RESEARCH ARTICLE

Wound Restoration Efficacy of the Extracts of *Lagenaria siceraria* and *Raphanus sativus*

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ABSTRACT

The process of healing a wound is intricate and dynamic, including several phases, including hemostasis, inflammation, proliferation, and remodeling. Natural extracts have gained attention in the management of healed wounds because of their bioactive compounds. These extraction derivatives from honey, turmeric, etcetera possess various properties like inflammation-reducing, antimicrobial and antioxidant potencies, which expedite the curing of wounds. The topical application of these natural remedies can enhance skin regeneration, reduce infection, and minimize scarring. Incorporating natural extracts into the treatment of wounds facilitates faster, safer alternatives to synthetic medications. This investigation reported the comparative ability of the extracts of *Lagenaria siceraria* leaves and *Raphanus sativus* seeds in the restoration of wounds.

Keywords: *Lagenaria siceraria*, *Raphanus sativus*, Restoration of wounds, Natural extracts.

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INTRODUCTION

A breach or damage to the skin's layers, especially the cell layers of the epithelium and breaking or loss of the cell parts, anatomic, or physiological continuity of live tissue[1] can be called a wound. Wound curing studies are mainly designed to identify numerous elements that influence the curing process, which might be used in clinical practice to help patients benefit more quickly.[2]

Wound care dates back to ancient civilizations, and most of these therapies relied heavily on herbal medicines.[3] There are several accounts in the scientific literature of medicinal plants changing many stages of wound curing, including clotting, epithelization, collagenation, swelling, wound contraction and fibroplasia.[4]

A wound is a sort of skin damage that can be ripped or punctured, closed wound caused by blunt-force trauma. Wound curing is an aspect of the body's homeostatic function, wherein the skin (or the other organ) heals after being injured.[5]

There are 2 sorts of wounds: closed wounds and open wounds. Wound curing comprises a complicated network of tissues, growth factors, cells (blood cells), and cytokines in case of either accidental damage or surgical intervention. In the wound-curing process, cellular activity appears to increase, resulting in a higher metabolic requirement for nutrients.[6] Deficits in some nutrients, viz vitamin C or A, can stymie cellular diversity, immunological role and collagen synthesis, causing wound curing to take longer.[7] In current biomedical sciences, research on medications that improve wound curing is indeed a growing field.[8] As a result, the current study will be conducted to discover novel natural herbs and phytochemical constituents from nature that enhance wound curing.

The hypothesis formulated in the present study is that herbal plant extract contains many phytoconstituents like antioxidants, polyphenols, and anti-aging agents, which work synergistically to enhance wound-curing processes. The existing study was planned to estimate the comparative effectiveness of the alcoholic extracts of a leaf of *Lagenaria siceraria* and seeds of *Raphanus sativus* on different wound models.

MATERIALS AND METHODS

Extractive Techniques

Leaves of *L. siceraria* and seeds of *R. sativus L* were acquired from resident market of Indore (M.P.). The leaves of *L. siceraria* were then dried in air and crushed in small pieces for extraction and extractive values. The seeds of *R. sativus L* were allowed to dry in air and indelicately powdered for extraction and extractive values.

In 50 gm of indelicately powdered drugs was kept for maceration in 200 mL alcohol for 7 days. It was macerated and obtained extracts were used for pharmacological evaluation.[9]

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Equipment's

- Tensiometer
- Glucometer

Animals

Albino Wistar rats with a weight range of 120 to 180 gm of weight were obtained from Oriental University, Indore Animal House. The animals spent a week in stabilization; they were kept in normal conditions and at ambient temperature. They had given free access for water and food. The animals adjusted to the lab setting before the experiments took place between 09:00 and 15:00 hours. The investigational procedure was authorized by the committee on institutional animal ethics of Oriental University, Indore (M.P.).[6-7]

Pharmacological studies

Acute dermal toxicity (fixed dosage)

Following the guideline, which is numbered 434 of the OECD (Organization for Economic Co-operation and Development), a "fixed dose procedure" was used to conduct acute dermal toxicity research on female albino rats. Plant extract 1 and 2 were administered topically at a 2000 mg/kg dosage.

