# The evidence supporting the use of honey as a wound dressing

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ABSTRACT

Some clinicians are under the impression that there is little or no evidence to support the use of honey as a wound dressing. This impression is reinforced by it being concluded in systematic reviews that the evidence is not of a high standard. But likewise the evidence for modern wound dressing products is of not of a high standard. For evidence-based medicine to be practised in wound care, when deciding which product to use to dress a wound it is necessary to compare the evidence that does exist, rather than be influenced by advertising and other forms of sales promotion. To allow sound decisions to be made, this review has covered the various reports that have been published on the clinical usage of honey. Positive findings on honey in wound care have been reported from 17 randomised controlled trials involving a total of 1965 participants, and 5 clinical trials of other forms involving 97 participants treated with honey. The effectiveness of honey in assisting wound healing has also been demonstrated in 16 trials on a total of 533 wounds on experimental animals. There is also a large amount of evidence in the form of case studies that have been reported. Ten publications have reported on multiple cases, totalling 276 cases. There are also 35 reports of single cases. These various reports provide a large body of evidence to support honey having the beneficial actions of clearing and preventing wound infection, rapidly debriding wounds, suppressing inflammation and thus decreasing oedema, wound exudate and hypertophic scarring, and stimulating the growth of granulation tissue and epithelialisation. It has been shown to give good results on a very wide range of types of wound. Clinicians should look for the clinical evidence that exists to support the use of other wound care products to compare with the evidence that exists for honey.

**Key words:** evidence, honey, infected wounds, surgical wounds, burns, ulcers, abscesses, skin grafts, moist dressings, non-stick, debriding, deodorising, antibacterial, anti-inflammatory, prevention of scarring

There is a rapidly increasing interest in the use of honey as a wound dressing, but it is common to hear clinicians express the opinion that there is no evidence to support the use of honey as a wound dressing. However, the impression upon which this opinion is based is most likely to be a reflection of the scarcity of advertising and other commercial promotion of honey for wound care relative to that of other wound care products. Even where reviews of clinical evidence for the use of honey have been published, a negative impression is often obtained from consulting these, as the conclusions stated are that the evidence is of low quality and/or that there is a need for more evidence.[1-6] But the myriad of advertisements for modern wound dressings possibly blinds people to the fact that only small, poor-quality trials exist to support the use of these products.[7] For example, if the PubMed database is searched for evidence to support the use of nanocrystalline silver dressings, which are very heavily promoted, it can be seen that there is in fact very little clinical evidence that has been published. A recent systematic review of publications on the use of advanced dressings in the treatment of pressure ulcers has found that their generalised use in the treatment of pressure ulcers is not supported by good research evidence.[8] In evidence-based medicine decisions should be made on the basis of the available evidence: where randomised controlled trials of the highest quality have not been conducted, then it is necessary to consider evidence of a lower quality. It is for these reasons that this review has been written, to allow clinicians to see the large amount of evidence that exists for the effectiveness of honey as a wound dressing. By comparing this with the evidence for other wound-care products clinicians can then judge for themselves the relative merits of honey as a treatment option for wounds.

The literature cited was found by searching the PubMed, BIOSIS and ISI Web of Science databases for the term ”honey”. Also, literature not included in the databases was found from citations in papers that were. Excluded were papers where honey was used in a mixture with other therapeutic substances, papers giving brief reports on the use of honey on cases where there was insufficient information on the cases given for the reader to judge if the positive outcomes were the result of honey being more effective than the prior treatment, and papers that were expressions of opinion rather than reports of treatment of wounds with honey. Conference presentations were also excluded.

## CLINICAL EVIDENCE

Many randomised controlled trials have been carried out comparing honey with various other wound treatments. These trials and the results obtained from them are summarised in Table 1. Other clinical trials have been conducted where the form of the trial has been other than a randomised controlled trial. In some of these the results for the group of patients treated with honey were compared retrospectively with those from the control treatment. In others the patients were crossed over to treatment with honey after a period of the treatment normally used for that type of wound. The details of these trials and the results obtained from them are summarised in Table 2. Some of the case studies reported for single cases have also involved a comparative study. In these the patient has had multiple wounds, so honey could be used on one side and the usual treatment on the other. The details of these are summarised in Table 3.

There have also been many non-comparative studies reported on the use of honey as a wound dressing. Since many of these cases were not responding to standard treatment for quite some time before dressing with honey was commenced, these provide evidence that is somewhat like that from a cross-over trial, although these studies involved no reverse change in treatment like would be done in a cross-over trial. Some of these studies have been with multiple cases. The details of these are summarised in Table 4. The details of studies of single cases are summarised in Table 5.

## EVIDENCE FROM ANIMAL EXPERIMENTS

Many studies have been carried on the effectiveness of honey in promoting the healing of standardised wounds created on experimental animals. These experiments have not only allowed there to be much more closely comparable controls in trials, but also have allowed histological examination of the healing wounds to provide additional data besides the usual measurements of decrease in wound size and time to heal. These experiments and the results obtained from them are summarised in Table 6.

## DISCUSSION

The evidence presented in this review amply demonstrates that honey, the oldest wound dressing material known to medicine, can give positive results where the most modern

products are failing. Because people generally are unaware of the historical usage of honey as a wound dressing, or know only of its ancient usage, its clinical usage is presumed to be a new development or something that has been "rediscovered".[9] However, a look at the reference list at the end of this paper will reveal reports of clinical usage published in the 1950s,[10,11] 1960s,[12] 1970s,[13-16] and 1980s[17-23] as well as the rapidly increasing number since it apparent "rediscovery". Clinicians need to decide if modern wound-care products are likely to give better results than this long-established wound dressing material.

The evidence presented here that supports the use of honey in wound care includes evidence from many clinical trials. However, none of the findings from these trials would be considered to be evidence of the very highest level, because even though they may have been randomised controlled trials they have not been double-blind. It is near impossible to conduct a double-blind trial of honey as a wound dressing, because of the difficulty of keeping obscured from the patients that a material as recognisable as honey is being used. Even if honey is applied in the form of a manufactured dressing, its aroma is immediately recognised. For this reason there is always the possibility that positive results achieved with honey will be partly due to a placebo effect.

