Practical Implementation of Nursing Science

Effectiveness of Complementary Therapies in the Management of Wounds Among Adult Patients

LITERATURE REVIEW

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ABSTRACT

Aims: To conduct a systematic review of complementary therapies for wound management.

Methods: An initial search of the literature was conducted using a machine-learning assisted instrument. Based on initial results, literature was hand reviewed by at least two team members for inclusion. Data were extracted and quality was assessed for included articles at the full text level.

Results: 67 articles were included on a variety of complementary therapies for wound management including original research such as randomized controlled trials, non-randomized controlled trials, case reports, and cohort studies that assessed the effectiveness of complementary therapies in the management of wounds among adult patients. Studies assessing the effectiveness of complementary therapies on patients with episiotomies, complementary therapies using body-mind therapies, studies for which the full text was inaccessible, and non-English language studies were excluded. Resulting treatments were honey, maggot debridement, Aloe vera, Calendula officinalis, Hypericum perforatum ointment, dragon's blood, curcumin, banana leaf dressing, potato peels, and tea tree oil.

Conclusion: Honey, maggot debridement, Aloe vera, Calendula officinalis, Hypericum perforatum ointment, dragon's blood, curcumin, banana leaf dressing, and tea tree oil show promise as low cost alternatives for wound management.

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KEYWORDS:

Wound management; complementary therapies; complementary alternative medicines; low-resource; low cost alternatives; systematic review

TO CITE THIS ARTICLE:

Msiska, G., Fu, C., Wella, K., Msosa, A., Mbirimtengerenji, N., Masache, G., Simbota, M., Banez, M. C., Chorwe-Sungani, G., & Sun, C. (2023). Effectiveness of Complementary Therapies in the Management of Wounds Among Adult Patients. *Practical Implementation of Nursing Science*, *2*(1), pp. 22–53. DOI: https://doi.org/10.29024/pins.31

INTRODUCTION AND BACKGROUND

Acute and chronic wounds remain a problem for both the developing and the developed world (Sibbald et al., 2012; Queen and Harding, 2012; Haagsma et al., 2016). In developed countries, the prevalence of skin breakdown from leg ulcers, pressure ulcers, and diabetic foot ulcers continues to grow as the population ages (Queen & Harding 2012; Posnett & Franks, 2008). In developing countries, injuries due to road traffic accidents and burns are major contributors to the wound care burden, and the unavailability of proper wound care and treatment is a critical challenge (World Health Organization 2009; World Health Organization 2019; World Health Organization 2015). Wound management is costly and therefore largely impractical for developing countries to implement (Benskin, 2013). While effective wound care is available in developing countries, advancements have been associated with escalating healthcare costs (Sen, 2019; Posnett & Franks, 2008). Thus, inexpensive and efficacious wound care strategies for developing countries are needed.

In Malawi, a developing country characterized by low resource clinical settings, the most commonly reported causes of injuries are animal bites (mostly dog bites), road traffic injuries, assaults, burns, and falls (National Statistics Office, 2017; Chokotho et al., 2014). Managing patients with traumatic wound injuries is a challenge in low income countries due to a lack of antiseptics and other materials for wound care. Extensive and infected wounds are common in surgical wards, including wounds that are clean initially and later become infected. Consequently, complementary therapies such as brown sugar, honey, pawpaw, tea, and Aloe vera are used for wound care. These locally available therapies are inexpensive and, if effective, could help mitigate wound care challenges faced by regional health sectors.

However, there is limited rigorous research to guide effective utilization of these complementary therapies (Erwin-Toth 2014). The lack of standardization of naturopathic products interferes with accuracy of dosage and leads to inconsistent delivery of the product, and differences in measured efficacy. These limitations make it difficult to ascertain the effectiveness of complementary therapies. Therefore, the purpose of this review is to evaluate the published evidence on the clinical effectiveness of complementary therapies in wound treatment, particularly for use in resource-poor countries, such as Malawi.

METHODS

This systematic review was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al., 2009).

INCLUSION AND EXCLUSION CRITERIA

Articles meeting the following criteria were included 1) randomized controlled trials, non-randomized controlled trials, and observational studies such as case reports and cohort studies which assessed the effectiveness of complementary therapies in the management of wounds among adult patients; 2) studies which assess the effectiveness of complementary therapies in the form of natural products such as honey, Aloe vera, and other similar products; 3) studies assessing the effectiveness of complementary therapies on patients with wound infections, burns, traumatic wounds, diabetic foot ulcers and surgical incisions, pressure sores, trophic ulcers, and venous ulcers; and 4) published from January 1, 2009, through October 31, 2018. The following exclusion criteria were applied: 1) systematic reviews and meta-analyses; 2) studies assessing the effectiveness of complementary therapies on patients with episiotomies; 3) studies assessing the effectiveness of complementary therapies in the form of body-mind therapies, alternative medical systems such as acupuncture, and manipulative and body-based methods such as massage therapy; 4) studies for which the full text was inaccessible; and 5) non-English language studies.

SEARCH STRATEGY

Digitally accessible full-text articles and abstracts were collected and systematized using Ediom's EvidenceEngine, a machine-learning assisted instrument intended to aid health systems in the

clinical value analysis process by providing comprehensive and objective analyses of the latest relevant information (D'Agostino et al., 2018; Rutkowski et al., 2018; Joanna Briggs Institute, 2014). Articles were identified via keyword searches of MedlinePlus, PubMed, Cochrane, Embase, and Google Scholar (Table 1). Hand searches were later conducted from the references lists of any meta-analyses and systematic reviews retrieved.

Table 1 List of Search Terms.

KEYWORD
complementary medicine wound infection
Aloe vera wound infection
"low resource" wound infection
low income intitle:wound
honey wound healing
honey wound infection
curcuma wound infection
curcumin wound healing
Tea tree wound infection
Calendula wound infection
Hypericum perforatum wound infection
potato peel dressing
Banana leaf dressing
Maggot therapy
curcumin healing randomized
curcumin wound randomized
"dragon's blood" + "wound"
Achillea millefolium wound
Salvia miltiorrhiza
Plantago major
Calendula officinalis
Thai Herbal
essential oils (cumin, cinnamon, cardamom and clove)
Lonicera japonica
Centella asiatica
Ixora coccinea
Arnebia euchroma
Embothrium coccineum
Commiphora (balsamowiec)
orange essential oil
Albizzia lebbeck
Justicia secunda
Nigella sativa L. seed oil
Gumbail tree (Cordia africana)
Lantana camara
Terminalia chebula
Pongamia pinnata
Moringa oleifera
Lavandula stoechas L.
Tap/saline water

DATA ANALYSES

Data were abstracted according to year, author, study design, sample size, peer-review status, conflict of interest statement, quality score, intervention, country, outcome measures, study results, strengths, weaknesses, and cost effectiveness. Studies were reviewed for quality at the full text level. This qualitative assessment included establishing the scientific merit of the evidence based on study type, publication date, sample size, peer review status, and conflict of interest. Each study was assessed by two independent reviewers and discrepancies were discussed until resolved.

RESULTS

Figure 1 shows the selection and evaluation process. A total of 67 studies met the inclusion criteria (Figure 1 and Table 2).

