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HERBAL COMPOUNDS AND THEIR MECHANISM IN WOUND MANAGEMENT

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ABSTRACT

The classical era, medicinal plants have already been employed as a resource for medicine and in the healing of wounds. Despite the use of standard medicines, chronic wounds are linked to significant healthcare and socioeconomic consequences. The mechanisms may result from the emergence of innovative wound-healing techniques utilizing medicinal plants in combination with nanotechnology. In this review, herbal formulations like biodegradable nanoparticles, films, fibers, hydrogels, and ointments with antibacterial, antioxidant, and anti-inflammatory characteristics are used in combination with herbal medicines to use in wound healing. Involved in skin healing. Commencement of a tissue lesion, a series of molecular and cellular actions take place to restore the injured tissue. This process is known as regeneration and tissue repair. Sequential events involving the integration of dynamic processes involving soluble mediators, blood cells, and parenchymal cells result in the exudative, proliferative, and extracellular matrix remodeling stages. The development of tissue edema is aided by exudative processes that happen after

damage. By recruiting myofibroblasts and fibroplasia, the proliferative stage aims to decrease the area of tissue damage.

KEYWORDS: Wounds healing; bandages; Hydrogels; Nanoparticles; Herbal Formulations; Aloe Vera.

1. INTRODUCTION

The human skin serves as the body's first line of defense and is the largest organ. Human skin is essential to our survival because it senses the outside world through ultraviolet radiation, regulates physicochemical and thermal homeostasis, stores vital nutrients, offers passive and active defense, and reacts to stress and harm.[1] With a Compound Annual Growth Rate (CAGR) of 6.6% over the analysis period of 2020–2027, it is anticipated that the global market for advanced wound care will reach $18.7 billion by 2027. The two other primary purposes of the skin, in addition to protection, are regulation and sensibility. More particularly, it protects against mechanical pressure and reduces the impact of temperature changes, fights microorganism infections, limits the effects of radiation, and prevents the entry of chemicals (Vadivel and Balasubramaniam). Being the largest organ in the body, the skin is crucial to many physiological processes, such as fluid balance, changes in peripheral circulation, and the regulation of body temperature (via perspiration and hair).[2,3] It serves as a reservoir for the synthesis of vitamin.D. The skin's dense network of nerve cells enables it to detect and transmit environmental changes (heat, cold, touch, and pain). effective wound management is required on both an individual and a communal level. To address wound healing, many treatments are employed. The various therapies have been applied both locally and systemically to promote wound healing. Antibiotics and antiseptics, desloughing agents (chemical debridement, such as hydrogen peroxide, eusol, and collagenase ointment), By increasing blood clotting, thwarting infection, and hastening the healing process, medicinal plants treat wounds.[4,5] Plants and the chemical substances derived from them indeed aid in healing and treatment. The benefits of medicinal plants on wound healing can be attributed to a variety of mechanisms, including modification of wound healing, reduction of the bacterial count, enhancement of collagen deposition, growth of fibroblasts and fibrocytes, etc.[6] Millions of people in Asia, Africa, and Latin America rely heavily on traditional treatments created from local plants, animals, and natural materials for wound care; for others, they are their only option. Since ancient times people have found cures in nature.