Using non-irritating tape and a porous gauze dressing, the test material was applied to an area that accounted for roughly 10% of the entire body surface area during the course of the 24-hour duration of exposure. Then, the animals were constantly monitored for changes in skin eyes, mucous membrane, cardiovascular system, respiratory system, nervous system, shakiness, seizures, loose stool, fatigue, unconsciousness, and coma. 30-minute intervals for the following three hours, and then every 24 hours to 14 days for mortality.[8]

Selection of dose

Rats were used for the assessment of the rate of healing wounds, and the dose level chosen was such that the dosage was around 1/10 of the highest dose taken during acute oral toxicity, which is reported in previous papers.[9]

Incision wound healing design

Four groups of six animals each were prepared. All four groups' animals were put to sleep using anesthetic ether. A 4 cm incision alongside the vertebrae through the skin and cutaneal muscle on the right side of the depilated back came into being, about 1.5 cm from the center. Using a needle labeled as Number 11 with a suture (No. 000), the two ends of the wound were brought closer together and stitched at intervals of 0.5 cm. Nine days after the wound, the sutures were removed. and the medication was still administered. Using a tensiometer, the breaking strength of the skin was measured after the passage of 10 days.[10,11]

Grouping of animals:

Group 1: Normal control
Group 2: Treatment group with extract of *L. siceraria* (PE1)
Group 3: Treatment group with extract of *R. sativus L* (PE2)
Group 4: Standard group with std. drug.

Method applied for Tensile Strength Quantification

The capability of a substance to withstand breaking upon the application of load is pronounced as Tensile strength. It is determined at least three times on each wound.[11]

To test the tensile strength, the selected group of rats was given anesthesia again and was positioned on the wooden platform, such the rats were individually in the board's center. The thickness of the platform was adjusted to align the wound with the points of the arms. The skin was gently pressed by the clamps on both sides of the wound till the opening of the wound occurred. The board was aligned in a manner for the provision of a steady source of water to the bottle. The weight of water in grams at which the incision opened enabled the calculation of the breaking strength.[11,12] (Figures 1 and 2)

Excision Treatment of Wounds in Rats

Wound contracture rate and the duration of epithelization were studied using excision wounds. Each rat's right side was shaved, and every wound had full thickness types that extended to the adipose tissue. The rats were sedated with anesthetic ether. A portion of the skin from the shaven region was taken away to create excision incisions that were almost all the same size. The wound remained exposed throughout. The animals were kept under strict observation in order to check for infection if any, and the ones who did show some signs were secluded, replaced, and kept out of a trial. In each case, the medication was applied topically. For sixteen days, the gel comprising plant extracts 1 and 2 was administered. A projector film and a permanent marker enabled the measurement of the areas of the wound on days 0, 4th, 8th, 12th, and 16th for every group.

Figure 1: Tensiometer

Figure 2: Measurement of tensile strength

On graph paper, the area of the wounds was recorded and measured. The day of epithelization was defined as when the scar ceases to appear after wounding and leaves no trace of the original wound.[13-15]

$$\text{Percentage of wound closure} = \frac{\text{Wound area on day 0} - \text{Wound area on day n}}{\text{Wound area on day 0}} \times 100$$

where n = number of days 4, 8, 12, and 16 day

Grouping of animals:

Group 1: Normal control
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Group 3: Treatment group with extract of *R. sativus L* (PE2)
Group 4: Standard group with std. drug.

Dead Space Wound Healing in Rats

Sterile cotton pellets (10 mg) were inserted into each rat's left groin and axilla on the ventral region to create dead space wounds. An oral dose of the said extract of 150 mg/kg was administered to the test group rats every day in their drinking water. Removal of granulation tissue that had developed on the subcutaneous cotton implants was meticulously taken out anesthetically on the tenth post-wounding day. Recording of the weight was done, which was followed by the addition of a few mL 6N Hydrochloric acid. A resting period of a day at a temperature of 110°C was given. Hydroxyproline was measured using the neutralized tissue acid extract.[16,17]

The Assay Procedure for Hydroxyproline Content

Before subjecting the tissues to hydrolysis in an acidic media for 4 hours using tubes, which were sealed at a temperature of 130°C, they were subjected to drying till they attained a weight that was steady at a lower temperature. After the hydrolysate's pH was adjusted to neutralization, it was allowed to undergo oxidation for the duration of twenty minutes using chloramine-T, followed by the termination of the reaction with the aid of perchloric acid. It was found that color was generated at 60°C with the aid of Ehrlich reagent and detected at 554 nm using an autoanalyzer.[17]

Grouping of animals:

Group1: Normal control
Group2: Treatment with extract of *L. siceraria* (PE1) (150 mg/kg p. o.).
Group3: Treatment with extract of *R. sativus L* (PE2) (150 mg/kg p. o.).

