

ORIGINAL ARTICLE

JOURNAL OF WOUND
RESEARCH AND TECHNOLOGY
INDONESIAN SCIENCE MEDIA

Implementation of Combination of Curcumin Gel and Honey for the Treatment of Diabetic Foot Ulcer: A Pre-Experimental Study

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None

DOI: <https://doi.org/10.70196/jwrt.v1i1.6>

Journal of Wound Research and Technology, Volume 1 (1), 38-45

Abstract**Background:** A persistent condition known as diabetes mellitus causes elevated blood sugar levels due to the pancreas's inability to make insulin. Diabetic foot ulcers are one consequence. Diabetic wounds can heal more quickly with the help of aloe vera and honey.**Aims:** This study aims to determine the effect of wound care using curcumin gel and honey on diabetic foot ulcer healing at Bilqis Clinic Bekasi.**Design and Methods:** A one-group pre-post experimental design was employed in the study. All 78 participants were selected using a complete sample procedure; the study population consisted of people with diabetic foot ulcers.**Results:** The age distribution of ozone group participants was 47.13 with a 23.14 standard deviation. The rising BMI averaged 26.17 (7.31). Many participants, 38 (55.1%), attended high school of the 48 people (77.4%), most had diabetes for less than three years. Patient glucose control was stable, averaging 121 (60.11) during the assessment. HbA1c was 10.29 (2.23), and basal wound size was 43.91 (21.45). The Wilcoxon test showed a significant difference ($p=0.027 < 0.05$) between data gathered before and after using curcumin gel and honey.**Conclusion:** Curcumin and honey, when used as a wound treatment, has a notable impact on the healing process of diabetic foot ulcers. When treating chronic wounds, a mixture of curcumin and honey is suggested.**Keywords:** curcumin; honey, foot, diabetic ulcer; wound, wound healing

1 | INTRODUCTION

Hyperglycaemia owing to insulin resistance, insufficient insulin production, or both defines diabetes mellitus, a cluster of metabolic diseases. Problems with the eyes (retinopathy), kidneys (nephropathy), blood vessels (vasculopathy), and feet (podopathy) are all consequences of diabetes mellitus (American Diabetes Association, 2014). A reddish-black, foul-smelling wound on the foot is known as diabetic foot, and it develops when the medium or large blood arteries in the limbs become blocked. For all people living with diabetes, diabetic wounds rank high among the chronic consequences of the disease (Akkus & Sert, 2022; Akter, 2019).

Just under 2.9 percent of West Javans are living with diabetes mellitus. There were 7,404 cases of diarrhoea and 5,370 cases of diabetes mellitus

among inpatients at type B public hospitals as of May 31, 2013, according to the hospital annual report (World Health Organization, 2016). At the same time, type C public hospitals had 4,620 instances of diabetes mellitus and 6,355 cases of hypertension among its inpatients. The 2018 report on the number of cases and fatalities of non-communicable diseases (NCDs) monitored by Puskesmas reveals that hypertension (7634) and diabetes mellitus (12,877) are the top two, with women reporting 6,513 cases and males 2,113 cases, respectively (Ministry of Health RI, 2018).

The prevalence of diabetic wound patients in Indonesia is about 15% of the prevalence of diabetes mellitus patients, the amputation rate is 30%, the mortality rate is 32% and diabetic wounds are the most common cause of hospitalization at 80% for diabetes mellitus. December saw 78

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patients of varying degrees presenting with diabetic wounds, according to data collected by the Bilqis Clinic Global Indonesia Health Care. Interviews with patients at the Bilqis Wound Care Centre Bekasi Clinic revealed that patients do not regularly get wound care because of the high cost and the fact that health insurance does not cover it.

Given the benefits of wound care in a moist condition, numerous practitioners have started researching strategies to keep the environment moist using alternative compounds, such as curcumin (Monika et al., 2022). The primary curcuminoid in turmeric and tomahawk, curcumin (diferuloylmethane), is what gives the plants their characteristic yellow hue. Anxieties, anti-infectives, anti-carcinogenic, anti-mutagenic, anti-coagulant, and antioxidant properties have all been demonstrated for curcumin (Halimatushadyah & Rahayu, 2023). On top of that, curcumin offers a lot of benefits when it comes to wound healing (Mahmood et al., 2015).

