Received: 13 October 2022 | Accepted: 10 November 2022

DOI: 10.1111/jocd.15536

JCD Journal of Cosmetic Dermatology WILEY

ORIGINAL ARTICLE

Efficacy and safety of innovative acne scar serum in Indian patients (ESTEEM India study)

Sanjiv Kandhari MD[1] | Anil Ganjoo MD[2] | Abhay Talathi MD, DNB[3] | Sanjeev Aurangabadkar MD[4] | Satish Bhatia MD[5] | Apratim Goel MD, DNB[6] | Chetan Y. Patil MD[7]

[1]Dr. Kandhari's Skin Clinic, New Delhi, India

[2]Skinnovation Clinics, New Delhi, India

[3]SkinSpace Clinic, Mumbai, India

[4]Dr. Aurangabadkar's Skin & Laser Clinic, Hyderabad, India

[5]Indian Cancer Society, Mumbai, India

[6]Cutis Skin Studio, Mumbai, India

[7]A. Menarini India Pvt Ltd, Mumbai, India

Correspondence
Chetan Y. Patil, A. Menarini India Pvt Ltd, Mumbai 400013, India.
Email: drchetanpatil.gmc@gmail.com

Funding information
A. Menarini India Pvt Ltd

Abstract

Background: Scarring is a common and undesirable outcome of acne vulgaris. There are limited effective topical formulations for acne scar treatment. The investigational product, acne scar serum (HEXILAK® Acne Scar Serum) is latest topical formulation developed for treatment of acne scar with unique ingredients, Kollaren and Exo-T.

Objective: Evaluate safety and efficacy of latest acne scar serum on the reduction of acne scars in Indian population.

Materials and Methods: Subjects, diagnosed clinically with acne scars with or without hyperpigmentation, of either gender in the age group of 15 to 45 years were enrolled in the study. The investigational acne scar serum was applied twice daily for 3 months with monthly follow for outcome evaluation.

Results: Out of 72 subjects enrolled, 67 completed the study. Most of the subjects, 79.1% showed improvement in acne scar at Day 90. Significant reduction of mean total post-acne hyperpigmentation index (PAHI) was seen at all follow up visits compared with baseline. Significant improvement in mean acne scar depth, mean acne scar volume, and mean L value using 3D imaging were observed at all visits compared with baseline. All side effects reported were mild and overall, it was well tolerated by all subjects.

Conclusion: We found that there was a significant reduction in acne scar and post-acne pigmentation with new acne scar serum as a monotherapy, this needs further confirmation in larger randomized controlled studies. Therefore, topical acne scar serum with unique ingredients Kollaren and Exo-T can be a safe, effective, and new option in the armamentarium of acne scar management.

KEYWORDS
acne scar, acne scar serum, scar, scar treatment

1 | INTRODUCTION

Acne vulgaris is one of the most common skin conditions and very often is seen in both adolescent and adult populations. Scarring is a common and undesirable outcome of acne vulgaris that can occur even in the setting of appropriate medical management. Acne scarring often occurs in highly visible areas such as the face.[1] Scarring on the face is equally common in males and females.[2] Hyperpigmentation after acne is also common and in an epidemiological study conducted in more than 6000 Indian acne patients there was a reported prevalence of post-acne scarring in 29% and hyperpigmentation in 35%.[3] Another Indian study for acne of all groups documented scarring and hyperpigmentation in 39.5% and 24.6% of the patients, respectively.[4] Post-acne scarring resulting not only in an undesirable cosmetic appearance but also detrimental effects on mental health, social functioning, and overall well-being.[5]

Various modalities have been used to treat acne scars like chemical peels, dermabrasion, laser resurfacing, skin needling, punch techniques, fat transplantation, platelet rich plasma, silicone dressings, other tissue augmenting agents, subcision etc. Their limited efficacy and problematic side effects can restrict their application and often combination of modalities are required to be used.[6] Therefore, in order to optimally treat a post-acne scar, it is important consider treatment either alone or in combination that can offers the satisfactory result, with better tolerance and which can be used easily. Moreover, there are limited effective topical formulations for acne scar treatment, which can be readily used by patients at their homes.[6,7]

The investigational acne scar serum (HEXILAK® Acne Scar Serum; A. Menarini India Pvt. Ltd.) is the latest topical formulation developed for the treatment of acne scars with unique ingredients, Kollaren and Exo-T.[8] Therefore, a prospective study was planned to assess its efficacy and safety in Indian population for treatment acne scars.

2 | MATERIALS AND METHODS

2.1 | Study objectives

The primary objective of the study was to evaluate the effect of acne scar serum on the reduction of acne scars and to assess its effect on the depth and volume of acne scars. The secondary objectives of the study were to evaluate the effect of acne scar serum on the reduction in post-acne hyperpigmentation and to evaluate the tolerance of acne scar serum.

2.2 | Study design

This was a multicenter, prospective, open label, and single arm study. This study was designed and conducted according to the Declaration of Helsinki, Good Clinical Practice (GCP), and Indian Council of Medical Research (ICMR) guidelines concerning medical research in human subjects. This study was initiated after approval by the independent ethics committee (dated September 21, 2021). Written informed consent from all the subjects was obtained before participation in this study and after being informed about the study procedures, expected outcomes, and side effects.

2.3 | Study population

Subjects, who were diagnosed clinically with acne scars with or without hyperpigmentation, of either gender in the age group of 15 to 45 years and who had not undergone any scar treatment in the past 6 months were included in the study. Subjects enrolled were willing to comply with the study protocol and willing to refrain from use of all other topical medications that would have significantly affected the results of the study.

Pregnant and lactating women, subjects with a history of allergic dermatitis or contact allergy to cosmetics, with known sensitivity to any of the ingredients in the study product, presence of any other skin conditions, diseases, or medical conditions in the investigator's opinion that might require concurrent therapy and interfere with the evaluation of the study medication or compromise patient's safety were excluded.

