

Honey and Wound Healing: An Update

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Table 2. Clinical Study Result Summary

<u>Author</u>	<u>Study Type</u>	<u>Wound Type</u>	<u>Honey Treatment: Sample Size; Outcome</u>	<u>Control Treatment: Sample Size; Outcome</u>	<u>Risk Difference (or equivalent) Honey- Control</u>	<u>P-Value</u>	<u>Potential for Bias</u>
Maghsoudi et al [44]	Prospective Randomized Trial	Partial Thickness Burn	<p><u>"Pure, unprocessed, undiluted honey</u> obtained from hives was applied in quantities of 16-30 mL, depending on the size of the burn, to the burn surface after this had been washed with normal saline. After spreading of the honey, the wound was covered with dry sterile gauze and bandaged. Honey was applied on alternate days...The wounds were inspected every two days until healing."</p> <p style="text-align: center;">n=50</p> <p>Satisfactory Epithelialization by day 7, 21: 84%, 100%</p>	<p>"...wounds were covered with pieces of <u>gauze impregnated with mafenide acetate</u> after being washed with normal saline. These were replaced every day. The wounds were inspected every two days until healing."</p> <p style="text-align: center;">n=50</p> <p>Satisfactory Epithelialization by day 7, 21: 72%, 84%</p>	<p>Day 7: +12%</p> <p>Day 21: +16%</p>	p<0.005	Study not blinded
Gupta et al [45]	Retrospective Review	1 st and 2 nd Degree Burns of <50% TBSA	<p>"Wounds examined carefully and washed with normal saline...dressed with <u>pure undiluted honey</u> daily. After dressing application, ...left the burn area open. Patients were followed up every fortnight for initial 2 months, monthly for next 4 months, and once in 6 months thereafter."</p> <p>Average Healing Time, n=51: 18.16 days</p> <p>In patients presenting within one hour of burn, # of wounds which became sterile within 14 days, n=8: 100% (8/8)</p> <p>Complete recovery from wound, n=51: 78.43% (40/51)</p>	<p>"Wounds examined carefully and washed with normal saline...dressed with <u>silver sulfadiazine cream</u> daily. After dressing application, ... left the burn area open. Patients were followed up every fortnight for initial 2 months, monthly for next 4 months, and once in 6 months thereafter."</p> <p>Average healing time, n=57: 32.68 days</p> <p>In patients presenting within one hour of burn, # of wounds which became sterile within 14 days, n=14: 14.29% (2/14)</p> <p>Complete recovery from wound, n=57: 47.39% (27/57)</p>	<p>Average healing time: -14.52 days</p> <p>Sterile wounds: +85.71%</p> <p>Complete recovery: +31.04%</p>	<p>Average healing time: p<0.05</p> <p>Sterile wounds: p<0.05</p> <p>Complete recovery: p<0.002</p>	The authors did not clarify if honey utilized in study was identical between patients and if it was medical grade
Subrahmanyam [48]	Prospective Randomized Trial	Split-thickness skin graft donor sites	<p><u>Unprocessed Syzygium cumini honey-impregnated gauze</u> applied to donor site; bandage changed if signs of infection present, otherwise removed at one week</p> <p style="text-align: center;">n=50</p> <p>Epithelialization by day 7: 96% (48/50)</p> <p>Healing by day 10: 100% (50/50)</p>	<p><u>Sterile Vaseline Gauze</u></p> <p style="text-align: center;">n=50</p> <p>Epithelialization by day 7: 78% (39/50)</p> <p>Healing by day 10: 76% (38/50)</p>	<p>Epithelialization by day 7: +18%</p> <p>Healing by day 10: +24%</p>	<p>Epithelialization: p<0.05</p> <p>Healing: p<0.05</p>	<p>Study not blinded</p> <p>The authors did not clarify if honey was medical grade</p>

