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Effect Of Aloe Vera Gel Phonophoresis On Venous Ulcer Healing

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ABSTRACT
Purpose*:The current study aimed to investigate the effectiveness of aloe vera gel phonophoresis on healing of venous ulcers.* ***Methods****: Sixty male and female patients with chronic lower limb venous ulcers participated in this study. Their ages ranged from 45to 60 years and were distributed randomly into group (A), 30 patients who received transdermal delivery of aloe vera (Phonophoresis) by low-intensity ultrasound in addition to regular medical care, and group (B), 30 patients who received topical aloe vera after receiving therapeutic ultrasound in addition to regular medical care. Imito wound mobile software and normal saline were used to evaluate ulcer surface area and volume, respectively. The evaluation was done pre-treatment, after 4 and 8 weeks of treatment.* ***Results:*** *There was a significant improvement in venous ulcer healing as there were reductions in wound surface and volume within each group. By comparing both groups post-treatment, results revealed that despite the difference between both groups not reaching a significant level, there was a clinical wound healing improvement in favor of group (A).* ***Conclusion*** *Aloe vera Phonophoresis (transdermal delivery of aloe vera) is a safe, non-invasive, and beneficial modality for lower limb venous ulcers and can be added to the treatment protocols for these debilitating conditions.*

Keywords: *Phonophoresis, Aloe vera, Low Intensity Ultrasound, Chronic Venous Ulcer.*

INTRODUCTION

Venous ulcers are injuries that occur due to dysfunction of the venous valves that lead to increased blood pressure in the veins of the legs, usually the legs (hence the leg ulcer) [1]. The causes are chronic venous insufficiency and/or congestive heart failure. Venous stasis causes an increase in pressure in the veins. Risk factors include deep vein thrombosis (DVT) or difficulty walking due to a problem such as osteoarthritis, leg injuries, obesity, paralysis, varicose veins., other circulation problems such as blood clots or phlebitis, smoking, and even more at risk if there is recent leg surgery such as a hip or knee replacement [2], [3] and [4].
The typical treatment is elastic compression and foot assessment known as the Bisgaard diet. Exercise combined with compression stockings improves healing. [5] and [6]. Antibiotics may also be used if the ulcer is infected, but they do not help the ulcer heal. [7] Therapeutic ultrasound is used to deliver high-frequency mechanical vibrations to facilitate healing at the cellular level. Therapeutic ultrasound is often used to reduce pain, increase circulation, and increase the mobility of soft tissues. In addition, the application of ultrasound can be beneficial for reducing inflammation, reducing pain, and promoting the healing of wounds and injuries [8]. Phonophoresis is the application of ultrasound to enhance the percutaneous absorption of a drug, usually an anti-inflammatory or anesthetic, for relieving pain and inflammation in musculoskeletal/sports injuries. [9].
Topical application of Aloe vera has been reported to prevent ulcers and improve the healing process of skin wounds (e.g . burns, frostbite, skin infections, surgical wounds, inflammation, ulcers of the 'herpes, diabetic foot ulcers, wounds, and chronic wounds) and it is very suitable for dressings. [10] . The current study aimed to investigate the effectiveness of aloe vera gel phonophoresis on venous ulcers.

MATERIALS AND METHOD

Patients:

Sixty (male and female) patients with chronic lower limb venous ulcers were recruited from Teaching Hospitals and Kasr Ini Hospitals, Cairo University. The subject selection was according to the following criteria:

Their age ranged between 45-60 years. All patients had a chronic venous ulcer and received the same medical care. All patients were assessed carefully by the physician before the study procedure started. They all received an explanation about the intervention and measurement devices, and the examination included a thorough physical evaluation. All patients have no evidence of Aloe Vera allergy. The participants were excluded if they met one of the following criteria:

Patients with evidence of local recurrence or distant metastasis, patients with severe lymphedema, patients with nerve injury, orthopedic limitation, and psychiatric condition, patients with multi-organ transplantation, patients with hypoxemia, and patients with arterial ulcers, circumferential ulcers, and diabetic ulcers. All patients were informed about the nature and the effect of the treatment and measurement devices. The patients were instructed to report any side effects during the management. All patients in the study were given his/her written informed consent. The included patients were divided randomly into two groups:

Phonophoresis group (A): Thirty patients received Aloe vera phonophoresis in addition to standard wound care. Ultrasound-preceded gel group (B). Thirty patients received therapeutic ultrasound followed by immediate topical aloe vera gel application in addition to standard wound care. During the study procedures, six patients withdrew, four from group A and two from group B, and were replaced by others and started with them again. This study was conducted during the period from September 2023 to October 2024.

