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Histopathologic Evaluation of Honey-Zinc Oxide Combination on Full-Thickness Experimental Wound Healing in Rats

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Abstract

Wounds are the creation of any defects and loss of connectivity of body tissues, both inside and outside the body. Researchers have always sought to find the most effective and least complicating factor to accelerate the wound healing process. The present study aimed to evaluate and compare the effectiveness of honey alone or in combination with zinc oxide on healing the experimental defect of skin full-thickness wound in rats. In this study, 48 adult male white Wistar rats were selected and randomly divided into four groups of 12 including the first group (control = C), the second group (honey = H), the third group (zinc = Z), and the fourth group (honey and zinc oxide= (ZH). A full-thickness skin defect with dimensions of 2 × 2 cm was created in the skin of the back, as well as the distance between the neck and the pelvic area. All animals received treatment appropriate to their group. Four rats from each group were prepared on histopathological samples on days 7, 14, and 21 and microscopic examination was performed. Axiovision software was used for macroscopic assessments. The highest healing rate on day 7 after wounding belonged to the Z group and the lowest to the H group. Also, the highest rate of healing on the 14th day after wounding belonged to the Z group and the lowest to the ZH group. However, no statistically significant differences were observed between the groups. On day 21 after wounding, the percentage of wound contraction in the ZH group was significantly higher than the C ($p = 0.001$), H ($p = 0.001$), and Z ($p = 0.013$) groups. Microscopic examination of the skin, 21 days after wounding, showed that the wound was completely covered by amplified keratinocytes in all rats in the ZH group. This was seen in two rats in the Z group and one in the C group. In all rats in the H group, the wound surface was still not completely covered and there was a scab on the wound. In the dermis of all ZH rats, regular clusters of collagens with a small number of fibroblasts and capillaries were observed. This study showed that the combination of zinc oxide and honey has a better effect on the wound healing process than other groups and accelerates the wound healing process. The combination of these two substances increases the formation of fleshy tissue and wound contraction and reduces inflammation and wound scarring.

Key words: Wound, Healing; Honey, Zinc oxide, Rat

Introduction

The skin is an important protective barrier for various tissues and organs of the body, which ultimately prevents the entry of pathogens and foreign bodies into the body. Moreover, it prevents the loss of body fluids and helps regulate body temperature (Cui et

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al., 2017). Damage to the skin disrupts the anatomical structure and function of the skin ultimately causing scarring (Oryan et al., 2019). Therefore, it is necessary to look for ways to accelerate the wound healing process while preventing scar formation as well as monitoring the wound healing process (Cui et al., 2017). Wounds are defined as any disorder in the integrity of the skin occurring for various reasons such as trauma, surgery, diabetes, and burns (Ehterami et al., 2019). Humans have been trying to find better ways to heal wounds to increase their chances of survival and minimize loss of function. Even when wounds are not life-threatening, it is a concern of modern medicine to minimize scarring and help patients return to conditions possibly closed to their original appearance and function (Auger et al., 2006). One of the evolving disciplines in modern medical sciences is research into the factors affecting wound healing. Moreover, trying to find more effective drugs may be one of the major challenges for researchers (Ghashghaii et al., 2017). An ideal topical material should be easily accessible and inexpensive, heal the wound with the best results in the shortest possible time, and reduce mortality by preventing bacterial contamination and infection. Since a combination with such properties has not yet been identified or constructed, studies attempt to discover the ideal agent (Arslan et al., 2012). Some natural compounds or extracts of traditional medicines have also been considered promising and cost-effective supplements and alternative approaches to wound healing and pain relief (Chen et al., 2019). Natural honey is a promising option in this regard as a result of its healing potential in infections and wounds, which has been used for a long time (Chaudhary et al., 2019). Honey has been used to treat infected wounds for many years, even before the discovery of bacteria (Latif et al., 2015). It increases the formation of granulation tissue, the density and activity of fibroblasts, keratinization of the wound surface, the thickness of the epidermis, and the thickness of collagen fibers (Ghaderi and Afshar., 2004). The greatest property of honey is its antimicrobial properties. Its action mechanism is high osmolarity, acidity, the presence of hydrogen peroxide inhibitors, flavonoids, and phenolic acids. Honey has the property of absorbing moisture, which can reduce inflammation and lead to faster healing and the initial reproduction phase of the inflammatory process (Latif et al., 2015). There have been many reports on the effectiveness of honey on a wide range of gram-positive and gram-negative bacteria, rapid wound infection clearance, and wound protection against infection (Khoo et al., 2010; Meo et al., 2017). Honey contains glucose oxidase; an enzyme converting glucose to hydrogen peroxide and possibly contributing to some of its antibacterial properties (Jull et al., 2008). The antibacterial activity of honey depends on the activity of peroxide and its non-peroxide mechanisms (Meo et al., 2017). Honey has anti-inflammatory properties. Beside granulation tissue, It has been also shown to accelerate epithelialization in the reproductive stage and reduce wound healing time (Lee et al., 2015). Honey reduces inflammation, edema, and exudate, improves wound healing, reduces wound scarring, and stimulates tissue regeneration (Vaghardoost et al., 2017). On the other hand, the benefits of using zinc (topical and topical) have been shown in the wound healing process (Arsalan et al., 2012; Cangul et al., 2006). Topical application of zinc accelerates the wound healing process with antibacterial activities, anti-inflammatory effects, reduction of tissue debris on the wound surface, and also accelerates epithelialization and activation of metalloenzyme by weak mechanisms. Zinc reduces the number of inflammatory cells and the duration of the inflammatory response in fleshy bud tissue and accelerates wound healing, especially in open wounds (Aksoy et al., 2010; Kogan et al., 2017; Arsalan et al., 2012). Zinc oxide (ZnO zinc oxide) has received a huge deal of attention as a result of its good catalytic activity, high stability, antibacterial properties, and non-toxicity (Gutha et al., 2017). Studies have shown that the use of zinc oxide speeds up the healing of chronic and acute wounds and also has antibacterial, antifungal, and anti-inflammatory properties (Vasile et al., 2014). Zinc oxide is as effective as an enzyme killer in wound healing and affects the epithelialization of wounds. It also has bacteriostatic properties, promoting it as an effective substance in local wound dressing. This substance can be used in the treatment of various dermatitis, blisters, and open wounds of the skin (Kumar et al., 2013). Topical zinc oxide ointment is inexpensive and easy to use with few side effects (Aksoy et al., 2010). It was found no published studies evaluating the effectiveness of the honey-zinc combination on the wound healing process. Therefore, the present study aimed to evaluate and compare the effectiveness of honey alone or in combination with zinc oxide powder on healing the experimental defect of full skin thickness in rats. It is assumed that after the simultaneous use of honey and zinc oxide ointment, the wound healing process will pass faster with appropriate quality.

