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REVIEW

Progress in the Application of Molecular Hydrogen in Medical Skin Cosmetology

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Abstract: Molecular hydrogen is a colorless, tasteless, biologically active small-molecule gas with reducing properties, demonstrating therapeutic and preventive effects across various human systems. Its mechanisms of action include selective antioxidation, anti-inflammatory effects, apoptosis inhibition, and the regulation of gene expression and signaling pathways. In the skin, molecular hydrogen reduces oxidative damage by scavenging free radicals and inhibiting oxidative stress, leading to improvements in texture and tone. It also regulates the inflammatory response, alleviating redness, itching, and discomfort, while promoting skin repair and regeneration. Moreover, hydrogen activates antioxidant enzymes in skin cells, boosting their antioxidant capacity and delaying aging. Clinical trials show that molecular hydrogen significantly improves conditions like acne, chloasma, and skin sensitivity. However, research in skin cosmetology remains in its early stages, with unanswered questions regarding mechanisms of action, optimal dosage, and long-term safety. Further investigation through clinical trials is essential for expanding its applications in this field. Molecular hydrogen holds significant promise in skin cosmetology, and as research and technology evolve, it is expected to drive innovations and breakthroughs in skin care. This review examines the therapeutic potential, mechanisms, and clinical applications of molecular hydrogen in skin cosmetology, addressing challenges and proposing pathways for future advancements in this field.
Keywords: molecular hydrogen, hydrogen, hydrogen-rich water, skin beauty

Introduction

Molecular hydrogen medicine, an emerging research field, has seen its potential applications in various medical fields gradually being verified and recognized, particularly in skin cosmetology. Traditional skincare methods, often limited to surface care and repair, are now being supplemented by molecular hydrogen medicine, which offers deeper treatment options. Hydrogen is a colorless, tasteless, and biologically active reducing small-molecule gas. As the simplest molecule in nature, hydrogen has long been mistaken by the biomedical community for being a physiologically inert gas. Since Ohsawa et al[1] demonstrated hydrogen's protective effects against cerebral infraction, there has been a surge in hydrogen medicine research worldwide. Since then, hydrogen, as a new type of medical gas, has been increasingly used in the medical field. By comprehensively reviewing and analyzing the application progress of molecular hydrogen medicine in skin beauty, we can gain a deeper understanding of its mechanisms of action on skin health and explore more potential applications in skin cosmetology.[2] Additionally, it can provide direction and ideas for future research, promoting the further development and application of molecular hydrogen medicine in skin cosmetology.

In recent years, researchers found that hydrogen has therapeutic effects on various diseases involving oxidative damage,[3,4] inflammation, apoptosis,[5] and vascular dysplasia. It has shown significant intervention effects on ischemia-reperfusion injury, ionizing radiation, allergies, and other diseases.[6] Hydrogen has been extensively applied in the treatment and prevention of diseases affecting various systems, including the central nervous,[7] cardiovascular,[8] digestive,[9] endocrine,[10] respiratory, urinary, reproductive, ocular, immune, and tumor systems,[11] with no adverse reactions reported. However, its specific mechanisms remain unclear. Therefore, this review provides a detailed exploration of the mechanisms, therapeutic applications, and advancements in molecular hydrogen medicine as applied to skin

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Table 1 Mechanisms and Effects of Hydrogen Therapy for Skin Injuries and Diseases

Hydrogen Function	Mechanism/Action	Type of Skin Injury	Effect on Skin	References
Inhibits oxidative stress	Selective antioxidant effect (MPO, malondialdehyde, 8-hydroxydeoxyguanosine, isoprostane 2α, thiobarbituric acid, SOD)	Cuts, burns	Skin repair, cosmetic	[1,12–16]
Anti-inflammatory effect	Reduces pro-inflammatory cytokines (IL-6, TNF-α, ICAM-1, NF-κB)	Cuts, burns, wounds	Skin repair, cosmetic	[14,15,17–20]
Apoptosis	Apoptosis inhibition (Bcl-2, Bcl-xl, Bax, caspase-3, caspase-8, caspase-12)	Cuts, burns	Skin repair	[2,21]
Gene expression	Promotes cell proliferation (NF-κB, JNK, VEGF, GFAP)	Cuts, burns	Skin repair	[2,22]
Treating atopic dermatitis	Anti-inflammatory effect (IL-2, IL-4, IL-5, IL-10, IL-12, GM-CSF, TNF-α)	Dermatitis, Skin I/R injury	Skin repair	[18,23,24]
Treating infections	Antiviral, antibacterial effect (TNF-α, IL-1, IL-6, IL-1β, bacterial species (eg, Staphylococcus aureus))	Infectious diseases	Skin repair	[25,26]
Treating radiodermatitis	Antioxidant effect (hydrogen-rich environment, oxidative stress reduction)	Radiodermatitis	Skin repair	[14,27,28]
Promotes skin regeneration	Promotes tissue regeneration (hydrogen-rich water, type I collagen synthesis, superoxide anion, hydrogen peroxide)	Cuts, burns	Skin repair, cosmetic	[14,25,29]
Maintains skin beauty	Reduces UV-induced damage (SOD, catalase, lipid peroxidation, malondialdehyde, isoprostane 2α, IL-6, IL-1β)	UV exposure	Skin repair, Cosmetic	[27,28,30–33,35]

cosmetology. By addressing its antioxidative, anti-inflammatory, and regenerative effects, the review seeks to bridge current knowledge gaps and inspire future clinical and research innovations in this emerging field (Table 1).

