acnes*). [45]. This skin disease, caused by the blockage of sebaceous glands due to hormonal changes associated with adolescence, has a prevalence rate of around 35% to 100% [46]. Treatment options typically include topical retinoids or benzoyl peroxide which often cause intolerance reactions such as skin dryness, peeling, redness, irritation, and even allergies [47]. Long-term use of oral or topical antibiotics, especially those that lead to bacterial resistance, can significantly affect patients' quality of life by causing nausea, diarrhoea, microbiome disruption, photosensitivity, drug reactions, and allergies [45, 47]. Due to these side effects, patient compliance and treatment adherence are also limited and are generally low. Therefore, alternative improvement treatments are necessary for compliance and limiting antibiotic use [46]. CAP, through the generation of bioactive species such as reactive oxygen and nitrogen species (RONS), exerts potent anti-inflammatory and antimicrobial effects, thereby positioning itself as a novel, non-invasive, painless, and clinically promising therapeutic modality for the management of diverse dermatological disorders. [45, 48].

Mariachiara et al. [45] applied plasma therapy (Argon-CAP, Adtec SteriPlas; Adtec Plasma Technology, Adtec Europe, Hunslow, UK) to two patients with acne, five sessions for the male patient and eight sessions for the female patient, with five minutes of skin exposure per session. At the end of the application, they reported a decrease of approximately 60% in skin lesions and clinical improvement in both patients. It was reported that no side effects or skin reactions were observed during or within the 3-month follow-up period. The treatment was well-tolerated, with patients reporting no pain or adverse sensations such as itching or burning during after plasma application. In a clinical study evaluating the safety and therapeutic efficacy of CAP in individuals presenting with moderate acne vulgaris, a total of 29 patients underwent CAP treatment over a period of 4 to 6 weeks, receiving 8 to 10 sessions each, with individual skin exposure durations not exceeding 10 seconds per session. [46]. Given the distinction between inflammatory and non-inflammatory acne lesions and the anticipated better

response of inflammatory lesions to treatment, the efficacy analysis was stratified by lesion type, as opposed to evaluating the total number of lesions. The study demonstrated a statistically significant reduction in inflammatory lesions following CAP treatment ( $p = 0.007$ ), whereas no significant change was observed in non-inflammatory lesions ( $p = 0.288$ ). The authors reported that CAP therapy achieved a continuous decline in acne, with an estimated 50% reduction in inflammatory lesions and a 36% reduction in non-inflammatory lesions. Cho et al. [49] conducted a study on 14 healthy individuals with oily facial skin, administering three sessions of non-thermal atmospheric pressure plasma (NTAPP) at one-week intervals and monitoring outcomes over an eight-week follow-up period. The study assessed daily sebum levels, sebum production rate, and porphyrin index, revealing a 26% and 24% reduction in sebum parameters by week four and a 38% decrease in porphyrin index by week two, relative to baseline. Mariachiara et al. [45] reported that CAP is a highly effective and well-tolerated option for patients with mild to moderate Acne vulgaris unresponsive to conventional therapies, although they emphasized that its high cost and limited accessibility currently preclude its use as a first-line treatment.

### 2.2. Atopic Dermatitis (Eczema)

Atopic dermatitis (AD) is a common chronic inflammatory dermatosis, clinically characterized by recurrent eczematous lesions accompanied by intense pruritus. [50]. Also known as eczema, atopic dermatitis typically begins in early childhood and can affect the entire family [51, 52]. In many parts of the world, more than 20% of children are affected by this disease at least once in their lifetime [53]. Atopic dermatitis patients are more susceptible to bacterial skin infections, which can lead to severe health problems and become systemic without proper treatment [54]. *Staphylococcus aureus*, a common disease-causing bacterium, frequently colonizes the skin of eczema patients, leading to infections. *S. aureus* contributes to cutaneous infection through the release of various virulence factors including superantigens, proteolytic enzymes, and cytolytic phenol-soluble modulins (PSMs) which trigger inflammatory responses within the skin [55]. Draining lesions, honey-colored crusts, and pustules are among the main signs of bacterial infections [54].

