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Natural Vs Therapeutic: An Insight On Wound Healing

Habibullah[1] , Muhammad Jamil[2] , Amar Nasir[1] , Muhammad Kashif[1] , Atta Ur Rehman[3] , Fateh Ullah[1] , Abdul Rahman[1] , Bibi Sadia[4] , Imtiaz Khan[5] , Imran Qazi[6] , Muhammad Rasheed[7] , Mubarik Ali[8]

[1]Department of Clinical Sciences, Sub Campus Jhang, University of veterinary and Animal Sciences, Lahore, 54000, Pakistan

[2]PARC Arid Zone Research Center, Dera Ismail Khan-29050-Pakistan

[3]Faculty of Veterinary and Animal Sciences, Gomal University, Dera Ismail Khan-29050-Pakistan

[4]Sardar Bahadur Khan Womenn,s University Quetta-87300-Pakistan

[5]PARC Adaptive Research Cum Demonstration Institute Miranshah- 28190-Pakistan

[6]PARC Adaptive ResearchCum Demonstration Institute Wana- 21776 -Pakistan

[7]Animal science Institute, National Agricultural Research Center, -Islamabad- 54000-Pakistan

Abstract

Wounds on the skin can heal on their own through a process known as cutaneous wound healing. Haemostasis, inflammation, proliferation, and remodelling are the four stages of wound healing that are usually recognised. To close the wound and restore homeostasis in humans and animals, keratinocytes create a functional epidermis (reepithelialisation) as quickly as feasible. "Granulation tissue" is formed when dermal fibroblasts move into the wound bed and multiply, allowing for the formation of new blood vessels. In the end, the wounded tissue is returned to its pre-injury form over an extended period. Various skin diseases, such as nonhealing or chronic ulceration, can result from wound healing cascade dysfunction. For more than half of all medicines used today, indigenous, and traditional treatments rely heavily on natural ingredients and their derivatives. A detailed literature review has been carried out recognising the importance of traditional medicine and the use of medicinal plants and plant-based products to treat cutaneous wounds. Curcuma longa, Aloe vera and Camellia sinesis are some of the most often utilised wound healing products throughout a wide range of countries and ethnicities. Traditional techniques still have a lot to teach us, as seen by their continuous use and popularity. Natural products and derivatives from natural products are full of unknown combinations, reagents, and adjunct chemicals that potentially have a position in today's therapeutic arsenal.

Keywords: Wound, Healing, herbal plants,Natural, Therapeutic

Introduction:

Most important functions of our bodies is the skin's ability to detect and respond to changes in our surroundings. It regulates our body's physiology and temperature, store nutrients for use, protect us from harm and heals us after injury. To execute these vital functions, the skin must have systems in place that can withstand trauma while also repairing and replacing any lost or damaged functions. For millennia, humans have used many methods to cure their wounds [2]. When it comes to wound care, traditional methods rely on what is at hand or can be procured locally: water; soil; plant/animal products. Thousands of people throughout the world rely on traditional remedies produced from local plants, animals, and natural items to treat their wounds [3]. For some, these medicines are their only option for treating wounds.

Cutaneous Wound Healing:

Skin must have a powerful and effective repair system in order to ensure the survival of the organism. Wound healing is the process through which the skin recovers from wounds inflicted by surgery, trauma, and burns [4]. Coagulation, inflammation, and proliferation (granulation), and remodeling (maturation) are the four stages of the healing process [5]. As soon as there are an injury, the blood vessel walls contract, and a blood clot forms [6, 7]. Wound healing begins when platelets in the bloodstream activate the clotting cascade and produce numerous growth factors. Neutrophils enter the wound, absorbing foreign debris and destroying bacteria through phagocytosis and the release of proteolytic enzymes [8, 9] in the subsequent inflammatory phase. When blood monocytes infiltrate an injury site, they change into macrophages, which release proteases to debride the wound and secrete a combination of bioactive chemicals, including TGF-1, that encourages the migration of fibroblasts and epithelial cells. Angiogenesis (by endothelial cells), granulation tissue development (by fibroblasts), and reepithelialization (by keratinocytes) are some of the actions that take place during the proliferation phase. A substantial amount of extracellular matrix (ECM), mostly collagen, is produced by fibroblasts to build the granulation tissue that replaces the injured tissue at this stage. During this time, the keratinocytes are regenerating a functional epidermis (reepithelialization) and seal the lesion to prevent additional damage to the underlying tissues [13]. Decreased dermal fibroblast cell populations in granulation tissue actively remodel ECM disorganization [14,15] that is characteristic of the wound as it progresses. Scar tissue (also known as a fibrosis) forms as a result of wound healing, with fibroblasts

