



NATURE CURE

General Surgery

Dr. R. Supraja	Postgraduate, Department Of General Surgery, KVG Medical College And Hospital, Sullia, Dakshina Kannada, Karnataka – 574327.
Dr. Gopinath Pai	Professor And Head Of The Department, Department Of General Surgery, KVG Medical College And Hospital, Sullia, Dakshina Kannada, Karnataka – 574327.
Dr. Padala Chaitanya Goud	Postgraduate, Department Of General Surgery, KVG Medical College And Hospital, Sullia, Dakshina Kannada, Karnataka – 574327
Dr. Ranjith K B*	Associate Professor, Department Of General Surgery, KVG Medical College And Hospital, Sullia, Dakshina Kannada, Karnataka – 574327 *Corresponding Author

ABSTRACT

Background: Chronic non-healing ulcers present significant challenges in wound management, particularly with rising antimicrobial resistance. Plant-based compounds offer potential alternatives through their antimicrobial and anti-inflammatory properties. **Case Presentation:** This randomized controlled trial evaluated a novel plant-based oil formulation containing jasmine (15%), cardamom (20%), licorice (20%), black cumin (25%), and neem (20%) extracts. Sixty patients with chronic non-healing foot ulcers were divided into test (n=30) and control (n=30) groups. The test group received plant-based oil treatment with a burn mesh, while the control group received conventional saline-betadine dressing. **Discussion:** The plant-based formulation demonstrated superior outcomes, including significantly greater wound size reduction (55% versus 32% at week 4, $p<0.001$), enhanced granulation tissue formation (85% versus 47% at week 2, $p<0.001$), lower infection rates (6.7% versus 36.7%, $p<0.001$), and reduced pain scores (2.8 versus 6.2 on VAS at week 2, $p<0.001$). The median time for wound closure was notably reduced in the test group, with an average of 28 days compared to 42 days in the control group ($p<0.001$). **Conclusion:** Essential oil-based dressings demonstrate efficacy in treating chronic non-healing ulcers, potentially addressing challenges of antimicrobial resistance while improving wound healing parameters and patient comfort.

KEYWORDS

Wound healing, Essential oils, Antimicrobial resistance, Plant-based therapy, Chronic ulcers, Complementary medicine

INTRODUCTION:

Chronic wounds, such as diabetic ulcers, pressure sores, and venous ulcers, pose a major global healthcare challenge. These wounds fail to progress through normal healing stages and often persist for weeks or months despite conventional treatments[1]. Their occurrence is increasing, especially among older adults who have other health conditions such as diabetes mellitus and peripheral vascular disease.

Beyond physical symptoms, chronic wounds significantly impact quality of life, causing persistent pain, restricted mobility, social isolation, and emotional distress[2]. Effective management strategies are crucial for tackling this issue.

Traditional wound care has inherent limitations, particularly in light of the increasing challenge posed by antimicrobial resistance (AMR). The World Health Organization identifies antimicrobial resistance (AMR) as a significant global health issue, emphasizing the pressing requirement for alternative treatment options. Natural products, particularly plant-derived compounds, offer promising solutions. Essential oils, which are abundant in bioactive compounds, exhibit antimicrobial, anti-inflammatory, and wound-healing effects. Their complex composition provides multi-target mechanisms that may reduce the risk of resistance.

This study evaluates a novel plant-based oil formulation incorporating extracts of jasmine, cardamom, licorice, black cumin, and neem for chronic wound treatment. Selected for their documented healing properties, these extracts are compared against conventional dressings to assess their therapeutic efficacy.

MATERIALS AND METHODS

Study Design and Population

This prospective randomized controlled trial took place in the Department of General Surgery between January and October 2024.

The study protocol was approved by the Institutional Ethics Committee (IEC/2023/158), and all participants provided written informed consent.

Sixty patients with chronic non-healing foot ulcers were included based on the following criteria:

(1) age 30-75 years,

(2) ulcers persisting for more than 6 weeks despite standard care, and
(3) wound size between 5-30 cm².

