

Review

Effect of Aloe vera on Wound Healing

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Abstract. Skin acts as a protective barrier of body. It keeps the internal body organs safe from external environmental conditions which can prove harmful for them. So, maintenance of skin integrity is very important for normal functioning of body. In our daily life body of both animals and humans encounter to different types of violence, some of them are of such a severity that they break the skin continuity. This breakage of skin continuity is termed as wound. Whenever, the skin continuity is broken, internal organs of body are exposed. This is a dangerous situation and can be fatal for life. Immediate response of skin after wound is the start of wound healing process which starts automatically. This process can be assisted in a number of ways by keeping the wound free from bacterial contamination, moisture and dirt. For this purpose a variety of antiseptic dressings are available which when applied topically support wound healing process. They prevent wound to be contaminated by any micro-organism and reduce wound healing time. Aloe vera is one of them, it possess significant wound healing properties. Herbs have been integral to both traditional and non-traditional forms of medicine dating back at least 5000 years. Herbal medicines, especially in wound management involve disinfection, debridement and provision of a suitable environment for aiding the natural course of healing. The super focus of this review is to summarize the findings of earlier scientists with authentic concluding verse for utilization of herbal medicines (Aloe vera) being safe, readily available and cheaper.

Keywords: Aloe vera, phyto-medicine, wounds, healing

Introduction

Wound is the break and discontinuation in the integrity of the skin and soft tissues as a result of any trauma and any physical, thermal and chemical injury. For restoration of the continuity of the skin integrity, appropriate management is essential to recover the anatomical and physiological status of the skin (Barreto *et al.*, 2014).

Wound healing is a complicated process including series of intercalated circumstances mediated through a number of phases of cellular and chemically coordinated processes along with hormonal influences (Chan *et al.*, 2008). Wound healing has four stages including coagulating, inflammatory, proliferative and remodelling phase, which determine the strength and healing of the tissue (Ayyanar and Ignacimuthu, 2009; Sumitra *et al.*, 2005).

Natural products including herbals and medicinal plants have been frequently used in the treatment of various

diseases worldwide, for centuries. Above 80% of the population throughout the world is still dependent upon these traditional medicines for cure of their maladies. Among these products, honey and Aloe vera have significance in wound healing (Kumara *et al.*, 2001).

Aloe vera contains enzymes such as bradykinase, carboxypeptidase which have analgesic and anti-inflammatory effects. (Fig. 1).

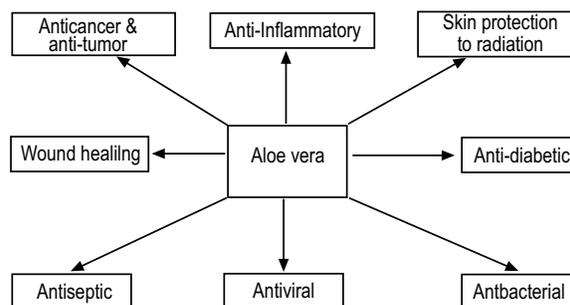


Fig. 1. Medical properties of Aloe vera (Ahmed and Hussain, 2013).

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In Aloe vera some polysaccharides, notably pectic acid or glucomannans are found to have wound healing properties, immuno-stimulatory, antimicrobial and antioxidant activities therefore, it is widely used for therapeutic purposes (Ahmed and Hussain, 2013).

Kaufman *et al.* (1988) studied the effects of gel and it was applied to experimental second degree burns in guinea pigs. Their effects were investigated on wound contraction, epithelialization, newly formed granulation tissue and regeneration of hair follicles. These effects were compared with 1% silver sulfadiazine cream (AgSD) treated wounds. Epithelialisation (%mean \pm SEM) on post burn day 8, 16 and 24 of the Aloe vera gel treated wounds was 38.72% \pm 2.71%, 60.34% \pm 3.28% and 92.46% \pm 2.26% respectively, whereas the AgSD-treated burns was 53.35% \pm 2.65%, 94.84% \pm 2.65% and 100%, respectively (P less than .001). Wound contraction of the Aloe vera gel treated wounds was significantly higher than that of the Ag SD-treated burns during the study of 24 days (P less than .001). The hair follicles count was significantly lower (P less than .001) as compared to the Ag SD-treated wounds. Newly

formed granulation tissue thickness was lower in the AgSD-treated wounds (P less than .001).

Rodriguez *et al.* (1988) studied an experiment on Hartley guinea pigs; they received full thickness burns covering 3% of their body surface area through direct contact with a hot plate. A total of 40 animals were randomly divided into four modalities of closed burn wounds management as follows: group one (I) was treated with silver sulfadiazine (Silva dine), group two (II) was treated with Aloe vera gel extract, group three (III) was treated with salicylic acid cream (aspirin), while group (IV) were served as dressing only with plain gauze. The size and appearance of each burn wound were recorded until complete healing and dressings and changed daily. On the sixth post burn day, quantitative burn wound cultures were prepared. In the control group, the average time to entire healing was 50 days and Aloe vera treated animals were found only significant difference, the complete healed on an average of 30 days (P less than 0.02). Wound bacterial counts were efficiently decreased by silver sulfadiazine (P = 0.015) and by Aloe vera extract (P = 0.015). According to their

Table 1. Chemical composition and properties of Aloe vera leaves (Rodríguez *et al.*, 2005)

Constituents	Number and identification	Properties and 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 body and muscle tissues
Anthraquinones	Provides Aloe emodin, Aloetic acid, alovin, anthracine	Analgesic, antibacterial
Enzymes	Antbranol, barbaloin, chrysophanic acid, smodin, ethereal oil, ester of cinnamonic acid, isobarbaloin, resistannol	Antifungal and antiviral activity but toxic at high concentrations
Hormones	Auxins and gibberellins	Wound healing and anti-inflammatory
Minerals	Calcium, chromium, copper, iron, manganese, potassium, sodium and zinc	Essential for good health
Salicylic acid	Aspirin like compounds	Analgesic
Saponins	Glycosides	Cleansing and antiseptic
Steroids	Cholesterol, campesterol, lupeol, sistosterol Antiseptic and analgesic properties	Anti-inflammatory agents, lupeol has
Sugars	Monosaccharides: Glucose and Fructose Polysaccharides: Glucomannans/polymannose	Anti-viral, immune modulating activity of acemannan
Vitamins	A, B, C, E, choline, B12, folic acid	Antioxidant (A, C, E), neutralises free radicals

data it appeared that Aloe vera gel extracts resulted in quick healing of burn wounds as compared to other treatments.

