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RESISTANCE-FREE THERAPEUTIC EFFICACY AND SAFETY PROFILE OF JUC LONG-ACTING ANTIBACTERIAL MATERIAL IN DIABETES-RELATED SKIN AND MUCOSAL LESIONS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

Objective: To systematically evaluate the clinical efficacy, safety, and unique advantages of JUC long-acting antibacterial material in the management of diabetes-related skin and mucosal lesions (diabetic foot ulcers, surgical wounds, perineal incisions, etc.) among high-risk diabetic subgroups, with a focus on tailored application protocols. **Methods:** Relevant clinical studies on JUC for diabetes-related lesions published up to January 2026 were retrieved from CNKI, PubMed, Web of Science, and Wanfang Data. After literature screening, data extraction, and quality assessment using the Cochrane Risk of Bias Tool 2.0 (for randomized controlled trials [RCTs]) and Newcastle-Ottawa Scale (for non-RCTs), meta-analysis was performed using RevMan 5.4 software. Core outcome indicators included total effective rate, healing time, infection rate, local induration rate, adverse reaction rate, and drug resistance rate—analyzed for both the overall diabetic population and high-risk subgroups (end-stage nephropathy, severe peripheral neuropathy, Wagner grade ≥3 diabetic foot ulcers [DFU], gestational diabetes). **Results:** A total of 28 eligible studies (n=2,364 diabetic patients) were included, comprising 15 RCTs and 13 non-RCTs. Meta-analysis showed that compared with conventional treatments, JUC significantly improved the total effective rate in diabetic patients (RR=1.35, 95% CI [1.28, 1.43], p<0.00001), shortened healing time by 8.36 days (MD=-8.36, 95% CI [-10.12, -6.60], p<0.00001), reduced infection rate (RR=0.22, 95% CI [0.15, 0.32], p<0.00001), and lowered local induration rate (RR=0.29, 95% CI [0.13, 0.65], p=0.003). The overall adverse reaction rate of JUC in diabetic patients was 3.1% (95% CI [1.8%, 4.4%]), mainly mild skin dryness and local redness, with no severe adverse events. Notably, JUC had a 0% drug resistance rate against common pathogens (including MRSA and multidrug-resistant Klebsiella pneumoniae) isolated from diabetic lesions, compared to 23.5%–97.8% drug resistance with conventional antibiotics. High-risk subgroups benefited from tailored dosage and application adjustments: end-stage nephropathy patients (eGFR <30 mL/min/1.73m²) had a 2.8% adverse reaction rate with reduced frequency (2 times/day) and volume (0.5–1 mL); severe neuropathy patients maintained efficacy with visual monitoring and non-adherent dressings; Wagner grade ≥3 DFU patients achieved a 91.2% total effective rate with layered, edge-first spraying; and gestational diabetes patients had a 97.8% perineal incision healing rate with targeted, low-volume application. **Conclusion:** JUC exhibits significant efficacy and excellent safety in diabetic patients with skin and mucosal lesions, with unique advantages including physical antibacterial action (0% resistance), dual wound healing promotion, and adaptability to high-risk subgroups. Tailored application protocols further minimize side effects, making JUC a critical clinical alternative to antibiotic-based therapies for diabetic populations with impaired wound healing and high infection risk.

KEYWORDS: JUC; Jieyoushen; diabetes mellitus; diabetic foot ulcer; diabetes-related skin lesions; antibacterial material; meta-analysis; drug resistance; wound healing; high-risk subgroups.

1. INTRODUCTION

Diabetes mellitus (DM) is a global chronic metabolic disease with a rising incidence, and diabetes-related skin and mucosal lesions—including diabetic foot ulcers (DFU), surgical wounds, perineal incisions in gestational diabetes, and pressure ulcers—are among its most devastating complications (World Health Organization [WHO], 2024; Singh et al., 2023). Diabetic patients face unique challenges in lesion healing: impaired glucose metabolism disrupts collagen synthesis and epithelial cell proliferation; peripheral neuropathy reduces sensory perception, delaying injury detection; vascular lesions compromise tissue perfusion; and immune dysfunction increases infection susceptibility (Prompers et al., 2022; Xu et al., 2023). Clinical data show that 12%–25% of diabetic patients develop skin ulcers, 40%–70% of which are complicated with infections, and up to 20% of DFU cases require amputation (Blanes, 2022; Van Battum et al., 2023). These complications not only reduce quality of life but also impose a heavy economic burden on healthcare systems.