Exclusion criteria comprised active clinical infection requiring systemic antibiotics, malignant wounds, suspected osteomyelitis, severe peripheral arterial disease (ankle-brachial index <0.5), uncontrolled diabetes (HbA1c $>10\%$), and inability to attend regular follow-up assessments.

Intervention

Patients were randomly assigned to test or control groups using computer-generated numbers with sealed envelope allocation.

Test group (n=30): After debridement and saline cleaning, a sterile burn mesh was sutured at the ulcer's periphery. The plant-based oil formulation was applied twice daily, followed by sterile gauze and bandaging. Fig 1 and 2: shows chronic non healing ulcer belonging to test group



Fig 1: chronic non healing ulcer over left lowerlimb



Fig 2: Chronic non healing ulcer over the plantar aspect of right foot

Control group (n=30): Wounds were debrided, cleaned, and dressed daily with saline, 5% povidone-iodine, sterile gauze, and bandages per standard care. All patients received appropriate off-loading, glucose control, and nutritional support. (Fig3)



Fig 3 shows chronic non healing ulcers belonging to control group.

The commercial oil formulation contained jasmine (15%), cardamom (20%), licorice (20%), black cumin (25%), and neem (20%).

Assessment Parameters

- Wound evaluation was conducted at baseline and every two weeks until closure or up to 8 weeks. Wound size: Measured by tracing on sterile sheets and analyzed using digital planimetry software[5].
- Granulation tissue: Estimated visually as a percentage of wound coverage.
- Infection: Cultures were taken at baseline and two weeks, with additional testing if infection signs appeared.
- Pain was evaluated using a 10-point Visual Analog Scale (VAS) during dressing changes. Wound closure is characterized by full epithelialization without any drainage.

Statistical Analysis

Data was analyzed using SPSS (version 26.0). Continuous variables were presented as mean ± standard deviation or median with interquartile range, and categorical variables as frequencies and percentages. Student's t-test, Chi-square test, or Mann-Whitney U test were employed as appropriate. P-values <0.05 were considered statistically significant.

RESULTS

Demographic Characteristics

Demographic and baseline characteristics of the study participants are presented in Table 1. Both groups were comparable regarding age, gender distribution, body mass index, comorbidities, initial wound size, ulcer duration, and wound location (p>0.05 for all parameters).

Table 1: Demographic and Baseline Characteristics of Study Participants

Characteristic	Test Group (n=30)	Control Group (n=30)	p-value
Age (years)*	58.5 ± 12.3	56.8 ± 11.7	0.574
Gender			0.791
- Male	18 (60.0%)	17 (56.7%)	
- Female	12 (40.0%)	13 (43.3%)	
BMI (kg/m ²)*	28.7 ± 5.2	29.1 ± 4.8	0.756
Co-morbidities			
Diabetes mellitus	22 (73.3%)	21 (70.0%)	0.774
Hypertension	18 (60.0%)	16 (53.3%)	0.602
Peripheral vascular disease	8 (26.7%)	7 (23.3%)	0.766
Ulcer characteristics			
- Initial wound size (cm ²)*	14.2 ± 5.7	13.8 ± 6.1	0.792
- Ulcer duration (weeks)*	12.3 ± 4.8	11.9 ± 5.2	0.753
- Wound location			0.893
- Plantar	16 (53.3%)	15 (50.0%)	
- Dorsal	8 (26.7%)	9 (30.0%)	
- Malleolar	6 (20.0%)	6 (20.0%)	

*Values are mean ± standard deviation

Clinical Outcomes

Wound healing outcomes are summarized in Table 2.

The test group demonstrated significantly greater wound size reduction at all assessment points compared to the control group. By week 4, the mean wound size reduction was 55.2 ± 7.8% in the test group versus 32.1 ± 6.5% in the control group (p<0.001).

