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Original Article

Effect of *Buchanania Lanzan* on wound healing potential in diabetic rats

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ABSTRACT

The purpose of this study was to assess the wound healing activities of Buchanania lanzan (B.lanzan) fruit extract in streptozotocin-induced diabetes mellitus rat. On each axilla of diabetic rats, dead space incisions were created. For eight days, the rats were randomly assigned to one of three treatment groups (Group I: Normal saline; Group II: Diabetic control; Group III: B.lanzan). Animals were euthanized on day 10, and cotton pellets and granuloma tissues were carefully collected and processed for further estimates. In all, 18 rats were utilized in the experiment.During the trial, the B.lanzan group had a substantial increase in dry and wet tissue weight when compared to the other groups. In addition, as compared to the control, treatment with B.lanzan dramatically enhanced Hydroxyproline, Hexosamines, Hexuronic acid, Tissue protein, and Lysyl oxidase. The increased hydroxyproline levels, as well as other important biochemicals, support the use of B.lanzan for topical wound healing treatment.

Key words: B.lanzan; Wound healing; Diabetic; Dead space wound; Granulation tissue; Streptozotocin.

INTRODUCTION

A wound is a break in the normal tissue continuity that causes a range of cellular and molecular consequences. For many years, the basic principles of optimum wound healing have been known, including avoiding tissue injury, debriding non-viable tissue, optimising tissue perfusion and oxygenation, appropriate nutrition, and a wet wound healing environment.[1] A variety of medicines, ranging from basic non cost analgesics to sophisticated and expensive chemotherapeutic

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treatments can have a favourable or negative effect on wound healing. Wound healing is frequently hindered in people with diabetes mellitus (DM), resulting in non-healing, delayed healing, or persistent skin ulcers.[2] 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.[3,4]

The rhizome of *B. lanzan* is used as an expectorant, diuretic, and carminative in traditional medicine.[5] It has also been discovered to have antihypertensive, anticancer, and larvicidal properties.[6-8] It is used to treat a variety of skin conditions, as well as rheumatism and diabetes mellitus.[9,10] However, to the best of our knowledge, no comprehensive investigation of *B.lanzan*'s wound healing activities in diabetic rats has been conducted. As a result, the current study was conducted to assess the wound healing properties of an alcoholic extract of *B. lanzan* rhizome in diabetic rats.

MATERIALS AND METHODS

Preparation of extracts: The shade dried fruits of *B.lanzan* plants were crushed into tiny bits and powdered. The powder was put into a soxhlet extractor in 8 batches of 250 g each and extracted for 30–40 hours with 95 percent ethanol. The extract was concentrated under decreased pressure on a water bath at a temperature below 50°C to a syrupy consistency after the solvent was distilled out. It was then dried in a dessicator. The yield was around 3%.

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 both sexes were divided into three groups, each with six animals: Group I: Normal control; Group II: Diabetic control; Group III: *B.lanzan* (300 mg/kg/day). The extracts were given to the various animal groups orally once a day.

Wound healing activity:

Dead Space wound model: Rathi et al. described a technique for creating dead space wounds.[11] 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.

For 8 days, the treatment groups were given extract or normal saline (1 ml/kg). Rats were euthanized on day 10 and 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 maintained at 110 ^{0}C for 24 hours. The hydroxyproline, hexosamine concentration, and hexuronic acid were determined using the neutralised acid hydrolyzate of the dry tissue. For the measurement of lysyl oxidase and tissue protein, a piece of the moist granulation tissue was utilised.[12]

Induction of diabetes: The overnight starved 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.e.) 15 minutes after receiving 110 mg/kg body weight nicotinamide (HiMedia labs Pvt. Ltd.). After 6 hours of STZ treatment, the rats were given a 10% glucose solution for additional 24 hours to prevent hypoglycemia caused by large pancreatic insulin secretion. Blood was collected from the tail veins of the rats 72 hours after the STZ injection, and rats with a fasting blood glucose level of more than 200 mg/dl were deemed diabetic and used in this investigation.[13]

Statistical analysis: The information is presented as a mean with a Standard Error Mean (SEM) (SEM). The differences between means were investigated using one way analysis of variance (ANOVA), with p values less than 0.05 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. P values less than 0.05 were deemed statistically significant.