However, there are trials and case studies in which the honey and the comparative treatment were used simultaneously on the same patient. These demonstrate that positive results achieved with honey are not just a placebo effect. One of these was a prospective randomised controlled trial of honey on split-thickness skin graft donor sites[24] (the last item in Table 1). On patients in this trial who had single donor sites (three groups of 14 patients), half of the donor site was treated with honey and half with the comparative treatment. On patients with two donor sites (three groups of 15 patients) one of the donor sites was treated with honey and one with the comparative treatment. (Honey was compared with three controls, saline-soaked gauze, paraffin gauze and a hydrocolloid.) In that trial, the significantly faster healing rates and lower pain scores achieved with honey compared with saline-soaked gauze and paraffin gauze clearly would have been due to physical effects of the honey and not to psychosomatic effects. Further evidence of a similar nature is seen in the results achieved in the case studies summarised in Table 3, although unlike with the trial with the skin graft donor sites where the wounds being compared were of a standard nature,

there is a possibility the wounds given different treatment for comparison may not have been identical when treatment was started.

The most convincing evidence for the results with honey not being due to a placebo effect comes from the many studies that demonstrated the effectiveness of honey on standard wounds inflicted on experimental animals. Although the participants in these trials may well have been able to detect by smell that honey was being used they would not have had any psychosomatic effects on healing resulting from beliefs that natural products would be more effective, or from hearing via the news media of the effectiveness of honey in wound treatment.

Another factor that many say may be the reason why honey gives good results in individual cases studied is that wound healing improves whenever wounds are receiving more attention, or that the prior treatment was less than ideal. However, in many of the cases summarised in Table 5 the wounds were receiving specialist care before honey was used. They changed to healing from non-healing only when treatment with honey was commenced. In many of these cases the wounds were not responding to best practice with modern dressings, although a recent systematic review of the evidence for the efficacy of modern wound dressings in the treatment of pressure ulcers has concluded that there is no evidence that these are any better than saline-soaked gauze.[8]

Further evidence to support the use of honey as a wound dressing comes from laboratory studies that have clearly demonstrated that honey has bioactivities that would be beneficial in wound care. In work with cultures of leukocytes, honey has been shown to stimulate cytokine production by monocytes.[25,26] The release of cytokines is what initiates the tissue repair process as well as the immune response to infection. Also, simulation by honey of other aspects of the immune response, the proliferation of B- and T-lymphocytes and the activity of phagocytes, has been shown.[27] Additional to this work with cells in culture, it has been demonstrated that honey stimulates the production of antibodies in mice in response to antigens from *Escherichia coli*.[28] These findings suggest that part of the effectiveness of honey in clearing and preventing infection in wounds that is so widely seen in the clinical evidence may be due to enhancement of the body's own immunity as well as being due to the antibacterial activity of honey.

The number of publications on laboratory studies showing that honey has antibacterial activity with a very broad spectrum is very large.[29] But what is often not taken into account is that honeys can vary as much as 100-fold in the potency of their

antibacterial activity.[30] More recent publications have reported on the sensitivity of various species of bacteria to honey with antibacterial potency near the median level found in surveys of large numbers of samples. (This level is a little below that of the various honey wound-care products now on sale manufactured from *Leptospermum* honey, but there are other wound-care products manufactured from honeys not selected to have high levels of antibacterial activity.[31]) Laboratory studies with *Leptospermum* (manuka) honey with antibacterial potency near the median level have shown the MIC (minimum inhibitory concentration, *i.e.* the concentration down to which honey could be diluted by wound exudate and still prevent bacterial growth) to be 2–3% for *Staphylococcus aureus*,[32] 3.3–4% for coagulase-negative staphylococci,[33] 5.5–9% for pseudomonads,[34,35] 2.7–3% for MRSA,[36] and 3.8–5% for VRE.[36]. (The effectiveness of honey in clinical usage in clearing infection with MRSA[37-41] and VRE[40] has been reported.) The slow clearance of infection, or failure to clear infection, in some of the cases reported may well reflect the use of honey with a low antibacterial potency. For example, this may have been the case in the randomised controlled trial where honey was found to be less effective than early tangential excision followed by autologous skin grafting in controlling infection in the treatment of burns.[42] The same author, publishing results comparing the MIC values for various types of honey available locally, reported that the MIC for the most potent honey against *Staphylococcus aureus* was 20–25%,[43] which means that the honey had only about one tenth of the antibacterial potency of the *Leptospermum* honey used in wound-care products now on sale.

Another reason for variability in results may have been that the honey in some cases was not being kept in place on the wound. The difficulty of achieving this has been commented on.[44,45] If the honey is flushed out of the dressing by wound exudate then its various bioactivities cannot be having any effect on the wound. A case which may be an example of this is where infection in a leg ulcer was reported to recur when compression was commenced.[46] Here it was noted that there was a problem with dressings adhering, which is a clear indication that honey has been flushed out of the dressing by wound exudate.[47] A similar occurrence was reported where honey-impregnated tulle dressings were being used.[48] These have very little absorbency so honey is easily flushed from them. It was noted in this case that the dressings became saturated with exudate within one hour. In another case where poor progress was occurring with honey it was found that much better progress with healing occurred when more frequent changes of the dressings were made.[49]

It has been noted that if sufficient honey is kept in place, by applying it by way of impregnated dressings and changing these frequently enough, then its anti-inflammatory activity will reduce the amount of exudate and thus remove the need for frequent dressing changes.[47] There is a very large amount of evidence for honey having significant anti-inflammatory activity. As well as the evidence that has come from the many clinical observations summarised in this review there is evidence from histological observation of biopsy samples taken in a clinical trial of honey on burns,[50] and from biochemical assays of indicators of inflammation in other clinical trials on burns.[51,52] One of these biochemical studies was in the form of a randomised controlled trial with 60 patients, comparing honey with silver sulfadiazine, and it was demonstrated that honey decreased oxidative stress by mopping up the free radicals arising from burns.[52] There is also histological evidence for the anti-inflammatory activity of honey from some of the studies on experimental animals summarised in Table 6. In some of the experimentally induced burns there was no infection evident, yet honey still brought about a decrease in inflammation. This indicates that the anti-inflammatory activity of honey is a direct action and not a secondary consequence of removal of infection through its antibacterial activity. This is confirmed also by honey giving a positive result in the standard guinea-pig wrist stiffness test for anti-inflammatory activity.[53] That honey has a direct anti-inflammatory activity is also indicated by it being found that honey was as effective as prednisolone in a trial on induced colitis in rats,[54] and by it being found to give a highly significant ($p<0.001$) reduction in peritoneal adhesions following surgery on the caecum and ileum in another trial on rats.[55] A laboratory study also demonstrated a direct anti-inflammatory activity in honey, as honey was shown to significantly ($p<0.001$) decrease the amount of reactive oxygen intermediates released from monocytes in culture that had been stimulated with *Escherichia coli* lipopolysachharide.