Davis *et al.* (1989) studied the influence of Aloe vera, orally and topically on wound healing. Wounds were introduced on both sides of the vertebral column of ICR mice with a biopsy punch. In the oral study, experimental animals were given Aloe vera in their drinking water for 2 months, while the control animals received only water. For the topical study, experimental animals were received 25% Aloe vera in Eucerin cream topically. The control group received cream only. Animals receiving 100 mg/kg/day oral Aloe vera reduced the wound diameter (62.5%) was noted in and animals receiving topical 25% Aloe vera a 50.8% reduction was recorded. Thus the data recommend that the Aloe vera is an effective by both routes of administration i.e. orally and topically.

Swaim *et al.* (1992) evaluated the Aloe vera extract gel and their effects on open wound healing created under anaesthesia in 15 Beagle dogs. Group (I) was treated with triple antibiotic ointment containing bacitracin, neomycin sulfate and polymixin B sulfate. Group (II) was treated with Aloe vera extract gel. The main difference between the 2 medications was noticed at 7 days when the Aloe vera extract gel treated wounds had a larger healed area than the wounds treated with antibiotics and untreated control wounds.

Heggers *et al.* (1996) examined the therapeutic effects of Aloe vera in preventing progressive dermal ischemia caused by burns, electrical injury, distal dying flap, frostbite and intra-arterial drug abuse in man and animal models. These injuries were analyzed by *in vivo* and results showed that thromboxane A2 was the mediator of progressive tissue damage. In this study, Aloe vera was compared to a variety of antithromboxane agents (such as U38450, a lodoxamide, a lazaroide and an Aloe wound gel). In the burn wound, Aloe vera was comparable to the lazaroide and lodoxamide with an 82 to 85% tissue survival when it was compared with the control and the Aloe wound gel. Tissue survival in the experimental frostbite injury was 28.2% when compared with the control. Same results were obtained from the intra-arterial drug abuse and electrical injury. Clinically burn wound patients were treated with Aloe vera; they healed without tissue loss as did those with frostbite. While in the intra-arterial drug abuse patients, Aloe vera inverted the tissue necrosis. This therapeutic

approach was used to stop progressive tissue loss in every injury by actively inhibiting the limited production of thromboxane A2. Aloe vera not only acts as a thromboxane A2 inhibitor but it maintains a homeostasis inside the vascular endothelium as well as the surrounding tissue.

Vazquez *et al.* (1996) studied the effects of aqueous, chloroform, and ethanol extracts of Aloe vera gel on carrageenan-induced edema in the rat paw and neutrophil migration into the peritoneal cavity stimulated by carrageenan. They also studied the capacity of the aqueous extract to inhibit cyclooxygenase activity. The aqueous and chloroform extracts decreased the edema induced in the hind-paw and the number of neutrophils migrating into the peritoneal cavity, whereas the ethanol extract only decreased the number of neutrophils. The anti-inflammatory agents in domethacin and dexamethasone also decreased carrageenan induced edema and neutrophil migration. The aqueous extract inhibited prostaglandin E2 production from (14C) arachidonic acid. The chemical tests performed in the aqueous extract for anthraglycosides, reductor sugars and cardio tonic glycosides were positive. In the ethanol extract, the chemical tests performed for saponins, carbohydrates naftoquinones, sterols, triterpenoids and anthraquinones were also positive. In the chloroform extract, the chemical tests performed for sterols type delta 5, and anthrax quinones were positive. These results demonstrated that the extracts of Aloe vera gel have anti-inflammatory activity and suggested its inhibitory action on the arachidonic acid pathway via cyclooxygenase.

Keith *et al.* (1996) studied the corneal epithelial lesions of 6 mm diameter were made mechanically in the eyes of anesthetized albino rabbits. At intervals of 6 or 24 h the lesions were photographed after the application of a 1% fluorescent solution. One eye received 50 μ L drops of bicarbonate Ringer three times daily while the contra lateral eye received Aloe vera gel obtained directly from freshly cut leaves at the same time intervals as the Ringer. No toxicity was observed to either aloe gel or Ringer with both pairs of eyes showing normality without redness or chemosis. Although a statistically significant difference existed between the eyes at 30 h, no difference was observed at any other time and healing was complete at 48 h in Ringer and Aloe treated eyes. Despite anecdotal reports of enhanced ocular healing, this quantitative examination showed no effect of Aloe on the healing rate of a mechanically induced corneal epithelial lesion.

Bunyapraphatsara *et al.* (1996) improved the Aloe cream and the Aloe stable preparations to overcome the instability of Aloe vera gel. For this purpose mice were selected and four regions of thermal burns wound were created on dorsal region for comparison and self-control. Aloe cream when applied on the first degree of the burn it delayed the damage and enhanced the healing efficacy more excellently than fresh Aloe vera gel. Sloughing of dead epidermis and damage of the skin was less in treated than in control (not treated). By applying the fresh Aloe gel and Aloe cream in second degree burns, it increased the healing rate and decreased the inflammation. When fresh Aloe gel and Aloe cream was applied on the third degree of burn, the result could not be estimated statistically due to the infection. It was detected that Aloe cream increased the epithelialization, but failed to display the anti-inflammatory action. All these findings evaluated that Aloe vera gel is effective for the treatment of the wound healing when it is well preserved.