RESULTS

The animals given the *B.lanzan* extract showed a substantial increase in wound-healing activity when compared to those given the placebo control treatments. The effects of the ethanolic extract of *B.lanzan* flower given orally at a dosage of 100 mg kg/day for 8 days on wound healing activity in rats with dead space wounds are shown in Table 1. When compared to diabetic and control rats, the *B.lanzan* therapy group had substantially higher granulation tissue breaking strength and wet and dry granulation tissue weight (table-1).

Table-1: 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	82.1 ± 6.2	242.5 ± 14.19	32.58 ± 5.90	288.39±15.37
Diabetic Control	274.18 ± 15.1[a]	164.5 ± 11.32[a]	23.5 ± 4.40[a]	176.41±1.30a
B.lanzan	264.37 ± 15.1[a]	281.5 ± 14.09[a]	37.5 ± 4.40[a]	317.49±15.37a

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

In streptozotocin-induced diabetic rats, the concentration of hydroxyproline in granulation tissue was dramatically reduced. The experimental group's glycosaminoglycan contents, such as hexuronic acid and hexosamine concentration, were considerably lower. When diabetic rats were compared to control rats, tissue protein content was quite low. The level of lysyl oxidase in the experimental group was considerably lower. When compared to diabetic and control rats (group II), all of the following metrics increased considerably in the *B.lanzan* 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	15.12 ± 4.12	11.59 ± 2.47	12.51 ± 3.89	42.58 ± 3.60	1713 ± 66
Diabetic Induced	11.18 ± 2.00[a]	8.1 ± 1.30[a]	9. ± 1.72[a]	26.5 ± 2.60[a]	1122 ± 46[a]
B.lanzan	14.62 ± 4.12[a]	13.59 ±2.47[a]	13.12 ±3.39[a]	43.58 ± 3.60[a]	1914 ± 62[a]

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

DISCUSSION

Granulation, collagen maturation, and scar formation are only a few of the numerous wound-healing stages that occur simultaneously yet independently. Because the herb *B.lanzan* has been known to have substantial wound healing activities, 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.

Granulation tissue is made up of largely fibroblasts, collagen, oedema, and new tiny blood vessels and forms in the last stages of the proliferative phase. Higher protein content is suggested by the rise in dry granulation tissue weight in test treated animals. The hydroxyproline content of the granulation tissue increased significantly after treatment with an ethanol extract of *B.lanzan*, indicating increased collagen turnover. Collagen is made primarily of the amino acid hydroxyproline, which has been utilised as a biochemical marker for tissue collagen. It is the main component that builds and maintains extracellular tissue.[14]

B. lanzan is an evergreen tree that grows in India's dry deciduous tropical woods and is used to cure cough, constipation, skin conditions, and stomach problems.[15] In the incision wound model, topical administration of *B.lanzan* methanol root extract (10% (w/w) ointment improved tensile strength substantially. In an excision wound model[16], *B.lanzan* demonstrated substantial wound healing activity. In comparison to the control in excision, incision, and dead space wound models, Chitra et al.[17] found that the methanol fruit extract of *B. lanzan* did not substantially enhance wound healing.

In the *B.lanzan* therapy group, the levels of hydroxyl proline, hexuronic acid, and hexosamine all increased. Enhanced lysyl oxidase activity in our study might result in increased granulation tissue cross linking and breaking strength. The wound healing ability of *B.lanzan* might be

ascribed to the phyto-constituents found in the plant, and the faster wound healing process could be due to the individual or cumulative actions of the phyto-constituents. We intend to do more research into the component phytochemical elements that contribute to *B.lanzan*'s pharmacological action in diabetic rats.

Conclusion: The current study found that an ethanol extract of *B. lanzan* flower possesses characteristics that allow it to promote faster wound healing in diabetic rats when compared to placebo controls. Increased hydroxyproline, hexosamines, hexuronic acid, tissue protein, and lysyl oxidase encourage further research into *B. lanzan's* use as a topical wound therapy.

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