

Honey as Topical Dressing in Chronic Wound: A Systematic Review

Komang Abdi Baskara Mayun¹, Ida Yustiana², IB Pramana Suaryasa³, I Made Adipta Adiputra⁴

^{1,2}General Practitioner, Bangli General Hospital, Bali, Indonesia

^{3,4}General Surgeon, Bangli General Hospital, Bali, Indonesia

Abstract: *Chronic wounds were still a great problem. It affected over 6 million people in US, and the number have increasing with increased of aging population and some chronic disease including diabetes mellitus, vascular disease, rheumatology, and others. Many substances had been studied in order to treat chronic wounds, one of them is honey. Honey is substances that have been known for medical used for centuries. In many countries, honey used as topical treatment of wide range of wound traditionally. The development of science has showing the bioactive compounds in honey that potentially have therapeutic effects in wound healing process. This systematic review is aimed to evaluate the role of topical honey in chronic wounds by studying 34 publications that obtained from electronic databases. Most studies report the positive outcome of using honey as topical chronic wounds treatment, including more rapid epithelization, it exhibits the anti-inflammatory effects, relieves pain, controls the infection, debridement properties, and has fewer side effects, thus shortening wound healing time.*

Keywords: Honey, Chronic Wound, Ulcer, Dressing

1. Introduction

Non-healing or chronic wounds have always been a big problem. Any kind of wound that does not heal for a long time, make patient felt unpleasant, impact the quality of life, as well as need more cost to manage [1]. It's estimated affected over 6 million people in US, and more often encountered in the elderly. In that population, the case increased may be explained by both involuntal changes by ageing process and increase the prevalence of comorbidities or immobility [2]. Some most common type of chronic wound such as diabetic foot ulcer, pressure ulcer (decubitus), venous-arterial ulcer, ulcer related to rheumatology or chronic inflammation disease, and other ulcers [1],[3].

Over years, various substances have been studied in wound care, and new products are developed. One of them is the product using honey. For thousands of years honey occupies an important role in traditional medicine worldwide and has been used to accelerate healing of wide range of wounds, including ulcers. Honey is a viscous solution, primarily contains 75–79% of sugar and about 20% of water. Other known components are proteins, B-complex vitamins, antioxidant substances, and also some minerals. Honey also contains some enzyme, the main enzyme is invertase, amylase and glucose oxidase. These enzymes convert sucrose into simple form of fructose and glucose, and then it produces gluconic acid. The presence of organic acids in honey (0.57%), such as ascorbic acid are responsible for its acidity feature. The specific concentration of metabolites component in honey, may vary depend on specific geographic location, type of plant source, harvest season, special treatment methods of honey and its age. [3],[4].

Honey is made from modified nectar extracted from honey juice by various bees all over the world. During production process of honey, it's easily contaminated. Over 26% of unsterilized honey contains *Clostridium botulinum* spores.

Therefore, medical used honey must be sterilized before being used as a therapeutic product. It is recommended to sterilize with 25-50 kGy gamma radiation instead of heat sterilization. Those radiation doses don't affect antibacterial activity of the medical honey, but the micro-organisms are killed [3].

In addition to its antibacterial effect, many other properties are also useful in the medical field, such as ability to reduce inflammation, as debridement agent, it can neutralize bad odors, promote tissue growth, and accelerated wound healing. Nowadays, Medihoney and Manuka honey are mainly used in clinical practice. Medihoney is a standard blend product of New Zealand and Australian honey. It has antibacterial activity equivalent to a phenolic acid strength of at least 18 (the strongest antibacterial medical honey currently available). Meanwhile, Manuka honey comes from *Leptospermum scoparium* trees in Australia and New Zealand [4].

There are several case reports, observational studies and clinical trials reported about topical honey treatment of chronic wounds. However, only few studies have systematically reviewed the use of topical honey to treat chronic wounds. Therefore, the review was aimed

2. Method

The literature sought in this systematic review was conducted in the PUBMED and Google Scholar databases. The keyword used are 'honey, 'topical honey', 'honey dressing', chronic wound', 'diabetic foot ulcer', 'venous ulcer', and 'pressure ulcer'. All clinical trials study, such as clinical controlled trials (CCTs), clinical trials (CTs), and randomized controlled trials (RCTs), were included in this study. Due to the lack of randomized controlled trials data, in this study also included all other studies evaluating the efficacy of honey, such as observational studies, case reports (or case series). The data were analyzed by four researchers.

The articles reviewed in this study were published between 2000 and 2020. Reviews, in vitro studies, animal studies, studies only in pediatric, study only in acute wound, and study not publish in English, were not included in this study.

