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INTEGRATING HERBAL EXTRACTS INTO WOUND MANAGEMENT: A PHYTOTHERAPEUTIC APPROACH

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ABSTRACT

Hemostasis, inflammation, proliferation, and remodelling are overlapping phases of the complicated biological process of wound healing that are controlled by complex cellular and molecular mechanisms. Tissue repair may be delayed if these mechanisms are disturbed by infection, ischemia, age, or systemic diseases. Using plant extracts in topical preparations has become a popular, cost-effective, and biocompatible way to aid with wound healing. Triterpenoids, flavonoids, alkaloids, and enzymes are among the bioactive components of medicinal plants including *Centella asiatica, Carica papaya, Ficus religiosa,* and *Calendula officinalis* that have a strong capacity to heal wounds. These substances lower inflammation and the microbial burden while promoting collagen production, angiogenesis, epithelialization, and antioxidant defence. Localized medication administration is further facilitated by formulations like hydrogels, ointments, and lotions, which guarantee ideal moisture balance and promote tissue regeneration. Comparative studies show that phytotherapeutic formulations perform better than traditional synthetic drugs due to their increased sustainability, safety, and patient compliance. As a result, herbal-based wound care is an environmentally responsible and scientifically supported development in contemporary therapeutic techniques.

KEYWORDS: Wound healing, Herbal extracts, *Centella asiatica*, *Carica papaya*, *Ficus religiosa*, *Calendula officinalis*, Phytotherapy.

1. INTRODUCTION

The term "loss of continuity of epithelium with or without the loss of underlying connective tissue" refers to harm to tissue that disrupts the normal anatomy and function of the skin. When the body's anatomy and physiology are damaged, a complex biological process known as wound healing takes place. It includes a number of intracellular and extracellular cellular and molecular processes that interact in accelerating the healing process of the injury. Hospitalised infants frequently sustain skin injuries due to the emphasis on skin care. Despite their differences, skin injuries all have a natural healing and repair mechanism.[1]

The physiological process of wound healing consists of a number of successive but overlapping phases. Haemostasis, the initial step, happens right after the damage. The victim's physiological state is a prisoner of many of the biochemical processes involved in wound healing. Any compromise of local perfusion and oxygenation significantly impairs the following reparative powers of macrophages, fibroblasts, and endothelial cells, even when the initial local events of inflammation occur normally in any live tissue.[2]

1.1 Overview of plants

Carica papaya (Papaya), *Ficus religiosa* (Peepal), *Centella Asiatica* (Gotu kola), and *Calendula Officinalis* (Marigold) all exhibit good wound-healing properties.

1.2 Factors affecting wound healing

Factors affecting are as follows.

Local Factors

1. **Oxygen Availability**: Adequate oxygen is essential for collagen synthesis, angiogenesis, and oxidative killing of microbes. Hypoxia delays epithelialization and granulation tissue formation. Hyperbaric oxygen therapy enhances collagen expression and angiogenesis, illustrating the central role of oxygen.[3]
2. **Infection**: Bacterial contamination prolongs inflammation, increases protease activity, and impairs extracellular matrix (ECM) deposition. Biofilm formation further hinders immune clearance and antibiotic efficacy. In diabetic wounds, infection alters immune gene expression and delays closure.[4]

3. **Foreign Bodies and Trauma**: Foreign material or repeated mechanical stress sustains inflammation and prevents epithelial migration. Necrotic tissue or debris must be removed to enable proper healing.
4. **Moisture Balance**: Optimal hydration supports keratinocyte migration and granulation tissue formation. Dry wounds inhibit epithelialization, while excessive exudate leads to maceration and tissue breakdown.[5]
5. **Ischemia**: Reduced perfusion limits oxygen and nutrient delivery, compromising collagen synthesis and angiogenesis. Peripheral vascular disease and diabetic microangiopathy are common causes.[6]

Systemic Factors

1. **Age**: Aging reduces fibroblast activity, angiogenesis, and collagen deposition, leading to delayed re-epithelialization. Elderly patients often experience slower and weaker repair.[7]
2. **Hormonal Influence**: Estrogen accelerates wound closure by modulating inflammation, enhancing keratinocyte activity, and promoting angiogenesis. Clinical trials demonstrate improved healing in estrogen-treated postmenopausal women.[8]

3. **Chronic Diseases**

- **Diabetes Mellitus:** Impairs repair through vascular dysfunction, defective angiogenesis, neuropathy, and immune dysregulation.
- **Obesity:** Excess adipose tissue reduces vascularity and increases inflammation, often coexisting with diabetes.
- **Nutritional Deficiency:** Protein, vitamin C, zinc, and iron are essential for collagen cross-linking, epithelialization, and immune competence. Deficiency delays proliferation and tensile strength development.[9]

4. **Medications and Immunosuppression**: Corticosteroids, cytotoxic drugs, and immunosuppressants inhibit fibroblast proliferation, reduce angiogenesis, and impair inflammatory responses, thereby slowing repair.

5. **Lifestyle Factors**

- **Smoking:** Nicotine causes vasoconstriction, while carbon monoxide reduces oxygen delivery. Smoke toxins impair fibroblast and endothelial proliferation, significantly delaying wound closure.