Chithra *et al.* (1998a) reported the influence of Aloe vera on the collagen content and its characteristics in a wound healing. Wound healing is a fundamental response to tissue injury that results in restoration of tissue integrity. This process is achieved mainly by the synthesis of the connective tissue matrix. Collagen is the major protein of the extracellular matrix and is the component which ultimately contributes to wound strength. It was observed that Aloe vera increased the collagen content of the granulation tissue as well as its degree of cross linking as seen by increased aldehyde content and decreased acid solubility. The type I, III collagen ratios of treated groups were lower than that of the untreated controls indicating enhanced levels of type III collagen. Wounds were treated either by topical application or oral administration of Aloe vera to rats and both treatments were found to be resulting in similar.

Chithra *et al.* (1998b) also reported the healing efficacy of the Aloe vera on the full thickness wound in diabetic rat. Incision (for tensile strength) and excision (for biological analysis) wounds were produced on the thoraco-lumbar region in diabetic rats. Topically application of Aloe vera gel was applied on wounds for fourteen days. The collagen, total protein, hexosamine and DNA contents were checked by removing the granulation tissues on various days. Period of epithelialization and rate of wound contraction were also determined. Tensile strength (incision wound) was measured in treated and untreated wounds. The result

showed that Aloe vera gel increased the process of healing by inducing the collagen synthesis, fibroplasia, inflammation, wound contraction and maturation. These results exhibit the hypo-glycemic properties of the Aloe vera gel.

Somboonwong *et al.* (2000) demonstrated the micro-circulatory and wound healing effects of Aloe vera on induced second degree burn wounds in rats. A total of 48 male Wistar rats were equally divided into 4 groups as follows: sham controls, untreated burn-wound rats, those treated with once daily application of normal saline (NSS) and those treated with once daily application of lyophilized Aloe vera gel. The animals in each group were equally subdivided into 2 sub groups for the study of cutaneous microcirculation and wound healing on day 7 and 14 after burn. Dorsal skin fold chamber preparation and intra vital fluorescence microscopic technique were performed to examine dermal micro vascular changes, including arteriolar diameter, post capillary venular permeability and leukocyte adhesion on post capillary venules. On day 7, the vasodilatation and increased post capillary venular permeability as encountered in the untreated burn were found to be reduced significantly ($P < 0.05$) in both the NSS and Aloe vera treated groups, but to a greater extent in the later. Leukocyte adhesion was not different among the untreated, NSS and Aloe vera treated groups. On day 14, vasoconstriction occurred after the wound had been left untreated. Only in the Aloe vera treated groups, was arteriolar diameter increased up to normal condition and post capillary venular permeability was not different from the sham controls. The amount of leukocyte adhesion was less as compared to the untreated and NSS treated groups. Besides, the healing area of the Aloe vera treated wound was better than that of the untreated and NSS treated groups during 7 and 14 days after burn. Aloe vera could exhibit the actions of both anti-inflammation and wound healing promotion when applied on a second degree burn wound.

Yun *et al.* (2003) determined the polysaccharide and flavonoid concentrations of 2,3 and 4 year old Aloe-vera plant and their antioxidant activities were evaluated compared to BHT and R-tocopherol by the DPPH radical scavenging method and the linoleic acid system at 100 μg of soluble solids per mL of ethanol. The results showed that three year old Aloe vera contained significantly higher levels of polysaccharides and flavonoids than two and four year old Aloe vera and no significant differences in flavonoid levels were found

between three and four year old Aloe vera. All the Aloe extracts showed significant antioxidant activity. The antioxidant activity of Aloe vera extracts and reference compounds followed the order: three year old Aloe vera > BHT > four year old Aloe vera > R-tocopherol > two year old Aloe vera. The three year old extract exhibited the strongest radical scavenging activity of 72.19%, which is significantly higher than that of BHT at 70.52% and R-tocopherol at 65.20%. These data suggest that the growth stage plays a vital role in the composition and antioxidant activity of Aloe vera.

Muller *et al.* (2003) designed an experiment to reveal the phenomenon that antimicrobial agents delay the wound contraction in burn wound. For this purpose full thickness burn wounds were produced on the dorsal region of the rat under the anaesthesia condition. By topical agents the wounds were treated twice daily for fifteen days, then observed until the wound healed. They were divided into different groups according to treatment criteria *viz.* placebo (aqueous cream) control, saline control, silver sulphadiazine (SSD) cream 1%, silver sulphadiazine 1% with Aloe vera, silver sulphadiazine 0.5%, silver sulphadiazine 1% with Nystatin and Nystatin. After every three days the wound areas were measured. 90 and 50% healing was compared by ANOVA. Wound healing times and half-life were shorter in Aloe vera/silver sulphadiazine and Nystatin groups ($P < 0.05$) and longer in the saline control and 1% silver sulphadiazine group. The placebo group (aqueous cream) cured in a very shorter time ($P < 0.05$) than the control group (saline). Wound contraction was delayed by silver sulphadiazine and saline group (control). Aloe vera and Nystatin when added to the silver sulphadiazine, they show the synergism. These investigations revealed that the dry wound (saline) heals slowly. Aloe vera with other anti- microbial agents plays a vital role in wound healing without infection.

Saeed *et al.* (2004) reported the importance of Aloe vera. It is a descriptive research. Aloe vera is a vitally important plant that has been used for different ointments *i.e.* geotrontestinal, gont boils, etc. It has several other properties or characteristics including antibacterial, anti inflammatory and antiseptic attributes. Easy growth, maintenance and multiple uses of Aloe plant's constituents have promoted several elaborated investigations in public and private sector.

