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Review

The Effect of Centella Asiatica for Wound Healing

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Abstract

Centella asiatica is a perennial creeper with a faint aroma and is a valuable medicinal herb in both the Old and New Worlds. It is found in tropical and subtropical regions around the world, including India, China, Nepal, Madagascar, Sri Lanka, and Indonesia. Centella's popularity in food and beverages stem from its functional properties. The plant's bioactive constituents have been linked to potential antioxidant, antimicrobial, cytotoxic, and neuroprotective activities, as reported in numerous studies. The plant's chemistry and pharmacology have been extensively studied for its efficacy in herbal preparations and chemical isolates, both ancient and modern. An intense effort has been made to develop new therapeutic approaches as well as technologies for more efficient and rapid wound healing. Research into plants that have long been used in traditional medicine to treat wounds has become a promising strategy for obtaining drugs that are therapeutically useful in acute and chronic wound management. Centella asiatica (Apiaceae) extracts and their active constituent, asiaticoside, have been shown to promote wound healing in both in vivo and in vitro models. We aim to create a formulation that promotes faster wound healing. This review provides a current and comprehensive analysis of the chemistry and health benefits of the Centella plant.

Keywords: Antioxidant, antimicrobial, wound healing, apiaceae, traditional medicine**,** Herbal medicine

INTRODUCTION

Centella asiatica is a popular herb in India for treating skin problems, healing wounds, and revitalizing nerves and brain cells. Its use in food and beverages has grown over the years due to its health benefits, which include antioxidant, anti-inflammatory, wound healing, memory enhancing, and many other properties. The potential of centella as an alternative natural antioxidant, particularly of plant origin, as well as its protection

against agerelated alterations in the brain antioxidant defense system, has grown significantly in recent years(1). Traditional medicine is valued globally, with treatment procedures, protocols, and standards established for ethnomedicine. Following a thorough analysis of etiology and traditional and alternative therapies for wound healing, we found Centella Asiatica (CA) species with promising results(2).

A wound refers to the disruption of the cellular, anatomical, or functional continuity of living tissue. Tissue injury can occur by physical, chemical, thermal, microbiological, or immunological means. Wound healing and repair are the body's natural processes for regenerating dermal and epidermal tissue. Healing needs collaboration among several tissues and cell lines. Platelet aggregation, blood clotting, fibrin production, inflammation, ground substance changes, angiogenesis, and re-epithelialization are all part of the wound healing process(3). Wounds are the breakdown of a tissue's anatomic continuity caused by physical, chemical, thermal, microbial, or immunological stressors. They can develop with or without microbial infection. The wound-healing process consists of four overlapping phases: hemostasis (immediate), inflammation (days 1-3), proliferation (days 4-21), and tissue remodeling (21days to 1 year). The stages and physiological activities must follow a specified order, timing, and intensity for best results. (1)

The plant components, asiaticoside, madecossoside, and centelloside have been separated. With the exception of centellic acid, It also contains volatile fatty acid which consists of steric, palmitic, oleic, lignoceric, linolenic and linoleic acids Triterpenoids Include centellose, asiatic, centellic, and madecassic a cids, as well as thankuniside, madecossoside, centelloside, and isothankunic acid. Asiaticoside and madecossoside predominated in the leaves with less in roots. From the dried plants, an alkaloid called hydrocotylin has been extracted. Centella asiatica is a significant medicinal plant in the global trade market, as reported by the Export and Import Bank of India. The wild stock of this plant species has been significantly depleted due to widespread exploitation, limited cultivation, and inadequate replacement efforts. The International Union for Conservation of Nature and Natural Resources (IUCN) has listed this plant species as Threatened and Endangered(4).

Centella contains vitamin C, B1, B2, niacin, carotene, and vitamin A. Total ash contains chloride, sulphate, phosphate, iron, calcium, magnesium, sodium, and potassium.

