Tikrit Journal for Dental Sciences 13(1) (2025) 153-167
https://doi.org/10.25130/tjds.13.1.16

Tikrit Journal
for
Dental Sciences
https://tjds.tu.edu.iq
ISSN:2073-1213

Histological Evaluation of the Effect of Squalane Oil /Rosehip Oil on Facial Wound Healing of Rat

Jwan Arkan Mohammed Saeed [(1)]
Enas Fadhil Kadhim [(2) *]

[(1)] Department of Oral Diagnosis (Oral histology), Dentistry, University of Baghdad, Baghdad, Iraq.
[(2)] Department of Oral Histology and Biology, Dentistry, University of Baghdad, Baghdad, Iraq.

Keywords:
squalane oil, rosehip oil, wound healing.

Article Info.:

Article History:
Received: 14/6/2024
Received in revised form: 13/7/2024
Accepted: 15/7/2024
Final Proofreading: 15/7/2024
Available Online: 1/6/2025

Citation: Mohammed JA, Kadhim EF. Histological Evaluation of the Effect of Squalane Oil /Rosehip Oil on Facial Wound Healing of Rat. Tikrit Journal for Dental Sciences. 2025; 13(1): 153-167.
https://doi.org/10.25130/tjds.13.1.16

***Corresponding Author:**
Email:
dr.enas.fadhil4@codental.uobaghdad.edu.iq

Prof. Dr. specialized in Oral Histology and Biology, Dentistry, University of Baghdad, Baghdad, Iraq.

Abstract

Background: Wound healing is achieved by 3 processes: hemostasis, inflammation, proliferation, and remodeling. squalene is considered a natural product with some ability to influence the immunomodulation of macrophages where it could help the "last stage remodeling and wound closure" because of its anti-inflammatory properties. Rosehip oil can shorten epithelialization time while decreasing the number of inflammatory cells that invade.

Objective: Study the efficacy of squalene oil and rosehip oil separately or as a combination in the healing of facial skin wounds of rats histologically.

Patients and Methods: forty-two rats were subjected to facial skin wounds.

They separated the animals into:

A. The control group on the left side left for spontaneous healing without any treatment.
B. Experimental group on the right side which were divided to three groups for each oil and their combination.

Then the specimens were taken on the 3rd and 7th day after wounding and prepared for histological examination (H&E stain).

Results: The greatest wound contraction was found in the squalane oil group on the 7th day. The histological evaluation showed that the control group had the greatest inflammatory cell count on day 3. Regarding the epithelial thickness it was found is where the combination group had the highest levels of epithelial thickness compared to the squalane oil and rosehip oil groups. As for blood vessel count, it was found that the greatest blood vessel counts in the rosehip oil group.

Conclusion: results showed that the use of squalane oil and rosehip oil separately or as a combination can be beneficial for wound healing.

Introduction:

Wounding is any violation of the live tissue integrity. Maintaining skin integrity and enabling effective wound healing are preconditions for healthy survival. Additionally, wound healing can be another challenge and burden to the healthcare system (1).

The skin primarily functions as a protective barrier against external factors; however, extensive damage or loss can lead to severe consequences, underscoring the necessity of an efficient wound healing system to restore tissue integrity and functionality to prevent complications such as disability or fatality (2, 3).

Healing of wounds is a complex process comprising regeneration and/or reconstruction of damaged tissue. The onset of the healing cascade is triggered by platelet-collagen interaction at the site of injury. This results in the accumulation of platelets and the production of clotting factors, which later on result in the formation of a fibrin clot at the injured area. Fibrin clot acts as a temporary framework, providing foundations for further healing events (4, 5).

Overall wound healing is achieved by 3 separate but overlapping biological mechanisms, including the consolidation of blood vessels, inflammation, cell division, and remodeling. This sequence of events is known as the wound-healing cascade, and if any one of these steps is missing, the body won't be able to repair the wounds (6, 7)

Squalene is oil-type liquid that is odorless and colorless. Squalene was first isolated from shark (Squalus milshamianai and other squaloids) liver oil, but it was subsequently discovered in several plant extracts as well, leading to its naming (8).

Squalane originated from nature and is one the major parts of polyunsaturated lipids found on the skin's surface; this is squalene in its saturated form, with the hydrogenation of two bonds eliminated. Squalane is more stable and therefore less likely to undergo oxidation, hence the reason why it is the preferred choice in personal care products (9).

It was not until the late decades of the 20th century that the presence of squalene in tiny quantities in the human body was not known. In humans, it is the newborns that have the highest lipid squalene in their blood. On the other hand, this reserve drastically declines after the ages of 30 and 40. Squalene in the human body made in the liver and then released into the skin by the sebaceous glands in large amounts. Squalene which is to be transported in the blood binds to small and very small-density lipoproteins (10, 11).

Rosehip oil is applied in the pharmaceutical, cosmetics, and the food industry. The essential fatty acids linolenic acid, linoleic acid, and oleic acid are isolated from the rosehip (Rosa canina L.) fruit by pressing it (12).

The anti-cancer effect is perhaps one of the most well-recognized health-promoting properties of rosehip oil among all other therapeutic benefits. Roship oil has been popular recently for cosmetic use due to its therapeutic impact on skin treatments. And because of its naturally occurring properties and wide range of uses rosehip oil is no longer limited to just health and beauty sectors where it is used as a natural remedy with potential skin-boosting and health-enhancing effects (13).

Materials and Methods

The research started at the Iraqi Center for Cancer Research and Medical Genetics. In this study, 42 male We utilized albino rats that were 200-350 grams in weight and roughly 4 to 6 months old. Housing the rats in plastic cages, they were kept at a temperature of 23±2 °C for a week before the surgical procedure. Before the experiment, all of the rats were examined by a veterinary doctor to assess their health and ensure that only healthy animals were included in the study.

forty-two rats were subjected to facial skin wounds.

The creatures were then categorized as follows:

A. The control group on the left side followed the number of the experimental group and left for

spontaneous healing without any treatment.

B. Experimental group on the right side.

Group 1: 14 rats were subjected to a wound on the right side of the facial skin and were treated daily with 30µl of squalene oil.

Group 2: 14 rats were subjected to a wound on the right side of the facial skin and were treated daily with 30µl of rosehip oil.

Group 3: 14 rats were subjected to a wound on the right side of facial skin and were treated daily with 15µl of squalene oil and 15µl rosehip oil as a combination.

Then each group was subdivided into 2 subgroups according to the healing intervals on days 3 and 7. Preparation for histological investigation began with the collection of specimens. (H&E stain).

