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Review Article

Phytochemical Diversity and Combined Therapeutic Potential of *Cucumis sativus* L. and *Centella asiatica* (L.) Urb. in Wound Healing: Mechanisms, Evidence, and Future Perspectives

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ABSTRACT

Wound healing is a complex physiological process involving haemostasis, inflammation, proliferation, and tissue remodelling. The increasing limitations of conventional wound-management therapies have encouraged the exploration of medicinal plants as alternative sources of bioactive compounds. Cucumis sativus L. (Cucurbitaceae) and Centella asiatica (L.) Urb. (Apiaceae) possess diverse phytochemical constituents with potential wound-healing properties. C. sativus contains flavonoids, phenolic compounds, and cucurbitacins, which are associated with antioxidant and anti-inflammatory activities. In contrast, C. asiatica is rich in triterpenoid saponins, particularly asiaticoside, madecassoside, asiatic acid, and madecassic acid, which have been investigated for their roles in collagen synthesis, fibroblast proliferation, angiogenesis, and tissue regeneration. This review highlights the botanical characteristics, pharmacognostic properties, phytochemical diversity, pharmacological activities, and molecular mechanisms associated with the wound-healing potential of both plants. Furthermore, it explores the scientific rationale for their combined therapeutic application, focusing on complementary antioxidant, anti-inflammatory, antimicrobial, and tissue-regenerative effects. The available evidence suggests that C. asiatica has a comparatively established preclinical wound-healing profile, whereas the direct wound-healing potential of C. sativus and the efficacy of their combined extracts require further investigation.

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Phytochemical standardization, formulation optimization, toxicity assessment, mechanistic validation, and well-designed clinical studies are essential to establish their therapeutic effectiveness and future applications in herbal wound management.

INTRODUCTION:

Wound healing is a complex and highly coordinated biological process that involves the restoration of tissue integrity following injury. It comprises four overlapping phases: haemostasis, inflammation, proliferation, and remodelling. These phases involve a series of cellular and molecular events, including platelet activation, inflammatory cell recruitment, fibroblast proliferation, extracellular matrix deposition, angiogenesis, and re-epithelialization. Any disruption in these processes may result in delayed healing, excessive scar formation, or the development of chronic wounds. Conditions such as diabetes mellitus, microbial infection, oxidative stress, and persistent inflammation further complicate wound management, highlighting the need for effective therapeutic interventions that promote tissue regeneration [1–3].

Conventional wound-management strategies include antiseptics, antibiotics, anti-inflammatory agents, and specialized wound dressings. Although these approaches are widely used, their effectiveness may be limited by microbial resistance, adverse effects, inadequate tissue regeneration, and the high cost of long-term treatment. Consequently, medicinal plants have attracted considerable attention as potential sources of bioactive compounds capable of modulating multiple biological pathways involved in wound repair. Phytochemicals such as flavonoids, phenolic acids, triterpenoids, and saponins have demonstrated antioxidant, anti-inflammatory, antimicrobial, and tissue-regenerative properties, making them promising candidates for the development of plant-based wound-healing formulations [2,3].

Cucumis sativus L. (Cucurbitaceae), commonly known as cucumber, is widely recognized for its traditional applications in skin conditioning, soothing, and hydration. Its phytochemical composition includes phenolic compounds, flavonoids, cucurbitacins, and other biologically active constituents that may contribute to antioxidant and anti-inflammatory effects. These properties suggest a potential role for C. sativus in supporting the wound-healing process, particularly through the maintenance of tissue integrity and modulation of oxidative stress. However, direct experimental evidence concerning its wound-healing efficacy remains comparatively limited and requires further investigation [4,5].

Centella asiatica (L.) Urb. (Apiaceae), commonly known as Gotu kola or Indian pennywort, is a medicinal plant traditionally used for the treatment of wounds, burns, ulcers, and various skin disorders. Its major bioactive constituents include asiaticoside, madecassoside, asiatic acid, and madecassic acid. These compounds have been investigated for their potential to stimulate collagen synthesis, promote fibroblast activity, modulate inflammatory responses, and enhance angiogenesis. Available preclinical and clinical evidence suggests that C. asiatica may contribute to improved wound contraction, re-epithelialization, and tissue repair, although further standardized clinical studies are required [2,3].

Considering the complementary phytochemical profiles of C. sativus and C. asiatica, their combined therapeutic potential represents an interesting area of investigation in wound management. The antioxidant and skin-conditioning properties associated with C. sativus, together with the collagen-promoting and tissue-regenerative activities attributed to C. asiatica, may provide a rationale for their combined application. Nevertheless, synergistic effects cannot be assumed without direct experimental validation. Therefore, this review aims to critically examine the phytochemical diversity, pharmacological properties, molecular mechanisms, and wound-healing evidence associated with both plants, with particular emphasis on their combined therapeutic potential, formulation strategies, research limitations, and future perspectives.

2. FUNDAMENTALS OF WOUND HEALING:

Wound healing is a complex physiological process involving the restoration of tissue integrity and function following injury. It requires the coordinated interaction of various cellular components, extracellular matrix (ECM), growth factors, cytokines, and signaling pathways. The healing process is conventionally

divided into four overlapping phases: haemostasis, inflammation, proliferation, and remodelling. Successful wound repair depends on the timely progression and regulation of these phases, whereas their disruption may result in delayed healing, chronic ulceration, or excessive scar formation [6–8].

2.1. Definition and Classification of Wounds

A wound is defined as a disruption in the anatomical structure and functional integrity of the skin or underlying tissues caused by physical, chemical, thermal, or pathological injury. Wounds are broadly classified according to their duration, depth, causative mechanism, and healing characteristics. Acute wounds generally heal within a predictable period through an organized repair process, whereas chronic wounds exhibit delayed or impaired healing due to persistent inflammation, infection, vascular insufficiency, or metabolic abnormalities [6,7].

