



# Evaluation of a Natural Ointment on Wound Healing

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## Abstract

**Introduction:** Traditional medicine may play an essential role in wound healing. This study aimed to assess the effect of a natural ointment on wound healing in the first stage of an open wound.

**Methods:** This randomized clinical trial study included 80 patients with pilonidal sinus referred to our hospital in Tehran from 2020 to 2021 who underwent open surgery. Patients were divided into two groups receiving medication and the control group using the block randomization method. Chi-square was used to describe qualitative variables, and T-test was used to describe quantitative variables. Parametric and non-parametric tests were used according to the type of variable distribution. It was used to compare the means of each group. A P-value less than 0.05 was considered significant.

**Results:** Wound healing time, pain intensity, need for analgesic compounds, and wound secretion were significantly shorter in the study group than in the control group ( $P < 0.001$ ).

**Conclusion:** The effect of this natural ointment on wound healing appears promising. Further studies are recommended.

**Keywords:** Wound Healing, Open Wound, Pilonidal Sinus.

## Introduction

Wound healing is one of the significant concerns and costly circumstances with a substantial global market for wound care products <sup>1</sup>.

The site of surgical wounds is a predisposing environment for bacterial colonization in medical centers. Among these, some factors that interfere with wound healing include underlying disease (including diabetes and uremia), wound classification and wound infection, Old age, malignancy, malnutrition, weakened immune system, smoking and infection in other parts of the body, use of steroid drugs and chemotherapy <sup>2</sup>, due to the improvement of wound healing methods to increase the quality of life and reduce Treatment costs will help patients a lot; Researchers have focused on determining a definitive drug to heal or heal wounds completely. The use of herbs is one of the essential methods of treatment that plays a critical role in the treatment of skin diseases, and wound healing with

drugs or substances with minor side effects, especially herbal compounds, is significant and valuable <sup>3</sup>.

ZOUSH ointment is prepared from a combination of extracts of Satureja Khuzestanica, Zataria multiflora, Origanum vulgare., honey, and Starch <sup>3</sup>; it should be noted that all plant extracts are identified by chromatographic technique, and this study aimed to investigate the effect of Zoush combination ointment on wound healing in the human sample, which in the first stage of the open wound due to pilonidal sinus surgery. In this study, macroscopic methods will evaluate patients during treatment following the use of Zoush combination ointment. The wound is washed and dressed without particular medication in the control group <sup>4</sup>.

A pilonidal cyst or sinus is a little skin sac containing hair on the lower back. The pilonidal disease occurs as an acute abscess or draining sinus in the sacral region of

the tail. This cyst or abscess usually develops at the end of the spine. This cyst is prone to infection. Pilonidal cysts are uncommon in black people. Both sexes are affected, but it is more common in men. Cyst infection usually begins in early adulthood (18-40 years). Most age groups are between 16 and 26. Statistically, 26 out of every 100,000 people get the disease<sup>4</sup>. In military populations, the pilonidal sinus is also essential regarding personnel and finances. For example, more than 77,000 soldiers were admitted to military hospitals from 1942 to 1945 due to the pilonidal sinus and were involved in the pilonidal sinus for an average of 44 days<sup>5</sup>.

In general, the wound healing mechanism includes two processes. The first phase in the wound healing process is the initial vascular response to damaged tissue. The response time is 10 minutes from the start of the injury to stop the bleeding. At this stage, the damaged cells at the wound site secrete substances that lead to the narrowing of the arteries and activation of the coagulation response, thus preventing bleeding<sup>6,7</sup>. The second phase of the healing process is the inflammatory response, which lasts up to a week. Clot formation is a repair signal that leads to the recall of monocytes to the wound site one day after the onset of injury, which then turns into macrophages. At the wound site, platelets begin to secrete transducer growth factor, fibroblast growth factor, and platelet-derived growth factor, stimulating the cell to grow and multiply. After the end of the third day and the inflammatory response, leukocytes migrate from the wound<sup>8-12</sup>.