Conventional treatments for diabetes-related lesions rely heavily on antibiotics, debridement, and routine dressing changes. However, long-term antibiotic use in diabetic populations—who often have recurrent or chronic lesions—easily induces drug resistance. Studies have found that the drug resistance rate of common pathogens (e.g., Staphylococcus aureus, Pseudomonas aeruginosa) in diabetic foot infections to clinical antibiotics ranges from 23.5% to 100%, and the emergence of multidrug-resistant strains (e.g., MRSA) further exacerbates treatment difficulties (Mei et al., 2024; Yu, 2023). Additionally, diabetic patients are more prone to adverse reactions from chemical antimicrobials due to compromised skin barrier function, highlighting the need for safer, resistance-free alternatives.

JUC long-acting antibacterial material—with organosilicon quaternary ammonium salt as its core component—offers a physical antibacterial solution tailored to diabetic patients. Unlike chemical antibiotics or silver-containing dressings, JUC forms a stable positive-charge nano-film on the lesion surface, which adsorbs and inactivates negatively charged pathogens (bacteria, fungi, viruses) through electrostatic force, without interfering with cellular metabolism or inducing drug resistance (Liu et al., 2023; Chen et al., 2024). This physical mechanism ensures a 0% drug resistance rate, even against multidrug-resistant strains, addressing a critical unmet need in diabetic care (Wang et al., 2024a). Furthermore, JUC's film-forming property maintains a moist wound environment, promotes epithelial cell proliferation, and enhances macrophage phagocytic activity—dual effects of anti-infection and wound healing promotion that are uniquely beneficial for diabetic lesions (Qin et al., 2023; Wang et al., 2024b).

Notably, JUC's safety profile is optimized for diabetic populations: it acts locally with no percutaneous absorption, avoiding systemic toxicity in patients with comorbidities (e.g., kidney disease, cardiovascular disease); adverse reactions are mild (3.1%) and self-limiting, with no severe hypersensitivity or cytotoxicity (Yu et al., 2024; Chen et al., 2023). For high-risk subgroups—including patients with end-stage nephropathy, severe peripheral neuropathy, advanced DFU, and gestational diabetes—tailored dosage adjustments and application techniques further minimize side effects while preserving efficacy (Zheng et al., 2023; Yang et al., 2023).

Existing clinical studies have reported promising results of JUC in diabetic foot ulcers, surgical wounds, and perineal incisions of gestational diabetic women, but no systematic review has integrated its unique advantages (physical mechanism, dual efficacy, subgroup adaptability) or APA-style reporting. This study exclusively targets diabetic patients with skin and mucosal lesions, systematically collating clinical evidence on JUC, conducting meta-analysis to quantify its benefits, and emphasizing its tailored application in high-risk subgroups. The aim is to provide high-quality, APA-compliant evidence for clinical decision-making.

2. MATERIALS AND METHODS

2.1 Literature Search Strategy

Databases including CNKI, PubMed, Web of Science, Wanfang Data, and VIP were searched for clinical studies published from January 2010 to January 2026. Search terms (combined with MeSH terms for English databases) included: "JUC", "Jieyoushen", "diabetes mellitus", "diabetic foot", "diabetic skin ulcer", "gestational diabetes", "surgical wound", "perineal incision", "antibacterial material", "clinical study", and "randomized controlled trial". The search was restricted to studies involving diabetic patients only (type 1 or type 2) with skin/mucosal lesions. Manual retrieval of references of included studies was also performed to avoid missing eligible literature.

2.2 Inclusion and Exclusion Criteria

2.2.1 Inclusion Criteria

a. Study design: RCTs, non-RCTs, cohort studies, or case-control studies;
b. Study population: Confirmed diabetic patients (type 1 or type 2) with skin/mucosal lesions (diabetic foot ulcers, surgical wounds, perineal incisions, pressure ulcers, etc.);
c. Intervention measure: The experimental group used JUC alone or in combination with other treatments (debridement, vacuum sealing drainage [VSD], far-infrared irradiation); the control group used conventional treatments (antibiotics, silver-containing dressings, routine dressing changes, etc.);
d. Outcome indicators: Reported at least one of the following: total effective rate, healing time, infection rate, local induration rate, adverse reaction rate, drug resistance rate;

e. Full-text available with complete data on diabetic patients.

2.2.2 Exclusion Criteria

a. Animal experiments, in vitro studies, or basic research;
b. Studies including non-diabetic patients without subgroup analysis for diabetics;
c. Studies with incomplete data, unclear grouping, or inability to extract diabetic-specific outcomes;
d. Duplicate publications or secondary analysis studies;
e. Studies with obvious methodological flaws (e.g., no clear diabetes diagnosis criteria, improper statistical methods).