Classification of wounds:

Table 01: Types of Wounds

Classification	Types	Description
According to duration	Acute wounds	Heal through an orderly physiological process within an expected period
	Chronic wounds	Exhibit delayed healing due to persistent pathological conditions
According to cause	Incisional wounds	Produced by surgical instruments or sharp objects
	Lacerations	Irregular tissue injuries caused by blunt or sharp trauma
	Abrasions	Superficial injuries involving epidermal damage
	Burns	Tissue injuries caused by thermal, chemical, electrical, or radiation exposure
According to depth	Superficial wounds	Involve the epidermis
	Partial-thickness wounds	Extend into the dermis
	Full-thickness wounds	Involve the entire dermis and may extend into underlying tissues
According to healing mechanism	Primary intention	Wound edges are closely approximated, generally with minimal tissue loss
	Secondary intention	Wounds heal through granulation tissue formation, contraction, and re-epithelialization
	Tertiary intention	Wounds are initially left open and subsequently closed after appropriate management

The classification of wounds is important for selecting suitable treatment strategies and evaluating the effectiveness of wound-healing agents. Experimental wound-healing studies commonly employ excision, incision, and burn models to investigate wound contraction, tensile strength, epithelialization, and tissue regeneration [7,9].

2.2. Phases of Wound Healing

Wound healing occurs through four interconnected phases. Although these phases are described separately for convenience, they overlap temporally and involve continuous communication between resident and recruited cells [6–8].

2.2.1. Haemostasis Phase:

Haemostasis begins immediately after tissue injury and prevents excessive blood loss. Following vascular disruption, transient vasoconstriction occurs, followed by platelet adhesion, activation, and aggregation. The coagulation cascade facilitates fibrin formation, resulting in the development of a provisional clot that provides a temporary protective barrier. Activated platelets release growth factors and mediators, including platelet-derived growth factor (PDGF) and transforming growth factor-beta (TGF-β), which initiate subsequent inflammatory and reparative responses [6,7].

2.2.2. Inflammatory Phase:

The inflammatory phase involves the recruitment of neutrophils, monocytes, and macrophages to the wound site. Neutrophils contribute to microbial elimination and the removal of cellular debris, whereas macrophages regulate inflammation and release growth factors that support tissue repair. Cytokines such as interleukin-1 (IL-1), interleukin-6 (IL-6), and tumour necrosis factor-alpha (TNF-α) participate in inflammatory regulation. Controlled inflammation is essential for healing; however, prolonged inflammatory activity may increase oxidative stress and protease-mediated tissue damage, thereby delaying wound closure [7,8].

2.2.3. Proliferative Phase:

The proliferative phase is characterized by the formation of granulation tissue, angiogenesis, fibroblast proliferation, collagen deposition, and re-epithelialization. Fibroblasts synthesize collagen and other ECM components, providing structural support to the developing tissue. Endothelial cells promote new blood vessel formation, while keratinocytes migrate and proliferate to restore the epidermal barrier. Myofibroblasts contribute to wound contraction and reduce the wound area. Growth factors such as vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), and TGF-β regulate these reparative events [6–8].

2.2.4. Remodelling Phase:

The remodelling phase involves the maturation and reorganization of newly formed tissue. During this phase, collagen type III is progressively replaced by collagen type I, and the extracellular matrix undergoes structural reorganization. The number of fibroblasts and newly formed blood vessels decreases as the tissue matures. Matrix metalloproteinases (MMPs) and their tissue inhibitors regulate ECM degradation and remodeling. The final scar gradually acquires tensile strength, although the healed tissue generally does not regain the complete mechanical strength of unwounded skin [6,8].

2.3. Cellular and Molecular Events in Wound Repair:

Wound repair is regulated by interactions among platelets, neutrophils, macrophages, fibroblasts, keratinocytes, endothelial cells, and the extracellular matrix. These components coordinate cellular migration, proliferation, inflammation, angiogenesis, and tissue remodelling. Growth factors and cytokines act as essential signaling molecules that regulate the progression of wound healing [8–10].

Table 02: Cellular and Molecular Events in Wound Repair

Cellular component	Major function in wound healing
Platelets	Initiate haemostasis and release growth factors
Neutrophils	Eliminate microorganisms and remove cellular debris
Macrophages	Regulate inflammation and stimulate tissue repair
Fibroblasts	Synthesize collagen and extracellular matrix
Keratinocytes	Promote re-epithelialization and restore the epidermal barrier
Endothelial cells	Facilitate angiogenesis and vascular regeneration
Myofibroblasts	Promote wound contraction and tissue closure

Major molecular mediators:

Table 03: Major Molecular Mediators

Molecular mediator	Role in wound repair
TGF-β	Regulates fibroblast activation, collagen synthesis, and ECM deposition
PDGF	Promotes fibroblast migration and proliferation
VEGF	Stimulates angiogenesis and vascular permeability
EGF	Promotes keratinocyte proliferation and epithelial regeneration
FGF-2	Supports fibroblast proliferation and angiogenesis
IL-1 and TNF-α	Regulate inflammatory responses
MMPs	Facilitate ECM degradation and remodelling

2.4. Factors Affecting Wound Healing:

Wound healing is influenced by several local and systemic factors that determine the rate and quality of tissue repair. These factors may interfere with cellular

proliferation, collagen synthesis, vascularization, and inflammatory regulation, ultimately resulting in delayed healing or chronic wound development [7,9,10].

