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# Rosa damascena extract is as effective as Centella asiatica in wound healing

## El extracto de Rosa damascena es tan eficaz como la Centella asiatica en la cicatrización de heridas

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## ABSTRACT

Since prolonged wound healing processes not only compromise patient comfort but also increase patient care costs, extracts obtained from various plants are preferred in clinical and experimental studies to accelerate wound healing and contribute to curation. The aim was to compare the efficacy of *Centella asiatica*, whose effectiveness on wound healing has been proven in previous studies, with that of *Rosa damascena,* for which research is still ongoing. Twenty-one Wistar albino rats aged 8-10 weeks were used in the study. The rats' back region was shaved with a shaving machine, cleaned with physiological serum, and a 2x2 cm incision was made to create a full-thickness excisional wound in the interscapular area. Group I: Control group, Group II: *Rosa damascena* group, *Rosa damascena* extract was applied once a day and dressed with gauze. Group III: *Centella asiatica* group received a similar application. The wound surface dimensions were measured on days 0, 7, 14, and 21 by drawing on acetate paper to calculate the surface area. On days 7, 14, and 21, punch biopsies were taken from different areas for histopathological examination. On day 14, no significant difference was observed between *Rosa damascena* and *Centella asiatica* in terms of wound surface area (P = 0.415). Again, no statistically significant difference was observed between the groups in terms of fibroblast activity on days 7 and 21, and neovascularization was also found to be insignificant on days 14 and 21. Collagen regularity and density increased in both the *Rosa damascena* group and the *Centella asiatica* group. VEGF retention did not show a significant difference between the two groups on day 21 (P = 0.762). It was concluded that *Rosa damascena* extract may contribute to wound healing more effectively than *Centella asiatica* ointment.

**Keywords:** Wound healing; Rosa damascena; Centella asiatica; VEGF.

## RESUMEN

Dado que la cicatrización prolongada de heridas no solo compromete la comodidad del paciente, sino que también incrementa los costos de atención médica, los extractos obtenidos de diversas plantas son los preferidos en estudios clínicos y experimentales para acelerar la cicatrización de heridas y contribuir a su curación. El objetivo fue comparar la eficacia de *Centella asiatica*, cuya eficacia en la cicatrización de heridas ha sido demostrada en estudios previos, con la de *Rosa damascena,* cuya investigación aún está en curso. Se utilizaron veintiún ratas albinas Wistar de 8 a 10 semanas de edad. Se afeitó la región dorsal de las ratas con una máquina de afeitar, se limpió con suero fisiológico y se realizó una incisión de 2 x 2 cm para crear una herida escisional de espesor completo en la zona interescapular. Grupo I: Grupo control. Grupo II: Grupo *Rosa damascena*. El extracto de *Rosa damascena* se aplicó una vez al día y se cubrió con una gasa. Grupo III: Grupo *Centella asiatica* recibió una aplicación similar. Las dimensiones de la superficie de la herida se midieron los días 0, 7, 14 y 21 dibujando en papel acetato para calcular el área superficial. Los días 7, 14 y 21 se tomaron biopsias por punción de diferentes áreas para su examen histopatológico. El día 14, no se observó diferencia significativa entre *Rosa damascena* y *Centella asiatica* en cuanto al área superficial de la herida (P = 0,415). De nuevo, no se observó diferencia estadísticamente significativa entre los grupos en cuanto a la actividad de fibroblastos los días 7 y 21, y la neovascularización también fue insignificante los días 14 y 21. La regularidad y la densidad del colágeno aumentaron tanto en el grupo de *Rosa damascena* como en el de *Centella asiatica*. La retención de VEGF no mostró una diferencia significativa entre los dos grupos el día 21 (P = 0,762). Se concluyó que el extracto de *Rosa damascena* puede contribuir a la cicatrización de heridas con mayor eficacia que el ungüento de *Centella asiatica*.