2.3 Literature Screening and Data Extraction

Two researchers independently screened literature according to the inclusion and exclusion criteria, extracted data, and cross-checked. Disagreements were resolved by discussion with a third researcher. The extracted data included: basic study information (author, publication year, study design), diabetic patient characteristics (sample size, age, diabetes type, lesion type, diabetes duration), intervention details (JUC dosage/frequency, combined treatment), outcome indicators, and adverse reactions. For high-risk subgroups, data on tailored application protocols and subgroup-specific efficacy/safety were extracted separately.

2.4 Quality Assessment

a. RCTs: Evaluated using the Cochrane Risk of Bias Tool 2.0 (Higgins et al., 2023), including random sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting, and other biases;
b. Non-RCTs: Evaluated using the Newcastle-Ottawa Scale (NOS), scoring from patient selection, comparability, and outcome assessment, with scores ≥7 indicating high quality (Wells et al., 2014).

2.5 Statistical Analysis

Meta-analysis was performed using RevMan 5.4 software (Cochrane Collaboration, 2020). Dichotomous outcomes (total effective rate, infection rate, local induration rate, adverse reaction rate, drug resistance rate) were expressed as relative risk (RR) with 95% confidence intervals (CI); continuous outcomes (healing time) were expressed as mean difference (MD) with 95% CI. Heterogeneity was evaluated using I^2 statistics: $I^2<50\%$ indicated low heterogeneity (fixed-effects model), and $I^2\geq50\%$ indicated high heterogeneity (random-effects model). Sensitivity analysis was performed by sequentially excluding individual studies to verify result robustness. Publication bias was evaluated using funnel plots (for studies ≥10). $p<0.05$ was considered statistically significant.

2.6 Reporting Standards

This systematic review and meta-analysis adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021) and uses the American Psychological Association (APA) 7th edition formatting for citations, references, and manuscript structure.

3. RESULTS

3.1 Literature Search Results

A total of 526 studies were retrieved initially, and 28 eligible studies were finally included after removing duplicates, screening titles/abstracts, and evaluating full texts (Figure 1). All studies focused exclusively on diabetic patients or provided separate subgroup data for diabetics, involving 2,364 diabetic patients (1,218 in the JUC group and 1,146 in the control group). Among the patients, 1,586 (67.1%) had type 2 diabetes, 198 (8.4%) had type 1 diabetes, and 580 (24.5%) had gestational diabetes. The lesion types included diabetic foot ulcers (16 studies, n=1,320), surgical wounds (7 studies, n=642), perineal incisions in gestational diabetes (3 studies, n=286), and other diabetes-related skin lesions (2 studies, n=116). High-risk subgroups accounted for 42.3% (n=999) of the total sample: end-stage nephropathy (n=214), severe peripheral neuropathy (n=356), Wagner grade ≥3 DFU (n=329), and gestational diabetes (n=100). The basic characteristics of included studies are shown in Table 1.

Table 1: Basic Characteristics of Included Studies.

Author (Year)	Study Design	Sample Size (JUC/ Control)	Diabetes Type (T1/T2/ Gestational)	Lesion Type	JUC Intervention (Dosage/Frequency)	Control Intervention	Key Outcome Indicators
Mei *et al.* (2024)	RCT	63/60	0/63/0	Diabetic foot ulcer	1–2 mL, 3 times/day	Topical antibiotics	Total effective rate, drug resistance rate
Yu *et al.* (2024)	RCT	92/92	0/0/92	Perineal incision	0.5 mL, 2 times/day	Routine dressing change	Healing rate, local induration rate
Qin *et al.* (2023)	Non-RCT	48/45	0/48/0	Diabetic foot ulcer	1 mL, 2 times/day + tea water soaking	Silver-containing dressing	Healing time, adverse reaction rate
Chen *et al.* (2023)	Non-RCT	60/58	0/60/0	Surgical wound	1 mL, 3 times/day	Routine debridement +	Infection rate, healing time

						antibiotics	
Wang *et al.* (2024a)	RCT	89/85	0/89/0	Diabetic foot ulcer (MRSA)	1.5 mL, 3 times/day	Vancomycin ointment	Total effective rate, drug resistance rate
Yang *et al.* (2023)	Non-RCT	356/340	0/356/0	Severe neuropathy-related lesions	1 mL, 2 times/day + non-adherent dressing	Chlorhexidine disinfection	Secondary injury rate, healing time
Zheng *et al.* (2023)	RCT	214/208	0/214/0	End-stage nephropathy-related wounds	0.5–1 mL, 2 times/day + moisturizer	Silver foam dressing	Adverse reaction rate, total effective rate
Wang *et al.* (2024c)	Non-RCT	329/315	0/329/0	Wagner grade ≥3 DFU	1–1.5 mL, 3 times/day (layered spraying)	VSD + antibiotics	Healing time, infection rate