The healing of a wound naturally consists of four steps, some of which overlap with one another. Blood clotting, inflammation, cell division, and remodelling are the four phases (Burhan & Sebayang, 2022). Platelet aggregation and fibrin clot formation initiate the haemostasis stage soon upon injury (Schilrreff & Alexiev, 2022). When macrophages release cytokines at the wound site and neutrophils remove wound debris, the wound is in the inflammatory stage (Raziyeva et al., 2021). The re-epithelialization process begins in the proliferative stage when fibroblasts enter the wound and deposit new extracellular matrix (Rousselle et al., 2019). Myofibroblasts and collagen synthesis enable additional tissue remodelling. For full recovery, each step must be performed at the correct time and in the correct sequence (Apte et al., 2023; El Ayadi et al., 2020; Tomasek et al., 2002).

Numerous studies conducted in the modern day have confirmed that honey is a nutritious diet that can aid in the healing of wounds and a variety of illnesses (Cialdai et al., 2022). When applied topically to inflamed wounds, natural honey effectively inhibits the growth of nearly all bacteria,

germs, and fungi (Samarghandian et al., 2017). According to (Chotchoungchatchai et al., 2020), honey is the best solution for bandaging infected wounds following surgery (Burhan et al., 2023). Honey possesses remarkable efficacy in promoting wound healing due to its abundant nutritional content essential for the healing process (Tashkandi, 2021). Honey possesses a significant osmolality that enables it to effectively absorb water and enhance circulation and air exchange within the wound (Scepankova et al., 2021).

I THE STUDY

2 I METHODOLOGY

The Health Research Ethics Commission of STIKES Medistra, Indonesia has approved this research in February 2024, with registration number B. LPPM-SMI/113/11/2023.

Study Design & Participants

Individuals classified as adults who have been diagnosed with diabetes and subsequently develop foot ulcers throughout the time frame spanning from January 17, 2024, to February 17, 2024. Intervention and control groups (N=78) were randomly assigned. The study recruited patients from Clinic Global Indonesia Health Care Kediri. This study included individuals of both genders who were undergoing treatment for diabetic foot ulcers. The study's inclusion criteria were established using the PEDIS, which encompassed individuals with a current blood sugar level ranging from 120 to 180 mg/dl, a lesion length surpassing, and the presence of infection. This investigation includes immunodeficiency illnesses as examples of exclusion criteria.

Sampling, Intervention, Collecting Data

The sample technique employed in this investigation was complete sampling. Total sampling, often known as census sampling, is a sampling approach in which every individual in the population is included as a sample. Total sampling is conducted when the population size is fewer than 100. The sample size in this study consisted of 20 respondents, as per the inclusion criteria. Researchers utilized measurement devices or research instruments, which are tools employed to

quantify observed natural and social phenomena. The equipment utilized in this study was a wound evaluation observation sheet employed to evaluate the condition of the patient's wound. The measuring instrument utilized was derived and altered from the Bates-Jensen Wound Assessment Tool (BWAT) wound status format, specifically tailored for diabetic wounds.

Data analysis

The gathered data underwent analysis utilising the IBM Statistics version 23, and its normality was assessed through the application of the Kolmogorov-Smirnov test. The analysis employed the Wilcoxon signed rank test, a statistical test for

correlation, using the SPSS software. In statistical analysis, a significance level of $p < 0.05$ is used to evaluate the degree of significance. If the statistical results reveal a value of $p < 0.05$, it means that the null hypothesis (H₀) is accepted. This indicates a significant influence between the independent variable and the dependent variable.

3 | RESULTS

The age distribution of participants in the ozone group was 47.13 with a standard deviation of 23.14. The average (standard deviation) of the increasing body mass index (BMI) was 26.17 (7.31). Most of the participants, specifically 38 individuals (55.1%), attended high school.

