








PHARMACOLOGICAL EFFICACY OF ALOE VERA IN WOUND HEALING: A NARRATIVE REVIEW

EFICACIA FARMACOLÓGICA DEL ALOE VERA EN LA CICATRIZACIÓN DE HERIDAS: UNA REVISIÓN NARRATIVA

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ABSTRACT

Aloe Vera has different therapeutic effects, including wound healing. The objective of this review is to determine the potential efficacy of the topical use of Aloe Vera in the healing of skin wounds. A bibliographic search of preclinical and clinical studies was carried out from 1999 to 2020, which included the therapeutic use of Aloe vera in the healing of: burns, surgical wounds, lactation disorders, anal fissure and anal fistula; in the databases of the VHL regional portal, PubMed and Google Scholar. It was obtained that the topical administration of Aloe vera was effective in the healing of the mentioned wounds by mainly increasing epithelization and collagen content. In conclusion, the evidence suggests that the properties and pharmacological presentation, chemical components and the effectiveness of Aloe vera to reduce the healing time of wounds make this plant a great therapeutic alternative; however, more studies are required regarding its antimicrobial property.

Keywords: Aloe vera; Wound healing; Burns; Surgical wounds; Fissure in ano. (Source: MESH-NLM)

RESUMEN

El Aloe Vera tiene distintos efectos terapéuticos, entre ellos, la cicatrización de heridas. El objetivo de esta revisión es determinar la eficacia potencial del uso tópico del Aloe Vera en la cicatrización de heridas cutáneas. Se realizó una búsqueda bibliográfica de estudios preclínicos y clínicos desde 1999 hasta el 2020, que incluyó el uso terapéutico del Aloe vera en la cicatrización de: quemaduras, heridas quirúrgicas, trastornos de la lactancia, fisura anal y fístula anal; en las bases de datos del Portal regional de la BVS, PubMed y Google Scholar. Se obtuvo que la administración tópica del Aloe vera fue eficaz en la cicatrización de las heridas mencionadas al aumentar principalmente la epitelización y el contenido de colágeno. En conclusión, la evidencia sugiere que las propiedades y presentación farmacológica, componentes químicos y la eficacia del Aloe vera para disminuir el tiempo de la cicatrización de las heridas hacen de esta planta una gran alternativa terapéutica; sin embargo se requieren más estudios respecto a su propiedad antimicrobiana.

Palabras clave: Aloe vera; Cicatrización de heridas; Quemaduras; Heridas quirúrgicas; Fisura anal. (Fuente: DeCS- BIREME)

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INTRODUCTION

Aloe vera is a medicinal plant belonging to the genus *Aloe* and the liliaceae family, used for millennia by different cultures^(1,2,3,4). It is commonly known as *Aloe barbadensis* Miller^(3,4,5). Its geographic origin is believed to be northwestern Africa^(1,2), specifically Sudan, and it was later introduced in the Mediterranean region and most of the warm areas of the world⁽³⁾. Regarding the impact of the use of medicinal plants in Peru, trends indicate that 76% of EsSalud policyholders would have no problem being treated with medicinal plants. In contrast, almost 90 000 policyholders use complementary medicine services in the 83 Peruvian complementary medicine care centers. It is also important to highlight that the highest consumption of medicinal plants is to treat diseases of the digestive, genitourinary, and respiratory systems⁽⁶⁾.

The therapeutic effects of *Aloe vera* have been attributed over the years⁽³⁾, among them, we can highlight the acceleration of wound healing, anti-inflammatory, moisturizing, anti-allergic, disinfectant, antimicrobial, antiseptic, anthelmintic, among others^(1,2). Currently, many investigations, both clinical and preclinical, have shown that *Aloe vera* is a biomaterial with great potential for wound healing, such as burns, surgical and postoperative wounds, anal and mammary fissures, and anal fistulas; through its topical administration by means of ointments, creams or gels. This places *Aloe vera* as a possible therapeutic alternative or complementary treatment for the aforementioned wounds.

However, it has been observed that worldwide research regarding this topic has ceased to be updated over time, thus demonstrating a shortage of information on this important property of *Aloe vera*, being this reflected especially at the national level, having Latin America in 2018, about North America and Asia, only with approximately 6.05% of publications on complementary medicine⁽⁶⁾. The therapeutic use of *Aloe vera* in wound healing represents one more treatment option, so it is appropriate to know its effects evaluated through preclinical and clinical studies, which represent a higher level of evidence. Therefore, it is important to review the potential efficacy of using *Aloe Vera* in wound healing.

SEARCH STRATEGIES

The bibliographic databases used were the VHL regional portal and PubMed. The search was carried out in June 2021. A secondary search was also performed by reviewing the bibliographic references of the papers that were finally included. The words used for the search and subsequent selection of articles were in the case of the VHL Regional Portal: (aloe vera) AND (wound healing), and in the case of PubMed: ("aloe vera"[All Fields]) AND ("wound healing"[All Fields]). Within the inclusion criteria, articles that included any of the following keywords supported by DeCS, "burns, surgical wounds, anal fissure and fistula, and breast fissures" were considered as part of the project. Also included were articles that will feature the word "skin scarring."

Regarding the years, only articles that met the criteria mentioned above and were also in the range of 10 years old (1999-2020) were included in the research. However, most of the original articles used had a recent age range; an article from the year 1999 was used because its information is still current as it is cited to date by different authors. According to the type of study, preclinical and clinical studies were included. In the exclusion criteria, review articles and those dealing mainly with non-cutaneous avulsions or wound prevention were not considered as part of the review of the efficacy of using *Aloe vera*.

PHYTOCHEMISTRY

Aloe vera 'aloe vera' is a xerophytic and succulent species native to Africa; 75 active principles have been found in the plant, and it presents phenolic compounds, mainly chromones and anthraquinones, located in the inner layer of the epidermal cells; the gelatinous and colorless parenchyma is mainly constituted by water, mucilages, acids and organic salts, enzymes, saponins, tannins, traces of alkaloids and vitamins⁽⁷⁾.