Table 04: Factors Affecting Wound Healing

Category	Factor	Effect on wound healing
Local factors	Wound infection	Prolongs inflammation and increases tissue damage
	Poor vascularization	Reduces oxygen and nutrient delivery
	Excessive moisture or dryness	Interferes with optimal wound-bed conditions
	Tissue necrosis	Delays granulation and epithelialization
	Repeated trauma	Disrupts newly formed tissue
Systemic factors	Diabetes mellitus	Impairs inflammation, angiogenesis, and collagen formation
	Advanced age	Reduces regenerative capacity
	Malnutrition	Limits protein synthesis and tissue repair
	Smoking	Reduces tissue oxygenation and vascular function
	Immunosuppression	Impairs inflammatory and reparative responses
	Chronic diseases	May interfere with vascular supply and cellular function

Among these factors, diabetes mellitus, persistent infection, and inadequate vascular supply are particularly important in chronic wound development. Therefore, the selection of wound-healing agents should consider their ability to support tissue repair while addressing the underlying factors responsible for delayed healing [7,9].

2.5. Limitations of Conventional Wound-Healing Therapies:

Conventional wound management includes antiseptics, antibiotics, anti-inflammatory agents, growth factors, and specialized wound dressings. These approaches are essential for infection control and wound protection; however, their effectiveness may vary depending on wound type, severity, patient condition, and treatment duration. Certain therapies may also produce adverse effects or fail to adequately address the multiple biological processes involved in tissue regeneration [9,10].

Table 05: Limitations of Conventional Wound-Healing Therapies

Conventional therapy	Major limitation
Topical antiseptics	Some agents may exhibit cytotoxicity toward regenerating cells when used inappropriately
Antibiotics	Prolonged or inappropriate use may contribute to antimicrobial resistance
Anti-inflammatory agents	Excessive suppression of inflammation may interfere with normal repair processes
Growth factor therapy	High cost, instability, and delivery limitations may restrict clinical application
Conventional wound dressings	May provide limited biological stimulation of tissue regeneration
Surgical wound management	May involve additional tissue trauma, cost, and risk of complications

These limitations have encouraged the investigation of plant-derived bioactive compounds with antioxidant, anti-inflammatory, antimicrobial, and tissue-regenerative properties. Medicinal plants may provide multiple bioactive constituents capable of influencing different wound-healing pathways. Nevertheless, their therapeutic effectiveness depends on appropriate extraction, phytochemical standardization, formulation development, and experimental validation [9,10].

3. BOTANICAL PROFILE AND PHARMACOGNOSTIC CHARACTERISTICS:

The botanical identification and pharmacognostic characterization of medicinal plants are essential for ensuring the authenticity, quality, and reproducibility

of herbal preparations. Variations in geographical distribution, environmental conditions, plant maturity, and morphological characteristics may influence the phytochemical composition and biological activity of medicinal plants. Therefore, the accurate identification and standardization of Cucumis sativus L. and Centella asiatica (L.) Urb. are important prerequisites for their investigation as potential wound-healing agents [11,12]. Both plants are traditionally used in herbal medicine and possess distinct botanical characteristics. C. sativus belongs to the family Cucurbitaceae, whereas C. asiatica belongs to the family Apiaceae. Their differences in morphology, plant parts, and phytochemical composition provide a basis for understanding their individual and potentially complementary pharmacological properties [11–13].

3.1. Botanical Profile of Cucumis sativus L.:

Cucumis sativus L., commonly known as cucumber, is an annual herbaceous plant belonging to the family Cucurbitaceae. It is widely cultivated in tropical and subtropical regions for its edible fruits and has a long history of use in traditional medicine and cosmetic preparations. The plant is characterized by a creeping or climbing growth habit, tendril-bearing stems, broad leaves, and elongated fruits. Its traditional applications include skin soothing, hydration, and the management of minor skin irritation [11,13].



Figure 01: ***Cucumis sativus L***

The pharmacological properties of C. sativus have been associated with several phytochemical constituents, including flavonoids, phenolic compounds, cucurbitacins, and other secondary metabolites. These constituents have been investigated for antioxidant, anti-inflammatory, antimicrobial, and skin-protective activities. However, the wound-healing potential of C. sativus requires further investigation through standardized experimental models and direct assessment of tissue repair [11,13].

3.2. Botanical Profile of Centella asiatica (L.) Urb.:

Centella asiatica (L.) Urb., commonly known as Gotu kola or Indian pennywort, is a perennial creeping herb belonging to the family Apiaceae (Umbelliferae). It is widely distributed in tropical and subtropical regions and commonly grows in moist habitats. The plant possesses slender creeping stolons, long-petioled leaves, small axillary flowers, and characteristic kidney-shaped or fan-shaped leaves with crenate margins. It has traditionally been used for the management of wounds, burns, ulcers, and various dermatological disorders [12,14].

The medicinal properties of C. asiatica are primarily attributed to its pentacyclic triterpenoids and triterpenoid saponins, particularly asiaticoside, madecassoside, asiatic acid, and madecassic acid. These constituents have been investigated for their effects on collagen synthesis, fibroblast activity, inflammation, and tissue regeneration. Pharmacognostic studies have also identified characteristic anatomical features, including palmate-actinodromous leaf venation, distinctive epidermal structures, calcium oxalate crystals, and vascular arrangements that support the identification and quality control of the plant [12,14,15].



Figure 02: ***Centella asiatica (L.) Urb***

3.3. Taxonomy:

Table 06: Botanical and Ethnomedicinal Characteristics of *Cucumis Sativus* and *Centella Asiatica*.

