

Hydrogen peroxide in dermatology

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Hydrogen peroxide (H₂O₂) is a reactive oxygen species produced by a variety of mammalian cells. It influences biological behaviour through several mechanisms which include alteration in cellular redox balance, changes in membrane potential or production of new molecules that regulate signalling transduction pathways.¹ Endogenous sources of hydrogen peroxide are the mitochondrial electron transport chain, enzymatic cellular reactions and respiratory burst in phagocytes. Ultraviolet light, ionising radiation, pollutants, chemotherapy and herbicides are its main exogenous sources.² Hydrogen peroxide can oxidatively damage proteins, lipids and nucleic acids directly or indirectly through the propagation of other reactive oxygen species.² Increased cellular hydrogen peroxide can overwhelm the antioxidant defence systems, contributing to the pathogenesis of dermatologic diseases. Topical hydrogen peroxide is used for therapeutic purposes at supraphysiologic concentrations.² This review discusses the pathogenic and therapeutic role of hydrogen peroxide in dermatology.

Role of hydrogen peroxide in the pathogenesis of skin diseases

Autoimmune connective tissue diseases

Environmental factors and genetically impaired free radical scavenging capacity cause increased cellular production of hydrogen peroxide. This results in lymphocyte apoptosis, glutathione depletion, impaired phagocytosis, increased autoantigen exposure and autoantibody formation. All these factors are implicated in the pathogenesis of systemic lupus erythematosus.³ Patients with systemic sclerosis express high levels of exhaled hydrogen peroxide which may indicate oxidative stress in the airways.⁴

Vitiligo and halo nevus

Elevated hydrogen peroxide was found in both serum and lesional skin of vitiligo patients. However, it was increased only in the lesions of patients with halo nevus but not in their serum. High hydrogen peroxide may increase CXCL10

expression resulting in CD8⁺ T-cell infiltration, leading to depigmentation in halo nevus and vitiligo.⁵

Photoaging and skin cancer

Dermal fibroblasts of sun-exposed skin have elevated hydrogen peroxide due to a decrease in catalase activity. Hydrogen peroxide-induced alteration in the mitogen-activated protein kinase pathway contributes to skin aging and photoaging.⁶ Ultraviolet B radiation can generate hydrogen peroxide in keratinocytes, which has a role in the formation of skin cancer due to its antiapoptotic effect.^{7,8}

Other dermatological diseases

Aquaporin-3-mediated hydrogen peroxide transport is required for nuclear factor-κB signalling in keratinocytes and the development of psoriasis.⁹ Hydrogen peroxide also has a role in the mediation of acne inflammation.¹⁰ Intrinsic deficiency of catalase in the hair bulb and bulge results in higher hydrogen peroxide levels, causing premature canities by the destruction of hair follicle melanocytes.¹¹ Macrophages and neutrophils in chronic widespread dermatophytosis patients had reduced *Trichophyton rubrum* phagocytic and killing abilities, and reduced hydrogen peroxide and nitric oxide release as compared to healthy donors.¹² Figure 1 summarises the pathogenic role of hydrogen peroxide in skin diseases.

Uses of hydrogen peroxide in dermatology

Low concentration hydrogen peroxide (1–6%)

Antimicrobial action

- Hydrogen peroxide acts as an antimicrobial against bacteria, fungi or viruses on open wounds or intact skin by the production of hydroxyl radicals which break down cell membranes and biofilms.^{13,14} Degradation of hydrogen peroxide to release oxygen, called effervescence, reduces pus and debris thereby reducing bacterial colonisation¹⁵
- Molluscum contagiosum in children has been treated effectively with 1.8% hydrogen peroxide gel applied twice daily for three weeks¹⁶

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- Mahran *et al.* reported the efficacy of 3% and 5% hydrogen peroxide solution in non-genital warts. Its antiviral effect is possibly mediated by apoptosis and membrane lipid peroxidation.¹⁷

Wound care

Hydrogen peroxide produced after cutaneous injury acts as a chemotactic signal.¹ It facilitates haemostasis by activating cell surface tissue factor, stimulating platelet aggregation and regulating endothelial cell contractility.¹⁸ It can also promote angiogenesis and tissue regeneration.¹⁹ For wound irrigation and disinfection, 3% hydrogen peroxide solution is commonly used. However, its use in wound care is limited as it may not decrease the bacterial burden and showed mixed results in clinical studies.²⁰ Venous ulcers treated by daily application of 1% lipid-stabilised hydrogen peroxide showed reduced ulcer area and improved microcirculation on laser doppler flowmetry.²¹

Hydrogen peroxide as a bleaching agent

Hair bleaching systems contain 3–6% hydrogen peroxide with ammonia.² Destructive oxidation of melanin by hydrogen peroxide in alkaline conditions forms the basis of cosmetic hair bleaching. Ferric and cupric ions in hair fibre may lead to Fenton or Fenton-like reactions, which decompose hydrogen peroxide during bleaching. This results in the generation of reactive oxygen species such as hydroxyl radicals, perhydroxyl radicals and superoxide anions.²²

