DOI: https://doi.org/10.52756/ijerr.2023.v32.032 *Int. J. Exp. Res. Rev.*, Vol. 32: 365-377 (2023)

Original Article | *Peer Reviewed* | *Open Access*

International Journal of Experimental Research and Review (IJERR)

ISSN: 2455-4855 (Online)
www.iaph.in
ISSN 2455-4855

Preclinical evaluation of the diabetic wound healing activity of phytoconstituents extracted from *Ficus racemosa* Linn. leaves

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Article History:

Received: 4th Jul., 2023
Accepted: 22nd Aug., 2023
Published: 30th Aug., 2023

Keywords:
Diabetes, Wound healing, Flavonoid, Wound

Abstract: Human body has several multi-layered organs, but skin is one of biggest and easiest to access. It serves as body's primary line of defense alongside various skin diseased conditions. Despite receiving sufficient and appropriate care, diabetes wounds heal slowly and may take a week to complete. A progression of connective tissue patch up is the body's natural defense against tissue damage. Fresh leaves of Ficus racemosa were utilized for the study. In this study, two distinct models were employed to compare how well different Ficus racemosa leaf extracts healed wounds. Excision wounds healed more quickly and to a greater extent after being treated with a flavonoid and tannin fraction of Ficus racemosa leaf extract, suggesting improved epithelization. The extract-treated groups also experienced an increase in breaking potency of incision wounds made; higher breaking strength indicates better wound healing. Complete closure of wound of flavonoid fraction and in fraction of Ficus racemosa extract occurred in 16 and 17 days respectively. Standard treatment increased tensile strength in the diabetic linear incision wound model, followed by treatment with the flavonoid fraction and tannin fraction of Ficus racemosa leaves extract. Ultimate finding and outcome of the present study experimentally demonstrates that extracts of the flavonoid and tannin fractions of Ficus racemosa have wound-healing properties and are effective in treating diabetic wounds. From this study, we state that Ficus racemosa flavonoid fraction and tannin fraction extract has a beneficial effect on blood glucose levels, which shows hypoglycaemic activity.

Introduction

The skin is an extensive organ composed of anatomically- epidermis, dermis and sub-cutaneous fat tissues. Human beings are constantly subjected to injuries that may result in cell death and tissue destruction. Thus, wounds are an inescapable event in the life of organisms and at times they are dangerous even life-threatening. Healing of wounds is a fundamental reaction to tissue damage that marks restitution of tissue integrity that occurs in different phases: Coagulation, contraction, epithelialization, granulation, collagenation, and tissue remodeling. Evidence suggests that the plant extract has

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medicinal promise as a wound-healing agent. Many plants are utilized to speed up the curative process of wounds in traditional medicine (Burgess et al., 2021). Healing is a physiochemical process that starts when a wound is hurt and usually ends when a scar forms (Albahri et al., 2023). Even with proper treatment, diabetic wounds often fail to heal completely. These are extremely difficult wounds to heal. Wounds often fail to heal properly in people with diabetes mellitus. Diabetic patients with ulcers are at increased risk for complications like infection and amputation. Most of these patients have severe complications after acquiring an infected wound. This review therefore examined a catalogue of plants traditionally employed in the treatment of wounds and diabetes. The text features a catalogue of plants, many of which have been experimentally shown to treat diseases and wounds while others have not (Sharma et al., 2013).

The use of medicinal flora for the management of different skin and dermatological disorders, including but not limited to cuts, wounds, and burns, dates back to the dawn of medicine. When there is a break in the cellular & anatomic continuity of live tissue, which is what we mean by "wound," the healing process begins and progresses through three overlapping phases: cellular proliferation, remodeling of the extracellular matrix, and remodeling of the extracellular matrix. Inflammation is a phase of 0-3 days, which involve the migration of neutrophil around incision.

From the literature survey, it was found that the leaves of Ficus racemosa Linn. (Moracease) an evergreen in Ayurveda; the entire plant is used for its therapeutic properties. Jaundice, diarrhoea, hyperglycaemia, dysentery, and inflammatory conditions have all benefited from its use (Pahari et al., 2022; Chopra, 2024). To treat bilious infection, try using a powdered honey and leaf mixture (Moses et al., 2023). In cases of dysmenorrhea, a douche containing a decoction is recommended for treating ulcers (Khaire et al., 2023). To keep hair from breaking, rub it with leaf juice. Boils, blisters, and the measles can all be treated using leaf latex, Ficus racemosa leaves contained Tetra triterpene, From the leaves, we were able to separate glauanolacetate and racemosic acid. Latex of the plant was used to extract a novel thermostable aspartic protease.

Ficus racemosa show Hypoglycaemic activity, Antioxidant, Hepatoprotective, Chemoproventive, Anti-inflammatory, Analgesic, Antibacterial, Gastroprotective, Antidiarrheal, Antifilarial, Larvicidal, Antipyrectic, Antitussive, Hypertensive activity (Pahari et al., 2022). Researchers found that an ointment made from its leaf powder and petroleum jelly (15 percent w/w) significantly increased the production of tissue DNA (1.76 mg/g), RNA (1.73 mg/g), and total protein (16.62 mg/g) in a rat model of an 8 mm full-thickness punch wound compared with untreated control rats (Chauhan et al., 2023). Therefore, the most important goal of understanding this study is to evaluate diabetic wound healing action of phytoconstituents extracted from *Ficus racemosa* Linn. leaves using animal models.

Methods

Plant and animals

Ficus racemosa leaves were freshly picked at the village of Sugaon, Maharashtra, India. Upon verification by scientist J. Jayanthi, the sample was sent to the Western Regional Centre of the Botanical Survey of India in Maharashtra, India, where a voucher specimen (SANFIR-1) was also deposited.

Both male and female Wistar albino (*Rattua norvegicus*) rats were procured from India's National Institute of Bioscience, Pune with weight ranging from 180g to 200g. The animals were housed in a controlled environment with a regular light/dark cycle, temperature, and humidity: 25ºC±3°C, 35-60%, 12 hours on and 12 hours off, respectively. Water and a standard pellet meal were provided. The Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) in India created guidelines with methodologies for animal experimentation, with approval from the Institutional Animal Ethics Committee (IAEC).

Drugs and chemicals

Alloxan monohydrate and chloramine T were purchased from LOBA Chemie PVT. LTD, Colaba, Mumbai 400005. INDIA for induction of diabetes. Ketamine was purchased from Aneket®, NEON Laboratories Ltd, Andheri East, Mumbai-400093. INDIA. and Povidon-Iodine from Cipladine, Cipla Ltd, Mumbai-400070, INDIA.

Extraction

In the shelter, the leaves were allowed to dry in the air before being pulverized into a powder. By a procedure known maceration, solvents were added to the powdered leaves to get the oil out of them. The extract was then put through a filter and the filtrate was evaporated to get a residue. Photochemical analysis was done on the *Ficus racemosa* extract that was gotten this way.