Therefore, angiogenesis results from the growth of pre-existing dermal vessels around the wound. In the third phase, fibroblast proliferation is stimulated by several mechanisms. At the wound site, various collagens are synthesized and secreted. Iron molecules such as cofactors, oxygen, and vitamin C are required to bind collagen molecules together. The presence of collagen in the extracellular matrix leads to tissue strength<sup>13</sup>. As migration begins, epithelial cells differentiate, migrating from the wound's edges to the center and covering the entire wound, stopping migration when the wound bed is completely covered. In the final phase, the tissue regains its natural state by changing the cellular arrangement, eventually leading to wound healing<sup>8</sup>.

The general purpose of this study was to evaluate the effect of natural ointment on open wound healing due to surgery in patients with pilonidal sinus.

## Methods

This study is a randomized clinical trial or RCT with the registration code IRCT20201106049283N1. This trial's statistical population included patients referred to Baqiyatallah Hospital in 2020 and 2021 for treatment of pilonidal sinus and who underwent open surgery. Inclusion criteria include patients with pilonidal sinus who have undergone open surgery, Conscious consent to participate in the project, Males under 45 years of age, and BMI less than 35. Based on the 2019 study, with an effect size of 0.3, a power test of 80%, and a significant level of 0.05, 80 samples were entered into two groups. Among patients with pilonidal sinus referred to Baqiyatallah Hospital in Tehran in 2020 and 2021, a sample of 80 people who underwent surgical resection was randomized. Using statistical software and the block randomization method (with block sizes of 4 and 6), patients were divided into two groups receiving medication and a control group (without receiving medication); the vital statistician arranged the order assigned to random groups, and each put the random position in an envelope. When each patient entered the study, an envelope was opened, and his treatment group was identified.

Group 1 includes surgical patients treated with Zoush ointment; Group 2 has patients operated on without ointment treatment.

### Formulation of Zoush ointment

The prepared ointment was received from a previous study by Dr. Davoud Esmaili et al.<sup>3</sup>.

The inclusion criteria were patients with second-degree burns. Exclusion criteria were reluctance to follow up, history of previous trauma or burn in the burned area, and facial burns that are important for beauty.

### Method of Zoush ointment

The ointment is applied in such a way that the day after the surgery, the wound site is first washed with water and baby shampoo, then the wound surface is completely covered with a layer of ointment, and a dressing is applied; this process continues once every 24 hours for up to 3 weeks.

In the group without ointment, only water washing baby shampoo, and wound dressing without any effective substance were used.

Patients in both groups were followed up at intervals of 7, 30, 60, and 90 days after surgery, and the results were recorded.

Finally, the two groups' information obtained during each visit and photographs during treatment were recorded in the relevant checklist, and treatment changes in the two groups were compared.

In this study, the Likert scale was used to determine patient satisfaction. This scale was confirmed by at least five surgeons in Baqiyatallah Hospital. The Likert scale is one of the most common measurement scales in research based on a questionnaire developed by Rennes Likert. The answers are multiple-choice; for example, in the case of 5 points, the options include "strongly disagree, disagree, have no opinion, agree, and strongly agree." Each item is then numerically evaluated, which is why it is also called the Score Sum.

#### Data analysis

Data were collected and analyzed by SPSS 22 software. Fisher exact test was used to describe qualitative variables, and a T-test was used for quantitative variables. According to the type of distribution of variables, parametric and non-parametric tests were used to compare the means of each group. A P-value less than 0.05 was considered a significant level in all statistical analyses.

#### Research limitations

Some patients did not have the necessary cooperation or were residents in the city or were not available due to the coronavirus pandemic so that we could follow them, so we tried as much as possible to provide the necessary information through Whatsapp and telephone calls.

The code of the Medical Ethics Study Committee is R.BMSU.BAQ.REC.1399.041

#### Results

In this study, 80 patients with pilonidal sinus who underwent open surgery were included in the study in the both control and Zoush groups.

The mean age was  $24.90 \pm 5.22$  in the Zoush group and  $27.92 \pm 6.56$  in the control group ( $P = 0.05$ ). The age difference between the two groups was not significant.