- **Alcohol and Stress:** Both reduce immune competence and alter cytokine balance, increasing susceptibility to infection and delayed healing. Chronic psychological stress elevates cortisol, suppressing immune and reparative functions.[10]

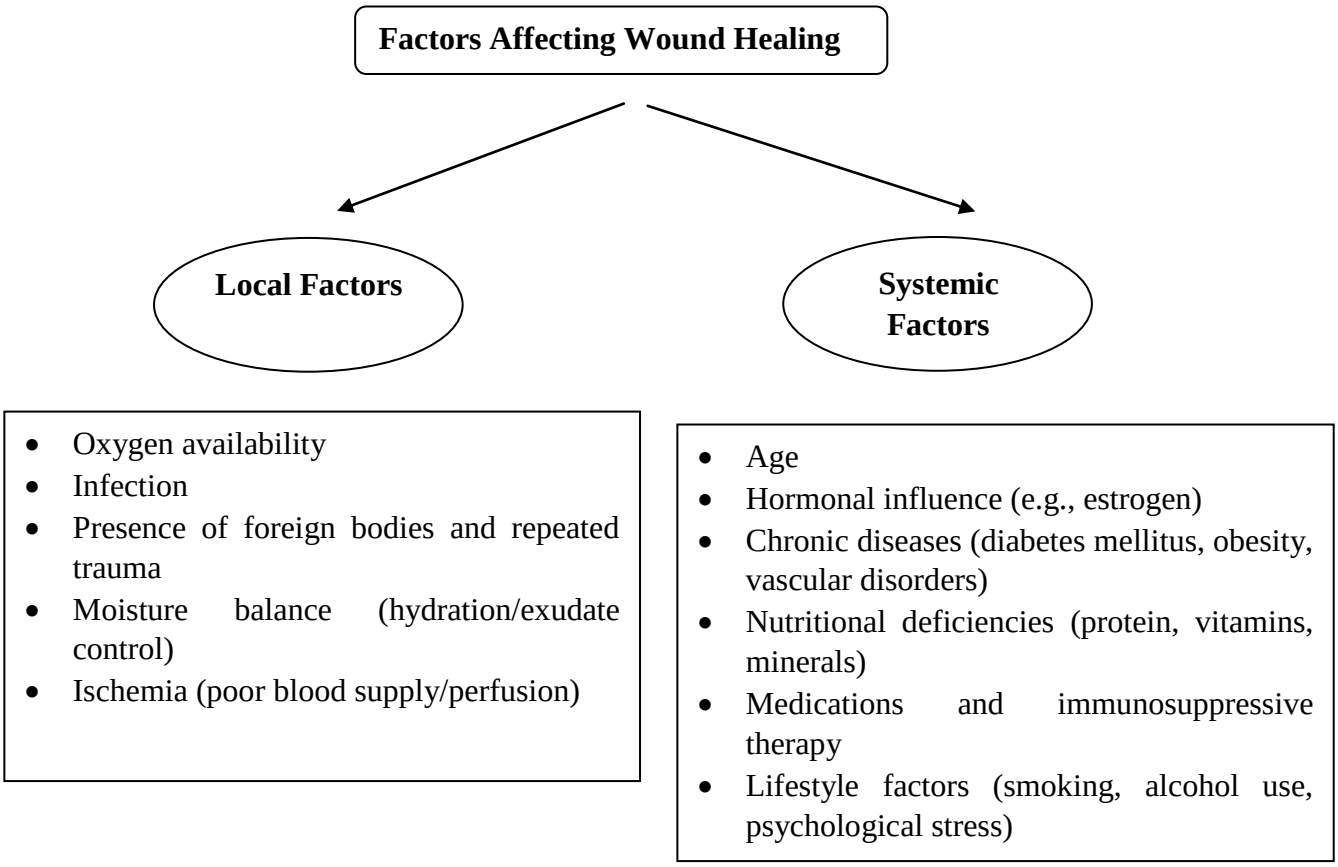

Fig 1: Factors affecting wound healing.

1.3 Mechanism of action of wound healing

The process of skin healing from wounds is a complex phenomenon that involves various cellular, humoral, and molecular pathways. It begins immediately after an injury occurs and can continue for a prolonged period, sometimes lasting several years. The condition being discussed involves instances where tissue is disrupted, leading to functional impairment. Injuries may occur either as open wounds, which affect the body's surface, or as closed wounds, where internal organs are damaged but the skin remains intact.[11]

There are four phases of wound healing.

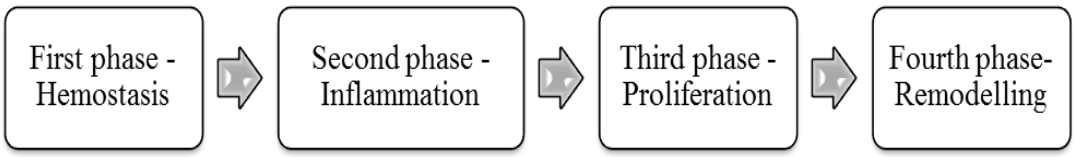

Fig 2: Stages of wound healing.

a. First phase – Hemostasis

Hemostasis is a process that helps stop bleeding by keeping blood within the damaged blood vessels. This process relies on the interaction of several components, including platelets, plasma coagulation cascades, fibrinolytic proteins, blood vessels, and cytokine mediators. When tissue is injured, the hemostatic mechanism uses a variety of vascular and extravascular receptors, along with blood components, to seal the damaged areas and prevent blood from escaping into surrounding tissues.[12]

The steps involved in hemostasis include: vasoconstriction, formation of a platelet plug, platelet adhesion, platelet activation, and platelet aggregation.