Phytochemical screening

Various phytochemical screening studies with different parts of plants extracts were done to find out if there were alkaloids, glycosides, tannins, flavonoids, carbohydrates, steroids, or saponins in the plant

DOI: https://doi.org/10.52756/ijerr.2023.v32.032

(Ghesmati et al., 2018; Khandelwal, 2006; Maalej et al., 2023)

Selection treatment group & doses

Group A –Normal control

Group B – Received alloxan monohydrate and vehicle (Diabetic control).

Group C – Glibenclamide (10 mg/kg orally) + Alloxan monohydrate as standard

Group D– Flavonoid fraction extract (400 mg/kg orally) + Alloxan monohydrate

Group E - Tannin fraction extract (400 mg/kg orally) + Alloxan monohydrate

Using a simple ointment IP as a base, the extract was made into an ointment for testing its wound healing efficacy in an excision and incision wound model. Two different formulations, one with a flavonoid fraction of 10% w/w (10g of extract in 100g of simple an ointment) and one with a tannin fraction of 10% w/w (10g of extract in 100g of simple ointment), were chosen for the investigation. Various animal groups were treated with a topical ointment containing 5% mg administered once daily.

Induction of diabetes

Prior to actually making the animals diabetic, they were weighed as well and their own fasting blood glucose levels were measured. Animals with glucose levels that were too low or too high were given new ones. One dose of Alloxan monohydrate was given to each animal (120 mg/kg, Sigma) in freshly made normal saline through their i.p. Normal saline was injected into the animals used as controls. After 3 days, the animals' fasting blood glucose levels were checked to make sure they were diabetic. To measure blood sugar, blood was taken from the tail vein (Criollo-Mendoza et al., 2023; Bhati et al., 2011; Zuber et al., 2013; Xiang et al., 2023).

Wound model (Circular excision)

The rats were split up into four groups of six. A dose of 100mg/kg i.p. ketamine was used to put each rat to sleep. The rat's back hair was successfully removed using depilation. Using 70% ethanol, we sterilized the cream and the newly shaven skin. Shaved rats had 20mm excision wounds produced on their backs; the test group was given 5% and 10% ointment, while the control group received Povidone iodine ointment. The untreated group served as the control. The size of the wound was measured on days 0, 3, 6, 9, 12, and 15 following surgeries. To get an accurate measurement, we laid a sheet of translucent tracing paper over the injury and sketched its perimeter using a fine-tipped marker. One mm2 graphed sheet was used to trace over the transferred tracing paper. For this study, we counted and recorded the total number of squares on the graphed sheet representing the healed area. At the end of each time period, the percentage of wound contraction was calculated (Pirbalouti et al., 2010).

Linear incision wound model

To calculate the tissue's tensile strength, this model was employed. Animals were separated into five groups. Rats had their back hairs removed with a depilatory lotion. Rats' shaved backs were cleaned with 70% ethanol. A sterile surgical blade (scalpel) was used to cut a 5 cm long paravertebral incision through the entire thickness of the skin. One-cm-apart interrupted sutures were used to seal the wound. Treatments for the test group included 5% and 10% ointments, respectively. The stranded group was given 5% povidone iodine ointment treatment. All sutures were removed on the ninth day following surgery, and the tensile strength of the tissue was assessed using the continuous water flow technique. The control group received no treatment, whereas the vehicle group received treatment with a sample ointment intravenously. (Gupta et al., 2008).

Evaluation parameters

Tensile strength

The force needed to open the repaired skin is referred to as the tensile strength of the skin. It reveals how much the restored tissue can withstand stress before breaking, and it may also reveal something about the quality of mended tissue. In order to assess the tensile strength, the recently healed tissue, including the scar, was removed. Constant water flow technique was utilised for the quantification of tensile strength.

Continuous water flow technique

A 6 × 12-inch board with a 4-inch post placed on each side of the longer ends served as the basic framework for the measurement of skin wound healing. The board was put on a table's end. On top of one of the poles was installed a pulley (with bearing). A piece of fishing line (20-tb. test monofilament) was linked to the tip of the post without a pulley to secure an alligator clamp with a clamp diameter of 1 cm so that it could extend to the middle of the board. A 1-L plastic bottle was fastened to one end of a longer fishing line with another alligator clamp attached. The animal was given ethyl ether under an open mask anaesthesia prior to testing. Scissors were used to remove the sutures from the incision. The pet was then placed in the centre of the board on a mound of paper towels. Towels could be added or subtracted to raise or lower the wound to the same plane as the poles. After that, the clamps were placed carefully on the skin on the sides of the wound, three centimeters apart. The polyethylene bottle was suspended in midair by adjusting

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the position of the board and placing longer piece of fishing line on the pulley. From the time the incision started to open, water was syphoned into the polyethylene bottle at a rapid yet steady pace from a huge reservoir (20-L bottle). The tensile strength of the injury was determined by measuring how much water was in the polyethylene bottle. Each injury was evaluated by two or three doctors. The tensile strength of the wound was calculated by averaging the results from both sides of the animal. All of the tensile strengths in this research were determined seven days following injury (Hu et al., 2023; Suresh and Karki, 2012).

Hydroxyproline estimation

On day 16, the wound was cut and dried in a hot air oven at 60-70° C until the weight was constant. Tissues were packed in tubes and heated to 130 degrees Celsius for four hours in 5N HCL. The skin hydrolysate was adjusted to a pH of 7.0. After soaking for 20 minutes, the solution undergoes chloramine T oxidation. After adding 0.4 M perchloric acid to stop the reaction, the Ehrlich reagent was used to develop the colour at 60°C, and absorbance was measured at 557 mm using a spectrophotometer. (Pandian et al., 2013).

Histopathology

After 16 days, the bandage was removed and the wound was dried in a hot air oven at 60-70 degrees Celsius until the weight was constant. Tissues were sealed in tubes and hydrolyzed in 5N HCL at 130°C for 4 hours. The skin hydrolysate was adjusted to a pH of 7.0. After soaking for 20 minutes, the solution undergoes chloramine T oxidation. Perchloric acid (0.4 M) was used to stop the reaction, Ehrlich reagent (60°C) was used to develop the colour, and a spectrophotometer recorded an absorbance of 557 mm. (Biswas and Mukherjee, 2003).

Hypoglycaemic activity

Anti- diabetic activity

Blood glucose levels were measured after subjects fasted for 16 hours despite having unrestricted access to water. An intravenous injection of 120 mg/kg of alloxan monohydrate (s.d. fine-chem. Ltd., Mumbai, India) in sterile saline was used to induce hyperglycemia. Three days after receiving alloxan injections, rats with high blood sugar (glucose level > 200 mg/dl) were separated and placed into groups of six for an anti-diabetic investigation. Except for the normal control and diabetic control groups, all medication was administered orally beginning on day 1. During this time period, all species enjoyed unrestricted access to a balanced diet and clean water. After 7 days of treatment, measurements of body fat and glucose levels were taken. (Pandian et al., 2013).