Each animal received a dose of 15mg/kg of ketamine hydrochloride and 0.15ml/kg of xylazine for general anesthesia, administered intramuscularly. The hair on the right and left cheeks of each rat was removed using a hair removal lotion. Subsequently, the skin of the cheek was disinfected with 70% ethyl alcohol.

An incision of full thickness of the skin with a length of 1.5 cm using blade no.11 was made externally on both sides of the cheeks of the rats, the right side was treated according to the groups mentioned above and the left side was left for spontaneous healing and considered the control group.

After 3 days of treatment, 7 rats from each group were sacrificed, and the remaining rats were sacrificed after 7 days. The rats were anesthetized using the same general anesthesia procedure mentioned earlier. Following the sacrifice procedure, a full-thickness skin biopsy was performed using surgical scissors. The excision border encompassed the wounded area and extended to the surrounding normal skin. The specimens were then placed in 10% formaldehyde for 24 hours for processing and then placed inside conventional paraffin blocks. To prepare the samples for H&E staining, the paraffin-embedded blocks were sliced into 4µm thick pieces and placed on glass slides (14-16)

Statistical analysis:

The statistical analysis approaches to assess and evaluate the present study results were used as follows:

1. **Descriptive statistic:**

a. Mean.
b. Standard deviation.
c. Standard error.
d. Numbers of the sample.
e. Two extreme values (min. and max.) respondents.
f. Graphical presentation by using line charts with markers.

2. **Inferential Statistics:**

a. Paired sample t-test: It was used for the comparison of the variables between the control and experimental groups in each duration.
b. One-way ANOVA test: It was used to compare the variables among the different durations in control and experimental groups.
c. Least Significant Difference test: It was used after the ANOVA test if it is significant to show the difference between two durations.

The following levels of significance in the statistical evaluation were used:

P> 0.05	Non-significant.
0.05 >P> 0.01	Significant.
P< 0.01	Highly significant.

Results

Estimation of wound contraction

Wound closure was calculated according to the following formula:

Wound closure percentage = [(D0-Dd)/D0]*100. Where D0 is the initial wound diameter (1.5 cm). Dd is the wound diameter on measurement day (day 3 or day 7).

On day 3, Wounds in the rosehip oil group were the largest, while those in the control group were the lowest. The rosehip oil group had the largest wound diameter on day 7, whereas the squalane oil group had the lowest, as shown in (Figure 1).

On day 3, the groups did not vary significantly according to the ANOVA test

findings in (Table 1), but on day 7, significant differences were found.
(Table 2) shows that wound diameter was greater significantly in the rosehip oil group compared to the squalane oil group and the combination group on day 7.

Inflammatory cell parameter
An optical microscope equipped with a square grid in the eyepiece was used to analyze tissue samples. Five random fields were selected under 40x magnification, and the number of inflammatory cells in each field was counted to determine the average count
There were significant differences in inflammatory cell counts between the groups on day 3, while on day 7 no significant differences were detected as seen in (Table 3).
The pairwise comparisons indicate that the inflammatory cell count on day 3 was significantly greater in the control group compared to the squalane oil and rosehip oil groups, as shown in (Figure 2).

Epithelial thickness parameter
The epithelial thickness was evaluated by measuring the distance between the topmost layer of the skin (keratin) and the deepest layer of the skin (basal layer of the epidermis) at the wound edges. The measurements were carried out using Image J computer software version 1.54.
Kruskal-Wallis test indicated that the differences in epithelial thickness between the four groups on day 3 were highly significant, while on day 7 there were no significant differences in epithelial thickness, shown in (Table 4).
A significant difference in epithelial thickness on day 3 was detected where the epithelial thickness was significantly greater in the combination group compared to the squalene oil group. The epithelial thickness was also significantly greater in the combination group compared to the Rosehip oil group, as shown in (Figure 3 &4).

Blood vessel count
The counting of blood vessels was conducted using Image J software version 1.54 in conjunction with a light microscope at a magnification of x40. five distinct visual fields per section were analyzed, after which the average values were calculated to determine the count of blood vessels accurately.
There were no significant differences in blood vessel count between the groups on day 3; while on day 7, a highly significant difference was detected as seen in (Table 5).
The blood vessel count in the rosehip oil group was significantly higher than that of the combination and control groups on day 7 as presented in (Figure 5).

Histological finding
Three days duration
I- Control group
Histological pictures show numerous inflammatory cells with blood vessels and newly formed hair follicles, as seen in(Figure 6).
II- Experimental group at three-day duration
Squalane oil application
The histological picture shows the formation of new epithelium with blood vessels and hair follicles, as shown in (Figure 7).
Rosehip oil application
Histological pictures show the migration of keratinocytes and the formation of new epithelium with new blood vessels and adipocytes, as presented in (Figure 8).
Squalene oil and rosehip oil application
Histological pictures show the thickening of the epithelium at the edge of the wound as a sign of mitotic activity; however, there was perfuse bleeding with numerous inflammatory cells and blood vessels, as shown in (Figure 9).

Seven-day duration
I- Control group
Histological pictures show incomplete closure of wound edges and the presence of granulation tissue with numerous inflammatory cells and fibroblasts, as presented in (Figure 10).

II- Experimental group at seven-day duration
a) **S**
Squalane oil application
Histological pictures show some cases with complete closure of the epithelium

and others have yet to close. There are also numerous new blood vessels within the granulation tissue, as seen in (Figure 11).

b)

Rosehip oil application

Histological pictures show the epithelial edges approaching each other with new blood vessels within the granulation tissue, as presented in (Figure 12).

c)

Squalene oil and rosehip oil application

Histological pictures show that most of the specimens have a complete epithelialization closing the surface and newly formed connective tissue with good remodeling of collagen fibers and fibroblasts, as shown in (Figure 13).

Discussion:

The complex healing process is tightly regulated and is necessary for the preservation of along with other skin functions, form the skin's barrier. There are a lot of variables, both adjustable and not, that might affect this process (1).

squalene can be good for tumor prevention (17), slowing down aging (18), and atherosclerotic lesions (19). squalene may be considered a successful natural product with some ability to influence the regulation of immune responses by macrophages primary cells comprising the innate immune system that is principally requested in wound healing. Its usefulness can be evident during the wound healing resolution, where it could help the “last stage remodeling and wound closure” because of its anti-inflammatory properties (20).

Rosehip oil has been demonstrated to shorten epithelialization time and reduce the enhanced collagen remodeling (basket weave meshwork of collagen), angiogenesis, fibroblast proliferation, inflammatory cell infiltration, and collagenation. These factors significantly impacted Rosehip oil's ability to heal wounds and improve the appearance of scars (21).

