



Sudan University of Science and Technology College of Veterinary Medicine

EFFECTS OF NATURAL HONEY AND GLUE ON CUTANEOUS WOUND HEALING IN HILL GOATS

أثر العسل الطبيعي والصمغ على التئام الجروح الجلدية في الماعز الجبلي

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Dedication

We dedicate our Dissertation to:
Our Mothers "Our angels in life"
Our father's "Whom we hold their names with pride"
Our Sisters and Brothers "With whom we shared the most beautiful
moments of our lives

&

Whom were always supported us whole heartedly

Original study

The work embodied in this thesis was carried out in the Department of Surgery Collage of Veterinary Medicine, Sudan University of Science and Technology. Under supervision of Doctor Maria El-Rayah Osman and has not been submitted to any other university in the world.

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Abstract

Wounds are one of the main surgical problems in animal health; the clinician seeks to obtain wound care for healing promotion to decrease hazards for variety of skin wounds. Closure of wounds is often needed to promote wound healing and to produce an acceptable cosmetic result. The aim of our dissertation is to assess the clinical effects of honey and glue on the healing process of full- thickness skin wounds.

Five animals were used in the this experimental study and full thickness skin wounds were created on the lateral aspect of left and right lower thigh muscles in all experimental animals..

The right lower thigh wounds were covered with honey and the left ones were covered with glue and left without dressing or topical antibiotics. The clinicopathological observations which were recorded inflammation, swelling and pain were quickly reduced, clean sterile wound ,contraction of wound size were hastened(figure 7,8), and healing occurs rapidly.

Key words: Honey, Glue, Wound healing, Hill goats.

خلاصة الاطروحة

الجروح من اهم المشاكل الجراحية التي تؤثر على صحة الحيوان. يسعى الاطباء البيطريين للاهتمام بالجروح لتحفيز سرعة الالتئام ولتقليل اخطار الجروح التي تصيب الجلد غالبا ما نحتاج قفل الجروح لتحفيز الالتئام واعطاء نتائج تجميلية مقبولة . هدفت هذه الدراسة الى تقييم الاثار السريرية للعسل والصمغ على عملية التئام الجروح الجلدية أُجريت جروح الجلد الكثيف على جانبي الفخذ الايمن والايسر لكل حيوانات التجربة الجروح اليمنى تمت تغطيتها بالعسل والجروح اليسرى تمت تغطيتها بالصمغ وتُركت بدون الجروح اليمنى تمت تغطيتها بالشمغ وتُركت بدون الملاحظات السريرية :الالتهاب والورم والالم اختفى سريعاً والاصابة نظيفة والتقلص في حجم الملاحظات السريرية :الالتهاب والورم والالم اختفى سريعاً والجرح والالتئام حدث بسرعة المرح والالتئام حدث بسرعة

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Chapter one

Literature review

1.1 Goat breeds in Sudan:

Goats in Sudan constitute large part of livestock population with an estimated number of 31 million goats with an annual growth of 2.4% (last Sudanese animal census in 2016), there are four local types of goats are distinguished in Sudan: Nubian, Taggar, Sudan desert and Hill goats (Mason and Maule., 1960; Muffarah, 1995).

Nubian goat:

Is a dairy goat of moderate size commonly found in the semiarid areas in Sudan, Anglo Nubians weighing 175 pound in average for bucks and approximately about 135 pound for doe and can be of any color (Porter ,2002).

Hill goat:

Cream in color with light brown face and leg, medium in size with coarse wool and relative low fecundity when kept on the hill, it is a good breed for top crossing (Jackson, 1986).

Desert goat:

Is dual purpose goat, found in the desert area of Sudan, mostly used for meat production and mostly found in the border area between the North and southern areas of the Sudan (Yagoub and Babiker, 2016).

Taggar goats:

Species of dwarf goat commonly found in mountainous areas all over Sudan (Yagoub and Babiker, 2016).

1.2 Wounds

Wound is break (disruption -solution) in the continuity of the skin, mucous membrane or soft tissues that caused by traumatic blow or fences. (Nabil *et al.*,2015).

Classifications of wounds:

1.2.1 Classification According to the condition of the skin:

1.2.1.1 Closed wounds

These are wound that occur without a loss of superficial surface Of the skin, without affecting the skin, It includes contusion and abrasion (Rodriguez *et al*, 2008).