If left untreated, bacterial skin infections in eczema can progress to life-threatening complications throughout the body, including sepsis, endocarditis, and bone and joint infections [56]. Eczema can cause severely uncomfortable symptoms such as itching and burning, leading to scarring and skin pigmentation changes [40]. In addition to bacterial skin infections, non-bacterial infections can also occur in dermatitis. It is crucial to pay attention to these in differential diagnosis as their symptoms can also be like bacterial infections. Eczema herpeticum (EH), a severe herpes simplex virus (HSV) infection, can develop in a subset of patients with eczema and may result in serious, potentially life-threatening complications. [50]. In affected patients, EH commonly involves the face, neck,

upper trunk, and flexural regions such as the antecubital and popliteal areas, and is often accompanied by systemic symptoms including fever, malaise, and lymphadenopathy [54, 57].

Therapeutic treatments for atopic dermatitis include topical treatment, phototherapy, or systemic treatment [58]. While some treatments, like topical medications or oral drugs, can offer relief, they may come with potential side effects, especially with long-term use. It's important to note that most atopic lesions are more likely to experience deterioration than complete disappearance. Therefore, an alternative, sustainable treatment method is recommended to treat localized atopic lesions. In this context, the CAP device can be used as a new treatment option for these indications [59]. In a study of twenty-two patients with mild to moderate atopic dermatitis with symmetric lesions, three treatment sessions were performed with cold atmospheric plasma application in weeks 0, 1, and 2. The patients' clinical severity indices and the lesions' microbial characteristics before and after treatment were analyzed at 0, 1, 2, and 4 weeks after the end of treatment. It was found that CAP could relieve the clinical severity of atopic dermatitis and significantly reduce the incidence of *S. aureus* in the treated group [59]. In their study, Gao et al. [60] treated a patient with chronic eczema for about three months with various methods (ointments, oral medications, and traditional Chinese medicine treatment). Still, they could not achieve practical results with these methods. They then applied two courses of CAP treatment to the patient and reported that the lesions improved. Another mouse model study found that CAP treatment reduced skin cell death, inflammation, and stress in atopic dermatitis. This improvement was linked to CAP increasing the expression of a protein called MANF, which protects against stress. The study reveals a potential mechanism for CAP's beneficial effects involving a protein called HIF-1 $\alpha$  that regulates MANF expression [61]. Choi et al. [62] applied CAP treatment to proinflammatory cytokine-stimulated keratinocytes and DNCB (2,4-Dinitrochlorobenzene)-induced atopic dermatitis mice. They observed a decrease in the expression levels of CCL11 (C-C motif chemokine ligand 11), CCL13, and CCL17 mRNA and NF- $\kappa$ B (Nuclear Factor kappa B) activity in CAP-treated HaCaT (human epidermal keratinocyte line) cells. The researchers reported that CAP significantly inhibited various immune responses of atopic dermatitis by regulating NF- $\kappa$ B activity.

### 2.3. Psoriasis

Psoriasis is a chronic, inflammatory autoimmune skin disorder marked by excessive keratinocyte proliferation, impaired skin barrier function, and dysregulated calcium homeostasis in affected areas [63, 64], clinically presenting as well-defined, scaly, reddish-pink plaques commonly located on extensor surfaces such as the elbows, back, scalp, and knees [2]. Psoriasis is a skin condition marked by two key features: a rapid buildup of skin cells (epidermal hyperplasia) and an influx of immune cells into the deeper layer of the skin (dermal infiltration). The pathogenesis of psoriasis is complex,

involving intricate interactions between keratinocytes, immune cells, and other resident skin cell populations [65]. Although there is no definitive cure for psoriasis, extensive research is ongoing to discover new and more effective treatments that can offer a lasting solution for patients [66, 67]. Existing treatments provide symptomatic relief for psoriasis, but a definitive cure is yet to be discovered [68, 69]. Psoriasis is a persistent autoimmune condition that primarily involves the skin, yet may also impact the joints and various systemic organs. It is frequently comorbid with metabolic and cardiovascular disorders such as hyperlipidemia, hypertension, coronary artery disease, and type 2 diabetes. [70, 71]. Psoriasis is thought to be linked to oxidative stress, an imbalance caused by reactive oxygen species. The severity of this stress dictates how cells react. Overwhelming stress can kill cells, while milder stress can promote abnormal cell proliferation. Consequently, low-level oxidative stress is considered a contributing factor in the development of epidermal hyperplasia observed in psoriasis. This finding also implies that augmenting local oxidative stress could potentially have antiproliferative effects [72].