From the first search by the keyword that has been determined, total 8.926 publications were reached from 2 databases. After several evaluation, 34 studies were examined (Figure 1).

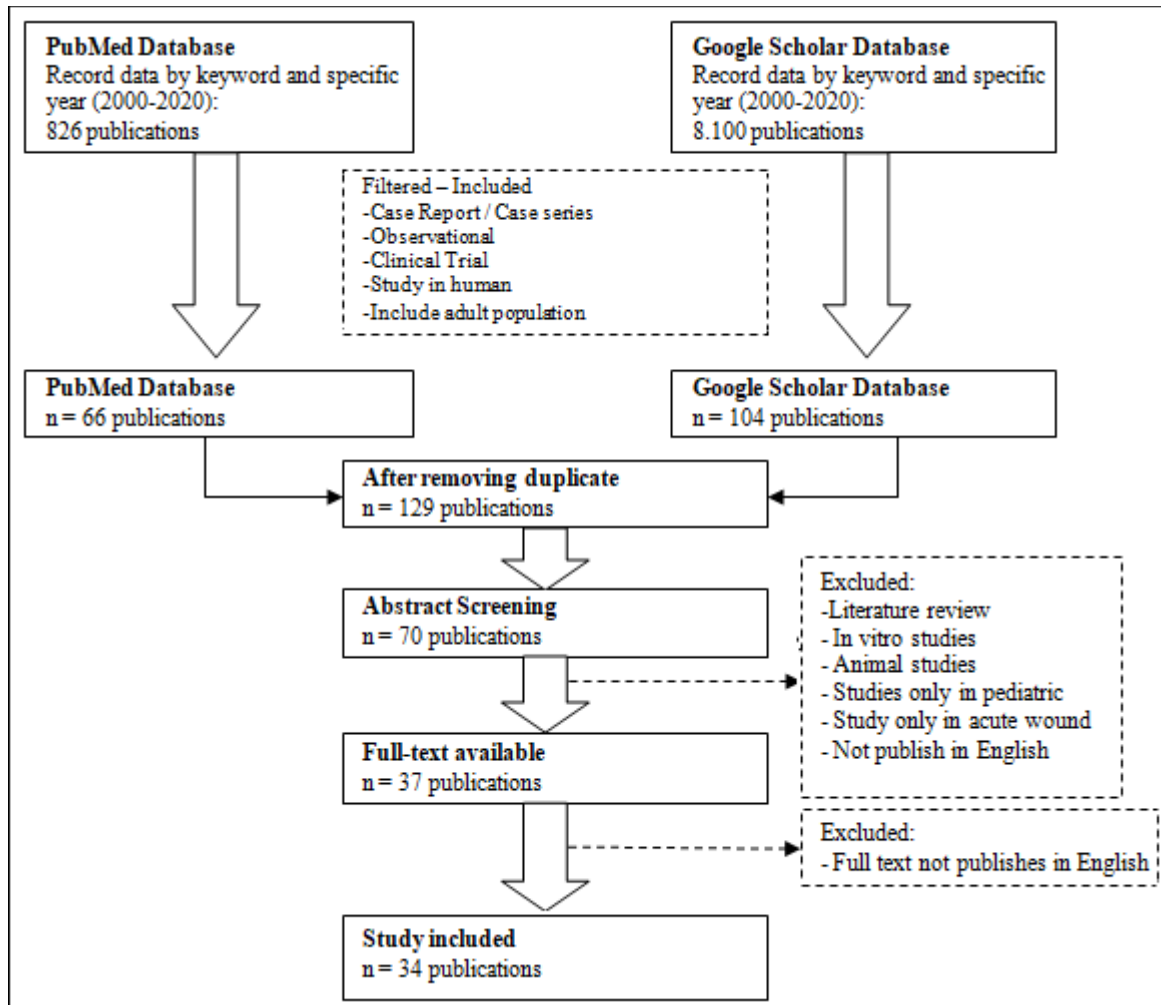


Figure 1: Flowchart of included studies

3. Results and Discussion

The research characteristics included in the evaluation are listed in Table 1. This study includes the results of using honey dressings for chronic wounds. This reviewed 34 full-text articles written in English. Fourteen RCTs reports, 13 care reports, and 4 observational studies publications included. The 34 included publications enrolled various chronic wound etiologies such as diabetic foot ulcer, venous-arterial ulcers, pressure ulcers, ulcerated tophaceous gout,

post-surgical infected wound, chronic atopic dermatitis, folliculitis decal vans, and others chronic wound.

