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EDITORIAL

Beyond Corticosteroids: Reconsidering the Role of Evidence-Based Herbal Medicine in Radiation-Induced Dermatitis

Shakiba Javadi

Radiation oncologist, Department of Radiation-Oncology, Faculty of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran.

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Dear Editor

Radiotherapy remains one of the most effective treatment modalities for breast cancer, substantially improving local control and survival across both early-stage and locally advanced disease. Despite remarkable advances in treatment planning, image-guided radiotherapy, moderate hypofractionation, and intensity-modulated techniques, radiation-induced dermatitis (RID) continues to affect most women receiving breast irradiation, with clinically significant (grade ≥2) reactions occurring in approximately one-quarter of patients. Although RID is usually self-limiting, it may compromise quality of life, treatment adherence, cosmetic outcomes, and healthcare utilization, underscoring the importance of effective supportive care in modern radiation oncology [1-8].

Current international guidelines, including those of the Multinational Association of Supportive Care in Cancer (MASCC), recommend gentle skin care, topical corticosteroids, barrier films, and selected silicone-based dressings for the prevention of acute RID [9, 10]. However, no single intervention has consistently demonstrated complete protection against radiation dermatitis, and considerable variability in treatment response persists across patient populations and radiotherapy techniques. This therapeutic gap highlights the need to explore additional evidence-based preventive strategies.

Contemporary understanding of radiation biology indicates that RID is a multifactorial process extending far beyond direct epidermal injury. Ionizing radiation initiates DNA damage and excessive production of reactive oxygen species, triggering activation of NF-κB, MAPK, and transforming growth factor-β signaling pathways, endothelial dysfunction, inflammatory cytokine release, extracellular matrix remodeling, and impaired tissue regeneration [11-14]. Because these mechanisms occur simultaneously, interventions capable of modulating multiple biological pathways may provide greater therapeutic benefit than agents targeting a single molecular process.

Within this context, interest in medicinal plants has increased considerably. Many botanical compounds including polyphenols, flavonoids, tannins, phenolic acids, and bioactive polysaccharides possess antioxidant, anti-inflammatory, antimicrobial, and wound-healing properties that closely correspond to the biological mechanisms involved in RID [15-18]. Importantly, reconsidering herbal medicine should not be interpreted as endorsing empirical or unregulated therapies. Rather, advances in pharmacognosy, phytochemistry, and pharmaceutical sciences now permit the development of standardized botanical preparations with reproducible concentrations of active constituents, enabling rigorous clinical evaluation comparable to that required for conventional pharmacological agents.

Among the botanical candidates, pomegranate peel has attracted particular attention because of its high concentrations of punicalagin, ellagic acid, gallic acid, and hydrolyzable tannins. Experimental studies have demonstrated potent antioxidant activity through reactive oxygen species scavenging and activation of the Nrf2/HO-1 pathway, together with suppression of NF-κB-mediated inflammatory signaling. These effects are associated with enhanced keratinocyte survival, improved collagen synthesis, and accelerated wound healing. Similarly, medical-grade honey has shown broad biological activity through antimicrobial effects, modulation of inflammation, promotion of angiogenesis, stimulation of fibroblast proliferation, and maintenance of an optimal wound-healing environment. Other traditional agents, including alum and Quercus infectoria (Mazoo), have received considerably less investigation but possess biological characteristics including high tannin content, astringent activity, and anti-inflammatory properties that

Corresponding Author:
Dr. Shakiba Javadi
Radiation oncologist, Department of Radiation-Oncology, Faculty of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran.
Email: Shakibaa89@gmail.com

justify further mechanistic and clinical evaluation.

Despite this encouraging biological rationale, current evidence remains insufficient to support routine clinical implementation. Most published studies are limited by small sample sizes, heterogeneous botanical formulations, inconsistent characterization of active constituents, inadequate blinding, and variability in toxicity assessment. Consequently, existing international guidelines appropriately refrain from recommending routine use of most herbal interventions until higher-quality clinical evidence becomes available [9, 10].

Equally important, herbal products should not be assumed to be inherently safe simply because they are natural. Batch-to-batch variability, differences in extraction methods, potential allergic reactions, herb–drug interactions, and inconsistent manufacturing quality remain important challenges. Therefore, future investigations should evaluate both efficacy and safety using chemically characterized botanical preparations manufactured according to Good Manufacturing Practice, together with standardized toxicity grading systems, validated patient-reported outcomes, and mechanistic biomarkers.

Future research should move beyond isolated evaluation of individual botanical products toward integrated, mechanism-based supportive care strategies. Rational combinations of complementary agents targeting oxidative stress, inflammation, microbial control, and tissue regeneration may prove more effective than single-compound interventions. Large multicenter randomized controlled trials incorporating standardized formulations and biomarker-guided patient stratification will be essential to determine whether selected natural products can complement established preventive approaches.

Supportive oncology has progressively evolved from symptom management toward mechanism-based prevention of treatment-related toxicity. Herbal medicine should be subjected to the same scientific standards as any other therapeutic intervention. Rather than asking whether natural products should replace established therapies, future research should determine whether standardized, evidence-based botanical preparations can safely complement current supportive care and improve outcomes for women undergoing breast radiotherapy.

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