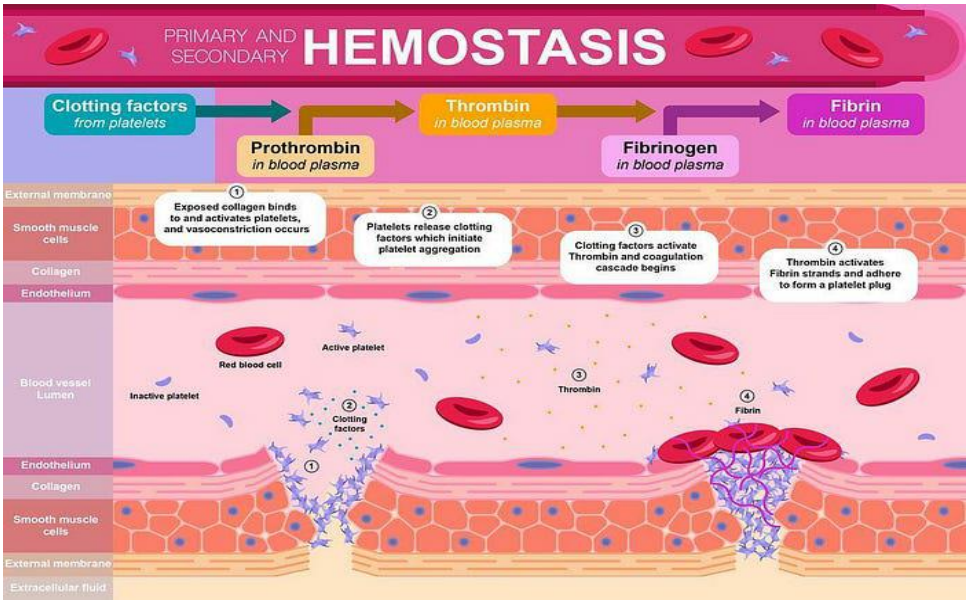

Fig 3: Various steps involved in hemostasis.

b. Second phase – Inflammation

The goal of this stage is to use neutrophils, the "first responders," to avoid infection. Within an hour, the wound is invaded by these extremely mobile cells, which peak over the first 48

hours. Chemotaxis, a mechanism in which they follow a chemical gradient set off by cues such as the interleukins, directs their arrival.

Three primary methods are used by neutrophils to remove debris and bacteria:
1. Phagocytosis: Direct ingestion of foreign particles is known as phagocytosis.
2. Degranulation: the release of harmful compounds that kill germs and dead host tissue, such as protease and elastase.
3. Free Radicals: Creating oxygen free radicals that are antibacterial and can also sterilize a wound when combined with chlorine.

As long as there are bacteria or debris present, this inflammatory phase will persist. After completing their task, neutrophils either die (apoptosis) or are removed by macrophages.[13]

c. Third phase – Proliferation

Tissue repair starts during the proliferation phase, also known as the granulation phase. It is distinguished by the development of granulation tissue, which includes the emergence of new blood vessels and the production and deposition of collagen and Extracellular Matrix (ECM) by fibroblasts that have been activated. Restoring the microvasculature is essential because it maintains the healing process, supplies the cytokines and growth factors required to start the construction of new vessels, and supplies oxygen and nutrients for cell metabolism.[14]

d. Fourth Phase – Remodelling

In the remodeling stage, immune cell infiltration is facilitated by newly produced, permeable blood arteries. The development of stable vasculature depends on vascular pruning, which involves the intentional death of endothelial cells (ECs). Vasohibin and Sprouty proteins are examples of negative feedback mechanisms that ECs use to control vessel formation. They also express CXCR3 to prevent the creation of endothelial tubes.[15]

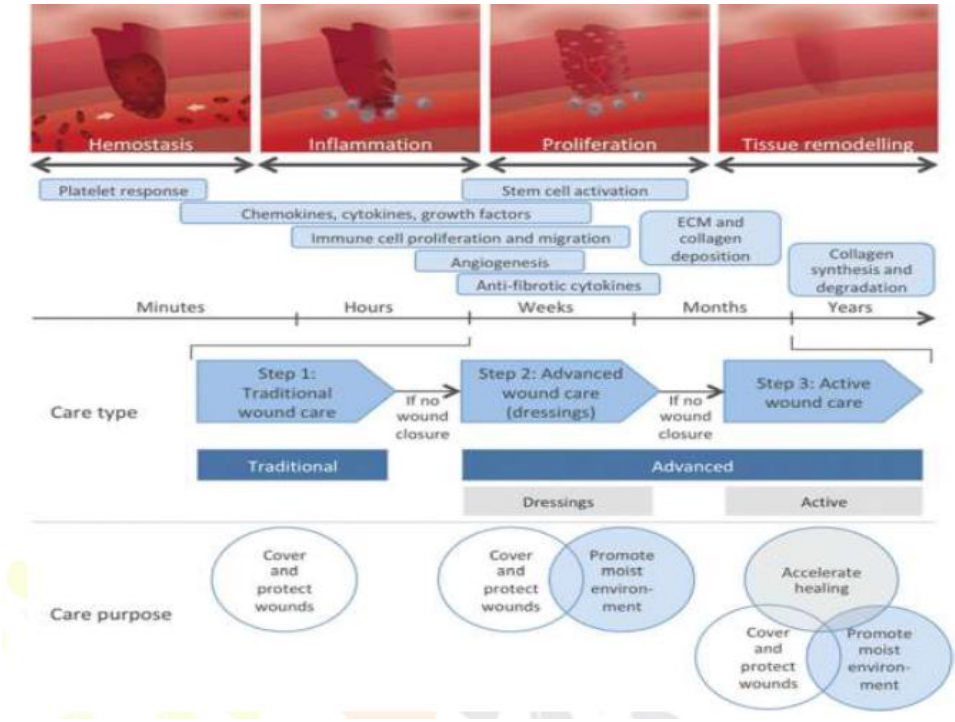

Fig 4: Overlapping phases involving distinct cells and effector mechanisms that all are required for efficient wound healing.[16]