The ethics

This research has been approved by the IAEC of Progressive Education Societies Modern College of pharmacy (Approval Number: MCP/IAEC/64/2012).

Statistical analysis

ANOVA is used to look at data from both models. The data are reported as mean ±SEM for each treatment group and compared to a control group; significance, defined as a value of $p < 00.01$, is assumed.

Results

Extraction of plant drug

The powdered were extracted with solvent by the maceration process. The extract was then filtered and the filtrate was evaporated to obtain residue.

The maceration involved significant a semisolid residue that was a dark greenish-black colour.

Phytochemical screening

Determination of total flavonoids

With a few tweaks, we were able to calculate the total flavonoids. The extract was diluted with 1.25 mL of distilled water, bringing the total volume to about 250 µL. Finally, 75 µl. of a 5% NaNO; solution was added to the pot. After waiting 6 minutes, we added 150 µL of a 10% AICT H0 solution and let the mixture stand for 5 minutes. Then we added 0.5 ml of 1 mol/L NaOH and brought the volume up to 25 ml with purified water. After a thorough mixing, the solution's absorbance was measured against a produced blank and quercetin at 510 nm. Quercetin equivalent milligrammes per gramme of extract were used to express the findings. The concentration of flavonoids in the *Ficus racemosa* Linn. leaves extract is 65.76±0.29 (mg of quercetin equivalent /g extract)

Determination of total tannins contents

The proportion of total weight that is tannins in Ficus racemosa leaves was determined (WHO, 1998). The dried powdered leaves were weighed (W) to ensure precision, then transferred to a 250 ml conical flask, where they were diluted with ethanol to make up the volume. The first 50 ml of the filtrate was discarded after the solids had settled and the liquid had been filtered using a piece of filter paper with a diameter of 12 cm.

The amount (T) of plant material extractable into ethanol was calculated by drying the remaining liquid in an oven set at 105 degrees Celsius for four hours. The percentage of plant material that can be extracted into ethanol without binding to the hide powder was measured by shaking together 80 ml of plant material extract and 6 gm of hide powder for 60 minutes, then evaporating the clear filtrate to dryness.

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Table 1. Phytochemical screening showed presences (+) and absences (-) of following constituents

Constituents	Test	Extract
Alkaloid	Dragendorff	+
	Mayer's	+
	Wagner	-
Flavonoids	Shinoda	+
	Lead acetate	+
	Sodium hydroxide	+
Tannins	Lead acetate	+
	5%$FeCl_3$ solution	+
	Dilute iodine solution	+
	Dilute potassium permanganate	+
Glycosides	Legal	+
	Keller killiani	+
Saponins	Foam	-
Steroids	Liebermann-Burchard reaction	-

To assess the solubility of hide powder, 6 g of hide powder was combined with 80 ml of ethanol and the resulting mixture was weighed (T) after drying in an oven at 105 °C for 4 hours. For an hour, the mixer was thoroughly shackled. We weighed (Ta) tannins in the extract after filtering and evaporating 50 ml of clear filtrate to dryness, then drying the residue in an oven at 105°C for 4 hours- [Ta-(T-To)]/ W 500.

The tannin contents were found to be 6 % w/w in the leaves.

Circular excision wound model

Progression in wound narrowing with healing by Ficus racemosa leaves extract (flavonoid fraction and tannin fraction ointment), the standard drug Povidone iodine ointment and untreated control groups of animals are revealed in Table 2. Observed wound contracting capacity of flavonoid fraction and tannin fraction ointment were considerably ($P<0.01$) superior than that of the control. Both flavonoid and tannin fraction extract ointment and standard treated group show significant wound healing activity by the 9th day on ward. Complete epithelisation period of all groups is shown in table 3. Standard treated group show complete wound closure (100%) in 16 days. Flavonoid and tannin fraction ointment treated group show complete wound closure in 17 and 18 days correspondingly while control group show total wound closure in 22 days.

Histopathology

Excision wound models treated with conventional medicine povidone iodine ointment, extract ointment (flavonoid fraction and tannin fraction), and control groups were subjected to histological analysis of regenerated tissue. The results are depicted in figures 1-7. Histological analysis showed that both the control and extract-treated rats exhibited extremely good tissue regeneration, including epidermal regeneration, fibroblast proliferation, increased collagen deposition, and hair follicle regeneration. In contrast, the rats in the control group displayed much-reduced epidermis and fibro collagenous stroma regrowth.

Linear incision wound model

Table 4 displays the tensile strength of an incision wound before and after treatment with extract ointment and regular ointment. Significant ($P<0.01$) increases in tensile strength relative to controls were seen across all treatment groups. Tensile strength is greatest in the control and flavonoid fraction ointment-treated groups, whereas the tannin fraction ointment-treated group shows a smaller but still substantial increase. Table 5 displays, however, the impact of extract on tensile strength in a model of a linear incision wound in a diabetic patient.

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Table 2. Effects of leaves extract on circular excision wound model

Days	Area of wound (mm^2) ± SEM		(% Contraction)	
	Control	Standard (Povidone iodine ointment)	Test I (Flavone in fraction ointment)	Test II (Tannin fraction ointment)
0	62.8	62.8	62.8	62.8
3	60.47±0.68	51.66 ± 1.78*	52.19 ± 1.96*	58.04 ± 1.31*
	(3.90)	(17.75)	(16.91)	(7.61)
6	47.24± 3.75	33.55 ± 2.53	34.74 ± 2.84	38.7 ± 2.41
	(24.80)	(46.60)	(44.71)	(35.90)
9	37.57± 4.99	21.55 ± 2.17*	24.47 ± 3.0*	28.22± 1.44*
	(40.20)	(65.70)	(60.70)	(55.11)
12	29.43± 4.16	10.96 ± 1.45*	15.63 ± 2.47*	15.99 ± 2.29*
	(53.15)	(82.56)	(75.11)	(74.55)
15	18.09± 3.39	1.9± 0.38*	7.24 ± 1.19*	11.02 ± 8.29*
	(71.21)	(97.91)	(90.41)	(86.81)

Values are mean ± SEM (% contraction of wound), n =6 in each group. SEM: Standard error of mean. *p<0.01 when compared to control.

Table 3. Complete epithelization period of circular excision wound model

Groups	Complete epithelizationperiod (days)
Control	22 ± 0 .50
Standard (Povidoneiodine)	16 ± 0.21*
Test I (Flavonoid fraction ointment)	17 ± 0.41*
Test II (Tannin fraction ointment)	18 ± 0.49*

Values are mean ± SEM (No. of days), n = 6 In each group. SEM: Standard error of mean. * p<0.01when compared to control

Hypoglycemic activity

Ficus racemosa leaf extract was investigated for its anti-diabetic effects using alloxan monohydrate in rats (120 mg/kg, i.p.).