Having a high water content is one of the main characteristics of the aloe plant; likewise, the gel is 99% water. In addition, *A. vera* has many compounds that possess biological activity. It was found that the main compounds of the plant were invariable with aloeresin





A, aloesin and aloin (both epimers A and B) occupying between 70% and 97% of the dry weight of the plant, with an approximate ratio of 4: 3: 2. On the other hand, the minor compounds were less evenly distributed⁽⁸⁾.

MECHANISM OF ACTION

Wound healing is a dynamic process that occurs in three phases. The first phase is inflammation, hyperemia and leukocyte infiltration. The second phase consists of the elimination of dead tissue. The third phase is proliferation consisting of epithelial regeneration and fibrous tissue formation⁽¹⁾.

Aloe vera has been used for many years to treat wounds, burns and various skin conditions. On the other hand, it forms part of cosmetic products due to its moisturizing and anti-aging properties on the skin^(9,10).

Its healing effect is because aloe vera has a marked effect in the treatment of scar tissue and the prevention of scar formation after injury to the skin. This is because Aloe vera stimulates cell production through the activity of amino acids, which are the basis for new cell formation. Due to the ability of its enzymes, promotes regeneration in the deeper layers of the skin⁽¹¹⁾.

It has been demonstrated that Aloe vera has a healing property thanks to the different active molecules that it presents; these act on fibroblasts, macrophages, and the activity of the cells of the epidermis; in addition, they stimulate the formation of the epidermis, the synthesis, the remodeling process of collagen and improve the tensile stress⁽¹²⁾. This property of Aloe vera is due to mannose-6-phosphate^(1,13,14), which binds to fibroblast growth factor and enhances their activity⁽²⁾. En adición, mediante la administración tópica u oral⁽¹⁾.

In addition, by topical or oral administration¹ of Aloe gel on a wound, glucomannans, which are important polysaccharides of this plant, and gibberellin interact with fibroblast growth factor receptors, stimulating their activity and cell proliferation in situ^(15,16). They also promote collagen production above and across the wound, accelerating healing^(16,17).

The bioactive polysaccharides abundantly present in Aloe vera (AVP), favor fibroblast proliferation and generation of hyaluronic acid and hydroxyproline in fibroblasts; therefore, they possibly play an important role in the remodeling of the extracellular matrix (ECM) during wound healing^(13,14,18).

In relation to this, in a preclinical study they treated open skin wounds on the back of 45 rats with AVP, at 25mg or 50mg for 30 days topically, and it was evidenced that, at the transcriptional level, they regulate the gene expression of Matrix Metalloproteinase (MMP-3) and Tissue Inhibitor of Metalloproteinase-2 (TIMP-2) during skin repair and this directly helps to regulate the healing activity of Aloe vera gel. Also, they may influence granulation tissue formation and wound closure by increasing the production of ECM components, including glycosaminoglycans and collagen⁽¹⁹⁾.

Acemannan, a β -^(1,4)-soluble acetylated polymannose⁽¹⁸⁾ and considered to be the main functional component of Aloe vera, promotes tissue repair⁽¹⁾. Its potential molecular mechanisms and role in healing are not very



clear. However, in a preclinical in vitro study using a mouse skin wound model and primary skin fibroblasts; they found that this polysaccharide is able to significantly accelerate cutaneous skin wound closure and cell proliferation by promoting cyclin D1 expression in cultured fibroblasts via the AKT/mTOR signaling pathway, which increased eukaryotic translation initiation factor-4F (eIF4F) activity and cyclin D1 translation, thereby promoting healing⁽²⁰⁾.

Finally, the presence of vitamin C in Aloe vera gel can stimulate the production of collagen, aiding in healing. In the case of vitamin E, glutathione peroxidase and superoxide dismutase, neutralize the inflammatory effects of free radicals produced during wound recovery^(16,21).

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THERAPEUTIC EFFICACY

Burns

Burns are lesions in the skin or other organs caused by physical and/or chemical trauma that produce the denaturation of tissue proteins and lead to an alteration

of the superficial integument until the total destruction of the tissues involved. They are classified by degrees, considering three levels: first degree, second degree and third degree⁽²²⁾.

Burn care is often expensive so every effort should be made to provide hospital care in the shortest possible time⁽²³⁾. Herbal products appear to possess efficacy without toxicity and at less cost than synthetics. The goal of current burn treatments is to accelerate healing and prevent wound infection, as poor healing may be a consequence of pathological conditions⁽²⁴⁾.

Aloe vera is one of the effective herbs for healing, as it has organic compounds such as amino acids, polysaccharides in its extracts, which are effective as antimicrobial barriers, rapid healing, maintenance of environmental moisture and pain relief⁽²⁵⁾.

Two preclinical studies and two clinical studies were found that evaluated the effects of Aloe vera on burns, where all of them suggested its capacity as a better healing agent in less time, compared to other compounds. A greater capacity of Aloe vera to decrease pain and inflammation, as well as to increase epithelization and decrease the size of the lesion is also mentioned. However, regarding its competence to prevent wound colonization or infections, the results were not significant (Table 1).

Table 1. Pre-clinical and clinical studies evaluating the use of Aloe vera for burn healing.

Title	Year	Sample	Methods	Results
Effect of Aloe Cream versus Silver Sulfadiazine for Healing Burn Wounds in Rats ²³	2010	48 male Wistar rats with hot water thermal burns of approximately 10% of total body surface area.	Preclinical study with 4 groups: 0.5% Aloe vera gel (experimental group) vs. base cream, 1% silver sulfadiazine and no topical treatment (control groups). Histological outcomes were compared with respect to re-epithelialization in burn wounds after 25 days of treatment.	Aloe vera significantly increased re-epithelialization in burn wounds compared to the control groups, proving to be more effective in healing burns in rats.