dispersed across a collagen-rich extracellular matrix (ECM). There are considerable differences between the original tissue and scar tissue in terms of biomechanical and functional aspects [16].

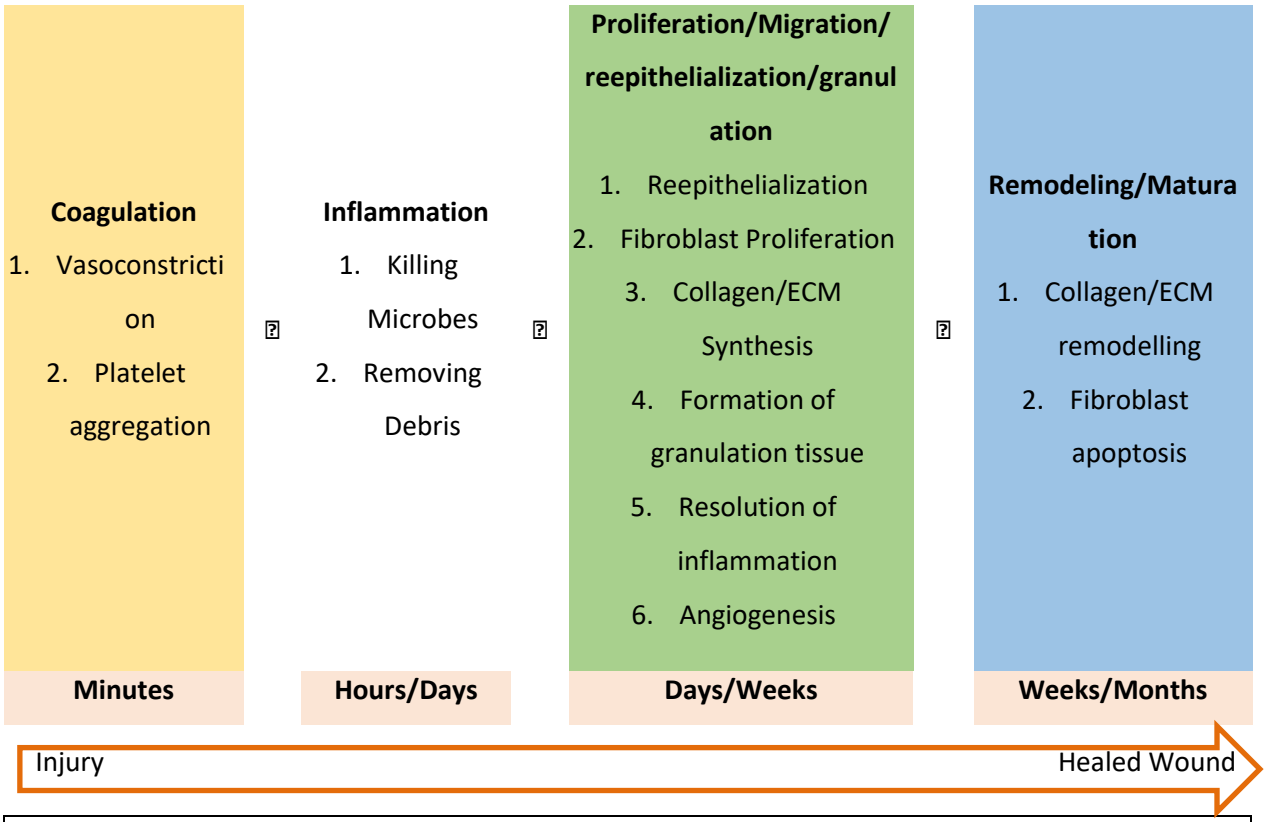

Figure 1:

Humans' wound-healing cascade. Coagulation, inflammation, proliferation, migration/reepithelialization/granulation, and remodeling/maturation are four separate phases of wound healing that overlap and interact with each other. Fluid loss and pathogen entry are temporarily prevented by the formation of an impermeable layer of the clot, which also provides bioactive factors and antimicrobials, as well as a provisional ECM that supports immune cell infiltration and migration. Tissue repair pathways are also triggered as a result of this process. An increase in the permeability of blood vessels, the release of antimicrobial substances, the production of alarmin (also known as DAMPs) signals by infiltrating immune cells, as well as the activation of keratinocytes and fibroblasts are all indicators of inflammation. There is an increase in the number of keratinocytes as well as fibroblasts and endothelial cells migrating and proliferating, as well as collagen and ECM synthesis, decreased blood vessel permeability, new capillary and lymphatic vessel angiogenesis, cell reepithelialization, and the formation of new granulation tissue. collagen/ECM turnover (production and breakdown), ECM remodeling and realignment, ECM contraction,

endothelia, and fibroblast death, and repigmentation are some of the remodeling/maturity processes that occur.

Injuries heal through an ordered progression of physiological mechanisms that overlap and interact (Figure 1). In juveniles, this process can take a few days to a few weeks, but in adults, it can take months. It takes fewer than four weeks for wounds to heal without complications and restore homeostasis, the skin's barrier function, flexibility, and physiological processes. Clinical evidence suggests that wound closure in a shorter period is related to less scarring and fibrosis. When a wound heals slowly or completely, it is more likely to cause fibrosis, which can lead to hypertrophic scars and keloids in some people. Wounds that don't heal within six weeks appear to "stall" and fail to advance through the stages of healing seen in Figure 1 (Figure 2). These wounds, which are difficult to heal, are referred to as "chronic" wounds. Chronic wounds can be caused by a variety of illnesses, including diabetes, vascular disease, hyperglycemia, ischemia, and neuropathy. These factors can make wounds difficult to heal. Diabetic foot ulcers, venous leg ulcers, arterial leg ulcers, and pressure ulcers are all terms used to describe wounds that have a specific underlying etiology.