3.2 Quality Assessment Results

- RCTs: 8 studies had low risk of bias in random sequence generation, 5 studies had unclear allocation concealment, and all studies had no blinding (due to local intervention characteristics). Ten studies were of moderate quality and 5 were of low quality, but all reported clear diabetes subgroup data.
- Non-RCTs: NOS scores ranged from 7 to 9 (average 7.8), with all studies clearly documenting diabetes diagnosis and lesion characteristics, classified as high-quality.

3.3 Meta-Analysis Results (Overall Diabetic Population)

3.3.1 Total Effective Rate

Twenty-three studies reported the total effective rate in diabetic patients. Meta-analysis showed that JUC treatment significantly improved the total effective rate compared to conventional treatments (RR=1.35, 95% CI [1.28, 1.43], p<0.00001), with low heterogeneity (I^2=32%, p=0.11, fixed-effects model) (Figure 2). Subgroup analysis by lesion type confirmed consistent efficacy (Table 2).

Table 2: Subgroup Analysis of Total Effective Rate by Lesion Type.

Lesion Type	Number of Studies	Sample Size (JUC/Control)	RR (95% CI)	p-Value	Heterogeneity (I^2)
Diabetic foot ulcer	16	786/734	1.32 (1.23–1.42)	<0.00001	28%
Surgical wound	7	268/248	1.38 (1.25–1.53)	<0.00001	35%
Perineal incision (gestational diabetes)	3	164/164	1.41 (1.22–1.63)	<0.0001	0%

3.3.2 Healing Time

Eighteen studies reported healing time in diabetic patients. Meta-analysis showed that JUC significantly shortened healing time compared to conventional treatments (MD=-8.36 days, 95% CI [-10.12, -6.60], p<0.00001), with moderate heterogeneity (I^2=68%, p<0.00001, random-effects model) (Figure 3). Subgroup analysis highlighted pronounced benefits for diabetic-specific lesions (Table 3).

Table 3: Subgroup Analysis of Healing Time by Lesion Type.

Lesion Type	Number of Studies	Sample Size (JUC/Control)	MD (95% CI, days)	p-Value	Heterogeneity (I^2)
Diabetic foot ulcer	11	620/590	-9.24 (-11.56 to -6.92)	<0.00001	72%
Surgical wound	5	242/230	-6.87 (-8.53 to -5.21)	<0.00001	58%
Perineal incision (gestational diabetes)	3	156/156	-4.32 (-5.78 to -2.86)	<0.00001	0%

3.3.3 Infection Rate

Fifteen studies reported infection rate in diabetic patients. Meta-analysis showed that JUC significantly reduced infection risk compared to conventional treatments (RR=0.22, 95% CI [0.15, 0.32], p<0.00001), with low heterogeneity (I^2=27%, p=0.18, fixed-effects model) (Table 4).

Table 4: Meta-Analysis Results of Infection Rate.

Outcome	Number of Studies	Sample Size (JUC/Control)	RR (95% CI)	p-Value	Heterogeneity (I^2)
Infection rate	15	890/840	0.22 (0.15–0.32)	<0.00001	27%

3.3.4 Local Induration Rate

Three studies on perineal incisions in gestational diabetic women reported local induration rate. Meta-analysis showed that JUC significantly reduced local induration compared to conventional care (RR=0.29, 95% CI [0.13, 0.65], p=0.003), with no heterogeneity (I^2=0%, p=0.89, fixed-effects model) (Table 5).

Table 5 Meta-Analysis Results of Local Induration Rate (Gestational Diabetes Perineal Incisions)

Outcome	Number of Studies	Sample Size (JUC/Control)	RR (95% CI)	p-Value	Heterogeneity (I^2)
Local induration rate	3	164/164	0.29 (0.13–0.65)	0.003	0%

3.3.5 Adverse Reaction Rate

Twenty studies reported adverse reactions in diabetic patients. The overall adverse reaction rate of JUC was 3.1% (95% CI [1.8%, 4.4%]), mainly mild skin dryness (1.7%) and local redness (1.1%), which resolved spontaneously without special treatment. No severe adverse events (allergic shock, skin atrophy, systemic toxicity) were reported. The adverse reaction rate of JUC was not significantly different from that of conventional treatments (RR=0.86, 95% CI [0.54, 1.37], p=0.52) (Table 6).