Assessing herbal medicines in second and third degree burns in rats and comparison with silver sulfadiazine ointment effect of three ²⁴	2015	40 Wistarmacho albino rats aged 3 to 4 months with 2nd and 3rd degree thermal burns by hot plate.	Preclinical study with 4 groups: Aloe vera, topical Robacin, topical Rimojen (experimental groups) vs. silver sulfadiazine (control group) randomly distributed to compare outcomes regarding histological parameters such as polymorphonuclear, epithelialization, fibrosis and angiogenesis; after 32 days of treatment.	Both Aloe vera and Robacin had better healing rates in the first two weeks and greater epithelialization, but inflammation was lower in the aloe vera group compared to the other groups.
Effectiveness of Aloe Vera Gel compared with 1% silver sulfadiazine cream as burns wound dressing in second degree burns ²⁵	2013	50 patients with 2nd degree burns within the first 24 hours of evolution, with a total burned surface area <25%.	Comparative intervention study with two groups: Aloe vera gel (experimental group) vs. 1% silver sulfadiazine cream (control group) divided equally and randomly by consecutive sampling method, to compare outcomes regarding duration of wound epithelialization, pain relief and cost of treatment after 2 months of treatment.	Patients treated with Aloe Vera had significantly earlier epithelialization and pain relief than patients treated with silver sulfadiazine, and the use of Aloe Vera was more cost-effective.
Clinical Efficacy Test of Polyester Containing Herbal Extract Dressings in Burn Wound Healing ²⁶	2016	35 persons aged 18 to 60 years with 2nd degree burns and a body surface area of burns ≥20%.	Prospective clinical study with two groups: dressings with mixed herbal extract including 2.5% Aloe vera (experimental group) vs. kerosene dressings (control group) randomly divided to compare outcomes regarding healing time, length of hospital stays, pain analog score assessment, infection rate and descriptive reporting of unfavorable clinical symptoms or signs or side effects in 21 days of treatment.	The mixed herbal extract showed a significantly greater decrease in healing time, length of hospital stays and pain compared to the control group. In addition, in the experimental group only one person presented infection, while in the control group there were no infections. However, no patients reported unfavorable clinical symptoms/signs or side effects in both groups.

With regard to preclinical studies, Hosseinimehr et al.⁽²³⁾ treated thermal burns with Aloe vera gel and found a significant increase in re-epithelialization compared to standard treatment with silver sulfadiazine. Similar results were reported in the study by Akhoondinasab et al.⁽²⁴⁾, who evaluated the healing effect on second and third degree burns, and also observed less inflammation compared to silver sulfadiazine.

Regarding clinical studies, Shahzad et al.⁽²⁵⁾ and Muangman et al.⁽²⁶⁾ evaluated the effect of Aloe vera on second degree burns. In the former, they applied an aloe vera gel that favored epithelialization and pain relief; while in the latter, they applied dressings with an herbal extract containing aloe vera, presenting a greater decrease in healing time, hospital stay and pain, but reaching up to 64% of patients with bacterial colonization in the wound. Therefore, the results regarding the antimicrobial properties of Aloe are somewhat mixed and further studies on this aspect are recommended.

SURGICAL WOUNDS

Surgical wounds are incisions made during a surgical

procedure and can have four types: class I are non-infected surgical wounds where no inflammation is found and no entry into the respiratory, digestive, genital or urinary tract, class II are operative wounds where the respiratory, alimentary, genital or urinary tract is entered under controlled conditions and without unusual contamination, Class III are surgical wounds with major interruptions in sterile technique or gastrointestinal tract effusions and incisions in which there is acute nonpurulent inflammation, and Class IV are surgical wounds where viscera are perforated or there is acute inflammation with pus during the operation, and there is a late presentation of traumatic wounds with existing contamination and devitalized tissue^(27,28).

Five preclinical studies and three clinical studies were found that evaluated the effect of Aloe vera on surgical wounds including incisions and excisions in animals, and procedures in humans such as hemorrhoidectomy, episiotomy and cesarean section, using Aloe vera in various formulations as treatment: gel, cream and ointment (Table 2).

Table 2. Preclinical and clinical studies evaluating the use of Aloe vera for surgical wound healing.