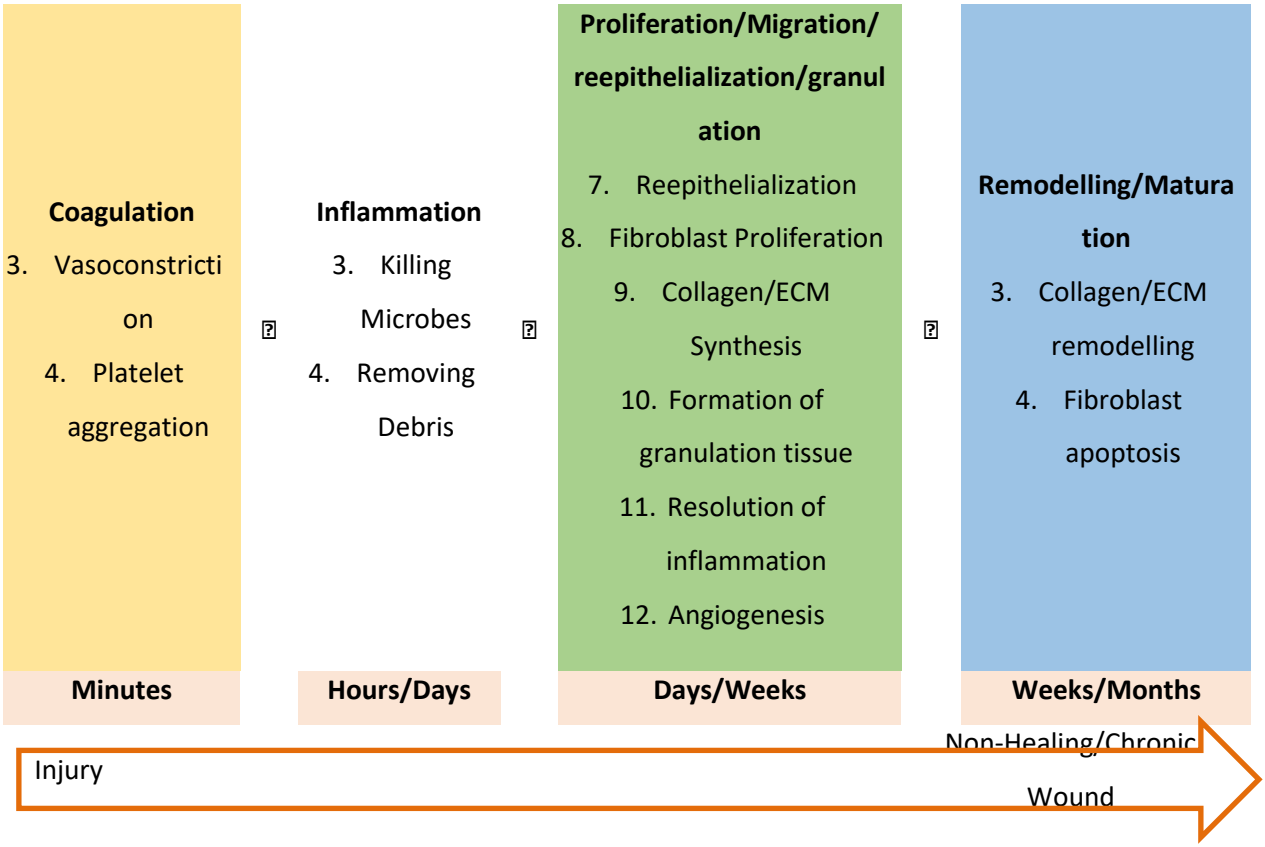

Figure 2:

Wounds that do not heal or are chronic—in humans. In chronic wounds, the orderly progression of overlapping and interconnected wound healing processes is typically hindered by a failure to resolve inflammation. In most cases, coagulation is unaffected. High pH; protease activation; keratinocyte and/or fibroblast senescence and/or damage-associated molecular patterns; free radicals and reactive molecular species; inflammation (vessel permeability sustained-aetiology specific). Angiogenesis, angiogenesis, angiogenesis, angiogenesis, angiogenesis, keratinocyte migration, keratinocyte reepithelialization, wound closure, inflammation, and ECM accumulation are all failures in wound healing. Reorganization and maturation of the ECM are not initiated

For individuals who have non-healing chronic wounds, the consequences can be devastating. They can lead to severe pain, restricted mobility, profuse exudates, wound malodor, and reduced quality of life, all of which can have an impact on the health and well-being of the individual. A chronic wound affects as many as 1-2 percent of the world's population at some point in their lives [20]. Chronic wounds harm 6.5 million people in the United States and cost more than $25 billion annually [21]. Alarmingly, global increases in cardiovascular disease, diabetes, obesity, metabolic syndrome, and general population aging are predicted to increase the burden of chronic wounds [21]. The pathophysiology of chronic wounds is still poorly understood, despite the fact that wound healing mechanisms are widely understood [22]. It is widely acknowledged that chronic wounds are caused by a malfunction in the normal healing process. Wound healing is slowed down in the inflammation phase by factors such as microbial biofilms, overexpression of inflammatory cytokines, high levels of proteases and reactive oxygen species (ROS), and diminished mitogenic activity. MMPs, which break down connective tissue, have also been shown to slow healing [23]. Wounds that are left open, do not heal, and eventually, turn into chronic [24].

Clinical decision-making in wound care is guided by the underlying aetiology of each wound. First, nonvital (necrotic) tissue is debrided; second, inflammation or infection may be present; third, managing moisture (too wet or too dry); and fourth, the state of surrounding tissue is taken into account. This method has its roots in Greek and Roman medicine [26], where it was prescribed to remove these "barriers to healing" so that the healing cascade could advance to completion. When a wound is debrided, the healing process can be restarted and brought back to an acute state. To promote cell growth and migration, debridement exposes healthy, well-perfused tissue. Damage-associated molecular patterns (DAMPs) and pathogen-associated molecular patterns (PAMP) can all be reduced or

eliminated through debridement, in addition to the removal of dead and necrotic tissue (PAMPs). Extracellular traps and bacteria from the wound are also removed during the process of debridement. Many years have passed since microorganisms in wounds were thought to be harmful [28], but new research shows that not all germs are harmful. There are many microorganisms commonly associated with infection, including Staphylococcus sp., Streptococcus sp, Propionibacterium a, and Pseudomonas a, but others, such as Malassezia p., Candida p., and Corynebacterium sp., can be isolated from non-infected wounds and may even help wound healing [29]. However, the ideal frequency and timing of debridement procedures are still a mystery [27]. An antibacterial agent can be delivered using dressings (e.g., honey or iodine), and some dressing designs absorb wound exudates, allowing for some control over moisture.

