

## HONEY AND WOUND HEALING

### Types of wound, care protocols and pharmaceutical requirements for the medicinal use of honey

Dr David LECHAUX, gastrointestinal surgeon - Hôpital Yves Le Foll 22000 ST-BRIEUC (France). Previously specialist in internal medicine at various hospitals in Rennes (Fr). Chairman of the Food and Nutrition Liaison Committee.

#### Introduction

The healing properties of honey have been known for hundreds of years. Honey was often used in the early decades of the 20th century, but after the Second World War it was gradually supplanted by more modern and sophisticated products, despite a plethora of literature describing the healing properties of honey and a wide consensus as to its effectiveness, particularly for the treatment of chronic wounds.

There are many possible reasons why the pharmaceutical industry has ignored this natural product - including a lack of knowledge about honey, a lack of any in-depth research into the medicinal use of honey, the difficulty of guaranteeing the stability of a perishable product of this nature, and the most effective type of honey to use for any purpose - and effectively pushed it into the realms of quackery.

However, in the University Medical Centre at Limoges (Fr), honey has been used successfully for the last twenty-five years as an aid to the healing by secondary intention of highly complex wounds.

This is mainly thanks to Professor Descottes, who between 2004 and 2010 treated more than 3000 deep wounds in the abdominal wall, some of them infected.

In the past fifteen years or so, more and more studies have been carried out, all over the world, to gain a better insight into the efficacious ingredients of honey. In the light of the current state of knowledge, honey deserves more than our passing curiosity; as clinicians we should give honey our full attention, especially in the hospital environment where we have to cope with the serious problem of strains of bacteria that have become resistant to antibiotics. The antimicrobial, healing and anti-inflammatory properties of honey,

which have been convincingly demonstrated in both the laboratory and in clinical tests, have prompted us to carry out more research into the effects of honey on the healing of various types of wounds, such as surgical wounds, chronic wounds, venous ulcers and decubitus ulcers. This is particularly important as the new treatment options have proved at best disappointing, at worst completely unsuccessful. Honey has been proven to create favourable conditions in the wound bed: autolytic debridement and the presence of substances that promote and accelerate the healing process.

#### Characteristics and efficacy of honey in wound-healing products

Thanks to the combination of three physical properties - a very high concentration of glucose and fructose (osmotic action), a low pH value (ranging between 3.2 and 5.4) and a low water content - and four important active ingredients, honey has three proven pharmacological characteristics: antimicrobial, wound-healing and anti-inflammatory. These characteristics - which have been objectified in numerous studies all around the world - prompt therapeutic indications for the healing of a variety of wounds, such as operation wounds, burns, ulcers and bedsores.

- Honey promotes healing by maintaining an environment which is moist (18% water) and acidic. Thanks to its osmotic properties, resulting from the high level of simple sugars (80%), honey helps clear away the necrotic tissue in the wound bed. This prevents the dressing sticking to the wound and protects the granulating edges, and this in turn stimulates cell division (mitosis).

- Because of this high glucose-fructose concentration (80%), honey deprives the inflammatory bacteria of their nourishment. Instead of metabolizing the amino acids - the amine- and sulphur-

containing decomposition products of the amino acids cause a putrid smell - the bacteria concentrate on producing lactic acid and acidifying the environment; through this mechanism honey is able to inhibit the development of the pathogenic bacteria that cause infections.

- The presence of the glucose oxidase (GOx) enzyme leads to the formation of hydrogen peroxide in the honey, in accordance with the following chemical reaction:

glucose + water = gluconic acid + hydrogen peroxide.

A particular characteristic of this process is that the hydrogen peroxide is released very gradually: after 12 hours, the concentration is 4 to 5 µg per gram of honey, rising to 25 µg/gram after 24 hours, and this is sufficient to disinfect the wound, to set autolytic debridement in motion and promote granulation, without any risk of the toxic effects that would be caused by too high a concentration of hydroxyl radicals.

- A second ingredient with antibacterial properties, this one a non-peroxide, was demonstrated by Professor Thomas Henle at Dresden University (Germany) in 2008. This is a substance which has been known to nutritionists for many years, because it is present in all foodstuffs with a high sugar content: methylglyoxal (MGO). This is one of the dicarbonyl components (5 references) that are formed during the Maillard reaction which occurs in all products that have a very high sugar content.

The MGO concentration varies according to the geographic origin and the type of the honey. The type of honey that is currently known to have the highest MGO content is manuka honey, or to be more precise the *Leptospermum scoparium* (family: Myrtaceae), which is very common in New Zealand. Depending on MGO content, which can range from 3 - 4 µg to 750 - 800 µg per gram honey, the honey will have a weaker or stronger effect on a narrower or wider spectrum of bacteria, particularly on the methicillin-resistant *Staphylococcus aureus* (MRSA) strains, the vancomycin resistant enterococci and *Pseudomonas aeruginosa*, which are unaffected by present-day

antibiotics. A high concentration does not seem necessary: MGO fulfils its antibacterial role at upwards of 10 µg per gram honey. However, biochemists know that MGO can cause damage at a cellular level: either via the blood where it leads to glycation, or via external pathways when it can lead to the malignant degeneration of young cells. MGO occurs in all types of honey, but the concentration ranges from 3 µg per gram in some types to 800 µg per gram in manuka honey. The important thing is that the effectiveness of the chosen honey in combating pathogenic bacteria (including resistant and non-resistant *Staphylococcus aureus*, *Pseudomonas* strains, etc.) has been proven.

- A third efficacious ingredient was demonstrated by Dr Zaat of the Medical Microbiology Department at the Academic Medical Centre of Amsterdam (NL) in November 2009. A minute quantity of this substance - ranging from 2 to 3 nanograms per gram honey - is present in all types of honey. The substance is similar to the human beta defensin 1 (HBD-1) protein: a peptide molecule with cationic properties which plays an antimicrobial role by the aggregation and destruction of the host cell, behaving like a true peptide antibiotic.

- A fourth group of substances which also play an important role in wound healing are the flavonoids, a group of molecules belonging to the polyphenols which are known to be effective against type 1 radicals (by neutralizing hydroxyl radicals).

At high concentrations, these substances reduce any inflammation present and moderate the pain; the importance of these effects during the wound healing process should not be underrated, as they make the episode more bearable for the patient.

A variety of methods have been used to study the antimicrobial effect of honey which has been found to be extremely effective against a broad spectrum of wound bacteria, both gram-positive and gram-negative. Moreover, no resistance has been detected to date. All these aspects make honey an impressive therapeutic aid to wound healing in the

hospital environment, where nosocomial infections are a major problem.