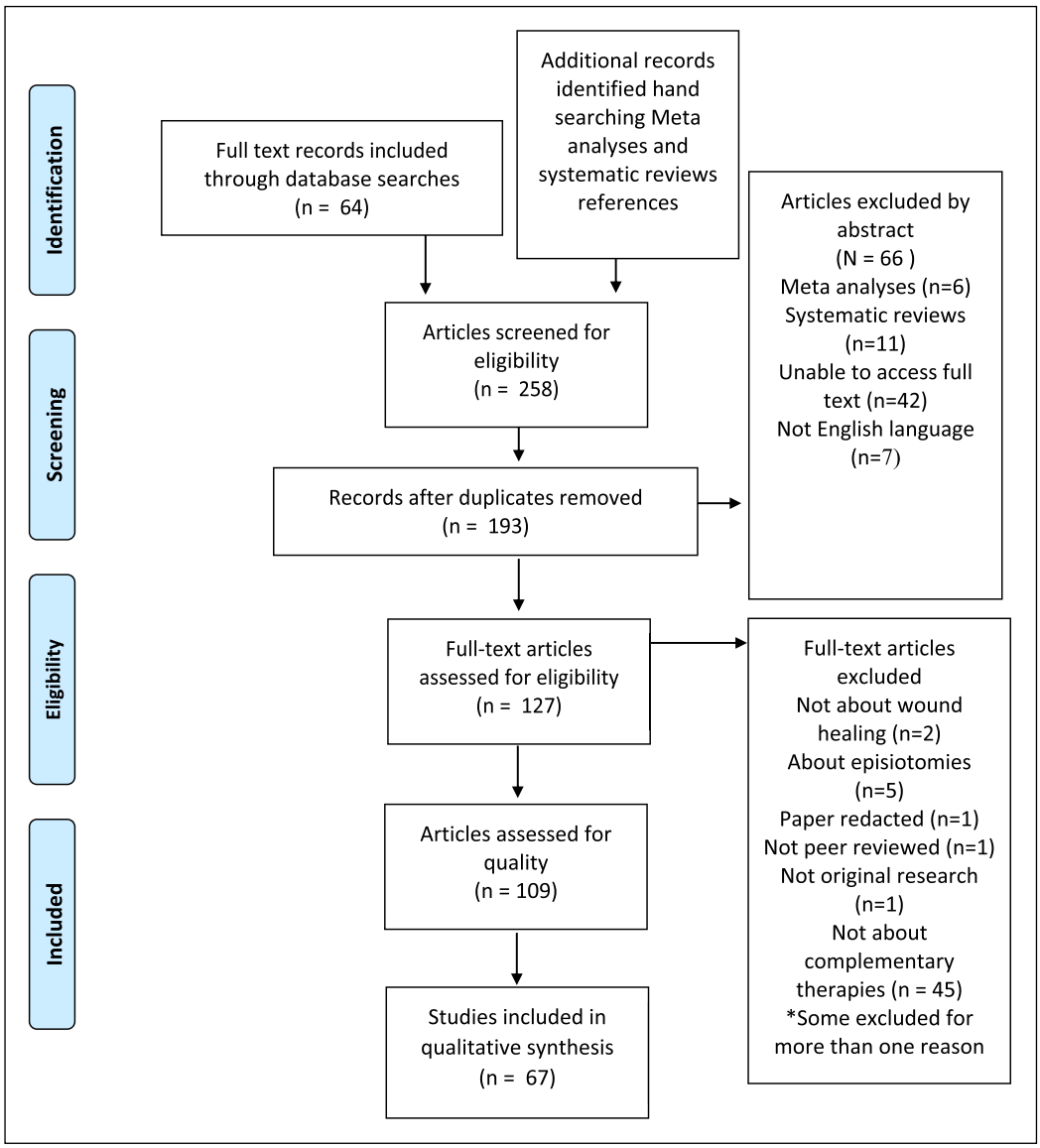

Figure 1 Article Selection Flow Diagram.

Table 2 Included studies for Each Complementary Therapy.

ALOE VERA							
AUTHOR, YEAR	**STUDY DESIGN**	**WOUND TYPE**	**N**	**OUTCOME MEASURE (UNITS)**	**EFFECT ESTIMATES**		
					CONTROL	**COMPARISON**	**TREATMENT**
						placebo	Aloe vera cream
Eshghi et al., 2010	RCT	hemorrhoidectomy	49	post-operative pain score, immediate		9.24 ± 0.66	9.29 ± 0.81
				post-operative pain score, 12 hr		8 ± 0.71	5.75 ± 0.9
				post-operative pain score, 24 hrs		6.3 ± 0.70	3.2 ± 0.83
				post-operative pain score, 48 hrs		5.2 ± 0.91	1.8 ± 0.64
				post-operative pain score, two weeks		2.56 ± 0.50	1.16 ± 0.38
				post-operative pain score, four weeks		1.04 ± 0.20	1 ± 0.00
				number completely healed at two weeks		24 per 24	1 per 25
						silver sulfadiazine	Aloe vera cream
Khorasani et al., 2009	RCT	burn	30	mean time to healing (days)		18.73 +/– 2.65	15.9 +/– 2
					control	placebo	Aloe vera cream
Khorasani et al., 2011	RCT	skin graft	45	mean time to epithelization (days)	17 +/– 8.6	9.7 +/– 2.9	8.8 +/– 2.8
						simple dressing	Aloe vera gel
Molazem et al., 2014	RCT	cesarean section	90	REEDA score,* 24 hrs		0.60 ± 1.30	0.00 ± 0.00
				REEDA score,* eight days		0.11 ± 0.49	0.29 ± 0.99
				percent with 0 REEDA score* (healed), 24 hrs		77.8	100
				percent with 0 REEDA score* (healed), eight days		91.11	93.33
						silver sulfadiazine	Aloe vera + herb cream
Panahi et al., 2012	RCT	burn	111	percent with skin dryness, day 2		27.3	12.5
				percent with skin dryness, day 7		25.5	12.5
				percent with skin dryness, day 14		10.9	7.1
				change in pain severity score, day 2		1.91 ± 2.25	2.61 ± 1.55
				change in pain severity score, day 7		3.78 ± 2.83	5.13 ± 2.82
				change in pain severity score, day 14		4.54 ± 2.83	5.68±3.2

(Contd.)

ALOE VERA							
AUTHOR, YEAR	STUDY DESIGN	WOUND TYPE	N	OUTCOME MEASURE (UNITS)	EFFECT ESTIMATES		
					CONTROL	COMPARISON	TREATMENT
						standard management	Aloe vera added
Schmidt & Greenspoon, 1991	Non-RCT	cesarean section	46	mean time to healing (days), vertical incisions		47 +/– 18	84 +/– 27
				mean time to healing (days), transverse incisions		53 +/– 24	83 +/– 35
				mean time to healing (days), all incisions		53 +/– 24	83 +/– 28
				number with adverse effects		0	0
						silver sulfadiazine	Aloe vera gel
Shahzad & Ahmed, 2013	RCT	burn	50	mean time to healing (days)		24.24 +/– 11.16	11 +/– 4.18
				mean time to total pain relief (days)		26	21
				number who developed wound colonization		22	16
						silver sulfadiazine	Aloe vera mucillage
Thamlikitkul et al., 1991	RCT	burn	38	percent with complete healing/epithelization		39	55
				percent with partial healing/epithelization		44	40
				percent with no healing/epithelization		17	5
				percent with side effects		44	40
				percent with no side effects		39	35
				percent with satisfactory patient rating		28	40
				percent with unsatisfactory patient rating		17	5
						moist saline gauze	Acemannan hydrogel (Aloe vera)
Thomas et al., 1998	RCT	pressure ulcer	30	percent completely healed		64	63

* Higher REEDA score indicates less healing.

BANANA LEAVES							
AUTHOR, YEAR	STUDY DESIGN	WOUND TYPE	N	OUTCOME MEASURE (UNITS)	EFFECT ESTIMATES		
					CONTROL	COMPARISON	TREATMENT
							banana leaves
Guenova et al., 2013	Prospective Case Series	post-surgical	43	number with pain score one			6 per 43
				number with infection, one week			0
				number with infection, two weeks			0

(Contd.)

CALENDULA OIL							
FIRST AUTHOR, YEAR	**STUDY DESIGN**	**WOUND TYPE**	**N**	**OUTCOME MEASURE (UNITS)**	**EFFECT ESTIMATES**		
					CONTROL	**COMPARISON**	**TREATMENT**
							Calendula oil
Buzzi et al., 2016	Prospective Case Series	pressure ulcer	41	mean healing time (weeks)			15.5 ± 6.7
				percent colonized, baseline			26.8
				percent colonized, 30 weeks			14.6
				percent infected, baseline			48.8
				percent infected, 30 weeks			2.4
CURCUMIN							
AUTHOR, YEAR	**STUDY DESIGN**	**WOUND TYPE**	**N**	**OUTCOME MEASURE (UNITS)**	**EFFECT ESTIMATES**		
					CONTROL	**COMPARISON**	**TREATMENT**
Choudhary et al., 2012	Self-controlled Case-control*	burn	228	percent with no infection, day 3		16.7	52.2
				percent with no infection, day 7		17.5	61.4
				percent with no infection, day 11		17.9	84.2
				percent with good epithelialization, day 7		17.5	61.4
				percent with fair epithelialization, day 7		34.2	29.8
				percent with poor epithelialization, day 7		48.2	8.7
				percent with good epithelialization, day 11		33.7	85.1
				percent with fair epithelialization, day 11		27.6	10.1
				percent with poor epithelialization, day 11		38.6	4.8
* Patients given both control and treatment (2 wounds per patient).							
DRAGON'S BLOOD							
AUTHOR, YEAR	**STUDY DESIGN**	**WOUND TYPE**	**N**	**OUTCOME MEASURE (UNITS)**	**EFFECT ESTIMATES**		
					CONTROL	**COMPARISON**	**TREATMENT**
Namjoyan et al., 2016	RCT	skin tag removal	60	mean percentage of wound healing at day 3		4.74	31.06
				mean percentage of wound healing at day 5		23.5	63.77
				mean percentage of wound healing at day 7		43.9	77.8
				mean percentage of wound healing at day 10		61.95	89.14
				mean percentage of wound healing at day 14		78.1	95.73
				number of wound infections per starting sample		1 per 55	0 per 45

(Contd.)

