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ORIGINAL ARTICLE

Natural Wound Healer: An Insights on Aloe Vera's Medical Importance

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ABSTRACT
Aloe vera has been used as a traditional therapy for a range of ailments, with the plant's inner gel being the most commonly studied and utilised. These plants are favoured because they are effortlessly available, affordable, and have rarer bad side effects than commercially available pharmaceutical compounds, say proponents. However, there hasn't been enough research done on the active components and the precise mechanisms by which they work. Identifying active ingredients and their functional mechanisms in wound healing is the focus of this review. Using A. vera gel for wound healing has been found to have a positive reaction, but this has only been demonstrated in the case of minor, uncomplicated lesions. Different active components including aloesin and aloin have been suggested to have a synergistic effect on the plant's actions, rather than a single chemical acting alone. For now, the plant should only be used in conjunction with other well-established, scientifically supported treatments.
Keywords: Wound, Natural, Inhaler, Aloe Vera, Wound Healing

INTRODUCTION
About 420 species of Aloaceae plants are classified as belonging to the Aloe barbadensis Miller genus, which is the botanic name for Aloe vera [1]. In contrast to the six other genera in the Aloe family, the Aloe genus has bright yellow flowers, thick leaves, and lengthy stamens. Aloe is a subfamily within the Aloaceae [2]. Additionally, Aloe vera and Aloe arborescens are two of the most extensively researched species. There is evidence that A. vera was used as a therapeutic medicine in Mesopotamia and other regions of the world as far back as 1750 B.C., despite the passage of time. As a result, they can be found all over the world, from South Africa to Malaysia to the subtropical and tropics, where they thrive in dry conditions [1].

Figure 1: Aloe Vera Plant

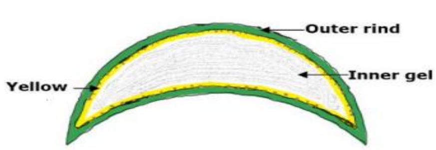

Figure 2: Aloe Vera Leaf Cross Section

Rhododendron rosette plants are known for their triangular, succulent leaves covered in spines (see Figure 1). In order to build a leaf, there must be three different layers (see Figure 2): Proteins and polyoses, i.e. highly acetylated glucomannans, are manufactured in the thick rind of 15-20 cells that forms the outermost layer [3]. Anthraquinones and glycosides predominate in the intermediate layer, which protects the gel surface and comprises the yellow fluid secreted by outer bundle sheath cells. Most of the innermost layer is made up of water, which comes from the clear centre mucilaginous pulp [4]. After initial harvesting and use as a bitter cathartic, the plant's inner transparent gel was discovered to have a broad range of curative applications.

Aside from its wound healing, ultraviolet protection, anti-seditious, purgative, antiviral and anticancer, oiling and anti-aging influences, as well as its antibacterial and antibacterial capabilities, the herb has been used historically [5]. A. vera, on the other hand, appears to have inconclusive effects on the human body as further research is conducted. Furthermore, there is a paucity of knowledge about the plant's biological components and how these components interact with humans. Researchers have worked harder to learn more about this topic, but their findings have been inconsistent, suggesting that its effects may not be due to a single active biochemical ingredient, but rather to the combination of multiple active components found in plants. Therefore, the primary goal of this research is to determine the active substances and the methods by which they work in areas where A. vera has already undergone extensive investigation (wound healing).

Wound Healing: Whenever the typical anatomical structure and function of the skin are disrupted, the wound healing process is prompted to begin. It is possible to break down the four steps into four distinct mechanisms. Scar tissue development and migration of fibroblasts characterise proliferation, whereas activation of the complement cascade and neutrophil infiltration into the wound site characterise acute inflammation during acute inflammation. We call this the ultimate stage of wound remodelling since scar tissue is formed during this time. [6]. Since mediaeval times, several herbs have been utilised to treat and heal wounds. Aloe vera, a species of the aloe genus, has demonstrated superior wound healing ability when compared to other aloe species, including Aloe ferox and Aloe marlothii [7]. Other plants that have been shown to have wound-healing properties, in addition to A. vera, comprise the leaves of Lafoensia pacari A. St.-Hil, a indigenous Brazilian tree [8], Sanguisorba officinalis L. [9], oat Avena sativa [10], Artemisia k [11]. A. vera has shown promising effects in a variety of wound types, according to the researchers. Burn wound models have shown favourable responses in second-degree burns involving damage to the cuticle and derma [12], and even 3rd degree burns including destruction to the derma and deeper tissues [12]. In addition, such consequences have been revealed in a full-texture excisional injury model [13, 14], a full-thickness incisional wound model [15], a shallow wound simulation concerning postdermabrasion injuries. It has also been proved that A. vera has the capability to cure wounds that are exemplified by prolonged recovery, i.e., those triggered by intense radiation or diabetic lacerations [16]. A probable, randomised, dual-blind, placebo-monitored experiment with post-operative patients has exposed that the treatment has a beneficial effect despite the fact that the majority of the positive responses were established in animal models [17]. In contrast, when the gel was administered that is supplemented with regular sore care, the recovery of vertical wounds was found to be delayed as equated to the group that received only traditional wound treatment. In this case, it is possible that the gel medication is not appropriate for people who have hurt issues that require recovery by a secondary aim. It is also noteworthy that more regular management may result in greater restorative capacity, as evidenced by twofold daily contemporary administration of the ointment as equated to just the once daily treatment of the gel [19].

