

#### ALTERNATIVE MEDICINE

# **Topical Application of Honey in The Treatment of Wound Healing: A Metaanalysis**

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#### Abstract

Honey has been extensively studied in the treatment of wound but efficacy in clinical practice is not fully established. The aim of the present study was to evaluate the efficacy of topical application honey in observational studies as well as in controlled clinical trials in the treatment of wound healing. A systematic literature search was carried out from 1966 to 31 July 2008 in Pubmed, Medline, Embase, Cochrane database using the appropriate search key words. We found 5 observational studies with 160 patients while 963 cases in 10 controlled clinical trials where 511 patients were treated with honey. Efficacy was found highly efficacious in observational studies but in controlled clinical trial showed its modest efficacy. Most of the patients reported with complete healing of 99% within 2-9 weeks in observational and 56% in controlled trials and healing was observed within 4-12 weeks time in controlled clinical trials however some of the recent double blind trial showed no superior benefit of honey compare to control. So base on above trials it can be concluded that topical application of honey is useful for the treatment for wound healing but to fully established its efficacy, larger prospective double blind study is required in near future.

#### Key words

Honey, Wound Healing, Alternative Medicine, Clinical Trial

## Introduction

Honey is a popular sweetener and a common household product throughout the world. It is nonirritant, nontoxic, easily available and cheap (1). It has been used from ancient times as a method of accelerating wound healing (2). During twentieth century, it was reported that honey as having good antimicrobial properties along with therapeutic potential in wound healing. Honey has been studied extensively and found most effective in wound healing, nearly all types of wounds, may be it is, an abrasion, abscess, amputation, burns, fistula, etc. are found to be responsive to honey therapy. Application of honey as wound dressing leads to rapid healing by stimulation of healing process, clearance of infection, cleansing action of wounds, stimulation of tissue regulation, reduction of inflammation and non adhesive tissue dressing (3,4). Several observational studies and controlled clinical trials (1-20) have been conducted so far to established the efficacy of honey in wound healing but the exact molecular mechanism of acceleration of wound healing using honey is yet to be elucidated however, recommendation are made regarding wound dressing with honey.

So, aim of study was to compare the efficacy of topical application of honey in the treatment of wound healing as demonstrated in observational studies and controlled clinical trials.

#### Material and Method

A systematic literature search was carried out from 1966 to 31 July 2008 in Pubmed, Medline, Embase, Cochrane database using the search words honey, wound

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healing, topical therapy, observational study, clinical trial and randomized controlled trial. Reference list of original reports and review articles were looked for finding desired studies. We also manually searched related journals in the National Medical Library (New Delhi), library of the institute and conference abstracts for 2003 to 2008 of international societies of plastic surgery.

#### Inclusion Criteria

We have included observational and randomized controlled clinical trials comparing honey with any standard topical therapy. Studies satisfying the following criteria were selected.

- Studies of open level, parallel group, observational study with honey and patients fail to other therapy for the treatment of wound healing.

- Randomized control clinical trial in treatment of wound, study with at least one arm is randomized to honey treatment.

## **Exclusion** Criteria

- Studies were excluded in case of patients using any other therapies along with topical honey therapy Data Extraction and Outcome Measure

Data was extracted in a specially designed format. The only outcome measure was percentage of wound healing and duration of wound healing at final scheduled follow up.

#### **Statistical Analysis**

From individual studies number of patients in treatment and control group, percentage of final wound healing and duration were obtained.

## **Results**

Out of 127 citations 72 were duplications. We identified 5 observational (Table 1) and 10 randomized controlled clinical trials (Table-2) among relevant publications. Another 14 studies were excluded as per inclusion criteria.

Table 1: Observational Studies of Topical Application of Honey in Wound Healing

S no.	Author	Year	Total patients	Treatment	Group	Remarks	Duration of Healing
1.	Efem et al (6)	1988	59	59	Showed	improvement(99%)	Within 2 weeks
2.	Phuapradit et al (7)	1992	15	15	Comple	te healing in all pts	Within 2 weeks
3.	Vardi et al (8)	1998	9	9	Improve	ement seen in all neon	ates 3 to 6 weeks
4.	Gethin (9)	2008	17	17	Improv	es with Honey	Within 2 weeks
5.	Abdelatif (10)	2008	60	60	Improv	ement in >90%	Within 9 weeks