HONEY							
AUTHOR, YEAR	STUDY DESIGN	WOUND TYPE	N	OUTCOME MEASURE (UNITS)	EFFECT ESTIMATES		
					CONTROL	COMPARISON	TREATMENT
Baghel et al., 2009	RCT	burn	78	mean time to healing (days)		32.68	18.16
				percent with complete healing, two months		37	81
				percent with wound sterilization, 21 days		36.5	100
						silver sulfladiazene	honey
Bangroo et al., 2005	RCT	burn	64	mean time to appearance of healthy granulation (days)		12.8	6.7
				number with infection, baseline		24 per 32	25 per 32
				number with infection, seven days		21 per 32	2 per 32
				number with contractures		5 per 32	2 per 32
							Medihoney
Biglari et al., 2012[a]	Prospective Case Series	pressure ulcer	20	percent with complete healing, four weeks			90
				percent with sterilization, one week			100
				number of negative effects			0
						none	Surgihoney
Dryden et al., 2014	non-RCT	oncology vascular lines	60	number with line colonization, baseline		4 per 30	2 per 30
				number with line colonization, during evaluation		6 per 30	0 per 30
				number with line colonization, end of evaluation		6 per 30	0 per 30
				number of pain events		2 per 30	2 per 30
				number of itching/irritation events		1 per 30	4 per 30
				number of rashes		1 per 30	3 per 30
				discharge at exit site		0 per 30	1 per 30
					saline	phenytoin	sterilized honey
Dubhashi & Sindwani, 2015	non-RCT	infections, ulcers	150	percent of wound reduction, three weeks	8.07	15.8	20.66
				mean time to wound sterilization (days)	14.94 ± 2.56	9.28 ± 2.03	8.4 ± 1.71
				mean pain score, day 5	6.72 ± 0.64	5.54 ± 0.68	5.10 ± 0.79
				mean pain score, day 10	5.02 ± 0.77	3.76 ± 0.77	3.06 ± 0.91
				mean pain score, day 15	4.32 ± 0.79	2.68 ± 0.65	2.06 ± 0.65

(Contd.)

HONEY							
AUTHOR, YEAR	STUDY DESIGN	WOUND TYPE	N	OUTCOME MEASURE (UNITS)	EFFECT ESTIMATES		
					CONTROL	COMPARISON	TREATMENT
				mean pain score, day 20	3.14 ± 0.76	1.20 ± 0.45	1.20 ± 0.45
				mean length of hospital stay (days)	4758 ± 10.19	29.6 ± 5.64	24.63 ± 5.20
						povidone iodine	honey
Gulati et al., 2014	RCT	chronic	42	percent with complete healing, six weeks		0	31.82
				median reduction wound surface area (cm^2), six weeks		2.3	3.8
				median reduction in pain score, baseline to six weeks		2	6
				median change in VAS* and comfort score (positive)		2	5
						silver sulfadiazine	honey
Gupta et al., 2011	Retrospective Cohort	burn	108	mean time to healing (days)		32.68	18.16
				percent with wound sterilization, 21 days		36.5	100
				percent with complete healing		37	81
						IntraSite Gel	monofloral aloe honey
Ingle et al., 2006[b]	RCT	shallow wounds, abrasions	82	mean healing time (days), shallow wounds		17.12 (11.7 – 22.5)	16.08 (12.3 – 19.9)
				mean healing time (days), abrasions		16.53 (12.3 – 20.8)	17.13 (13.1 – 21.1)
				percent of patients reporting itching		31	27
				cost per gram (Rand)		0.433	0.014
				cost per patient (Rand)		12.06	0.49
						usual care	Manuka honey dressing
Jull et al., 2008[c]	RCT	venous ulcer	368	percent with complete healing, 12 weeks		49.7	55.6
				mean time to healing (days)		65.3	63.5
				mean reduction from baseline ulcer area (%)		65.5	74.1
				percent patients with infection episodes		22.1	17.1
				number of patients reporting adverse events		84 per 181	111 per 187
				number of patients reporting pain		18 per 181	47 per 187
				mean total cost per patient (NZD)		972.68	917

(Contd.)

HONEY							
AUTHOR, YEAR	STUDY DESIGN	WOUND TYPE	N	OUTCOME MEASURE (UNITS)	EFFECT ESTIMATES		
					CONTROL	COMPARISON	TREATMENT
						conventional dressing (saline)	Medihoney tulle
Kamaratos et al., 2012	RCT	diabetic ulcer	63	percent healed during follow-up period		90	97
				mean time to healing (days)		43 ± 3	31 ± 4
				number with infection, baseline		31 per 31	32 per 32
				number with infection, one week		20 per 31	7 per 32
				number with infection, two weeks		8 per 31	2 per 32
				number with infection, four weeks		4 per 31	0 per 32
				percent needing antibiotics		29	0
						silver-coated bandage	honey-coated bandage
Lund-Nielsen et al., 2011[d]	RCT	malignant (cancer)	69	median decrease in wound size (cm2)		8	15
				number with improved wound cleanliness		17 per 35	23 per 34
						mafenide acetate	honey dressing
Maghsoudi et al., 2011[e]	RCT	burn	100	percent completely healed, day 7		72	84
				percent completely healed, day 21		84	100
				number with infection (out of 50), baseline		44	46
				number with infection (out of 50), day 7		12	16
				number with infection (out of 50), day 21		6	1
						silver sulfadiazine	honey
Malik et al., 2010	RCT	burn	150	mean time to healing (days)		15.62 ± 4.40	13.47 ± 4.06
				number with infection		29 per 150	6 per 150
				number who “failed to heal”		29 per 150	8 per 150
				number needing skin graft, two weeks		29 per 150	8 per 150
						povidone iodine	honey
Marshall et al., 2005	RCT	toenail surgery	51	mean time to healing (days), all		25 ± 8.70	33 ± 15.71
				mean time to healing (days), total avulsion		30 ± 10.62	44 ± 7.88
				mean time to healing (days), partial avulsion		24 ± 7.23	18 ± 8.45
				number of patients who developed infection		0 per 24	1 per 27
				mean VAS* value for pain (cm)		1.99 ± 1.41	1.86 ± 1.67

(Contd.)

