A Study on the Multidimensional Effects of Hydrogen-Rich Materials in Wound Healing and the Alleviation of Skin Fibrosis

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Background:

Wound healing disorders and skin fibrotic lesions (e.g., keloids) are complex clinical challenges often leading to functional impairments. Hydrogen-rich materials, known for their antioxidant, anti-inflammatory, and metabolic regulatory properties, have emerged as promising therapeutic agents. This study evaluates the effects and molecular mechanisms of hydrogen-rich saline (HRS) and hydrogen-rich water (HRW) in wound repair and scar management.

Methods:

Animal Model: A full-thickness skin defect model was created in rabbits, divided into five groups: control, saline, HRS, VSD+saline, and VSD+HRS. Wound healing was assessed via closure rate and histopathological evaluation.

Cell Experiment: Human keratinocyte HaCaT cells were used in vitro to evaluate cell viability.

Metabolomics Analysis: Wound tissue samples underwent untargeted metabolomics analysis to identify differential metabolites and oxidative stress markers.

Clinical Trial: A double-blind randomized controlled trial involved 21 keloid patients, randomized into HRW (11 patients) and control groups (10 patients). Cytokine expression levels and keloid appearance were assessed using Western blotting, qPCR, ELISA, and the Vancouver Scar Scale (VSS).

Ethical Approval: The animal study protocol was approved by the Ethics Committee of Peking Union Medical College Hospital (Approval No.: XHDW-2023-063), and the clinical study passed ethical review (Review No.: ZS-3373). All participants provided informed consent.

Results:

Animal Experiment: The VSD+HRS group showed significantly higher wound healing rates and shorter closure time ($p < 0.05$). HE staining revealed superior epidermal regeneration and granulation tissue formation.

Cell Viability: The VSD+HRS group exhibited significantly higher HaCaT cell viability ($p<0.05$).
Metabolomics Analysis: Forty-five differential metabolites were identified, with biotin metabolism pathways emerging as potential targets.
Oxidative Stress: VSD+HRS treatment reduced local oxidative stress in wound tissues.
Clinical Trial: HRW significantly reduced postoperative pain and pruritus frequency ($p<0.05$) and improved VSS and pigmentation scores ($p<0.05$).
Molecular Mechanisms: HRWT downregulated TRPV1 and HIF-1α expression ($p<0.05$) and upregulated anti-inflammatory IL-10 ($p=0.003$), while pro-inflammatory factors IL-6, TGF-β, and VEGF decreased ($p=0.030$, $p=0.002$, and $p=0.063$).

Conclusion:
Hydrogen-rich materials show therapeutic potential in wound healing and keloid management. HRS combined with VSD accelerates wound closure, while HRW therapy alleviates pruritus and promotes inflammation resolution. These findings provide scientific support for the application of hydrogen-rich materials in wound management and skin fibrosis treatment, though further optimization and mechanistic validation are needed.