Materials and Methods

Ethics

The project was approved by the local Committee of the Institutional Animal Care and Use of Shahid Chamran University of Ahvaz.

Animals

In this study, 48 adult male Wistar rats with an average weight of 250-300 g were used. The animals were prepared from the animal house of the Faculty of Veterinary Medicine of the Shahid Chamran University of Ahvaz. The temperature of the animal housing was adjusted to 23 ± 3 ° C with appropriate humidity. Animals were exposed to 12 hours of light and 12 hours of darkness. This darkness-light cycle was regulated by an automatic system. During this period, the rats were fed with a special rat food in the form of compressed capsules prepared from the same animal house. The individual cages were thoroughly washed and disinfected with alcohol before surgery. An independent 120 ml drinking bowl was provided for each cage. All surgeries were performed by one person at a specific time of day. The animals were divided into four equal groups as follows: Control group (C): Saline treated; group H: receiving 2 g honey; group Z: receiving 2 g zinc oxide ointment (Pharma-Shimi, Tehran, Iran); and group ZH: receiving a mixture of honey and zinc oxide in a ratio of 1 to 1.

Surgery

All animals were anesthetized by intraperitoneal administration of a combination of 2% xylazine (10 mg/kg) (Kela, Belgium) and 10% ketamine (100 mg/kg) (Bremer, Germany). Then, the region between the neck and pelvic was clipped and prepared for aseptic surgery. Using a sterile stencil ruler and a surgical blade, a 2 × 2 cm full-thickness skin defect was created in the skin of the back (Fig.1). The wounds were washed with normal saline and each animal received appropriate treatment. Treatments were applied daily until the end of the assessment. The animals were transferred to the veterinary school animal house and kept in separate cages until the end of the study. Four rats of each group on days 7, 14, and 21 after wound creation were sacrificed with overdose intraperitoneal injection of ketamine and xylazine for further investigations.

Macroscopic evaluation (wound contraction):

Four rats from each group on days 7, 14, and 21 after wound creation were sacrificed with overdose intraperitoneal injection of ketamine and xylazine. The wound site of each animal was then imaged on a given day. The images were assessed with computer software (Axiovision). The area of each wound was measured. Then, the percentage of wound contraction (Vakilian, et al. 2019) was calculated using the following equation:

Wound contraction=100 * [Primary wound area / (Secondary wound area - primary wound area)]

