

Article Review

SUCRALFATE AND HONEY IN BURN WOUND HEALING: AN ARTICLE REVIEW

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ABSTRACT

Introduction : Several studies stated that sucralfate and honey typically promote wound healing process. Sucralfate has been used for stomatitis, excoriation in perianal and peristomal, ulcers, and burn wounds. Honey as a food which is taken orally, is also used topically for several kind of wounds including burn wounds. However, there is no study reviewing sucralfate and honey in burn wounds.

Method : Literature review was conducted from 1st until 6th of June 2022 using the terms of "honey", "sucralfate", "burns" and "wound healing". Pubmed, Cochrane, Science Direct, Scopus, and Google Scholar were the online data bases we used. We identified eight studies, three trials evaluated the effects of sucralfate in burn wounds and five trials evaluated the effects of honey in burn wounds.

Result : 3 Randomized Controlled Trials (RCTs) (n=170) about the effects of sucralfate and 5 RCTs (n=474) reported the effects of honey in burn wounds. Both Sucralfate and Honey group had similar wound healing duration around 18 days and had early sign of wound healing by day 7. Honey has faster complete wound healing compared to sucralfate by day 21. Honey has remarkable antimicrobial effect within one hour. No side effects were reported in both trials. Both honey and sucralfate reduce the necessity for skin grafting.

Conclusion: Both sucralfate and honey have similar rapid re-epithelization in burn wounds, but honey has faster complete wound healing by day 21. Both has similar antimicrobial effect, no side effects, and reduce the necessity for skin grafting.

Keywords: *Sucralfate; Honey; Burns; Wound Healing*

Latar Belakang: Beberapa studi menyatakan bahwa sucralfate dan madu secara topikal dapat mempercepat proses penyembuhan luka. Sucralfate telah digunakan untuk stomatitis, ekskoriasi pada area perianal dan peristomal, ulkus, serta luka bakar. Madu, yang biasanya dikonsumsi secara oral, juga digunakan secara topikal untuk berbagai jenis luka termasuk luka bakar. Namun, belum ada studi yang mengulas penggunaan sucralfate dan madu dalam mengatasi luka bakar.

Metodologi: Tinjauan literatur dilakukan dari tanggal 1 hingga 6 Juni 2022 menggunakan istilah "madu", "sucralfate", "luka bakar", dan "penyembuhan luka". Kami menggunakan basis data online seperti PubMed, Cochrane, ScienceDirect, Scopus, dan Google Scholar. Kami mengidentifikasi delapan studi, di mana tiga uji coba mengevaluasi efek sucralfate pada luka bakar dan lima uji coba mengevaluasi efek madu pada luka bakar.

Hasil: Tiga RCTs dengan total 170 peserta membahas efek sucralfate, sedangkan lima RCTs dengan total 474 peserta melaporkan efek madu pada luka bakar. Baik kelompok sucralfate maupun madu menunjukkan durasi penyembuhan luka yang serupa sekitar 18 hari dan menunjukkan tanda-tanda penyembuhan luka awal pada hari ke-7. Madu menunjukkan penyembuhan luka yang lebih cepat dibandingkan sucralfate pada hari ke-21. Madu memiliki efek antimikroba yang signifikan dalam waktu satu jam. Tidak ada efek samping yang dilaporkan dalam kedua uji coba tersebut. Baik madu maupun sucralfate mengurangi kebutuhan untuk cangkok kulit.

Kesimpulan: Baik sucralfate maupun madu memiliki re-epitelisasi yang cepat dan serupa pada luka bakar, namun madu menunjukkan penyembuhan luka yang lebih cepat pada hari ke-21. Keduanya memiliki efek antimikroba yang serupa, tidak ada efek samping yang dilaporkan, dan mengurangi kebutuhan untuk cangkok kulit.

Kata Kunci: *Sucralfate; Madu; Luka Bakar; Penyembuhan Luka*

Conflicts of Interest Statement:

The author(s) listed in this manuscript declare the absence of any conflict of interest on the subject matter or materials discussed.