Fig 1: centella asiatica

Scientific research have shown that Centella asiatica has a number of biochemical components, including secondary metabolites, making it useful in modern medicine as well. (4,14)
Centella Asiatica is known to contain the following chemicals.
compounds:

- ♦ Triterpenoids
- ♦ Volatile and Fatty acids
- ♦ Alkaloids
- ♦ Glycosides
- ♦ Flavanoids
- ♦ Others- Vitamin B, C, G and some amino acids etc

PREPARATION OF HERBAL WOUND HEALING CREAM

The creams were made using the fusion proces The oil phase materials (extract, maize oil, GMS, and cetyl alcohol) were weighed and combined with a mechanical stirrer at 100 rpm and 80°C to create a homogeneous liquid. Similarly, the water phase ingredients were weighed and stirred continuously using a mechanical stirrer at 80°C. The phases were combined using a mechanical stirrer at 100 rpm (Remi motor RQT-127 HP1/8) for 30 minutes to ensure equal distribution of materials. All batches were left to equilibrate for 24 hours at room temperature(3).

PREPARATION OF HERBAL WOUND HEALING GEL

Using carbomer as a gelling agent, topical herbal gels with either 1% plant extracts were made. Table 1 displays the formulation's composition. Using a magnetic stirrer set to 1500 rpm, carbomer powder was dissolved in an adequate amount of deionized water to create carbomer gel. After adding the medication or plant extract to a 1% concentration, the pH was raised to a pH of 7 to 7.5 using 10% NaOH while being constantly stirred until gel was formed. A similar procedure was used to prepare the ciprofloxacin gel. Prior to being administered to animals, the obtained gel preparations underwent testing.(5)

EVALUATION OF HERBAL WOUND HEALING CREAM

A) DETERMINATION OF PH

After dispersing 0.5 g cream in 50 ml of distilled water, the PH was measured using a digital PH viscosity meter. (7)

B) HARDNESS

Hardness of formulation was determined using a texture analyzer (Brookfield CT-3) cream (20 gm) was filled in conical probe (up to plane surface of top) and Hardness was measured. This apparatus shows Hardness into the comparison of spreadablity and adhesive force.

C) DERMINATION OF MEAN GLOBULE DIAMETER

The mean globule diameter was determined by using the method of optical microscopy using 1% dispersion of cream in water.

D)VISCOSITY

The viscosity of prepared creams was determined using viscometer (Brookfield digital viscometer RVDV Pro) equipped with ULE adapter. The spindle (S06) was rotated at 0.5 rpm. Samples of the cream were allowed to settle over 30 min at the temperature (25±10C) before the measurements were taken. Viscosity was reported in (cP).

E) INVITRO DRUG RELEASE

The release of drug from the cream was determined using Franz diffusion cell apparatus for 6h.The receptor medium was phosphate buffer pH 6.8, maintained at 370C. The membrane filter (cellulose acetate) pore size 0.45µ was soaked in phosphate buffer pH 6.8 for 1h and mounted between the donor and receptor compartment. The gel was placed on receptor compartment and both the compartments were clamped together. The phosphate buffer pH 6.8 in the receptor compartment (8 ml) was stirred using magnetic stirrer 60 rpm. The samples (1ml) were withdrawn at different time intervals and replaced with an equal volume of buffer. The samples were analyzed spectrophotometrically at 297 nm. The % cumulative drug releases were calculated.(3,5)

F) SPREADIBILITY

The spreadability of a herbal gel refers to how easily it spreads on the skin. This is an important feature for topical applications because it determines how evenly and comfortably the gel can be applied. A spreadability test helps to evaluate this property, ensuring that the gel is both user-friendly and effective.

G) SKIN IRRITATION TEST

To test a herbal gel for skin irritation, you can conduct an in-vivo or in-vitro study. In-vivo methods, such as the Draize test, involve applying the gel to animal skin and looking for irritation signs. In-vitro methods, such as the SkinEthic Skin Irritation Test, assess irritation potential using reconstructed human epidermis models.(5)

SKIN FOR WOUND HEALING

The skin is a specialized organ composed of three structural and functional layers. The epidermis, or outermost layer, is avascular and impermeable, consisting of dead cells, immune system cells, melanocytes, sebaceous glands, sweat glands, and hair follicles. The dermis, or middle layer, contains extracellular matrix (ECM), vasculature, mechanoreceptors, connective tissue, nerve endings, hair follicles, and glands. The deepest layer, subcutaneous tissue, is mostly composed of fat, connective tissues, bigger blood arteries, and nerves . The skin performs numerous important homeostatic functions, including regulating thermostability and fluid balance. Furthermore, the skin serves as the body's primary protective barrier, shielding inside components from infections as well as physical, mechanical, and chemical harm.

