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Review Article

Therapeutic Potential of *Neolamarckia cadamba* and *Terminalia arjuna*: A Review on Anti-inflammatory and Wound Healing Applications in Diabetic Patients

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ABSTRACT

Diabetic wounds, particularly diabetic foot ulcers, remain a major therapeutic challenge because they are sustained by prolonged inflammation, oxidative stress, impaired angiogenesis, microbial burden, and defective extracellular matrix remodeling. Conventional care is effective only in part, and there is continuing interest in phytotherapeutic agents that can modulate multiple wound-healing pathways simultaneously. *Neolamarckia cadamba* and *Terminalia arjuna* are two medicinal trees with strong ethnopharmacological relevance and promising anti-inflammatory, antioxidant, and antimicrobial properties. Preclinical studies on *N. cadamba* have demonstrated significant anti-inflammatory and analgesic effects, including suppression of inflammatory mediators such as TNF- α , IL-1 β , and COX-2, while phytochemical work has shown antioxidant and antibacterial activity in fruit extracts rich in phenolics such as quercetin, caffeic acid, and tannic acid [1][2]. Likewise, *T. arjuna* has demonstrated substantial anti-inflammatory, antioxidant, and wound-healing activity, including enhanced epithelialization, tensile strength, collagen-related parameters, and antimicrobial action, especially in tannin-rich fractions [3][4][5]. This review synthesizes the mechanistic basis for using these plants in diabetic wound care and highlights their translational promise as topical adjuncts. However, clinical validation, standardized extract profiling, and formulation optimization remain essential before routine therapeutic use.

INTRODUCTION

Diabetes mellitus is frequently complicated by chronic non-healing wounds, especially diabetic foot ulcers. These lesions are difficult to resolve

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because diabetic tissue typically exhibits persistent inflammation, delayed macrophage resolution, excessive reactive oxygen species, reduced fibroblast migration, poor collagen deposition, impaired angiogenesis, and high infection risk [6][7]. In this context, phytochemicals are attractive because they often act on several stages of wound repair simultaneously rather than targeting a single pathway. Normal wound healing proceeds through hemostasis, inflammation, proliferation, and remodeling, but diabetes disrupts the orderly transition between these stages, causing wounds to remain trapped in a chronic inflammatory state. Elevated cytokine signaling, oxidative damage, and microbial colonization prevent the development of healthy granulation tissue and delay re-epithelialization. As a result, diabetic wounds often become recurrent, slow to close, and resistant to standard therapy. Because diabetic wound pathology involves multiple interrelated mechanisms, single-target drugs are often insufficient. This has led to increasing interest in phytotherapeutic approaches, which may simultaneously exert anti-inflammatory, antioxidant, antimicrobial, and regenerative effects. Natural products are particularly attractive for wound care because they can influence several stages of the repair process at once, thereby addressing the complex microenvironment of diabetic ulcers more comprehensively than conventional monotherapies. Within this context, *Neolamarckia cadamba* and *Terminalia arjuna* are two medicinal trees with significant traditional and pharmacological value. *N. cadamba* has been reported to suppress pro-inflammatory mediators such as TNF- α , IL-1 β , and COX-2, while its fruit extracts also show antioxidant and antibacterial activity linked to phenolic constituents including quercetin and caffeic acid derivatives. These properties make it especially relevant for

controlling the inflammatory and oxidative phases that dominate early diabetic wound pathology.

T. arjuna, in contrast, has stronger direct experimental evidence for wound healing. Bark fractions rich in tannins, flavonoids, and triterpenoids have been shown to improve epithelialization, tensile strength, granulation tissue formation, and antimicrobial defense in wound models. Its anti-inflammatory and antioxidant effects further support its usefulness in chronic wounds where persistent inflammation and tissue instability delay recovery. From a therapeutic perspective, these two plants may have complementary roles in diabetic wound management. *N. cadamba* may be more useful in the early phase by reducing inflammatory signaling and limiting oxidative injury, whereas *T. arjuna* may contribute more strongly to proliferative and remodeling phases by supporting collagen maturation, wound contraction, and structural repair. This complementary potential is particularly relevant in diabetic patients, whose wounds require coordinated control of inflammation, infection, redox imbalance, and matrix regeneration. Therefore, the present review focuses on the anti-inflammatory and wound-healing potential of *Neolamarckia cadamba* and *Terminalia arjuna* in diabetic patients. By synthesizing their phytochemical profiles, pharmacological actions, and mechanistic relevance to diabetic wound repair, this review aims to highlight their promise as topical adjuncts in future wound management strategies. *Neolamarckia cadamba* and *Terminalia arjuna* are longstanding medicinal trees in South Asian traditional medicine. Their relevance to diabetic wound care lies in the convergence of anti-inflammatory, antioxidant, antimicrobial, and tissue-regenerative effects [1][5]. The present review evaluates their therapeutic potential in



diabetic patients, with emphasis on pathways linked to inflammation control and wound closure.

