Volume 10, Issue 07, July 2024,
Publish Date: 24-07-2024
Doi https://doi.org/10.55640/ijmsdh-10-07-03

International Journal of Medical Science and Dental Health (Open Access)

THE POTENTIAL OF CROCUS SATIVUS IN THE TREATMENT OF BURNS—MINI REVIEW

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ABSTRACT

This article under review summarizes clinical and animal model studies that prove the potential of ingredients of saffron including safranal, crocetin and crocin's extracts and their admixtures in treating of burn wound because of treating of burns still a receive attention in contemporary medicine, notably in developing nations that cannot supply costly and progressive medicines. Reviews presented in databases such as Google Scholar, Scopus, Pub-Med, Web of Science and Science Direct, published in English in 2008–2022, were considered. According to medical trials which described, it was shown that saffron extracts have notable effectiveness in treating of burn wounds, including reducing inflammation and speeding up the healing process than the conventional treatment used hitherto. This current review emphasis on the aspect of the main active compounds of saffron, on healing burn and the mechanisms investigated by researchers in treating. Researches on animal pattern indications that saffron preparation may have potential beneficial in the treatment burn wounds. According to antibacterial activity, mechanism of action, low toxicity and mild cost, saffron extracts can compete with conventional treatment.

INTRODUCTION

Tissue damage carried out by flam, electricity, radiation, chemical materials, etc. is defined as burn. Consistent with the complexity of damage, burn wounds are classified as full-thickness, partial thickness and superficial [(1)]. Healing of burn wound consider a difficult process begin with inflammation, re-epithelialization that start after injury in hours, repossession of the extracellular matrix, neovascularization which connect to extracellular matrix in the base of wound, furthermore immigration and activation of mitogenic of endothelial cells and contraction of wound as a consequence of interaction among cells, extracellular matrix and cytokines[(2)(3)]. Drugs of current medicaments are reported to be operative on both typical and injured skin in approximately (1-3%); In contrast to nearly, one to third of herbal medicines are for such use [(4)]. Since ancient times, ointments and poultices were deemed as current forms of herbal medicine that have been used. Medicinal plants act as wound medicinal agents because of their contain of different active ingredients like phenolic compounds, alkaloids, fatty acids, saponins, flavonoids, terpenoids, tannins and essential oils, which are confirm ability to healing of burn wound, as well as other advantages of herbal remedies like affordable,

abundance and fewer side effects. In these years, detect and isolate the active components from remedial plants that accountable for wound healing properties are getting world attention. Saffron represent a good example of plant category used as herbal treatment of burn wounds [5][6][7].

Saffron, scientifically known as Crocus sativus (C. sativus), it's from Iridaceae family, saffron is mainly produced and grown in Turkey Iran, Morocco, Greece, India and Spain. The growth cycle of saffron takes 220 days at least; summer and autumn are the top seasons for its growth. Saffron is usually utilize as a spice, food flavour, as well as for numerous medicinal purposes. Saffron has been used as flatulence, diaphoretic, aphrodisiac, appetizer, sedative, antispasmodic, carminative, tranquilizer, expectorant and eupeptic. C.sativus displayed numerous pharmacological properties such as antidiabetic, cardioprotective, immunomodulatory, anticancer, analgesic, antiatherogenic, antimicrobial and antioxidant. The therapeutic properties of saffron may be belong to its constituents, such as crocin, safranal and crocetin, which are consider the main biologically active compounds [8][9].

Phytochemical Components of Saffron

Saffron main constituents are nitrogenous compounds, water, anthocyanins, monoterpenes, glycosides, aldehydes, flavonoids, vitamins (in particular , thiamine and riboflavin and little amounts of β-carotene), proteins, , amino acids ,volatile oil, minerals, carbohydrates, gums and raw fibers.Also, in the bulbs petroleum ether extract, linolenic , linoleic and essential fatty acids, are present .Sterols(stigmasterol, β-sitosterol and camp sterol) plus oleanolic, palmitic, ursolic, oleic acids and palmitoleic. Moreover, the products of bio oxidative cleavage of zeaxanthin (picrocrocin and apocarotenoids) compounds like crocin, safranal, crocetin are found [10].