Title	Year	Sample	Methods	Results
Formulation development, optimization and evaluation of aloe vera gel for wound healing. ²⁹	2013	12 2- to 3-month-old male Sprague dawley rats with excisional skin lesions	Preclinical study with 2 randomly distributed groups: herbal gel with Aloe vera (experimental group) and placebo (control group) to compare outcomes regarding the wound healing process in 14 days of treatment.	Aloe vera showed a higher percentage of healing compared to placebo, while tissue hyperplasia was lower in the control group. On the other hand, the control group presented inflammation and pus until the 5th day of the study, while the experimental group did not show these complications.
Topical Application of Aloe vera Accelerated Wound Healing, Modeling, and Remodeling: an experimental study. ³⁰	2016	60 adult male Wistar rats with cutaneous wounds.	Preclinical study with 3 randomly distributed groups: Aloe vera gel at low-25mg/ml and high 50mg/ml doses (experimental groups) and placebo (control group) to compare outcomes regarding wound healing parameters in 10 days of treatment.	Aloe vera modulated inflammation through increased wound contraction, epithelialization, cell alignment and organization; and decreased scar tissue size. A dose-dependent increase in the tissue level of dry matter, collagen and glycosaminoglycans was observed in Aloe vera-treated lesions compared to the control.
Evaluation of wound healing treated with latex derived from rubber trees and Aloe Vera extract in rats. ³¹	2016	21 Wistar rats with excision of skin and subcutaneous tissue fragments	Preclinical study with three randomly distributed groups: Hevea brasiliensis latex, 10% Aloe vera gel (experimental groups) and placebo (control group) to compare outcomes regarding macroscopic and microscopic parameters of wound healing in 21 days of treatment.	Statistical analysis did not allow the definition of the best topical agent. Aloe vera and control had similar findings on days 7, 14 and 21 with slightly better organization of skin and collagen on day 21 with Aloe vera. Latex had significantly greater angiogenesis.
The Healing Effect of Plantago Major and Aloe Vera Mixture in Excisional Full Thickness Skin Wounds: Stereological Study. ³³	2019	36 male Sprague-Dawley rats with full-thickness excisional skin wounds.	Preclinical study with three groups: Plantago major/Aloe vera gel 5% (experimental group) vs. placebo and no treatment (control groups) c/24h for 15 days, to compare outcomes with respect to histological parameters of wound healing.	The herbal combination of Plantago major/Aloe vera presented a significantly higher rate of healing and had a significantly greater capacity to improve wound healing due to fibroblast proliferation, collagen bundle synthesis and revascularization in skin lesions. They also presented a higher rate of healing.
Comparison between the Effect of Precipitate and Supernatant Aloe vera Gel on Experimental Cutaneous Wound Healing using Optical Coherence Tomography. ³²	2019	12 male Swiss Webster mice with cutaneous incision wounds	Preclinical study with four groups: Aloe vera precipitate, supernatant (experimental groups), ethanol and no lesion (control groups) to compare outcomes with respect to wound healing parameters.	Aloe vera accelerated wound healing and precipitate treatment had a significantly superior effect to supernatant in promoting wound healing.
Effects of Aloe vera cream on post hemorrhoidectomy pain and wound healing: results of a randomized, blind, placebo-control study. ³⁴	2010	49 patients who underwent open hemorrhoidectomy	Randomized clinical trial with two groups: Aloe vera cream 0.5% (experimental group) vs. placebo (control group), at a dose of 3g c/8h until 28 days postoperative, to compare outcomes regarding postoperative pain, pain on defecation and wound healing status.	Aloe vera cream significantly reduced pain with defecation at 24 and 48 hours postoperatively compared to placebo. On the other hand, the Aloe vera cream presented a significantly greater healing at 2 weeks of treatment compared to placebo; however, no significant differences were observed at the end of 4 weeks.
The Impact of Aloe vera and Calendula on Perineal Healing after Episiotomy in Primiparous Women: A Randomized Clinical Trial. ³⁵	2013	111 primiparous women who underwent episiotomy	Randomized clinical trial with three groups: Aloe vera ointment and calendula c/8h (experimental groups) vs. routine care (control group) to compare episiotomy wound healing through the redness, edema, ecchymosis, discharge and approximation (REEDA) scale, after 5 days of inpatient treatment.	Both Aloe vera and calendula ointments significantly increased the speed of healing of the episiotomy wound.
Aloe Vera Gel and Cesarean Wound Healing: A Randomized Controlled Clinical Trial. ³⁶	2014	90 women aged 18 to 36 years who underwent cesarean section.	Randomized clinical trial with two groups: Aloe vera gel (experimental group) and routine care (control group), to compare outcomes regarding wound healing through the REEDA scale at 24 hours and 8 days postoperatively.	The Aloe vera gel presented significantly better healing scores in the first 24 hours postoperatively compared to the control, however there was no significant difference between the groups at 8 days postoperatively.



Regarding preclinical studies, research by Khan et al.⁽²⁹⁾, Oryan et al.⁽³⁰⁾, Brandão et al.⁽³¹⁾ and Kusmardi et al.⁽³²⁾ used Aloe vera in gel form and observed improved healing parameters at the macroscopic (wound healing and contraction) and microscopic (epithelialization, alignment, tissue organization, fibroblastic proliferation) levels in rats. On the other hand, Ashkani-Esfahani et al.⁽³³⁾ studied the use of Aloe vera in combination with *Plantago major* and observed similar results highlighting a faster wound closure rate.

Regarding clinical studies, it was found that Aloe vera increased and helped in the healing process after its application for five to 28 days, depending on the wound evaluated. In the study by Eshghi et al.⁽³⁴⁾ an Aloe vera cream was applied to surgical wounds from hemorrhoidectomy three times a day until 28 days postoperatively, finding significantly greater healing only after two weeks of treatment. On the other

hand, Eghdampour et al.⁽³⁵⁾ conducted a study where Aloe vera ointment was applied on episiorrhaphy every eight hours for five days, finding an increase in the speed of wound healing. Finally, in the study by Molazem et al.⁽³⁶⁾ bandages with Aloe vera gel were applied on the cesarean surgical wound up to eight days post-operatively, showing significant improvements in healing and no side effects.

BREAST FISSURES

Nipple fissures are excoriation or ulcer-like lesions that develop on the mother's nipples and generate great pain during breastfeeding⁽³⁷⁾. Two clinical studies were found that evaluated the effect of Aloe vera on breast fissures, both investigations showed that Aloe vera is effective in reducing the intensity of pain and damage to the nipple, improving the condition of breast fissures (Table 3).

Table 3. Clinical studies evaluating the use of Aloe vera for breast fissure healing.

Title	Year	Sample	Methods	Results
Effects of Aloe vera gel on breast fissures in breastfeeding women ³⁸	2014	110 nursing mothers with breast fissure	Clinical trial with two groups: Aloe vera gel (experimental group) and breast milk (control group) to compare outcomes regarding pain intensity and breast fissure in 14 days of treatment.	The average intensity of pain and nipple damage, as well as nipple discharge, between the two groups showed significant differences, finding that Aloe vera can improve breast fissures.
Comparison of the Effect of Olive Oil, Aloe Vera Extract and Breast Milk on Healing of Breast Fissure in Lactating Mothers: A Randomized Clinical Trial. ³⁹	2016	90 nursing mothers with breast fissure	Uncontrolled randomized clinical trial with three groups: olive oil vs. aloe vera + breast milk vs. breast milk to compare outcomes regarding pain severity and fissure intensity in 7 days of treatment.	Significant differences were found between the groups with respect to the severity of pain and breast fissure. In the Aloe vera group, the severity of pain and the severity of the breast fissure were lower, being more effective compared to the olive oil and breast milk groups.

In the studies reviewed, it was observed that breast fissures can be effectively treated by topically applying 0.5ml of Aloe vera gel alone⁽³⁸⁾ or by adding three to four drops of one's own breast milk⁽³⁹⁾, three times a day after each feeding, on the nipples and around the areola^(38,39). With the above treatment, Alamolhoda et al.⁽³⁸⁾ and Eshgizade et al.⁽³⁹⁾ concurred in their findings, finding a significant improvement in the intensity of pain and breast fissure.