Traditional Medicine

Those practicing "modern" (western) medicine frequently describe traditional medicine with sceptical terms such as "alternative," "conventional," "indigenous," and" complementary medicine, when in fact many of the techniques and practices of "modern" medicine are little different from those used by traditional healers when it comes to wounds. Water, plants, animals, and minerals are among the natural resources that traditional ways rely on nearly exclusively. Traditional approaches continue to be highly regarded and widely practiced by the majority of the world's population [3]. Traditional Chinese medicine (TCM) is founded on the theories of the Five Phases and Yin-Yang, which are documented in ancient Chinese medical texts such as the "ShenNong Ben Cao Jing" and the "Ben Cao Gang Mu." Traditional Chinese medicine is a branch of medicine that originated in China. Several types of TCM, although not all, make substantial use of herbs, ensuring that it is effective, inexpensive, and easily accessible [30]. It is noteworthy that around 54 percent of the new anticancer medications discovered between 1940 and 2002 were derived from natural ingredients [31], which is a significant proportion. [32] According to the findings of another study, approximately 73 percent of all currently available pharmaceutical medications contain components derived from natural sources. Because the therapeutic activity of many traditional medicines is given by natural chemicals produced inside the plant, the efficacy of TCM preparations can vary significantly and is influenced by the genotype, environmental, and growth factors that each source plant is exposed to [30, 32]. The urbanization of the world and the industrialization of pharmaceutical engineering have raised the need for TCM products that are "off the shelf" and have uniform composition, quality, and clinical efficacy, among other things. In parallel with industrialization, thorough product testing for evidence of biological activity and clinical efficacy has been introduced.

Aloe vera

The Egyptians, Romans, and indigenous peoples of Africa, Asia, and the Americas have all utilised Aloe vera to cure wounds for over 5000 years [34].It is still considered a first-line treatment for burns, ulcers, and surgical wounds. A variety of natural bioactive compounds are found in aloe vera [35], including pyrocatechol, saponins, acemannan, anthraquinones, glycosides, oleic acid, phytol, and a variety of simple and complex water-soluble polysaccharides. Pyrocatechol is a bioactive compound that has been shown to have antioxidant properties. Acetone extracts from the leaves of Aloe vera have been shown to have greater antibacterial activity than both alcohol and aqueous extracts of the plant. Aloe vera appears to be more toxic to Gram-positive bacterial species than it is to Gram-negative bacterial species [36]. Saponins, acemannan, and anthraquinone derivatives are examples of compounds having demonstrated antibacterial action [37], [38]. Acemannan, a significant mucopolysaccharide (mesoglycan) derived from the plant Aloe vera, is a powerful activator of macrophage and T-cell activity and stimulates the transcription of proinflammatory mRNAs (such as interleukin 1a and 1b, interleukin 6a, TNF-a, PGE2, and nitrous oxide) [38]. In addition to binding and capturing endogenous mitogen inhibitors and reactive oxygen species, mesoglycan moieties also stimulate phagocytosis (the capture and retention of foreign substances). Glycans, by coincidence, help to maintain the stability of released cytokines, growth factors, and other bioactives, allowing them to remain active for longer periods. Using a rat wound healing model, it has been shown that topically applied acemannan can drastically reduce the time it takes for a wound to close by acting on the cyclin D1 and AKT/mTOR signal pathways [39]. It has also been observed that aloe veraglycans considerably increase the de novo development of granulation tissue, while the exact mechanism is uncertain [40].

