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Research Article
Irradiated Honey and Medical Vaseline: A Comparative Study for Full-Thickness Burns on Rats *in vivo*

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Abstract

Background and Objective: Burns may lead to some psychological and physical problems, while several treatments such as silver sulfadiazine and sophisticated dressings, vaseline and honey have been approved as a medication. The current research aimed to study the morphological investigations of full-thickness burn healing impacts of irradiated honey and medical vaseline ointments. **Materials and Methods:** A total of 60 (3 months old) albino rats weighing 250-350 g b.wt., were divided into 6 sets of 10, including (1) vaseline set, (2) positive control set and (4 sets) treated with four honey types which coded as *Nigella sativa* honey (NSH), Moringa honey (MOH), sidr honey (SIH) and pumpkin honey (PUH), respectively. After the anesthetizing, the 2nd-degree burns were made on the animal's back and each set was treated topically twice a day. Several clinical evaluations were applied on the 1st, 5th, 10th and 15th days. **Results:** On the 15th day, the greatest granulation tissue rate was related to PUH, which reached 4.55. The MOH caused the lowest inflammation level 1.02 (the highest rate) compared to those sets PUH (0.99), SIH (0.87) and NSH (0.77). The highest wound secretion rate was detected for the treated rats with NSH (3.23), followed by PUH (3.21), SIH (3.18) and MOH (3.05), while the vaseline-treated rats reached (2.01) as the lowest rate. The highest dermal stuffiness rate was detected for the treated rats with SIH (3.22), followed by MOH (3.15), NSH (2.99) and PUH (2.23), while the vaseline-treated rats reached (2.03) as the lowest rate. The shrinkage rate was the highest in the treated rats with SIH (95.21), followed by PUH (92.39), MOH (89.22) and NSH (84.97). The MOH-treated rats reported the lowest tissue damage rate compared to vaseline-treated rats which detected some collagen deposited around circular muscle fibers in the inner muscular layer and reported 3.42. **Conclusion:** According to the morphological results, it is concluded that the traditional honey types as ointments are rich in therapeutic biomaterials and have many healing effects on burned skin.

Key words: Irradiated honey, medical vaseline, full-thickness burns, ointments, healing wounds

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Several options against antibiotic resistance emerge to prevent and combat sepsis, resolve in ammation and maintain homeostasis. Honey is considered a nutritional healthy product of the ancient well-known treatments for several diseases worldwide[1]. The rich composition of honey is well-known as immunomodulatory due to the presence of sugars, minerals, multivitamins, proteins, enzymes, flavonoids, phenols, hydrogen peroxide, methylglyoxal and bee defensin-1[2]. It can be employed for the healing of respiratory, urinary, gastrointestinal, diabetes, hypertension, sexual dysfunction, arthritis and skin diseases especially ulcers, wounds, eczemas, psoriasis and dandruff[3]. Honey efficiently can decrease inflammations, edemas, microbes, viruses and analgesics, promote healing, diminish scar sizes and stimulate tissue regeneration[4]. Studies reported that honey efficiently acts as anti-hyperlipidemic, hepato-protective for the liver, cardio-protective for the heart and a general sedative effect[5,6]. Several types of honey can be varied according to several factors such as the bee species, geographical origin, botanical source, nectar, environmental condition, pollen, flowers and leaves[7]. Comparative studies *in vivo* and *in vitro* delineated the anti-inflammatory mechanisms of honey with NF-κB, cytokines, nitric oxide, tumor necrosis factors, cyclooxygenase isoenzymes, COX-1 and COX-2[8]. High sugar concentrations, low water activities and acidity might cause osmotic stresses to the microorganisms[9,10]. Burns are observed due to emergency conditions which can lead to some psychological and physical problems with an increased rate of mortality[11]. Several treatments have been presented for healing wounds in the medicinal literature such as silver sulfadiazine and sophisticated dressings against bacterial infections in burned areas[12,13]. Manuka honey has been approved as a medical coating for the treatment of wounds and burns[14].