A Possible Mechanism of Action for Hydrogen Therapy

Selective Antioxidant Effect

Molecular Hydrogen (H_2) has emerged as a promising antioxidant, with both preventive and therapeutic potential.[1] It primarily neutralizes hydroxyl radicals (HO•), the most cytotoxic among ROS, by donating electrons and converting them into water (H_2O), thus preventing oxidative damage in cells.[12,13] In addition to hydroxyl radicals, H_2 also neutralizes peroxynitrite ($ONOO^-$), a potent oxidant that can cause significant damage to mitochondrial proteins and lipids. This is particularly important in preserving mitochondrial function, as peroxynitrite can inhibit oxygen consumption and disrupt cellular respiration.

Hydrogen also neutralizes peroxynitrite ($ONOO^-$), a potent oxidant,[14–16] and activates the Nrf2 pathway, which regulates antioxidant enzymes like superoxide dismutase (SOD), catalase, and glutathione peroxidase (GPx).[17] This pathway helps cells respond to oxidative stress by producing antioxidants that eliminate ROS (Figure 1).[17,18] However, excessive Nrf2 activation can disrupt cellular balance, highlighting the need for regulated activity.[19]

Anti-Inflammatory Effects

The inflammatory response is a protective mechanism activated by infection or injury, involving immune cells like neutrophils and monocytes.[20] However, ROS can lead to prolonged activation of the NF-κB pathway, exacerbating inflammation. H_2 has been shown to limit this process by reducing the infiltration of neutrophils and macrophages, and by decreasing proinflammatory cytokine secretion. Specifically, H_2 inhibits the expression of adhesion molecules like ICAM-1 and cytokines such as IL-1β, IL-6, IL-8, IL-10, and TNF-α,[5,21] promoting a balanced immune response and supporting tissue recovery (Figure 2).

Additionally, H_2 stabilizes mast cells (MCs) and prevents their degranulation, inhibiting the release of histamine and other inflammatory mediators.[22] This action helps reduce inflammation, particularly in allergic conditions like atopic

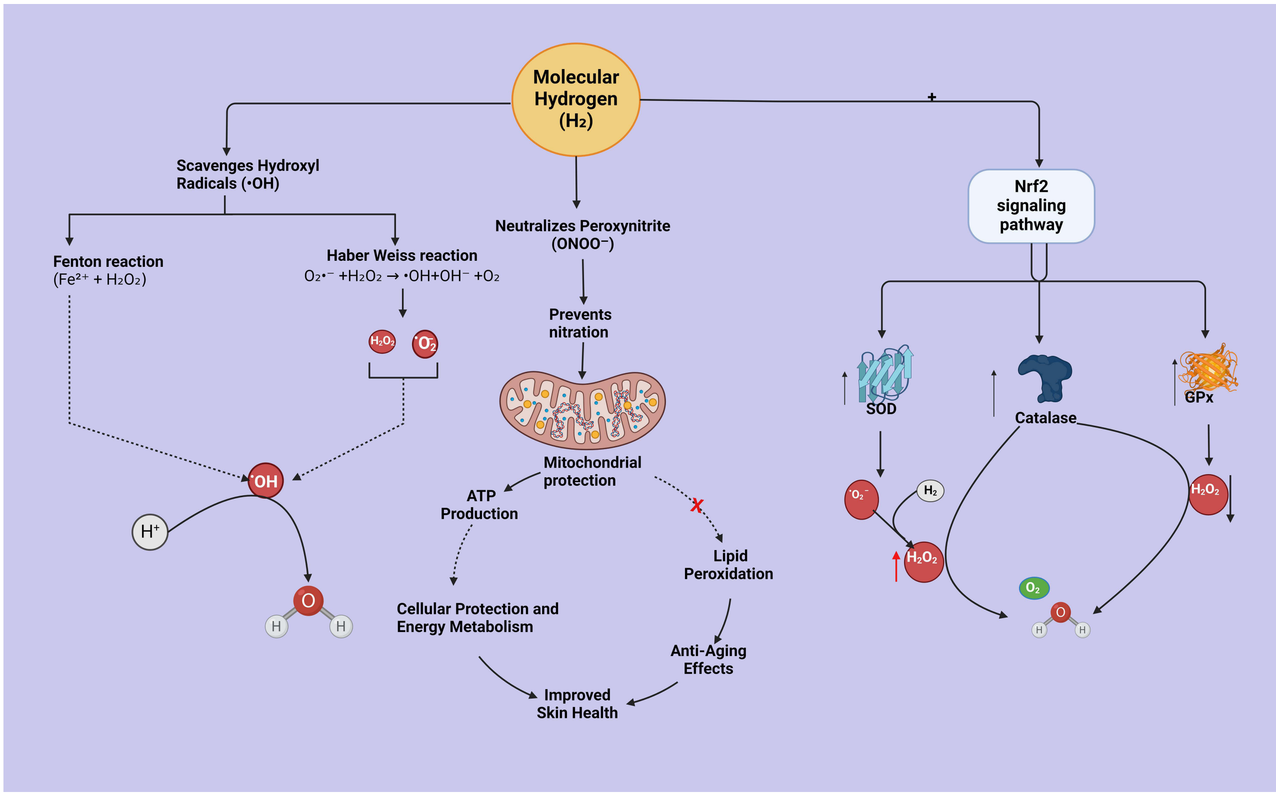

Figure 1 Antioxidant effect of hydrogen. Hydrogen selectively scavenges harmful ROS, such as hydroxyl radicals and peroxynitrite, while activating the Nrf2 pathway to enhance antioxidant defense and protect skin from oxidative damage.

dermatitis, by limiting histamine-driven responses such as itching, swelling, and redness.[22–24] Through its antioxidant properties, hydrogen modulates the activity of MCs, offering a potential strategy for controlling inflammation in specific tissue microenvironments.[25,26]