2. Wounds

Wounds are described as injuries to live tissue that cause its normal anatomical composition and purpose to be disrupted. They develop asa result of tissue harm resulting from physical, chemical, thermal, microbiological, or immunological factors Wounds, regardless of their source or nature, can harm the tissue and alter the surrounding environment. The damage can compromise the reliability of the epithelial layer of the skin, as well as spread into the subcutaneous tissue, affecting tendons, muscles, and nerves. Chronic wounds develop when wounds do not heal naturally. Chronic wounds are a secret pandemic that claims the lives of countless people across the world. Chronic wounds have been estimated to affect 6 million persons worldwide in the last decade. Wounds have a significant detrimental influence on patients' and their families' economic and social life. They induce extreme pain, physical handicaps such as immobility and loss of function, as well as loss of self-esteem, depression, anxiety, and early mortality.[6,7,8] Wounds not only disrupt patients' social lives, but they also affect patients as well as healthcare systems by money. Chronic wounds gobble up a lot of healthcare resources all around the world. Chronic wounds are most commonly associated with the elderly, but their frequency is predicted to rise across the board as the incidence of illnesses that hinder wound healing, such as diabetes, obesity, and vascular disorders, rises. An organized succession of overlapping, interconnected wound healing processes in chronic wounds frequently fails to advance because it is difficult to control inflammation. Coagulation is seldom harmed Inflammation has high pH, free radicals, and damage-related molecular patterns; functional activation of proteases, fibroblast senescence, as well as keratinocyte senescence, will occur at that site Failure to maintain proliferation, start angiogenesis, prompt keratinocyte movement and re-epithelialization, end inflammation, and deposit ECM. Remodeling/maturation ECM does not begin reorganization or maturation.[9,10,11]

2.1.Cellular aspects of wound repair

Wound repair is the normal physiologic response to any injury but it takes some time to heal completely hence the main goal of wound repair therapies is to achieve tissue integrity and homeostasis rapidly and completely. Hemostasis and remodeling, proliferation, and inflammation are the three steps that make up the typical wound healing process.[12,13] The cellular process of wound healing is shown in Hemostasis is Just after the trauma, the clotting cascade gets activated and leads to platelets and fibroblast aggregation along with fibrin network formation which blocks the exit of erythrocytes out of the wound at the first stage of

wound healing, which causes the formation of clots and momentarily seals the defect.[14] During Inflammation, Inflammatory cells such as macrophages, neutrophils, monocytes, and mast cells are drawn to the formed clot and release cytokines and other substances that activate the inflammatory phase and clear the wound bed to create an ideal environment for tissue repair. In this phase, fibroblast cells are differentiated into myofibroblasts, and keratinocytes get activated which ultimately leads to wound contraction. In the matrix remodeling phase, the immature collagen gets converted into mature collagen by crosslinking and Myofibroblasts regenerate tissue when there is a wound.[15,16]

