The Effect of Honey on Treatment for Chronic Wounds Compared to Standard Therapy: A Systematic Review

Silvia Ochoa Sosa
Pacific University

Recommended Citation
https://commons.pacificu.edu/pa/200
The Effect of Honey on Treatment for Chronic Wounds Compared to Standard Therapy: A Systematic Review

Abstract
Background: Honey is the oldest known wound dressing. Its uses date back to ancient Greece, Egypt, and parts of India. Composed of 80% sugar and 17% water, this supersaturated natural substance makes a splendid wound dressing. Its high osmolarity, phytochemicals, and enzymatic production of hydrogen peroxide inhibit bacterial growth, while its acidic pH and autolytic debridement, decrease inflammation and improve blood circulation to enhancing epithelialization and healing with minimal scar tissue. The subject of this review is whether studies show that honey's wound healing properties make it a better wound dressing by decreasing the healing time of chronic wounds, compared to standard therapy.

Methods: An exhaustive search of available medical literature using search engines MEDLINE, CHINAHL, and Web of Science was conducted with honey, treatment, therapy, and wounds as key words. JADAD score was used to determine the validity of each study.

Results: Three studies were identified meeting the exclusion and inclusion criteria established. All studies were consistent in that honey reduces the healing rate of chronic ulcers but only one study reached statistical significance. All studies had weak JADAD scores of three due to their lack of blinding the participants. The studies were also of poor quality design in that much of the treatment was determined by the clinician and no standard protocol was used across the groups tested.

Conclusion: Honey is an effective wound treatment agent but no additional benefit is gained over standard therapy.

Degree Type
Capstone Project

Degree Name
Master of Science in Physician Assistant Studies

First Advisor
Anya Hill, PA-C, MS

Second Advisor
Annjanette Sommers MS, PAC

Third Advisor
Rob Rosenow PharmD, OD

Keywords
Honey, treatment, therapy, wounds

Subject Categories
Medicine and Health Sciences

This capstone project is available at CommonKnowledge: https://commons.pacificu.edu/pa/200
Copyright and terms of use

If you have downloaded this document directly from the web or from CommonKnowledge, see the “Rights” section on the previous page for the terms of use.

If you have received this document through an interlibrary loan/document delivery service, the following terms of use apply:

Copyright in this work is held by the author(s). You may download or print any portion of this document for personal use only, or for any use that is allowed by fair use (Title 17, §107 U.S.C.). Except for personal or fair use, you or your borrowing library may not reproduce, remix, republish, post, transmit, or distribute this document, or any portion thereof, without the permission of the copyright owner. [Note: If this document is licensed under a Creative Commons license (see “Rights” on the previous page) which allows broader usage rights, your use is governed by the terms of that license.]

Inquiries regarding further use of these materials should be addressed to: CommonKnowledge Rights, Pacific University Library, 2043 College Way, Forest Grove, OR 97116, (503) 352-7209. Email inquiries may be directed to: copyright@pacificu.edu
NOTICE TO READERS

This work is not a peer-reviewed publication. The Master’s Candidate author of this work has made every effort to provide accurate information and to rely on authoritative sources in the completion of this work. However, neither the author nor the faculty advisor(s) warrants the completeness, accuracy or usefulness of the information provided in this work. This work should not be considered authoritative or comprehensive in and of itself and the author and advisor(s) disclaim all responsibility for the results obtained from use of the information contained in this work. Knowledge and practice change constantly, and readers are advised to confirm the information found in this work with other more current and/or comprehensive sources.