Microscopic evaluation

For Microscopic evaluation, the wound area of sacrificed rats was isolated along with approximately 2 mm from adjacent healthy areas of skin. Then, it was washed with a normal sterile saline solution. Subsequently, the tissue sample was placed in 10% formalin buffer solution and after 24 hours the formalin solution was changed again. The samples were routinely prepared and stained with hematoxylin and eosin and examined microscopically. In microscopic studies of tissues, histological parameters were evaluated semi-quantitatively. Epithelialization (X 10 and X 40) was scored as follows: absence (0), the thickness of cut edges (1), migration of cells (2), bridging the excision (3), and keratinization (4). Granulation tissue scores (X 10 and X 40) were defined as follows: immature and inflammatory tissue more than 70% (0), thin immature and inflammatory tissue more than 60% (1), moderate remodeling more than 40% (2), thick granulation tissue, and well-formed collagen matrix more than 60% (3) and complete tissue organization more than 80% (4). Angiogenesis (X 10 and X 40) was scored as lack of vascular formation (0), large and dilated vessels and full of RBCs (1), regular capillaries and perpendicular to the direction of the collagen fibers (2), and reduced number of capillaries (3). Inflammation (X 40) was defined when a mean number of neutrophils in 5 microscopic fields was more than 75% (1), between 50-75% (2), between 25-50% (3), and less than 25% (4).

Data analysis

SPSS software V.26 (IBM Corporation, NY, USA) was used to review the data. One-way analysis of variance (ANOVA) with Tukey post-test was used to compare the obtained data between the study groups. Repeated measures ANOVA following LSD post-test was also used for differences within the groups. Nonparametric data were analyzed using the *Kruskal–Wallis* test. The results were presented as mean ± standard deviation or median (minimum-maximum) and values of $p < 0.05$ were considered significant.

Results

Macroscopic results

Inflammation and infection were observed in three and one animals, respectively, in the control group. In the second and third weeks of evaluation, no evidence of inflammation or infection was observed at the wound site of the animals in the control group. In the honey group, mild inflammation was observed in two samples during the first week. However, no evidence of infection was observed in the first week. In the second and third weeks of evaluation, there were no infection and inflammation. No signs of infection and inflammation were found in the zinc oxide group as the most stable group in terms of heal process. In the honey and zinc oxide combination group, there was mild inflammation in the first week, similar to the honey group, while no signs of infection were observed. In this group, where the healing process was started with a delay, in the third week, the healing process was obviously ahead.

Wound contraction and healing percentage

By evaluating the wound healing percentage parameter, the highest healing rate on day 7 after wounding belonged to the zinc oxide group while the lowest rate was related to the honey group. Despite the higher wound healing percentage in the zinc oxide group than the other groups, this difference was slightly significant compared to the honey group ($p = 0.041$) (Table 1 and Fig.1).

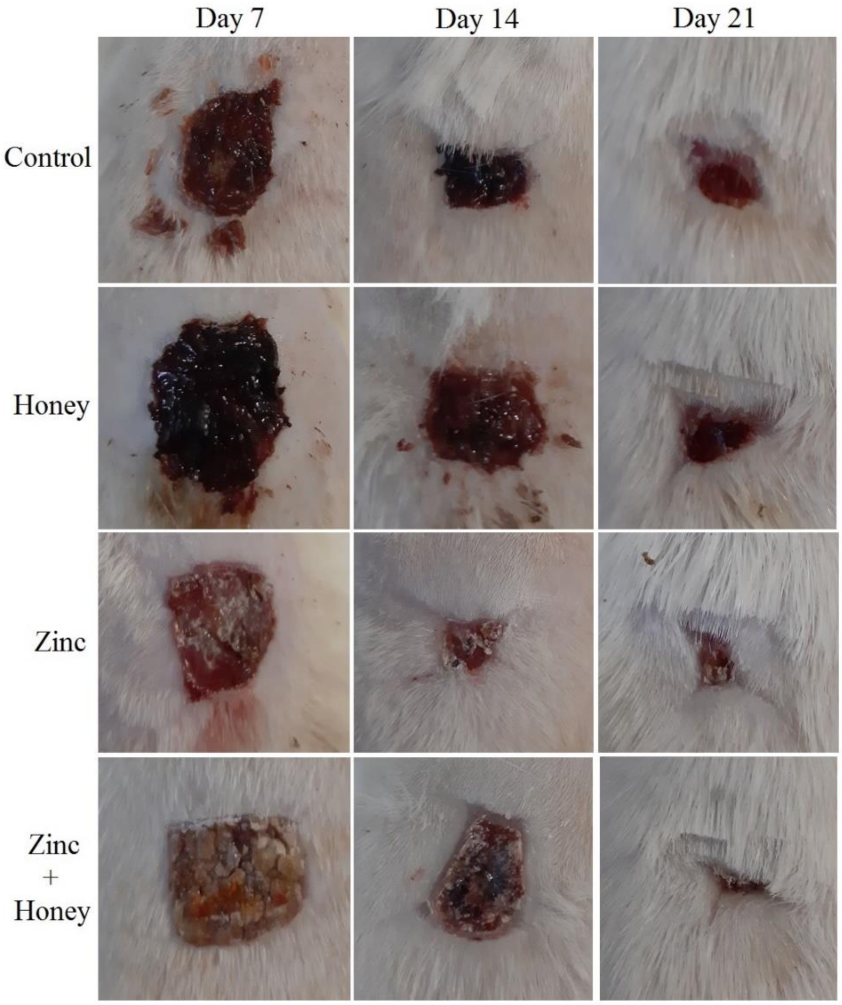

Figure 1: Macroscopic images of the wound site at the time of evaluation and in different groups

