The Efficacy of Aloe Vera Gel in Postprocedural Wound Care after Fractional 1,550 nm Erbium-Doped Fiber Laser

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Objective: To evaluate clinical efficacy and the safety of aloe vera gel in postprocedural wound care after fractional 1,550 nm erbium-doped fiber laser treatment.

Material and Method: Thirty Thai participants with mild to moderate, photoaging skin, categorized by Glogau's classification were enrolled. All participants were treated with fractional 1,550 nm erbium-doped fiber laser. After laser treatment, the participants randomly assigned to apply one side with aloe vera gel and contralateral side with placebo. Clinical erythema score, erythema index, melanin index by Mexameter, transepidermal water loss (TEWL) by Tewameter, and skin capacitance by Corneometer were assessed. The daily self-assessment report for wound recovery and global satisfaction score for treatment were assessed by participants. The present study was followed for five visits, at the baseline, immediately after laser, at day 3, day 7, and day 14.

Results: Aloe vera group had significantly better improvement for clinical erythema score than the placebo at day 3 and day 7 after laser (p-value = 0.005 and 0.011, respectively). Aloe vera group had also significantly lower TEWL than the placebo group at day 7 and day 14 after laser (p-value = 0.03 and 0.04, respectively). Additionally, the aloe vera group had significantly better global satisfaction score than the placebo group at day 7 and day 14 after laser (p-value = 0.03 and 0.04, respectively). Additionally, the aloe vera group had significantly better global satisfaction score than the placebo group at day 7 and day 14 after laser (p-value = 0.05 and 0.05, respectively). However, there was no significant difference between the two groups for erythema index, melanin index, and skin capacitance. Median duration of wound recovery was similar between the two groups (6 days vs. 7 days, p = 0.11).

Conclusion: Aloe vera gel for postprocedural wound care after fractional 1,550 nm erbium-doped fiber laser treatment is effective for the reduction of skin redness and the preservation of TEWL or skin barrier function with better global satisfaction score. Aloe vera gel could be considered as an alternative treatment.

Keywords: Aloe vera, Wound care, Fractional laser, Photothermolysis, Laser resurfacing

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Facial resurfacing with laser is one of the procedures for skin photorejuvenation. Both conventional ablative and fractional photothermolysis laser have been proven for clinical efficacy in photoaging and acne scarring treatment⁽¹⁻³⁾.

Complications after laser treatment are commonly found as prolong skin redness and post-inflammatory hyperpigmentation^(4,5). Therefore, postprocedural wound care is needed to diminish these side effects and improve patient's satisfaction.

Aloe vera has several therapeutic properties such as anti-inflammatory and anti-microbial effects. Aloe vera gel affect by down regulation of proinflammatory cytokines such as Interleukin-1 β (IL-1 β), IL-6, IL-8, Tumor necrotic factor- α (TNF- α), and inhibition of activated macrophages⁽⁶⁾. The compositions of aloe vera gel include mannose-6-phosphate⁽⁷⁾,

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 β -sitosterol⁽⁸⁾, magnesium lactate⁽⁹⁾, and bradykininase enzyme⁽¹⁰⁾ that mainly contains anti-inflammatory effects.

Aloe vera gel promotes wound healing by inhibition of collagenase and matrix metalloproteinases (MMPs) enzymes activity⁽¹¹⁾. A polysaccharide fraction of Aloe barbadensis Miller leaves, is reported for its ability to enhance the proliferation of human fibroblasts in vitro study⁽¹²⁾. Moreover, previous clinical studies demonstrated that aloe vera gel could help promoting wound healing process and had been used for the treatment of burn wound⁽¹³⁻¹⁵⁾.

Concerning anti-microbial effect, aloe vera has been shown for antibacterial⁽¹⁶⁻¹⁸⁾, antifungal⁽¹⁹⁾, and anti-viral activities^(20,21). This compound had an anti-oxidant effect and immune-modulation that enhance the wound healing process^(22,23).

However, the clinical evidence to confirm an efficacy of aloe vera gel for the treatment of post-laser wound care has not been investigated. Hence, the objectives of the present study were to evaluate the efficacy and the safety of aloe vera gel in postprocedural wound care after fractional 1,550 nm erbium-doped fiber laser treatment.

