Review Article

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Indian dermatological experts' consensus on topical peptides for revising acne scars

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ABSTRACT

Acne scars are the common and one of the challenging conditions to treat that are often encountered at dermatologist's clinic. Peptides in cosmetics have gained popularity due to their potential benefits in promoting skin health and anti-aging properties. These small protein fragments can help stimulate collagen production, reduce fine lines and wrinkles, and improve overall skin elasticity. When incorporated into skincare products, peptides work by sending signals to the skin cells, encouraging them to function optimally and maintain a youthful appearance. However, it is essential to choose products from reputable brands, as the efficacy of topical peptides can vary significantly among different formulations. This article discusses the potential role of topical peptides in acne scar management. Experts group meeting was conducted across the four zones and faculty part of acne scar forum discussed the role of peptides along with evidence-based data sharing on peptides was done. Following the meeting the dermatologist were asked to share their opinion and insights on using peptides in their practice and the data was captured to better understand the product. It was found that dermatologists believed that Peptides are valuable topical agents that can be beneficial in various scenarios where it can be utilized as home-based treatment or an adjutant to the various office-based treatment to expedite overall treatment outcome. Since peptides do not irritate or dry up the skin like other topical medicines do, most doctors believed they have an advantage over them.

Keywords: Acne scar serum, Topical peptides, Acne scars, Peptides for acne scar, Topical peptides consensus

INTRODUCTION

Acne is a common condition that affect up to 80% of adolescents at varying degree of severity. Acne scarring is common sequel of acne that can affect up to 95% of

individuals.² Severe scarring has been reported in 30% of acne patients, although mild to moderate scarring has been reported in up to 95% of these patients.³ The pathogenesis of atrophic acne scarring is most likely related to inflammatory mediators and enzymatic degradation of collagen fibres and subcutaneous fat.⁴

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Impaired cosmetic appearance is not the only negative impact of acne scars. Rather, there is evidence linking acne scars to mental health conditions such as melancholy and suicidal thoughts, emotional exhaustion, humiliation, low self-esteem, and overall social impairment.⁵

The necessity to treat different forms of acne scars, the variety of reactions observed in different skin types, and the growing popularity of minimally disruptive techniques has been observed, while several treatments might lessen the visibility of acne scars, none can eliminate them. For the best cosmetic outcomes, scar treatment usually requires a multimodality approach. The kind and severity of acne scars, patient choice, side effects, cost, and accessibility to treatments are all taken into consideration when choosing a treatment plan.

Topical peptides have emerged as a promising new adjuvant modality of routine treatment. Clinical studies have demonstrated the beneficial effects of topical peptides when used as monotherapy or as an adjunctive treatment for acne scarring.⁶

NEED FOR CONSENSUS

Although topical peptides have been increasingly utilised in dermatology for various indication like Acne scars and anti-ageing etc., there is still scarcity in terms a proper randomised controlled trials or comprehensive reviews regarding its effectiveness. The purpose of this consensus document is to provide dermatologists with a comprehensive, evidence-based guide on use of topical peptides for patients suffering from acne scars based on the clinical experience of a dermatologists throughout India who have used topical peptides in their practice.

METHODOLOGY USED IN STUDY

A panel of 120 dermatologists, each with over 12 years of professional experience, having used peptides in their practice participated in the scar forum 2024, held in Mumbai and Kolkata, Lucknow, and Delhi. These experts were engaged in a series of in-depth discussions focused on the various aspects of acne scars, including their etiopathogenesis (origin and development), clinical features, diagnostic methods, and the potential therapeutic role of peptides in managing these scars.

Set of question were drafted in deliberation with panellist and following the discussions, all responses and opinions of dermatologists participated in Scar forum 2024 were systematically recorded and transcribed. This transcript served as the foundation for the development of the consensus document. The experts then thoroughly reviewed the compiled manuscript, offering feedback and suggesting specific revisions. These suggestions were carefully incorporated to enhance the accuracy, clarity, and authenticity of the document. By critically refining the document, the expert group ensured that the final

version would serve as a reliable and scientifically supported reference for dermatologists, helping them make informed treatment decisions for patients with acne scars.

