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Original Article

Role of Aloe Vera aqueous extract in dead space wound in diabetic rats

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ABSTRACT

Physical impairments are frequently caused by wounds. Wound healing is the orderly evolution of a set of processes that restore the injured tissue integrity. Constipation, colitis, asthma, irritable bowel syndrome, diabetes, peptic ulcer, inflammation, heart burn, stress, and other ailments are treated using Aloe vera leaves pulp from Aloe arborescens species. The purpose of this study was to evaluate the effect of Aloe vera leaf pulp on wound healing activity using an oral route on a dead space wound model. On an excision wound model, Aloe vera leaf pulp was discovered to have a superior and faster wound healing effect. In the current study, in a dead space wound model, wet and dry granulation tissue weights, granulation tissue breaking strength, and hydroxyl proline, hexuronic acid, tissue protein, and lysyl oxidase content all increased statistically significantly.

Key words: Aloe Vera, Wound healing; Diabetic; Dead space wound; Granulation tissue; Streptozotocin

INTRODUCTION

Wounds are a common source of physical restrictions. Healing is a survival mechanism that attempts to maintain as normal anatomical structure and connections as feasible.[1] Immunosuppressants, cytotoxins, and nonsteroidal anti-inflammatory drugs all delay wound healing. Wound healing is a time-consuming and expensive procedure.[2] The repair of damaged tissue (wounds) is a crucial process that is essential for survival. It's on the verge of becoming the standard for all surgical procedures.[3] In a variety of conditions, several plants have been demonstrated to have significant wound healing properties. Plants with antiseptic, astringent, anti-inflammatory, and antibacterial qualities can help speed up the healing process.[4] Such a plant can hasten tissue regeneration by providing several essential chemicals necessary at various phases of wound healing. Plants are less expensive and safer than allopathic medications, therefore they might be useful in veterinary

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medicine, especially in India, where they are abundant.[5] Constipation, colitis, asthma, irritable bowel syndrome, diabetes, peptic ulcer, inflammation, heartburn, and stress are among the diseases that *Aloe vera* pulp is used to cure.[6-8]

The wound healing ability of *Aloe vera* was investigated in diabetic rats utilising a dead space wound model. Wound healing is frequently hindered in people with diabetes mellitus (DM), resulting in non-healing, delayed healing, or persistent skin ulcers.[9] In diabetes, delayed wound healing can be caused by an imbalance in the inflammatory response, changed cytokine production, altered collagen synthesis, insufficient angiogenesis, extracellular matrix differentiation, lower tensile strength, or diminished growth factors.[10,11] Incision and excision wound models were used to study the impact of *Aloe vera* on wound healing activities. The *Aloe vera* effect in a diabetic rat with dead space wound model, on the other hand, is unknown. As a result, the goal of this study is to see how *Aloe vera* affects diabetic wound.

MATERIALS AND METHODS

***Aloe vera* Preparation:** Fresh *Aloe vera* mature leaves were obtained from a nearby nursery yard. Fresh mature leaves were washed with distil water from the exterior to eliminate any dirt or other contaminants. The rind was removed with the assistance of a sanitised knife. The gel was dried in an oven at 600°C to produce powder. The powder was dissolved in distilled water and centrifuged for 10 minutes at 5000 rpm. The filtered supernatant was collected. After drying the filtrate, powdered *Aloe vera* was obtained. Before oral administration to the experimental animals, the extract was reconstituted in double distilled water.

Animals: Healthy wistar rats of either sex (150–200 g) were utilised in this study with no prior pharmacological treatment. The animals were fed a commercial pellet diet and given unlimited access to water. The animals were acclimatised to laboratory hygienic conditions for 10 days prior to the start of the trial. The therapy was carried out with the approval of the animal ethics committee of King Khalid University, as well as the National Institute of Health's standards for the care and use of laboratory animals in the United States (NIH Publication No. 85-23, revised 1996). For the dead space wound model, animals of either sex were divided into three groups, each with six animals: Group I- Normal control; group II received diabetic control; and group III received *Aloe vera* (50 mg/kg/day). The extracts were administered orally to the individual animal groups once a day.

Wound healing activity:

Dead Space wound model: Rathi et al. described a technique for creating dead space wounds.[12] Eighteen rats were divided into three groups of six individuals each. Subcutaneous dead space wounds were produced in the area of the axilla by creating a pouch through a tiny nip in the skin under general anaesthesia (achieved with 10 mg/kg body weight of xylazine hydrochloride and 50 mg/kg ketamine hydrochloride). The development of granulomas was induced by implanting sterile cotton pellets (30 mg) in each axilla. Sutures were used to close the wounds, which were then cleaned with an alcoholic swab. After being grouped together, the animals were placed individually in a metal cage to prevent them from biting each other's wounds.