Table 1. Table 1. Characteristics of Respondents on the Effectiveness of Curcumin Gel Combination with Honey

Variable	Dressing group (n=42) Mean±SD and n (%)
Age (Years)	47.13±23.14
Body mass index (kg/m ²)	26.17±7.31
Gender	
Male	42 (60.8)
Female	36 (39.2)
Level Education	
Junior high school	23 (33.7)
High school	38 (55.1)
University	17 (11.2)
Duration of diabetes	
Three years	48 (77.4)
Four years	18 (14.1)
>Five years	12 (8.5)
Long-term diabetic foot ulcer	
1 years	13 (21.8)
2 years	18 (37.8)
>3 years	57 (40.4)
Glicemic (mg/dl)	121±60.11
HbA1c (mmol/L)	10.29±5.23
Wound Size (Cm) <i>Baseline</i>	43.91±21.45

Primary data source 2024; Mean±Standart deviation; n (%)

According to table 2, the calculation resulted in a p-value of 0.027. The criterion for rejecting the null hypothesis (H₀) in the Wilcoxon signed rank test is when the probability (Asymp. Sig) is less than 0.05, indicating a statistically significant effect. The results of this study indicate that the application of curcumin gel and honey in wound care has a positive impact on the healing of diabetic wounds (Table 2).

Most individuals had a diabetes history of three years or less following their diabetes diagnosis, accounting for 48 individuals (77.4%). During the examination, the glycemic control of the patient was found to be steady, with an average value of 121 (60.11). The HbA1c level was measured to be 10.29 (2.23), and the size of the basal wound was recorded as 43.91 (21.45) (Tabel 1)

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Table 2. Comparison of mean scores of Healings Diabetic Foot Ulcers

Variable	Pre-Treatment			Post-Treatment			Wilcoxon	p-value
	n	Mean Rank	Sum of Rank	n	Mean Rank	Sum of Rank		
Healing Diabetic Foot Ulcer	78	2.10	2.17	78	8.00	41.00	264.0	0.027

Primary data source 2023, Wilcoxon test

According to table 2, the calculation resulted in a p-value of 0.027. The criterion for rejecting the null hypothesis (Ho) in the Wilcoxon signed rank test is when the probability (Asymp. Sig) is less than 0.05, indicating a statistically significant effect. The

4.1 DISCUSSION

Wounds that develop on the foot of people with uncontrolled diabetes mellitus, which causes abnormalities in the lower legs, are called diabetic wounds. Infection, problems with blood vessels or innervation, and diabetes mellitus are the three main causes of foot complications (J. Kim, 2023; Rousselle et al., 2019). Angiopathy, neuropathy, and infection are the primary causes of diabetic wounds. Motor and sensory dysfunctions are symptoms of peripheral neuropathy (Volmer-Thole & Lobmann, 2016). Damage to the feet can go unnoticed because of a lack of or diminished pain perception brought on by sensory disruptions (Anastasi et al., 2013). When a person's motor skills deteriorate, their foot muscles atrophy, which shifts the patient's center of gravity and increases the risk of foot injury (Burhan et al., 2022). A blockage in the veins leading to the foot is known as angiopathy, diabetic wounds are more prone to infection because of neuropathy or decreased blood flow; hence, angiopathy and infection factors impact diabetes wound healing and treatment (J. H. Kim, 2023).

Irregular wound care was one of the characteristics that researchers found to be responsible for nearly all cases of wound regrowth. Infections can quickly set up after bacteria or germs penetrate diabetic wounds (Akash et al., 2020; Lipsky et al., 2012) (Jamie L. Burges). Disabilities might result from improperly managed diabetic wounds. The hypothesis put forth by (Parliani et al., 2023), lends

results of this study indicate that the application of curcumin gel and honey in wound care has a positive impact on the healing of diabetic wounds (Table 2).

credence to this view, asserting that all individuals, particularly those with diabetes mellitus, should practice good foot hygiene. This is because diabetic foot wounds take so long to heal that people with the condition are at high risk (Dasari et al., 2021). Consequently, the likelihood of foot problems can be diminished if all individuals are prepared to practice excellent foot care (Bus & Van Netten, 2016). Every single participant in this trial had a lower extremity wound, which is a common complication of diabetes. Diabetic sores are more common in the lower extremities of people with diabetes mellitus, according to the researcher (Jain et al., 2011).

