

SYSTEMATIC REVIEW

The efficacy and safety of Polyhexanide compared to other wound dressings in patients with various wound types: a systematic review and meta-analysis

Vannia Christianto Teng^{1*}, Asnawi Madjid¹, Widya Widita¹, Khairuddin Djawad¹

¹Department of Dermatology and Venereology, Faculty of Medicine, University of Hasanuddin, Makassar, Indonesia

*Corresponding author email vanniacteng@gmail.com

Abstract

Aims This study aims to evaluate the efficacy and safety of polyhexanide or polyhexamethylene biguanide (PHMB) for management of various wound types compared to other dressings.

Methods A literature search was conducted in journal databases including PubMed, Google Scholar, ScienceDirect, Cochrane, CENTRAL, and Clinicaltrials.gov. We included intervention studies that evaluated the use of polyhexanide topical preparations in wound healing until November 2024. Risk of bias was assessed using Cochrane Risk-of-Bias tool 2 (RoB2) and ROBINS-I. Quantitative analysis was carried out using Review Manager version 5.4.

Results Eighteen studies were included, comprising randomised controlled trials and cohort studies with sample sizes ranging from 12 to 146 patients. Five studies were eligible for meta-analysis. Healing time was significantly faster in polyhexanide group compared to controls (MD -14.84 days; 95% CI -31.30, 1.62; p=0.08). While there was no significant difference (Odds ratio 0.76; 95% CI 0.23, 2.48; p=0.65), the bacterial burden reduction was higher in PHMB-treated wounds (p=0.04).

Conclusion Polyhexanide demonstrated significantly faster healing time in treatment of various types of wounds. It also had multiple advantages, such as its transparent properties, antimicrobial activity, and reduced pain compared to other treatments. Further studies may be needed to assess long-term efficacy and safety of PHMB for various wound types.

Keywords polyhexanide, meta-analysis, wound.

For referencing Teng VC et al. The efficacy and safety of polyhexanide biguanide compared to other wound dressings in patients with various wound types: a systematic review and meta-analysis. *Wound Practice and Research* 2025;33(3):122-138.

DOI <https://doi.org/10.33235/wpr.33.3.122-138>

Submitted 13 December 2024, Accepted 9 April 2024

Introduction

Wound healing is a complex process to restore destroyed or damaged tissue, which includes multiple overlapping processes: hemostasis, inflammatory response, proliferation of connective tissues and its precursors (such as keratinocyte, fibroblast, macrophage, and endothelial cell migration), and tissue remodeling.^{1,2} Disruption in any stage of wound healing may result in chronic, non-healing wounds, which may be attributable to multiple risk factors, such as advancing age, obesity, presence of comorbidity (for example diabetes mellitus, malignancy), repeated insults, and poor treatment choice and its adherence.^{1,3} Treatment may also be more complicated in cases in which there is contamination of

drug-resistant bacteria and biofilm formation, which may further hinder the process of wound healing.^{4,5}

Administration of topical disinfectants and wound dressing has been the choice of treatment in various wound types to replace the barrier function in intact skin, such as polyhexanide or polyhexamethylene biguanide (PHMB). Polyhexanide is a positively charged polymer with a hydrophobic backbone and cationic groups spaced by hexamethylene chains. This structure enables polyhexanide to attach to negatively charged molecules to bacterial surfaces, compromising the bacterial cell membrane and ultimately causing cell death.⁶ Polyhexanide has been widely used in wound care because of its effectiveness in reducing microbial loads and its high

tolerability by cells and tissues and several other advantages, including a broad antimicrobial range, the capacity to bind to an organic matrix, and a positive impact on wound healing.^{7,8} Previous study has reported the use of PHMB-containing dressings in various wound types, such as burn injury, pressure ulcers, and venous ulcers.^{5,9,10} However, systematic evidence of polyhexanide use as main treatment in various wound types was still scarce. This study aimed to evaluate the efficacy and safety of polyhexanide for management of various wound types compared to other dressings.

Methods

Search strategy

This systematic review and meta-analysis followed the guidelines from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). A literature search was carried out in multiple journal databases, such as PubMed, Google Scholar, ScienceDirect, Cochrane, CENTRAL, and Clinicaltrials.gov until November 2024. The search was conducted independently by two authors to ensure thoroughness.

We included intervention studies (randomised controlled trials, non-randomised controlled trials, cohort studies) that evaluated the use of polyhexanide topical preparations in wound healing. We used Boolean operators with the following keywords: “wound”, “polyhexanide”, and outcomes with its synonyms. Outcomes of this study included efficacy and safety. Efficacy consisted of healing time, re-epithelialisation time and change in wound size, pain (by scores or overall quality of life assessment), antimicrobial effect (such as changes in bacterial load, infection rate, regression rate), and alterations of wound characteristics (including wound assessment scores, odor). Assessment of safety was evaluated with number of adverse events in included studies.

Data extraction

Four authors were involved in study selection and data extraction. Inclusion criteria of this study were:

- therapeutic study design evaluating the efficacy and/or safety of Polyhexanide Biguanide wound dressings;
- human-based studies involving patients with acute or chronic wounds; randomised controlled trials (RCTs) and cohort studies with a control group;
- studies comparing Polyhexanide Biguanide wound dressings to other standard wound dressings;
- studies reporting at least one quantitative clinical/microbiological outcomes;
- published in peer-reviewed journals with full-text availability;
- written in English (or with an available English translation).

We excluded studies with non-human subject research, case report or case series, review articles, meta-analyses,

systematic reviews, narrative reviews, or expert opinions, evidence summaries (such as guideline summaries, clinical practice summaries, or consensus statements), and irretrievable full-text articles. Duplicate records were manually removed using Microsoft Excel. Data extraction was performed by Authors 1, 2, and 3 and included patient age, sample size, wound type, intervention details, and study outcomes (wound healing time, pain score, adverse reactions, antimicrobial effect, antiseptic effect, and alteration of wound characteristics). Any discrepancies in data extraction were resolved by Author 4.

Risk of bias assessment

Risk of bias in included studies was evaluated using Cochrane Risk of Bias (ROB) tool for randomised controlled-trials and ROBINS-I for non-randomised clinical trials.^{11,12} Risk of bias was assessed independently by two authors, in which discrepancy between two authors were resolved by third author. Publication bias was assessed using a funnel plot for outcomes, with more than ten studies included for quantitative analysis.

Data synthesis and analysis

Data were presented in tables and figures. Meta-analysis was performed using Review Manager version 5.4 software. Outcomes were measured using mean difference (MD) for continuous variables and odds ratio (OR) for categorical variables, any study that did not report specific outcomes were not included in quantitative analysis. Random-effect meta-analysis model was used as we judged that each study may use different dosage and frequency of polyhexanide as treatment for wounds. Heterogeneity was assessed using chi-square analysis with I-squared statistics. A *p* value of less than 0.05 was considered as statistically significant. Synthesis and analysis was done by two authors and was further reviewed by a third and fourth author.

Results

Study characteristics

A total of 257 records were identified in the initial search (Figure 1). Removal of duplicates resulted in a total of 254 records, of which 194 records were excluded after title and abstract screening. Of 38 full-text articles, we excluded 20 articles due to difference in PICO. A total of 18 included studies^{5,7-10,13-25} in this review can be seen in Table 1, which consisted of five studies for quantitative review. The included studies varied in design, with most being randomised controlled trials (RCTs), but also including cohort studies and non-randomised clinical trials. Sample sizes ranged from 12 to 146 participants, and study participants were generally adults with various wound types, including pressure ulcers, venous leg ulcers, burns and surgical wounds. Outcome measures included healing time, pain scores, bacterial load, odor, infection rates, wound size reduction, and quality of life assessments. A detailed breakdown of each study's characteristics can be found in the table. Efficacy outcomes between studies can be seen in Table 2.