Kilic (2005) described the effect of gel in the wound healing process is known. Because peritoneal healing

is a kind of wound healing process, it was hypothesized that post-operative peritoneal adhesion (PPA) may be reduced with intra-peritoneal gel administration. The study was conducted with 45, 6 month old, out bred female Sprague-Dawley rats with a mean weight of 236 ± 17 g. The rats were divided into three equal groups. An adhesion model was constituted in the caecum and terminal ileum of all rats in each group. After above process, the Sham group received no further treatment. The remaining rats received a 5 mL intra peritoneal injection of either saline (Na Cl 0.9%, control group) or gel (treated group) before the abdomen was closed. Ten days later, rats were sacrificed and the adhesions were graded according to their degree of severity. The mean adhesion score of gel treated rats was 3.0 ± 2.3 while it reach 10.2 ± 4.6 in the sham group and 9.6 ± 4.2 in the control group. This study strongly suggests that intra-peritoneal gel administration can reduce PPA in rats. Aloe vera has been traditionally used for burn healing but clinical evidence remains unclear. We conducted a systematic review to determine the efficacy of topical Aloe vera for the treatment of burn wounds. Only controlled clinical trials for burn healing were included. There were no restrictions on any language of publication. Two reviewers independently extracted data on study characteristics, patient characteristics, intervention, and outcome measure. Four studies with a total of 371 patients were included in this review. Based on a meta analysis using duration of wound healing as an outcome measure, the summary weighted mean difference in healing time of the Aloe vera group was 8.79 days shorter than those in the control group ($P = 0.006$). Due to the differences of products and outcome measures, there is paucity to draw a specific conclusion regarding the effect of Aloe vera for burn wound healing. However, cumulative evidence tends to support that Aloe vera might be an effective interventions used in burn wound healing for first to second degree burns. Further, well designed trials with sufficient details of the contents of Aloe vera products should be carried out to determine the effectiveness of Aloe vera.

Moghbel *et al.* (2007) explained that Aloe vera has useful properties in various conditions. The plan of this study was to prepare a topical cream by Aloe vera and to conduct its clinical trials. A total of 30 patients (10 females and 20 males aging 25-45 years old) effected with second degree of burn wounds on both hands were selected. Topical application of Aloe vera and 1%

sulfadiazine cream was applied on each hand as a control and test, respectively. The speed of healing was observed and compared after the treatment on 0-18 days. The healing with Aloe vera was 90.6 and 29.8% with silver sulfadiazine 10 days post treatment. According to patient responses during post treatment period, there was no swelling, redness, itching, rashes, inflammation, irritation and no other toxicity signs in Aloe vera treated group. On the basis of these findings, the researchers concluded that Aloe vera has no dermal toxic effects on burn wound.

Medhi *et al.* (2008) evaluated the efficiency of topical use of honey in experimental studies in addition to restricted experimental trials in the treatment of wound curing. They create 5 experimental studies with 160 animals whereas 963 cases in 10 controlled experimental trials wherever 511 animals were treated through honey. Efficiency was observed extremely effective in experimental studies however in controlled experimental examination it reported poor effectiveness. The majority of the animals showed total curing of 98% within 2-9 weeks in experimental and 57 % in controlled experiment and curing was reported within 4-12 week's time in controlled experimental trials. Therefore, based on over experiment it can be accomplished that topical utilization of honey is supportive for the treatment for wound curing.

Hamman and Josias (2008) studied the combination and applications of Aloe vera gel. Aloe vera is associated with many health benefits which have been accredited to the polysaccharides found in the gel of the Aloe vera. These organic actions improved the wound healing, anti-inflammatory, antifungal activity, anti-diabetic effects or hypoglycaemic, immunomodulatory, anti-cancer and gastro protective effects. Whereas, the well-known natural behaviour of Aloe vera was completely observed; the main plan of this study was to more underline recently exposed properties and applications of the Aloe vera gel. These properties contain the possible of entire leaf or inner fillet gel fluid formation of Aloe vera and it can also enhance the intestinal assimilation and bioavailability of co-administered complex in addition to improvement of skin penetration.

Rajar *et al.* (2008) compared the efficacy of Aloe vera gel and placebo in the topical management of vulval lichen planus. Thirty four female patients were randomized into two groups to receive Aloe vera gel or placebo for local application for 8 weeks. Clinical data

and treatment response was graded according to Thongprasom criteria. Z-test was used for comparing response between the groups. Thirty-four consecutive patients participated in the study. We found erosive and ulcerative lesions in 83 and 17%, respectively. The most common site of vulval lichen planus was the labia minora. Fourteen (82%) out of 17 patients treated with Aloe vera had a good response i.e. clinically improved by at least 50% after 8 weeks of treatment, while one (5%) of 17 placebo-treated patients had a similar response ($P < 0.001$). Furthermore, one patient (5%) treated with Aloe vera had a complete clinical remission. No side effects were found in both groups. Aloe vera gel was a safe and effective treatment for patients with vulval lichen planus.

Nasrin *et al.* (2009) investigated the study of topical influence of Aloe vera, on the wound healing process. A total of 63 male rats with microscopic and cell count methods. On the day of surgery a round wound, of diameter 20 mm, was created on the back of rats necks under sterile conditions. The surgery day was determined as day zero. Then the rats were divided randomly into control and experimental groups (1) and (2). Animals in each group were subdivided to three smaller groups, investigated every 4, 7 and 14 days. From day zero, wound surfaces were covered with gel once daily in experimental group (1) and twice daily, for 12 h interval in experimental group (2). Each rat received 30 g of the gel. The wound surface and healing were assessed on days 4, 7, and 14, and then a sample from the wound was prepared and investigated microscopically. The results show that the number of neutrophil, macrophage, and fibroblast cells and the wound thickness in the control group were statistically different from the experimental groups. It was found that the wound diameter thickness in the experimental group was greatly lower due to twice administration of gel and the power of wound healing was more than other groups.

Mendonca *et al.* (2009) investigated the effects of topical application of an Aloe vera gel combined or not with micro current application on the healing of skin wounds surgically induced in Wistar rats. The animals were randomly divided into the following groups: control group, animals topically treated with Aloe vera, animals treated with a micro current and animals receiving topical application of Aloe vera combined with micro current application. The results indicated differences in wound healing between the various treatments when compared to the control group. Tissue hyperplasia was

lower in the control group compared to the other treated groups. Accelerated wound healing was observed in the group treated with Aloe vera compared to control. Animals submitted to micro current application only and the group treated with micro current plus Aloe vera presented an earlier onset of the proliferative phase compared to the control group and animals treated with Aloe vera gel alone. Morphometric data confirmed the structural findings. Simultaneous application of Aloe vera gel and micro current is an excellent choice for the treatment of open wounds thus indicating a synergistic action of these two applications.