The student author attests that this work is completely his/her original authorship and that no material in this work has been plagiarized, fabricated or incorrectly attributed.
The Effect of Honey on Treatment for Chronic Wounds Compared to Standard Therapy: A Systematic Review

Silvia Ochoa Sosa

A Clinical Graduate Project Submitted to the Faculty of the

School of Physician Assistant Studies

Pacific University

Hillsboro, OR

For the Masters of Science Degree, August 14, 2010

Faculty Advisor: Anya Hill
Clinical Graduate Project Coordinators: Annjanette Sommers MS, PAC & Rob Rosenow PharmD, OD
Biography

[Redacted for privacy]
Abstract

Background: Honey is the oldest known wound dressing. Its uses date back to ancient Greece, Egypt, and parts of India. Composed of 80% sugar and 17% water, this supersaturated natural substance makes a splendid wound dressing. Its high osmolarity, phytochemicals, and enzymatic production of hydrogen peroxide inhibit bacterial growth, while its acidic pH and autolytic debridement, decrease inflammation and improve blood circulation to enhancing epithelialization and healing with minimal scar tissue. The subject of this review is whether studies show that honey’s wound healing properties make it a better wound dressing by decreasing the healing time of chronic wounds, compared to standard therapy.

Methods: An exhaustive search of available medical literature using search engines MEDLINE, CHINAHL, and Web of Science was conducted with honey, treatment, therapy, and wounds as key words. JADAD score was used to determine the validity of each study.

Results: Three studies were identified meeting the exclusion and inclusion criteria established. All studies were consistent in that honey reduces the healing rate of chronic ulcers but only one study reached statistical significance. All studies had weak JADAD scores of three due to their lack of blinding the participants. The studies were also of poor quality design in that much of the treatment was determined by the clinician and no standard protocol was used across the groups tested.

Conclusion: Honey is an effective wound treatment agent but no additional benefit is gained over standard therapy.

Keywords: Honey, treatment, therapy, wounds.
Acknowledgements

To my parents Alfonso and Maria Elena Ochoa: Thank you always desiring the best for me and for guiding me in the right direction, even if you didn’t know what that direction was. Thank you for allowing me to grow and discover my passion for helping others. Thank you for all your love and support.

To my brothers Gerardo & Leo, to my sister Elena and Nancy and Bianca: Thank you for being the shoulder I needed to cry on and for always willing to listen. Thank you for your kind words and advice I needed to make it through the program.

To my love Benjamin Lopez: Thank you for all your unconditional love and support I needed to make it through the program. Thank you for sticking by me to the end and for what is to come.
## Table of Contents

Biography ................................................................................................................. 2
Abstract .................................................................................................................... 3
Acknowledgements .................................................................................................. 4
Table of Contents .................................................................................................... 5
List of Tables ........................................................................................................... 6
List of Abbreviations ............................................................................................... 6
Background .............................................................................................................. 7
Methods .................................................................................................................... 12
Results ..................................................................................................................... 12
Discussion ................................................................................................................. 16
Conclusion ................................................................................................................. 20
References ............................................................................................................... 22
Tables ....................................................................................................................... 24
List of Tables

Table 1: Summary of Reviewed Studies
Table 2: Comparison of Healing Rate of Honey vs. Standard Wound Therapy

List of Abbreviations

IL................................................................................................................ Interleukin
MRSA.......................................................... Methicillin-resistant Staphylococcus aureus
VRE................................................................. Vancomycin-resistant enterococci
The Effect of Honey on Treatment for Chronic Wounds Compared to Standard Therapy: A Systematic Review

BACKGROUND

Honey has many purposes in medicine. Historically it has been used to treat coughs, asthma symptoms, and even blood pressure. Long before the discovery of bacteria, it was considered to be the oldest wound dressing as it dates back to ancient medical writings of Egypt, Greece and parts of India. Its use on skin wounds has been documented on skin grafts, trauma wounds, necrotizing fasciitis, pilonidal sinuses, pressure ulcers, lacerations, burns, surgical wounds, herpetic lesions, atopic dermatitis, animal bites, and rheumatoid ulcers. The use of honey had been forgotten with the discovery of antibiotics however, with antibiotic resistance on the rise in recent years, honey has been newly discovered and its uses once again investigated.