Traditionally, vitamin C has been attributed to healing as collage synthesis requires it as a co-substratum of hydroxylase enzymes among other activities. Rosehips are rich in vitamin C (262–213 mg/100g) on a dry weight basis (1, 13). **R**

a. Wound contraction

On day 7, the greatest wound contraction was found in the squalene oil group, this may be due to its anti-inflammatory effect, and this agrees with a study conducted by Sánchez-Quesada *et al* (20) recently it was discovered that squalene oil, a natural substance, may regulate the healing of wounds by influencing the innate immune response of macrophages, the primary cells involved in the healing process. Its anti-inflammatory characteristics may make it useful in the later phases of wound healing, when the wound is being modelled and closed.

In our study, the least wound contraction was found in the rosehip oil group as compared to the other groups, this may be due to the late action of rosehip oil as was shown in the study conducted by da Costa Cavalcante *et al* (22) where the effect of rosehip was mostly noticeable after the 14th day of the experiment.

As for the combination group, there may have been an anti-synergic effect of each oil when mixed together as a combination and the effect was almost similar to the control group.

b. Inflammatory cell count

According to the results of this study, it was shown that mean values of the control group had a greater inflammatory cell count than the experimental groups on day 3, but by day 7, there was no meaningful difference.

Similar results were found in a study done to evaluate the anti-inflammatory and wound-healing properties of squalene by Ulrikh and Smolovskaya(23) as they found that squalene appears in order to regulate inflammation by the use of pro- and anti-inflammatory signals, which aid in wound healing, reduce swelling, and protect tissues from damage remodeling after regenerating and that squalene has anti-inflammatory and wound healing effect.

While on day 7 the inflammatory cell count did not vary significantly between the control group and the group that received squalane oil which may be due to the continuous use of the oil at high concentrations.

This coincides with a study done by Ulrikh and Smolovskaya (23) where they found that when its concentration ranges from 10 to 100 μM, it no longer has a therapeutic function and instead produces inflammation (above 100 μM concentration it becomes much more harmful). While they did touch on the topic of squalene's anti-aging benefits, they stressed that "the ratio risk and benefit effect of applying squalene in high concentrations is rather high, consequently it is not recommended for the treatment of skin tissue aging."

As for the use of rosehip oil in this study, it was shown that the oil significantly reduces the inflammatory cell count by day 3 as compared to the control group, Similar results have been obtained in a prior study, where they examined the effect of rosehip oil on excisional wound healing and their histopathological study of the wound sections revealed that the wounds of the control group had a distinct denser infiltration of inflammatory cells compared to the rosehip group on day 2 (21).

It is thought that the underlying mechanism through which rosehip enhances the healing process by influencing the shift to macrophages of the M2 subtype. Inflammation is linked to M1 macrophages, while M2 macrophages help repair the extracellular matrix and bring inflammation under control. The disruption of this transition may cause non-healing or chronic wounds (12).

The Studies on rosehip have identified three significant bioactive fatty acid compounds: a galactolipid, linoleic acid, and α-linolenic acid. These compounds have demonstrated anti-inflammatory properties in research (24).

As for the combination group, the combined action of both oils showed a slight increase of inflammatory cells over the rosehip oil group and a slight decrease compared to the squalane oil group. Nevertheless, still many fewer inflammatory cells compared to the control group.

c. Epithelial thickness

In our study, day 3 showed a notable disparity in epithelial thickness, with considerably thicker epithelial layers in the combination group compared to the squalene oil group and rosehip oil group. Indicating that the epithelialization started earlier in the combination group and the increase in epithelial thickness continued to day 7.

A study was done to evaluate the effect effects of a topical agar-based emulgel scaffold loaded with squalene on the ability of a full-thickness burn model to heal wounds, they came to the conclusion that the squalene-loaded emulgel scaffold-treated group appeared to show the best granular tissue formation rate amongst other controls such as negative control and agar gel and on 12th day studies confirmed that the tissue sections of the squalene-loaded emulgel scaffold-treated revealed the excellent reepithelization activity along with the neovascularization (25).

On the other hand, another study was done to assess the healing of incisional surgical wounds in rats following the application of rosehip oil. and they observed that there were no statistical differences between groups at different times as far as the degree of re-epithelialization and the presence of granulation tissue (22).

So, in our study, the effect of both oils combined showed promising results regarding re-epithelialization.

d. Blood vessel count

In our study, there was a slight increase in blood vessel count in the squalane oil group over the course of the wound healing process when compared to the control group. This agrees with a study done to evaluate the effect research on the effects of a squalene-loaded emulgel scaffold on the ability of a burnt rat wound to heal in a full-thickness burn model revealed that, compared to agar gels and a negative control, the rats treated with the squalene-loaded emulgel scaffold exhibited superior reepithelization,

neovascularization, and angiogenic response (25).

As for rosehip oil, there was a significant increase in blood vessel count from day 3 to day 7 when compared to the control group which agrees with a study done by Lei et al.(21) where they discovered that on day 7, wounds treated with rosehip showed more proliferation of fibroblasts, collagen formation, and angiogenesis, while in the control group, only a few capillaries were present.

But unlike the skin, there are several types of wounds that can heal very fast and without or barely noticeable scars. As a starting point, we have prenatal skin damage. It is well-documented that early foetal skin has a scarless healing phenotype, which includes less inflammation and fibrosis. Within the mouth, on the oral mucosa, there is another kind of lesion that heals quickly with little scarring. This area is well-known for its ability to heal quickly and, similar to embryonic skin, to have low inflammation. Alternatively, in contrast to typical adult skin wounds, lesions that heal entirely during pregnancy or in the mouth have less angiogenesis. Inflammation, capillary development, and the establishment of a capillary network are all reduced in wounds that heal more quickly and with fewer scars (26).

Conclusions:

- **Results** obtained in this study showed that the topical application of squalane oil increased wound contraction over time compared to the control groups while the rosehip oil needed more time to show its effect on wound contraction.

-**On** the third day, the control group had a much greater inflammatory cell count than the experimental groups. By the seventh day, however, no such distinction was apparent.

-**Histomorphometric** assessment of epithelial thickness showed a significant difference on day 3 was detected where the epithelial thickness was significantly greater in the combination group compared to the squalene oil group and rosehip oil group indicating there was a synergic effect between the two oils. While on day 7, there was no significant difference between groups.

-**Results** for blood vessel count showed that the highest value was recorded for the combination group on day 3, while on day 7, the highest value was recorded for the rosehip oil group. As for the control group, there was no significant increase in blood vessel count over time.