In the research work, irradiated four types of honey such as (*Nigella sativa* honey, *Moringa* honey, sidr honey and pumpkin honey) and medical vaseline ointments were investigated on the full-thickness second-degree burns wound on rats *in vivo*.

MATERIALS AND METHODS

Study duration: The current study was carried out from June to December, 2023 under the Ethics Committee Number (HAO-02-T-105).

Irradiation process of honey samples: Four honey types which varied according to their origin were purchased from Elshifa in Taif City, Saudi Arabia. Honey types were coded as *Nigella sativa* honey (NSH), *Moringa* honey (MOH), sidr honey (SIH) and pumpkin honey (PUH), respectively. Honey types were sterilized and subjected to a cobalt-60 irradiator with a Co-60 source measuring 24,000 at King Abdulaziz City for Science and Technology, Saudi Arabia. Approximately 2 kg of honey samples were stored in sealed, Teflon-coated plastic vials and kept in a cool place for further use.

Animals and experiment design: The current experimental research was performed in the College of Sciences, Taif University, Saudi Arabia. All the rats were randomized and transferred to the Department of Food Science and Nutrition. A total of 60 (3 months old) albino rats weighing 250-350 g b.wt., were required for experimental research and divided into six sets. Rats were healthy with clean fur and clear sights. Before the experiment work the rats had been received humane care for seven days and kept in separate enclosures with a temperature of ±20-23°C. Rats were fed with a commercial diet and water during the whole study period. Treatments were begun directly after burning on the 8th day. Rats in the (third, fourth, fifth and sixth) sets were treated with (NSH, MOH, SIH and PUH) as ointments daily, while the first set was treated with the medical vaseline, respectively. The negative control set was kept without any treatment.

Full-thickness second-degree burns process: Rats were anesthetized with 40 mg/kg anesthesia and waited for 2 min. Approximately 400 mm^2 areas were shaved with shaving cream on the backs of rats with an electric clipper. The shaved areas were sterilized with methylene blue. Briefly, the full-thickness second-degree burns were applied by using hot aluminum plaques (10 mm diameter) heated over the stove for 30 sec to reach 120°C then pressed on the back skin for 10 sec.

Animal treatments: Rats were treated by using a sterile cotton swab twice a day with a span of 12 hrs based on the set, namely (NSH, MOH, SIH and PUH) as ointment coatings daily, while the first set was treated with the medical vaseline, respectively. Treatments were continued for 15 days.

Determination of granulation tissue and inflammation response rates: For the histological analysis, the burned skins were washed with some normal sterile saline solutions; then, approximately 2% of lidocaine was injected subcutaneously and the biopsy was extracted according to the previous protocol for the burn wound healing scale[15]. The samples were applied with 10% buffered formalin for 2 days after 24 hrs, the

formalin solution was changed again. The samples were prepared with Hematoxylin and Eosin (H&E). The histological analysis with an optical microscope (Leica RDM 2000 LED, Shanghai, China) and a digital camera (Leica RMC 170 HD, Shanghai, China). Granulation tissue rate was evaluated by (X 10 and X 40), while Inflammation rate was evaluated by (X 40) as the mean number of neutrophils in 5 microscopic fields[16].

Determination of wound secretion and dermal stuffiness rates: The secretion rate was evaluated according to secretion types as the following sequence: 1 refers to purulent; 2 refers to sanguineous; 3 refers to serous; while 4 is none secretion. Secretion amount was considered heavy in case of 1, low in case of 2, moderate in case of 3 and none in case of 4[17]. The dermal stiffness was evaluated according to the following sequence: 1 refers to none; 2 refers to stiff; 3 refers to moderate and 4 is soft[18].