Interventions:

Measurement Procedures:

Measurement of ulcer area**:**

Smartphone application (imito wound software) automatically calculates the wound area (length, width, and area) after taking a photograph **[11] and [12].**

Measurement of ulcer volume:

The patient was positioned in a relaxed position with the ulcer directed upwards. The sterilized syringe was filled with saline (0.9%soudium chloride in distilled water). The saline was then ejaculated into the ulcer cavity to fill it to the surface, considering not losing any saline drops. In the case of curved ulcers, the saline was injected into the ulcer through a sheet of transparent paper till filling. The measured saline that filled out the ulcer cavity represented the ulcer volume **[13] and [14].** Both groups were evaluated pre-treatment, after 4 and 8 weeks from the beginning of the treatment. The measurement process was conducted three times for each wound and at each measurement phase to establish the reliability of the measurement. Then, the average of the three measurements was taken and expressed as ulcer area or volume.

Treatment Procedures:

Group (A):

The patients in this group received Aloe Vera phonophoresis sessions and standard wound care.

Aloe Vera phonophoresis Procedure:

The patient was in a relaxed position during the treatment. The wound was cleaned and sterilized (with alcohol or petadine). Low-intensity US (Ultrasound stimulator BTL- 4000 (IFU**), USA**) was used and applied with the following parameters; low-frequency ultrasound penetrates deeper and supports healing, low intensity and pulsed ultrasound (0.5 W/cm2) was transmitted at a low frequency of 1 MHz to facilitate topical drug diffusion (aloe vera gel) using aloe vera gel **[15].**

The wound ulcer was filled with Aloe vera gel (Bio Soft, license: 1646, Registration:77801/2022) and covered with a sterilized plastic film to prevent cross-contamination. The ultrasonic gel was applied under the ultrasonic transducer head, and the device started and adjusted with the mentioned parameters. Then, the ultrasound head was moved slowly through plastic film and on the periphery and the area of the ulcer in overlapping circles to cover the ulcer. Treatment time in minutes equaled the ulcer area in cm^2 (1 minute of treatment/ 1 cm2 area)

Group (B):
The patients in this group received therapeutic ultrasound therapy followed by immediate topical aloe vera gel application (Ultrasound-preceded gel) in addition to standard wound care.
Ultrasound-preceded gel Procedure:
The patient was in a relaxed position during treatment. The wound was cleaned and sterilized (with alcohol or petadine).
Ultrasound therapy was applied first using the same parameters and same time equation (1 minute of treatment/ 1 cm2 area) in group A. The wound ulcer was covered with a medical gel in a sterilized plastic bag. The ultrasonic transducer head moved slowly over the gel bag and on the periphery and area of the ulcer in overlapping circles to cover the ulcer. Then, immediately after treatment, the wound was cleaned and dried, and the wound ulcer was filled with aloe vera gel and covered with a sterilized plastic film for a duration equal to the ultrasound treatment time. Both groups received treatment at a frequency of two times weekly and for 8 weeks (two months).

Statistical analysis
Data were expressed as mean± SD. Shapiro-Wilk test was used for testing the normality of data distribution. Chi-square was used to compare non parametric data. An unpaired t-test was used to compare the characteristics and outcome measures of the two groups. The One-way repeated- measures ANOVA test was used to compare the mean values of different treatment phases in each group. The statistical package for the social sciences computer program (version 18 for Windows; SPSS Inc., Chicago, Illinois, USA) was used for data analysis. *P-value* less than 0.05 was considered significant.