Risk of bias can be seen in Figure 2, in which 13 studies^{7,8,13-22,25} had moderate risk of bias due to bias arising from randomisation processes in RCT studies and bias due to confounding, missing data, and measurement outcomes in non-randomised clinical trials.

Healing time

A total of 4 studies^{7,9,14,16} reported the outcome of healing time with a total sample of 248 patients (Figure 3). Mean difference of healing time was 14.84 days (95% CI 31.30, 1.62; $p=0.08$), and meta-analysis showed significantly faster healing time in polyhexanide compared to controls. However, Ceviker et al⁷ found no significant difference in wound healing time between polyhexanide (15±5 days) and Ringer's Lactate Solution (RLS) (16±3 days; $p=0.462$) groups.⁷ Heterogeneity was substantial in this outcome (I-squared=98%).

Bacterial load

Five studies^{7-9,18,20} reported the outcome of bacterial load with a total sample of 140 patients (Figure 4). Meta-analysis of this outcome showed a non-significant difference

in presence of bacterial load in PHMB treated wounds compared to controls (OR 0.76; 95% CI 0.23, 2.48; $p=0.65$), although lower bacterial load was seen in patients receiving PHMB. Heterogeneity was substantial in this outcome (I-squared=75%). The timing of bacterial load assessment varied, with some studies measuring it at different follow-up intervals, which may influence pooled estimates.

Bacterial burden reduction rate

Three studies^{8,21,23} reported bacterial burden reduction rates following polyhexanide administration. Eberlein et al⁸ found significantly higher bacterial clearance in polyhexanide treated wounds compared to silver ($p=0.0009$). Motta et al²¹ reported significant reductions in bacterial colony count ($p<0.05$), supporting the efficacy of polyhexanide in reducing bacterial burden. Sibbald et al²³ observed a decrease in bacterial burden in wounds treated with polyhexanide dressings. Pooled analysis of this outcome showed a non-significant difference between polyhexanide and controls (OR 1.44; 95% CI 0.17, 12.45; $p=0.74$), with substantial heterogeneity (I-squared=78%) (Figure 5). The follow-up duration for

