


# Is aloe vera effective for wound healing? The state of the art

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## Abstract:

**Introduction:** *Aloe vera* is a herbal plant that has been used widely for centuries as a natural medicine. Its therapeutic activity is based on the numerous beneficial pharmacological properties induced by the parenchyma. It is easy to access, manipulate and is low-cost; these properties have led to a progressive increase in its consumption. However, its action in the cicatricial process is not fully known, which has driven research into new discoveries in this context. **Aim:** The purpose of this literature narrative review was to discuss the current information available on the benefits of using *Aloe vera* in the wound healing process. **Materials and methods:** Scientific articles were selected from the PubMed and LILACS databases between February 2018 and July 2018, by using the English and Portuguese words of “Aloe Vera”, “Wound healing”, “Healing” and “Tissue repair”. In total, 229 articles were found in PubMed and 63 articles were found in LILACS. After reading the abstracts, 30 articles that reported how the pharmacological properties of *Aloe vera* influence the healing process were selected. **Results:** *Aloe vera* exerted positive effects on the treatment of oral ulcers and protection of the mucous membranes, with reductions in these lesions and the painful symptomatology. In addition, it was effective for the prevention and treatment of oral mucositis and the reduction of candidiasis in patients with cancer. Promising results have also been reported from the treatment of symptomatic oral lichen planus. In the treatment of plaque-induced gingivitis, *Aloe vera* provided a significant improvement in inflammation. **Final considerations:** The literature supports the anti-inflammatory and cicatricial potential of *Aloe vera*, which has a wide indication for the treatment of several conditions. Therefore, additional clinical studies based on scientific evidence are needed to gain a better understanding of *Aloe vera*, its compounds and therapeutic indications.

**Keywords:** Aloe; Wound healing; Plants, medicinal

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## INTRODUCTION

Herbal medicines are a form of treatment that is based on the use of plants with a high potential for bioactivity. These therapies have been used throughout history for the treatment of various diseases; recipes have been passed down through generations to become common knowledge that is associated with culture, health, and improvements in the quality of life of people with illnesses<sup>1,2,3</sup>.

Despite the vast production of synthetic substances used in the pharmaceutical industry, the concept of plant-based therapies remain popular and their market share has continued to increase. This was justified by the idea that the use of natural products is directly linked to greater benefits and fewer undesirable side effects<sup>4</sup>. The low cost, which results from easy access and manipulation, is often associated with medicinal plants; often, they are the only viable treatment option for patients, especially in populations with low social economic power<sup>5</sup>. Studies indicate that approximately 82% of Brazilians make use of healing herbs; however, the efficiency of many of these herbs have not been scientifically confirmed<sup>2</sup>.

One of the medicinal plants in the Brazilian territory is *Aloe barbadensis*, popularly known as *Aloe vera*, is characterized as a shrubby plant with medicinal power of extreme importance for the treatment of various skin diseases. *Aloe vera* belongs to the Liliaceae family, originates from South Africa and Asia and exhibits favorable growth patterns in tropical areas. The plant spread to Brazil during the colonial period, where it adapted to different regions. Currently, there are more than 300 known species of *Aloe*, but only four are considered safe for medical use; the others are regarded as harmful<sup>1,5</sup>.

*A. barbadensis* is the species that contributes to the greatest amount of nutrients in the gel (*Aloe vera*), which justifies its choice as the species of choice for curative medicine<sup>1</sup>. The gel is contained in your and parenchyma, corresponding to the main scar residue, and is able to induce the proliferation of fibroblasts, macrophages, and angiogenesis. It also contains anthraquinones known to have antibacterial, antiviral, and antifungal action<sup>6</sup>.

The therapeutic activity of *Aloe vera* can be used to treat skin lesions, such as burns, irradiation damage, and ischemic ulcers. The gel has healing, analgesic, and anti-inflammatory activity, in addition to being a powerful hydrating and skin-protective agent, contain vitamins C and E, essential amino acids, and polysaccharides that stimulate the growth of tissues and cell regeneration<sup>7</sup>.