Parmar et al [49]	Technical Note	Split-thickness skin graft donor sites	<p>“Donor sites are...dressed with Allevyn non-adhesive dressing, OpSite and bandaged...At the first clinic appointment, the <i>dressing</i> is changed to one with <i>impregnated honey</i>, (which are) re-applied on a weekly basis.”</p> <p>Subjective: “patients report reduced pain and less concerns than previously with standard dressings... superior management of the wound, pain and healing, with reduced rates of infection and over-granulation... earlier epithelialization and healing”</p>	<p>“<i>Standard dressings</i>, e.g. Jelonet, Kalsostate or non-adhesive foam dressings”</p>	N/A	N/A	<p>Subjective findings with no statistical support</p> <p>The authors did not clarify if the honey utilized in the study was identical between patients and if it was medical grade</p>
Anyanechi & Saheeb [50]	Prospective Randomized Trial	Segmental mandibular resections resulting in wound dehiscence where primary closure was not possible	<p>“Same treatment regimen as control group except that wounds were dressed at weekly intervals for three consecutive weeks with <i>Obudu honey</i>, and discontinued. The <i>Obudu honey</i>... was smeared on the wound surfaces and then impregnated on ribbon gauze before tucking it into the wounds.”</p> <p>n=36</p> <p>Healing at week 5: 52.8% (19/36)</p> <p>Healing at week 9: 100% (36/36)</p>	<p>“Wounds debrided with <i>dilute hydrogen peroxide alternated with normal saline</i>, repeated twice at weekly intervals”</p> <p>n=36</p> <p>Healing at week 5: 36.1% (13/36)</p> <p>Healing at week 9: 100% (36/36)</p>	<p>Healing at week 5: +16.7%</p> <p>Healing at week 9: 0%</p>	<p>Healing at week 5: no p-value provided</p> <p>Healing at week 9: p=0.23 (not statistically significant)</p>	<p>All patients treated by same physician without blinding</p> <p>No statistical analysis at week 5 healing point</p>
Nikpour et al [51]	Triple-blind Prospective Randomized Trial	Post-Cesarean section abdominal wounds	<p>“<i>25% honey gel (coriander and Goat’s thorn honey)</i>...with a specific code was given to the mothers and they were trained to use it twice daily (12 ± 2 hours) for 14 days.”</p> <p>n=37</p> <p>Total REEDA* score: Day 7: 2.27 +/- 2.46 Day 14: 0.47 +/- 0.84</p> <p>Redness: Day 7: 1.02 +/- 0.98 Day 14: 0.30 +/- 0.52</p> <p>Edema: Day 7: 0.72 +/- 0.87 Day 14: 0.16 +/- 0.37</p> <p>Ecchymosis: Day 7: 0.45 +/- 0.76 Day 14: 0</p> <p>Discharge: Day 7: 0.02 +/- 0.16 Day 14: 0</p>	<p>“<i>Placebo gel</i>... with a specific code was given to the mothers and they were trained to use it twice daily (12 ± 2 hours) for 14 days”</p> <p>n=38</p> <p>Total REEDA* score: Day 7: 3.91 +/-2.74 Day 14: 1.59 +/- 1.95</p> <p>Redness: Day 7: 1.59 +/- 1.01 Day 14: 0.78 +/- 0.78</p> <p>Edema: Day 7: 1.27 +/- 0.76 Day 14: 0.51 +/- 0.69</p> <p>Ecchymosis: Day 7: 0.86 +/- 0.91 Day 14: 0.29 +/- 0.61</p> <p>Discharge: Day 7: 0.10 +/- 0.31 Day 14: 0</p> <p>Approximation: Day 7: 0.08 +/- 0.27 Day 14: 0</p>	<p>Mean differences:</p> <p>Total REEDA* score: Day 7: -1.64 Day 14: -1.12</p> <p>Redness: Day 7: -0.57 Day 14: -0.48</p> <p>Edema: Day 7: -0.55 Day 14: -0.35</p> <p>Ecchymosis: Day 7: -0.41 Day 14: -0.29</p> <p>Discharge: Day 7: -0.08 Day 14: 0</p> <p>Approximation: Day 7: -0.06 Day 14: 0</p>	<p>Total REEDA: Day 7: p=0.008 Day 14: p=0.002</p> <p>Redness: Day 7: p=0.017 Day 14: p=0.003</p> <p>Edema: Day 7: p=0.006 Day 14: p=0.010</p> <p>Ecchymosis: Day 7: p=0.043 Day 14: p=0.006</p> <p>Discharge: Day 7: p=0.017 Day 14: -</p> <p>Approximation: Day 7: p=0.311 (not statistically significant) Day 14: -</p>	<p>Positives: Attempts to maintain similar nutrition between treatment and control groups were undergone</p> <p>One pharmacist prepared drug and placebo gels</p>

