Clinical Research

Natural remedies in burn care: a systematic review and network meta-analysis

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ABSTRACT

BACKGROUND Burn injuries are a global public health issue that impact healing time and cause complications. While silver sulfadiazine (SSD) cream is commonly used for treatment, research indicates that SSD can hinder the wound healing process. Natural alternatives like *Aloe vera*, honey, and amniotic membranes have shown promise in promoting wound healing. This study aimed to evaluate their efficacy by their wound healing time and infection rate.

METHODS 3 independent reviewers conducted a literature search across 6 databases (Cochrane Central Register of Controlled Trials, PubMed, ScienceDirect, Taylor & Francis, Wiley, and ProQuest). Quality assessment was conducted using the Cochrane Risk of Bias 2 tool, while network meta-analysis was performed using the netmeta package in R. The variable in this study is the average time to burn wound healing and infection occurrence by analyzing MD data or OR of each intervention, with 95% CI to calculate the efficacy.

RESULTS A total of 3,434 patients from 37 studies were included. In the analysis of 26 studies comparing the healing time to SSD, *A. vera* has the best efficacy (MD: −4.75; 95% CI: −8.67 to −0.86), followed by amniotic membrane (MD: −4.71; 95% CI: −7.45 to −1.97), and honey (MD: −4.25; 95% CI: −6.76 to −1.73). Meanwhile, the occurrence of infection analysis in burn wounds across 24 studies highlighted that honey has the lowest infection rate (OR: 0.09; 95% CI: 0.04 to 0.23) and was the only statistically significant finding when compared to SSD.

CONCLUSIONS *Aloe vera* and amniotic membrane are effective for wound healing, while honey is particularly effective in preventing wound infection in patients with burn injuries.

KEYWORDS *Aloe vera*, amniotic membrane, burns, honey, silver sulfadiazine

Burn injuries pose a major public health concern, especially in low- and middle-income countries, with higher rates in Africa and Southeast Asia. They are classified as first-, second-, or third-degree.[1,2] Abnormal scarring from burns may result from factors such as burn severity, affected surface area, healing time, skin type, burn location, and wound healing process. The primary topical antimicrobial for burn injuries is 1% silver sulfadiazine (SSD) cream, which can cause delayed healing, resistance, renal toxicity, and leukopenia.[3] Studies confirm that prolonged SSD cream use on large wounds should be avoided.[4]

Aloe vera is widely used topically for various skin conditions, as it inhibits thromboxane, reduces inflammation, and promotes healing.[5,6] Honey, rich in beneficial compounds, offers antibacterial, anti-inflammatory, immune-boosting, and wound-healing properties, with its composition depending on the nectar source.[7,8] These effects result from honey's acidic pH and high sugar content, which causes

osmotic effects, hydrogen peroxide production, and bioactive compounds.[9] The human amniotic membrane's antibacterial properties arise from antimicrobial peptides (AMPs) secreted by its cells.[10,11] AMPs like α- and β-defensins exhibit antibacterial, antiviral, and antifungal effects. Antimicrobial agents in amniotic fluid, including transferrin, lysozyme, IgA, globulin β1C/β1A, 7S immunoglobulin, and peptides such as α-defensins and calprotectin, also enhance its antimicrobial properties.[12] Side effects of SSD in patients with burns are well-documented, with common issues like leukopenia, itching, rashes, and skin discoloration (1–10% of patients). Severe side effects include anaphylaxis, Stevens-Johnson syndrome, toxic epidermal necrolysis, kidney failure, and liver toxicity.[3,13]

In Indonesia, honey is more accessible and affordable than SSD, with local honey priced around 25,000–40,000 IDR per bottle, depending on quality and source. In contrast, SSD requires a prescription or must be bought from pharmacies, making it harder to obtain, especially in rural areas with limited medical supplies. Its high cost as a regulated medication also makes it less affordable.[14,15] In Indonesia, *A. vera* products are widely available online and in retail shops, while SSD, a regulated medication, requires a prescription, limiting its accessibility outside urban centers and specialized healthcare institutions.[16] Onion extracts, like Mederma, are more accessible than SSD and commonly used for wound healing and scar reduction, available in traditional and retail stores.[17]

While SSD is widely available, amniotic membrane is mainly limited to specialized medical settings, with increasing studies on its preparation and use in wound healing. Amniotic membrane use in hospitals and research highlights its specialized medical availability. This study aimed to evaluate the effectiveness of *A. vera*, honey, and amniotic membrane *versus* SSD for superficial and partial-thickness burns, focusing on healing time, wound sterility, and infection rates. Secondary outcomes included a network meta-analysis of how these dressings performed compared to SSD. This review may inspire further research, promoting broader use of natural remedies as a wound dressing.