Inhibition of Apoptosis

Apoptosis is a controlled cell death mechanism that helps maintain the homeostasis of cell populations by regulating cell formation and death rates. An imbalance in this system can result in excessive cell proliferation or autoimmune issues. Apoptosis is essential throughout embryonic development, supporting tissue renewal and clearing inflammatory cells as the organism grows.[27] Hydrogen inhibits apoptosis by upregulating anti-apoptotic factors and downregulating pro-apoptotic factors. Anti-apoptotic factors include B cell lymphoma-2 (Bcl-2) and Bcl-xL, while pro-apoptotic factors include Bcl-2-associated X protein (Bax), and caspase 3, caspase 8, and 12.[28] H2-rich medium showed notable reductions in ROS formation, protection of cell viability, and inhibition of both caspase-3 and caspase-9 within intestinal epithelial cells. H2 helps in normalizing the expression of Bax and Bcl-2 (Figure 3).[29]

H_2 inhibits apoptosis through three key oxidative stress-mediated, mitochondria-dependent pathways.[30] First, H2 prevents high glucose-induced apoptosis in Schwann cells by suppressing poly (ADP-ribose) polymerase-1 (PARP-1) activation, which is involved in both caspase-independent and caspase-dependent apoptosis.[29] Second, H2 activates the Nrf2/ARE pathway, increasing the expression of antioxidant genes like HO-1 and proteins such as SIRT1 and Bcl-2, which inhibit apoptotic signals by reducing Bax expression, p53 acetylation, and cytochrome c release.[30] Lastly, H2 modulates the PI3K/Akt/Foxo3a pathway, protecting cells from apoptosis caused by oxidative stress.[31]

Regulation of Gene Expression

Hydrogen influences gene expression by modifying the free radical-driven oxidation of phospholipids. In a cell-free system, H_2 reduced the autoxidation of key phospholipids.[32]

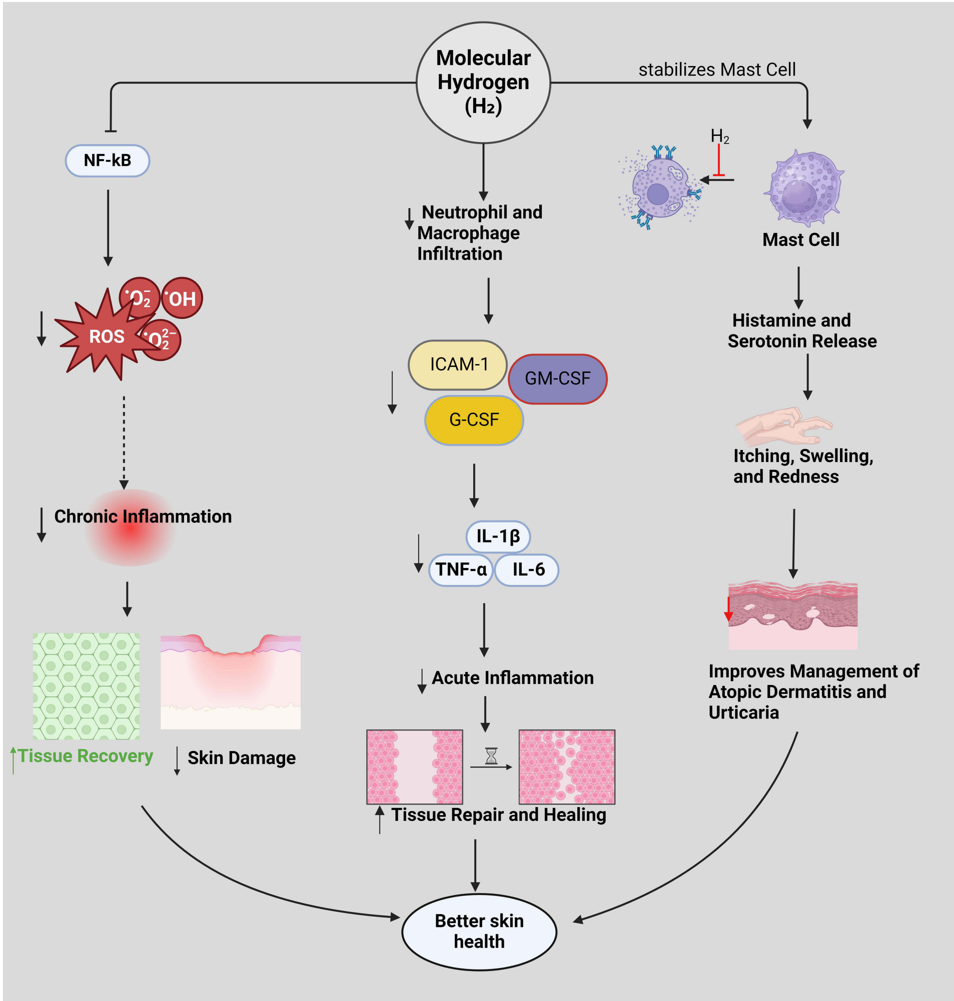

Figure 2 Anti-inflammatory effects of hydrogen. Hydrogen inhibits NF-κB, reduces ROS, and stabilizes mast cells, suppressing inflammation and promoting tissue recovery in inflammatory skin disorders.