Andrographispaniculata

Green chiretta, also known as andrographispaniculata, is a traditional Chinese, Indian, and Southeast Asian medicine for fever, snakebite, diarrhoea, infections, wounds, and itching [41–44]. Antioxidant [45], anti-inflammatory [46], antidiabetic [47], anticancer [43], antimicrobial [48], antiviral [49], antimalarial [50], hypotensive [51], immunostimulatory [43], and hepatoprotective [52] actions have been reported for Andrographispaniculata extracts. Wound repair in rats was greatly improved after treatment with a 10% aqueous leaf extract of Andrographispaniculata in one study [53]. In healed wounds, animals treated with Andrographispaniculata showed reduced inflammation, scarring, enhanced angiogenesis, and a higher amount of collagen fibres [53]. Andrographolide, a bicyclic diterpenoid derived from Andrographispaniculata leaves, has been formally investigated in clinical trials and shown to have beneficial benefits on a number of autoimmune illnesses [54].

Blumeabalsamifera (Camphor)

Blumeabalsamifera (also known as ngai camphor) is a plant that is found throughout Asia's tropics and subtropics, and it is widely utilized as a traditional medicinal herb. Blumeabalsamifera, also known as sambong in the Philippines, is a diuretic herb that is commonly utilized. Blumeabalsamifera is referred to as kakoranda in Ayurvedic medicine, and it is used to cure fevers, coughs, pains, and rheumatism. Leaf extracts are administered topically to treat eczema, dermatitis, skin injury, bruising, beriberi, lumbago, menorrhagia, rheumatism, and skin injury [55]. Leaf extracts are also used topically to treat rheumatism and skin injury. Blumeabalsamifera extracts have been shown to have a wide range of bioactivities, including antimalarial [56], antitumor [57], antifungal [58], and antiobesity [59] effects, among other things. Based on their findings, Pang et al. concluded that oils derived from the flowering plant Blumeabalsamifera promote wound healing in mice by increasing angiogenesis and perfusion, as well as collagen deposition and the formation of well-organized granulation tissue as well as reepithelialization and wound closure [60].

Camellia sinensis (Green Tea)

For its purported health advantages [61], green tea, an aqueous extract prepared from the leaves of the Camellia sinensis plant, has long been treasured throughout Asia. Century-old anecdotal evidence has been experimentally validated by showing that Camellia sinensis has antioxidant [62], anti-inflammatory [63], antimicrobial [64] activities, and that it also has anti-carcinogenic [65] activities, as well as anti-obesity [66-68] activities, as well as cardioprotective [69] and neuroprotective [70] activities. Catechins, the polyphenolic chemicals derived from the Camellia sinensis plant, are thought to be the primary catalysts for these pharmacological effects [71]. EGCG [61], the most abundant catechin, increases the proliferation and differentiation of keratinocytes [72]. EGCG is the most abundant catechin in nature. The researchers discovered that EGCG reduces TGF-receptors in human dermal fibroblasts by changing TGF-beta signaling, lowering MMP-1 and MMP-2 expression, and attenuating the synthesis of collagen type 1 in the cells, among other things. These characteristics suggest that EGCG may have potential as an anti-scarring agent [73]. Additionally, it has been proven that EGCG can cause keloid shrinking [74] as well as decrease the growth and degenerative characteristics of keloids by inhibiting STAT3 signaling [75]. According to certain reports, methanol extracts from the Camellia sinensis plant stimulate fibroblast proliferation and collagen formation [65]. Further evidence suggests that Camellia sinensis considerably improves wound healing in rats by boosting angiogenesis [71, 76]. This has been established in animal research. It has also been found that extracts from the Camellia sinensis plant can promote wound healing in a diabetic mice model [77].

Carthamustinctorius (Safflower)