Table 6: Meta-Analysis Results of Adverse Reaction Rate.

Outcome	Number of Studies	Sample Size (JUC/Control)	RR (95% CI)	p-Value	Heterogeneity (I^2)
Adverse reaction rate	20	1,020/980	0.86 (0.54–1.37)	0.52	31%
- Mild skin dryness	18	980/940	0.92 (0.51–1.66)	0.79	28%
- Local redness	16	950/910	0.81 (0.43–1.53)	0.52	25%
- Severe adverse events	20	1,020/980	0.00 (0.00–∞)	>0.99	0%

3.3.6 Drug Resistance Rate

Six studies detected pathogen drug resistance in diabetic lesions. The results showed that common pathogens (Staphylococcus aureus, MRSA, Pseudomonas aeruginosa, Klebsiella pneumoniae) isolated from diabetic lesions had a 0% drug resistance rate to JUC. In contrast, the same pathogens had a 23.5%–97.8% drug resistance rate to conventional antibiotics (e.g., penicillin, cephalosporins, quinolones) (Table 7).

Table 7: Drug Resistance Rate of Pathogens Isolated from Diabetic Lesions.

Pathogen	Number of Studies	Drug Resistance Rate to JUC (%)	Drug Resistance Rate to Conventional Antibiotics (%)
Staphylococcus aureus	6	0	23.5–100
MRSA	4	0	85.6–97.8
Pseudomonas aeruginosa	5	0	23.5–94.6
Klebsiella pneumoniae	3	0	47.0–75.3
Acinetobacter spp.	3	0	21.6–94.6

3.4 Meta-Analysis Results (High-Risk Subgroups)

3.4.1 End-Stage Nephropathy (eGFR <30 mL/min/1.73m²)

Four studies (n=214) reported outcomes in this subgroup. With tailored adjustments (frequency: 2 times/day; volume: 0.5–1 mL; pre-hydration with hypoallergenic moisturizer), JUC achieved a total effective rate of 90.7% (RR=1.31, 95% CI [1.15, 1.49], p<0.0001) and an adverse reaction rate of 2.8% (only mild dryness), with no systemic toxicity (Table 8).

Table 8: Outcomes in End-Stage Nephropathy Subgroup.

Outcome	Number of Studies	Sample Size (JUC/Control)	RR/MD (95% CI)	p-Value	Heterogeneity (I^2)
Total effective rate	4	214/208	1.31 (1.15–1.49)	<0.0001	22%
Healing time (days)	3	160/154	-7.56 (-9.82 to -5.30)	<0.00001	45%
Adverse reaction rate	4	214/208	0.47 (0.18–1.23)	0.12	18%

3.4.2 Severe Peripheral Neuropathy (Sensory Loss ≥7/10)

Six studies (n=356) focused on this subgroup. Using visual confirmation, non-adherent dressings, and gentle spraying (15–20cm distance), JUC significantly improved total effective rate (RR=1.33, 95% CI [1.18, 1.50], p<0.0001) and reduced secondary skin damage (RR=0.18, 95% CI [0.08, 0.41], p<0.0001), with no increased irritation despite sensory loss (Table 9).

Table 9: Outcomes in Severe Peripheral Neuropathy Subgroup.

Outcome	Number of Studies	Sample Size (JUC/Control)	RR/MD (95% CI)	p-Value	Heterogeneity (I^2)
Total effective rate	6	356/340	1.33 (1.18–1.50)	<0.0001	30%
Healing time (days)	5	284/270	-8.12 (-10.45 to -5.79)	<0.00001	52%
Secondary skin damage rate	4	240/228	0.18 (0.08–0.41)	<0.0001	0%

3.4.3 Wagner Grade ≥3 DFU

Five studies (n=329) reported outcomes for deep ulcers with bone/tendon exposure. With layered, edge-first spraying (3 times/day, 1–1.5 mL/application; pre-debridement of necrotic tissue), JUC achieved a total effective rate of 91.2% (RR=1.36, 95% CI [1.20, 1.54], p<0.00001) and shortened healing time by 10.1 days (MD=-10.10, 95% CI [-12.45, -7.75], p<0.00001), with only 1 case of transient stinging (0.3%) (Table 10).

Table 10: Outcomes in Wagner Grade ≥3 DFU Subgroup.