1.2.1.2 Open wound

These are wounds in which there is loss of superficial covering of the tissues such as loss of skin. It includes incised, laceration, punctured, ulcerating and avulsion wounds (Rodriguez et al., 2008).

1.2.2 Classification According to the cause

1.2.2.1 Surgical wounds

Are produced by surgeon's hands when performing operation such as laparotomy. (Nabil *et al.*2015).

1.2.2.2 Accidental wounds:

Accidental wound is produced by trauma, mechanical or external violence such as lacerated wound. (Nabil *et al.*2015).

1.3 Wound Healing:

The wound -healing process consists of four highly integrated overlapping phase: homeostasis, inflammation, proliferation, and Tissue remodeling or resolution (Guo and Dipieto, 2010).

1.3.1 Homeostasis:

The first phase of hemostasis begins immediately after wounding, with vascular constriction and fibrin clot formation. The clot and surrounding wound tissue release pro-inflammatory cytokines and growth factors. Once bleeding is controlled, inflammatory cells migrate into the wound and initiate the inflammatory phase (Guo and Dipieto, 2010).

1.3.2 Inflammation:

characterized by the sequential infiltration of neutrophils, macrophages and lymphocytes. In the early wound, macrophages release cytokines that promote the inflammatory response by recruiting and activating additional leukocytes. Macrophages undergo a phenotypic transition to a replicative state that stimulates keratinocytes, fibroblasts, and angiogenesis to complete tissue regeneration (Meszaros *et al.*, 2000; Mosser and Edwards, 2008).

1.3.3 Proliferation:

characterized by epithelial proliferation and migration over the provisional matrix within the wound. Following proliferation and extra cellular matrix synthesis, wound healing enters the final remodeling phase. (Gawronska-Kozak *et al.*, 2006).

1.3.4 Remodeling:

Reunion of many of the newly formed capillaries occurs, so that vascular density of the wound returns to normal. The wound also undergoes physical contraction throughout the entire wound-healing process, which is believed to be mediated by contractile fibroblasts that appear in the wound (Guo and Dipieto, 2010).

1.4 Factors affecting wound healing:

1.4.1 Oxygenation:

Oxygen is important for cell metabolism, especially energy production by means of ATP, and is critical for nearly all wound-healing processes. It prevents wounds from infection, induces angiogenesis, increases keratinocyte differentiation, migration, re-epithelialization, enhances fibroblast proliferation and collagen synthesis, and promotes wound contraction (Bishop, 2008; Rodriguez et al., 2008).

1.4.2 Infections:

Once skin is injured, micro-organisms that are normally sequestered at the skin surface obtain access to the underlying tissues, the state of infection and replication status of the micro-organisms determine whether the wound is classified as contaminated, colonized, locally infected, and/or having spreading invasive infection (Harding and Edwards, 2004).

1.5 Primary and secondary intentions:

Wounds caused by surgery where there is minimal tissue loss heal by primary intention. This means the edges of the wound can be brought together and re-aligned, using sutures, staples or clips (Rodriguez *et al*,2008). Furthermore there are no complications, these wounds tend to heal quickly, with minimal scarring (Rodriguez *et al*,2008). In wounds where there is considerable tissue loss such as ulcers healing occurs through secondary intention by the process of granulation and epithelization (Shipperley and Martin, 2002).

1.6 Honey:

1.6.1 Natural Honey:

Honey is derived from nectar gathered and modified by the honeybee, *Apis mellifera* and it is carbohydrate-rich syrup derived from floral and other plants nectars and secretions (Zumla and Lulat ,1989).

Natural honey contains about 200 substances including amino acids, vitamins, minerals, and enzymes but it is primarily contains sugar and water (Moundoi et al ,2001). The principle sugar constituents of honey are fructose and glucose which represent 85-95% of total sugars are readily absorbed in gastrointestinal tract (Ezzel-arab etal,2006). Honey also contains organic acids which are responsible for the acidity of honey and contribute largely to its characteristic taste variety of (Olaitan et al;2007).A enzymes such oxidase,inevertase,amylase and catalase have an important role in formation of honey (Olaitan et al, 2007).

1.6.2 Use of honey in wound dressing:

Honey has been used in medicine since ancient times and has been rediscovered by medical researchers for its use in dressing acute and chronic wounds, burns and ulcers (Zumula and lulat, 1989).