Hydrogen peroxide in hair dyes

Semi-permanent and permanent hair dyes have 2% and 6% hydrogen peroxide, respectively. Hydrogen peroxide and para dyes combine in an oxidation reaction liberating oxygen. The primary intermediates enter the cortex and combine with couplers to produce the desired colour molecules.²³

Anti-acne effect of hydrogen peroxide

Milani *et al.* observed the therapeutic effect of 1% hydrogen peroxide cream used twice daily in acne for eight weeks. Hydrogen peroxide reduced the total lesions, inflammatory lesions as well as comedones. It acts by reducing cutibacterium

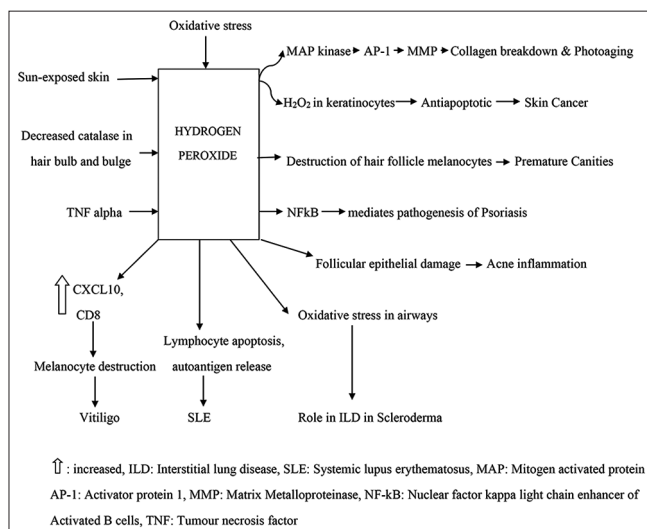


Figure 1: Schematic diagram showing the pathogenetic role of H₂O₂ in skin diseases

acnes colonisation and was as effective as benzoyl peroxide with a better tolerability profile.^{24,25}

Use of hydrogen peroxide in photodynamic therapy

About 1% hydrogen peroxide cream increased the photodynamic reaction during photodynamic therapy for cutaneous malignancies.²⁶

Hydrogen peroxide as a radiosensitiser

Intratumoral injection of 3% hydrogen peroxide and sodium hyaluronate administered weekly before radiation had radiosensitising effect on non-superficial neoplasms.²⁷ For superficial non-resectable neoplasms, 3% hydrogen peroxide soaked gauze was applied to the tumour after electron beam radiation. Hydrogen peroxide may increase the efficacy of radiation by increasing the synthesis of reactive oxygen species.²⁸

High concentration hydrogen peroxide

As neoadjuvant in excision of non-melanoma skin cancers

Cervicofacial non-melanoma skin cancers were treated with 33% hydrogen peroxide solution. The solution was applied with a cotton tip applicator till blanching was observed. A statistically significant decrease in the size of skin malignancies such as squamous and basal cell carcinoma was observed with a single application of the chemical. This led to simpler excisions and reduced need for flap reconstruction or skin grafting.²⁹ The action of hydrogen peroxide can be explained by the Warburg effect which refers to increased susceptibility of malignant cells to oxidative stress due to a shift from oxidative to glycolytic metabolism.³⁰

Seborrhoeic keratosis

Food and drug administration (FDA) has approved 40% hydrogen peroxide solution for the treatment of seborrhoeic keratosis.³¹ It presumably causes cell death by causing oxidative damage to cells.³² It is applied to the lesion four times, one minute apart and the unit dose applicator is discarded after use. Retreatment can be done at three weeks for lesions that do not improve.³¹

Actinic keratosis

Sulindac gel combined with 25% hydrogen peroxide was applied daily for three weeks on lesions of actinic keratosis. Six out of ten lesions demonstrated a partial or complete reduction in size.³³

Pregnancy and lactation

Hydrogen peroxide when applied topically is not absorbed systemically. It is not expected to result in the exposure of the foetus or breastfeeding infant to the drug.³¹

Adverse Effects

Low hydrogen peroxide concentrations cause transient symptoms such as erythema, burning, hypopigmentation, blanching, paraesthesia and blistering.^{16,17,34} High concentrations are known to result in concentration and length-dependent effects which in addition include vesiculation, erosion, crusting, hypopigmentation, hyperpigmentation and scarring.^{2,31} High concentrations used to bleach hair can cause chemical burns.³⁵ Fatal oxygen embolism due to wound irrigation has been reported.³⁶ Inhalation of highly concentrated solutions can cause irritation and inflammation of the mucosa with coughing and dyspnoea.³⁷ Ocular exposure may cause immediate stinging, lacrimation and blurred vision.³⁸

Conclusion

Hydrogen peroxide regulates multiple signalling transduction pathways and can even trigger autoimmunity, thereby influencing the pathogenesis of numerous skin diseases. It also has a therapeutic role when used topically at supraphysiologic concentrations and is a new, promising and cost-effective alternative in a variety of dermatological conditions.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

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