



ALOE VERA-THE HEALING WONDER TRADITIONAL PLANT FOR CUTANEOUS WOUND HEALING: AN INSIGHTFUL REVIEW

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Abstract

Aloe vera is an ancient, succulent plant which has been used for medicinal purposes for centuries. This versatile plant is known for its many healing properties, including the ability to promote cutaneous wound healing. Aloe vera is a well-researched medicinal plant that has been the subject of numerous studies for its wound healing potential. A cutaneous wound is a common type of wound that occurs on the skin, and it can vary in severity from minor cuts and scrapes to deep lacerations or puncture wounds. Aloe vera has been found to be an effective natural remedy for the management of cutaneous wounds, aiding in both the prevention of infection and promotion of healing. In conclusion, aloe vera is a traditional medicinal plant with remarkable wound healing abilities. Its effectiveness in the management of cutaneous and other wounds is well-established, and it is considered to be a safe and cost-effective alternative to conventional wound healing agents. A growing body of evidence supports the use of aloe vera as a natural remedy for promoting cutaneous wound healing

Keywords: aloe vera, cutaneous, wound, healing.

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INTRODUCTION

Aloe vera, also known as Aloe vera Linn or Aloe vera barbadensis Mill. It is a one type of tropical plant that may be grown within hot, dry areas, such as Thailand. The mucilaginous tissue, known as aloe vera gel, found in core of aloe vera leaf is used to make a variety of cosmetics and pharmaceuticals. Since the Roman era, and maybe much before, aloe vera gel is utilised for a variety of purposes. One of the most benefits of using aloe vera gel in many nations is the healing of burn wounds. Aloe vera gel was included to Thailand's list of fundamental public health herbs as a treatment for burn wounds. According to several studies, aloe vera or one or more of its components may aid in the healing of wounds in a variety of animal models.^[1]

A recent systematic evaluation of 10 clinical research investigating the therapeutic efficacy of aloe vera for a range of conditions was conducted. They discovered that aloe vera which is used for oral may be helpful for lowering glucose or cholesterol levels. Its topical form useful for treating genital herpes and psoriasis, however it is ineffective as a radiation injury preventative.^[2]



Fig. 1.1



Fig.1.2

Fig.1.1: Aloe Vera Plant **1.2:** Aloe Vera Flower

Aloe vera's effectiveness for treating burn wounds was not included in the study, though. This systematic review sought to establish aloe vera's effectiveness in the treatment of burn wounds. A promising plant with numerous pharmacological effects is Aloe vera (L.). This plant is well-known as a therapeutic plant or slow healer and has historically been used in clinical settings to cure a variety of ailments.^[3]

Numerous active substances found in aloe vera plants, such as terpenoids, lectins, anthraquinones, tannins, saponins, and flavonoids, aid in the healing of skin burns and wounds and also have anti-bacterial and anti-inflammatory qualities. Aloe vera gel is frequently castoff as a moisturiser and in the creation of cosmetic items. Aloe vera extracts have additionally been utilised to treat hyperglycemic illnesses.^[4]

The organ which is largest in the body and the first line of defence against harm from the outside is the skin. It has distinct immunological networks and neuroendocrine functions and aids in the maintenance of bodily fluids and temperatures in humans. Also, the organism's sensory capabilities are crucial to how it interacts with its surroundings. Skin conditions are the fourth greatest cause of disability in the world, harming patients' bodies and minds as well as placing a heavy financial burden on society.^[5]

There are two types of skin injuries: acute and chronic. Whereas chronic wounds are alkaline (pH: 7.2–8.8), acute wounds are neutral or alkaline (pH: 6.5–8.5). Burns, blunt wounds, and piercing wounds, for example, tend to heal fast while chronic wounds like bedsores, venous leg ulcers, and diabetic foot ulcers take longer time to heal and are more prone to infection and inflammation. The most important aspects of treating skin injuries are to protect the epidermis, the skin's outermost barrier, halt bleeding, moisturize, and reduce discomfort. However, the issues of wound contraction, fraft fragility and scar formation cannot be resolved by the epidermis cover alone. Therefore, it is important to support epidermal transplantation with suppleness and strength as well as to encourage wound healing and skin regeneration.^[6]

HISTORY

Aloe vera has been used medicinally for millennia in a number of cultures, including India, Greece, Egypt, China, Japan, and Mexico. Cleopatra and Nefertiti, two Egyptian princesses, used it

frequently as part of their beauty routines. Alexander the Great and Christopher Columbus both used it to treat the wounds of soldiers. Aloe vera first appeared in a written form in John Goodyew's translation of Dioscorides' medical text *De Materia Medica* in A.D. 1655. By the early 1800s, Americans were already using aloe vera as a laxative, but something changed in the central of the 1930s when it was successfully utilised to treat severe and chronic radiation dermatitis. [7]

In recent decades, there has been a serious debate and challenge regarding the treatment for the patients with dermal wounds and skin healing among with dermatologist surgeons and experts in plastic surgery. The development of contemporary wound healing methods on the one hand, and the propensity to use the curative capabilities of medicinal herbs as a supplemental medicine on the other, have given rise to this controversy. [8]

