Comparative Evaluation of Argan Oil as a Post-Operative Agent Versus Placebo Following Laser Gingival Depigmentation: A Randomized Controlled Clinical Trial

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Abstract

Background: Gingival hyperpigmentation is a common esthetic condition that, although benign, may adversely affect patient self-confidence and smile attractiveness. Laser-assisted gingival depigmentation is widely used due to its precision, minimal invasiveness, and favorable healing profile. Nevertheless, optimization of postoperative wound healing and pain control remains a clinical priority. Prostaglandin E_2 in the post-operative inflammatory response as it is closely related to postoperative pain perception, vasodilation, and consequent tissue inflammation. Argan oil is a natural bioactive substance rich in antioxidants, polyphenols, and unsaturated fatty acids, and has demonstrated anti-inflammatory and wound-healing properties. These characteristics suggest a potential role for argan oil as a postoperative adjunct following periodontal laser procedures.

Materials and Methods: This randomized, parallel-group, single-blind controlled clinical trial evaluated the effect of topical argan oil compared with placebo following laser gingival depigmentation. Forty patients were randomly allocated into two equal groups (n = 20 each). All patients underwent standardized laser depigmentation procedures. Postoperatively, the test group received topical argan oil, while the control group received a placebo formulation. Clinical outcomes included wound healing assessment, pain evaluation at predetermined follow-up intervals, and levels of PGE_2 in the gingival crevicular fluid measured by ELISA. Statistical analysis was performed to compare outcomes between groups. Data were analyzed using IBM SPSS version 27, and statistical significance was set at $p < 0.05$.

Results: Patients treated with topical argan oil demonstrated statistically significantly better wound-healing scores and lower postoperative pain levels compared with the placebo group at the assessed time points. Visual analogue scale (VAS) scores were also significantly lower in the argan oil group, indicating improved patient comfort during the postoperative healing phase. PGE_2 levels in gingival crevicular fluid decreased significantly in patients treated with topical argan oil as compared with the placebo group at all evaluation periods, with a significantly greater reduction in the argan oil group at 1 and 2 weeks.

Conclusion: Within the limitations of this study, topical application of argan oil was associated with improved postoperative wound healing, reduced pain, and lowered inflammatory response as reflected by PGE2 levels following laser gingival depigmentation when compared with placebo. These findings suggest that argan oil may represent a promising

natural adjunct in postoperative periodontal care. Further large-scale, well-designed randomized clinical trials are recommended to confirm these results and establish standardized clinical application protocols.
Trial registration: The trial was approved by the Faculty of Dentistry, Cairo University Ethics Committee (Approval No. 38-10-25)- Clinical trial registration number: NCT073557883
Keywords: Argan oil; Gingival depigmentation; Laser therapy; Postoperative pain; Wound healing.

BACKGROUND

Gingival hyperpigmentation is a multifactorial condition influenced by genetic, physiological, environmental, and pathological factors (KOPPOLU; ALMUTAIRI; YOUSEF; ANSARY *et al.*, 2024). Although clinically benign, its esthetic impact may be considerable, particularly in individuals with a high smile line, where gingival display plays a critical role in smile harmony (GULATI; DUTT; GUPTA; TYAGI, 2016). A clear understanding of the esthetic implications of gingival pigmentation is essential for appropriate patient counseling and treatment planning (GUL; HAMEED; NAZEER; GHAFOOR *et al.*, 2019).
Various treatment modalities have been proposed for the management of gingival hyperpigmentation (FARID; SHINWARI; KHAN; TANWIR, 2017). Conventional surgical techniques are effective but are often associated with increased postoperative discomfort and longer healing periods (ALTAYEB; HAMADAH; ALHAFFAR; ABDULLAH *et al.*, 2021). In contrast, laser-assisted gingival depigmentation has gained popularity due to its precision, reduced intraoperative bleeding, minimal tissue trauma, and favorable postoperative healing profile, making it a preferred modality in contemporary periodontal esthetic therapy (ALTAYEB; HAMADAH; ALHAFFAR; ABDULLAH *et al.*, 2021)
Despite these advantages, postoperative discomfort and wound healing remain relevant clinical concerns following laser procedures. Adjunctive therapies aimed at enhancing tissue repair and reducing postoperative pain may therefore improve patient experience and treatment outcomes (ALTAYEB; LUK; ARNABAT-DOMINGUEZ; ABDULLAH *et al.*, 2025).
Argan oil is a natural product derived from *Argania spinosa* kernels and is rich in bioactive compounds, including tocopherols, polyphenols, sterols, and unsaturated fatty acids. These components have been shown to exert antioxidant, anti-inflammatory, antimicrobial, and wound-healing effects. Such properties support its potential use as a topical adjunct in oral and periodontal wound management (RABBAA; BOUCHAB; LAAZIOUEZ; LIMAMI *et al.*, 2025)
Prostaglandin E2 (PGE2) is a key mediator of pain and inflammation in periodontal tissues. It induces vasodilation, promotes edema formation, and sensitizes peripheral nociceptors, thereby contributing to postoperative discomfort. Clinical periodontal studies have shown that PGE2 levels are elevated in inflamed gingival tissues and decline following successful periodontal therapy (CHENG; HUI *et al.*, 2021). Beyond pain generation, prostaglandins also influence the wound-healing microenvironment through interactions with cytokines, fibroblasts, and local vascular responses. Laser irradiation has been reported to activate cyclooxygenase pathways in gingival fibroblasts, potentially increasing prostaglandin production and amplifying inflammatory signaling (KUMAR; REDDY; BABU; KUMAR *et al.*, 2013). Consequently, topical agents capable of reducing oxidative stress and modulating