Honey is a natural, sweet substance produced by honey bees of the genera *Apis* and *Meliponinae*. The bees collect nectar from a variety of flowers and process it by adding their own body’s enzymes and deposit it into wax cells of the hive where it is concentrated by evaporation through fanning of the bees’ wings. The final result is a supersaturated sweetener composed of 80% sugar and 17% water. The remainder of the honey is made up of proteins, enzymes, and non-essential amino acids. The high sugar concentration is primarily composed of simple sugars which include 38.2 % fructose and 31.3 % glucose that are readily absorbed by the body and the other sugars maltose 7.35%, sucrose 1.3% and isomaltose make up the additional 30%.
The enzymes found in honey, play an important role in its antibiotic properties. Invertase produced by the bee converts sucrose to glucose and fructose, amylase breaks down starch, glucose oxidase converts glucose to gluconolactone which in turn yields gluconic acid and hydrogen peroxide. Trace amounts of vitamin B, calcium, iron, zinc, potassium, phosphorus, magnesium, selenium, and chromium are also found in the composition of honey. The low pH of honey comes from the organic acids acetic, butanoic, formic, citric, succinic, lactic malic, pyroglutamic, and gluconic acid.

Although the exact composition of honey varies depending on the geographical source and the plants on which the bees have been feeding, this supersaturated mixture of sugars with small quantities of enzymes, amino acids, vitamins, minerals and organic acids holds many desired properties for an impressive antibacterial dressing for wounds. Several studies have shown it to inhibit over 60 species of bacteria including, anaerobes, gram-positive and gram-negative bacteria, and even some yeast species of Aspergillus, and Penicillium.

The super-saturated solution of honey, containing only 17% water inhibits bacterial growth primarily due to this high osmolarity. Water is essential for the survival of bacteria but with a low availability the microorganisms cannot survive and reproduce. When honey is applied to wounds, the high solute concentration creates an osmotic effect drawing lymph and other fluid out of the wound bed diluting the honey. As, the osmolarity decreases by the wound drainage, the antibiotic activity is not lost and at times is increased as Sackett noted in his study. It is the enzymatic effect from glucose oxidase’s production of hydrogen peroxide that brings about the continuous additional antimicrobial effect after the sugar saturation is lost. Glucose oxidase secreted from the hypopharyngeal glands of the bee, converts glucose to gluconic acid and
hydrogen peroxide. The bactericidal effect of hydrogen peroxide, further decreases the number of microorganisms available on the wound bed. The release of hydrogen peroxide is slow and continuous for a constant antibacterial effect successfully eliminates microorganisms but is not cytotoxic to the surrounding tissue.

Another factor associated with the antibiotic effect of honey is thought to be due to the phytochemicals in the nectar. The phytochemicals found in honey mostly consist of complex phenol and organic acids that further serve an antibacterial function. They also aid in reducing the risk of oxidative damage in the tissue. The concentration of phytochemicals varies depending on the plant source of the nectar and makes some honey’s more effective than others in terms of their antimicrobial activity.

Cooper et al tested three honeys against 17 strains of *Pseudomonas Aeruginosa* isolated from wound patients to compare its antimicrobial effects. They tested Medihoney which works primarily using phytochrome as an antibiotic compared to mixed pasture honey which used hydrogen peroxide as its antibiotic activity and an artificial honey which uses the high osmolar concentration of sugar as an antibiotic source. The results showed no difference in the antibacterial effect of the natural honeys with a minimum inhibitory concentration of 6.8-7.5% but a significantly higher concentration of 17-22% for artificial sugar is needed to inhibiting all 17 strains. This demonstrates that there is an additional antibiotic characteristic aside from the high osmolarity concentration but no difference in effectiveness between the hydrogen peroxide over the phytochrome honey.