Determination of shrinkage and tissue damage rates: Rats were frequently detected for shrinkage rate by using a digital camera 20 cm above the animals in their cages[19]. The tissue damage rate was evaluated by scoring the sub-mucosal collagen intensity according to secretion types as the following sequence: 0 refers to no damage; 1 refers to mild; 2-3 refers to severe damage[20].

Statistical analysis: Statistical analyses for results were applied to IBM SPSS version 26. Descriptive statistical methods were used to express results by (mean and standard deviation). The differences between rat sets were applied by ANOVA test and considered as significant case $p \leq 0.05$.

RESULTS AND DISCUSSION

Effect of various treatments on granulation tissue rate: The NSH caused the greatest results for granulation rate to reach (2.02 and 3.43) on days 5 and 10, respectively, Fig. 1. On the 15th day, the greatest granulation tissue rate was related to PUH, which reached 4.55. After healing wounds, rats treated with honey showed complete covering with proliferated keratinocytes. Also, it was observed clusters of collagens and a small number of fibroblasts and capillaries in the dermis. Compared with the vaseline set, the surfaces of the wound were still not completely covered and there were some scabs. Meo *et al.*[21], reported the efficient role in healing wounds by increasing the body's immune system and motivating the granulation rate. Another study reported the combination of topical honey use on wounds with oral zinc sulfate can increase the growth of fleshy bud tissues, enhance angiogenesis and increase the tensile strength of wounds[22]. Therefore, it is recommended to take oral zinc sulfate as a medication, especially with people with zinc deficiency to help in stimulating the epidermal migration.

Effect of various treatments on inflammation response rate: On the 15th day, MOH caused the lowest inflammation level 1.02 (the highest rate) compared to those sets PUH (0.99), SIH (0.87) and NSH (0.77), while rats treated with vaseline reported (0.47), Fig. 2. Khoo *et al.*[23], reported the combination of honey and zinc oxide to reduce the inflammation responses with no infection on wound sites compared to using them individually. Therefore, that combination will heal full-thickness wounds faster and with better quality.