		Approximation: Day 7: 0.02 +/- 0.16 Day 14: 0					
Dryden et al [53]	Retrospective observational study	Post-Cesarean section abdominal wounds	10 g single-application of <i>Surgihoney with prophylactic antibiotics around time of Cesarean section</i> with patients monitored for 30 days post-op n=186 Surgical site infections: 2.15% (4/186)	<i>Prophylactic antibiotics around time of Cesarean section</i> with patients monitored for 30 days post-op N=590 Surgical site infections: 5.42% (32/590)	Surgical site infections: -3.27%	Surgical site infections: p=0.042	Timing of antibiotic dose was not uniform for all patients Study was not randomized or blinded
Heidari et al [54]	Prospective Randomized Trial	Post-Cesarean section abdominal wounds	"...Iranian <i>Astragalus gossypinus honey</i> place(d) on Caesarean wound by pressing it in a way that the entire wound was covered...asked to continue using the tubes twice a day until 16 consecutive days post caesarean" n=44 Total REEDA* Score, Day 40: 0.18 (SD: 0.58)	"... <i>placebo gel</i> place(d) on Caesarean wound by pressing it in a way that the entire wound was covered...asked to continue using the tubes twice a day until 16 consecutive days post caesarean" n=42 Total REEDA* Score, Day 40: 0.10 (SD: 0.30) " <i>Control</i> received neither local honey nor any of the local disinfectant materials (such as povidone iodine)." n=46 Total REEDA* Score, Day 40: 0.55 (SD: 0.64)	Mean differences: Honey vs. Control: -0.37 Placebo vs. Control: -0.45 Honey vs. Placebo: +0.08	Honey vs. Control: p=0.005 Placebo vs. Control: p=0.001 Honey vs. Placebo: p=0.76 (not statistically significant)	Authors attempted blinding as much as possible, but placebo and honey topicals were not identical Inability to accurately assess wounds through sampling due to wounds being cleaned
Johnson et al [55]	Open-label Prospective Randomized Trial	Peritoneal Dialysis (PD) Exit Site	"Daily topical exit-site application of 10 mg of gel containing of 80% <i>Leptospermum sp</i> Medihoney plus standard exit-site care" n=186 Note: Primary study outcome- First infection related to PD	"Participants without nasal carriage of <i>S aureus</i> at baseline received <i>standard exit-site care</i> and underwent nasal swab screening every 6 months thereafter. Participants with nasal carriage of <i>S aureus</i> at initial or subsequent screens received 2% mupirocin ointment for self-application twice daily to both anterior nares for 5 consecutive days each month plus standard exit-site care for the duration of the trial." n=185	Diabetic participants with PD in honey group: Primary composite outcome Hazard ratio: 1.85 (1.05-3.24) Peritonitis Hazard ratio: 2.25 (1.16-4.36)	Overall, no significant differences in infection-free survival time, serious adverse events, and deaths. Diabetic patients' primary outcome in honey group: p=0.03 Diabetic patients and peritonitis in honey group: p=0.002	Only blinded to microbiology staff, but not clinical staff High patient dropout of study due to multitude of reasons (i.e. renal transplant, death, conversion to hemodialysis)
Dina Jarjis et al [56]	Case Report	Post-bariatric abdominoplasty with wound infection and dehiscence	"Conservative wound treatment with <i>topical Manuka Honey</i> " Outcome: "significant clinical improvement and effective healing concurrently with good patient satisfaction"	N/A	N/A	N/A	Case report with subjective results (low level of evidence)
Majtanova et al [57]	Case Report	Infected corneal ulcer	"Combination of topical levofloxacin and <i>irradiated honeydew honey solution</i> ... applied as a sterile 25% (w/v) solution directly to the affected eye... five times a day."	N/A	N/A	N/A	Case report with subjective results (low level of evidence)