HONEY							
AUTHOR, YEAR	STUDY DESIGN	WOUND TYPE	N	OUTCOME MEASURE (UNITS)	EFFECT ESTIMATES		
					CONTROL	COMPARISON	TREATMENT
						silver sulfadiazine	pure honey
Mashhood et al., 2006	RCT	burn	50	percent healed, two weeks		20	52
				percent healed, four weeks		60	100
				time to all patient wounds healed (weeks)		6	4
				time to all patients relieved of pain (weeks)		4	3
				percent with bacterial growth, baseline		76	80
				time to all patient wounds sterilized (weeks)		5	3
						paraffin tulle gras	active Manuka honey
McIntosh & Thomson, 2006[f]	RCT	toenail surgery	100	mean time to healing (days), all		39.98 ± 25.42	40.30 ± 18.21
				mean time to healing (days), total avulsion		52.03 ± 21.3	45.28 ± 18.03
				mean time to healing (days), partial avulsion		19.62 ± 9.31	31.76 ± 18.8
				mean VAS* value for pain (cm)		1.57 ± 1.3	1.60 ± 1.22
				mean pain score during dressing change		1.23 ± 0.84	1.26 ± 1.09
						silver sulfadiazine	pure undiluted honey
Memon et al., 2005[g]	RCT	burn	80	time to all patients healed (days)		46	30
				mean time to healing (days)		20	15.3
				percent with infection (bacteria colonization)		80	0
				number with minor complications after healing		30 per 40	9 per 40
						intralesionalglucantime	topical honey added
Nilforoushzadeh et al., 2007[h]	RCT	Leishmaniasis ulcer	90	percent with complete healing		71.1	51.1
				mean time to healing (weeks)		6.3 ± 2.29	7.04 ± 3.09
				attrition rate		10 per 45	13 per 45
						conventional treatment	Medihoney™ antibacterial honey
Robson et al., 2009[i]	RCT	secondary intention	105	median time to healing (days)		140	100
				healing rate, 12 weeks (%)		34.0 (22.3, 49.5)	46.2 (32.9, 61.7)
				healing rate, 24 weeks (%)		63.3 (48.6, 77.9)	72.7 (57.3, 86.1)
				median time to 50% reduction in wound area (days)		46	32

(Contd.)

HONEY							
AUTHOR, YEAR	STUDY DESIGN	WOUND TYPE	N	OUTCOME MEASURE (UNITS)	EFFECT ESTIMATES		
					CONTROL	COMPARISON	TREATMENT
				percent with 50% reduction in wound area, 12 weeks		70.5 (57.1, 82.8)	68.2 (54.4, 81.2)
				percent with 50% reduction in wound area, 24 weeks		80.1 (66.4, 90.9)	94.0 (79.1, 99.4)
				attrition rate		3 per 53	4 per 52
				number with adverse events		5 per 53	7 per 52
						povidone iodine	pure honey
Shukrimi et al., 2008[j]	RCT	diabetic ulcer	30	mean time to healing (days)		15.4	14.4
						Eusol dressing	honey
Subrahmanyam & Ugane, 2004	RCT	gangrene	30	mortality rate		2 per 16	1 per 14
				number with clearance of slough, day 7		8 per 16	8 per 14
				number with clearance of slough, day 10		2 per 16	1 per 14
				number with clearance of slough, day 14		3 per 16	5 per 14
				percent with healthy granulation, one week		18.7	28.5
				number requiring secondary suturing		9 per 16	9 per 14
				mean length of hospital stay (days)		32	28
						silver sulfadiazine	pure undiluted honey
Subrahmanyam, 1991	RCT	burn	104	mean time to healing (days)		13.4	7.4
				number with infection, baseline		41 per 52	43 per 52
				number with infection, seven days		38 per 52	4 per 52
				number of complications		16 per 32	2 per 52
						OpSite®	honey gauze
Subrahmanyam, 1993a[k]	RCT	burn	92	mean time to healing (days)		15.3	10.8
				number with infection, baseline (day 1)		9 per 46	10 per 46
				number with infection, after seven days (day eight)		17 per 46	8 per 46

(Contd.)

HONEY							
AUTHOR, YEAR	STUDY DESIGN	WOUND TYPE	N	OUTCOME MEASURE (UNITS)	EFFECT ESTIMATES		
					CONTROL	COMPARISON	TREATMENT
						amniotic membrane	honey gauze
Subrahmanyam, 1994[l]	RCT	burn	64	mean time to healing (days)		17.5	9.4
				number with infection, baseline		19 per 24	28 per 40
				number with infection, seven days		11 per 24	4 per 40
				percent with moderate or severe pain		45.9	17.5
				percent with mild or no pain		54.1	82.5
				percent with residual scarring, three months		16.6	8
						boiled potato peels	honey
Subrahmanyam, 1996a	RCT	burn	100	mean time to appearance of granulation (days)		9.2	6.8
				mean time to healing (days)		16.2	10.4
				number with infection, baseline		42 per 50	40 per 50
				number with infection, day 7		42 per 50	4 per 50
						pure undiluted honey	PEG 4000, vitamins C, E added
Subrahmanyam, 1996b	RCT	burn	84	mean time to healing (days)		8.3	6.4
				number with infection (out of 42), baseline		12	10
				number with infection (out of 42), after seven days		14	12
						silver sulfadiazine	honey
Subrahmanyam, 1998b	RCT	burn	50	number with fluid exudation, seven days		8 per 25	4 per 25
				number who formed an eschar (complication)		15 per 25	0 per 25
				number with fluid exudation, 21 days		4 per 25	1 per 25
				percent with clinical evidence of healing, seven days		72	84
				percent with histological evidence of healing, seven days		52	80
				percent with clinical evidence of healing, 21 days		84	100
				percent with histological evidence of healing, 21 days		84	100
				number with infection, baseline		22 per 25	23 per 25

(Contd.)

HONEY							
AUTHOR, YEAR	STUDY DESIGN	WOUND TYPE	N	OUTCOME MEASURE (UNITS)	EFFECT ESTIMATES		
					CONTROL	COMPARISON	TREATMENT
				number with infection, seven days		6 per 25	8 per 25
				number with infection, 21 days		3 per 25	1 per 25
						honey dressing	tangential excision and graft
Subrahmanyam, 1999[n]	RCT	burn, skin graft		mean blood replaced units (% blood volume)		21±15	35±12
				mortality rate		3 per 25	1 per 25
				number with 100% graft take (of those who received grafts)		2 per 11	19 per 24
				rate of infection per swab cultures taken		42 per 123	7 per 71
				mean length of antibiotic treatment (days)		32±18	16±3
				mean length of hospital stay		46±19	21±4
				number with excellent or good wound appearance, three months		12 per 22	22 per 24
						Vaseline gauze	raw honey (Jambhul)
Subrahmanyam, 2015	RCT	skin graft	100	percent with pain assessment none or mild		88	90
				percent with excellent wound appearance patient rating		68.1	69.5
				number with epithelization/healing, day 7		39 per 50	48 per 50
				number with epithelization/healing, day 10		38 per 50*	50 per 50
							Manuka honey
Thomas et al., 2011	Retrospective Cohort	post-surgical	17	number with complete healing			15 per 17
				mean time to healing (days)			65
				median time to healing (days)			49
				number of adverse events			3 per 17
					paraffin tulle (standard)	Manuka honey	nanocrystalline silver
Tsang et al., 2017[o]	RCT	diabetic ulcer	31	wound size reduction rate (%/week)	76.91	86.24	97.45
				slope of wound reduction over time	2.883	9.337	20.573
				number of microorganism species, baseline	2.00 ± 1.25	1.56 ± 1.59	1.00 ± 1.00

(Contd.)

HONEY							
AUTHOR, YEAR	STUDY DESIGN	WOUND TYPE	N	OUTCOME MEASURE (UNITS)	EFFECT ESTIMATES		
					CONTROL	COMPARISON	TREATMENT
				estimated marginal mean number of microorganisms	1.36	1.17	0.86
				number of adverse events	4 per 10	1 per 10	1 per 11

* VAS = Visual analogue scales.
a. Negative effects included blood sugar derailment in diabetic patients, allergies.
b. Only compared non-infected wounds, outcome differences not significant between treatment.
c. All patients received compression bandaging, for usual care, RNs determined appropriate dressing (alginate, hydrofibre, hydrocolloid, foam, hydrogel, non-adherent, iodine or silver dressings), quality of life scores (4 scales) at 12 weeks not significantly different between groups.
d. Patients with reduced wound size had longer median survival, 387 days vs 134.
e. 50 patients per treatment arm.
f. Healing = complete re-epithelialization, VAS = Visual analogue scales, 100mm.
g. Unprocessed (raw) honey; reported different time points for healing response for different arms.
h. Reason given for attrition was "progression of their lesions."
i. Analyzed data from patients up to point of leaving study, adverse events included death, pain, wound deterioration.
j. Found similar outcomes for both groups, described adverse events (infections, pain, discharge) and cost did not provide all numbers for comparison.
k. OpSite® is a bio-occlusive, moisture-permeable polyurethane dressing.
l. Forty patients treated with honey gauze, 24 treated with amniotic membrane, inconsistency in results reported in text versus table.
m. No allergies or other side effects observed; similar pain relief observed.
n. Language unclear regarding mortality.
o. The percentage of area reduction in "week y" was (ulcer area of week 0 – ulcer area of week y)/ulcer area of week 0 × 100%.