The mean BMI was  $29.6 \pm 2.02$  in the Zoush group and  $27.40 \pm 1.62$  in the control group ( $P < 0.001$ ). The mean BMI was significantly higher in the Zoush group than in the control group.

The mean wound volume was  $7.87 \pm 2.59$  ml in the wart group and  $6.27 \pm 1.82$  in the control group ( $P = 0.008$ ). The mean wound volume was significantly higher in the zoush group than in the control group (Table 1).

Table 1: Distribution of age, BMI, and wound volume of patients by group, independent t-test.

Characteristic	P-value	Control	Zoush
age	0.05	$27.92 \pm 6.56$	$24.90 \pm 5.22$
BMI	0.001	$27.40 \pm 1.62$	$29.60 \pm 2.02$
Wound volume	0.008	$6.27 \pm 1.82$	$7.87 \pm 2.59$
Independent t-test.			

The mean of pain seven days later was  $2.05 \pm 0.71$  in the Zoush group and  $3.65 \pm 1.23$  in the control group ( $P < 0.001$ ). The mean pain seven days later was significantly lower in the Zoush group than in the control group (Table 2). The mean pain 30 days later was significantly lower in the Zoush group than in the control group. The mean pain 60 and 90 days later was not significantly different between the control and Zoush groups (Table 2). Four patients (10.0%) in the Zoush group and 11 patients (27.5%) in the control group needed analgesic compounds in the first week ( $P < 0.001$ ). The need for analgesic compounds was

significantly lower in the Zoush group in the first week than in the control group.

0 patients (0.0%) in the Zoush group and 4 patients (10%) in the control group needed analgesic compounds in the first month ( $P < 0.001$ ). The need for analgesic compounds was significantly lower in the Zoush group in the first month than in the control group. In the second and third months, there was no need for analgesic compounds between the two groups. (Table 3).

The mean patient satisfaction was  $3.47 \pm 0.50$  in the zoush group and  $0.85 \pm 2.85$  in the control group ( $P < 0.001$ ). The mean of satisfaction was significantly

higher in the Zoush group than in the control group (Figure1).

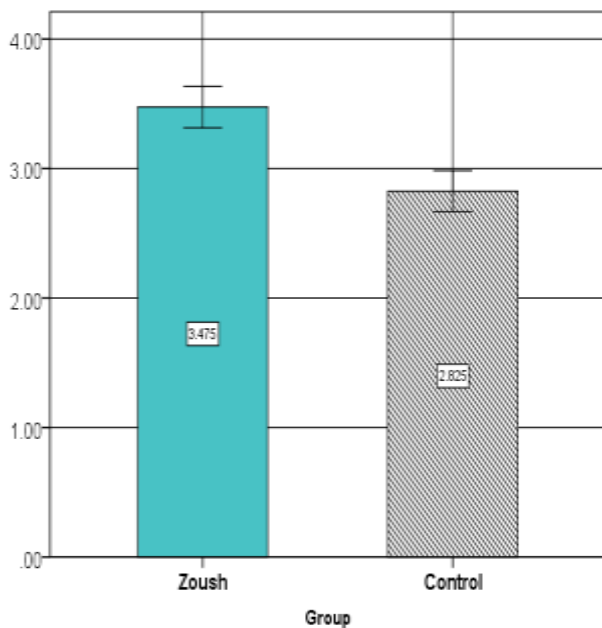


Figure 1: Mean patient satisfaction in the two groups

Two patients (5.0%) in the Zoush group and 12 patients (30.0%) in the control group had ulcer secretion ( $P < 0.001$ ). Wound discharge was significantly lower in the first week in the Zoush group than in the control group (Table 4).

At subsequent visits, there was no significant difference between the two groups in wound discharge.

In addition, there was no need for antibiotic treatment in both groups' wound secretion.

The mean recovery time was  $47.27 \pm 7.47$  in the Zoush group and  $56.62 \pm 9.28$  in the control group ( $P < 0.001$ ). The mean recovery time was significantly shorter in the Zoush group than in the control group (Figure 2).