Three main biologically active compounds are

1. Crocin($C_{44}H_{64}O_{24}$): a carotenoid glycoside which give the orange - yellow pigment of the spice. Crocin is consist of a crocetin-di-gentiobiose ester ($C_{20}H_{24}O_4$), with a β-glyosidic bond which can be hydrolyzed by emulsine (beta glucosidase). Crocetin (the aglycon of crocin) is responsible for the antioxidant properties of Crocin due to its chemical structure. Because of the ability crocetin of to rise the speed and diffusivity of oxygen transport in vivo and vitro, crocin have been attributed most compound have remarkable effects of saffron what makes crocetin beneficial therapeutic applicant in many medical conditions [11] [12].
2. Picrocrocin: responsible for bitter taste and the flavor of saffron. Picrocrocin have ability to convert into volatile compound known as safranal by hydrolysis in water [13].
3. Safranal: cyclical terpenic-aldehyde. Safranal is made from volatile element in percentage70%, so it's mostly responsible for the smell of saffron. Because of picrocrocin is resistant to demolition, odor on the fresh stigmata is absent. The characteristic aroma appears during the storage stage and drying of saffron [14].

MATERIALS AND METHODS

The collected researches of this review were taken from electronic databases, in particular, Google Scholar, Scopus, PubMed, Web of Science, and Science direct. Selected articles were published in English language in the years 2008–2023. Search word were "burn wound" and "Saffron" in the headline or abstract, and "plant extract", "plants", and "herbals" in the full text. The papers demonstrate the effect

of extract of Saffron on treating the first, second and third-degree burn wounds was included. Studies on one of chemical compounds isolated from saffron were be considered.

Basic studies and clinical findings

In 2008–2023, more than a few medical trials were conduct to confirm the effectiveness of saffron extract in healing burns wounds. These studies are described according to the mechanisms investigated by researchers in treating burns.

Two mechanisms inspected in research

1-Induse Oxidative stress and inflammatory response.

Unbalance between the creation and exclusion of reactive oxygen species (ROS) is named Oxidative stress. In normal situation, our body has a powerful antioxidant defense system, struggle against exaggerated creation of ROS. Nevertheless, during either antioxidant defense system is damaged or excessive ROS is generated, oxidative stress occurs [15]. ROS is intended constituents of cell membrane that induces lipid-peroxidation, degeneration of membrane, and damage of endothelial cells, and thus raises micro-vascular permeability, which sequentially leads to the revitalization and adhesion of polymorpho-nuclear neutrophils (PMNs) and the pro-inflammatory material liberation [16]. The PMN accumulation additionally contributes to ROS formation and damage in intestinal tissue, resulting in translocation of bacteria, systemic complications, and subsequently, multi-organ collapse [17] [18].

Zhou et al., investigate the impact and potential mechanisms of crocetin from gardenia fruits and saffron in burn-induced intestinal injury. Inflammation and oxidative stress signify the main roles in burn-induced intestinal injury. A carotenoid compound called crocetin, has been shown to decrease inflammatory reaction and oxidative stress.

Generation of free radical and lipid-peroxidation models were used to scientifically estimate, in vitro, the antioxidant actions of crocetin. To promote intestinal injury in rats, an ordinary model of burn was used. To assess a 30% of total body surface area, burn, animals were located into a template constructed injury and then immediately received a transcutaneous injection of 1.5mL buprenorphine dissolved in normal saline for fluids revival and control of pain. Crocetin intra-peritoneal injection (100 and 200 mg/kg) was performed directly after than burn injury. Level Changes of, malondialdehyde, catalase, glutathione peroxidase, super oxidase dismutase, interleukin 6, poly-morpho-nuclear neutrophil accumulation, intestinal histology, and intestinal permeability were checked

Crocetin exposed remarkable inhibitory action towards free radicals and lipid peroxidation in several antioxidant activity models. Crocetin increased antioxidant enzyme levels, so, as a result, intestinal oxidative damage was reduced in burn models. In addition, crocetin inhibited poly-morphonuclear-neutrophil accumulation, limited tumor necrosis factor-a and levels of interleukin 6, intestinal permeability, and histological changes [19].

