
COMBINATION-BASED TOPICAL THERAPIES IN WOUND MANAGEMENT: MECHANISTIC INSIGHTS INTO NEOSPORIN, LAVENDER, AND VITAMIN E

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ABSTRACT

Wound healing is a highly coordinated biological process involving inflammation, cellular proliferation, angiogenesis, and tissue remodeling. Delayed or impaired healing remains a significant clinical challenge due to factors such as microbial infection, oxidative stress, and prolonged inflammation. Conventional topical antibiotics are effective in controlling infection but often lack regenerative and antioxidant support, highlighting the need for combination therapeutic approaches. This review critically examines the pharmacological and mechanistic basis of a topical formulation combining Neosporin, lavender (*Lavandula angustifolia*) extract, and vitamin E for enhanced wound healing. Neosporin provides broad-spectrum antibacterial activity, while lavender extract and vitamin E contribute anti-inflammatory, antioxidant, and tissue-regenerative effects. Experimental evidence from preclinical excision wound models demonstrates that this combination therapy significantly improves wound contraction, accelerates epithelialization, enhances collagen deposition, and reduces inflammatory cell infiltration when compared with untreated controls and single-agent therapies. Mechanistically, the synergistic action of the formulation promotes infection control, modulation of inflammatory mediators, scavenging of reactive oxygen species, stimulation of fibroblast proliferation, angiogenesis, and extracellular matrix remodeling. Histopathological observations consistently support improved tissue architecture and faster wound closure in treated groups. Overall, the reviewed evidence suggests that the combined topical use of Neosporin, lavender extract, and vitamin E represents a promising multimodal strategy for wound management. This integrative approach may offer superior therapeutic outcomes compared to conventional monotherapies and warrants further clinical evaluation for its potential application in acute and chronic wound care.

KEYWORDS: Wound healing, hair follicles, skin, burns.

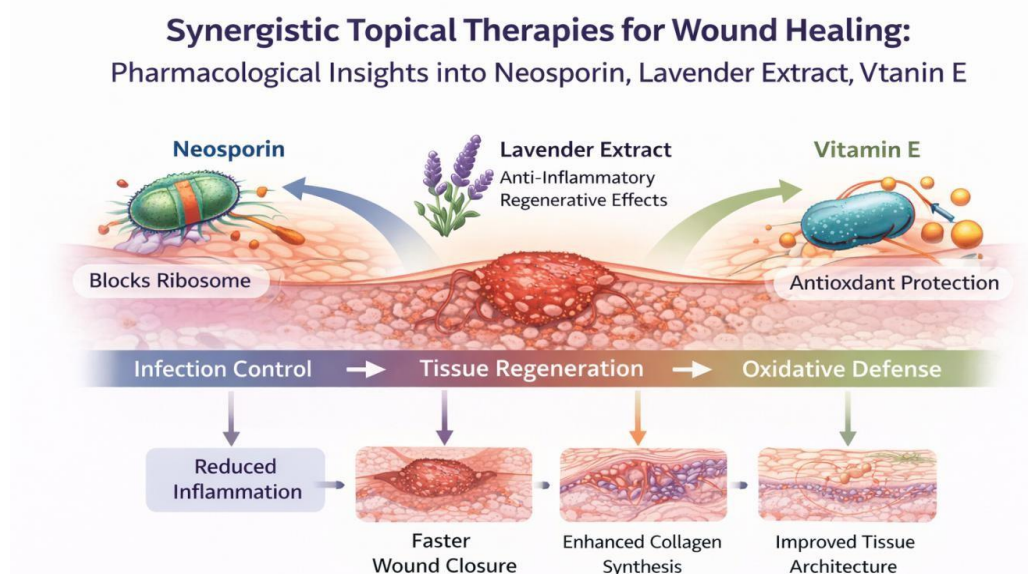


Fig.1: Graphical abstract for wound healing.

INTRODUCTION

The largest organ in the human body both mass-wise and area-wise is skin. Its whole size comes to more than 16,000 square meters. About 8% of an adult's entire body mass consists of their skin. Every living entity has an epidermis, the outermost tissue or layer. The skin forms a protective layer to guard itself from possibly harmful environmental elements. Sunlight may help the skin create vitamin D, a useful molecule. [1,2] Apart from being a sensory organ, The skin assists the body to keep its core temperature constant. The skin consists of melanocytes, erythrocytes, keratinocytes, and many other cell types. Its many constituents—cells and fibers among them—have produced a multi-layered architecture.[3]

THE SKIN CONSISTS OF LAYERS

A. The Epidermis: The skin plays an important role in regulating the body's internal temperature. The thickness of the epidermis changes with bodily location.[4,5] The bulk of the epidermis consists of keratinocytes and dendritic cells. It also features melanocytes, Langerhans cells, and others. The metabolically active tissue is the layer of the skin on its outside.[6]

The outermost layer is classified into five sub-layers, and these are:

- 1) Stratum corneum
- 2) Stratum lucidum
- 3) Stratum granulosum
- 4) Stratum spinosum
- 5) Stratum Basale

1) Stratum corneum: The stratum corneum is the stratum most exterior of the epidermis. With a thickness between 8 and 15µm, it is also called the stratum corneum. The layer with a hexagonal form helps to shield the skin from extreme dryness. Water retention depends critically on its main component, ceramide.[7]

2) **Stratum lucidum:** The delicate, see-through stratum lucidum is the skin's dead cell layer. It is exclusively present on the thickest parts of the body, such the palms and soles of the feet.[8]

3) **Stratum granulosum:** Another name for the three μm -thick layer is the granular cell layer. Its granular cells are stacked two to four times. KeraFiber fibers flatten their shape when more and more of them are included in the cells. [9]

4) **Stratum spinosum:** Another term for it is the 50 to 150 μm thick prickly cell layer. The numerous cells that comprise it might differ in size, form, and content.[10]

5) **Stratum basale:** Just one layer makes up Stratum Basale, the deepest sublayer of the epidermis. Beginning their trip to the surface from their stratum basale, keratinocyte Turnover is the keratinocyte mobility.[11] Over each cycle, keratinocytes change both structurally and functionally; these changes might span many days. Comprising eight percent of the water in the epidermis, this layer is also called the basal cell layer.[12]

B. The Dermis

1) At least in human skin, the bulk of the activity occurs in the dermis. Mostly consisting of fibroblasts, collagen, and elastin, the dermis is the layer that finds numerous applications.

2) The dermis of the skin is teeming with lymphatic veins and blood that remove waste and nutrients.[13]

3) Sweat glands inhabit the dermis. They cool the body down, and draining toxins from the skin causes sweating to exit.

4) The hair follicles—the structural units that enable hair to grow—as well as the sebaceous glands—the real structures that give your skin its silky and smooth feel—are found in the dermis; an excess of these glands can lead to rashes and oily skin.[14]

C. The Subcutaneous layer

1) Lining the spaces between your bones and muscles is the fat that lies beneath the skin's surface. It penetrates to a level where the active ingredients in your skin care products can never reach.[15]

2) A thermostat is provided by the layer immediately under the skin. It protects the body and supplies energy as needed.

3) Before they get to your important organs, muscles, and bones, fat filters toxins.

4) The deepest oil-producing sebaceous glands are located in the fourth and final layer, which is home to nerve endings, hair follicular roots, extra blood vessels, and the subcutaneous layer.[16,17]

IMPORTANCE OF WOUND HEALING

Healing of wounds is a fundamental physiological process required for tissue integrity and functioning to return following an injury.[18] Maintaining the body's defences against infection, reducing inflammation, and encouraging tissue regeneration depend on it. Restoring the structural and functional integrity of wounded tissue is the goal of the carefully 8 orchestrated process known as wound healing. Among the several different but overlapping phases it passes through are haemostasis, inflammation, proliferation, and remodelling.[19,20] After an injury, haemostasis starts right away to

stop bleeding and create a temporary matrix for later healing. While platelets gather at the wound site to create a haemostatic plug, blood arteries narrow to reduce blood loss.[21] Comprising fibrin and other clotting agents, this plug stabilises the wound and offers a scaffolding for the latter phases of healing.[22]

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Inflammatory cells, including neutrophils and macrophages, go to the wound site to collect and degrade dead cells, pathogens, and foreign particles. [25]

In addition to coordinating the recruitment of other immune cells, these cells produce cytokines and growth factors that encourage the proliferation of endothelium and fibroblast cells. Usually spanning many days to weeks, the proliferative phase overlaps with inflammation and indicates tissue regeneration. [26,27] Arriving into the wound bed, fibroblasts start synthesis of extracellular matrix (ECM) proteins and collagen. Granulation tissue produced by this process saturates the wound and stimulates angiogenesis, the growth of fresh blood vessels supplying the healing tissue with nutrients and oxygen. [28] Epithelial cells at its boundaries move simultaneously across the granulation tissue to close the wound (epithelialisation). Furthermore crucial for wound contraction are fibroblasts as they compress the wound's boundaries and reduce its size.[29]

Rationale for Combination Therapy in Wound Healing

Wound healing requires a coordinated balance between microbial control, inflammatory regulation, and tissue regeneration. Single-agent therapies rarely target all these processes effectively. Combination topical formulations can provide synergistic benefits by acting on multiple biological pathways simultaneously.[30]

Neosporin, a widely used topical antibiotic containing neomycin, bacitracin, and polymyxin B, offers broad-spectrum antibacterial coverage.[51] However, prolonged use may be associated with hypersensitivity reactions and lacks regenerative support. Natural products such as lavender extract and antioxidants like vitamin E complement antibiotics by reducing inflammation, scavenging reactive oxygen species (ROS), and promoting collagen synthesis and epithelialization.[31]