METHODS

This systematic review and network meta-analysis adhered to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines with network meta-analysis.[18] Disagreements were resolved through discussion.

Search strategy and eligibility criteria

Inclusion and exclusion criteria were set before the search to ensure specificity. Inclusion criteria covered human trials, peer-reviewed publications, and comparative studies of burn wound interventions. Exclusion criteria excluded non-human trials, non-burn wound studies, and gray literature. No language restrictions were applied.

The literature search was conducted from February 27 to April 29, 2024, by three reviewers (MAI, KT, and GSW) across six databases: Cochrane Central Register of Controlled Trials, PubMed, ScienceDirect, Taylor & Francis, Wiley, and ProQuest. Key search terms were ("silicone gel" OR "silicone wax" OR "silicone elastomer") AND ("onion extract" OR "Allium Cepa") AND ("Burn" OR "Burn management" OR "Burn care" OR "Burn treatment"). A full search strategy report is available. Results were screened for duplicates, followed by title and abstract reviews. Selected studies were then evaluated using inclusion and exclusion criteria before data extraction.

Data extraction and outcome of interest

Three reviewers (MAI, KT, and GSW) extracted data using a spreadsheet (Microsoft Excel V.16; Microsoft, USA). Discussions were held with the supervisor (YS) regarding unclear data. Extracted information included author, study design, location, injury severity, treatment, and comparative data.

The primary outcomes extracted were average healing time and the percentage of wounds achieving sterility. These metrics, commonly used as primary outcomes in randomized controlled trials, assessed the efficacy of *A. vera*, honey, and amniotic membrane compared to SSD.

Assessment of quality and inconsistency

The three reviewers verified all included studies and assessed potential bias using the Cochrane Risk of Bias 2 tool.[19] The tool evaluates five domains: outcome measurement, treatment variations, missing data, randomization method, and reported result selection.

The domains were rated as low, moderate, or high risk of bias to assess study quality. Local and global

consistencies were evaluated using a loop-specific approach, with local inconsistency assessed through indirect and direct evidence methods.[20] Inconsistencies were shown using a net heat plot, where red elements indicate evidence inconsistencies and blue elements indicate consistency.

Data analysis

Quantitative analysis was performed using the Netmeta package in R version 3.0.0 (R software, USA).[21] Dichotomous outcomes were estimated using odds ratios (ORs) with 95% confidence intervals (CIs), while mean differences (MDs) were used for continuous data. Statistical heterogeneity in pairwise and network meta-analysis comparisons was expressed using I^2 and t^2. Cochran's Q statistics assessed heterogeneity across studies and indirect comparisons. Higgins' I^2 calculation classified the score as insubstantial (0–25%), low (25–50%), moderate (50–75%), or high (75–100%).[22]

Treatments were ranked using the surface under the cumulative ranking curve and P-score. Results are shown in forest plots for all studies and for high- and middle-low-income studies. Connections between analyzed triages are displayed in a network graph using R.