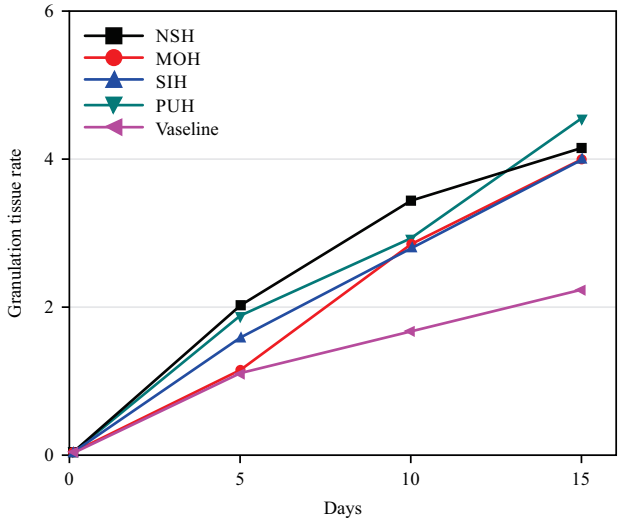

Fig. 1: Granulation tissue rate among vaseline and honey types

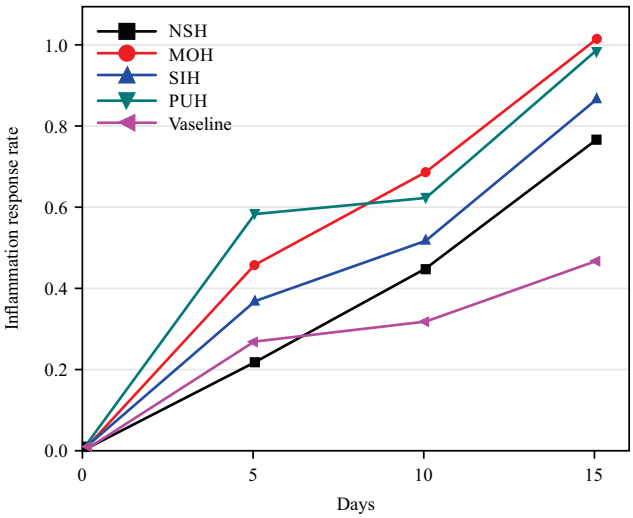

Fig. 2: Inflammation response rate among vaseline and honey types

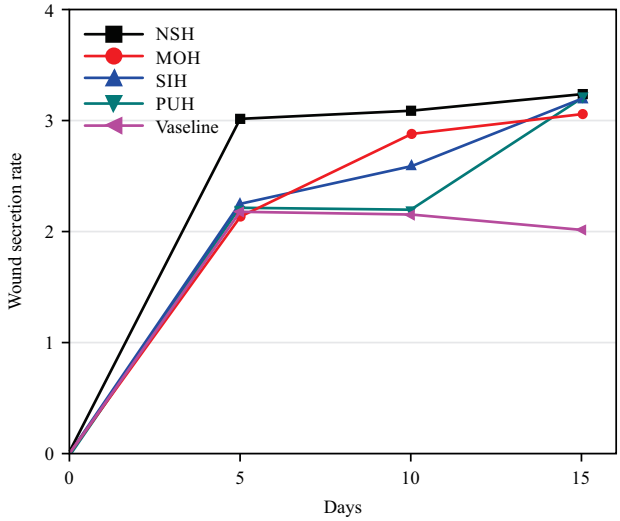

Fig. 3: Wound secretion rate among vaseline and honey types

However, more studies are recommended to supply such as clinical advice on that combination.

Effect of various treatments on wound secretion rate: The highest wound secretion rate was detected for the treated rats with NSH (3.23), followed by PUH (3.21), SIH (3.18) and MOH (3.05), while the vaseline-treated rats reached (2.01) as the lowest rate, Fig. 3. The results also reported showed that the scar tissues were not stiff or coarse on treated honey rats compared with the vaseline rats. The current results were in agreement with the previous study by Emsen[24] on wound secretion and improved the skin to be reddish with low inflammation.

Effect of various treatments on dermal stuffiness rate: The highest dermal stuffiness rate was detected for the treated rats with SIH (3.22), followed by MOH (3.15), NSH (2.99) and PUH (2.23), while the vaseline-treated rats reached (2.03) as the lowest rate, Fig. 4. Furthermore, the current study was in agreement with the previous study by Bergman *et al.*[25], who found that the dermal stuffiness and wound color in rats treated with honey as ointment were better and bright red color compared the control which was worth and dark-creamy color. Oryan and Zaker[26], reported that honey can improve anti-inflammatory activities and support the growth of tissues. Emsen[24], reported the use of a combination of milk and honey for healing burned skin with increasing catalase activities.