Received: 19-02-2024, Revised: 01-03-2024, Accepted: 26-06-2024

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INTRODUCTION

Various types of dressings and topical therapy have been used for burn injuries. Several studies stated that sucralfate and honey topically promote wound healing process in burn wounds. Sucralfate is an aluminium salt of sucrose octa sulphate which is orally taken as a mucoprotective agent for gastrointestinal diseases.¹ Sucralfate is beneficial for skin protection and wound repair by accelerating cell proliferation leading to thickening of the epidermis and dermis.¹ Recent trials also observed about the anti-inflammatory, bacteriostatic, and pain relief of Sucralfate by binding to bFGF (basic Fibroblast Growth Factor).¹ Topical sucralfate has been used for stomatitis, excoriation in perianal and peristomal, wound ulcers, even burn wounds.¹ On the other hand, honey is also known as a treatment option for burn wounds.² Honey is a sweet food substance produced by bees from sugar secretion of plants or insects.³ Honey as a food which is taken orally, is also used topically for several kind of wounds.² Honey facilitates wound healing by its anti-inflammatory action and its ability to create a viscous barrier as anti-bacterial agent.² High osmolarity topical agent has been considered a valuable option in the treatment of infections, specifically burn wounds.⁴ High osmolarity topical agent prevents the growth of bacteria and encourages wound healing, which can be achieved topically by honey.⁴ Honey is proven having specific antibacterial properties where its osmolality ceased to be completely inhibitory to prevent the growth of *Staphylococcus aureus*.⁴ Several studies stated that in burn wounds, honey promotes re-epithelialization and complete wound healing.² However, there is no study reviewing between sucralfate and honey in burn wound healing.

METHOD

This article will review between sucralfate and honey in burn wound healing. Literature review was conducted from 1st until 6th of June 2022 using the terms of "honey", "sucralfate", "burns" and "wound healing". Pubmed, Cochrane, Science Direct, Scopus, and Google Scholar were the online data bases we used. This article qualitatively summarize the effect of sucralfate and honey in burn wounds healing.

RESULTS

The articles were divided into two groups, the effects of sucralfate in burn wounds and the effects of honey in burn wounds. We identified eight studies in total, three trials evaluated the effects of sucralfate in burn wounds and five trials evaluated the effects of honey in burn wounds.

From **Table 1**, we conclude that most of the patient population of the trials were superficial partial thickness of burns with less than 50% TBSA, only few patients with full thickness of burns were included. Godhi, A., et al⁶ is the only study that mentioned scald and thermal as their etiology of burns, while other studies did not mention their burn etiology. Banati, A., et al⁵ and Koshariya et al⁷ included pediatric patients as their patient population, while Godhi, A., et al⁶ only included adult patients. This means that there is a risk of bias in patient characteristics due to wide age range and unknown etiology of burns explained in two studies.

The intervention applied between studies were similar using sucralfate cream as dressings, but the control group were different in each studies. Banati A., et al⁵ used antimicrobial cream in the control group, while Godhi, A. et al⁶ and Koshariya et al⁷ used SSD (Silver sulfadiazine) cream as their control treatment. All studies changed the wounds dressings daily and regularly observed the outcome of the wounds.

All studies concluded that rate of re-epithelialization and wound healing is significantly faster in Sucralfate group compared to other control treatment group.^{5,6,7} Banati A., et al⁵ reported that rate of re-epithelialization was faster in 18.8 days compared to control group. Both superficial partial thickness of burns and full thickness of burns were having rapid re-epithelialization in sucralfate group compare to other treatment group.⁵ The incidence of secondary infection was also less frequently found in Sucralfate group compared to other control treatment group.⁷ There were also no side effects of Sucralfate reported in the trials, such as aluminium in blood samples, local or systemic adverse reaction.^{5,7}

From **Table 2**, we can conclude that all patients of the trials were superficial partial thickness of burns with less than 50% TBSA. There was no full thickness of burns included in

these studies. Subrahmanyam et al⁸ (1997) and Subrahmanyam et al⁹ (1991) mentioned thermal injuries as their burn etiology, but the rest of the studies did not mentioned their burn etiology. All studies except Malik et al¹² included pediatric patients as their patient population, while Malik et al¹² only included adult patients. This means that there is a risk of bias in patient characteristics due to wide age range between Malik et al¹² study and the other studies.

