SKIN

# ORIGINAL RESEARCH

## Comparison of Safety and Efficacy of a Silicone-Based Gel Containing Pracaxi Oil (*Pentaclethra macroloba*) Versus a Silicon-Based Gel Containing Cepalin Onion Extract for the Treatment of Post-Surgical Hypertrophic Scars

Mark S. Nestor MD, PhD[1,2,3], Brian Berman MD, PhD[1,2], Jessica L. Jones DO[1]

[1]Center for Clinical and Cosmetic Research Aventura, FL
[2]Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, FL
[3]Department of Surgery, Division of Plastic Surgery, University of Miami Miller School of Medicine, Miami, FL

## ABSTRACT

Scars are an unavoidable consequence of cutaneous surgery. Healing with an excellent cosmetic outcome is a crucial component to any surgical wound to avoid any negative impact on quality of life. Various products exist which claim to improve post-surgical scar appearance and texture. In this blinded, randomized pilot study, we compared the efficacy of a silicone-based topical gel containing Pracaxi oil (PO Gel; Serica™ Moisturizing Scar Formula; Cynova Laboratories, Houston, TX) against a second silicone-based gel containing Cepalin onion extract (OE Gel; Mederma® Advanced Scar Gel, Merz, North America). The Vancouver Scar Scale (VSS), Physician and Subject Global Assessment of Scar Treatment, and digital photography were used to determine efficacy and superior post-surgical care treatment outcomes. Forty healthy subjects (18-75 years old) with recent surgical scar (1 to 4 months old) were randomized to PO gel or OE gel and asked to apply a topical solution three times daily for 8 weeks. There were six study visits (Baseline and Weeks 2, 4, 8, 12 and 16). The results of this study showed that subjects with post-surgical scars achieved significant improvements at 8 and 12 weeks following application of a product with either Pracaxi oil or onion extract gel, based on mean Vancouver Scar Scale scores. Both products generally improved the individual scar signs and symptoms. Subjects using the onion extract product did not achieve improvement in Pain or Itch at the 8-week evaluation or Pain at the 12-week evaluation.

## INTRODUCTION

Scarring is an unfortunate and unavoidable consequence of cutaneous surgery.[1] Scar outcomes vary widely from a spectrum of fine and asymptomatic to unappealing keloids. Raised hypertrophic scars exist within this scar spectrum and occur by the over-expression of extracellular matrix molecules during the proliferative and remodeling phases of wound healing.[2]

Hypertrophic scars often occur on the shoulders, central chest, upper arms and upper back[1] where their increased visibility may be associated with substantial

psychological distress [3], potentially having a significantly negative impact on quality of life.[4,5]

Silicone gel sheeting and silicone-based gels have been shown to mitigate the development of post-operative scars[6-8] and, depending on the anatomical location, silicone gels may offer an advantage over silicone sheeting.[9] The use of silicone sheeting or gels is generally considered as a first-line option for extenuating and treating hypertrophic scars.[10] Current guidelines for treating hypertrophic scars include silicone-based products,[3] although the results of a large systematic review concluded clinical trials evaluating silicone gel sheeting as a treatment for hypertrophic scarring are of poor quality and highly susceptible to bias.[11]

A unique silicone-based gel containing pracaxi oil has been developed for improving the appearance of post-surgical scars (Serica™ Moisturizing Scar Formula; Cynova Laboratories, Houston, TX). Pracaxi oil is derived from the seed of *Pentaclethra macroloba*, a tree native to South America. It contains the fatty acids oleic acid, linoleic acid, and behenic acid[12] which have been shown to enhance wound healing.[13,14] An anhydrous silicone-based product containing pracaxi oil was recently shown to have beneficial effects on wound healing[15] and scar development.[12] The ability of Pracaxi oil to improve wound healing may be partly due to its antibiotic activity.[16]

Another alternative silicone-based product, containing the active ingredient Cepalin, which is extracted from the Allium Cepa onion, has also suggested improved post-surgical care outcomes after use (Mederma® Advanced Scar Gel, Merz, North America). The onion extract contains cepanes which have shown anti-inflammatory properties and anti-infective properties due to the thiosulfinates.[25]

The objective of this 16-week, randomized, double-blind comparison study was to determine the safety and efficacy of a unique silicone-based gel containing Pracaxi oil versus a silicone-based gel containing Cepalin onion extract for improving the appearance of hypertrophic surgical scars.