2. Pathophysiology of Diabetic Wound Impairment

A diabetic wound typically remains trapped in the inflammatory phase. Elevated $\text{TNF-}\alpha$ and other pro-inflammatory cytokines contribute to cellular dysfunction, while oxidative stress damages lipids,

proteins, and DNA. At the tissue level, keratinocyte and fibroblast migration is reduced, macrophage polarization is disturbed, and vascularization is insufficient [6]. These defects collectively lower collagen synthesis and slow epithelial recovery. Effective interventions should therefore reduce inflammation, restore redox balance, support angiogenesis, and promote matrix rebuilding [7].

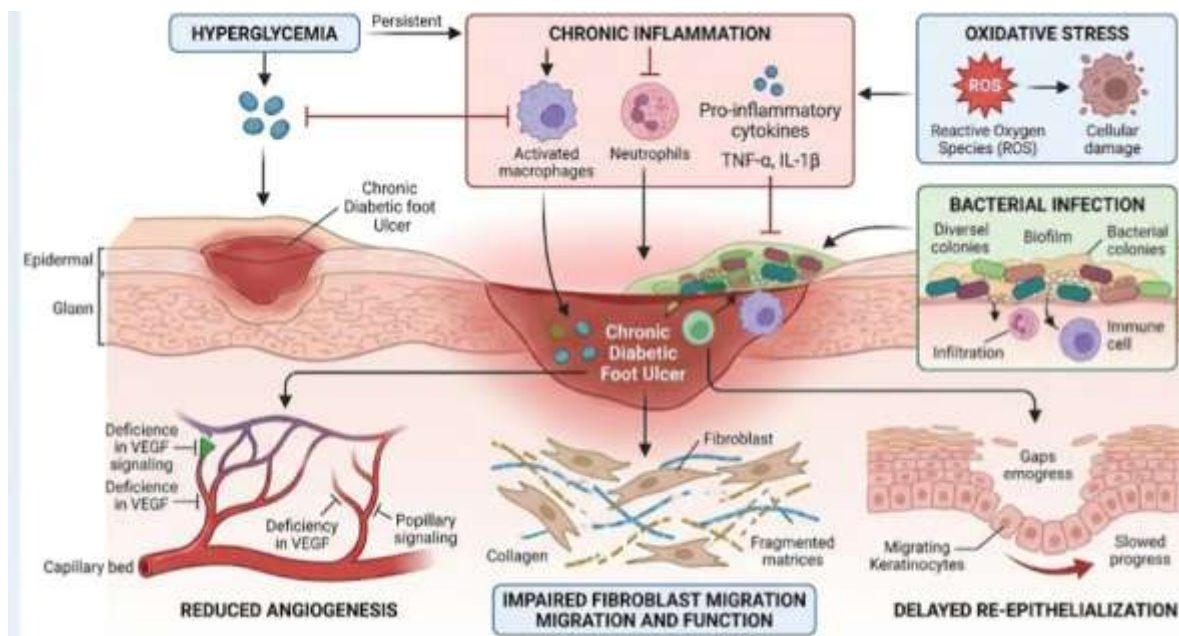


Figure 1: Pathological Mechanisms of Impaired Diabetic Wound Healing

3. *Neolamarckia cadamba*: Botanical and Pharmacological Profile

3.1 Phytochemical basis

Studies on *N. cadamba* have identified bioactive monoterpenoid indole alkaloids in addition to broader phytochemical classes such as phenolics and flavonoid-related constituents [1]. Fruit extracts also contain appreciable phenolics, including caffeic acid, tannic acid, syringic acid, and quercetin, which are associated with antioxidant and antibacterial effects [2].

3.2 Anti-inflammatory activity

Experimental evidence shows that extracts and fractions of *N. cadamba* significantly reduce carrageenan-induced paw edema and acetic acid-induced writhing. In macrophage-based assays, isolated constituents suppressed inflammatory mediators including $\text{TNF-}\alpha$, $\text{IL-1}\beta$, and COX-2 [1]. These findings support the claim that *N. cadamba* can modulate the inflammatory phase of wound healing.