**Palabras clave:** Cicatrización de heridas; Rosa damascena; Centella asiática; VEGF.

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## INTRODUCTION

Wound healing is a process involving interactions between cellular and molecular events, consisting of the stages of hemostasis, inflammation, proliferation, and remodeling, which are necessary to maintain tissue functionality and continuity after tissue damage. This process begins with wound formation and can take a long time depending on the effects of local and systemic factors that influence healing and cause chronicity. A prolonged wound healing process not only compromises patient comfort but also increases patient care costs [1 , 2 , 3].

In recent years, increasing chronic diseases, poor nutrition, and a sedentary lifestyle have been among the factors that disrupt the wound healing process. For this reason, extracts obtained from various plants are preferred in clinical and experimental studies to accelerate wound healing and contribute to wound healing [4 , 5 , 6].

*Centella asiatica* is more commonly known as gotu kola, tiger grass, or Asian pennywort. It is a flowering plant belonging to the umbellifer family that grows in tropical countries and humid regions, primarily in Southeast Asia and Australia. It is used in both the food industry and traditional medicine [7 , 8 , 9]. Studies on *Centella asiatica* have shown that its hydrogel form enhances epithelialization and possesses anxiolytic, anti-inflammatory, antioxidant, anti-ulcer, anti-cancer, neuroprotective, and wound-healing properties [10].

*Rosa damascena,* commonly known as Damask rose, is an ornamental plant belonging to the Rosaceae family, originating from the Middle East. It grows to an average height of 1 to 2 meters and has colorful flowers. It is cultivated all over the world, particularly in Türkiye, Iran, and India. In traditional medicine, *Rosa damascena* is said to have anti-inflammatory and wound-healing effects, and it has been observed to be effective for coughs, abdominal pain, and dysmenorrhea. *Rosa damascena* is also known to be effective in vasorelaxation, antidepressant, analgesic, anti-diabetic, anti-inflammatory, bronchodilator, antioxidant, antimicrobial, anti-aging, skin repair, and aphthous stomatitis treatment [11 , 12 , 13 , 14].

As a result of the literature review, it was determined that there are limited studies based on concrete data from a methodological perspective regarding the effects of *Rosa damascena* on wound healing. Therefore, in this study, the potential effects of *Centella asiatica* and *Rosa damascena,* which have proven efficacy on wound healing, on congestion, collagen density and irregularity, fibroblast activity, neovascularization, mononuclear cell infiltration, immunohistochemical density, and changes in wound surface area.

## MATERIALS AND METHODS

### Ethics committee approval

Approval was obtained with the ethical committee decision No. 2023/17, which was decided at the meeting of the Dicle University Animal Experiments Local Ethics Committee on November 30, 2023. The experimental animals were obtained from the Sabahattin Payzın Research Center (DUSAM) at Dicle University. The experimental procedures were conducted at the DUSAM animal care center, while tissue analyses were performed at the Pathology Laboratory of the Diyarbakır Gazi Yaşargil Health Application and Research Center at the University of Health Sciences.

### Obtaining Rosa damascena extract

Commercially available *Rosa Damascena* extract, bottled as Rose Hydrosol, is obtained by distilling *Rosa Damascena* roses in chrome-made (inox) stills at the rose factory (Sincer rose oil factory, Isparta, Türkiye), without separating the rose oil, resulting in a 100 % pure and natural rose hydrolate. After opening the bottles, they are stored at a temperature of 4-6 *°C, away from sunlight.*

### Wound model and formation of experimental groups

The study used 21 Wistar albino rats (*Rattus norvegicus*) weighing 200-300 grams (g) and aged 8-10 weeks.The rats were housed in stainless steel cages (temperature 22±2 °C, humidity 60 %) with a 12-hour (h) light/dark cycle and without food or water restrictions.

After being randomly divided into 3 groups of 7 rats each, the rats were sedated on days (d) 0, 7, 14, and 21 with intramuscular (i.m.) injections of 90 mg/kg Ketamine (Ketalar®, Pfizer Inc., USA) and 10 mg/kg Xylazine (Rompun®, Bayer HealthCare AG, Germany). The depth of sedation and the need for additional doses were assessed by observing limb responses.