## METHODS

*Inclusion Criteria*

Healthy male and female subjects, 18 to 75 years old, were enrolled. Subjects were required to have a recent surgical scar, 1 to 4 months old, which was located in an area that could be easily accessed for evaluation and readily allow topical application of the study product by the subjects three times daily. Each subject expressed their willingness to complete all study requirements. Women of childbearing potential were required to have a negative urine pregnancy test at the baseline study visit and agree to use an accepted method of birth control throughout the study.

*Exclusion Criteria*

Reasons for exclusion from study participation included an allergy history or hypersensitivity to any components of the investigational products; uncontrolled diabetes or collagen vascular disorders that affect normal wound healing such as scleroderma, systemic lupus erythematosus or Ehler-Danlos syndrome; anticipated need for surgery or hospitalization during the study; a target scar which spanned a joint, required the use of a pressure bandage, or was <1 month or >4 months old; pregnancy,

lactation or planned pregnancy during the study; a condition or situation which, in the Investigator's opinion, put the subject at significant risk or would confound the study results; or enrollment in a study involving an investigational drug or device study within the past 30 days.

*Study Procedures*

Two test articles were utilized in this study, each with a different active ingredient to compare efficacy outcomes. One test article was a translucent, silicone-based gel containing Pracaxi oil (PO Gel; Serica™ Moisturizing Scar Formula; Cynova Laboratories, Houston, TX). The comparator product was a similar-appearing gel containing Cepalin, an onion extract (OE Gel; Mederma® Advanced Scar Gel, Merz, North America). Each subject received a randomly assigned product in the exact same 30-mg pump bottle labeled with the proper storage conditions and a statement regarding the investigational nature of the product. Subjects were randomized in a 1:1 ratio to be treated with the PO Gel or OE Gel. Both investigators and subjects were blinded to which product subjects were assigned. Each product was to be applied to the target area three times daily, approximately 8 hours apart, for 8 weeks. The study included up to six study visits, which included a Baseline (Day 0) visit and follow-up visits at Weeks 2, 4, 8, 12 and 16. Changes in scar appearance were documented with digital photographs obtained at baseline and each follow-up visit.

*Efficacy Assessments*

A modified Vancouver Scar Scale (VSS) was used to assess three specific characteristics of scars often observed throughout the remodeling process: vascularity, pliability, and height. The vascularity category was determined upon exam and described as normal, pink, red, or purple then assigned a value of 0, 1, 2, or 3 respectively. Additionally, pliability and scar height were quantified with the same scoring system. Pliability was assessed as normal (score of 0), supple (score of 1), yielding (score of 2) or firm (score of 3). The height assessment was broken down into flat (score of 0), <2mm (score of 1), 2-5mm (score of 2), or >5mm (score of 3). This study did not assess melanin pigmentation as the VSS remains widely applicable to evaluate therapy and as a measure of outcomes.[17] Using the Global Assessment of Scar Treatment, investigators provided an overall assessment of each product's efficacy for improving scar appearance as Very Good, Good, Moderate or Unsatisfactory at each visit. Subjects were asked to provide scar-associated symptoms of itching and pain and a Global Assessment of Scar Treatment which provided an overall satisfaction with the results as Very Good, Good, Moderate or Unsatisfactory at each visit.

*Safety Assessments*

Reports of adverse events (AEs) were recorded throughout the trial using Medical Dictionary for Regulatory Activities Terminology (MedDRA® MSSO, Version 15.1; McLean, VA) and summarized by system organ class, preferred-term, severity, relatedness and seriousness. Each subject was counted only once within a system organ class or a preferred term using the event with the greatest relationship and greatest severity.

*Statistical Analysis*

All subjects were included in the summaries of demographic and baseline characteristics. The safety population included subjects

exposed to any investigational product and who provided any post-application safety information. The efficacy population included subjects who completed the study including the Week 16 evaluation. Report summaries were generated by biostatistics personnel (Agility Clinical, Carlsbad, CA) using SAS® Software, Version 9.3 (SAS Institute, Inc., Cary, NC). Quantitative variables were summarized to indicate sample sizes (n), mean, standard deviation (SD), and range (min, max). When applicable, significance testing was performed to assess equivalence between the two treatment groups. Confidence intervals were presented to assess equivalence between the two treatment groups. All confidence intervals were two-sided and performed using α=0.05. No formal sample size calculations were performed for this trial.