Hemostasis is the first step in wound healing, during which a platelet plug stops blood loss and a precursory fibrin matrix is created. Together with bacterial products, platelets also generate platelet-derived growth factor, which draws inflammatory cells to the site of damage. Unless the wound becomes infected, the inflammatory phase lasts for two to five days and begins during the first twenty-four hours after the injury.(6)

Your body instantly begins the extraordinary process known as wound healing. While this natural reaction works diligently to mend and restore, some wounds may need specific treatment to heal effectively. This is where advanced wound care techniques come into play. From small injuries to chronic wounds, these skilled treatments speed up recovery and lessen the chance of consequences. Let us look at the four stages of wound healing and how to best help your body's recovery. Any implant will inevitably result in wound healing, which includes hemostasis, inflammation, repair, and remodeling. Repair and remodeling of nondegradable smooth-surfaced implants results in tissue encapsulation, which isolates them. The encapsulation tissue and the cellular participants in the immune reaction leading to this outcome vary depending on the site of implantation and the type of tissue that hosts.(8)

TYPE OF WOUND HEALING

1) Acute wound healing

Acute wound healing (as seen in primary healing) is a carefully regulated, systemic cascade of overlapping processes that require the coordinated completion of a variety of cellular activities, such as phagocytosis, chemotaxis, mitogenesis, and extracellular matrix component synthesis. These actions occur in a cascade that corresponds to the development of different cell types in the wound at various phases of healing

2) Chronic wound healing

A chronic wound is one in which the normal healing process is disrupted at one or more points during the haemostasis, inflammation, proliferation, or remodelling phases, resulting in a longer than expected healing time. (9)

Wound healing stages

1. Hemostatsis {stopping the bleed}

Stopping the bleeding is your body's top priority. Hemostasis is the process used to accomplish this. To slow the blood flow, the blood vessels close to the wound first constrict. Platelets then rush to the injury site. To create a clot, they adhere to one another. By sealing the wound and acting as a plug, this clot prevents the entry of foreign objects. Later, the clot solidifies and becomes the scab's base. For a few minutes during this phase, you may notice bleeding from the wound. Since your body is still forming the clot, this is normal. The wound appears red or swollen once the bleeding has stopped. Additionally, you might notice some transparent fluid seeping out. There is currently nothing to be concerned about.(10)

2. Inflammation-defending against infection

In order to prevent infection, your immune system takes over when the bleeding stops. To combat any bacteria, debris, and dead cells that shouldn't be there, white blood cells called neutrophils and macrophages travel to the wound site. Imagine this as the cavalry entering to drive out dangerous intruders. Your body increases blood flow once more to make more oxygen and nutrients available to support the immune system.(11)

3. Proliferation – Rebuilding Tissue

The wound Your body switches gears to rebuilding as it regains control. We call this proliferation. Granulation tissue, a type of new tissue, starts to grow over the wound. Due to the growth of tiny blood vessels inside, it is typically pink or red and has a slightly bumpy or shiny appearance. Fibroblasts are another type of cell involved in this process. They create collagen, a protein that strengthens the newly formed tissue by serving as a scaffold. Meanwhile, the wound's edges begin to draw together. site and the surrounding area will swell as a result of all these changes. Additionally, there might be pain, some warmth, and redness. Even though it may seem like things are getting worse, this is just your body's normal reaction for the time being.(10)

Stages of a Scab

You will observe that the wound is progressively becoming smaller over time. However, as a thin scab forms on top, the surface will appear uneven and discolored. Around the scab, you might experience some itching. The scab will fall off, exposing the scar tissue underneath, as soon as the skin underneath has fully healed. The wound has now completely healed. It is not entirely healed, though. One more step remains to be completed.(11)

4: Maturation – Strengthening the Skin

To make the previously injured tissue as resilient as possible, it is now time to strengthen it. The wound site becomes stronger and more elastic as a result of the collagen fibers created during the preceding stage fitting in. But it takes time a few weeks to several months, at most. If your wound is deep or covers a larger area, it might even take a year or longer. The scar tissue will begin to relax after initially feeling constricted or stretched. It will also gradually flatten and change color, frequently fading to the color of your natural skin.