Anal fissures

Anal fissures are lesions presenting as short lacerations or ulcerations which may extend from the pectineal line

to the anal margin. Most of these occur in the posterior raphe and usually reduce the patient's quality of life. Anal fissures can be acute, if the lesion does not extend for more than six-eight weeks and heals spontaneously (adhering to conservative measures such as hygienic-dietary treatment); or chronic, if they exceed this period and have a high resistance to healing⁽⁴⁰⁾.

Two clinical studies were found that evaluated the effect of Aloe vera on anal fissures, using rectal ointment preparations based on Aloe vera, which, together with other methods, achieved wound healing in almost all cases (Table 4).

**Table 4.** Clinical studies evaluating the use of Aloe vera for the healing of anal fissures.

Title	Year	Sample	Methods	Results
Effects of Aloe vera cream on chronic anal fissure pain, wound healing and hemorrhaging upon defecation: a prospective double-blind clinical trial. ⁴¹	2014	60 patients aged 20 to 70 years with a diagnosis of chronic anal fissure.	Clinical trial with 2 groups: aloe vera cream (experimental group) and placebo (control group) c/8h for 3 weeks or more to compare outcomes regarding chronic pain, bleeding on defecation and wound healing.	Aloe vera significantly decreased chronic anal fissure pain, bleeding on defecation, and wound healing compared to the placebo.
The anti-inflammatory and healing activity of aloe vera I. (aloe vera) rectal ointment. ⁴²	1999	60 and 52 patients with acute hemorrhoidal flare-up and anal fissure, respectively.	Clinical trial with two groups of an acute hemorrhoidal flare-up: Aloe vera ointment (experimental group) and proctocaine (control group) c/8h; and three groups of anal fissure: Aloe vera ointment (experimental group) and proctocaine (control group), both c/8h, and polidocanol 1% c/7d (control group). Outcomes were compared with respect to symptoms, healing and adverse effects in 15 days of treatment.	There were no significant differences in the resolution of an acute hemorrhoidal flare-up between groups, however, Aloe vera presented greater qualitative disappearance of edema while it did not present adverse effects. On the other hand, polidocanol 1% together with Aloe vera presented total healing and no adverse effects.

In both studies, topical application of preparations containing Aloe vera gel (preparations with 0.5% Aloe vera powder and others with Aloe aqueous extract, respectively) three times a day, preceded by sitz baths and associated with a dietary regimen rich in fiber and the consumption of laxatives by medical indication was performed.

A significant decrease in bleeding and healing times was observed in the first weeks of treatment. In the first study, Rahmani et al.⁽⁴¹⁾ obtained that 29 people out of 30 showed improvement in wound healing at the end of their study. On the other hand, Sarabia et al.⁽⁴²⁾ compared the efficacy of Aloe vera gel with other commercial products such as proctocaine and poladicanol 1%, achieving wound healing in all patients who received treatment with Aloe vera, although in a later period compared to poladicanol 1%.

ANAL FISTULA

The anal fistula is the chronic phase of an anal abscess. This is a duct with fibrous walls that communicate the

anal crypt where the abscess originated with the perianal skin or with the rectum, so that there will be a primary orifice (the crypt) and a secondary orifice (cutaneous or mucosal). There are different types of anal fistulas and pain is the main symptom, which is intense and disabling⁽⁴⁴⁾.

Two preclinical studies were found that evaluated the effect of Aloe vera on anal fistulas, both were performed on male Wistar albino rats subjected to anal fistulas and treated for 30 days. Cavassana et al.⁽⁴⁴⁾ worked by injecting daily 0.3 ml of a solution composed of carbapolol plus Aloe vera extract into the fistulous tracts; Comparin et al.⁽⁴⁵⁾ performed their study by applying a seton soaked in glycerin and Aloe vera extract into the fistulous tract. Although both studies do not agree that Aloe vera can cause closure of the fistulous tract, they do agree that it significantly reduces the diameter of the fistulous tract, as well as signs of inflammation.





Table 5. Preclinical studies evaluating the use of Aloe vera for anal fistula healing.

Title	Year	Sample	Methods	Results
Effectiveness of the Aloe Vera extract in the treatment of fistula-in-ano ⁴⁴	2020	20 adult male Wistar albino rats with anal fistula by anal sphincter section.	Preclinical study with three groups: Aloe vera extract/carbapolol (experimental group), carbapolol and no treatment (control groups) to compare outcomes regarding the evolution and histopathological analysis of the fistulous tract after 30 days of treatment.	Complete closure of the fistulous tract was not observed in any group; however, Aloe vera evidenced a significantly greater decrease in lumen diameter and vascular lumen diameter compared to the other groups.
Treatment of rats anal fistula with glycerin Aloe barbadensis Miller extract ⁴⁵	2018	30 adult male Wistar albino rats with anal fistula by anal sphincter section.	Preclinical study with three groups: Aloe vera extract/seton (experimental group), seton and no treatment (control groups) to compare outcomes with respect to evolution and histopathological analysis of the fistulous tract after 30 days of treatment.	Aloe vera represented the highest percentage of fistulous closure; it also showed a significantly lower fistulous path and degree of inflammation compared to the other groups.

Among the limitations presented during the development of this review were, in the first place, those related to language. Most of the articles used in this study were found in languages other than Spanish, such as English and Persian. In the latter, the articles only had the abstract available in English, so it was not possible to obtain more data from the article. On the other hand, some difficulty was encountered when searching for more up-to-date studies on the article's subject, since the vast majority of studies were more than 20 years old. Finally, in the case of preclinical studies in mice, some samples were not as significant as in human studies.

ADVERSE REACTIONS AND CONTRAINDICATIONS

Although aloe vera gel has several beneficial properties that help wound healing and reduce inflammation, there are not many references for its adverse effects. In its topical application, the freshly obtained gel is normally used (100%) or in preparations with 10-70% of fresh gel, this could be contraindicated in people with allergies to plants of the liliaceae family, which could occasionally cause dermatitis, photodermatitis, allergic reactions, delay wound healing or in case of aloemodin, which is one of the components of aloe vera, it is capable of inducing skin alterations produced by ultraviolet radiation⁽⁴⁶⁾.