*Ethics*

The protocol used in this study and associated materials were approved by a commercial institutional review board (U.S. Institutional Review Board, Inc., Miami, FL). Written informed consent was obtained from each subject including authorization to release health information prior to participating in any study-related activities.

## RESULTS

Enrolled subjects (*N*=40) were randomized to receive the PO Gel (n=20) or OE Gel (n=20). Over the course of the study, three patients did not complete the study. The study was completed through Week 16 by 19 subjects in the PO Gel group (95%) and 18 subjects in the OE Gel group (90%). Reasons for not completing the study were withdrawal due to AEs of pruritus (n=1) and redness (n=1) and loss to follow-up (n=1). Demographics and baseline characteristics of the enrolled subjects are summarized in **Table 1**. Both groups were well-balanced except for mean scar age, which was significantly older in the OE Gel group despite being blindly randomized.

*Efficacy Analysis*

The change in mean composite modified Vancouver Scar Scale scores for PO Gel and OE Gel groups over the course of the study were calculated and are shown in **Table 2**. Change in values can also be seen as a graph in **Graph 1**. Average VSS scores were calculated for each visit- baseline, 8 weeks/End of Treatment, and 12 weeks/End of study for both the PO and OE gel groups.

**Table 1: Demographics and Baseline Characteristics.**

| | Pracaxi Oil Gel n (%) | Onion Extract Gel n (%) |
|---|---|---|
| **Mean Age, years** | 53.2 | 54.8 |
| **Gender** | | |
| Male | 10 (50) | 10 (50) |
| Female | 10 (50) | 10 (50) |
| **Race** | | |
| Caucasian | 15 (75) | 17 (85) |
| African-American | 4 (20) | 3 (15) |
| Other | 1 (5) | -- |
| **Ethnicity** | | |
| Hispanic/Latino | 2 (10) | 1 (5) |
| Non-Hispanic/Non-Latino | 19 (90) | 19 (95) |
| **Mean Scar Age, days** | 49.5 | 70.2[a] |
| 28-57 | 15 (75) | 9 (45) |
| 58-87 | 5 (25) | 6 (30) |
| 88-118 | -- | 5 (25) |

[a] Significantly different, *p*=0.008.

Baseline average scores were then compared to average scores recorded at 8 weeks/End of Treatment, and again with average scores observed at 12 weeks/End of Study. The PO Gel scores were significantly different from OE Gel scores at each time point although both groups achieved significant improvements in baseline scores.

A total -1.8 reduction in score was seen with Pracaxi oil at the end of the 12 week study period. Additionally, a -2.0 score reduction was demonstrated for the onion extract cohort. It is important to keep in mind, because the VSS scale uses very low values, a significant change is needed in any of the individual scores for vascularity, pliability, and scar height in order to produce even a slight change in average VSS scores. Therefore, it is impressive that both groups experienced nearly a -2.0 score reduction from baseline to end of study.

Average VSS scores for the individual subcategories (vascularity, pliability, and height) were also calculated for both the PO gel and OE gel groups (data not shown).

**Table 2: Change in Mean Vancouver Scar Scale Scores.**

| | Pracaxi Oil Gel | Onion Extract Gel |
|---|---|---|
| Total Score | | |
| Day 0 (Baseline)[a] | 3.90 | 3.30 |
| Week 8 (End of Treatment)[b] | 2.60 | 1.50 |
| Week 12 (End of Study)[c] | 2.10 | 1.33 |
| Change in VSS Score | | |
| Day 0 – Week 8 | -1.2[d] | -1.8[e] |
| Day 0 – Week 12 | -1.8[f] | -2.0[g] |

Between-group comparisons: [a]$p<0.01$; [b]$p=0.01$; [c]$p<0.05$. Baseline comparisons: [d]$p=0.005$; [e]$p=0.001$; [f]$p=0.0001$; [g]$p=0.0001$.

Baseline average scores were compared against end of study average scores. Pracaxi oil proved to be superior at reducing scar vascularity with a -1.1 overall reduction versus an average of -0.85 score reduction seen with Onion extract. However, greater score reductions were calculated for pliability and scar height for those subjects using onion extract.