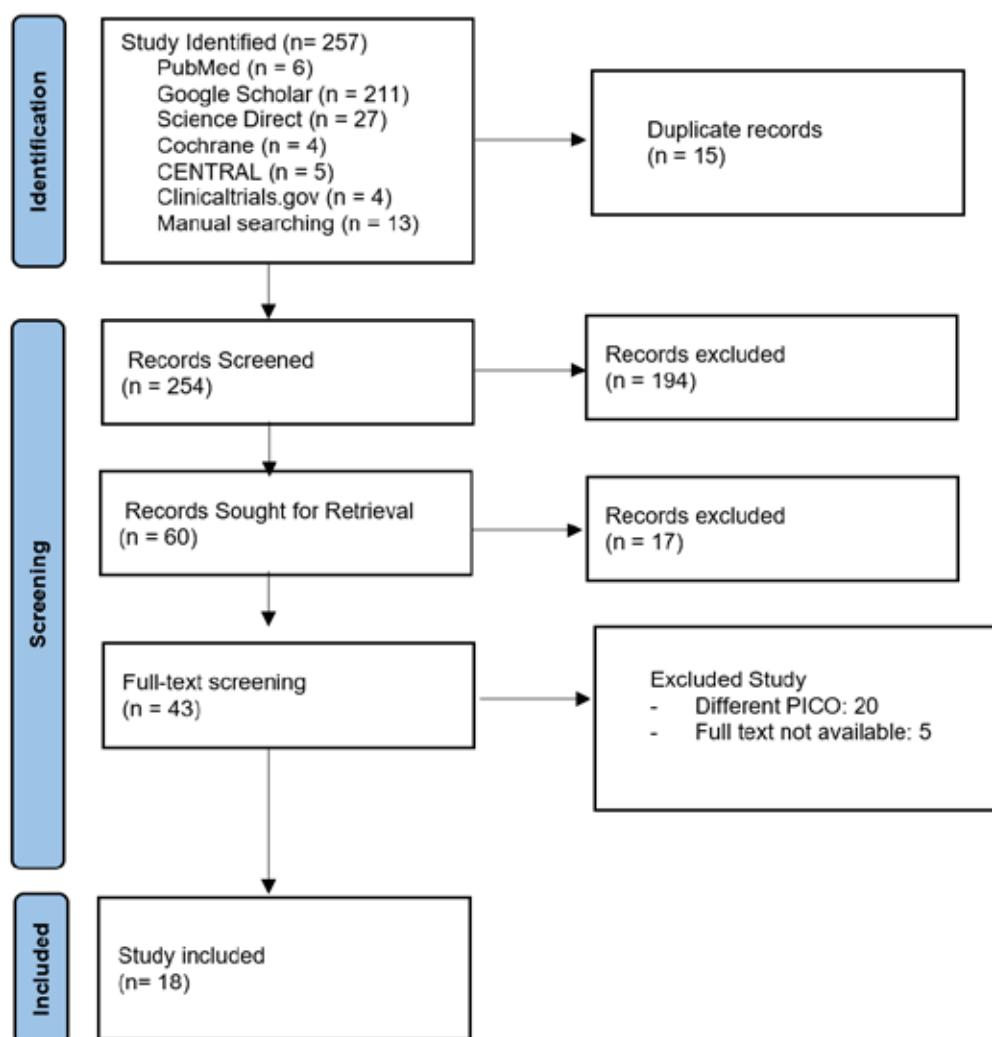


Figure 1. PRISMA flow diagram²⁶

Table 1. Study characteristics

Lead author, year	Study design	Country	Intervention	Details	Control	Sample size (n)	Age (year)	Wound type	Outcomes reported
Wattanapoy, 2017 ⁹	RCT	India	Polyhexanide/betaine gel	Protosan® Wound Gel X	Silver sulfadiazine	Intervention: 23 Control: 23	Intervention: 26.9±6.9 Control: 31.3±6.4	Partial-thickness burn injury	(1) Healing time (2) Pain score (VAS) (3) Bacterial load (4) Infection rate
Bellingeri, 2016 ¹⁰	RCT	Italy	Propylbetaine 0.1% and polihexanide 0.1% solution	Protosan®	Normal saline	Intervention: 143 Control: 146	Intervention: 79.8 Control: 77.2	Pressure ulcers or vascular leg ulcers	(1) Bates-Jensen Wound Assessment Tool (BWAT) score (2) Pain score (VAS) (3) Adverse event
Romanelli, 2010 ⁵	RCT	Italy	Propylbetaine 0.1% and polihexanide 0.1% solution	Protosan®	Normal saline	Intervention: 20 Control: 20	62±3	Painful chronic leg ulcer	Pain score (VAS)
Kiefer, 2018 ¹³	Cohort study	Germany	Polyhexanide/betaine gel	Protosan® Wound Gel X	NA	51	43±16.6	Deep partial or full-thickness burn injury requiring STSG	(1) Time to re-epithelialisation (2) Adverse reaction
Borges, 2018 ¹⁴	RCT	Brazil	Propylbetaine 0.1% and polihexanide 0.1% solution	Protosan®	Normal saline	Intervention: 22 Control: 22	Intervention: 55.92±5.9 Control: 60.9±13.9	Venous leg ulcers	(1) Healing time (2) Wound size
Ceviker, 2015 ⁷	Cohort study	Turkey	0.5% polyhexamethylene biguanide (PHMB) solution	Actolind®	Ringer's lactate solution	Intervention: 15 Control: 16	Intervention: 64±12 Control: 60±10	Pressure ulcer or surgical site infection with non-healing wound in patient underwent cardiac surgery	Bacterial load
Lenslink, 2011 ²⁵	Cohort study	Netherlands	Polyhexanide-containing biocellulose dressing	Suprasorb X + PHMB	NA	16	60.9±21.6	Non-healing wounds	(1) Wound size (2) Pain score (VAS) (3) Alteration of wound characteristics
Saleh, 2016 ¹⁵	Non-randomized clinical trial	Sweden	Propylbetaine 0.1% and polihexanide 0.1% solution	Protosan®	Sterile water	Intervention: 20 Control: 20	NI	Post facial full-thickness skin grafting	(1) Bacterial load (2) Infection rate (such as surgical site infection) Healing time
De Decker, 2024 ¹⁶	Cohort study	Belgium	Polyhexanide/betaine gel	Protosan® Wound Gel X	Alginate-based dressing (Flaminal or Forte®)	Intervention: 29 Control: 31	Intervention: 32.34±26.10 Control: 39.77±30.83	Burn injury (superficial burn or full-thickness burn injury)	Healing time
Eberlein, 2012 ⁸	RCT	Austria and Switzerland	Polyhexanide-containing biocellulose dressing	Suprasorb X + PHMB	Silver sulfadiazine	Intervention: 21 Control: 17	Intervention: 72.8±11.8 Control: 70.3±12.7	Primary venous leg ulcer (PVLU) with some arterial components and diabetic foot ulcers	Pain score (VAS)

Lead author, year	Study design	Country	Intervention	Details	Control	Sample size (n)	Age (year)	Wound type	Outcomes reported
Lorincz, 2024 ¹⁷	Cohort study	Hungary	0.04% Polyhexamethylene biguanide (PHMB) gel betaine	LAVANID®	NA	27	3.74±4.73	II/1 Partial-thickness burn injury with 1–10% TBSA	Time to re-epithelialisation
Findlay et al, 2013 ²⁰	RCT	UK	PHMB	Prontosan wound gel	Mupirocin (Antibiotic Ointment)	Intervention: 53 Control: 53	Intervention: 59.9±1.7 Control: 58.0±1.9	Peritoneal dialysis exit site infections	(1) Exit site infection (ES) rate (2) Peritonitis rate (3) Bacterial load (organisms isolated)
Gentile, 2012	RCT	Italy	PHMB-based gynecological Solution	Monogin®	No Treatment (Control Group)	Intervention: 50 Control: 50	30–45	HPV infection	(1) HPV regression rate (2) HPV clearance at 3 and 6 months
Gerli, 2012 ²²	RCT	Italy	PHMB vaginal suppositories	Monogin®/ Biguanelle® ovuli, Lo.Li. Pharma, Italy	Chlorhexidine digluconate vaginal suppositories	50	20–40	Postoperative cervical lesions after CO ₂ laser therapy for CIN II & III	(1) Bacterial vaginosis (BV) occurrence (2) Healing rate (Incision defect recovery) (3) Irritation, bleeding (4) Infection (5) Prevention
Lee, 2011 ¹⁸	RCT	Malaysia	PHMB-impregnated Gauze	Excilon™ AMD™ I.V. Sponges, 0.2% PHMB	Plain Gauze (Excilon™ I.V. Sponges) Wetted with Normal Saline	Intervention: 22 Control: 18	26.3 (5–68)	Pin site infections in external fixation	(1) Pin site infection rate (Grade 1–3) (2) Infection risk reduction (3) Comparison of infection rates by pin/wire interface
Motta, 2004 ²¹	RCT	US	PHMB-impregnated gauze dressing	Kerix® A.M.D. gauze dressing	Plain gauze dressing (no PHMB)	24	68.5±10.2	Delayed closure surgical wounds, pressure ulcers, diabetic foot ulcers requiring packing	(1) Wound healing time (days) (2) Healing rate (%) (3) Bacterial load reduction (4) Antimicrobial effect (bacterial culture) (5) Alteration of wound characteristics (6) Pain score (VAS scale)
Sibbald, 2011 ²³	RCT	Canada	PHMB-impregnated foam dressing	Kendall AMD antimicrobial foam dressing	Non-antimicrobial foam dressing	45	55.8±13.13	Chronic wounds (leg ulcers=23, foot ulcers=22)	(1) Wound healing rate (wound size reduction %) (2) Bacterial burden (3) Pain reduction (4) Infection rate
Villela-Castro, 2023 ²⁴	RCT	Brazil	0.2% PHMB solution, applied during dressing changes twice daily for 8 days	Prontosan, B. Braun, Brazil	0.8% Metronidazole solution	Intervention: 12 Control: 12	62.4±15.1	Malignant wounds	(1) Odor intensity (2) Odor quality (3) Impact of odor on patients (4) Pain during dressing changes (5) HRQOL (Ferrans and Powers Quality of Life Index: FPQUJ-WV)

Table 2. Efficacy outcomes in patients receiving polyhexanide

Lead author, year	Intervention	Control	Healing time (days) mean±SD		p	Time to re-epithelialisation (days) mean±SD		p	Wound size (cm squared) mean±SD		p	Pain score (VAS) mean±SD		p
			Control	Intervention		Control	Intervention		Control	Intervention		Control	Intervention	
Wattanaploy, 2017 ⁹	Polyhexanide/betaine gel	Silver sulfadiazine	18.8±2.1	17.8±2.2	0.013					0.8±1	0.5±0.7	0.0472		
Bellingeri, 2016 ¹⁰	Propylbetaine 0.1% and polihexanide 0.1% solution	Normal saline								3	3	NS		
Romanelli, 2010 ⁵	Propylbetaine 0.1% and polihexanide 0.1% solution	Normal saline								Week 1:10 Week 2:9 Week 3:9 Week 4:8	Week 1:9 Week 2:8.2 Week 3:7.8 Week 4:4.2	<0.05		
Kiefer, 2018 ¹³	Polyhexanide/betaine gel	NA				7.1±0.2	NA							
Borges, 2018 ¹⁴	Propylbetaine 0.1% and polihexanide 0.1% solution	Normal saline	73.3±20.7	24.25±5.4	0.6885			22.95 ± 4.69	17.68 ± 4.48	0.882				
Ceviker, 2015 ⁷	0.5% polyhexamethylene biguanide (PHMB) solution	Ringer's lactate solution												
Lenslink, 2011 ²⁵	Polyhexanide-containing biocellulose dressing	NA								NA	Day 0:7.4 Week 24:3.2	NA		
Saleh, 2016 ¹⁵	Propylbetaine 0.1% and polihexanide 0.1% solution	Sterile water												
De Decker, 2024 ¹⁶	Polyhexanide/betaine gel	Alginate-based dressing (Flaminal or Forte®)	20.60±7.76	22.60±12.54	0.288									
Eberlein, 2012 ⁸	Polyhexanide-containing biocellulose dressing	Silver sulfadiazine								Baseline 5.42±1.43 Day 28 significantly reduced (p<0.001)	Baseline 6.13±1.43 Day 28 significantly reduced (p<0.001)	NA		