The third antimicrobial property of honey is due to glucose oxidase converting glucose to gluconic acid which gives honey its low pH. Honey has an acidic composition with a pH
between 3.2-4.5, which is acidic enough to inhibit many pathogens.\textsuperscript{2,5,7} The more acid the pH the more the pathogen growth is inhibited. In addition to decreasing the pathogens in the wound, the acidic environment is beneficial to epithelialization. The acid environment increases the amount of oxygen released from the hemoglobin in the wound bed, which, in turn, increase the rate of granulation.\textsuperscript{7}

Honey has been shown to microscopically reduce inflammatory cells in acute and chronic inflammation. Although its exact mechanism is not understood, it stimulates peripheral blood to draw B and T lymphocytes to the surface and activates phagocytes even at honey concentrations as low as 0.1\%.\textsuperscript{13} It also stimulates monocytes to release cytokines, Tumor necrosis factor-1, and IL 1 and 6.\textsuperscript{13} Reducing inflammation is very important in wound healing as it improves circulation and delivers more oxygen and nutrients to help the tissue repair and heal.\textsuperscript{5} The anti-inflammatory effects of honey also reduce the hypertrophic scarring during the maturation phase of wound healing resulting in less scar tissue.\textsuperscript{14}

The high osmolar concentration of honey not only works as an antimicrobial property but also as aids in debridement of the wound. The strong osmotic action draws exudates and lymph fluid from the wound out towards the surface to add the moisture needed for autolytic debridement.\textsuperscript{5} This osmotic autolytic debridement, action washes the wound base from beneath as it removes debris and sloughs off necrotic tissue that would normally slow down healing process.\textsuperscript{3,8,10} Honey on the wound bed not only draws material out of the wound, but also prevents biofilm formation and cross-contamination. It provides a barrier effect on an open wound preventing further infection from external contamination.\textsuperscript{15}
Honey has a unique feature in that it can reduce and eliminate the malodorous nature of wounds. First its antibacterial action against odor producing anaerobes such as *bacterioides spp*, *prevotella ssp*, *peptostertococcus ssp*. destroys the bacteria that typically produces malodor.\(^5\)

Secondly, the glucose provided by honey is used by the bacteria, as an alternative to using amino acids from the metabolism of serum and dead cells. The end result, is therefore, the production of lactic acid, instead of malodorous ammonia, amines, and sulfur compounds which give a wound the unpleasant foul smell.\(^3,5\)

With the rise in antibiotic resistance the US FDA gave clearance for the use of Medihoney as a wound dressing product in 2007. Medihoney contains Manuka honey from *Leptospermum scaparium* derived from New Zealand tea trees.\(^15\) The honey is sterilized with \(\gamma\) radiation to remove the spores but retain its biologic properties.\(^3\) Manuka honey has a high level of phytochemical components and has been found to be very effective in clearing wounds.\(^12\) It is known that honey’s antibacterial activities are slower than those of traditional antiseptics which decrease bacteria count in mere minutes but balancing the speed against honey’s other properties is the question and issue here. The subject of this review is whether studies show that its combination of longer lasting bactericidal activity, its autolytic debridement activity, moist environment formed by the lymph preventing the dressing from adhering to the wound, and the sugar content and acidic environment promoting epithelialization through the increased availability of oxygen and nutrients to the cells decrease the healing time and make it a better wound dressing.

Many studies have looked at the affects of honey on burns, but few have a primary focus on chronic wounds. The focus of this study is to perform a literature search on randomized control
trials assessing the healing time of chronic wounds using honey as a wound therapy in comparison to standard therapy. Standard therapy for ulcers require debridement of necrotic tissue, the use of an occlusive or semipermeable dressings to maintain a moist wound environment, and treatment of wound infection if present.\textsuperscript{16}

**METHODS**

An exhaustive literature search was performed using the search engines MEDLINE, CINAHL, and Web of Science databases. Honey, treatment and therapy, and wounds were used as the keywords. The results were further limited to English only journals with Medihoney as the choice of honey used in treatment. The 239 articles found were read to determine the eligibility for the criteria. The inclusion criteria was, all randomized clinical trials, using patients with chronic skin wounds who were not receiving treatment with antibiotics, and must have had no other comorbidities or poorly controlled diabetes influencing the healing of the wound. Studies must have tested Manuka honey in comparison to standard therapy with the primary outcome of measuring healing time. Exclusion criteria were articles not in English, not available in full text and studies done in-vitro.