inflammatory mediator release may enhance healing quality and postoperative comfort (GAUTAM; SUSHAMA; ASHANK *et al.*, 2017)

While argan oil has been investigated in dermatologic and experimental wound-healing contexts, clinical evidence regarding its use in oral surgical procedures remains limited. The present study was therefore designed to evaluate the effect of topical argan oil on postoperative wound healing and pain following laser gingival depigmentation.

MATERIALS AND METHODS

Study Design

This study was designed as a randomized, parallel-group, single-blind controlled clinical trial to evaluate the effect of topical argan oil compared with placebo following laser gingival depigmentation.

Sample Size and Sampling Process

Sample size calculation was based on data reported by (FOUDA; SEIFALLAH; ELDESSOUKY; BISSAR, 2024). Assuming a mean difference of 0.30, a statistical power of 80%, and a significance level of 5%, the required sample size was estimated to be 40 participants, with 20 patients allocated to each group.

Participants were recruited using a convenience sampling method from patients attending the outpatient clinics of the Faculty of Dentistry, Cairo University, and were screened for eligibility according to predefined inclusion and exclusion criteria.

Participants:

Inclusion criteria:

- Patients aged 18–40 years
- Presence of moderate to severe physiological gingival pigmentation
- Good general and periodontal health

Exclusion criteria:

- Systemic diseases affecting healing (e.g., uncontrolled diabetes).
- Smokers or tobacco chewers.
- Pregnant/lactating women.
- Previous depigmentation procedures in the last 2 years.

Outcome:

Outcome Measures

Primary outcome:

- Postoperative wound healing (FOUDA; SEIFALLAH; ELDESSOUKY; BISSAR, 2024)

Secondary outcomes:

- Patient-reported VAS scores
- Prostaglandin E2 (PGE_2) level in the gingival crevicular fluid (GCF)

Methods:

Test Methods: Preparation of the Argan Oil Formulation

Purified argan oil was combined with natural beeswax to obtain a topical formulation suitable for clinical use. Five grams of pure medical-grade beeswax were added to 100 mL of argan oil. The mixture was gently heated to allow uniform dispersion of the beeswax and then cooled gradually to achieve a homogeneous topical preparation (RABBAA; BOUCHAB; LAAZIOUEZ; LIMAMI *et al.*, 2025).

Surgical Procedure

All patients underwent laser gingival depigmentation using a diode laser[1] (wavelength 810–980 nm) in continuous mode, with a power setting of 1.5–2 W and a 400-μm initiated fiber tip. All procedures were performed by a single calibrated periodontist.

Postoperative Protocol

- Test group: Topical argan oil applied twice daily for 14 days using a sterile cotton swab.
- Control group: Placebo formulation consisting of normal saline applied using the same protocol.

All patients received standardized postoperative instructions, which included rinsing with chlorohexidine 0.12% twice a day for one week. The application of 5mm oil was twice a day using a sterile gauze supplied by the surgeon.

Gingival Crevicular Fluid Analysis for PGE2

- To assess the inflammatory response during healing, prostaglandin E2 (PGE2) levels were measured in gingival crevicular fluid (GCF) from both groups.
- Timing of GCF Collection
- Since PGE2 indicates the inflammatory response and can detect changes in the early as well as medium-term following laser treatment, GCF was obtained at these time points:

- Baseline (before laser depigmentation).
- 7 days after treatment.
- 14 days after treatment.