Material and Method *Patients*

The present study was a randomized, doubleblinded, split-face, controlled trial, was approved by the Ethic Committee of Human Research, Srinakharinwirot University. Thirty participants with mild to moderate severity for skin photoaging, classified by Glogau's classification were enrolled. Photoaging with Glogau's classification defines mild severity as mild pigmentary changes, no keratosis with minimal wrinkle and moderate severity as early visible brown spots, and palpable keratosis but not visible and parallel smile lines. Concurrent skin conditions or any underlying diseases that may affect wound healing process were excluded. All of the study participants underwent fractional 1,550 nm erbium-doped fiber laser using Finescan Pulse Pro (TNC Spectronics Co., Ltd., Bangkok, Thailand) with the fluence of 10 milli-Joule (mJ) and the density of 1,500 micro-thermal zone (MTZ)/cm²⁽²⁴⁾ as standard protocol. The study participants were randomly assigned to receive either aloe vera gel treatment on one side of the face and contralateral side with identical placebo gel immediately after laser treatment, and daily application at bedtime. The present study was double-blinded to the study participants and clinical assessors. A compound of aloe vera gel contains 87.40% of inner leaf gel, edetate disodium, bronopol, sodium meta-bisulfite, methylparaben, propylparaben, butylene glycol, carbomers, triethanolamine, and purified water (Burnova Gel manufactured by BeRich (Thailand) Co., Ltd.).

The present study followed clinical outcomes for four visits (at baseline, day 3, day 7, and day 14). Clinical erythema score was assessed by two independent dermatologists and graded as: 0 = none, 1 = slightly redness, 2 = moderately redness, and 3 =strongly redness. Erythema index and melanin index was measured by Mexameter® MX 16 (Courage & Khazaka Electronic GmbH, Germany), transepidermal water loss (TEWL) by Tewameter® TM 300 (Courage & Khazaka Electronic GmbH Germany), and skin capacitance by Corneometer® CM 825 (Courage & Khazaka Electronic GmbH, Germany). Global satisfaction score for wound recovery was evaluated by participants, graded as 0 to 4 points (unsatisfied if score between 0 to 2 points and satisfied if score = 3to 4 points). The daily self-assessment report for

wound recovery was done by comparing the two sides. The duration from the date of laser treatment to time of complete wound recovery was determined. The adverse events were also evaluated.

Statistical analysis

The primary outcome was median duration of wound recovery period (days) between the two groups. From the previous study, the difference in days for median duration of wound recovery period for crusting was 4.1 days and variance of difference was $56.0^{(25)}$. The sample size of 27 patients was required, with 95% confidence interval and 80% power. With a dropout rate of 10%, samples of 30 patients had to be recruited.

Descriptive for demographics and baseline data was reported. The comparison of study measurements between two groups were analyzed by using independent student t-test. Median duration of wound recovery period was analyzed by Kaplan-Meier method and log-rank test. The *p*-value of 0.05 or less was considered as statistical significance. Statistical data analysis using IBM statistical package for the social sciences (SPSS) version 19.0 (SPSS, Chicago, IL, USA) was used.

Results

Thirty Thai participants, 15 male and 15 female were enrolled between September and November 2015. Average age (mean \pm SD) was 34.8 \pm 5.1 years (range 28 to 50 years). There were 63.3% with mild and 36.7% with moderate skin photoaging by Glogau's classification. There were 53.3% with type III and 46.7% with type IV Fitzpatrick's skin type (Table 1).

Aloe vera gel group had statistically significantly better improvement for clinical erythema

Table 1. Dermographics characteristics of participants (n = 30)

(1 20)	
Volunteer characteristics	n (%)
Sex	
Male	15 (50.0)
Female	15 (50.0)
Age (years)	
Mean \pm SD	34.8±5.1
Range	28 to 50
Glogau's classification	
Mild severity	19 (63.3)
Moderate severity	11 (36.7)
Fitzpatrick Skin type	
Type III	16 (53.3)
Type IV	14 (46.7)



Fig. 1 Comparing the clinical erythema score between aloe vera group and placebo group; * $p \le 0.05$.



Fig. 2 Comparing transepidermal water loss (TEWL) between aloe vera group and placebo group; * $p \le 0.05$.