All of the the intervention applied between studies were similar using pure, unprocessed, undiluted honey as wound dressings, except Malik et al¹² using 'Langnese' as their

commercially natural honey. The control group were also different in each studies. All studies using SSD cream as their control treatment, except for Subrahmanyam et al¹⁰ (1993) using polyurethane film OpsiteR as their control treatment. The dressings change was varies between studies following a risk of bias in different duration of dressing change and follow up.

Table 1. The effects of sucralfate in burn wounds

Author(s)	Patient Population	Age Range	Intervention	Dressings Evaluation	Outcome
Banati, A. et al ⁵ (2000)	60 patients with less than 50% TBSA, 41 patients had superficial partial thickness burns and 19 patients had full thickness burns	9 months - 63 years old	Phase I: 30 patients treated with sucralfate cream and the other 30 patients treated with antimicrobial cream Phase II: Double blind trial with 25 patients of Sucralfate group treated with sucralfate cream in one site and placebo in another site	Changed daily, swab culture was taken twice a week	<ul style="list-style-type: none"> In phase I, the rate of re-epithelization of superficial partial thickness of burns in Sucralfate group was faster (18.8 days) compared with antimicrobial group (24.6 days) (P value < 0.00001). In full thickness burns, healthy granulation formed at 16.3 days in Sucralfate group compared with antimicrobial group (22.9 days) (P value = 0.0002). In phase II, healing site treated with Sucralfate was faster than healing site treated with placebo (P value = 0.00067). Histopathology result shows that Sucralfate cream promotes rapid epithelialization in superficial partial thickness of burns with minimal side effects. None of the 10 patients showed any detectable amount of aluminium in blood samples.
Godhi, A. S. et al ⁶ (2017)	60 patients with thermal and scald superficial partial thickness of burns less than 50% TBSA	Adult patients (>18 years old)	30 patients treated with topical sucralfate dressing and the other 30 patients treated with 1% SSD dressing	Changed daily for maximum 21 days	<ul style="list-style-type: none"> A total of 15 (50%) patients in sucralfate group had faster wound healing within 7 days, compared with SSD group, 17 (56.67%) patients healed between 15 and 20 days (P value = 0.149). The mean day of granulation was 8.11 ± 3.92 days in sucralfate group, faster than SSD (8.93 ± 3.29 days, P value = 0.396). The wound culture on day 1,7, and 14 did not differ significantly in both groups (P value > 0.050).
Koshariya et al ⁷ (2018)	50 patients with less than 50% TBSA, 45 patients with superficial partial thickness of burns and 5 patients with full thickness of burns	Adult and paediatric patients (>12 years old)	25 patients treated with sucralfate and the other 25 patients had bilaterally symmetrical wounds that were treated with Sucralfate in one site and the other site treated with SSD	Not mentioned in the article, only stated that the wounds were regularly reviewed	<ul style="list-style-type: none"> Rate of re-epithelialization was faster in Sucralfate group (11-22 days) compared to SSD group (15-30 days). By the end of the 3rd week, 50-75% of wound was healed in sucralfate group compared to 35-50% in SSD group. The incidence of secondary infection was less frequently found in sucralfate group (25%) than in SSD group (66.66%). There were no local or systemic adverse reactions to the topical application of sucralfate.

