



Quercetin and low level laser therapy promote wound healing process in diabetic rats *via* structural reorganization and modulatory effects on inflammation and oxidative stress



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ABSTRACT

This study aimed to evaluate the effect of quercetin and the photo-stimulatory effect of low energy 632.8 nm laser irradiation on excisional wound healing in non-diabetic and diabetic rats. Streptozotocin (45 mg/kg body weight) was intraperitoneally applied for diabetes induction. A full-thickness skin wound ($2 \times 2 \text{ cm}^2$) was aseptically created with a scalpel in non-diabetic and diabetic rats on the shaved back of the animals. The wounded non-diabetic and diabetic rats were treated every other day with quercetin by oral gavage at dose 25 mg/kg body weight and/or with low level laser therapy (LLLT) for 14 days. The wound closure percent calculated during the course of the experiment at days 1, 7 and 14 was remarkably increased as a result of treatment of non-diabetic and diabetic wounded rats with quercetin and LLLT; the treatment with both was the most potent. The elevated blood glucose and the lowered serum insulin levels were significantly improved in diabetic wounded rats treated with quercetin and LLLT as compared to the diabetic wounded control. The histological findings indicated that the wounded skin showed a marked increase in collagen fibers which become well oriented in sub-epidermal tissue, intact epidermis and presence of hyperplasia covering well-developed granulation tissue in the wounded rats treated with quercetin and LLLT as compared to the corresponding wounded control. The elevated levels of serum pro-inflammatory cytokines, IL-1 β and TNF- α , as well as PGE-2 and LTB-4 were decreased in non-diabetic and diabetic wounded rats with quercetin and LLLT while the lowered level of serum anti-inflammatory cytokine, IL-10, was increased. The augmented oxidative stress represented by increased serum lipid peroxides level was decreased and the serum level of non-enzymatic anti-oxidant glutathione was increased as a result of treatment with quercetin and LLLT. Thus, it can be suggested that the improvements in glycemic state, cytokines involved in inflammation and antioxidant defense system as well as structural reorganization after treatment with quercetin and LLLT may play pivotal roles in promoting the wound healing process. The study also concluded that the treatment with quercetin in association with LLLT was better in improving wound healing in non-diabetic and diabetic rats than the use of either of each.

1. Introduction

Wounds are major cause of physical disabilities [1]. Current estimates indicate that nearly 6 million people suffer from chronic wounds worldwide [2]. A wound which is disturbed state of tissue is caused by chemical, physical, microbial or immunological insults or typically associated with loss function [3]. According to the wound healing society, wounds are physical injuries that results in an opening or break of the

skin that cause disturbance in the normal skin function and anatomy [4].

Diabetes mellitus (DM) is a complex metabolic chronic disorder involving many organs and tissues and continue to devastate the lives of affected individuals [5]. Impaired wound healing is one of complications of DM and it is a serious problem in clinical practice [6]. It was estimated that 15% of individuals with DM will develop foot ulceration and wounds, and 3% will require lower-extremity amputation [7]. In

