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CLITORIATERNATEA: A MAGICAL HERB IN WOUND HEALING TREATMENT

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ABSTRACT

Clitoria ternatea is a seasonal floral herbaceous plant that can probably heal the wounds faster by providing oxygen and nutrients for tissue repair that results in enhancement of blood flow to the wounds. The goal of this review is to comprehend and investigate the important phytochemical and pharmacological facts that will help to improve the wound healing processes. Wound healing is a complex mechanism, comprises of four phases- hemostasis, inflammation, proliferation remodeling. Clitoria ternatea can facilitate to reduce inflammation and speed up the wound healing process due to its high flavonoid content. It has long been used to treat skin aggravation, and minor burns due to its diverse wound healing properties.

KEYWORDS: *Clitoria ternatea, phytochemical tests, wound healing mechanism, Tissue regeneration.*

1. INTRODUCTION

The greatest common dermatitis consideration is a wound on the body surface that entails a loss in cell functioning due to prolonged access to atmospheric as well as related causes.Components that induce skin wounds produce reactive oxygen species (ROS) that promote inflammatory cytokines like interleukin-6 and -8 and tissue destruction.This inflammatory reaction speeds up the production of dermal enzymes (elastase, hyaluronidase, matrix metalloproteinases, and so on), resulting in extracellular network deterioration (ECM)[1].Fibrin, elastin, hyaluronan (glycosaminoglycan), type I and type III collagen, and other fibers make up the ECM, that produce a thread matrix to sustain anatomical stability[2].

Elastase shatters down fibrin and elastin fibers, while hyaluronandepolymerization through hyaluronidase and matrix metalloproteinases-1 shatters down type I collagen.Loss of skin flexibility, transepidermal fluid, and elastic modulus are the prominent side effects.These findings imply that dermal enzyme expression and thread synthesizingderegulation perform a significant effect in the healing of skin wounds[3].

Herbal extracts, vitamins, and antioxidant food additives are the foremost beneficial treatments for skin wounds because they consume free radicals and lower the concentration of dermal enzymes, restoring regular skin integrity and slowing the inflammatory response.

Clitoriaternatea is an elevated, protein-rich, robust, leading, scurrying, rising legume, sometimes known as a "tropical alfalfa" and a moderate protein source [4].

Plant Information

The plant has been distributed in the tropical areas of tropical places and subcontinents of Asia. Clitoriaternatea has antibacterial, antioxidant, anticancer, hypolipidemic, cardiovascular, central nervous, respiratory, immunological, anti-inflammatory, analgesic antipyretic, and numerous pharmacological actions [5].

The plant belongs to the family of Fabaceae (Pipilionaceae) and is known by vernacular names such as, Aparajita,ClitoriaalbifloraMattei,ClitoriabracteataPoir.Clitoriamearnsii De Wild, etc. It is a traditional herbal medication that is said to alleviate disorders with the central nervous system (CNS), such as stress, agitation, melancholy, and tremors etc. [6].

Scientific Classification [7]

Kingdom: Plantae
Order: Fabales
Family: Fabaceae
Genus: Clitoria
Species: C. ternatea
Binomial name: Clitoriaternatea L
Synonyms: Clitoriaprincipissae

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Phytochemicals Presents in the Plant [8]

Sn.	Phytochemicals	Plant Part				
		Leaf	Root	Shoot	Flower	Seed
1	Alkaloids	Negative	Negative	Positive	Negative	Positive
2	Tannins	Positive	Negative	Positive	Positive	Positive
3	Glycosides	Positive	Negative	Positive	Positive	Positive
4	Resins	Positive	Negative	Positive	Positive	Positive
5	Steroids	Positive	Negative	Negative	Negative	Negative
6	Saponins	Negative	Positive	Negative	Negative	Negative
7	Flavonoids	Positive	Positive	Positive	Positive	Positive
8	Phenols	Negative	Positive	Negative	Negative	Negative

Traditional uses of the Medicines [9]

The plant consists of verity of the phytochemicals which makes this plant so important in the treatment of the various diseases. Some of traditional uses of this drug enlisted below:

1. **Dye production**- Flower
2. **Tea production** – Flower
3. **Reproductive Diseases**- Whole plant
4. **Ayurvedic Medicine**- Whole Plant
5. **Memory enhancer**-Whole Plant
6. **Anti-stress**- Whole Plant
7. **Anti-depressant**- Whole Plant
8. **Anticonvulsant**- Whole Plant
9. **Sedative Agent**- Whole Plant

The tradition uses of the plants have been immersed greatly in recent days. The plant and its potential uses have been examined through the studies i.e. in vitro and in vivo. Precisely, the various parts of the plants have got tremendous effect in the various diseases related to CNS, ANS and Cardiovascular.

Phytochemicals and Its function [10]

Sn.	Plant Part	Phytochemicals	Functions
1	Flower	Saponin, Tannins, Alkaloids, Glycosides, Phytosterols, Carbohydrates	Anti-diabetic, Anti-spasmodic, Anti-Inflammatory
2	Leaf	Alkaloids, reducing sugars, flavonoids, steroids, glycosides	Anti-diabetic, Anti-neurodegenerative
3	Root	1,1-diphenyl-2-picrylhydrazyl (DPPH)	Anti-Oxidant, Diuretic, Laxative
4	Seed	The seeds contain essentialamino-acids, pentosan, water-soluble mucilage, adenosine, an anthoxanthinglucoside, greenish yellow fixed oil a phenol glycoside, 3,5,7,4-tetrahydroxy-flavone-3-rhamoglycoside, an alkaloid , ethyl Dgalactopyranoside, p-hydroxycinnamic acid polypeptide, a highly basic proteinfinotin, a bitter acid resin, tannic acid, 6% ash and a toxic alkaloid	Anti-inflammatory, cathartic and purgative

THE DIFFERENT STAGES OF THE WOUND HEALING MECHANISM

Wound healing occurs throughout the body's tissues and organs. A large number of theserestorative processes can be identified in all body tissues [11].Healing is a continuous process encompassing multiple immunological and biological mechanisms interacting in conjunction.A range of rigorously and perfectly regulated mechanisms

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and functions that correlate to the emergence of distinct cell forms in the wound bed are required at particular phases of the healing mechanism.Followingare four timereliant stages that emerge in acute tissue healing as a response of tissue trauma- hemostasis, inflammation, proliferation, and restructuring[12].

a. Hemostatis

While the skin is injured, the body's natural approach is to tighten the artery borders to prevent the haemorrhage.After that, two concurrent and mechanistically associated systems facilitate fundamental and subsequent hemostasis [13].Platelet clumping and the development of platelet stumps underneath the sub-endothelial composite are necessary for principal hemostasis.Secondary hemostasis occurs when the coagulation pathway is activated, resulting in the conversion of absorbable fibrinogen into insoluble threads which constitute the fibrin lattice[14].The platelet clog and fibrin grid combine to form a thrombus, which inhibits bleeding, emits complements and growth regulators, and serves as a provisional substrate for wound-healing tissues to infiltrate[15].

b. Inflammation

The inflammatory response occurs shortly after the trauma and can endure somewhere between 24 and 48 hours, with certain incidences enduring up to two weeks [16]. The inflammatory stage initiates hemostatic mechanisms to reduce bleeding at the wound area soon. As an outcome swelling, skin irritation, redness, and discomfort, are therapeutically recognizable primary indicators [17]. Vasoconstriction and platelet agglomeration induce blood clotting, which is followed by vasodilation and phagocytosis, which tends to cause inflammation at the wound area [18].

c. Proliferation

Once the enduring injury has completed, hemostasis has been accomplished, and an immunological response has been adequately developed the acute wound progresses toward tissue regeneration. The proliferative phase of the inflammation consists of migration of the certain fibroblasts [19]. That fibroblast used to contains in the freshly produced ECM (Extra cellular matrix) and act as the substitute for the protein fibers such as fibrin and fibronectin. These protein fibers are interlinked through the certain channels of the collagen which act as filling over the particular muscles [20]. This phase starts on the third day following the lesion and would last for around two weeks.An enormous amount of granulation tissue production can be seen at the macroscopic phase of wound healing.

d. Remodeling

The last phase of wound healing phase consistsof deterioration. The deterioration continues takes place in the tissue while other i.e. epidermis of the skeleton muscles, dermal vasculature, nerves, and myofibers being altered during this process. This process makes the tissue being raptured and malfunctioned [21].