Table 1: Mean ± standard deviation of wound contraction percentage in the studied groups (Four rats)

Groups/Day	7	14	21
Control (C)	28.95 ± 3.72 a	69.00 ± 4.92 b	78.56 ± 7.60 c, ZH
Honey (H)	22.26 ± 2.44 a, Z	64.66 ± 4.55 b	79.30 ± 4.24 c, ZH
Zinc oxide (Z)	31.90 ± 7.13 a, H	77.84 ± 3.38 b	84.99 ±3.48 c, ZH
Zinc oxide + Honey (ZH)	23.46 ± 2.37 a	61.42 ± 5.32 b	97.42 ± 1.48 c, H, ZH

Inserting the group name at the top of each number indicates a significant difference with that group in each day ($p \leq 0.05$).
Mismatched letters indicate a significant difference between the studied days in each of the studied groups ($p \leq 0.05$).

The highest healing rate on day 7 after wounding belonged to the zinc oxide group and the lowest rate was related to the honey group. Despite the higher wound healing percentage in the zinc oxide group than the other groups, this difference was only significant compared to the honey group (p = 0.041) (Table 1 and Fig.1). Also, the highest rate of healing on day 14 after wounding belonged to the zinc oxide group, and the lowest rate was related to the zinc-honey group (Table 1). However, there was no statistically significant difference between the groups. On the 21st day after wound formation, the percentage of wound healing in the zinc-honey group was significantly higher than the control (p = 0.001), honey (p = 0.001), and zinc oxide groups (p= 0.013) (Table 1 and Fig. 1). Also, an increasing trend of wound healing percentage was observed in each group so that the healing rate was significant between the studied days (p = 0.049) (Table 1 and Fig.1).

Microscopic assessment

Examination of skin sections seven days after wounding indicated the presence of scabs (remnants of dead cells and necrotic nuclei on the wound, which are dried when exposed to air) on the wound. Keratinocytes began to proliferate on both sides. Flesh bud tissue was formed on both sides of the wound but not covering the entire wound site. Inflammatory exudates were also visible in the central part of the wound. These cases were seen in all rats of all three control, honey, and zinc and honey groups. In three rats in the zinc oxide group, fleshy bud tissue occupied the entire wound site (Fig.2). In these cases, inflammatory cells were found in the upper and labia of fibroblasts of fleshy bud tissue. Collagen fibers were also formed in the deeper parts. Blood capillaries also wore collagen fibers perpendicular to each other.

Fourteen days after wounding, histopathological examination of the samples showed the complete formation of fleshy bud tissue in all parts of the wound. In three rats in the control group and all four rats in the honey group, numerous neutrophils were seen above the upper parts of the fleshy bud tissue. In the deep parts, newly expanded capillaries were observed along with a large number of erythrocytes. However, in the rats receiving zinc, zinc, and honey, the fleshy bud tissue had a small number of neutrophils and the blood capillaries were arranged perpendicular to the collagen fibers. More collagen fibers were also formed in the deeper parts. Moreover, proliferated keratinocytes migrated to a large area of the wound (Fig.3). Microscopic examination of the samples, 21 days after wounding, showed complete wound covering by proliferated keratinocytes in all rats in the zinc and honey groups. This was seen in two rats in the zinc group and one in the control group. In all rats in the honey group, the wound surface was still not completely covered and there was a scab on the wound (Fig. 4). In the dermis of all rats receiving zinc and honey, regular clusters of collagens with a small number of fibroblasts and capillaries were observed. Such a condition was also found in two rats in the zinc group and one in the control group. In other cases, fleshy bud tissue with multiple fibroblasts and capillaries was observed (Fig.3).

Semi-quantitative assessments

The median scores of epithelialization were not significant between groups on any days of assessments. At the end of the study, the highest score of epithelialization was related to the ZH group. However, the difference was not significant to the groups C (p = 0.099), H (p = 0.053), and Z (p = 0.489), respectively (Table 2). Zinc oxide (Z) caused the best results of granulation growth at days 7 and 14 (Table 2). The difference of granulation growth in the group Z was significant compared to the groups H (p = 0.011) and ZH (0.013) at day 7, as well as the groups C (p = 0.002), H (p = 0.001) and ZH (0.039) (Table 2). On day 21, the best granulation tissue score was related to the group ZH, which was significant compared to the groups C (p = 0.023) and H (p = 0.001) (Table 2). The severest status of inflammation was related to day 7 for all groups (Table 2). On day 14, zinc oxide (Z) caused the least inflammation status (the highest score) which was significant compared to those of the groups H (p = 0.031) and ZH (p = 0.031) (Table 2). The highest score (the least) of inflammation at day 21 was associated with group Z, which was significant only compared to group H (p = 0.007). The best and highest scores of angiogenesis were related to the group ZH which was significant compared to the group H (p=0.007), at the end of the study (Table 2).