			Outcome: “Treatment was effective... honeydew honey was shown to be highly effective in vitro against ocular isolates, in particular <i>S.</i> <i>maltophilia</i> ”				
Okeniyi et al [58]	Prospective Randomized Trial	Pyomyositis abscesses excision sites	“Twice daily “ <i>Crude undiluted honey</i> ” wound dressings with packing following fresh surgical incision & drainage and 21-day course of ampicillin, cloxacillin, and gentamicin” n=23 Completion of epithelialization at day 21: 87% (20/23)	“Twice daily “ <i>Edinburgh University solution of lime (EUSOL)</i> ” soaked- gauze with packing following fresh surgical incision & drainage and 21- day course of ampicillin, cloxacillin, and gentamicin” n=20 Completion of epithelialization at day 21: 55% (11/20)	Healing at day 21: +22% mean length of hospital stay: -2.50 days	Completion of epithelialization at day 21: RR: 1.58 CI: 1.03-2.42 p=0.047 Mean length of hospital stay: p=0.019	Type of honey and medical quality unknown Not blinded
Biglari et al [59]	Prospective Observational Study	Chronic pressure ulcers	“ <i>Medihoney</i> dressings were changed daily in a sterile environment...for more than 6 weeks” n=20 After day 7: No bacterial growth in swabs from 100% of patients (20/20) Complete wound healing after day 28: 90% (18/20)	N/A	N/A	N/A	Observational study with no direct comparison to standard treatment
Khadanga et al [60]	Randomized observational cross-sectional study	Decubitus Ulcers	“ <i>Honey</i> ” n=20 Mean VAS** Score +/- SD: 3.30 +/-0.47	<i>Povidone Iodine</i> n=20 Mean VAS** Score +/- SD: 3.70 +/- 0.47	Mean VAS** Score: - 0.40	Mean VAS** Score: p=0.010 Reduction in wound size: p=0.459	Type of honey and medical grade not specified Duration and dose of honey treatment not specified Not Blinded
Saha et al [61]	Prospective Randomized Trial	Decubitus Ulcers	“ <i>Honey</i> ” + <i>Metronidazole Powder</i> applied daily n=20 Mean VAS** Score: Day 1: 8.5 Day 7: 6.0 Bates Jensen Wound Assessment: Day 1: 50.1 Day 10: 34.1	<i>Metronidazole Powder</i> applied daily n=20 Mean VAS** Score: Day 1: 7.7 Day 7: 8.7 Bates Jensen Wound Assessment: Day 1: 47.7 Day 10: 51.6	Mean VAS** Score: Day 1: +0.8 Day 7: -2.7 Bates Jensen: Day 1: +2.4 Day 10: -17.5	VAS F value (critical difference): 6.638 (1.667) (statistically significant) Bates Jensen Wound Assessment F value (critical difference): 6.523 (14.03) (statistically significant)	Type of honey and medical quality unknown Study not blinded
Imran et al [62]	Prospective Randomized Controlled Trial	Diabetic foot ulcers	<i>Beri (Ziziphus jujuba) honey- impregnated dressings</i> . All patients were admitted in surgical ward for at least first 2 dressings. Wound dressing was sealed with 2nd layer for protection. Dressing was performed twice daily for three days and then, depending on the wound condition, either once/ twice daily or after 48 hours. Patients were followed-up for a maximum 120 days.	<i>Control (Saline)</i> : All patients were admitted in surgical ward for at least first 2 dressings. Wound dressing was sealed with 2nd layer for protection. Dressing was performed twice daily for three days and then, depending on the wound condition, either once/ twice daily or after 48 hours. Patients were followed-up for a maximum 120 days. n=169	Complete healing: +18.58% Median healing time: -11.00 days No serious side effect in both groups	Complete healing: p=0.001 Mean healing time: p<0.001	Study not blinded Study subjects mostly belonged to lower socioeconomic class. Wound healing was observed only clinically. Isolation of microorganisms or histopathological aspects of wounds not