Analysis Using Statistics

The performance of analysis using Statistics was conducted with the aid of Graph Pad Prism program, and the findings were presented as mean ± SEM. The results were compared using Dunnet's test, which reported p less than 0.05, $p < 0.01$, and $p < 0.001$.

RESULT

Acute Dermal Toxicity

Over the course of 14 days, acute cutaneous toxicity in female rats at a dose of 2000 mg/kg did not cause any deaths. No indications of a skin allergy were present. Examined were the behavioral, neurological, and autonomic responses during the 6-hour toxicity examination. During the whole research project, the rats did not exhibit any noticeable behavior (Table 1).

Tensile Strength (g)

In the incision wound healing model, the plant extract-treated animals showed better breaking strength in comparison to animals treated as controls. The animals that were treated with the standard showed the best breaking strength in comparison to all the groups treated with the plant extract as well as the control (Table 2, Figure 3).

Excision wound healing:

Wound area:

The following result was obtained when wound healing was studied using normal, extract treated and standard treated rats.

Standard group animals showed better wound healing efficacy in comparison to all 3 groups but *L. siceraria (PE1)* treated groups showed superior wound healing ability in comparison to normal and *R. sativus L (PE2)* group. (Table 3, Figures 4, 5 and 6)

Figure 4: (a)=0 day wound area measurements, (b)=4th day wound area measurements, (c) 8th day wound area measurements, (d)=12th day wound area measurements and (e)16th day wound area measurements.

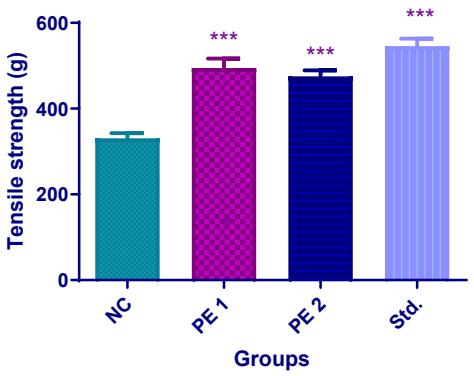


Figure 3: Tensile strength

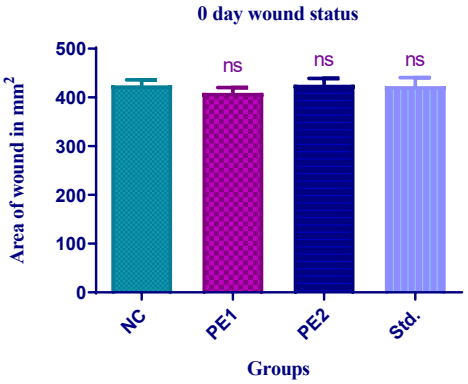


Figure 4(a): 0 day wound area measurements

Table 1: Mortality in determination of acute dermal toxicity

Drug	*Dosage (mg/kg)*	*Animals' number*	*Rate of death*			*Profile for toxicity*
			Post 24 hours	*After 7 days*	*Post 14 days*	
L. siceraria (PE1)	2000	5	0	0	0	Safe
R. sativus L (PE2)	2000	5	0	0	0	Safe

Table 2: Tensile strength (g)

Group I Normal Control	*Group II L. siceraria (PE1)*	*Group III R. sativus L (PE2)*	*Group IV Std.*
330.84 ± 11.90	495.75 ± 21.78***	475.73 ± 14.03 ***	545.80 ± 17.58 ***

N = 6, The values are in mean ± SEM, *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$, (Dunnet's test preceded by ANOVA).

Table 3: Wound area (mm^2)

Days	*Groups*			
	Normal control	*L. siceraria (PE1)*	*R. sativus L (PE2)*	*Std.*
0	424.6 ± 11.56	409.2 ± 11.18 ns	426.2 ± 12.63 ns	423.0 ± 17.46 ns
4	388.2 ± 6.12	335.4 ± 9.79**	391.6 ± 8.75 ns	353.2 ± 14.62 ns
8	289.2 ± 12.69	209.4 ± 6.68***	288.00 ± 6.41ns	224.6 ± 8.23***
12	130.80 ± 3.30	115.8 ± 8.70***	147.40 ± 4.04*	100.40 ± 6.36**
16	84.80 ± 3.32	21.40 ± 3.14***	34.60 ± 4.63***	13.08 ± 1.07***

N = 5, The values are in mean ± SEM, *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$, (Dunnet's test preceded by ANOVA).