VERNACULAR NAMES

Table 1: Vernacular Names

LANGUAGE	NAME
Hindi	Giloya
Kannada	Lolesara
Sanskrit	Kumari
Malayalam	Kattarvazha
Tamil	SoththuKathalai
English	Aloe
Assamese	Musabhar,Machamber
Bengali	Ghritakalmi, Ghrit-Kumari, Musabhar Kanya
Gujrat	Eliyo, Eariy, Kunvar, Kumarpathy
Marathi	Korphad, Korkand
Oriya	Mushaboro, Kumari
Punjabi	Kalasoehaga, Mussubar, Alua
Urda	Musabbar, Ailva, Sibr

TAXONOMICAL CLASSIFICATION

A. barbadensis Mill., *Aloe indica* Royle, *Aloe perfoliata* L. var. *vera*, and *A. vulgaris* Lam. are a few synonyms for the species. Chinese aloe, Indian aloe, true aloe, barbados aloe, burn aloe, and first aid plant are some of its common names.

"True" or "genuine" are the meanings of the species name *vera*. It has been suggested that the spotted variety of *Aloe vera* may be conspecific with *A. massawana*, despite the fact that the species can vary widely in terms of leaf spots. Some literature names the white-spotted variant of *Aloe vera* as *Aloe vera* var. *chinensis*. *Aloe perfoliata* var. *vera* was the species' original name when it was originally reported by Carl Linnaeus in 1753. Ten years later, in 1768, *Aloe vera* was the name given to the plant by Nicolaas Laurens Burman for it in *Flora Indica*, and ten days later, Philip Miller named it *Aloe barbadensis* in the *Gardener's Dictionary*. [9]

Aloe vera is thought to be rather closely related to the Yemeni indigenous *Aloe perryi* species, according to methods based on DNA comparison. *Aloe forbesii*, *Aloe scobinifolia*, *Aloe inermis*, *Aloe sinkatana*, and *Aloe striata* are all believed to be close relatives of this plant based on similar methodologies such chloroplast DNA sequence comparison and also ISSR profiling. All of these *Aloe* species which are indigenous to Socotra (Yemen), Somalia, and Sudan with the exception of the South African species *A. striata*. Because there aren't any evident natural populations of the species, several writers have hypothesised that *Aloe vera* might be a mixtureherbal.

CHEMICAL COMPOSITION OF ALOE VERA

Because aloe vera is a juicy plant and can stock a significant amount of water in its interior tissue, water makes up between 99 and 99.5% of its chemical components. The remaining portion is made up of a variety of fat- and water-soluble elements, such as vitamins, polysaccharides, phenols, sterols, minerals, amino acids, enzymes, and other organic compounds. About 55% of aloe gel is made up of polysaccharides, 17% of it is sugar, 16% of it is mineral, 7% is amino, 4% is fatty, and 1% is phenolic. Anthraquinones and glycosides make up the majority of the yellow bitter latex's chemical makeup.

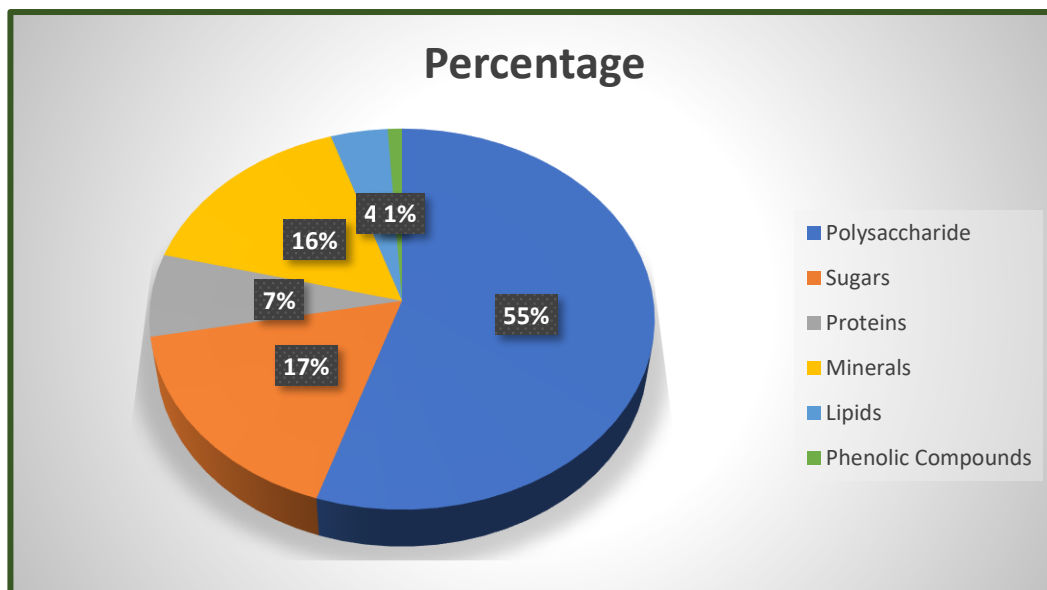


Fig.2: Chemical Composition of Aloe Vera

Species, climatic circumstances, and the growth environment all affect the chemical composition of aloe vera plant. It had been hypothesised that Aloe vera gel's diverse composition may be a factor in both its medicinal and psychoactive characteristics. The leaves of aloe vera contain more than 240 bioactive compounds with therapeutic and dietary benefits.[10] Complex chemical composition can be found in aloe vera gel. In addition to vitamins, enzymes, minerals, carbohydrates, lignin, saponins, salicylic acids, and amino acids, aloe vera also contains 75 potentially active substances. [11]