Carthamustinctorius is a Latin name for a thorny cactus. Safflower seeds, also known as Carthamustinctorius or safflower seeds, are a major source of cooking oil in many parts of the world. Carthamustinctorius, a plant that is less well-known, has a long history of use as a component in Traditional Chinese Medicine formulations for the treatment of blood problems. According to recent research, this compound is related to a wide range of biological actions, including vasodilation, immunological modulation, anticoagulation and thromboprophylaxis, antioxidation, anti hypoxia, antiaging, antifatigue, anti-inflammation, anti-cancer, and analgesia [78]. The safflower seed oil has also been demonstrated to prevent melanogenesis in B16 melanoma cells, which makes it a good candidate for skin whitening applications [79]. There has been evidence that hydroxysafflor yellow A (HSYA), the primary water-soluble monomer of safflower yellow pigments, can protect against cerebral and cardiac ischemia [80], and that it possesses anti-inflammatory, proangiogenic, and apoptosis-inhibiting activities [81-84]. Streptozotocin-induced diabetic rats were given a topical application of HSYA at a modest dose (4 mg/mL), and the results showed that it improved diabetic wound healing by encouraging neovascularization, reepithelialization, and granulation tissue development. Wound healing, on the other hand, is hindered at high levels (more than 10 mg/mL) [85, 86].

Cinnamomum cassia (cinnamon)

A common spice and flavoring agent, Cinnamomum cassia bark is also used to enhance blood circulation and as an analgesic [87]. Cinnamomum cassia is also used to treat pain and inflammation [88]. As one of the seven botanical components of ShexiangBaoxin pill (SBP), a well-known Traditional Chinese Medicine (TCM) medication indicated for chest pain and discomfort associated with coronary artery disease [88], Cinnamomum cassia is commonly combined with other herbs. Current clinical trials are investigating the use of SBP in the treatment of coronary artery disease that is not susceptible to revascularization [89] and is presently enrolling participants. SBP's anti-inflammatory [90] and anticancer [91, 92] properties, as well as its effects on hypertension, insulin resistance, and noninsulin-dependent diabetic Mellitus [93], have all been studied in depth. According to in vitro and in vivo studies, the bioactive component of Cinnamomum cassia, which is a natural insecticide, is also an antimicrobial, anti-diabetic, anti-lipidemic, anti-inflammatory, and neuroprotective agent [94], and activates the PI3K/AKT and MAPK signaling pathways, increasing VEGF expression, and stimulating angiogenesis in human umbilical vein endothelial cells [87]. Cinnam [54] It has also been observed that cinnamon aldehyde can speed up wound healing in zebrafish.

Curcuma longa (Turmeric)

In traditional Chinese medicine, curcumin, an active chemical found in the root of the Curcuma longa plant, which is a member of the ginger family, has been used as a medication and as a food seasoning for centuries [95]. Curcumin is used to treat inflammation, respiratory problems, liver disorders, and diabetes by practitioners of traditional Ayurvedic medicine [96]. Curcumin, a compound found in turmeric, is a popular therapy for stomach pain in traditional Chinese medicine. Since it has been used by many ethnic groups for ages, curcumin has been one of the most widely investigated nutraceuticals available today. At the transcriptional, translational, and posttranslational levels, it has been proven that this highly pleiotropic protein interacts with critical physiological pathways. Proinflammatory cytokines, apoptosis, nuclear factor–B, cyclooxygenase-2, 5-LOX, STAT3, C-reactive protein, prostaglandin E2, prostate-specific antigen, cell adhesion molecules, phosphorylase kinase, transforming growth factor-beta, triglycerides, ET-1, creatinine, heme oxygenase-1, AST, and ALT are all targets [97] Curcumin has been the subject of more than 100 clinical trials and in vivo investigations, the majority of which have focused on it as a therapy for epithelial malignancies. These in vivo and in vitro studies have revealed that curcumin exerts the majority of its positive effects through changing the pericellular and extracellular matrix [96], consistent with previous findings. The fact that curcumin increases fibroblast proliferation, granulation tissue development, and collagen deposition in cutaneous wound healing may therefore come as no surprise [98].\

Honey

Honey is a naturally occurring product that has just lately been incorporated into modern medical practise as a therapeutic agent. Researchers have exhaustively researched honey's antimicrobial qualities, as well as its effects on the healing of wounds. Honey has been demonstrated to be an efficient broad-spectrum antibacterial agent in both laboratory and clinical trials, according to the findings. It is evidenced that natural honey is useful in wound healing and that it has the power to sterilise infected wounds. A review of studies on the therapeutic effects of honey gathered from various geographical locations on skin wounds, skin and gastric ulcers, and burns is presented, as well as a discussion of the mechanisms of action. Ulcers and burns are included as examples of wounds that are difficult to treat. According to the research, honey's wound healing qualities include the promotion of tissue growth, the enhancement of epithelialization, and the reduction of scar formation. Honey's acidity, hydrogen peroxide content, osmotic action, nutritional and antioxidant contents, activation of immunity, and the presence of undiscovered chemicals are all thought to be responsible for these effects. Prostaglandins and nitric oxide are important mediators of inflammation, microbial death, and