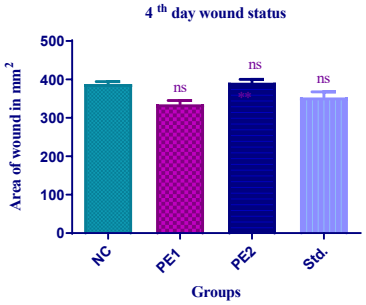


Figure 4 (b): 4th day wound area measurements

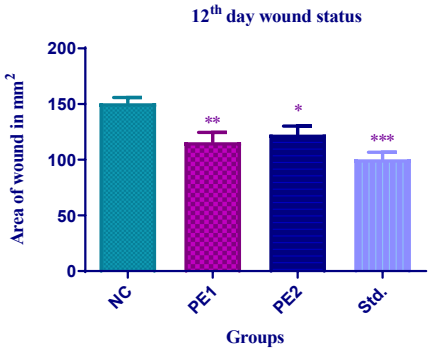


Figure 4 (d): 12th day wound area measurements

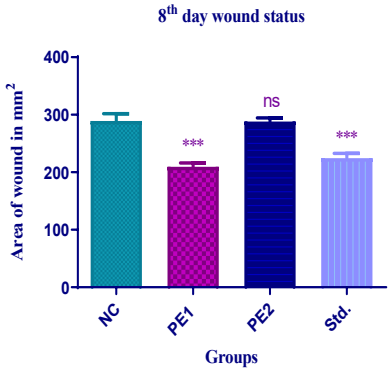


Figure 4 (c): 8th day wound area measurements

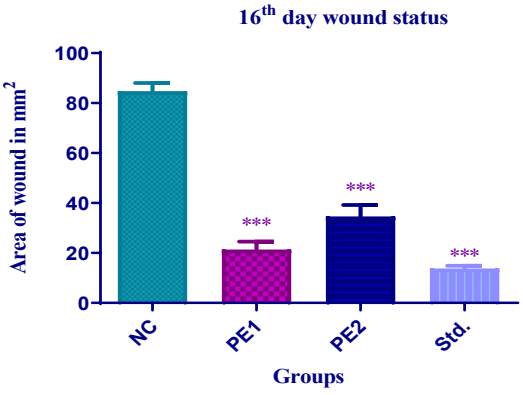


Figure 4 (e): 16th day wound area measurements

Figure 5: 0 day wound status

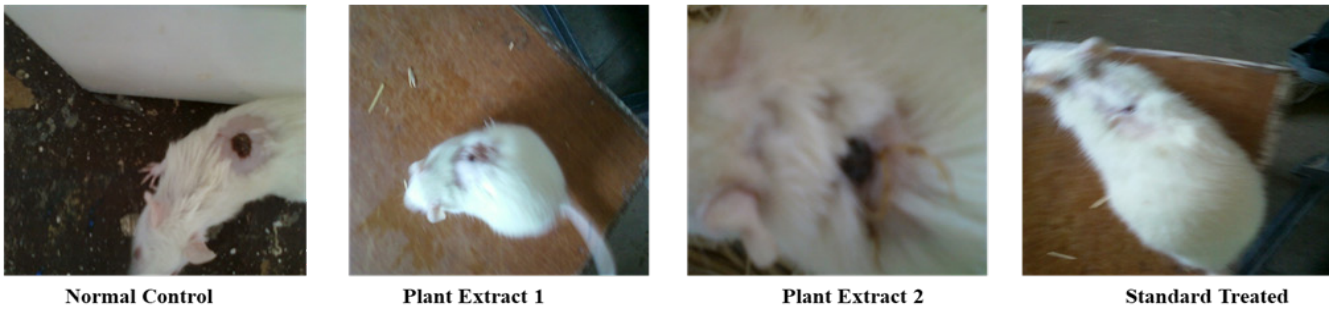


Figure 6: 16th-day wound status

Percentage Wound Closure

Using a clear tracing paper every four days, the measurement of the wound edge was done. The healed space was then computed by deducting the initial wound area. When compared to the group considered as normal control, the wound contraction in the groups treated with drug and standard groups was found to be significant on days 8 and 12. The most significant healing was found in the wounds of the standard treated group on the 16th day, while the wounds of the PE 1 and PE 2 groups showed significant healing rates of 94.77 and 91.97%, respectively, in comparison to the normal and control groups. (Table 4)