## CONCLUSIONS

There is a large body of evidence to support the use of honey as a wound dressing for a wide range of types of wound. Its antibacterial activity rapidly clears infection and protects wounds from becoming infected, thus it provides a moist healing environment without the risk of bacterial growth occurring. It. also rapidly debrides wounds and removes malodour. Its anti-inflammatory activity reduces oedema and exudate, and prevents or minimises hypertrophic scarring. It also stimulates the growth of granulation

tissue and epithelial tissue so that healing is hastened. Furthermore, it creates a non-adherent interface between the wound and the dressing so that dressings may be easily removed without pain or damage to newly re-grown tissue

The barrier to using honey that has existed for many clinicians who have been constrained to using only licensed products has been removed now that honey is available in the form of various sterile products licensed for use in wound care. To practise evidence-based medicine, clinicians involved in wound care thus should check what evidence exists for other wound dressing products they may be considering using, and weigh this up against the evidence that exists to support the use of honey.

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**Table 1.** Randomised controlled trials that have been carried out on honey as a wound dressing

| Type of wound | Control treatment | No. in trial | Results<br>Honey *cf* control | Statistics | Other findings | Ref. no. |
|---|---|---|---|---|---|---|
| Superficial burns | Silver sulfadiazine | 104 | Proportion of wounds becoming sterile within 7 days: 91% *cf* 7% | $p < 0.001$ | Honey gave better relief of pain, less irritation of the wound, less exudation, a lower incidence of hypertrophic scar and post-burn contracture, acceleration of epithelialisation, a chemical debridement effect and removal of offensive smell. | 56 |
| | | | Mean time that healthy granulation tissue first observed: means 7.4 *cf* 13.4 days | Not given | | |
| | | | Proportion of wounds healing within 15 days: 87% *cf* 10% | Not given | | |
| | | | Mean healing time: 9.0 days *cf* 24.6 days | $p < 0.001$ | | |
| Fresh partial-thickness burns | OpSite® | 92 | Mean healing time: 10.8 days *cf* 15.3 days | $p < 0.001$ | Honey gave debridement and deodorisation, a soothing effect, and ease of removal of dressings with little pain. | 57 |
| | | | Cases infected after 8 days: 8 *cf* 17 | $p < 0.001$ | | |
| Fresh partial-thickness burns | Amniotic membrane | 64 | Mean healing time: 9.4 days *cf* 17.5 days | $p < 0.001$ | | 58 |
| | | | Proportion of patients with residual scars: 8% *cf* 16.6% | $p < 0.001$ | | |
| | | | Number of cases infected after 7 days: 4 *cf* 11 | $p < 0.001$ | | |
| Partial-thickness | Conventional (90 with | 900 | Mean healing time: 9 days *cf* 13.5 days | Not given | | 59 |

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| | | | Proportion of wounds infected: 5.5% *cf* 12% | Not given | | |
| | | | Proportion of cases resulting in scars: 6.2% *cf* 20% | Not given | | |
| Fresh partial-thickness burns | Boiled potato peel | 82 | Mean healing time: 10.4 days *cf* 16.2 days | $p < 0.001$ | | 60 |
| | | | Proportion of those with positive swab cultures becoming sterile within 7 days: 100% *cf* 0% | $p < 0.001$ | | |
| Superficial burns | Silver sulfadiazine | 50 | Proportion showing epithelialisation by 7th day: 84% *cf* 72%; by 21st day: 100% *cf* 84% | $p < 0.001$ | Honey gave early subsidence of acute inflammatory changes, better control of infection and quicker wound healing. There was eschar in 60% of the cases treated with silver sulfadiazine, none with honey.<br><br>With silver sulfadiazine, 4 of the superficial burns converted to deep burns requiring skin grafting, none with honey. | 50 |
| | | | Proportion showing evidence of reparative activity (on histological examination of biopsy samples):<br>on Day7: 80% *cf* 52%<br>on Day21: 100% *cf* 84% | $p < 0.005$ | | |
| Moderate burns, half of the total burn area being full-thickness | Tangential excision 3–6 days post-burn, then skin grafting | 50 | Mean percentage blood volume replaced: 21% *cf* 35% | $p<0.01$ | Skin grafting was required on only 11 of the 25 treated with honey cf all of the tangentially excised group. | 42 |
| | | | Mean period antibiotics needed: 32 days *cf* 16 days | $p<0.001$ | | |
| | | | Proportion of swab cultures positive: 34% *cf* 10% | $p<0.05$ | | |

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| | | | Mean length of hospital stay: 46 days *cf* 21 days | p<0.001 | | |
| | | | Proportion with excellent or good wound appearance after 3 months: 55% *cf* 92% | p<0.01 | | |
| Moderate burns, 1/6$^{th}$ total burn area being full-thickness | Silver sulfadiazine | 100 | Mean healing time:15.4 days *cf* 17.2 days | p<0.001 | With honey, 4 required grafting *cf* 11 with silver sulfadiazine, and there was one case of contractures *cf* 5 with silver sulfadiazine. | 51 |
| | | | Number of swab cultures positive after 7 days: 4 (from 44 at start) *cf* 42 (from 42 at start) | p<0.001 | | |
| | | | Lipid peroxidation (a measure of inflammation):<br>4.3 *cf* 5.3 on day 7<br>3.8 *cf* 4.4 on day 14<br>3.2 *cf* 4.1 on day 21 | <br><br>p<0.01<br>p<0.01<br>p<0.005 | | |
| | | | Mean length of hospital stay: 22.0 days *cf* 32.3 days | p<0.005 | | |
| Paediatric burns | Silver sulfadiazine | 64 | Mean healing time: 11.0 days *cf* 16.1 days | p<0.001 | There were 2 cases of contractures with honey *cf* 5 with silver sulfadiazine.<br><br>Honey gave a decrease in oedema and exudate, and no eschar. | 61 |
| | | | Mean time to form healthy granulation: 6.7 days *cf* 12.8 days | Not given | | |
| | | | Number of swab cultures positive after 7 days: 24 (from 25 at start) *cf* 21 (from 24 at start) | p<0.001 | | |