Ali *et al.* (2009) conducted an experiment to compare the effects of ointment and silver sulfadiazine (SSD) on burned wounds for healing in rats. Sixty male Wistar albino rats were divided into three equal groups. A burned model was constituted on the back of all rats. The burned areas in the first, second and third groups were covered daily with collagens, SSD skin cream and cold cream (control), respectively. Ten and 21 days later the rats were anaesthetized and the burned skin tissue samples of ten cases of each group were collected for histo-pathological examinations. In conclusion, application of collagens ointment is significantly effective in healing of burned skin wounds in rat model ($P < 0.0001$).

Jagtap *et al.* (2009) evaluated the different parts of the plants such as the aerial parts of *Centella asiatica* (L.) Urban and rhizomes *Curcuma longa* (L.) were collected, dried under shade and extracted with ethanol and water respectively. These extracts were dried. Aloe barbadensis concentrated gel powder was obtained as free sample. Each extract and Aloe gel was added with appropriate proportion in cream base and evaluated for wound healing activity against povidone iodine ointment. In excision wound model the complete wound healing was observed with cream formulation I and II treated rats was observed in 18 days where as povidone iodine ointment took 16 days. In incision wound model tensile strength of formulations I and II was found to be 366.08 ± 2.32 and 351.35 ± 3.29 gm respectively. Tensile strength of povidone iodine ointment was found 379.98 ± 2.95 gm. Herbal formulation I and II took two days more for complete wound healing as compared to povidone iodine ointment.

Mendonca *et al.* (2009) explored in another experiment the efficacy of the Aloe vera combined or in combination form in wound healing in rat model. For this purpose

40 rats were selected, they were divided in to four groups (A), (B), (C) and (D). In each group there was assigned 10 rats. In anesthetized condition, burn wound was created by the hot water (100 °C) on the thoracolumbar region. Group (A) was treated by Aloe vera; Group (B) was treated by micro current (10 μ A/2 min). Group (C) was treated by the combination of the Aloe vera and the micro current and the group (D) was control and remained un-treated. The parameters were contraction rate, healing time and histopathology. The results were compared to each other. Group (C) which was treated by the combination of Aloe vera and the micro current showed the synergism effect. The healing was completed only in 10 days. Histopathology examination showed the more collagen contents in this group as compared to the other group.

Fariborz *et al.* (2010) studied the Aloe vera plant as an herbal medicine, which has wound healing effects in burn injury. This study assessed the effects of Aloe vera cream in reducing post-operative pain, post defecation pain, and its promotion of wound healing after open hemorrhoidectomy. A prospective, randomized, double-blind, placebo controlled trial was conducted comparing the effects of a cream containing Aloe vera versus a placebo cream on post hemorrhoidectomy pain. The study preparations were applied by patients to the surgical site 3 times per day for 4 weeks after hemorrhoidectomy. Pain was assessed with a visual analog scale immediately postoperatively and at hours 12, 24, and 48 after surgery and at weeks 2 and 4. Wound healing was examined and evaluated at the end of 2 and 4 weeks. The use of analgesics was recorded. Forty-nine (49) patients were randomly assigned to receive aloe ($n=24$) or placebo ($n=25$). Patients in the topical aloe cream group had significantly less postoperative pain at hours 12, 24, and 48 h and at 2 weeks. Aloe cream reduced the pain after defecation in 24 and 48 h post-surgery ($P < 0.001$). Wound healing at the end of the second post-operative week was significantly greater in the aloe group compared with the placebo group ($P < 0.001$). Patients required fewer additional analgesics post hemorrhoidectomy ($P < 0.001$). Application of Aloe vera cream on the surgical site is effective in reducing postoperative pain both on resting and during defecation, healing time and analgesic requirements in the patients compared with the placebo group.

Himanshu *et al.* (2010) evaluated the wound healing activity of gel containing cow ghee and Aloe vera in rats. Incision wounds for tensile strength and excision

wounds contraction along with the histopathological examination of the regenerated tissues were employed to investigate the wound healing potential. Topical application of the test formulation alone promoted the tensile strength (incision wounds) and wound contraction (excision wounds) showing healing potential comparable to framycetin sulphate cream (1%w/w). Histological examination reveals good keratinisation, epithelisation, fibrosis and collagenation indicative of the wound healing potential of gel. The present study thus offers a valuable proves into the claimed wound healing potential of the test formulation.

Kumar *et al.* (2010 a and b) investigated the dose dependent effect of Aloe vera gel on repolarization state of myocardium, heart rate, QRS complex and QT interval using electro cardiograph in albino rats. Aloe vera is a well-known medicinal plant contents with over 75 different ingredients, anthraquinones, saponins, and sterols. Recent studies showed that it is a potently polipedimic, hypoglycaemic and antioxidant. A total of 24 male albino rats were divided into four groups, one control and three experimental. An aqueous solution of Aloe barbadensis was prepared by taking fresh leaf of aloe plant. Animals of all the groups were anesthetized and were treated (i.p.) with Aloe vera gel extract in doses of 100, 200 and 30 mg/kg body weight in experimental groups me, II and III, respectively. Electro cardio grams were recorded at 0 (basal), 15 and 30 min after injection of Aloe vera/ saline. Aloe vera in doses of 200 mg increases TCU from 73.10 ± 3.25 (mv) to 75.04 ± 1.93 (mv) and in 300 mg, TCU increased from 72.10 ± 1.85 to 76.10 ± 1.56 which is statistically significant ($P < 0.05$). Higher doses of Aloe vera cause prolongation of TCU interval in albino rat.