The detail is as follows:

1. CARBOHYDRATE FRACTION

The complex polysaccharides polyhexoses and a few more trace amounts of xylose, hexans, arabinose, galactose, mannose, and glucose are found in the aloe vera gel fraction. Hexuronic acid is present in high concentrations in a number of pectic polysaccharides, including mannuronic, glucuronic, and galacturonic acid, which when hydrolyzed yields glucose, mannose, and minute amounts of galactose, arabinose, and xylose. The predominant polysaccharide is acetylated glucomanan, which has a roughly 15:1 mannose: glucose ratio. [12] The primary therapeutic component of aloe vera gel is acemanan, which is the juice's core. Its average molecular weight is 105 daltons. It is only possible to appropriately describe items as aloe vera if they include acemanan or 1-4 acetylated glucomanans. The degree of acetyl substitution in the glucomanan is larger than 0.71 per sugar residue. In glucomanan, some sugar residues have undergone double or

even triple substitution. In a polysaccharide that is typically hydrophilic, they become extremely hydrophobic. [13]

2. CHROMONES

Chromones are leaf exudations compounds predominantly reside in pericyclic cells beneath of the leaf skin. Because of their colour and GI irritability, chromones are disregarded as contaminants. Derivatives of 8-Cglucosyl-7 hydroxy-5 methyl 2-propyl-4-chromone are chromones. Cinnamoyl, coumaroyl, caffeoyl, feruloyl, and tiglyl are examples of substituted acyl groups. The degree of oxidation in propyl side chain, the methylation of -OH groups in the C7 side chain, and esterification of the glucose fraction cause variations in chromones. Aloesin is thought to be the parent substance of all aloe chromones. Numerous structures with anti-inflammatory and anti-ulcer properties can be found in aloe chromones. Laxative action, protection of the skin. [15]

3. ALKALOIDS

Aloe vera has been said to contain a few alkaloids. Dragendroff responds well to an aloe vera distillation extract. [14]

4. ANTHRAQUINONE GLYCOSIDES

When a fresh leaf is split open from the base, several anthraquinone glycosides are present. These are hydrophobic and have low molecular weights. Because they are related, these substances work better together. Barbaloin (aloe emodinanthrone C10 glycoside) is the essential one. It acts as a harsh purgative. According to some authors, aloin's impact might result from its

biotransformation into aloe emodin (1, 8-dihydroxy-3-(hydroxymethyl)-9, 10-anthracenedione) in the gut.^[16] Aloe species include free anthraquinones and anthrones, with roots and underground stems making up the majority of these compounds. Aloe roots contain the anti-helminthosporine anthraquinone. Aloe saponaria contains aloesaponarin II, an isomer of chrysophanol in which the positions of the groups on the carbon atoms 1 and 3 are switched. Aloe saponaria also contains deoxyerythrolaccin, a 6-hydroxy derivative. Flowers from aloe plants contain chrysophanolanthrone. It is uncommon to have anthrone -O-glycosides listed as an aloe component. Aloe emodin-o-galactoside and aloe emodin-11O-rhamnoside are two of the few O glycosides discovered. 11-O-rhamnosyl aloe emodin and 7-O glucosylnataloe - emodin.^[17]

5.LECTINS

Aloe was originally shown to have a lectin-like protein in 1978. Lectins are distinguished by their hemoagglutinating (cell agglutinating) abilities. Polysaccharides, glycoproteins, and glycol lipids are precipitated by lectins that have at least two sugar binding sites. Lectins are mostly used for analysing the chemical composition of cell surfaces and malignant cell transformations. The lectins Aloctin A and Aloctin B were isolated from *Arborescens*, one of the most extensively researched lectins in aloe.^[19] Hemagglutinating and mitogenic ac are present in alotin A. Aloe extracts form an acidic precipitate known as alotin A. Aloctin B is a component of aloe extracts' acidic supernatant that has hemagglutinating properties.

6.PHYTOSTEROLS

The three most prevalent examples are campesterol (4-desmethyl sterol), stigmasterol, and sitosterol. The suppression of absorption and subsequent compensatory promotion of cholesterol production is one of the main roles of phytosterols in diet. In general, they are thought to be a type of functional factor that could lower blood cholesterol and LDL-C levels. With regard to decreasing serum cholesterol, -sitosterol is the most effective type of phytosterol. ^[18]

7.OTHER COMPONENTS

The Aloe Vera leaf gel contains a variety of compounds, including cardiotoxic, saponins, tannins, cardiotoxic glycosides, terpenoids (limonene, myrecene), isoprenoids, polyphenols, sulphur derivatives, salicylic acid, organic acids such as succinic, malic, lactic, and p-coumaric

acid, aloctin, magnesium lactate, and biological growth factors like auxins and gibberellins. Among the amino acids present in this substance are arginine, histidine, lysine, aspartic acid, threonine, serine, glutamic acid, proline, glycine, alanine, valine, methionine, isoleucine, leucine, tyrosine, and phenylalanine. Vitamins A, B1, B2, B4, B6, and B12 are present. Both the inside gel and the outside skin of aloe leaves include isoenzymes, such as superoxide dismutase.^[20]