			n=179 Complete healing at day 120: 75.97% (136/179) Median healing time: 18.00 days (6-120)	Complete healing at day 120: 97/169 (57.39%) Median healing time: 29.00 days (7-120)			performed frequently due to lack of facilities High patient loss-to- follow-up: Beri-honey group: 16 of 195 (179 included in analysis) Control group: 11 of 180 (169 included in analysis)
Kamaratos et al [63]	Prospective Randomized Double-Blind Study	Neuropathic diabetic foot ulcers in Caucasian type 2 diabetes mellitus patients	“ <u>Manuka-impregnated honey dressings</u> (Medihoney Tulle) were applied... initially on a daily basis and then with declining frequency as wound healing progressed.” n=32 Mean healing time: 31+/- 4 days Sterile ulcers at day 7: 78.13% (25/32) Patients requiring antibiotic therapy: 0% (0/32) % of ulcers which healed at 16 weeks: 97% (31/32)	“ <u>Saline-soaked gauze</u> were applied... initially on a daily basis and then with declining frequency as wound healing progressed.” n=31 Mean healing time: 43 +/- 3 days Sterile ulcers at day 7: 35.5% (11/31) Patients requiring antibiotic therapy: 29.03% (9/31) (four hospitalized) % of ulcers which healed at 16 weeks: 90% (28/31)	Mean healing time: -12 days Sterile ulcers: +42.63% Antibiotic therapy: -29.03% % of ulcers which healed: +7%	Mean healing time: p<0.05 Sterile ulcers: No stats provided Antibiotic therapy: No stats provided % of ulcers which healed: Not statistically significant	
Gulati et al [66]	Prospective Randomized Trial	Clean, non-infected chronic wounds of ≥ six weeks’ duration (majority: venous etiology, 40/42 on lower extremity)	“ <u>Gamma-sterilized honey from a bee hive on a neem tree (Azadiracta indica)</u> ... wound dressing changed every other day until complete healing or up to 6 weeks... venous leg ulcers were reinforced with elastic compression garments” n=22 Complete healing at week 6: 31.82% (7/22) Median wound surface area (cm ²) (range): Week 0: 4.35 (1.8-12.1) Week 6: 0.55 (0-12.1) Median VAS** Score (Range): Week 0: 7 (0-10) Week 6: 1 (0-4)	“ <u>Povidone Iodine</u> wound dressing changed every other day until complete healing or up to 6 weeks... venous leg ulcers were reinforced with elastic compression garments” n=20 Complete healing at week 6: 0% (0/20) Median wound surface area (cm ²) (Range): Week 0: 4.25 (0.8-8.6) Week 6: 3.2 (0.3-8.1) Median VAS** Score (Range): Week 0: 7 (0-10) Week 6: 5 (0-9)	Complete healing at week 6: +31.82%	Complete healing at week 6: p<0.05 Median wound surface area: p<0.001 Median VAS** Score: p<0.001	Study not blinded All the subjects were not followed until complete healing
Thomas et al [70]	Retrospective case note review of prospectively collected patient database which underwent treatment	Recurrent or chronic pilonidal sinus disease	“Skin surrounding wound was first protected with a barrier cream. <u>Active Manuka Honey</u> then applied directly to base of wound as a gel. Gauze swabs impregnated with further Manuka honey then placed over this to fill wound cavity. In the absence of a cavity, honey impregnated gauze was applied	N/A	One patient developed an erythematous rash around the wound after 48 days (delayed local reaction)	N/A	Retrospective study with no control group