In one study, a 5.5 kDa glycoprotein was found as having cell-proliferation activity. However, Veracylglucan C, which has been demonstrated to have anti-proliferative properties, may be able to counteract this impact. According to another investigation, a heavy molecular mass polypeptide has been identified as the component accountable for the phenomenon. Aloesin [14] and aloin [13], which are two of the primary elements of Aloe vera exudation, may also play a part in the acceleration of wound treatment, according to the research (Figure 3). When it comes to wound healing, it is most likely that the underlying processes of the increased wound-therapy procedure begin in the second phase of the healing process (inflammation) [14] observed greater quantities of neutrophiles and macrophages in the cured group at this point. These levels then reduced on Day 7. Increased neutrophil numbers improved the clearance of microorganisms and cellular wastes from the lesion, but neutrophils too create chemical compounds that may possibly trigger some harm, i.e., reactive oxygen species and peptidases, when they are in the wound. Moreover, when the wound progresses into the proliferative phase, macrophages contribute to the provocative response by the release of cytokines and the induction and clearance of apoptotic cells, which include neutrophils [19].

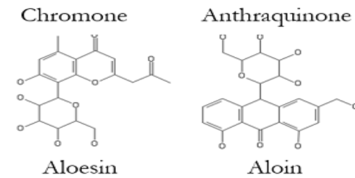

Figure 3: Purposed Wound Healing Compounds in Aloe Vera Chromone (Wahedi et al. 2017) and Anthraquinone (Li et al. 2017)

Following that, it was discovered that the proliferative phase had been accelerated while still taking place in a regulated manner. According to the findings, a reduction in the duration of the Gap 0 (resting phase) / Gap 1 (interphase) of the cell cycle, which resulted in an increase in the length of the S phase (DNA synthesis) of the cell cycle [13, 14], was responsible for an increase in cell proliferation. Additionally, the increased proliferation of fibroblasts was accompanied by an increase in migration, which was mediated by the phosphorylation of Cdc42 and Rac1, as well as the overexpression of -PAK, both of which are migration-related proteins, and the overexpression of phosphorylated Cdc42 and Rac1, both of which are migration-related proteins. Increased levels of extracellular matrix (ECM) components such as glycosaminoglycan (GAG), hyaluronic acid (HA), proteoglycan (PG), and dermatan sulphate (DS) may be generated when a large number of fibroblasts are present. It was also found that the freshly generated collagen fibres had better alignment than the older collagen fibres, which indicates that the production of collagen, another component of the extracellular matrix, was boosted as well when equated to the alignment of the collagen fibres in the untreated wounds, suggesting that the formation of scar tissue may be prevented [13, 14].

However, in another study, no similar proliferative influence on fibroblasts was detected, but the fibroblasts were extra mature and well aligned as a result of the treatment. Also reported to be enhanced in A. vera-treated groups were the quantities of glycohydrolases identified in sore granulation tissue. In addition to beta-glucuronidase and N-acetyl glucosaminidase, several glycohydrolases have been examined, including beta-glucosidase and beta-galactosidase, both of which are involved in the return of the extracellular substance. Also activated were signalling proteins such as Smad (an abbreviation formed from the fusion of Caenorhabditis elegans Sma genes and the Drosophila Mad, Mothers against decapentaplegic) and mitogen activated protein kinase (MAPK), which are important players in cell migration, angiogenesis, and tissue development. Angiogenesis, defined as the formation of new vessels from active vasculature in granulation tissue, was observed to be improved with A. vera therapy, which was associated with the activation of angiogenic growth factors in the tissue [13, 14]. In addition, increased representation of the development features vascular endothelial growth factor (VEGF) [16], transforming growth factor-1 (TGF-1) and basic [16, 20]. According to the findings, the effect of A. vera on the expression of TGF—1 and bFGF was shown to be dosage- and time-dependent, with the expression decreasing markedly after 24 hours. Since the buildup of matrix peptides and the subsequent creation of a hypertrophic trauma appears to be a reaction mechanism to avoid overrun of these development factors, it appears to be an effective method [20]. The collagen fibres in the last segment of the injury-recovery process were shown to have a greater degree of cross-linking, which resulted in increased lesion strength. Therefore, investigators have tried to add A. vera having chemical composition (Table 1) into formulations to make wound dressings that are both effective and safe to use.