H_2 can potentially interact directly with potent oxidants like hydroxyl radicals (•OH) within the body. Hydroxyl radicals may play a physiological role by initiating free radical chain reactions and influencing the regulation of calcium or ATP-dependent potassium channels in mitochondria.[33]

Calcium ions (Ca^{2+}) and their concentration gradient across the epidermis are vital for regulating key skin functions, such as keratinocyte differentiation, skin barrier formation, and maintaining the permeability barrier. Recent research indicates that intracellular Ca^{2+} reserves, particularly in the endoplasmic reticulum (ER), are significant contributors to the epidermal calcium gradient. Proper ER calcium balance is essential for processes like keratinocyte differentiation, intercellular junction development, antimicrobial defense, and maintaining the permeability barrier (Figure 4).[32]

H_2 suppressed free radical-induced lipid peroxidation, leading to the recovery of Ca^{2+} levels. This restoration of Ca^{2+} signaling subsequently regulated Ca^{2+}-dependent gene expression. Thus, H_2 may modulate gene expression by affecting Ca^{2+} signal transduction through its antioxidant effects.[35] It also up-regulates the expression of genes like Kcnc3, regulated by H3K27 methylation, in various organs. H_2 also alters the methylation status of H3K27 by inducing Jmjd3, an H3K27 demethylase, and activates mitochondrial unfolded protein response (mtUPR)-related genes. These findings suggest that H_2 promotes beneficial effects through mtUPR activation, driven by epigenetic histone modifications and gene expression changes (Figure 4).[34]

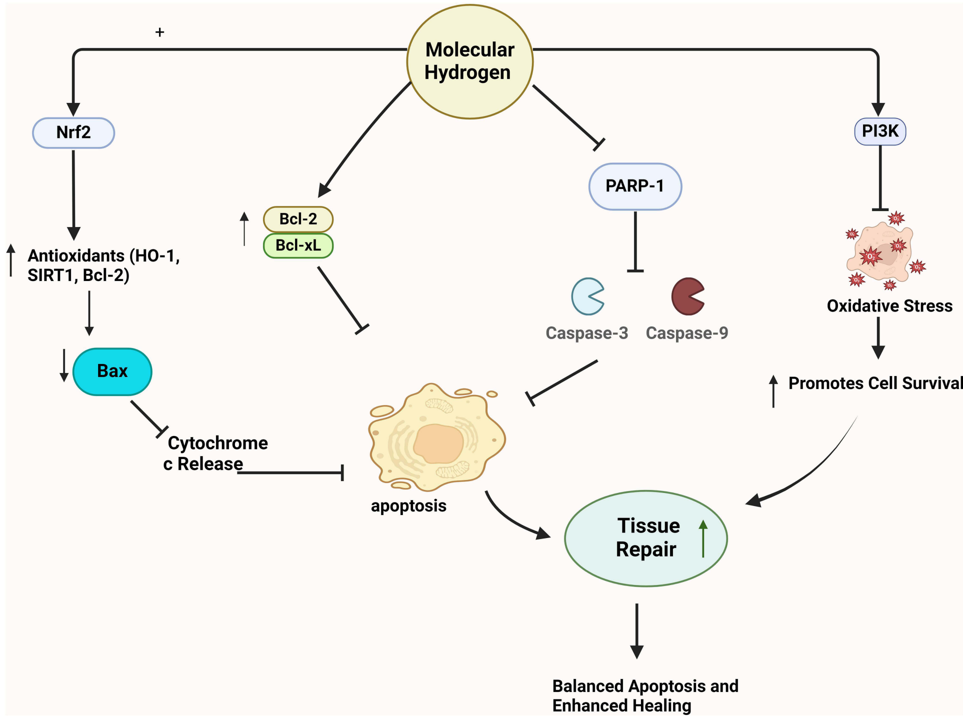

Figure 3 Protective effect of hydrogen. Hydrogen protect cells from apoptosis by inhibiting several factors including casepase 3/9, activation of Bcl-2, Bcl-xL, and Nrf2.