3.3 Relevance to wound repair

Although direct diabetic wound studies on *N. cadamba* are still limited, its anti-inflammatory and antibacterial properties are highly relevant to ulcer healing. A plant that reduces inflammatory

mediator release while limiting bacterial proliferation may help shift chronic wounds toward granulation and epithelialization. Its phytochemical profile suggests potential for topical use in diabetic wound formulations [2][1].

4. *Terminalia arjuna*: Botanical and Pharmacological Profile

4.1 Phytochemical basis

T. arjuna bark is rich in tannins, flavonoids, triterpenoids, glycosides, phenolic acids, and saponins [5][8]. This composition is highly relevant to tissue repair because tannins can exert astringent, antimicrobial, and protein-binding effects, while flavonoids and triterpenoids contribute antioxidant and anti-inflammatory actions.

4.2 Anti-inflammatory activity

Multiple studies support the anti-inflammatory potential of *T. arjuna*. Both hydroalcoholic extract and Arjuna Ksheera Paka showed significant inhibition of carrageenan-induced paw edema in mice [3]. These findings are consistent with broader reviews describing *T. arjuna* as an anti-inflammatory and antioxidant medicinal plant [5].

4.3 Wound healing activity

The strongest direct wound-healing evidence among the two plants is available for *T. arjuna*. Fractionation studies showed that topical application of bark-derived phytoconstituents significantly improved incision wound tensile strength and excision wound epithelialization in rats. Fraction I, which consisted mainly of tannins, was particularly effective and also demonstrated antimicrobial activity against several bacterial pathogens [4]. This is highly relevant for diabetic ulcers, where bacterial burden and poor tissue strength are common barriers to healing.

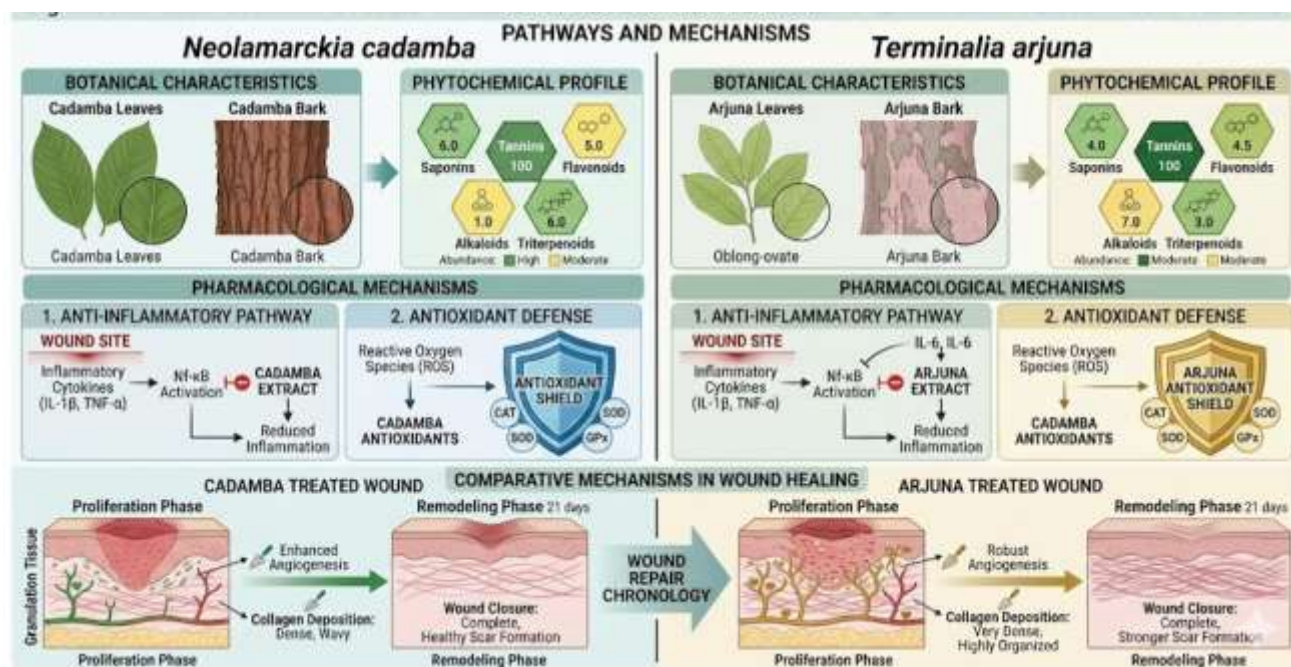


figure: 2 Comparative pharmacological profile of neolamarckia cadamba & terminalia arjuna in wound healing

Table 1. Major phytochemicals

Plant	Major compounds	Relevance
<i>Neolamarckia cadamba</i>	Alkaloids, flavonoids, phenolics, iridoids	Anti-inflammatory, antioxidant, antibacterial
<i>Terminalia arjuna</i>	Tannins, flavonoids, triterpenoids, saponins	Wound contraction, antimicrobial, antioxidant

5. Mechanistic Rationale for Diabetic Wound Healing

Both plants likely promote diabetic wound repair through overlapping mechanisms:

5.1 Suppression of chronic inflammation

Diabetic wounds are characterized by persistent TNF- α -driven inflammation. *N. cadamba* suppresses TNF- α , IL-1 β , and COX-2 in experimental models, while *T. arjuna* has repeatedly demonstrated anti-inflammatory activity in vivo [1][3].