ACNE SCARS

Acne vulgaris is an inflammatory process localized to the pilosebaceous units of the face, chest, upper arms, and back. Most often, acne affects the face, and many patients have some scarring, the severity of which varies with acne grade. An impaired wound healing response to epidermal inflammation causes acne scars; inflammatory cell infiltrates are present in 77% of atrophic scars. Different kinds of acne scars are caused by abnormal collagen synthesis and breakdown throughout the healing process. Atrophic scars are the result of a net breakdown of collagen in the dermis, which occurs in 80 to 90 percent of cases. Less frequently, hypertrophic or keloid scars are the result of a net collagen gain. 10

Atrophic scars are classified according to the depth and size of destruction; however, different scar types are typically seen on the same person, making differentiation difficult.¹⁰ Between 60 and 70 percent of atrophic scars are icepick scars. The sharp border of these V-shaped, narrow, less than 2 mm epithelial tracts continue vertically to the deep dermis or subcutaneous tissue. Icepick scars are resistant to traditional skin resurfacing techniques due to their depth of involvement. Twenty to thirty percent of atrophic scars are boxcar scars. These scars are circular to oval, 1.5 to 4.0 mm in width, and their vertical edges are clearly defined. Deep boxcar scars (≥0.5 mm) are resistant to skin resurfacing procedures, but shallow boxcar scars (0.1-0.5 mm) respond well to them. Fifteen to twenty-five percent of atrophic scars are rolling scars. These scars are the largest, with a maximum diameter of 5 mm. Scars appear undulating and have superficial shadowing due to fibrous anchoring of the dermis to the subcutis.¹⁰

CONSENSUS POINT 1: PREFERENCE FOR TOPICAL PEPTIDES IN CLINICAL PRACTISE

When Doctors were asked do, they prefer utilising peptides, in nearly 98 (82%) of the doctors agreed that they prefer using topical peptides in their practice. Most of the doctors believe that peptides have gained lot of popularity in the recent times in the cosmeceuticals because of their ability to modulate extracellular matrix proteins and improving pigmentation that are especially beneficial in the patients with atrophic acne scars.

Topical peptides

A peptide is a group of amino acids connected by peptide bonds. In terms of chemical complexity, peptides fall somewhere between larger proteins and typical small molecule compounds. 11,12 It is well recognized that naturally occurring peptides have a wide range of

biological functions, chief among them being as signaling/regulatory molecules in numerous physiological processes like as growth, homeostasis, immunity, defense, and reproduction. Dermatology and cosmetics industries have lately developed short, stable, synthetic peptides that are involved in inflammation, innate immunity, pigmentation, and creation of extracellular matrix. 13

CONSENSUS POINT 2: UTILIZATION OF TOPICAL PEPTIDES IN VARIED DERMATOLOGICAL INDICATION

Since bioactive peptides have varied function, they have been utilized in dermatology for various indications like to improve the signs of aging, in management of the acne scars, pigmentations etc. Forum was asked where exactly they prefer utilizing topical peptides and had to choose between the options like antiaging, acne scars, both, and none. There was mixed opinion regarding use of topical peptides where 82 (71%) of doctor agreed they prefer using peptides for both antiaging and acne scar management and 25 (29%) doctors believed that peptides are better when used in management of acne scars.

Topical peptides in varied dermatological indications

Peptides are new active components that increase the production of collagen, promote the growth of skin cells, or reduce inflammation. They can be categorized as signal peptides, carrier peptides, neurotransmitter inhibitor peptides, and enzyme inhibitor peptides according to how they work.¹⁴

Figure 2 shows various dermatological indications where topical peptides are being used.¹⁵ Their primary function as anti-wrinkle agents has made them extraordinary substances. Cosmetic peptides work in several ways to minimize wrinkles and stop new ones from developing; these mechanisms can work in concert to produce better effects.

