

Comparative Effects of Phenolic Extract As an Ointment Dosage Form in Inducing Wound Healing in Mice and β -sitosterol in Experimentally Induced Acute Wound Healing in Mice

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Abstract

Background: Wound healing is a multi-phase and well-organized dynamic process involving the coordinated use of numerous cell types and biological processes to repair damaged tissue, which relies on many inter-related factors. The failure of traditional healing protocols in many cases of acute wound healing that may progress to gangrene or lead to chronic wounds and amputation provides a strong stimulus to discover a neoteric, relatively long-term, safe, and effective treatment. Antioxidant, anti-inflammatory, and anti-microbial mechanisms are used. As is widely known, plant secondary metabolites such as phenolic compounds, besides their beneficial impact on the plant host, can be effective for humans in treating a variety of disorders. The most common properties of polyphenols—antioxidant, anti-inflammatory, and antimicrobial—indicate that they deserve recognition in natural medicine and may be highly effective in the treatment of various skin problems. Those three mentioned properties constitute the main potential mechanisms of action against various skin disorders.

Aim: To compare the effects of phenolic extract from Iraqi *Petroselinum crispum* to β -sitosterol on wound size reduction, histological outcome, and biomarkers of collagen III, and epidermal growth factor, as well as identify the most likely mechanism of action in experimentally induced acute wounds in mice.

Methodology: Phenolic compounds are extracted from Iraqi *Petroselinum crispum* plants by universal methanol (80%) solvent, followed by fractionation by ethyl acetate to obtain phenolic compounds. The dose of phenolic compound will be (13,22%) w/w of extract and the phenolic extract powder mixed with Vaseline to obtain the ointment. **In vivo study:** Fifty male albino mice were enrolled in this study, and they were divided into five groups (N = 10/group). Group I: served as normal control. Group II served as an induced control, receiving only a petrolatum base (negative control). Mice with induced wounds were treated topically with β -sitosterol ointment (0.25% w/w) as a standard drug (positive control). Group IV and V: mice with induced wounds were treated topically with a phenolic extract of *Petroselinum crispum* ointment (13% and 22%w/w), respectively. These products were applied twice daily for 10 consecutive days.

Results: Phenolic extract ointment produced a highly significant reduction in wound size in comparison with petrolatum base ($P \leq 0.001$).

In this histological study, re-epithelization and angiogenesis scores of all treatment groups showed a significant increase in comparison with the petrolatum base group ($P \leq 0.05$), but in collagen scores, the significant increase just occurred with the highest concentration of phenolic extract ointment (22% w/w) in comparison with the petrolatum base group ($P \leq 0.05$). In cytokine outcome at the end of the experiment, phenolic extract from *Petroselinum crispum* (22% w/w) groups produced a significant increase in epidermal endothelial growth factor. Phenolic extract from *Petroselinum crispum* (22%) produced a significant increase in collagen III in comparison with the β -sitosterol group ($P \leq 0.05$).

Conclusion: According to the present findings, we can conclude that phenolic extract from *Petroselinum crispum* ointment is more efficient than petrolatum base and comparable in efficacy to β -sitosterol ointment in accelerating wound healing.

Keywords: Attention, concentration, referee.

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INTRODUCTION

Wound healing is a crucial homeostatic mechanism that entails several coordinated and multi-phase processes, such as (1) the processes of hemostasis, inflammation, proliferation, and remodeling (2,3). Tissue damage occurs during acute inflammation, which is afterwards resolved. Whereas with chronic inflammation, damage and repair occur over an extended period of time. (4). Neutrophils, an example of an inflammatory cell, phagocyte invading pathogens, remove waste and debris, and also promote angiogenesis, which may accelerate the recruitment of inflammatory cells and the subsequent laying down of extracellular matrix to repair tissue injury. (5). Long-lasting inflammation may cause tissue injury, and aberrant or insufficient healing may result in fibrosis and poorly ordered matrix deposits that alter the normal architecture of the tissue (6).

Bioactive compounds content and nutritional potential of different

Parsley

(*Petroselinum crispum*) parts

In subtropical and tropical regions, *P. crispum* is a brilliant green annual plant. Leaves are used to flavor cuisine (7). as well as for the treatment of skin disorders (8).