### Indications and protocols for the use of honey to promote wound healing

The protocols below describe various methods for caring for acute and chronic wounds, and are intended to optimize the quality of care through the implementation of practices that are the subject of consensus in the clinical world.

The healing of a wound is a natural, biological process that occurs in 3 phases:

- the exudation or drainage phase, which serves to clean the wound;
- the proliferation or rebuilding phase, with the formation of granulation tissue;
- the differentiation phase, when cells mature, scar tissue forms and re-epithelialization takes place.

Tissue is capable of repairing localized wounds itself, but this ability is influenced by various factors. The speed and the quality of wound healing depend on the general condition of the patient, the aetiology of the wound, the condition and site of the wound, and whether or not infections occur.

Other factors that can hinder wound healing are diabetes, malnutrition, obesity, smoking, advanced age, the use of corticosteroid-based medication and the use of immunosuppressants. The primary consideration for optimal care is always the aetiology of the wound, e.g. reducing localized pressure in the case of bedsores, and using support stockings to relieve the symptoms of venous insufficiency in venous ulcers.

**Preparation.** The risk of infection can arise during the preparations for wound care as a result of poor organization, non-compliance with protocols or unfamiliarity with the method to be used. Moreover, the risk of persistent sepsis increases if the patient is uncooperative, poorly informed or has poor personal hygiene.

**What elementary precautionary measures should be taken in the hospital environment?**

- **Nursing care plans** should be made known in advance, so that staff are not interrupted while changing the dressings. If staff need to attend to the dressings of multiple patients, the work should be organized so that they begin with the simple dressings and end with the more complicated dressings, i.e. infected wounds and all wounds infected with resistant bacteria. Of course, account must be taken of each patient's needs and the local rules of the hospital. During doctors' rounds, it is recommended that dressings are removed only at the last minute. If the dressing is removed in advance, however, the wound must be protected with a sterile non-adhesive dressing. All the material that will be needed should be available to hand on the treatment trolley unnecessary trips to collect additional items.

The *dressing trolley* should be kept in the hallway. The top surface should be wiped clean with a cloth dampened with disinfectant cleaner at the end of each shift, and the entire trolley should be cleaned once a week.

The *treatment trolley* is wheeled into the patient's room, except in the case of patients with infections in which case the materials for those individuals is stored in the room itself. The treatment trolley should contain the minimum of products and materials. The *top surface* must be clear. After the treatment of each patient, the top surface should be wiped clean with disinfectant cleaner, and the entire trolley should be cleaned at the end of each shift. Dressings waste carries a risk of infection; after treating a patient, and while still in the patient's room, the waste should be packed into a sealable bag and disposed of in the designated sack on the dressing trolley or in the sluices.

*Preparing the patient:* ensure that the patient knows what is going to happen, and explain any possible undesirable consequences. Pain levels should be assessed before, during and after each dressing change and relief given if necessary.

- **Before the treatment**, the patient should have showered and the bedding been changed if possible. The nurse will check that the patient has been washed with special attention to the area of skin

around the wound; a series of standard procedures need to be carried out, irrespective of the type of wound.

*Clean uniform:* is sufficient for the care of simple wounds where there is no risk of spatter or contact between the wound and the nurse's clothing.

*Protective clothing:* is recommended in the case of infected or extensive wounds, heavy or complex dressings, or if there is a risk of spatter (during irrigation for example).

*Hand hygiene:* it is absolutely essential that hands should be disinfected by the six-step technique using 2 applications of a hydroalcoholic gel. This method is preferable to washing the hands with antiseptic soap, because it is more effective and better for the skin. During treatment, this sanitizing procedure should be repeated after every action that involves the risk of contamination (e.g. removal of the dressing) and before any action with a risk of infection (e.g. cutting a sterile dressing).

It is recommended that *gloves should be worn* for any treatment in which there is contact with blood or bodily fluids.

- *Non-sterile gloves:* should be worn for the removal of dressing.

Generally speaking, such gloves are used when dressing chronic wounds.

- *Sterile gloves:* should only be used when changing dressings on acute wounds if no sterile medical aids are available. Such gloves can be used to directly handle sterile compresses, but are not necessary if sterile medical aids are available.

- *Wearing a facemask and eye protection:* is advised so as to prevent oropharyngeal transmission and to protect the nurse or carer from airborne bacteria. It is recommended that a facemask and eye protection should always be worn during the irrigation of wounds and where highly pathogenic and antibiotic-resistant bacteria are present.

### **A) Care of chronic wounds**

First of all, a few important principles that nurses/carers should be aware of when dressing chronic wounds:

- A moist environment promotes wound healing. A dry wound delays healing, as does too much moisture, so it is important to achieve the optimum environment.

- Wounds should be cleansed with a normal saline solution or with non-sterile water and a mild soap.

- No local antibiotics and no antiseptics may be used.

All wounds are colonized and the dressing must be affixed in such a way that the bacterial ecosystem remains intact.

- The aetiology of the wound must be ascertained in all patients with chronic wounds; a nutritional assessment should be made, pain assessed and relieved and, finally, appropriate hygiene must be maintained.

Hands must be sanitized before treatment, after removing soiled dressings, and again at the end of treatment.

Subsequently, a series of additional procedures should be carried out:

*Decubitus ulcers:* care must be taken that the pressure is taken off the wound by changing the patient's position regularly and by using the appropriate aids.

*Venous ulcers:* correct pressure promotes venous return. Walking and mobilization of the ankle and foot joints have a positive effect. Specialist advice is always desirable.

*Arterial ulcers:* necrosis must be borne in mind, and the possibilities for restoring the blood supply should be examined.

*Neurotrophic ulcer:* neurotrophic foot ulcers should be relieved by wearing suitably adapted footwear or support insoles.

### **Venous ulcers**

It is generally acknowledged that compression therapy is the best treatment for venous ulcers. Nonetheless, a honey dressing can have a place in the treatment of inflamed or complex leg wounds that are resistant to treatment or are not suitable for compression therapy.

This type of therapy makes it possible for patients to be cared for in their own homes, thus reducing the need for hospitalization. In complex leg ulcers it is important to carry out a thorough assessment of the wound by means of a direct bacteriological examination followed

by a tissue culture and a biopsy to confirm the diagnosis. To increase the chance of success in the absence of devitalized or fibrinous tissue, debridement should be carried out before the dressing is applied.

#### **- inflamed ulcers:**

A honey dressing can be used for patients with inflamed ulcers; this will help prepare the wound bed prior to final operative closure or deferred secondary healing. These patients have wounds that are difficult to heal, and an increased risk that skin grafts will be rejected. Such ulcers can occur in the following situations: scleroderma, systemic lupus erythematosus, hypercoagulability, polyarthritis rheumatica, vascular lesions.