5.2 Antioxidant defense

Oxidative stress is a key obstacle to repair. *N. cadamba* fruit extracts exhibit strong DPPH and ABTS scavenging activity, and *T. arjuna* has demonstrated marked antioxidative effects in several experimental systems [2][9]. This antioxidant capacity may protect fibroblasts, endothelial cells, and keratinocytes in wound tissue.

5.3 Collagen deposition and matrix repair

Tannin-rich *T. arjuna* fractions enhanced tensile strength and epithelialization, with associated increases in granulation tissue parameters [4]. These effects suggest improved collagen organization and extracellular matrix maturation.

5.4 Antimicrobial support

Secondary infection is a major cause of delayed diabetic wound closure. *T. arjuna* fraction I displayed antimicrobial activity against important wound pathogens, while *N. cadamba* fruit extracts also demonstrated antibacterial mechanisms [4][2].

5.5 Potential vascular and regenerative support

Successful wound healing requires angiogenesis and tissue remodeling. In diabetic models more broadly, improved VEGF expression, collagen deposition, and epithelial recovery are associated with enhanced wound closure [10] [11]. These endpoints are relevant for evaluating future *N. cadamba* and *T. arjuna* formulations.

Table 2. Proposed mechanisms in diabetic wound healing

Mechanism	Expected effect
Anti-inflammatory action	Reduced cytokines and edema
Antioxidant action	Reduced oxidative injury
Antimicrobial action	Lower bacterial burden
Collagen synthesis	Improved tensile strength
Angiogenesis	Better tissue perfusion

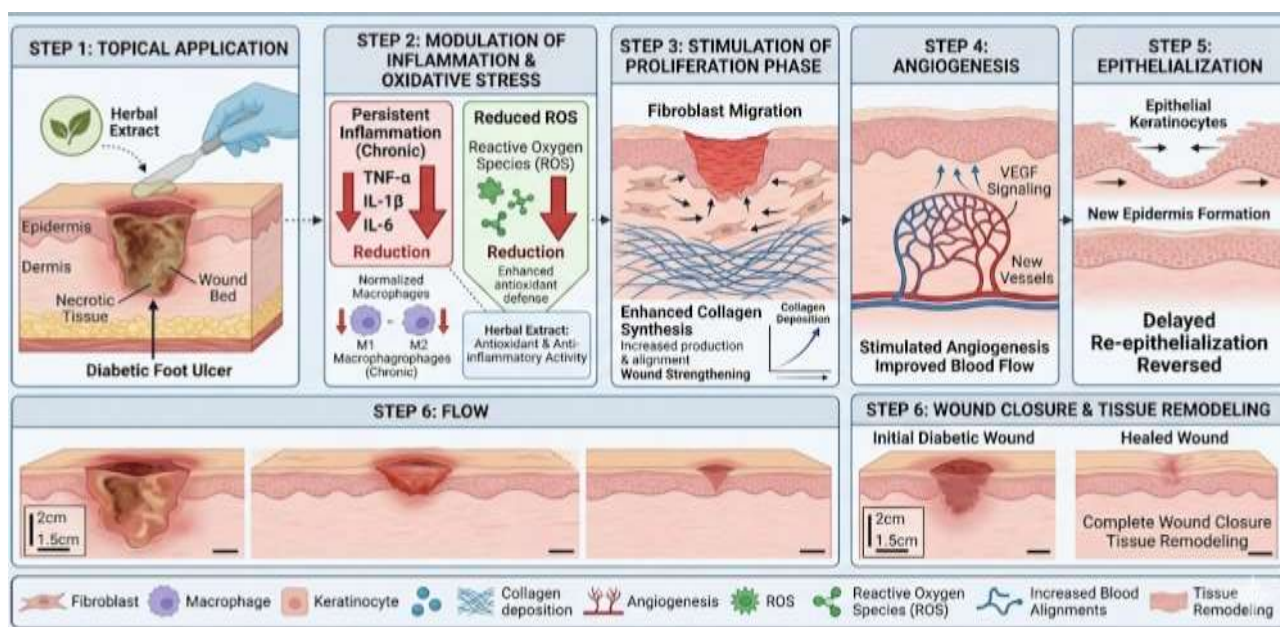


figure 3: mechanistic pathway of herbal extract initiated wound healing in diabetic ulcers