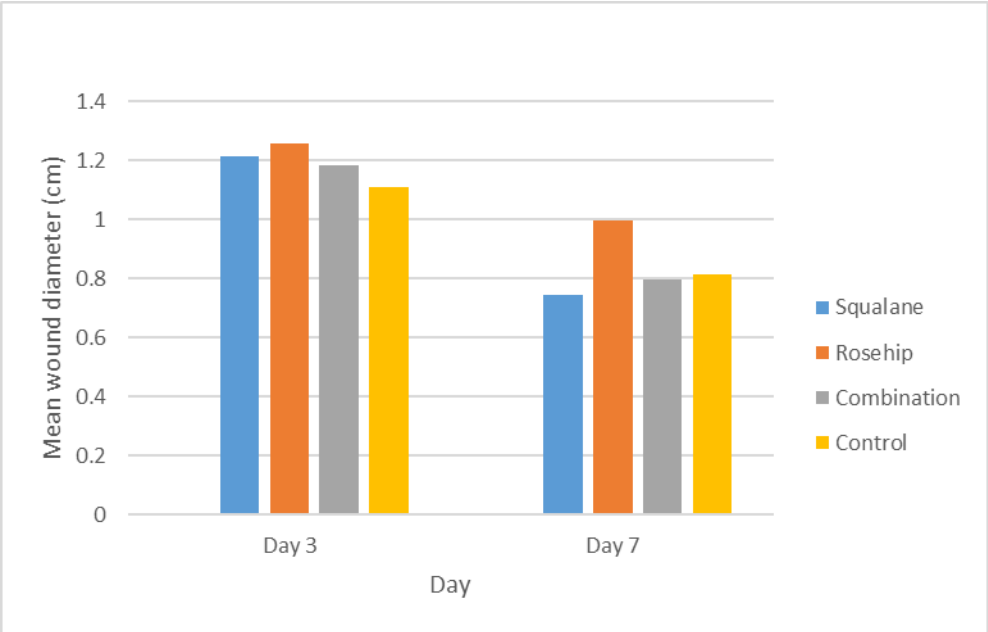

Figure 1: Mean wound diameter values on days 3 and 7.

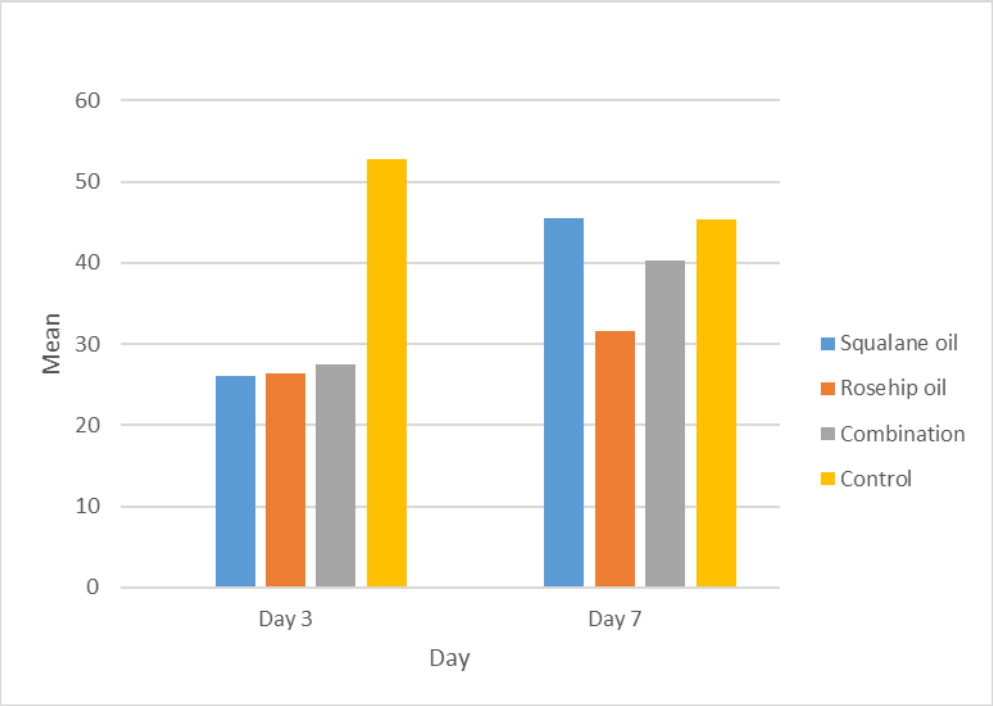

Figure 2: Mean inflammatory cell count for each group and healing period.

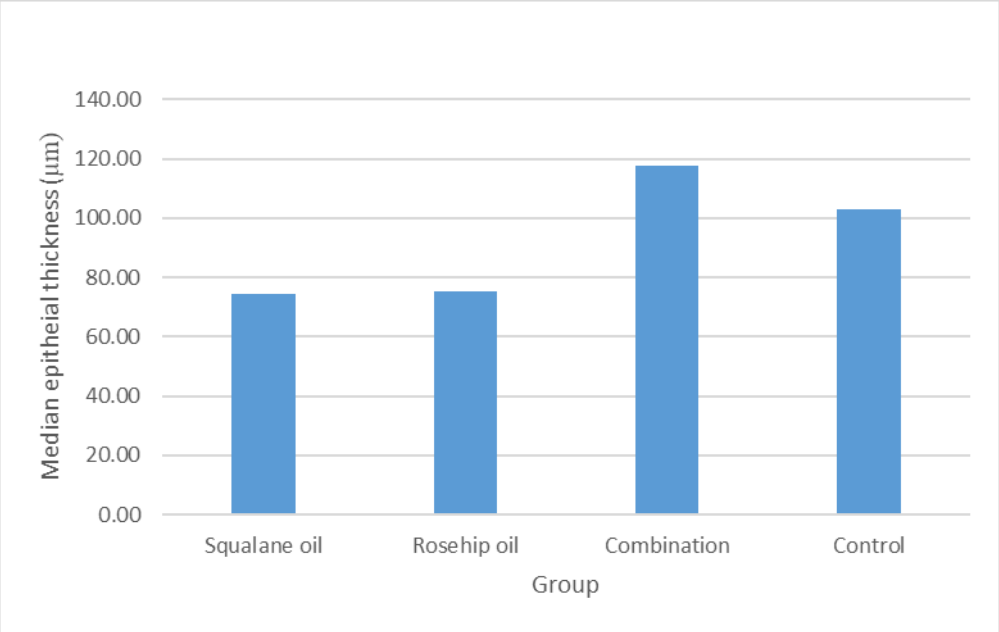

Figure 3: Median epithelial thickness scores on day 3.