If the underlying clinical pathology is resistant, or incorrectly treated, inflamed ulcers generally fail to heal despite optimum care of the wound.

Moreover, wound healing can be delayed if the overall treatment includes the administration of NSAIDs. In the case of non-inflamed ulcers, a honey dressing could perhaps be used for a short while to ascertain whether it is having a beneficial effect. Treatment should then be carried out for 4 to 8 days, after which it can be evaluated and if the results are good it can be continued.

#### **- complex ulcers:**

Use of a honey dressing could be considered in the treatment of complex ulcers. These include:

- wounds producing a great deal of exudate, possibly in combination with vacuum therapy (VAC);
- ulcers that are anatomically difficult to treat (if it is difficult to place and stabilize the dressing);
- ulcers that are infected with multiresistant organisms (there is no known resistance to the antibacterial effect of honey);
- wounds that require a skin graft.

#### **- diabetic foot:**

It is sometimes thought that all ulcers on a diabetic foot are identical in terms of treatment targets. In reality there are large differences between cases, and any decision to use a honey dressing will

depend on the type of wound. A honey dressing can be considered for complex and deep wounds, for post-operative wounds and equally for superficial wounds. In the case of ischemic wounds, the advice of a vascular surgeon should be sought before the use of honey is considered.

*Complex and deep ulcers of the diabetic foot that are not inflamed or ischemic*, can benefit from treatment with honey in order to reduce the surface area of the wound because honey stimulates the formation of granulation tissue on bone, tendons or exposed tissue. This can avoid the necessity for a more complex technique such as operative closure.

In the case of plantar wounds, a pressure-relieving dressing technique should be applied to avoid the formation of lesions as a result of the extra pressure.

Honey dressings can sometimes be used for an extended period, in conjunction with systemic antibiotics, in order to allow full resolution of underlying osteomyelitis before skin closure. This prevents the problem of ulcer recurrence due to residual osteomyelitis when the skin heals before the underlying bone.

*In poorly perfused wounds, and when revascularization is not possible*, honey can be used for a trial period during which the physician can observe the response to treatment and assess tissue viability. The application of honey has provided unexpected and encouraging results and in some cases allowed more distal amputations to be carried out with a better functional outcome.

In many cases an initial treatment period of one to two weeks is recommended. After that period, the situation can be evaluated to see whether it has improved or deteriorated.

*If the outcome is favourable*: if healthy granulation tissue has formed, the depth of the wound has decreased, vascularization is satisfactory and no infection has arisen, the honey treatment can be continued until the treatment target has been achieved.

*If the outcome is unfavourable or deterioration occurs:* in this case an alternative treatment method should be chosen in line with the characteristics of the wound.

*Comments:*

- *In the case of chronic non-healing ulcers for which other treatments have failed, it is possible that granulation tissue will first be observed two weeks after the start of treatment with medicinal honey.*

- *There is no contraindication to the local use of honey in diabetics; honey can be used in various ways to treat a diabetic foot ulcer, irrespective of its complexity.*

- *On the other hand, in certain wounds, the use of medicinal honey may occasionally lead to hypergranulation which then hinders epithelialization. In such cases it is sufficient to apply a corticoid cream which will allow epithelialization to resume within a few days, and the wound can then heal.*

**- Decubitus ulcers**

Decubitus ulcers are skin lesions, ischemic in origin, that occur because soft tissue has been compressed between a hard surface and a bony prominence. Such ulcers can be described as wounds that occur from the inside out, they are conical in shape with a deep base and multiple points of origin, thus distinguishing them from superficial abrasions. Decubitus ulcers fall into three categories:

**incidental decubitus ulcers:** resulting from a temporary reduction of mobility and/or consciousness; **neurological decubitus ulcers:** resulting from a chronic locomotory and/or sensory disorder; **multifactorial decubitus ulcers:** occurring in patients with multiple pathology who are confined to a bed or chair.

**The main purpose of the honey treatment** for decubitus ulcers is to reduce the volume of the wound cavity. The treatment also has important benefits for the patient in terms of increased comfort (e.g. fewer dressing changes, less exudate and less smell) and improved quality of life, and for nursing staff and carers in terms of simplifying the care of

these complex wounds. The therapy is not generally recommended in second degree decubitus, and it may not be used if there is any suspicion of lesions in deeper tissues under intact skin.

**Honey therapy** is also possible, in certain circumstances, for the treatment of third and fourth degree decubitus, and should then be part of a comprehensive treatment plan. The entire wound bed must be visible and must be examined before the honey is applied. Such ulcers are often complex wounds with discrete subcavities. In such cases, before the honey is applied, the wound should be cleaned by the surgical removal of any necrotic tissue and pseudomembranes, and fully exposed in order to offer access to the deepest cavities.

**Honey therapy** can be used pre-operatively to prepare wounds for reconstruction or to make it possible to use a smaller and/or less complex skin graft. This will help reduce the duration of the operation, post-operative risks and morbidity of the donor site. The effect of the treatment should be evaluated continually for a period of up to two weeks.

**The duration of the treatment** is determined by the original size of the wound and the volume of tissue available for reconstruction. Honey dressings can be used post-operatively to treat a minor dehiscence and to promote the healing of an inflamed wound. Tissue regeneration will quickly be stimulated.

For patients who develop decubitus ulcers after a serious accident (e.g. if an active patient suffers traumatic lesions of the spinal cord), the frequent changing of dressings and lengthy confinement to bed can have an adverse effect on overall wellbeing. **Honey dressings** can allow these patients to progress to wheelchair mobility and rehabilitation sooner. Some patients with decubitus ulcers (especially those who have had a large number of skin grafts) benefit from a longer period of treatment (e.g. three weeks) in order to bring their symptoms under control. Extended treatment can mean less exudate and increased comfort in the

period before conservational measures are taken to treat the wound.

**Honey therapy** can also play a palliative role in that it can improve the quality of life for terminal patients with decubitus ulcers. It helps make dressing changes painless and eliminates unpleasant wound odour. It should be noted that the treatment is more likely to fail if debridement is inadequately carried out. Under no circumstances should honey dressings take the place of good quality basic care. No extra skill is needed to apply the dressing to sacral decubitus ulcers situated near the anus.

### **B) Care of acute and surgical wounds**

#### **Superficial wounds**

These are wounds whereby the outer and/or middle dermis layers of the skin have been damaged. This can be caused by erosion, an ulcer, a decubitus ulcer with loss of the epidermis, or a superficial first or second degree burn. This type of wound has a characteristic appearance: it exudes a clear liquid (plasma) and its bed is pink or bright red. The area around the wound is inflamed, sometimes oedematous and painful. There may be sharp pain as a result of the exposure of sensory receptors. The wound is superficial and small in size. The wound will heal naturally if vascularization is adequate, if appropriate hygiene measures are taken, and the localized care is non-aggressive.