Diabetic rats' fasting blood glucose levels were much higher than those of normal rats'. Flavonoid and fraction of tannin of Ficus racemosa extract show a dose-dependent momentous anti-hyperglycemicaction in 7-day treatment. The antihyperglycemic effect of flavonoid fraction and tannin fraction effectiveness of Ficus racemosa extract was found to be lower than that of the gold standard, Glibenclamide. When compared to diabetic control, glibenclamide resulted in a marked decrease in blood glucose. Table 6 displays the obtained data.

The body weights of the normal controls remained consistent, but those of the diabetes controls dropped dramatically over the course of a week. In a dose-dependent manner, Ficus racemosa extract prevented the weight loss induced by alloxan. The test extract also had a substantial impact on the animals' body weight. Table 7 displays the results.

DOI: https://doi.org/10.52756/ijerr.2023.v32.032

Table 4. Effects of leaves extract on linear incision wound model

Groups	Tensile strength (gms)
Control	296.21 ± 14.43
Standard (Povidone iodine)	644.61 ± 16.18*
Test I (Flavonoid fraction ointment)	621.25 ± 9.26*
Test II (Tannin fraction ointment)	606.9 ± 6.76*
Values are mean ± SEM (n=6), tensile strength, tensile strengths are expressed in grams. *p<0.01 when compared to control.	

Table 5. Effects of leaves extract on diabetic linear incision wound model

Groups	Tensile strength (gms)
Control	298.65 ± 5.61
Standard (Povidone iodine)	645.3 ± 7.66*
Test I (Flavonoid fraction ointment)	606.7 ± 6.19*
Test II (Tannin fraction ointment)	519 ± 6.06*
Values are mean ± SEM (n=6), tensile strengths are expressed in grams. *p<0.01 when compared to control.	

Table 6. Effect of Leaves Extract on Blood Glucose Level in Diabetic Rats

Days	Blood glucose level				
	Normal control	Diabetic control	Standard	Test-I	Test–II
1	91 ± 1	410.6 ± 33.73	445.6 ± 48.78	412.8 ± 22.61	391.2 ± 45.8
2	89.6 ± 0.67	410.6 ± 36.22	390.4 ± 36.43	401 ± 17.84	380.2 ± 38.23
3	87.6 ± 0.83	420 ± 22.62	389.4 ± 53.43	399.2 ± 16.88	379 ± 40.25
4	85 ± 0.63	408.6 ± 31.72	371 ± 50.13*	381.4 ± 32.26*	350.8 ± 39.7*
5	83 ± 0.31	435 ± 21.69	345.2 ± 42.74*	367.2 ± 25.19*	362 ± 53.07*
6	88 ± 1.3	400 ± 20.37	341 ± 48.94*	357.6 ± 25.29*	350.4 ± 46.67*
7	89 ± 0.37	440 ± 19.34	333 ± 47.37*	336.4 ± 22.64*	339 ± 45.43*
n=6; values are mean ±SEM; * p<0.01 when compared to control.					

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Table 7. Effect of Leaves Extract on Body Weight in Diabetic Rats

Days	Body weight (gms)				
	Normal control	Diabetic control	Standard	Test– I	Test–II
1	204.6 ± 1.07	203.4 ± 0.5	205.8 ± 0.86	204 ± 0.7	203 ± 0.7
2	205 ± 1.22	177 ± 2.09	202.3 ± 0.37	198.4 ± 1.03	171.2 ± 3.68
3	206 ± 1.18	167.2 ± 3	188.8 ± 2.03	188.8 ± 2.51	163.6 ± 1.86
4	206.6 ± 1.6	154 ± 2.09	182.4 ± 4.27*	181.4 ±2.97*	152.8 ±0.86*
5	209.2 ± 1.15	142.4 ± 1.5	177.6 ± 4.38*	176.8 ±1.98*	147.4 ±2.18*
6	207.8 ± 1.28	136.4 ± 2.11	179.6 ± 2.04*	168.4 ±1.43*	133.6 ±2.73*
7	209.2 ± 1.06	128.4 ± 2.54	175.2 ± 2.35*	164.8 ±1.77*	122 ± 2.55*
n=six; values are mean ±SEM; * p<0.01 when compared to control.					