Carrier peptides provide vital trace elements to support skin repair; neurotransmitter inhibitor peptides relax facial muscles, minimizing expression wrinkles; signal peptides stimulate fibroblast cells to increase collagen production and improve skin elasticity; and enzyme inhibitor peptides decrease collagen breakdown, maintaining the integrity of the skin. 15,16

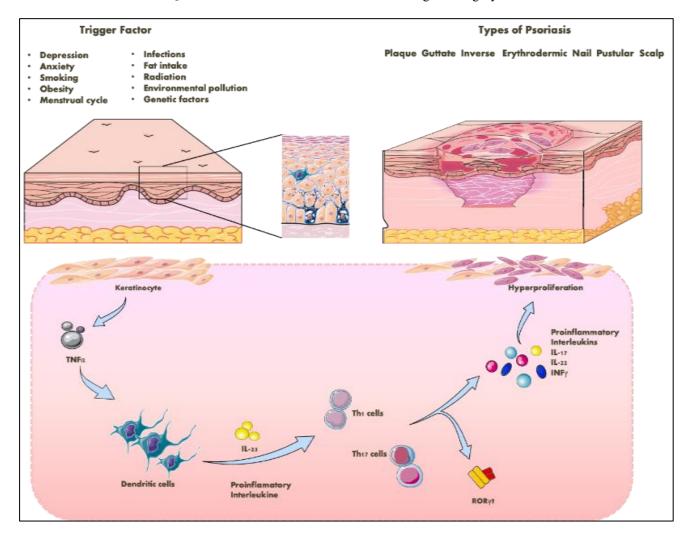


Figure 1: Trigger factor and types of psoriasis.

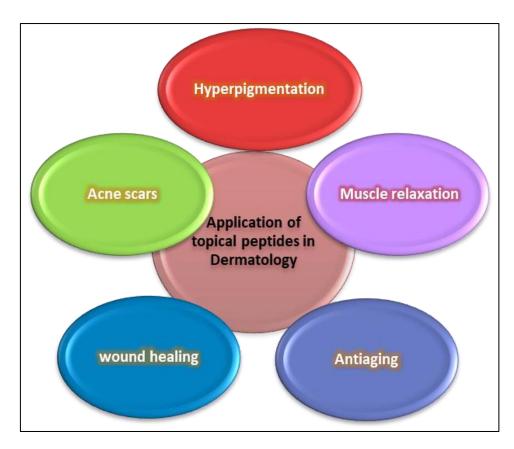


Figure 2: Dermatological indications where topical peptides are utilized.

Enhancing the stimulation of collagen formation is one of their most important benefits. The ability of signal peptides to imitate the transmitted signal during the manufacture of extracellular matrix proteins, such collagen and elastin, is primarily responsible for this trait. This mimicry leads to increased fibroblast activity, which in turn produces collagen and elastin.

To produce more elastic, firm, and smoother skin, peptide s are used to restore collagen levels that have been impact ed by fibroblast senescence. This slows down the prolifer ation of fibroblasts and decreases the manufacture of coll agen, particularly type I, while also addressing the destruction of collagen by proteolytic enzymes.¹⁷

Additionally, several peptides may have antioxidant qualities that prevent the overproduction of reactive oxygen species (ROS). Its detrimental effects can be exacerbated by a variety of exogenous or endogenous stimuli, including inflammation, toxins, ultra violet radiation, as well as others. By scavenging free radicals via several mechanisms, peptides help to reduce the oxidative stress in the skin and postpone the aging process of the skin.¹⁸

One promising novel adjuvant technique for routine treatment is topical peptides. Topical peptides have been shown in clinical studies to have positive benefits on acne scarring when used either as a monotherapy or as an adjuvant.¹⁹

CONSENSUS POINT 3: TOPICAL PEPTIDE IN RECENT OR CHRONIC ACNE SCARS

Topical peptides work by modulating extracellular matrix protein. When the dermatologists were asked to share their experience on utilisation of peptides in recent and chronic acne scars, most of the dermatologists who were part of forum believed that topical peptides have role in both recent and the chronic acne scar. Nearly 72 (60%) doctors agreed that when used in the recent acne scar, they have better ability to modulate the collagen and prevent prevents further breakdown of extracellular matrix and thus prevent further scar progression. Doctors were also of opinion that topical peptides have ability to reduce erythema associated with the early acne scars specially in cases where patient cannot afford devicebased treatment. The 36 (30%) of the doctors believed that they are beneficial in chronic acne scar but not as a monotherapy but when used in conjunction with devicebased therapies to expedite the overall treatment outcome