The rats' back region was shaved with a razor without irritating the skin, cleaned with physiological serum, and marked with a 2x2 cm ruler. The area to be operated on was cleaned with alcohol and a 2x2 cm full-thickness (epidermis, dermis) excisional wound was created in the interscapular area with a No. 15 scalpel. This wound model is simple and widely used. Thus, the rate of wound closure over time can be observed. Important stages such as granulation tissue development, collagen accumulation, re-epithelialization process, and wound contraction can be examined in detail with this model [15 , 16]. After the wounds were created, Paracetamol (Atabay Pharmaceuticals, Istanbul, Türkiye) was added to the rats' drinking water at a dose of 2 mg/ml/d to control pain.

Group I (n=7): Control group, no other procedures were performed except for d dressing with gauze.

Group II (n=7): After creating a 2x2 cm excisional wound in the rats in the *Rosa damascena* group, *Rosa damascena* extract was applied once a d and dressed with gauze.

Group III (n=7): This was the *Centella asiatica* group, where *Centella asiatica* ointment was applied once d, followed by dressing care.

The wound surface areas of rats were measured on d 0, 7, 14, and 21 by drawing the wound surfaces on acetate paper. Punch biopsies were taken from different areas of the wounds on d 7, 14, and 21 for histopathological examination.

### Histopathological examination

Tissue samples were obtained by punch biopsy from the upper left corner on d 7, the upper right corner on d 14, and the lower right corner on d 21. The samples were fixed in 10

% formalin for 24 h, then rinsed in running water, dehydrated, and embedded in paraffin blocks. Sections 4–5 microns (μ) thick were taken from the paraffin blocks and subjected to routine histological examination. The sections were stained with hematoxylin and eosin (H&E) and examined under a light microscope (Zeiss microscope, Germany) [16].

### Immunohistochemical examination

For immunohistochemical examinations, sections 4-5 µm thick were prepared following routine histological tissue follow-up, and the prevalence of Vascular Endothelial Growth Factor (VEGF) (Santa Cruz, USA) expression (brown areas) was evaluated. Gill Hematoxylin was used in the counterstaining protocol. The sections were examined under a light microscope (Zeiss microscope, Germany), and the degree of damage was determined according to the method developed by Erdogan and Yalcin [17].

### Statistical analysis

Statistical Package for Social Sciences (SPSS, Inc., Chicago, IL, USA) for Windows 24.0 was used for statistical analysis of the obtained data. The Kolmogorov Simirnov test was used to check the distribution of the data. ANOVA test was used for multiple group comparisons of normally distributed data, and the relationship between groups was evaluated using the Posthoc Tukey test. For data that did not show a normal distribution, the Kruskal-Wallis test was used for multiple group comparisons, and the Mann-Whitney U test was used to compare groups. Data were considered significant when $P < 0.05$.

## RESULTS AND DISCUSSIONS

### Macroscopic evaluation results

When the wound surface areas were calculated on d 7, 14, and 21,it was found that the *Centella asiatica* group was lagging behind in wound healing on d 7 and had a larger wound area. No statistically significant difference was observed between the control group and the *Rosa damascena* group ($P = 0.08$). A statistically significant difference was calculated between the control group and the *Centella asiatica* group ($P = 0.033$).

No significant difference was observed between wound surface areas on d 14 ($P = 0.415$).

On d 21, the *Centella asiatica* group had the largest wound surface area, and the difference between it and both the *Rosa damascena* and control groups was statistically significant ($P^{C-B} = 0.017$, $P^{A-B} = 0.009$). The *Centella asiatica* group had a larger wound surface area and was morphologically behind in wound healing (TABLE I) (FIG. 1).