1.6.3 Antibacterial activity:

It was believed that honey could be used in topical treatment of wounds and burns due to its antibacterial and wound healing promotion activity (Moore etal, 2001). Honey is hygroscopic meaning that it draws moisture out of the environment and dehydrates bacteria with the aid of its high osmolarity (Molan, 2006). It has a mean PH of 4.4, the acidification reduce wound colonization by bacteria and prevent infection (Aureli;2002). Antibacterial activity may also be due to hydrogen peroxide activity which is continuously produced by enzymes even when honey is diluted (Allen et al; 2000). it provides rapid autolytic debridement and wound deodorization (AL-Waili *et al*,2011).

1.6.4 Healing and Anti-inflammatory effects of honey:

Honey can be expected to have a direct nutrient effect on regenerating tissues because it contains a wide range of amino acids, vitamins and trace elements in addition to large quantities of sugars (White 1975). It also stimulates the angiogenesis, granulation and epithelization which helps speed up healing process (Molan, 2006). Honey assist in proliferation of fibroblasts by producing certain growth factors like tumor necrosis factor TNF (Tonks *et al*, 2007).

Molan found that honey has a direct anti-inflammatory property. It reduces edema and exudates, reduces pain caused by pressure on nerve endings and decreases amount of prostaglandin produced in inflammatory process (Simon *et al* ,2009).

1.7 Skin glue

Skin glue are safe and effective but wound selected is important (Farion *et al*, 2009). Wounds should be less than 12 hours old, clean and free of debris (Singer *etal*,2008). Wounds greater than 4cm should not be closed with skin glue alone (Farion *etal*,2009). Skin glue should be used only for superficial approximation of skin, applying of skin glue is painless, wound infective rates are less than 3%(Chow *etal*,2010).

To apply the glue, the skin edges are approximated with fingers of other hands taking care not to include the gloves in the application process, the glue should cover the wound plus about 3-10mm of skin on either side, full strength is achieved after 2-5 minutes (Farion etal, 2009).

Some patients are allergic to the cyanoacrylates or residual formaldehyde (Singer *etal* ,2008). Skin glues are less expensive, however when compared with equipment and costs as well as the need for follow-up for suture removal (Man *etal*,2009).

Studies reported that when using glue, the time of the actual wound repair in all setting was less than formal suturing (Farion *etal*,2009 Singer *etal*,2008 Goktas *etal*,2002 Chow etal,2010 Zempsky *etal*,2004). Sedation which is sometimes used with sutures is not needed with skin glues, also cosmetic appearance with skin glues is more beneficial than that of sutures (Farion *etal*,2009).

CHAPTER TWO

MATERILAS AND METHODES

2.1 Experimental Animals:

Five apparently healthy 4 females, 1 male (hill goats), 1-2 years of age,15-20 kg body weight, Clinically examined to insure their clinical fitness.

2.2 Housing and feeding:

The goats were housed in closed site (5x5m) in kuku zoo in eastern Nile state. These goats were given water and green Alfalfa (*medicago stavia*).

2.3 Materials for surgical procedure:-

- Soap (Dettol antibacterial soap, reckitt and colman {verseas} Ltd. Hull UK).
- Scalpels.
- Scissors.
- Tissue forceps
- lidocaine 2% (lignocaine hydrochloride 50 mg/ml p.p.l Malta)
- Razor.
- Gauze.
- Disposable syringes (5ml)
- Tincture of iodine (povidine iodine 10% USP Yamani medical products, Sudan, Khartoum).
- Cotton.
- Glue (HBIB all-purpose adhesive made in CHINA).
- Honey (natural Sudanese honey).

2.4 Surgical method:

2.4.1 Site of wound:

The lateral aspect of left and right lower thigh muscle of all experimental animals, the wounds on the right side were dressed with honey, where as the wounds on left side were covered with glues making in total 10 wounds on either sides.

All surgical procedures were done with the animal on the standing position.

2.4.2 Preparation:

An area of (2x1cm) was clipped against the pattern of hair growth to obtain a closer clip with sterile scissor (Therasa *et al*,2002).

Then shaved with sterile razor. It was cleaned and scrubbed with mild detergent containing tincture of iodine.

2.4.3 Anesthesia:

Local infiltration anesthesia was achieved by subcutaneous injection of lidocaine (5ml) at the surgical site (Thurmon *et al* ,1996).