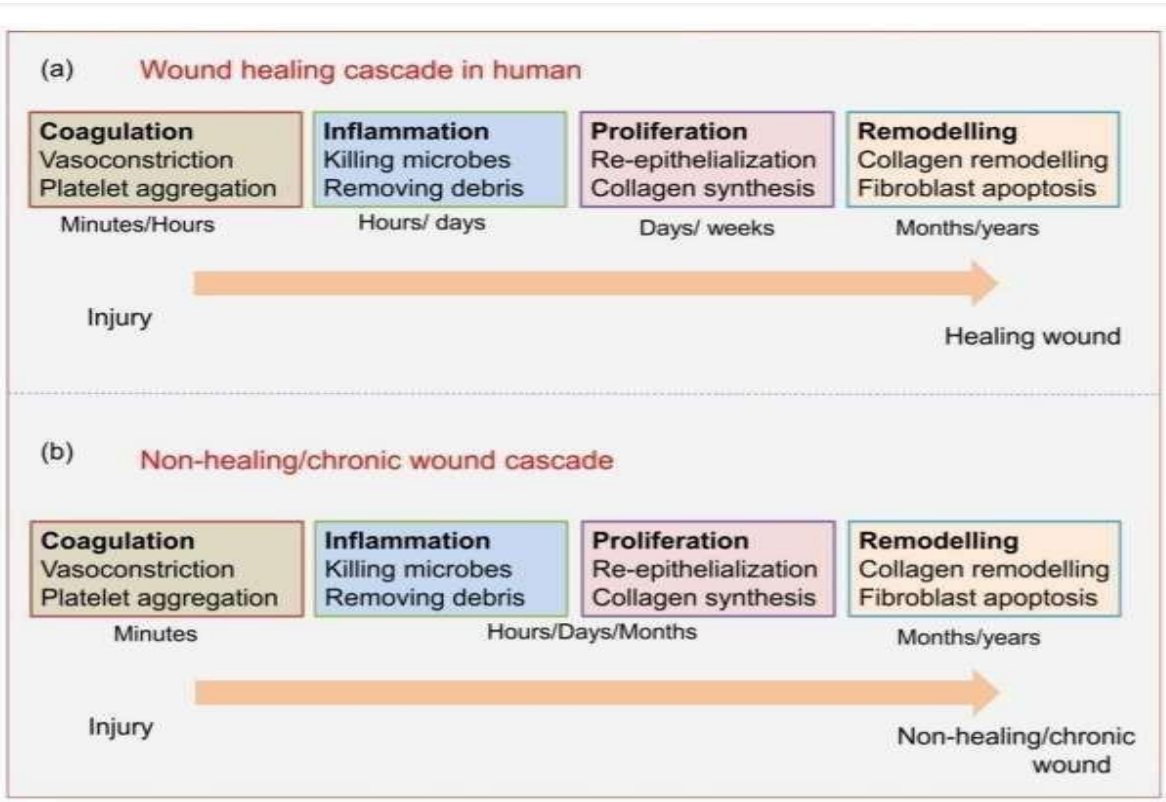

Figure 1: Healing and Nonhealing/chronic wounds cascades in humans.

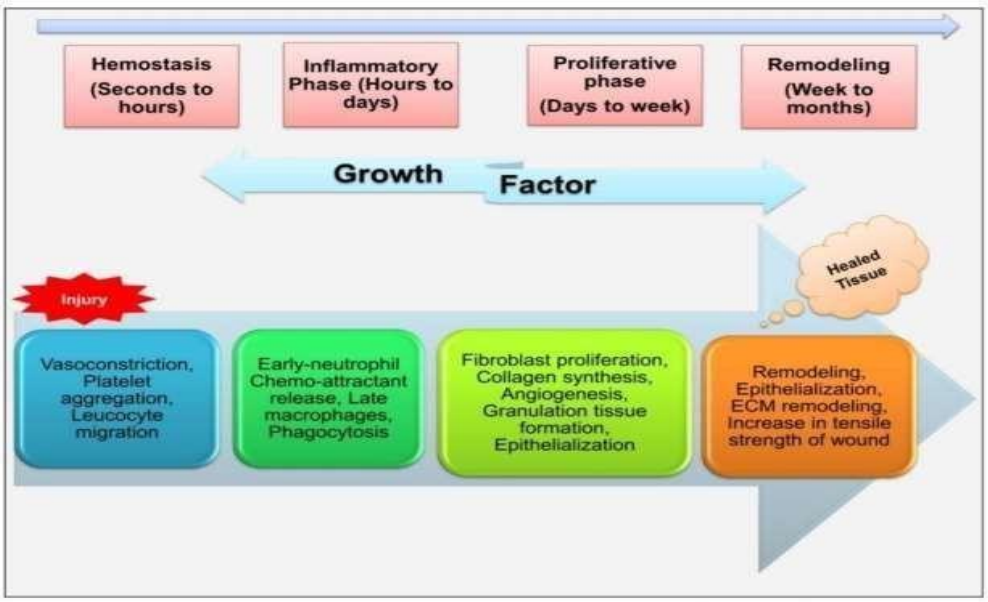

Figure 2: Cellular aspects of acute wound repair

Wound healing activity of some medicinal plants A good wound healing agent is that to be effective to modulate inflammation, accelerating fibroplasia, and enhancing remodeling of the healing tissue in minimum time with the least adverse effects. An ideal wound healing dressing or agent should prevent bacterial infection on the wound tissue, should reduce inflammation, promotes the proliferation of new cells which leads to the reconstruction of the damaged tissues, and should have antioxidant action because the main cause of inflammation is free radicals. A list of medicinal plants used for wound healing is provided in table 1. Here, we'll talk about a few therapeutic plants and their main chemical constituents.[17,18]

Table No: medicinal plants used to cure many sorts of wounds.