References were evaluated for additional studies that fit the eligible criteria. No articles were identified from the references provided. The JADAD scoring system was used on each trial to evaluate the validity of the study, although this was not used as a basis for exclusion.

**RESULTS**

Using the three search engines Medline, CINAHL, and Web of Science, 239 articles were identified using the key words honey, therapy, and wounds. Limiting the 239 articles to English and studies done on humans left 76 articles to review. Of those, 34 studies looked at honey on
wounds but 16 case reports were excluded leaving 18 articles for screening. After further evaluation of the articles only three studies fit the inclusion and exclusion criteria as randomized controlled clinical trials using honey in comparison to standard therapy in patients with chronic wounds who had not received antibiotic therapy and had no other comorbidities affecting the healing of the wound. The studies are summarized in table 1 and their finding are summarized in Table 2.

Robson et al\textsuperscript{4} conducted a open-label randomized clinical trial between September 2004 and May 2007 with the aim of comparing Medihoney with conventional treatment on wounds healing by secondary intention. A total of 105 patients from a large district general hospital in the United Kingdom were recruited to participate in the study. Fifty-two patients were randomized to receive 3mm of Medihoney covered with a low adherent dressing and an absorbent dressing followed by compression bandage. Fifty-three were randomized to receive standard local practice wound care from the hospital’s formulary, leaving the practitioner to choose the dressing and compression bandage. The hospital protocol dictated hydrogel be added to the wound in the presence of slough or necrotic tissue. Patients were excluded if they had diabetes or other health problems, wounds exposing tendons, muscle, or bone, and if they had received any antibiotics in the preceding two weeks. The groups were similarly placed with regard to gender, age, size and location of the wound, with 70\% of the patients having leg ulcers. The median time of complete healing in the honey group was 100 days compared to 140 days in the control group with a hazard ratio of 1.3 and 95\% CI of 0.77-2.19 and a p-value of 0.321. Although the honey showed to be 30\% more likely to heal, the wide confidence interval showed not to be statistically significant. In the honey treated group, two patients were lost to follow up
and eight discontinued interventions mostly due to indications from the clinician. The control group had similar results in that one was lost to follow up and 7 discontinued treatment. They concluded that healing rates with honey are reduced but the sample size was too small for the study to reach statistical significance.\textsuperscript{4}