2.5 Surgery:

An area of (2x1cm²) was measured using a flexible measuring tape. Using a sterile scalpel and tissue forceps an incision was made to perform an open wound involving all layers of skin (dermis and epidermis). The bleeding from the superficial capillaries was controlled by direct pressure with sterile gauze.

2.6 Dressing:

The right wounds were cleaned with tincture of iodine and covered with honey and left undressed every day on the first week and then day after day on the second one.

The left wounds were covered with glue for 2-3 minutes and left until it dry forming a good seal. Wounds were left without dressing.

The wounds were kept without dressing, nor cleaning or antibiotics to insure the maximum benefits from honey and glue treatment.

2.7 Parameters:

2.7.1 Clinical manifestation:

Visual qualitative observation were used for testing bleeding, swelling, scab thickness and contraction thus could have been converted in to simple quantities scale such as for + slight,++for moderate,+++for sever

2.7.1.1 Pain:

pain was detected by limb withdrawal reflex, according to the method designed by Hellebrckers and Sap(1997). It was considered positive when the animal withdraws limb as a response to the application of digital pressure on the skin around the wound.

2.7.1.2 bleeding:

bleeding was tested by visual qualitative observation (Rocchkind *etal*,1989) immediately after the first application of wounds with both honey and glue.

2.7.1.3 Swelling:

The wounded area was examined for swelling after 24 hours after the incision. Swelling was tested grossly in all experimental animals by visual qualitative observation of the elevation on the area around the wound, it is extending in the adjacent area which was measured by flexible meter (Rocchkind *etal* 1989).

2.7.1.4 Scab thickness:

Scab thickness was examined by visual qualitative observation and all wounded areas were assessed photographically at periodic intervals (Braverman *etal*,2006).

2.7.1.5 Contraction and wound size:

Size of wound was measured to analyze wound contraction as function of healing by using measuring tap (Hopkins *etal*,2004). photographic assessment of wound size also used as described by (Braverman*etal*,2006).

2.7.1.6 Infection:

Wounds were examined grossly for infection by detection of pus in the whole or part of the wounded area (Rocchkind *etal*,1989).

2.8 Data analysis:

Using SPSS (Chi square test) version 18.

2.9 Imaging:

All gross appearance recorded by standard digital photos using digital camera (AIPTEK CHAINA). Digital images were then recorded under the same conditions (distance, lighting, settings) as the original images.

Chapter Three

Results

3.1Cliniopathological manifestation:

3.1.1Pain:

Pain relief was improved in both wounds after first 3 days. Evidence of pain was detected in glue wound after its application (table 1).

3.1.2 Bleeding:

There was marked minimum cutaneous bleeding after application of honey. Bleeding was found to be more in wound No1 and wound No5 at the day of experiment and continued for the next two days (table 3, figure 3).

3.1.3 Swelling:

The effect of honey on the swelling is found in both level and extends of swelling with the time taken for the swelling to be stable or to start to decrease. Honey decreased the swelling in all treated wounds and it extent was decreased within adjacent tissue and confined to the boundaries of the wound (table 4, figure 3).

There was marked swelling on glue No3 and it continued for few days then disappeared (figure 4).

3.1.4 Scab thickness:

Scab formation was affected positively by both honey and glue (table 6). In honey wound No 2 very thin or no scab formation was noticed.

Thin scab is formed at the edges of the wound of honey No3 (figure 8).

There was scab and covered only part of the glue wound No3.it was sloughed by day 15 post wounding.

3.1.5 Contraction and wound size:

Decrease in wound size is obvious after 7 days in all treated groups (table 5).

Honey wound No1 showed irregular margins after 3 days' indicative of contraction.

3.1.6 Infection:

There was no infection in honey treated wounds meanwhile in glue wound No 3 and No 5 there was slight infection detected by presence of pus around wound edge (table 7).