- **Saponins**-When combined and stirred with water, these produce soapy lathers. They are antimicrobial and have been used as foaming agents and detergents.
- **Lignin**- The only known medical benefit of this cellulose component, which is included in the gel, is that it can penetrate human skin.
- **Anthraquinones**-Aloin, Isobarbaloin, Emodin, Anthracene, Ester of Chrysophanic Acid, Cinnamonic Acid, Barbaloin, Anthranol, Aloetic Acid, Aloe Emodin, Ethereal Oil, and Resistannol are the 12 substances that can be found in aloe vera sap. These have potent antibacterial, antifungal, and virucidal activities in addition to acting as natural painkillers, laxatives and analgesics.
- **Minerals**-The following minerals are found in aloe vera: Calcium is necessary for healthy bone and tooth density. A constituent of enzymes required for the initiation of other enzymes is manganese. Sodium: (assures that the body's fluids don't become either acidic or very alkaline). Copper: (allows iron to function in red blood cells as oxygen transporters. Magnesium is a mineral that helps the membranes of the neurons and muscles conduct electrical impulses. Potassium: (controls the amounts of acidity or alkalinity in bodily fluids). Zinc: (helps in the breakdown of proteins, carbs, and lipids); Chromium: (important for insulin's efficient operation, which in turn regulates blood sugar levels). Iron: (manages red blood cells' ability to carry oxygen throughout the body. ^[21]

Table 2: Percentage of Minerals In Aloe Vera

S. No.	Minerals	Aloe Vera(Whole Leaf) %
I	Sodium	3.67
II	Calcium	3.6
III	Magnesium	1.22
IV	Iron	0.2
V	Potassium	0.01
VI	Copper	0.05
VII	Zinc	0.03
VIII	Phosphorous	0.01

- **Sugars**-Both monosaccharides, such as fructose and glucose, and polysaccharides can be found in aloe vera. The most significant sugars are those that contain polysaccharides. They support healthy digestion, keep cholesterol levels in check, enhance liver functions, and encourage bone growth.
- **Vitamins**-Many vitamins are found in aloe vera, including vitamins A, C, and E (vital antioxidants that protect the body from harmful free radicals). Vitamin B and choline (important for generating energy, metabolising amino acids, and building muscular mass). Vitamin B12 and folic acid both aid in the development of new blood cells and the creation of red blood cells, respectively.
- **Sterols**- Important anti-inflammatory compounds include sterols. Cholesterol, Sitosterol, Campesterol, and Lupeol are the ones that can be found in aloe vera. These sterols

have analgesic and antibacterial qualities. They also possess aspirin-like painkilling effects.

- **Enzyme**-Enzymes are naturally occurring protein molecules with very specialised catalytic roles in biological reactions that are formed by all living things, including microbes, plants, animals, and people. Like all other proteins, enzymes are comprised of amino acids, yet unlike other proteins, they have the rare ability to speed up metabolic processes without altering their own structure or nature. The most significant enzymes in aloe vera include catalase, peroxidase, amylase, lipase, cellulose, carboxypeptidase, and alkaline phosphates. [8]
- **Amino Acids**-Protein's amino acids serve as the building blocks for muscle tissue growth and repair. The human body needs 22 amino acids, of which 8 are essential. Aloe vera contains 7 of the 8 essential amino acids and 20 of the necessary amino acids.

Table 3:Percentage of Amino Acids In Aloe Vera

S. No.	Amino acid	Aloe vera(whole leaf)
A	Glutamic acid	4.7
B	Asparagines	3.29
C	Aspartic acid	1.75
D	Glycine	1.00
E	Glutamine	0.80
F	Serine	1.25
G	Threonine	0.34
H	Valine	0.36
I	Alanine	0.92
J	Proine	0.25
K	Methionine	0.02
L	Histidine	0.04
M	Tryptophane	0.00
N	Tyrosine	0.07
O	Cystine	0.05
P	Lysine	0.18
Q	Leucine	0.10
R	Isoleucine	0.07
S	Arginine	0.13
T	Phenylalanine	0
Total	Concentration	(nMol/mg dry mass) 15.33

WOUND HEALING, CELL SIGNALING AND CLASSIFICATION

Burning is a type of tissue trauma caused by exposure to heat, chemicals, electricity, sunshine, and/or radioactive radiation, among other things. The majority of burning incidents are brought on by structure fires, contact with hot liquids, steaming water, and flammable gases. The primary cause of death and disability in the victims is thought to be burning brought on by heat, accidents, and other similar events. Every year, two million persons who experienced scorching trauma required medical care. To stop

infectious materials from penetrating the wound, the common of initial therapies, including medicine topical dosage, are used. Patients who have experienced scorching trauma may live longer and experience better quality of life thanks to advancements in wound care and tissue regeneration techniques.[8]