Psoriasis treatments have pro-oxidant properties [73, 74]. Pro-oxidant treatments also play a role in increasing oxidative stress. Plasma, a source of external RONS, offers a promising approach to psoriasis treatment. It can deliver controlled amounts of RONS to cells, suppressing hyperproliferative keratinocyte growth and triggering apoptosis (programmed cell death). This targeted action could lead to the regression of psoriatic hyperplasia [75]. In a study investigating the role of ROS in psoriasis, it was reported that psoriatic dermatitis induced by imiquimod could be regulated by increasing the function of regulatory T cells [76].

In a cellular model of psoriasis, Zhong et al. [77] demonstrated that CAP treatment led to apoptotic activity, disruption of mitochondrial function, and lysosomal membrane destabilization in human keratinocytes, alongside a reduction in IL-12 expression. In their study, Gareri et al. [78] applied a Plasma Coagulation Controller (PCC) device to a 20-year-old woman with psoriasis for 30 seconds on the 0<sup>th</sup> day and 3<sup>rd</sup> day of treatment under standard conditions (7 kV voltage; 5 kHz frequency; 1 cm distance). They reported that the patient showed improvement without any side effects during the 14-day follow-up period. In an *in vivo* study utilizing an imiquimod (IMQ)-induced psoriasiform dermatitis model, commonly employed to simulate human psoriasis, Atmospheric Pressure Plasma Jet (APPJ) was directly administered to the lesional skin of mice. The animals were assigned to four groups: control, IMQ, IMQ + plasma, and plasma only. Within three days of IMQ application, mice in the IMQ group exhibited characteristic psoriatic changes such as erythema, scaling, and epidermal thickening, which became more pronounced with prolonged exposure. In contrast, mice in the plasma-only group received 2-minute daily APPJ treatments without developing any visible skin damage. Notably, APPJ exposure in the IMQ + plasma group led

to a marked attenuation of psoriatic skin manifestations compared to the IMQ-only group [75].

#### 2.4. Rosacea

Rosacea is a multifactorial chronic skin disorder, primarily characterized by recurrent facial erythema, with a global prevalence of approximately 10% [79]. Although it most commonly presents between the ages of 30 and 50, it can occur at any age. Reported prevalence rates may vary depending on study design, population characteristics, geographic region, and sociocultural factors influencing disease perception [80, 81]. Lesions of this disease can manifest as erythema, papules, and pustules resembling acne, telangiectasia, tissue fibrosis, and rhinophyma (enlargement of the nose) [82]. Certain external factors such as sunlight, extreme temperatures, alcohol, and spicy foods can trigger rosacea flare-ups, while avoiding these triggers may help alleviate symptoms and reduce recurrence [83]. Additionally, underlying conditions like obesity, *H. pylori* infection, smoking, and inflammatory bowel disease have been identified as risk factors that may increase susceptibility to rosacea [84]. In recent years, a range of therapeutic approaches has been developed for rosacea, encompassing topical agents, systemic medications, light-based therapies, skincare regimens, and lifestyle modifications [85-87]. In addition to these treatments, clinical studies on rosacea are also ongoing [87, 88]. It is known that current treatment methods help alleviate rosacea symptoms, but they do not completely eliminate the disease [79]. Hofmeyer et al. [89] performed a randomized controlled trial to evaluate the effectiveness of dielectric barrier discharge plasma therapy in patients with erythematotelangiectatic (ETR) and/or papulopustular rosacea (PPR). Daily CAP treatment (90 seconds per area) over six weeks significantly reduced papulopustular lesions and erythema size on the treated side compared to the untreated side. The therapy was well tolerated and led to improvements in quality of life. The authors concluded that CAP may be a promising treatment option for rosacea but emphasized the need for larger-scale studies to validate these findings. They also highlighted the importance of future research focusing on inflammatory lesion management and the potential benefits of combining CAP with other therapeutic agents.