Botanical characteristics	Cucumis sativus L.	Centella asiatica (L.) Urb.
Common name	Cucumber	Gotu kola, Indian pennywort
Family	Cucurbitaceae	Apiaceae
Genus	Cucumis	Centella
Habit	Annual herbaceous climber or creeper	Perennial creeping herb
Stem	Branched, creeping or climbing, tendril-bearing	Slender, creeping stolons
Leaves	Broad, rough, palmately veined	Kidney-shaped or fan-shaped, crenate margins
Flowers	Yellow, unisexual or occasionally bisexual	Small, pinkish to reddish or white
Fruit	Elongated or cylindrical pepo	Small, dry schizocarpic fruit
Distribution	Widely cultivated in tropical and subtropical regions	Tropical and subtropical regions, particularly moist habitats
Traditionally used plant parts	Fruits, leaves, seeds	Leaves, aerial parts, whole plant
Ethnomedicinal applications	Skin soothing, hydration, traditional skin care	Wound healing, burns, ulcers, skin disorders
Major phytochemical groups	Flavonoids, phenolics, cucurbitacins	Triterpenoid saponins, triterpenic acids, flavonoids

3.4. Pharmacognostic and Microscopic Characteristics:

Pharmacognostic evaluation involves the systematic examination of the morphological, microscopic, and physicochemical properties of medicinal plants. These characteristics are useful for detecting adulteration, confirming botanical identity, and establishing quality-control parameters for herbal raw materials [14,15]. For C. sativus, pharmacognostic assessment may include the examination of leaf morphology, epidermal structures, stomatal characteristics, trichomes, vascular tissues, and physicochemical parameters such as ash values, moisture content, and extractive values. Such investigations provide preliminary standards for the authentication and quality assessment of plant materials [11,13]. In C. asiatica, characteristic pharmacognostic features include palmate-actinodromous venation, distinctive leaf epidermal structures, calcium oxalate crystals, and characteristic vascular arrangements in the leaf, petiole, stolon, and root. Powder microscopy may reveal fragments of epidermis, mesophyll, trichomes, collenchyma, parenchyma, and tracheary elements. These features are useful for the identification and standardization of crude plant materials [14,15]. The pharmacognostic standardization of both plants is particularly important for wound-healing research because variations in plant identity, extraction procedures, and raw-material quality may influence the biological activity and reproducibility of herbal formulations.

4. PHYTOCHEMICAL DIVERSITY AND PHARMACOLOGICAL PROPERTIES:

The therapeutic potential of medicinal plants is closely associated with their phytochemical composition, which includes primary and secondary metabolites responsible for various biological activities. Cucumis sativus L. and Centella asiatica (L.) Urb. contain diverse phytochemical constituents, including flavonoids, phenolic compounds, triterpenoids, saponins, and other bioactive molecules. These compounds have been investigated for their antioxidant, anti-inflammatory, antimicrobial, and tissue-regenerative properties [16–18]. Although both plants possess potentially beneficial pharmacological properties, their phytochemical profiles differ considerably. C. sativus is associated with phenolic compounds, flavonoids, cucurbitacins, and other metabolites, whereas C. asiatica is particularly rich in pentacyclic triterpenoids and triterpenoid saponins. Understanding these differences is important for evaluating their individual contributions to wound healing and establishing a scientific

rationale for their combined therapeutic application [16–19].

4.1. Phytochemical Constituents of Cucumis sativus L.:

Cucumis sativus contains a diverse range of phytochemicals distributed across its leaves, fruits, seeds, stems, and roots. The major reported phytochemical groups include flavonoids, phenolic compounds, cucurbitacins, saponins, phytosterols, and other secondary metabolites. The distribution and concentration of these constituents may vary according to plant part, cultivar, geographical origin, maturity, and extraction conditions [16,17].

Flavonoids and phenolic compounds are important constituents of C. sativus because of their potential antioxidant properties. These compounds may contribute to the neutralization of reactive oxygen species (ROS), thereby supporting the maintenance of cellular integrity under oxidative stress. Cucurbitacins, which are characteristic tetracyclic triterpenoids of the Cucurbitaceae family, have also been investigated for their diverse biological activities. However, their contribution to wound healing requires further compound-specific investigation [16,17]. The phytochemical composition of C. sativus suggests its potential application in skin-care and wound-management formulations. Nevertheless, the biological activity of an extract cannot be attributed to a single phytochemical group without appropriate analytical and experimental evidence. Therefore, phytochemical characterization and standardization are essential for establishing reproducible pharmacological outcomes [16,17].

4.2. Phytochemical Constituents of Centella asiatica (L.) Urb.:

Centella asiatica is a well-characterized medicinal plant containing several classes of secondary metabolites, including triterpenoid saponins, triterpenic acids, flavonoids, phenolic acids, phytosterols, and volatile constituents. Its pharmacological activities are primarily associated with four major pentacyclic triterpenoids: asiaticoside, madecassoside, asiatic acid, and madecassic acid [18–20].

Asiaticoside and madecassoside are glycosidic triterpenoids, whereas asiatic acid and madecassic acid represent their corresponding aglycone forms. These compounds have attracted considerable attention because of their potential effects on fibroblast activity, collagen synthesis, inflammatory regulation, and tissue regeneration. Their biological activities are influenced by their chemical structures, concentrations, and the characteristics of the extracts in which they occur [18–20]. In addition to triterpenoids, C. asiatica contains phenolic acids and flavonoids that may contribute to its antioxidant properties. These constituents may complement the biological activities of the major triterpenoids by influencing oxidative stress and inflammatory responses. However, the relative contribution of individual compounds to the wound-healing activity of whole-plant extracts remains an important area for further investigation [18,20].

4.3. Major Bioactive Compounds and Their Biological Activities:

Table 07: Comparative Phytochemical Constituents and Pharmacological Properties of *Cucumis Sativus* and *Centella Asiatica*.