The intricate process of treating cutaneous wounds is the consequence of cooperative function among the many tissues with numerous cellular colonies. Each type of functional cell has had its behaviour described using a combination

of migration, proliferation, matrix creation and contraction, phases and growth factors, and the current matrix signals in the wound site. [22] To treat injury following trauma, a variety of typical occurrences may take place. The cells behind dermis begin to generate collagen as a result of an inflammatory reaction brought on by trauma, and this process continues all the way up to the completion of the epithelium's growth. Any form of trauma to the skin or other body tissues can cause a sequence of molecular and cellular reactions. Thrombosis, inflammation and proliferation and the growth of new tissue, and tissue retrieval are the three stages of wound healing. [23]

Growth factors of different sorts, such as epidermal growth factors (EGFs), fibroblastic growth factors (FGFs), transforming growth factors (TGFs), and insulin-like growth factors (IGFs), regulate crucial cellular signalling processes and extracellular matrix activities in the healing process. The peptides in the insulin-like growth factor are known as somatomedin-C because they stimulate the release of growth factor hormone and have a structural sequence that is extremely similar to that of insulin. These substances function in a variety of paracrine, autocrine, and endocrine ways. [24] In healthy skin, only a small percentage of the dermis and epidermis cells secrete insulin-like growth factors (IGFs), but with dermal trauma, they are secreted by the majority of epidermal cells, including platelets and macrophages. This group of growth factors also affect the angiogenesis trend in addition to stimulating mitogenic fibroblasts. Other studies have demonstrated that IGFs play a

significant part in the process of wound healing by increasing the thickness of the epidermis and dermis, together with other substances including platelet-derived growth factors (PDGFs). In the epidermal basal layer, the rate of IGF gene expression is minimal, but it significantly grows for one to three days after the wound happens. [26]

CLASSIFICATION OF WOUND

Acute wounds and chronic wounds are the two categories into which wounds are classified based on the quality and length of the healing trend. Acute wounds are referred to as a set of injuries since they are often superficial and heal entirely in 8 to 12 weeks. The term "chronic wounds" refers to a collection of wounds that heal slowly and take more than 12 weeks to do so. These wounds continue and frequently recur. These wounds are caused by certain diseases, such as cancer and chronic infections, as well as by certain physiological situations, such as wounds that diabetes individuals experience. This category includes foot wounds with ischemic, venal and traumatic aetiology. [27]

PHASES OF THE WOUND HEALING

Cellular, subcellular, physiological, and biochemical processes all work together as part of the healing mechanism to heal wounds. [28] It involves four main phases: Hemostasis Phase, inflammatory phase, proliferative phase, and tissue remodeling phase. These stages aren't discrete under usual circumstances. However, when they begin because of a physical ailment, they must continue all the way through in order to fully heal. [29]

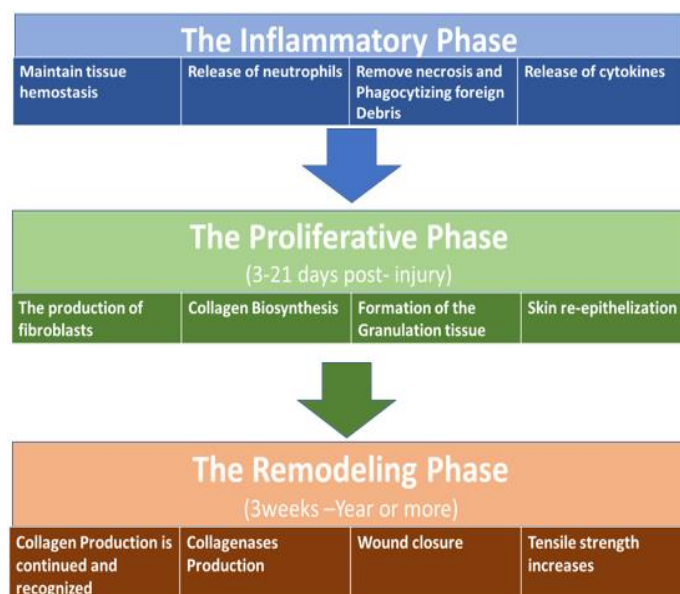


Fig No.3: Phases of the Wound Healing

1. The Hemostasis Phase

Hemostasis, which begins as soon as an injury occurs and is the initial step of healing, aims to stop the bleeding. At this point, the body starts to clot the blood, kicks on its emergency repair system, and builds a dam to stop the drainage. Activation and aggregation are brought on by the interaction of platelets with collagen during this phase. An enzyme called thrombin, which is present in the centre, kick starts the formation of a fibrin mesh and strengthens the platelet clumps into a stable clot.^[30]

2. The Inflammatory phase

The inflammatory phase begins right after the injury incident and lasts for around four days. It primarily achieves two key objectives. The first is to maintain tissue hemostasis, which can be done through smooth muscle cell contraction, sealing of the big blood vessels that have burst, and platelet build up to thrombose the smaller injured capillaries. The removal of impurities, germs, and other harmful debris from the wound is the second objective.^[31] Immediately after the occurrence of a wound, polymorphonuclear leukocytes (neutrophils) migrate from the nearby microvasculature and carry out this task. At the site of wounds, neutrophils appear to be transient cells that die within a few hours. However, some researchers hypothesised that neutrophil behaviour is more complex and that they might return to the local vascular. About two days after the injury, a different type of cell called macrophages emerges at the wound site. These cells function to clear out foreign debris, phagocytizing bacteria, and necrotic tissue. Angiogenesis and fibroplasia, two significant processes in the healing process, are also started by macrophages. The cytokines that the activated macrophages produce are responsible for mediating these actions.