Bardaa *et al.* [18] created an excisional wound model in diabetic rats and compared the wound surface area of Ginkgo biloba and *Centella asiatica*, observing that *Centella asiatica* had a smaller wound surface area. According to Kim *et al*. [19] experimental study, the *Rosa damascena* group showed faster wound closure compared to the control group. Nie *et al*. [20] created skin ulcers in diabetic rats and found that the *Centella asiatica* and nitric oxide mixture resulted in a significantly smaller wound area on d 3 and 14 compared to the control group.

**TABLE I**
**Comparison of wound surface areas on days 7, 14, and 21**

| | | Control | *Rosa damascena* | *Centella asiatica* | *p* |
|---|---|---|---|---|---|
| 7th d | | 2.77±0.18 | 2.89±0.44 | 3.2±0.34 | |
| | Intragroup comparisons p-value[x] | [A-C]0.800 | [C-A]0.800 | **[B-A]0.033** | **0.033[a]** |
| | | **[A-B]0.033** | [B-C]0.114 | [B-C]0.114 | |
| 14th d | | 0.8±0.6 | 0.9±0.27 | 0.91±0.12 | 0.415[a] |
| 21th d median (IQR) | | 0.24(0.07) | 0.25(0.09) | 0.36(0.20) | |
| | Intragroup comparisons P-value[y] | [A-C]0.847 | [C-A]0.847 | **[B-A]0.009** | **0.014[b]** |
| | | **[A-B]0.009** | **[C-B]0.017** | **[B-C]0.017** | |

[A-C]: P-value in the comparison between the control group and the Rosa damascena group, [A-B]: P-value in the comparison between the control group and the Centella asiatica group, [B-C]: In the comparison between the Rosa damascena group and the Centella asiatica group, the p-value was, IQR: Inter Quantile Range, a: ANOVA test, x: Evaluation according to the intra-group post hoc Tukey test on day 7, b: Kruskal Wallistest, y: Evaluation according to the Mann Whitney-U test in the subgroup analysis on day 21.

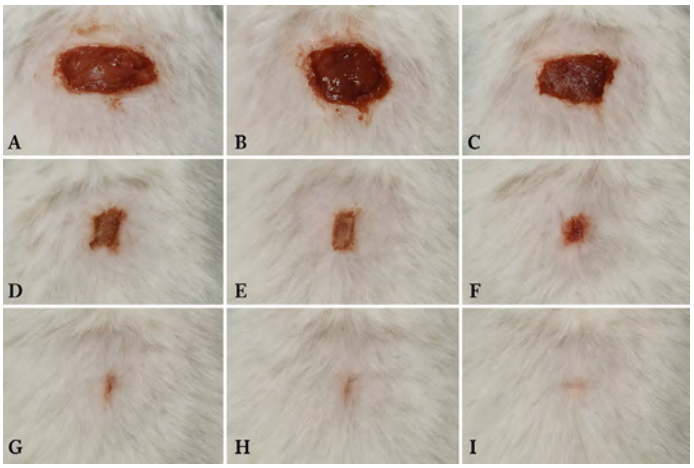


**FIGURE 1.** A; Rosa damascena, B; Centella asiatica, C; Wound images taken on the 7th day of the control groups. D; Rosa damascena, E; Centella asiatica, F; Wound images from control groups on day 14. G; Rosa damascena, H; Centella asiatica, I; Wound images from control groups on day 21.

In the wound surface area comparison on d 7, we observed that the control group had the smallest wound area, while the *Centella asiatica* group had the largest wound area. No statistically significant difference was observed between the control group and the *Rosa damascena* group. On d 14, *Centella asiatica* was calculated to be behind in wound healing according to wound surface area calculations. On d 21, when evaluating wound surface areas, *Centella asiatica* was found to have a higher wound surface area than both the *Rosa damascena* group and the control group.The morphological findings were not consistent with the literature for *Centella asiatica* but showed more meaningful results for *Rosa damascena*.

### Histopathological examinations

Tissue samples taken on d 7, 14, and 21 were stained with H&E and examined under a light microscope to assess collagen

regularity, collagen density, fibroblast activity, myofibroblast density, congestion, neovascularization, and mononuclear cell infiltration were scored on a scale of 1 to 4 by a blinded pathologist (FIG. 2).