2.4 | Study procedure

The investigational product acne scar serum (HEXILAK® Acne Scar Serum; by A. Menarini India Pvt. Ltd.)[8] was instructed to apply with sufficient quantity to cover the entire face, twice daily (morning after bath and night before bedtime) for 3 months. Subjects were instructed to wash their face with mild soap or face wash and pat dry before applying the acne scar serum. It had to be applied in a circular motion in the same direction 1 or 2 times without any massage. Follow-up of subjects was done monthly that is on Day 30, Day 60, and Day 90.

2.5 | Study outcome parameters

2.5.1 | Efficacy evaluation

Primary efficacy endpoint was the percentage of subjects showing improvement in acne scars on Clinical Quartile Grading System at all visits compared with baseline. Secondary efficacy endpoint was mean change in Post Acne Hyperpigmentation Index (PAHPI) at all follow-up visits compared with baseline. Total PAHPI (Min 6 to Max- 22) was calculated based on addition of three different scores as,

Score of number of lesions: 1–15, score 1; 16–30, score 2; 31–45, score 3; 46–60, score 4; >60, score 5. Score of median lesion size: <3 mm, score 2; 3–6 mm, score 4; 7–10 mm, score 6; and > 10 mm,

score 8. Score of median lesion intensity: slightly darker than surrounding skin- score 3; moderately darker than surrounding skin—score 6; significantly darker than surrounding skin—score 9.[9]

Other secondary efficacy parameters were instrumental evaluation using 3D imaging and non-invasive ultrasound biomicroscopy (UBM).[10,11] 3D imaging evaluation was done to assess mean reduction in acne scars depth and volume of acne and reduction in post-acne hyperpigmentation, by measuring L* value at all visits compared with baseline.[10] Non-invasive UBM of the acne scars was done at baseline and 90 days to confirm the changes in texture, thickness, and measurements of acne scars.[11]

Subject self-assessment was done (strongly disagree, disagree, neither agree nor disagree, agree, strongly agree) to understand the subject perception about reduction on acne scar number, intensity and pigmentation, and overall satisfaction of study subjects at all follow-up visits compared with baseline.

2.5.2 | Safety assessment

Safety was assessed using adverse drug reaction reporting, physical examinations, and recording of vital signs at each visit. All safety endpoints were summarized descriptively for the safety population. To further clinically evaluate the tolerance of the acne scar serum following scales were used.

2.6 | Statistical analysis

Statistical analysis was done using SPSS 10.0. Descriptive statistics were derived. Categorical data were presented as frequency and percentages. Continuous data were presented as mean and standard deviation. Parametric paired data were analyzed using a two-tailed paired t-test, whereas the Wilcoxon signed-rank test was used to analyze non-parametric matched data. p value <0.05 was considered statistically significant for all comparisons.

3 | RESULTS

Seventy-two subjects were included in the study. Out of that, sixty-seven subjects completed the study (mean age 29.03 ± 7.68 years, range: 17 to 43 years; males: 43.3% and females: 56.7%) and five subjects were lost to follow-up. Subjects with acne scar hyperpigmentation were 91% ($n = 61$) of all the participants.

3.1 | Efficacy evaluation

3.1.1 | Clinical improvement in acne scar

A total of 62.7% subjects showed improvement in acne scar at Day 30. While total 79.1% of subjects showed improvement at Day 60 and Day 90. Moreover, percentage of subjects showing 26–50% improvement in acne scars was 28.4% at Day 90 compared with 11.9% at Day 60 (Figure 1). Mean total PAHI score significantly reduced at all follow-up visits (Days 30, 60, 90) compared with baseline (P-0.001 at all visits vs baseline). At Day 90, mean total PAHI score reduced significantly by 20.9% from baseline (Figure 2). Similarly, mean scores of the number of lesions, median lesion size, and median lesion intensity reduced significantly at all follow-up visits (Days 30,60,90) compared with baseline ($p < 0.05$, at all visits vs baseline, for all three parameters). Moreover, percentage mean score reduction of the number of lesions, lesion size, and lesion intensity at Day 90 were 29.1%, 23%, and 13.8%, respectively (Figure 3–5).

3.1.2 | Instrumental evaluation using 3D imaging

Significant improvement of mean acne scar depth, mean acne scar volume, and mean L value (hyperpigmentation index) were noted at all follow-up visits (Days 30,60,90) compared with baseline ($p < 0.05$, at all visits vs baseline, for all three parameters). The mean percentage improvement at Day 90 compared to baseline was 14.3%,

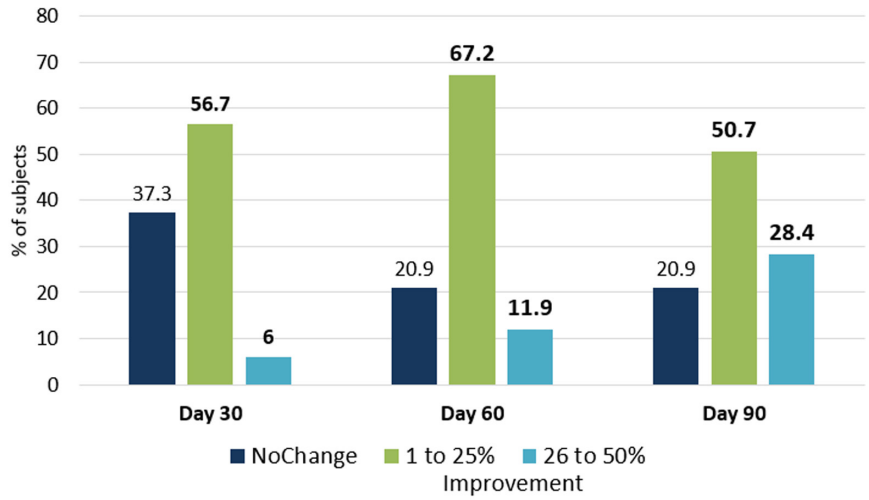


FIGURE 1 Percentage of subjects showing improvement in acne scar ($N = 67$)