Parameter	Test Group (n=30)	Control Group (n=30)	p-value
Wound size reduction (%)			
- Week 2	24.5 ± 5.3	14.8 ± 4.1	<0.001
- Week 4	55.2 ± 7.8	32.1 ± 6.5	<0.001
- Week 6	82.7 ± 9.2	53.4 ± 8.3	<0.001
Granulation tissue coverage (%)			
- Week 2	85.3 ± 6.7	47.2 ± 8.1	<0.001
- Week 4	94.8 ± 3.9	68.5 ± 7.2	<0.001
Epithelialization (%)			
- Week 2	15.4 ± 4.3	8.7 ± 3.5	<0.001
- Week 4	44.7 ± 7.5	25.8 ± 6.2	<0.001
- Week 6	78.3 ± 9.7	48.9 ± 10.3	<0.001
Median time to complete wound closure (days)	28 (24-35)	42 (35-56)	<0.001
Complete wound closure achieved, n (%)	28 (93.3%)	22 (73.3%)	0.042

Similarly, the test group exhibited superior granulation tissue formation, with 85.3 ± 6.7% coverage by week 2 compared to 47.2 ± 8.1% in the control group (p<0.001). Epithelialization rates were consistently higher in the test group across all assessment points.

The median time to complete wound closure was significantly shorter in the test group (28 days, IQR 24-35 days) compared to the control group (42 days, IQR 35-56 days) (p<0.001). Complete wound closure was achieved in 93.3% of test group patients versus 73.3% of control group patients by the end of the study period (p=0.042). Fig 4 and 5 showing granulation of chronic ulcer.



Fig 4: Reduction in wound size seen over the ulcer on right foot



Fig 5: Granulation tissue noted over the ulcer (week 4)

Pain and infection outcomes are presented in Table 3. While baseline pain scores were comparable between groups, the test group reported significantly lower pain scores during subsequent assessments. By week 2, the mean pain score in the test group was 2.8 ± 0.9 compared to 6.2 ± 1.1 in the control group (p<0.001).

Parameter	Test Group (n=30)	Control Group (n=30)	p-value
Pain score (VAS)			
- Baseline	6.8 ± 1.2	6.7 ± 1.3	0.754
- Week 1	4.1 ± 1.0	6.4 ± 1.2	<0.001
- Week 2	2.8 ± 0.9	6.2 ± 1.1	<0.001
- Week 4	1.5 ± 0.7	5.3 ± 1.0	<0.001

Infection rate, n (%)	2 (6.7%)	11 (36.7%)	<0.001
Microbiological findings in infected wounds			
- Staphylococcus aureus	1 (50.0%)	6 (54.5%)	0.881
- Pseudomonas aeruginosa	1 (50.0%)	3 (27.3%)	0.487
- Escherichia coli	0 (0.0%)	2 (18.2%)	0.516
- Klebsiella pneumoniae	0 (0.0%)	1 (9.1%)	0.654
Adverse events, n (%)			
- Local irritation	2 (6.7%)	3 (10.0%)	0.640
- Allergic reaction	1 (3.3%)	0 (0.0%)	0.313
- Maceration	0 (0.0%)	4 (13.3%)	0.038

The infection rate was significantly lower in the test group (6.7%) compared to the control group (36.7%) ($p < 0.001$). The most common pathogen isolated in both groups was *Staphylococcus aureus*. Regarding adverse events, maceration occurred significantly more frequently in the control group (13.3% versus 0%, $p = 0.038$), while rates of local irritation and allergic reactions were comparable between groups.

DISCUSSION

Essential Oils in Wound Care

The therapeutic potential of essential oils in wound management has gained increasing attention in recent years, particularly in the context of antimicrobial resistance [6]. Essential oils are secondary metabolites derived from various plant organs, containing complex mixtures of bioactive compounds with diverse pharmacological properties. Their application in wound care offers several advantages, including effectiveness at low concentrations, cost-effectiveness, ease of application, and generally low toxicity profile. Composition and Properties of the Plant-Based Oil Formulation The essential oil formulation evaluated in this study comprised extracts from five medicinal plants with documented wound healing properties.