Various honey product from pure until ready to used was studied in publications. The most used types were Manuka honey and Medihoney. In controlled trial study, honey was frequently compared with other clinical substance such as normal saline solution, hydrogel, silver sulfadiazine and povidone iodine. There's also study combined honey with thus substance.

Table 1: Information of the included studies evaluating the used of honey in chronic wound treatment

<i>Authors, Study's Year</i>	<i>Study's type/ Sample</i>	<i>Wound's type</i>	<i>Treatment Used</i>	<i>Result</i>
Ahmed et al., 2003 [5]	Observational n = 60	-Chronic wound (n=21) -Surgical wound (n=23) -Acute traumatic wound (n=16)	H: honey-medicated dressing	Treatment duration average of 3 weeks (range 1-28 weeks). Wound healing was achieved in 57 patients, 2patients show wound not get worsening, 1 patient stop the treatment due to pain sensation. No allergic reactions.
Dunford et al., 2004 [6]	Observational, multicentre (4) n = 40	Chronic venous and/ arterial ulcer	H: Medihoney dressings	12-weeks study period 50% patients experienced a decrease inreported pain levels. 21/26 patients experienced decrease in odor, 3 patients perceived an increase in odor, 2 patients had been no change. (average total wound area decreased steadily (p<0.002)
Alangari et al., 2017 [7]	Observational n = 14	<i>Bilateral Atopic Dermatitis</i> (n = 28 lesions)	H: manuka honey C: untreated as possible	After 7 days of the study, there was no significant change of <i>Staphylococcus</i> in skin of both groups.
Moghazy et al., 2010 [8]	Observational n = 30	Infected diabetic foot	H: pure raw untreated commercial honey, applied the form of impregnated gauze	After 1-week study period, bacterial load of all ulcers was significantly reduced. 3-months study period Complete healing achieved in 43.3% ulcers significantly. Size reduction was observed in 43.3% of patients. Treatment failure observed in 6.7% ulcers.
Biglari et al., 2011 [9]	Observational n = 20	Pressure ulcer	H: Medihoney	After 4-weeks study period, 90% patients showed complete wound healing. No negative effect was documented.
Bilgari et al., 2012 [10]	Observational n = 121	Various chronic wound	H: combination of Medihoney with diverse dressings (calcium alginate, hydrofiber dressings, sodium chloride solution)	2-years study period Wound size decreased significantly, many wounds healed after relatively short time periods, pain levels decreased significantly, and the wounds showed noticeably less slough/necrosis.
Dreyfus et al., 2018 [11]	Observational n = 50.866	Various chronic wound	H: medicinal honey C: clostridial collagenase ointment (CC)	Compared with medicinal honey treatment, patients receiving CCO treatment have a lower chance of being hospitalized and re-admitted (OR = 0.86, 95% CI 0.80-0.94).
Gunes & Eser, 2007 [12]	RCT n = 26	Pressure ulcer (50 stage II / III)	H: honey dressing C: ethoxy-iaminoacridine plus nitrofurazone dressings	5-weeks study period The pressure ulcer healing scale (PUSH) tool score of patients receiving honey dressing was significantly higher than that of patients receiving ethoxydiaminoacridine and nitrofurazone dressing (6.55±2.14 vs 12.62±2.15, P <.001).
Mphande et al., 2007 [13]	RCT n = 40	Infected wound	H: Mzuzu Honey (Smallholders Coffee Farmers Trust, Mzuzu, Malawi) C: sugar by Ilova Sugar (Limbe, Malawi).	After 2-weeks study period, the median rate of healing in the honey group was 3.8cm ² /week and the sugar group about 2.2cm ² /week After 3 weeks of treatment, 86% of the patients treated with honey felt no pain when changing the dressing, while 72% of patients treated with sugar felt no pain.
Jull et al., 2008 [14]	RCT n = 368	Venous ulcer	H: manuka honey dressings (ApiNate™ UMF 12+; Comvita New Zealand, Te Puke, New Zealand), impregnated into calcium alginate dressing C: silver dressings, hydrogel, iodine, hydrofibre, foam, iodine, or hydrocolloid	12-weeks study period 55.6% ulcers in the group that treated by honey and 49.7% ulcers that handle by usual treatment had healed, absolute increase 5.9% (95% confidence interval (CI) -4.3- 15.77; P = 0.258). Treatment with honey may be associated with more adverse events and become more expensive (relative risk 1.3)
Gethin & Cowman, 2008 [15]	RCT n = 108	Venous ulcer	H: manuka honey C: hydrogel	After 4 weeks of treatment, 70% of the wounds treated with Manuka honey (n = 7) and 16% of the wounds treated with hydrogel (n = 1) were eradicated from MRSA
Shukrimi et al., 2008 [16]	RCT n = 30	Diabetic foot Ulcers - Wagner type II	H: pure, clean, non-sterile honey; C:10% povidone-iodine	The average healing time of the honey group was 14.4 days (7-26 days) (p <0.005), while the standard dressing group was 15.4 days (9-36 days)