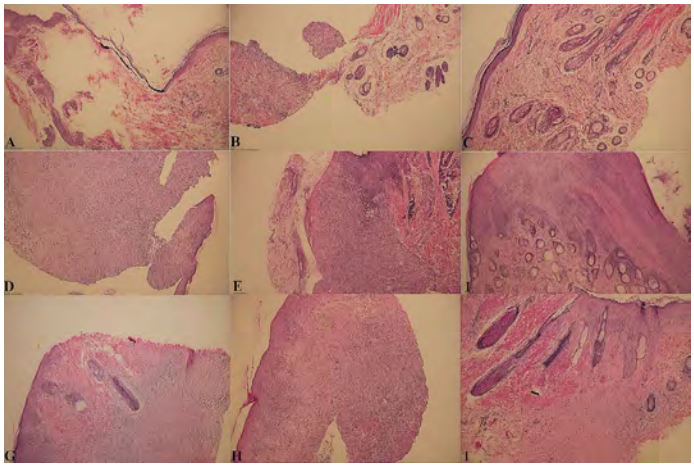


**FIGURE 2.** A; Rosa damascena, B; Centella asiatica, C; Hematoxylin & Eosin staining images of control groups on day 7. D; Rosa damascena, E; Centella asiatica, F; Hematoxylin & Eosin staining images of control groups on day 14. G; Rosa damascena, H; Centella asiatica, I; Hematoxylin & Eosin staining images of control groups on day 21.

No statistically significant difference in collagen regularity was found between the groups on d 7 and 21. On d 14, collagen regularity was found to be higher in the *Rosa damascena* group than in both the control group and the *Centella asiatica* group ($P^{C-B}$ = 0.028, $P^{C-A}$ = 0.001).

Similarly, collagen density was observed to be higher in both the *Rosa damascena* group and the *Centella asiatica* group compared to the control group on d 14 ($P^{C-A}$ = 0.049, $P^{B-A}$ = 0.003).

In terms of fibroblast activity, no statistically significant difference was observed between the groups on d 7 and 21, while on d 14, the control group was found to have higher fibroblast activity than both the *Rosa damascena* group and the *Centella asiatica* group, with the difference between them being statistically significant ($P^{A-C}$ = 0.011, $P^{A-B}$ = 0.034). No significant difference was observed between the *Rosa damascena* and *Centella asiatica* groups(P = 0.849) (TABLE II).

**TABLE II**
**Comparison of collagen regularity, collagen density, and fibroblast activity on days 7, 14, and 21**

| | | Control | *Rosa damascena* | *Centella asiatica* | P |
|---|---|---|---|---|---|
| 7th d | | 1.86±0.690 | 1.71±0.488 | 2.00±0.816 | 0.737[a] |
| 14th d | | 1.14±0.378 | 2.29±0.488 | 1.57±0.535 | **0.001[a]** |
| | Intragroup comparisons p-value[x] | **$^{A-C}$0.001** | **$^{C-A}$0.001** | $^{B-A}$0.232 | |
| | | $^{A-B}$0.232 | **$^{C-B}$0.028** | **$^{B-C}$0.028** | |
| 21th d | | 1.86±0.378 | 2.29±0.488 | 2.43±0.535 | 0.088[a] |

| | | Control | *Rosa damascena* | *Centella asiatica* | *p* |
|---|---|---|---|---|---|
| 7th d | | 2.86±0.690 | 2.14±0.690 | 2.29±1.11 | 0.279[a] |
| 14th d | | 2.29±0.488 | 2.86±0.378 | 3.14±0.378 | **0.004[a]** |
| | Intragroup comparisons p-value[x] | **$^{A-C}$0.049** | **$^{C-A}$0.049** | **$^{B-A}$0.003** | |
| | | **$^{A-C}$0.003** | $^{C-B}$0.424 | $^{B-C}$0.424 | |
| 21th d | | 3.14±0.378 | 3 | 3 | 0.387[a] |