			<p>directly to wound...Patients were instructed to bathe and dress wounds twice daily in the early stages of management. As wound exudate reduced, they could reduce the dressings to daily.”</p> <p>n=17</p> <p>Complete wound healing: 88.24% (15/17)</p> <p>One patient stopped treatment due to adverse effect and two patients experienced recurrence after completing honey treatment</p> <p>Mean time of healing: 65 days</p> <p>Median time of healing: 49 days</p> <p>Range time of healing: 14-262 days</p>				
Haidari et al [71]	Retrospective study	Fournier’s gangrene	<p>“In week one, cleansing was done using normal saline under anesthesia in the OR every other day and <u>30-50cc of honey</u> was used on the site after it was dried, and then the wound was dressed. This method was taught to the patients and their attendants so that they... continue the treatment at home. Patients were asked to report to hospital every other day after discharge for follow-up.”</p> <p>n=17</p> <p>Mean hospitalization time (days): 12 +/- 6</p>	N/A	N/A	N/A	<p>Retrospective study with no control group</p> <p>Type of honey and medical quality unknown</p>
Biglari et al [72]	Prospective Observational Multicenter Trial	Wounds of varying etiologies	<p>“Combination of <i>Medihoney</i> with diverse dressings for exudate management. Local investigators were advised to change the honey dressings after 1–3 days depending on the individual level of wound exudation.”</p> <p>Total n=104 Post-operative wound n=26 Decubitus Ulcers n=20 Soft tissue infections n=8 “undergoing treatment for cancer” n=32</p> <p>Significant decrease was seen in the wound size, perceived pain levels, and wound sloughing/necrosis</p>	N/A	N/A	Decrease in the wound size, perceived pain levels, wound sloughing/necrosis: p<0.05	Observational study with no comparison group
Dryden et al [73]	Prospective multi-institutional observational study	Acute and chronic wounds with established delayed healing	<p>“Dressings and <i>Surgihoney gel</i> were changed at the discretion of the attending clinician and patient circumstances, but the recommendation was for gel change every 2-3 days. The gel is applied to</p>	N/A	N/A	Adverse effects: Two patients reported stinging sensation post-application in two patients	Limitations: Subjective reporting by patients

			<p>the wound bed in an even layer up to approximately 2mm thick and covered with a suitable sterile secondary dressing (highly absorbent if the wound is heavily exuding).”</p> <p>Total n= 104 total patients with 114 wounds n= 33 patients with leg ulcers n= 18 patients with pressure ulcers n= 14 patients with surgical wounds n= 5 patients with diabetic ulcers n= 20 patients with traumatic/surgical wounds from developing world</p> <p>Mean duration of wounds before treatment= 3.7 months Mean duration of treatment= 25.7 days</p> <p>21% (24/114) of wounds healed completely</p> <p>79% (90/114) of wounds improved clinically</p> <p>0% (0/114) of wounds demonstrated clinical deterioration</p> <p>In 37 leg ulcer wounds, 68% (25/37) demonstrated reduction in size and 92% (34/37) demonstrated improvement in healing</p> <p>In 19 pressure ulcer wounds, 63% (12/19) demonstrated reduction in wound size and 89% (17/19) demonstrated improvement in healing</p> <p>In 47 wounds exhibiting wound exudation, 100% (47/47) of wounds demonstrated change from green-tinged/purulence to clear serous exudate with Surgihoney treatment</p> <p>Reduction in patient pain and devitalized tissue consistently reported</p> <p>97.5% (39/40) of wound cultures demonstrated reduction in bacterial load</p>	Two elderly patients died of causes unrelated to the dressing or chronic wound	<p>No statistical analysis of significance of wound changes</p> <p>Observation time varied by patient</p> <p>Sampling bias (patients enrolled at discretion of clinician)</p> <p>No randomization</p> <p>No control treatment</p> <p>Biofilm not assessed histologically</p> <p>Wound cultures were semi-quantitative and not undertaken in every patient</p> <p>First author became shareholder in Surgihoney manufacturer after study completion</p>		
Maiti et al [74]	Prospective study	Patients with head and neck cancer requiring radiation therapy	<p>In addition to chemoradiation, patients advised to take 20 mL of “<i>natural honey</i>” 15 minutes before, 15 minutes after, and similar amount at bed time.</p> <p>n=28</p>	Chemoradiation n=27	Grade 3 mucositis: -23%	P-value not provided	Study not randomized or blinded
				Grade 3 mucositis: 41% (11/27)	Grade 4 mucositis: -18%	One patient discontinued honey treatment due to loss of glycemic control, while another discontinued treatment due to “unknown reason”	No statistical indicators of significance (i.e. p-value) provided
				Grade 4 mucositis: 22% (6/27)			