the healing process, among other things. Honey has been shown to reduce prostaglandin levels while simultaneously increasing nitric oxide end products. These characteristics may contribute to the explanation of some of the biological and therapeutic capabilities of honey, including its effectiveness as an antibacterial agent and wound healer. The studies provided here reveal that honeys sourced from various geographical locations had significant therapeutic effects on chronic wounds, ulcers, and burns when applied topically. The findings support the use of honey in clinical practise as a wound healer that is both natural and non-toxic.

Zinc Oxide

Zinc is a vital trace element in the human body, and its significance in both health and sickness has long been recognised and acknowledged. Numerous transcription factors and enzyme systems, including zinc-dependent matrix metalloproteinases that are involved in wound repair use zinc as a cofactor to enhance autodebridement and cell migration. Zinc gives resistance to epithelial apoptosis through cytoprotection against reactive oxygen species and bacterial toxins, which may be mediated through the antioxidant activity of the cysteine-rich metallothioneins, according to the findings. Pathological alterations and delayed wound healing can occur as a result of zinc deficiency, which can be caused by inherited or nutritional factors. Oral zinc supplementation may be effective in the treatment of zinc-deficient leg ulcer patients, although its role in the treatment of surgical patients requires further investigation. Topical zinc administration appears to be superior to oral zinc administration due to its ability to reduce superinfections and necrotic material through enhanced local defence systems and collagenolytic activity, as well as the sustained release of zinc ions that stimulates epithelialization of wounds in individuals who are not hypozincemic (low zinc levels). Protective and soothing properties of zinc oxide in paste bandages (Unna boot) are provided for peri-ulcer skin that is irritated. Even though the systemic effects of zinc from these formulations appear to be modest, zinc is delivered through the skin from these formulations. The role of topical zinc therapy in autodebridement, anti-infective activity, and the development of epithelialization has been overlooked despite clinical evidence demonstrating its effectiveness.

Conclusion

We reviewed the evidence that explains why numerous medicinal plants are used to heal cutaneous wounds and clinical skin problems. Medicinal herbs have been used to treat trauma, infection, sickness, and injury since ancient times. Humans have learned to detect and transform botanical resources from their immediate surroundings as food and medicine throughout millennia. Uncontrolled clinical

experiments have proven the therapeutic advantages of many of these “ancient” and traditional medicinal herbs. Unexpectedly, many medicinal plants synthesise the same or similar chemicals. As a result, many biological traits are shared by unrelated species. Many of the same biological targets and pathways are involved in the mammalian wound healing cascade. These chemicals target mitogenic pathways (AKT, PI3K, SMAD, and cyclins), proinflammatory NF-B pathways (caspases, interleukins, TNF-, and TGF-1) and differentiation pathways (e.g., -SMA).

On the basis of their bioactivities, medicinal practices have been evaluated for their clinical efficacy and economic viability. While each plant has been tested in vitro or in vivo, not every mechanism of action has been confirmed. Several compounds, including acemannan (Aloe vera), hydroxysafflor yellow A (Carthamustinctorius), polysaccharide (Ganodermalucidum), phthalide lactones, and alkaloids (Ligusticum striatum), saponins (Panax ginseng), shikonin and arnebin-1 (Lithospermumerythrorhizon), Curcuma longa, Aloe vera and Camellia sinesis are popular therapeutics worldwide.

In our opinion, traditional traditions still have much to teach us, some of which could lead to innovative reagents and therapies for today's therapeutic difficulties. Unavoidably, modern medicine and medications remain inaccessible (and pricey) to the majority of humanity. For this reason alone, traditional medicine is the first, and often only, treatment option for many. More individuals will appreciate and benefit from traditional methods as they become more understood. We hope that “modern medicine” does not reject this information but rather uses it to benefit all.

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