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| Superficial burns | Silver sulfadiazine | 50 | 100% of cases healed in 10 days *cf* 70% in 15 days | Not given | Honey gave early subsidence of acute inflammation, and better control of infection. Honey reduced the period of hospital stay and expenses by 30%. | 62 |
| Severe post-operative wound infections following abdominal surgey | Washing wounds with 70% ethanol then applying povidone-iodine | 50 | Mean time to get negative swab cultures: 6 days *cf* 14.8 days | p<0.05 | With honey there was mild wound dehiscence in 4 cases, with no need for re-suturing: in the control group there was wound dehiscence in 12 cases, 6 requiring re-suturing under general anaesthetic. | 63 |
| | | | Mean number of days antibiotics were required: 6.88 *cf* 15.4 | p<0.05 | | |
| | | | Mean healing time:10.73 days *cf* 22.04 days | p<0.05 | | |
| | | | Mean size of post-operative scars: 3.62 mm *cf* 8.62 mm | p<0.05 | | |
| | | | Mean period of hospitalisation required: 9.36 days *cf* 19.91 days | p<0.05 | | |
| Surgically drained pyomyositis abscesses | EUSOL-soaked gauze | 32 (43 wounds) | Proportion on Day 7 with clean wounds: 100% *cf* 65.5% | p=0.007 | | 64 |
| | | | Proportion on Day 7 with granulating wounds: 100% *cf* 50% | p<0.001 | | |
| | | | Proportion on Day 7 with epithelialising wounds: 86.9% *cf* 35% | p=0.001 | | |
| | | | Proportion on Day 21 with complete epithelialisation: 86.9% *cf* 55.0% | p=0.047 | | |

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| | | | Mean length of hospital stay: 16.08 days *cf* 18.61 days (medians 14 days *cf* 22 days) | p = 0.019 | | |
| Chronic leg ulcers (mean duration of 56.5 months) | Phenytoin paste | 50 | Mean reduction in ulcer size: 27.0% *cf* 35.5% | Not significant | | 65 |
| | | | Mean pain score (on a scale of 1 to 10): 1.8 *cf* 3.6 | Not significant | | |
| Pressure ulcers on orthopaedic patients | Saline-soaked gauze | 40 | Proportion healed in 10 days:100% *cf* 70% | p<0.05 | | 66 |
| | | | Mean healing time for ulcers that healed in 10 days: 8.2 days *cf* 9.9 days | p<0.001 | | |
| Exit sites of central venous catheters | Povidone-iodine | 49 | Incidences of blood-stream infections: 12 *cf* 19 episodes per 1000 catheter-days | Not significant | | 67 |
| Exit sites of tunnelled, cuffed central venous catheters | Mupirocin | 101 | Incidences of catheter-associated bacteraemias: 0.97 *cf* 0.85 episodes per 1000 catheter-days | Not significant | | 68 |
| Split-thickness | Saline-soaked | 87 (174 | Mean healing time: 9.1 days *cf* 13.2 days with saline | p<0.05 | Leakage occurred on 22 dressing changes with the hydrocolloid: no fluid accumulated | 24 |

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| | | | Mean healing time: 9.4 days *cf* 12.4 days with paraffin, | p<0.001 | | |
| | | | Mean healing time: 9.6 *cf* 9.4 days with hydrocolloid | Not significant | | |
| | | | Mean pain scores, honey *cf* saline:<br>Day 1: 4.8 *cf* 7.2<br>Day 2: 2.9 *cf* 4.2<br>Day 3: 2 *cf* 3.1 | p<0.05 | | |
| | | | Mean pain scores, honey *cf* paraffin:<br>Day 1: 4.6 *cf* 6.7<br>Day 2: 3.2 *cf* 3.9<br>Day 3: 1.8 *cf* 2.8 | p<0.05 | | |
| | | | Mean pain scores, honey *cf* hydrocolloid:<br>Day 1: 4.4 *cf* 4<br>Day 2: 2.9 *cf* 2.6<br>Day 3: 1.8 *cf* 1.6 | Not significant | | |

**Table 2.** Other types of clinical trials that have been carried out on honey as a wound dressing

| Type of wound | Form of trial | No. in trial | Results | Statistics | Other findings | Ref. no. |
|---|---|---|---|---|---|---|
| Disrupted abdominal wounds from Caesarean section | Results from 15 patients treated with honey application and wound approximation by micropore tape were compared retrospectively with 19 similar cases who had their dehisced wounds cleaned with hydrogen peroxide and Dakin solution and packed with saline-soaked gauze prior to resuturing under general anaesthesia. | 15 *cf* 19 | Period of hospitalisation required: 2 - 7 days (mean 4.5) with honey *cf* 9 - 18 days (mean 11.5) with control | Not given | With honey, 11 healed within 7 days, the other 4 within 2 weeks.<br><br>With honey, slough and necrotic tissue were replaced by granulation and advancing epithelialisation within 2 days, wounds were made odourless and sterile within 1 week, and no re-suturing was required. | 69 |

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| Fournier's gangrene (necrotising fasciitis on the scrotum) | 20 consecutive cases of Fournier's gangrene managed conservatively with honey plus systemic antibiotics (oral amoxicillin/clavulanic acid and metronidazole), were compared with 21 cases managed in the same period by another consultant, using surgical debridement. | 41 | With honey, within 1 week malodour, oedema and discharge had subsided, all necrotic tissues had separated, rapid epithelialisation was occurring.<br><br>Within 1 week with honey all swabs were negative: there was no need to change from the routine antibiotics to ones to which the bacteria were found to be sensitive, as was done with the surgically debrided cases. | Not given | A second operation for secondary suturing was needed for all cases surgically debrided, with plastic reconstruction needed for two of these With honey no surgery was needed, and most healed with very little or no scars.<br><br>3 deaths occurred in the surgically treated group, none in the honey-treated group. | 70 |