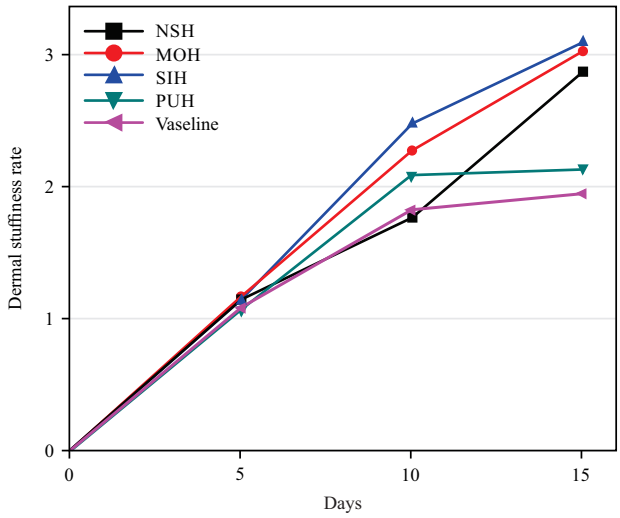

Fig. 4: Dermal stuffiness rate

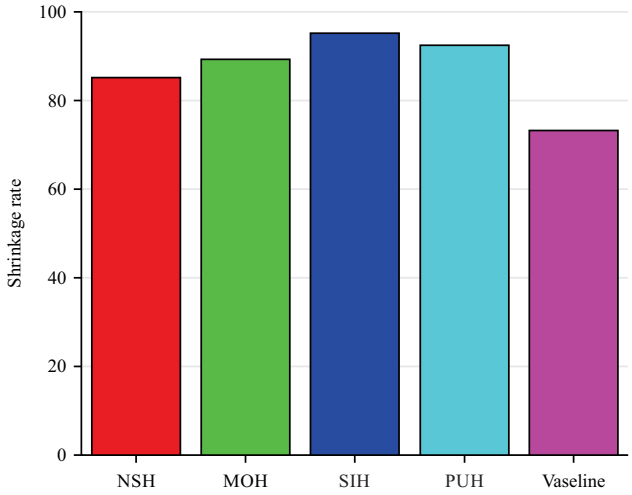

Fig. 5: Shrinkage rate among vaseline and honey types

Mao *et al.*[27] results were in agreement with current study results due to the reduction of collagen fibers with no scar tissues.

Effect of various treatments on shrinkage rate: Indeed, the shrinkage rate was the highest in the treated rats with SIH (95.21), followed by PUH (92.39), MOH (89.22) and NSH (84.97), whereas that group treated with the vaseline only reached (73.15), Fig. 5. Some ancient civilizations such as the Aztecs, Egyptian and Chinese used honey bee wax to close wounds, reduce burns and prevent bleeding processes to avoid the contracting infections associated with the entry of microbial loud in those lesions[28]. Dassamiour *et al.*[29], reported the use of honey and honey wax in the absorption of edema by dehydration, granulations and closing edges of wounds. Also, the presence of saponins in honey can boost the blood vessel counts with the blood supply in burned areas[30]. Honey can increase the epithelial thickness of burned areas and fibroblast counts leading to tissue regeneration[31,32].

Effect of various treatments on tissue damage rate: According to the microscopic images, vaseline-treated rats detected some collagen deposited around circular muscle fibers in the inner muscular layer and reported 3.42 as a tissue damage rate, Fig. 6. Moreover, the muscle fibers appeared irregular and degenerate. The MOH-treated rats reported the lowest tissue damage rate (1), followed by NSH (1.92), while SIH and PUH-treated rats reported similar values (2.51 and