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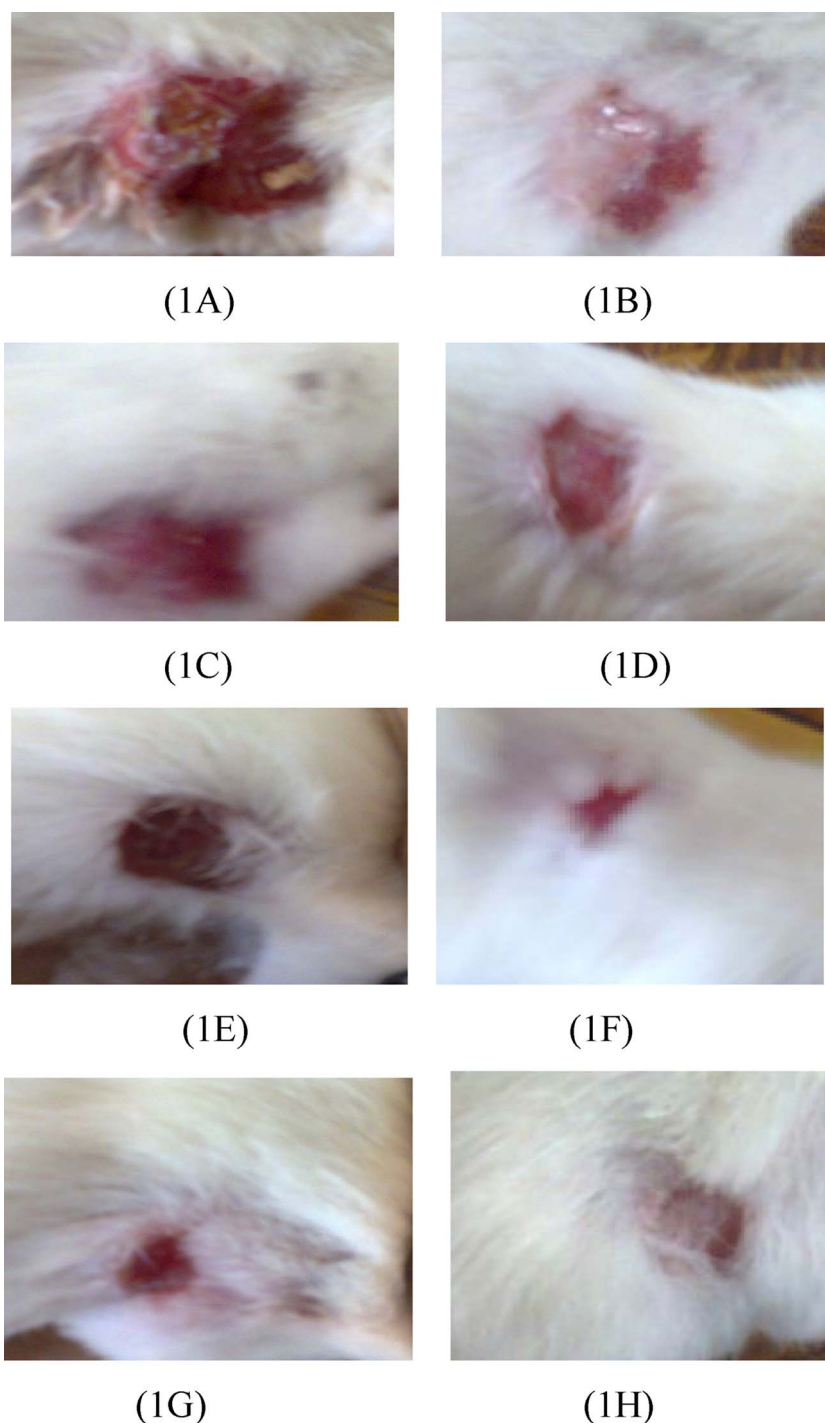


Fig. 1. Photographs showing wound healing and wound closure in untreated and treated non-diabetic wounded rats. 1A: wound at the 7th day in untreated non-diabetic rat. 1B: wound at the 14th day in untreated non-diabetic rat. 1C: wound at the 7th day in non-diabetic wounded rat treated with quercetin. 1D: wound at the 14th day in non-diabetic wounded rat treated with quercetin. 1E: wound at the 7th day in non-diabetic wounded rat treated with LLLT. 1F: wound at the 14th day in non-diabetic wounded rat treated with LLLT. 1G: wound at the 7th day in non-diabetic wounded rat treated with quercetin and LLLT. 1H: wound at the 14th day in non-diabetic wounded rat treated with quercetin and LLLT.

addition, an increased incidence of wound complications in surgical patients with DM increases the general surgical risks due to the metabolic abnormalities associated with DM [8]. In our previous publication, it was demonstrated that although DM slows wound healing, daily administration of natural product, camel whey protein, after wounding hastens wound closure in both diabetic and non-diabetic rats [9].

It has been found that more than 80% of the world population is dependent on the drugs from natural origin for the treatment of skin related problems [10]. Many of the synthetic drugs are associated with problems like drug resistance, allergy and other side effects making the

scientists to seek alternative drugs [11]. Natural healing process of wound management involves disinfection, debridement and providing a moist environment [9], thereby hastening the healing process. Plant based therapy not only accelerates wound healing process but also maintains the aesthetics in a natural way [12]. More than 70% of wound healing pharmaceutical products are derived from plants, 20% are mineral based and the remaining are animal-derived products [13]. Plant-derived materials are used as first aid-antiseptic coagulants and wound wash [2]. In recent times, focus on plant researches has increased all over the world and large body of evidence has collected to

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