			Grade 3 mucositis: 18% (5/28)				Unknown if honey is medical grade
			Grade 4 mucositis: 4% (1/28)				
Hawley et al [75]	Prospective double-blind randomized placebo-controlled trial	Radiation-induced mucositis in head and neck cancer patients	Patients told to “swish, hold, and swallow” <i>irradiated Manuka honey</i> 4x daily during radiation tx, and seven days post-radiation tx n=54 Highest RTOG*** score Total evaluable patients: 40 <3: 26 (65%) ≥3: 14 (35%)	Patients told to “swish, hold, and swallow” <i>placebo Gel</i> 4x daily during radiation tx, and seven days post-radiation tx n=52 Highest RTOG*** score Total evaluable patients: 41 <3: 23 (56%) ≥3: 18 (44%)	N/A	Highest RTOG*** score: p=0.4126 Manuka honey was not tolerated very well by the patients	High dropout rate mostly due to nausea (57% in honey group, 52% in placebo gel group)
Bardy et al [76]	Prospective double-blind randomized placebo-controlled trial	Patients with head and neck cancer undergoing radiation therapy	Rinse mouth with 20 ml of <i>Manuka honey</i> , and to swallow it slowly, 4x daily for duration of radiotherapy (4 weeks) and for 2 weeks after treatment (42 days in total) n=64 Incidence of grade 3 mucositis: 79.69% (51/64)	Rinse mouth with 20 ml of <i>golden syrup placebo</i> , and to swallow it slowly, 4x daily for duration of radiotherapy (4 weeks) and for 2 weeks after treatment (42 days in total) n=63 Incidence of grade 3 mucositis: 74.60% (47/63)	Incidence of grade 3 mucositis: 5.09% “Patients reports problems with the taste and texture of the products and cited the effort required to take them as reason for discontinuation”	Incidence of grade 3 mucositis p=0.64	
Lund-Nielsen et al [77]	Prospective blinded randomized trial	Malignant wounds and advanced cancer	<i>Manuka honey-coated bandages</i> and absorbent dressing for four weeks. Wound treatments took place on average every 2–3 days with approximately 1.5 hours per visit. n=34 Median decrease in wound size: 15 cm ² VAS** malodor rating: 1.4 +/- 2.1 VAS** exudation rating: 1.9 +/- 2.2	<i>Nanocrystalline silver-coated bandages</i> and foam bandages for four weeks. Wound treatments took place on average every 2–3 days with approximately 1.5 hours per visit. n=35 Median decrease in wound size: 8 cm ² VAS** malodor rating: 2.3 +/- 3.0 VAS** exudation rating: 3.5 +/- 2.7	Median decrease in wound size: +7 cm ² Malodor VAS**: -0.9 Exudation VAS**: -1.6	Median decrease in wound size: p=0.63 Malodor: p=0.007 Exudation: p<0.0001	
Drain & Fleming [78]	Case report	Oral Squamous Cell Carcinoma	“Calcium alginate impregnated with <i>medical grade Manuka honey</i> was applied to external wound and <i>Manuka honey paste</i> was applied twice daily with a swab in the oral cavity.” “decrease in wound size... and the odor and inflammation which the patient experienced”	N/A	Wound size: Decreased from 2 cm x 2cm to 1 cm x 1 cm	N/A	Case report (low level of evidence)
Lund-Nielsen et al [79]	Prospective single- blind randomized trial	Malignant wounds	“ <i>Manuka honey-coated primary dressing</i> was administered in the patient’s home every 2 to 3 days. Each visit lasted approximately 90 minutes.” n=34	“ <i>Silver-coated primary dressing</i> was administered in the patient’s home every 2 to 3 days. Each visit lasted approximately 90 minutes.” n=33	N/A	“No statistically significant differences were found between the type and number of different wound pathogens in the wounds during the course of the study or	No untreated control group