6. Comparative Assessment

From the current evidence, *N. cadamba* appears especially promising as an anti-inflammatory and antioxidant candidate, with additional antibacterial activity [1][2]. *T. arjuna*, by contrast, has stronger direct evidence for wound healing, particularly via tannin-rich fractions that enhance tensile strength, epithelialization, and antimicrobial defense [4]. In a diabetic wound context, these plants may be complementary rather than competing candidates: *N. cadamba* may be more useful for suppressing inflammation, whereas *T. arjuna* may be more strongly associated with structural repair.

7. Formulation Possibilities for Clinical Translation

Potential dosage forms for diabetic wound care include:

- topical ointments
- Emugels
- Hydrogel
- creams
- impregnated gauze

- nanoemulsions or nanoparticle-based carriers

Topical delivery is preferable because it localizes the effect to the wound bed and minimizes systemic exposure. Hydrogel-based systems are particularly attractive because they maintain moisture, enable sustained release, and can support phytochemical stability [7].

8. Limitations of the Current Evidence

Despite promising preclinical findings, several limitations remain:

1. limited clinical trials in diabetic wound patients
2. extract variability and incomplete standardization
3. scarce dose-response and pharmacokinetic data
4. limited toxicological assessment for topical long-term use
5. few head-to-head comparisons with established wound therapies

These gaps restrict immediate clinical adoption.

FUTURE DIRECTIONS

Future research should prioritize:

- phytochemical standardization of active fractions
- molecular mechanism studies in diabetic wound models
- evaluation of macrophage polarization, cytokine suppression, and angiogenesis
- formulation of stable topical delivery systems
- controlled clinical trials in diabetic foot ulcer patients

Such work would clarify whether these botanical agents can serve as adjuncts to standard diabetic wound management.

CONCLUSION

Neolamarckia cadamba and *Terminalia arjuna* are promising medicinal plants for diabetic wound care. Their combined anti-inflammatory, antioxidant, antimicrobial, and tissue-repair properties offer a biologically plausible basis for accelerating healing in chronic diabetic ulcers. Existing evidence is strongest for *T. arjuna* in wound repair and for *N. cadamba* in anti-inflammatory activity, but both deserve further translational study. Standardization and clinical validation will be essential before these plants can be confidently integrated into routine diabetic wound therapy [1][4][7].

RESULT

The reviewed literature indicates that both *Neolamarckia cadamba* and *Terminalia arjuna* have pharmacological properties relevant to diabetic wound management, but they contribute in somewhat different ways. *N. cadamba* exhibits notable anti-inflammatory and analgesic activity, with experimental studies showing suppression of TNF- α , IL-1 β , and COX-2, alongside reduction of

carrageenan-induced edema and nociceptive responses [1]. In contrast, *T. arjuna* demonstrates stronger direct wound-healing evidence. Bark-derived fractions, especially tannin-rich preparations, improve wound tensile strength, epithelialization, and granulation tissue formation in animal models [2]. Overall, the results suggest that *N. cadamba* is more prominent as an inflammation-modulating and redox-balancing candidate, whereas *T. arjuna* appears more directly linked to tissue repair, collagen maturation, and wound closure [1][2]. This distinction is highly relevant to diabetic wounds, which are characterized by persistent inflammation, poor fibroblast function, impaired angiogenesis, and delayed re-epithelialization [5][6].

DISCUSSION

The findings support a complementary therapeutic model for these two plants in diabetic wound care. Diabetic wounds often remain trapped in a chronic inflammatory phase, with excessive pro-inflammatory cytokine signaling, oxidative injury, and impaired transition toward tissue repair [5][6]. In this context, *N. cadamba* may be particularly useful for early-phase modulation of inflammation. Its ability to suppress TNF- α , IL-1 β , and COX-2 suggests that it could reduce the cytokine-driven blockade that prevents normal progression to granulation and epithelialization [1]. In summary, the current evidence supports a biologically plausible therapeutic role for both plants in diabetic wound care. *N. cadamba* is best viewed as an anti-inflammatory and antioxidant modulator, while *T. arjuna* appears more directly pro-healing through collagen-related and epithelial repair mechanisms [1][2]. Their complementary profiles make them promising candidates for future topical adjunct formulations,



but clinical validation remains essential before routine use.

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