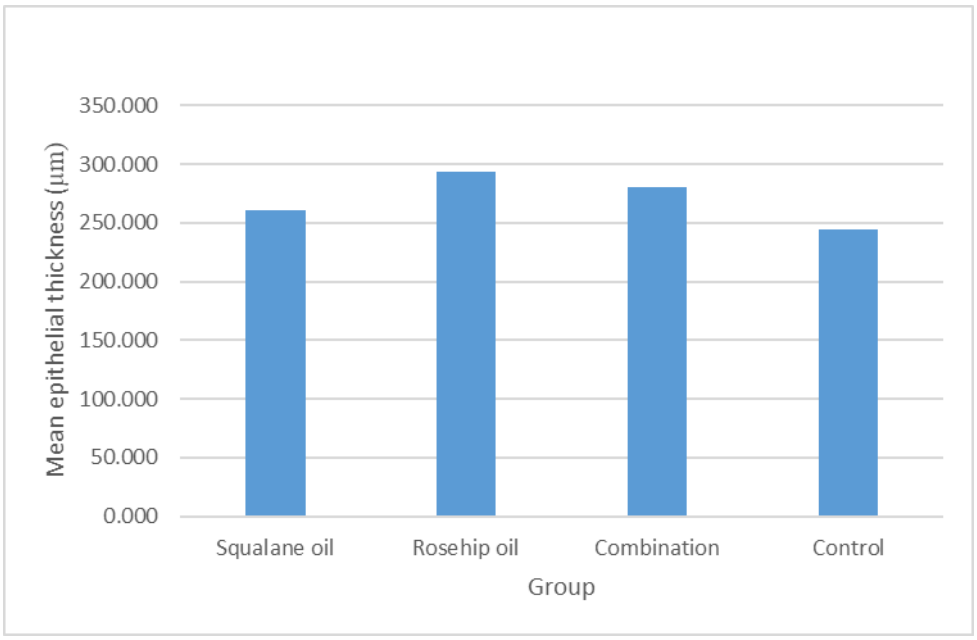

Figure 4: Mean epithelial thickness scores for each group on day 7.

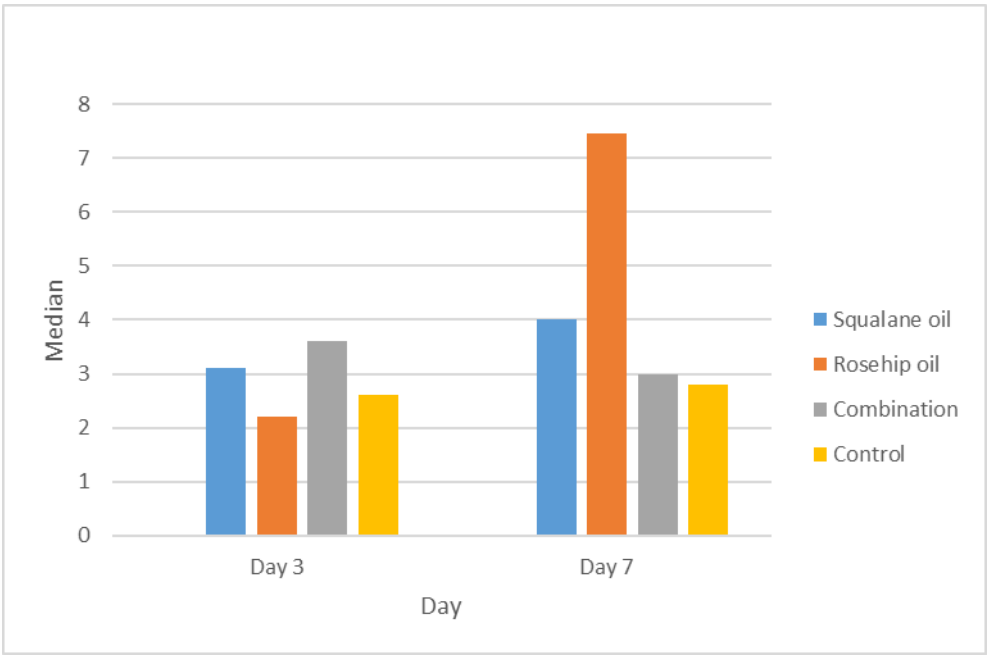

Figure 5: Median values of blood vessel count for each group and healing period.

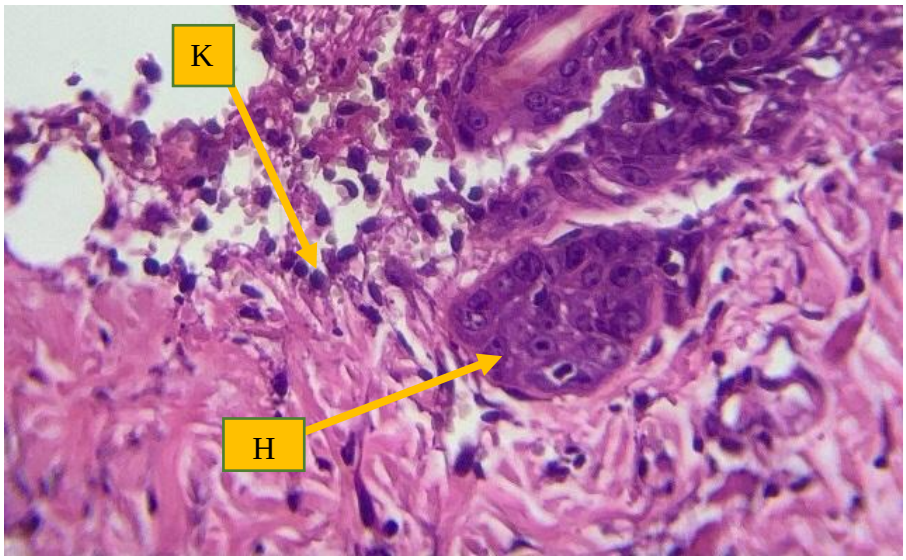

Figure 6: histological picture at the wound edge that shows the migration of keratinocytes (K) and the new hair follicle (HF.)

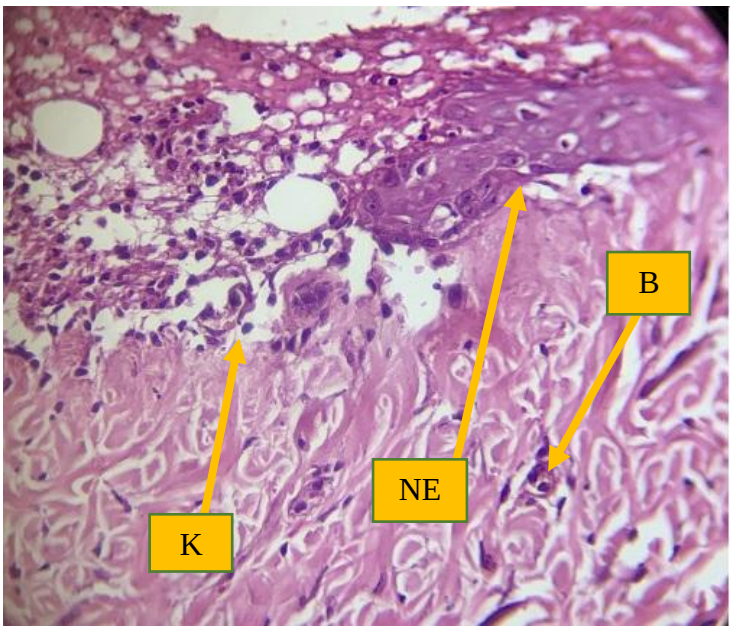

Figure 7: histological picture at the wound edge that shows the formation of new epithelium (NE), the migration of keratinocytes (K), and new blood vessel (BV).