Parsley is a leafy vegetable that is mostly used as a culinary aromatic herb to enhance the overall sensory qualities of foods. Aromatic herbs, including parsley, are high in phytochemicals that have powerful antioxidant, anti-inflammatory, antibacterial, and anticarcinogenic properties (9).

Bioactive compounds content

Vitamin C (ascorbic acid) is one of the most important essential compounds for the human organism. It's specific to exhibit a strong antioxidant activity and has recently become one of the most popular vitamins in human nutrition (10).

Phenols are also important compounds in the development of organoleptic (sensory) characteristics of food, such as those responsible for specific color development and food taste (11).

Toxicity of *Petroselinum crispum*

The toxicity of *P. crispum* and its essential oil have been claimed to be abortifacient. Photodermatitis due to furocoumarins, particularly 55, is responsible for its contact photodermatitis activity in pigs exposed to *P. crispum* (12).

The leaf ethanol extract of *Petroselinum crispum* was mildly hepatotoxic and nephrotoxic at continued oral doses equal to or more than 1000 mg/kg. It was concluded that the extract does not cause any obvious toxicity when used at lower doses, and it is therefore expedient for users to exercise caution in its administration to avoid overdosing. Its use should be avoided in the presence of potential

contraindications such as pregnancy, lithium ingestion as seen in psychiatric patients, warfarin, and opiate therapies. In addition, the plant's source should not be from soil irrigated with waste water (13).

The role of phenolic extract in the healing of wounds

Skin lesions heal faster as a result of the anti-inflammatory, antioxidant, antibacterial, and angiogenic properties of polyphenols. Whether used alone, in conjunction with other treatments, or as phenolic extracts, which are rich in various polyphenols that may have synergistic effects, these substances make up an appealing therapeutic approach for wound healing. Clinical trials are necessary to confirm these findings in humans and to understand the mechanisms behind the actions of these medications. (14)., By over-expressing Nrf2, phenolics improve antioxidant defense and enzyme function in cells and increase collagen formation in fibroblasts. Applying certain extracts topically helps avoid dermal damage. According to these results, phenolic compounds may promote fibroblast activity, hasten healing, and guard against UV-induced photoaging. protection. (15).

The effects of phenolic extract on inflammation

The inflammatory reaction starts happening right away after the damage. By triggering a local inflammatory response that attracts diverse inflammatory cell types to the site of the wound, the innate immune system is triggered. (16).The potent antioxidant effects of phenolic compounds are mediated by scavenging free radicals like ROS, suppressing the formation of ROS by inhibiting specific enzymes or chelating trace minerals required for their production, and finally by up-regulating or protecting the antioxidant defense system (17).

The effect of phenol on fibroblasts

Plants are abundant sources of a wide variety of compounds, many of which are metabolically active. The phenolics are a large class of secondary compounds that function, among other things, as powerful reactive oxygen scavengers in cells, including fibroblasts. The synthesis of extracellular matrix elements like collagen and the preservation of connective tissue integrity are both very important functions performed by these ubiquitous dermis residue cells. Chronic wounds or skin exposure to UV radiation impair fibroblast function by producing reactive oxygen species, which have the potential to harm cell components and alter numerous communication pathways. By acting as antioxidants, phenolic chemicals obtained from plants may be able to correct the resultant imbalance. Phenolics are good candidates for eliminating the causes of skin damage, including wounds and aging, and acting as skin care agents (18).

Materials and methods

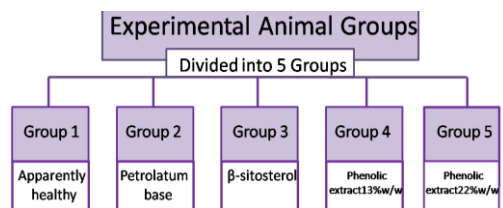
Materials

Phenolic extract powder was purchased from al Razi center for alternative medicine; B-Sitosterol ointment was obtained

from Philadelphia/Jordan; Formalin (MW=30.3) was provided by SOLVOCHEM/UK; castor oil was obtained from Jayant Agro-organics LTD, India; and petrolatum base was provided by Regent chemicals, India.