The vascular elements of granulation tissue fibroblast and myofibroblast are decreased, and PBMC cells drop dead or depart the region. Consequently, the concentrations of glycosaminoglycans and proteoglycans that are complex and hydration-related are diminishing[22].Type III collagen in granulation tissue is destroyed by collagen metalloproteinase which are developed by fibroblasts and macrophages, and are replaced by Type I collagen, which is then reorganized into parallel strands, leading in a low-cellularity scar. It will require months to finish the last phase [23].

PATHOPHYSIOLOGY OF WOUND HEALING

Wound healing treatment through ClitoriaTernatea Plant

There has been an upsurge in research in evaluating the efficacy of plant extracts in wound healing throughout the last two years, as well as discovering more about the bioactive elements that stimulate or regulate the curing mechanism[24]. Following are the primary impacts of the efficient elements of plant extracts on wound healing:

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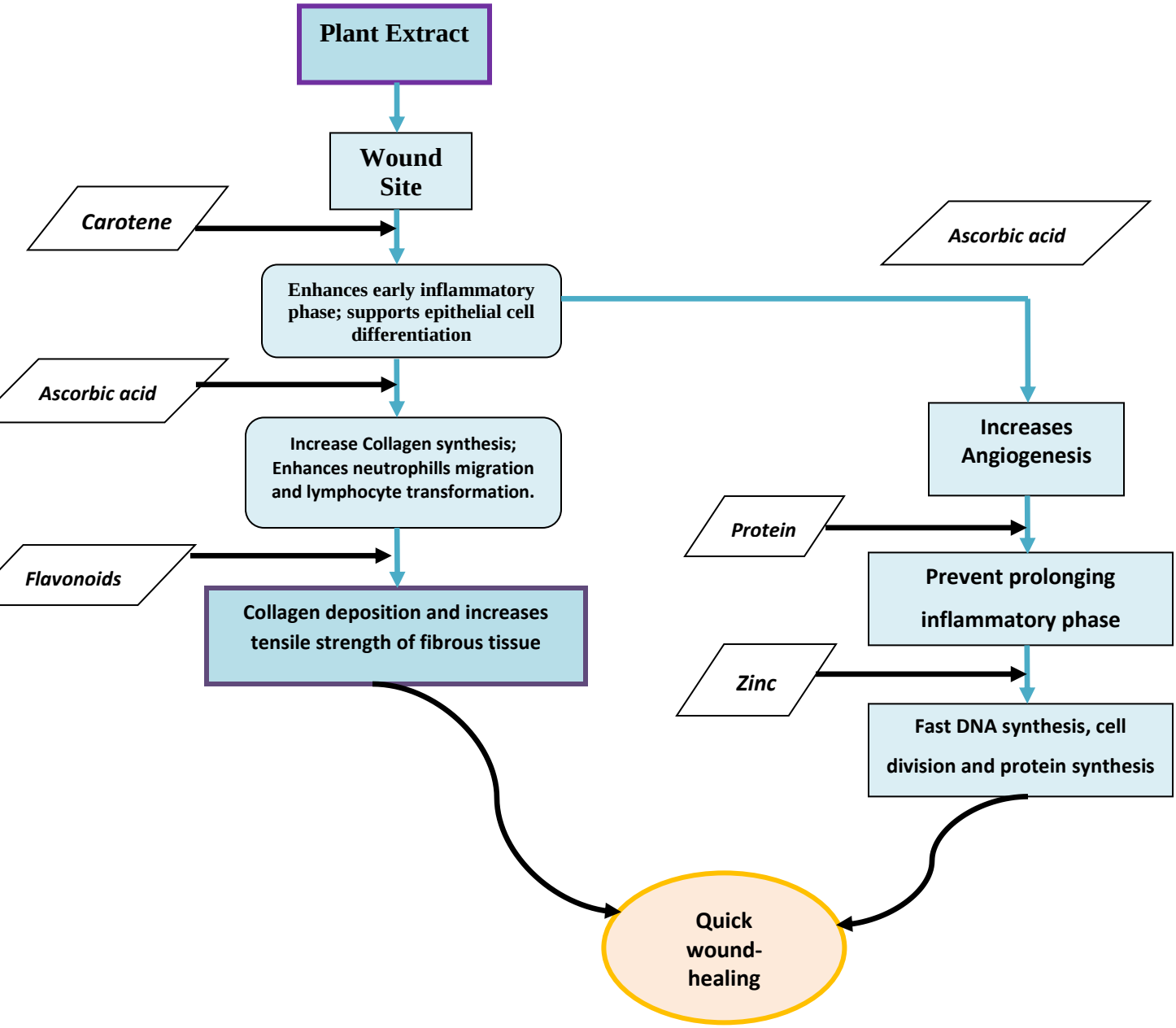