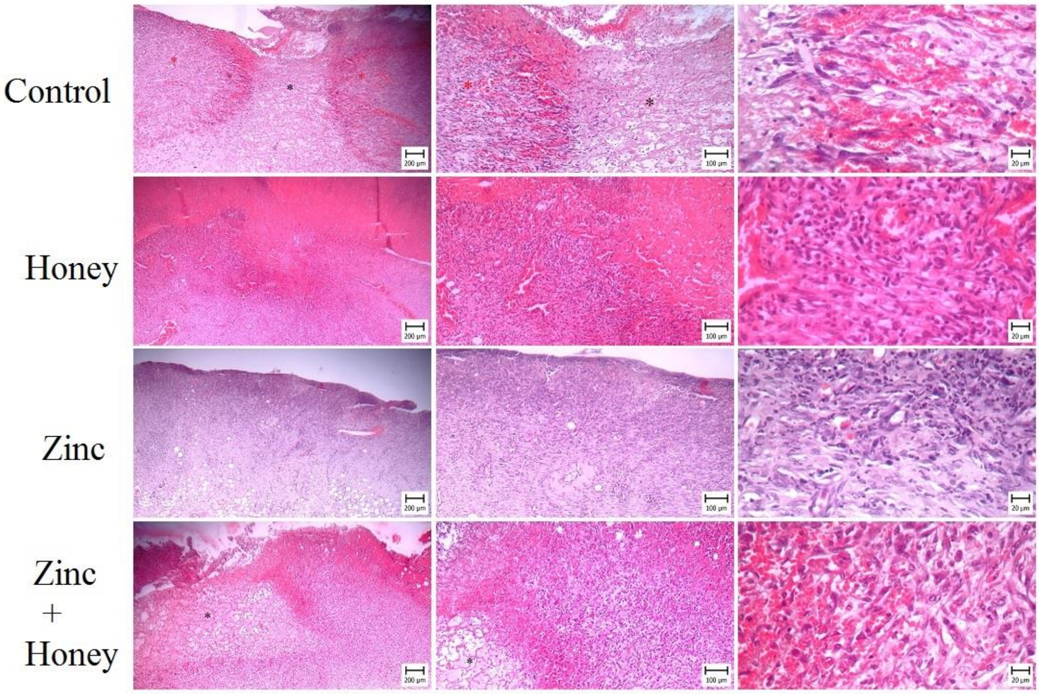

Figure 2: Day 7. In the control group, honey and zinc and honey, inflammatory exudate (star) was still visible at the wound site. While in the zinc group, fleshy bud tissue was seen completely at the wound site (hematoxylin and eosin staining) (Four rats).

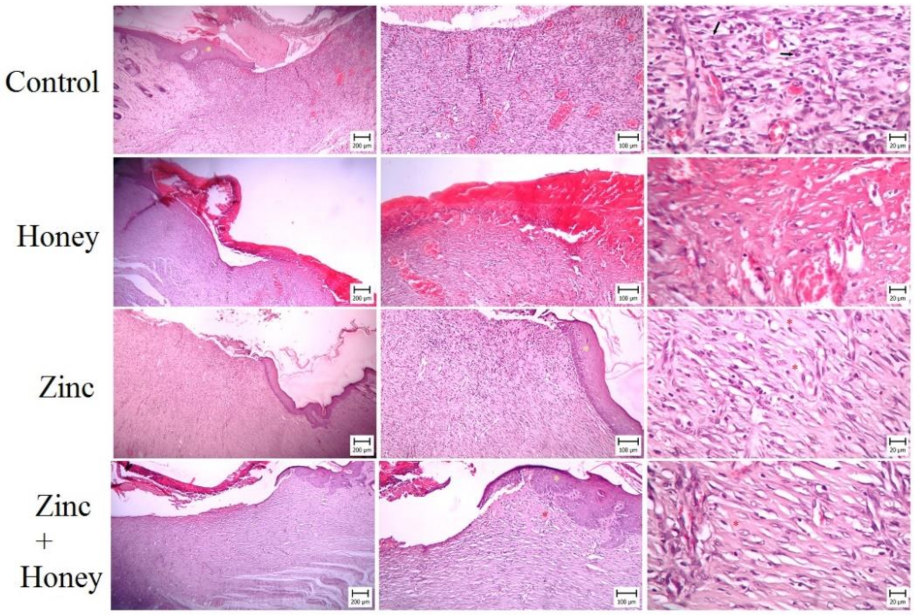

Figure 3: Day 14. In the control and honey groups, a large number of inflammatory cells were visible on the superficial parts and more immature fleshy bud tissue was observed. In the zinc, zinc, and honey groups, keratinocytes migrated more to the wound and the fleshy bud tissue matured more. In this way, more collagen fibers are produced and the arrangement of capillaries is perpendicular to the fibers and the number of vessels is reduced (hematoxylin and eosin staining) (Four rats).