RESULTS

I)Patient demographic data:
There were no significant difference (P >0.05) between both groups regarding, age, gender (type and number), and characteristics of ulcer (type, grades, and dimensions) .

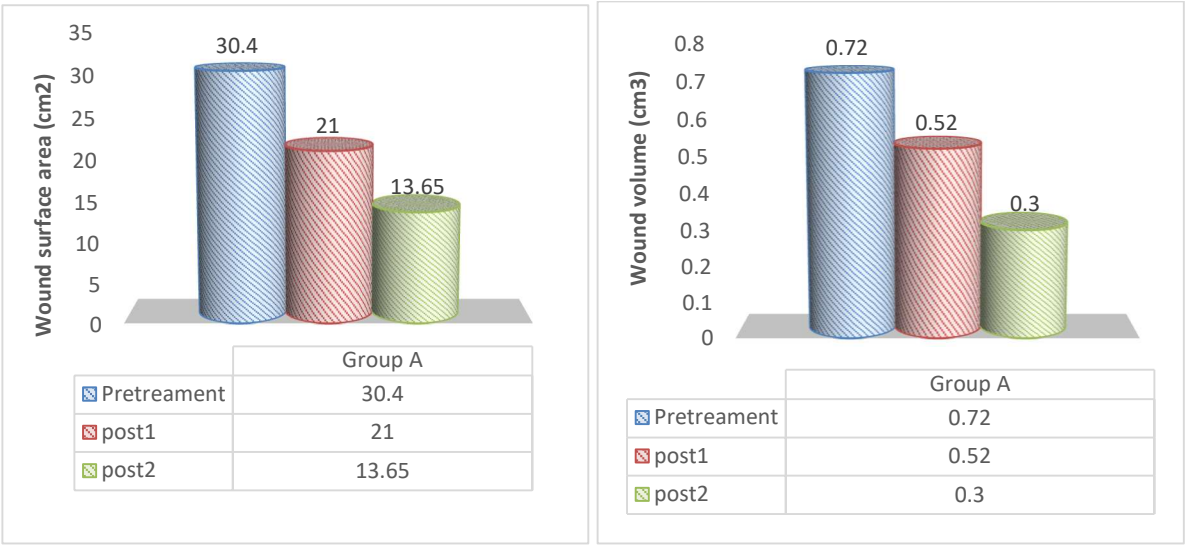
II) Within-group results:

Group (A):
Table (1) and Figure (1) demonstrated the mean values of wound surface area and wound volume at different treatment phases in group (A). The pre-treatment, post1, and post2 mean values of surface areas were (30.4±20.98), (21 ±15.19), and (13.65±11.2), respectively. The pre treatment, post1 and post2 mean values of volumes were (0.72 ± 0.40), (0.52 ± .34), and (0.3 ± 0.26), respectively. One-way repeated- measures ANOVA test revealed statistically significant differences (decreases) between mean values of wound areas and volumes of different treatment phases as the p-value was (**0.0001**) for all.

Table (1) shows comparison of mean values of wound surface areas and wound volumes between diffrerent treatment phases in each group.
WSA: Wound Surface Area WV: Wound Volume X : Mean SD: Standard Deviation MD: Mean difference

Group	Outcome measure	Pre treatment	Post (1)	Post (2)	F-value	p-value	Sig
Group(A)	WSA.(cm^2)	30.4±20.98	21 ±15.19	13.65±11.2	42.3	0.0001	S
	WV.(cm^3)	0.72 ± 0.40	0.52 ± .34	0.3 ± 0.26	54.08	0.0001	S
Group(B)	WSA.(cm^2)	29.95 ± 19.6	21.35±13.6	14.5 ±9.69	52.34	0.0001	S
	WV.(cm^3)	(0.66± 0.36)	(0.48±0.26)	(0.31±0.2)	78.8	0.0001	S