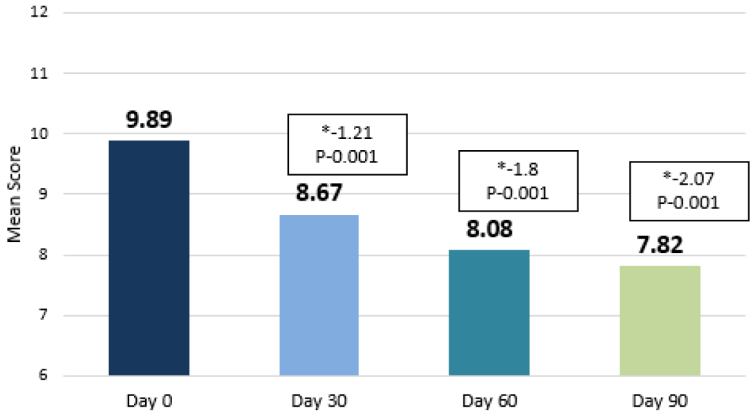


FIGURE 2 Changes in mean total PAHI score ($N = 61$); * mean score difference; p value compared with baseline by Wilcoxon signed rank test, $p < 0.05$- significant

(N = 61); * mean score difference; p value compared to baseline by Wilcoxon signed rank test, P<0.05- significant.

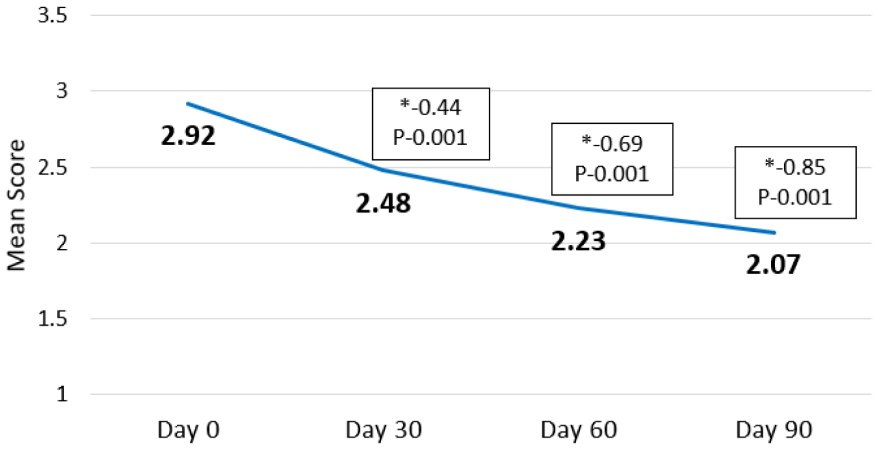


FIGURE 3 Mean changes in score of number of lesions- PAHI ($N = 61$); * mean score difference; p value compared with baseline by Wilcoxon signed rank test, $p < 0.05$- significant

(N = 61); * mean score difference; p value compared to baseline by Wilcoxon signed rank test, P<0.05- significant.

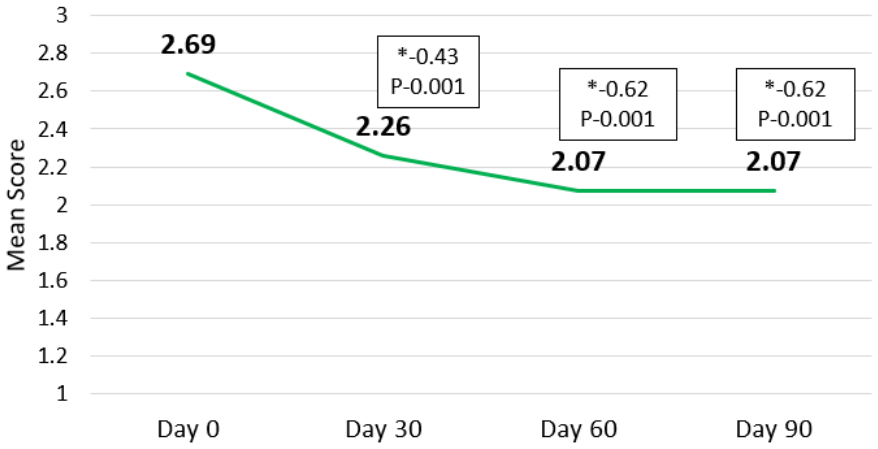


FIGURE 4 Mean changes in score of median lesion size- PAHI ($N = 61$); * mean score difference; p value compared with baseline by Wilcoxon signed rank test, $p < 0.05$- significant

(N = 61); * mean score difference; p value compared to baseline by Wilcoxon signed rank test, P<0.05- significant.

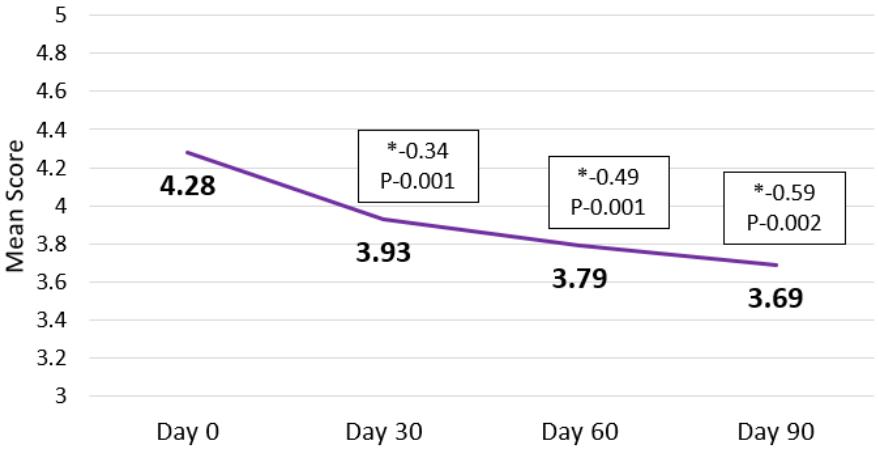
22.5%, and 1.5% for acne scar depth, acne scar volume, and L value, respectively (Figures 6–8).