#### **Deep and cavity wounds**

The deeper dermis has been affected, sometimes even the hypodermis and underlying tissue (fascia, tendons, muscles, blood vessels, bone). This type of wound - an ulcer, deep decubitus ulcer, deep second or third degree burn, bite wound or open traumatic surgical wound - will not heal of its own accord, but must be managed.

*Care:* the skin around the wound should be washed with soap and water or with a normal saline solution, after which the wound itself should be rinsed out with a normal saline solution. The areas of pseudomembranes or necrotic tissue should be carefully removed, either

directly or with the aid of a compress. The underlying granulation tissue must be accessible, but care should be taken that the wound does not bleed. The application of the dressing depends on the appearance of the wound. Honey is effective in all three phases of wound healing whereby loss of tissue has occurred: in the debridement phase, the granulation phase and in the epithelialization phase.

- During the debridement phase, the wound becomes covered with a fibrinous deposit. There may also be necrotic tissue. Clean the wound with a normal saline solution and rub it gently with a surgical toothbrush (type: Inava). Subsequently, as soon as the fibrin has been completely removed, apply a honey dressing. The dressing should be changed every 48 hours.

- In the granulation phase: clean with a saline solution, then apply a honey dressing.

- In the epithelialization phase, the wound closes from the edges and the epidermis grows back over the entire wound. Clean by irrigating with normal saline solution, followed by a honey dressing. The skin should not be covered in the final phase of the wound healing process. In this type of wound, a dose of medicinal honey is applied to the wound bed after which it is covered with an absorbent gauze dressing. On flat wounds, a honey dressing is applied so that it overlaps the surrounding healthy skin by a good margin.

Follow-up of the wound is necessary in order to determine the phase of wound healing, to prevent the skin around the wound becoming affected and to monitor local signs of inflammation (redness, oedema, heat, discharge) which are often accompanied by heightened pain.

#### **Treatment of wounds using negative pressure therapy**

The vacuum-assisted closure method (known as VAC) makes use of local and controlled negative pressure and is combined with a multilayer dressing incorporating a compress impregnated

with medicinal honey (honey dressing\*) in the middle. The benefits of negative pressure wound therapy lie in the promotion of granulation tissue formation, the removal of superfluous exudate and possibly infected tissue from the wound, the creation of a sealed and moist environment that stimulates wound healing, and improved blood flow to the wound. A layer of foam dressing creates a barrier and, consequently, offers mechanical protection.

To this, the **honey dressing in the sandwich layer** adds powerful antibacterial protection in case of contamination, it prevents the foam dressing sticking to the wound, makes changing the dressing less painful and creates an environment that promotes the rapid growth of skin and subcutaneous tissue. All these factors serve to accelerate the wound healing process.

**Indications for VAC:** chronic wounds such as decubitus ulcers, venous ulcers and diabetic wounds, but also subacute wounds, dehiscence, wounds that have opened, acute wounds and traumatic wounds.

**Contraindications:** necrosis, untreated osteomyelitis, exposed blood vessels and/or organs, fistula, bleeding wounds, tumour wounds.

**In the Yves Le Foll hospital in Saint Brieuc (Fr),** abdominal dermolipectomy operations (abdominal reduction) are carried out during which the navel is repositioned. This is an operation which is accompanied by the risk of poor wound healing as a result of the large incision and the tension on the tissue. The surgery consists of resecting a large section of skin and subcutaneous fat, often weighing as much as several kilograms. The reconstruction of the abdominal wall requires the patient to be kept in a half-sitting position in order to bring the upper and lower wound edges together. The operation wound is always between 80 and 90 cm long. Vascularization around the edges of the wound is vulnerable in both the skin tissue and the subcutaneous tissue. The aim is to introduce a dressing system that will guarantee that the wound edges are perfectly approximated and, at

the same time, to create an environment that is conducive to wound healing. The wound-healing properties of honey, in combination with the vacuum-assisted closure system, are proving to be particularly suited to this type of wound.

- **Characteristics of the wound:** abdominal dermolipectomy with repositioning of the navel will leave two scars: one running from one hipbone to the other over the axial plane of the patient, and one running circularly around the navel. The subcutaneous tissue will be closed with soluble sutures, and the skin with staples. Immediately after surgery, the wound must be protected to allow the patient to wear a tight support belt. A dry dressing is usually applied over the wound, and the belt worn over it.

- **Dressing technique:** the first dressing is applied under general anaesthetic at the end of the surgical operation. The materials needed are: the motor, the sterile polyurethane foam dressing (cut to size to fit the wound), the reservoir, sterile scissors or scalpel, a set of sterile dressings, sterile gloves, saline solution, sterile compresses or wadding, sterile drapes, and the 8 cm wide honey-impregnated dressing\* that will be used to cover the entire length of the wound and protect the surrounding skin.

- **Procedure:** clean the wound with a saline solution; sanitize the hands using 2 applications of hydroalcoholic gel or put on new gloves; lay out the necessary material on a sterile field; rinse with saline solution and dry the surrounding area; protect fragile surrounding skin: use a honey dressing of 8 x 8 or 10 x 20 cm; using sterile scissors, cut polyurethane foam dressing to fit the size of the wound; place foam dressing on wound, ensuring it is in contact with the honey compress; cover the dressing with polyurethane film that overlaps the surrounding skin by approx. 5 cm. To make the polyurethane film easier to fit, it can be cut into smaller pieces. Make an incision, 1.5 cm long, in the film where it makes contact with the foam dressing and place the suction pad directly on top of this hole, ensuring that it is well affixed; the suction tube can now



be attached to the reservoir. Check that all clamps are open.

Switch the system on. When in operation, it must be possible to see that the foam dressing is being compressed.

*- Adjusting the system:*

Start with a constant pressure of 125 mm Hg; maintain this level for 4 days. The continuous pressure mode can be maintained, depending on medical requirements.

*- Checks:*

It is not necessary to measure the amount of exudate removed daily. The reservoir (single use) must be replaced as and when necessary. Any leakage will trip an alarm; the system must then be checked for leaks.

*- Changing the dressing:*

The dressing must be changed on the fourth post-operative day. The new dressing will be affixed without the VAC system, but still using a honey compress as a sandwich layer. For optimum effect, the honey dressing should be changed every 48 hours.