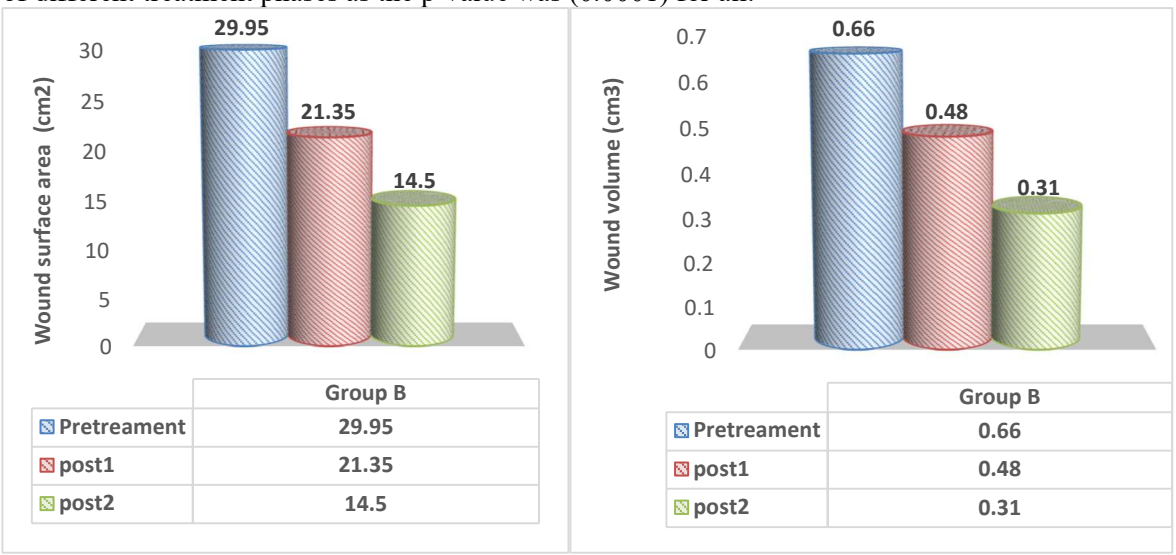
p value: Probability value S: Significant



Figure(1) shows mean values of wound surface areas and wound volumes in diffrerent treatment phases for group (A).

Group (B):

Table (1) and Figure (2) demonstrated the mean values of wound surface area and wound volume at different treatment phases in group (A). The pre-treatment, post1, and post2 mean values of surface areas were (29.95 ± 19.6), (21.35±13.6), and (14.5 ±9.69), respectively. The pre-treatment, post1, and post2 mean values of volumes were (0.66 ± 0.36), (0.48 ± 0.26), and (0.31 ± 0.21) respectively. One-way repeated- measures ANOVA test revealed statistically significant differences (decreases) between mean values of wound areas and volumes of different treatment phases as the p-value was (0.0001) for all.



Figure(2) shows mean values of wound surface areas and wound volumes in diffrerent treatment phases for group (B).

III) Between-group results:

Table (2) and Figures (3&4) revealed the independent t-test results for the surface area and wound volume pre-, post-1and post-2 treatment between groups A and B. Unpaired t-test revealed there was no significant difference between the two groups, regarding the pre-treatment surface area and volume values, where the p-value was (**0. 945**) and (**0.748**), respectively. Also, there was no significant difference between the two groups,

regarding the post-1-treatment surface area and volume values, as the p-values were (**0.939**) and (0.611) respectively. Finally, there was no significant difference between the two groups, regarding the post-2-treatment surface area and volume values, as the p-values were (**0.799**) and (0.894), respectivel

Table (2) shows comparison of mean values of wound surface areas and wound volumes between groups at each treatment phase.