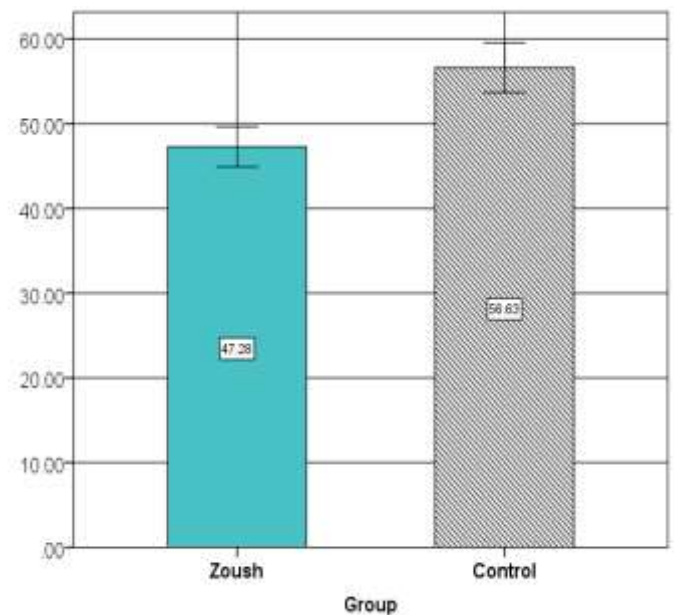


Figure 2: Mean recovery time in the two groups.

Table 2: Distribution of patients' pain by group.

Characteristic	P-value	Control	Zoush
Pain after 7 days	0.001	$3.65 \pm 1.23$	$2.05 \pm 0.71$
Pain after 30 days	0.001	$0.6 \pm 0.1$	$0.05 \pm 0.01$
Pain after 60 days	---	$0.0 \pm 0.0$	$0.0 \pm 0.0$
Pain after 90 days	---	$0.0 \pm 0.0$	$0.0 \pm 0.0$

Table 3: Distribution: Analgesic compounds, Fisher exact test.

Characteristic	Control	Zoush	P-value
Analgesic compounds up to one week	11(%27.5)	4(%10)	<b>0.001</b>
Analgesic compounds for up to one month	4(%10)	0(%0)	<b>0.001</b>





Figure 3: An example of Zoush group photos

Table 4: Distribution: Wound discharge status, Fisher exact test.

Characteristic	Control	Zoush	P-value
Wound discharge first week	12(%30)	2(%5)	0.001
First month wound discharge	2(%5)	0(%0)	0.07
Second month wound discharge	1(%2.5)	0(%0)	0.14



Figure 4: An example of control group photos

## Discussion

Despite the scientific advances in wound healing, wound healing and its infections, especially postoperative infections, were still a significant health problem in surgical centers, including several factors. They interfere with wound healing, including underlying diseases (diabetes and uremia), wound classification, and wound infection. Old age, malignancy, malnutrition, weakened immune system, smoking, infection in other parts of the body, use of steroid drugs and chemotherapy, etc., due to the improvement of wound healing methods to increase the quality of life and reduce costs of Therapy in patients will help a lot; Researchers have focused on determining a definitive drug to heal or heal wounds completely<sup>13-18</sup>. The use of herbs is one of the most important methods of treatment that plays an essential role in the treatment

of skin diseases, and wound healing with drugs or substances with minor side effects, especially herbal compounds, is significant and valuable<sup>15-21</sup>.

Pilonidal disease, by inducing a sinus or cyst in the sacral region of the tailbone, causes problems and an inability to perform daily tasks and infects these patients by causing various symptoms. Various methods have been proposed for the proper treatment of these patients<sup>20-22</sup>. A typical old practice is removing and bandaging the area to heal the surgical site and the wound over time. Today, due to the importance of time and the need for a quick return to work and life for patients, finding a treatment solution to accelerate this process is essential. Materials and medicines are listed for fast and convenient repair<sup>23</sup>.

This study aimed to investigate the effect of Zoush combination ointment on wound healing in a human

sample. In the first stage, the open wound caused by pilonidal sinus surgery (secondary repair method) was used. The use of Zoush combination ointment was evaluated. The wound was washed and bandaged in front of the control group without any particular medication<sup>24</sup>.