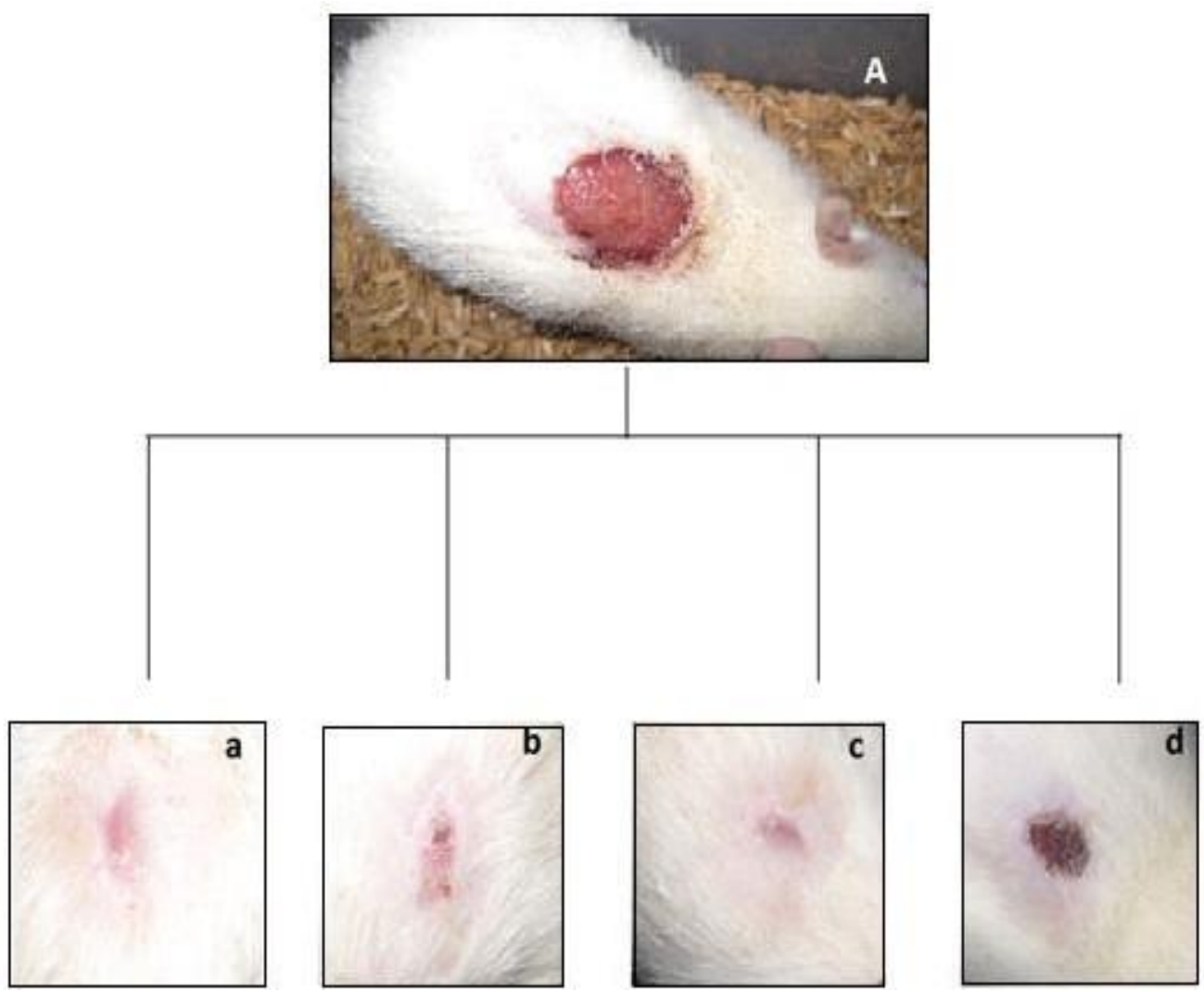

Figure 1. Excision wound model A: Excision wound at day1; a: Excision wound of standard treated rat at day 15, b: Excision wound of test I (tannin fraction ointment) treated rat at day 15; c: Excision wound of test II (flavonoid fraction ointment) treated rat at

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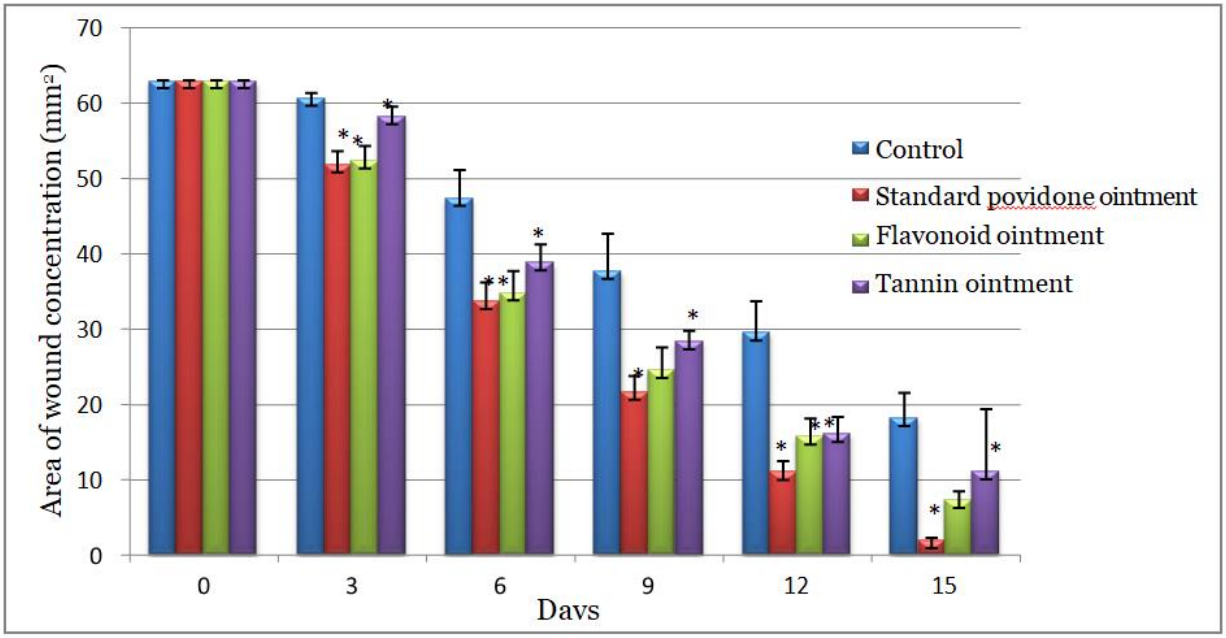