HYPERICUM PERFORATUM							
AUTHOR, YEAR	STUDY DESIGN	WOUND TYPE	N	OUTCOME MEASURE (UNITS)	EFFECT ESTIMATES		
					CONTROL	COMPARISON	TREATMENT
					NO TREATMENT	PLACEBO OINTMENT	*H. PERFORATUM* OINTMENT
Samadi et al., 2010	RCT	Cesarean section	125, 114*	REEDA score,[a] day 10 postpartum	0.79 ± 1.17	0.75 ± 1.08	0.19 ± 0.50
				hypertrophic scar VSS score[b], day 40 postpartum	5.50 ± 0.92	5.03 ± 1.29	3.32 ± 1.54
				patient satisfaction with scarring rate (%)	68	76	90
				attrition rate due to treatment**	0 per 32	0 per 40	1 per 44

*19 lost to follow up on day 10 (n = 125); nine more lost to follow up on day 40 (n = 114).
**Mentions one patient withdrawal due to H. perforatum ointment but not at what stage of the study.
a.REEDA score includes redness, edema, ecchymosis, discharge, and approximation.
b.VSS, Vancouver scar scale.

(Contd.)

MAGGOT WOUND THERAPY							
AUTHOR, YEAR	STUDY DESIGN	WOUND TYPE	N	OUTCOME MEASURE (UNITS)	EFFECT ESTIMATES		
					CONTROL	COMPARISON	TREATMENT
							larvae
Azad, 2016	Case Series	diabetic ulcer	11	mean duration of treatment (days)			30.27
				number healed after treatment			10 per 11
				attrition rate (unrelated complications)			1 per 11
					hydrogel	bagged larvae	loose larvae
Dumville, 2009c	RCT	ulcer	267	average estimated cost per application (£)	1.50 ± 0	111.90 ± 33.6	71.79 ± 13.40
				mean number of applications per patient	9.2 ± 27.78	1.46 ± 1.06	1.44 ± 1.22
				mean duration of treatment (days)	43.17 ± 51.76	12.84 ± 11.47	11.95 ± 9.11
				mean annual cost (£)[d]	1976.4 (1521.4 to 2500.2)		2073.1 (1724.4 to 2433.4)
				mean time to healing (days)[d]	206.5 (202.7 to 260.2)		204.1 (207.9 to 248.3)
				QALYs[d]	0.540 (0.489 to 0.589)		0.551 (0.505 to 0.591)
				mean unadjusted utility weights, baseline (value, %)	0.539, 0.313	0.434, 0.342	0.534, 0.301
				mean unadjusted utility weights, three months (value, %)	0.559, 0.317	0.562, 0.33	0.551, 0.343
				mean unadjusted utility weights, six months (value, %)	0.566, 0.301	0.588, 0.339	0.596, 0.334
				mean unadjusted utility weights, nine months (value, %)	0.628, 0.315	0.561, 0.381	0.608, 0.345
				mean unadjusted utility weights, 12 months (value, %)	0.615, 0.322	0.565, 0.382	0.630, 0.329
						larvae, caged application	larvae, direct application[w]
Gilead, 2012	Prospective Case Series	ulcer	435[v]	percent of cases		9.4	90.6
				mean number of treatments			2.9
				median number of treatments			2
				mean duration of treatment (days)			4.6
				median duration of treatment (days)			3

(Contd.)

MAGGOT WOUND THERAPY							
AUTHOR, YEAR	STUDY DESIGN	WOUND TYPE	N	OUTCOME MEASURE (UNITS)	EFFECT ESTIMATES		
					CONTROL	COMPARISON	TREATMENT
				percent with complete debridement			82.1
				percent with partial debridement			16.8
				percent reporting increase pain			38
				attrition rate (due to pain)			5 per 435
							bagged larvae
Hwang, 2011	Case Series	post-surgical and infected[x]	5	mean duration of treatment (weeks)			5.2
				mean number of treatment cycles			8.8
				mean wound size before treatment (cm)			24.2 ± 3.3
				mean wound size after treatment (cm)			11.8 ± 4.5
				mean difference in wound size, before-after (cm)			12.4
				mean healed scar size (cm)			10.4 ± 4.6
							larvae
Marineau, 2011	Prospective Case Series	diabetic ulcer	23	mean duration of treatment (days)			11.09
				median duration of treatment (days)			10
				number with complete debridement			17 per 23
						hydrogel	larvae
Mudge, 2014	RCT	ulcer	88 (64)[i]	rate of complete debridement		11 per 42	31 per 46
				attrition rate, any reason		10 per 42	14 per 46
				attrition rate, infection or increased slough		9 per 42	3 per 46
				attrition rate, pain or discomfort		1 per 42	8 per 46
				attrition rate, patient request to stop treatment		0 per 42	3 per 46
				mean pain score (VAS), baseline		30.17 ± 26.44	41.54 ± 28.80
				mean pain score (VAS), final evaluation		21.80 ± 27.98	19.26 ± 21.48j
				mean number of dressing changes		5.40 ± 1.795	2.83 ± 1.102
				incidence of reappearance of slough		11 per 42	31 per 46
				number that remained debrided after complete debridement		2 per 11	9 per 31

(Contd.)

MAGGOT WOUND THERAPY							
AUTHOR, YEAR	STUDY DESIGN	WOUND TYPE	N	OUTCOME MEASURE (UNITS)	EFFECT ESTIMATES		
					CONTROL	COMPARISON	TREATMENT
						conventional (surgical)	bagged maggots
Opletalova, 2012	RCT	ulcer	105	mean wound surface area, baseline day one (cm^2)		11.4 ± 8.1	11.5 ± 9.3
				mean percent change in wound surface, day 8[k]		−1.5 ± 34.3	−10.9 ± 38.1
				mean percent change in wound surface, day 15[k]		8.2 ± 37.9	−14.6 ± 59.6
				mean percent change in wound surface, day 30[k]		12.9 ± 53.0	−5.3 ± 104.3
				mean percent slough, baseline (day 1)		78.7 ± 23.5	79.7 ± 22.3
				mean percent slough, day 8		66.5 ± 25.2	54.5 ± 31.6
				mean percent slough, day 15		53.8 ± 33.6	55.4 ± 30.0
				mean percent slough, day 30		60.0 ± 36.4	55.4 ± 30.4
				rate of MRSA-positive, baseline day 1		7 per 50	9 per 49
				rate of MRSA-positive, day 15		13 per 48	6 per 48
				rate of pseudomonas-positive, baseline day 1		5 per 50	4 per 50
				rate of pseudomonas-positive, day 15		5 per 48	4 per 49
				mean pain score (VAS) overall		2.7 ± 2.6	2.3 ± 2.6
				number with crawling sensation		101 per 49	10 per 49
						standard dressing (saline)	live maggots
Paul, 2009	Prospective Case-Control	diabetic ulcer	54	attrition rate		1 per 30	4 per 29
				number healed		18 per 29	14 per 25
				mean length of hospital stay (days)		19.8	12.5
				number with at least one microorganism		23 per 29	18 per 25
							larvae
Pinheiro, 2015	Case Report	diabetic ulcer	1	decrease in wound area (cm^2)			0.7
				duration of treatment (days)			43
						conventional (prior to treatment)[p]	larvae
Sherman, 1995	Self-controlled Case-control	pressure ulcer	20	number of patients observed		8 per 20	20 per 20
				mean time to complete debridement (weeks)		–	1.4
				mean change in surface area (%/week)[q]		21.8	−22

(Contd.)