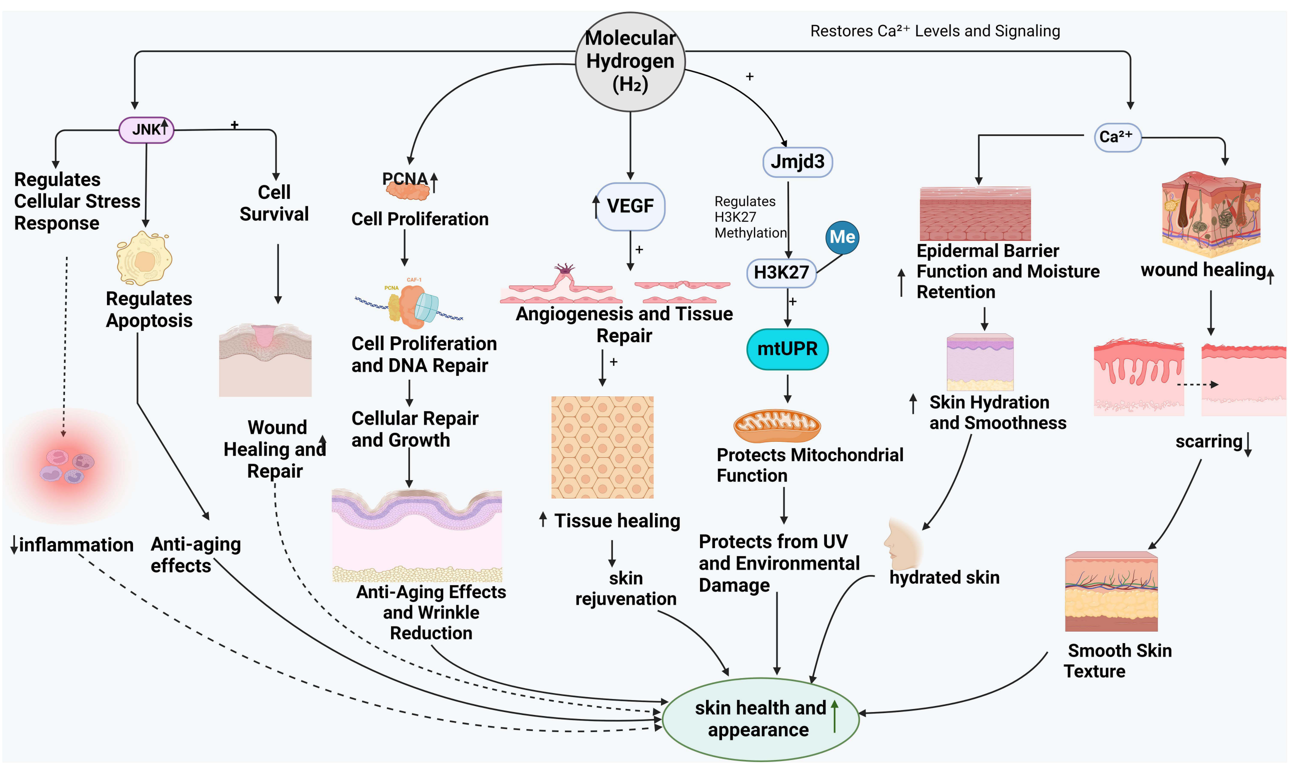

Figure 4 The role of molecular hydrogen in gene expression and its mechanisms in skin cosmetology. Molecular hydrogen modulates key pathways—such as JNK, Ca^{2+} signaling, and gene expression—to reduce inflammation, promote cell repair, and improve skin texture, hydration, and overall appearance, contributing to anti-aging and enhanced skin health. Created with Biorender.com.

Methods of Hydrogen Administration in Medicine

Currently, several convenient and effective methods for administering hydrogen have been reported, including inhalation, hydrogen-rich baths, oral administration, hydrogen-rich saline intravenous infusion.[36] The application of hydrogen medicine in dermatology includes nearly all of the above routes, though each has its own advantages and disadvantages. A comprehensive selection should be made based on the disease characteristics and the patient's age.

Inhalation

Hydrogen inhalation is a rapid method for delivering hydrogen to the bloodstream and tissues, especially useful for acute oxidative stress.[37] A mixture of hydrogen and oxygen in a two-to-one ratio can be produced by passing a low-voltage current through water containing an electrocatalyst, such as potassium hydroxide.[38] During this process, hydrogen is generated at the cathode, and oxygen at the anode. These gases can be delivered separately (hydrogen/oxygen) or inhaled together as a combined gas mixture, known as oxy-hydrogen. Both hydrogen and oxy-hydrogen inhalation therapies have demonstrated positive effects on the respiratory and cardiovascular systems, likely because of their direct interaction with these tissues. The inhalation method is non-invasive, making it an efficient and effective way to deliver hydrogen for treating both acute and chronic conditions.[37,39]

Wet Compress, Bubble Bath, and Oral Administration

Hydrogen-rich water, with a concentration of more than 1. 6 mg/L dissolved at normal temperature and pressure, can be used in wet compresses and baths. It is absorbed through the skin and distributed throughout the body via blood flow, making it suitable for localized treatment. Oral administration of hydrogen-rich water is convenient, safe and portable, but the absorbed dose cannot be accurately controlled.[6]

Venous Inflow

Hydrogen-rich injections are prepared by dissolving hydrogen into normal saline at high pressure (0.4MPa) for 6 hours to reach saturation concentration. An effective therapeutic hydrogen concentration, detected by gas chromatography, should exceed 0.6mmol/L. The infusion of hydrogen-rich solution allows for precise control of the hydrogen dose.[22]

Preparation Methods for Hydrogen Application in Skin Cosmetology

The application of hydrogen in skin cosmetology requires various preparation methods to maximize its therapeutic benefits. These range from traditional techniques, such as hydrogen-rich water, to more advanced methods like electrospinning, electrospray, and nano-bubble technology.[40–42] Each technique offers unique advantages in enhancing hydrogen's effectiveness for skin health and cosmetic use (Figure 5).

Hydrogen-rich water, produced by dissolving molecular hydrogen in water, is a common method in skin cosmetology. Typically reaching a concentration of 1.6 mg/L, this solution can be used orally, topically, or as a compress. Its non-invasive nature makes it ideal for clinical and consumer use. Research shows that hydrogen-rich water significantly reduces oxidative stress and inflammation, improving conditions like atopic dermatitis, acne, and UV-induced pigmentation.[43,44] It also enhances skin appearance by promoting cell viability and reducing sensitivity.[45,46]

Advanced methods, such as electrospinning and electrospray, are being explored for creating hydrogen-loaded nanofibers and nanoparticles. These techniques use high-voltage electric fields to shape polymer solutions into fibers or particles, providing controlled hydrogen release. This sustained delivery promotes wound healing and accelerates tissue regeneration.[47,48] For example, electrospun hydrogen nanofibers have shown promise in wound dressings, improving skin repair and reducing scarring in animal models.[49]

Nano-bubble technology is another emerging technique. It generates stable hydrogen nano-bubbles in liquid, enhancing solubility and retention. Nano-bubble hydrogen solutions penetrate deeper skin layers than conventional hydrogen water, offering superior antioxidant effects and reduced inflammation.[40,50] This method shows promise for treating conditions like erythema and photoaging.