Fig. 3 Comparing the erythema index between aloe vera group and placebo group.

score than the placebo at day 3 and day 7 after laser (p-value = 0.005 and 0.011, respectively). However, there was no significant difference between the groups at day 14 (Fig. 1).

Aloe vera group also had lower TEWL than the placebo at day 7 and day 14 with statistically significant difference (p-value = 0.03 and 0.04, respectively) but did not differ at day 3 (Fig. 2). However, there were





Skin capacitance



group and placebo group.



Fig. 6 The median time to wound recovery between aloe vera group and placebo group.

no significant difference for erythema index, melanin index, and skin capacitance (Fig. 3-5).

The median duration of post-laser wound recovery was six days (interquartile range, IQR = 5 to 9 days) for aloe vera group and a bit longer with seven days (IQR = 4 to 10 days) for the placebo; however, there was no significant difference (log-rank test, p-value = 0.11) (Fig. 6).

Global satisfaction score	Percentage	Percentage of satisfied	
	Aloe vera	Placebo	
Day 3 post laser	60.0	50.0	0.44
Day 7 post laser	80.0	56.6	0.05*
Day 14 post laser	90.0	70.0	0.05*
* <i>p</i> ≤0.05			

 Table 2. Comparing global satisfaction score between aloe vera group and placebo group

Aloe vera group had significantly better satisfaction score than the placebo at 7 and 14 days after laser treatment (p-value = 0.05) (Table 2). No adverse event was reported.

Discussion

Currently, facial resurfacing lasers have been used for the treatment of photoaging skin and importantly for atrophic acne scar. Due to the occurrence of adverse effects such as prolonged erythema, pigmentary changes, infection, and permanent skin scarring from full ablative conventional lasers, the novel of laser technology with fractional photothermolysis eventually has been developed to improve treatment efficacy, reduce side effects, and shorten the period of wound recovery after laser treatment.

The active ingredients of aloe vera extracts contain polysaccharides (mannose-6-phosphate) to promote wound healing and anti-inflammation; glyco-proteins to promote wound healing; anthraquinones (aloin, aloe-emodin) have anti-microbial and anti-oxidant properties; minerals (magnesium lactate), and β -sitosterol to activate anti-inflammatory process. Aloe vera extracts have been used as a traditional herbal medicine for the treatment of burn wound for a long time^(14,15).

Previous studies^(14,15) found that aloe vera gel could improve burn wound process. However, there was lack of evidence to confirm the benefit of aloe vera gel in post-laser wound care setting. The present study demonstrated that aloe vera gel significantly improve clinical erythema of the skin after laser treatment and minimize TEWL, which indicate the restoration of skin barrier function⁽²⁶⁾. Hence, this is the first study to demonstrate the clinical efficacy of aloe vera gel for post-laser wound treatment.

The present study found the median duration of wound recovery in aloe vera group was slightly faster than placebo (6 days vs. 7 days) without significant difference. In contrast to the study of Khorasani et al⁽¹⁴⁾, it was demonstrated that aloe vera gel could shorten the duration of wound recovery period in second degree burn patients. There was no adverse event observed from this research. The negative result for wound recovery effect in the present study may due to a small sample size.

Conclusion

Aloe vera gel for postprocedural wound care after fractional 1,550 nm erbium-doped fiber laser treatment is highly effective for reduction of skin redness and restoration of TEWL or skin barrier function with better global satisfaction score and safety profile. Aloe vera gel could be considered as an alternative treatment.

What is already known on this topic?

Aloe vera has been used as a traditional herbal medicine for the treatment of burn wounds for a long time. Several demonstrations have appeared in many years covering various therapeutic properties of aloe vera gel such as anti-inflammation, anti-microbial effect, and wound healing promotions.

What this study adds?

The clinical evidence to confirm an efficacy of aloe vera gel for the treatment of post-laser wound care has not been investigated. The present study showed that aloe vera gel is highly effective for the reduction of skin redness and the restoration of skin barrier function for post-laser wound care.

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Potential conflicts of interest

None.

References

- 1. Alexiades-Armenakas MR, Dover JS, Arndt KA. The spectrum of laser skin resurfacing: nonablative, fractional, and ablative laser resurfacing. J Am Acad Dermatol 2008; 58: 719-37.
- Meduri NB. Facial resurfacing: an overview. Operat Tech Otolaryngol Head Neck Surg 2007; 18: 172-80.
- Rerknimitr P, Pongprutthipan M, Sindhuphak W. Fractional photothermolysis for the treatment of facial wrinkle in Asians. J Med Assoc Thai 2010; 93 (Suppl 7): S35-40.
- 4. Manuskiatti W, Fitzpatrick RE, Goldman MP.

