



## Review Article

## Wound Healing Efficacy of Honey, Aloe Vera, And Turmeric

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## ABSTRACT

Skin naturally acts as a body's protective layer and external environmental factors that can harm internal body organs are protected by it. So, maintaining skin integrity is vital for normal physiological functioning. In our daily lives, the bodies of both animals and humans are subjected to various forms of violence, some of which are severe enough to destroy the skin's continuity. A wound is a breakdown in the continuity of the skin. When the skin's continuity is disrupted, the body's interior organs are exposed. There's a risk of death in this case. There's a risk of death in this case. The skin's immediate response to a wound is the first step in the healing process, which begins automatically after the injury has been inflicted. It is possible to speed up this process in a variety of ways, including keeping the wound free of bacterial infection, moisture, and dirt. A number of antiseptic dressings are available for this purpose, and when applied topically, they help to speed up the healing process of wounds. They protect the wound from contamination by microorganisms and speed up the healing process. Among these are Aloe vera, honey, and turmeric, all of which have considerable wound healing capabilities. Turmeric, honey, and Aloe vera are all considered good for promoting wound healing. They are involved in the prevention of platelet aggregation, myocardial infarction, tumour formation, inflammatory cytokine release, oxidative stress, and metastasis. Several studies have demonstrated that they play a critical function in the promotion of wound healing. Their use for wound dressing has proven to be a successful method. The primary goal of this review is to summarise previous scientists' findings with authentic concluding verse for the use of Aloe vera, Turmeric and Honey that are safe, readily available, and less expensive.

## INTRODUCTION

An external or internal insult can cause a wound. External assaults such as mechanical trauma, thermal, UV, or gamma radiation therapy produce many acute wounds. Inadequate circulation deprives tissues of nutrients and elevates pro-inflammatory cytokines, resulting in necrosis in chronic injuries (leg, pressure ulcers, and diabetic). Wound curing is

traditionally separated into 4 phases: hemostasis, inflammation, proliferation, and remodeling. The above steps overlap a lot [2]. During the inflammatory phase, waste and germs are eliminated from the injury. In the proliferation phase, blood vascular invasion, connective tissue, and epithelial regeneration wound contraction, and wound

healing occur. Apoptosis is used to remove superfluous tissue during the rebuilding period [3]. Infection, aging, and deprived circulation are thought to slow healing. Wound care involves removing the harmful insult first, then providing the best possible environment for wound healing. Controlling a wound's bacterial burden is critical to promoting healing. Bacterial counts of over 10<sup>5</sup> organisms per gram of wound tissue have been shown to impair wound healing in surgical and chronic wounds [4,5]. Many topical treatments with diverse qualities are now used to promote wound healing. Surprisingly, most of these products lack convincing evidence to support their usage [6-9]. To help clinicians better understand the complexities of clinical use of medical-grade honey, Aloe Vera and turmeric, evidence indicators like Cochrane reviews can be used to evaluate the lack of evidence to support their use, as well as select clinical entities in patients who may benefit from treatment with these therapeutic agents based on their clinical outcomes. All of these medicinal therapies' biochemical properties, their independent wound healing, and bacterial/inflammatory processes will also be discussed.

**HONEY:** Honey is gaining popularity in wound care, especially for burn wounds. Honey has been utilized for nourishment and healing since prehistoric times [6]. Between 2600 and 2200 BCE, ancient Egyptians used honey to treat wounds [6]. Although the actual mechanism for honey's wound healing benefits is uncertain, research has concentrated on honey's antimicrobial properties. Honey's high sugar content makes it hygroscopic, which prevents the development of microorganisms. Honey's antimicrobial qualities are complex than merely greater sugar content, according to research [10]. In addition to its antibacterial qualities, oxidation of glucose to hydrogen peroxide occurs naturally in honey. [6,11,12] And the antimicrobial effects of honey seem to vary by floral source. Hydrogen peroxide was not necessary for the antibacterial properties of manuka and viper's bugloss honey [13]. The antibacterial characteristics of honey are thought to be due to an unknown component [14]. Manuka honey also inhibits vancomycin-resistant enterococcus, MRSA, and *P. aeruginosa* species [15,16] In a study, ulmo honey outperformed manuka honey against MRSA [17]. Finally, honey had antifungal action [14,18]. Honey increased wound healing in animals, according to histological research. Histologically, honey reduced edoema, inflammation, necrosis, improved epithelialization, and wound contraction in rabbits. [19] Honey also increased wound healing on cutaneous wounds in mice [20] Human studies found that honey-treated wounds [21,22] promoted granulation tissue formation, [21-24] enhanced epithelialization, [21,22] and decreased inflammation [22,25]. This was in line with the

earlier animal study data, but clinical observation without histological proof is limited.