2- Possible impacts of saffron on cell migration and proliferation.

The study of Alizadeh and Oryan was consummate to estimate the saffron effectiveness in healing burn wounds in vivo model. The wound closure percentage, reduction of the wound, cytokines levels, and growth factors were calculated. The extract of saffron was also practical to assess the migration and proliferation of human dermal fibroblast (HDF) cells. Saffron-treated wounds show clear enhanced healing in comparison with groups of the silver sulfadiazine and negative control. Decreasing

interleukin-1β expression and growth factor-β1 transforming (TGF-β1) throughout the inflammatory stage confirmed the possibility of saffron in wound healing promote. Also, enhanced expression of TGF-β1 through the phase of proliferative and fibroblast growth factor throughout the remodeling phase describes the anti-scarring and regenerative function of saffron, correspondingly. Biochemical and histological results also established that saffron appreciably motivated the healing of burn wounds by healing phase modulation. For that reason, saffron able to be the best choice for enhancing skin fix and renewal [20].

Khorasani et al., research was to estimate the effectiveness of cream made with an extract of saffron pollen in the healing of thermal-induced burn wounds in comparison with sil¬ver-sulfadiazine (SSD) in rats. Thermal burn wounds are the skin tissue damage caused by hot surfaces, liquid, fumes, and fire. Following a burn injury that was caused by hot water, animals administrate a current cream including saffron (20%) at 24 hours. After 25 days, the wound size of the model that was treated with saffron was much smaller than other groups (control, base, or SSD (1%)). Histological assessment has exposed that saffron significantly increases reepithelialization in wounds of burn with fulfilled reepithelialisation of epidermis, dermis fibrosis, and mild inflammatory cell penetration, as compared to wounds treated with other cream. Examination with microscopic of the his to-pathological slides, discovered that the wounds treated with cream of saffron contained smaller amount of inflammatory cells competition with another groups. Wound closure was also estimated and found that treatment burn wounds with 20% saffron cream induce the epidermis to close in normal structure [21].

Burak Ozdemir et al., evaluate the usefulness treating of thermal-induced burn wounds with the extract of saffron stamen and compare the results with silver sulfadiazine (SSD). In this study, researchers was designed to encapsulate of Saffron stamen aqueous extract (SSAE) with CNPs(chitosan-nanoparticles) to be used locally on thermal burn wounds. Tests of biological activity such as DNA cleavage, DNA binding and antibacterial activity were carry out to establish the efficiency of encapsulated SSAE. in addition, a test of genotoxicity was performed for the dependability of SSAE. DNA binding showed interaction between SSAE and DNA electro-statically. It was indomitable that all doses of SSAE used in hydrolysis and oxidative DNA of cleavage experiments cleave DNA. Antibacterial findings exposed that CNPs were loaded via SSAE were more efficient against bacteria than blank SSAE [22].

saffron toxicity

Saffron is well known as a food complementary for more than a few centuries. The results of previous studies exposed that saffron and its derivates didn't pose a danger to the body organs at minor concentration or even at pharmacological doses. According to the lethal dose (LD50) value of saffron, 1.5g per day has been consider to be harmless, at 5 gr as toxic and 20gr as fatal dose. Nevertheless, in a number of reports, 4gr/day of saffron did demonstrate side effect in pregnant women where dosage of on top of 10g was enough to stimulating the uterus and cause abortion [23]. In preceding investigations, administered 20–200 mg/day of saffron for 10–16 weeks were tolerable in treating a variety of body problems. Mild toxicity with saffron causes nausea, vomiting, diarrhea and dizziness, whereas toxicity with high concentration may cause deadness, itchy in the feet and hands and yellowing of the skin and eyes and the spontaneous bleeding, conjunctiva can also be an indication [24].

CONCLUSION

As a result of the various mechanisms of action, antimicrobial activity, and safety, saffron extract can compete with conservative medication in treating wound of burns. The rising attention in herbal medicine and substitute therapies is also creating insist for those products. Conversely, creating a new solution for burn wounds treatment that could substitute the common use of usual treatment is a challenge for modern medicine. In this review, the researchers suggest that preparations in which plant ingredients are included have a strong competition for synthetic compounds.

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