Treatment phase	**Wound surface area (cm²) X ± SD**		**MD**	**t- value**	**p-value**	**Sig**
	Group A	**Group B**				
Pre	30.40± 20.98	29.95±19.61	.45	.070	.945	**NS**
Post (1)	21 ±15.19	21.35±13.62	- 0.35	- 0.077	0.939	**NS**
Post (2)	13.65±11.2	14.5 ± 9.69	- 0.85	- 0.26	0.799	**NS**
Treatment phase	**Wound volume (cm³) X ± SD**		**MD**	**t- value**	**p-value**	**Sig**
	Group A	**Group B**				
pre	0 .72±0.4	0 .66 ± 0.37	.04	.324	0.748	NS
Post (1)	0.52±0.34	0.48±0.26	0.048	0.513	0.611	NS
Post (2)	0.3± 0.26	0.31±0.21	-0.01	-0.134	0.894	NS

X: Mean SD: Standard deviation MD: Mean difference t value: Unpaired t value p value: Probability value NS: Non significant

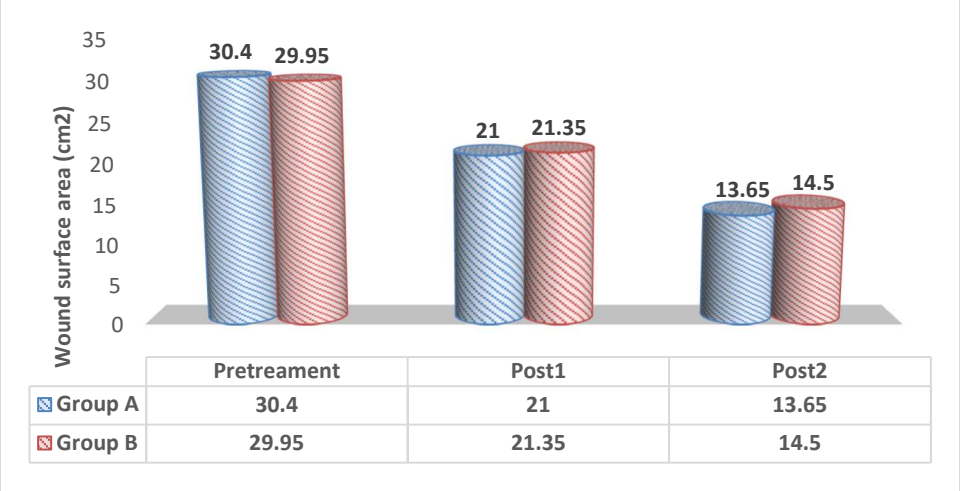


Figure (3) shows mean values of wound surface areas at each treatment phases in both group.

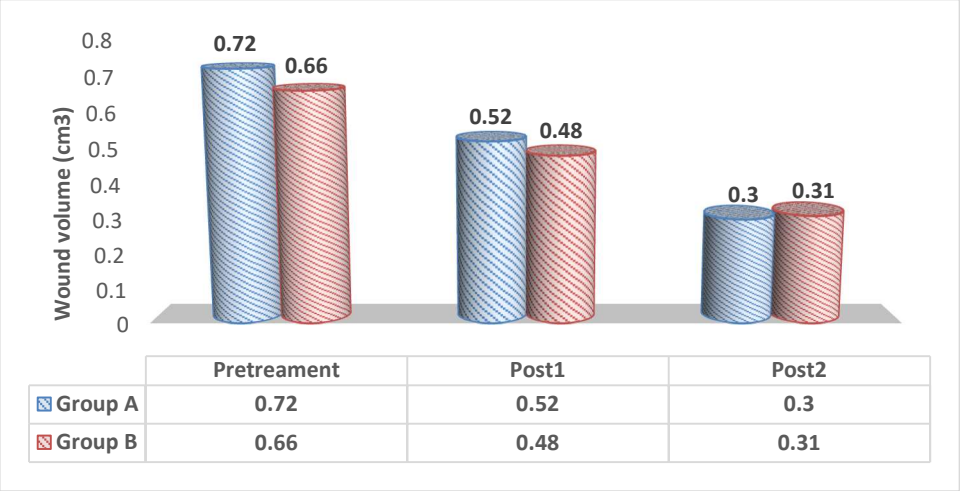


Figure (4) shows mean values of wound volumes at each treatment phases in both group.