Plant	Phytochemical group	Representative constituents	Reported pharmacological properties	Potential relevance to wound healing
Cucumis sativus	Flavonoids	Apigenin, luteolin, quercetin derivatives	Antioxidant and anti-inflammatory activities	May support cellular protection against oxidative stress
Cucumis sativus	Phenolic compounds	Caffeic acid, ferulic acid, other phenolic derivatives	Antioxidant activity	May contribute to oxidative stress regulation
Cucumis sativus	Triterpenoids	Cucurbitacins and related compounds	Diverse biological activities, including anti-inflammatory effects reported for selected compounds	Potential modulation of inflammatory responses; requires wound-specific validation
Cucumis sativus	Saponins and other metabolites	Various glycosides and secondary metabolites	Reported biological activities vary with extract and compound	Potential contribution to the overall activity of plant extracts
Centella asiatica	Triterpenoid saponins	Asiaticoside, madecassoside	Tissue-regenerative and anti-inflammatory activities	May promote collagen synthesis and tissue repair
Centella asiatica	Triterpenic acids	Asiatic acid, madecassic acid	Anti-inflammatory and tissue-regenerative properties	May support fibroblast activity and extracellular matrix formation
Centella asiatica	Flavonoids	Quercetin, kaempferol derivatives	Antioxidant and anti-inflammatory activities	May contribute to the regulation of oxidative stress
Centella asiatica	Phenolic acids	Caffeoylquinic acid derivatives and related compounds	Antioxidant activities	May contribute to protection against oxidative damage

The reported phytochemical diversity of C. sativus and C. asiatica is supported by published phytochemical and pharmacological reviews. The wound-healing relevance shown in the table represents potential biological contributions and should not be interpreted as proof of clinical efficacy for every listed compound [16–20].

4.4. Comparative Phytochemical Profile of Both Plants:

The phytochemical composition of C. sativus and C. asiatica demonstrates differences in their major bioactive constituents. C. sativus contains diverse phenolic compounds and flavonoids, whereas C. asiatica is characterized by its triterpenoid saponins and corresponding aglycones. These differences may provide a rationale for investigating their complementary biological activities in wound-healing formulations [16–20].

The antioxidant constituents of C. sativus may contribute to the regulation of oxidative stress, while the triterpenoids of C. asiatica have been investigated for their effects on collagen synthesis and tissue regeneration. Nevertheless, the combined therapeutic potential of these plants remains a hypothesis that requires direct experimental investigation. Comparative phytochemical profiling, quantitative estimation of marker compounds, and evaluation of individual and combined extracts are necessary to establish their potential contributions to wound healing [16–20].

5. MECHANISTIC INSIGHTS INTO WOUND-HEALING ACTIVITY:

5.1. Antioxidant Activity and Regulation of Oxidative Stress: Phytochemicals present in Cucumis sativus and Centella asiatica may help neutralize excessive reactive oxygen species (ROS), protect cellular

components, and maintain the oxidative balance required for wound repair [16–20].

5.2. Modulation of Inflammatory Mediators: Bioactive constituents of both plants may regulate inflammatory mediators such as TNF-α, IL-1β, and IL-6, thereby supporting the transition from inflammation to tissue regeneration [18–20].

5.3. Enhancement of Fibroblast Proliferation and Migration: Selected phytoconstituents, particularly triterpenoids of C. asiatica, may promote fibroblast proliferation and migration, contributing to granulation tissue formation and wound closure [18,19].

5.4. Stimulation of Collagen Synthesis and Extracellular Matrix Formation: Asiaticoside, madecassoside, asiatic acid, and related compounds may enhance collagen synthesis and extracellular matrix organization, supporting tissue strength and structural restoration [18–20].

5.5. Promotion of Angiogenesis and Re-epithelialization: The bioactive constituents of both plants may support vascular regeneration and keratinocyte migration, facilitating oxygen delivery, epidermal restoration, and wound closure [16–20].

5.6. Antimicrobial Activity and Prevention of Wound Infection: Selected phytochemicals may exhibit antimicrobial effects against wound-associated microorganisms, potentially reducing microbial burden and supporting an environment conducive to tissue repair [16–20].

5.7. Regulation of Growth Factors and Molecular Signalling Pathways: Plant-derived compounds may influence growth factors and signalling pathways, including TGF-β, VEGF, and PI3K/Akt, which regulate fibroblast activity, angiogenesis, collagen deposition, and tissue regeneration; however, these mechanisms require direct validation for the combined extracts [18–20].