Additionally, PO Gel-treated subjects achieved improvement in the signs and symptoms of each individual Vancouver Scar Scale score, which were greater than OE Gel for Pain and Itch scores at Week 8 and Pain and Vascularity scores at Week 12. Based on Physician and Subject Global Assessment of Scar Treatment, both groups rated their appearance results as Good.

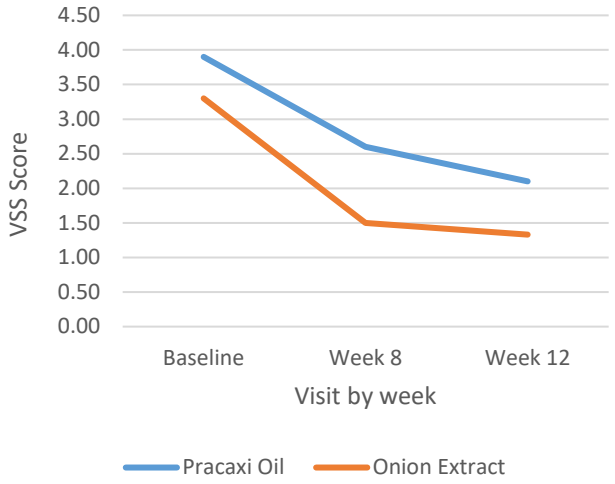
*Safety Analysis*

No significant adverse events were reported during the study. Two patients from the OE gel group withdrew due to redness and loss to follow-up, and one patient from the PO gel group withdrew secondary to intense itching.

## DISCUSSION

Pracaxi oil is derived from seeds of the *Pentaclethra macroloba* tree. It contains high concentrations of fatty acids[18] with known emollient and medicinal effects including antibacterial activity,[16,19,20] enhancing wound healing,[13,14] antiproteolytic and antihemorrhagic properties[21,22] and are essential to the formation and maintenance of cell membranes within the stratum corneum. Cepalin onion extracts have also demonstrated similar wound healing benefits due to anti-inflammatory properties and anti-microbial properties. These benefits are attributed to the biochemical thiosulfinates.[25]

**Figure 1:** Change in Mean Vancouver Scar Scale Scores over study length.




Cepalin is extracted from the Allium Cepa onion. Data from in vitro studies suggested that the onion extract exhibits anti-inflammatory, antiproliferative, bacteriostatic, and collagen down regulatory properties by its effect on fibroblast and mast cell.

The therapeutic effects of topical anhydrous silicone base containing Pracaxi oil was initially demonstrated in a case series of patients with surgical, traumatic, or burn wounds and scars.[12] The product was applied two to four times daily based on the size and severity of the scar or wound. The mean duration of application of the Pracaxi oil product was 11 days and ranged from 48 hours to 3 weeks. Among the 21 enrolled patients, self-reported questionnaire results and clinical photographs were obtained for seven. Using an 11-point (0-10) satisfaction scale, the mean (SD) score was 10 (1.15). One patient with a 1-year old hypertrophic surgical scar reported the thickness, color, and overall scar severity were improved after 1 week of treatment.

The overall objective of this study was to compare the efficacy and safety of a silicone-based gel containing Pracaxi oil against a gel containing onion extract for treating hypertrophic scars. The ability of onion extract to improve the appearance of surgical scars has previously been assessed in several clinical studies. However, in those studies OE gel was compared against silicone sheeting, and ultimately demonstrated mixed results. Two randomized studies showed silicone gel containing onion extract was more effective than the silicone gel vehicle for treating post-surgical hypertrophic scars.[23,24] One study showed that onion extract gel significantly improved post-surgical scar softness, redness, texture, and global appearance.[25] In another study, onion extract reduced the height of hypertrophic scars but did not improve redness and overall appearance.[26] Two studies found onion extract had no effect on post-surgical scars[27,28] while one reported it was less effective than silicone gel sheeting.[29]

The VSS was a critical component of this study in measuring the efficacy of treatment outcomes by assessing vascularity, height/thickness and pliability of each scar. Reduction in VSS scores were calculated from each group for weeks 0-8 and again weeks 8-12. A -1.8 reduction in score was seen with Pracaxi oil at the end of the 12 week study period. Additionally, a -2.0 score reduction was demonstrated for the onion extract cohort.