Figure 2. Decrease in area of wound contraction of circular excision wound model

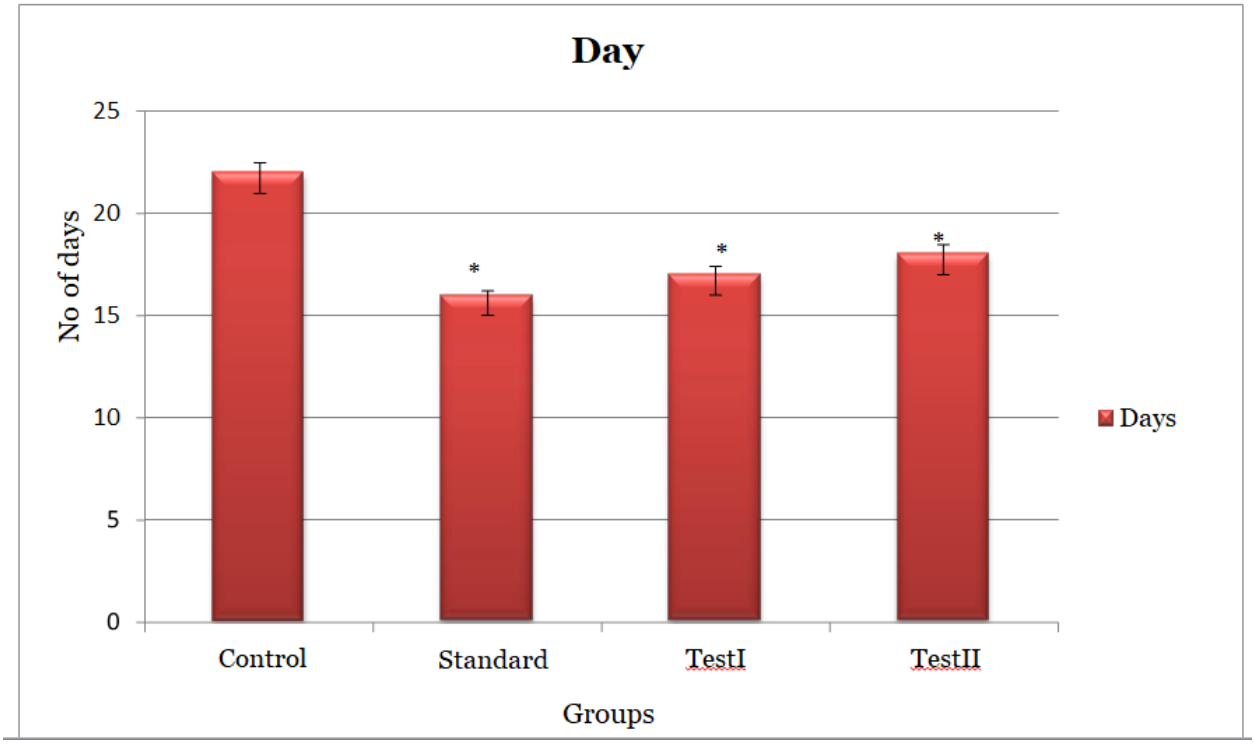

Figure 3. Complete epithelization period of circular excision wound model

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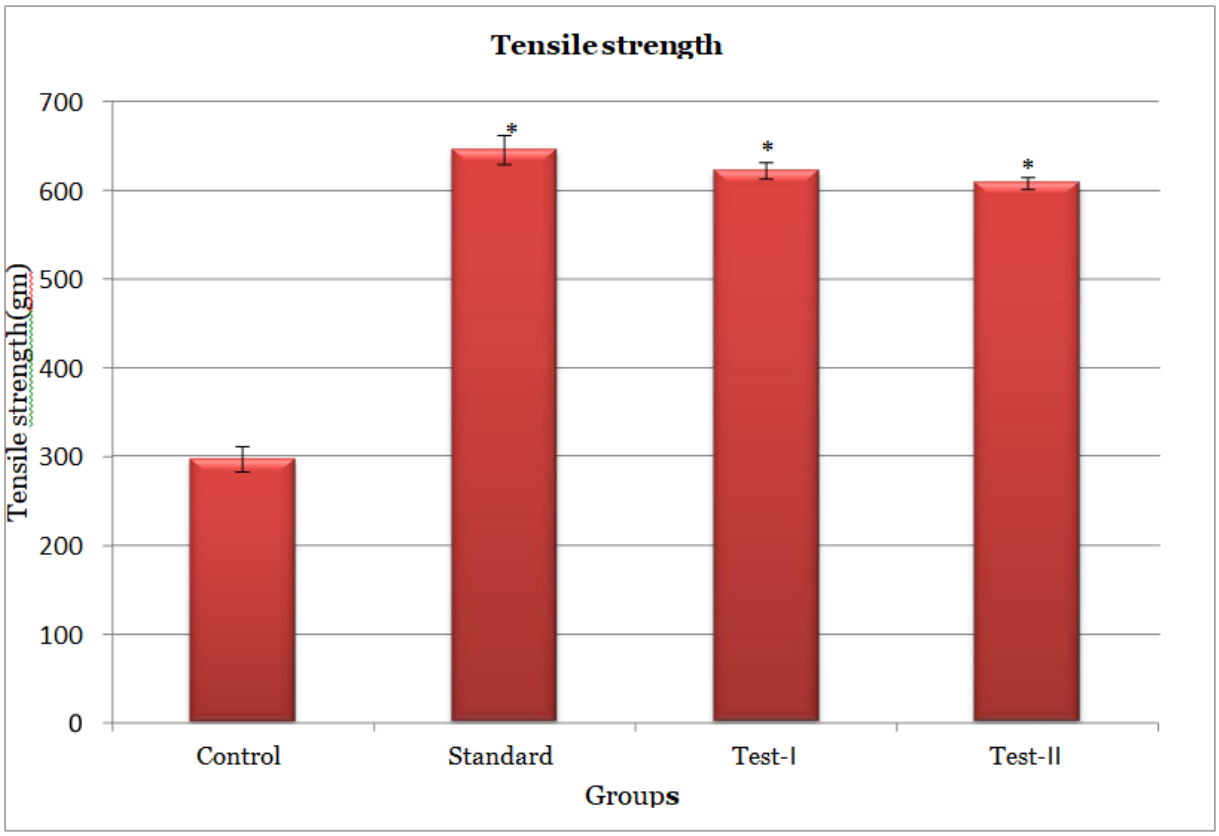