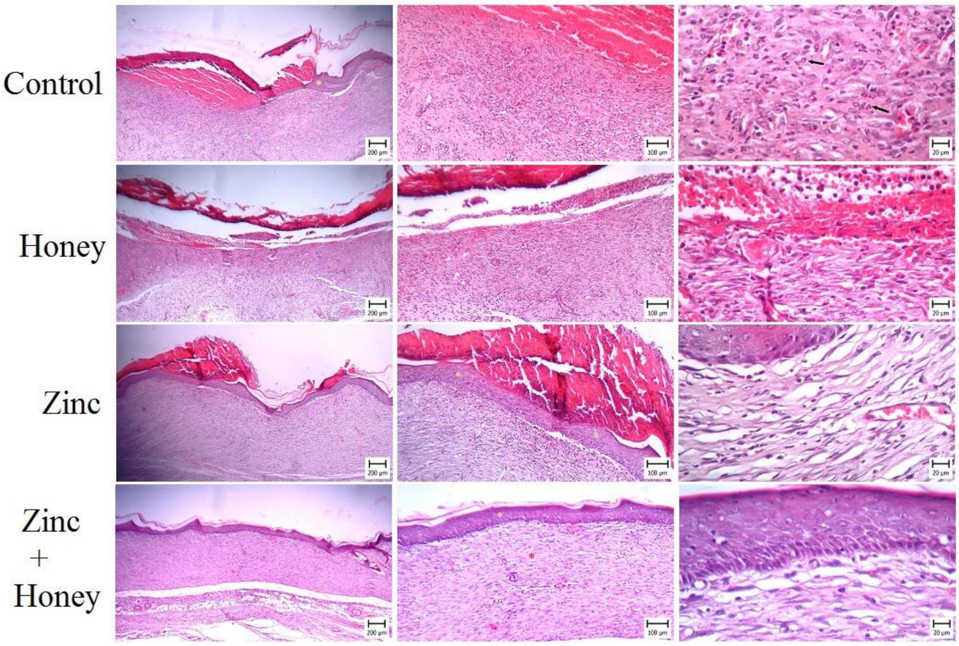

Figure 4: Day 21. In the zinc, zinc, and honey groups, the wound surface is covered by proliferated keratinocytes, and in the dermis, connective tissue containing pink filaments and a small number of fibroblasts and capillaries can be seen. In the control and honey groups, fleshy bud tissue containing numerous fibroblasts, blood capillaries and inflammatory cells (staining of hematoxylin and eosin) was also seen (Four rats).

Table 2: Median (Minimum-Maximum) of some histopathologic parameters of wounds under treatment of saline control (C), honey (H), zinc Oxide (Z) and combination of zinc oxide and honey (ZH) in Four rats

Parameters	Groups/Day	7	14	21
Epithelialization	Control (C)	2 (1-2)	1.5 (1-2)	2 (1-4)
	Honey (H)	1 (1-2)	1 (1-2)	2 (2-2)
	Zinc oxide (Z)	2 (2-2)	2 (1-2)	3 (2-4)
	Zinc oxide + Honey (ZH)	2 (0-2)	2 (2-2)	4 (2-4)
Granulation tissue	Control (C)	1 (1-2)	2 (1-2) Z	2 (2-4) ZH
	Honey (H)	1 (1-1) Z	1.5 (1-2) Z, ZH	1.5 (1-2) Z, ZH
	Zinc oxide (Z)	2 (1-2) H, ZH	3 (3-3) C, Z, ZH	3 (3-4) H
	Zinc oxide + Honey (ZH)	1 (1-1) Z	2 (2-3) H, Z	4 (3-4) C, H
Inflammation	Control (C)	1 (1-1)	2 (1-2)	2 (1-4)
	Honey (H)	1 (1-1)	1 (1-2) Z	1 (1-2) Z, ZH
	Zinc oxide (Z)	1 (1-1)	2 (2-2) H, ZH	4 (2-4) H
	Zinc oxide + Honey (ZH)	1 (1-1)	1 (1-2) Z	3.5 (2-4) H
Angiogenesis	Control (C)	1 (1-2) ZH	2 (1-2)	2 (2-3)
	Honey (H)	1 (0-1) Z	1 (1-2)	1.5 (1-2) Z, ZH
	Zinc oxide (Z)	2 (1-2) H, ZH	2 (1-2)	2.5 (2-3) H
	Zinc oxide + Honey (ZH)	0 (0-1) C, Z	1 (1-2)	3 (2-3) H

Group name at the top of each data indicates a significant difference with that group in each day ($p \leq 0.05$).