Studies have reported the use of *Aloe vera* gel for the treatment of rheumatoid arthritis, eye diseases, and intestinal disorders<sup>6,7</sup>. The pharmacokinetics also include hypoglycemic, detoxifying, antioxidant, and antimicrobial (antibacterial, antifungal, and antiviral) properties, and anticancer, immunomodulatory, and gastroprotective activities<sup>8,9</sup>.

It is known that all individuals are prone to injuries and, when attacked, the human body begins the process of tissue repair. This process is systemic, complex, and dynamic, and is dependent on the environmental and physiological conditions. During the healing period, complications from contamination by infectious agents or metabolism imbalance, or insufficient vascularity may occur. The healing process is characterized by the formation of new tissue and consists of three phases: proliferative, inflammatory, and remodeling, in which the migration of leukocytes and early cascade of tissue, the production of reparation fibrous tissue, angiogenesis, reepithelization, and increased resistance to damaged occurs<sup>10,11</sup>.

Although many technological advances have occurred in the field of healthcare owing to the development of new materials and medicines, questions remain on the existence of an ideal dressing for the treatment of wounds and on the ability of *Aloe vera* to stimulate healing<sup>6</sup>. Given the importance of studying the curative potential of medicinal plants, this literature review aims to collect concise and current information in the scientific literature about the benefits of *Aloe vera* use in the wound healing process.

## MATERIALS AND METHODS

This study was a narrative literature review based on the search of scientific articles in the Pubmed and LILACS databases between February 2018 and July 2018. The following descriptors were used in English and Portuguese: "Aloe Vera", "Wound healing", "Healing", and "Tissue Repair".

The selection of articles was based on titles that determined how the *Aloe vera* was able to influence or exert a modulatory role in the inflammation and/or in the healing process, as well as their constituent compounds, phytochemicals, functions during repair, clinical applicability, cellular changes, and other general aspects of the plant.

Initially, we collected the summaries available in databases. An initial search identified 229 articles in the Pubmed and 63 in the LILACS databases. Only articles

that contained scientific evidence about *Aloe vera* in the area of health and therapeutic potential in the tissue healing process were selected. The following inclusion criteria were used: relevant articles written in English and Portuguese that were published between 1979 and 2018. The selection was started in the year 1979, as the existence of articles relevant to the subject started this year. The articles that did not have complete summaries were excluded from this study.

After analysis of the articles, only 30 were included in this narrative literature review (Figure 1).

## LITERATURE REVIEW

### HISTORY of the *ALOE VERA*

The first evidence for the use of *Aloe vera* was found in ancient Mesopotamia, documented in a clay tablet at approximately 2100 BC. It is believed that the name is derived from the Arabic word *alloe*, which is defined as bitter and brilliant product<sup>12</sup>.

The Egyptians pioneered the use of this herb for medicinal purposes, such as to cure skin diseases, burns, and infections, followed by the Greeks, Spaniards, and Africans<sup>13</sup>. Despite their African roots, the *Aloe vera* was taken to many regions of the world, and adapted to them all, but flourished in hot and dry locations<sup>5,13</sup>.

*Aloe vera* was referenced in the encyclopedia *Natural history of Pliny, the elder* (23–79 AD) and in the *Medical Materia of Dioscorides*, who alluded to the strong smell, bitter taste, and use for curing skin disorders. However, despite the range of uses, this herb was only officially recognized by the British Pharmacopoeia in the year 1932<sup>14</sup>. Over the years, owing to its many healing properties, *Aloe* has been given several popular names, such as “wand of heaven”, “blessing of heaven”, and “the silent healer”<sup>15</sup>.

### CHEMICAL COMPOSITION

The extract of *Aloe Vera* leaf yields two parts: the first, located in the outermost region, which is a bitter yellow exudate, popularly known as “Aloe juice”; and the second, present in the area inner sheet, called parenchyma, is the mucilaginous gel of Aloe<sup>16</sup>. The outer fraction contains a large amount of anthracenes, which possess laxative properties<sup>17</sup>, whereas the mucilaginous gel contains biologically active molecules that function during the process of wound healing wounds and burns, to relieve painful symptoms, and moisturizing properties<sup>18</sup>.