1.4 Role of topical formulations in wound healing

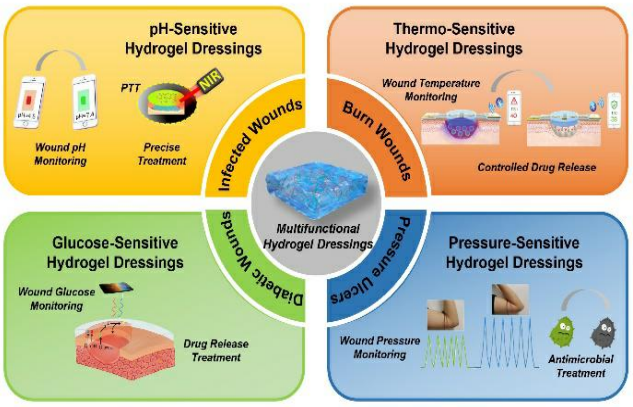

Fig 5: Role of Topical formulations.

Topical formulations play a pivotal role in wound management by delivering therapeutic agents directly to the injury site, thereby enhancing local drug concentration and minimizing systemic side effects. These formulations, including creams, ointments, gels, and hydrogels, create a moist environment that facilitates cell migration, proliferation, and efficient tissue regeneration.[17] Moist wound healing promoted by topical agents accelerates angiogenesis and collagen synthesis, essential phases in wound repair. Advanced formulations such as "smart" hydrogels enable controlled drug release and real-time wound monitoring, enhancing

healing outcomes.[18] Herbal-based topical preparations leverage bioactive phytochemicals imparting antimicrobial, anti-inflammatory, and antioxidant effects, which synergistically support various healing phases.[19] Moreover, topical delivery bypasses systemic metabolism, reducing risks such as nephrotoxicity linked to systemic drugs. Patient compliance improves due to ease of application and targeted action, making topical therapies indispensable for effective and safe wound management.

1.5 Available formulations

- **Hydrogels**: Provide excellent moisture vapor permeability and sustain a moist wound environment. They promote quicker re-epithelialization and more seamless healing and are non-adhesive and hypoallergenic. When compared to ointments, hydrogels are especially renowned for their increased patient comfort and healing rates.[20,21]
- **Ointments:** conventional formulations that include components like herbal extracts or antibiotics. Although ointments are stable and might hasten healing, study suggests gels frequently produce superior outcomes in terms of wound contraction and recovery speed.[22]
- **Creams:** Emulsified semi-solids are frequently utilized for dispersing plant extracts or bioactive substances. Certain specialty creams, such as "knowledgeable" or plant extract-based creams, show encouraging wound healing effects and actual time wound monitoring capabilities.[23]
- Silver sulfadiazine, povidone-iodine, and other medications that aid in infection control include examples of antimicrobial/antiseptic topicals.

2. Plant review

2.1. *Centella asiatica*

Centella asiatica (Gotu Kola, Indian pennywort, Tiger Grass) is a perennial herb of the Apiaceae family, widely distributed across Asia, Africa, and tropical regions.[24] It thrives in humid wetlands, along riverbanks, and in forest undergrowth, demonstrating remarkable adaptability.[25] Known for centuries in Ayurveda, Unani, and South-East Asian traditional medicine, its use encompasses treatment of skin disorders, cognitive enhancement, and wound management.[26] The leaves, roots, and stems are employed for medicinal purposes, and it is commonly consumed as a culinary and medicinal plant in Malaysia and India.[27]

Fig 6: Gotu kola plant.

2.1.1 Scientific classification of *Centella asiatica.*

Table 1: Taxonomic classification of *Centella asiatica.*

Rank	Classification
Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Apiales
Family	Apiaceae (Umbelliferae)
Genus	Centella
Species	*Centella asiatica* (L.) Urb.

2.1.2 Morphological Characteristics of *Centella asiatica*

Centella asiatica is described as having kidney-shaped to fan-shaped leaves with crenate or scalloped margins. The leaves are carried on slender, creeping stems, rooted at the nodes.[28] Flowers are small, pink to purple, borne in solitary axillary umbels, and the plant produces minute, compressed ribbed fruits.[29] The root system consists of thin, tufted roots emerging from nodes. Its entire aerial parts are commonly harvested for pharmacological usage, with much of the plant's identity established by leaf morphology and axillary inflorescence.[30]

2.1.3 Chemical Constituents of *Centella asiatica*

The primary bioactive compounds are triterpenoids (asiaticoside, madecassoside, asiatic acid, and madecassic acid), flavonoids (quercetin, kaempferol, rutin), alkaloids, phytosterols, essential oils, and polyacetylenes. Glycoside-rich extracts (asiaticoside and madecassoside) are especially noted for wound healing and anti-aging effects.[31]

Table 2: various plant parts showing different phytoconstituents.

Constituent	Key Biological Action
Asiaticoside	Collagen synthesis, anti-inflammatory
Madecassoside	Tissue regeneration, angiogenesis
Asiatic acid	Proliferative, antioxidant
Flavonoids	Antioxidant, skin protection

2.1.4 Pharmacological Actions of *Centella asiatica*

Centella asiatica and its triterpenoids impact multiple cellular and molecular mechanisms for wound healing.