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| Large infected surgical wounds on infants | Treatment was crossed over to honey dressings after wounds had failed to heal with treatment of at least 14 days using intravenous antibiotics (vancomycin plus cefotaxime, subsequently changed according to bacterial sensitivity), fusidic acid ointment, and wound cleaning with aqueous 0.05% chlorhexidine solution. | 9 | After starting dressing with honey a marked clinical improvement was seen in all cases after 5 days, and all wounds were closed, clean and sterile after 21 days. | Not given | Six of the patients had systemic antibiotic treatment discontinued when treatment with honey started. | 71 |
| Venous leg ulcers, non-healing after at least 12 weeks of compression | Treatment was crossed over to honey dressings used under compression from standard treatment for venous ulcers | 40 | Pain decreased from an average McGill score of 1.6 to 1.08 in 12 weeks. | $p<0.02$ | In the 12 week study period, complete healing occurred in 7 cases, with a significant reduction in ulcer size for the rest (mean reduction 32%).<br><br>There was a high level of patient satisfaction with honey dressings. | 72 |
| | | | Linear decrease in pain with time | $p<0.001$ | | |
| | | | Decrease in pain correlated with reduction in wound size | $p<0.05$ | | |
| | | | Decrease in pain correlated with healing rate | $p<0.05$ | | |

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| | | | The 26 malodorous wounds decreased in odour mean score (on a scale of 1 to 3) in two weeks from 1.58 to 0.69. | p<0.001 | | |
| Burns | A review of all the burns cases in a hospital over the preceding 5 years | 156 | 90.5% of the cases were treated with silver sulfadiazine, 8.5% with honey: the outcomes were similar. | Not given | | 73 |

**Table 3.** Case studies on the use of honey as a wound dressing where a comparison with other treatments was conducted on multiple wounds within single cases

| Type of wounds | Status of wounds before using honey | Comparison | Results | Ref. no. |
|---|---|---|---|---|
| Multiple chronic leg ulcers, on both legs | 20 year history of multiple ulcers on the legs and feet resulting from chronic venous hypertension with secondary lymphoedema | The ulcers on one leg were dressed with honey, those on the other leg with *Aquacel*, | At the time of discharge 10 days later the ulcers dressed with honey had a cleaner wound bed, signs of infection had cleared and the green exudate had ceased, whereas with the *Aquacell* there was copious leakage of green fluid. | 44 |
| Multiple chronic leg ulcers, on both legs | Ulcers had been there for >5 years. They had features of stasis dermatitis. There was no arterial disease. | The ulcers on one leg were dressed with honey, those on the other leg were debrided with fibrinolysin (*Elase R*) then dressed with *Sorbosan R.* | Initially healing was much more rapid with honey. After I month both legs were healing well. | 74 |
| Broken-down wound from abdominal surgery | Areas of dehiscence at each end of the wound, of similar appearance | The dehiscence at one end was dressed with honey, on the other end with *Debrisan.* | Healing was complete in 24 days with honey, 32 days with *Debrisan.* | 75 |
| Third-degree burns to both arms | | Burns on one arm were dressed with honey, the other arm with EUSOL. | Granulation was “much nicer” with honey, reducing time to skin grafting. | 76 |

**Table 4.** Reports on the use of honey as a wound dressing: studies with multiple cases

| Type of wound | Status of wounds before using honey | No. of cases | Outcome from treatment with honey | Ref. no. |
|---|---|---|---|---|
| 16 acute traumatic wounds, 23 complicated surgical wounds and 21 chronic non-responding wounds | The chronic non-responding wounds had all been subjected to other regimens before honey dressings were used. | 60 | One patient withdrew from the trial because the honey was causing pain. Two wounds did not change. The rest healed in a mean time of 3 weeks (range 1–28 weeks). One patient was treated with silver sulfadiazine and antibiotics instead of honey for one week because of an infection with *Staphylococcus aureus*.<br><br>Advanced epithelialisation and a decrease in exudate, oedema and wound odour were observed. | 77 |
| Recalcitrant wounds and ulcers of varied aetiology, such as Fournier's gangrene, burns, cancrum oris, diabetic ulcers, traumatic ulcers, decubitus ulcers, sickle cell ulcers and tropical ulcers | 47 of the patients had been treated for 1–24 months with conventional treatment (such as Eusol toilet and dressings of Acriflavine, Sofra-Tulle, or Cicatrin, or systemic and topical antibiotics) with no signs of healing, or the wounds were increasing in size. | 59 | The 51 wounds with bacteria present became sterile within 1 week and the others remained sterile. In one of the cases, a Buruli ulcer, treatment with honey was discontinued after 2 weeks because the ulcer was rapidly increasing in size. The 58 other cases "showed remarkable improvement". Sloughs, necrotic and gangrenous tissue separated so that they could be lifted off painlessly, and were rapidly replaced with granulation tissue and advancing epithelialisation. Surrounding oedema subsided, weeping ulcers dehydrated, and foul-smelling wounds were rendered odourless within 1 week. Burn wounds treated early healed quickly, not becoming colonised by bacteria. | 17 |

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| Wounds from radical vulvectomy with lymphadectomy | Wounds had broken down | 12 | Wounds became free from bacteria in 3–6 days. Complete healing was achieved in 3–8 weeks. Clean healthy granulation was achieved, requiring minimal surgical debridement. Skin grafting was unnecessary. | 13 |
| Wounds of mixed aetiology: surgical, accidental, infective, trophic, and burns. The average size of the wounds was 57 $cm^2$. | Half of the cases had been treated with "the usual topical measures" (an antiseptic) which had failed. One third of the wounds were purulent, the rest were red with a whitish coat. | 40 | Honey delimited the boundaries of the wounds and cleansed the wounds rapidly to allow skin grafting. Of the 33 patients treated only with honey dressings, 29 were healed successfully, with good quality healing, in an average time of 5–6 weeks. Two of the four who did not heal were suffering from immunodepression, one was withdrawn from treatment with honey because of a painful reaction to the honey, and one burn remained stationary after a good initial response. | 78 |
| Septic wounds, chronic ulcers, burns, pyogenic abscesses | 6 patients were diabetic, 5 with a septic foot and 1 with an abscess. | 11 | Healing time was 7–15 days apart from one diabetic who took 56 days and one, who was ill, in which there was no improvement. Clean healthy granulation was achieved which allowed skin grafting in 14 days (30 for one diabetic), with prompt graft taking. | 18 |
| A variety of wounds, including ulcers of various aetiologies, pressure ulcers, burns, skin tears and traumatic wounds | | 20 | In 80% of cases the wound bed improved (it was cleaner, with less slough and malodour, with movement along the healing continuum). In 20% of cases there was no improvement.<br>65% found honey dressings easy to apply, 75% found them easy to remove, 85% found the dressings stayed in place, 65% found them comfortable. | 79 |