The second study was also an open label randomized clinical trial conducted by Gethin and Cowman\textsuperscript{17} between February 2003 and January 2006. They measured the healing rate at 12 weeks and the ability of Manuka honey to deslough venous leg ulcers in comparison to standard therapy. A total of 108 patients with venous leg ulcers less than 100 mm\textsuperscript{2} were recruited from 10 different centers including acute and community hospitals, and vascular and leg clinics. Patients were excluded if their Ankle Brachial Pressure Index was \( \geq 0.8 \), if they had poorly controlled diabetes, or if they had been taking antibiotics or an immunosuppressant at the time of the study. Fifty-four patients were randomized to the honey group and received 5g/20 cm\textsuperscript{2} of honey weekly while 54 patients in the control group received 3 g/20 cm\textsuperscript{2} weeks followed by compression therapy for a total of 4 weeks. Clinical assessment was conducted thereafter on an as needed basis which varied from patient to patient, and a final follow up was conducted at 12 weeks. The honey group had a median of 34\% reduction in wound size at 4 weeks compared to a 13\% reduction in the control group with a p-value < 0.001. The healing rate at 12 wks was 39\% in the honey group compared to 33\% in the control group with a p-value of 0.03. No patients were lost to follow up in either group but 9 withdrew from the honey group and 17 from the control group with infection being the number one reason for withdrawal. They concluded that the healing rate was significant at 12 weeks for the honey group and had less infection rates compared to standard wound therapy.\textsuperscript{17}
The third study was an open-label multicenter randomized controlled trial conducted by Jull et al\textsuperscript{18} in which 368 patients with leg ulcers were recruited from four community based nursing services in New Zealand between May 2004 and September 2005. Patients were excluded if they had any history of diabetes, rheumatoid arthritis, or peripheral arterial disease. Of the study participants, 187 patients were randomized to receive manuka honey impregnated into calcium alginate dressings and covered by compression bandage. The honey was changed with frequency determined by the clinician. A total of 181 patients were randomized to the control group receiving a dressing covered by compression bandage. The dressing of choice was decided by the district nurse and consisted of alginate, hydrofibre, hydrocolloid, foam, hydrogel, non-adherent, iodine, or silver dressings. Patients in both groups were similar in gender, ABPI, and ulcer size at the beginning of the trial. Results showed that at 12 weeks, 104 (55.6\%) ulcers had completely healed compared to 90 (49.7\%) in the control group giving a 5.9\% increase in healing (95\% CI -4.3 to 15.7, p=0.258). Mean healing time was 63.5 days in the honey group and 65.3 days in the control group with a difference of -1.8 days (95\% CI -7.7 to 4.1 days, p= 0.553). In the honey group 32 patients had an infection during the trial compared to 40 in the control group giving an absolute decrease of 5.0 (95\% CI -3.1 to 13.1, p=0.228), although pain intensity was not recorded. Of the patients in the treated group, 47 reported pain compared to 18 in the control group with a RR 2.5 (95\% CI 1.5 to 4.2, p=0.001). No patients were lost to follow up in the honey group and 6 were lost in the control group. However, 31 patients in the honey group discontinued their treatment compared to none in the control group mostly due to problems at the ulcer site, including, pain, infection, bleeding, and wound deterioration. Jull et al\textsuperscript{18} concluded
that honey did not have a significant enough effect to consider it clinically relevant, and therefore there is no additional benefit from using honey impregnated dressings for ulcerations.\textsuperscript{18}

\textbf{DISCUSSION}

The antibacterial, anti-inflammatory, and debridement qualities give honey the potential to be a good treatment option for chronic wounds. The objective of this paper was to evaluate the healing rate of Manuka honey as a therapy for chronic wounds in comparison to standard therapy. The exhaustive systematic review identified three studies that looked at groups of patients who participated in randomized clinical trials to receive honey or a hydrogel plus a wound dressing. Two of the studies showed to have a small decrease in healing rate in the honey treated groups, but the difference was too small and confidence interval too large making the results not statistically significant.\textsuperscript{4,18} The third study showed to have a slight larger difference with a statistically significant difference by 6\% healing rate with a \( p \) value of 0.03.\textsuperscript{17} However, all three studies were poorly conducted with several limitations in the study design. Table 2 demonstrates each had a weak JADAD score of 3 due to their potential for bias as they were all open label studies where none of the participants or the medical professionals was blinded to the treatment type and much of the treatment seems to have been left to the individual practitioner’s discretion rather than being of standardized design.

\textbf{Limitations of Study}

Robson et al\textsuperscript{4} in addition to having a small sample size without blinding, did not treat the two groups equally. The honey treated group received honey and compression only. In the control group, in addition to the initial treatment, as their facility protocol recalled, the patients also
received hydrogel only when the presences of slough or necrosis was present on the wound. Honey being an autolytic debridement they felt no need to provide additional assistance when slough or necrosis was presence.\textsuperscript{4} The ability of honey to debris the wound is one of its great qualities in wound healing. In order to properly assess the superiority over standard treatment the groups should have been handles with a standardized protocol. Due to the lack of blinding, their randomization efforts failed, as two of the patients randomized to the honey group did not receive honey and 6 of the patients in the control group did not adhere to treatment and received honey as a result of patient’s decision from external pressure.\textsuperscript{4} “Unfortunately, however, because of the lack of blinding, a small number of patients allocated to conventional treatment did not adhere to treatment and received honey as a result of either patient pressure or external clinical decision.”\textsuperscript{4} Although patients were accounted for based on their assigned group as well as their final group and the results were similar, it appears that those conducting the study sabotaged their own efforts to some degree to please their patients.