The results of the present study showed that subjects with post-surgical scars achieved significant improvements at 8 and 12 weeks following application of a product with either Pracaxi oil or onion extract gel, based on mean Vancouver Scar Scale scores, and both products generally improved the individual scar signs and symptoms. Subjects using the onion extract product did not

achieve improvement in Pain or Itch at the 8-week evaluation or Pain at the 12-week evaluation; however, the baseline scores for these symptoms were already very low. Neither product achieved any improvement in the Physician or Subject Global Assessment of Scar Treatment Scores.

## LIMITATIONS

One of the main limitations to this study is the fact that this is a pilot study, as the sample size is small with 40 total subjects. A limitation to the study was the significant difference in mean scar age at baseline. Despite randomization, scars were significantly older for subjects in the onion extract group. This might account for the higher baseline composite Vancouver Scar Scale scores scale for the Pracaxi Oil Gel group (3.9 *vs*. 3.3) and possibly lower Pain and Itch scores. As this imbalance was probably due to small sample sizes, a larger randomized study is likely to be more balanced.

## CONCLUSION

The results of this study indicate a topical silicone-based Pracaxi Oil Gel is as effective as an Onion Extract Gel for improving the appearance of hypertrophic post-surgical scars. Larger controlled studies will be necessary to further evaluate the overall potential of this product for improving the unsightly appearance of hypertrophic scars.

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**Corresponding Author:**
Mark S. Nestor, MD, PhD
Center for Clinical and Cosmetic Research
2925 Aventura Boulevard, Suite 205
Aventura, FL
Email: nestormd@admcorp.com

**References:**

1) Clayton AS, Stasko T. Surgical Complications and Optimizing Outcomes. In: Bolognia JL, Jorizzo JL, Schaffer JV, eds. *Dermatology.* Vol 3. Atlanta: Elsevier Inc; 2016.
2) Sidgwick GP, McGeorge D, Bayat A. A comprehensive evidence-based review on the role of topicals and dressings in the management of skin scarring. *Arch Dermatol Res.* 2015;307:461-477.
3) Meaume S, Le Pillouer-Prost A, Richert B, Roseeuw D, Vadoud J. Management of scars: updated practical guidelines and use of silicones. *Eur J Dermatol.* 2014;24:435-443.
4) Bock O, Schmid-Ott G, Malewski P, Mrowietz U. Quality of life of patients with keloid and hypertrophic scarring. *Arch Dermatol Res.* 2006;297:433-438.
5) Choi Y, Lee JH, Kim YH, Lee YS, Chang HS, Park CS, Roh MR. Impact of postthyroidectomy scar on the quality of life of thyroid cancer patients. *Ann Dermatol.* 2014;26:693-699.
6) Kim JS, Hong JP, Choi JW, Seo DK, Lee ES, Lee HS. The efficacy of a silicone sheet in postoperative scar management. *Adv Skin Wound Care.* 2016;29:414-420.
7) Medhi B, Sewal RK, Kaman L, Kadhe G, Mane A. Efficacy and safety of an advanced formula silicone gel for prevention of post-operative scars. *Dermatol Ther (Heidelb).* 2013;3:157-167.
8) Spencer JM. Case series: evaluation of a liquid silicone gel on scar appearance following excisional surgery--a pilot study. *J Drugs Dermatol.* 2010;9:856-858.

9) Kim SM, Choi JS, Lee JH, Kim YJ, Jun YJ. Prevention of postsurgical scars: comparsion of efficacy and convenience between silicone gel sheet and topical silicone gel. *J Korean Med Sci.* 2014;29(Suppl 3):S249-253.

10) Monstrey S, Middelkoop E, Vranckx JJ, Bassetto F, Ziegler UE, Meaume S, Téot L. Updated scar management practical guidelines: non-invasive and invasive measures. *J Plast Reconstr Aesthet Surg.* 2014;67:1017-1025.

11) O'Brien L, Pandit A. Silicon gel sheeting for preventing and treating hypertrophic and keloid scars. *Cochrane Database Syst Rev.* 2006;1:CD003826.

12) Banov D, Banov F, Bassani AS. Case series: the effectiveness of fatty acids from pracaxi oil in a topical silicone base for scar and wound therapy. *Dermatol Ther (Heidelb).* 2014;4:259-269.

13) Ruthig DJ, Meckling-Gill KA. Both (n-3) and (n-6) fatty acids stimulate wound healing in the rat intestinal epithelial cell line, IEC-6. *J Nutr.* 1999;129:1791-1798.