The extract or normal saline (1 ml/kg) was given to the treatment groups over an 8 day period. After the rats were euthanized on day 10, the cotton pellets and granuloma tissues were carefully removed, dried in a 60°C oven, weighed, and compared to the control. 5mL 6 N HCl was applied to the dry tissue and stored at 1108C for 24 hours. Hydroxyproline, hexosamine concentration, and hexuronic acid were measured using the neutralised acid hydrolyzate of dry tissue. Lysyl oxidase and tissue protein were determined using a sample of moist granulation tissue.[13]

Induction of diabetes: The rats were given a newly produced solution of streptozotocin (STZ) (Sigma, St. Louis, MO, USA) dissolved in citrate buffer pH 4.5 at a dosage of 65 mg/kg intraperitoneally (i.p.) 15 minutes after receiving 110 mg/kg body weight nicotinamide (HiMedia labs Pvt. Ltd.). The rats were given a 10% glucose solution after 6 hours of STZ treatment for additional 24 hours to prevent hypoglycemia owing to large pancreatic insulin secretion. Blood was collected from the tail veins of the rats 72 hours after the STZ injection, and those with a fasting blood glucose level of more than 200 mg/dl were classified as diabetic and used in this investigation.[14]

Statistical analysis: The data is presented as a mean with a standard deviation (SEM). The differences between means were investigated using one way analysis of variance (ANOVA), with p values less than 0.05 being deemed significant. The data was analysed using one way analysis of variance (ANOVA) with a post hoc Scheffe's test in Graph Pad, and the mean and standard deviation were calculated. Statistical significance was defined as a p value of 0.05 or less.

RESULTS

Animals treated with *Aloe vera* showed a substantial increase in wound-healing activity when

compared to those that received placebo control treatments. The effects of *Aloe vera* given orally for 8 days on wound healing activity in rats with a dead space wound are shown in Table 1. When compared to diabetic and control rats, the breaking strength of granulation tissue and the weight of wet and dry granulation tissue were considerably higher in the *Aloe vera* therapy group. (table 1).

Table1: Physical and biochemical analysis of granulation tissue in streptozotocin induced diabetic rats

Groups	Blood glucose (mg/dl)	Wet tissue weight (mg/ 100g rat)	Dry tissue weight (mg/ 100g rat)	Tissue breaking strength (g)
Wounded Control	83.1 ±6.2	239.1 ± 12.29	34.18 ± 4.30	282.19±12.07
Diabetic Control	276.38 ± 14.1[a]	169.5 ± 10.32[a]	22.5 ± 4.50[a]	176.36±1.10[a]
Aloe vera	272.38 ± 13.1[a]	270.5 ± 12.09[a]	36.5 ± 4.60[a]	317.43±15.07[a]

Values are mean ± SD of 6 replications. p values: [a]:<0.01vs control.

In diabetic rats produced by streptozotocin, the concentration of hydroxyproline in granulation tissue was substantially lower. The experimental group had considerably lower levels of glycosaminoglycan contents such as hexuronic acid and hexosamine. When diabetic rats were compared to control rats, tissue protein content was extremely low. In the experimental group, the amount of lysyl oxidase was substantially lower. When compared to diabetic and control rats (group II), all of the above metrics dramatically improved in the *Aloe vera* therapy group (table 2).

Table 2: Biochemical analysis of granulation tissue in streptozotocin induced diabetic rats

Groups	Hydroxyproline (mg/g tissue)	Hexosamines (mg/g tissue)	Hexuronic acid (mg/g tissue)	Tissue protein (mg/g tissue)	Lysyl oxidase (SFU)
Wounded control	16.12 ± 3.92	12.45 ± 3.17	13.51 ± 3.19	44.68 ± 4.40	1723 ± 62
Diabetic Induced	12.18 ± 3.20a	7.4 ± 1.40a	9.2 ± 1.12a	25.5 ± 2.60a	1129 ± 46a
Aqueous extract of Aloe vera	14.74± 4.62	11.39 ± 2.47	15.21 ± 3.19	41.18 ± 4.10	1910 ± 61

Values are mean ± SD of 6 replications. (SFU- Spctroflourimetric units), p values: [a]:<0.01 vs control.

DISCUSSION

Numerous researches have been done to establish the effectiveness of *Aloe vera* in treating wounds and burns, cancer, diabetes, indigestion, ulcers, and diabetes, among other conditions. The synergistic effect of many components contained in Aloe vera, rather than a single isolated molecule, may be responsible for its diverse biological functions.[15] The presence of phytoconstituents including alkaloids, triterpenoids, tannins, and flavonoids in the extracts may be responsible for the wound healing benefits.

Flavonoids and triterpenoids are also known to aid wound healing, owing to their astringent and antibacterial properties, which appear to be responsible for wound contraction and epithelialization. In the incision and dead space wound models, increased skin breaking strength and tissue breaking strength suggested increased collagen maturation. The high collagen turnover was indicated by an increase in granulation tissue dry weight and hydroxyl proline content, which could be due to the activity of some phyto-constituents like flavonoids, which are known to reduce lipid peroxidation not only by preventing or slowing the onset of cell necrosis but also by improving vascularity.[16] Because *Aloe vera* has been shown to have substantial wound healing properties, the current study looked at its efficacy in diabetic wound healing. Streptozotocin is commonly used to cause diabetes in a number of animals by causing pancreatic β-cell degeneration and necrosis. Similarly, the current investigation utilised STZ induced diabetes and a dead space wound model to assess wound healing capacity. In the *Aloe vera* therapy group, the levels of hydroxyproline, hexuronic acid, and hexosamine increased. Enhanced lysyl oxidase activity in our study might lead to increased granulation tissue cross linking and breaking strength.

Conclusion: The wound healing properties of *Aloe vera* aqueous extracts can be linked to the phyto constituents found in them, which may have an individual or additive impact on wound healing.

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