Period of Epithelization

In comparison to animals in a group considered to be normal control, the epithelization duration for the excision wound healing model was considerably decreased in the animals in the standard treatment and PE 1 and PE 2 treated groups. (Table 5, Figure 7)

Dead Space Wound Model

Wet and dry tissue granule weight

Groups when subjected to drugs taking into consideration the dead space wound healing framework displayed noticeably greater amounts of both wet and dry granulation weight when compared to a group considered to be normal control (Table 6, Figure 8)

Hydroxyproline Content

Hydroxyproline was found to be higher in drug-treated animals, in the dead space wound healing model, than in animals of control normal (Figures 9 and 10).

DISCUSSION

The body's defensive mechanism for wound restoration involves the immune system. The mechanism wherein the skin (or another organ) heals itself following damage is known

Table 4: Percentage wound closure

Days	*Groups*			
	Normal control (%)	*L. siceraria (PE1) (%)*	*R. sativus L (PE2) (%)*	*Standard (%)*
0	0	0	0	0
4	8.57	18.04	8.11	16.50
8	31.88	48.83	32.42	46.90
12	69.19	71.70	65.41	76.26
16	80.02	94.77	91.97	96.90

Table 5: Period of epithelization in days

	Groups			
	Normal control	*L. siceraria (PE1)*	*R. sativus L (PE2)*	*Std.*
Days	23.2 ± 0.447	18 ± 0.316***	19.2 ± 0.372***	17 ± 0.447**

*The values are in mean ± SEM, when N=5, ***p < 0.001, **p < 0.01, *p < 0.05, (Dunnet's test preceded by ANOVA).*

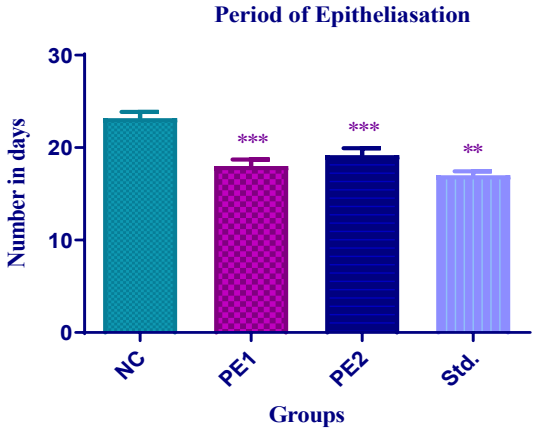


Figure 7: Period of epithelization

as the homeostatic mechanism. The surface layer of skin, the epidermis, and the layer next to it, the dermis, are stably in homeostasis in normal skin, which forms a barrier against the external world. As soon as the barrier is broken, the body's natural healing process for wounds starts.[14-20]

In the incision wound model, the PE1 (495.75 ± 21.78) treated animal showed greater wound tensile strength compared to PE2 (475.73 ± 14.03) as compared with the standard (See Table 2 and Figure 3). The greater tensile strength might be attributed to increased collagen formation and cross-linking between newly produced tissue and cells. Both plant extracts are supposed to increase ulcer healing and cell proliferation[21]. Hence there may be chances with PE1 and PE2 extracts having ulcer-healing, proliferating, and antioxidant[22] properties to increase tensile strength.

The PE1 treatment group demonstrated more wound contraction and improved healing of the surface in the excision wound model in relation to PE2 and groups considered as normal control. Wound area on 16th day was reduced significantly in PE1 (21.40 ± 3.14) as as compared to PE2 (34.60 ± 4.63). (Table 3 and Figure 4,5,6). Percentage wound closure was found to be 94.77% in PE1 and 91.97% in PE2 as compared with standard 96.90%. (Table 4). The period of