MAGGOT WOUND THERAPY							
AUTHOR, YEAR	STUDY DESIGN	WOUND TYPE	N	OUTCOME MEASURE (UNITS)	EFFECT ESTIMATES		
					CONTROL	COMPARISON	TREATMENT
						conventional[s]	larvae[s]
Sherman, 2002	Prospective Cohort	pressure ulcer	103 (67)[r]	number of adverse events		(not reported)	3 per 50[t]
				percent of wounds completely debrided		48 (26, 70)	80 (65, 95)
				mean time to 50% debridement (weeks)		4.0 (2.6, 5.4)	1.4 (1, 1.7)
				mean time to total debridement (weeks)		17 (7, 28)	8 (6, 10)
				mean rate of change in surface area (cm2/week)		0.3 (-0.9, 1.6)	-1.6 (-2.6, -0.6)
				percent with > = 50% granulation		18 (7, 29)	51 (36, 66)
				mean time to 50% granulation (weeks)		4.7 (2.1, 7.3)	2.1 (1.7, 2.6)
				mean rate of change in granulation (%/week)		3.3 (0.9, 5.7)	13 (7, 19)
				mean total change in surface area (cm2)		6.3 (2.5, 10.1)	-7.3 (-10.4, -4.2)
				mean rate of change in surface area (cm2/week)		1.4 (0.5, 2.3)	-1.5 (-2.3, -0.7)
				mean time to complete healing (weeks)		13.4 (8. 19)	12.0 (7, 17)
					conventional only	conventional then maggot	maggot larvae
Sherman, 2003	Retrospective Cohort	diabetic ulcer	18[a]	time to 50% reduction in necrotic surface area (days)	29	–	9
				percent necrotic tissue, two weeks	39	–	7
				percent necrotic tissue, four weeks	33[b]	–	0
				mean debridement rate (cm2), two weeks	0	–	4.1
				percent of healthy granulation area, four weeks	15	-	56
				difference in weekly change of surface area, maggot vs conventional (cm2/week)		1.9	
				difference in percent necrotic tissue area remaining, one week	–	22	–
Sherman, 2004	Case-control	soft tissue	25[u]	number of wounds infected		6 per 19	0 per 10
				rate of postoperative infection (%, 95% CI)		38 (13, 62)	0
				number of adverse events		(not reported)	2 per 12

(Contd.)

MAGGOT WOUND THERAPY							
AUTHOR, YEAR	STUDY DESIGN	WOUND TYPE	N	OUTCOME MEASURE (UNITS)	EFFECT ESTIMATES		
					CONTROL	COMPARISON	TREATMENT
					hydrogel	loose larvae	bagged larvae
Soares, 2009	RCT	ulcer	267	mean number of applications	9.2 ± 27.78	1.44 ± 1.22	1.46 ± 1.06
				mean duration of treatment (days)	43.17 ± 51.76	11.95 ± 9.11	12.84 ± 11.47
				mean estimated cost per application (£)	1.50 ± 0	71.70 ± 13.40	111.90 ± 33.6
				mean estimated total cost per patient (£)[l]	1596 ± 1861	1833 ± 1978	1696 ± 1948
				mean adjusted annual costs (£)[m]	1976.4 (1521.4, 2500.2)	–	2073.1 (1724.4, 2433.4)
				mean time to healing (days)[m]	206.5 (2.02.7, 260.2)	–	204.1 (207.9, 248.3)
				mean QALYs[m]	0.540 (0.489, 0.589)	–	0.551 (0.505, 0.591)
							larvae
Turkmen, 2010	Case Series	chronic (mix)	34	number with satisfactory debridement			29 per 34
				number with granulation			29 per 34
				number healed by 10 days			27 per 34
				number of adverse events (treatment intolerance)			1 per 34
						conventional dressing	larvae
Wang, 2010	Retrospective Cohort	diabetic ulcer, pressure ulcer	25, 18[h]	mean time to granulation, diabetic ulcer (days)		6.3 ± 1.2	3.1 ± 1.2
				mean time to sterilization, diabetic ulcer (days)		16.1 ± 3.8	12.0 ± 2.5
				mean time to healing, diabetic ulcer (days)		39.6 ± 13.4	26.4 ± 12.6
				mean time to granulation, pressure ulcer (days)		4.8 ± 1.0	2.5 ± 1.0
				mean time to sterilization, pressure ulcer (days)		13.1 ± 2.2	10.4 ± 1.8
				mean time to healing, pressure ulcer (days)		30.6 ± 12.2	18.7 ± 10.4
						Intrasite hydrogel	larvae
Wayman, 2000[e,f]	RCT	ulcer	12	mean number of nurse visits		22.17	3
				median number of nurse visits		19	3
				mean nursing time (hrs)[g]		426.7	86.7
				median nursing time (hrs)[g]		375	75
				mean nursing costs (£)		66.74	12.44

(Contd.)

MAGGOT WOUND THERAPY							
AUTHOR, YEAR	STUDY DESIGN	WOUND TYPE	N	OUTCOME MEASURE (UNITS)	EFFECT ESTIMATES		
					CONTROL	COMPARISON	TREATMENT
				median nursing costs (£)		53.85	0.77
				mean dressing costs, dressing only (£)		106.52	11.69
				median dressing costs, dressing only (£)		89.55	9.87
				mean total costs (£)		173.26	81.98
				median total costs (£)		136.23	78.64
							larvae
Wollina, 2002n	Prospective Case Series	ulcer	30	mean wound score before treatment[o]			13.5 ± 1.8
				mean wound score after treatment[o]			6.3 ± 2.7
				mean difference in wound score (before-after)[o]			7.23
				median number of treatments			1
				mean application time (days)			3.3 ± 2.2
							larvae
Wu, 2012	Case Report	burn	1	time to granulation (days)			6

a. 20 wounds in 18 patients.
b. At five weeks vs 100% debrided for maggot group at four weeks.
c. Focused on cost-benefit analysis.
d. Larval therapy arms combined.
e. 30-day treatment period for all; only one larval treatment was administered.
f. One control patient switched from control to larval therapy at end of study because of persistent necrotic slough (which was then quickly healed).
g. Discrepancy between results text (hours) and table (min).
h. 25 patients with diabetic foot ulcers; 18 with pressure ulcers.
i. Started with 46 in larvae arm and 42 in hydrogel; 32 completed larvae arm; 32 completed hydrogel arm; statistics based on starting number.
j. Three patients with no data for final evaluation.
k. Wound surface area increased for conventional arm and decreased for maggot (negative percent indicates decrease).
l. 77-85% of costs due to nurse consultations and hospital visits.
m. Hydrogel compared to combined larval therapy arms.
n. Mentions that mild pain/burning sensation was common but not in how many patients.
o. Wound score calculated as a combined score for sloughy coverage, exudation, malodor, inflammation, granulation, each marked 0-3; maximum score 15.
p. Conventional treatment as determined by patients' primary care providers observed in eight out of 10 patients three to four weeks prior to larvae treatment.
q. Positive indicates increase in wound area, negative indicates decrease.
r. 103 patients (with 145 wounds) evaluated for adverse events; 92 wounds in 67 patients analyzed for debridement and healing.
s. Results represented as estimate (95% confidence interval); for surface area, positive values show increase in wound area and negative show decrease.
t. Two reported pain, one reported anxiety about treatment.
u. 29 wounds in 25 patients.
v. 723 wounds in 435 patients.
w. Combined results reported on all outcome measures.
x. Scoliosis patients with infected wounds; antibiotic treatment concurrent with maggot debridement.

(Contd.)

POTATO PEEL							
AUTHOR, YEAR	**STUDY DESIGN**	**WOUND TYPE**	**N**	**OUTCOME MEASURE (UNITS)**	**EFFECT ESTIMATES**		
					CONTROL	**COMPARISON**	**TREATMENT**
Manjunath, 2015	Case Report	necrotizing fasciitis	1	reduction in wound surface area, one week (cm2)			12

TEA TREE OIL							
AUTHOR, YEAR	**STUDY DESIGN**	**WOUND TYPE**	**N**	**OUTCOME MEASURE (UNITS)**	**EFFECT ESTIMATES**		
					CONTROL	**COMPARISON**	**TREATMENT**
Lee, 2014	RCT	ulcer infected with MRSA	32	quantity of MRSA, baseline (CFU/ml)		6437±1209	7093±1356
				quantity of MRSA, one week (CFU/ml)		8125±1821	4531±1783
				quantity of MRSA, two weeks (CFU/ml)		8937±2174	2375±1284
				quantity of MRSA, three weeks (CFU/ml)		9875±2610	468±590
				quantity of MRSA, four weeks (CFU/ml)		10312±3054	93±201
				PUSH score, baseline		8.1	7.9
				PUSH score, one week[a]		7.6	5.5
				PUSH score, two weeks[a]		6.9	5.4
				PUSH score, three weeks[a]		5.5	1
				PUSH score, four weeks[a]		4.6	0
							3.3% tea tree oil
Edmondson, 2011	Case Report	MRSA	11[b]	number reporting pain			3 per 11
				attrition rate after treatment started (adverse events)			1 per 11
				mean wound size, baseline (mm^2)			2553.36
				mean wound size, last measurement (mm^2)			2101.18
				mean duration of treatment, last measurement (weeks)			5.82
				median duration of treatment, last measurement (weeks)			6
				number still MRSA-positive at last measurement			12 per 12
				mortality rate			1 per 12
				mean degree of pain, baseline			4.45
				mean degree of pain, last measurement			5.09

a. Pressure Ulcer Scale for Healing (PUSH) tool 3.0 score combines scores on surface area, exudate, and wound tissue type, each on a 0-4 scale.
b. 12 eligible, 11 received treatment, two completed study; 11 analyzed.