Preparation of topical phenolic extract ointment from *Petroselinum crispum*

Since petroselinum is not available in a topical dosage form, I buy from the market 1 kelo of fresh petroselinum crispum and then wait for it to dry (the aerial part). Then I blend it in a blender machine to get a powder of about 200g. It was defatted with hexane (1400 ml). The defatted plant material was further extracted with ethanol (1500 ml) using a soxhlet extractor. The ethanolic extract was concentrated by evaporation under reduced pressure using a rotary evaporator. Then distilled water (35ml) was added to the ethanol extract and the extract portion with ethyl acetate (50 ml) was allowed to stand over night. The phenolic compounds were extracted from the *Petroselinum crispum* plant. The extraction by universal methanol (80%) solvent was followed by fractionation by ethyl acetate to obtain phenolic compound powder. Afterwards, the powder was mixed well with petrolatum base by the incorporation method to achieve the required weight of 100 gm. In the incorporation method, a small amount of petrolatum base was mixed carefully with a small volume of phenol powder for about 5 minutes until a clear, homogenized ointment was obtained. The prepared phenolic extract ointment was then transferred into clean and sterile plastic cups, which were closed tightly and stored at normal room temperature.



Experimental animal groups

Fifty mice were involved in the experiment. Each group contained ten mice, which were selected randomly from the total number of mice involved in the experiment, as illustrated in Figure 1.



Figure 1. Experimental Animal Groups

model of a murine wound

Mice were anesthetized by intraperitoneal injection of "ketamine (100mg/kg)" and "xylazine (10mg/kg)". Afterwards, the back-skin hair was shaved using shaving cream, and a 1-cm full-thickness excisional wound was then made on the back of each mouse using a sterile 10-mm biopsy punch (19), as shown in Figure 2.



Figure 2. Experimental Wound induction by punch biopsy

Measurement of Wounds

The wound size areas for 6 mice from each group were randomly selected and measured by a ruler from edge to edge on the 5th and 10th days of the experiment. The difference in wound size reduction between the experimental groups was compared using the following equation:

$$\% \text{ Wound Closure} = (\text{primary wound area} - \text{end wound area}) / 100\% \text{ of the primary wound area}$$

The primary wound area (on day 0) was defined as 1 cm (20). The wounds on the tenth day were carefully dissected by a sharp, sterile surgical blade. Tissues were collected

without folding by forceps, which were stabilized in 10% buffered formalin solution and stocked into a sterile plastic container for storage, ready for embedding in paraffin wax for histopathological and immunological study.

As shown in Table 1, zero-day data revealed no significant differences between each group in wound size reduction (P_a , P_b , and $P_c > 0.05$) respectively.

On the other hand, the data obtained revealed a highly significant reduction in the wound size of the treatment groups as compared with induced control group ($P_a \leq 0.001$), but there were no significant differences in comparisons between the treatment groups (P_b , $P_c > 0.05$) as shown in Table 1.

Table 1: Comparison of wound size reduction in milli meter between induced control and each other treatment groups and among other treatment groups by un paired t-test.

day	Wound reduction %	Vaseline N=6	β -Sitosterol N=6	Phenolic extract from <i>Petroselinm crispum</i> 13 % N=6	Phenolic extract from <i>Petroselinum crispum</i> 22 % N=6
Day0	Mean±SE	0.00 +0.00	0.00 +0.00	0.00 +0.00	0.00 +0.00
	Median	0.00	0.00	0.00	0.00
	P-value <i>a</i>		1.000	1.000	1.000
	P-value <i>b</i>			1.000	1.000
	P-value <i>c</i>				1.000
Day5	Mean±SE	32.00+1.67	48.17+0.79	47.67+0.92	48.17+0.79
	Median	31.50	48.50	48.00	48.50
	P-value <i>a</i>		0.000	0.000	0.000
	P-value <i>b</i>			0.689	1.000
	P-value <i>c</i>				0.689
Day10	Mean±SE	73.50+1.61	97.33 +1.31	97.33 +1.31	97.67 +1.20
	Median	74.00	98.50	98.50	99.00
	P-value <i>a</i>		0.000	0.000	0.000
	P-value <i>b</i>			1.000	0.885
	P-value <i>c</i>				0.885

- Data represented as Mean±Standard error(SE).
- N=number of animals from each group tested per day.
- (a) Comparison between the petrolatum base (vaseline) group and each treatment group, (b) Comparison between β -Sitosterol and both petroselinum crispum (13% and 22% w/w). (c) Comparison between phenolic extracts from Petroselinum crispum (13% and 22% w/w).

