

The Emerging Role of Quercetin in the Treatment of Diabetic Foot Ulcers

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Dear Editor,

Diabetic Foot Ulcers (DFU) are the leading cause of non-traumatic lower extremity amputations, placing a huge burden on the entire healthcare system and significantly reducing patient's quality of life (Yarahmadi *et al.*, 2021). Despite many efforts to address this issue and treat patients suffering from DFU, there is no satisfactory treatment that can prevent long-term complications of DFU (Hu *et al.*, 2025). Wound healing is a process involving many intricate signaling pathways that occur upon tissue damage (Yarahmadi *et al.*, 2021). Wound healing is divided in four well-organized phases named homeostasis, inflammation, proliferation and remodeling (Yarahmadi *et al.*, 2021). In DFU, into these four phases of wound healing are disrupted mainly due to inflammation and oxidative stress resulting from the long-term hyperglycemia of diabetes (Yarahmadi *et al.*, 2021).

Recently, there has been growing evidence showing the potential use of natural polyphenol compounds in the treatment of DFU (Hagde, *et al.*, 2022). One of these well-studied polyphenolic compounds is quercetin (Hagde, *et al.*, 2022). It has been shown that quercetin has various pharmacological effects in body such as antioxidant, anti-inflammatory, angiogenesis, antimicrobial and immunomodulatory effects which is of importance in wound healing process (Hagde, *et al.*, 2022; Yarahmadi *et al.*, 2017).

Previous studies have shown that quercetin can modulate the high oxidative stress and inflammation in the body through its strong antioxidant and anti-inflammatory effects (Askari *et al.*, 2012). Furthermore, one of the major challenges in the treatment of DFU is that wounds in these patients, especially chronic ones, remain in the inflammatory phase due to defects in macrophage polarization (Zhou *et al.*, 2024). The balance of M1 and M2 macrophages is critical for normal wound healing (Zhou *et al.*, 2024). It is more likely that in DFU, more macrophages remain in the pro-inflammatory M1 form and prevent from the normal wound healing process (Zhou *et al.*, 2024). Thus, modulating the immune system response and reducing the high inflammation associated with DFU via quercetin may help to achieve faster and more efficient wound healing in these patients (Fu *et al.*, 2020).

Interestingly, recent studies have reported promising results showing that quercetin demonstrates a suitable antimicrobial effect against the

most common bacteria found in wounds, including *Staphylococcus Aureus* and *Pseudomonas aeruginosa* (Almuhanna *et al.*, 2024; Najim *et al.*, 2024).

Considering the increasing number of patients with diabetes and its complications, including DFU, and due to the extensive potential of quercetin in wound healing process at the cellular and molecular level, it seems that it might be a good candidate for future studies to better demonstrate its possible clinical application in the treatment of DFU.

CONFLICT OF INTEREST

The author declares that there is no conflict of interest.

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