

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

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

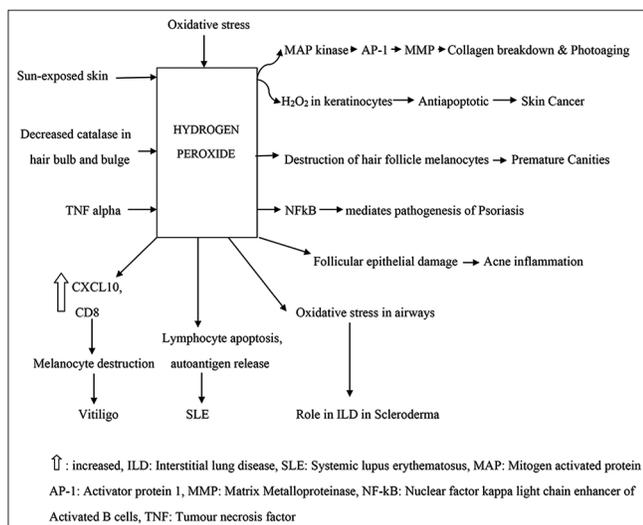


Figure 1: Schematic diagram showing the pathogenetic role of H₂O₂ in skin diseases

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.

References

- Zhu G, Wang Q, Lu S, Niu Y. Hydrogen peroxide: A potential wound therapeutic target? *Med Princ Pract* 2017;26:301-8.
- Murphy EC, Friedman AJ. Hydrogen peroxide and cutaneous biology: Translational applications, benefits, and risks. *J Am Acad Dermatol* 2019;81:1379-86.
- Pravda J. Systemic lupus erythematosus: Pathogenesis at the functional limit of redox homeostasis. *Oxid Med Cell Longev* 2019;2019:1651724.
- Łuczyńska M, Szkudlarek U, Dziańkowska-Bartkowiak B, Waszczykowska E, Kasielski M, Sysa-Jedrzejowska A, *et al.* Elevated exhalation of hydrogen peroxide in patients with systemic sclerosis. *Eur J Clin Invest* 2003;33:274-9.
- Yang Y, Li S, Zhu G, Zhang Q, Wang G, Gao T, *et al.* A similar local immune and oxidative stress phenotype in vitiligo and halo nevus. *J Dermatol Sci* 2017;87:50-9.
- Shin MH, Rhie GE, Kim YK, Park CH, Cho KH, Kim KH, *et al.* H₂O₂ accumulation by catalase reduction changes MAP kinase signaling in aged human skin *in vivo*. *J Invest Dermatol* 2005;125:221-9.
- Masaki H, Sakurai H. Increased generation of hydrogen peroxide possibly from mitochondrial respiratory chain after UVB irradiation of murine fibroblasts. *J Dermatol Sci* 1997;14:207-16.
- Ibuki Y, Akaike M, Toyooka T, Mori T, Nakayama T, Goto R. Hydrogen peroxide is critical for UV-induced apoptosis inhibition. *Redox Rep* 2006;11:53-60.
- Hara-Chikuma M, Satooka H, Watanabe S, Honda T, Miyachi Y, Watanabe T, *et al.* Aquaporin-3-mediated hydrogen peroxide transport is required for NF-κB signalling in keratinocytes and development of psoriasis. *Nat Commun* 2015;6:7454.
- Akamatsu H, Horio T, Hattori K. Increased hydrogen peroxide generation by neutrophils from patients with acne inflammation. *Int J Dermatol* 2003;42:366-9.
- Shi Y, Luo LF, Liu XM, Zhou Q, Xu SZ, Lei TC. Premature graying as a consequence of compromised antioxidant activity in hair bulb melanocytes and their precursors. *PLoS One* 2014;9:e93589.
- de Sousa Mda G, Santana GB, Criado PR, Benard G. Chronic widespread dermatophytosis due to *Trichophyton rubrum*: A syndrome associated with a *Trichophyton*-specific functional defect of phagocytes. *Front Microbiol* 2015;6:801.
- Richardson BW. On the introduction of peroxide of hydrogen as a medicine. *Lancet* 1866;87:300.
- Richardson BW. On peroxide of hydrogen, or ozone water, as a remedy. *Lancet* 1891;137:707-9.
- Rodeheaver GT. Wound cleansing, wound irrigation, wound disinfection. In: Krasner DL, Rodeheaver GT, Sibbald RG, Woo KY, editors. *Chronic Wound Care: A Clinical Source Book for Healthcare Professionals*. 2nd ed. Wayne, PA: Health Management Publications, Inc.; 1997. p. 97-108.
- Schianchi R, Nazzaro G, Veraldi S. Treatment of molluscum contagiosum with hydrogen peroxide. *Clin Exp Dermatol* 2018;43:66-7.
- Mahran AM, Twisy HO, Elghazally SA, Badran AY. Evaluation of different concentrations of hydrogen peroxide solution (3% and 6%) as a potential new therapeutic option of non-genital warts: A randomized controlled triple-blinded clinical trial. *J Cosmet Dermatol* 2020;19:416-22.
- Sen CK, Roy S. Redox signals in wound healing. *Biochim Biophys Acta* 2008;1780:1348-61.
- Loo AE, Wong YT, Ho R, Wasser M, Du T, Ng WT, *et al.* Effects of hydrogen peroxide on wound healing in mice in relation to oxidative damage. *PLoS One* 2012;7:e49215.