Lead author, year	Intervention	Control	Healing time (days) mean±SD		p	Time to re-epithelialisation (days) mean±SD		Wound size (cm squared) mean±SD		Pain score (VAS) mean±SD		p	
			Control	Intervention		Control	Intervention	Control	Intervention	Control	Intervention		
Lorincz, 2024 ¹⁷	0.04% Polyhexamethylene biguanide (PHMB) gel betaine	NA				NA	8.78±2.64	NA					
Findlay, 2013 ²⁰	PHMB	Mupirocin (Antibiotic Ointment)											
Gentile, 2012 ¹⁹	PHMB-based gynecological solution	No Treatment (Control Group)	3 months: 28/50 (56%) 6 months: 35/50 (70%)	3 months: 33/50 (66%) 6 months: 45/50 (90%)	0.023								
Gerli, 2012 ²²	PHMB vaginal suppositories	Chlorhexidine digluconate vaginal suppositories	NA	NA	Faster recovery in intervention group								
Lee, 2011 ¹⁸	PHMB-impregnated gauze	Plain Gauze (Exiclon™ I.V. Sponges) wetted with normal saline											
Motta, 2004 ²¹	PHMB-impregnated gauze dressing	Plain gauze dressing (no PHMB)	1 wound healed in 5 weeks	2 wounds healed in 5 weeks							Mean decrease from 7.4 to 3.2	<0.05	
Sibbald, 2011 ²³	PHMB-impregnated foam dressing	Non-antimicrobial foam dressing						50% reduction	100% reduction	0.85	33.3% with no pain	78.9% with no pain	0.02
Villela-Castro, 2023 ²⁴	0.2% PHMB solution, applied during dressing changes twice daily for 8 days	0.8% Metronidazole solution									Day 0: 2.08±3.37 Day 4: 1.58±2.84	Day 0: 2.0±3.22 Day 4: 1.58±2.84	No significant difference

Abbreviations: NA=not applicable, NS=not significant, p=p value, SD=standard deviation, VAS=visual analog scale

Table 2. Efficacy outcomes in patients receiving polyhexanide (cont)

Lead author, year	Intervention	Control	BWAT score mean±SD		Bacterial load n (%)		Infection n (%)		Alteration of wound characteristics (%)		
			Control	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	p
Wattanaploy, 2017 ⁹	Polyhexanide/betaine gel	Silver sulfadiazine			6 (26.1)	6 (26.1)	0 (0)	0 (0)			1.00
Belingeri, 2016 ¹⁰	Propylbetaine 0.1% and polihexanide 0.1% solution	Normal saline	Total score Day 0 : 25 Day 7: 25 Day 14: 24 Day 21: 23 Day 28: 22	Total score Day 0 : 25 Day 7: 25 Day 14: 20 Day 21: 18 Day 28: 14							
			Inflammatory score Day 0: 10 Day 7: 9.8 Day 14: 9 Day 21: 8 Day 28: 8.8	Inflammatory score Day 0: 11 Day 7: 9.9 Day 14: 8 Day 21: 5 Day 28: 4							
Romanelli, 2010 ⁵	Propylbetaine 0.1% and polihexanide 0.1% solution	Normal saline									
Kiefer, 2018 ¹³	Polyhexanide/betaine gel	NA									
Borges, 2018 ¹⁴	Propylbetaine 0.1% and polihexanide 0.1% solution	Normal saline									
Ceviker, 2015 ⁷	Polyhexamethylene biguanide (PHMB) 0.5% solution	Ringer's lactate solution			6 (16)	6 (15)					0.336
Lenselink, 2011 ²⁵	Polyhexanide-containing biocellulose dressing	NA							NA	Granulation tissue present in the wound bed (%) Day 0: 38.2+34.6 Day 2: 77.4+36.0	<0,04
Saleh, 2016 ¹⁵	Propylbetaine 0.1% and polihexanide 0.1% solution	Sterile water					8 (20)	2 (20)			0.028

Lead author, year	Intervention	Control	BWAT score mean+SD			Bacterial load n (%)			Infection n (%)			Alteration of wound characteristics (%)		
			Control	Intervention	p	Control	Intervention	p	Control	Intervention	p	Control	Intervention	p
Decker, 2024 ¹⁶	Polyhexanide/betaine gel	Alginate-based dressing (Flaminal or Forte®)												
Eberlein, 2012 ⁸	Polyhexanide-containing biocellulose dressing	Silver sulfadiazine												
Lorincz, 2024 ¹⁷	0.04% Polyhexamethylene biguanide (PHMB) gel/betaine	NA												
Findlay, 2013 ²⁰	PHMB	Mupirocin (antibiotic ointment)				S. aureus: 0 Pseudomonas: 0	S. aureus: 4 Pseudomonas: 6	0.001	3.3	3.7	Not significant			
Gentile, 2012 ¹⁹	PHMB-Based Gynecological Solution	No Treatment (control group)												
Gerli, 2012 ²²	PHMB vaginal suppositories	Chlorhexidine digluconate vaginal suppositories												Fewer cases of persistent irritation and bleeding
Lee, 2011 ¹⁸	PHMB-impregnated Gauze	Plain Gauze (Exilon™ I.V. Sponges) wetted with normal saline							38/864 (4.5%)	11/1068 (1%)	<0.001			
Motta, 2004 ²¹	PHMB-impregnated gauze dressing	Plain gauze dressing (no PHMB)				Reduction 50%	Reduction 100%	< 0.05						
Sibbald, 2011 ²³	PHMB-impregnated foam dressing	Non-antimicrobial foam dressing				33%	5.3%	0.04						
Villela-Castro, 2023 ²⁴	0.2% PHMB solution, applied during dressing changes twice daily for 8 days	0.8% Metronidazole solution												

Abbreviations: BWAT=Bates-Jensen Wound Assessment Tool, NA=not applicable, p=p value, SD=standard deviation

Table 2. Efficacy outcomes in patients receiving polyhexanide (cont)

Lead author, year	Intervention	Control	Odor Control		Bacterial Vaginosis Occurrence		HRQOL Improvement			
			Control	Intervention	Control	Intervention	Control	Intervention	p	
Wattanaploy, 2017 ⁹	Polyhexanide/betaine gel	Silver sulfadiazine								
Bellingeri, 2016 ¹⁰	Propylbetaine 0.1% and polihexanide 0.1% solution	Normal saline								
Romanelli, 2010 ⁵	Propylbetaine 0.1% and polihexanide 0.1% solution	Normal saline								
Kiefer, 2018 ¹³	Polyhexanide/betaine gel	NA								
Borges, 2018 ¹⁴	Propylbetaine 0.1% and polihexanide 0.1% solution	Normal saline								
Ceviker, 2015 ⁷	Polyhexamethylene biguanide (PHMB) 0.5% solution	Ringer's lactate solution								
Lenselink, 2011 ²⁵	Polyhexanide-containing biocellulose dressing	NA								
Saleh, 2016 ¹⁵	Propylbetaine 0.1% and polihexanide 0.1% solution	Sterile water								
Decker, 2024 ¹⁶	Polyhexanide/betaine gel	Alginate-based dressing (Flaminal or Forte®)								
Eberlein, 2012 ⁸	Polyhexanide-containing biocellulose dressing	Silver sulfadiazine								
Lofincz, 2024 ¹⁷	0.04% Polyhexamethylene biguanide (PHMB) gel betaine	NA								