Medicinal Plant (Common Name and Scientific Name)	**Part** Used	**Main Chemical** Constituents	**Uses (Wound** Healing Type)	**References**
Indian Mulberry (*Morinda citrifolia*)	Leaves and fruit	Anthraquinones, steroids, phenol, tannin, and terpenoids	Closed wound healing	(Manjunatha, Krishna et al. 2007)
Club Moss (*Lycopodium serratum*)	Spores and whole fern	Alkaloids, steroids, tannins	Acute/chronic wound healing	(Nayak et al., 2006)
Madagascar periwinkle (*Catharanthus roseus*)	Leaves	Monoterpenoids alkaloids, vinblastine, Vincristine	Acute/chronic wound healing	(Arun et al., 2013)

Asthma Weed (*Euphorbia hirta*)	Leaves	Saponins, tannins, flavonoids, alkaloids, glycosides	Chronic wound healing	(Sharma et al., 2021)
Red sandalwood (*Pterocarpus santalinus*)	Bark wood	Santalin A and B, savinin, calocedrin, pterolinus K and L, and pterostilbenes	Acute/chronic wound healing	(Asif, Kakub et al. 2007)
Lawsonia alba	Leaves	Coumarins,	Chronic	(Manjunatha,
(*Lawsonia*	and roots	naphthoquinone,	wound healing	Krishna et al.
inermis)		flavonoids, sterols,		2007)
		triterpene, and xanthones		
Aloe vera (*Aloe vera*)	Leaves	Anthraquinone, C and E vitamins, amino acids	Open wound healing	(Galehdari, Negahdari et al. 2016)
Bay (*Sphagneticola trilobata*)	Leaves	Flavonoids, terpenoids, alkaloids, and saponin	Incision wound healing	(Garcia-Orue, Gainza et al. 2017)
Adusa (*Adhatoda vasica*)	Leaves	Flavonoids, tannins	Excision wound healing	(Osunwoke Emeka, Olotu Emamoke et al. 2013)
Humble plant (*Mimosa pudica*)	Whole plant	Mimosine (an alkaloid), sitosterol, amino acids, linoleic acid, tannins, polyphenols, and oleic acid	Excision wound healing	(Saini, Dhiman et al. 2016)
Papaya (*Carica papaya*)	Latex, fruit	Papain	Diabetic, burn, soft tissue wounds	(Osunwoke Emeka, Olotu Emamoke et al. 2013)
Jungle flame (*Ixora coccinea*)	Leaves	Triterpenes, Geranyl acetate, Ursolic acid	Excision wound healing	(Saini, Dhiman et al. 2016)
Betle Piper (*Piper betle L.*)	Leaves	Phenolic complex, Betal-phenol, chavicol	Excision wound healing	(Yogesh, Jeyabalan et al. 2013)
Common wireweed (*Sida acuta*)	Whole plant	Alkaloids, terpenes, and flavonoids	Excision, incision wound healing	(Soni and Singhai 2012)
Drumstick tree (*Moringa oleifera*)	Leaves	Vitamins vicenin-2, beta-carotene, phenolics, amino acid	Excision, incision wound healing	(Gozubuyuk, Aktas et al. 2014)
Indian olive (*Olea europaea*)	Leaves, oil	Biophenolics, Oleuropein, Secoiridoid, Luteolin	Incision wound healing	(Sharma, Khanna et al. 2021)
Honey (*Apis mellifera*)	Secretion from hive	5-Hydroxyimidacloprid, imidacloprid, 4,5dihydroxyimidacloprid, desnitro-imidacloprid, 6-chloronicotinic acid, olefin	Acute wound healing	(Sharma, Khanna et al. 2021)
Theaceae	Leaves	Flavonoids, theanine, and	Excision wound	(Yang, Song et