	Table 2: Controlled Clinical Trials of Topical Application of Honey in Wound Healing									
S N	o. Author	Year	No of patients	Honey	Control	<b>Remarks &amp; Duration of Wound Healing</b>				
1.	Subrahman yam (11)	1991	104	52	52	- Improvement occurred in 87% with honey &10 % control groupComplete healing in 16-30 days				
2.	Subrahmanyam (12)	1994	64	40	24	- Wounds healed between 11 to 30 days				
3.	Subrahmanyam (13)	1998	50	25	25	- Wound healed within 21 days				
4.	Waili et al (14)	1999	50	26	24	- 22 patients showed complete wound healing in between 10-20 days				
5.	Molan (15)	2004	59	47	12	- Improvement occurred in 80% of patients Complete healing within 15 days				
6.	Subrahmanyam (16)	1999	50	25	25	- 92% of the tangential excision patients healed				
7.	McIntosh (17)	2006	100	52	48	<ul> <li>Patients may benefit more from paraffin tulle grass. Healing with honey group within 40.3 &amp; paraffin impregnated tulle grass in 39.98 days</li> </ul>				
8.	Ingle (18)	2006	82	42	40	- 78% of patients were satisfied with honey while 71% in intrasite gel Group. Healing with Honey was in 16.6 days and with Intrasite gel was 16.8 days.				
9.	Yapucu G (19)	2007	36	15	11	<ul> <li>With ethoxy-diaminoacridine plus nitrofurazone) Efficacy with honey was 4 times superior the control Healing with honey was within 5 weeks</li> </ul>				
10.	Jull A (20)	2008	368	187	181	- 56.6% healed in honey group and 49.9% in control in 12 weeks.				



Ten studies fulfilled all the specified criteria (Table 2). All the studies are in English language and published in index journal. Observational studies which included total no of 160 patients, they were treated with honey, was found highly efficacious. The patients reported complete healing within 2-9 weeks time; it indicate 99% patients showed improvement in term of wound healing (Table 1), while in controlled clinical trials improvement was there but the time taken for improvement was from 5 to 30 days with modest efficacy of 56 % of improvement compare to control group duration of healing was ranged from 7 days to 17 months, in controlled clinical trials, total 963 patients were included in 10 randomized controlled clinical trials with honey (total 511 patients were treated with honey) (Table 2). In controls group patients treated with silver sulfadizine, antiseptic, soframycin and acriflavin etc.

## Discussion

It has been for a long time that honey is using to accelerate the wound healing (6). It is an excellent adjuvant for acceleration of wound healing, is widely accepted in folk medicine. The exact molecular mechanism of wound healing using honey is yet to be elucidated. Studies showed that it act by reducing ROS levels, besides this it exert antibacterial activity and low pH and high free acid content may assist wound healing (7). However, several recommendations are made regarding appropriate wound dressing with honey. Type of wound and degree of severity will effect efficacy. Selected honey should be used in sufficient quantities so that it remains there if diluted with wound exudates. It should cover and extend beyond the wound margins. Better results occur when applied on dressing than on wound. All the cavities should be adequately filled with honey and occlusive dressing applied to prevent oozing from the wound (4).

The effect of honey in wound healing is the result of the combined effects of chemical debridement of dead and devitalized tissues from ulcers by catalase, absorption of edema by the hygroscopic properties of honey, the promotion of granulation and epithelization from wound edges, the bactericidal and fungicidal properties of honey, its nutritional properties and the production of hydrogen peroxide (2). Honey comprises 40% glucose, 40% fructose, 20% water, with organic acids, vitamins, enzymes, and minerals; it has specific weight of 1.4 and pH of 3.6 (2,4). The treatment with honey is simple and in expensive, and honey need not to be sterile as it already possesses a bactericidal property (6), because of its high viscosity it forms a physical barrier, creating a moist environment which appears to be helpful and accelerates wound healing1. In observational groups, complete healing was present in this group of patients within two weeks, a good improvement was there in most of the cases, while in case of controlled clinical trials patients reported improvement but the time of improvement varies compare to control groups.

Till date several non comparative studies have been conducted for the use of honey as a wound dressing, there are no report of cross over trial, though only few double blind trials have been conducted since it is difficult because of properties of honey, so there is a need for more number of double blind randomized controlled clinical trial. Most of the earlier randomized studies conducted in the past have not given detail of statistical analysis so meta-analysis cannot be plan to make a conclusive remarks. Some of the important factors are not taken in to consideration in most of the studies is composition of honey, underlying etiology of wound, nutritional status, age of patients and efficacy of honey in wound healing in different anatomical site of body. So the real efficacy of honey only can be established from more number of double blind RCT with adequate number patients of honey in the treatment of wound healing (17). Ingle *et al* (18), reported a prospective, randomized, double-blind study comparing the effect of honey and Intrasite gel. The mean healing times of shallow wounds treated with honey or with Intrasite gel did not differ significantly. When adjusted for wound size, the 2.8-day difference in favour of honey was not significant. In the case of abrasions there was also no significant difference. In conclusion of the study, there was no evidence of a real difference between honey and IntraSite gel as healing agents. Another double blind controlled study with 100 patients was carried out by McIntosh (17), revealed that conventional treatment was superior to topical honey



application in partial avulsion wounds. Similarly Jull *et al* (20) also showed modest efficacy 56.6% with honey treatment and most of the patients reported healing in 12 weeks time.

## Conclusion

From this analysis, we can concluded that application of honey has significant efficacy in treatment of wounds as it demonstrated in observational studies but in controlled clinical studies observed, its modest efficacy, so clinicians and researchers should look for clinical evidence and more randomized double blind trials that will provide the scientific evidence to support the use of honey in wound healing management. So base on above observations it can be concluded that topical application of honey is useful for the treatment for wound healing but to fully established its efficacy larger prospective double blind study is required in near future.

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