The following complementary therapies were evaluated: honey, maggot debridement, Aloe vera, Calendula officinalis, Hypericum perforatum ointment, dragon's blood, curcumin, banana leaf dressing, potato peels, and tea tree oil. Nearly all evaluated complementary therapies were found to be potentially effective, but the quality of the evidence varied widely between different treatments. The richest body of evidence was identified for honey dressing, maggot debridement, and Aloe vera.

ALOE VERA

Nine articles met the inclusion criteria (Eshghi et al., 2010; Khorasani et al., 2009; Khorasani et al., 2011; Molazem et al., 2014; Panahi et al., 2012; Schmidt & Greenspoon, 1991; Shahzad & Ahmed, 2013; Thamlikitkul et al., 1991; Thomas et al., 1998). The studies used Aloe vera as creams or gel. Four studies compared Aloe to silver sulfadiazine dressings for treatment of burn wounds (Khorasani et al., 2009; Panahi et al., 2012; Shahzad & Ahmed, 2013; Thamlikitkul et al., 1991); three studies used standard management, simple dressings, or gauze moistened with saline as a comparison (Molazem et al., 2014; Schmidt & Greenspoon, 1991; Thomas et al., 1998); and two studies compared Aloe to a placebo (Eshghi et al., 2010; Khorasani et al., 2009). Aloe vera cream reportedly decreased pain for haemorrhoidectomy but may have increased healing time (Eshghi et al., 2010). Aloe hydrogel produced a similar outcome to moist saline gauze when treating pressure ulcers (Thomas et al., 1998). There was mixed evidence for whether Aloe improved healing time for post-operative Caesarean section wounds (Molazem et al., 2014) or increased healing time (Schmidt & Greenspoon, 1991). For burns, Aloe vera reportedly improved skin dryness, pain severity (Panahi et al., 2012) and had a high patient satisfaction rating (Thamlikitkul et al., 1991) compared to silver sulfadiazine dressings. Healing time for burn wounds for those treated with Aloe vera was similar or shorter than silver sulfadiazine dressings (Khorasani et al., 2009; Panahi et al., 2012; Shahzad & Ahmed, 2013).

Comparison of the effectiveness of nanocrystalline silver (nAg) and Aloe vera as complementary therapies

Tsang et al. (2017) conducted a randomized controlled study of nanocrystalline silver (nAg) and manuka honey (MH) compared to conventional dressing (paraffin tulle and gauze) in healing diabetic foot ulcer (DFU) in terms of ulcer healing, ulcer infection, and inflammation (listed under "Honey" in Table 2). Estimated healing potential was highest in the nAg group followed by the MH group, and both were higher than the conventional group. The ulcer size reduction rate measured by percentage of area reduction was highest in the nAg group and second highest in the MH group, both of which were at least 10 percentage points higher than the conventional group.

BANANA LEAVES

One study was included on sterilized banana leaves, which focused on direct application to surgical incision wounds (Guenova et al., 2013). Banana leaves were tested in a clinical setting in postsurgical patients in Uganda and were reported to have wound-dressing properties that equaled those of petroleum jelly gauze dressings. No additional pain during the first dressing change and no infections were reported during the two-week follow-up period.

CALENDULA OFFICINALIS

Buzzi et al. (2016) examined the effects of Calendula officinalis on patients with venous leg ulcers. The proportion of patients achieving complete epithelialization was 72% and 32% in the treatment and control groups, respectively. The average healing time was approximately 12 weeks in the treatment group and 25 weeks in control patients. Patients with ulcers treated with Calendula officinalis extract had a significant four-fold increase in percentage healing velocity per week, 7.4%, compared with 1.7% in the control group. No adverse events were observed during the Calendula officinalis extract treatment.

CURCUMIN OINTMENT (TURMERIC)

One clinical trial of high quality conducted in India was identified (Choudhary et al., 2012). Turmeric (ethanol extract of turmeric in Vaseline base after proper sterilization applied topically along with Vaseline gauze (Jelonet)) was found to be effective as an antiseptic treatment with local application for superficial burns. Patients in the test group were consistently found to have a lower rate of infection and positive swab cultures throughout the time points measured in the course of study compared to the control group (Vaseline gauze (Jalonet) alone). Also, the study found a progressive decrease in the number of positive cultures in the test group from the third day onward. No side effect was noted in either group.

DRAGON'S BLOOD TOPICAL CREAM

One clinical trial from Iran investigated whether dragon's blood was an effective and safe healing agent (Namjoyan et al., 2016). At the end of the trial, there was a significant difference in the mean duration of wound healing between the two groups, and no irritations or wound infections were reported among those in the therapy arm.

HONEY

Thirty-one studies of high to moderate quality were identified. Most were clinical trials. The efficacy of the topical use of honey was evaluated for a wide range of wound types including burns, acute, chronic, pressure, malignant, post-traumatic, and post-operative wounds.

The highest quality studies reported evidence that treating superficial and partial thickness burns with honey reduced mean time to healing in comparison with conventional non-antibacterial treatments. Additional moderate quality evidence suggested that burns treated with honey were more likely to heal over time as compared to topical antibiotics (Mashhood et al., 2006; Subrahmanyam, 1998). Some moderate quality evidence suggested that honey was more effective than antiseptics followed by gauze for post-operative infected wounds, while lower quality evidence suggested wounds treated with topical honey were less likely to get infected compared to treatments with silver-based antiseptics or topical antibiotics (Gulati et al., 2014).

Many studies including several randomized controlled trials found that the antibacterial effect of honey dressing differed depending on wound type. Studies investigating the impact of honey on diabetic and pressure foot ulcers strongly supported an antibacterial effect of honey dressing (Shukrimi et al., 2008; Dubhashi & Sindwani, 2015; Tsang et al., 2017; Kamaratos et al., 2012). Studies examining malignant wounds reached mixed conclusions; some found honey-coated and silver-coated bandages to have no effect while others showed improved outcomes (Lund-Nielsen et al., 2011). Honey dressing reportedly performed comparably to phenytoin cream and even superior to silver sulfadiazine (Mashhood et al., 2006; Subrahmanyam, 1998). Studies also referenced numerous other benefits associated with the use of honey dressing, including increase of patient comfort, better pain management, faster and more efficient removal of malodor, decrease in wound size, and fast disinfection (Dorai, 2012; Dubhashi & Sindwani, 2015; Gulati et al., 2014; Kamaratos et al., 2012). Several trials highlighted an improved aesthetic outcome of the wound by using honey dressing (Dorai, 2012).

HYPERICUM PERFORATUM

Only one study on Hypericum perforatum was included (Samadi et al., 2010). Hypericum perforatum ointment was compared to placebo as a treatment for Caesarean section wounds. There were significant differences in wound healing on the 10th day and scar formation on the 40th day postpartum between the treatment group and the placebo and control groups. The placebo group had no differences in wound healing and scar formation from the control group. In addition, significantly lower pain and pruritus were reported by the treatment group compared with the placebo and control groups on the 40th day postpartum.

MAGGOT DEBRIDEMENT

Nineteen studies varying in quality were identified, with high prevalence of meta-analyses, systematic reviews, and case reports. The majority of available evidence investigated patients with different types of ulcers and other chronic wounds.