Collagen synthesis and fibroplasia take place between the third and fifth day after wounding, while angiogenesis starts three days after injury and is necessary to meet the metabolic requirements of the healing process.^[32]

3. The Proliferative phase

Three weeks after the injury, the proliferative phase might continue. Angiogenesis factors (AGF) and fibroblast stimulating factors are released by the activation of macrophages. The proliferative phase of the cell cycle depends on the proliferation of fibroblasts, which is facilitated by fibroblast stimulating substances. The

fibroblasts in turn create proteoglycans and collagen. AGF encourages the development of capillary buds and new blood capillaries. The granulation tissue that fills wound defects is made up of neovasculature, collagen, and proteoglycans. Collagen synthesis boosts the tensile strength of wounds.^[33]

Due to the wound's contraction, the wound's boundaries are closer to one another, reducing the damaged area. Myofibroblasts, a particular variety of fibroblast with a contractile character, mediate this process. The re-epithelization procedure, in which the surrounding epithelial cells actively proliferate and migrate over the granulation tissue to join both ends of the wound, is also a part of the proliferative phase. Re-epithelialization is an essential step in the healing process because the newly formed epithelial tissue serves as a physical barrier against microbial and pollutant incursions from the outside environment as well as preventing body fluid leakage. The size of the wound has an immediate impact on how quickly it closes since larger flaws take longer to repair because migrating epithelial cells must^[34]

Additionally, epithelial cell migration is facilitated on a moist wound surface, whereas it is inhibited on a dry surface. Therefore, the main objective of novel wound dressing chemicals is to give the wound a moist milieu to encourage re-epithelization.

4. The Remodeling phase

The healing process ends with the remodelling or maturation phase. It starts about three weeks after the wound and could linger for over a year. During this stage, fibroblasts continue to produce collagen. Collagenases are a set of enzymes secreted during this phase that work to lyse collagen bundles made during the proliferative phase and re-arrange them in a parallel layout. During this stage, the wound is still healing and the tensile strength is gradually increasing. The amount of collagen production and the degree of crosslinking between adjacent collagen bundles determine the final strength of a healed wound. The wound reaches its maximum tensile strength at the conclusion of the maturation phase, which is generally^[35]

Wounds usually recover between four to six weeks. Chronic wounds, however, do not heal in this time frame. Diabetes, hypoxia, ischemia, bacterial infection, errors in collagen synthesis,

malnutrition, smoking, and dehydration are just a few of the conditions that can hinder healing.

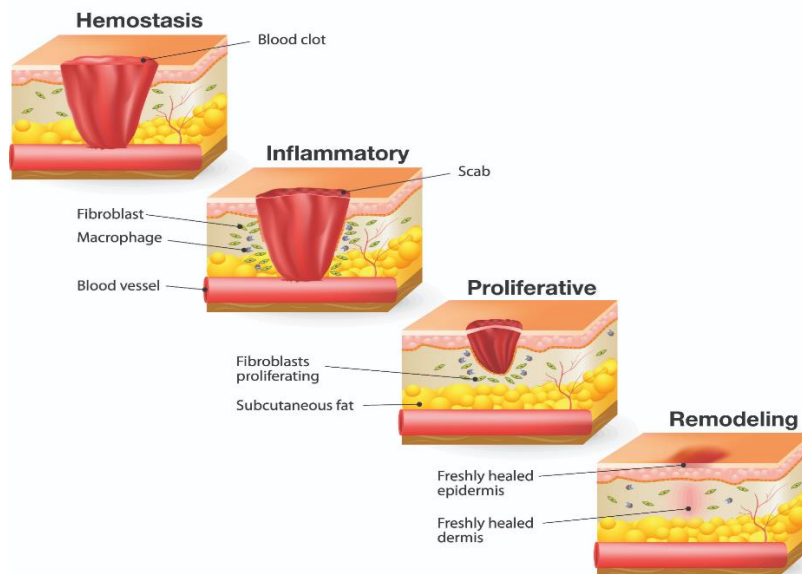


Fig.4: Four Phases Of Wound Healing [41]

ROLE OF ALOE VERA IN WOUND HEALING

Numerous research are taking into account the usage of aloe vera in wound healing. This plant has been used medicinally for millennia. saccharides, anthraquinones, vitamins C and E, zinc, acetyl salicylic, enzymes, and other substances are present. The primary carbohydrate

fraction removed from aloe vera leaves is acemannan. This fraction possesses immune-stimulating, antiviral, and anticancer properties that aid in wound healing. Aloe vera influences a number of wound-healing variables and encourages healing. [42]