The motor should be switched off one hour before the dressing is to be removed; the foam dressing must be dampened with saline solution 20 minutes before it is removed.

*- Comments*

After the wound has been closed with staples, a strip of honey dressing\*, 5 cm wide, should be placed over the entire length of the wound and over the navel. Before the foam dressing is applied, a check should be made that the honey dressing is properly aligned along the staples. The absorbent foam dressing of the VAC system is cut into a 4 x 4 cm strip. This is placed over the honey compresses\*, precisely over the line of staples.

Transparent adhesive foil (type: Opsite) can be used to prevent slippage of the dressing.

After this step, the entire black foam dressing must be covered with the transparent film that will ensure that there are no leaks in the suction system.

One problem is proper placement of the dressing over the hips. To connect the

suction system, it is sufficient to cut a 1 x 1 cm opening into the plastic film which is in contact with the foam dressing and affix the tubing that has been shaped for this purpose. The pump is activated and the foam dressing compresses and is pressed on to the wound. The equipment (pump) indicates the presence or absence of leaks. The elastic belt is tightened when the patient is moved transferred from the operating table to a bed. Since June 2012, this operation has been carried out on 20 patients at the gastrointestinal unit of the hospital in Saint Brieuc. The results of the study are currently being evaluated.

*\* The honey dressings (Revamil®) were chosen after the characteristics of the various types of honey had been studied; preference was given to a honey variety that had the right properties and quality for medical use.*

## **Quality requirements of honey for medical use**

The honey that we have in our store cupboards is not immediately suitable for use in the treatment of open wounds, burns and decubitus ulcers. After all, honey is a perishable product; depending on the method used for conservation, it can undergo a large number of changes and consequently lose many of its most important properties. In addition, depending on its region of origin, it might have been exposed to contamination from various sources (dispersion of substances such as weed killer and pesticides in the ground or through the air). The collection site, the extraction method and the processing carried out during the production process can all have undesirable and sometimes harmful effects. Therefore, a range of processes need to be carried out and precautionary measures taken to make the honey suitable for medical purposes. Ensuring constant and reproducible effectiveness for medical use demands:

## **Control of the physicochemical and microbiological properties of medicinal honey**

Each production batch must undergo a series of physicochemical and microbiological tests in order to check the bactericidal properties and the operational

spectrum in a reproducible way. First of all, just as with medication, an initial batch must be subject to the battery of tests necessary to determine the bactericidal properties and operational spectrum.

This initial batch must be characterized by the maximum physicochemical indices that must be present in each batch subsequently produced, so as to ensure that they include the same medicinal properties and a bacterial burden that complies with the pharmaceutical norm of  $\leq 30$  CFU/gram, as the level in honey is usually around 600 CFU/gram.

Constant therapeutic effectiveness can be guaranteed by measuring the peroxidase activity and the antibacterial properties against a selection of bacteria. Since the active ingredient content of honey depends on the production area and the way in which the honey is collected and processed, the bee-keeping, production and collection of honey needs to be carried out under strictly controlled conditions.

The quality and reproducibility of the production batches can be assured with the aid of quality assurance procedures and a series of physicochemical and microbiological analyses on each such batch.

#### **Ensuring absolute harmlessness**

Absence of pesticides and heavy metals: the repeated use of pesticides in areas where intensive agriculture is practised makes it essential that only honey that is produced in protected natural areas (such as regional parks) is selected, and that it is systematically tested for pesticides and heavy metals (such as lead, mercury and cadmium). Expertise in procedures to remove such contamination is required.

Absence of bacterial contamination, yeasts and botulinum spores: honey is quickly contaminated when it is exposed to the air, especially in the polluted atmospheres found in a hospital. In the presence of moisture, yeast fermentation can occur. Honey can also cause botulism due to the

presence of spores of the Clostridium botulinum bacteria. Sterilization with gamma rays is necessary to produce honey with a bacterial burden of no more than 30 CFU/gram.

Minimal presence of pollen: although there are only a very few cases known, pollens can cause allergies in some patients; they can also be a source of pollution (lead, cadmium, pesticides, etc.).

#### **Ensuring the stability of the active ingredients by storing the honey in a dry, dark place**

The honey must firstly be marked with a "use before" date; a constant bacteriological effect must be assured up to that date. The water content must be between 17 and 18%; this serves to prevent the fermentation which can occur after approx. three months as a result of the hygroscopic properties of honey, which in turn reduces peroxidase activity. In moderate climate regions, honey can be stored at room temperature, but temperatures above 25° C should be avoided (optimum storage temperature: between 12° and 25° C). Honey undergoes changes under the influence of UV rays, so the product must be protected against exposure to UV light.

*Honey for medicinal use is currently included in the regulatory categories of medical aids and devices in class II (EU: II B).*

*Because of the criteria that honey must fulfil if it is to be deemed suitable for medicinal use, physicians are advised to make certain that the prescribed honey complies with the same standards for preparation and control as any medication, and its efficacy has been demonstrated.*

This article is the result of a literature review of more than a hundred and fifty recent scientific publications. It is based on the latest scientific data on the use of honey for the purpose of wound healing, from a biological and therapeutic perspective.