DISCUSSION

The results obtained from the current study revealed that there was a significant improvement in venous ulcer healing in the form of a reduction of wound surface and volume within each group (phonophoresis, and ultrasound-preceded gel groups) after two months of treatment as the p-value was<(0.05). By comparing both groups post-treatment, results revealed that despite the difference between both groups did not reach a significant level, as There was no significant difference in post-treatment in both groups there was a clinical wound healing improvement (reduction in venous ulcer area and volume) in favor of group (A). The patient number in this study may be a limitation factor that could affect the study's statistical results. Increasing the number of patients in upcoming studies could enhance clinical improvement in group A (phonophoresis group) to more obvious significant results.

This study is consistent with a study comparing the effect of aloe vera gel phonophoresis and silver nanoparticle (SNP) phonophoresis on the healing of second-degree burns, which reported that there was a very significant reduction in wound surface area between phonophoresis in aloe vera gel. (Group A) compared to that of phonophoresis in SNP (group B). It was concluded that aloe vera gel phonophoresis is more effective than PNS phonophoresis on second-degree burns. [16].

In a study comparing topical application of Aloe vera gel, pulsed ultrasound (US), and phonophoresis of Aloe vera in a mouse paw affected by collagenase-induced tendinitis, topical application of Aloe vera gel did not show any statistically significant improvement in the inflammatory process, while phonophoresis improved the action of the gel, reducing edema and the number of inflammatory cells, promoting the rearrangement of collagen fibers, and also promoting the recovery of tensile strength. [17].

The results are also consistent with another study that aimed to determine the effects of Aloe vera, a potential wound-healing agent, on wound contraction in excisional wounds treated with topical antimicrobials. Aloe vera accelerates wound contraction and counteracts the wound-slowing effect seen with topical mafenide acetate alone. [18].

Stephen Cook et al., reported that low-intensity pulsed ultrasound improved cartilage repair of the interface of autologous osteochondral plugs compared to controls in a canine model. Improvements of the quality and repair rate of autologous osteochondral plugs may reduce postoperative recovery time and improve functional outcomes.[19] **Davood Hekmatpou et al.**, said that Aloe vera has been used to prevent skin ulcers and treat wounds, postoperative wounds, and chronic wounds, including pressure ulcers, and may improve wound healing.[20] .And finally, **Mahran et al.**, investigated that ultrasound waves significantly increase the effect of topical Aloe Vera gel in the full-thickness wound model in diabetic animals. [21].

CONCLUSION:

Despite the difference between both groups not reaching a significant level, there was a clinical wound healing improvement in favor of group (A). The patient number in this study may be a limitation factor that could affect the study's statistical results. Increasing the number of patients in upcoming studies could enhance clinical improvement in group A (phonophoresis group) to more obvious significant results. Aloe vera Phonophoresis (transdermal delivery of aloe vera) is a safe, non-invasive, and beneficial modality for lower limb venous ulcers and can be added to the treatment protocols for these debilitating conditions.