Figure 4. Effect of extracts on tensile strength of linear incision wound

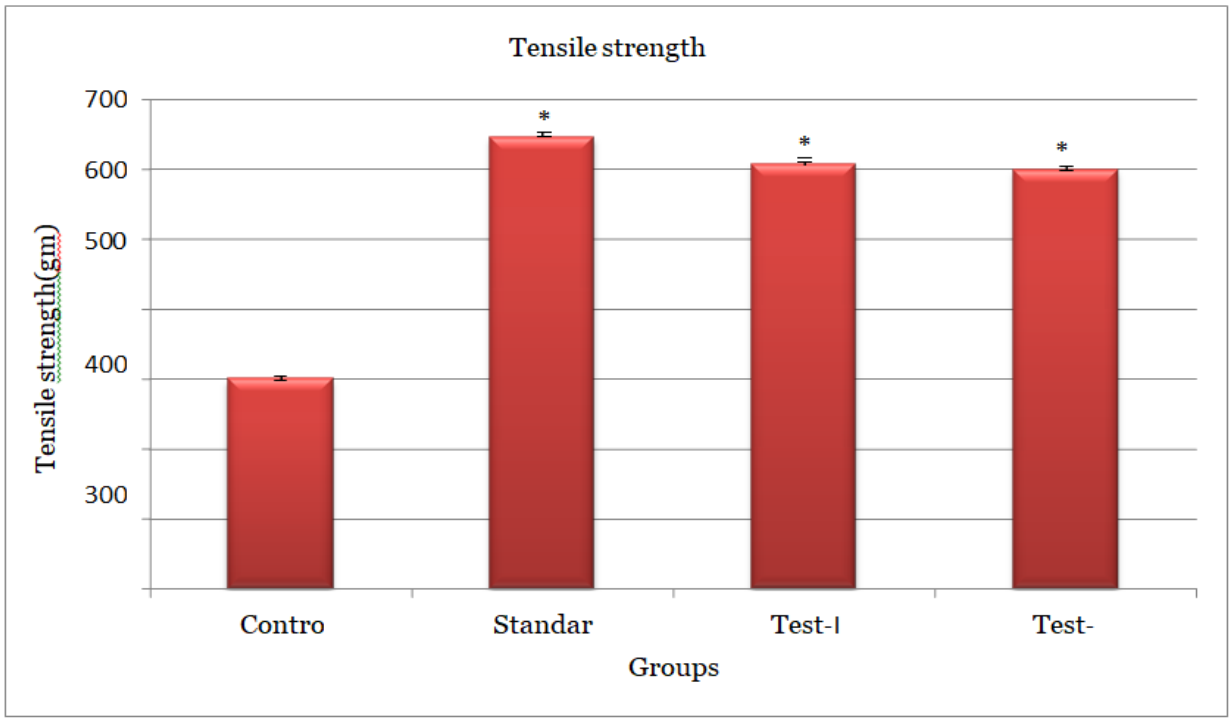

Figure 5. Tensile strength of diabetic linear incision wound model

DOI: https://doi.org/10.52756/ijerr.2023.v32.032

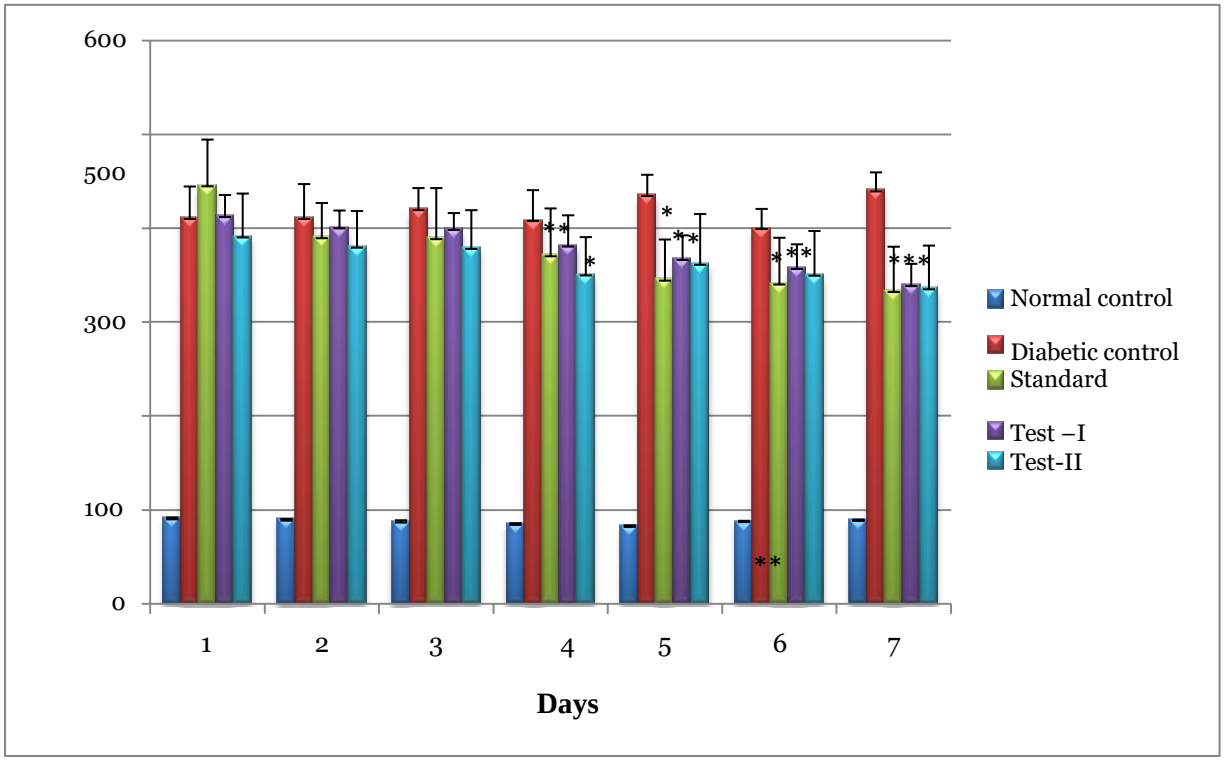

Figure 6. Effect of leaves extract on blood sugar level in diabetic rats based on Diabetic Linear Incision Wound Model

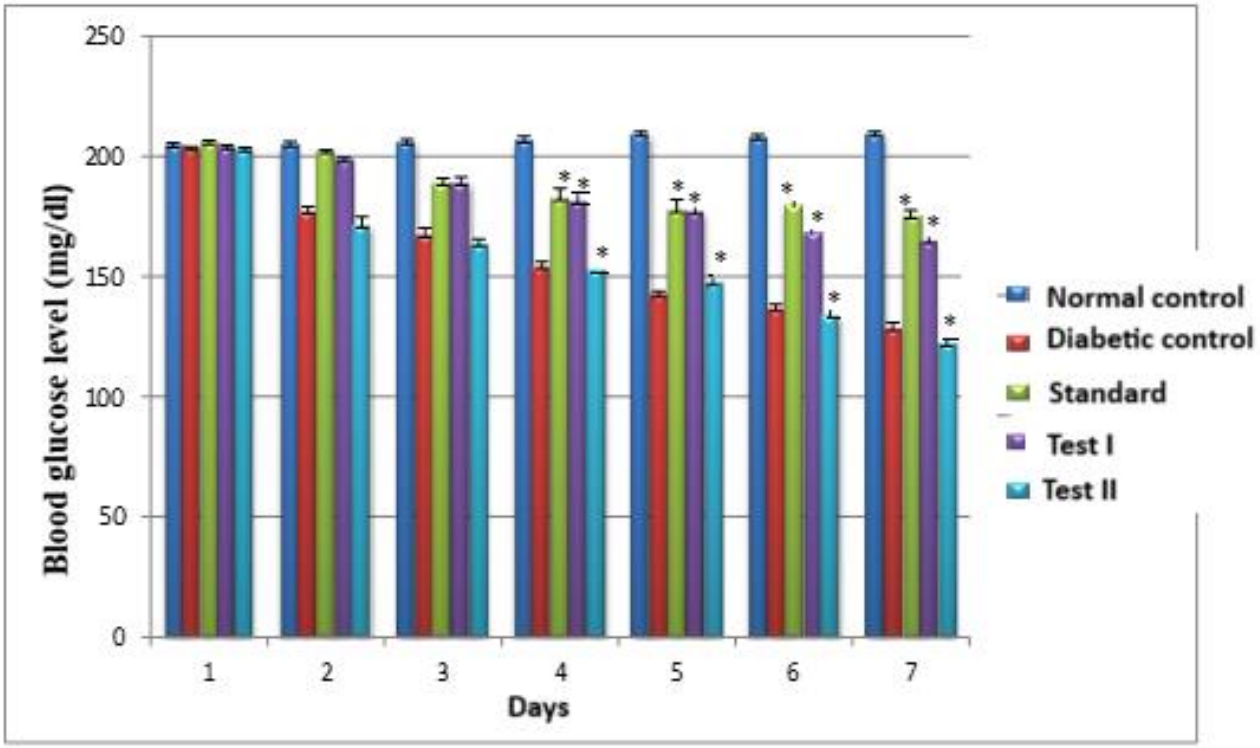

Figure 7. Effect of leaves extract on body weight in diabetic rats

DOI: https://doi.org/10.52756/ijerr.2023.v32.032

Conclusion

The preclinical assessment of phytoconstituents derived from the leaves of Ficus racemosa Linn. has established a robust basis for further investigation into the potential of these compounds in the context of healing diabetic wounds. The results of this study offer potential for the advancement of innovative treatments that have the potential to greatly enhance the well-being of those affected by diabetes and facing challenges related to persistent wounds. Nevertheless, further research is required in order to completely comprehend the therapeutic capabilities of these phytoconstituents within clinical environments. The current study's final observation and results provide experimental proof that the flavonoid fraction and tannin fraction extract of Ficus racemosa have wound healing activity and is useful in treating diabetic wounds. Hypoglycaemic activity was seen in the Ficus racemosa flavonoid fraction and tannin fraction, as determined by the results of this investigation.