Fig.1- Wound healing mechanism of ClitoriaTernatea

- Components of phytochemical that contribute to antibacterial activity.
- Antioxidants and free radical scavengers in phytochemical components.
- Mitogenic activity (which contributes to accelerated cell reproduction), angiogenesis, collagen formation, and DNA replication are all significant constituents [25].

To demonstrate enhanced potency, active compounds contained in plant extracts should be expected to conflict with one or more stages of the wound healing mechanism in a constructive approach in the genuine essence and at an opportune moment (fig.1) [26].

Recently, the discovery of secondary metabolites in plant extracts which could connect to cellular receptors at the wound area and trigger wound healing mechanism regulation has been investigated. The plant possesses pro-anthocyanidins, polyphenolic flavonoids, and polyphenols, which are thought to support the healing procedure by reducing superoxide anions and eventually by increasing

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the manifestation of vascular endothelial growth factor (VEGF), which improves angiogenesis and blood flow as the repair develops [27].

Because of elevated fibroblast function in rejuvenated wound tissues, CT extract is thought to accelerate wound contraction. During the initial phases of wound healing, there has been a record of an elevation in the fabrication and concentrations of extracellular matrix protein and substances such as collagen, hexosamine, and uric acid, accompanied by a restoration toward routine amounts [28].CT enhanced the dynamic rigidity of the wound, resulting in greater collagen generation and accumulation. The tensile strength of triple halix collagen is determined by the Vander Waals forces interference among the hydrogen ion bonds that causes winding of the collagen fibers [29]. The stronger the winding of such fibers, the higher the compressive stiffness and hence the quicker the wound healing [30].

OTHER MAJOR PHARMACOLOGICAL USES OF CLITORIATERNATEA PLANT

Nootropic Activities

Several studies have reported that this plant contains the phytochemical which act as the booster for the brain Clitoriaternateawhen the extract administered orally to the animals Uddin, M. S., et al, 2001)[31]. In other study the Jain, N. et al, 2003 has demonstrate the effects of methanolic extract of the Clitoriaternateaoncognitive behavior, anxiety, depression induced by the maximum electroshock [32]. The extract of Clitoriaternateawas found nootropic, anti-stress and anti-depressant. Furthermore, Damodaran, T., et al, 2020 identified the Clitoriaternatea is the potential treatment for the cognitive decline using root extract of the Clitoriaternateain the Sprague Dawley rats. The doses were given to the animals for 28 days and subjected to the behavioral assessments. The root extract at 200 and 300 mg/kg restored the memory impairments [33].