Lead author, year	Intervention	Control	Odor Control		Bacterial Vaginosis Occurrence		HRQOL Improvement	
			Control	Intervention	p	Control	Intervention	p
Findlay, 2013 ²⁰	PHMB	Mupirocin (Antibiotic Ointment)						
Gentile, 2012 ¹⁹	PHMB-based gynecological solution	No Treatment (Control Group)						
Gerli, 2012 ²²	PHMB vaginal suppositories	Chlorhexidine digluconate vaginal suppositories		7/22	1/21	0.04		
Lee, 2011 ¹⁸	PHMB-impregnated gauze	Plain Gauze (Excilon™ I.V. Sponges) wetted with normal saline						
Motta, 2004 ²¹	PHMB-impregnated gauze dressing	Plain gauze dressing (no PHMB)						
Sibbald, 2011 ²³	PHMB-impregnated foam dressing	Non-antimicrobial foam dressing						
Villela-Castro, 2023 ²⁴	0.2% PHMB solution, applied during dressing changes twice daily for 8 days	0.8% Metronidazole solution	Day 0: 2.67±0.89 Day 4: 0.33±0.65	Day 0: 2.58±0.79 Day 4: 0.08±0.29	<0.01	Baseline: 13.04±1.48 Final: 14.22±1.27	Baseline: 13.00±2.42 Final: 14/21±2.11	

Abbreviations: HRQOL=Health-Related Quality of Life, NA=not applicable, p=p value, SD: standard deviation

		Risk of bias domains					
		D1	D2	D3	D4	D5	Overall
Study	Eberlein et al. (2012)	-	+	+	+	+	-
	Saleh et al. (2016)	-	+	+	+	+	-
	Borges et al. (2018)	-	+	+	+	+	-
	Romanelli et al. (2010)	+	+	+	+	+	+
	Bellingeri et al. (2016)	+	+	+	+	+	+
	Wattanaploy et al. (2017)	+	+	+	+	+	+
	Findlay et al., 2013	-	+	-	-	+	-
	Gentile et al., 2012	-	+	+	+	+	-
	Lee et al., 2011	-	+	+	+	+	-
	Motta et al., 2004	-	+	+	+	+	-
	Sibbald et al., 2011	+	+	+	+	+	+
	Villela-Castro et al., 2023	+	+	+	+	+	+
	Gerli et al., 2012	-	+	+	-	+	-

Domains:
 D1: Bias arising from the randomization process.
 D2: Bias due to deviations from intended intervention.
 D3: Bias due to missing outcome data.
 D4: Bias in measurement of the outcome.
 D5: Bias in selection of the reported result.

Judgement
 - Some concerns
 + Low

(a)

		Risk of bias domains							
		D1	D2	D3	D4	D5	D6	D7	Overall
Study	Kiefer et al., 2018	-	+	+	+	+	+	+	-
	Lensenink et al., 2011	-	+	+	+	+	+	+	-
	Ceviker et al., 2015	-	+	+	+	+	-	+	-
	Lorincz et al., 2024	-	+	+	+	+	-	+	-
	De Decker et al., 2024	-	+	+	+	-	-	+	-

Domains:
 D1: Bias due to confounding.
 D2: Bias due to selection of participants.
 D3: Bias in classification of interventions.
 D4: Bias due to deviations from intended interventions.
 D5: Bias due to missing data.
 D6: Bias in measurement of outcomes.
 D7: Bias in selection of the reported result.

Judgement
 - Moderate
 + Low

(b)

Figure 2. Risk of bias of included studies: (a) RoB 2.0 for RCT studies¹²; (b) ROBINS-I for cohort studies.¹¹

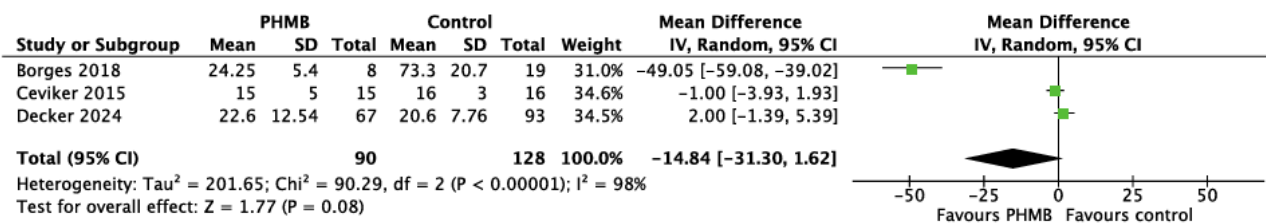


Figure 3. Pooled analysis of healing time

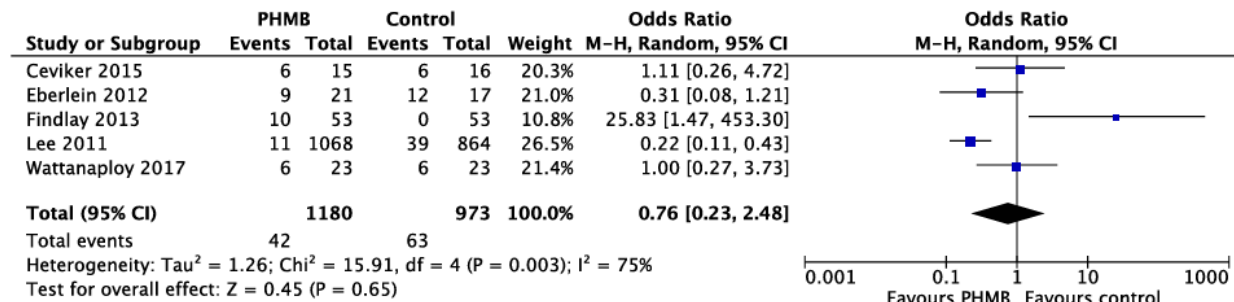


Figure 4. Pooled analysis of bacterial load

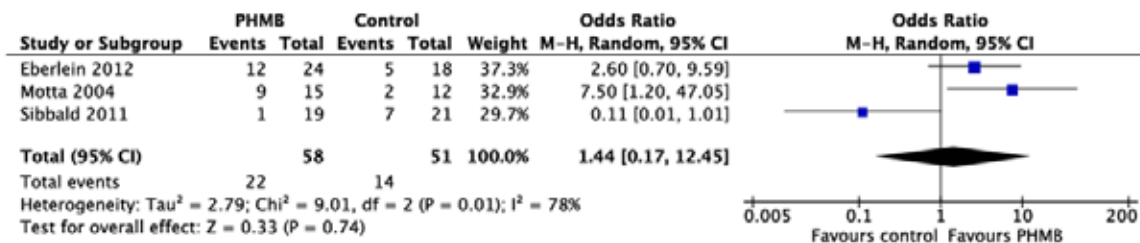


Figure 5. Pooled analysis of bacterial burden reduction rate

bacterial burden reduction varied between studies, ranging from days to weeks: Eberlein et al⁸ measured outcomes at seven days, Motta et al²¹ at 14 days, and Sibbald et al²³ at 21 days, which may impact the observed effects.

Time to re-epithelialisation

Two studies^{13,17} reported time to re-epithelialisation in which Kiefer et al¹³ reported time to re-epithelialisation of 7.1±0.2 days in deep partial or full-thickness burn injury requiring split thickness skin graft (STSG) in adult subjects, while Lorincz et al¹⁷ reported longer time (8.78±2.64 days) in pediatric burn injury patients.