Discussion

Although many studies have been performed on the effect of honey and zinc on the wound healing process, there have been no studies on the effect of topical application of their combination. In this regard, the present study investigated the effect of topical and simultaneous use of honey and zinc oxide on full-thickness experimental wound healing in rats. Investigating the antibacterial, antiviral, anti-inflammatory, and antioxidant effects, it was stated that honey could be used as a wound dressing to accelerate wound healing (Yaghoobi et al., 2013). These effects are caused by the antibacterial effect of honey, high acidity, osmotic effect, antioxidant content, and hydrogen peroxide. The use of honey improves the wound healing process in acute cases, relieves pain in burn patients, and reduces the inflammatory response in such patients (Yaghoobi et al., 2013). According to the results of the present study, the use of honey causes no allergic reactions and no significant side effects. Honey quickly eliminates wound odor, improves fleshy bud tissue and epithelialization, and reduces the secretion and sterilization of wounds from microbes (Al-Waili et al., 2011). Furthermore, honey has significant effects on cellular element immunity and antibody production (Al-Waili et al., 2011). It was showed that the wound healing potential of honey has an effective role in wound closure, re-epithelialization, and collagen I / III expression (Chaudhary et al., 2019). The chemotactic activities and pro-angiogenic potential of honey have proven its effectiveness as a natural healing agent for diabetic wound healing. Recent studies have shown that honey can clear the infection of chronically infected wounds and accelerate the healing process, especially in wounds resistant to conventional treatments. In the present study, the best and highest score of angiogenesis was related to group ZH. There is also evidence that honey may reduce inflammation, reduce scarring, and aid in cell regeneration processes (Lusby et al., 2002). Although the highest score (the least) of inflammation at day 21 was associated with group Z, no abnormal discharge, infection, or major inflammation was observed in group ZH.

In 2004, Ghaderi and Afshar studied the effect of topical use of honey on skin wound healing in rats. They found that honey increases the formation of fleshy bud tissue, density and activation of fibroblasts, keratinization at the wound surface, the thickness of the basement membrane and epidermis, and the thickness of collagen fiber (Ghaderi and Afshar., 2004). It also reduces infection, inflammation, swelling, and wound opening and increases flexibility, ultimate tensile strength, and stiffness of wound tissue, and generally wound healing speed. Zinc ions are very important in cellular and biological processes. Zinc deficiency has several clinical manifestations, such as impaired wound healing. The observation of inadequate wound healing in people with zinc deficiency has led to several studies on the role of zinc in wound healing. Moreover, treatment methods have been developed to strengthen and accelerate the wound healing process (Kogan et al., 2017). Topical administration of zinc seems to be preferable to oral treatment as a result of its function in reducing severe infections and necrotic residues. This is achieved by strengthening local defense systems, collagenolytic activity, and continuous release of zinc ions at the wound site stimulating wound epithelialization (Lansdown et al., 2007). In the present study, better healing and non-observation of infection symptoms in zinc oxide groups and the combination of honey and zinc oxide revealed that zinc oxide has an effective role in wound healing by strengthening the body's defense system and stimulating epithelialization. Zinc plays a vital role in all stages of wound healing.

The lower zinc levels in the cellular environment affected all four stages of healing (Marriage-Arcari., 2016). Zinc oxide was as effective as a topical enzymatic agent in treating pressure ulcers (Agren et al., 1991), and also significantly increased wound contraction (Cangul et al., 2006). Similarly, in the present study, a higher percentage of wound contraction was observed in the zinc oxide-containing groups during the evaluation period. Abdullah et al. (2019) investigated the effect of topical application of zinc oxide ointment and platelet-rich plasma on the experimental defect of full skin thickness in New Zealand rabbits. They concluded that zinc reduces wound debris and increases epithelialization in surgical wounds. Aksoy et al. (2010) evaluated the effectiveness of the topical application of zinc oxide in the development of hypertrophic scars in rabbits. They revealed that zinc oxide ointment can be used therapeutically to accelerate wound healing and to prevent hypertrophic ulcers in patients with a high probability of developing hypertrophic ulcers such as patients with deep second-degree burns and patients undergoing heart surgery (Aksoy et al., 2010).

Topical zinc oxide could accelerate the healing of leg wounds and skin grafts, which are mainly closed by epithelialization. This drug accelerates the wound healing process in both full-thickness and part-thickness wounds (Lansdown et al., 2007). Topical zinc oxide had no significant effect on reducing the time required for open surgical pilonidal sinus wounds to close. This discrepancy can be explained by stimulated epithelialization overwound contraction in experimental wounds (Agren et al., 2006). In an experimental study comparing the effects of silver sulfadiazine and zinc oxide on burn wounds in New Zealand rabbits, it was concluded that zinc oxide ointment was more effective than silver sulfadiazine in healing burn wounds (Arslan et al., 2012). Zinc oxide has a more effective role in epithelialization, wound maturation, and reducing scar formation. Zinc oxide further accelerates recapitalization for 4 to 5 days. It also reduces the colonization of bacteria at the wound site. This is probably the most recent reason for the lack of clinical observation of infection in groups containing zinc oxide. The simultaneous effect of topical honey use on wounds and oral sulfate consumption was examined in rats. It was indicated that co-administration of these two substances increases the growth of fleshy bud tissue, enhances angiogenesis at the wound site, stimulates epidermal migration and increases wound tensile strength (Sazegar et al., 2011). Oral administration of zinc sulfate and natural honey (administered topically) can also affect wound healing in people with zinc deficiency. Since re-epithelialization is an important mechanism in wound closure, it was suggested that topical honey and oral zinc may accelerate healing not only in animals with low serum zinc levels but also in animals with normal zinc status.