Anti-inflammatory and analgesic Activity

Both the activities of Clitoriaternatea was examined by the Devi, B. P., et al, 2003. Ethanolic extract of the root was administered to the mice and observed the effects. Writhing response was induced by the acetic acid and was subjected to examine the number of writing. Less number of writhing was noted in the groups which were administered root extract at 200 and 400 mg/kg (p.o.) in mice [34]. The one more investigation was done by Swathi, K. P., et al, 2021 in the Wistar rats. The inflammatory model was used to assess the activity of the Clitoriaternatea. Ethanolic extract of Clitoriaternatea was prepared and administered in arthritic induced Wistar rats. The arthritis was induced by single injection of Freund's complete adjuvant. The results showed the significant improvement in the arthritis after examined the biochemical parameters (TNF alpha and interlukins), hematologicalsuch as hemoglobin, red blood cells and white blood cells and anti-oxidant parameters. The results showed the significant improvement at 200 and 400 mg/kg dose when compare to Diclofenac[35].

Antioxidant

Antioxidant activity ofClitoriaternatea was assessed by the Kamkaen, N., & Wilkinson, J. M. (2009). Clitoriaternatea plant flower is used in the cosmetic in many regions of the Asia and other parts of the world. Aqueous extract was prepared of flower petals and examined the antioxidant properties using DPPH scavenging activity. Results suggested that the antioxidant properties was less to the reference standard but comparable to the marketed cosmetics [36]. Furthermore, Iamsaard, S.,et al, 2014 assessed the antioxidant activity of the Clitoriaternatea leaves against the ketoconazole induced toxicity in the male rats. The result showed the significant increase in the sperm concentration, diameter of testis, and testicular tyrosine phosphorylation by immunoblotting[37].

Antidiabetic activity

Antidiabetic activity of the Clitoriaternatea was performed by the Rajamanickam, M., et al, 2015, in alloxan induced diabetes in albino rats. The blood glucose level and biochemical level was analyzed and compared the results with standard. The analysis was supporting the hypothesis as it can lower the blood glucose level in the diabetic rats [38]. Another study was performed by the Minelko, M., et al, 2020, as Clitoriaternatea was also used in the ayurvedic medicines in the treatment of diabetes for long time. This study was done to evaluate the inhibition of α-amylase activity in vitro and blood glucose monitoring in vivo. The results indicated the Clitoriaternatea plant does have the potential benefits in the treatment of type-2 diabetes[39].

Anthelmintic Activity

Alnaz, A. R. M., et al, 2021 examined that apart from the other benefits of the Clitoriaternatea flower, it does possess the anthelmintic activity too. As the flower contains majorly alkaloids, flavonoids and glycosides which possess the other activities besides that these phytochemicals works against the parasites by paralyzed them. Flowers extract were prepared and diluted 1:10 ratio for each dose concentrations. The results showed the significant increase in the Anthelmintic activity [40].

Other treatment options for Wound healing

In the beginning chronic wounds are often treated and covered with bandages and dressings for wounds. If the

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wound isn't healed for a long period despite all the wound treatment specific treatments like skin grafts or closures using vacuum are utilized. If someone is suffering from an injury that lasts lasting more than eight weeks and there is no sign of healing, it's thought to be an ongoing wound [41].

These types of wounds typically are the result of inadequate blood circulation or diabetes, or an insufficient immune system. Wounds that are open in the leg's lower part are called venous leg ulcers. Alongside taking care of the condition that is causing it and attending to the wound, relief from pain is essential. Certain people who have complex badly healing wounds can are also able to benefit from psychological counseling [42].

Cleaning the wound

The wound needs to be cleaned before the dressing is going to be changed or dressing up. The wound generally cleaned by the sterile water or saline solution which contains the salt. However, the cleaning solution does not help in the filling the wound but it can clean all the dead cells and other foreign particles [43]. Sterile water could be used if normal saline is not available, as it is not clear whether it does have effects or not. Cleaning wound often considered the cleaning of the cells and tissue so that outer layer of the wound comes out easily and filling of the wound by the medication starts quickly [44].