Assessment of the histopathological changes of tissue sections. (H & E stains)

were used for the staining of paraffin wax sections (21). The skin histopathological changes for each mouse were scored (22). The amounts of collagen, angiogenesis, and re-epithelization scores were made and evaluated as: 0 = absent or a few, 1 = moderate presence, and 2 = plenty.

Type III Collagen (Col III) ELISA Kit

Type III collagen has been suggested to play a major role in development and wound healing and contributes to the visco elastic properties of most connective tissues. Type III collagen is found co-localized with Type I collagen in tissues, blood vessels, and skin. Type III collagen is a homo trimeric pro collagen comprised of three identical pro $\alpha 1$ (III) chains. Collagen III is important for the development of skin and the cardiovascular system and for maintaining normal physiological functions in adult life. Collagen III has been

used for studies of collagen I fibrillogenesis in normal cardiovascular development. Many of the same properties and functions of animal derived collagens can be duplicated using recombinant human collagens.

Epidermal growth factor ELISA Kit (EGF)

Epidermal growth factor, or EGF, is a growth factor that plays an important role in the regulation of cell growth, proliferation, and differentiation by binding to its receptor EGFR. Human EGF is a 6045-Daprotein with 53 amino acid residues and three intramolecular disulfide bonds. EGF acts by binding with high affinity to the epidermal growth factor receptor (EGFR) on the cell surface and stimulating the intrinsic protein-tyrosine kinase activity of the receptor. EGF results in cellular proliferation, differentiation, and survival. It also has a profound effect on the differentiation of specific cells in vivo and is a potent mitogenic factor for a variety of cultured cells of both ectodermal and mesodermal origins. EGF has strong expression in the kidney, salivary gland, cerebrum, and prostate, moderate expression in the trachea and thyroid; and low expression in bone marrow, heart, spleen, thymus, uterus, and colon. No expression was detected in the adrenal gland, liver, lung, cerebellum, placenta, and small intestine.

Results and discussion

Preparation of topical phenolic extract from petroselinum crispum ointment

Since phenolic extract from petroselinum crispum is not yet

available in a topical dosage form, the challenge of developing a successful semi-solid topical ointment formulation has been more promising than other topical dosage forms, taking into account the properties of the active ingredient (phenol), which is water insoluble, and the attractive properties of the ointment base (petrolatum), including its ability to cover the site of application for a long time, and it will act as a barrier that prevents foreign substances and microorganisms from penetration into the tissue through the wound. In addition, the ointment base increases the hydration of the skin due to its oil nature, which prevents moisture evaporation, leading to an increase in drug penetration (23). Furthermore, the prepared phenolic extract ointment will be in a similar dosage form when compared to the positive control β -sitosterol ointment, since both of them have been used in an ointment dosage form. This will minimize any influence of the dosage form type on the wound healing process.

Wound size reduction:

The data obtained has revealed a highly significant reduction in the wound size of the treatment groups as compared with the induced control group ($P_a \leq 0.001$), but there were no significant differences in comparisons between the treatment groups ($P_b, P_c > 0.05$) as shown in Table 1 and figure 3. This shows how effective phenolic extract ointment is at minimizing wound size and accelerating wound closure. Researchers have found that phenolic compounds, especially flavonoids, are potent antioxidants that outperform carotenoids, vitamin C, and vitamin E. (24).