- Lau WY, Wong SH. Randomized, prospective trial of topical hydrogen peroxide in appendectomy wound infection. High risk factors. *Am J Surg* 1981;142:383-97.
- Belcaro G, Cesarone MR, Nicolaidis AN, Geroulakos G, di Renzo A, Milani M, *et al.* Improvement of microcirculation and healing of free venous hypertension and ulcers with Crystacide. Evaluation of free radicals, laser Doppler flux and PO₂. A prospective-randomized-controlled study. *Angiology* 2003;54:325-30.
- Smith RA, Garrett B, Naqvi KR, Fülöp A, Godfrey SP, Marsh JM, *et al.* Mechanistic insights into the bleaching of melanin by alkaline hydrogen peroxide. *Free Radic Biol Med* 2017;108:110-7.
- Madhani N, Khan K. Hair cosmetics. *Indian J Dermatol Venereol Leprol* 2013;79:654-67.
- Veraldi S, Micali G, Berardesca E, Dall'Oglio F, Sinagra JL, Guanziroli E. Results of a multicenter, randomized, controlled trial of a hydrogen peroxide-based kit versus a benzoyl peroxide-based kit in mild-to-moderate acne. *J Clin Aesthet Dermatol* 2016;9:50-4.
- Milani M, Bigardi A, Zavattarelli M. Efficacy and safety of stabilised hydrogen peroxide cream (Crystacide) in mild-to-moderate acne vulgaris: A randomised, controlled trial versus benzoyl peroxide gel. *Curr Med Res Opin* 2003;19:135-8.
- Manifold RN, Anderson CD. Increased cutaneous oxygen availability by topical application of hydrogen peroxide cream enhances the photodynamic reaction to topical 5-aminolevulinic acid-methyl ester. *Arch Dermatol Res* 2011;303:285-92.
- Ogawa Y, Kubota K, Ue H, Kataoka Y, Tadokoro M, Miyatake K, *et al.* Phase I study of a new radiosensitizer containing hydrogen peroxide and sodium hyaluronate for topical tumor injection: A new enzyme-targeting radiosensitization treatment, kochi oxydol-radiation therapy for unresectable carcinomas, Type II (KORTUC II). *Int J Oncol* 2009;34:609-18.
- Ogawa Y, Ue H, Tsuzuki K, Tadokoro M, Miyatake K, Sasaki T, *et al.* New radiosensitization treatment (KORTUC I) using hydrogen peroxide solution-soaked gauze bolus for unresectable and superficially exposed neoplasms. *Oncol Rep* 2008;19:1389-94.
- Mundi N, Jordan K, Doyle P, Moore C. 33% hydrogen peroxide as a neo-adjuvant treatment in the surgical excision of non-melanoma skin cancers: A case series. *J Otolaryngol Head Neck Surg* 2020;49:33.
- Liberti MV, Locasale JW. The Warburg effect: How does it benefit cancer cells? *Trends Biochem Sci* 2016;41:211-8.
- Hydrogen peroxide 40% (Eskata) for seborrheic keratoses. *JAMA* 2019;321:99-100.
- DuBois JC, Jarratt M, Beger BB, Bradshaw M, Powala CV, Shanler SD. A-101, a proprietary topical formulation of high-concentration hydrogen peroxide solution: A randomized, double-blind, vehicle-controlled, parallel group study of the dose-response profile in subjects with seborrheic keratosis of the face. *Dermatol Surg* 2018;44:330-40.
- Resnick L, Rabinovitz H, Binnering D, Marchetti M, Weissbach H. Topical sulindac combined with hydrogen peroxide in the treatment of actinic keratoses. *J Drugs Dermatol* 2009;8:29-32.
- Dickson KF, Caravati EM. Hydrogen peroxide exposure-325 exposures reported to a regional poison control center. *J Toxicol Clin Toxicol* 1994;32:705-14.
- Maguina P, Shah-Khan M, An G, Hanumadass M. Chemical scalp burns after hair highlights. *J Burn Care Res* 2007;28:361-3.
- Beattie C, Harry LE, Hamilton SA, Burke D. Cardiac arrest following hydrogen peroxide irrigation of a breast wound. *J Plast Reconstr Aesthet Surg* 2010;63:e253-4.
- Watt BE, Proudfoot AT, Vale JA. Hydrogen peroxide poisoning. *Toxicol Rev* 2004;23:51-7.
- Pandit RT, Farjo AA, Sutphin JE. Iatrogenic corneal and conjunctival toxic reaction from hydrogen peroxide disinfection. *Arch Ophthalmol* 2003;121:904-6.