Gethin and Cowman\textsuperscript{17} was the only study of the three that showed a statistically significant healing rate in the honey treated group, but this study design also lacked the validity of blinding, and they failed to recruit the desired number of participants with a total of 108 participants in the trial. Of their patients, 24\% (n=26) withdrew from the study, six in the honey treated group and 12 in the control group due to infection at the wound site.\textsuperscript{17} This is important to note as it is the only trial that included patients with diabetes that was well controlled. Although, their diabetes was controlled at the start of the trial they did not monitor their diabetes throughout the 12 weeks. An incidental finding could have been made had they determined if the patients with diabetes accounted for the ones that developed the infections but interestingly they do not appear
to have followed up on this issue. The other two trails completely excluded patients that had a
diagnosis of diabetes.4,18 Future studies should place the diabetic population in a separate group
and monitor their glucose levels throughout the trial.

Gethin and Cowman17 evaluated their patients on a weekly basis up to 4 weeks and thereafter
on an as needed basis determined by the health care provider that was not blinded to the
treatment and a final evaluation at 12 weeks. Not having a standardized follow up protocol
allowed for extensive variability in the frequency of dressing change. We know that honey’s
osmotic affect draws lymph fluid to the surface diluting the honey and its antimicrobial
properties. The other two studies could have potentially also been influenced by the dressing
frequency change as they do not mention how often the dressings were changed.4,18 The healing
rate can be affected either by too frequent or too late of a dressing changes. This study was
terminated at 12 weeks and stopping the trial at this stage fails to demonstrate complete healing
outcomes.17

Jull et al18 included the largest sample size of the three studies with 368 participants
randomized to receive honey or standard therapy for venous leg ulcers. The study was also an
open label study failing to blind the patients and involved clinical staff. Another limitation in this
study is that the control group varied in the “standard” therapy they received. It was left to the
nurses’ choice to use alginate, hydrofibre, hydrocolloid, foam, hydrogel, non-adherent, iodine, or
silver dressing. The dressing differed in the absorption and adherence to the wound, which in
turn could have had a treatment affect influencing the final healing rate of the wound.18 There
was no standard dressing change for either group, it was left up to the clinical staff to determine
the type and frequency of dressing change. Due to funding, this study failed to follow all patients
to complete healing and also terminated the evaluations at 12 weeks, which has an effect on its validity.

**Adverse events**

Jull et al\(^{18}\) was the only study that directly evaluated adverse events. The honey group had a 17% (n=31) discontinuation of treatment due to adverse effects of deterioration of the skin surrounding the ulcer (n=8), pain (n=4), infection (n=8). The control group had no patients discontinue treatment.\(^{18}\) The reason for the difference is not explained but could be related to the lack of blinding.

Pain and infection were the top two adverse events experienced by the participants in both experimental groups of the three studies.\(^{4,17,18}\) Robson et al\(^{4}\) reported one patient (1.9%) in the treatment group with pain. The second study by Gethin and Cowman\(^{17}\) reported 6 (11%) patients in the treatment group withdrew due to infection at the wound site and 12 (22%) in the control group. Jull et al\(^{18}\) reported a higher incidence of pain in the honey group with 47 (25%) compared to 18 (10%) in the control group but only 32 (17.1%) compared to 40 (22.1%) in the control group reported infection. The difference in infection rate was not significant (p=0.228).\(^{18}\) It does appear that pain is a problem with the honey protocol but none of the studies measured or reported the degree of pain. The pain was likely a result of the acidity of honey and varied according to the size of the wound and frequency of application.