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| Surgical wounds, mostly dehiscent or infected | Pediatric patients receiving chemotherapy, making wounds hard to heal because of profound immunosuppression | 16 | Wounds became sterile within 1–4 days. The average healing time was 25 days. Four patients undergoing prolonged immunosuppression healed in an average time of 27 days. Healing occurred without complication apart from one small keloid. | 41 |
| Venous leg ulcers that had undergone split-skin grafting | Ulcers were of 12 months or more duration, and were not responding to normal treatment such as compression. They were of borderline suitability for grafts. Five had conditions characteristic of insufficient tissue perfusion. | 6 | The mean healing time was 22 days. There were no post-operative infections or other complications. No re-grafting or revision of grafts was needed. There was no recurrence of the ulcers on follow-up (average of 19 months later). | 80 |
| Fournier's gangrene | Honey was used following aggressive surgical debridement and triple antibiotic therapy. | 38 | Honey gave rapid healing changes in an average period of 10 days. | 81 |
| Gangrene in the genitals and perineum | | 14 | The mean time for the debriding action of the honey to cleanse the wounds was 5.2 days, for granulation to be seen was 9.4 days, and for complete healing was 28.7 days. | 82 |

**Table 5.** Reports on the use of honey as a wound dressing: studies of single cases

| Type of wound | Status of wound before using honey | Outcome from treatment with honey | Ref. no. |
|---|---|---|---|
| Bilateral leg ulcers of mixed aetiology | 88 year old patient with marked lower leg oedema and peri-wound maceration of skin | Within 4 weeks there was a dramatic improvement in the maceration, and the ulcer beds were much healthier.* | 79 |
| Venous ulcer | Five-year history of intermittent infected venous ulcers. The ulcer was inflamed, with necrosis, oedema and exudate. There had been no improvement with 4 weeks of treatment with hydrogel. | The exudate was decreased, so a compression stocking could then be used. The necrosis was debrided in 10 days. Complete healing was achieved in 28 weeks. The skin integrity had been maintained 18 months later. | 49 |
| Extensive leg ulcers | 75 year old patient. Ulcers had increased in size over the past 4 years without signs of permanent healing despite ongoing attention. | The foul smell disappeared. Granulation and islands of epithelialisation were seen within 3 weeks.* | 77 |
| Leg ulcers | 85 year old patient with a history of numerous small sloughy leg ulcers not reducing in size despite 3-layer compression bandaging. There were calcium deposits subcutaneously and in the ulcer beds with associated chronic inflammation. The deposits had been removed by sharp debridement every 3 months. | After 2 weeks, atraumatic removal of the calcium deposits was occurring. This continued with further use of honey, with reduction in wound size, slough and inflammation.* | 83 |

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| Hydroxyurea-induced leg ulcer on an immunosuppressed patient | No change in the ulcer had occurred over three months of treatment with a range of topical therapies. It was sloughy, and MRSA was present. | MRSA was cleared in 14 days. Healing was complete within 21 days. Treatment with hydroxyurea and cyclosporin continued through this period. | 38 |
| Multiple bilateral venous ulcers | 25 year history of venous ulceration with recurrent infections. Ulcers were deep, highly exuding, sloughy and malodorous. There was widespread varicose eczema in the region of the ulcers | The malodour was removed within 1 day. After 10 days all signs of eczema had gone. But when compression bandaging was commenced there was within two days another outbreak of bacterial infection.* | 84 |
| Mixed arterial/venous ulcers on calf and median malleolus | The ulcers, on an 80 year old patient, had occasionally shown signs of improvement in the past but they had never healed. Sharp debridement and removal of calcification was carried out before starting treatment with honey. | After 4 weeks there was a 23.6% reduction in area of the large ulcer on the calf, and full epithelialisation of the small ulcer on the malleolus.* | 48 |

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| Extensive venous ulcers | The ulcers, on an 80 year old patient, were of $2^{1}/_{2}$ years duration, with compression being used. Recurrent infections had occurred, soon after each course of antibiotics had finished, that silver dressings did not prevent. The ulcers on one leg had got cellulitic, very wet, painful, and covered with soft necrotic tissue. They were debrided before starting treatment with honey. The ulcer on the other leg was clean but static and over-granulating | Over the next 6 weeks no further infection occurred. (A low dose of Flucoxacillin was used for the first 3 weeks.) Then, coinciding with compression being started, infection recurred in the wet ulcers.* The over-granulating static ulcer on the other leg was healed, level with the skin, after 3 weeks treatment with honey. | 48 |
| Venous ulcer | Painful, sloughy, highly exuding, malodorous. Initial debridement was done with maggots. | Complete deodorisation was achieved within 24 hours.* | 48 |
| Diabetic foot ulcers, 8 x 5 cm and 3 x 3 cm | 79 year old patient. The ulcers remained unhealed after 14 months treatment with an orthotic device, antibiotics, topical therapies by a wound care expert and four lots of surgery. MRSA, VRE and Pseudomonas were present in wound tissue. | The ulcers were granulating within 2 weeks, and healed within 6 and 12 months. There had been no recurrence 2 years later. | 40 |