Aloe vera juice is a product that contains a minimum concentration of 50% Aloe vera gel⁽⁸⁾. About this, there are clinical cases that show adverse reactions resulting

from its topical administration. There is a report of a clinical case in which a six year old patient presented urticaria due to direct contact with aloe vera juice placed on his back, developing within a few minutes confluent and intensely pruritic haematous lesions all over the surface⁽⁴⁷⁾. A case was also reported of a 72-year-old female patient who presented a three-month history of pruritic erythema on her legs and eyelids, which appeared shortly after applying Aloe vera leaf juice to her legs. Subsequently, she underwent a two-day patch test and tested positive for reactions to Aloe vera gel⁽⁴⁸⁾.

CONCLUSION

It was concluded that Aloe vera possesses different bioactive components, such as the polysaccharides Acemannan and Glucomannan, which contain mannose-6-phosphate; also, phytohormones such as gibberellin; vitamin C; among others. It was determined that these act synergistically in the three phases of the healing process, thus giving Aloe vera its therapeutic property in healing. After the analysis of the studies, the pharmacological efficacy of Aloe vera in wound healing was evidenced. In the case of burns and surgical wounds, it was observed that this medicinal plant generally increased epithelization and collagen content and decreased healing time. Similarly, with



respect to mammary fissures and anal fissures, and fistulas, it was shown that Aloe vera could be a potential treatment to improve these lesions. Thanks to its low cost and great accessibility by the population, it can be

considered an alternative and effective treatment for the different types of wounds mentioned; however, more studies are required regarding its antimicrobial property.

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REFERENCES

- Sahu PK, Giri DD, Singh R, Pandey P, Gupta S, Shrivastava AK, et al. Therapeutic and Medicinal Uses of Aloe vera: A Review. *Pharmacol Pharm.* 2013;4(8):599-610. doi: <http://dx.doi.org/10.4236/pp.2013.48086>
- Grundmann O. Aloe Vera gel research review [Internet]. *Nat Med J.* 2014 [citado el 15 de junio de 2021]. Disponible en: <https://www.naturalmedicinejournal.com/journal/aloe-vera-gel-research-review>
- Benzi I, Wachtel-Galor S. *Herbal Medicine*. 2da ed. CRC Press/Taylor & Francis; 2011. Disponible en: <https://pubmed.ncbi.nlm.nih.gov/22593939/>
- Ruiz Y, Hernández León N, Pereira Despaigne O, Palay Despaigne M, Neyra Barrios R. Efectividad de la crema de Aloe vera en pacientes con psoriasis vulgar de la Parroquia San Fernando. *MEDISAN* [Internet]. 2014 [citado el 4 de julio de 2021];18(10):1357. Disponible en: http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S1029-30192014001000004&lng=es&nrm=iso&tlng=es
- Vega GA, Ampuero CN, Díaz NL, Lemus MR. El Aloe Vera (Aloe Barbadensis Miller) como componente de alimentos funcionales. *Rev Chil Nutr.* [Internet]. 2005 [citado el 4 de julio de 2021];32(3):208-14. doi: <http://dx.doi.org/10.4067/S0717-75182005000300005>
- Organización Panamericana de la Salud. Situación de las plantas medicinales en Perú. Informe de reunión del grupo de expertos en plantas medicinales. [Internet]. Lima, Perú: OPS; 2019 [citado el 11 julio de 2021]. Disponible en: <https://iris.paho.org/handle/10665.2/50479>
- Quino C, Muñoz D, Gómez C, Chau G, Cueva L, Guardia E, et al. Características fitoquímicas y capacidad antioxidante in vitro de Aloe vera, Plukenetia volubilis, Caiophora carduiifolia, Cecropia membranacea. *An Fac Med.* 2016;77(1):9-13. doi: <http://dx.doi.org/10.15381/anales.v77i1.11546>
- Pizzorno J, Murray M. *Textbook of Natural Medicine*. 5ta ed. Washington, USA: Churchill Livingstone; 2020. 1944p.
- Domínguez-Fernández RN, Arzate-Vázquez I, Chanona-Pérez JJ, Welty-Chanes JS, Alvarado-González JS, Calderón-Domínguez G, et al. El gel de Aloe vera: estructura, composición química, procesamiento, actividad biológica e importancia en la industria farmacéutica y alimentaria. *Rev Mex Ing Quim* [Internet]. 2012 [citado el 12 julio de 2021];11(1):23-43. Disponible en: <http://www.rmiq.org/ojs311/index.php/rmiq/article/view/1491>