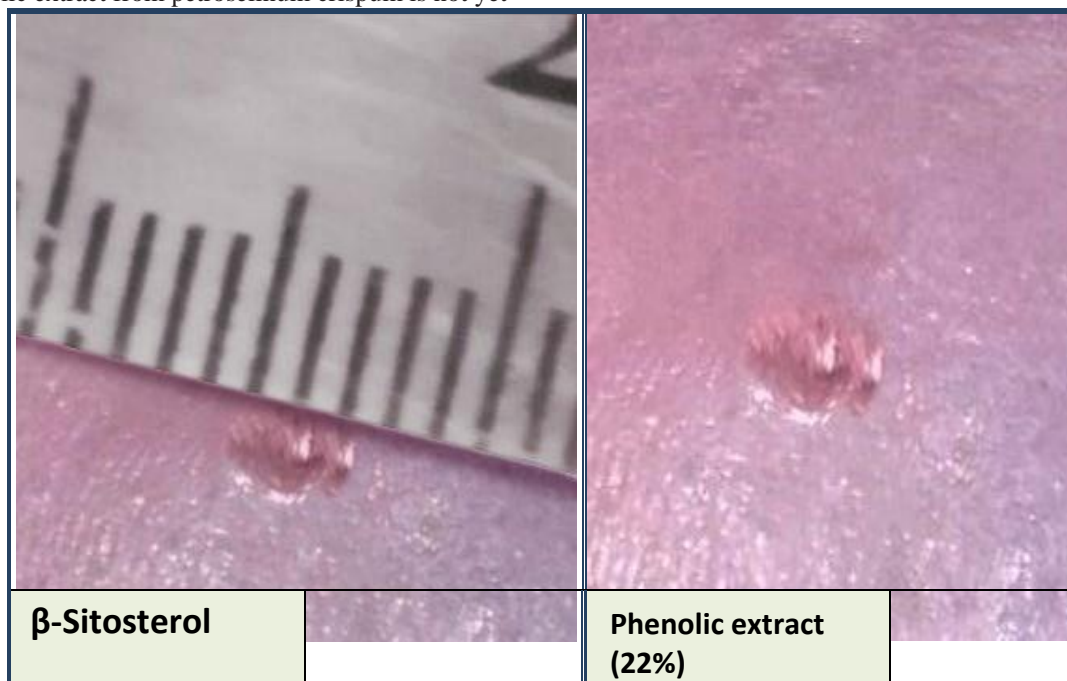


Figure 3: Wound images on the tenth day, showed completely wound closure in treatment groups, but incomplete wound closure in the petrolatum base group.

Histopathological scores on the tenth day

Inflammatory cell infiltration score.

Apparently a healthy group when compared with other groups,

at the tenth-day, the results have shown that there was a significant decrease in the petrolatum base (Vaseline) group ($P_a \leq 0.05$), while, in all treatment groups, there were no

significant differences with the apparently healthy group ($P_a > 0.05$), as illustrated in Table 2. In a comparison of the Vaseline group with each treatment group, on the tenth day, all treatment groups have a significant difference in inflammatory score as compared to the petrolatum base (Vaseline) group ($p_b \leq 0.05$) as demonstrated in Table 2. There were no significant differences in a comparison between the treated groups (P_c and $P_d > 0.05$) on the tenth day as shown in Tables 2.

Table (2): Comparisons of histopathology at tenth day between healthy, induced control, and each other treatment groups and among each treatment group by Mann Whitney test.

Histopathology		Control N=6	Vaseline N=6	β - Sitosterol N=6	Phenolic extract from <i>Petroselinu m crispum</i> 13 %N=6	Phenolic extract from <i>Petroselinu m crispum</i> 22 %N=6
Fibroblasts	Mean±SE	0.00+0.00	1.67+0.21	0.33+0.21	0.83+0.17	0.50 +0.22
	Median	0.00	2.00	0.00	1.00	0.50
	P-value a		0.002	0.394	0.015	0.015
	P-value b			0.009	0.041	0.394
	P-value c				0.180	0.699
	P-value d					0.394
Inflammatory cell	Mean±SE	0.00+0.00	1.67+0.21	0.50 +0.22	0.33+0.21	0.67 +0.21
	Median	0.00	2.00	0.50	0.00	1.00
	P-value a		0.002	0.180	0.394	0.065
	P-value b			0.015	0.009	0.026
	P-value c				0.699	0.699
	P-value d					0.394

- Data represented as Mean±Standard error(SE).
- N=number of animals from each group tested per day.
- (a) Comparison between healthy and all other groups.
- (b) Comparison between petrolatum base and treatment groups.
- (c) Comparison between β -sitosterol and both phenolic extract from petroselinum crispum .
- (d) Comparison between both phenolic extract from petroselinum crispum (13 and 22 % w/w).

In the inflammatory stage, the main aim is the removal of debris, damaged tissue, and bacteria by neutrophils and macrophages, which have a role in anti-microbial defense and debridement of devitalized tissue by the production of proteolytic enzymes and reactive oxygen species (ROS) (25). ROS is produced in high amounts at the site of a wound as a defense mechanism against invading bacteria (26).