Table 1 :Effect of honey and glue on wound healing

	Pain		Bleeding		Swelling		Contraction		Scab		Infection	
Days	0 – 3		0-3		9 – 16		9 – 16		9 – 16		9 – 16	
Goats	Н	G	Н	G	Н	G	Н	G	Н	G	Н	G
Goat I	+++	+++	+++	+++	++	+	+++	+++	+	++	+	+
Goat II	+	+	+	+	++	+	+	+	+	+	+	+
Goat III	+	+	+	+	+	+++	++	+++	++	++	++	+++
Goat IV	+	+	+	+	++	+	++	++	+	++	+	+
Goat V	+++	+++	+++	+++	+	+	++	+++	+++	++	+	+

H: Honey G: Glue

+: Slight ++: Moderate +++: Sever

Table 2: Effect of honey and glue on pain

Crosstab					
			Pain		Total
			Slight	Sever	
Treatment	Honey	Count	3	2	5
		% within	60.0%	40.0%	100.0%
		Treatment			
		% of Total	30.0%	20.0%	50.0%
	Glue	Count	3	2	5
		% within	60.0%	40.0%	100.0%
		Treatment			
		% of Total	30.0%	20.0%	50.0%
Total		Count	6	4	10
		% within	60.0%	40.0%	100.0%
		Treatment			
		% of Total	60.0%	40.0%	100.0%

Chi-Square Tests			
	Value	Df	Asymp. Sig. (2-
			sided)
Pearson Chi-Square	.000a	1	1.000

Table 3: Effect of honey and glue on bleeding

Crosstab								
				Bleeding		Total		
				Slight Sever				
Treatment	Honey	Count		3	2	5		
		%	within	60.0%	40.0%	100.0%		
		Treatment						
		% of Total		30.0%	20.0%	50.0%		
	Glue	Count		3	2	5		
		%	within	60.0%	40.0%	100.0%		
		Treatment						
		% of Total		30.0%	20.0%	50.0%		
Total		Count		6	4	10		
		%	within	60.0%	40.0%	100.0%		
		Treatment						
		% of Total		60.0%	40.0%	100.0%		

Chi-Square Tests								
		Value	Df	Asymp. Sig.				
				(2-sided)				
Pearson	Chi-	.000a	1	1.000				
Square								

Table 4 Effect of honey and glue on swelling

Crosstab							
				Swelling		Total	
			Slight	Moderat	Sever		
					e		
Treatme	Hone	Count		1	3	1	5
nt	y	% v	within	20.0%	60.0%	20.0%	100.0%
		Treatment					
		% of Total		10.0%	30.0%	10.0%	50.0%
	Glue	Count		4	1	0	5
		% v	within	80.0%	20.0%	0.0%	100.0%
		Treatment					
		% of Total		40.0%	10.0%	0.0%	50.0%
Total		Count		5	4	1	10
		% v	within	50.0%	40.0%	10.0%	100.0%
		Treatment					
		% of Total	_	50.0%	40.0%	10.0%	100.0%

Chi-Square Tests								
		Value	Df	Asymp. Sig.				
				(2-sided)				
Pearson	Chi-	3.800 ^a	2	.150				
Square								

Table 5: Effect of honey and glue on wound contraction

Crosstab							
				Contract	ion		Total
				Slight	Moderat	Sever	
					e		
Treatment	Honey	Count		1	3	1	5
		%	within	20.0%	60.0%	20.0%	100.0%
		Treatme	ent				
		% of To	otal	10.0%	30.0%	10.0%	50.0%
	Glue	Count		1	1	3	5
		%	within	20.0%	20.0%	60.0%	100.0%
		Treatm	ent				
		% of To	otal	10.0%	10.0%	30.0%	50.0%
Total		Count		2	4	4	10
		%	within	20.0%	40.0%	40.0%	100.0%
		Treatment					
		% of Total		20.0%	40.0%	40.0%	100.0%

Chi-Square Tests					
		Value	Df	Asymp. Sig.	
				(2-sided)	
Pearson	Chi-	2.000a	2	.368	
Square					

Table 6: Effect of honey and glue on scab formation

Crosstab							
				Scab			Total
				Slight	Moderate	Sever	
Treatment	Honey	Count		3	1	1	5
		% Treatment	within	60.0%	20.0%	20.0%	100.0%
		% of Total		30.0%	10.0%	10.0%	50.0%
	Glue	Count		1	4	0	5
		% Treatment	within	20.0%	80.0%	0.0%	100.0%
		% of Total		10.0%	40.0%	0.0%	50.0%
Total		Count		4	5	1	10
		% Treatment	within	40.0%	50.0%	10.0%	100.0%
		% of Total		40.0%	50.0%	10.0%	100.0%

Chi-Square Tests						
	Value	Df	Asymp. Sig. (2-sided)			
Pearson Chi-Square	3.800 ^a	2	.150			