All three studies proved honey to be an effective wound treatment choice but not a better choice for faster healing than standard treatments.\(^{4,17,18}\) Honey showed to cause no harm, and the only known adverse event is a variable degree of pain that could be possible reduced by the frequency of dressing change. As Robson et al\(^{4}\) demonstrated, honey is a well accepted natural
regimen in our society and people are open to the idea of using it as a medical treatment. The antimicrobial properties could take honey’s use to a deeper level. Studies have proven honey to be sensitive to MRSA and VRE,\textsuperscript{5,19} without gaining resistance. Blair et al were not successful in generating a honey resistant strain of \textit{pseudomonas aeruginosa} or \textit{staph aureus} using subleathel doses over longer periods of time when Tetracycline, Oxacillin, and Ciprofloxacin were all resistant to the pathogens.\textsuperscript{20} Jull et all\textsuperscript{18} also looked at the cost effectiveness of using honey. When considering nursing, materials, appointments, and hospitalization, there was a -$9.45 (95% CI -$39.63 to $16.07) in New Zealand dollars favoring the honey treated group. The difference was attributed to only three patients requiring hospitalization for a total of 10 days in the honey group compared to 6 patients in the control group hospitalized for a total of 40 days.\textsuperscript{18}

CONCLUSION

There continues to be limited evidence supporting the medical use of honey and the studies published are of poor quality. This systematic review evaluated three studies comparing sterilized Manuka honey to standard therapy for chronic wounds. All articles had weak validity scores using JADAD grading system where none of them receiving more than a three due to the potential of biases from the lack of blinding the all participants. The two studies that excluded patients with controlled diabetes are consistent in that they demonstrate no additional benefit from using honey on the treatment of chronic wounds in comparison to standard therapy. However the results were not significant perhaps due to the small population size. All three studies are consistent with past studies in demonstrating that honey is effective in treating wounds with the only adverse event of pain experienced by the participants.
Future studies should focus on testing honey on chronic wounds with a better study design. The randomized control trial should focus on obtaining a large sample size, double blinded participants, and using well developed standard protocol in both groups with same treatment in type and frequency of dressing change. Honey should be further investigated as it could be the answer to cutting down cost and treating many complicated wounds infected with MRSA or VRE and decrease further antibiotic resistance.
REFERENCES


### TABLE1: Summary of Reviewed Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Title</th>
<th>Journal/ Yr. published</th>
<th>Patients/ Population</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Outcome(s)</th>
<th>Study type</th>
<th>Validity (JADAD score)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Robson, Dodd, Thomas</td>
<td>Standardized antibacterial honey with standard therapy in wound care</td>
<td>Journal of Advanced Nursing: 2008</td>
<td>Adults with wound infections greater than 12 wks.</td>
<td>Manuka Honey</td>
<td>Conventional dressing from hospital protocol</td>
<td>1. Time for complete healing of the wound. 2. Time for 50% reduction of the wound area.</td>
<td>RCT</td>
<td>3</td>
<td>(-) Not blinded. (-) Pts were allowed to switch treatment groups.</td>
</tr>
</tbody>
</table>
**TABLE 2: Comparison of Healing Rate of Honey vs. Standard Wound Therapy**

<table>
<thead>
<tr>
<th>Study</th>
<th>Participants</th>
<th>12 week healing rate</th>
<th>p-value 12wk healing rate</th>
<th>Mean healing time</th>
<th>p-value healing time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Robson, Dodd &amp; Thomas</td>
<td>52 Honey</td>
<td>46.2%</td>
<td></td>
<td>100 days</td>
<td>0.321</td>
</tr>
<tr>
<td></td>
<td>53 Control</td>
<td>34.0%</td>
<td></td>
<td>140 days</td>
<td></td>
</tr>
<tr>
<td>Grethin &amp; Cowman</td>
<td>54 Honey</td>
<td>24%</td>
<td>0.03</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>54 Control</td>
<td>18%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jull et al</td>
<td>187 Honey</td>
<td>55.6%</td>
<td>0.258</td>
<td>63.5 days</td>
<td>0.553</td>
</tr>
<tr>
<td></td>
<td>181 Control</td>
<td>47.9%</td>
<td></td>
<td>65.3 days</td>
<td></td>
</tr>
</tbody>
</table>