Fibroblasts' infiltration score

In a comparison of the apparently healthy skin group with other groups, at the tenth-day Vaseline and both phenolic extract from petroselinum crispum (13 and 22 % w/w) were significantly higher than the apparently healthy ($P_a \leq 0.05$), but β -sitosterol groups showed no significant differences with that group ($P_a > 0.05$) as shown in Table 2.

In a comparison of the Vaseline group with β -sitosterol and both phenolic extract from petroselinum (13 and 22% w/w) groups, on the tenth-day, the results have shown that the Vaseline has significant deference with β -sitosterol and phenolic extract from petroselinum (13 mg) and no significant deference with phenolic extract from petroselinum (22 %).

There were no significant differences in comparisons between β -sitosterol and both phenolic extract from petroselinum (13 and 22%) groups (P_c and $P_d > 0.05$) on the tenth day as shown in Tables 2.

A wide variety of cells make up fibroblasts. There can be a wide range of functions within one organ system. Dermal fibroblasts play distinct roles in different parts of the

integument. The deeper lineage is in charge of ECM production, whereas the surface lineage is involved in the creation of the hair follicle and is in charge of re-epithelization after wound healing (27).

ELISA expression of Collagen III scores on the tenth day

Apparently healthy skin group compared with other groups, at the tenth day, there were significant difference in all groups ($P_a \leq 0.05$). A comparison of β -sitosterol and both phenolic extract from petroselinum (13 and 22 % w/w) with vasaline group, at the tenth day, there were significant difference in both phenolic extract from petroselinum groups ($P_b \leq 0.05$) but no significant difference with β -sitosterol ($P_b > 0.05$). The comparison of β -sitosterol group with both phenolic extract from petroselinum (13 and 22%) w/w groups on the tenth day revealed that there was an insignificant difference in petroselinum (22%) groups ($P_c \leq 0.05$) and no significant difference in phenolic extract from petroselinum (13%) groups ($P_c > 0.05$). In the comparison between phenolic extract from petroselinum (13 and 22% w/w), there was a significant difference in phenolic extract from petroselinum at 22% ($P_d \leq 0.05$).

Type III collagen serves as a foundation for wound healing as well as a matrix for the re-establishment of blood vessels to supply future healing activities (28).

ELISA expression of epidermal growth factor scores on the tenth day

Apparently healthy skin group when compared with other groups. On the tenth day, β -sitosterol and Vaseline and phenolic extract from petroselinum 13 % groups were not significant ($P_a > 0.05$), but there was significant difference in the phenolic extract from petroselinum 22 % group ($P_a \leq 0.05$) as shown in Table 3. A comparison of β -sitosterol and both phenolic extract from petroselinum (13 and 22%) groups with the Vaseline group on the tenth day showed a significant increase in both phenolic extract from petroselinum groups ($P_b \leq 0.05$) but no significant difference in β -sitosterol ($P_b > 0.05$). The comparison between β -sitosterol with both phenolic extract from petroselinum (13 and 22%) groups on the tenth day has revealed that there was an insignificant increase in the petroselinum (22%) group only ($P_c \leq 0.05$) as illustrated in Table 3. In comparison between petroselinum (13 and 22 % w/w), there was significant difference in phenolic extract from petroselinum at 22% ($P_d \leq 0.05$).

EGF is a powerful protein that, when applied to the skin, accelerates healing and increases the rate of skin renewal in aging skin. We are able to produce this protein with a high level of expertise, and the end result is a high-quality product made specifically for skin care applications. This also means that we are able to offer EGF at extremely competitive prices, Accelerates healing of skin and cornea Increases the rate of skin renewal (helping aging skin) and will help slow down skin thinning, which occurs as we age (29).

Table (3) Comparison of cytokines parameters levels on the tenth day between healthy, induced control, and each β -sitosterol and both Phenolic extract from petroselinum crispum (13 and 22% w/w) by Mann Whitney test.

Parameter		Control N=6	Vaseline N=6	β - Sitosterol N=6	Phenolic extract from <i>Petroselinum crispum</i> 13 %N=6	Phenolic extract from <i>Petroselinum crispum</i> 22 %N=6
Collagen	Mean±SE	292.60 +30.2	173.26 +12.61	128.96 +21.4	114.33 +11.03	72.37+5.56
	Median	305.12	175.7	120.69	115.71	75.05
	P-value a		0.004	0.004	0.002	0.002
	P-value b			0.132	0.015	0.002
	P-value c				0.937	0.041
	Pvalue d					0.009
EGF	Mean±SE	169.54 +18.01	137.32 +4.32	118.43+6.80	113.41 +6.11	94.62+3.45
	Median	174.65	139.57	116.15	111.32	97.21
	P-value a		0.065	0.065	0.065	0.026
	P-value b			0.132	0.026	0.002
	P-value c				0.485	0.004
	P-value d					0.015

- Data represented as Mean±Standard error(SE).
- N= number of animals from each group tested per day.