#### 2.5. Vitiligo

Vitiligo is a pigmentary skin disorder characterized by the loss of melanocytes, with a global prevalence estimated between 0.5% and 1% [90]. Non-segmental vitiligo, the most prevalent form of the disease, presents as sharply defined, milky white depigmented patches and is considered a multifactorial condition arising from the interplay between genetic predisposition and environmental triggers [91]. The abnormalities that impair melanocyte regeneration and proliferation indicate a fundamental defect within the melanocytes [92, 93]. It is known that silent inflammation and autoimmunity play an important role, especially in the advanced stages of the disease [93-96]. Current treatments for vitiligo (topical and systemic steroids, and topical calcineurin inhibitors)

focus on stimulating melanocyte regeneration or suppressing inflammation and the immune system. However, these limited treatments may not always be effective and can cause side effects. Advancements in understanding the immune mechanisms underlying vitiligo have facilitated the development of targeted therapies that specifically act on melanocytes while minimizing adverse effects [97]. Oxidative stress, immune inflammation, and T cell-mediated destruction of melanocytes play essential roles in the development of vitiligo [98, 99]. CAP treatment can suppress these processes by producing low levels of ROS. Therefore, it is thought that CAP will strengthen antioxidant responses and inhibit immune reactions in vitiligo [99]. In their studies investigating the efficacy of CAP in the treatment of vitiligo in mice and humans, Zhai et al. [7] found that CAP applied at 8 kV and 9 kHz was able to improve vitiligo lesions and accelerate the redistribution of melanocytes to hair follicles. The authors also reported that CAP could prevent the migration of immune cells (CD8+ T cells, CD3+, and CD11c+ cells) to lesions and reduce the release of immune cytokines.

In conclusion, Table 1 summarizes some studies on the usability of CAP for various skin diseases. As can be seen from the table, CAP shows promise as a safe and effective treatment for various skin diseases.

**Table 1.** Efficacy of CAP against various skin diseases

<b>Acne</b>				
<b>Method</b>	<b>Number or Name of Samples</b>	<b>Application Condition</b>	<b>Decrease in Lesions</b>	<b>References</b>
Argon-CAP plasma	2	5-8 sessions/ for 5 minutes	%60	[45]
CAP	29	8-10 sessions/ less than 10 seconds	Inflammatory lesion %50, Non-inflamantory lesion %36	[46]
NTAPP	14	3 sessions	sebum levels 26% sebum production rate 24% porphyrin index %38	[49]
<b>Atopic Dermatitis (Eczema)</b>				
CAP	22	3 sessions/ for 4 weeks	Decrease in clinical severity indices, significant reduction in <i>S. aureus</i> bacteria	[59]
CAP	1	2 cycles/ for about three months	Healing of lesions	[60]
CAP	-	-	Reducing skin cell death, inflammation and stress by increasing the expression of the stress-reducing MANF protein	[61]
CAP	6-week-old male Nc/Nga mice	-	Significantly reducing the inflammation response by regulating NF- $\kappa$ B activity	[62]
<b>Psoriasis</b>				
DBD	HaCaT cells	2, 3, and 4 minutes	Causes apoptosis, mitochondrial dysfunction and lysosomal leakage in keratinocytes, reduces IL-12 expression	[77]
PCC	1	2 sessions/ for 30 seconds/ during the 14-day	Improvement in lesions at 14-day follow-up	[78]
APPJ	8-10 weeks old Balb/C female mice	2 minutes once a day	Significantly reducing lesions in mice induced with psoriatic dermatitis with IMQ	[75]
<b>Rosacea</b>				
DBD	12	90 seconds/ 6 weeks	Significant reduction in papulopustular lesions and erythema size	[89]
<b>Vitiligo</b>				
CAP	-	-	Inhibiting the migration of immune cells to lesions and reducing the release of immune cytokines	[7]

### 3. CONCLUSION

Plasma is a partially ionized gas composed of free electrons, charged particles, and neutral atoms or molecules in ground or excited states. It contains multiple biologically active components, such as reactive species, electric currents, and UV radiation, that can act synergistically. The advent of cold atmospheric plasma has significantly advanced its biomedical applications, enabling safe and effective use in various clinical settings. CAP has the potential to be widely used in modern clinical applications. Current studies show that cold plasma therapy is beneficial in many areas of medicine, with no significant adverse effects on healthy cells. Conventional dermatology treatments, while effective, often come with limitations like side effects, limited targeting, and resistance. While challenges remain, CAP's versatility, minimal side effects, and potential for treating and optimizing skin health paint a promising future for this

innovative technology. Cold plasma therapy is emerging as a new treatment option for various skin conditions. Using this treatment as an alternative or complementary to traditional treatments is a significant advancement for patients with skin conditions. Despite the need for further research, cold plasma therapy has emerged as a safe and effective option for treating skin conditions. As research continues and hurdles are addressed, CAP has the potential to revolutionize the way it approaches skin health, offering patients safer, more effective, and personalized treatment options.

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