Long-term effectiveness and side effects of carbon dioxide laser resurfacing for photoaged facial skin. J Am Acad Dermatol 1999; 40: 401-11.

- Graber EM, Tanzi EL, Alster TS. Side effects and complications of fractional laser photothermolysis: experience with 961 treatments. Dermatol Surg 2008; 34: 301-5.
- Budai MM, Varga A, Milesz S, Tozser J, Benko S. Aloe vera downregulates LPS-induced inflammatory cytokine production and expression of NLRP3 inflammasome in human macrophages. Mol Immunol 2013; 56: 471-9.
- Tabandeh MR, Oryan A, Mohammadalipour A. Polysaccharides of Aloe vera induce MMP-3 and TIMP-2 gene expression during the skin wound repair of rat. Int J Biol Macromol 2014; 65: 424-30.
- Duansak D, Somboonwong J, Patumraj S. Effects of Aloe vera on leukocyte adhesion and TNFalpha and IL-6 levels in burn wounded rats. Clin Hemorheol Microcirc 2003; 29: 239-46.
- 9. Vázquez B, Avila G, Segura D, Escalante B. Antiinflammatory activity of extracts from Aloe vera gel. J Ethnopharmacol 1996; 55: 69-75.
- Bautista-Pérez R, Segura-Cobos D, Vázquez-Cruz B. In vitro antibradykinin activity of Aloe barbadensis gel. J Ethnopharmacol 2004; 93: 89-92.
- Barrantes E, Guinea M. Inhibition of collagenase and metalloproteinases by aloins and aloe gel. Life Sci 2003; 72: 843-50.
- Yao H, Chen Y, Li S, Huang L, Chen W, Lin X. Promotion proliferation effect of a polysaccharide from Aloe barbadensis Miller on human fibroblasts in vitro. Int J Biol Macromol 2009; 45: 152-6.
- Heggers JP, Kucukcelebi A, Stabenau CJ, Ko F, Broemeling LD, Robson MC, et al. Wound healing effect of aloe gel and other topical antibacterial agents on rat skin. Phytother Res 1995; 9: 455-7.
- Khorasani G, Hosseinimehr SJ, Azadbakht M, Zamani A, Mahdavi MR. Aloe versus silver sulfadiazine creams for second-degree burns: a randomized controlled study. Surg Today 2009; 39: 587-91.
- Visuthikosol V, Chowchuen B, Sukwanarat Y, Sriurairatana S, Boonpucknavig V. Effect of aloe vera gel to healing of burn wound a clinical and histologic study. J Med Assoc Thai 1995; 78: 403-9.

- 16. Reynolds T, Dweck AC. Aloe vera leaf gel: a review update. J Ethnopharmacol 1999; 68: 3-37.
- 17. Ndhlala AR, Amoo SO, Stafford GI, Finnie JF, Van Staden J. Antimicrobial, anti-inflammatory and mutagenic investigation of the South African tree aloe (Aloe barberae). J Ethnopharmacol 2009; 124: 404-8.
- Habeeb F, Shakir E, Bradbury F, Cameron P, Taravati MR, Drummond AJ, et al. Screening methods used to determine the anti-microbial properties of Aloe vera inner gel. Methods 2007; 42: 315-20.
- Das S, Mishra B, Gill K, Ashraf MS, Singh AK, Sinha M, et al. Isolation and characterization of novel protein with anti-fungal and anti-inflammatory properties from Aloe vera leaf gel. Int J Biol Macromol 2011; 48: 38-43.
- 20. Lin CW, Wu CF, Hsiao NW, Chang CY, Li SW, Wan L, et al. Aloe-emodin is an interferoninducing agent with antiviral activity against Japanese encephalitis virus and enterovirus 71. Int J Antimicrob Agents 2008; 32: 355-9.
- 21. Syed T, Afzal M, Ashfaq Ahmad S, Holt A, Ali Ahmad S, Ahmad S. Management of genital herpes in men with 0.5% Aloe vera extract in a hydrophilic cream: a placebo-controlled doubleblind study. J Dermatol Treat. 1997; 8: 99-102.
- Kang MC, Kim SY, Kim YT, Kim EA, Lee SH, Ko SC, et al. In vitro and in vivo antioxidant activities of polysaccharide purified from aloe vera (Aloe barbadensis) gel. Carbohydr Polym 2014; 99: 365-71.
- Yu Z, Jin C, Xin M, JianMin H. Effect of Aloe vera polysaccharides on immunity and antioxidant activities in oral ulcer animal models. Carbohydr Polym 2009; 75: 307-11.
- 24. Rahman Z, Alam M, Dover JS. Fractional Laser treatment for pigmentation and texture improvement. Skin Therapy Lett 2006; 11: 7-11.
- 25. Batra RS, Ort RJ, Jacob C, Hobbs L, Arndt KA, Dover JS. Evaluation of a silicone occlusive dressing after laser skin resurfacing. Arch Dermatol 2001; 137: 1317-21.
- Sotoodian B, Maibach HI. Noninvasive test methods for epidermal barrier function. Clin Dermatol 2012; 30: 301-10.