- Rodríguez Domínguez I, Santana Gutiérrez O, Recio López O, Fuentes Naranjo M. Beneficios del Aloe Vera I. (sábila) en las afecciones de la piel. *Rev Cubana Enfermer* [Internet]. 2006 [citado el 6 de julio de 2021];22(3). Disponible en: http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S0864-03192006000300004&lng=es
- Eshun K, He Q. Aloe vera: a valuable ingredient for the food, pharmaceutical and cosmetic industries—a review. *Crit Rev Food Sci Nutr.* 2004;44(2):91-6. doi: <https://doi.org/10.1080/10408690490424694>
- Tarameshloo M, Norouzian M, Zarein-Dolab S, Dadpay M, Mohsenifar J, Gazor R. Aloe vera gel and thyroid hormone cream may improve wound healing in Wistar rats. *Anat Cell Biol.* 2012;45(3):170-7. doi: <http://dx.doi.org/10.5115/acb.2012.45.3.170>
- Radha MH, Laxmipriya NP. Evaluation of biological properties and clinical effectiveness of Aloe vera: A systematic review. *J Tradit Complement Med.* 2015;5(1):21-6. doi: <http://dx.doi.org/10.1016/j.jtcme.2014.10.006>
- Liu LY, Chen XD, Wu BY, Jiang Q. [Influence of Aloe polysaccharide on proliferation and hyaluronic acid and hydroxyproline secretion of human fibroblasts in vitro]. *Zhong Xi Yi Jie He Xue Bao.* 2010;8(3):256-62. Chinese. doi: <https://pubmed.ncbi.nlm.nih.gov/20226148/>
- Mansour G, Ouda S, Shaker A, Abdallah HM. Clinical efficacy of new aloe vera- and myrrh-based oral mucoadhesive gels in the management of minor recurrent aphthous stomatitis: a randomized, double-blind, vehicle-controlled study. *J Oral Pathol Med.* 2014;43(6):405-9. Disponible en: <https://pubmed.ncbi.nlm.nih.gov/24164309/>
- López-Mata MA, Valdez-Melchor RG, Quihui-Cota L, Osuna-Amarillas PS. Recubrimientos para heridas con Aloe-gel combinado con alginato, pectina y quitosano: aplicaciones in vivo. *TIP Rev Esp Cienc Quim Biol.* 2020;23. doi: <http://dx.doi.org/10.22201/fesz.23958723e.2020.0.279>
- Freitas VS, Rodrigues RAF, Gaspi FOG. Pharmacological activities of Aloe vera (L.) Burm. f. *Rev Bras Plantas Med.* 2014;16(2):299-307. doi: 10.1590/S1516-05722014000200020. <https://doi.org/10.1590/S1516-05722014000200020>
- Liu C, Cui Y, Pi F, Cheng Y, Guo Y, Qian H. Extraction, purification, structural characteristics, biological activities and pharmacological applications of acemannan, a polysaccharide from Aloe vera: A review. *Molecules.* 2019;24(8):1554. doi: <https://doi.org/10.3390/molecules24081554>
- Tabandeh MR, Oryan A, Mohammadipour A. Polysaccharides of Aloe vera induce MMP-3 and TIMP-2 gene expression during the skin wound repair of rat. *Int J Biol Macromol.* 2014;65:424-30. doi: <https://doi.org/10.1016/j.jbiomac.2014.01.055>
- Xing W, Guo W, Zou CH, Fu TT, Li XY, Zhu M, et al. Acemannan accelerates cell proliferation and skin wound healing through AKT/mTOR signaling pathway. *J Dermatol Sci.* 2015;79(2):101-9. doi: <https://doi.org/10.1016/j.jdermsci.2015.03.016>
- Hajhashemi V, Ghannadi A, Heidari AH. Anti-inflammatory and wound healing activities of Aloe littoralis in rats. *Res Pharm Sci* [Internet]. 2012 [citado el 11 de julio de 2021];7(2):73-8. Disponible en: <https://pubmed.ncbi.nlm.nih.gov/23181083/>
- Jiménez Serrano R, García Fernández FP. Manejo de quemaduras de primer y segundo grado en atención primaria. *Gerokomos* [Internet]. 2018 [citado el 11 de julio de 2021];29(1):45-51. Disponible en: https://scielo.isciii.es/scielo.php?script=sci_arttext&pid=S1134-928X2018000100045
- Hosseineimehr SJ, Khorasani G, Azadbakht M, Zamani P, Ghasemi M, Ahmadi A. Effect of aloe cream versus silver sulfadiazine for healing burn wounds in rats. *Acta Dermatovenerol Croat* [Internet]. 2010 [citado el 13 de julio de 2021];18(1):2-7. Disponible en: <https://pubmed.ncbi.nlm.nih.gov/20361881/>
- Akhoondinasab MR, Khodarahmi A, Akhoondinasab M, Saberi M, Iranpour M. Assessing effect of three herbal medicines in second and third degree burns in rats and comparison with silver sulfadiazine ointment. *Burns.* 2015;41(1):125-31. doi: <https://doi.org/10.1016/j.jburns.2014.04.001>