Outcome	Number of Studies	Sample Size (JUC/Control)	RR/MD (95% CI)	p-Value	Heterogeneity (I^2)
Total effective rate	5	329/315	1.36 (1.20–1.54)	<0.00001	25%
Healing time (days)	5	329/315	-10.10 (-12.45 to -7.75)	<0.00001	60%
Infection rate	4	264/252	0.19 (0.09–0.40)	<0.00001	15%
Adverse reaction rate	5	329/315	0.31 (0.10–0.96)	0.04	22%

3.4.4 Gestational Diabetes (Perineal Incisions)

Three studies (n=100) reported outcomes in this subgroup. With targeted, low-volume application (2 times/day, 0.5 mL/incision; 20cm spray distance), JUC achieved a 97.8% 甲级 healing rate (RR=1.43, 95% CI [1.21, 1.69], p<0.0001) and a 2.0% adverse reaction rate, with no fetal risks (Table 11).

Table 11: Outcomes in Gestational Diabetes (Perineal Incisions) Subgroup.

Outcome	Number of Studies	Sample Size (JUC/Control)	RR/MD (95% CI)	p-Value	Heterogeneity (I^2)
Grade A healing rate	3	100/100	1.43 (1.21–1.69)	<0.0001	0%
Healing time (days)	3	100/100	-4.85 (-6.32 to -3.38)	<0.00001	0%
Local induration rate	3	100/100	0.22 (0.07–0.68)	0.008	0%
Adverse reaction rate	3	100/100	0.33 (0.08–1.36)	0.13	0%

3.5 Comparative Analysis of JUC vs. Commonly Used Antibacterial Materials

JUC's unique advantages for diabetic wounds are further highlighted by comparison with mainstream antibacterial materials (Table 12).

Table 12: Comparative Summary: JUC vs. Commonly Used Antibacterial Materials for Diabetic Wounds.

Comparison Factor	JUC	Topical Antibiotics (e.g., Penicillins, Cephalosporins)	Silver-Containing Dressings (e.g., Silver Foam/Gauze)	Chemical Disinfectants (e.g., Chlorhexidine, Povidone-Iodine)
Antibacterial Mechanism	Physical: Positive-charge nano-film inactivates pathogens via electrostatic force	Chemical: Targets bacterial cell wall synthesis/enzymes	Chemical: Silver ion oxidation of bacterial proteins/nucleic acids	Chemical: Oxidation/denaturation of bacterial cell membranes
Drug Resistance Rate	0% (even for MRSA/multidrug-resistant strains) (Mei et al., 2024)	23.5%–97.8% (diabetic foot pathogens) (Yu, 2023)	Low (but emerging silver resistance) (Tang et al., 2023)	Not applicable (broad-spectrum, no resistance pressure)
Wound Healing Impact	Promotes healing: Moisture retention + barrier protection; shortens DFU healing by 9.24 days (Wang et al., 2024b)	Neutral: No healing benefits; may disrupt wound microbiome (Yu, 2023)	Inhibits healing: Silver ion cytotoxicity to fibroblasts/keratinocytes (Tang et al., 2023)	Delays healing: Dries wounds + damages granulation tissue (Ma et al., 2024)
Systemic Toxicity	None (no percutaneous absorption) (Chen et al.,	Yes (GI distress, drug-drug interactions with	Yes (silver accumulation → kidney toxicity in	None (local action only)

	2023)	hypoglycemics) (Yu et al., 2024)	renal-impaired diabetics) (Chen et al., 2023)	
Adverse Reaction Rate	3.1% (mild dryness/redness, self-resolving) (Yu et al., 2024)	8%–12% (contact dermatitis, rash) (Yu, 2023)	7%–15% (skin irritation, argyria) (Tang et al., 2023)	15%–20% (pain, itching, severe dryness) (Ma et al., 2024)
Biofilm Inhibition	Effective (74.4% reduction) (Zhang et al., 2023)	Ineffective (cannot penetrate biofilm matrix) (Mei et al., 2024)	Limited (silver ions trapped in biofilm) (Tang et al., 2023)	Ineffective (only kills surface bacteria) (Ma et al., 2024)
Formulation & Applicability	Spray: Easy to apply to irregular lesions (DFU, perineal incisions) (Zheng et al., 2023)	Ointment: Greasy; poor for exudative wounds (Yu, 2023)	Rigid gauze/foam: Difficult for deep/irregular lesions (Tang et al., 2023)	Liquid: Requires frequent reapplication; poor adherence (Ma et al., 2024)
Subgroup Suitability	Safe for gestational diabetes, end-stage nephropathy, severe neuropathy (Yang et al., 2023)	Contraindicated in antibiotic-allergic/gestational diabetes patients (Yu et al., 2024)	Unsafe for renal-impaired diabetics; irritates neuropathic skin (Tang et al., 2023)	Exacerbates neuropathy; unsafe for fragile incisions (Ma et al., 2024)
Cost-Effectiveness	High: Reduces total costs by 23%–37% (shorter hospitalization) (Li et al., 2024)	Low: High long-term cost (resistance → repeat treatments) (Yu, 2023)	Low: 3–5x more expensive than JUC; no healing time savings (Tang et al., 2023)	Low upfront cost; high indirect costs (delayed healing/adverse reactions) (Ma et al., 2024)
Combination Compatibility	Synergistic with debridement, VSD, far-infrared, antibiotics (Wang et al., 2024c)	Risk of antagonism with other antimicrobials (Yu, 2023)	Incompatible with some dressings (silver leaching) (Tang et al., 2023)	Inactivates topical growth factors/products (Ma et al., 2024)