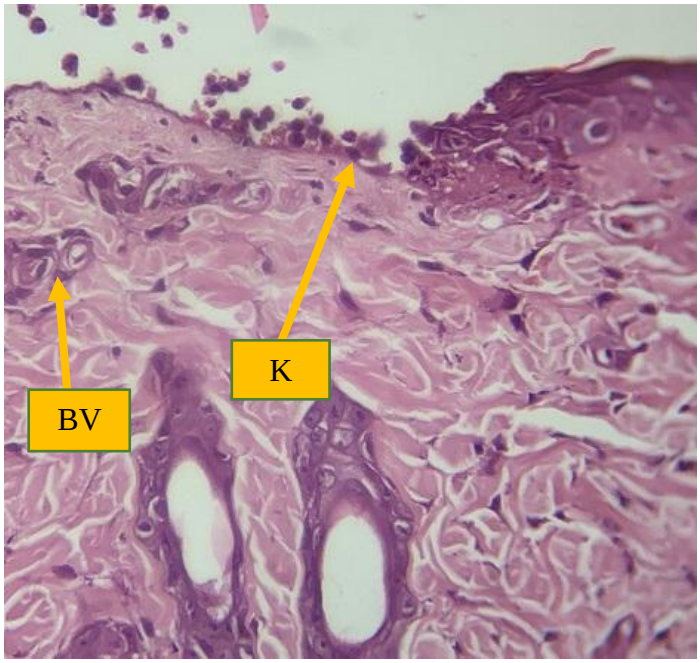

Figure 8: histological picture at wound edge that shows the migration of keratinocytes(K) and new blood vessels (BV).

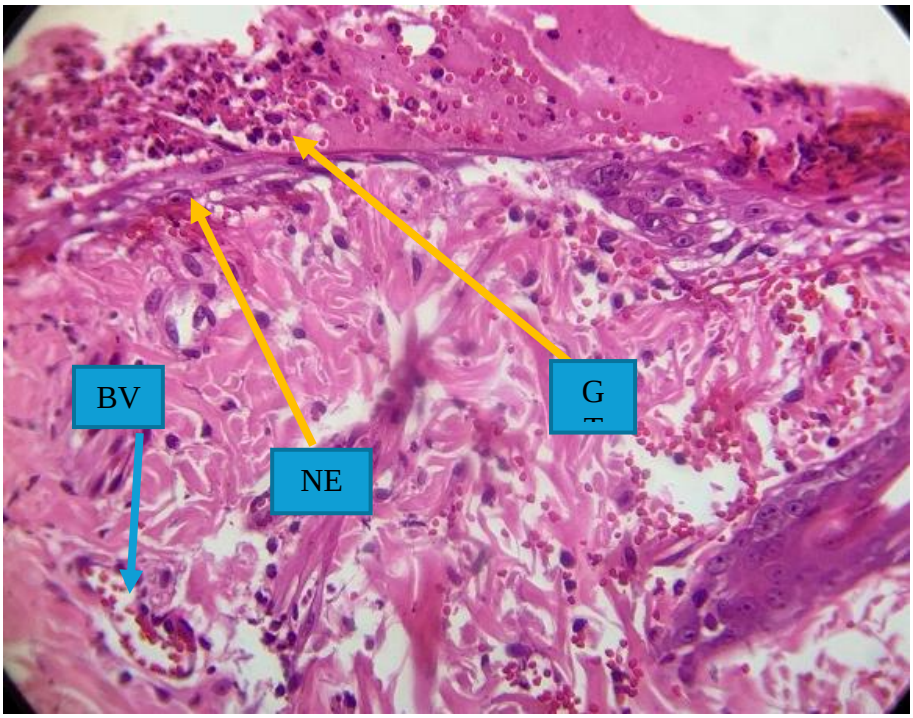

Figure 9: histological picture at the wound edge that shows the formation of new epithelium (NE), granulation tissue (GT), and blood vessels (BV).

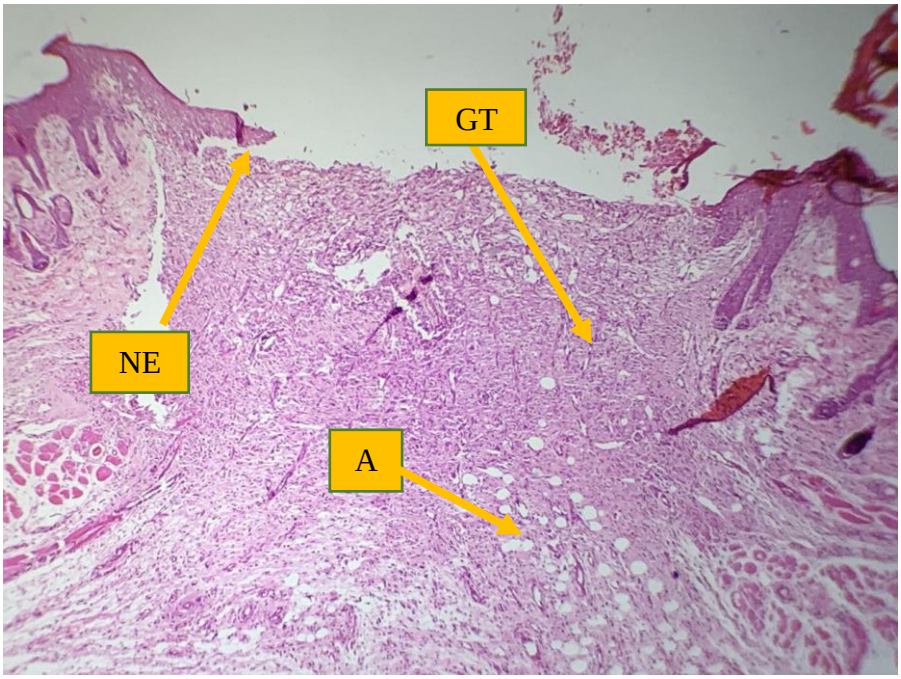

Figure 10: histological picture of the wound that shows the new epithelium (NE), granulation tissue (GT) and adipocytes (A).