Kamaratos et al., 2014 [17]	RCT n = 63	Diabetic foot ulcer	H: Group I, with Manuka honey-impregnated dressings C: Group II, with conventional type dressing	After 16-weeks study period, the number of healed ulcers did not differ significantly between two groups I and II (97% and 90%) The average cure time of group I was 31±4 days, while the average cure time of group II was 43±3 days (P<0.05).
Siavash et al., 2013 [18]	RCT n = 25	Diabetic foot ulcer (n=60ulcer)	H: sterile 5% royal jelly (product of a worker honey bee) C: Placebo	3-months study period. All the parameters between the two groups (depth, length and width reduction rate, the duration and number of complete recoveries showed no significant differences (respectively P = 0.69, 0.95, 0.7, 0.74 and 0.6)
Imran et al., 2015 [19]	RCT n = 348	Diabetic foot Ulcers - Wagner type I & II	H: Beri-honey-impregnated dressing (group A) C: normal saline dressing (group B)	About 75.97% of patients were completely cured with honey dressings, and 57.39% with saline dressings were completely cured (p = 0.001). In group A found that the median wound healing time was 18.00 (6-120) days (median IQR), and the median wound healing time in group B was 29.00 (7-120) days (median IQR) (p <0.001).
Tsang et al., 2016 [20]	RCT n = 31	Diabetic Foot Ulcer	H: Manuka honey (MH) C1: Nanocrystalline silver (nAg) C2: Conventional dressing with paraffin tulle and gauze	Proportions of complete healing in the nAg, MH, and conventional groups were 81.8%, 50%, and 40% Ulcer size reduction rate was 97.45% in nAg group, 86.21% in MH group and the conventional group was 75.17%
Goharshenasan et al., 2016 [21]	RCT n = 72	Surgical incision	H: pure, sterilized by gamma irradiation (25kGY) C: petrolatum-impregnated gauze	After the third and sixth study period, the average scar width was 3.64 ± 0.83 mm and 3.49 ± 0.87 mm on the side receiving the honey dressing, and in in the control group about 5.43 ±0.05 mm and 5.30 ± 1.35 mm.
Bashir et al., 2018 [22]	RCT n : 95	Diabetic foot ulcer	H: pure, sterilized honey C: Vacuum Assisted Closure (V.A.C)	The healing rate of the V.A.C group was faster than that of the honey dressing. The average V.A.C was 18.2 days and the honey was 28.8 days.
Saeed, 2019 [23]	RCT n : 71	Diabetic foot ulcer	H: 35 g of Unique Manuka honey Factor-13 C: Silver hydrogel	The average eradication time of the silver treatment group was faster than honey treatment group, but the difference was not statistically significant (P>0.05). The mean time required for complete ulcer healing was shorter in honey treatment group than the silver treatment (P > 0.05, insignificant)
Suryaprakash, 2017 [24]	RCT n : 90	Chronic wound (ulcer)	H: Dabur Honey 10-30ml C: Mechanical debridement + povidone iodine	Healthy granulation tissue formation was faster in honey group (14.7±5.4 days) than in debridement group (17.9±7.5days). (significant, p=0.025).
Zeleníková & Vyhřídálová, 2019 [25]	RCT n :40	Chronic wound (ulcer)	H: Actilite (99% manuka honey, 1% of manuka oil) C: nanocrystalline silver, povidone-iodine, or hydrogel	After 3-months study period, 80% individuals in honey group had their wounds completely healed, as compared with only 30% controls group
Alcaraz & Kelly, 2002 [26]	Case Report n = 1	Venous leg ulcer (n=2 ulcers)	H: Right leg with Sterile manuka honey (MediHoney) spread on to N-A Dressing C: Left leg with Aquacel sized to cover wound beds	Honey was found to have a noticeable deodorizing action, led to cessation of the green exudate, honey dressings were easier to remove, wound beds appeared cleaner and less sloughy.
Weyden, 2003 [27]	Case Report n = 2	Pressure ulcer	H: honey impregnated alginate dressing (API-NATE™, Apimed New Zealand Ltd)	Case 1: After 11-weeks of study period, the first patients, that wound treat with honey, had healed completely and no need for protective dressings, fully regain mobility of the feet without pain Case 2: In the second patient, by 2 months, there was almost no scar, no pain and the wound were completely healed.
Weyden, 2005 [28]	Case Report n = 1	Venous ulcer	H: Manuka honey-impregnated alginate dressing (ApiNate, Comvita Medical Ltd).	After 28 weeks, the wound was completely healed, oedema was greatly reduced.
Visavadia et al., 2006 [29]	Case Report n = 2	Infected post-surgical wound	H: Manuka honey tulle dressings (Activon)	Case 1: the wound that infected by MRSA had healed 2 weeks later