Carrier systems such as hydrogels, liposomes, and microneedle patches are being developed to optimize hydrogen delivery. Hydrogen-loaded hydrogels create a moist environment that supports healing and ensures gradual hydrogen

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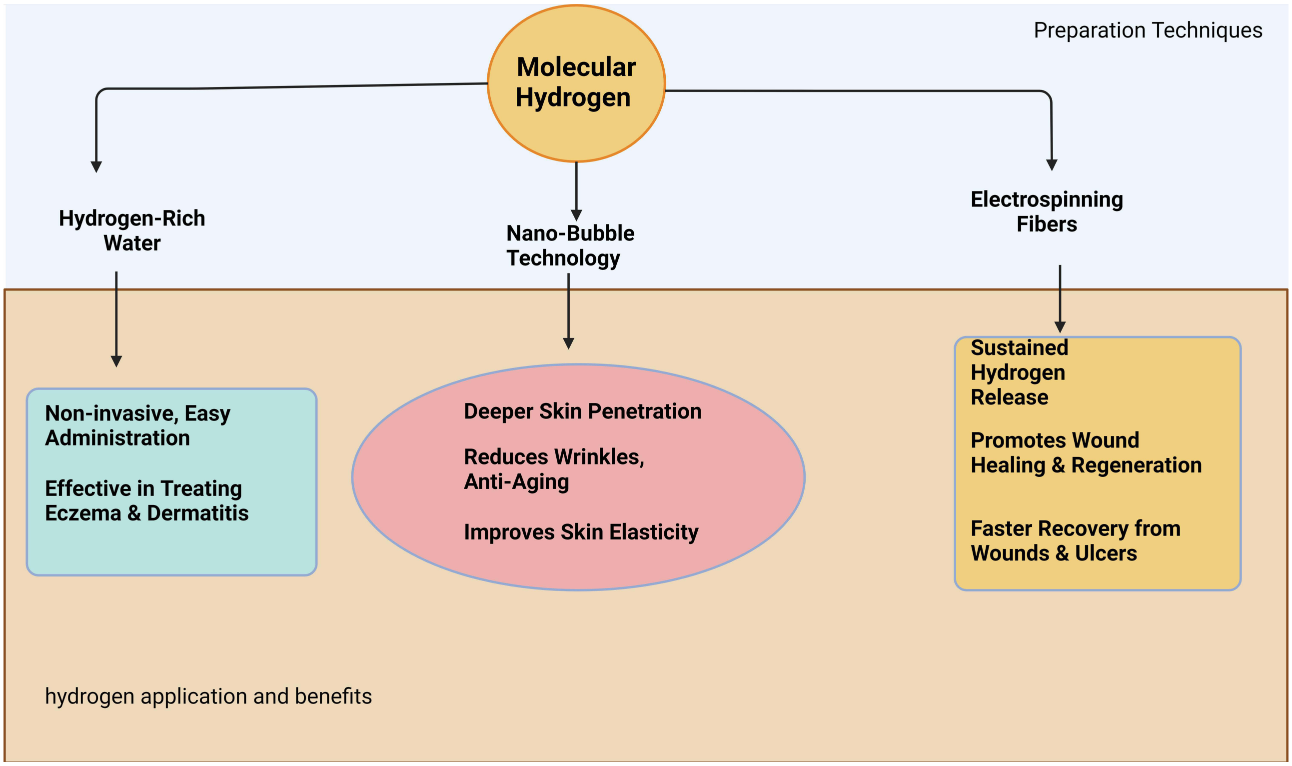

Figure 5 Preparation methods for hydrogen and their applications and benefits in skin care.

release, effective in treating oxidative stress and promoting tissue repair.[51] Similarly, microneedle patches deliver hydrogen directly into the dermal layers, offering a minimally invasive option for chronic skin conditions like psoriasis and eczema.[52] These innovations enhance therapeutic outcomes and broaden hydrogen's application in clinical and cosmetic dermatology.

Overall, the development of advanced hydrogen preparation methods is essential for unlocking its full potential in skin cosmetology. As research progresses, these techniques are expected to lead to more targeted treatments for various skin conditions, enhancing both therapeutic and aesthetic benefits.

Application of Hydrogen Medicine in Skin Disorders and Skin Cosmetic Medicine

Hydrogen-rich water and topical hydrogen purification have shown positive effects in various clinical applications.[53] For instance, studies have demonstrated that hydrogen-rich water baths can significantly improve skin conditions like eczema and atopic dermatitis by reducing oxidative stress and enhancing skin barrier function. Similarly, topical hydrogen purification has proven to be a safe and effective treatment for acne vulgaris,[54] with patients showing improvements in skin parameters and reduced inflammation, demonstrating hydrogen's therapeutic potential for common dermatological conditions.[55,56]

The clinical use of hydrogen for skin regeneration has also been demonstrated in clinical settings. For example, hydrogen-rich water and hydrogen inhalation have been found to help accelerate recovery from ischemia-reperfusion injury and burn wounds. Additionally, clinical studies have reported the benefits of hydrogen therapies in treating photoaging, where hydrogen-rich water helps reduce UV-induced oxidative damage, wrinkles, and skin aging by mitigating free radical damage.[57]

While the clinical use of hydrogen in dermatology is advancing, particularly in countries like China, where it is widely adopted in dermatology and cosmetology clinics, there remains a significant gap between clinical practice and the scientific evidence supporting its widespread application.[37] Many dermatology clinics are increasingly incorporating hydrogen-based therapies for skin conditions, but the scientific literature is still limited. Further clinical trials are needed to provide conclusive evidence on the long-term safety and efficacy of hydrogen therapies for skin health, and to establish standard protocols for their use in cosmetic dermatology.[53,56]

Infectious Diseases

Hydrogen-rich water wet compresses were used to treat skin ulcers in patients with pemphigus vulgaris, leading to significant improvement within one week and complete healing within 10 weeks.[58] In 2012, Ono et al[59] reported the use of a hydrogen-containing glucose electrolyte injection in a patient with left facial herpes zoster. The patient presented with left buccal and frontal erythema, edema, ulceration, and pain, along with left ptosis, and an inability to open the eyes and open mouth.