14) Cardoso CR, Souza MA, Ferro EA, Favoreto S Jr, Pena JD. Influence of topical administration of n-3 and n-6 essential and n-9 nonessential fatty acids on the healing of cutaneous wounds. *Wound Repair Regen.* 2004;12:235-243.

15) Simmons CV, Banov F, Banov D. Use of a topical anhydrous silicone base containing fatty acids from pracaxi oil in a patient with a diabetic ulcer. *SAGE Open Med Case Rep.* 2015;3:2050313X15589676.

16) Guimarães AL, Cunha EA, Matias FO, Garcia PG, Danopoulos P, Swikidisa R, Pinheiro VA, Nogueira RJ. Antimicrobial activity of copaiba (Copaifera officinalis) and pracaxi (Pentaclethra macroloba) oils against Staphylococcus aureus: importance in compounding for wound care. *Int J Pharm Compd.* 2016;20:58-62.

17) Nedelec B, Shankowsky HA, Tredget EE. Rating the resolving hypertrophic scar: comparison of the Vancouver Scar Scale and scar volume. *J Burn Care Rehabil.* 2000;21:205-212.

18) dos Santos Costa MNF, Muniz MAP, Negrao CAB, et al. Characterization of *Pentaclethra macroloba* oil. *J Therm Anal Calorim.* 2014;115:2269-2275.

19) Oliveira AA, Segovia JF, Sousa VY, Mata EC, Gonçalves MC, Bezerra RM, Junior PO, Kanzaki LI. Antimicrobial activity of Amazonian medicinal plants. *Springerplus.* 2013;2 371.

20) Leal ICR, Junior II, Pereira EM, Laport MS, Kuster KM, dos Santos KRN. Pentaclethra macroloba tannins fractions active against methicillin-resistant staphylococcal and gram negative strains showing selective toxicity. *Rev Bras Farmacogn.* 2011;21:991–999.

21) da Silva JO, Coppede JS, Fernandes VC, Santana CD, Ticli FK, Mazzi MV, Giglio JR, Pereira PS, Soares AM, Sampaio SV. Antihemorrhagic, antinucleolytic and other antiophidian properties of the aqueous extract from *Pentaclethra macroloba*. *J Ethnopharmacol.* 2005;100:145-152.

22) da Silva JO, Fernandes RS, Ticli FK, Oliveira CZ, Mazzi MV, Franco JJ, Giuliatti S, Pereira PS, Soares AM, Sampaio SV. Triterpenoid saponins, new metalloprotease snake venom inhibitors isolated from *Pentaclethra macroloba*. *Toxicon.* 2007;50:283-291.

23) Jenwitheesuk K, Surakunprapha P, Jenwitheesuk K, Kuptarnond C,

Prathanee S, Intanoo W. Role of silicone derivative plus onion extract gel in presternal hypertrophic scar protection: a prospective randomized, double blinded, controlled trial. *Int Wound J.* 2012;9:397-402.

24) Wananukul S, Chatpreodprai S, Peongsujarit D, Lertsapcharoen P. A prospective placebo-controlled study on the efficacy of onion extract in silicone derivative gel for the prevention of hypertrophic scar and keloid in median sternotomy wound in pediatric patients. *J Med Assoc Thai.* 2013;96:1428-1433.

25) Draelos ZD. The ability of onion extract gel to improve the cosmetic appearance of postsurgical scars. *J Cosmet Dermatol.* 2008;7:101-104.

26) Chanprapaph K, Tanrattanakorn S, Wattanakrai P, Wongkitisophon P, Vachiramon V. Effectiveness of onion extract gel on surgical scars in Asians. *Dermatol Res Pract.* 2012;2012:212945.

27) Jackson BA, Shelton AJ. Pilot study evaluating topical onion extract as treatment for postsurgical scars. *Dermatol Surg.* 1999;25:267-269.

28) Chung VQ, Kelley L, Marra D, Jiang SB. Onion extract gel versus petrolatum emollient on new surgical scars: prospective double-blinded study. *Dermatol Surg.* 2006;32:193-197.

29) Karagoz H, Yuksel F, Ulkur E, Evinc R. Comparison of efficacy of silicone gel, silicone gel sheeting, and topical onion extract including heparin and allantoin for the treatment of postburn hypertrophic scars. *Burns.* 2009;35:1097-1103.