Nevertheless, it is imperative to recognize that the research is now in the preclinical phase, and more inquiries, such as clinical studies, are imperative to substantiate the safety and effectiveness of these phytoconstituents in human subjects. In addition, it is important to comprehend the exact mechanisms of action and ascertain any adverse effects or interactions with other drugs, as these are pivotal stages in the progression of this study into clinical implementation.

Conflicts of interest

It has been confirmed by the authors that there are no competing interests associated with this work.

References

Albahri, G., Badran, A., Hijazi, A., Daou, A., Baydoun, E., Nasser, M., & Merah, O. (2023). The therapeutic wound healing bioactivities of various medicinal plants. *Life*, *13*(2), 317. https://doi.org/10.3390/life13020317

Bhati, R., Singh, A., Saharan, V. A., Ram, V., & Bhandari, A. (2011). Pharmacognostical standardization, extraction and anti-diabetic activity of Smilax china L. rhizome. *Asian J. Tradit. Med.*, *6*(5), 218-223.

Biswas, T. K., & Mukherjee, B. (2003). Plant medicines of Indian origin for wound healing activity: a review. *The International Journal of Lower Extremity Wounds*, *2*(1), 25-39.

Burgess, J. L., Wyant, W. A., Abdo Abujamra, B., Kirsner, R. S., & Jozic, I. (2021). Diabetic wound-healing science. *Medicina*, *57*(10), 1072. https://doi.org/10.3390/medicina57101072

Chopra, D. (2014). Anaphylaxis: case report. Reactions, *1503*, 38-31.

Chauhan, S., Chalotra, R., Rathi, A., Saini, M., Deol, S., Lard, M., & Gupta, S. (2023). Current Approaches in Healing of Wounds in Diabetes and Diabetic Foot Ulcers. *Current Bioactive Compounds*, *19*(3), 104-121. https://doi.org/10.2174/1573407218666220823111344

Criollo-Mendoza, M. S., Contreras-Angulo, L. A., Leyva-López, N., Gutiérrez-Grijalva, E. P., Jiménez-Ortega, L. A., & Heredia, J. B. (2023). Wound healing properties of natural products: Mechanisms of action. *Molecules*, *28*(2), 598. https://doi.org/10.3390/molecules28020598

Ghesmati, F., Firoozi, M., & Varaeii, S. (2018). Studying the effect of Aloe vera ointment on wound healing of CABG surgery in diabetic patients. *J. Res. Med. Dent. Sci.*, *6*, 256-260. https://doi.org/10.24896/jrmds.20186141

Gupta, A., Upadhyay, N. K., Sawhney, R. C., & Kumar, R. (2008). A poly-herbal formulation accelerates normal and impaired diabetic wound healing. *Wound Repair and Regeneration*, *16*(6), 784-790. https://doi.org/10.1111/j.1524-475X.2008.00431.x

Hu, N., Cai, Z., Jiang, X., Wang, C., Tang, T., Xu, T., ... & Cui, W. (2023). Hypoxia-pretreated ADSC-derived exosome-embedded hydrogels promote angiogenesis and accelerate diabetic wound healing. *Acta Biomaterialia*, *157*, 175-186. https://doi.org/10.1016/j.actbio.2022.11.057

Khaire, M., Bigoniya, J., & Bigoniya, P. (2023). An Insight into the Potential Mechanism of Bioactive Phytocompounds in the Wound Management. *Pharmacognosy Reviews*, *17*(33), 43-68. https://doi.org/10.5530/097627870153

Khandelwal, K.R. (2006). Practical pharmacognosy: techniques and experiments. 10th edition, Nirali Prakashan, Pune, 149-150.

Maalej, H., Maalej, A., Bayach, A., Zykwinska, A., Colliec-Jouault, S., Sinquin, C., ... & Nasri, M. (2023). A novel pectic polysaccharide-based hydrogel derived from okra (Abelmoschus esculentus L. Moench) for chronic diabetic wound healing. *European Polymer Journal*, *183*, 111763. https://doi.org/10.1016/j.eurpolymj.2022.111763

Moses, R. L., Prescott, T. A., Mas-Claret, E., Steadman, R., Moseley, R., & Sloan, A. J. (2023). Evidence for natural products as alternative wound-healing therapies. *Biomolecules*, *13*(3), 444. https://doi.org/10.3390/biom13030444

Pahari, N., Majumdar, S., Karati, D., & Mazumder, R. (2022). Exploring the pharmacognostic properties and pharmacological activities of phytocompounds present in Ficus Racemosa Linn.: a concise review. *Pharmacological Research-Modern Chinese Medicine*, 100137.
https://doi.org/10.1016/j.prmcm.2022.100137

Pandian, C., Srinivasan, A., & Pelapolu, I. C. (2013). Evaluation of wound healing activity of hydroalcoholic extract of leaves of Stachytarpheta jamaicensis in streptozotocin induced diabetic rats. *Der Pharmacia Lettre*, *5*(2), 193-200.

Pirbalouti, A. G., Azizi, S., Koohpayeh, A., & Hamedi, B. (2010). Wound healing activity of Malva sylvestris and Punica granatum in alloxan-induced diabetic rats. *Acta Pol. Pharm.*, *67*(5), 511-516.

Sharma, Y., Jeyabalan, G., Singh, R., & Semwal, A. (2013). Current aspects of wound healing agents from medicinal plants: a review. *Journal of Medicinal Plants Studies*, *1*, 2320-3862.

Suresh Babu, A. R., & Karki, S. S. (2012). Wound healing activity of calotropis gigantea leaves in albino wistar rats. *International Journal of Pharmacy*, *2*(1), 195-199.

Xiang, Y., Qi, X., Cai, E., Zhang, C., Wang, J., Lan, Y., ... & Hu, R. (2023). Highly efficient bacteria-infected diabetic wound healing employing a melanin-reinforced biopolymer hydrogel. *Chemical Engineering Journal*, *460*, 141852. https://doi.org/10.1016/j.cej.2023.141852

Zuber, M., Rajesh, V., Anusha, K., Reddy, C. R., & Tirupathi, A. (2013). Wound healing activity of ethanolic extract of Allium sativum on alloxan induced diabetic rats family (Liliaceae). *International Journal of Science Inventions Today*, *2*(1), 40-57.

How to cite this Article:

Sadhana Pawar, Kajal Pawade, Sonali Nipate, Aishawarya Balap, Bhushan Pimple, Vijay Wagh, Ramanlal Kachave and Asmita Gaikwad. *International Journal of Experimental Research and Review*, *32*, 365-377.

DOI : https://doi.org/10.52756/ ijerr.2023.v32.032