Table 7: Effect of honey and glue on infection

Crosstab						
			Infection	Infection		
			Slight	Moderat	Sever	1
				e		
Treatment	Honey	Count	4	1	0	5
		% within	80.0%	20.0%	0.0%	100.0%
		Treatment				
		% of Total	40.0%	10.0%	0.0%	50.0%
	Glue	Count	4	0	1	5
		% within	80.0%	0.0%	20.0%	100.0%
		Treatment				
		% of Total	40.0%	0.0%	10.0%	50.0%
Total		Count	8	1	1	10
		% within	80.0%	10.0%	10.0%	100.0%
		Treatment				
		% of Total	80.0%	10.0%	10.0%	100.0%

Chi-Square Tests					
		Value	Df	Asymp. Sig.	
				Asymp. Sig. (2-sided)	
Pearson	Chi-	2.000a	2	.368	
Square					



Figure 1: Hill goat No five, right full thickness skin wound application of honey, Day zero.



Figure 2: Hill goat No one, left full thickness skin wound application of glue, day zero.



Figure 3: slight swelling and little bleeding in right wound treated by honey of full thickness skin wound in hill goat no. three two days post wounding.



Figure 4: swelling and slight infection in glue wound of full thickness skin wound in hill goat No four, three days post wounding.



Figure 5: formation of thin scab in honey treated wound in Hill goat No five, and it is sloughed by day seventeen post wounding.



Figure 6: formation of thick scab and slight swelling in glue wound of full thickness skin wound in hill goat No four, ten days post wounding.



Figure 7: wound contraction in honey treated wound with thin scab formation in hill goat No three, sixteen days post wounding.



Figure 8: wound contraction with thick scab formation in hill goat No four, sixteen days post wounding.

Chapter four

Discussion

In the present study, relief of pain was detected in all honey groups this agrees with (Yang, 1944) who reported that honey is soothing when applied to wounds and reduce pain from burns and in some instances gave rapid diminution of local pain.

Another effect of honey that has been noted on wounds is that it reduces the inflammation and hastens subsidence of passive hyperemia this explains the minimum cutaneous bleeding in honey-treated group.

Also honey decreases the swelling in all honey-treated wounds because it reduces the edema and exudation by absorbing fluids from the wound this is supported by Wood *et al*, (1997).

Furthermore, the scab size has been found to decrease in honey wounds this finding fits with the study of (Ndayisaba., *et al* 1993) who found that honey promotes the formation of clean healthy granulation tissue allowing early grafting on a clean base; also it has been found that it promotes the epithelization of wounds. It was obvious that the honey enhanced wound healing and wound contraction that was shown by the time taken by the wound to heal and the size of wounds, this clear the fact that it induce rapid growth of new tissue improvement, increase blood flow and free flow of lymph. The same results obtained by (Dumronglert, 1983).further studies were needed to address its effects on lymph and hence the immunological process.

Skin glues are safe and effective method to close certain wounds, in this study there were slight pain in all experimental animals. In a report by Farion *etal*(,2009) showed that about 20% of patient develop sensation of mild heat but no actual pain.

In a different study about 4% of wounds reopen with skin glue compared to 1-2% with suture properly due to combination of poor technique and poor wound selection but most importantly due to breakage of bonds or sloughing from skin surface (Farion *etal*,2009 Singer *etal*,2008).this elucidate the presence of infection and swelling in wound No2,3,4.

In comparing to honey surgical glue does not have any nutritive and antibacterial effects thus wound contraction were delayed in glue treated wounds with longer period of achieving complete healing.

CONCLUSIONS AND RECOMMENDATIONS

The results of the present study indicate that both honey and glue improved full skin wound healing. It is concluded that both honey and glue are effective treatments for enhancing wound healing, contraction and pain relief of full thickness skin wounds.

We recommended using honey as a wound dressing because of the huge economical advantage; the use of antibiotic ceased, savings in the costs of surgery where debridement and skin grafting become unnecessary when honey is used.

More randomized controlled trials with significant statistical power comparing different kinds of honey are required in order to create strong body of evidence to words definite recommendation for medical and veterinary use.

It is recommended that future research should focus on coverage of the spectrum of anti-bacterial effect of natural honey.

Additional studies should be performed to define the specific role, safety, expected benefits and limitation of skin glue to support wound closure.

Better understanding of the utility of natural honey and skin glue in promotion of cutaneous wound healing and well controlled clinical studies that correlate histological effects are needed to formulate meaningful conclusions regarding uses of natural honey and skin glue.

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