RESULTS

Study selection and characteristics

The search of six databases yielded 286 papers from the last 10 years (Figure 1). After a full-text review, 231 studies were excluded due to comorbidities or unrelated interventions. After data extraction, 37 studies were deemed suitable for quantitative analysis.[10,23–58] The characteristics and

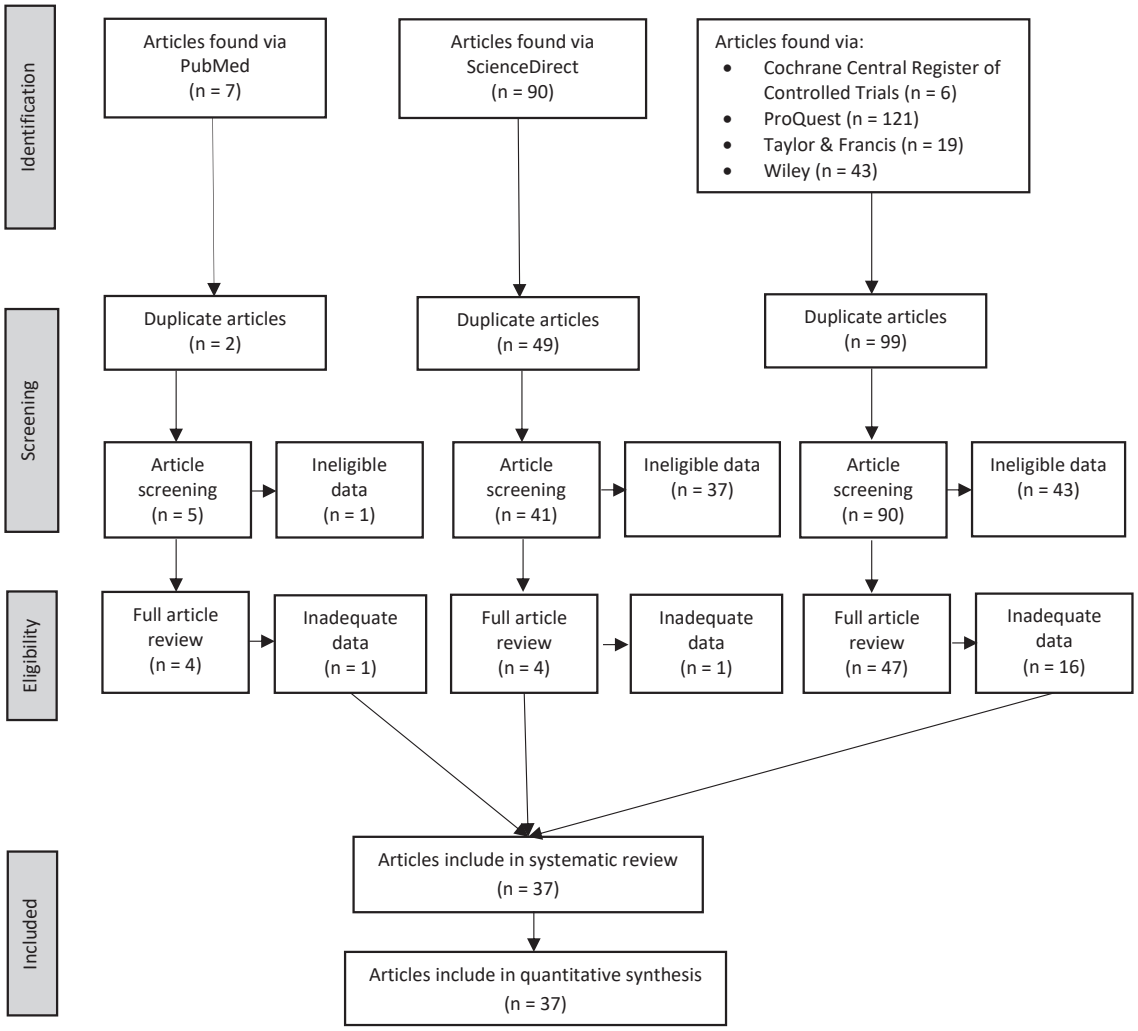

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart of literature search

Table 1. Summary of studies

First author, year	Study design	Country	Wound degree	Treatment used	Sample (n)	Endpoint		
						Healing duration (days), mean (SD)	Infected wound rate	
							Event	Total sample
Amnion								
Sharma,[24] 1985	Controlled trial	India	2nd degree	SSD	5	NA	5	5
				Amniotic membrane	5		0	5
Subrahmanyam,[45] 1994	RCT	India	Partial skin thickness	Honey	28	24.0 (9.40)	4	28
				Amniotic membrane	19	17.5 (9.08)	11	19
Andonovska,[40] 2008	RCT	Macedonia	Dermal & subdermal wound	SSD	30	NA	16	30
				Amniotic membrane	30		9	30
Branski,[46] 2008	RCT	USA	Partial skin thickness	Antibiotic	49	8.0 (2.00)	2	49
				Facial amnion + antibiotic	53	6.0 (2.00)	1	53
Mohammadi,[41] 2009	RCT	Iran	2nd & 3rd degree	SSD	107	14.3 (2.60)	NA	
				Amniotic membrane	104	9.5 (2.13)		
Mohammadi,[47] 2009	RCT	Iran	2nd & 3rd degree	SSD	61	30.5 (8.59)	40	61
				Amniotic membrane	63	20.7 (5.00)	30	63
Adly,[10] 2010	RCT	Egypt	2nd & 3rd degree	Polyurethane membrane	23	16.1 (6.69)	3	23
				Amniotic membrane	23	11.9 (6.08)	1	23
Mostaque,[42] 2011	RCT	Bangladesh	2nd degree	SSD	51	13.4 (5.13)	NA	
				Amniotic membrane	51	10.7 (6.08)		
Mohammadi,[48] 2013	RCT	Iran	2nd & 3rd degree	Skin graft	54	13.9 (1.66)	NA	
				Skin graft + amniotic membrane	54	7.0 (1.35)		
Eskandarlou,[43] 2016	Controlled trial	Iran	NA	SSD	32	NA	0	32
				Amniotic membrane	32		2	32
Soleimani,[44] 2022	RCT	Iran	2nd degree	SSD	33	4.4 (2.94)	0	33
				Amniotic membrane	33	2.9 (1.18)	1	33
Moghimi,[49] 2023	RCT	Iran	2nd degree	SSD	25	21.2 (3.45)	NA	
				Amniotic membrane	25	17.6 (2.56)		
Firos KA,[51] 2020	RCT	India	1st & 2nd degree	SSD	34	21.6 (4.40)	NA	
				Amniotic membrane	36	14.5 (3.50)		