						between treatment groups.”
Jull et al [80]	Cochrane Systematic Review	All wounds	<p>“High quality evidence”: Honey dressings (compared to conventional dressings) heal partial thickness wounds more quickly (2 trials, n=992)</p> <p>“Moderate quality evidence” that honey healed infected post-operative wounds more rapidly than antiseptic washes and gauze with fewer adverse effects (One trial, n=50)</p> <p>“Very low quality evidence” on honey’s effects on adverse effect rates and “low quality evidence” on honey’s effects on infection</p>	<p>“High quality evidence” that there is no difference in overall healing within six weeks when comparing honey to silver sulfadiazine. A decrease in the overall risk of adverse effects with honey treatment was found (6 trials, n=462)</p>	N/A	N/A
Lindberg et al [81]	Systematic Review and Meta-analysis	Burns	<p><u>Honey</u></p> <p>“Unequivocal” results that honey’s effectiveness as an antibacterial dressing is superior to that of silver when utilized in burns (6 RCTs, n=512)</p>	<u>Silver</u>	Application of honey resulted in quicker healing, increased number of wounds which healed, and better antimicrobial effects	N/A
Vandamme et al [82]	Systematic Review	All wounds	<p><u>Honey</u></p> <p>Randomized studies show a clear antimicrobial effect and faster wound healing with honey treatment in burns</p> <p>Antimicrobial properties of honey in burns should be further examined, as five of seven randomized controlled trials are by the same investigator. In six trials, “pure, undiluted” honey is used without composition specifications</p> <p>With other wound types, a link with honey and healing is “not always obvious”</p>	N/A	N/A	N/A
Norman et al [83]	Cochrane Systematic Review	Surgical wounds healing by second intention (pyomyositis abscess excision sites, by Okeniyi et al (see above))	<p>“<u>Crude undiluted honey</u>” following fresh surgical incision & drainage and 21-day course of ampicillin, cloxacillin, and gentamicin</p> <p>“moderate quality evidence” (due to the small sample size, n=43)</p>	<u>Edinburgh University solution of lime (EUSOL)</u> following fresh surgical incision & drainage and 21-day course of ampicillin, cloxacillin, and gentamicin	N/A	N/A
Amaya [100]	Multi-center retrospective chart review	Neonatal and pediatric wounds	<p><u>Active Leptospermum honey</u></p> <p>n=115 patients, 121 wounds</p> <p>Successful debridement (overall): 86.0% (104/121)</p> <p>Successful debridement (neonatal): 86.1% (31/36)</p>	N/A	N/A	Only two patients experienced an adverse effect (“transient stinging sensation on application”), with none in neonatal patients

Mohr et al [101]	Case series	Neonatal wounds of varying etiologies, including ischemia and intravenous solution extravasation	<u>Active Leptospermum honey</u> (treatment regimen varied by case) n=3 Conclusion: "Active Leptospermum honey is a viable wound management option... and should be considered when treating wounds in the neonatal population."	N/A	N/A	N/A	Case report with subjective results (low level of evidence)
Boyar et al [99]	Case series	Neonatal stage 3 pressure ulcer, dehiscent and infected sternal wound, and full thickness wound from extravasation injury	<u>Medihoney (Leptospermum honey)</u> (treatment regimen varied by case) n=3 “(Honey products) demonstrated ease of use, decreased pain with dressing changes, timely wound closure and no side effects in our patients.”	N/A	N/A	N/A	Case report with subjective results (low level of evidence)
Dryden et al [102]	Case report	Neonatal surgical site infected with MRSA	“Topical Medihoney failed to clear MRSA after four days. <u>Surgihoney</u> eradicated MRSA after four days of topical application, and the wound healed without recourse to antibiotics.”	N/A	N/A	N/A	Case report with subjective results (low level of evidence)
Gray & Ishii [103]	Case series	Wounds requiring debridement	“ <u>Active Leptospermum honey</u> was covered with foam dressing and changed every three days” n=6 After 9 to 20 days of treatment, wounds were completely (or almost completely) debrided, with a 75% average increase in wound bed granulation tissue	N/A	N/A	N/A	Case report with subjective results (low level of evidence)

*REEDA Scale Assesses Redness, Edema, Ecchymosis, Discharge, Approximation of Wound Edges

**VAS Score: Visual Analogue Score

***RTOG score: Radiation Therapy Oncology Group assessment of severity of oral mucositis

Abbreviations: Tx- Treatment

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