Following the use of a combination of honey and zinc oxide, a higher percentage of wound contraction, angiogenesis, epithelialization, and granulation tissue growth are observed compared to using them individually. Collagen bunches will also have a more regular arrangement, much less inflammation, and no infection at the wound site. In other words, following the use of this combination, wound healing will be faster with better quality. Therefore, it can be concluded that the topical and simultaneous use of a combination of honey and zinc oxide is relatively effective in healing full-thickness wounds in the rat in terms of macroscopic and microscopic use compared to their separate use. However, further studies are needed to provide clinical advice on this combination.

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Conflict of interest

The authors declare that they have no competing interests.

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ارزیابی هیستوپاتولوژی ترکیب عسل و پماد زینک اکساید بر ترمیم زخم تجربی تمام ضخامت پوست در موش صحرایی

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چکیده

اساساً زخم به ایجاد هرگونه شکاف و از بین رفتن پیوستگی بافت‌های بدن چه در داخل و چه در سطح خارجی بدن گفته می‌شود. همواره تلاش برای یافتن اثربخش‌ترین و کم عوارض‌ترین عاملی که روند ترمیم زخم را تسریع کند مورد نظر محققین بوده است. هدف از انجام مطالعه‌ی حاضر، بررسی و مقایسه‌ی میزان اثربخشی عسل به تنهایی یا در ترکیب با پودر زینک اکساید بر ترمیم نقیصه‌ی تجربی تمام ضخامت پوست در موش صحرایی می‌باشد. در این تحقیق، تعداد ۴۸ موش صحرایی سفید نر بالغ از نژاد ویستار انتخاب شدند. حیوانات به صورت تصادفی به چهار گروه ۱۲تایی تقسیم شدند: گروه اول (کنترل=C)، گروه دوم (عسل=H)، گروه سوم (روی=Z) و گروه چهارم (عسل و روی=ZH). یک نقیصه پوستی تمام ضخامت با ابعاد ۲×۲ سانتی‌متر در پوست ناحیه پشت، حدفاصل بین گردن و ناحیه لگنی ایجاد گردید. تمامی حیوانات درمان متناسب با گروه خود را دریافت نمودند. از هر گروه، چهار موش در روزهای ۷، ۱۴ و ۲۱ نمونه هیستوپاتولوژی تهیه گردید و بررسی میکروسکوپی انجام شد. بررسی ماکروسکوپی نیز با استفاده از نرم‌افزار Axiovision صورت گرفت. با ارزیابی پارامتر درصد بهبودی زخم، بالاترین میزان بهبودی در روز ۷ پس از ایجاد زخم به گروه Z و کمترین آن به گروه H تعلق داشت. همچنین بالاترین میزان بهبودی در روز ۱۴ پس از ایجاد زخم به گروه Z و کمترین آن به گروه ZH تعلق داشت. اما از نظر آماری هیچ‌گونه اختلاف معنی‌داری بین گروه‌ها مشاهده نگردید. در روز ۲۱ پس از ایجاد زخم، درصد بهبودی زخم در گروه ZH به طور معنی‌داری بیشتر از گروه‌های کنترل (p=۰/۰۰۱)، عسل (p=۰/۰۰۱) و زینک اکساید (p=۰/۰۱۳) بود. در روز ۲۱ پس از جراحی، در قسمت درم در تمام موش‌های گروه ZH، دستجات منظم کلاژن همراه با تعداد کمی فیبروبلاست و مویرگ قابل مشاهده بود. این شرایط در دو موش از گروه Z و یک موش از گروه C نیز دیده شد. در سایر موارد بافت جوانه‌ی گوشتی با فیبروبلاست‌ها و مویرگ‌های خونی متعدد رؤیت گردید. این مطالعه نشان داد ترکیب زینک اکساید و عسل نسبت به سایر گروه‌ها در فرآیند ترمیم زخم تاثیر بهتری دارد و روند ترمیم زخم را تسریع می‌کند. ترکیب این دو ماده باعث افزایش تشکیل بافت جوانه‌گوشتی، افزایش انقباض زخم، کاهش التهاب، کاهش اسکار زخم می‌شود.

کلمات کلیدی: ترمیم، زخم، عسل، زینک اکساید، موش صحرایی

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