Although these studies suggest that hydrogen therapies may play a beneficial role in treating infectious skin conditions, it is important to note that such case reports often lack control groups, and the sample sizes are typically small. Therefore, while these results provide valuable early data, they must be interpreted with caution. Further clinical studies, particularly those with larger sample sizes and control groups, are necessary to better understand the mechanisms of hydrogen in treating infections and to establish optimal treatment protocols. In a study with 100 rats, hydrogen-rich saline (post-herpetic neuralgia -H2 group) reduced pro-inflammatory cytokines (TNF-α, IL-1β, IL-6) and increased autophagy markers (LC3, beclin 1, P62) in post-herpetic neuralgia, suggesting that hydrogen-rich saline mitigated inflammation and infection-related tissue damage by activating autophagy.[60]

Atopic Dermatitis

Atopic dermatitis (AD) is an allergic inflammatory skin disease characterized by dysregulation of the immune response. Th1 and Th2 cytokines, along with pro-inflammatory factors such as IL-2, IL-4, IL-5, IL-10, IL-12, p70, GM-CSF, TNF-α, play crucial roles in its pathogenesis.[61] Although there are no current clinical reports on the use of hydrogen-rich drinking water for atopic dermatitis treatment, there are clinical reports supporting its use for allergies.[62] Ignacio et al[63] used NC/Nga male mice to construct an animal model of AD to study the effects of hydrogen-rich water on the condition. In this study, 11 mice were fed hydrogen-rich water, 9 mice with mild atopic dermatitis were given pure water, and 9 healthy mice were used as blank controls. After 4 weeks, the severity score of atopic dermatitis in the hydrogen-rich water group was significantly lower than in the pure water group. The hydrogen-rich group also showed significant reductions in transcutaneous water loss, regulator activation, mast cell infiltration, and IL-1β and IL-33 release, suggesting promising clinical treatment prospects for AD with hydrogen-rich water.

Drug Eruption

Ono et al[59] reported a case of facial erythema and burning after an enhanced CT examination, where a contrast allergy was suspected. Treatment with compound glycyrrhizin injection showed no relief, and the patient developed a fever (38.5°C), headache and nausea. However, after administering 500 mL of hydrogen-rich saline, the patient's symptoms improved within 30 minutes. Within an hour, the erythema and body temperature had decreased significantly, with no recurrence. Ono et al[59] also reported a patient with aneurysm rupture and coma, who developed multiple system infections, erythema, and blisters after treatment with antibiotics and anticonvulsant drugs, with suspected Stevens-Johnson syndrome. Due to the patient's thrombocytopenia and fungal infection, systemic glucocorticoids could not be used, and there was no remission with external glucocorticoids and antifungal ointment. Therefore, 500 mL of hydrogen-rich saline injections were administered twice daily. After 3 days of continuous use, the skin rash improved significantly, and his body temperature returned to normal. The rash had almost disappeared after one week of treatment. No recurrence was observed during a 4-month of follow-up. However, similar to other case reports, this study is limited by its lack of a control group and the small number of patients involved.

Radiodermatitis

Studies using a rat model of radiodermatitis showed that hydrogen accelerates wound healing in acute radiation dermatitis, with higher concentrations of hydrogen gas reducing the healing time. In a study by Ke Mei et al[64], n = 6 rats were exposed to 15 Gy and 20 Gy of radiation, and n = 4 rats were exposed to 25 Gy. The rats pretreated with hydrogen showed faster recovery and less severe dermatitis compared to the control group. This suggests that hydrogen-rich saline can help protect against radiation-induced skin damage, promoting wound healing and reducing inflammation. In another study, Zhou et al[65] used 60 male SD rats, divided into three groups of 20 rats each: (1) the control group (distilled water treatment), (2) the HRW 1.0 ppm group (treated with hydrogen-rich water at 1.0 ppm), and (3) the HRW 2.0 ppm group (treated with hydrogen-rich water at 2.0 ppm). The rats inhaled hydrogen-containing gas (HCG: hydrogen 1.3%, oxygen 20.8%, nitrogen 77.9%) at a flow rate of 2 L/min for 2 hours daily before radiotherapy. This significantly reduced oxidative damage in the X-ray irradiated skin area and promoted the healing of radiation-induced skin damage. The mechanism is likely due to the reduction of cytotoxicity from oxidative stress, inhibition of apoptosis in epidermal keratinocytes, and the promotion of growth factor expression, suggesting that HCG could be an effective skin protectant during clinical radiotherapy.

Eryatous Ous Disease

Zhu et al[53] treated 41 patients with psoriasis using hydrogen-enriched baths for 8 weeks. The Psoriasis Area and Severity Index(PASI) score was significantly lower in the treatment group compared to the control group. PASI improvement was observed in 75% of the hydrogen group versus 24.4% in the control. Moreover, 56.1% of hydrogen group patients reported improved symptoms, including significant relief from itching.

Ishibashi et al[66] reported three cases of psoriasis with psoriatic arthritis, using various hydrogen administration methods: intravenous hydrogen saline, inhalation of 3% hydrogen, and oral consumption of hydrogen-rich water. Significant reductions were noted in PASI and Disease Activity Score (DAS 28), with decreases in TNFα, IL-6, and IL-17. These cytokine levels were measured pre- and post-treatment. Before treatment, IL-6, TNF-alpha, and IL-17 levels were ~50 pg/mL, ~55 pg/mL, and ~45 pg/mL, respectively. After 12 weeks of hydrogen-gas therapy, these levels reduced significantly to ~6 pg/mL (IL-6), ~5 pg/mL (TNF-alpha), and ~4 pg/mL (IL-17). The reductions were also observed with hydrogen-rich saline, where after 5 days of treatment, IL-6 levels dropped to ~25 pg/mL, TNF-alpha to ~40 pg/mL, and IL-17 to ~30 pg/mL.

These findings highlight the anti-inflammatory effects of hydrogen therapies, as evidenced by significant reductions in pro-inflammatory cytokine levels pre- and post-treatment.