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| Pressure ulcer on ankle, 4 x 2.5 cm, down to tendon | 83 year old patient. There was no commencement of healing when treated with *SoloSite* and hydrocolloids for 3 weeks. The ulcer was highly exudative, with a strong malodour, and painful. | After 13 days there was much less malodour and less slough. The ulcer was healed in 11 weeks. | 85 |
| Sacral pressure ulcer | 84 year old patient. The 5.5 x 5 cm ulcer had an area of necrosis 2 x 1 cm. The surrounding area was red and painful. There had been no improvement after 4 weeks of debriding treatment with *SoloSite* then a hydrocolloid then *Solugel.* | The ulcer was debrided after 2 weeks, and was healed by 8 weeks, almost without scarring. | 85 |
| Sacral pressure ulcer | The ulcer was15–20 cm in size, exposing bone. | The ulcer became closed, without surgery, after 21 days, and completely re-epithelialised in 10 weeks | 19 |
| Pressure ulcers | There was one 10 x 5 cm ulcer, on the buttocks, with a deep centre, and two smaller ulcers. There was some discharge from the ulcers. | Granulation was seen after 7 days. The smaller ulcers completely healed in 4 weeks, the larger one in 8 weeks. | 12 |
| Pressure ulcers | The ulcer on one hip was deep. The large ulcer on the other hip and the linking ulcers in the sacral region had black slough. All ulcers were discharging and becoming offensive. The patient had disseminated sclerosis and was weak and ill. | Within 6 weeks all slough had separated, there was no purulent discharge or malodour, and healthy granulation was seen at the edges of the ulcers. | 12 |

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| Broken area of skin on calf | The 6 x 2 cm wound, on an obese patient, was colonised, sloughy, with minimal exudate, and with a macerated peri-wound area | Healed in 4 weeks | 86 |
| Unhealed biopsy wound in groin | Immunocompromised patient, with lymphoma, undergoing chemotherapy: wound at risk of becoming infected | The wound was completely healed in 4 weeks. | 39 |
| Non-healing split-thickness skin graft donor site | The donor site was not healing 9 months after a skin graft had been harvested. There was some over-granulation, and moderate exudate. | Healing was evident after 2 weeks, with exudate and pain reduced. Complete healing was achieved in 4 weeks. | 87 |
| Abscess following orthopaedic surgery | The wound was unhealed 9 months after the surgery, despite courses of antibiotics and many types of dressings being tried. The abscess was recalcitrant, with a small amount of slough. | After 4 weeks the surrounding redness was settling and there was some debridement. After a further 20 weeks the wound was the size of a pin-head, with no redness. | 87 |
| Lymphorrhoea in the groin resulting from a voluminous lymphocele following surgery on the iliac artery | The patient refused the further surgery that was advised. | Placing honey in the inguinal cavity daily reduced the liquid discharge to a minor amount within a few days, with a notable reduction in the size of the cavity. No discharge was occurring after 11 days.* | 88 |
| Cavity wounds from broken-down haematomas, also infected split-thickness skin graft donor site | There were two large wounds on the lower leg of an obese patient with chronic lymphoedema, on which skin grafting had failed. MRSA was present. | The MRSA was eliminated, and complete healing was achieved in 8 weeks without further grafting, the donor sites healing first. Elimination of the offensive wound odour was also noted. | 37 |

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| Broken-down wound from amputation of toe | Amputation was because of gangrene in the big toe of an 83 year old patient. No improvement seen in the wound after 6 weeks of EUSOL and paraffin dressings. A hard crust, 2.5 x 4 cm, covered the wound. | The crust started to separate and granulation was seen after 7 days. By 2 weeks a lot of the crust had been removed and improvement in granulation had occurred.* | 12 |
| Recalcitrant wound in the axilla, from surgical treatment of hidradenitis suppurativa | The wound had failed to heal for 36 months despite trying a wide range of therapeutic dressings and systemic and topical antimicrobial agents and three attempts at treatment by surgery. | There was removal of bacteria and a noticeable improvement in the wound in one week, and complete healing in one month. | 89 |
| Grossly infected wound from Caesarian section | There was pus pouring from an open 12 cm wound. Infection had not responded to several courses of antibiotics. | The wound was clean and granulating after 7 days, and completely healed in 2 weeks. | 19 |
| Broken-down surgical wound after breast reduction | Wound break-down started 6 weeks after surgery and deteriorated over the following 2 weeks. There was some granulation and some small areas of necrosis. The exudate was distressing. | After 2 weeks the necrosis and slough had cleared, the malodour had gone, there was healthy granulation, and the exudate was manageable. There was complete healing in 13 weeks. | 90 |
| Non-healing surgical wound | The wound was not healing after 4 weeks of daily dressing with calcium alginate. | Complete healing was achieved in 6 weeks. | 77 |
| Non-healing traumatic wound | The 4 x 4 cm wound, on the lower arm, was clean but had no signs of granulation (no capillary buds were present). | Granulation and epithelialisation were visible within 1 week, and complete healing was achieved in 6 weeks. | 37 |

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| Extensive infected skin lesions resulting from meningococcal septicaemia | These lesions had a heavy growth of *Pseudomonas, Staphylococcus aureus* and *Enterococcus,* and had remained non-healing for 8 months despite a wide range of treatments being tried. Additional lesions had resulted from graft donor sites becoming infected. | Within a few days, signs of epithelialisation were seen, skin grafting became possible as the pathogens were cleared, and complete healing was achieved within 10 weeks. | 91 |
| Ulcer between breasts from radiation necrosis | The wound had initially appeared 13 months after mastectomy and radiotherapy and had then healed 13 months after that, then had re-ulcerated a few months later and enlarged to 4 x 3 cm with necrotic bone and costal cartilage at its base. The wound was painful, with thick, offensive pus exuding. The peri-wound area was sore and excoriated. | Complete healing occurred in 10 months. | 90 |
| Spontaneously erupted abscess (of unknown cause) on cheek | After surgical drainage and antibiotics the lump arose again. | After 3 lots of honey dressing of less than 24 hours each, on unbroken skin, the lump had reduced in size.* | 48 |
| Burn on upper arm | 88 year old patient. The burn had dried out, but after $1^{1}/_{2}$ weeks of treatment with hydrogel the eschar was still dry, so the wound was tight and painful | The eschar was softened within 1 week, so the wound became less painful. Debriding was occurring within 3 weeks and was complete within 10 weeks, with extensive epithelialisation.* | 79 |