				Case 2: the wound that infected by MRSA had healed 5 weeks later
Lotfy et al., 2006 [30]	Case Report	Infected diabetic foot ulcer	H: MPH paste (800 mg bee propolis, 50 g myrrh)	The wound had cured well and the patient returned to work after 4-weeks
Sare, 2008 [31]	Case Report n =3	Chronic leg ulcer	H: Medihoney™ antibacterial wound gel	Case 1: mixed arterial and venous ulcer, the wound improved significantly within a two-week period Case 2: Venous ulcer, debris and erythema were significantly reduced after 4 days Case 3: venous ulcer, after 16 days therapy, healing progressed, debris decreased, pain reduced and exudate diminished.
Hampton et al., 2011 [32]	Case Report n = 1	Venous ulcer	H: combination of the superabsorbent KerraMax® (Crawford Healthcare) with the antibacterial honey Algivon® (Advancis Medical)	The wound has an improvement and the pain had diminished after a month.
Mohamed, 2014 [33]	Case Report	Diabetic foot ulcer	H: pure, commercial honey, covered with a glycerin-based dressing	Ulcer completely healed after 16-weeks of treatment
Filanovsky et al., 2015 [34]	Case Report n : 1	Ulcerated tophaceous gout	H: MediHoney	After 1 week, the wound show improvement. But, after 1-month of treatment, severe pain is still felt.
Yeh et al., 2019 [35]	Case Report n : 1	Folliculitis decalvans	H: Manuka Honey	There's reduction of wound after 1 month therapy.
Astrada et al., 2019 [36]	Case Report n : 1	Diabetic foot ulcer	H: pure, Trigona honey	After 2-months, wound edge has complete re-epithelialization
Woodward, 2019 [37]	Case Report n : 5	Various chronic wound	H: Medihoney® Barrier Cream	Case 1: incontinence-associated dermatitis, reduced the inflammation and pain Case 2: incontinence-associated dermatitis, after 13days the wound completely healing Case 3: incontinence-associated dermatitis, after 13 days there are evidenced of healing Case 4: incontinence-associated dermatitis, after 7 days the wound showed evidence of epithelialization Case 5: excoriation around the suprapubic catheter, after 7 days the redness was greatly reduced
Henry et al., 2019 [38]	Case Report n :4	Various chronic wound	H: Revamil wound dressing (Polyacetate sheet dressing with pure honey)	Case 1: Scalding Case 2: Graft after burn injury Case 3: Scalding Case 4: Toxic epidermal necrolysis In all cases, there is very little wound exudate and the skin around the wound remains intact after treatment, this may due to the dressing was easy to apply and remove.
n = number of samples, H = honey, C= control, RCT = randomized control trial				

3.1 Diabetic Foot Ulcer

According to reports, diabetic foot ulcers occur in 15% of diabetic patients (either type I or type II) and related to most reason of diabetes-related amputations (84% of all cases). In order to prevent amputations and increase wound healing rate, honey is now frequently used in diabetic foot injuries. In this systematic review, seven RCT study from total 688 samples have been done to evaluate the benefit of using honey in treat diabetic foot. Most of that study report positive outcome in using honey, and no adverse events were reported in any clinical trials. The healing rate in those study range from 7- 120days based on ulcer stage and other medical condition [16]-[20], [22]-[23]. It is reported that compared with normal saline, the healing speed of honey dressing is better than normal saline, and the antibacterial effect is stronger. The median wound healing time in the honey group was observed in 18.00 (6-120) days, and the median wound healing time of the saline group was 29.00 (7-120) days (p <0.001) [19]. Others study compared honey

with povidone iodine, placebo, and other conventional dressing also reports improvement of wound healing in honey group but most parameters (depth, length and width reduction rate, duration and incidence of sustained healing) did not show any significant differences [17]. There was no uniformity ingrade of ulcer included and efficacy parameters. Hence the results cannot be pooled.