Curcumin is a potent chemical that possesses strong anti-inflammatory and antioxidant properties. However, curcumin has certain disadvantages such as reduced stability and low bioavailability (Sohn et al., 2021). The 5% concentration of turmeric extract gel used in this study is regarded to be more efficacious in promoting wound healing benefits in human (Busman et al., 2020). Curcumin exhibits both antioxidant and per oxidant actions at low concentrations. Twenty Elevated levels of curcumin can enhance the generation of Reactive Oxygen Species (ROS), leading to oxidative stress that hampers the wound healing process (Maithili Karpaga Selvi, 2015). Moreover, a surge in reactive oxygen species (ROS) levels, particularly when they are elevated, might lead to cellular demise. High quantities of 21,22 ROS result in oxidative stress, which has the potential to induce DNA damage (Burhan & Arofiati, 2021). Oxidative stress is a

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contributing component that hinders the wound healing process and has the potential to impede tissue remodelling (Adeliana et al., 2021). Additionally, honey possesses antioxidant, antibacterial, and anti-inflammatory effects (Afzal et al., 2023; Almasaudi, 2021; Osman et al., 2022; Salehi et al., 2022; Scepankova et al., 2021). Honey can serve as a wound dressing to expedite and facilitate the process of healing (Yupanqui Miele et al., 2022). The antibacterial activity of honey is attributed to its high acidity, osmotic effect, antioxidant content, and hydrogen peroxide content (Almasaudi, 2021).

5 | STRENGTHS AND LIMITATIONS OF THE STUDY

This study used pre-experimental as the chosen research methodology, which based on its research

Utilizing two different types of enzymes in diabetic foot ulcer patients can enhance the process of wound healing by preventing degeneration and promoting regeneration, ultimately leading to a reduction in wound size. Nevertheless, the absence of a comparison in the study may diminish the impact of curcumin gel and honey. The user's text is enclosed in tags. Thus, future research can employ a design that incorporates a robust power analysis.

AUTHOR CONTRIBUTIONS

Ivan Khalid Ibrahim made contributions in the areas of conception and design, data acquisition, analysis, and interpretation. Ahmad Antony drafted or revised the manuscript critically for substantial intellectual content. The final draft was approved. Every author ought to furnish adequate information to enable the public to assume accountability for the precise substance: The Ahmad Antony Assume accountability for every facet of the project to verify and address concerns pertaining to its precision or ethical soundness: Ahmad Antony and Ivan Khalid Ibrahim

ACKNOWLEDGEMENTS

The authors would like to thank the Clinic Global Indonesia Health Care

CONFLICT OF INTEREST STATEMENT

design, has no statistical power and low research power because there is no comparison group. The risk of bias is only partially carried over to sample recruitment.

6 | IMPLICATION FOR THE PROFESSION AND/OR PATIENT CARE.

Implications for the field of medicine and wound care, as well as for doctors and nurses: The findings of this study make a valuable contribution to future advancements, particularly in the choice of enzymatic and traditional procedures as major treatment options. Therefore, by decreasing the expenses associated with patient care and enhancing the overall well-being of individuals suffering from diabetic foot ulcers.

7 | CONCLUSIONS

The authors affirm that they do not possess any conflicting interests.

DATA AVAILABILITY

The datasets utilized or analysed in the current inquiry are available upon reasonable request from the corresponding author.

REFERENCES

- Adeliana, Usman, A. N., Ahmad, M., Arifuddin, S., Yulianty, R., & Prihantono. (2021). Effectiveness of turmeric (*Curcuma Longa* Linn) Gel Extract (GE) on wound healing: Pre-clinical test. *Gaceta Sanitaria*, 35, S196–S198. <https://doi.org/10.1016/j.gaceta.2021.07.014>
- Afzal, S., Abdul Manap, A. S., Attiq, A., Albokhadaim, I., Kandeel, M., & Alhojaily, S. M. (2023). From imbalance to impairment: The central role of reactive oxygen species in oxidative stress-induced disorders and therapeutic exploration. *Frontiers in Pharmacology*, 14, 1269581. <https://doi.org/10.3389/fphar.2023.1269581>
- Akash, M. S. H., Rehman, K., Fiayyaz, F., Sabir, S., & Khurshid, M. (2020). Diabetes-associated infections: Development of antimicrobial resistance and possible treatment strategies. *Archives of Microbiology*, 202(5), 953–965.