| | | Control | Rosa damascena | *Centella asiatica* | *p* |
|---|---|---|---|---|---|
| 7th d | | 2.43±0.535 | 2.71±0.756 | 3±0.577 | 0.263[a] |
| 14th d | | 3 | 2.14±0.378 | 2.29±0.756 | **0.009[a]** |
| | Intragroup comparisons p-value[x] | **$^{A-C}$0.011** | **$^{C-A}$0.011** | **$^{B-A}$0.034** | |
| | | **$^{A-B}$0.034** | $^{C-B}$0.849 | $^{B-C}$0.849 | |
| 21th d | | 2.14±0.378 | 2 | 2.43±0.535 | 0.126[a] |

$^{A-C}$: P-value in the comparison between the control group and the Rosa damascena group, $^{A-B}$: P-value in the comparison between the control group and the Centella asiatica group, $^{B-C}$: In the comparison between the Rosa damascena group and the Centella asiatica group, the p-value was, a: ANOVA test, x: Evaluation according to the intra-group post hoc Tukey test on day 14.

Fibroblasts are known to be effective in contraction, cell migration, and collagen production, and to play a role in all stages of wound healing [21]. On the 14th d of the proliferation phase, fibroblasts transform into myofibroblasts [22]. In a study comparing the effect of *Centella asiatica* on the proliferation of human dermal fibroblasts with that of retinoic acid, it was found to have a stronger effect than retinoic acid [23].

A systematic review of *Centella asiatica* indicates that it has an activating effect on fibroblasts and contributes to granulation tissue formation by increasing angiogenesis [24]. *Rosa damascena* has been shown to increase the lifespan of human fibroblast cells by inducing morphological changes [25].

It is known that saponins, flavonoids, tannins, and terpenoids in plants support wound healing by activating fibroblasts and increasing their growth [26]. On the 14th d of this study, fibroblast activity was statistically higher in the control group, which is in favor of *Rosa damascena* and *Centella asiatica* and is consistent with the literature data.

Collagen density and regularity are important indicators that determine granulation tissue formation and the wound healing process. During the remodeling phase of skin wounds, collagen accumulation is a critical process and serves as a criterion for evaluating wound healing [27].

According to an *in vitro* study examining human collagen 1 and fibroblast activity, asiaticoside in *Centella asiatica* has been shown to increase collagen 1 and fibroblast synthesis separately

[28]. In an experimental study by Maquart *et al*.[29], triterpenes derived from *Centella asiatica* were found to increase collagen matrix and hydroxyproline in rat wound healing.

In another study, it was shown that topical application of *Centella asiatica* gel contributes to an increase in collagen content [30]. In their study on radiation-induced skin aging, Park *et al.* [31] found that *Rosa damascena* improves collagen synthesis by reducing matrix metalloproteinases through TGF-β stimulation, thereby providing protection against skin aging. According to our study, we observed that *Rosa damascena* is as effective as *Centella asiatica* in collagen synthesis.

In the intergroup comparison of collagen regularity and density, we found that the *Rosa damascena* group was statistically significantly superior to both the control group and the *Centella asiatica* group on d 14.

The severity of congestion increased in the *Centella asiatica* group compared to the control group on d 7 (P = 0.018), while no statistically significant difference was found with the *Rosa damascena* group (P = 0.233) (TABLE III).

No statistically significant difference was observed between the groups in the comparison of neovascularization on d 14 and 21 (TABLE III).