Table 2. The effects of honey in burn wounds

Author(s)	Patient Population	Age Range	Intervention	Dressings Evaluation	Outcome
Subrahmanyam et al ⁸ (1997)	50 patients with superficial partial thermal burns less than 40% TBSA	3 – 60 years old	25 patients treated with pure, unprocessed, undiluted honey and the other 25 patients treated SSD impregnated gauze	Changed every two days until healed. Biopsies were collected on days 7 and 21	<ul style="list-style-type: none"> In honey treated patients, all the wounds healed by day 21 (100%) and in the SSD treated group in 21 patients (84%) (P value < 0.001). Granulation tissue was formed in 21 patients in honey group compared to 18 patients in SSD group by day 7. Honey-treated patients had less positive swab culture for bacteria in one patient compared to SSD treated group had three positive swab cultures in day 21. All honey treated patients healed completely and did not need skin grafting compared to four patients in SSD group that required skin grafting.
Subrahmanyam et al ⁹ (1991)	104 patients with superficial thermal burns with less than 40% TBSA	1 – 65 years old	52 patients treated with pure, unprocessed, undiluted honey and the other 52 patients treated with SSD impregnated gauze	Changed daily and swabs taken on day 7 and 21	<ul style="list-style-type: none"> Healthy granulation tissue was observed earlier in honey treated patients (7.4 days vs 13.4 days). In honey treated group, 87% patients healed within 15 days vs 10% in the control group. The time taken for wound healing differed significantly between the groups (P value < 0.001). In honey group, 91% of wounds were rendered sterile compared to SSD group 7% of wounds rendered sterile within 7 days.
Subrahmanyam et al ¹⁰ (1993)	92 patients with partial thickness of burns less than 40% TBSA	3 – 65 years old	46 patients treated with (unprocessed undiluted) honey impregnated gauze and 46 patients treated with polyurethane film Opsite ^R	In honey group, the dressing changed on day 2 and repeated on alternate days until the wound healed. In polyurethane group, the dressings were removed on day 8	<ul style="list-style-type: none"> Signs of healing earlier shown in Honey group compared to polyurethane group (mean 10.8 days vs 15.3 days) (P value < 0.001). In honey group, 38 cases were sterile and 8 were infected at the end of day 8, compared to polyurethane group, 29 remained sterile and infection was found in 17 cases.
Baghel et al ¹¹ (2009)	78 patients with superficial partial thickness of burns less than 50% TBSA	10 – 50 years old	37 patients in honey group and 41 patients in SSD group	Changed every third and seventh day and on the day of completion of study	<ul style="list-style-type: none"> Honey group has faster average duration of healing compared to SSD group (18.16 days and 32.68 days) (P value = 0.05). Wound of all honey group patients reported within 1 hour became sterile compared to none with SSD (P value = 0.01).
Malik et al ¹² (2010)	150 patients with partial thickness of burns less than 50% TBSA	Adult patients (>18 years old)	One site was treated with SSD cream and the other site of the same patient was treated with commercially natural honey 'Langnese'	The dressing was applied twice daily until the burn wounds were fully healed and epithelialized	<ul style="list-style-type: none"> The mean duration of healing was significantly faster in the sites treated with honey than in the sites treated with SSD (13.47 ± 4.06 versus 15.62 ± 4.40 days, P< 0.0001). The site treated with honey healed completely faster in less than 21 days vs 24 days for the site treated with SSD. In honey group, six patients had positive culture for <i>Pseudomonas aeruginosa</i>, whereas 27 patients had positive culture in SSD group. In honey group, eight patients required skin grafting, whereas 29 patients in SSD group were grafted.

All studies reported that wound healing is significantly faster in Honey group compared to other control treatment group.⁸⁻¹² Subrahmanyam et al⁸ (1997) reported that granulation formed by day 7 and the burn wounds completely healed in day 21 in Honey group. Subrahmanyam et al⁹ (1991) reported that

healthy granulation tissue found earlier in honey treated patients and all wounds healed by day 21. The time taken for wound healing differed significantly between honey and control group (P value < 0.001)⁹. Subrahmanyam et al¹⁰, Baghel et al¹¹, and Malik et al¹² also reported that honey treated patient healed significantly faster than

patients in control group. All honey treated patients healed completely and did not need skin grafting in Subrahmanyam et al⁸ (1997) study and less patients needed skin grafting in Honey group (8 vs 27 patients) in Malik et al¹² study. Honey treated patients also had less positive swab culture compared to each control group in all studies⁸⁻¹². The side effects of honey was not mentioned in the trials, local nor systemic adverse reaction.