C,[52] 2021	Clinical trial	India	Partial thickness burn	Collagen sheet	50	24.2 (4.00)	32	50
				Amniotic membrane	50	19.9 (4.04)	19	50
Dhanaraj,[53] 2013	RCT	India	1st & 2nd degree	SSD	47	NA	14	47
				Amniotic membrane	47		20	47

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Table 1. (Continued)

First author, year	Study design	Country	Wound degree	Treatment used	Sample (n)	Endpoint		
						Healing duration (days), mean (SD)	Infected wound rate	
							Event	Total sample
Honey								
Bangroo,[32] 2005	RCT	Delhi, India	Superficial thermal burns	SSD	32	12.8	NA	
				Honey	32	6.7		
Baghel,[56] 2009	RCT	Indore, India	1st & 2nd degree <50% TBSA	SSD	41	32.6	NA	
				Honey	37	18.1		
Bagheri,[25] 2017	RCT	Tehran, Iran	Superficial secondary degree burns	SSD	12	5.5 (2.38)	0	12
				Honey	17	6.4 (3.24)	0	17
Malik,[50] 2010	RCT	Wah Cantt, Pakistan	Superficial & partial thickness burns <40% body surface	SSD	150	15.6 (4.40)	27	150
				Honey	150	13.5 (4.06)	6	150
Memon,[54] 2005	RCT	Pakistan	Superficial & mid dermal burn injuries	SSD	40	20.0 (20.00)	32	40
				Honey	40	15.3 (0)	0	40
Subrahmanyam,[27] 1991	RCT	India	Superficial thermal burns	SSD	52	17.2 (0)	38	52
				Honey	52	9.4 (2.30)	4	52
Subrahmanyam,[55] 1998	RCT	India	Partial thickness burns	SSD	25	8.2 (8.30)	5	25
				Honey	25	4.9 (3.60)	0	25
Subrahmanyam,[35] 2001	RCT	India	Thermal injury <40% TBSA	SSD	50	17.2 (4.30)	42	50
				Honey	50	15.4 (3.20)	4	50
Gümüş,[28] 2017	Experimental	Turkiye	2nd degree burn	Antibiotic	33	14.4 (7.79)	2	33
				Honey	31	8.2 (3.05)	0	31
Gupta,[29] 2011	Retrospective	India	1st & 2nd degree burn	SSD	57	32.6 (3.60)	NA	
				Honey	51	18.1 (2.30)		
Honeypalsinh H ,[30] 2019	Cross-sectional	India	Chronic wound, infected, or burns	SSD	20	16.0 (5.78)	NA	
				Honey	20	12.5 (4.15)		
Liche,[31] 2018	RCT	Zambia	Partial superficial burn, children under 12 less than 20% TBSA	SSD	32	15.2 (5.92)	NA	
				Honey	32	11.4 (3.95)		
Okeniyi,[33] 2005	Clinical trial	India	Partial thickness burn	SSD	12	18.6 (2.08)	NA	
				Honey	15	14.2 (4.58)		
Maghsoudi,[34] 2011	RCT	Iran	Superficial thermal burn	Mafenide acetate	50	32.3 (2.00)	10	50
				Pure unprocessed honey	50	22.0 (1.20)	0	50