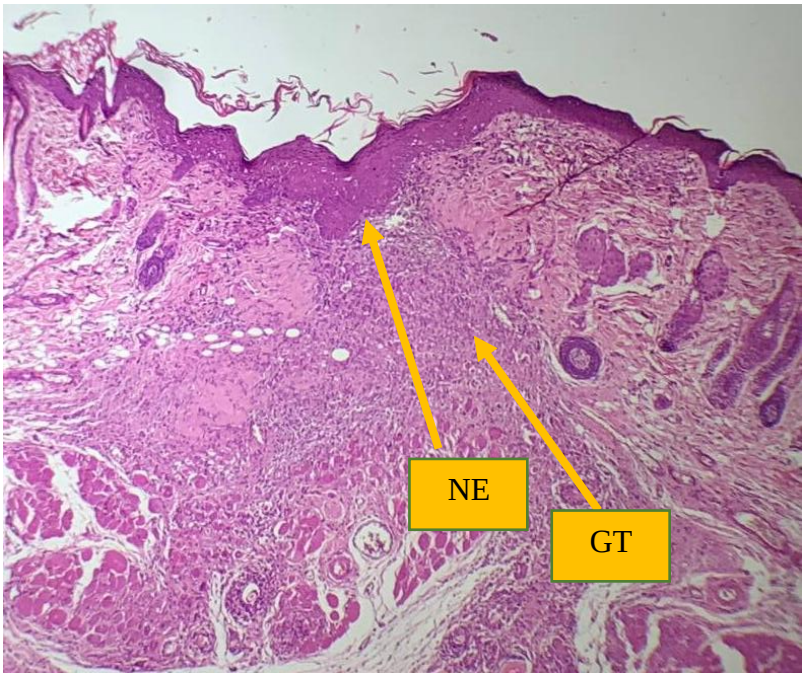

Figure 11: histological picture of the wound at low power that shows complete closure of the epithelial bridge (NE) and the granulation tissue (GT).

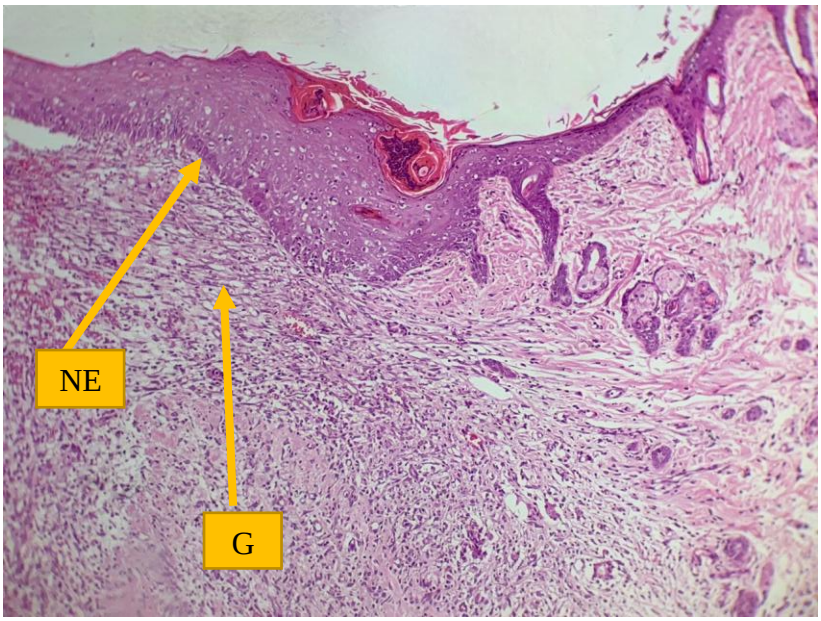

Figure 12: histological picture of the wound showing the new epithelium (NE) covering the granulation tissue (GT)

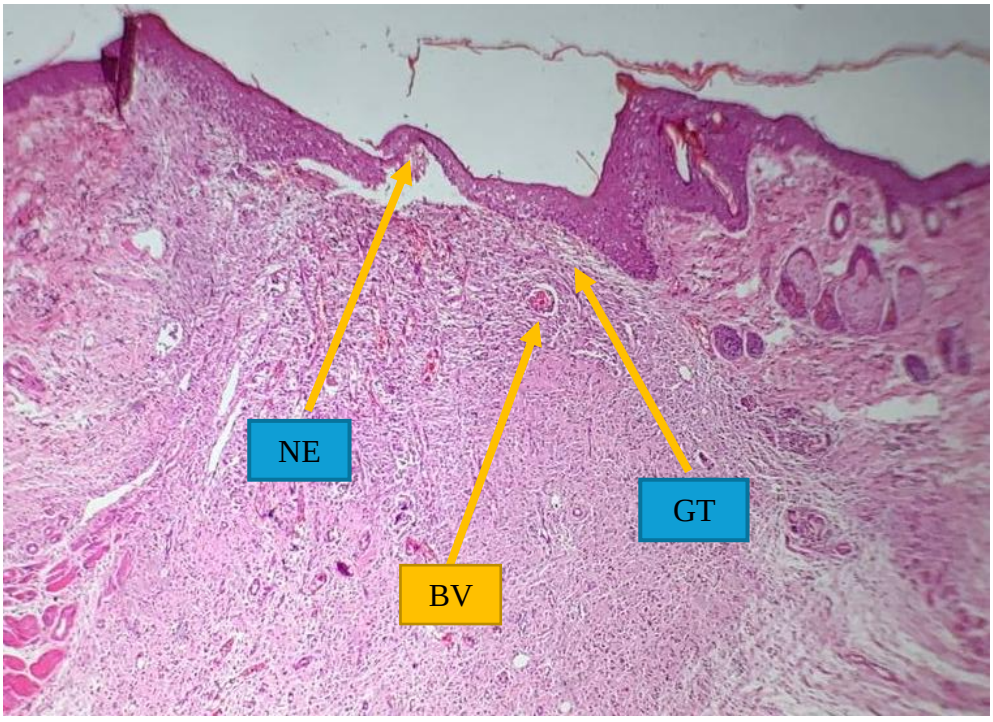

Figure 13: Histological picture of the wound showing the complete epithelialization (NE) covering the granulation tissue (GT) and new blood vessels (BV).

Table 1: Comparison of wound diameter across groups for each healing period

Variable	Group comparison	
	F	*p*-value
Day 3	1.46	0.247
Day 7	6.135	0.004

Table 2: Pairwise comparisons for wound diameter values on day 7.