Your wound has now fully healed. The once-damaged area will never be as strong as it was prior to the injury, despite the fact that the process is complete.(9,10,11)

Other Pharmacological activity

1.**Cytotoxocity And Antitumour**

Oral administration of C. asiatica crude extract and partially purified fractions led to apoptosis in solid and Ehrlich Ascites tumors, extending their life span. Asiatic acid has been shown to have anticancer properties on skin cancer. Oral administration of C. asiatica crude extract and partially purified fractions led to apoptosis in solid and Ehrlich Ascites tumors, extending their life span. Asiatic acid was discovered to have an anticancer effect on skin cancer. (1,4)

2.Cardioprotective: The plant's alcoholic extract effectively prevents myocardial infarction caused by ischemia-reperfusion.

3.Radio protective: Centella asiatica may help prevent radiation-induced behavioral changes during clinical radiotherapy.

4.Antidepressant: The total triterpenes demonstrated antidepressant activity and significantly reduced corticosterone levels in serum.

5. Antiprotozoa: The plant's alcohol extract effectively inhibited Entamoeba histolytica.(1,4)

6. Diabetes mallitus and obesity

Extracts of C. asiatica show promise in treating endocrine disorders, including type 2 diabetes and obesity. In terms of specific substances, asiatic acid has been shown to be effective in treating obesity, while made cassoside may be useful in treating osteolytic bone disorders. Centella asiatica extracts significantly increased cyclic adenosine monophosphate levels in human adipocytes, followed by increases in non-esterified fatty acids. Diabetes type 2 (T2DM) is defined by high blood sugar, insulin resistance, and a decreased insulin-stimulated response when blood sugar levels are high(12).

7. Neuroprotective Effect

The neuroprotective properties of C. asiatica and its main triterpene saponosides have been thoroughly investigated using a variety of animal testing paradigms, including passive avoidance and elevated-plus labyrinth tests for memory enhancement. The effects of C. asiatica's aqueous extract on intracerebrovascular streptozocin-induced memory associated with the sporadic type of Alzheimer's disease were investigated in rats by administering the extract at doses of 100, 200, and 300mg/kg (b.w.)26. C.asiatica enhances the nervous system's performance. It degrades in water, ethanol, and methanol. According to relevant research on the nervous system, C. asiatica and its triterpenes can treat a number of neurological conditions, but Alzheimer's disease (AD) and Parkinson's disease have received the most attention.(1.4,13)

8. Effects on Digestive Diseases

C. asiatica and its triterpenoids not only improve liver fibrosis, colitis, and gastric mucosal damage, but they also help with digestive issues. These effects include a decrease in Helicobacter pylori colonization of the stomach. The current study found that C. asiatica extract significantly repaired gastric mucosal injury, reduced H. pylori infection, and effectively mitigated drug-induced liver toxicity. Research indicates that madecassoside can effectively reduce inflammatory factors (TNF-, IL-1b, IL-6, IFN-, and IL-17) in arthritis model rats. Madecassoside (30mg/kg) taken orally has been shown in animal studies to significantly reduce the signs and symptoms of arthritis and stop the release of inflammatory cytokines(13).

9. Memory Enhancing

The herb's aqueous extract improved learning and memory while decreasing levels of norepinephrine, dopamine, 5-HT, and their metabolites in the brain. Centella asiatica includes brahmicacid, isobrahmic acid, brahminoside, and brahmoside. It possesses psychotropic, sedative, and anticonvulsant effects. It also helps with dementia, mental illnesses, and anxiety. Mentat, a polyherbal composition that works synergistically, improves memory, attention, and focus in children with learning disabilities.

TRADITIONAL USES

It is a well-known rasayana medication in Ayurveda, used as medhyarasayana to treat epilepsy, schizophrenia, and cognitive impairment. It is a so effective in treating leprosy, skin conditions, anorexia, and asthma. It has also been used as an antipyretic, analgesic, and anti-inflammatory in other traditional systems to

treat diarrhoea, cholera, measles, jaundice, leukorrhea, haematemesis, hepatitis, urethritis, toothache, syphilis, smallpox, neuralgia, rheumatism, toothache, and varices. Poultices were used to treat sprains, fractures with closed ends, and contusions. Andfurunculos. (13)

CONCLUSION

The literature study suggests that C. asiatica has promise for wound healing treatment due to its antidiabetic, antiinflammatory, antioxidant, and antibacterial properties. These features have been established in preclinical and clinical studies, indicating possibilities for developing nature-based pharmaceuticals to heal wounds.

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