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Table 1. (Continued)

First author, year	Study design	Country	Wound degree	Treatment used	Sample (n)	Endpoint		
						Healing duration (days), mean (SD)	Infected wound rate	
							Event	Total sample
				Mafenide acetate	20		19	20
Zahmatkesh,[36] 2015	RCT	Iran	2nd degree burn	Olea ointment contains 33.4% honey, 33.3% olive oil, and 33.3% sesame oil	10	NA	1	10
Sami,[26] 2011	RCT	Pakistan	5–40% TBSA burn	1% SSD cream	25	NA	6	25
				Honey	25		5	25
Aloe vera								
Muangman,[57] 2016	RCT	Salaya, Thailand	2nd degree burn	Impregnated gauze with soft paraffin containing 0.5% chlorhexidine acetate	18	20.1 (2.51)	NA	
				Herbal extract dressing containing *Aloe vera* and *Centella asiatica* combined with lipidocolloid dressing	17	18.5 (1.66)		
Shahzad,[37] 2013	RCT	Multan, Pakistan	2nd degree burns	1% SSD cream	25	24.2 (11.20)	4	25
				Aloe vera gel	25	11.0 (4.18)	3	25
Khorasani,[38] 2009	RCT	Mazandaran, Iran	2nd degree burns	1% SSD cream	30	18.7 (2.65)	0	30
				Aloe vera cream	30	15.9 (2.00)	0	30
Ullah,[58] 2022	RCT	Dhaka, Bangladesh	Superficial burn	1% SSD cream	20	8.3 (2.40)	2	20
				Aloe vera gel	20	5.2 (1.56)	1	20
Akhtar,[59] 1996	RCT	Nagpur, India	2nd degree burns	Framycetin cream every 3 days	50	30.9 (0)	NA	
				Aloe vera cream	50	18.0 (0)		
Panahi,[39] 2012	RCT	Tehran, Iran	2nd degree burns	1% SSD cream	55	NA	0	55
				Herbal combination cream containing *Aloe vera* gel and essential oils of *Lavandula stoechas* and *Pelargonium roseum*	56		1	56

NA=not available; RCT=randomized controlled trial; SD=standard deviation; SSD=silver sulphadiazine; TBSA=total body surface area

summary of these 37 studies are shown in the table (Table 1).

Average time to burn wound healing

The 26 studies compared the healing time between SSD and other interventions, including honey, *A. vera*, and amniotic membrane. Details on all observed interventions are shown in Figure 2a. *A. vera* showed the best efficacy (MD: −4.75; 95% CI: −8.67 to −0.86), followed by amniotic membrane (MD: −4.71; 95% CI: −7.45 to −1.97), and honey (MD: −4.25; 95% CI: −6.76 to −1.73) (Figure 3a).