In this clinical trial, after randomly dividing the patients based on the entry and exit criteria, they were divided into two groups of 40 recipients of Zoush combined ointment and the control group. The differences and similarities between the two groups were statistically examined.

The two groups were similar in terms of many demographic variables and the characteristics of the surgery. They did not have a significant difference, indicating the appropriate patient distribution in these two groups.

The variables evaluated after surgery to assess the extent of improvement under the influence of Zoush combined ointment and postoperative control group include:

- The patient's satisfaction after surgery.
- The severity of postoperative pain.
- The need for analgesic compounds.

Results were better in the Zoush group.

Panahi et al. (2015) showed that Aloe vera/olive oil combination ointment affects chronic wounds<sup>25</sup>. The effect of this drug was compared with phenytoin ointment. The results showed that although both treatments positively affected the healing process, the results obtained according to the VAS criteria were better for the amount of pain in the group receiving aloe vera/olive oil combination cream. The results obtained from this group in reducing pain were consistent with those obtained in the present study after 30 days<sup>21-25</sup>.

The appearance of the wound in terms of secretion was also examined. The data obtained from the evaluation of wound condition seven days after surgery showed that purulent secretions in wounds of patients of Zoush's combination ointment group were less, and this difference was statistically significant. Less purulent discharge at the site of the pilonidal sinus surgery wound can be considered a positive factor in patients in the combination cream group compared to patients in the placebo group.

One of the most important variables of this study was the mean recovery time, which was  $47.27 \pm 7.47$  in the Zoush group and  $56.62 \pm 9.28$  in the control group ( $P < 0.001$ ). Therefore, the mean recovery time was

significantly shorter in the Zoush group than in the control group.

In 2005, Agren et al. conducted a randomized, double-blind study of the therapeutic effect of zinc oxide on wound healing from open pilonidal sinus surgery. In this study, 64 patients were divided into two groups receiving a placebo and zinc oxide. Although the results of this group showed a positive effect of zinc oxide on the treatment of these wounds, the average duration of Therapy in this treatment strategy was 54 days, which was longer than the duration of wound healing in the present study<sup>24</sup>.

## Conclusion

Positive results were seen, including reduced discharge and the amount of pain and duration of wound healing using Zoush natural ointment. It is recommended that more studies should be done to confirm the outcomes.

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None.

## Conflict of Interest Disclosures

There is on Conflict of Interest.

## Funding Sources

None.

## Authors' Contributions

All authors contributed equally in this study.

## Ethical Statement

The code of the Medical Ethics Study Committee is R.BMSU.BAQ.REC.1399.04. This study is a randomized clinical trial or RCT with the registration code IRCT20201106049283N1.

## References

1. Haridas M, Malangoni MA. Predictive factors for surgical site infection in general surgery. *Surgery*. 2008 Oct 1;144(4):496-503.
2. Brunicaudi FC. Schwartz's principles of surgery. McGraw-Hill Education.; 2019.
3. Meskini M, Ghorbani M, Esmaeili D. The Importance of Using ZOUSH Ointment in Burn Wound Infection Treatments. *Adv Vaccines Vaccin Res*. 2018;1(1):16-8.