- **Collagen Synthesis:** Asiaticoside and madecassoside "stimulate type I and III collagen production in fibroblasts by activating TGF-Smad signaling," supporting granulation and matrix formation. Enhanced hydroxyproline content demonstrates increased collagen maturation and tensile strength.[32]
- **Angiogenesis:** Active constituents raise levels of VEGF and FGF, promoting capillary formation and new tissue vascularization.[33]
- **Anti-inflammatory Effects:** Reduction of neutrophil infiltration and cytokines (TNF-α, IL-1, IL-6), with asiaticoside and madecassoside inhibiting NF-κB, COX-2, and iNOS pathways.[34]
- **Antioxidant Activity:** Flavonoids and saponins "scavenge reactive oxygen species, boost SOD and catalase, and protect against lipid peroxidation in wound tissue".
- **Epithelialization and Remodeling**: Increased cellular migration, proliferation, and accelerated epithelial closure are consistently observed in experimental burn and chronic wound models. Enhanced remodeling results from improved collagen crosslinking and matrix reorganization.[35]
- **Antimicrobial Activity**: Methanolic and ethanolic extracts demonstrate efficacy against Gram-positive and Gram-negative bacteria and fungi.
- **Synergistic Effects**: Studies highlight that whole-plant extracts, combining multiple triterpenoids and flavonoids, yield superior wound contraction, granulation tissue development, and clinical outcomes compared to isolated compounds or standard wound care.[36]

2.2. *Carica papaya*

Among the most popular and commercially significant Caricaceae species, the papaya (*Carica papaya Linn.*) is one of the most extensively farmed plants in tropical climates. This flowering plant species is indigenous to Oman, Malaysia, Indonesia, the Philippines, Sri Lanka, and India. Papaya has been grown commercially in a number of Asian nations. Papaya is also grown as a garden plant in various tropical nations. Polysaccharides, vitamins, minerals, enzymes, alkaloids, glycosides, saponins, sterols, and other phytochemicals are all found in papaya. The plant is easily identified by its soft, fragile, and typically unbranched

stem that produces a lot of white latex. It also grows quickly and can reach a height of 20 meters.[37]

Fig 8: Papaya fruit.

2.1 Scientific classification of *Carica papaya*

Table 3: Taxonomic classification of *Carica papaya.*

Rank	Classification
Kingdom	Plantae
Division	Magnoliophyte
Class	Magnoliopsida
Order	Brassicales
Family	Caricaeae
Genus	Carica
Species	Papaya L.

2.2.2 Morphological characteristics of *Carica papaya*

Reaching 5 to 10 meters in height, the *Carica papaya* is a fast-growing, semi-perennial plant with a hollow stem and huge, palmately lobed leaves that form an umbrella-like canopy. The plant is polygamous, producing tubular, hermaphrodite flowers that yield the majority of commercial fruits, female flowers that are larger and have a functional pistil, and male flowers that are smaller and have many stamens.[38]

Tropical and subtropical regions of the world are home to Carica papaya L. crops and fruits. On roughly 389,990 hectares, more than 6.8 million tons of papaya fruit were harvested worldwide in 2004. In 2004, 47% of the United States, 30% of Asia, and 20% to 22% of Africa were growing carica papaya. Brazil has the greatest papaya industry in the world, and it is still growing. The *Carica papaya* originates in southern Mexico and other parts of Mesoamerica. In the 16th century, Malaysian plantation selection brought the *Carica papaya* to India. Papaya trees, which range in height from 2 to 10 meters, are difficult to distinguish between male and female species in Australia, the Hawaiian Islands, the Philippines, Sri Lanka, and South Africa. 12 Carica papaya grows in the shape of a pear.[39]

2.2.3 Chemical constituents of *Carica papaya*

Table 4: Various plant parts showing different phytoconstituents.[40]

Parts	Constituents
1. Fruit	Minerals, calcium, phosphorus, iron, vitamin C, thiamine, protein, fat, fiber, and carbohydrates. amino acids, citric acids, melic acid (found in green foods), riboflavin, niacin, and cacoxene, volatile Compound: cis, trans, benzylisothiocynate, and linalool 2-octen-2-ol, 2, 6-dimethyl-3,6 expoxy-7. Benzyl-B-d glucoside, 2-phenylethi-B-D glucoside, alkaloid, carpaine, and 4-hydroxyl-phenyl-2
2. Juice	Lipids that include myristic, palmitic, stearic, linoleic, linolenic, vacenic, and oleic acids; n-butyric, n-hexanoic, and n-octanoic acids.
3. Seed	Papaya oil, caprine, benzylisothiocynate, benzyl glucosinolate, glucotropacolin, benzylthiourea, hentriacontane, B-sitosterol, fatty acids, crude proteins, crude fiber,
4. Root	Apposite and an enzyme myrosin
5. Leaves	Choline, carnosine, vitamin C and E, carpain, pseudocarp in, and dehydrocarpaine I and II are alkaloids.
6. Bark	Xylitol, galactose, fructose, sucrose, glucose, and B-sitosterol.
7. latex	Papain and chymopapain, glutamine acyltransferase, chymopapain A and B, proteolytic enzymes, and lysozymes.

2.2.4 Pharmacological actions of *Carica papaya*

1.Wound Healing activity: Papaya's papain content, which has an ulcer-preventive effect, is what gives it its wound-healing qualities. Papain has the ability to decompose dead tissue without endangering living cells. Experiments have demonstrated that extracts from the leaves of the carica papaya plant reduce the inflammatory cytokine IL-1β and boost collagen density (Col1A1) in wound tissues, promoting quicker tissue remodeling and epithelialization. Carica papaya ethanol extract significantly improves wound healing in rats, confirming its traditional use and promoting additional research in people. In postoperative extraction socket repair, topical administration of Carica papaya leaf extract outperformed Hem coagulase in wound healing efficacy, suggesting potential clinical application. Carica papaya latex has been used historically to treat skin conditions by encouraging tissue regeneration. Its wound-healing qualities have been confirmed in in vivo mouse burn models. Flavonoids, saponins, tannins, alkaloids, and antioxidants are among the bioactive substances found in the plant that have anti-inflammatory, antibacterial, analgesic, and antimicrobial effects. These chemicals promote fibroblast migration and collagen synthesis, which are necessary for wound healing and skin restoration.[41]

2. Anti-microbial activity: When it comes to Enterococcus faecalis, carica papaya leaf extracts have demonstrated antibacterial activity, frequently with greater potency than seed extracts.