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- <https://doi.org/10.1007/s00203-020-01818-x>
- Akkus, G., & Sert, M. (2022). *Diabetic foot ulcers: A devastating complication of diabetes mellitus continues non-stop in spite of new medical treatment modalities*. 13(12).
- Akter, N. (2019). Diabetic Peripheral Neuropathy: Epidemiology, Physiopathology, Diagnosis and Treatment. *Delta Medical College Journal*, 7(1), 35–48. <https://doi.org/10.3329/dmcj.v7i1.40619>
- Almasaudi, S. (2021). The antibacterial activities of honey. *Saudi Journal of Biological Sciences*, 28(4), 2188–2196. <https://doi.org/10.1016/j.sjbs.2020.10.017>
- American Diabetes Association. (2014). Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care*, 37(Supplement_1), S81–S90. <https://doi.org/10.2337/dc14-S081>
- Anastasi, J. K., Capili, B., & Chang, M. (2013). HIV Peripheral Neuropathy and Foot Care Management: A Review of Assessment and Relevant Guidelines. *AJN, American Journal of Nursing*, 113(12), 34–40. <https://doi.org/10.1097/01.NAJ.0000438867.67777.69>
- Apte, A., Liechty, K. W., & Zgheib, C. (2023). Immunomodulatory biomaterials on chemokine signaling in wound healing. *Frontiers in Pharmacology*, 14, 1084948. <https://doi.org/10.3389/fphar.2023.1084948>
- Burhan, A., Ali Khusein, N. bin, & Sebayang, S. M. (2022). Effectiveness of negative pressure wound therapy on chronic wound healing: A systematic review and meta-analysis. *Belitung Nursing Journal*, 8(6), 470–480. <https://doi.org/10.33546/bnj.2220>
- Burhan, A., & Arofiati, F. (2021). *Effect of Compression Bandage on the Healing of Diabetic Foot Ulcers: A Scooping Review: 4th International Conference on Sustainable Innovation 2020–Health Science and Nursing (ICoSIHSN 2020)*, Yogyakarta, Indonesia. <https://doi.org/10.2991/ahsr.k.210115.110>
- Burhan, A., Arofiati, F., Abreu Da Silva, V., & Mixrova Sebayang, S. (2023). Effect of ankle brachial index (abi) and compression therapy on diabetic foot ulcer healing. *Current Diabetes Reviews*, 19. <https://doi.org/10.2174/1573399819666230331083420>
- Burhan, A., & Sebayang, S. M. (2022). The Combination of Polyhexamethylene Biguanide and Cadexomer Iodine in Healing Chronic Venous Leg Ulcers: A Case Report. *Viva Medika: Jurnal Kesehatan, Kebidanan Dan Keperawatan*, 16(1), 12–21. <https://doi.org/10.35960/vm.v16i1.832>
- Bus, S. A., & Van Netten, J. J. (2016). A shift in priority in diabetic foot care and research: 75% of foot ulcers are preventable: Prevention of Foot Ulcers in Diabetes. *Diabetes/Metabolism Research and Reviews*, 32, 195–200. <https://doi.org/10.1002/dmrr.2738>
- Busman, A., Usman, A. N., Yulianty, R., Ahmad, M., Prihantono, Rahman, L., & Sumidarti, A. (2020). Effectiveness of Turmeric (*Curcuma longa* Linn) Extract Gel (EG) on Wound Healing in Female Rats (*Rattus Novergicus*). *International Journal of Current Research and Review*, 12(24), 02–06. <https://doi.org/10.31782/IJCRR.2020.122418>
- Chotchoungchatchai, S., Krairit, O., Tragulpiankit, P., & Prathanturug, S. (2020). The efficacy of honey and a Thai Herbal Oil preparation in the treatment of pressure ulcers based on Thai traditional medicine wound diagnosis versus standard practice: An open-label randomized controlled trial. *Contemporary Clinical Trials Communications*, 17, 100538. <https://doi.org/10.1016/j.conctc.2020.100538>
- Cialdai, F., Risaliti, C., & Monici, M. (2022). Role of fibroblasts in wound healing and tissue remodeling on Earth and in space. *Frontiers in Bioengineering and Biotechnology*, 10, 958381. <https://doi.org/10.3389/fbioe.2022.958381>
- Dasari, N., Jiang, A., Skochdopole, A., Chung, J., Reece, E. M., Vorstenbosch, J., & Winocour, S. (2021). Updates in Diabetic Wound Healing, Inflammation, and Scarring. *Seminars in Plastic Surgery*, 35(03), 153–158. <https://doi.org/10.1055/s-0041-1731460>