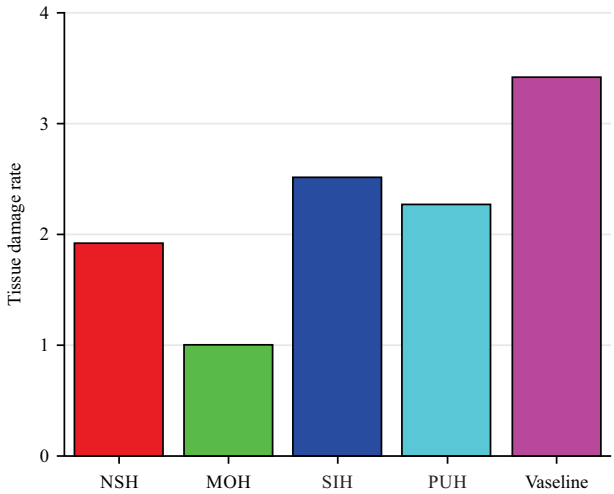

Fig. 6: Tissue damage rate among vaseline and honey types

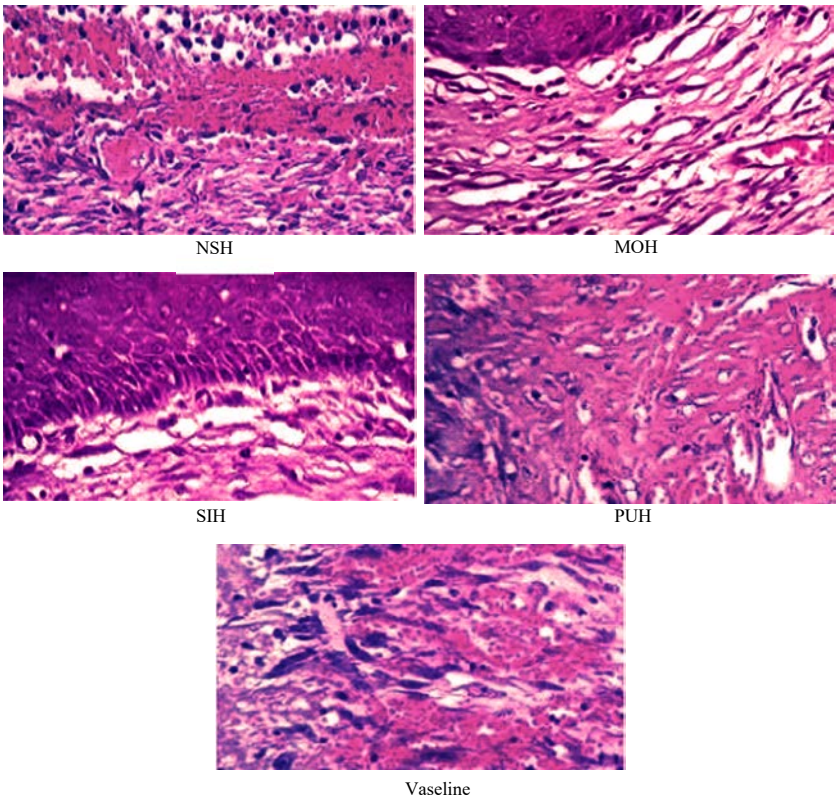

Fig. 7: Histological examinations of full-thickness burns on rats by using various treatments
NSH: *Nigella sativa* honey, MOH: *Moringa* honey, SIH: Sidr honey and PUH: Pumpkin honey

2.27), respectively. Honey showed a significantly greater histopathological effect in preventing fibrosis and stricture formation compared to prednisolone. Molan[33], reported the anti-bacterial and anti-inflammatory agents in honey which can accelerate epithelialization and reduce edema and tissue damage rate. Molan[33], compared fifty patients after various treatments with Savlon antiseptic and honey as coating, honey gave 60% recovery against 36% Savlon antiseptic in the

same period. Honey also has some chemical barriers to prevent cross-infections[34]. The current results were in agreement with Jull *et al.*[35], who used honey as a dressing for burns by differentiation, re-epithelializing, tissue debriding, proliferation of monocytes and fibroblast counts.

Histological examinations: The histological examinations of the progress of healing wounds of burned areas are presented after the 15th day, Fig. 7. In the vaseline set, a huge number of inflammatory cells were visible on the superficial parts and more immature fleshy bud tissue was observed. In the other honey sets, keratinocyte components had migrated more to the wounds and the fleshy bud tissues matured more. Also, more collagen fibers were formed and the display of capillaries was perpendicular to the fibers; while the vessel numbers were reduced.

CONCLUSION

In the current study, the positive effects of several irradiated honey types produced in Saudi Arabia compared to the medical vaseline to heal full-thickness burns on rats have been investigated. Sidr honey reported the highest shrinkage and dermal stuffiness rates; *Nigella sativa* honey reported the highest granulation tissue and wound secretion rates and pumpkin honey reported the highest inflammation response and the lowest tissue damage rates, compared with the vaseline-treated rat.

SIGNIFICANCE STATEMENT

Wounds and burns are serious problems, consequently, a treatment for wounds and burns are essential to improve up the healing processes. Using some natural products as honey varieties is extremely considerable for repairing skin. Saudi is considered one of the main countries in honey production, therefore extra qualified researchers are needed to determine such potential medical uses in accurate ways.

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