At higher extract concentrations, the inhibition zones against S. aureus and E. coli reached around 23.5 mm, demonstrating dose-dependent antibacterial effectiveness.

A wide range of Gram-positive and Gram-negative bacteria, such as Salmonella Typhi, Bacillus subtilis, Klebsiella pneumoniae, and Pseudomonas aeruginosa, have been shown to be inhibited by methanol and ethanol extracts of both the leaf and the seed, with the seed extracts frequently having a stronger effect.[42]

3. Anti-oxidant activity: Unripe papaya seed extracts have the highest DPPH radical scavenging activity, followed by ripe seed and peel-pulp extracts. Papaya seed extracts have more powerful antioxidant activities than peel-pulp extracts. Papaya leaf extracts' ability to scavenge free radicals and lessen oxidative damage is attributed to the polyphenols and caprine they contain.[43]

2.3. *Ficus religiosa*

The "peepal tree," or Ficus religiosa Linn, is regarded as a sacred tree. In Indian culture, it is believed to have mythological, religious, and therapeutic significance. With more than 800 species of shrubs, trees, and epiphytes that can be found in both tropical and subtropical regions around the globe, Ficus is one of the largest angiosperm genera. There are currently over 500 species of Ficus in the Asian-Australasian region.[44] The peepal tree was referred to as Ashwattha all through the Vedic era. Among trees, this one is considered as the the king.[45]

Fig 10: Peepal plant.

2.3.1 Scientific classification of *Ficus religiosa*.

Table 5: Taxonomic classification of *Ficus religiosa*.[46]

Rank	Classification
Kingdom	Plantae
Subkingdom	Viridae plantae
Phylum	Tracheophyte
Subphylum	Euphyllopsida
Class	Magnoliopsida
Subclass	Dilleniidae
Order	Urticales
Family	Moraceae
Tribe	Ficeae
Genus	*Ficus*
Specific epithet	Religiosa Linnaeus
Botanical name	*Ficus religiosa*

2.3.2 Morphological characteristics of *Ficus religiosa*

This large, ancient tree is thirty meters long. They are either brown or white, and they break bark. The slender, glossy leaves have five to seven veins. Fruits have a diameter of around ½ inch, which is comparable to an eye pupil. It is compacted and has a round form. The leaves have a roughly sigmoid growth pattern; after emerging from the spathe, each leaf grows in size over the course of nine days, from 425 to 4025 mm2 (based on the average mature leaf size). The leaf features anomocytic and paracytic stomata between polygonal epidermal cells and is hypostomatic. From 33.3 to 400, there are more stomata per square millimeter. per mm2 as the leaves expand, however the quantity of top epidermal cells drops from 5600 to 1110.[46]

2.3.3 Chemical constituents of *Ficus religiosa*

The plant contains tannins, phenols, saponins, sugars, alkaloids, methionine, terpenoids, flavonoids, glycosides, and steroids, in accordance to the preliminary phytochemical research.[47]

Table 6: various plant parts showing different phytoconstituents.[48]

Plant parts	Bioactive compounds
Bark	Tannins, leucocyanidin-3-O-β-D-glucopyrancoside, Lupeol, lupeol acetate, α-amyrin acetate, saponins, polyphenolic compounds, sterols.
Leaves	Gallic acid, Rutin, α-amyrin, Campestrol, isofucosterol, phenylacetaldehyde, n-nonanal, palmitic acid
Fruits	dendrolasine, α-ylangene, α- thujene, α-copaene, β-bourbonene, terpenoids, glycosides, flavanoids

2.3.4 Pharmacological actions of *Ficus religiosa*

1. Nootropic effects: An established challenge in learning new knowledge (anterograde amnesia) and/or restoring information from the past is referred to as amnesia, a type of cognitive dysfunction. Because F. religiosa fruits have a high serotonin content, it was thought that curing them might modify the brain's serotonergic processes and be beneficial for addressing amnesia.

2. Antibacterial activity: Utilizing aqueous leaf extracts, it was discovered that the leaves of F. religiosa possessed antimicrobial properties against *Shigella dysenteriae, Salmonella typhi, Salmonella typhimurium, P.Aeruginosa, E. Coli, Bacillus subtillis, S. Aureus, S. Typhimurium, S. Staph aureus, and Staphylococcus*. Furthermore, making use of fruit chloroform extract has an antibacterial effect against *Obacter chroococcum*, B. cereus, Streptococcus faecalis, Bacillus megaterium, Klebsiella pneumonia, and Streptomycin lactis.

3. Wound healing activity: Excision, incision, and burn wounds all exhibit dose-dependent wound-healing activity when rats using experimentally generated wounds employing various wound models are treated with hydroalcoholic extract of F. religiosa leaves. Increased contraction of the wound rate, shortened epithelial growth length, and high skin breaking strength were all signs that treatment with 5 and 10% extract ointment accelerated wound healing in a dose-dependent manner.[49]

4. Antioxidant activity: Different solvents have been utilized for the fruit and bark of F. religiosa. They were assessed based on their capacity for neutralizing radicals against 1, 1-diphenyl-2-picrylhydrazyl (DPPH) as well as their oil stability index. Diabetes patients lost weight as a result of decreased glucose absorption, free fatty acid removal from the bloodstream, and increased β-oxidation in adipose tissue.