In study compared honey with Vacuum Assisted Closure (V.A.C) [22], or Nanocrystalline silver [20], honey group shows inferior in rate of wound healing. Honey seems have faster wound healing rate than silver hydrogel [23], but insignificant differences. The mean time to eradicate infection in the silver treatment group were faster than honey treatment group, but not significantly different (P > 0.05) [23]. In one observational study, the used of pure raw untreated commercial honey in infected diabetic foot shows reduced bacterial load in 30 patients significantly after 1 week of treatment and after 3 months uses the complete healing achieved in 43.3% ulcers significantly [8]. There're

3 case report study found completely healed wound in 1-4 months treatment [30], [33], [36]. In the study of Kamaratos et al. (2014) that investigate the effect of wound healing, concluded that with manuka honey impregnated dressing the duration of hospital stay and antibiotic requirements decreased [17].

The honey's antibacterial effect is based on multiple mechanisms. First is the present of hydrogen peroxide, the product of glucose oxidase activity, it produced when the wound exudate dilutes honey. It activates the neutrophils that stimulate inflammatory response. Neutrophil recruiting and activating other leucocytes. Second are phytochemicals (flavonoids), its direct inhibition of phagocytosis, and it prevent formation superoxide free radicals. The third is honey has a low water activity, this property plays role in prevents bacteria's growth. The high sugar content in honey absorbs water from the wound through osmosis, and then extracts water from the bacteria, causing the bacteria to die. Finally, the acidity (pH between 3.2-4.5) of honey inhibits the growth of microorganisms [3],[4].

3.2 Venous-Arterial Ulcer

Leg ulcers are deep wound, below the knee. Typically, leg ulceration is a chronic-relapsing and the most common cause is venous insufficiency. The standard treatment of venous ulcers is compression technique by tight bandaging on the lower leg to reduce hydrostatic pressure [14]. Adjuvant treatment by honey, have been found to be effective. In study of Dunford et al., (2004) the used of Medihoney relief pain in 50% patient, decrease malodor in over 90% patient, as far as decreased total wound sized [6]. In RCTs study by Gethin & Cowman (2008) with honey and hydrogel, the treatment report showed that 70% of wounds treated with Manuka honey (n = 7) and 16% of wounds treated with hydrogel (n = 1) had eradicated MRSA after 4 weeks. In the case report of total 6 patients, the use of honey product in venous ulcer showed good outcome [26],[27],[31],[32]. Honey was found to have a noticeable deodorizing action, led to cessation of the green exudate, honey dressings were easier to remove, wound beds appeared cleaner and less sloughy [26]. The wound in those study start reduced debris and erythema after 4 days [31]. High honey's osmolarity stimulates the outflow of fluid from the deeper wound compartments to the surface area, this property aiding the wound cleansing and contributing to wound debridement [26].

3.3 Pressure ulcer

Pressure ulcer or decubitus or a bedsore happen due to long time immobilization. That makes one site of body area have long term high pressure, when the soft tissue it that area can no longer withstand the pressure and, in conjunction with poor wound healing, a pressure ulcer may result [9]. As the population ages and increasing number of patients receiving acute disease treatment, the prevalence of pressure ulcers continues to rise. In addition to relieving pressure and providing good nutritional support related patient's health problems, the local wound management is also essential to increase the healing process of pressure sores. A case series reported 2 positive results using honey (Manuka honey) as a

topical pressure ulcer treatment. After 11-weeks of study period, the wound of the first patients treated with honey, had healed completely, no need for protective dressings, full mobility of the feet is restored, and there is no pain. The second patient, by 2 months, had almost no scars, no pain and the wound were completely healed [27]. In RCT study by Gunes & Eser (2007), report that the patients who were treated by honey dressing compared with subjects treated with ethoxydiaminoac pyridine and nitrofurazone dressings, the pressure ulcer healing scale (PUSH) score was significantly better (6.55 ± 2.14 vs 12.62 ± 2.15 , $P < .001$) after 5-weeks study period [12]. Two observational study not documented negative effect [9], [11]. But one study found that the use of clostridial collagenase ointment better than medicinal honey in patient readmissions [11].