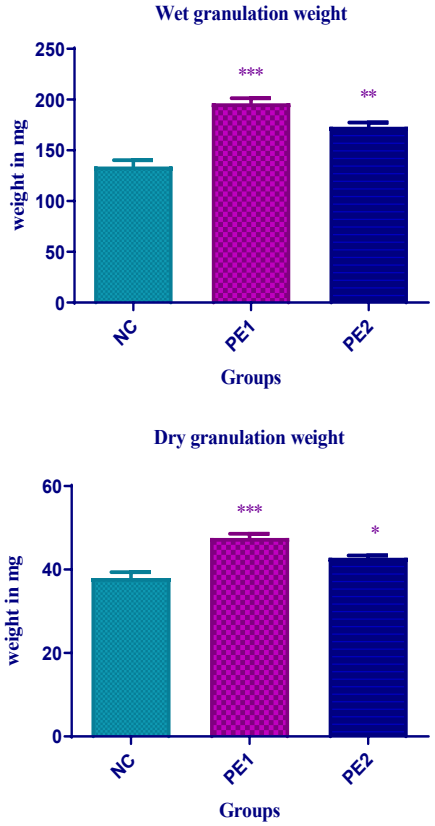


Figure 8: Comparison of wet and dry granulation weight in all 3 groups

epithelization was found to be 18 ± 0.316 days in PE1 and 19.2 ± 0.372 days in PE2, whereas the standard group showed 17 ± 0.447 days period of epithelization, which is very near to PE1 results (Table 5 and Figure 7).

The dead space model showed a discernible rise in the hydroxyproline content, indicating higher collagen deposition.[23] *L. siceraria* (PE1) and *R. sativus L* (PE2) treated group showed promising increases in the amount of hydroxyproline as it is a major part of collagen.[24] (Table 6). Both *L. siceraria* (PE1) and *R. sativus L* (PE2) treated groups shoed A rise in the dry granuloma weight,, signifying an

Table 6: Wound parameter

Parameters	*Groups*		
	Normal Control	*L. siceraria (PE1)*	*R. sativus L (PE2)*
Wet granulation (mg)	133.96 ± 6.31	196.37 ± 4.90 ***	173.14 ± 4.22 **
Dry granulation (mg)	37.95 ± 1.39	47.58 ± 0.98***	42.81 ± 0.58*
Hydroxyproline (µg/mL)	5.27 ± 0.12	8.14 ± 0.20***	7.06 ± 0.26**

N = 5 the values are in mean ± SEM, ***p < 0.001, **p < 0.01, *p < 0.05, (Dunnet's test preceded by ANOVA).

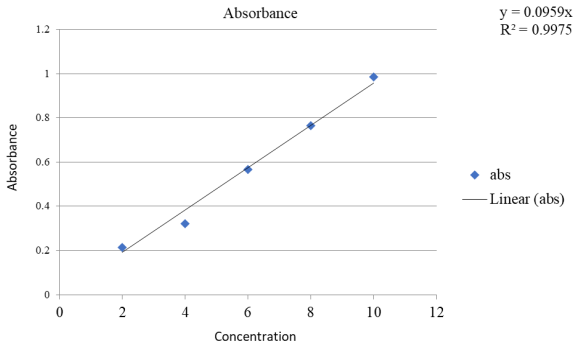
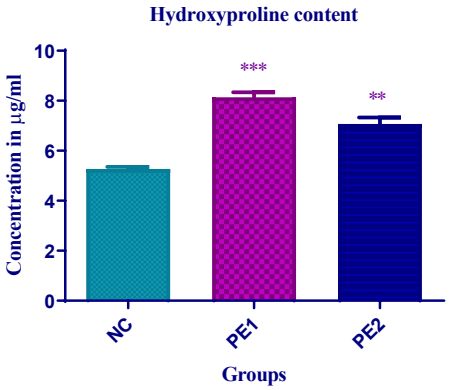


Figure 9: Standard curve of hydroxyproline



N = 5 the values are in mean ± SEM, ***$p < 0.001$, **$p < 0.01$, *$p < 0.05$, (Dunnet's test preceded by ANOVA)

Figure 10: Comparisons of hydroxyproline in all 3 groups

increase in protein content.[25] (Figure 8). Based on the afore mentioned findings, we conclude that in various wound healing models, both plant extracts accelerate the rate of collagen turnover, the time of epithelization, and the contraction of the wound.[26-28]

CONCLUSION

The wound-restoring potential and acute dermal toxicity pertaining to both plant extracts *L. siceraria* (PE1) and *R. sativus L* (PE2) have been studied. During a 14-day period, female rats administered with 2000 mg/kg showed no mortality from acute cutaneous toxicity, and no signs of skin allergy were seen. On the basis of results obtained from the incision, excision and dead spave wound model we can state that both plants extracts *L. siceraria* (PE1) and *R. sativus L* (PE2) showed appreciable wound-restoring efficacy in animal models could be attributed to its antioxidant, antimicrobial activity and angiogenic activity. The exact mechanism requires more intensive research work in this context to reach a final conclusion.

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