Wound size

Two studies^{14,25} reported final wound size following polyhexanide administration. Lenseink et al²⁵ reported smaller wound size in week 24 after patients received polyhexanide-containing dressings. Borges et al¹⁴ compared polyhexanide to normal saline for wound dressings, which showed smaller wound size (17.68±4.48 vs 22.95±4.69cm-squared; p=0.882)

in polyhexanide group, although the difference were not statistically significant. The follow-up duration in these studies differed, with Lenseink et al²⁵ assessing outcomes at 24 weeks and Borges et al¹⁴ at 12 weeks.

Wound closure rate

Two studies^{7,21} reported the rate of wound closure following polyhexanide treatment. Ceviker et al⁷ found improved epithelialised scar tissue length in polyhexanide-treated wounds (10.4±4.09mm) compared to RLS (4.22±2.81mm; p=0.015). Motta et al²¹ also observed improved wound closure in polyhexanide-treated wounds. Pooled analysis of these studies found a non-significant improvement in wound closure rate with polyhexanide (OR 2.47; 95% CI 0.70, 8.78; p=0.16), with no heterogeneity (I-squared=0%) (Figure 6). Follow-up periods in these studies ranged from weeks to months, with Ceviker et al⁷ assessing outcomes at four weeks and Motta et al²¹ at 12 weeks, potentially influencing the comparability of findings.

Pain score

Six studies^{5,8-10,24,25} reported pain scores on a VAS scale. Lenselink et al²⁵ reported decreases on a pain scale in week 24 in patients receiving polyhexanide-containing dressings (7.4 vs 3.2). Romanelli et al⁵ reported significantly lower pain score in polyhexanide group ($p < 0.05$) compared to normal saline, while Bellingeri et al¹⁰ reported a non-significant difference in final pain scores. Eberlein et al⁸ found that pain reduction before dressing change was significantly better in polyhexanide ($p = 0.03$). Villela-Castro et al²⁴ also reported a significant reduction in pain scores following polyhexanide treatment.²⁴ The timing of pain assessment varied across studies, with Romanelli et al⁵ assessing at 4 weeks, Villela-Castro et al²⁴ at 8 weeks, and Lenselink et al²⁵ at 24 weeks.

Two studies^{8,9} compared polyhexanide (either used as wound dressing solution or gel) with silver sulfadiazine. Wattanaploy et al⁹ showed significantly lower pain scores in patients treated with polyhexanide gel ($p = 0.0472$). However, Eberlein et al⁸ reported higher pain score in polyhexanide-containing biocellulose dressings compared to silver sulfadiazine (6.13 ± 1.43 vs 5.42 ± 1.43), although both showed significantly decreased pain following treatment ($p < 0.001$ in both groups). Pooled analysis of pain scores showed a mean difference of 1.36 (95% CI 0.28, 2.43; $p = 0.01$), with low heterogeneity ($I^2 = 0\%$) (Figure 7).

BWAT score

Bates-Jensen Wound Assessment Tool (BWAT) score was used as outcome in one study.¹⁰ BWAT score consisted of several items: wound size, depth, edges, type of exudate, amount of exudate, skin color surrounding wound, peripheral tissue edema and induration, and granulation tissue; in which higher value indicated more severe wounds. Wound dressing using polyhexanide solution was associated with significantly lower total BWAT score and inflammatory signs characterised with BWAT scoring tools compared to normal saline ($p = 0.0248$ and $p = 0.03$ respectively).

Infection rate

Four studies^{7,9,15,18} reported infection rates in wounds. Wattanaploy et al⁹ reported no infection in patients receiving either polyhexanide gel or silver sulfadiazine for burn injury treatment. However, Saleh et al¹⁵ reported significantly higher infection rate in patients treated with dressings soaked with polyhexanide compared to normal saline. Ceviker et al reported fluctuating infection rates over four weeks with no significant differences.⁷ Lee et al found that polyhexanide significantly reduced overall infection rate ($p < 0.001$) compared to the control group.¹⁸ Follow-up durations for infection rates varied, with Wattanaploy et al⁹ assessing at two weeks, Saleh et al¹⁵ at six weeks, Ceviker et al⁷ at four weeks, and Lee et al¹⁸ at 12 weeks, which could influence variability in results.

Alteration of wound characteristics

One study²⁵ reported alteration of wound characteristics, which were reported as presence of granulation tissue in wound bed. Polyhexanide-containing biocellulose dressings resulted in significantly higher granulation tissue on Day four compared to initial assessment (77.4 ± 36 vs 38.2 ± 34.6 ; $p < 0.04$).

Human Papilloma Virus (HPV) regression rate

One study, by Gentile et al,¹⁹ assessed HPV regression rate following polyhexanide administration. The study found a notable reduction in HPV-related lesions, suggesting that polyhexanide may contribute to improved viral clearance in affected patients.¹⁹

Odor control

One study, by Villela-Castro et al,²⁴ evaluated the effect of polyhexanide on odor control in wound care. The study reported a significant reduction in wound-related odor in patients treated with polyhexanide dressings, contributing to improved patient comfort and overall wound management.

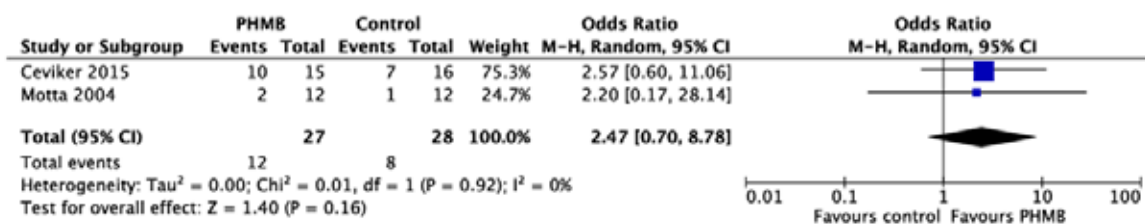


Figure 6. Pooled analysis of wound closure rate

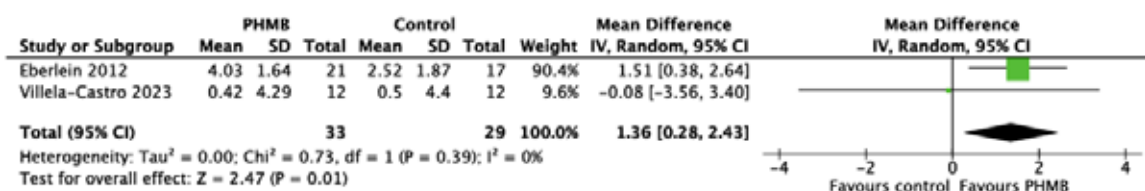


Figure 7. Pooled analysis of pain score

HRQOL & HRQOL subscale improvement

The study by Villela-Castro et al²⁴ also assessed health-related quality of life (HRQOL) and its subscales in patients receiving polyhexanide treatment. The study found significant improvements in overall HRQOL, with notable enhancements in pain relief, mobility, and emotional well-being subscales, indicating a positive impact of polyhexanide on patient outcomes.