Infection occurrence

Twenty-four studies compared infection rates between SSD and other interventions, mainly focusing

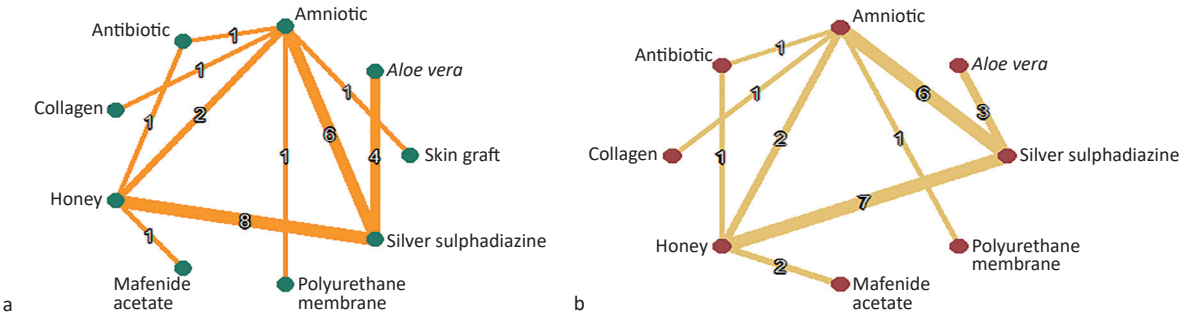

Figure 2. Network graph of studies. (a) Healing time; (b) infection occurrence

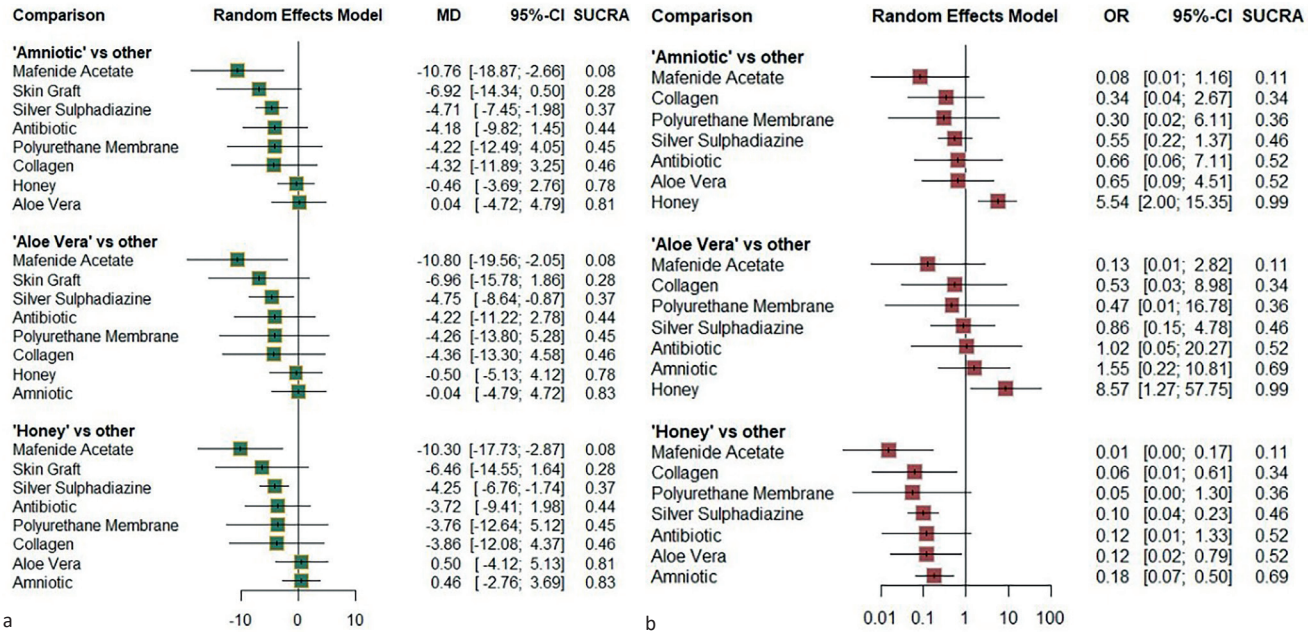

Figure 3. Forest plot of studies. (a) Healing time; (b) infection occurrence. CI=confidence interval; MD=mean difference; OR=odds ratio; SUCRA=surface under the cumulative ranking curve