This plant contains 75 phytochemicals compounds with biological properties, which demonstrate that it is a medicinal herb<sup>15,8</sup> (Table 1). Among its components are vital nutrients such as vitamins A, C and E, which act

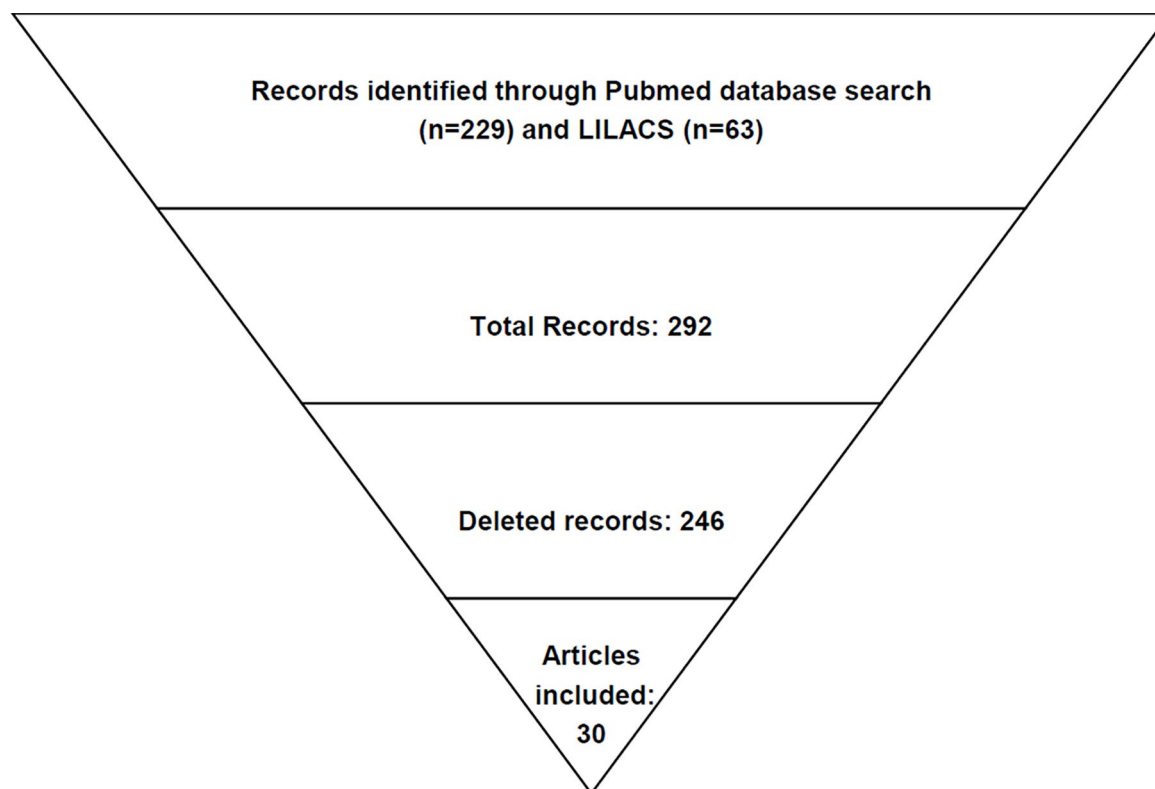


Figure 1. Flow chart of the literature review.