Fig.5: Role of Aloe Vera in Wound Healing

The Role of Growth Factors

The majority of cells create growth factors, which are large proteins that start paracrine and auto

crine auto cascading mechanisms in a variety of cellular activities as they are secreted. One might mention the transforming growth factor TGF- as

one of several efficient growth factors in the tendency of wound healing. TGF- is released from the site of the wound after tissue trauma by platelets degranulating. Cutaneous damage results in the appearance of TGF-1 with platelet origin on the wound point, which led to advancement in the trend of wound healing.^[43]

TGF-1 has increased the ability of human skin fibroblasts to undergo mitosis. TGF- increases the appearance of angiogenetic factors like VEGF in epithelial and fibroblast cells, which increases the angiogenesis tendency in different tissues. TGF-promotes angiogenesis, fibroblast growth, my ofibroblast differentiation, and extracellular matrix synthesis. On the site of a skin wound, TGF-1 controls and boosts 2- FGF genetic expression. Throughout this course, other studies have demonstrated how -sitosterol, one of the components of aloe vera mucilage, has improved healing of damaged tissues by accelerating the rate at which VEGF and its receptor are expressed genetically at the site of injury. The mannose sugar present in the aloe vera compound excites

these cells to produce cytokines and advance in some stages of wound curing after connection with the specific receptor located on the surface of skin macrophages, according to in vitro experiments on the stimulation of macrophages in damaged tissues. In this regard, Trade Name of Acemenan has been regarded as a medicinal compound for a class of mannose-rich polysaccharides found in aloe vera mucilage.^[8]

Rats exposed to a form of radiation may produce more bFGF and TGF-1 in the wound on their skin after taking an oral dose of aloe vera mucilage. Aloe vera mucilage applied topically to rats' wound points has sped up wound healing, thrombosis, and wound point contraction. In this study, it was discovered that applying aloe vera to the skin improved angiogenesis, granulation tissue, and collagen placement at the site of wounds. ^[44]The shear wounds in desert rats and rabbits have healed after topical application of aloe vera mucilage.

Table 4: The Role of Growth Factors

Compositions	Effects on gene levels and cytokine	Functions on cells and tissues	Effects on collagen levels and glycosaminoglycan
Aloe vera	bFGF↑ TGF-β1↑ MDA↓ TNF-α↓ VEGF↑ IGF-1↑ FGF-2↑GLUT-1↑	Promote fibroblast proliferation and angiogenesis Reduce inflammation period	Promote collagen deposition and synthesis
Acemannan	Cyclin D1↑ VEGF↑	Change the cell cycle from the G1 phase to S phase Promote the proliferation of skin fibroblasts	Promote the fusion of type I collagen
Aloe Polysaccharides	IL-10↓ IL-5↓ MMP-9↓ MMP-3↓TIMP-2	Affect the development of granulation tissue and wound healing	Promote the production of collagen and glycosaminoglycan
Mannose-6-phosphate	TGF-1↓ TGF-2↓	Promote skin regeneration, fibroblast proliferation and Reduce scarring	Promote collagen synthesis and deposition
Aloe emodin	COX-2↓EGF↑ VEGF↑ iNOS↓	Inhibit inflammation and promote wound healing	
Aloin	EGF↑ GSH↑ SOD↑ TNF-α↓ COX-2↓ caspase-3↓	Promote angiogenesis and fibroblast proliferation Decrease the formation of scars Inhibit inflammatory response	Make the collagen fibers of skin more regular
Glycoprotein		Promote epidermal cell proliferation	
Rhein		Anti-inflammatory, antioxidant, and regulation of cell cycle	
Aloesin	Phosphorylation of Cdc42 andRac1	Promote angiogenesis and granulation tissue formation	Promote collagen deposition
β-sitosterol	VEGF↑ PGN↓TNF-α↓ NLRP3 inflammasome↓ caspase-1↓	Promote angiogenesis and wound healing Anti-inflammation	

The Role of Vitamins and Others

Aloe vera gel contains substances like vitamin C, vitamin E, and some amino acids that can show a significant role in accelerating the healing trend of wounds. Experiments have shown that vitamin C rises the production of collagen and inhibits the synthesis of these strands, while vitamin E acts as a potent antioxidant and also enters the healing trend. Aloe vera mucilage's antibacterial and anti-inflammatory properties contribute to the advancement of the wound healing trend. Glutathione peroxidase and superoxide dismutase are two antioxidant enzyme systems found in aloe vera mucilage that speed up the healing process by neutralising the effects of the free radicals produced on wound site and by acting as an anti-inflammatory. The diabetic foot wound in rats was lessened by application of aloe vera gel ethanolic extract. Aloe vera may be the best treatment for burn wounds, according to a different article. Topical administration of aloe vera improved the morphological, biochemical, and biomechanical characteristics of rats' healing cutaneous lesions. According to a clinical study analysis, aloe vera and calendula ointment hastens the healing of episiotomy wounds; as a result, it may be used to hasten the healing of episiotomies.^[8]

HEALING MECHANISM OF ALOE VERA

Its medicinal value is connected to glucomannan, a substance that is rich in polysaccharides like mannose. As a result of the glucomannan's impact on fibroblast growth factor and stimulation of these cells' activity and proliferation, collagen formation and secretion are enhanced. Aloe vera's mucilage speeds wound healing by both increasing the amount of collagen at the location of the injury and the transversal connections between these bands rather than changing the structure of the collagen.^[37]