3.1.3 | Non-invasive ultrasound biomicroscopy

Non-invasive ultrasound assessment was done in 11 subjects as an exploratory assessment to confirm the any changes after the application of acne scar serum for 90 days compared to baseline. The echotexture of the acne scar in 63.6% of subjects changed from inhomogeneous to homogenous. The mean full skin thickness was increased in 81.8% of subjects. Mean scar transverse diameter was reduced in 54.5% of subjects at Day 90 compared with baseline. Overall improvement was recorded in 72.7% of subjects at the end of study.

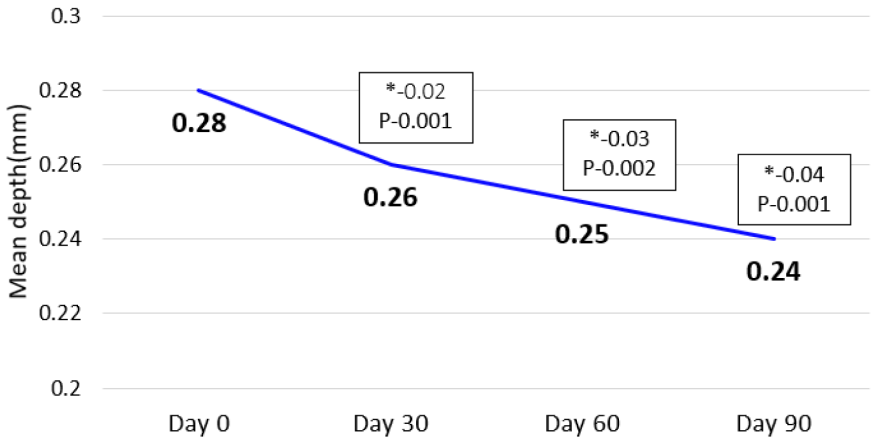
3.1.4 | Self-assessment of efficacy and overall Satisfaction of subjects

Percentage of subjects, who either agreed to strongly agreed that there was a visible in reduction in number of scars, scar intensity, and scar pigmentation at Day 90 compared with baseline were 73.1%, 61.2%, and 71.6%, respectively (Figure 9). Moreover, at Day 90, no subject either disagreed or strongly disagreed regarding the visible in reduction in scars, numbers, intensity, and pigmentation. No subject strongly disagreed about improvement at any follow-up visit. Overall, 69% of subjects were satisfied with treatment. Subjects, who had very good to excellent satisfaction were 34.4% and none of the subject was dissatisfied with treatment.



(N = 61); * mean score difference; p value compared to baseline by Wilcoxon signed rank test, P<0.05- significant.

FIGURE 5 Mean changes in score of median lesion intensity- PAHI (*N* = 61); * mean score difference; *p* value compared with baseline by Wilcoxon signed rank test, $p < 0.05$- significant



(N = 43); * mean difference; p value compared to baseline by two tailed paired 't' test, P<0.05- significant.

FIGURE 6 Changes in mean acne scar depth (*N* = 43); * mean difference; *p* value compared to baseline by two tailed paired "*t*" test, $p < 0.05$- significant

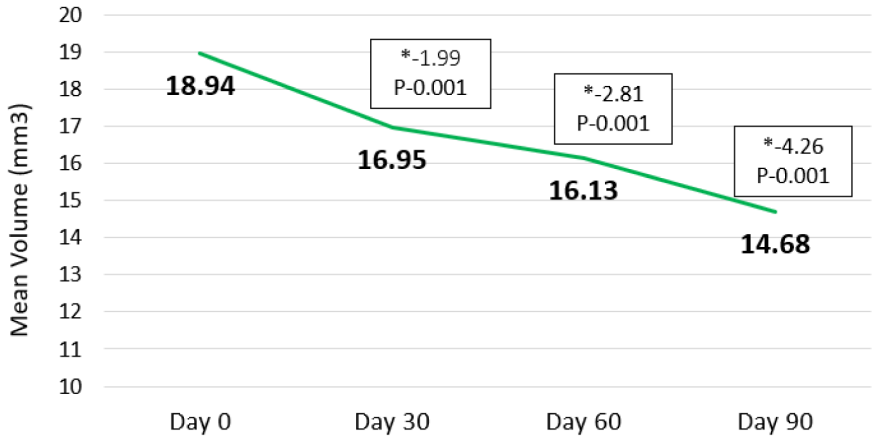


FIGURE 7 Changes in mean acne scar volume ($N = 43$); * mean difference; p value compared with baseline by two tailed paired "t" test, $p < 0.05$- significant

(N = 43); * mean difference; p value compared to baseline by two tailed paired 't' test, P<0.05-significant.

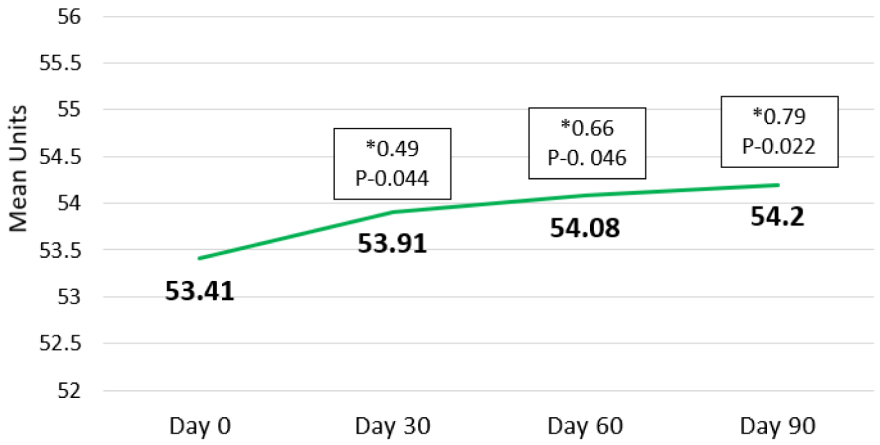


FIGURE 8 Changes in Mean post acne hyperpigmentation, L Value ($N = 43$); * mean difference; p value compared to baseline by two tailed paired "t" test, $p < 0.05$- significant

(N = 43); * mean difference; p value compared to baseline by two tailed paired 't' test, P<0.05-significant.