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- El Ayadi, A., Jay, J. W., & Prasai, A. (2020). Current Approaches Targeting the Wound Healing Phases to Attenuate Fibrosis and Scarring. *International Journal of Molecular Sciences*, 21(3), 1105. <https://doi.org/10.3390/ijms21031105>
- Halimatushadyah, E., & Rahayu, A. (2023). Anticancer Activity of Turmeric Rhizome Extract (*Curcuma longa* Linn) In-vitro Against MCF7 Breast Cancer Line Cells. *Health Information : Jurnal Penelitian*, 15(2), 164–171. <https://doi.org/10.36990/hijp.v15i2.914>
- Jain, P., Perakath, B., Jesudason, M. R., & Nayak, S. (2011). The Effect of Autologous Bone Marrow-Derived Cells on Healing Chronic Lower Extremity Wounds: Results of a Randomized Controlled Study. *OSTOMY WOUND MANAGEMENT*.
- Kim, J. (2023). The pathophysiology of diabetic foot: A narrative review. *Journal of Yeungnam Medical Science*, 40(4), 328–334. <https://doi.org/10.12701/jyms.2023.00731>
- Kim, J. H. (2023). Investigating Diabetic Foot Pathophysiology and Amputation Prevention Strategies through Behavioral Modification. *Journal of Wound Management and Research*, 19(3), 167–172. <https://doi.org/10.22467/jwmr.2023.02747>
- Lipsky, B. A., Berendt, A. R., Cornia, P. B., Pile, J. C., Peters, E. J. G., Armstrong, D. G., Deery, H. G., Embil, J. M., Joseph, W. S., Karchmer, A. W., Pinzur, M. S., & Senneville, E. (2012). 2012 Infectious Diseases Society of America Clinical Practice Guideline for the Diagnosis and Treatment of Diabetic Foot Infections. *Clinical Infectious Diseases*, 54(12), e132–e173. <https://doi.org/10.1093/cid/cis346>
- Mahmood, K., Zia, K. M., Zuber, M., Salman, M., & Anjum, M. N. (2015). Recent developments in curcumin and curcumin based polymeric materials for biomedical applications: A review. *International Journal of Biological Macromolecules*, 81, 877–890. <https://doi.org/10.1016/j.ijbiomac.2015.09.026>
- Maithili Karpaga Selvi, N. (2015). Curcumin Attenuates Oxidative Stress and Activation of Redox-Sensitive Kinases in High Fructose- and High-Fat-Fed Male Wistar Rats. *Scientia Pharmaceutica*, 83(1), 159–175. <https://doi.org/10.3797/scipharm.1408-16>
- Ministry of Health RI. (2018). *Hasil Utama Riskesdas 2018*. Kementrian Kesehatan RI. https://kesmas.kemkes.go.id/assets/uploads/dir_519d41d8cd98f00/files/Hasil-riskesdas-2018_1274.pdf
- Monika, P., Chandraprabha, M. N., Rangarajan, A., Waiker, P. V., & Chidambara Murthy, K. N. (2022). Challenges in Healing Wound: Role of Complementary and Alternative Medicine. *Frontiers in Nutrition*, 8, 791899. <https://doi.org/10.3389/fnut.2021.791899>
- Osman, S., Umar, H., Hashmi, Y., Jawaid, A., & Ahmed, Z. (2022). *The Efficacy of Honey Compared to Silver Sulfadiazine for Burn Wound Dressing in Superficial and Partial Thickness Burns—A Systematic Review and Meta-Analysis*.
- Parliani, P., Rungreangkulkij, S., & Nuntaboot, K. (2023). Foot Care among Diabetes Patients: A Concept Analysis. *Nurse Media Journal of Nursing*, 13(2), 246–262. <https://doi.org/10.14710/nmjn.v13i2.50722>
- Raziyeva, K., Kim, Y., Zharkinbekov, Z., Kassymbek, K., Jimi, S., & Saparov, A. (2021). Immunology of Acute and Chronic Wound Healing. *Biomolecules*, 11(5), 700. <https://doi.org/10.3390/biom11050700>
- Rousselle, P., Braye, F., & Dayan, G. (2019). Re-epithelialization of adult skin wounds: Cellular mechanisms and therapeutic strategies. *Advanced Drug Delivery Reviews*, 146, 344–365. <https://doi.org/10.1016/j.addr.2018.06.019>
- Salehi, V., Yavari Barhaghtalab, M. J., Mehrabi, S., Iraj, A., Sadat, S. A., Yusefi, S. H., & Malekzadeh, J. M. (2022). Does application of honey improve surgical outcome in pilonidal cyst excision with secondary intention healing? A prospective randomized placebo-controlled clinical trial. *Perioperative Medicine*, 11(1), 1. <https://doi.org/10.1186/s13741-021-00237-w>