3.4 Other Chronic Wound

Other chronic wound included chronic infected post-surgical wound, ulcerated tophaceous gout, folliculitis decal vans, chronic dermatitis atopic, incontinence-associated dermatitis, excoriation around the suprapubic catheter, toxic epidermal necrolysis, and scalding skin were have been studied to evaluate the outcome of topical honey treatment. Most study report good outcome in using honey as topical treatment. One case series in 2 patient that had infected post-surgical wound report the wound that infected by MRSA had healed 2 weeks after treatment in first patient and 5 weeks after treatment in second patient [29]. In RCT study by Reddy (2017) in various chronic ulcer, found that healthy granulation tissue formation was faster in honey group (14.7 ± 5.4 days) than in debridement group (17.9 ± 7.5 days; $p=0.025$) [24]. In one case report of topical honey use in ulcerated tophaceous gout, after 1 week, the wound show improvement. But, after 1-month of treatment, severe pain is still felt. A case report that enrolled toxic epidermal necrolysis patient and treat with honey Revamil wound dressings (Polyacetate sheet dressing with pure honey) showed that there is very little wound exudate, the skin around the wound remains intact after treatment, and the dressing is easy to apply and remove [38]. Honey has osmosis properties, it can produce solution in contact with the wound surface, thereby preventing the dressing from adhering to the wound bed or the area around the wound, thereby causing limited damage to the tissue when changing the dressing and reducing pain [12].

4. Conclusion

Most studies report the positive outcome of using honey as topical chronic wounds treatment, including more rapid epithelization, showed anti-inflammatory effects, relieves pain, controls the infection, debridement properties, and has fewer side effects, thus shortening wound healing time. However, there are not enough good quality data to fully draw conclusions about the efficacy of topical honey in the treatment of chronic wounds. This review at least shows that honey dressings can treat diabetic foot ulcers safely.

References

- [1] Zeleníková, Renáta, and Dana Vyhídalová. "Applying honey dressings to non-healing wounds in elderly