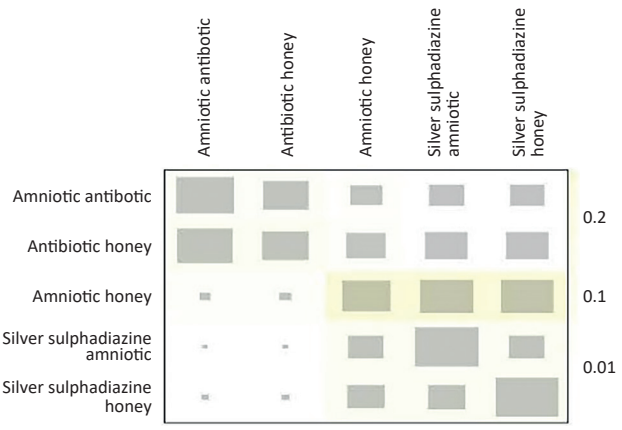

Figure 4. Net heat plot describing inconsistencies of included studies indicated by the warm color. Larger rectangle: direct evidence (studies directly comparing those treatments) has a stronger influence; smaller rectangle: direct evidence is weak, meaning it has a weaker influence

on honey, amniotic membrane, or *A. vera* (Figure 2b). Honey showed the lowest infection rate (OR: 0.09; 95% CI: 0.04 to 0.23) and was the only intervention with a statistically significant difference (Figure 3b).

Studies inconsistencies and quality appraisal

Inconsistencies across studies were shown using a net heat plot (Figure 4), indicating low inconsistencies in direct and indirect interventions of the available treatments acquired from the quantitative analysis.

DISCUSSION

This meta-analysis included 37 studies on healing time, 24 on infection rates, and 3,434 patients with burns to compare natural remedies with SSD. *A. vera*

can accelerate healing compared to other remedies, including SSD. It is cost-effective, widely available, and generally safe.[59] The exact mechanism of *A. vera* in wound repair is not fully understood. Still, studies suggest its gel contains polysaccharides, amino acids, tannins, and enzymes, which can stimulate cell proliferation *in vitro*.[60] *A. vera* stimulates fibroblast and keratinocyte proliferation and migration while positively regulating growth factors and cytokines.[61] Some studies suggest topical *A. vera* may cause redness, burning, stinging, and rarely generalized dermatitis in sensitive patients, particularly due to anthraquinones like aloin and barbaloin. It is recommended to apply *A. vera* to a small area first to test for allergic reactions.[62]

Honey reduces infection rates and accelerates healing compared to SSD. Honey is a traditional treatment in the Indian subcontinent. Its viscosity, osmolarity, acidic pH, and nutrients inhibit bacterial growth and promote healing.[62,63] Honey is effective against antibiotic-resistant bacteria and more affordable.[64] Precautions are needed when using honey to avoid allergic reactions, contaminated honey infections, or inadequately cleaned wounds.[34]

Due to their fragile nature, amniotic membranes have drawbacks, such as burn wound dressings. They may lack mechanical support for large or deep wounds, and improper application can lead to detachment or complications requiring further intervention. Natural shedding of the membrane can cause odor, requiring frequent dressing changes and discomfort. amniotic membrane's efficacy varies by patient response and wound characteristics, meaning benefits may differ.[65]

This meta-analysis highlights the benefits of *A. vera* and honey for treating burns, considering potential side effects. These alternatives are accessible and cost-effective, particularly in low-income countries, but further research on side effects is needed. A limitation of this study is its reliance on published studies, which may underrepresent those with negative or inconclusive results that are less likely to appear in peer-reviewed journals. Excluding patients with comorbidities limits the study's real-world applicability, where patients with burns often have other health conditions. Additionally, the analysis focused mainly on efficacy, such as healing time and infection rates, without addressing the safety or side effects of the interventions, which are crucial for clinical decision-making.

In conclusion, *A. vera* accelerates healing, while honey is superior to SSD in preventing infections. However, these results come from a study with a small sample and high heterogeneity. We encourage further research on natural remedies for burn treatment, following the Consolidated Standards of Reporting Trials to improve trial quality.

Conflict of Interest

The authors affirm no conflict of interest in this study.

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