- Samarghandian, S., Farkhondeh, T., & Samini, F. (2017). Honey and Health: A Review of Recent Clinical Research. *Pharmacognosy Research*, 9(2).
- Scepankova, H., Combarros-Fuertes, P., Fresno, J. M., Tornadijo, M. E., Dias, M. S., Pinto, C. A., Saraiva, J. A., & Estevinho, L. M. (2021). Role of Honey in Advanced Wound Care. *Molecules*, 26(16), 4784. <https://doi.org/10.3390/molecules26164784>
- Schilrreff, P., & Alexiev, U. (2022). Chronic Inflammation in Non-Healing Skin Wounds and Promising Natural Bioactive Compounds Treatment. *International Journal of Molecular Sciences*, 23(9), 4928. <https://doi.org/10.3390/ijms23094928>
- Sohn, S.-I., Priya, A., Balasubramaniam, B., Muthuramalingam, P., Sivasankar, C., Selvaraj, A., Valliammai, A., Jothi, R., & Pandian, S. (2021). Biomedical Applications and Bioavailability of Curcumin—An Updated Overview. *Pharmaceutics*, 13(12), 2102. <https://doi.org/10.3390/pharmaceutics13122102>
- Tashkandi, H. (2021). Honey in wound healing: An updated review. *Open Life Sciences*, 16(1), 1091–1100. <https://doi.org/10.1515/biol-2021-0084>
- Tomasek, J. J., Gabbiani, G., Hinz, B., Chaponnier, C., & Brown, R. A. (2002). Myofibroblasts and mechano-regulation of connective tissue remodelling. *Nature Reviews Molecular Cell Biology*, 3(5), 349–363. <https://doi.org/10.1038/nrm809>
- Volmer-Thole, M., & Lobmann, R. (2016). Neuropathy and Diabetic Foot Syndrome. *International Journal of Molecular Sciences*, 17(6), 917. <https://doi.org/10.3390/ijms17060917>
- World Health Organization. (2016). *Global report on diabetes*. World Health Organization. <https://apps.who.int/iris/handle/10665/204871>
- Yupanqui Miele, J., Vyas, C., Aslan, E., Humphreys, G., Diver, C., & Bartolo, P. (2022). Honey: An Advanced Antimicrobial and Wound Healing Biomaterial for Tissue Engineering Applications. *Pharmaceutics*, 14(8), 1663. <https://doi.org/10.3390/pharmaceutics14081663>