**Table 1.** Chemical constituent of *Aloe vera*.

Class	Chemical Composition
Anthraquinones	Aloin, Barbaloin, Laobarnaloin, Anthranol, Aloetic acid, Anthracene Ester of cinnamic acid, Aloe-emodin Emodin, Chrysophanic acid Etheral oil, Resistanol
Inorganic	Calcium, Sodium, Chlorine, Manganese, Sorbate magnesium, Zinc, Copper, Chromium, Potassium
Saccharides	Cellulose, Glucose, Mannose, L-Rhamnose, Aldopentose
Enzymes	Oxidase, Amylase, Catalase, Lipase, Alkaline phosphatase
Vitamins	Vitamin B1, Vitamin B2, Vitamin B6, Choline, Folie acid, Vitamin C Alpha-tocopherol, Beta carotene
Essential amino acids	Lysine, Threonine, Valine, Leucine, Methionine, Isoleucine, Phenylalanine
Non-essential amino acids	Histidine, Arginine, Hydroxyproline, Aspartic acid, Glutamic acid, Proline, Glycerin, Alanine, Tyrosine
Miscellaneous	Cholesterol, Triglycerides, Steroids, Beta-sitosterol, Lignins, Uric acid, Gibberellins, Lectin-like substance, Salicylic acid

as antioxidants, minerals (calcium, copper, magnesium, potassium, and zinc), enzymes, glycoproteins, amino acids, carbohydrate constituents, such as polysaccharides and salicylic acid. The polysaccharides include galactose, xylose, arabinose, and acetylated mannose<sup>8,15,19</sup>.

As seasonal changes, changes in the cultivation, extraction, and processing, and geographical location, are modifiers of the composition of *Aloe vera* gels. Plants that receive greater irrigation tend to have lower levels of polysaccharides than in plants that receive lower irrigation. Therefore, plants that receive lower irrigation tend to have greater medicinal effects<sup>8, 12</sup>.

### **ALOE VERA IN TISSUE HEALING**

After injury, the human body starts a dynamic cascade of cellular and molecular events that aim to restore the integrity of the injured tissue through a process called scarring. To achieve the ultimate goal of successful healing, some mediators of inflammation, such as anti-inflammatory drugs, are common in pharmaceutical or medicinal plants. It is believed that *Aloe vera* is able to exert an anti-inflammatory role in these processes. The likely mechanism for the anti-inflammatory action is mediated through the reduction of vasoconstriction and platelet aggregation, with a subsequent improvement in the oxygenation of the wound, the elimination of free radicals, and the increased formation of collagen. In addition, it appears to be able to inhibit cyclo-oxygenase,

reduce leukocyte adhesion, and reduce the activity of pro-inflammatory cytokines, such as TNF- $\alpha$  (tumor necrosis factor alpha) and IL-6 (interleukin-6)<sup>20-22</sup>.

Some studies have suggested another possible mechanism of action of *Aloe vera*, which supported the potential anti-inflammatory. It is believed that the presence of the enzyme carboxypeptidase in the plant degrades bradykinin, a substance involved in the inflammatory process<sup>15,23</sup>.

The curative property of *Aloe vera* was also related to the presence of the constituent polysaccharides, which are the most important constituents in the healing of cutaneous wounds<sup>20</sup>. Mannose-6-phosphate and acemannan are active components present in the skin of plants and are able to bind to receptors on the surfaces of macrophages and fibroblasts, which induces the proliferation and growth of these cells. As a consequence of the increase in fibroblasts, there will be greater collagen synthesis, by the tensile strength of the wound<sup>24,25</sup>. In 2012, Tarameshloo *et al.*, evaluated the effects of the gel of this phytotherapeutic during the healing process of sutured incisions in Wistar rats in comparison with those of thyroid hormone cream and silver sulfadiazine cream. The results of the study showed that *Aloe vera* gel exerted positive effects on wound healing, as it was able to increase the production of fibroblasts, optimize reepithelialization, angiogenesis, and accelerate wound closure. These authors also confirmed the existence of mannose-6-phosphate as an important structural component of *Aloe vera* and was capable of increasing the activity of macrophages and inducing the proliferation of fibroblasts<sup>25</sup>.

In 1998, Chithra *et al.*, assessed the presence of high levels of hyaluronic acid and dermatan sulfate in the granulation tissue in wounds treated with *Aloe vera*, and suggested that the two compounds helped significantly in healing the injury, because they were responsible for the stimulation of the synthesis of collagen and fibroblastic activity<sup>26</sup>.