Kumar *et al.* (2010 b) in another experiment explored that Aloe vera contains several amino acids, enzymes, vitamins, minerals, natural sugars and substances which may be antimicrobial and anti- inflammatory. It is also used as antiseptic, antibacterial and is good for the restoration of tissue. It is generally used for minor cuts, burns, skin cancer treatment and vaginal yeast infections. Washing of eyes by Aloe vera provides the protection from the ultra violet rays of sun. It provides the healthy and flexible appearance to the skin by reducing wrinkles.

Singh *et al.* (2010) determined the health benefits associated with Aloe vera have been attributed to the polysaccharides contained in the gel of the leaves. These biological activities include effects promotion of wound

healing, antifungal activity, hypo glyceemic or anti diabetic effects, anti-inflammatory, anticancer, immunomodulatory and gastro protective properties. While the known biological activities of Aloe vera will be briefly discussed, aim of this review is to highlight recently discovered effects and applications of the leaf gel. These effects include the potential of whole leaf or inner fillet gel liquid preparations of Aloe vera to enhance the intestinal absorption and bioavailability of co-administered compounds as well as enhancement of skin permeation. In addition, important pharmaceutical applications such as the use of the dried Aloe vera gel powder as an excipient in sustained release pharmaceutical dosage forms will be outlined.

Oran *et al.* (2010) conducted a study to estimate the efficiency of Aloe vera on cutaneous wound healing. Forty rats were selected into two equal groups (control untreated and experimental treated) to meet the objectives. 1.5 mL aqueous extract of Aloe vera was applied on the wounds of experimental group. Wound contraction was observed after every 5 days (5, 10, 15 and 20 days). Twenty rats (10 of each group) were selected on day 10 and then biochemical and histopathological sampling were performed. Remaining 20 rats were selected on day 20th. Histopathological results of treated animals on 10th days were non-significant. A significant wound contraction started at day 15th onwards. The tissue samples of the treated animals showed a better arrangement and less inflammatory cells penetration on the day 20th. These results recommended that application of aqueous extract of Aloe vera on cutaneous wounds produce better wound contraction and enhance healing process.

Hosseini-mehr *et al.* (2010) concluded the effectiveness of the Aloe vera cream in the cure of burn wound and match these results with 1% silver sulphadiazine. For this purpose 48 male Wister rats weight 180-200 g were selected. Animals were divided into four groups (A), (B), (C) and (D). In each group there was assigned 12 rats. They were treated respectively by Aloe vera, 1% silver sulphadiazine, base cream (without effecting agent) and control (non-treated). On the thoracic region burn wounds were created by the hot water (100 °C). After 4 h of inducing the burning, the treatment was applied. After every 3 days wound contraction was measured. The wound size mean was 4.5 cm in control, 3 cm in base, 0.70 cm in Aloe and 4.1 cm in silver treated group at three days. The wound size was appreciably

smaller in Aloe treated group as compare to the other groups. Histopathology was performed after 8, 12 and 16 days. Histological evaluation showed the Aloe treated group enhanced the re-epithelialization in the burn wounds appreciably as compared to the other cream treated wounds. The conclusion of this study is Aloe vera enhanced the wound contraction and the re-epithelialization in burn wound as compared to the 1% silver sulphadiazine.

Reddy *et al.* (2011) described the use of Aloe vera in wound healing is being considered in many studies. The aim of this comprehensive review is to present an update about the mechanism of action of Aloe vera in wound healing. Aloe vera contains important ingredients necessary for wound healing, such as vitamin C and E, amino acids and zinc. Aloe vera affects various factors involved in wound healing and promotes healing. In conclusion, Aloe vera on its own and through its constituents promotes wound healing. It being a natural substance, has less side effects. Clinical recommendations warrant further research.

Babak *et al.* (2011) analyzed the effects of different levels of Aloe vera gel as an alternative to antibiotic, on performance and ileum morphology in broilers. Three hundred one day old Ross 308 male broilers were used on a completely randomized design in 5 groups with 4 replicates, each consisting of 15 broilers. The groups included the control group (basal diet) and three groups with basal diet mixed with different levels of Aloe vera gel (1.5, 2 and 2.5%). Finally, there was a group with basal diet plus 15 ppm antibiotic virginiamycin. Their results obtained regarding performance of the broilers showed that Aloe vera gel groups brought about higher body weight gain and feed intake compared to the control group; however, no significant difference was observed in feed conversion ratio between the groups treated by Aloe vera gel and the control group ($P > 0.05$). Although the antibiotic group showed better performance and heavier dressing percentage than the Aloe vera gel and control groups, no significant difference was seen between the group treated by 2% Aloe vera gel and the antibiotic group regarding body weight gain, feed conversion ratio and dressing percentage ($P > 0.05$). Among the Aloe vera gel groups, the 2% Aloe vera gel group had the largest villus height and the greatest villus height to crypt depth ratio compared to the antibiotic group ($P < 0.05$). In general, 2% Aloe vera gel treatment may be recommended to

achieve the best performance in broilers as an alternative to antibiotic growth promoter.

Sharrif *et al.* (2011) explained the special characteristic of Aloe vera gelatin that is extracted from this plant is continuously used to treat burns, cuts and inflamed scars since many years. It was known to people in Egypt and also Greece for example Aristotle. It is useful for skin damaged from X-ray as reported in many researches in journals related X-rays. On the other hand concentration of glucose in gelatine, results in high osmotic pressure that protect skin from live bacteria.

Sharrif *et al.* (2011) also explained that Aloe vera has "Antrokinon" chemicals that are known as antivirus, antibacterial and anticancer. Aloe vera has 400 species but just 2 species; *A. Barbadosis* is used for trade in the world. This plant needs very less water for living and also can survive on saline soils, beaches and is resistant to diseases and insects. It can live in very hot regions, but cannot tolerate cold.