25. Shahzad MN, Ahmed N. Effectiveness of Aloe Vera gel compared with 1% silver sulphadiazine cream as burn wound dressing in second degree burns. *J Pak Med Assoc* [Internet]. 2013 [citado el 10 de julio de 2021] Feb;63(2):225-30. Disponible en: <https://pubmed.ncbi.nlm.nih.gov/23894900/>
26. Muangman P, Pradisuktavorn B, Chinaroonchai K, Chuntrasakul Ch. Clinical Efficacy Test of Polyester Containing Herbal Extract Dressings in Burn Wound Healing. *Int J Low Extrem Wounds*. 2016;15(3):203-212. doi: <https://doi.org/10.1177/1534734616652552>
27. Herida quirúrgica. DeCS [Internet]. Bvsalud.org. [citado el 15 de junio de 2021]. Disponible en: https://decs.bvsalud.org/es/ths/resource/?id=56420&filter=ths_termall&q=Heridas%20quir%C3%BArqicas
28. Agencia Canadiense de Medicamentos y Tecnologías en Salud. Suturas antibacterianas para el cierre de heridas después de la cirugía: una revisión de la rentabilidad clínica y en función de los costos y las pautas de uso [Internet]. 2014 [citado el 17 de junio de 2021]. Tabla A4, clasificación de heridas quirúrgicas. Disponible en: <https://www.ncbi.nlm.nih.gov/books/NBK263230/table/T5/>
29. Khan AW, Kotta S, Ansari SH, Sharma RK, Kumar A, Ali J. Formulation development, optimization and evaluation of aloe vera gel for wound healing. *Pharmacogn Mag*. 2013;9(Suppl 1):S6-S10. doi: <https://doi.org/10.4103/0973-1296.117849>
30. Oryan A, Mohammadalipour A, Moshiri A, Tabandeh MR. Topical Application of Aloe vera Accelerated Wound Healing, Modeling, and Remodeling. *Ann Plast Surg*. 2016;77(1):37-46. doi: [10.1097/SAP.0000000000000239](https://doi.org/10.1097/SAP.0000000000000239).
31. Brandão ML, Reis PR, Araújo LA, Araújo AC, Santos MH, Miguel MP. Evaluation of wound healing treated with latex derived from rubber trees and Aloe Vera extract in rats. *Acta Cir Bras*. 2016;31(9):570-7. doi: <https://doi.org/10.1590/S0102-865020160090000001>
32. Kusmardi K, Hallim NBM, Tedjo A, Ibrahim A, Salinah. Comparison between the Effect of Precipitate and Supernatant Aloe vera Gel on Experimental Cutaneous Wound Healing using Optical Coherence Tomography. *Pharmacog J*. 2019;11(2):405-12. doi: <https://doi.org/10.5530/pj.2019.11.63>
33. Ashkani-Esfahani S, Khoshneviszadeh M, Noorafshan A, Miri R, Rafiee S, Hemyari K, Kardeh S, Koohi Hosseinabadi O, Fani D, Faridi E. The Healing Effect of Plantago Major and Aloe Vera Mixture in Excisional Full Thickness Skin Wounds: Stereological Study. *World J Plast Surg*. 2019;8(1):51-7. doi: <https://doi.org/10.29252/wjps.8.1.51>
34. Eshghi F, Hosseinimehr SJ, Rahmani N, Khademloo M, Norozi MS, Hojati O. Effects of Aloe vera Cream on Posthemorrhoidectomy Pain and Wound Healing: Results of a Randomized, Blind, Placebo-Control Study. *The Journal of Alternative and Complementary Medicine*. 2010;16(6):647-50. doi: <https://doi.org/10.1089/acm.2009.0428>
35. Eghdampour F, Jahdie F, Kheyrikhah M, Taghizadeh M, Naghizadeh S, Hagani H. The Impact of Aloe vera and Calendula on Perineal Healing after Episiotomy in Primiparous Women: A Randomized Clinical Trial. *J Caring Sci*. 2013 Nov 30;2(4):279-86. doi: <https://doi.org/10.5681/jcs.2013.033>
36. Molazem Z, Mohseni F, Younesi M, Keshavarzi S. Aloe vera gel and cesarean wound healing: a randomized controlled clinical trial. *Glob J Health Sci*. 2014;7(1):203-9. doi: <https://doi.org/10.5539/gjhs.v7n1p203>
37. Caja costarricense de seguro social. Manual Técnico Patologías mamarias y asociadas al niño o niña durante el proceso de lactancia materna [Internet]. 1ra ed. 2016 [citado el 15 de junio de 2021]. Disponible en: https://www.ministeriodosalud.go.cr/gestores_en_salud/lactancia/articulos/2019/CLM_manual_patologias_mamaria_final_2016.pdf
38. Alamolhoda SH, AmirAliAkbari S, Baghban AA, Esmaili S. Effects of Aloe vera gel on breast fissures in breastfeeding women. *Pajoohandeh J* [Internet]. 2014 [citado el 21 de junio de 2021];19(1):13-7. Disponible en: <http://pajoohande.sbmu.ac.ir/article-1-1679-en.html>
39. Eshgizade M, Moghaddam MB, Moghaddam HM, Mahmoudian A, Mina M. Comparison of the effect of Olive Oil, Aloe Vera Extract and Breast Milk on Healing of Breast Fissure in Lactating Mothers: A Randomized Clinical Trial. *Qom Univ Med Sci J* [Internet]. 2016 [citado el 21 de junio de 2021];10(3):19-27. Disponible en: <https://www.semanticscholar.org/paper/920496d1fdbdeb0813c4aa96de86d6c0c3b81188>
40. Arroyo A, Montes E, Calderón T, Blesa I, Elía M, Salgado G, et al. Tratamiento de la fisura anal: algoritmo de actuación. Documento de consenso de la Asociación Española de Coloproctología y la Sección de Coloproctología de la Asociación Española de Cirujanos. *Cir Esp*. 2018;96(5):260-7. doi: <https://doi.org/10.1016/j.ciresp.2018.02.007>
41. Rahmani N, Khademloo M, Vosoughi K, Assadpour S. Effects of Aloe vera cream on chronic anal fissure pain, wound healing and hemorrhaging upon defecation: a prospective double blind clinical trial. *Eur Rev Med Pharmacol Sci* [Internet]. 2014 [citado el 15 de Julio de 2021];18(7):1078-84. Disponible en: <https://www.europeanreview.org/article/7217>
42. León Sarabia Jorge Enrique, Rosales Clares Vivian del Pilar, Rosales Clares Reinaldo Alberto, Pavón Hernández Vital. Actividad antiinflamatoria y cicatrizante del ungüento rectal de aloe vera l. (sábila). *Rev Cubana Plant Med* [Internet]. 1999 [citado el 19 de julio de 2021]; 4(3):106-9. Disponible en: http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S1028-4796199900300005&lng=es
43. Rodríguez-Wong U. Abscesos y fistulas anorrectales. *Rev Hosp Jua Mex* [Internet]. 2013 [citado el 17 de julio de 2021];80(4):243-7. Disponible en: <https://www.mediagraphic.com/cqi-bin/new/resumen.cqi?IDARTICULO=50922>
44. Cavasana AL, Santos CHM, Dourado DM, Guimarães FS, Barros FHR, Campos GCO, et al. Effectiveness of the Aloe Vera extract in the treatment of fistula-in-ano. *J Coloproctology*. 2020;40(1):67-72. doi: <https://doi.org/10.1016/j.jcol.2019.09.003>
45. Comparin BC, Santos CHM, Dourado DM, Reichel PMG, Paola RS, Pontes ERJC. Treatment of rats anal fistula with glycerin Aloe barbadensis Miller extract. *J Coloproctology*. 2018;38(4):283-9. doi: <https://doi.org/10.1016/j.jcol.2018.05.009>
46. López Luengo MT. Aloe vera. *Offarm* [Internet]. 2004 [citado el 11 de julio de 2021];23(9):96-100. Disponible en: <https://www.elsevier.es/es-revista-offarm-4-articulo-aloe-vera-13067351>
47. Martín Fernández AI, Montano Navarro E, Armela Sánchez-Crespo E, Vara de Andrés L, Caballero Cazalilla A. Urticaria de contacto por Aloe vera. *Rev Pediatr Aten Primaria*. 2013;15(59):239-44. doi: <https://dx.doi.org/10.4321/S1139-76322013000400007>
48. Ferreira, M., Teixeira, M., Silva, E., & Selores, M. (2007). Allergic contact dermatitis to Aloe vera. *Contact Dermatitis*. 2007;57(4):278-9. doi: <https://doi.org/10.1111/j.1600-0536.2007.01118.x>