* Details of subsequent progress were not reported

**Table 6.** Animal experiments carried out on the use of honey as a wound dressing

| Type of wound | Control treatment | Species of animal | No. in trial | Results | Statistics | Other findings | Ref. no. |
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| Deep dermal burns (6.7 x 6.7 cm) made with a 170°C brass block | Silver sulfadiazine: also sugar | Yorkshire pigs | 3 (36 wounds) | Complete epithelialisation achieved within 21 days with both honey and sugar, *cf* 28 - 35 days with silver sulfadiazine | Not given | | 92 |
| | | | | Histological examination revealed less inflammation in wounds treated with honey than in those treated with sugar and with silver sulfadiazine, and a more advanced stage of healing. | Not given | | |
| Dermal burns (1.3 x 3 cm) made with a 170°C brass block | Silver sulfadiazine: also untreated (other than a daily saline rinse) | Pigs | 2 (27 wounds) | First granulation was observed (histologically) after 5 days with honey, 10 days with the controls. | Not given | | 93 |
| | | | | Less oedema and inflammation was observed (histologically) with honey than with the controls. | Not given | | |
| Third-degree dermal burns (made with steam), 8.5 $cm^{2,}$, inoculated with | Silver sulfadiazine : also acetate mafenid | Piglets | 60 | After 30 days, the mean reduction in wound area was 62% with honey *cf* 29% with silver sulfadiazine and 22% with acetate mafenid. | p = 0.000 for honey *cf* the other treatments | | 94 |

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| | | | | After 10 days, the proportion of wounds with good granulation covering the major part, suitable for grafting, was 90% with honey *cf* 44% with silver sulfadiazine and 35% with acetate mafenid. | $p < 0.003$ for honey *cf* the other treatments | | |
| | | | | The proportion of biopsy samples, taken after 10 days, giving positive microbial cultures was 20% with honey *cf* 100% with silver sulfadiazine and 95% with acetate mafenid. | $p = 0.000$ for honey *cf* the other treatments | | |
| Superficial burns, created on the skin with a red-hot pin (15 $mm^2$) | No treatment: also, solution of sugars as in honey | Rats | 60 (120 wounds) | The mean time to complete healing was 20.4 days with honey *cf* 30.3 days with no treatment. | $p < 0.01$ | Healing was seen histologically to be more active and advanced with honey, and honey was also clearly seen to give attenuation of inflammation and exudation, and less serious necrosis. | 16 |
| | | | | The mean time to complete healing was 20.4 days with honey *cf* 28.5 days with sugar. | $p < 0.01$ | | |

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| Wounds created by cutting away 2 x 4 cm pieces of skin on the back | Nitrofurazone ; also sterilised petrolatum | Buffalo calves | 6 (24 wounds) | Granulation, scar formation, and complete healing occurred faster with honey, with more proliferation of fibroblasts and angioblasts. | Not given | Attenuation of inflammation by honey was also seen (by histological observation). | 95 |
| Wounds created by cutting away 2 x 4 cm pieces of skin on the back, infected by subcutaneous injection of *Staphylococcus aureus* two days prior to wounding | Ampicillin ointment: also saline | Buffalo calves | 9 (90 wounds) | Honey gave the fastest rate of healing compared with the other treatments, also (observed histologically) the most rapid fibroblastic and angioblastic activity in the wounds and the fastest epithelialisation. | Not given | Attenuation of inflammation by honey was also seen (by histological observation). | 96 |
| Wounds created by excising skin (1 x 1 cm) | Saline | Mice | 24 | Histological examination showed that the thickness of granulation tissue was greater with honey. | $p<0.001$ | | 20 |
| | | | | Histological examination showed that the distance of epithelialisation from the edge of the wound was greater with honey. | $p<0.001$ | | |

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| Wounds created by excising skin (1 x 1 cm) | Saline | Rats | 15 (30 wounds) | The area of the wound ($mm^2$) with the honey treatment *cf* the area with saline was:<br>after 4 days: 47.5 *cf* 71.4<br>after 8 days: 33.3 *cf* 52.2<br>after 12 days: 9.1 *cf* 40.5 | p<0.01 | With honey, epithelialisation was more rapid and there was less oedema (both assessed histologically). | 97 |
| | | | | The thickness of granulation tissue (mm, assessed histologically) with the honey treatment *cf* the thickness with saline was:<br>after 4 days: 0.52 *cf* 0.389<br>after 8 days: 1.17 *cf* 0.53<br>after 12 days: 1.917 *cf* 0.995 | p<0.01 | | |
| Wounds created by excising skin (2 x 2 cm) | Saline | Rats | 20 | The mean contraction in size of the wounds was 80% with honey, 55% with saline. | p = 0.001 | | 98 |
| Wounds created by excising skin (2 x 2 cm) | Saline | Rats | 20 | After 10 days the mean area of the wounds was 1.15 $mm^2$ with honey, 2.38 $mm^2$ with saline. | p = 0.002 | There was histological evidence of greater granulation with honey. | 99 |
| Wounds created by excising skin (2 x 2 cm) | No treatment | Rats | 12 | The quantity of collagen synthesised was increased by honey *cf* the control. | p<0.001 | | 100 |
| | | | | The degree of cross-linking of the collagen in the granulation tissue was increased by honey increased by honey *cf* the control | p<0.05 | | |

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| Wounds created by excising skin (2 x 2 cm) | No treatment | Rats | 12 | The content in granulation tissue of various markers of connective tissue metabolism increased by honey *cf* the control:<br>protein<br>collagen<br>hexosamine<br>uronic acid | <br><br>p<0.01<br>p<0.01<br>p<0.01<br>p<0.001 | | 101 |
| | | | | The rate of healing was increased by honey *cf* the control:<br>contraction of wound<br>epithelialisation | <br><br>p<0.001<br>p<0.05 | | |
| Incision (6 cm long) made in skin, then sutured | No treatment | Rats | 12 | The tensile strength of the wounds was increased by 21% with honey *cf* the control. | p<0.05 | | 101 |
| Full-thickness incisions (3 cm long) made in the skin | No treatment | Rabbits | 40 | Honey increased the strength of the healed wounds compared with the untreated control:<br>tensile strength (measured after 14 days)<br>ultimate strength<br>yield strength | <br>p<0.001<br>p<0.05<br>p<0.02 | Less oedema was observed with the honey treatment, and histological examination revealed that honey gave less inflammation and necrosis and more fibroblasts and collagen present. | 102 |

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| Full-thickness incisions (1.5 cm long) made in the skin | No treatment | Rats | 6 | Histological examination of biopsy samples showed:<br>with honey, on Day 7 there was epithelial bridging *cf* inflammatory exudate and no epithelialisation with the control;<br>with honey, on Day 14 there was complete epithelial bridging with honey *cf* epithelium yet to cover wound with the control. | Not given | | 103 |