Pairwise comparison	Mean difference	*p*-value*
Control-squalane oil	0.1119	> 0.99
Control-rosehip oil	-0.1867	0.443
Control-combiation	0.0819	> 0.99
Squalane-rosehip	-0.2986	0.05
Squalane-combination	-0.0300	> 0.99
Rosehip-combination	0.2686	0.013

*The *p*-value was adjusted by the Bonferroni correction of multiple comparisons.

Table 3: Comparison of inflammatory cell counts across groups for each healing period by ANOVA test.

Day	Group comparison	
	F	*p*-value
Day 3	3.941	0.02
Day 7	2.330	0.1

Table 4: Comparisons of epithelial thickness across groups for each healing period.

Day	Statistical test	Statistic	*p*-value
Day 3	Kruskal-Wallis	16.24	0.001
Day 7	ANOVA	0.97	0.423

Table 5: Across group comparison of blood vessel count by Kruskal-Wallis test.

Day	Group comparison	
	H	*p*-value
Day 3	2.911	0.405
Day 7	18.985	<0.001

References

1. Almadani YH, Vorstenbosch J, Davison PG, Murphy AM, editors. Wound healing: A comprehensive review. Seminars in plastic surgery; 2021; 35(3);141-144.
2. Nanci A, Wazen RM. Ten Cate's oral histology: repair and regeneration of oral tissue. Elsevier health sciences. 2018;9:320-244.
3. Singer AJ, Clark RA. Cutaneous wound healing. New England journal of medicine. 1999;341(10):738-46.
4. Sharma A, Khanna S, Kaur G, Singh I. Medicinal plants and their components for wound healing applications. Future Journal of Pharmaceutical Sciences. 2021;7(1):1-13.

5. Hasan AA, Majid OW. The Impact of Aloe Vera Gel on Healing of Surgically Made Maxillary Mucosal Wounds in Rabbits. Tikrit Journal for Dental Sciences. 2021;9:137-46.
6. Almadani YH, Vorstenbosch J, Davison PG, Murphy AM, editors. Healing, Inflammation, and Fibrosis: Wound Healing: A Comprehensive Review. Seminars in Plastic Surgery; 2021:35(3):141-144.
7. Wang P-H, Huang B-S, Horng H-C, Yeh C-C, Chen Y-J. Wound healing. journal of the chinse medical association. 2018;81(2):94-101.
8. Micera M, Botto A, Geddo F, Antoniotti S, Bertea CM, Levi R, et al. Squalene: More than a step toward sterols. Antioxidants. 2020;9(8):688.
9. Oliveira AL, Valente D, Moreira HR, Pintado M, Costa PJC. Effect of squalane-based emulsion on polyphenols skin penetration: Ex vivo skin study. Colloids Surfaces B: Biointerfaces. 2022;218:112779.

10. Reddy LH, Couvreur P. Squalene: A natural triterpene for use in disease management and therapy. Advanced drug delivery reviews. 2009;61(15):1412-26.
11. Popa O, Băbeanu NE, Popa I, Niță S, Dinu-Pârvu CE. Methods for obtaining and determination of squalene from natural sources. BioMed research international. 2015;2015:367202.
12. Belkhelladi M, Bougrine A. Rosehip extract and wound healing: A review. Journal of Cosmetic Dermatology. 2024;23(1):62-7.

13. Kiralan M, Yildirim G. Rosehip (Rosa canina L.) oil. Fruit Oils: Chemistry and Functionality. 2019:803-14.

14. Suvarna KS, Layton C, Bancroft JD. Bancroft's theory and practice of histological techniques E-Book: Elsevier health sciences; 2018.
15. Hadi RJ, AL-Ghaban NMH, A.Fadhil A. Immunohistochemical Localization of Substance P in Pulp Tissue After In-Office Bleaching Technique in Rats. Tikrit Journal for Dental Sciences.. 2022;10:160-6.
16. Hadi RJ, Kamil NB, AL-Ghaban NM, Ghani BA, Izzat AW. Vascular Endothelial Growth Factor Expression in Pulp Regeneration Treated By Hyaluronic Acid Gel in Rabbits. Iraqi Journal of Pharmaceutical Sciences. 2023;32(3):156-64.

17. Warleta F, Campos M, Allouche Y, Sánchez-Quesada C, Ruiz-Mora J, Beltrán G, et al. Squalene protects against oxidative DNA damage in MCF10A human mammary epithelial cells but not in MCF7 and MDA-MB-231 human breast cancer cells. Food and chemical toxicology. 2010;48(4):1092-100.

18. Kim S-K, Karadeniz FJAif. Biological importance and applications of squalene and squalane. Advances in food and nutrition research. 2012;65:223-33.

19. Guillén N, Acín S, Navarro MA, Perona JS, Arbonés-Mainar JM, Arnal C, et al. Squalene in a sex-dependent manner modulates atherosclerotic lesion which correlates with hepatic fat content in apoE-knockout male mice. Atherosclerosis. 2008;197(1):72-83.
20. Sánchez-Quesada C, López-Biedma A, Toledo E, Gaforio JJ. Squalene stimulates a key innate immune cell to foster wound healing and tissue repair. Evidence-based Complementary and Alternative Medicine: eCAM. 2018;2018(1).
21. Lei Z, Cao Z, Yang Z, Ao M, Jin W, Yu L. Rosehip oil promotes excisional wound healing by accelerating the phenotypic transition of macrophages. Planta Medica. 2019;85(07):563-9.
22. da Costa Cavalcante LC, Pessôa TCP, Júnior RFGR, Yasojima EY, Soares RHdFC, Brito MVH, et al. Healing incisional surgical wounds using Rose Hip oil in rats. International Archives of Medicine. 2017;10.

23. ULRIKH EV, SMOLOVSKAYA OV. Evaluation of anti-inflammatory and wound healing properties of Squalene: An important phytochemical component of amaranth oil. International Journal of Chemical and Biochemical Science. 2022;21:54-60.

24. Winther K, Sophie Vinther Hansen A, Campbell-Tofte J. Bioactive ingredients of rose hips (Rosa canina L) with special reference to antioxidative and anti-inflammatory properties: in vitro studies. Botanics: Targets and Therapy. 2016:11-23.

25. Shanmugarajan T, Selvan NK, Uppuluri VNVA. Development and characterization of squalene-loaded topical agar-based emulgel scaffold: wound healing potential in full-thickness burn model. The International Journal of Lower Extremity Wounds. 2021;20(4):364-73.
26. DiPietro LA. Angiogenesis and wound repair: when enough is enough. Journal of Leucocyte Biology. 2016;100(5):979-84.