From the early beginning, the use of medicinal herbs in wound care has been noted. People are aware of these plants because of the decreased financial burden and its therapeutic properties. Many skin lesions and burns are traditionally treated with a variety of plants around the world^[38]; They include plants like mountain germander, jujube, olibanum, and portulaca, whose effectiveness has been demonstrated through a trend in the recovery of burning wounds in rats. Aloe vera, among other plants, has a very long history of being used to treat burns and skin ailments. The results show that aloe vera treatment has faster the rising rate of expression in the genes

for vascular endothelial growth factor (VEGF) and TGF-1 in the area of wound in the skin of rats. It has been demonstrated that oral administration of aloe vera mucilage by the rat with diabetes type-II has faster the trend of healing of skin wounds in these animals. In this instance, TGF-1 spurred fibroblasts to more effectively than ever repair the extracellular matrix at the site of the wound.^[39]

Following the development of a skin wound, cells in the dermal area begin to produce more collagen and respond to inflammatory stimuli, which is followed by a reorganisation of the epithelial tissue. This is a physiological process, and a variety of factors, such as growth factors and cytokines, may affect the way it develops. The goal of wound healing is to treat it as quickly as possible while causing the patient as little pain, discomfort, and scarring as feasible.^[40]

• Effect on epithelisation

A key component of wound healing is epithelization; healthy epithelization is ensured by properoxygenation, hydration, and clearance of dead tissue. The water content of aloe vera is high (96%). This delays wound desiccation and promotes epithelial cell migration. Aloe increases oxygenation by enhancing the microcirculation of the wound. Catecholamines hinder the speed of wound healing. By reducing catecholamine activity, aloe improves epithelization. A histology investigation found that aloe vera improves the vascularity of the lesion, which promotes wound healing by eliminating dead tissue. Epithelial cell migration from the surrounding skin is encouraged by each of these pathways. Epithelization serves as a catalyst for ground substance depositing.^[41]

• Effect on collagenisation

Early closure, tensile strength, and the fate of the scar are all influenced by collagenization. Collagen's cross-linking is accelerated by aloe vera. Aloe-treated wounds had a low Type I/Type III collagen ratio, which suggests more Type III collagen. Aloe-treated wounds had high concentrations of dermatan sulphate and hyaluronic acid, the two primary components of ground material. Aloe may also promote the synthesis of macrophage cytokines, which may boost collagenization. Acemmamman stimulates macrophage activity. Through the growth factors it contains, aloe vera may also be able to prevent some substances like sterols and amino acids that hinder the healing of wounds. Aloe vera contains

ascorbic acid, which promotes collagen synthesis and balances collagen degradation. Aloe enhances wound healing by inducing the processes of inflammation, fibroplasias, collagen synthesis, maturation, and wound contraction, according to studies on diabetic rats. Additionally, it improves wound tensile strength. Aloe vera is utilised to treat herpes simplex infection, lichen planus, and gingivitis, according to other studies. Aloe toothpastes have been proven to reduce root irritation, according to reports. Aloe vera stimulates wound healing both on its own and through the actions of its ingredients. Given that it is natural, its adverse effects are minimal. Clinical suggestions demand additional study.^[42]

SIDE EFFECTS

Aloe vera is commonly regarded as an effective herbal remedy with therapeutic applications for both diabetic and non-diabetic wounds because of its remarkable healing properties. When compared to the alternative therapies which are currently available, aloe vera is thought to be significantly more successful and cost-efficient in terms of consistency and speed of wound healing. With topical use of Aloe vera, no severe adverse responses were seen. Yet, according to recent studies, aloe vera extracts may include hazardous substances and might have some negative effects.

- When Aloe vera is applied topically to cutaneous wounds, sensitive people may experience little, passing discomfort, stinging, burning, redness, and extremely uncommon cases of dermatitis. Anthraquinones are the principal cause of allergic responses. So, it would be wise to test any potential allergic reaction on a tiny area first.
- On the other hand, oral use of aloe preparations has been connected to a number of issues, including phototoxicity, hypokalemia, diarrhoea, pseudomelanosis coli, nephrotoxicity, and hepatotoxicity, in addition to phototoxicity and hypersensitive reactions.
- Moreover, Aloe vera whole leaf extract was identified as a potential carcinogen for Humans by the International Agency for Cancer Research. Since it causes cancer in rats.^[10]

CONCLUSION

The study focuses on remarkable effectiveness of aloe vera in wound healing and thoroughly examines how it has been used as a wound dressing for a long time. Aloe vera contains many compounds that can aid in wound healing. Aloe vera can be combined with various biomedical polymers to create new types of wound dressings

that have better anti-inflammatory and anti-bacterial, decreased cytotoxicity, promoted fibroblast collagen synthesis, proliferation, and angiogenesis, increased dressing stability, and decreased scar formation properties.

Aloe vera is also still being used more and more as a skin remedy. Novel scaffolds based on Aloe vera gel extracts were generated recently using tissue engineering techniques for applications in the treatment of wounds. Aloe vera may lessen the negative effects of natural and synthetic polymers created to resemble the original structure of the human body.

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