Gingival Crevicular Fluid Sampling Procedure

- Under standardized conditions, GCF samples were obtained from the treated gingival sites. To minimize saliva contamination, the sampling area was gently isolated with cotton rolls and carefully air dried. Supragingival plaque, if any were present, was removed without inducing bleeding. Standardized absorbent paper strips were then gently inserted into the selected site in the gingival crevice or sulcus until light resistance was felt and left for a defined time. Blood- or saliva-smeared strips were tossed and replaced.
- The strips were transferred directly into labeled sterile microtubes after collection and frozen at −80°C until biochemical analysis (KADAYIF; TAŞÇI; KARADUMAN,2025).

Biochemical Analysis of PGE2

PGE_2 levels in GCF samples were measured according to the manufacturer's instructions using a commercial enzyme-linked immunosorbent assay (ELISA) kit. The assay relied on a competitive binding principle, in which PGE2 in the sample competed with a constant amount of enzyme-labeled PGE2 for binding sites on a monoclonal antibody adsorbed to the microplate. After incubation and washing, the substrate solution was added to the wells, and the optical density was measured at 450 nm using a microplate reader. The color intensity was inversely correlated with the concentration of PGE_2 in the sample. PGE_2 levels were determined from the standard calibration curve and reported as described in the assay protocol. The results were expressed as pg/μL (KUMAR; REDDY; BABU; KUMAR *et al.*, 2013).

[1] Woodpecker, woodpecker limited China.

Blinding

This study was conducted as a single-blind trial, in which outcome assessors were blinded to group allocation. The argan oil and placebo formulations were dispensed in identical amber containers to minimize patient awareness of treatment assignment.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics version 27.0 (IBMCORP IBM, 2017 USA). Quantitative variables were tested for normality using the Shapiro–Wilk test. Normally distributed data were analyzed using Student's *t*-test, while non-normally distributed data were analyzed using the Mann–Whitney *U* test. Friedman and Wilcoxon signed-rank tests were used for repeated measures where appropriate. Statistical significance was set at $p \leq 0.05$.

Results:

Forty patients completed the study, with 20 participants in each group. Demographic characteristics were comparable between groups.

Demographic Data :

The two study groups were comparable with respect to demographic and clinical baseline characteristics. No statistically significant differences were observed between the argan oil and placebo groups in terms of gender distribution ($p = 0.204$), age ($p = 0.158$), medical history ($p = 0.411$), smoking status, or dental history ($p = 0.604$). These findings indicate that the study groups were well matched at baseline.

Table (1): Comparison between the two studied groups according to demographic data

	Argan (n = 20)	**Placebo (n = 20)**	**Test of Sig.**	**p**
Gender				
Male	7 (35.0%)	11(55.0%)	χ^2= 1.616	0.204
Female	13 (65.0%)	9 (45.0%)		
Age (years)				
Min. – Max.	14.0 – 42.0	19.0 – 41.0	t= 1.440	0.158
Mean ± SD.	27.55 ± 8.27	30.90 ± 6.32		
Median	24.5 (21.5 – 35.0)	32.5 (26.5 – 35.5)		
Medical history				
Not reported	2 (10.0%)	0 (0.0%)	χ^2= 2.289	^{MC}p= 0.411
Medically free	16 (80.0%)	16 (80.0%)		

Smoker	2 (10.0%)	4 (20.0%)		
None	3 (18.8%)	5 (31.3%)		
Scaling	2 (12.5%)	3 (18.8%)		
Restoration	0 (0.0%)	2 (12.5%)		
Scaling +restorations	1 (6.3%)	0 (0.0%)	χ^2= 5.181	^{MC}p= 0.604
Ortho	7 (43.8%)	4 (25.0%)		
Ortho referral	1 (6.3%)	0 (0.0%)		
Ortho + scaling	2 (12.5%)	2 (12.5%)		

Wound healing: Wound-healing scores were significantly better in the argan oil group compared with the placebo group at both one week and one month postoperatively ($p < 0.001$). Within-group analysis showed no statistically significant change in wound-healing scores between one week and one month in either group ($p > 0.05$). Table 2 demonstrates wound healing results.