5. Anticonvulsant activity: In a laboratory model of convulsions caused by maximal electroshock (MES), picrotoxin, and pentylenetetrazol (PTZ), F. religiosa shown promising anticonvulsant effects. The high serotonin content of F. religiosa's figs and its use in ethnomedical treatment of epilepsy led to the assumption that the figs may have anticonvulsant qualities via regulating the brain's serotonin levels, which will be beneficial in clinical settings.[50]

6. Hypoglycemic activity: β-Sitosterol-d-glycoside was isolated from the root bark of *F. religiosa*, which has a peroral hypoglycemic activity. Oral administration of *F. religiosa* bark extract at the doses of 25, 50, and 100mg/kg was studied in normal, glucose-loaded, and STZ (streptozotocin) diabetic rats. *F. religiosa* also showed significant increase in serum insulin, body weight, and glycogen content in liver and skeletal muscle of STZ-induced diabetic rats,

while there was significant reduction in the levels of serum triglyceride and total cholesterol.[51]

2.4. *Calendula officinalis*

More than 6,000 plants are utilized in traditional, herbal, and folk medicine in India. About 500 of the 1500 known medicinal herbs are used often. One of the most widely used medicinal plants in China, India, Europe, and the United States is calendula officinalis L., also known as pot marigold. The term marigold comes from the fact that calendula, which was known as "gold's" in old English, was connected to Queen Mary and the Virgin Mary. Because of its lengthy blossoming season, this plant's name is derived from the Latin word "Calend," which means the first day of every month. "Leo" has become an astronomical sun sign because flowers go in the direction of the sun's light. Approximately 80 cm tall, calendula is an annual herb with a corymbosely branching stem, a long tap root with hispid, sharp, oblanceolate, alternating, and sessile leaves; a large number of secondary roots; and an inflorescence of flower heads encircled by two rows of hairy bracts. The plant features curved, sickle-shaped, ringed achenes, as well as yellow to orange flowers with female ray ûorets and hermaphrodite, tridentate, tubular, disc florets.[52]

Fig 12: Marigold flower.

2.4.1 Scientific classification of *Calendula officianlis*

Table 7: Taxonomic classification of *Calendula Officinalis.*

Rank	Classification
Kingdom	Plantae
Subkingdom	Tracheobionta
Division	Magnoliophyta
Class	Magnoliophyta

Subclass	Asteridae
Order	Asterales
Family	Asteraceae
Tribe	Calenduleae
Genus	*Calendula*
Species	*officinalis*

2.4.2 Morphological characteristics of *Calendula Officinalis*

The annual or biennial plant C. officinalis Linn. can grow to a height of 30 to 60 cm. Marginal flowers in cultivated plants are multi-seriate, with corolla oblong spatulate, 15-25 mm long and 3 mm wide; corolla of disc flowers is rounded, with the top tridentate, 1.5-2.5 cm long, 4-7 mm in diameter, and 5 mm long tubular florets. Lower spatulate leaves are 10-20 cm long and 1-4 cm wide, whereas higher oblong and mucronate leaves are 4-7 cm long. The stem is angular, hairy, and solid. Fragments of the corolla, anomocytic stomata in the apical region of the outer epidermis, covering and glandular trichomes, elongated sclerenchymatous cells, pollen grains, and wall fragments are all present in the yellowish brown powdered C. officinalis, which has a distinctive, aromatic odor and a slightly bitter taste of the ovaries with brown pigment, pieces of the fibrous layer of the others, and pieces of the stigma.[53]

2.4.3 Chemical constituents of *Calendula officinalis*

Table 8: Various plant parts showing different phytoconstituents.

Plant parts	**Bioactive compounds**
Flower	
Terpenoids	Lupeol, Erythrodiol, Calenduloside, *Calendula officinalis* glycoside, *Calendula officinalis* glycoside B, Cornulacic acid acetate
Flavonoids	Isoquercitrin, Rutin, Calendoflavoside, Quercetin, Isorhamnetin, Isorhamnetin-3-O-β-D-glycoside, Narcissin
Coumarins	Esculetin, Scopoletin, Umbelliferone
Volatile oils	Cubenol, α-cadinol, Oplopanone, Methyllnoleate, Sabinene, Limonene, p-cymene, Carvacrol, Geraniol, Nerolidol
Leaves	
Quinones	Phylloquinone, α-tocopherol, Ubiquinone, Plastoquinone
Root	
Terpenoid	Calenduloside
Petal and Pollens	
Carotenoids	Flavoxanthin, Luteoxanthin, Auroxanthin, 9Z-antheraxanthin, Violaxanthin