**Literatuur**

- Adams CJ, Boulton CH, Deadman BJ, Farr JM, Grainger MNC, Manley-Harris M, Snow MJ (2008) Isolation by HPLC and characterisation of the bioactive fraction of New Zealand manuka (*Leptospermum scoparium*) honey. *Carbohydr Res* 343(4):651–659
- Adams CJ, Manley-Harris M, Molan PC (2009) The origin of methylglyoxal in New Zealand manuka (*Leptospermum scoparium*) honey. *Carbohydr Res* 344(8):1050–1053
- Adesunikanmi, K. and Oyelami, O.A. 1994. The pattern and outcome of burn injuries at Wesley Guild Hospital, Ilesha, Nigeria: a review of 156 cases. *J. Trop. Med. Hyg.* 97: 108-112.
- Al Waili NS, Saloom KY. Effects of topical honey on post-operative healing. *J Altern Complement Med* 9: 267–73
- Allen, K.L., Molan, P.C. and Reid, G.M. 1991. A survey of the antibacterial activity of some New Zealand honeys. *J. Pharm. Pharmacol.* 43: 817-822.
- Allen, K.L., Molan, P.C. and Reid, G.M. 1991. The variability of the antibacterial activity of honey. *Apiacta* 26: 114-21.
- Allen, K.L., Hutchinson, G. and Molan, P.C. 2000. The potential for using honey to treat wounds infected with MRSA and VRE. Presented at the First World Healing Congress, Melbourne, Australia, Sept. 10-13.
- Assie, Descottes B. (dir.). *Le miel comme agent cicatrisant*. 115 p. Thèse d'exercice : Médecine. Toulouse : Toulouse III : 2004.
- Babacan, S., Pivarnik, L.F. and Rand, A.G. 2002. Honey amylase activity and food starch degradation. *J. Food Sci.* 67(5): 1625-1630.
- Basson, N.L. and Grobber, S.R. 1997. The effect of honey on human tooth enamel and oral bacteria. In "Proceedings of the International Conference on Bee Products: Properties, Applications and Apitherapy" held in Tel Aviv, Israel, May 26-30, wound infections due to gram positive and gram negative bacteria following caesarean sections and hysterectomies. *Eur J Med Res* 1999;4: 126–30.
- Bera A, Almeida Muradian LB, Sabato SI S.F. Effect of gamma radiation on honey quality control. *Radiation physics and chemistry*, 2009, vol. 78, n°7-8, p. 583-584.
- Berenbaum, M., Robinson, G. and Unnevehr, L. 1995-1996. Antioxidant properties of •
- Subrahmanyam, M. 1991. Topical application of honey in treatment of burns. *Br. J. Surg.* 78: 497-498.
- Bergman, A., Yanai, J., Weiss, J., Bell, D. and Menachem, P.D. 1983. Acceleration of wound healing by topical application of honey, an animal model. *Am. J. Surg.* 145: 374-376.
- Blair SE, Cokcetin NN, Harry EJ, Carter DA (2009) The unusual antibacterial activity of medical-grade *Leptospermum* honey: antibacterial spectrum, resistance and transcriptome analysis.
- Blaser G, Santos K, Bode U, Vetter H, Simon A (2007) Effect of medical honey on wounds colonised or infected with MRSA. *J Wound Care* 16(8):325–328
- Blomfield, R. Honey for decubitus ulcers. *JAMA* 224(5): 905.
- Bogdanov, S. 1989. Determination of pinocembrin in honey using HPLC. *J. Apicultural Res.* 28(1):
- Bogdanov S, Ruoff K, Oddo LP (2004) Physico-chemical methods for the characterisation of unifloral honeys: a review. *Apidologie* 35:S4–S17
- Bourne, I.H.J. 1991. Honey and the healing of leg ulcers. *J. R. Soc. Med.* 84: 11.
- Brudzynski K (2006) Effect of hydrogen peroxide on antibacterial activities of Canadian honeys. *Can J Microbiol* 52: 1228–37
- Chambers J (2006) Topical manuka honey for MRSA-contaminated skin ulcers. *Palliat Med* 20:557
- Cooper RA (1999) Antibacterial activity of honey against strains of *Staphylococcus aureus* from infected wounds. *J R Soc Med* 92: 283–5
- Cooper, R. 2001. How does honey heal wounds? In "Honey and Healing," ed. P. Munn and R. Jones. International Bee Research Association, Cardiff, UK.

Cooper RA, Fehily AM, Pickering JE, Erusalimsky JD, Elwood PC, Honey, Health and Longevity. Centre for Biomedical Sciences, Cardiff School of Health Sciences, University of Wales Institute, Cardiff, Western Avenue, Cardiff CF5 2YB, UK. rcooper@uwic.ac.uk. *Curr Aging Sci.* 2010 Jul 5. [Epub ahead of print]

Cooper, R.A., Molan, P.C. and Harding, K.G. 1999. Antibacterial activity of honey against strains of *Staphylococcus aureus* from infected wounds. *J. R. Soc. Med.* 92: 283-285.

Cooper, R.A., Halas, E., Davies, R. Molan, P.C. and Harding, K.C. 2000. The inhibition of Gram-positive cocci of clinical importance by honey. Presented at the First World Healing Congress, Melbourne, Australia, Sept. 10-13.

Cooper RA, Halas E, Molan PC. The efficacy of honey in inhibiting strains of *Pseudomonas aeruginosa* from infected burns. *J Burn Care Rehabil* 2002; 23:366-70.

Cooper RA, Molan PC, Harding KG. The sensitivity to honey of gram positive cocci of clinical significance isolated from wounds. *J Appl Microbiol* 2002; 93:857-63.

Descottes B. Cicatrisation par le miel, l'expérience de 25 ans. *Phytothérapie*, 2009, vol. 7, n°2, p. 112-116.

Descottes B. Miel et cicatrisation. *Apithérapie : la science de l'abeille pour l'énergie et le bien-être*, 1997, n°57950, p. 33-40.

Dunford, C., Cooper, R.A. and Molan, P.C. 2000. Case Report: Using honey as a dressing for infected skin lesions. *Nursing Times* 96(14): 7-9.

Efem, S.E.E. Clinical observation on the wound healing properties of honey. *Br. J. Surg.* 75: 679-681.

Efem, S.E.E., Udoh, K.T. and Iwara, C.I. 1992. The antimicrobial spectrum of honey and its clinical significance. *Infection* 20(4): 228-229.

Frankel, S. Robinson, G.E., and Berenbaum, M.R. 1998. Antioxidant capacity and correlated characteristics of 14 unifloral honeys. *J. Apicultural Res.* 37(1): 27-31.

Flodhazi, G. 1994. Analysis and quantification of sugars in honey of different botanical origin using high performance liquid chromatography. *Acta Alimentaria* 23(3): 299-311.

Gheldof, N., Wang, X. and Engeseth, N.J. 2001. Characterization of the antioxidants in honeys from different floral sources. Presented at Ann. Mtg., Inst. of Food Technologists, New Orleans, LA, June 23-27.

Gheldof, N. and Engeseth, N.J. 2002. Antioxidant capacity of honeys from various floral sources based on the determination of oxygen radical absorbance capacity and inhibition of in vitro lipoprotein oxidation in human zout samples. *J. Agric. Food Chem.* 50(10): 3050-3055.

Gheldof, N., Wang, X. and Engeseth, N.J. 2002. Identification and quantification of antioxidant components of honeys from various floral sources.

Gheldof, N. and Engeseth, N. 2002. In vitro and ex vivo antioxidant effect of honey. Presented at Ann. Mtg., Inst. of Food Technologists, Anaheim, CA, June 15-19.

Goethe P. Le miel comme traitement local désinfectant et cicatrisant des plaies. *Phytothérapie*, 2009, vol. 7, n°2, p. 91-93. • HUTT N., DE BLAY F., HOYET C. [et al.]. Allergie alimentaire par ingestion de pelotes de pollen. *Revue française d'allergologie et d'immunologie clinique*, 1989, vol. 29, n°3, p. 147-148.

Grange, J.M. Reply: honey and propolis as possible promoters of the healing of ulcers in leprosy. *Lepr. Rev.* 61(2): 195.