**TABLE III**
**Comparison of congestion severity and neovascularization on days 7, 14, and 21**

| | | Control | *Rosa damascena* | *Centella asiatica* | *p* |
|---|---|---|---|---|---|
| 7th d | | 1.71±0.488 | 2.43±0.976 | 3±0.816 | |
| | Intragroup comparisons p-value[X] | [A-C]0.233 | [C-A]0.233 | **[B-A]0.018** | **0.023[a]** |
| | | **[A-B]0.018** | [C-B]0.383 | [B-C]0.383 | |
| 14th d | | 2.71±0.756 | 2.43±0.535 | 2.86±0.690 | 0.487[a] |
| 21th d | | 2.43±0.535 | 2.14±0.378 | 2 | 0.126[a] |

| | | Control | *Rosa damascena* | *Centella asiatica* | *p* |
|---|---|---|---|---|---|
| 7.d | | 1.71±0.756 | 2.43±0.787 | 3±1 | |
| | Intragroup comparisons p-value[X] | [A-C]0.286 | [C-A]0.286 | **[B-A]0.029** | **0.037[a]** |
| | | **[A-B]0.029** | [C-B]0.440 | [B-C]0.440 | |
| 14th d | | 3.29±0.756 | 2.43±0.787 | 3.43±0.976 | 0.83[a] |
| 21th d | | 2.71±0.488 | 2.14±0.690 | 2.57±0.787 | 0.274[a] |

[A-C]: P-value in the comparison between the control group and the Rosa damascena group, [A-B]: P-value in the comparison between the control group and the Centella asiatica group, [B-C]: In the comparison between the Rosa damascena group and the Centella asiatica group, the p-value was, a: ANOVA test x: Evaluation according to the intra-group post hoc Türkiye test on day 7.

Congestion limits damage to the wound during the inflammatory phase through hemostasis, chemotaxis, and increased vascular permeability. It aids cell migration to clear cellular debris and bacteria, thereby playing an important role in wound healing [27]. Cesarone *et al*. [32] reported that *Centella asiatica* increases microcirculation and improves venous hypertensive microangiopathic patients. The severity of congestion was better in the *Centella asiatica* group on d 7, and there was no significant difference between it and the *Rosa damascena* group.

It has been shown that oral administration of *Centella asiatica* in rats increases angiogenesis compared to the control group by activating the kinase-independent pathway through collagen type 1, fibroblast increase, and VEGF increase [33]. In their experimental studies comparing *Polypodium vulgare* and *Centella asiatica* in rats, Batur *et al.* [34], demonstrated that *Centella asiatica* contributed to greater new vessel formation and granulation tissue development compared to the control group.

**Immunohistochemical studies**

Tissue samples taken on d 7, 14, and 21 were subjected to VEGF antibody testing. Following VEGF antibody testing, VEGF binding intensity (graded from 1 to 3) and VEGF density (weak = 1, strong = 2) were calculated. Immunohistochemical staining images are shown in FIG. 3.

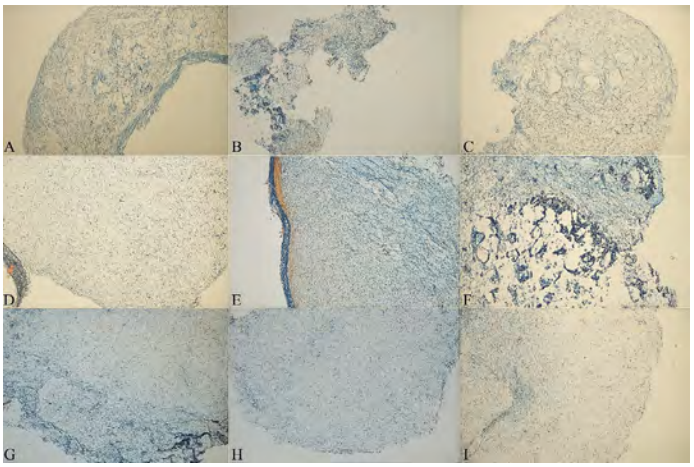


**FIGURE 3.** A; Rosa damascena, B; Centella asiatica, C; VEGF staining images of control groups on day 7. D; Rosa damascena, E; Centella asiatica, F; VEGF staining images of control groups on day 14. G; Rosa damascena, H; Centella asiatica, I; VEGF staining images of control groups on day 21. VEGF: Vascular Endothelial Growth Factor.