REFERENCES

1. Bonkemeyer Millan S, Gan R, Townsend PE. Venous Ulcers: Diagnosis and Treatment. Am Fam Physician. 2019; 100 (5): 298 - 305. PMID : 31478635.
2. Santler B, Goerge T. Chronic venous insufficiency - a review of pathophysiology, diagnosis, and treatment. J Dtsch Dermatol Ges. 2017 May;15(5):538-556. doi: 10.1111/ddg.13242.
3. Zhu R, Hu Y, Tang L.Reduced cardiac function and risk of venous thromboembolism in Asian countries. Thrombosis Journal. 2017;15 (1): 12. PMC 5404284. PMID 28450810.doi:10.1186/s12959-017-0135-3.
4. Moreo K. Understanding and overcoming the challenges of effective case management for patients with chronic wounds. The Case Manager. 2005;16 (2): 62–3, 67. doi:10.1016/j.casemgr.2005.01.014.
5. Jull A, Slark J, Parsons J. Prescribed Exercise With Compression vs Compression Alone in Treating Patients With Venous Leg Ulcers: A Systematic Review and Meta-analysis. JAMA Dermatology. 2018;154 (11): 1304–131. PMC 6248128. doi:10.1001/jamadermatol.
6. Van Gent WB, Wilschut ED, Wittens C. Management of venous ulcer disease.BMJ. 2010; 341: c6045. doi:10.1136/bmj.c6045.
7. O'Meara S, Al-Kurdi D, Ologun Y, Ovington LG, Martyn-St James M, Richardson R. Antibiotics and antiseptics for venous leg ulcers. Cochrane Database Syst Rev. 2014 Jan 10;2014(1):CD003557. doi: 10.1002/14651858.CD003557.pub5. PMID: 24408354; PMCID: PMC10580125
8. Schönenberger K. Ultrasound therapeutic device. J Acoust Soc Am. 2005; 118(2):600 .
9. Joel M. Press, and Deborah A. Physical modalities. Clinical Sports Medicine. 2007: 207-226.doi: 10.1016/B978-141602443-9.50019-2
10. Joseph B and Justin RS. Pharmacognostic and phytochemical properties of Aloe vera Linn. - An overview. Int.J. Pharmaceut. Sci. Review and Res.2010; 2: 106-110.
11. Ivan Miguel Pires and Nuno M. Garcia. Wound Area Assessment using Mobile Application. International Conference on Health Informatics. 2015; 2: 271-282. doi:10.5220/0005236502710282.
12. Jun YJ, Shin D, Choi WJ, Hwang JH, Kim H, Kim TG, Lee HB, Oh TS, Shin HW, Suh HS, Lee AY, Hong JPJ. A Mobile Application for Wound Assessment and Treatment: Findings of a User Trial. Int J Low Extrem Wounds. 2016;15(4):344-353. doi: 10.1177/1534734616678522. Epub 2016 Nov 23. PMID: 27881691.
13. Jørgensen LB, Sørensen JA, Jemec GB, Yderstraede KB. Methods to assess area and volume of wounds - a systematic review. Int Wound J. 2016; 13(4):540-53. PMID: 26250714; PMCID: PMC7949796.B doi:10.1111/iwj.12472.
14. Schubert V, Zander M. Analysis of the measurement of four wound variables in elderly patients with pressure ulcers. Adv Wound Care. 1996;9:29– 36.
15. Byl, N. N. The Use of Ultrasound as an Enhancer for Transcutaneous Drug Delivery: Phonophoresis. Physical Therapy.1995;75(6):539–553. doi:10.1093/ptj/75.6.539.
16. Ereny S. Wahba . Comparing the effect of aloe vera gel phonophoresis and silver nanoparticle (SNP) phonophoresis on the healing of second-degree burns .Bulletin of Faculty of Physical Therapy.2018; 23:30–35.
17. Maia Filho AL, Villaverde AB, Munin E, Aimbire F, Albertini R. Comparative study of the topical application of Aloe vera gel, therapeutic ultrasound and phonophoresis on the tissue repair in collagenase-

induced rat tendinitis. Ultrasound Med Biol. 2010;36(10):1682-90. doi: 10.1016/j.ultrasmedbio.2010.06.012. PMID: 20800944.

18. Heggers JP, Kucukcelebi A, Listengarten D, Stabenau J, Ko F, Broemeling LD, Robson MC, Winters WD. Beneficial effect of Aloe on wound healing in an excisional wound model. J Altern Complement Med. 1996;2(2):271-7. doi: 10.1089/acm.1996.2.271. PMID: 9395659
19. Cook SD, Salkeld SL, Patron LP, Doughty ES, Jones DG. The effect of low-intensity pulsed ultrasound on autologous osteochondral plugs in a canine model. Am J Sports Med. 2008 Sep; 36(9):1733-41. doi: 10.1177/0363546508316766. Epub 2008 May 15. PMID: 18483198.
20. Hekmatpou D, Mehrabi F, Rahzani K, Aminiyan A. The Effect of Aloe Vera Clinical Trials on Prevention and Healing of Skin Wound: A Systematic Review. Iran J Med Sci. 2019 Jan;44(1):1-9. PMID: 30666070; PMCID: PMC6330525.
21. Mahran H.G., Aborehab M.A.S. Ultrasonic Enhancement of Aloe Vera Gel Effect on Full-thickness Wound Healing in Diabetic Rats. Annals of R.S.C.B. 2021: 25(6):9169 – 9181.