4. da Silva JH. Pilonidal cyst: cause and treatment. *Diseases of the colon & rectum*. 2000 Aug 1;43(8):1146-56.
5. Corman ML. *Corman's colon and rectal surgery*. Wolters Kluwer Health/Lippincott Williams & Wilkins; 2013.
6. Clark RA, editor. *The molecular and cellular biology of wound repair*. Springer Science & Business Media; 2013 Nov 11.
8. Eming SA, Krieg T, Davidson JM. Inflammation in wound repair: molecular and cellular mechanisms. *Journal of Investigative Dermatology*. 2007 Mar 1;127(3):514-25.
9. Martin P. Wound healing--aiming for perfect skin regeneration. *Science*. 1997 Apr 4;276(5309):75-81.
10. Ghaderi R, Afshar M, Akhbarie H, Ghalipour MJ, Ghaderi R, Afshar M. Comparison of the efficacy of honey and animal oil in accelerating healing of full thickness wound of mice skin. *Int J Morphol*. 2010 Mar 1;28(1):193-8.
11. Cutting KF. Honey and contemporary wound care: an overview. *Ostomy Wound Management*. 2007 Nov 1;53(11):49.
12. Yaghoobi R, Kazerouni A. Evidence for clinical use of honey in wound healing as an anti-bacterial, anti-inflammatory anti-oxidant and anti-viral agent: A review. *Jundishapur journal of natural pharmaceutical products*. 2013 Aug;8(3):100.
13. Esmaeelian B, Najafi O, Aldavood SJ, Jalali FS, Farshid AA, Rahmani S. Clinical and histopathological evaluations of local honey application in the healing of experimental wounds in dog. *Journal of Veterinary Research*. 2012;67(3):265-71.
14. Lusby PE, Coombes A, Wilkinson JM. Honey: a potent agent for wound healing?. *Journal of WOCN*. 2002 Nov 1;29(6):295-300.
15. Gethin GT, Cowman S, Conroy RM. The impact of Manuka honey dressings on the surface pH of chronic wounds. *International wound journal*. 2008 May;5(2):185-94.
16. Smirnov SV, Shakhlov MV, Litinsky MA, Yanshin DV, Sachkov AV, Obolensky VN. Polyurethane foam covering for wounds, burns and ulcers. *Wound medicine*. 2013 Nov 1;2:6-8.
17. Heo DN, Yang DH, Lee JB, Bae MS, Kim JH, Moon SH, Chun HJ, Kim CH, Lim HN, Kwon IK. Burn-wound healing effect of gelatin/polyurethane nanofiber scaffold containing silver-sulfadiazine. *Journal of biomedical nanotechnology*. 2013 Mar 1;9(3):511-5.
18. Meskini M, Esmaeili D. The study of formulated Zoush ointment against wound infection and gene expression of virulence factors *Pseudomonas aeruginosa*. *BMC complementary and alternative medicine*. 2018 Dec;18(1):1-0.
19. Meskini M, Ghorbanalizadegan M, Esmaeili D. Importance of Herbal Ointment for *Pseudomonas aeruginosa* infection in burn patients. *International Journal of Medical Investigation*. 2015 Jun 10;4(2):257-61.
20. Meskini M, Ghorbani M, Bahadoran H, Zaree A, Esmaeili D. ZOUSH ointment with the properties of antibacterial moreover, burn wound healing. *International Journal of Peptide Research and Therapeutics*. 2020 Mar;26:349-55.
21. Meskini M, Korani M, Esmaeili D. Herbal Therapy for Burn Wound Infections. *Medical Laboratory Journal*. 2019 Jul 1;13(4).
22. Mehrvarz S, Mohebbi HA, Manoochehry S, Arjmand S, Rasouli HR. Comparison of outcomes in four different surgical methods for sacral pilonidal sinus with long-term follows-up. *Tehran University Medical Journal TUMS Publications*. 2019 Jan 10;76(10):660-4.
23. Mackowski A, Levitt M. Outcomes of the house advancement flap for pilonidal sinus. *ANZ Journal of Surgery*. 2017 Sep;87(9):692-4.
24. Egren MS, Ostenfeld U, Kallehave F, Gong Y, Raffn K, Crawford ME, Kiss K, Friis-Møller A, Gluud C, Jorgensen LN. A randomized, double-blind, placebo-controlled multicenter trial evaluating topical zinc oxide for acute open wounds following pilonidal disease excision. *Wound repair and regeneration*. 2006 Sep;14(5):526-35.
25. Panahi Y, Izadi M, Sayyadi N, Rezaee R, Jonaidi-Jafari N, Beiraghdar F, Zamani A, Sahebkar A. Comparative trial of Aloe vera/olive oil combination cream versus phenytoin cream in the treatment of chronic wounds. *Journal of wound care*. 2015 Oct 2;24(10):459-65.