DISCUSSION

Patient Population

There are eight high quality evidences including 3 RCTs (n=170) reported the effects of sucralfate in burn wounds and 5 RCTs (n=474) reported the effects of honey in burn wounds. Most of the patient population of the trials were superficial partial thickness of burns with less than 50% TBSA, only few patients with full thickness of burns were included in Sucralfate trials. None of Honey trials included full thickness of burns in their study. Most mentioned burn etiology in the trials were thermal injuries and most trials included pediatric and adult patients as their patient population, except for Godhi A., et al⁶ and Malik et al¹² only included adult patients. Heterogenous of patient populations, burn etiology, patient's comorbid between studies are the bias factor that may affect the result of this study.

The form of the dressings and follow up

We should take a note that form of the dressing also takes a role in burn wound healing. The topical treatment applied between studies were similar using sucralfate cream as dressings in Sucralfate trials and pure, unprocessed, undiluted honey as dressings in Honey trials. Only one study, Malik et al¹², using 'Langnese' as their commercially natural honey. The dressings changed daily in all of the Sucralfate trials, but varies between Honey trials following a risk of bias in different duration of dressing change and monitoring.

The effects of Sucralfate and Honey in Burn Wounds

The effects of Sucralfate and Honey that we discuss in this study are about the rate of re-epithelialization of the wound, complete wound healing, the antimicrobial, the side effects, and the necessity for skin grafting after the application of the topical treatment.

Regarding rate of re-epithelialization, Banati A., et al⁵ reported that rate of re-epithelialization was faster in Sucralfate group in 18.8 days and Godhi, A., et al⁶ reported that 50% of patients in Sucralfate group healed faster within 7 days. On the other hand, Baghel et al¹⁰ reported that Honey group has faster average duration of healing in 18.16 days and Subrahmanyam et al⁸ (1997) reported that granulation formed by day 7. Both Sucralfate and Honey group had similar wound healing duration around 18 days and had early sign of wound healing by day 7. Both Sucralfate and Honey had similar duration of wound healing around 18 days and reported to have early sign of wound healing by day 7. Kosyariya et al⁷ also reported early rate of re-epithelialization in Sucralfate group in 11-12 days while Malik et al¹² also reported duration of healing in Honey group in 13.47 ± 4.06 days (P value < 0.0001).

In Sucralfate trials, both superficial partial thickness of burns and full thickness of burns were having rapid re-epithelialization.⁵ Full thickness burn patients were not included in all of honey trials, so there were no evidences about the effect of Honey in full thickness burns.

Regarding complete wound healing, Kosyariya et al⁷ reported that by the end of the 3rd week, 50-75% of wound was healed in sucralfate group while Subrahmanyam et al⁹ (1991) reported that all wounds healed by day 21 in Honey group. This means that honey has faster complete wound healing compared to sucralfate group only had 50-75% wound healed by day 21.

Regarding antimicrobial effects, the incidence of secondary infection was also less frequently found in Sucralfate group.⁷ Honey treated patients also had less positive swab culture compared to each control group in all studies⁸⁻¹². Both sucralfate and honey have similar antimicrobial effects to the wounds. But, Baghel et al¹¹ reported that wound of all honey group patients reported within 1 hour became sterile (P value = 0.01). This is remarkably fast for the wound to become sterile within one hour.

Regarding its side effects, there were also no side effects of Sucralfate reported in the trials, such as aluminium in blood samples, local or systemic adverse reaction.^{5,7} The side effects of honey also did not mentioned in the trials, local nor systemic adverse reaction.

All honey treated patients healed completely and did not need skin grafting in Subrahmanyam et al⁸ (1997) study and less patients needed skin grafting in Honey group (8 vs 27 patients) in

Malik et al¹² study. In sucralfate trials, the need of skin grafting did not mention in the trials assuming that all of the patients in sucralfate group did not need skin grafting after the application of sucralfate. Both of Honey and Sucralfate reduce the necessity for skin grafting after the application of the topical treatment.

CONCLUSION

Both sucralfate and honey have similar rapid re-epithelization in burn wound healing, but honey has faster complete wound healing by day 21. Honey and Sucralfate have similar antimicrobial effect, no side effects, and reduce the necessity for skin grafting after the application of the topical treatment.

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