- (a) Comparison between healthy and all other groups.
- (b) Comparison between petrolatum base and β -sitosterol, phenolic extract from petroselinum crispum (13 and 22 % w/w).
- (c) Comparison between β -sitosterol and both petroselinum crispum(13% and 22% w/w) (d) Comparison between phenolic extract from petroselinum crispum 13% and 22% w/w)
- E G F epidermal growth factor, and col III =collagenIII.

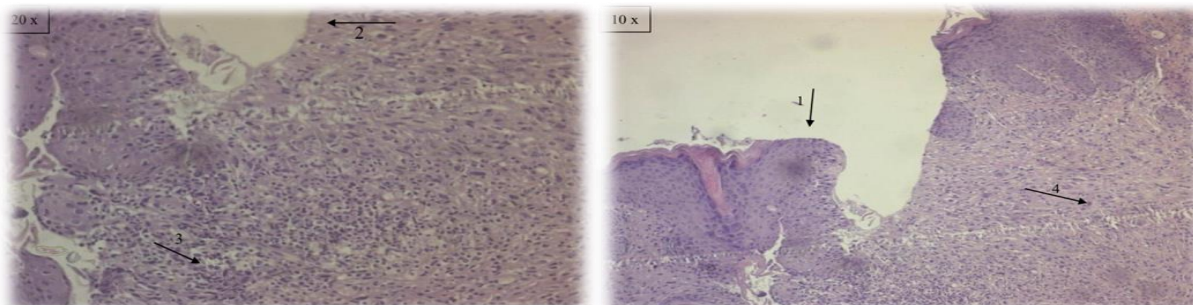


Figure (4A) Cross-section of wound tissue at tenth day for vasaline group; Showed high presence of inflammatory cells and fibroblasts but mild collagen, angiogenesis, and re-epithelization on microscopical examination (H&E staining) (10x) and (20x). 1.Re-epithelialization. 2.Collagen. 3.Inflamatory cell. 4.Fibroblast.

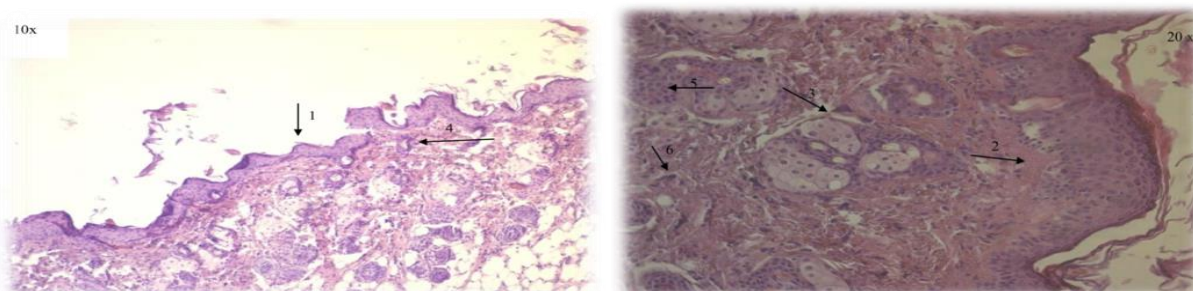


Figure (4B) Cross-section of wound tissue at tenth day for β -sitosterol group; Showed the presence of few inflammatory cells, fibroblasts ,high angiogenesis, collagen and completed re-epithelization on microscopical examination (H&E staining) (10x) and (20x). 1.Re-epithelialization. 2.Collagen. 3.Hair follicle. 4.Blood vessels. 5.Inflamatory cell.6.Fibroblast.