In 2016, Oryan *et al.*, investigated the healing effect of topical *Aloe vera* on skin wounds on the backs of mice; after application, modulation of inflammation, stimulation of fibroplasia, and increased production of collagen and glycosaminoglycans were observed. It was noticed that the improvements in the lesions occurred dose dependently in the different stages of healing, and the wounds treated with *Aloe vera* exhibited greater acceleration of contraction, faster reepithelization processes, and less scarring<sup>27</sup>. Another study conducted by Mercès

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*et al.*, in 2017, assessed the healing ability of *Aloe vera* on wounds induced on the back of rats and their results showed that for 100% of the animals treated with these herbal medicines, complete healing occurred on the 21st day post wounding<sup>1</sup>.

In 2011, Atiba *et al.*, exposed rats orally administered *Aloe vera* to radiation and observed that wound contraction was accelerated in the treated animals compared with the control animals. In addition, the authors observed the largest formation of vessels, greater proliferation of fibroblasts, and maximum deposition of collagen deposition, with the expression of TGF-1 (transforming growth factor 1) and BFGF (basic fibroblasts growth factor) significantly higher in the group of irradiated animals treated with *Aloe vera* compared with the group that did not receive the medication<sup>28</sup>. In the study of Oliveira *et al.*, in 2010, progressive improvement in an injury diagnosed as an ischemic bruise was observed. In this case study, the authors treated the patient with the use of a non-conventional coverage of a base of *Aloe vera* and collagen. During treatment, there was a great reduction in the dimensions of the wound, with contraction of the edges and a significant formation of granulation tissue and epithelial cells, with complete healing of the wound after 10 weeks of treatment<sup>7</sup>. In 2009, Faleiro *et al.*, contacted a controlled study in which the glycolic extract of *Aloe vera* was found to facilitate the healing process through the retraction of the wounds in the skin of animals. Moreover, the histological analysis revealed that the reepithelization and restructuring of the dermis occurred in rats treated with this herbal medicines, whereas in the untreated rats, reepithelization was retarded<sup>5</sup>.

In dentistry, some studies have demonstrated positive results for the use of *Aloe vera* for oral complications and oral diseases. In 2013, Ajmera *et al.*, conducted a study of patients diagnosed with gingivitis induced by bacterial biofilms. The treatment consisted of mouthwash with *Aloe vera*, and the authors concluded that washing with 15 mL of mouthwash containing of Aloe for 1 minute twice per for 90 days led significant improvement was observed in inflammation. Thus, it was concluded that this rinse can be used as an auxiliary therapy to mechanical treatments for gingivitis<sup>29</sup>.

According to Ahmadi, in 2012, in a literature review on the impact of the use of *Aloe vera* in the reduction of radiation-induced oral mucositis in patients with head and neck cancer, the use of mouthwash with 94.5% Aloe juice not only proved to be effective for

the prevention of mucositis induced, but also for the prevention of candidiasis, owing to its antifungal and immunomodulatory properties. There was a significant improvement in the delivery of nutrition to the patients, and a consequent improvement in the quality of life<sup>21</sup>.

As reported from the use of *Aloe vera* in oral mucositis, in a study by Garnick *et al.*, in 1998, the authors evaluated the effectiveness of acemannan gel on the treatment of recurrent oral ulcers. The results showed that there was a reduction in the number and painful symptoms of the lesions, as well as increased time between the appearance of ulcers in the patients treated with the gel, by 3 to 4 months<sup>30</sup>.

## FINAL CONSIDERATION

The use of different forms of *Aloe vera* appears to be promising; it is easy to access, low cost, and highly effective for the treatment of various injuries in different areas of health owing to its peculiar pharmacological properties, such as potential anti-inflammatory, antimicrobial, and immunomodulatory activities. Therefore, additional clinical studies based on scientific evidence are needed to gain a better understanding of *Aloe vera*, its compounds and therapeutic indications.

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