Clinical evidences of topical peptides in acne scars

Topical peptides have emerged as a promising new adjuvant modality of routine treatment. Clinical studies have demonstrated the beneficial effects of topical peptides when used as monotherapy or as an adjunctive treatment for acne scarring. It has been shown in the studies that topical peptides following invasive resurfacing procedures promote healing and reduce

downtime, leading to better patient outcomes and improved patient satisfaction.¹⁹

In a study by Jordan et al it was found that addition of tripeptide/hexapeptide serum as a peri-procedural adjunct to non-ablative fractional laser resurfacing improved various clinical measures of photodamage and cutaneous aging and the immediate postprocedural recovery. The tripeptide/hexapeptide serum was demonstrated to be safe, well-tolerated, and well-liked by subjects.²⁰

In another study by Weinstein et al who evaluated the efficacy and safety of a topical tripeptide/hexapeptide anhydrous gel when used pre- and post- hybrid fractional laser for the treatment of acne scars. The use of RSN pre- and post-laser resurfacing significantly decreased postprocedural TEWL and erythema, and increased aesthetic improvement in acne scars and patient satisfaction, when compared with bland moisturizer. ²¹

About 80% of participants in a study by Kandhari et al who were on Kollaren and exo-T, a combination peptide (HEXILAK® acne scar serum) in Indian patients showed a significant reduction in their acne scars within three months. Apart from scar gradings, there was also a significant reduction in pigmentation.¹⁹

In a study by Vanaman et al peptide/hexapeptide serum was added as a peri-procedural adjunct to non-ablative fractional laser resurfacing, which enhanced the immediate postprocedural recovery as well as several clinical measures of photodamage and skin aging. It was shown that the peptide/hexapeptide serum was well-liked, well-tolerated, and safe.²²

In a review by Angra et al mentioned that tripeptide/hexapeptide modulates the extracellular matrix by upregulating matrix metalloproteinases, tissue inhibitor of metalloproteinases, decorin, dermatopontin, elastin, and collagen and believed that peptides can reduced post–laser-resurfacing erythema, exudation, tenderness, burning/stinging, and bruising; additionally, there was an improved rate of wound healing and cosmetic outcome.²³

CONSENSUS POINT 4: TOPICAL PEPTIDE BENEFITS ACCORDING TO TYPE OF ACNE SCAR

As each type of acne scar respond differently to different treatment options whether same thing will imply to topical peptides? In consensus we tried to understand that will topical peptide has different effects on different types of acne scars? When the forum was asked for their opinion regarding topical peptides benefits differently with each type of scar? we got different opinions. Nearly 14 (12%) of doctors said that it works well in the box scar, 14 (12%) doctors agreed that it works better in the icepick scars, 24 (20%) of doctors opined that it is beneficial in rolling scars, 62 (52%) doctors said it works

well in all the types of the scars and 2 (1%) of doctors said it does not have any benefits. Over all 118 (99%) agreed that topical peptides have benefits in acne scars. Most of the doctors said that topical peptide has a benefit over different types of acne scars but the extent to which patient can get benefit is variable and is influenced by several factors like severity of the scar, patient compliance etc.

CONSENSUS POINT 5: MECHANISM BY WHICH TOPICAL PEPTIDE HELPS IN ACNE SCARS

As acne scars are atrophic and often associated with pigmentation, we asked the doctors how exactly they benefit in acne scars. Doctors opined that topical peptides are biomimetic peptides and possess anti-inflammatory activity due to which it is been able to reduce inflammation that is associated with the acne and prevent post inflammatory hyperpigmentation. As peptides are signalling molecules, they also have effect on the collagen modulation because of which it helps in pluming atrophic acne scar by improving the scar associated pigmentation and collagen modulation topical peptides can overall improve the outcome.