Table (2): Comparison between the two studied groups according to wound healing

Wound healing	**Argan (n = 20)**	**Placebo (n = 20)**	**U**	**p**
1week				
Min. – Max.	1.0 – 2.0	2.0 – 4.0	31.50*	<0.001*
Mean ± SD.	1.35 ± 0.49	2.75 ± 0.79		
Median	1.0 (1.0 – 2.0)	3.0		
1month				
Min. – Max.	1.0 – 2.0	2.0 – 3.0	65.00*	<0.001*

Mean ± SD.	1.65 ± 0.49	2.50 ± 0.51		
Median	2.0 (1.0 – 2.0)	2.50		
Z	1.732	1.232		
p_0	0.083	0.218		

Postoperative pain: Postoperative pain scores were significantly lower in the argan oil group at all assessed time points. VAS scores also demonstrated significantly reduced pain perception among patients receiving argan oil. Table 3 demonstrates VAS scores

Table (3): Comparison between the two studied groups according to pain

Pain	**Day 1**	**Day 3**	**One month**	**Fr**	**p_0**
Argan (n = 20)					
Min. – Max.	1.0 – 3.0	1.0 – 2.0	0.0 – 3.0	18.918*	= <0.001*
Mean ± SD.	1.75 ± 0.55	1.50 ± 0.51	0.65 ± 0.75		
Median	2.0 (1.0 – 2.0)	1.50 (1.0 – 2.0)	1.0 (0.0 – 1.0)		
Sig. bet. period.	p_1=0.385, p_2=<0.001*,p_3=0.006*				
Placebo (n = 20)					
Min. – Max.	5.0 – 9.0	3.0 – 5.0	1.0 – 4.0	39.077*	<0.001*
Mean ± SD.	6.45 ± 1.0	4.05 ± 0.89	2.15 ± 0.74		
Median	7.0 (6.0 – 7.0)	4.0 (3.0 – 5.0)	2.0 (2.0 – 2.53)		
Sig. bet. period.	p_1=0.004*,p_2=<0.001*,p_3=0.001*				
p	=<0.001*	=<0.001*	=<0.001*		

PGE2 Levels in GCF: At baseline, PGE2 levels were comparable between the argan and placebo groups, with no statistically significant difference (U = 187.5, p = 0.664). The mean PGE2 values were 146.80 ± 15.90 pg/mL in the argan group and 149.50 ± 16.80 pg/mL in the placebo group.

At 7 days, a statistically significant reduction in PGE2 levels was observed in both groups compared to baseline (p_0 < 0.001 for both). However, the argan group demonstrated significantly lower PGE2 levels than the placebo group (U = 116.5, p = 0.012), with mean values of 104.90 ± 15.20 pg/mL and 118.80 ± 14.10 pg/mL, respectively.

By 14 days, the reduction in PGE2 levels remained statistically significant within both groups compared to baseline (p_0 < 0.001 for both). Intergroup comparison continued to show significantly lower PGE2 levels in the argan group relative to the placebo group (U = 103.0, p = 0.006), with mean values of 84.60 ± 14.90 pg/mL and 97.90 ± 15.70 pg/mL, respectively. Table 4 demonstrates PGE2 levels in GCF.

Table (4): Comparison between the two studied groups according to PGE2 level in gingival crevicular fluid (pg/mL)

PGE2 (pg/mL)	Argan (n = 20)	Placebo (n = 20)	U	p
Baseline			187.5	0.664
Min. – Max.	118.0 – 178.0	120.0 – 182.0		
Mean ± SD.	146.80 ± 15.90	149.50 ± 16.80		
Median (IQR)	145.0 (135.0–158.0)	148.0 (137.0–161.0)		
7 days			116.5	0.012*
Min. – Max.	78.0 – 136.0	96.0 – 152.0		
Mean ± SD.	104.90 ± 15.20	118.80 ± 14.10		
Median (IQR)	104.0 (94.0–116.0)	119.0 (108.0–129.0)		
Z	3.92*	3.74*		
p0	<0.001*	<0.001*		
14 days			103.0	0.006*
Min. – Max.	58.0 – 115.0	72.0 – 131.0		
Mean ± SD.	84.60 ± 14.90	97.90 ± 15.70		
Median (IQR)	84.0 (74.0–96.0)	97.0 (87.0–109.0)		

PGE2 (pg/mL)	Argan (n = 20)	Placebo (n = 20)	U	p
Z	3.87*	3.81*		
p0	<0.001*	<0.001*		

DISCUSSION

The present randomized controlled clinical trial evaluated the effect of topical argan oil as a postoperative adjunct following laser gingival depigmentation. The findings indicate that the application of argan oil was associated with improved wound-healing outcomes and reduced postoperative pain compared with placebo. To the authors' knowledge, this is the first clinical trial to assess the effect of argan oil intraorally

The two studied groups were comparable with respect to demographic variables, including age, gender, medical history, and dental history, indicating appropriate group matching and minimizing the influence of confounding demographic factors on the outcomes.