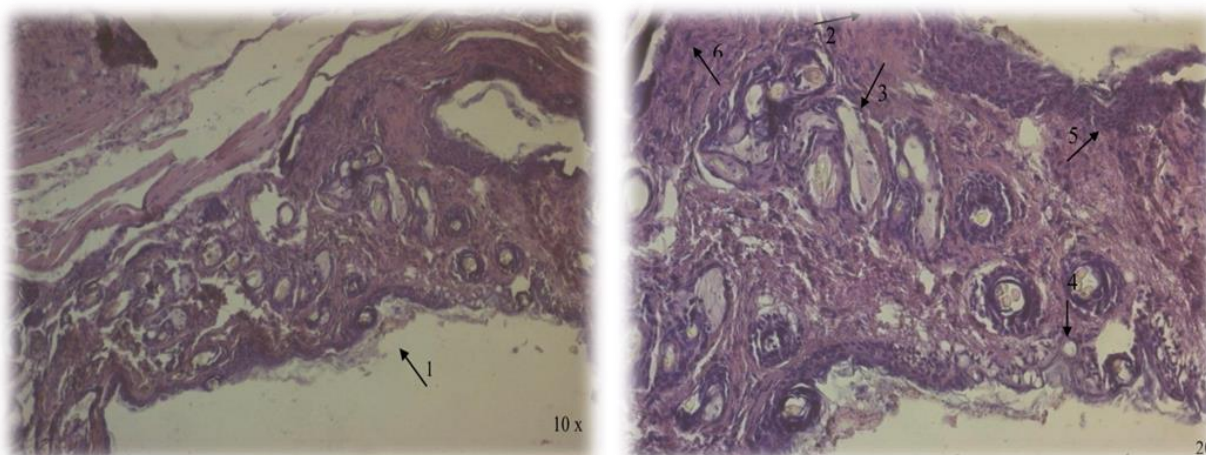


Figure (4C): Cross-section of wound tissue at tenth day for petroselinum crispum 13 % group; Showed the presence of few inflammatory cells, fibroblasts, high angiogenesis, dense collagen and completed re-epithelization on microscopical examination (H&E staining) (10x) and (20x). 1.Re-epithelialization. 2.Collagen. 3.Hair follicle. 4.Blood vessels. 5.Inflamatory cell.6.Fibroblast.

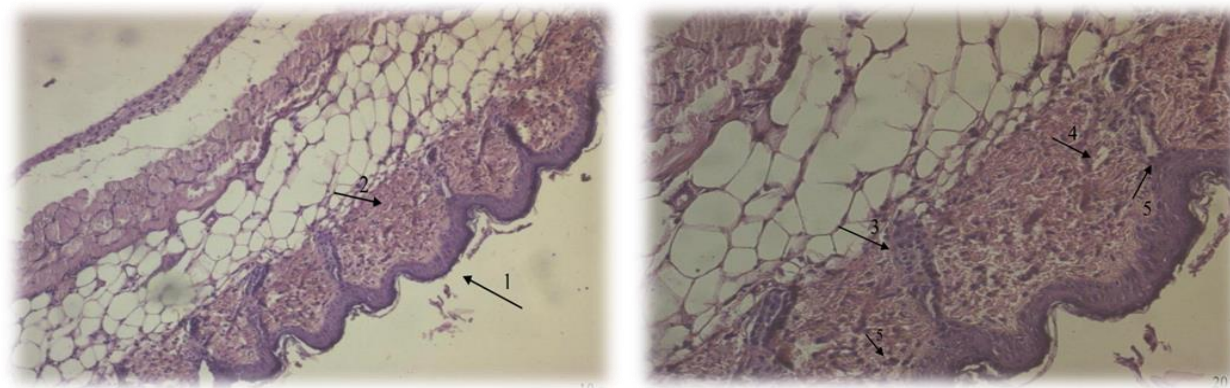


Figure (4D): Cross-section of wound tissue at tenth day for petroselinum crispum 22 % group; Showed the presence of few inflammatory cells, fibroblasts, high angiogenesis, very dense collagen and completed re-epithelization on microscopical examination (H&E staining) (10x) and (20x). 1. Re-epithelialization. 2. Collagen. 3. Hair follicle. 4. Blood vessels. 5. Inflammatory cell. 6. Fibroblast.

CONCLUSION

In all parameter scores that have been measured, topical application of phenolic extract ointment from *Petroselinum crispum* twice daily for 10 days on induced wounds appears to be more effective in accelerating wound healing than petrolatum base and comparable in efficacy to β -sitosterol ointment.

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INTEREST CONFLICT

None

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