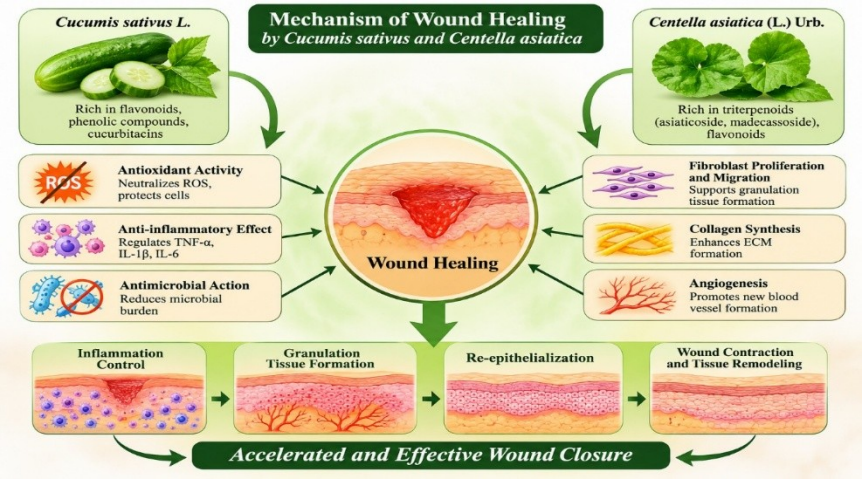


Figure 03: ***Mechanism of wound healing***

5.8. Mechanism of wound healing:

6. COMBINED THERAPEUTIC POTENTIAL OF CUCUMIS SATIVUS AND CENTELLA ASIATICA:

The combined therapeutic potential of Cucumis sativus L. and Centella asiatica (L.) Urb. represents an emerging area of research in plant-based wound management. Both plants contain diverse bioactive constituents that may influence different phases of wound healing. C. sativus is associated with flavonoids and phenolic compounds possessing antioxidant and anti-inflammatory properties, whereas C. asiatica contains triterpenoids, including asiaticoside, madecassoside, asiatic acid, and madecassic acid, which have been investigated for their tissue-regenerative and collagen-promoting activities [21,22].

The combination of these plants may provide a multi-target approach to wound healing by addressing oxidative stress, inflammation, microbial burden, fibroblast activity, and extracellular matrix formation. However, the potential benefits of combined therapy must be distinguished from the established pharmacological activities of the individual plants. Direct experimental evidence is necessary to determine whether the

combination produces additive, synergistic, or antagonistic effects [21–23].

6.1. Rationale for Combined Phytotherapy:

The combination of Cucumis sativus and Centella asiatica may provide a complementary approach to wound healing by targeting multiple biological processes involved in tissue repair. The antioxidant properties of C. sativus may help regulate oxidative stress, whereas the triterpenoid constituents of C. asiatica may support collagen synthesis, fibroblast proliferation, and tissue regeneration [21–23].

The rationale for combining these plants is based on their potentially complementary pharmacological activities rather than established synergistic efficacy. Therefore, comparative studies involving individual extracts and their combinations are necessary to determine whether the combined formulation offers additional therapeutic benefits [21,22].

6.2. Complementary Phytochemical and Pharmacological Actions:

The phytochemical constituents of both plants may contribute to different aspects of wound repair, including oxidative stress regulation, inflammatory modulation, collagen deposition, and tissue regeneration [21–23].

Table 08: Complementary Phytochemical and Pharmacological Actions

Plant	Major bioactive constituents	Potential complementary action
Cucumis sativus	Flavonoids, phenolic compounds, cucurbitacins	Antioxidant activity and potential inflammatory regulation
Centella asiatica	Asiaticoside, madecassoside, asiatic acid, madecassic acid	Fibroblast activity, collagen synthesis, and tissue regeneration

6.3. Potential Synergistic and Additive Effects:

Synergistic or additive effects may occur when bioactive constituents influence different molecular targets involved in wound healing. The combination of antioxidant-rich C. sativus with collagen-promoting C. asiatica may potentially support multiple stages of tissue repair. However, the presence of complementary phytochemicals does not independently establish pharmacological synergy [21–23].

Synergistic activity should be evaluated through dose-response studies, appropriate combination ratios, and comparison with individual extracts. Experimental assessment may include wound contraction, epithelialization period, collagen content, tensile strength, histopathological examination, and inflammatory biomarkers [21,22].

6.4. Challenges in Combination Therapy:

The development of combined herbal formulations may be affected by variations in phytochemical composition, extraction methods, extract ratios, bioavailability, stability, and potential interactions between constituents. Standardized extraction procedures and quantitative estimation of marker compounds are therefore necessary to ensure reproducibility and establish the safety and efficacy of combined formulations [21–23].

6.5. Standardization and Optimization of Combined Herbal Formulations:

The standardization of combined C. sativus and C. asiatica extracts should involve botanical authentication, phytochemical screening, chromatographic fingerprinting, quantitative estimation of selected marker compounds, and optimization of the extract ratio. Formulation development should also include physicochemical evaluation, stability studies, skin irritation assessment, and appropriate preclinical wound-healing models [21–23].

The optimized formulation should be compared with individual plant extracts and a suitable standard treatment to establish its relative efficacy and determine whether the combination provides an additional therapeutic advantage.

7. COMPARATIVE EVALUATION OF WOUND-HEALING EVIDENCE:

The wound-healing potential of Cucumis sativus L. and Centella asiatica (L.) Urb. has been investigated

through various experimental and clinical approaches. The available evidence suggests that C. asiatica possesses comparatively stronger wound-healing evidence, particularly regarding collagen synthesis, wound contraction, and re-epithelialization. In contrast, the wound-healing potential of C. sativus remains less extensively investigated, with much of its pharmacological rationale based on antioxidant, anti-inflammatory, and skin-protective properties [24–27].

A comparative assessment of these plants is important for identifying the strengths and limitations of existing research. In particular, the distinction between individual plant efficacy and combined extract efficacy is essential because the therapeutic advantages of combining C. sativus and C. asiatica have not been established through sufficient direct experimental evidence.

7.1. *In-Vitro* Studies:

In vitro studies provide preliminary information regarding the biological activities of plant extracts and isolated phytoconstituents. Commonly employed approaches include antioxidant assays, antimicrobial testing, fibroblast proliferation assays, cell migration studies, and cytotoxicity evaluation. These methods are useful for investigating the potential contribution of plant-derived compounds to wound repair [24,25].

The antioxidant and anti-inflammatory properties of C. sativus may support its investigation in cellular wound-healing models, whereas C. asiatica and its triterpenoid constituents have been examined for their effects on fibroblast proliferation, collagen synthesis, and cellular repair mechanisms [25–27].

However, in vitro findings cannot independently establish wound-healing efficacy in living organisms because tissue repair involves complex interactions among immune cells, blood vessels, extracellular matrix, and systemic physiological factors.