The observed improvement in wound-healing outcomes in the argan oil group may be attributed to the biological activity of its constituent compounds, which are known to modulate key phases of tissue repair. This is consistent with (AVSAR; HALICI; AKPINAR; YAYLA *et al.*, 2016) who stated that Tocopherols and polyphenols present in argan oil play a role in reducing oxidative stress at the wound site, thereby limiting excessive inflammatory responses and supporting epithelial regeneration. In addition, (DAğLıOğLU; YAKAN; ERDOğAN; KöKSAL *et al.*, 2024) reported that the high content of unsaturated fatty acids may contribute to stabilization of cell membranes and promotion of extracellular matrix remodeling, which are essential processes in effective wound healing.

The reduction in postoperative pain observed in the argan oil group may similarly be explained by its anti-inflammatory and analgesic properties. This could be explained by the fact that argan oil attenuates inflammatory mediator release and reduces local oxidative damage; argan oil may decrease peripheral nociceptor sensitization during the early healing period (GHARBY; CHARROUF, 2022). Although pain perception is inherently subjective, the consistent reduction in pain and VAS scores across multiple postoperative time points suggests a potential supportive role for argan oil in enhancing patient comfort following laser gingival depigmentation.

The results of this analysis concluded that Argan oil had a statistically significant decreasing effect on Prostaglandin E_2, which is a key player in the recovery process, acting as one of the main mediators of the inflammatory response to cutaneous challenges in post-surgical management, including pain sensation, vasodilation, and local tissue inflammation (KUMAR; REDDY; BABU; KUMAR ET *al.*,2013). These results are in line with previous reports on propolis-based preparations and manuka honey, suggesting that argan oil may have similar healing effects (GONZáLEZ-SERRANO; SERRANO; SANZ; TORRES *et al.*, 2023; GHALWASH; EL-GAWISH; ABOU-BAKR, 2025)

These findings are biologically plausible and consistent with experimental and preclinical evidence demonstrating the antioxidant and anti-inflammatory properties of argan oil. Its rich content of tocopherols, polyphenols, and unsaturated fatty acids may contribute to the modulation of inflammatory responses and support epithelial regeneration, thereby facilitating wound healing and reducing postoperative discomfort (MENNI; BELARBI; MENNI;

BENDIAB *et al.*, 2020). Several recent reviews summarize these protective and reparative properties and propose mechanisms by which argan compounds may accelerate tissue repair (EL KEBBAJ; RIAD *et al.,* 2024)

Argan oil's analgesic and healing effects can be explained by several overlapping mechanisms. Its antioxidant components, particularly phenolic compounds and tocopherols, reduce oxidative damage at the wound site, thereby attenuating inflammatory cascades that contribute to pain and delayed healing (RABBAA; BOUCHAB; LAAZIOUEZ; LIMAMI *et al.*, 2025)

In addition, the unsaturated fatty acids and sterols present in argan oil have been shown to modulate inflammatory mediators and support epithelial regeneration and extracellular matrix remodeling (MANCA; MARIA; LETIZIA *et al.*, 2021). Collectively, these effects may shorten the inflammatory phase, reduce nociceptor sensitization, and promote earlier progression to the proliferative and remodeling phases of healing, which is consistent with the lower pain scores and improved wound healing observed in the Argan group.

Comparable improvements in wound healing and pain reduction have been reported with other natural bioactive agents, such as propolis (GONZáLEZ-SERRANO; SERRANO; SANZ; TORRES *et al.*, 2023) and medical-grade honey (GHALWASH; EL-GAWISH; ABOU-BAKR, 2025), which share similar biological properties. However, clinical evidence supporting argan oil use in oral wound healing remains limited, and direct comparisons with other agents should be interpreted cautiously.

Several limitations should be acknowledged. The relatively modest sample size may limit generalizability, and pain-related outcomes are inherently subjective. Additionally, as this was a single-blind study, the subjects could not be blinded due to the aromatic nature of the argan oil. Future studies employing double-blind designs, objective wound-healing measures, and larger sample sizes are recommended.

CONCLUSIONS

Within the limitations of this randomized controlled trial, topical argan oil application following laser gingival depigmentation was associated with improved wound healing and reduced postoperative pain compared with placebo. These results suggest that argan oil may serve as a promising natural adjunct in postoperative periodontal care. Further well-designed clinical trials are required to confirm these findings and establish standardized clinical protocols.

Declarations

Ethical Committee Approval:

Ethical committee approval was obtained from the Faculty of Dentistry, Cairo University IRB, with approval number 38-10-25.

Consent for publication

Written informed consent was obtained from patients regarding the screening, clinical examination, participation in the study, and taking photos during the trial for publication without revealing their identity. A verbal assent was obtained from participants before doing any step.

Availability of data and materials: Upon request from the corresponding author.

Declaration of interests: The authors declare no conflict of interest.

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