Dermatoma

The use of hydrogen for the treatment of malignant tumors has been widely reported. Chen et al[67] treated 82 patients with stage I and stage II cancers for 4 weeks and conducted a prospective follow-up study using a "real-world evidence" approach. The results showed significant improvements in respiration, appetite, fatigue, and insomnia, along with an increase in the core quality of life questionnaire score. After 3 months of treatment, 36% of patients showed decreased tumor marker expression, with the highest reduction rate reaching 75%. Imaging findings showed that 83% of stage I patients and 48% of stage II patients had controlled tumors. In a study on a squamous cell carcinoma model in mice, Dole et al[68] conducted a high-pressure hydrogen treatment and found that mice with skin squamous cell carcinoma showed significant tumor volume reductions after continuous treatment with high-pressure hydrogen (97.5% hydrogen, 2.5% oxygen) for two weeks, demonstrating the effectiveness of high-pressure hydrogen treatment for skin malignancies.

In 2008, Saitoh et al[69] demonstrated through in vitro experiments that neutral hydrogen-rich electrolytic water could inhibit both the colony formation efficiency and size of human HSC-4 tongue cancer cells, as well as the growth and migration capacity of human HT-1080 fibrosarcoma cells. In 2009, Saitoh et al[70] further reported that platinum colloidal hydrogen-containing water inhibited colony formation and size of human HSC-4 tongue cancer cells, with no significant effect on normal epithelial cell growth.

Skin Regeneration

Animal studies have shown that hydrogen-rich water can effectively reduce ischemia-reperfusion injury following flap transplantation. Zhou et al[71] performed flap surgery on rats and administered hydrogen-rich saline or normal saline for

2 weeks before and after the procedure. The experimental group showed significantly improved blood flow and higher flap survival rates, indicating that hydrogen-rich water protects against ischemia-reperfusion injury.

In a separate study, Li et al[51] treated bedridden patients with hydrogen-rich water via gastric tube. The treatment accelerated the healing of bedsores, likely due to increased collagen synthesis and enhanced mitochondrial activity in keratinocytes.

Wang et al[72] established a post-burn rat model to evaluate the effects of hydrogen-rich saline. The treated rats survived significantly longer (9 days on average) compared to the control group (2 days), suggesting hydrogen's potential to reduce inflammation and mortality following burns. This effect is likely due to hydrogen's selective antioxidant properties, which mitigate oxidative damage by neutralizing superoxide anions and hydrogen peroxide.

Skin Beauty

Long-term ultraviolet (UV) radiation, particularly UV that penetrates the dermis, causes significant oxidative damage to dermal fibroblasts, leading to wrinkles, skin laxity, telangiectasia, and uneven pigmentation. Exposing primary human fibroblasts to increasing intensities of UVB radiation results in a marked reduction in cell viability. Hydrogen treatment at various stages can mitigate UVB-induced inhibition of cell proliferation, enhance superoxide dismutase and catalase activity, and reduce lipid peroxidation products such as malondialdehyde and 8-isoprostanin 2α, thereby protecting cells and minimizing damage. Additionally, hydrogen pretreatment offers better protection than post-treatment.[73]

Kato et al[74] observed six healthy volunteers who consumed hydrogen-rich electrolyzed warm water (0.2–0.4 mg/L dissolved hydrogen, redox potential: −741 mV, 41°C) daily for 3 months. They found a significant reduction in neck and back wrinkles. This effect may be attributed to the effective removal of reactive oxygen species (ROS) by hydrogen, promoting type I collagen synthesis and inhibiting UVA-induced skin damage, suggesting that hydrogen-rich electrolyzed warm water could be a valuable addition to daily skincare.

Despite advancements in the application of molecular hydrogen in skin cosmetology, several challenges remain.[75] These include determining the optimal concentration, method of use, and long-term safety of hydrogen.[56,75] In addition, variations in skin types and the specific needs of different populations pose challenges for its widespread application.

Current Research and Future Directions for Hydrogen Therapy in Skincare

Current Research Status

Hydrogen therapy has garnered significant attention in skincare for its potent antioxidant and anti-inflammatory effects. Studies have shown that hydrogen can effectively reduce oxidative stress, decrease inflammation, and promote skin repair in conditions such as atopic dermatitis, psoriasis, and UV-induced skin damage.[6,76] Despite these positive findings, the research is still in its infancy, with variations in efficacy due to differing administration routes and dosages.

Key Challenges

Establishing the optimal dosage and delivery methods for hydrogen therapy remains a major challenge. Current studies employ various forms such as hydrogen-rich water, topical gels, and inhalation, but there is no consensus on the most effective approach for specific skin conditions. Additionally, the long-term safety of these treatments, particularly systemic applications, is under-explored. Furthermore, individual variability in skin type and condition complicates the development of standardized treatment protocols.[20,37]

Future Directions

Future research should focus on large-scale clinical trials to develop standardized protocols for hydrogen use in skincare. Investigating the molecular mechanisms of hydrogen, including its role in gene expression and cellular signaling during skin regeneration, will provide deeper insights into its therapeutic potential. Combining hydrogen therapy with other dermatological treatments, such as antioxidants or retinoids, may enhance its effectiveness. Moreover, advancements in delivery systems, such as nano-carriers and microneedle patches, could significantly improve hydrogen's stability and bioavailability, expanding its applications in both clinical and cosmetic dermatology.[77,78]

Conclusion

In conclusion, hydrogen is a gas molecule with significant biological activity, and its administration is a promising treatment option widely applied in disease prevention and the treatment of various systems, with no obvious toxic side effects observed. However, most current experiments are still limited in preliminary exploration in animal models and small-scale clinical trials. Research has mainly focused on the phenomenon of hydrogen's preventive and therapeutic effects, with limited investigation into its mechanism, which requires more in-depth study in the future.

Data Sharing Statement

All datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

This study wasn't involved in any ethic event.

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Disclosure

The authors declare that they have no competing interests.

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