7.2. *In-Vivo* Experimental Studies:

In vivo wound-healing studies provide important evidence regarding the effects of medicinal plant extracts on wound contraction, epithelialization, collagen deposition, tensile strength, and histopathological changes. Animal models commonly used in wound-healing research include excision, incision, burn, and diabetic wound models [26–29].

Experimental studies involving C. asiatica have demonstrated improvements in collagen content, tensile strength, cellular proliferation, and wound contraction. Suguna et al. reported enhanced collagen synthesis and improved maturation of granulation tissue following administration of C. asiatica extract in rats. Similarly, Shukla et al. investigated asiaticoside in normal and delayed wound-healing models and reported improvements in hydroxyproline content, tensile strength, collagen formation, and epithelialization [26,27].

Topical formulations of C. asiatica have also been evaluated in experimental wound models. Different formulations, including ointments, creams, and gels, demonstrated improvements in wound contraction and collagen synthesis, with the gel formulation showing comparatively favorable healing outcomes in the reported study [28].

These findings support the preclinical wound-healing potential of C. asiatica. Nevertheless, the results should be interpreted in relation to the experimental model, extract composition, dose, formulation, and study design.

7.3. Comparative Evidence for Individual Plant Extracts

The available evidence for C. sativus and C. asiatica differs in terms of the number of experimental investigations, the characterization of active constituents, and the strength of wound-healing outcomes.

Table 09: Comparative Evidence for the Wound-Healing Potential of *Cucumis Sativus* and *Centella Asiatica*.

Parameter	Cucumis sativus L.	Centella asiatica (L.) Urb.
Major investigated constituents	Flavonoids, phenolics, cucurbitacins	Asiaticoside, madecassoside, asiatic acid, madecassic acid

Parameter	Cucumis sativus L.	Centella asiatica (L.) Urb.
Antioxidant evidence	Reported antioxidant potential associated with phenolic compounds and flavonoids	Antioxidant activity reported for extracts and selected constituents
Anti-inflammatory evidence	Potential inflammatory modulation associated with selected phytochemicals	Investigated in relation to inflammatory regulation and tissue repair
Fibroblast proliferation	Requires further wound-specific investigation	Supported by experimental studies
Collagen synthesis	Direct wound-specific evidence remains limited	Supported by preclinical studies
Wound contraction	Requires further standardized experimental evaluation	Reported in animal and selected clinical studies
Re-epithelialization	Requires further direct evidence	Investigated in experimental and clinical wound studies
Clinical evidence	Limited direct wound-healing evidence	Available but requires further high-quality clinical validation
Combined extract evidence	No established direct evidence for combination with C. asiatica	No established direct evidence for combination with C. sativus

The comparative evidence indicates that C. asiatica has a more established preclinical wound-healing research profile, whereas C. sativus may provide a complementary phytochemical basis for further investigation. However, the potential benefits of combined therapy remain to be demonstrated experimentally [24–29].

7.4. Evidence Gaps in Combined Extract Therapy:

Despite the promising pharmacological properties of both plants, several research gaps remain regarding their combined wound-healing application. The major limitations include the insufficient characterization of combined phytochemical profiles, absence of optimized extract ratios, limited mechanistic validation, and inadequate comparative evaluation against individual extracts [30–32].

Future investigations should include standardized extraction procedures, quantitative phytochemical analysis, in vitro cell migration assays, antimicrobial studies, and appropriate in vivo wound-healing models. Comparative assessment of individual extracts, combined extracts, vehicle control, and standard treatment is essential to establish whether the combination provides an additional therapeutic advantage [31–33].

Furthermore, the evaluation of collagen deposition, hydroxyproline content, wound contraction, epithelialization period, tensile strength, and histopathological parameters may provide a comprehensive understanding of the wound-healing activity of the combined formulation. Safety assessment and formulation stability should also be incorporated before considering clinical translation [32–35].

The existing evidence therefore supports further investigation of C. sativus and C. asiatica as individual wound-healing agents and provides a rationale for exploring their combined therapeutic potential. However, direct experimental evidence is required to establish the efficacy, safety, and possible synergistic effects of their combination.

9. SAFETY, TOXICITY, AND QUALITY STANDARDIZATION:

The safety and quality standardization of herbal wound-healing formulations are essential for ensuring their therapeutic effectiveness, reproducibility, and suitability for topical application. Although Cucumis sativus L. and Centella asiatica (L.) Urb. have been traditionally used in skin care and wound management, their safety depends on the plant part, extraction method, phytochemical composition, concentration, and formulation characteristics. Therefore, systematic toxicity assessment, phytochemical standardization, and stability evaluation are necessary before developing combined herbal formulations for wound healing [36–38].

9.1. Phytochemical Standardization and Quality Control

Phytochemical standardization involves the identification, characterization, and quantitative estimation of bioactive constituents present in herbal extracts. For C. sativus and C. asiatica, standardization may include

preliminary phytochemical screening, chromatographic fingerprinting, and quantitative estimation of selected marker compounds. High-performance thin-layer chromatography (HPTLC), high-performance liquid chromatography (HPLC), and liquid chromatography–mass spectrometry (LC-MS) may be employed to establish the identity and consistency of herbal extracts [36,37].

The quality assessment of combined herbal formulations should also include physicochemical parameters such as pH, viscosity, homogeneity, moisture content, microbial limits, and extractive values. These parameters help ensure batch-to-batch consistency and maintain the quality of herbal wound-healing preparations [36–38].

9.2. Acute and Subacute Toxicity Assessment:

Toxicity assessment is an important step in evaluating the safety of herbal extracts before their application in wound-healing formulations. Acute toxicity studies provide preliminary information regarding the adverse effects associated with a single or limited exposure, whereas subacute toxicity studies evaluate the effects of repeated administration over a defined period. The assessment may include mortality, behavioural changes, body weight, food consumption, haematological parameters, biochemical markers, and histopathological examination of major organs [37,38].