- persons receiving home care." *Journal of tissue viability* 28.3 (2019): 139-143.
- [2] Powers, Jennifer G., et al. "Wound healing and treating wounds: Chronic wound care and management." *Journal of the American Academy of Dermatology* 74.4 (2016): 607-625.
- [3] Yilmaz, Ayse Celik, and Dilek Aygin. "Honey dressing in wound treatment: a systematic review." *Complementary Therapies in Medicine* (2020): 102388.
- [4] Vandamme, Lynn, et al. "Honey in modern wound care: a systematic review." *Burns* 39.8 (2013): 1514-1525.
- [5] Ahmed, A. Kalam J., et al. "Honey-medicated dressing: transformation of an ancient remedy into modern therapy." *Annals of plastic surgery* 50.2 (2003): 143-148.
- [6] Dunford, C. E., and R. Hanano. "Acceptability to patients of a honey dressing for non-healing venous leg ulcers." *Journal of wound care* 13.5 (2004): 193-197.
- [7] Alangari, Abdullah A., et al. "Honey is potentially effective in the treatment of atopic dermatitis: Clinical and mechanistic studies." *Immunity, inflammation and disease* 5.2 (2017): 190-199.
- [8] Moghazy, A. M., et al. "The clinical and cost effectiveness of bee honey dressing in the treatment of diabetic foot ulcers." *Diabetes research and clinical practice* 89.3 (2010): 276-281.
- [9] Biglari, B., et al. "Use of Medihoney as a non-surgical therapy for chronic pressure ulcers in patients with spinal cord injury." *Spinal cord* 50.2 (2012): 165-169.
- [10] Biglari, B., et al. "Use of Medihoney as a non-surgical therapy for chronic pressure ulcers in patients with spinal cord injury." *Spinal cord* 50.2 (2012): 165-169.
- [11] Dreyfus, Jill, et al. "Clostridial collagenase ointment and medicinal honey utilization for pressure ulcers in US hospitals." *Journal of medical economics* 21.4 (2018): 390-397.
- [12] Günes, Ülkü Yapucu, and Ismet Eser. "Effectiveness of a honey dressing for healing pressure ulcers." *Journal of Wound Ostomy & Continence Nursing* 34.2 (2007): 184-190.
- [13] Mphande, A. N. G., et al. "Effects of honey and sugar dressings on wound healing." *Journal of wound care* 16.7 (2007): 317-319.
- [14] Jull, Andrew, et al. "Randomized clinical trial of honey-impregnated dressings for venous leg ulcers." *British Journal of Surgery* 95.2 (2008): 175-182.
- [15] Gethin, Georgina, and Seamus Cowman. "Bacteriological changes in sloughy venous leg ulcers treated with manuka honey or hydrogel: an RCT." *Journal of wound care* 17.6 (2008): 241-247.
- [16] Shukrimi, A., et al. "A comparative study between honey and povidone iodine as dressing solution for Wagner type II diabetic foot ulcers." *Med J Malaysia* 63.1 (2008): 44-6.
- [17] Kamaratos, Alexandros V., et al. "Manuka honey-impregnated dressings in the treatment of neuropathic diabetic foot ulcers." *International wound journal* 11.3 (2014): 259-263.
- [18] Siavash, Mansour, et al. "The efficacy of topical royal jelly on healing of diabetic foot ulcers: a double-blind placebo-controlled clinical trial." *International wound journal* 12.2 (2015): 137-142.
- [19] Imran, Muhammad, Muhammad Barkaat Hussain, and Mukhtiar Baig. "A randomized, controlled clinical trial of honey-impregnated dressing for treating diabetic foot ulcer." *J Coll Physicians Surg Pak* 25.10 (2015): 721-725.
- [20] Tsang, Ka-Kit, et al. "A pilot randomized, controlled study of nanocrystalline silver, manuka honey, and conventional dressing in healing diabetic foot ulcer." *Evidence-Based Complementary and Alternative Medicine* 2017 (2017).
- [21] Goharshenasan, Peiman, et al. "Topical application of honey on surgical wounds: a randomized clinical trial." *Complementary Medicine Research* 23.1 (2016): 12-15.
- [22] Maqsood, Rasikh, Umar Bashir, and Hassan Shabbir. "Comparing negative pressure wound treatment with honey dressing in healing of foot ulcers in diabetics." *Pakistan Armed Forces Medical Journal* 68.1 (2018): 34-38.
- [23] Al Saeed, Mohammed. "Prospective randomized comparison of controlled release ionic silver hydrophilic dressings and medicated honey-impregnated dressings in treating neuropathic diabetic foot ulcer." *Saudi Journal for Health Sciences* 8.1 (2019): 25.
- [24] A Suryaprakash, Reddy. "Efficacy of honey dressing versus mechanical debridement in healing of ulcers with biofilms a comparative study. Diss. BLDE (Deemed to be University), 2017.
- [25] Zeleníková, Renáta, and Dana Vyhlídalová. "Applying honey dressings to non-healing wounds in elderly persons receiving home care." *Journal of tissue viability* 28.3 (2019): 139-143.
- [26] Alcaraz, Antonia, and Jennifer Kelly. "Treatment of an infected venous leg ulcer with honey dressings." *British journal of nursing* 11.13 (2002): 859-866.
- [27] A van der Weyden, Elizabeth. "The use of honey for the treatment of two patients with pressure ulcers." *British Journal of Community Nursing* 8.Sup6 (2003): S14-S20.
- [28] van der Weyden, Elizabeth A. "Treatment of a venous leg ulcer with a honey alginate dressing." *British journal of community nursing* 10.Sup2 (2005): S21-S27.
- [29] Visavadia, Bhavin G., Jan Honeysett, and Martin H. Danford. "Manuka honey dressing: An effective treatment for chronic wound infections." *British Journal of Oral and Maxillofacial Surgery* 46.1 (2008): 55-56.
- [30] Lotfy, M., et al. "Biomedical Science in Brief." *British journal of biomedical science* 63.4 (2006): 171.
- [31] Leigh Sare, Janice. "Leg ulcer management with topical medical honey." *British journal of community nursing* 13.Sup4 (2008): S22-S32.
- [32] Hampton, Sylvie, et al. "Using a superabsorbent dressing and antimicrobial for a venous ulcer." *British Journal of Nursing* 20.Sup8 (2011): S38-S43.
- [33] Mohamed, Hashim, et al. "Honey based therapy for the management of a recalcitrant diabetic foot ulcer." *Journal of tissue viability* 23.1 (2014): 29-33.

- [34] Filanovsky, Michelle Gita, Kumar Sukhdeo, and Megan Cunnane McNamara. "Ulcerated tophaceous gout." *Case Reports 2015* (2015): bcr2015210707.
- [35] Yeh, Jennifer E., et al. "Resolution of folliculitis decalvans with medical honey." *Dermatology online journal* 25.8 (2019).
- [36] Astrada, Adam, et al. "Successful treatment of a diabetic foot ulcer with exposed bone using Trigona honey: a case study." *Journal of Wound Care* 28.Sup12 (2019): S4-S8.
- [37] Woodward, Sue. "Moisture-associated skin damage: use of a skin protectant containing manuka honey." *British Journal of Nursing* 28.6 (2019): 329-335.
- [38] Henry, Nader, Steven Jeffery, and Ishan Radotra. "Properties and use of a honey dressing and gel in wound management." *British journal of nursing* 28.6 (2019): S30-S35.