Greenwood, D. 1993. Honey for superficial wounds and ulcers. *Lancet* 341(8837): 90-91.

Gubin, A.F The beekeeping institute during the war: honey in medicine. *Pchelovodstvo* (1): 25-29.

Johnson DW, van Eps C, Mudge DW, et al. Randomized, controlled trial of topical exit-site application of honey (Medihoney) versus mupirocin for the • Bang LM (2003) The effect of dilution on the rate of hydrogen peroxide production in honey and its implications for wound 1996, p. 65-71. Plenum Press, New York.

Jonard L, Banu L, Pressac M, Just J, Bahua M. Les défensines en physiopathologie humaines. *pédiatrie*, 2010, vol. 17, n°9, p. 1288-1292.

Jones, C. 1992. Bad language. *The Veterinary Record* 130(9): 192.

Jones, K.P. 2001. The role of honey in wound healing and repair. In "Honey and Healing," ed. P. Munn and R. Jones. International Bee Research Association, Cardiff, UK.

King L-A, Popoff M-R, Mazuet C. [et al.]. Le botulisme infantile en France. Archives de

Kwakman, PH, AA te Velde, L Boer, Speijer D, Vandenbroucke – Grauls CM, Zaat SA. How honey kills bacteria: Département de microbiologie médicale, Academic Medical Center, Université d'Amsterdam, 1105 AZ Amsterdam, Pays-Bas FASEB J. 2010 juillet; 24 (7) :2576-82.

Kwakman, P.H, Te Velde A, DeBoer L. [et al.]. How honey kills bacteria. *FASEB journal*, 2010, vol. 24, n°7, p. 2576-2581.

Lachman J, Orsak M, Jtmankova AK, Kovarova. Evolution of antioxidant activity and total phenolics of selected Czech honeys. *Food Science and Technology*, 2010, vol.43, n°1, p. 52-58.

Le Cerf JM. Effets métaboliques du fructose et du miel. *Phytothérapie*, 2009, vol.7, n°2, p. 83-86.

Lehrer RI, Barton A, Daher KA, Harwig SS, Ganz T, Selsted ME. Interaction of human defensins with *Escherichia coli*: mechanism of bactericidal activity. *J Clin Invest* 1989; 84:553-61.

Levy SB. The antibiotic paradox: how misuse of antibiotics destroys their curative powers. Cambridge: Perseus Publishing, 2002.

Levy SB, Marshall B. Antibacterial resistance worldwide: causes, challenges and responses. *Nat Med* 2004; 10:S122-9.

Marceau E, Yaylayan VA., Profiling of alpha-dicarbonyl content of commercial honeys from different botanical origins: identifications of 3,4-dideoxyglucosone-3-ene (3,4-DGE) and related compounds. Department of Food Science and Agricultural Chemistry, McGill University, 21,111 Lakeshore, Ste. Anne de Bellevue, Quebec, Canada H9X 3 V9. *J Agric Food Chem*. 2009 Nov 25;57(22):10837-44.

Mavric E, Wittmann S, Barth G, Henle T (2008) Identification and quantification of methylglyoxal as the dominant antibacterial constituent of Manuka (*Leptospermum scoparium*) honeys from New Zealand. *Mol Nutr Foods Res* 52(4):483-489

McInerney, R.J.F. Honey—a remedy rediscovered. *J. R. Soc. Med.* 83(2): 127.

Meda A A, Lamien CE, Marco R [et al.]. Determination of the total phenolic, flavonoid and proline contents in Burkina Faso honey, as well as their radical scavenging activity. *Food Chemistry*, 2005, vol. 91, n°3, p. 571-577.

Midura, T.F., Snowden, S. Wood, R.M. and Arnon, S.S. 1979. Isolation of *Clostridium botulinum* from honey. *J. Clin. Microbiol.* 9(2): 282-283.

Molan, P.C. 2001, Potential of honey in the treatment of wounds and burns. *Am. J. Clin. Dermatol.* 2(1): 13-19. University of Waikato—Honey Research Unit.

Molan, P.C. 2001. Why honey is effective as a medicine. 1. Its use in modern medicine. In "Honey and Healing."

Molan, P.C. 2002. Selection of honey as a wound dressing. Waikato Honey Research Unit, University of Waikato.

Molan, P.C. 1992. The antibacterial activity of honey. 1. The nature of antibacterial activity. *Bee World* 73: 5-28

Molan, P.C. 1992. The antibacterial activity of honey. 2. Variation in the potency of the antibacterial activity. *Bee World* 73: 59-76.

Molan, P.C. 1996. Honey for treatment of infections. *Bee Informed* 3(2): 6-9.

Molan, P.C. 1992. The antibacterial activity of honey. 1. The nature of antibacterial activity. *Bee World* 73: 5-28.