Pharmacological Profile of Key Components 1 Neosporin

Neosporin exerts its antibacterial effect by inhibiting bacterial cell wall synthesis and disrupting membrane integrity. [32] By preventing microbial colonization at the wound site, it reduces infection-induced inflammation and facilitates an optimal healing environment. However, its role is primarily antimicrobial, with limited influence on tissue regeneration.[33,50]

2 Lavender (*Lavandula angustifolia*) Extract

Lavender extract contains bioactive compounds such as linalool and linalyl acetate, known for their antimicrobial, anti-inflammatory, analgesic, and antioxidant activities.[34] Experimental studies demonstrate that topical lavender enhances fibroblast proliferation, angiogenesis, and collagen deposition while reducing inflammatory cell infiltration. These properties make lavender an effective

regenerative adjunct in wound management.[35,48]

3 Vitamin E

Vitamin E (tocopherols and tocotrienols) is a potent lipid-soluble antioxidant that protects cellular membranes from oxidative damage.[36,49] It enhances collagen synthesis, accelerates epithelialization, and improves cosmetic outcomes by reducing scar formation. Vitamin E also modulates inflammatory mediators, thereby supporting both early and late stages of wound repair.[37]

Experimental Evidence from In Vivo Studies

Preclinical evaluation using Wistar albino rat excision wound models provides strong evidence for the synergistic wound-healing efficacy of the Neosporin–lavender–vitamin E combination. Animals treated with combination ointments demonstrated significantly higher wound contraction rates, reduced epithelialization periods, and superior histopathological outcomes compared to control and single-agent groups.[38,52]

Histological examination revealed dense collagen bundles, well-formed epithelial layers, minimal inflammatory infiltration, and enhanced neovascularization, particularly in higher- concentration combination formulations. These findings indicate that the formulation effectively accelerates all phases of wound healing.[39, 40]

Mechanistic Insights into Synergistic Action

The enhanced efficacy of the combination formulation can be attributed to complementary mechanisms:

- **Antimicrobial protection:**Neo sporin prevents infection and microbial-induced inflammation.[41]
- **Anti-inflammatory modulation:** Lavender extract suppresses pro-inflammatory cytokines and reduces leukocyte infiltration.[47,55]
- **Antioxidant defense:** Vitamin E neutralizes ROS, preventing oxidative damage to fibroblasts and keratinocytes.[42]
- **Enhanced tissue regeneration:** Lavender and vitamin E stimulate fibroblast activity, collagen synthesis, angiogenesis, and epithelial migration.[43,53]



Fig.2: Synergistic therapies for wound healing.

Comparison with Existing Wound-Care Strategies

Traditional wound treatments often rely on antibiotics or antiseptics alone, while modern approaches increasingly favor bioactive dressings, herbal formulations, and antioxidant-based therapies. [44,54] The reviewed combination aligns with contemporary trends emphasizing multimodal treatment strategies. Compared to silver sulfadiazine and single-agent antibiotics, the combination therapy offers superior regenerative outcomes with reduced inflammation. [45,46]

Clinical Relevance and Future Perspectives

Although current evidence is largely preclinical, the demonstrated efficacy of this combination formulation suggests strong translational potential. Further clinical trials are required to evaluate safety, optimal dosing, and long-term outcomes in human subjects. Integration of such combination therapies into wound-care protocols may significantly improve healing outcomes while reducing complications and healthcare costs.

CONCLUSION

The available scientific evidence highlights the therapeutic advantage of combination-based topical formulations in wound management. The integration of Neosporin with standardized lavender (*Lavandula angustifolia*) extract and vitamin E demonstrates a clear synergistic potential in enhancing wound healing outcomes when compared with monotherapy approaches. By simultaneously targeting microbial control, inflammation modulation, oxidative stress reduction, and tissue regeneration, this multimodal formulation addresses the key pathological factors that delay wound repair.

Neosporin contributes effective broad-spectrum antibacterial protection, creating an optimal wound environment by minimizing infection-related complications. Lavender extract provides additional antimicrobial and anti-inflammatory benefits while promoting fibroblast proliferation, angiogenesis, and collagen synthesis. Vitamin E further complements this activity through its potent antioxidant properties, supporting cellular integrity, extracellular matrix remodeling, and improved epithelial regeneration. The combined action of these agents results in accelerated wound closure, enhanced epithelialization, improved collagen organization, and reduced inflammatory responses.

Comparative analysis indicates that combination formulations, particularly at optimized concentrations, exhibit superior wound-healing efficacy compared with conventional antibiotic treatments alone. These findings underscore the importance of integrative therapeutic strategies in modern wound care and support the growing interest in combining synthetic antimicrobials with natural bioactive compounds and antioxidants.

Overall, the reviewed evidence suggests that topical formulations incorporating Neosporin, lavender extract, and vitamin E represent a promising and effective approach for wound management. Further clinical investigations are warranted to

validate their safety, efficacy, and applicability in human wound care, particularly for chronic and infection-prone wounds.

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