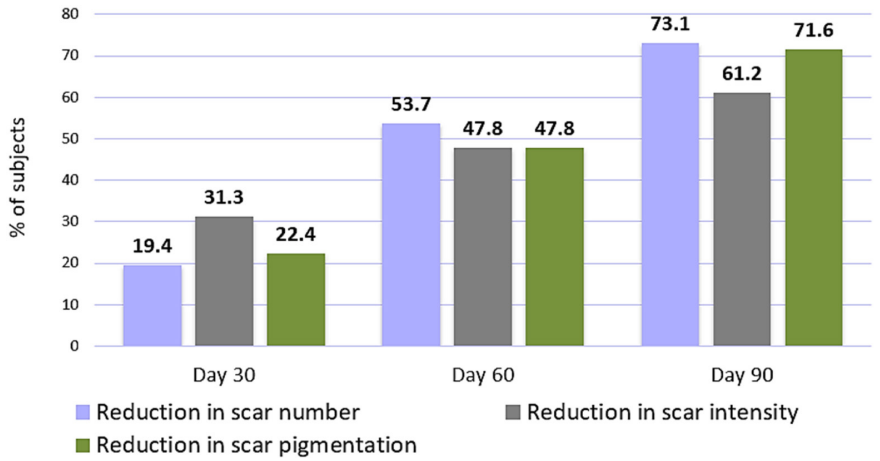


FIGURE 9 Percentage of subjects reporting agree to strongly agree for reduction in scar number, intensity, and pigmentation ($N = 67$)

(N = 67)

3.2 | Safety assessment

Erythema (1.4%), localized itching (2.8%), and cutaneous dryness (5.6%) was reported with initial application of acne scar serum, which resolved spontaneously within a few hours to few days of onset. All side effects reported by subjects were mild. One more subject developed slight erythema after Day 30 visit which also resolved spontaneously within few days.

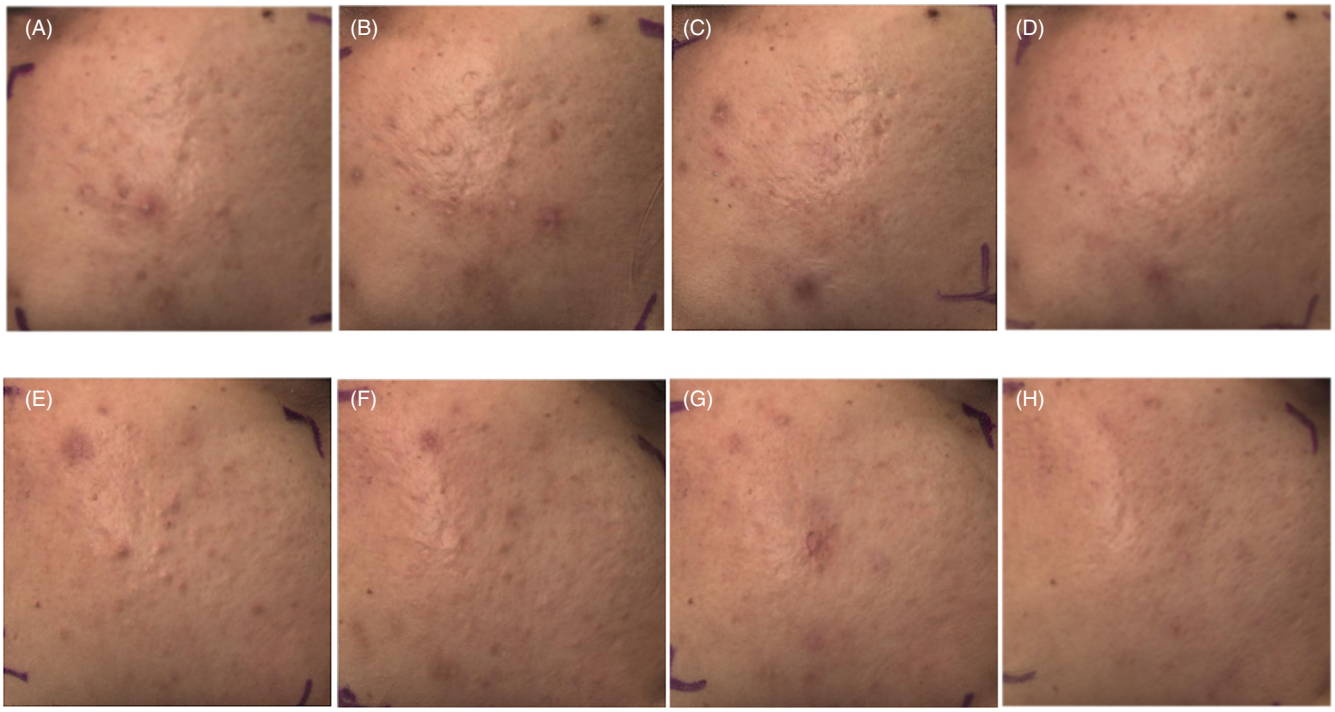


FIGURE 10 31-year-old female patient, (A–D) left cheek area. (A) Day 0 before treatment, and (B) Day 30, (C) Day 60, (D) Day 90 after treatment showing clinical improvement. (E–H) right cheek area. (E) Day 0 before treatment, and (F) Day 30, (G) Day 60, (H) Day 90 after treatment showing clinical improvement

Changes in acne scar appearance of 31-year-old female patient in clinical and 3D imaging photographs at all study visits are shown in Figures 10 and 11, respectively. Changes in acne scar appearance of 20-year-old female patient at Day 0 before treatment, and at Day 90 after treatment are shown in Figure 12.