**ACUTE WOUNDS :** Although medical-grade honey has been shown to speed up healing in animal trials, human outcomes have been mixed. Three small randomized single-blind [27-29] and one small randomized nonblinded controlled trial [30] showed that honey may safeguard cancer patients from radiation-induced mucositis. Using honey and hydrogel dressings to treat abrasions and minor lacerations were shown to not affect on healing time in a blind, randomized study [31]. An unblinded study [32] found no difference in average healing times between paraffin gauze, honey, and iodofom gauze for patients who had toenail avulsions. Analysis of these 3 studies found no statistical difference between honey and standard treatment in mild acute wounds [6]. Compared to traditional dressings like silver sulfadiazine dressing [25,34-36] and clear polyurethane film dressing, using honey on minor burns (superficial to partial-thickness burns) speeds up healing time [23]. Honey also outperformed unconventional treatments like potato peels [37] and amniotic membrane [38]. Because of the lack of a description of randomization, the validity of these studies has been called into doubt [6,39]. Meta-analyses demonstrated that honey quickened minor burn healing relative to the comparator [6,39,40]. A randomized controlled experiment found that early excision beat honey dressing in mild burns [41]. However, the study's strength is questioned due to the lack of clarity regarding randomization. When selecting burn wound coverings, clinicians must assess the evidence.

**CHRONIC WOUNDS:** As previously indicated, many chronic wounds result from circulation issues. Because topical medications do not effectively address the primary circulatory impairment, many currently utilized products have limited evidence to support their use. Honey was used to treat venous leg ulcers in two randomized open-label trials. At 12 weeks, the honey-impregnated dressing did not affect venous leg ulcers compared to standard dressing [42]. Both groups used compression. Another study compared honey dressing to hydrogel in soggy intravenous ulcers. At 80 days, honey had a slightly higher healing rate (44%) than hydrogel (33 percent). Both studies reported the randomization approach. Based on these two investigations, a meta-analysis indicated that honey and traditional dressing treat venous leg ulcers equally well [6]. A low-quality randomized controlled experiment indicated that honey dressing accelerated recovery in Stage I and II strain ulcers. Another low-quality study indicated honey to hasten the healing of stage II or III pressure ulcers. The honey plaster was observed to be equally effective as iodine treatment in Wagner type II diabetic foot ulcers. None of the

preceding cited research revealed their randomization process, raising concerns about their validity.

**ALOE VERA PHARMACOLOGY:** Wound healing is aided by a perennial green herb from the Liliaceae family, Aloe vera, which is the most effective. Located at the top of the stem, the thick and juicy leaves form clusters. Slightly toothed lanceolate leaves cover the plant. Red, yellow, or speckled with red are the colors of the flowers. A versatile crop, it is currently farmed all over the world [43,44]. These include cancer prevention, antioxidation, anti-bacteria, and lipid-lowering. Antihypertensive. Antioxidant. Antibacterial. Anti-inflammatory. Antiulcer. Antiviral. These are only a few examples [45-47]. It is also frequently used in the treatment of wounds, burns, ulcers, tumors, constipation, dental difficulties, metabolic syndrome, AIDS, herpes, diabetes, and psoriasis. For its cosmetic properties, it is utilized in cosmetics and skincare products, as well as in the food business, to make health drinks [48-50]. As a medicinal herb, A. vera's leaves are the most commonly utilized portion of the plant. Synergistic effects of more than 200 physiologically active compounds, including carbohydrates, anthraquinones, and chromones and flavones, and alkaloids as well as amino acids and lipids have been proven to be responsible for numerous pharmacological activities [51,52]. Three sections make up the Aloe leaf. Photosynthesis occurs in the green leaf epidermis, which is the outermost layer. Phloem and xylem make up the layer's structure. The xylem transports water, whereas the phloem transports carbohydrates and other tiny organic materials, such as cellulose. Leaf epidermis pericyclic cells secrete the reddish-yellow latex in the center of the structure. As a laxative, latex can be applied to the skin. Chrysophanol, emodin, and anthraquinone make up the bulk of the active component list [53-55]. Tubular cells in the parenchyma form a clear and smooth gel at the heart of the Aloe leaf. Skin wounds can be treated with gel. With a water concentration of 98%, polysaccharides are the primary active ingredient in this formula. In addition, organic acids, vitamins, and minerals abound in gels [56-58].