Table 1: Chemical Composition of A. Vera and it properties (Zhang and Tizard 1996) [21]

Constituents	Number & Identification	Properties & Activity
Amino acids	Provides 20 of the 22 required amino acids and 7 of the 8 essential ones.	Basic building blocks of proteins in the production and muscle tissues.
Anthraquinones	Provides aloe emodin, aloetic acid, alovin, anthracine.	Analgesic, antibacterial
Enzymes	Anthranol, barbaloin, chrysophanic acid, smodin, ethereal oil, ester of cinnamonic acid, isobarbaloin, resistannol.	Antifungal & antiviral activity but toxic at high concentrations.
Hormones	Auxins and gibberellins	Wound healing & anti-inflammatory.
Minerals	Calcium, chromium, copper, iron, magnesium, manganese, potassium, sodium, zinc.	Essential for good health.
Salicyclic acid	Aspirin like compounds	Analgesic
Saponins	Glycosides	Cleansing & antiseptic
Steroids	Cholesterol, campesterol, lupeol, sistosterol	Anti-inflammatory agents. Lupenol has antiseptic and analgesic properties.
Sugars	Monosaccharides: Glucose & Fructose Polysaccharides: gluco-mannans / polymannose	Antiviral,immune modulating activity of acemannan
Vitamins	A,C,E,B, choline, B_{12}, folic acid	Antioxidant(A,C,E) Neutralises free radicals

Electrospinning has been used to make nanofibrous dressings with polylactic-co-glycolic acid (PLGA) as the polymeric matrix [22] or polyvinyl alcohol (PVA) as the polymeric matrix in the past [23]. This was followed by the electrospinning process, which was used to incorporate recombinant human epidermal growth factor (rhEGF) into the dressings. When combined with A. vera, this resulted in an increase in fibroblast proliferation, demonstrating that the synergistic effect of these two compounds was not compromised by the electrospinning process. A. vera extract was added to the polymeric solution, which resulted in an increase in viscosity and conductivity, which made the electrospinning process easier [23]. The membranes were also given higher flexibility and tensile strength as a result of this [22]. Because of the varied mechanisms involved, the incorporation of A. vera into numerous types of substances resulted in a variation in the release rate of A. vera. Researchers discovered an opposite relationship concerning the amount of A. vera present and the ratio at which the film was released. This was attributable to the fact that the diameter of the fibres increased as the A. vera content increased, resulting in a decline in the external area of the films. On the antithesis, increased concentrations of the active ingredient in hydrogel sheets resulted in faster release rates. As the amount of A. vera in the hydrogel films rose, pore expansion increased, which made it easier for water to enter the films [23]. In the meantime, in another exploration project, aloin-loaded chitosan-alginate (CA) and chitosan-xanthan (CX) tissues have also been produced for use as wound bandages in a variety of applications. CA membranes exhibited the features of being extra stable in fluid media and exhibiting higher standards of extension at break, whereas CX membranes exhibited continual release of aloin for up to 5 hours, which was a result of the cross-linking progression with calcium ions during the fabrication process [24].

CONCLUSION

Currently available evidence supports the use of A. vera, which has demonstrated incredible powers in the area of wound healing. This is an optimistic first step toward widespread adoption of the plant. Moreover, a favourable reaction to the Aloe Vera gel has been exhibited, which supports the application of A. vera in wound-healing gel; nevertheless, it should only be applied to small, uncomplicated wounds. Its activities have been attributed to a range of distinct active components, including chromone and anthraquinone, and this can be translated as the result of an interaction between several compounds more accurately than the activity of a particular substance. In order to achieve a concentrated concentration of active compounds in Aloe vera formulations, researchers are increasingly investigating the influence of processing processes on the active compounds. This research is important in order to inhibit the deprivation of the active agents and the loss of the anticipated effect. In light of the increasing number of A. vera uses in diverse fields, more research should be conducted in this area.

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