การศึกษาประสิทธิภาพของเจลว่านหางจระเข้ในการดูแลแผลหลังการทำเลเซอร์ 1,550 นาโนเมตร เส้นใยเออร์เบียม มนตรี อุดมเพทายกุล, เทพ เฉลิมชัย, อุดมศักดิ์ บุญนริสรางกูร

วัตถุประสงค์: เพื่อศึกษาถึงประสิทธิภาพทางคลินิกและความปลอดภัยของเจลว่านหางจระเข้ในการดูแลแผลหลังการทำเลเซอร์ 1,550 นาโนเมตร เส้นใยเออร์เบียม

วัสดุและวิธีการ: อาสาสมัครจำนวน 30 คน ที่มีความเสื่อมสภาพของผิวระดับเล็กน้อยถึงปานกลางตาม Glogau's classification ที่ได้รับการรักษาด้วยเลเซอร์ 1,550 นาโนเมตร เส้นใยเออร์เบียม ภายหลังการทำเลเซอร์ผู้ป่วยจะได้รับเจลว่านหางจระเข้ทาที่ บริเวณใบหน้าด้านหนึ่ง และใบหน้าอีกด้านที่เหลือจะทาด้วยยาหลอกซึ่งใช้วิธีการสุ่มจากผู้ช่วยการศึกษา มีการประเมินการวัดระดับ ความแดงทางคลินิกโดยแพทย์ วัดค่าระดับความแดงของผิว วัดค่าระดับความเข้มของสีผิว วัดค่าการสูญเสียน้ำทางผิวหนัง วัดค่า ปริมาณน้ำที่ผิวหนัง การหายของแผลในแต่ละวัน การวัดระดับความพึงพอใจของอาสาสมัคร รวมทั้งอาการไม่พึงประสงค์ โดยมี การติดตามผลภายหลังการทำเลเซอร์ทันที, วันที่ 3, 7 และ 14 หลังทำเลเซอร์

ผลการสึกษา: เจลว่านหางจระเข้สามารถช่วยในการลดระดับความแดงทางคลินิก ลดค่าการสูญเสียน้ำทางผิวหนัง และมีระดับ ความพึงพอใจในการรักษามากกว่ายาหลอกอย่างมีนัยสำคัญ (p≤0.05) แต่อย่างไรพบว่าไม่มีความแตกต่างกันในเรื่องของค่ามัธยฐาน ของการหายของแผล (p = 0.11) รวมทั้งค่าระดับความแดงของผิว ค่าระดับความเข้มของสีผิว และค่าปริมาณน้ำที่ผิวหนัง (p-value >0.05)

สรุป: เจลว่านหางจระเข้มีคุณสมบัติช่วยในการลดระดับความแดงทางคลินิกและลดค่าการสูญเสียน้ำทางผิวหนังได้ดีภายหลังการ ทำเลเซอร์ 1,550 นาโนเมตร เส้นใยเออร์เบียม ดังนั้นเจลว่านหางจระเข้อาจนำมาใช้เป็นอีกทางเลือกหนึ่งในการดูแลแผลหลัง การทำเลเซอร์ได้