**ALOE VERA AND SKIN WOUND HEALING:** Aloe vera is a mature medicinal plant for treating skin sores. Aloe gel and Aloe extract can be used for wound healing in the same way [59,60]. Glucomannan and acetylated polymannan are two examples of polysaccharides that are essential for wound healing. Aloin, rhein, emodin, and aloesin are also important. These compositions have antibacterial, antioxidant, immunomodulatory, and anti-inflammatory effects [61-63]. Wound healing is facilitated by these qualities. Different growth factors i.e., FGF, epidermal, TGF, VEGF, and interleukin (IL), influence cell signaling and ECM activity during wound healing (IGF). The migration and proliferation

of epithelial, endothelial, and fibroblast cells are all influenced by basic FGF (bFGF). TGF- $\beta$ 1 inhibits degradation of the extracellular matrix (ECM), regulates fibroblast spread, and stimulates the formation of elastin, collagen, and fibronectin (collagen-like proteins). A. vera's enhanced synthesis of bFGF and TGF- $\beta$  promotes collagen deposition, fibroblast proliferation, and angiogenesis [64,65]. It is believed that IL-1 $\beta$ , an anti-inflammatory cytokine abundant in phagocytes, epithelial cells, and vascular endothelial cells, is responsible for activating T lymphocytes. The anti-inflammatory action of A. vera is due to the reduction of proinflammatory cytokines such as IL-1 $\beta$  [66]. For example, the inflammatory period can be significantly shortened and malondialdehyde, tumor necrosis factors (TNF-A) levels are reduced. glucose transporter 1, IGF-1, VEGF, and FGF-2 can also be considerably increased, which promotes cell production, collagen production, and angiogenesis [67]. The anti-inflammatory and immunomodulatory properties of aloe polysaccharides found in A. vera make them ideal for wound healing. Glucomannan, acetylated poly-mannan, and acemannan are anti-inflammatory polysaccharides that lower MMP-9, IL-10, and IL-05 [68]. Aloe polyose impacts granulation tissue development and wound healing by enhancing glycosaminoglycan and collagen synthesis [69]. The AKT/mTOR signaling pathway enhances the synthesis of cyclin D1, which not only stimulates skin fibroblast proliferation but also shifts the cell cycle from the G1 to the S phase. Increased VEGF and type I collagen synthesis are two mechanisms through which Acemannan enhances wound healing [70-72]. M6P is an aloe polyose involved in epithelialization. Adiponectin promotes collagen deposition and skin regeneration via binding to mannose-6-phosphate receptors. It also inhibits TGF-1 and TGF-2 activation, reducing fibrosis and encouraging epithelialization [73,74]. Anthraquinone also helps protect the skin and cure wounds. The ability to heal wounds and promote angiogenic growth. Anthraquinone is an antibacterial agent that inhibits the dehydrogenation and oxidation of bacterium sugars and metabolic intercedes, as well as the production of protein and nucleic acid. Aloin can improve wound healing by increasing angiogenesis and fibroblast proliferation via increasing EGF expression. Aloin also makes the skin's collagen fibers more regular after healing, minimizing scarring [75,76]. Aloin also protects the skin by decreasing lipid peroxidation and reactive oxygen species while enhancing SOD and glutathione peroxidase activity [77,78]. Aloin reduces IL-6, TNF- $\alpha$ , iNOS, and cyclooxygenase-2 expression in response to LPS (COX-2). Aloin also suppresses caspase-3 activation and apoptosis generated by LPS. Aloin reduces inflammation by decreasing NF- $\kappa$ B signaling [79,80]. Aloe-emodin can aid wound