Adverse events

Five studies^{7,8,10,13,20} evaluated adverse events in patients receiving polyhexanide. Kiefer et al¹³ reported that 12 patients (23.5%) had one to four adverse events following administration of gel containing polyhexanide and betaine, which include tachycardia, eye irritation, gastrointestinal symptoms (constipation, abdominal pain, nausea), postprocedural hemorrhage and transplant failure, hyperglycemia, musculoskeletal symptoms (arthralgia, back pain, pain in extremity), dizziness, anxiety disorder, anuria, pneumonia, hypertension, and others. Mild to moderate pruritus was seen in two patients. Bellingeri et al¹⁰ reported no adverse events following polyhexanide in propylbetaine 0.1% and polyhexanide 0.1% as wound cleansing solution. Ceviker et al⁷ reported two cases of pruritus and erythema in the polyhexanide group and one death (stroke). Eberlein et al⁸ found no serious adverse events but reported slightly higher periwound maceration in the polyhexanide group ($p < 0.0001$). Findlay et al²⁰ reported cardiovascular and rheumatological adverse events as well as transient skin erythema in polyhexanide-treated patients.

Discussion

This study aims to evaluate the efficacy and safety of polyhexanide for management of various wound types compared to other dressings. We found significantly faster healing time in patients receiving polyhexanide compared to controls in the treatment of wounds. However, substantial heterogeneity (I-squared = 98%) among studies suggests that differences in study design, wound types, and treatment protocols may influence the observed effects, warranting further investigation into the optimal application of PHMB for different wound types. Lower risk of bacterial load was also seen, although not statistically significant, which may be attributed to the range of variability of bacterial species and differences in the bacterial load assessment methods. Multiple adverse events (mild to moderate) were reported in five studies with ranging adverse effects, although other study reported no adverse events.

Treatment using simple solution (i.e., normal saline, RLS) may remove necrotic tissues and destroy adhesion bridges between biofilm formed by bacteria and wound bed to aid wound healing, although it may be less efficacious as there was no active agent in simple isotonic solution. In our findings, the administration of polyhexanide reduced healing time, wound size, BWAT score, and resulted in higher granulation tissue in the wound bed. The mechanism

of action of polyhexanide may be attributable to its antimicrobial properties. Polyhexanide has been shown effective to both Gram-negative and Gram-positive bacteria, such as strains of *Escherichia coli*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Pseudomonas aeruginosa*, and fungi such as *Candida albicans*.^{1,27,28} In vitro study conducted by Zhang et al²⁹ reported sensitivity of 60%, 45%, and 80% to *Staphylococcus aureus*, *Acinetobacter baumannii*, and *Klebsiella pneumoniae*, and its cytotoxicity increased with increasing exposure time and drug concentration. The mechanism of action involved disruption of cell membranes and inhibition of internal metabolic process of pathogens.³⁰ Polyhexanide also has antibiofilm property, in which a previous study reported good efficacy against biofilm in 63% patients treated with polyhexanide-containing dressing for non-healing wounds.²⁵ Improvement in wound healing processes was also suitable in pediatric populations, as shown in Lorincz et al¹⁷, in which there was rapid wound closure and time to re-epithelialisation following administration of lower concentration of polyhexanide gel (0.04%) betaine in burn injuries.

The effects of polyhexanide on bacterial load may also be explained by reduction in inflammatory markers (such as CRP and leukocyte counts) reported by Ceviker et al,⁷ which may indicate reduce in inflammatory and infection processes involved in wounds. An in vitro study³¹ also suggested the role of polyhexanide in inhibiting the formation of reactive oxygen species (ROS) and reactive nitrogen species responsible for inflammation. Polyhexanide treatment has also been associated with improved HRQOL, including better mobility and emotional well-being, underscoring its holistic benefits in wound management beyond physical healing.²⁴

It is also important to assess patient-reported outcomes, such as pain scores. Use of polyhexanide, either in gel or solution in wound dressings, resulted in decreased in pain scores.^{8,9,25} Pain scores were reported to be significantly lower compared to other agents, such as normal saline and silver sulfadiazine.^{5,9} Eberlein et al⁸ highlighted that the use of polyhexanide was associated with significantly reduced pain scores from baseline while also it promoted faster and better removal of bacterial load compared to silver sulfadiazine. The use of biocellulose dressings in the study may exert a physical cooling effect and help lower pain scores.⁸

The use of polyhexanide also exhibits other advantages compared to other active agents. For instance, silver sulfadiazine has been associated with delayed healing, tissue irritation caused by nitrate, and the formation of pseudo-eschar.³² Use of polyhexanide may also cause less mechanical stimuli resulting in pain perception in burn wounds compared to silver sulfadiazine. This was attributed to its moist properties and non-toxic main ingredients to human cells; thus resulting in faster healing time and lower pain scores.^{9,30} Also, the transparency of polyhexanide (particularly gel preparations) was beneficial as it may facilitate direct wound assessment, which ensures effective

wound management and handling.¹⁶ Polyhexanide treatment was also found to significantly reduce wound-related odor, enhancing patient comfort and quality of life, particularly in chronic wounds prone to malodor.²⁴

In a study conducted by Saleh et al¹⁵ higher infection rate with no effect on bacterial load was reported in wound dressings soaked with polyhexanide solution compared to silver sulfadiazine. The study highlighted that use of polyhexanide may possibly reduce some specific commensal flora, and potentially led to colonization of pathogenic bacteria (such as *S. aureus*). For instance, specific bacteria such as *S. epidermidis* has been reported to produce antimicrobials that inhibit growth of other pathogenic bacteria,³³ and the absence of *S. epidermidis* was associated with higher spread of bacterial levels and detection of Gram-negative bacteria.¹⁵ Further studies with larger populations are needed to evaluate the association of bacterial species present in patients' wounds and polyhexanide efficacy.

However, routine administration of antiseptics as cleansing solution for wounds may result in potential toxicity to adjacent cells with the risk of inactivation of essential organic material.¹⁴ Although, an in vivo study reported that following polyhexanide administration, there was no significantly different level in erythema and melanin with absence of edema, papule, and vesicle/bullae with no toxic effect to adjacent cells in in vitro study; which suggested that polyhexanide was non-irritant and safe to use as routine dressings.³⁴ Despite these findings, concerns remain regarding potential adverse events, such as pruritus and erythema in some patients, highlighting the need for further safety evaluations.

There were some limitations in our review. Firstly, quantitative analysis to perform comprehensive statistical comparisons was limited due to variability in the parameters reported across included studies following polyhexanide treatment. Also, the studies included in the review used different control groups, which potentially affects outcome interpretation and comparability of results. There was also no data regarding long-term safety and potential cytotoxic effect. Future studies should focus on standardising protocols and assessing the long-term benefits and risks of polyhexanide use in wound management. Furthermore, the follow-up duration varied across studies, with some studies measuring outcomes at different time points, which may impact comparability. Clarification on when specific variables, such as pain scores, were measured is necessary to ensure consistency in evaluating polyhexanide efficacy over time.

Conclusions

Polyhexanide demonstrated significantly faster healing time in treatment of various types of wounds. It also possessed multiple advantages, such as its transparent properties, antimicrobial activity, and reduced pain compared to other treatments. Further studies may be needed to assess long-term efficacy and safety of polyhexanide in various wound types.

Conflict of interest

None.

Ethics statement

An ethics statement is not applicable.

Funding

The authors received no funding for this study.

Author contribution

All authors made substantial contributions regarding literature searching, data extraction, statistical analysis, interpretation, drafting and final approval of the manuscript.