For topical wound-healing formulations containing C. sativus and C. asiatica, toxicity evaluation should consider the intended route of administration, concentration, duration of exposure, and possibility of systemic absorption. The safety of the combined formulation should not be assumed solely from the traditional use or individual safety profiles of the plants [37,38].

9.3. Skin Irritation and Sensitization Potential:

Topical herbal formulations should be evaluated for their potential to cause skin irritation, inflammation, or allergic sensitization. Skin irritation studies assess local reactions such as erythema, oedema, and tissue damage following topical application. Sensitization studies investigate the potential development of allergic responses after repeated exposure. These assessments are particularly important for wound-healing formulations because damaged skin may exhibit increased permeability and sensitivity to formulation components [37–39].

Appropriate validated methods, including OECD test guidelines, should be considered for evaluating the dermal safety of herbal preparations. The selection of suitable testing methods should follow applicable ethical and regulatory requirements [38,39].

9.4. Stability and Reproducibility of Herbal Formulations:

Stability evaluation is necessary to determine whether the phytochemical constituents, physical properties, and biological activity of herbal wound-healing formulations remain consistent during storage. Parameters such as appearance, colour, odour, pH, viscosity, drug or marker content, microbial quality, and packaging compatibility should be monitored under appropriate storage conditions [36,40].

The reproducibility of herbal formulations depends on the consistency of plant materials, extraction procedures, extract ratios, and manufacturing processes. Therefore, standardized extraction methods and appropriate quality-control procedures are essential for developing reliable combined formulations of C. sativus and C. asiatica [36–40].

10. FUTURE PERSPECTIVES AND RESEARCH DIRECTIONS:

The wound-healing potential of Cucumis sativus L. and Centella asiatica (L.) Urb. provides an opportunity for developing innovative plant-based therapeutic formulations. Although C. asiatica has demonstrated promising wound-healing properties in preclinical and selected clinical investigations, the therapeutic contribution of C. sativus and the efficacy of their combined extracts remain insufficiently explored. Future research should focus on phytochemical standardization, mechanistic validation, formulation optimization, safety assessment, and clinical evaluation to establish the therapeutic relevance of these plants [41–43].

10.1. Identification of Active Phytochemical Markers:

Future studies should employ advanced analytical techniques, including HPLC, HPTLC, LC-MS/MS, and nuclear magnetic resonance (NMR) spectroscopy,

to identify and quantify the bioactive constituents of C. sativus and C. asiatica. The identification of suitable marker compounds, such as asiaticoside and madecassoside in C. asiatica, may improve extract standardization and facilitate the establishment of reproducible pharmacological outcomes [41,42].

10.2. Mechanistic Validation of Combined Extracts:

Further investigations should examine the molecular mechanisms underlying the wound-healing activity of individual and combined extracts. Studies should evaluate oxidative stress markers, inflammatory cytokines, collagen synthesis, fibroblast migration, angiogenesis, and relevant signaling pathways, including TGF-β/Smad, PI3K/Akt, and VEGF-mediated pathways. Such investigations may help determine whether the combined extracts produce additive, synergistic, or antagonistic effects [42–44].

10.3. Advanced Formulation Development:

The development of advanced topical formulations, including hydrogels, nanoemulsions, nanofibers, and biodegradable wound dressings, may improve the stability, penetration, and localized delivery of phytoconstituents. Incorporating standardized extracts of C. sativus and C. asiatica into suitable delivery systems may enhance wound-bed hydration, maintain sustained release, and support tissue regeneration. However, formulation development should be guided by compatibility studies, release kinetics, stability evaluation, and biological performance [43–45].

10.4. Translational Research and Clinical Evaluation:

Future research should progress from preliminary in vitro investigations to standardized animal models and well-designed clinical trials. Clinical studies should evaluate wound closure time, wound area reduction, epithelialization, infection rates, pain, scar formation, and treatment tolerability. Randomized controlled trials with appropriate comparators and adequate sample sizes are required to establish the safety and clinical effectiveness of combined C. sativus and C. asiatica formulations [41,44,46].

10.5. Challenges in Clinical Standardization and Commercialization:

The clinical translation of combined herbal formulations may be limited by variations in botanical identity, phytochemical composition, extraction procedures, formulation characteristics, and manufacturing quality. Establishing standardized raw materials, validated analytical methods, reproducible manufacturing processes, and appropriate regulatory documentation is essential for commercialization. Furthermore, long-term safety assessment and clinical validation are necessary to support the development of reliable and evidence-based herbal wound-healing products [42,45,47–49].

CONCLUSION:

Wound healing is a complex physiological process involving coordinated cellular and molecular events that restore tissue integrity and function. Cucumis sativus L. and Centella asiatica (L.) Urb. possess diverse phytochemical constituents with promising antioxidant, anti-inflammatory, antimicrobial, and tissue-regenerative properties. The phenolic compounds and flavonoids of C. sativus may contribute to oxidative stress regulation and cellular protection, whereas the triterpenoids of C. asiatica, particularly asiaticoside, madecassoside, asiatic acid, and madecassic acid, have been investigated for their roles in collagen synthesis, fibroblast activity, and tissue repair. Their complementary pharmacological properties provide a scientific rationale for exploring combined herbal formulations in wound management. However, the synergistic efficacy of these plants has not been sufficiently established. Future investigations should emphasize phytochemical standardization, mechanistic validation, formulation optimization, comprehensive safety assessment, and well-designed clinical studies to determine their therapeutic relevance and establish evidence-based applications in wound healing.

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