3.6 Sensitivity Analysis and Publication Bias

Sensitivity analysis by sequentially excluding individual studies showed no significant changes in the combined RR and MD of total effective rate, healing time, and infection rate, indicating robust results. Funnel plots of total effective rate (23 studies) were symmetric, suggesting no significant publication bias.

4. DISCUSSION

Diabetes-related skin and mucosal lesions are clinically challenging due to impaired healing, high infection risk, and antibiotic resistance—all of which are exacerbated by the unique pathophysiological characteristics of diabetes (Prompers et al., 2022; Xu et al., 2023). This meta-analysis of 28 studies (n=2,364 diabetic patients) provides compelling evidence that JUC is uniquely suited to address these challenges, with distinct advantages over conventional antibacterial materials and tailored efficacy for high-risk subgroups.

4.1 Unique Mechanistic Advantages of JUC for Diabetic Lesions

JUC's physical antibacterial mechanism—forming a stable, non-leachable positive-charge nano-film—sets it apart from chemical antibiotics and silver-containing dressings (Liu et al., 2023; Chen et al., 2024). Unlike antibiotics that target bacterial metabolism (inducing resistance) or silver ions that rely on chemical oxidation (causing cytotoxicity), JUC inactivates pathogens via electrostatic adsorption, avoiding selective pressure on bacteria. This explains the 0% drug resistance rate observed in diabetic lesions, even against multidrug-resistant strains like MRSA—addressing a critical unmet need in diabetic care (Mei et al., 2024; Wang et al., 2024a). For diabetic patients with chronic, recurrent lesions (e.g., grade Ⅲ–Ⅳ DFU), this resistance-free property eliminates the risk of treatment failure due to antibiotic overuse, a major limitation of conventional therapies (Yu, 2023).

Additionally, JUC's film-forming property provides dual benefits for diabetic wound healing: it maintains a moist environment (reducing transepidermal water loss by 45% in diabetic skin) and acts as a protective barrier against external pathogens and friction (Qin et al., 2023; Wang et al., 2024b). Diabetic wounds heal poorly in dry environments due to impaired epithelialization, and JUC's moisture-retention effect directly addresses this by promoting collagen synthesis and epithelial cell proliferation (Zhang et al., 2023). In contrast, chemical disinfectants (e.g., povidone-iodine) dry out wounds, and silver-containing dressings can be cytotoxic to fibroblasts—further delaying healing in diabetic patients (Tang et al., 2023; Ma et al., 2024).

4.2 Tailored Efficacy for High-Risk Diabetic Subgroups

High-risk diabetic subgroups (end-stage nephropathy, severe neuropathy, advanced DFU, gestational diabetes) face amplified healing challenges and safety risks, but JUC's adaptability—via dosage adjustments and application techniques—ensures optimal outcomes:

a. **End-stage nephropathy**: Patients with impaired fluid/electrolyte balance are prone to skin dryness, but reducing JUC frequency (2 times/day) and volume (0.5–1 mL) plus pre-hydration with

moisturizer minimized adverse reactions (2.8%) while maintaining a 90.7% total effective rate (Zheng et al., 2023). JUC's lack of systemic absorption is critical for this subgroup, as it avoids kidney toxicity associated with silver accumulation or antibiotic excretion (Chen et al., 2023).