Agarwal *et al.* (2011) explained that Aloe vera (*Aloe Barbadosis*) is commonly used in sunburn, minor cuts, insect bites and used as wound healing, anti-inflammatory, antiviral, antitumor, laxative and in the treatment of frostbite and psoriasis. The whole plant as well as its specific parts (leaves, roots), plant extracts and its active constituent muco polysaccharides (MPS) (long chain sugars) have been widely used as antiseptic, anti-inflammatory, anti-viral, anti-tumour and immunomodulator. Several epidemiological, clinical and experimental studies have demonstrated the multiple biological activities of Aloe vera. This review summarizes the most interesting studies on the various biological activities of Aloe vera.

Mahsa *et al.* (2012) investigated the effects of topical application of an Aloe vera gel, thyroid hormone cream and a silver sulfadiazine cream on the healing of skin wounds surgically induced in Wistar rats for determining the treatment of choice. Many research studies report the healing effects of Aloe vera, thyroid hormone cream and silver sulfadiazine. However, the effects of these therapeutic agents are not well understood and have not been compared in one study. In a randomized controlled trial, twelve male rats and aged 120 days and with a mean weight of 250 to 300 g, were divided randomly into 5 groups based on drug treatments: Aloe vera gel (AV), thyroid hormone cream (TC), silver sulfadiazine 1% (S), vehicle (V) and control. To evaluate

the efficacy of each treatment technique, a biomechanical approach was used to assess tensile stress after 14 days of treatment. Tensile stress was significantly improved in the Aloe vera gel group as compared with the other four groups ($P=0.05$), while the other treatment options resulted in better healing than the control group, this difference was not significant. We conclude that Aloe vera topical application accelerated the healing process more than thyroid hormone, silver sulfadiazine and vehicle in surgically induced incisions in rats.

Yadav *et al.* (2012) evaluated the effect of Aloe vera gel on wound healing by wound excision model and histopathology was used to study the effect on wound healing. Aloe vera gel of 50% and 96.4% were tested for its wound healing activity by topical application in experimental rats. The effect produced by Aloe vera gel with reference to wound contraction, wound closure, decrease in surface area of wound, tissue regeneration at the wound site and histopathological characteristics were significant in treated rats. The effect of Aloe vera gel on biochemical studies revealed significant increase in collagen and decreased hexosamine content and malondialdehyde levels when compared with control. The present study thus provided scientific rationale for the traditional use of Aloe vera gel for management of wounds.

Fani *et al.* (2012) explained Aloe vera is a medicinal plant with anti-inflammatory, antimicrobial, antidiabetic and immune-boosting properties. In the present study we investigated the inhibitory activities of Aloe vera gel on some cryogenic (*Streptococcus mutans*), periodontopathic (*Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*) and an opportunistic periodontopathogen (*Bacteroides fragilis*) isolated from patients with dental caries and periodontal diseases. Twenty isolates of each of these bacteria were investigated for their sensitivity to Aloe vera gel using the disk diffusion and microdilution methods. *S. mutans* was the species most sensitive to Aloe vera gel with a MIC of 12.5 µg/mL, while *A. actinomycetemcomitans*, *P. gingivalis*, and *B. fragilis* were less sensitive, with a MIC of 25-50 µg/mL ($P < 0.01$). Based on our present findings it is concluded that Aloe vera gel at optimum concentration could be used as an antiseptic for prevention of dental caries and periodontal diseases.

Yadav *et al.* (2012) tested the efficacy of the Aloe vera gel of 96.4 and 50% on wound healing in experimental rats. The effect of the Aloe vera gel was evaluated on

the excision wound and the histopathology was performed to check the effect. Wound closure, wound contraction, tissue regeneration, decrease in the surface area of the wound and histopathological features were significant in treated rats. Biochemical studies exposed the decrease in hexosamine and increased in collagen contents as compared to the control (not treated). It enhances the traditional uses of Aloe vera gel in the treatment of the wound healing.

Fani *et al.* (2013) designed an experiment to observe and judge the efficiency of Aloe vera extract on wound healing. For this purpose, 2 cm long incisions were made over the back side of 18 rabbits. The rabbits were divided equally into three groups (A), (B) & (C); each was treated with mixture of Xylo Aid & Aloe vera extract respectively every day for 12 days, and gradually marked with green, black and blue. At 11th post incision day the whole wound area besides with 3-5 mm of the nearby skin was excised and fixed in 10% formaldehyde. The processed sections of the tissues were stained with hematoxylin and eosin (H&E) and examined under microscope; fibroblasts were counted to observe the value of healing. Microscopic examination showed that at 11th day post incision the healing was 75% with Aloe vera extract while 30% and 50% with Xylo Aid and mixture application respectively. Application of Aloe vera for 11th days on wound showed better healing efficiency as compared to Xylo Aid and mixture.

Sahu *et al.* (2013) evaluated the importance and composition of the Aloe vera. Broadly it is used in allopathic and homoeopathic medicines. It is also used as food preservative. The leaves of the Aloe vera contain the numerous enzymes, vitamins, minerals, natural sugars and amino acids. It also contains the other bioactive compounds with purgative, emollient, antioxidant, anti-microbial, anti-inflammatory, antiseptic, antifungal and anti-helmenthic. It is used for cosmetic purpose in health care.

Atiba *et al.* (2014) evaluated the efficacy of the Aloe vera gel in the treatment of second degree of burn wound in dog model and compared the result with silver sulfadiazine 1% cream. Five dogs were selected and three groups of second degree burn wounds were produced on thoraco-lumbar region in each dog. They were treated gradually with Aloe vera, silver sulphadiazine 1% cream and one group of wound was controlled (no topical therapy). The effect of the treatment was based on the percentage of wound healing,

degree of inflammation and time of completeness of wound healing. Wound contraction was superior in Aloe vera treated group as compared to silver sulfadiazine and control group after 14, 21 and 27 days. The mean times of complete wound healing were 25.7 ± 2.31 and 22.9 ± 2.56 days for silver sulfadiazine and Aloe vera, respectively.