healing by increasing cutaneous vascular-related growth factor expression. Aloe-emodin is a potent anti-inflammatory. It reduces inflammation by inhibiting iNOS and COX-2 expression. Allergic to [48,81] Rhein? It influences cell cycle and death via MAPK and PI3K-AKT signaling pathways [82]. Other compounds in *A. vera* aid in wound healing. 5.5 kDa glycoprotein has been demonstrated to enhance keratinocyte proliferation and epidermal tissue formation in vitro and in vivo. This glycoprotein improved wound healing in bald mice [83]. b-Sitosterol enhances injury healing and angiogenesis by boosting VEGF and its receptor gene expression [84]. It also possesses anti-inflammatory properties, inhibiting TNF- $\alpha$ , LPS-induced keratinocytes, peptidoglycan, and macrophages from secreting inflammatory factors, and inhibiting caspase-1 activation [85]. Aloesin promotes wound curing by activating Smad and MAPK/Rho signaling pathways. It promotes cell motility by phosphorylating Cdc42 and Rac1 and modulates growth factors and cytokine release in macrophages. Aloesin promotes collagen deposition, angiogenesis, and granulation tissue development in hairless mice [86]. The vitamins in *A. vera* help heal wounds. Vitamin E is a strong antioxidant that can reduce ROS damage. It also modulates transcription and expression of the gene to protect wounds against infections like methicillin-resistant *Staphylococcus aureus*. Vitamin C enhances collagen formation by hydroxylating proline and lysine residues in procollagen. Its ability to boost immunological activity is also vital in wound healing [87,88].

**TURMERIC:** *Curcuma odora* is the common name for this plant. Species of curcumin are known as wild turmeric (vanaharidra) or yellow zedoary (Salisb) (*Curcuma longa* Linn.). The plant is indigenous to India, where it is commonly grown in Kerala and West Bengal [89]. It is both an aromatic medicinal cosmetic as well as a potential therapeutic drug. Traditional Chinese medicine uses *Curcuma aromatic* (CA) as a powerful anti-cancer herb. Uses in traditional medicine include treating skin conditions, sprains, bruises, snake venom, and enhancing the appearance of skin. The Chemical and aroma attributes of the volatile oil are different from *Curcuma long* it's (4-8%) volatile oil. CA's volatile oil includes camphene, camphor, and high-boiling alcohol that *C. longa* does not [90].

**CHEMICAL COMPOSITION:**  $\alpha$  and  $\beta$  (turmerone and curcumin), d-camphor, germacrene D, p-methoxycinnamic acid, curzerene,  $\alpha$ , and  $\beta$  pinenes, germacrene, borneol,  $\alpha$ , and  $\beta$  Terpeniol,  $\gamma$ -Terpenolene, Myrcene, and  $\beta$ -Thujonene, limonine,  $\beta$ -thujone,  $\alpha$ , and  $\beta$  Copoanes and  $\beta$ -Bisabolene are also present. A total of eighteen different compounds were detected in the oil: alpha and beta-pinene, isofurano-germacrene, 1,8-cineol, borneol, and its isoforms,  $\beta$ -

curcumene,  $\alpha$ -curcumene, germacrene, xanthorrhizol, and curzerenone.

**MEDICINAL IMPORTANCE:** Skin, cardiovascular, and respiratory system ailments are among the conditions for which the medication is prescribed in Ayurveda. There are many uses for CA in cosmetics and traditional medicine, including as an anti-inflammatory agent, a stimulant of blood flow, and an anti-cancer agent. It is common to utilize rhizomes with astringent and fragrant herbs in the treatment of a variety of ailments, such as bruising and skin eruptions. There are many uses for CA rhizomes, including in snake poison. Home remedies for headaches include a paste of CA rhizomes [91]. Carbamazepine (CA) is conventionally used as an anti-provocative medication. According to several research, Wild turmeric has immunological, anti-tumor, anti-inflammatory, wound healing, antifungal, antioxidant, anti-microbial, antiplatelet, and insect repellent properties. Preventing coronary heart disease, treating epilepsy, acting as an anti-allergy, and treating auto-immune disease are all uses of CA. In the therapy of cholecystitis, biliary calculi, and other related illnesses extracts of CA roots are used. In mice with Ehrlich ascites tumor cells, ethanol extract had powerful anti-angiogenic and pro-apoptotic actions. Anti-proliferative activity against human cancer cells was established by methanol extracts of CA. An in vitro estrogenic effect was also seen. Rhizomes produce 6.1 percent essential oil and have been shown to have anti-tumor properties. Rhizomes. Cervical cancer in its early stages can also be treated with oil. An in vivo inhibitory impact of volatile oil on hepatocellular growth was observed in mice. In vitro antihelmintic action was also demonstrated using essential oil [92]. Curcumin's anti-inflammatory properties, the anti-diabetic effects of (4S,5S)-(+)-germacrene-4,5-epoxide, and the antiarrhythmic properties of aqueous extract due to the presence of dipotassium magnesium dioxalatedihydrate are just some of the other activities that have been linked to essential oils. The oil and the methanol extract have powerful radical-scavenging properties. - In addition, the extracts showed impressive superoxide radical scavenging properties. A number of the curcuminoids in CA have been shown to have antibacterial, antifungal, antioxidant, and antitumor properties [91]. In the following part, we'll go into more detail about each of these. Mice tested the anti-inflammatory effects of aqueous and alcoholic extracts. In arachidonic acid-induced ear inflammations, the ethanol extracts and formulations showed considerable anti-inflammatory action. The anti-inflammatory activity was attributed to the impacts on various mediators and arachidonic acid metabolism including the cyclo-oxygenase pathway [93]. An investigation of the volatile oil from