b. **Severe peripheral neuropathy**: Sensory loss increases the risk of unrecognized irritation and secondary damage, but visual monitoring, non-adherent dressings, and gentle spraying (15–20cm distance) reduced secondary skin damage by 82% (RR=0.18) and maintained a 92.4% total effective rate (Yang et al., 2023). JUC's mild adverse reactions (no severe pain or irritation) are particularly beneficial for patients with neuropathy-related hypersensitivity.

c. **Wagner grade ≥3 DFU**: Deep ulcers with necrotic tissue and exposed nerve endings are prone to infection and stinging, but layered, edge-first spraying (avoiding direct contact with nerve endings) and pre-debridement achieved a 91.2% total effective rate and shortened healing time by 10.1 days (Wang et al., 2024c). JUC's ability to penetrate exudate and inhibit biofilm formation (74.4% reduction) addresses the key drivers of DFU recurrence (Zhang et al., 2023).

d. **Gestational diabetes**: Hormonal skin sensitivity and fetal safety concerns limit treatment options, but targeted, low-volume application (0.5 mL/incision) achieved a 97.8% perineal incision healing rate with no fetal risks (Yu et al., 2024). JUC's lack of systemic absorption and mild adverse reactions (2.0%) make it superior to antibiotics (which carry fetal exposure risks) and silver dressings (which may cause skin irritation).

4.3 Safety Advantages in Diabetic Populations

Diabetic patients are more vulnerable to adverse reactions from topical treatments due to skin barrier impairment and comorbidities, but JUC's safety profile is optimized for this group.

a. **Localized action**: No percutaneous absorption eliminates systemic toxicity (e.g., kidney/liver damage) in patients with organ impairment (Chen et al., 2023).

b. **Mild adverse reactions**: Only 3.1% of patients reported mild dryness or redness (self-resolving), with no severe hypersensitivity or cytotoxicity (Yu et al., 2024).

c. **No drug-drug interactions**: Does not interfere with hypoglycemic agents (e.g., insulin, metformin) or antihypertensives, avoiding risks of glucose fluctuations (Ma et al., 2024).

d. **Subgroup tolerance**: Safe for gestational diabetes, elderly diabetics, and patients with neuropathy—populations often excluded from conventional antimicrobial trials (Yang et al., 2023; Yu et al., 2024).

4.4 Practical Application and Cost-Effectiveness

JUC's spray formulation and versatility make it suitable for diverse diabetic care settings.

a. **In-hospital care**: Combinable with debridement, VSD, and far-infrared irradiation for severe lesions (e.g., grade Ⅲ DFU) (Wang et al., 2024c);

b. **Community/home care**: Easy self-administration by patients/caregivers, improving adherence for chronic lesions (Zheng et al., 2023);

c. **Cost-effectiveness**: Reduces total medical costs by 23%–37% vs. antibiotics/silver dressings via shorter hospitalization and lower recurrence, critical for long-term diabetic care (Li et al., 2024).

4.5 Limitations and Future Directions

This study has some limitations: (1) Some RCTs lacked allocation concealment and blinding, potentially introducing bias; (2) Most studies were from China, limiting generalizability to other regions; (3) Few studies reported long-term outcomes (e.g., lesion recurrence rate) in high-risk subgroups; (4) JUC dosage and frequency varied across studies, contributing to heterogeneity.

Future research should focus on: (1) Large-scale, multicenter RCTs with adequate blinding and long-term follow-up (≥1 year) to evaluate recurrence rate in high-risk subgroups; (2) Head-to-head comparisons with advanced wound care products (e.g., growth factors, bioengineered dressings) in diabetic patients; (3) International multicenter studies to verify efficacy in diverse ethnic and socioeconomic groups; (4) Development of standardized application guidelines for specific diabetic lesions (e.g., DFU, perineal incisions).

5. CONCLUSION

JUC long-acting antibacterial material exhibits significant efficacy and excellent safety in diabetic patients with skin and mucosal lesions, with unique advantages including physical antibacterial action (0% drug resistance), dual wound healing promotion, and adaptability to high-risk subgroups. Tailored dosage adjustments and application techniques—such as reduced frequency/volume for end-stage nephropathy, visual monitoring for severe neuropathy, layered spraying for advanced DFU, and targeted low-volume use for gestational diabetes—further minimize side effects while preserving efficacy. JUC's localized action, mild adverse reactions, and lack of drug-drug interactions make it particularly suitable for diabetic populations with impaired wound healing, comorbidities, and high antibiotic resistance risk. As an APA-compliant, evidence-based alternative to conventional antimicrobial therapies, JUC is worthy of widespread clinical promotion in diabetic care.

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