Mechanism by which topical peptides work

Acne scars, especially atrophic types, form due to collagen loss and impaired skin repair.²³ Topical peptides-short amino acid chains-act as biological messengers that trigger collagen production, reduce inflammation, and promote healthy tissue remodelling. This makes them a promising, non-invasive option for improving scar texture and appearance.²⁴

A. Collagen stimulation and ECM remodelling

Topical peptides such as GHK-Cu (Copper tripeptide), Kollaren® (Tripeptide-1), and palmitoyl pentapeptide-4 stimulate fibroblast activity and promote the synthesis of collagen types I and III, elastin, and fibronectin, leading to improved dermal structure and reduced scar depth.²⁵⁻²⁷

B. Cell renewal and keratinocyte proliferation

Exo-TTM (Exot), a peptide that promotes keratinocyte differentiation and desquamation. It supports skin renewal by accelerating epidermal turnover and reducing the appearance of post-inflammatory hyperpigmentation and textural irregularities. It is particularly beneficial in acne-prone and scarred skin due to its gentle exfoliating and regenerative properties.²⁸

C. Matrix metalloproteinase (MMP) regulation

Excessive MMP activity leads to ECM breakdown in acne scars. GHK-Cu and tripeptide-1 modulate MMPs, preventing over-degradation of dermal structures and allowing a balanced matrix remodeling, crucial for effective scar reduction. 25-27

D. Inflammation modulation

Peptides such as GHK-Cu and Kollaren have demonstrated anti-inflammatory effects by reducing cytokine expression (e.g., IL-6, TNF-α).

This limits prolonged inflammation-a key contributor to scar formation-and allows more organized collagen deposition during healing.^{27,29} Figure 3 depicts various mechanisms by which topical peptides work in acne scars

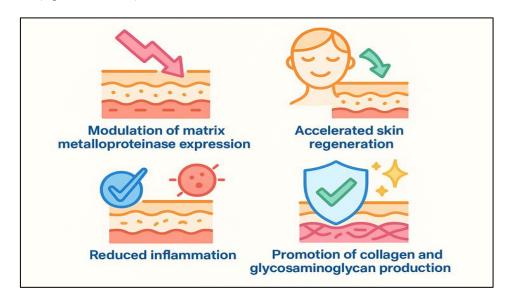


Figure 3: Mechanisms by which topical peptides work in acne scars.

CONSENSUS POINT 6: TOPICAL PEPTIDES AS MONOTHERAPY OR AS ADJUTANT TO VARIOUS TREATMENT MODALITIES

Nearly 48 (40%) of doctors were of opinion that it is better if used post procedure as it decreases procedure associated erythema or inflammation and help to expedite the outcome. The 51 (43%) of doctors said there are beneficial in both the cases as in monotherapy in early cases or in combination or adjutant to procedures but one should know that the outcome is not going to be dramatic.

CONSENSUS POINT 7: TOPICAL PEPTIDES ON TREATMENT OUTCOME WHEN USED WITH OTHER DEVICE-BASED PROCEDURES

Deeper ablative therapies occasionally associated with side effects including delayed healing, infection, scarring, erythema, acne, milia, oedema and dyspigmentation.³⁰ Doctors opined that post procedures they always ask patient to take utmost care with use of proper sunscreen, moisturisers, or other topical medications to prevent any irritation that occurs but there are no topicals medications that can work in synergy of procedure where the topical product can mitigate the side effects like erythema, or inflammation. In these kind situations it is great to have products that can mitigate after procedure side effects. The 96 (80%) of the participants agreed that peptides when used in conjunction with the conventional clinicbased procedure promote healing and reduce downtime, leading to better patient outcomes and improved patient satisfaction.