4 | DISCUSSION

Post-acne scarring is a very distressing and difficult problem for physician and patient alike and can affect the mental health and quality of life of patient significantly. Therefore, it is important to treat acne scarring early and possibly prevent their formation by effective and early acne management. However, some degree of post acne facial scarring has been reported to occur in up to 95% of acne patients with severe scarring in 30% of these patients.[1,2,12] Moreover, scarring will occur in almost all types of acne, not just limited in nodulocystic acne.[1,12]

Patho-physiologically post acne **scarring** occurs when there is a delayed and extended inflammatory process that is not as effective at repairing tissue. Chronic inflammation can be damaging to the skin tissue and cause acne scarring.[13] Once inflammation subsides, the body begins repairing the tissue damage, by stimulating the production of important extracellular matrix (ECM) proteins such as collagens.[14] The ECM plays important role, by providing structure, organization, and orientation to cells and tissues and controlling cellular metabolism by acting as a template for cell migration, proliferation, differentiation, and adhesion.[2,15] Atrophic scarring is more common and is characterized by an overall localized reduction in collagen content. It can be further divided into various subtypes based on morphologic criteria (e.g., size and depth), such as boxcar, ice pick, and rolling scars.[1,2,14]

Hyperpigmentation often accompanies scaring after the acne, especially in darker skinned individuals and those living in areas of intense sun exposure.[16,17] Pigmentation changes following active acne lesions are usually transient; however, when permanent, are a great cosmetic concern. Topical agents for treating hyperpigmentation include retinoids, azelaic acid, and hydroquinone. Hydroquinone, a topically applied bleaching agent, is often the first-line and but has potential adverse effects include hypopigmentation of surrounding normal skin (the "halo effect") and the development of contact dermatitis.[16]

Current aesthetic medicine practice can offer a wide range of treatment options for reducing acne scars, depending on the type of scar, its location, the depth of the lesions. Though many options are available, repeated treatment is often necessary with many of these modalities and often in combinations. Moreover, many of these modalities have limited efficacy and undesired side effects have restricted their application. Therefore, in order to optimally treat a post-acne scar, it is important to consider treatment that offers the satisfactory result with ease of application.[1,6,7,16]

Investigational acne scar serum is a new topical formulation of unique ingredients viz.

Kollaren (15%) and Exo-T (2%).[8] Kollaren (Butylene Glycol, Dextran, and Tripeptide-1) is a biomimetic peptide. Being a biomimetic peptide, which is similar to the skin's peptides, it acts on

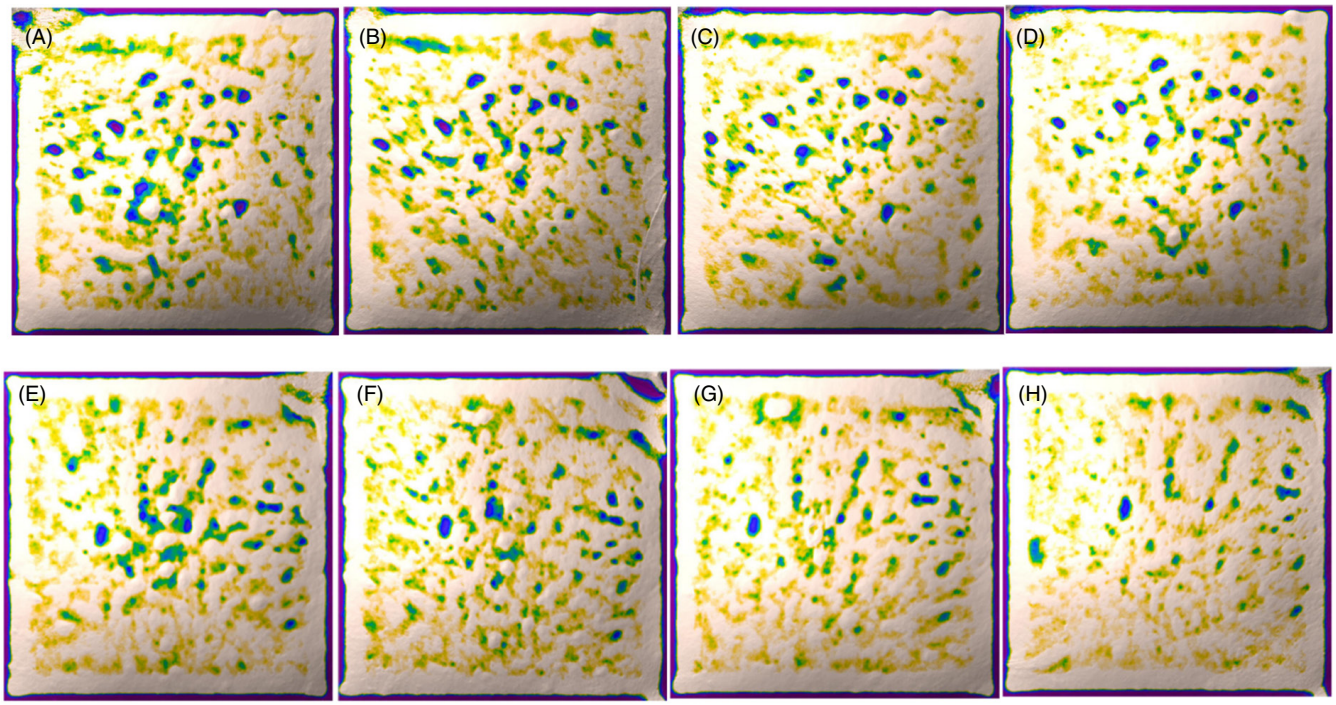
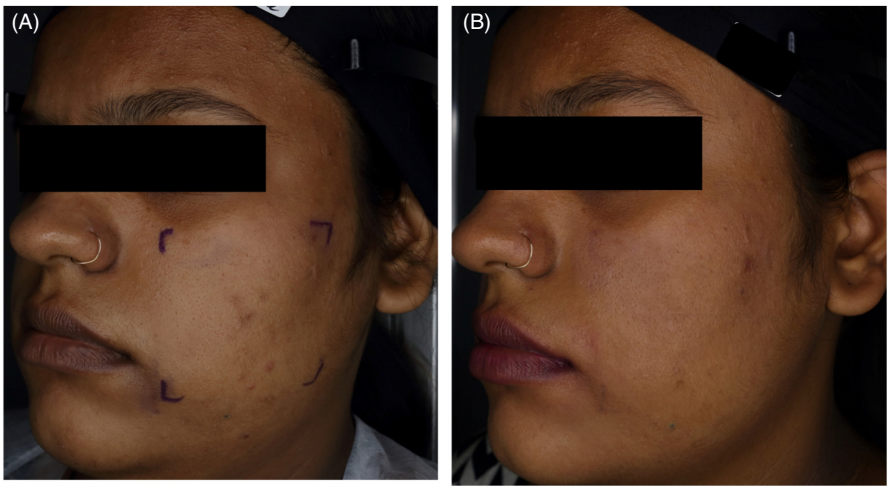