Sajjad and Sajjad (2014) reviewed the clinical applications, actions and composition of Aloe vera in dentistry and to set up its efficiency as valuable addition in the treatment of dental problem. Aloe vera has many medicinal properties such as antibacterial, antitumor, anti-inflammatory and anti-viral. These properties enhance the healing and help to treat the lesions in oral cavity. To check the efficacy of Aloe vera in the treatment of gingivitis a study was conducted. For this purpose 120 subjects were selected. They were requested to give up the tooth brushing for 15 days. Then, they were divided into three groups. Group (A), (B) and (C). Group (A) was standard group and was treated by 100% pure Aloe vera. Group (B) was negative control group and was treated by the placebo (distilled water). Group (C) was positive control group and was treated by the 0.2% chlorhexidine. The plaque growth was observed by plaque index (PI), Gingivitis was observed by the gingival index (GI) while, bleeding was assessed by bleeding index (BI) at 6th, 12th and 18th days. Group (A) which was treated by the Aloe vera containing mouth wash showed the significant reduction in gingivitis and plaque. The group (C) which was treated by the chlorhexidine showed the less significant effects as compared to the group A. The result showed that Aloe vera is the effective anti-plaque agent.

Adnan *et al.* (2015) suggested the function of Aloe vera extract on generally induced and contaminated wounds with *Staphylococcus aureus*. Twenty male rabbits were selected in the experiment. They were equally divided into four groups and burning was induced by sulphuric acid. After one hour of washing with water, group (I) was control, group (II) was treated by Aloe vera extract for 8 days, group (III) was contaminated by *Staphylococcus aureus* and group (IV) was contaminated by *Staphylococcus aureus* and was treated with Aloe vera extract for 15 days. To identify the progress of infectivity and healing, swabs were taken from all burns every day before and after treatment. Non infected and non-treated group (I) showed the signs of infection such as ulceration, redness, thickness of skin tissue and oedematous after

24-48 h of infection. Group (II) of non-infective animals treated by extract showed some signs of infections after 2 days. After 7 days the wound started to heal and there was no ulceration and swelling. The skin started to soften and there was no broken tissue. Group (III) which was infected with *Staphylococcus aureus* and not treated; there was swelling and thickening areas with pus cells. Group (IV) was infected with *Staphylococcus aureus* and was treated by Aloe vera extract for 15 days; there were no inflammation, swelling and pus cells. A degree of healing was observed in this group. Histo-pathological sections of group (IV) showed granulation tissues, unequal fibrous connective tissues with packed blood vessels and penetration of mononuclear cells in some areas. These results proved that Aloe vera extract have the capacity to increase the speed of wound healing and act as antibacterial. *Staphylococcus aureus* was affected by Aloe vera extract, therefore Aloe vera extract was recommended in the treatment of burn wound healing.

Lakhanpal *et al.* (2015) evaluated the healing efficacy of different formulations of Aloe vera in burn wound in rat model and compare these formulations healing with the Framycetin sulphate. Fifty rats of either sex and weighing 120-180 g were selected. They were divided into five groups each group contains 10 rats. Group (I) was control and remained untreated. Group (II) was treated by Aloe gel. Group (III) was treated by Aloe pulp. Group (IV) was treated by Aloe-powder. Group (V) was treated by Framycetin cream. The second degree burn wounds were created under anaesthesia by pouring the boiling water (above 100 °C) in thoraco-lumbar region. The study formulations were topically applied twice a day till the day of the complete healing. Two parameters (period of re-epithelialization and wound contraction) were measured. In burn model, Framycetin and Aloe pulp showed the excellent healing on the day 20th. They showed the shorter period of re-epithelialization and maximum wound contraction as compared to other groups. Aloe pulp has the greater efficacy of healing of wound. In house hold burn, it can be easily recommended as a safe and faster healing agent.

Ahmad *et al.* (2015) explored the efficacy of the Aloe vera on angiogenesis process during burn wound healing. For this process seventy rats were selected. They were divided into three groups (A), (B) and (C). full thickness burn wound were induced on the thoraco-lumbar region

under anaesthesia condition. Group (A) was control and was untreated. Group (B) and (C) were treated by the Aloe vera gel. Further group (B) and (C) were divided into three subgroups. Skin specimens were collected after a specific interval at 4th, 8th and 12th days. They were prepared for immuno-histochemical and histological study by Masson's trichrome (MT), hematoxylin and eosin (H&E) and alpha smooth muscle actin (α -SMA). All data were statistically analyzed. The initial inflammation and necrosis slowly swapped by enhancing the granulation tissues (GT) on 8th and 12th day specimens. To create coarse dense bundles, the collagen deposition of granulation tissues improved gradually. The freshly formed capillaries of granulation tissues were bounded by pericytes that exhibited widespread appearance of alpha smooth muscle actin (α -SMA) on 4th and 8th day specimens and declined on 12th day specimens. Aloe vera treated groups exposed comparative reduction of alpha smooth muscle actin (α -SMA) particularly in 8th and 12th day specimens. It also showed a significant reduction in the inflammatory infiltrate and provides mature granulation tissues that speed up the healing process and create a comprehensive well-remodelled scar.

Conclusion

Wound healing is an intricate process where the skin or other body tissues repairs itself after the injury but some time healing may fail because of interruption at any stage. There are many factors including diabetes, anaemia, nutritional deficiency, local infections, haematoma etc can slow the healing process of wound. Many herbal plants like neem, turmeric, Aloe vera etc are found useful in treating of wound. The wound healing by Aloe vera are inexpensive, affordable and safe because having no side effects. These herbal ointments induce healing and regeneration of the lost tissues by multiple mechanisms. However, there is a need for scientific evaluation, standardization and safety evaluation of these herbal ointments. The previous studies revealed that wounds treated with Aloe vera healed promptly and the hyper tonicity and acidic pH of the Aloe vera are considered to be the main factors responsible for accelerating the healing of wounds. Aloe vera may accelerate the wound healing by enhancing glycolytic enzyme activities and delivering enough energy for cellular restoration. Aloe vera can be regarded as economical, easily available, safe, and potent topical agent in treatment of wounds.

Conflict of Interest. The authors declare have no conflict of interest.

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