Debridement

During the infection the dead cells and tissues are often kept putting the layers on the wound and do not allow the wound to get cured. Before putting the medicines the wound needs to be get cleaned thoroughly [45]. The process of the removing the dead cells and tissue called as debridement. The dead cells and tissue are used clear by the surgical instruments i.e. curette and scalpel [46]. During this process the wound needs to be cleaned before and after. An enzyme based gel can be an option for the for this wound healing process, it helps to get clean wound easily [47].

Sometimes, the wound are painful and cleaning through the surgical instruments is not easy then ananesthetic is used to get rid of the pain [48]. Local anesthetic agents are used to numb the area to clean and remove the tissue and cells from the wound [49].

More extensive wounds can be cleaned with general anesthetic. There isn't enough research into the advantages and drawbacks of different methods of debridement to be able to determine the effectiveness of these techniques [50].

a. Wound dressings

Once the area has been cleansed and covered, it's covered with the bandage. The majority of wounds are treated with damp compressions. However, some dressings can be utilized in addition to:[51]

- Films
- Gauze
- Hydrogel dressings
- Hydrocolloid dressings
- Dressings that contain alginates or silver
- Foam dressings

The dressings are used to remove excess fluids from the wound as well as protect the wound from infection. They're typically kept on for a few hours. Dressings need to be changed if they are unable to absorb additional wound fluids, or should they fall off from the wound or leaks through the wound dressing. It's difficult to decide the appropriate dressings for wounds the best for different types of wounds because of the absence of reliable research on this issue[52].

There are other dressings that contain substances known as growth factor. These hormone-like products are designed to aid in healing processes by increasing the growth of cells in the body. However, there aren't enough scientific studies to determine whether treatment using the growth factor is superior to conventional treatment in treating diabetic foot ulcers, as well and any other chronic injuries of every kind[53].

Honey is typically used to treat wounds. However, applying honey specifically made before dressing the wound won't help to any degree. The effects of using honey for treating wounds on the legs have been investigated only by those suffering with ulcers in the leg however[54].

b. Antibiotics

Wounds are also more difficult to heal when they're contaminated by the bacteria. If the situation is how serious the condition is, antibiotics may be an option. It is possible to cover the wound using an ointment or apply it to the wound with compresses [55]. Initial findings from an investigation show that the wounds in people suffering from the condition known as diabetic feet heal more quickly. It's not clear whether this is the case for other injuries that are caused by other ailments [56].

It's not clear whether antibiotic tablets are beneficial. However, studies haven't shown that they're effective in healing wounds as compared with other options [57].

c. Hyperbaric Oxygen Therapy

The patient with the injured area is placed in a room to breathe oxygen under extremely high Pressure. This will increase the oxygen levels in their blood, as well as to increase the flow of blood towards the area of wound [58].

Research suggests that oxygen therapy using hyperbaric pressure can aid in the healing process for injuries suffered by patients with the foot condition known as diabetes [59].

d. Skin grafting

Skin grafts are thought of as an option for treatment if the wound is too large that it's not able to close by itself. In this method, the skin is extracted from another area of your

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body - typically the thigh area - and then transplanted to the wound [60].

Grafts are also available that are made of human cell components or synthetic material. Studies have proven that they improve the likelihood of healing leg ulcers, which heal quicker [61].

The wounds completely healed in six months

- 40 out of 100 patients treated with conventional methods, using wound dressings and
- 61 of 100 who received a skin graft.

The chronic foot wounds heal quicker after a graft to the skin than traditional treatment [62].

CONCLUSION

In this review article we have provided the comprehensive details of the Clitoriaternateaplant and its uses in several diseases. This plant used to grow in different habitats and cropping also done in many regions of Asia and other countries of the world. Clitoriaternateaplant itself a magical plant as it exhibits the significant roles in Ayurveda. Prominently, the cosmetic industry and food colorant industries are already approved its necessity. The approach of this review was identifying the relevance of the novel phytochemicals which are presents in this plant (root, shoot, leaves and flower). We anticipate the further development of novel approach of this plant in some other diseases which are not mentioned here. We anticipate the extracted enzymes and extracted phytochemicals from this plant shall encourage the more research on relatable diseases.

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