Maggot therapy was found to influence three processes: tissue granulation, debridement, and infection. An increase in wound granulation tissue and quicker debridement (average within one week) were shown in numerous studies (Wayman et al., 2000; Wollina et al., 2002; (Marineau et al., 2011; Turkmen et al., 2010). Studies reached mixed conclusions regarding disinfection; some seem to confirm the disinfecting properties of this therapy (Sherman et al., 1995; Sherman & Shimoda, 2004), while the others found no difference in infection rates between larval and conventional therapies (Opletalová et al., 2012). Bio-surgical properties of maggot therapy such as healing time, complete healing rate, and amputation rate were evaluated. Their translation into clinical outcomes varied. The evidence showed a consistent significant decrease in amputation rate only regarding time to heal; most of the studies found larval therapy groups with significantly shorter healing time (Sherman, 2003; Azad et al., 2016; Wu et al., 2012), but other studies showed no difference (Paul et al., 2009; Dumville et al., 2009; Soares et al., 2009). While some studies showed improvement in full healing rate after implementation of larval therapy, numerous other reviews and meta-analyses failed to show any significant improvement in complete healing rate following maggot debridement therapy.

Studies performing cost-effectiveness analyses also reached mixed conclusions. Most of them found larval therapy to be more cost-effective than conventional therapies due to shortening the length of hospital stay and reducing the need for amputation. Increase in wound granulation tissue and quick debridement (average within one week) were shown in numerous studies. A few studies (Soares et al., 2009) suggested the costs of larval therapy may be similar to those of hydrogel-based therapies.

POTATO PEELS

Only two studies focused on potato peels as a potential wound treatment. One study included 100 patients with burn injuries and compared treatment with potato peels to honey (Subrahmanyam, 1996a, listed under "Honey" in Table 2), and the other was a case study (Manjunath et al., 2015). In the patients treated with honey, 90% of wounds were rendered sterile within seven days, but infections persisted in patients treated with potato peels in the same period. Potato peels were also not found to improve total healing time compared to treatment with honey; 100% of patients with burn wounds treated with honey healed within 15 days versus only 50% with wounds treated with boiled potato peel dressings. Potentially positive results of potato peels that were reported included a fast rate of formation of healthy granulation tissue and good marginal healing.

TEA TREE OIL

There were only two studies on tea tree oil as a wound treatment for patients with stage II or higher MRSA-colonized wounds. In the tea tree oil group, all chronic wounds that had previously been delayed in healing were healed within the study period without adverse reaction. In the study by Lee et al. (2014), MRSA was also completely eradicated in 87% of wounds in the group receiving the 10% topical tea tree oil preparation by the end of the study period. Sixteen MRSA colonized wounds in the tea tree oil group were closed skin by 28 days. After treatment, eight of the 11 treated wounds had begun to heal and reduced in size. In another study, no participants were MRSA negative after treatment (Edmondson et al., 2011), but this study had a smaller sample size, used a lower dose of tea-tree oil, and a "rinse-off" treatment, rather than "leave-on" treatment.

DISCUSSION

ALOE VERA

The results suggest that Aloe vera improved pain, was well tolerated, and had similar or better wound healing rates compared to silver sulfadiazine dressings in treating burn wounds. Aloe vera also improved healing time after haemorrhoidectomy and skin graft. On the other hand, in chronic wounds such as pressure ulcers, there was no statistical difference in the healing process, and in post-Caesarean wounds, adding Aloe to standard treatment sometimes extended healing time. The results suggest that there is need for more studies to understand for which types of wounds Aloe vera can improve healing and for which it either makes no difference or slows healing.

BANANA LEAVES

The study on sterilized banana leaves used as wound dressings could serve as a proof of concept. Though there was limited evidence to support the hypothesis that a special chemical found in the leaves could proactively promote healing and reduce infectious bacteria, in application, the rate of discomfort and complications for banana leaf dressings were found to be comparable to conventional dressings, suggesting they could be used as a lower cost alternative.

CALENDULA OFFICINALIS

Calendula oil (or Calendula officinalis extract) may aid in wound healing by promoting epithelial growth and by enhancing immune responses. While the studies suggest efficacy for venous and diabetic leg ulcers and post-cesarean section wounds, further research is needed to validate this result.

CURCUMIN OINTMENT (TURMERIC)

The study on turmeric cream reported this to be a painless treatment, even suggesting that turmeric was soothing on local application for superficial burn would patients. Although the one randomized controlled trial identified suggested that it could be a safe and effective treatment for wound healing, further studies are needed to support this statement.

DRAGON'S BLOOD TOPICAL CREAM

While the results for the use of dragon's blood were promising, these were from only one clinical trial. Also, there is no clear understanding of the role of pathogenesis of wound healing. As such, there is need to conduct more studies to test its effectiveness on stimulation or hindering of mediators in wound healing. Additionally, there are a number of studies published in Chinese that were not evaluated in this systematic review.

HONEY

Honey had the largest body of literature studying its effectiveness for wound therapy. Most studies found that it was effective for burn wounds and diabetic ulcers; this may be especially important in resource-limited settings. Notably, nine studies on honey therapy were conducted by one researcher (Subrahmanyam).

HYPERICUM PERFORATUM

Evidence on the effectiveness of Hypericum perforatum in wound healing was scant. The primary benefit found in one study was that Hypericum perforatum may increase patient comfort. More research would help determine the usefulness of Hypericum perforatum in wound healing.

MAGGOT DEBRIDEMENT

There was a large body of literature evaluating the efficacy of maggot debridement therapy, and most studies showed it was effective particularly in treating chronic ulcers and preventing

amputations. Also, many studies concluded that larval therapy was more cost-effective than conventional treatments.

POTATO PEELS

The limited evidence on potato peels suggests they are not an efficacious wound treatment. In a direct comparison, honey, which also had a larger evidence base, was shown to be more effective.

TEA TREE OIL

There was some evidence showing that tea tree oil could be helpful in treating MRSA colonized wounds; however, neither complete healing nor eradication of MRSA was achieved. Further research is need to support the use of tea tree oil for a treatment for MRSA colonized wounds, though it may have utility when conventional treatments are unavailable.

CONCLUSION

This review evaluated the available published evidence on the clinical effectiveness of complementary therapies in wound treatment and identified several that may be therapeutically effective and more cost-effective than conventional treatments. All complementary therapies reviewed except for potato peels had at least one study that found them to be potentially effective, though the quality of the evidence varied. Out of the studies identified, few contained high quality evidence, and some articles were case studies. The richest bodies of evidence were identified for honey dressing, maggot debridement, and Aloe vera, which all demonstrated effectiveness in the treatment of chronic wounds. While additional high-quality studies are needed across settings to understand effectiveness, best practices, and indications, the results of this systematic review can assist in guiding practitioners to identify options for lower-cost, potentially efficacious wound treatments.

ACKNOWLEDGEMENTS

We gratefully acknowledge the support of Ediom's EvidenceEngine, Ray Liu, and Sally Yin for their support of our project. We also thank Columbia University School of Nursing's Global Innovation Fund for the Writing to Improve Nursing Science in Malawi grant that supported this work, as well as the partnership and contribution from University of Malawi Kamuzu University of Health Sciences, formerly Kamuzu College of Nursing. We are grateful for all the staff and faculty that supported this project from University of Malawi Kamuzu College of Nursing. Finally, we thank Yu-Hui Ferng for arranging and supporting our in-person writing workshop, Drs. Ana Kelly and Maureen George for serving as co-investigators on the Writing to Improve Nursing Science in Malawi grant, and Dr. Tonda Hughes and Dr. Jennifer Dohrn for their insight and support for the project.

FUNDING INFORMATION

This study was funded by the Columbia University School of Nursing's Global Innovation Fund.

COMPETING INTERESTS

The authors have no competing interests to declare.

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TO CITE THIS ARTICLE:
Msiska, G., Fu, C., Wella, K., Msosa, A., Mbirimtengerenji, N., Masache, G., Simbota, M., Banez, M. C., Chorwe-Sungani, G., & Sun, C. (2023). Effectiveness of Complementary Therapies in the Management of Wounds Among Adult Patients. *Practical Implementation of Nursing Science*, *2*(1), pp. 22–53. DOI: https://doi.org/10.29024/pins.31

Submitted: 19 April 2022
Accepted: 23 May 2023
Published: 08 June 2023

Practical Implementation of Nursing Science is a peer-reviewed open access journal published by Levy Library Press.

Levy Library Press