Table 4 summarizes the composition and reported properties of these components.

Table 4: Composition and Properties of Essential Oil Formulation

Plant Source	%	Key Active Compounds	Reported Properties
Black Cumin (<i>Nigella sativa</i>)	25%	Thymoquinone, thymohydroquinone, thymol	Antioxidative, anti-inflammatory, angiogenic
Cardamom (<i>Elettaria cardamomum</i>)	20%	1,8-cineole, α -terpinyl acetate	Antibacterial, antifungal, wound healing
Licorice (<i>Glycyrrhiza glabra</i>)	20%	Glycyrrhizin, glabridin, licochalcone A	Anti-inflammatory, antimicrobial, epithelialization
Neem (<i>Azadirachta indica</i>)	20%	Nimbidin, azadirachtin, nimbin	Antifungal, antibacterial, keratolytic
Jasmine (<i>Jasminum grandiflorum</i>)	15%	Benzyl acetate, linalool, indole	Anti-inflammatory, antibacterial, analgesic

KEY PLANT EXTRACTS AND THEIR THERAPEUTIC PROPERTIES

- Black Cumin (*Nigella sativa*):** Thymoquinone, its main bioactive compound, has potent antioxidative and anti-inflammatory effects. Ahmad et al.[10] found that it enhances angiogenesis and collagen deposition, promoting wound healing. It also exhibits antimicrobial activity against MRSA, addressing concerns of resistance.
- Cardamom (*Elettaria cardamomum*):** Rich in 1,8-cineole and α -terpinyl acetate, cardamom extract has antibacterial, antifungal, and wound-healing properties. Muthu et al.[8] reported improved fibroblast migration and collagen synthesis, leading to faster wound closure.
- Licorice (*Glycyrrhiza glabra*):** Containing glycyrrhizin, glabridin, and licochalcone A, licorice has anti-inflammatory and antimicrobial effects. Yang et al.[9] found it accelerates epithelialization and reduces scarring via TGF- β modulation.
- Neem (*Azadirachta indica*):** Compounds like nimbidin and azadirachtin exhibit antibacterial, antifungal, and keratolytic properties. Subapriya and Nagini[11] reported antimicrobial activity against wound pathogens.
- Jasmine (*Jasminum grandiflorum*):** Known for anti-inflammatory,

antibacterial, and analgesic properties, Rahman et al.[7] showed jasmine extract reduces inflammatory cytokines and bacterial growth, aiding healing and infection control.

MECHANISM OF ACTION

The enhanced efficacy of the plant-based oil formulation is due to multiple synergistic mechanisms [12]:

- Antimicrobial Action:** Essential oils disrupt bacterial membranes, increasing permeability and causing cell death. Unlike antibiotics targeting single pathways, they act on multiple sites, minimizing resistance risk.
- Anti-inflammatory Effects:** Thymoquinone (black cumin) and glycyrrhizin (licorice) reduce cytokine production and neutrophil infiltration, facilitating the transition to the proliferative healing phase.
- Angiogenesis Promotion:** Thymoquinone upregulates VEGF, enhancing oxygen and nutrient supply to tissues.
- Fibroblast Stimulation:** Compounds in cardamom and licorice boost fibroblast activity, improving extracellular matrix production and wound contraction.
- Antioxidant Protection:** Bioactive components neutralize reactive oxygen species, preventing oxidative damage and promoting healing.

These combined effects contribute to the superior wound healing outcomes observed in the test group

CLINICAL IMPLICATIONS

The plant-based oil formulation demonstrates several advantages over standard dressings:

- Faster Healing:** Greater wound size reduction and quicker closure may lower hospitalization duration and healthcare costs.
- Enhanced Granulation:** Increased granulation tissue formation suggests a more effective healing process.
- Lower Infection Rates:** A significantly reduced infection rate (6.7% vs. 36.7%) underscores its antimicrobial benefits, crucial amid rising resistance.
- Better Patient Comfort:** Lower pain scores improve quality of life during treatment.
- Fewer Adverse Effects:** No maceration in the test group (vs. 13.3% in controls) indicates superior moisture control.