- Molan, P.C. 2002. Honey as an antimicrobial agent. Waikato Honey Research Unit, University of Waikato,
- Molan, P.C. 2002. What's special about active manuka honey. Waikato Honey Research Unit, University of Waikato,
- Molan, P.C. 2001. Why honey is effective as a medicine. 2. The scientific explanation of its effects. In Cardiff, UK.
- Molan, P.C. 2002. The evidence for honey promoting wound healing. Univ• Molan, P.C. and Allen, K.L. 1996. The effect of gamma-irradiation on the antibacterial activity of honey. *J. Pharm.Pharmacol.* 48: 1206-1209.
- Molan, P.C. 2002. Re-introducing honey in the management of wound and ulcers—theory and practice. *Ostomy Wound Manage.* 48(11). In press.
- Molan, P.C. 2002. Where to get honey for medical use. Waikato Honey Research Unit, University of Waikato,
- Molan, P.C. and Russell, K.M. 1988. Non-peroxide antibacterial activity of some New Zealand honeys.*J. Apicultural Res.* 27(4): 252-256.
- Molan, P.C., Smith I.M. and Reid, G.M. 1988. A comparison of the antibacterial activities of some New Zealand honeys.*J. Agric. Res.* 27(4): 252-256.
- Moolenaar O (2006) The effect of honey compared to conventional treatment on healing of radiotherapy induced skin toxicity in breast
- Morse, R.A. and Flottum, K. 1990. "The ABC & XYZ of Bee Culture," 40th ed. The A.I. Root Co., Medina, OH.
- Mundo, M.A., Padilla-Zakour, O.I. and Worobo, R.W. 2002. Antimicrobial activity of honey against food pathogens and food spoilage microorganisms. Presented at Ann. Mtg., Inst. of Food Technologists, Anaheim, CA, June 15-19.
- Munn, P. and R. Jones, 2001, editors of "Honey and Healing," International Bee Research Association.
- Munstedt, K. and Lang, U. 1997. Honey's wound healing properties. *Am. Bee J.* 137(4): 296-297.
- Nakano, H., Yoshikuni, Y., Hashimoto, H. and Sakaguchi, G. 1992. Detection of *Clostridium botulinum* in natural sweetening. *Int. J. Food Microbiol.* 43: 183-195.
- Nakano, H. and Sakaguchi, G. 1991. An unusually heavy contamination of honey product with *Clostridium botulinum* Type F and *Bacillus alvei*. *FEMS Microbiology Letters* 79: 271-178.
- Ndayisaba, G., Bazira, L. and Habonimana, E. 1992. Treatment of wounds with honey. 40 cases.*Presse-Med.* 21(32): 1516-1518. (Abstract only - French.) -113.
- Pawlowska, M. and Armstrong, D.W. 1994. Evaluation of enantiomeric purity of selected am Illinois honeys. Grant Proposal for National Honey Board. University of Illinois at Urbana-Champaign.
- Phuapradit, W. and Saropala, N. 1992. Topical application of honey in treatment of abdominal wound disruption.*J.Obstet.Gynaecol.* 32(4): 381-384.
- Pichichero E, Cicconi R, Mattei M, Muzi MG, Canini A., Acacia honey and chrysin reduce proliferation of melanoma cells through alterations in cell cycle progression. Department of Biology, Honey Research Center, University of Rome 'Tor Vergata' Via della Ricerca Scientifica 1, I-00133 Rome, Italy. *Int J Oncol.* 2010 Oct;37(4):97381.
- Postmes, T. 2001. The treatment of burns and other wounds with honey. In "Honey and Healing," ed. P. Munn and R.Jones. International Bee Research Association, Cardiff, UK.
- Postmes, T.J., Bosch, M.M.C., Dutrieuex, R., van Baare, J. and Hoekstra, M.J. 1997. Speeding up the healing of burns with honey.
- Radwan, S.S., El-Essaway, A.A. and Sarhan, M.M. 1984. Experimental evidence for the occurrence in honey of specific substances active against microorganisms. *Zid. Mikrobiol.* 139: 249-255.
- Rashad UM, Al-Gezawy SM, El-Gezawy E, Azzaz AN., Honey as topical prophylaxis against radiochemotherapy-induced mucositis in head and neck cancer. Department of Otolaryngology,

Oncology, Faculty of Medicine, Assiut University, Egypt. *J Laryngol Otol.* 2009 Feb;123(2):223-8. Epub 2008 May Bactericidal Activity of Medical-Grade Hon

Rosenblat G., Angonnet, S., Goroshit, A. Tabak, M. and Neeman, I. 1997. Antioxidant properties of honey produced by bees fed with medical plant extracts. In "Proceedings of the International Conference on Bee Products: Properties, Applications and Apitherapy" held in Tel Aviv, Israel, May 26-30, 1996, p. 49-55. Plenum Press, New York.

Roth LA (1986) Use of a disc assay system to detect oxytetracycline residues in honey. *J Food Prod* 49: 436-41

Safdar N, Kluger DM, Maki DG. A review of risk factors for catheter-related bloodstream infection caused by percutaneously inserted, noncuffed central venous catheters: implications for preventive strategies. *Medicine (Baltimore)* 2002; 81:466-79.

Schramm, D.D. and Keen, C.L. 2002. Buckwheat honey, a natural sweetener, conveys antioxidant protection to healthy human subjects. Presented at Ann. Mtg., Inst. of Food Technologists, Anaheim, CA, June 15-19. National Honey Board. University of Illinois at Chicago.

Snowdon JA Cliver D. Microorganisms in honey. *International journal of Microbiology*, 1996, vol. 31, n°1-3, 1996, p. 1-26.

Somerfield, S.D. 1991. Honey and healing. *J. R. Soc. Med.* 84(3): 179. a prospective randomised study. *Br. J. Plast. Surg.* 46: 322-323

Subrahmanyam, M. 1993. Honey impregnated gauze versus polyurethane film (OpSite®) in the treatment of burns- 25(11): 86-87.

Subrahmanyam, M. 1993. Storage of skin grafts in honey. *Lancet* 341: 63-64.

Subrahmanyam M 1993 Honey impregnated gauze versus polyurethane film (OpSite) in the treatment of burns—a prospective randomised study. *Br J Plast Surg* ; 46:322-3.

Subrahmanyam, M. 1994. Honey impregnated gauze versus amniotic membrane in treatment of burns. *Burns* 24(4): 331-333.

Subrahmanyam, M 1994 A prospective randomised clinical and histological study of superficial burn wound healing with honey and silver sulfadiazine. *Burns* 24: 157-161.

Subrahmanyam, M. 1996. Honey dressing versus boiled potato peel in the treatment of burns: a prospective randomized study. *Burns* 22(6): 491-49

Subrahmanyam M 1998 A prospective randomised clinical and histological study of superficial burn wound healing with honey and silver sulfadiazine. *Burns* 24:157-61.

Sugiyama, H., Mills, D.C. and Kuo, L.J.C. 1978. Number of *Clostridium botulinum* spores in honey. *J. Food Prot.* 41(11): 848-850.

Taormina PJ (2001) Inhibitory activity of honey against foodborne pathogens as influenced by the presence of hydrogen peroxide and level of antioxidant power. *Int J Food Microbiol* 69: 217-25

Taormina, L.R., Niemara, B.A. and Beuchat, L.R. 2001. Inhibitory activity of honey against foodborne pathogens as influenced by the presence of hydrogen peroxide and level of antioxidant power. *Int. J. Food Microbiol.* 69: 217-225.

Temnov, V.A. Bactericidal properties of honey and utilization of honey and other beekeeping products for healing of wounds. *Bee World in acids in honey. Chirality* 6: 270-27

Tomlinson, J.T. and Williams, S.C. 1985. Antibiotic properties of honey produced by the domestic honey bee *Apis mellifera* .

Visavadia BG, Honeysett J, Danford MH (2008) Manuka honey dressing: an effective treatment for chronic wound infections. *Br J Oral Maxill Surg* 46:55-56

White, J.W., Subers, M.H. and Schepartz, A.I. 1963. The identification of inhibin the antibacterial factor in honey, as hydrogen peroxide and its origin in a honey glucose-oxidase system. *Biochem. Biophys. Acta* 73: 57-79.

Willix, D.J., Molan, P.C. and Harfoot, C.G. 1992. A comparison of the sensitivity of wound-infecting species to the antibacterial activity of manuka honey and other honey. *J. Appl. Bacteriol.* 73: 388-394.