FIGURE 11 31-year-old female patient, (A–D) left cheek area. (A) day, and (B) Day 30, (C) Day 60, (D) Day 90. (E–H) right cheek area. (E) Day 0, and (F) Day 30, (G) Day 60, (H) Day 90 with 3D color photo-analysis. Purple to dark shade of blue indicates large depressions, lighter shade of blue to green indicates smaller depressions with lesser depth, and yellow to white represents relatively flat surface. Thus, indicating reduction in scar depth and intensity on follow-up visits compared with Day 0

FIGURE 12 20-year-old female patient, left cheek area. (A) Day 0 before treatment, and (B) Day 90 after treatment showing clinical improvement



the physiological mechanisms of the skin with a higher specificity. Kollaren stimulates synthesis of ECM Proteins such as Type I and III Collagen, Fibronectin, Laminin, and Elastin. In vitro placebo-controlled study conducted using Kollaren, reported stimulation of the ECM proteins, Type I collagen (+305%) and III collagen (+105%), Fibronectin (+155%), Laminin (+85%), and Elastin (+15%). Another invitro study conducted on excised human skin with topical application of 15% of Kollaren daily for 5 days improved tensile strength of the scar by 31%. Thus, indicating improvement in the skin regeneration and faster tissue repair.[18]

Exo-T (Butylene Glycol, Vibrio Alginolyticus Ferment Filtrate) is a purified exopolysaccharide derived from kopara microorganisms vibrio alginolyticus found in islands of French Polynesia.[19] Skin desquamation is required for shedding of old cells at the skin surface and is essential for the continuous regeneration of the skin; and Exo-T has been found to stimulate the desquamation process.[19,20] In vitro study has demonstrated increased levels of desquamation markers Kalikreins; KLK5 (+60%), KLK6 (+280%), KLK7(+307%) with Exo-T.[19] Involucrin and filaggrin are markers of cell differentiation and both proteins are expressed in the outermost layers of the epidermis. Increased expression of involucrin and filaggrin has been associated with accelerated recovery after skin barrier disruption.[19,21] It was noted in the in vitro study that Exo-T increases levels of involucrin (+136%) and filaggrin (+103%). Transglutaminases (TGM) are found at

the outmost layer of the epidermis, where its activity is required for the formation of the cornified envelope to improve skin barrier function.[19,22] Application of Exo-T for 3 hrs at the surface of skin explants immediately after delipidation was found to restores TGM levels.[19]

Thus, Kollaren one of the ingredients in new acne scar serum, can regenerate and stimulate the production of the essential ECM proteins thus increasing tissue regeneration and healing process of the skin. While, another key ingredient, Exo-T can help in regulating cell differentiation and desquamation in the skin and protects the collagen network and thus contributes to skin rejuvenation. Therefore, investigational acne scar serum with these unique ingredients can help in reducing the appearance of acne scars and can promote smoother and healthier looking skin.[8,18,19]

Current prospective study, which was conducted in Indian patients using innovative acne scar serum showed majority of participants (79.1%) showing improvement in acne scar at day 90 based on clinical assessment. Clinical grading of scar pigmentation also showed significant reduction at all follow up visits compared with baseline. Similarly, there was a significant reduction of individual PAHI, mean score of number of lesions, median lesion size, and median lesion intensity at all follow-up visits compared with baseline. Instrumental analysis using 3D imaging revealed that there was significant improvement in mean acne scar depth and mean scar volume at all follow-up visits. Moreover, significant improvement in pigmentation was also seen at all follow-up visits compared with baseline. Based on non-invasive ultrasound biomicroscopy, though conduced in limited number showed the similar improvement in acne scar. Overall, this new acne scar serum was well tolerated by all subjects and all the side effects were mild and self-limiting.

There are some limitations to the present study. The current study is a single-arm. Therefore, larger randomized control studies would be required to confirm the findings of this study. Future studies with longer-multiple follow-ups will be required to assess the long-term effect of acne scar serum. Current study was done using the monotherapy of acne scar serum, and considering its outcomes as monotherapy, and in further studies, it will be interesting to assess possible synergistic effect with routinely performed treatment modalities.

5 | CONCLUSION

There was a significant improvement in acne scar as well as post-acne pigmentation with new acne scar serum as a monotherapy. Based on encouraging results of new acne scar serum as a monotherapy, its application also needs to be evaluated as an adjunctive to conventional treatment options. Overall, it was well tolerated. Thus, topical acne scar serum with unique ingredients Kollaren and Exo-T can be a safe, effective, and new option in the armamentarium of acne scar management.