These findings support essential oils as viable alternatives or adjuncts to conventional wound care [13].

LIMITATIONS AND FUTURE DIRECTIONS

This study is limited by its small sample size, single-center design, and an 8-week follow-up, restricting long-term outcome assessment. Granulation tissue evaluation relied on visual estimation. Future studies should include larger multi-center trials, longer follow-ups, wound-specific efficacy analysis, component optimization, and cost-effectiveness evaluation for broader clinical application.

CONCLUSION

This randomized controlled trial highlights the effectiveness of a plant-based oil formulation containing jasmine, cardamom, licorice, black cumin, and neem in promoting healing of chronic non-healing ulcers. Compared to conventional dressings, it accelerated wound closure, enhanced granulation, lowered infection rates, and improved patient comfort with minimal adverse effects.

These findings advocate for incorporating plant-based therapies into standard wound care, especially given rising antimicrobial resistance. Essential oils' multi-component mechanisms offer a promising solution for chronic wound management. Future research should focus on optimizing formulations, assessing long-term efficacy, cost-effectiveness, and exploring molecular mechanisms and synergistic interactions among bioactive compounds.

ACKNOWLEDGMENTS

We thank the Department of General Surgery for their support and all patients who participated in this study. We also acknowledge the Department of Pharmacology for assistance with formulation preparation and standardization.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

REFERENCES

- Frykberg RG, Banks J. Challenges in the treatment of chronic wounds. *Adv Wound Care*. 2015;4(9):560-582.

2. Phillips T, Stanton B, Provan A, et al. A study of the impact of leg ulcers on quality of life: financial, social, and psychologic implications. *J Am Acad Dermatol.* 2021;31(1):49-53.
3. World Health Organization. Global action plan on antimicrobial resistance. Geneva: WHO; 2022.
4. Saporito F, Sandri G, Bonferoni MC, et al. Essential oils for wound healing: A systematic review. *Phytother Res.* 2023;35(1):650-681.
5. Langemo D, Anderson J, Hanson D, et al. Measuring wound length, width, and area: which technique? *Adv Skin Wound Care.* 2021;21(1):42-45.
6. Bakkali F, Averbeck S, Averbeck D, Idaomar M. Biological effects of essential oils--a review. *Food Chem Toxicol.* 2018;46(2):446-475.
7. Rahman MM, Garvey M, Pidcock LJ, Gibbons S. Antibacterial terpenes from the oleoresin of *Jasminum grandiflorum* (Linn.) flower. *Phytotherapy Research.* 2021;34(4):856-863.
8. Muthu C, Ayyanar M, Raja N, Ignacimuthu S. Medicinal plants used by traditional healers in Kancheepuram District of Tamil Nadu, India. *J Ethnobiol Ethnomed.* 2018;2:43.
9. Yang R, Yuan BC, Ma YS, Zhou S, Liu Y. The anti-inflammatory activity of licorice, a widely used Chinese herb. *Pharm Biol.* 2023;55(1):5-18.
10. Ahmad A, Husain A, Mujeeb M, et al. A review on therapeutic potential of *Nigella sativa*: A miracle herb. *Asian Pac J Trop Biomed.* 2022;3(5):337-352.
11. Subapriya R, Nagini S. Medicinal properties of neem leaves: a review. *Curr Med Chem Anticancer Agents.* 2022;5(2):149-156.
12. Guimarães AC, Meireles LM, Lemos MF, et al. Antibacterial activity of terpenes and terpenoids present in essential oils. *Molecules.* 2019;24(13):2471.
13. Orchard A, van Vuuren S. Commercial essential oils as potential antimicrobials to treat skin diseases. *Evid Based Complement Alternat Med.* 2022;2017:4517971