It was observed that VEGF retention was best in the *Rosa damascena* group on d 7, and that the *Rosa damascena* group and *Centella asiatica* group were better than the control group, with a statistically significant difference between them ($P^{C-A}$ = 0.001, $P^{B-A}$ = 0.020). No statistically significant difference was observed between groups on d 14 and 21 (P = 0.510, P = 0.093) (TABLE IV).

It was determined that VEGF density showed a significant increase in the *Centella asiatica* group compared to the control group only on d 14 (P = 0.029). On d 21, no significant difference was observed between the *Rosa damascena* group and the *Centella asiatica* group (P = 0.762) (TABLE IV).

**TABLE IV**
**Comparison of VEGF retention and density on days 7, 14, and 21**

| | | Control | *Rosa damascena* | *Centella asiatica* | *p* |
|---|---|---|---|---|---|
| 7th d | | 1.14±0.378 | 2 | 1.71±0.488 | **0.001[a]** |
| | Intragroup comparisons p-value[x] | [A-C]**0.001** | [A-C]**0.001** | [B-A]**0.020** | |
| | | [A-B]**0.020** | [C-B]0.314 | [B-C]0.314 | |
| 14th d | | 2.14±0.9 | 2±0.577 | 2.43±0.535 | 0.510[a] |
| 21th d | | 1.86±0.690 | 1.57±0.535 | 2.29±0.488 | 0.093[a] |

| | | Control | *Rosa damascena* | *Centella asiatica* | *p* |
|---|---|---|---|---|---|
| 7th d | | 1.29±0.488 | 1.43±0.535 | 1.57±0.535 | 0.598[a] |
| 14th d | | 1.43±0.535 | 1.86±0.378 | 2 | **0.029[a]** |
| | Intragroup comparisons p-value[x] | [A-C]0.114 | [C-A]0.114 | [B-A]**0.029** | |
| | | [A-B]**0.029** | [C-B]0.762 | [B-C]0.762 | |
| 21th d | | 1.57±0.535 | 1.71±0.488 | 1.57±0.535 | 0.840[a] |

[A-C]: P-value in the comparison between the control group and the Rosa damascena group, [A-B]: P-value in the comparison between the control group and the Centella asiatica group, [B-C]: In the comparison between the Rosa damascena group and the Centella asiatica group, the p-value was, a: ANOVA test, x: Evaluation according to the intra-group post hoc Tukey test on day 14. VEGF: Vascular Endothelial Growth Factor.

In Zang and Lineweaver [35] study on the effect of VEGF on the survival of flaps and skin grafts, they reported that VEGF levels increased and new blood vessel formation occurred in the *Centella asiatica* group.Instead of Kim *et al*. [19] reported that *Rosa damascena* triggered more new blood vessel formation than the control groups in an excisional wound model. In a study comparing the effect of *Centella asiatica* on skin flap survival in rats with a control group, it was demonstrated that *Centella asiatica* had improved microcirculation and exhibited higher VEGF expression [36]. It was revealed that the findings of our study were consistent with the literature.

In this study, VEGF uptake was found to be optimal in the *Rosa damascena* group on d 7, and the *Rosa damascena* group and *Centella asiatica* group were found to be statistically significantly superior to the control group. VEGF density was found to be statistically significantly higher in the *Centella asiatica* group compared to the control group on d 14.

## CONCLUSION

Macroscopic examinations revealed that *Rosa damascena* extract yielded better results than *Centella asiatica* in wound healing. Microscopic evaluation showed that the group treated with *Rosa damascena* extract yielded similar results to the *Centella asiatica* group. When evaluating our macroscopic and microscopic findings as a whole, we believe that *Rosa damascena* extract may contribute to wound healing more effectively than *Centella asiatica* ointment, and we recommend that studies in this field be supported by more comprehensive studies.

**Conflict of interest**

The authors declare no conflicts of interest regarding this article's research, authorship, and/or publication.

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