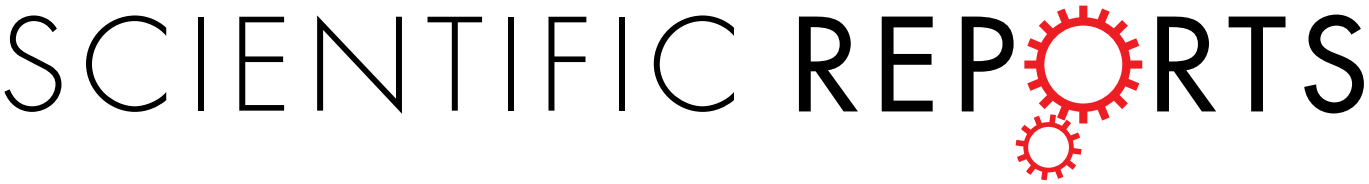

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Additive enhancement of wound healing in diabetic mice by low level light and topical CoQ10

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Diabetes, a highly prevalent disease that affects 9.3% of Americans, often leads to severe complications and slow wound healing. Preclinical studies have suggested that low level light therapy (LLLT) can accelerate wound healing in diabetic subjects, but significant improvements must be made to overcome the absence of persuasive evidence for its clinical use. We demonstrate here that LLLT can be combined with topical Coenzyme Q10 (CoQ10) to heal wounds in diabetic mice significantly faster than LLLT alone, CoQ10 alone, or controls. LLLT followed by topical CoQ10 enhanced wound healing by 68~103% in diabetic mice in the first week and more than 24% in the second week compared with untreated controls. All wounds were fully healed in two weeks following the dual treatment, in contrast to only 50% wounds or a fewer being fully healed for single or sham treatment. The accelerated healing was corroborated by at least 50% higher hydroxyproline levels, and tripling cell proliferation rates in LLLT and CoQ10 treated wounds over controls. The beneficial effects on wound healing were probably attributed to additive enhancement of ATP production by LLLT and CoQ10 treatment. The combination of LLLT and topical CoQ10 is safe and convenient, and merits further clinical study.

There are an estimated 371 million cases of diabetes worldwide, putting patients at serious risk for wound healing complications that reduce both quality and length of life. In particular, foot ulcers hamper 15% of all diabetics, accounting for the majority of non-traumatic lower limb amputations in the United States[1]. These complex wounds result from a combination of diminished immune function, peripheral neuropathy, arterial occlusion, and miscellaneous factors such as limited joint mobility and improper footwear[1–3]. Small sores are readily healed in healthy individuals but frequently develop into deep ulcers, leading to infections of underlying tissues and bones that sometimes necessitate amputation in diabetic patients. Treatment of these chronic wounds in diabetic patients mainly relies on conventional wound bed preparation, mechanical and surgical debridement, and antibiotic therapy to battle infections[4,5]. However, these managements have extremely limited efficacy, leading to a high 5-year mortality rate following amputation[6].

Considering the toll on patients and $11 billion cost to American health care payers[7], there is a substantial demand for better approaches to diabetic wound management. The potential of low-level laser therapy (LLLT), a non-invasive treatment that some studies have shown to successfully accelerate wound healing in specific circumstances, is particularly attractive[8]. LLLT does not cause a noticeable temperature change in subjects, yet seems to stimulate tissue repair and relieve pain[8–10]. While their efficacy in clinical settings has long been disputed[11], an increasing number of studies have contended that LLLT can increase fibroblast proliferation, collagen production, angiogenesis, granulation formation, and other positive effects[12]. As for diabetes specifically, a study proved that 633nm laser at 10 J/cm^2 accelerated wound healing in diabetic rats by ~38%[1]. Systematic reviews have been hindered by lack of adequate sample sizes and consistent methodologies in clinical studies, but demonstrate plausibility and safety of using LLLT to treat diabetic wounds[2].

Therapeutic mechanisms of LLL are not well understood to date. Considering that thermal increases are absent following LLLT, photobiomodulation may be the major contributor of the reported acceleration in tissue repair[8,12,13]. For example, one event suspected to contribute significantly to wound healing is the absorption of far red or near infrared light (600–1100 nm) by the redox active metal centers of cytochrome c oxidase, also known as complex IV of the electron transport chain at mitochondria[12]. Such absorption is thought to increase

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