California's anti-inflammatory properties was also conducted. In rabbits, the powdered rhizome of CA was found to have wound-healing properties. Studies using excision wound models, which were used to evaluate the wound healing activity of topical application of CA rhizome extracts and its cream formulations [93], likewise revealed considerable wound healing activity. A key bioactive component of CA, Germacrone has been shown to have anti-tumor activities. CA's most essential bioactive component is this. An investigation into the anti-proliferative and molecular mechanisms of germacrone's cytotoxicity on glioma cells found that germacrone inhibits the proliferation of cancerous cells by causing apoptosis and cell cycle arrest in the cells. By regulating the expression of proteins associated with apoptosis and G1 cell cycle arrest, Germacone may be an effective and new chemopreventive treatment for gliomas [94]. Researchers also looked at the anti-tumor properties of beta-elemene, which was extracted from the roots of agave plants in California. Two tumor inhibitory tests on hepatoma in mice were carried out as part of the study to investigate the inhibitory effects of Curcuma aromatic oil (CAO) on hepatoma in mice's cell proliferation. Proliferating cell nuclear antigen (PCNA) immunohistochemical labeling was utilized to assess the effects of CAO on hepatocarcinoma proliferation in mice (PCNA). In two experiments, the tumor inhibitory rates of CAO were 52 percent and 51 percent, respectively, as a result of the consequent tumor inhibitory rates. Both variations were statistically substantial (P 0.01) when compared to the results of the saline-treated control groups. [95]. The researchers concluded that CAO's prevention of hepatoma growth in mice may be connected with its suppression of cellular proliferative activity.

## CONCLUSION

When it comes to healing skin wounds, there is a wide range of medicinal plants and natural therapies that are used. These have been utilized for centuries to treat trauma, infection, disease, and damage. For millennia, humans have mastered the art of harvesting and preparing edible and medicinal plant materials from their local surroundings. Medicinal practices have been examined for clinical efficacy and economic viability based on their bioactivities. As a result, not all the mechanisms of action of each plant have been established. For the most part, we believe that traditions still have a lot to offer us, including the potential for developing novel drugs and treatments for today's therapeutic challenges. There is no escaping the fact that modern medicine and pharmaceuticals remain out of the reach of most people. Traditional medicine is often the primary and only therapy choice for many people because of

this. Traditional ways will become more widely accepted and appreciated as people grow more familiar with them. This information should not be rejected by "modern medicine," but rather put to good use for the benefit of humanity. There are no adverse effects associated with using Aloe vera, turmeric, and honey to cure wounds. Healing and regeneration of lost tissues are facilitated by numerous processes in these herbal creams. However, these herbal ointments must be evaluated scientifically, standardised, and evaluated for safety. Aloe vera's high tonicity and acidic pH are thought to be the major elements that speed up wound healing in earlier studies, which found that wounds treated with Aloe vera healed quickly. The wound healing process may be accelerated by Turmeric, Honey and aloe vera's ability to boost glycolytic enzyme activity and provide enough energy for cell repair. To treat wounds, Turmeric, Honey and Aloe vera can be a cost-effective option that is safe, readily available, and has powerful healing properties.

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