References

1. Guiomar AJ, Urbano AM. Polyhexanide-releasing membranes for antimicrobial wound dressings: a critical review. *Membranes (Basel)*. 2022;12(12):1281.
2. Kumar Jha K, Raj A, Shreyasi, Bishnoi H, Raj M, Thakur V. Chronic wound healing: A Review of current management and treatments. *Asian J Pharm Res Dev*. 2023;11(3):95–102.
3. Guo S, DiPietro LA. Factors affecting wound healing. *J Dent Res*. 2010;89(3):219–229.
4. Zhou M, Liu Y, Fang X, Jiang Z, Zhang W, Wang X. The effectiveness of polyhexanide in treating wound infections due to methicillin-resistant staphylococcus aureus: a prospective analysis. *Infect Drug Resist*. 2024;17:1927–1935.
5. Romanelli M, Dini V, Barbanera S, Bertone MS. Evaluation of the efficacy and tolerability of a solution containing propyl betaine and polyhexanide for wound irrigation. *Skin Pharmacol Physiol*. 2010;23(Sup1):41–44.
6. To E, Dyck R, Gerber S, Kadavil S, Woo KY. The effectiveness of topical polyhexamethylene biguanide (PHMB) agents for the treatment of chronic wounds: a systematic review. *Surg Technol Int*. 2016;29:45–51.
7. Çeviker K, Canikoğlu M, Tatlıoğlu S, Bağdatlı Y. Reducing the pathogen burden and promoting healing with polyhexanide in non-healing wounds: a prospective study. *J Wound Care*. 2015;24(12):582–586.
8. Eberlein T, Haemmerle G, Signer M, Gruber-Moesenbacher U, Traber J, Mittlboeck M, et al. Comparison of PHMB-containing dressing and silver dressings in patients with critically colonised or locally infected wounds. *J Wound Care*. 2012;21(1):12–20.
9. Wattanaploy S, Chinaronchai K, Namviriyachote N, Muangman P. Randomized controlled trial of polyhexanide/betaine gel versus silver sulfadiazine for partial-thickness burn treatment. *Int J Low Extrem Wounds*. 2017;16(1):45–50.
10. Bellingeri A, Nurse CS, Falciani F, Care W, Nurse S, Wound C. Effect of a wound cleansing solution on wound bed preparation and inflammation in chronic wounds: a single-blind RCT. *J Wound Care*. 2016;25(3):160–168.
11. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ*. 2016;355:i4919.
12. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019;366:i4898.
13. Kiefer J, Harati K, Möller-Seubert W, Fischer S, Ziegler B, Behr B, et al. Efficacy of a gel containing polyhexanide and betaine in deep partial and full thickness burns requiring split-thickness skin grafts: A noncomparative clinical study. *J Burn Care Res*. 2018;39(5):685–693.

14. Borges EL, Frison SS, Honorato-Sampaio K, Guedes ACM, De Araújo Nogueira Lima VL, De Oliveira OMM, et al. Effect of polyhexamethylene biguanide solution on bacterial load and biofilm in venous leg ulcers. *J Wound Ostomy Continence Nurs.* 2018;45(5):425–431.
15. Saleh K, Sonesson A, Persson K, Riesbeck K, Schmidtchen A. Can dressings soaked with polyhexanide reduce bacterial loads in full-thickness skin grafting? A randomized controlled trial. *J Am Acad Dermatol.* 2016;75(6):1221–1228.e4.
16. De Decker I, Janssens D, De Mey K, Hoeksema H, Simaey M, De Coninck P, et al. Assessing antibacterial efficacy of a polyhexanide hydrogel versus alginate-based wound dressing in burns. *J Wound Care.* 2024;33(5):335–347.
17. Lőrincz A, Nudelman H, Lamberti AG, Garami A, Tiborcz KA, Kovács TZ, et al. Management of pediatric superficial partial-thickness burns with polyhexamethylene biguanide: outcomes and influencing factors. *J Clin Med.* 2024;13(11):3074.
18. Lee CK, Chua YP, Saw A. Antimicrobial gauze as a dressing reduces pin site infection: a randomized controlled trial. *Clin Orthop Relat Res.* 2012 Feb;470(2):610–615.
19. Gentile A, Gerli S, Di Renzo GC. A new non-invasive approach based on polyhexamethylene biguanide increases the regression rate of HPV infection. *BMC Clin Pathol.* 2012;12:17.
20. Findlay A, Serrano C, Punzalan S, Fan SL. Increased peritoneal dialysis exit site infections using topical antiseptic polyhexamethylene biguanide compared to mupirocin: results of a safety interim analysis of an open-label prospective randomized study. *Antimicrob Agents Chemother.* 2013;57(5):2026–2028.
21. Motta GJ, Milne CT, Corbett LQ. Impact of antimicrobial gauze on bacterial colonies in wounds that require packing. *Ostomy Wound Manage.* 2004;50(8):48–62.
22. Gerli S, Bavetta F, Di Renzo GC. Antisepsis regimen in the surgical treatment of HPV generated cervical lesions: polyhexamethylene biguanide vs chlorhexidine. A randomized, double blind study. *Eur Rev Med Pharmacol Sci.* 2012;16(14):1994–1998.
23. Sibbald RG, Coutts P, Woo KY. Reduction of bacterial burden and pain in chronic wounds using a new polyhexamethylene biguanide antimicrobial foam dressing-clinical trial results. *Adv Skin Wound Care.* 2011;24(2):78–84.
24. Villela-Castro DL, Santos VLC de G, Woo K. Polyhexanide versus metronidazole for odor management in malignant (fungating) wounds. *J Wound Ostomy Continence Nurs.* 2018;45(5):413–418.
25. Lenselink E, Andriessen A. A cohort study on the efficacy of a polyhexanide-containing biocellulose dressing in the treatment of biofilms in wounds. *J Wound Care.* 2011;20(11):534–539.
26. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Syst Rev.* 2021;10(1):89.
27. Alves PJ, Barreto RT, Barrois BM, Gryson LG, Meaume S, Monstrey SJ. Update on the role of antiseptics in the management of chronic wounds with critical colonisation and/or biofilm. *Int Wound J.* 2021;18(3):342–358.
28. Worsley A, Vassileva K, Tsui J, Song W, Good L. Polyhexamethylene biguanide:polyurethane blend nanofibrous membranes for wound infection control. *Polymers (Basel).* 2019;11(5):915.
29. Zhang M, Jin J, Liu Y, Ben C, Li H, Cheng D, et al. Analysis of povidone iodine, chlorhexidine acetate and polyhexamethylene biguanide as wound disinfectants: in vitro cytotoxicity and antibacterial activity. *BMJ Nutr Prev Health.* 2023;6(1):21–27.
30. Hübner NO, Kramer A. Review on the efficacy, safety and clinical applications of polyhexanide, a modern wound antiseptic. *Skin Pharmacol Physiol.* 2010;23(SUPPL. 1):17–27.
31. Dissemmond J, Gerber V, Kramer A, Riepe G, Strohal R, Vassel-Biergans A, et al. A practice-oriented recommendation for treatment of critically colonised and locally infected wounds using polyhexanide. *J Tissue Viability.* 2010;19(3):106–115.
32. Muangman P, Pundee C, Opananon S, Muangman S. A prospective, randomized trial of silver containing hydrofiber dressing versus 1% silver sulfadiazine for the treatment of partial thickness burns. *Int Wound J.* 2010;7(4):271–276.
33. Christensen GJM, Brüggemann H. Bacterial skin commensals and their role as host guardians. *Benef Microbes.* 2014;5(2):201–215.
34. Napavichayanun S, Yamdech R, Aramwit P. The safety and efficacy of bacterial nanocellulose wound dressing incorporating sericin and polyhexamethylene biguanide: in vitro, in vivo and clinical studies. *Arch Dermatol Res.* 2016;308(2):123–132.