4.4 Pharmacological action of *Calendula Officinalis*

1. **Wound healing Activity:** Calendula officinalis is highly regarded in Ayurvedic medicine for its emollient, wound-healing, and scar-reducing characteristics. According to studies, its extracts—particularly the ethanolic fraction—significantly enhance angiogenesis, collagen metabolism, and epithelialization in wound regions. In accordance with Hill et al., calendula flower extract performs well as a massage emollient and enhances the appearance of scars. The extract diminished wound size and measures of tissue injury and inflammation, including as ALT, AST, and ALP, while increasing blood vessel development, collagen production, and blood flow in experimental animals. Its antibacterial and antioxidant effects aid in the healing process even more. Notably, 2% calendula gel applied daily has demonstrated positive effects in encouraging tissue regeneration and wound closure.[54]
2. **Antioxidant activity:** Particularly in its flowers, which are abundant in flavonoids (such as isorhamnetin and quercetin), saponosides, carotenoids, sterols, organic acids, and saccharides, calendula officinalis demonstrates potent antioxidant action. The solvent utilized determines how well these chemicals are extracted; extracts with enhanced antioxidant activity are produced by lipophilic and medium-polarity solvents, as opposed to water or 50% ethanol. By preventing lipid peroxidation brought on by ascorbic acid and Fe2+, residual aqueous extracts also shown antioxidant properties.
3. **Antimicrobial Activity of *Calendula officinalis:*** Strong inhibitory effects against important periodontal bacteria, such as Porphyromonas gingivalis, Prevotella spp., Fusobacterium nucleatum, and others, were demonstrated by a 10% decoction and methanol extract of C. officinalis flowers. Additionally, the essential oil showed significant antifungal action against a variety of human-derived yeasts and Candida species, such as Rhodotorula spp., C. albicans, C. glabrata, and C. krusei.
4. **Genotoxic and Antigen-toxic Activity:** Calendula flower aqueous-ethanolic extract has anti-genotoxic effects at low concentrations and genotoxic effects at high concentrations. Propylene glycol extract of calendula was also discovered to have an anti-genotoxic effect throughout the assessment that included measuring excretory 24-hour urinary 8-hydroxy2'-deoxyguanosine (8-OHdG) and lymphocyte DNA fragmentation in young pigs. In addition to being a key indicator for assessing the endogenous impact of oxidative damage to DNA and a factor in the beginning and progression of carcinogenesis, urine 8-OHdG functions as a biomarker for carcinogenesis and a number of degenerative diseases.[55]

5. Table 9: Summary of properties of the plant species

Plant species	***Centella asiatica***	***Carica papaya***	***Ficus religiosa***	***Calendula officinalis***
Synonyms	Gotu Kola, Indian pennywort, Tiger Grass	Pawpaw, Pepita, Erandkarkati.	Pipal, Pimpal, Ahant, Arayal, Ranji, Basri	Calendula aurantiaca Kotschy ex Boiss., Calendula eriocarpa DC., Calendula hydruntina(Fiori) Lanza
Geographical distribution	Asia, Africa, and tropical regions.	Brazil, Mexico, and Central America India, Philippines, and other Southeast Asian countries.	India, Nepal, Pakistan, and Bangladesh, as well as the Assam area, the Eastern Himalaya, and the Nicobar Islands.	Originally from the Mediterranean region, calendula has now spread throughout many temperate nations.
Chemical constituents	Asiaticoside, madecassoside, asiatic acid, and madecassic acid	**Alkaloids:** Carpaine **Enzymes:** Papain, cystatin, chymopapain Vitamins: Ascorbic acid (vitamin C), tocopherol (vitamin E) **Folic acid** Phenolic compounds and Flavonoids	bergapten, bergaptol, lanosterol, campestrol, stigmasterol, isofucosterol, α-amyrin, lupeol, tannic acid, arginine, serine, aspartic acid, tetradecane	terpenoids, flavoinoids, coumarins,volatile oil,quinones, carotenoids
Pharmacological activity	Collagen Synthesis, Angiogenesis, Anti-inflammatory Effects, Antioxidant Activity, Epithelialization and Remodeling, Antimicrobial Activity	Anti-inflammatory, immunostimulant effect, wound healing, antifungal effect, antibacterial effect, antioxidant activity, Collagen Synthesis	Hypoglycemic activity, Hypolipidemic activity, Anticonvulsant activity, Antioxidant activity, Wound-healing activity, Immunomodulatory activity	Anti-inflammatory, immunostimulant effect, wound healing, antifungal effect, antibacterial effect, antioxidant activity
Method of extraction	Soxhlet extraction	Soxhlet extraction, steam distillation, solvent	Ethanolic or methanolic extraction using hydroalcoholic	Homogenizer assisted (HAE), maceration, soxhlet, and

		extraction, percolation, maceration, infusion	mixture in Soxhlet apparatus	ultrasound assisted (UAE)
Synergistic effects	Centella asiatica, when combined with other medicinal plants such as Aloe vera or Calendula officinalis, demonstrates pronounced synergistic effects in wound healing.	Papaya peel is combined with honey to provide calming hydrating and skin lightening properties like sunscreen as cosmetic. Papaya peel can combine with lemon juice and applied 20 minutes prior to shampooing to treat dandruff.	While limited specific research exists on the synergistic effects of *Ficus religiosa* with many other individual plant species, it has been shown to have synergistic properties in polyherbal formulations, particularly within the Ayurvedic system. Scientific studies have identified enhanced effects when combined with other *Ficus* species and with *Lantana camara*.	1.Combined wound healing activity of Calendula officinalis and Basil leaves. 2. Calendula officinalis and Echinacea purpurea as antimicrobial agent**.**

CONCLUSION

The application of plant extracts to wound care represents a promising development in phytotherapy backed by recent research findings. The bioactive components of *Calendula officinalis*, *Ficus religiosa*, *Centella asiatica*, and *Carica papaya* demonstrate a variety of wound-healing mechanisms, such as enhancing antioxidant and antimicrobial defense, promoting angiogenesis, reducing inflammation, and stimulating collagen synthesis. Together, these phytochemicals speed up tissue remodeling and epithelialization. In contemporary wound-care therapies, herbal-based topical formulations are emerging as viable and effective substitutes for traditional synthetic medicines due to their greater biocompatibility, low toxicity, and affordability.

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