AUTHOR CONTRIBUTIONS

S.K., A.G., A.T., S.B., and A.G. designed the research study. A.T. performed the research. S.K., A.G., A.T., S.A., and S.B. analyzed the data and interpreted the results. C.P., A.G., and A.T. wrote the paper. All authors have read and approved the final manuscript.

ACKNOWLEDGMENT

We acknowledge Dr Mukta Sachdev for guiding us on study designing. We would also like to acknowledge C.L.A.I.M.S. PVT. LTD, Dr. D. Nagaraju, and Dr. Kalpana Bhatt for their assistance with the trial conduction.

FUNDING INFORMATION

This study was funded by A. Menarini India Pvt Ltd, Mumbai.

CONFLICT OF INTEREST

There are no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

The study was carried out in accordance with the ethical guidelines and principles of the 1975 Declaration of Helsinki, Good Clinical Practice (GCP) and Indian Council of Medical Research (ICMR) guidelines concerning medical research in human subjects. Study was approved by the independent ethics committee on September 21, 2021 (ECR/245/Indt/MH/2015/RR-18).

REFERENCES

1. Lanoue J, Goldenberg G. Acne scarring: a review of cosmetic therapies. *Cutis*. 2015;95(5):276-281.
2. What causes a pimple to scar? - Acne.org. Accessed on 30 September 2022 https://www.acne.org/what-causes-a-pimple-to-scar.html
3. Budamakuntla L, Parasramani S, Dhoot D, Deshmukh G, Barkate H. Acne in Indian population: an epidemiological study evaluating multiple factors. *IP Indian J Clin Exp Dermatol*. 2020;6(3):237-242.
4. Adityan B, Thappa DM. Profile of acne vulgaris-a hospital-based study from South India. *Indian J Dermatol Venereol Leprol*. 2009;75(3):272-278.
5. Halvorsen JA, Stern RS, Dalgard F, Thoresen M, Bjertness E, Lien L. Suicidal ideation, mental health problems, and social impairment are increased in adolescents with acne: a population-based study. *J Invest Dermatol*. 2011;131:363-370.
6. Gozali MV, Zhou B. Effective treatments of atrophic acne scars. *J Clin Aesthet Dermatol*. 2015;8(5):33-40.
7. Goodman GJ. Management of post-acne scarring. What are the options for treatment?. *Am J Clin Dermatol*. 2000;1(1):3-17.
8. HEXILAK® Acne Scar Serum, Package insert. A. Menarini India Pvt. Ltd. 2022.
9. Savory SA, Agim NG, Mao R, et al. Reliability assessment and validation of the postacne hyperpigmentation index (PAHPI), a new instrument to measure postinflammatory hyperpigmentation from acne vulgaris. *J Am Acad Dermatol*. 2014;70(1):108-114.
10. Linming F, Wei H, Anqi L, et al. Comparison of two skin imaging analysis instruments: the VISIA® from canfield vs the ANTERA 3D® CS from Miravex. *Skin Res Technol*. 2018;24(1):3-8.
11. El-Zawahry MB, Abdel El-Hameed El-Cheweikh HM, Abd-El-Rahman Ramadan S, et al. Ultrasound biomicroscopy in the diagnosis of skin diseases. *Eur J Dermatol*. 2007;17(6):469-475.

12. Layton AM, Henderson CA, Cunliffe WJ. A clinical evaluation of acne scarring and its incidence. *Clin Exp Dermatol*. 1994;19:303-308.
13. Holland DB, Jeremy AH, Roberts SG, Seukeran DC, Layton AM, Cunliffe WJ. Inflammation in acne scarring: a comparison of the responses in lesions from patients prone and not prone to scar. *Br J Dermatol*. 2004;150(1):72-81.
14. Fabbrocini G, Annunziata MC, D'Arco V, et al. Acne scars: pathogenesis, classification and treatment. *Dermatol Res Pract*. 2010;2010:893080.
15. Xue M, Jackson CJ. Extracellular matrix reorganization during wound healing and its impact on abnormal scarring. *Adv Wound Care (New Rochelle)*. 2015;4(3):119-136.
16. Levy LL, Zeichner JA. Management of acne scarring, part II: a comparative review of non-laser-based, minimally invasive approaches. *Am J Clin Dermatol*. 2012;13(5):331-340.
17. Spann CT. Ten tips for treating acne vulgaris in Fitzpatrick skin types IV-VI. *J Drugs Dermatol*. 2011;10(6):654-657.
18. KOLLAREN™ Technical File - Lucas Meyer Cosmetics. Accessed on 2 October 2022. https://www.lucasmeyercosmetics.com/sites/lucasmeyer-corp-v2/files/Lucasmeyer/documents-downloads/kollaren-techfile.pdf
19. EXO™ - T technical file - Lucas Meyer Cosmetics. Accessed on 2 October https://www.ulprospector.com/documents/1044879.pdf?bs=4498&b=124788&st=1&sl=143289116&crit=a2V5d29yZDpbZXhvLXRd&k=exo-t&r=asia&ind=personalcare
20. Nauroy P, Nyström A. Kallikreins: essential epidermal messengers for regulation of the skin microenvironment during homeostasis, repair and disease. *Matrix Biol Plus*. 2019;21(6-7):100019.
21. Lee WJ, Park KH, Cha HW, et al. The expression of involucrin, loricrin, and filaggrin in cultured sebocytes. *Ann Dermatol*. 2014;26(1):134-137.
22. Hasegawa T, Shimada H, Uchiyama T, Ueda O, Nakashima M, Matsuoka Y. Dietary glucosylceramide enhances cornified envelope formation via transglutaminase expression and involucrin production. *Lipids*. 2011;46(6):529-535.

How to cite this article: Kandhari S, Ganjoo A, Talathi A, et al. Efficacy and safety of innovative acne scar serum in Indian patients (ESTEEM India study). *J Cosmet Dermatol*. 2023;22:880-889. doi:10.1111/jocd.15536