(*Camellia pubipetala*)		caffeine	healing	al. 2020)
Forest Champa (*Spermadictyon suaveolens*)	Roots	Triterpenes, sesquiterpenes, alkaloids	Chronic wound healing	(Shalu, Amanjot et al. 2016)

3. Current Technology of wound Healing

To improve the activity of medicinal plants, nanotechnology has been used to integrate them. Plants have been used to effectively produce a variety of nanoparticles, including silver, gold, titanium dioxide, and selenium. Silverbasedwound creams have a long history of use in the management of chronic wounds. It has been demonstrated that substances that release silver stop the development of fungus, ram-positive and Gram-negative bacteria, and other microbes on wounds.[19,20] This is because silver interferes with the electron transport system or binds to and inhibits microbe DNA replication. Furthermore, because silver treatments may be neutralized by anions in bodily fluids, they have low systemic toxicity. Silver alginates are included in products such as Askina Calgitrol Ag, Aquacel Ag Dressing, 3M Tegaderm Alginate Ag Dressing, and Systagenix Silvercel antimicrobial alginate dressing, whereas Silvadene, Thermazene, and SSD Cream contain silver sulfadiazine.[21,22] Certain dressings, such as Aquacel Ag Dressing, might irritate the skin and create allergies. Negative pressure wound therapy, growth factor administration, hyperbaric oxygen, and skin grafts more comprehensive techniques of chronic wound management, have been documented to be expensive, dangerous, and harmful to surrounding healthy tissues. As a result, new wound healing treatments that are more effective and have fewer adverse effects are continually being developed. Nanotechnology has played a significant influence in the development of better diagnostic and treatment approaches for diseases. Too far, the US Federal Drug Administration has licensed 51 nano- pharmaceuticals made M from liposomes, polymers, nanocrystals, proteins, micelles, and inorganic reducing agents, and they may be found in clinical settings, while several more are under clinical trials.[23,24]

4.1 Biogenic Nanocomposite in Wound Healing

Although numerous chemical and physical synthesis methods for producing nanoparticles are known and employed, biological models for nanoparticle formation have significant benefits over existing approaches. This is because physio-chemical techniques for nanoparticle production use organic solvents and toxic reducing agents, resulting in hazardous waste products When it comes to industrial and human health care goods, biologically produced nanoparticles have a significant. advantage. Several biological ways of nanoparticle

production use various natural resources such as plants, microbes, and algae. Although microorganisms are commonly employed to decrease metallic salt solutions to create nanoparticles, the method involves toxic and expensive reactants, making the platform unsuitable for biocompatible synthesis.[25,26]

4.2 for delivery of Plant-based constituents

Plant-based dressings continue to be important in basic health care. Many plants and preparations of them have traditionally been utilized in wound care, owing to their enormous capacity to influence the wound healing process. Healing and tissue regeneration are induced by plant-derived extracts and/or isolates through numerous interconnected processes, which typically have a synergistic influence on overall healing efficiency. Many plant-derived medications (also known as phytomedicines) are inexpensive and have few negative side effects.[27]

4. CONCLUSION

Numerous plants promote the skin's natural repair processes, offering great potential for therapeutic application in wound treatment. Due to the immense cellular diversity, complexity, and flexibility, wound healing is incredibly challenging to fully comprehend. All of the skin's cells, tissues, cytokines, and growth factors are involved in the interactions between several cellular and extracellular wound-healing participants. The steps of tissue repair-re- epithelialization of the wound, creation of granulation tissue, wound contraction, and scar formation as well as the short-lived inflammatory phase all happen appropriately when cells are healthy, according to current knowledge. The inflammatory process is prolonged, the integrity of the skin is not restored, and an ulcer or pathological fibrosis develops when cells are defective, as in diabetes. In all stages of tissue repair, macrophages predominate over other types of cells. They have a crucial regulatory role, making them significant therapeutic targets for the future management of the wound healing process. By combining traditional and current knowledge, it is possible to create unique wound healing medications with greatly reduced undesired side effects.

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