ADVANTAGES AND LIMITATIONS OF THE PEPTIDES

Signal peptides act as messengers to fibroblasts in the dermis, encourage the creation of collagen and elastin, which results in smoother, firmer skin and less wrinkles and fine lines.³² Many peptides help heal wounds, calm irritated skin, and lower inflammation. Additionally, several of them have antimicrobial qualities that can aid in acne treatment.³³ Topical peptides demonstrate several limitations: Without delivery modifications, they find it challenging to penetrate the lipid-rich stratum corneum due to their poor skin penetration, which is caused by their high molecular size, hydrophilicity, and numerous amide linkages.¹⁴ Strong, long term efficacy in practical application is currently unknown due to the paucity of clinical evidence, the majority of which comes from in vitro or small-scale research.¹⁴

ENHANCEMENT TECHNIQUES FOR TRANSDERMAL DELIVERY OF OLIGOPEPTIDE

Since different proteolytic enzymes can break down oligopeptides quickly and peptides can be charged at physiological pH, passive transdermal administration of peptides presents difficulties. To overcome the stratum corneum barrier, several enhancement techniques have been used. 33,34 Penetration enhancers change the stratum corneum's lipid structure, which decreases its barrier qualities and increases its permeability for medications that would not normally pass through the skin. A variety of substances can increase penetration, such as alcohols, azones, hexanoates, pyrrolidones, urea, sugar esters,

surfactants, and unsaturated fatty acids like oleic acid. Peptide encapsulation has also been shown to improve peptide distribution through the skin. The surfactants in various particle types, including liposomes, transferosomes, niosomes, and ethosomes, help to

localize the fluidization of the lipids, which enables the particles to stay in the upper layers of the stratum corneum where they create a depot for a sustained effect. Since liposomes are made of naturally occurring lipids found in the skin. 12,34

Table 1: Summary of the experts' consensus.

| Consensus point | Key points from experts' consensus |
|--|---|
| Preference of topical | 82% of doctors prefer using peptides in clinical practice, viewing them as effective for modulating |
| peptides | extracellular matrix proteins and improving pigmentation, particularly beneficial for atrophic acne scars. |
| Utilization in varied dermatological indications | Peptides are used for multiple purposes, including anti-aging and acne scar management. 71% of doctors prefer peptides for both indications, while 29% focus on acne scars. Studies show peptides improve skin wrinkles and acne scar characteristics significantly. |
| Efficacy in recent vs. chronic acne scars | Effective for both recent and chronic acne scars. 60% agree they help in recent scars by modulating collagen and preventing further scar progression, while 30% suggest their use for chronic scars in conjunction with device-based therapies. |
| Benefits according to type of acne scar | Opinions vary on peptide effectiveness for different scar types: 12% for box scars, 12% for icepick scars, 20% for rolling scars, and 52% found peptides effective on all types. Overall, 99% agree peptides have benefits, though patient outcomes may vary based on scar severity and compliance. |
| Mechanism of action | Topical peptides reduce inflammation associated with acne, prevent post-inflammatory hyperpigmentation, and help improve collagen modulation, which overall enhances the appearance of atrophic scars. |
| Monotherapy vs. adjuvant use | While some studies support peptides as effective monotherapy (17% favor), 43% believe they are beneficial in both early treatments and as adjuncts. 40% prefer using peptides post-procedure for reducing erythema and expediting outcomes. |
| Impact on treatment outcomes with device- based procedures | 80% of participants report that peptides improve healing and reduce side effects from invasive procedures, ultimately enhancing patient outcomes and satisfaction. Peptides help manage side effects like erythema and inflammation post-treatment. |

CONCLUSION

The integration of home-based topical peptides into acne scar management represents a significant advancement in dermatologic care. These bioactive compounds, which promote cellular communication and extracellular matrix remodeling, offer a scientifically grounded adjunct to inoffice procedures such as microneedling, laser resurfacing, and chemical peels. When incorporated into long-term treatment regimen, topical peptides contribute to enhanced dermal repair, improved skin texture, and reduced scar visibility. This patient-centred, non-invasive approach not only reinforces and prolongs the clinical benefits achieved through professional interventions but also empowers individuals to actively participate in their own skin rehabilitation process, ultimately supporting more sustainable and personalized therapeutic outcomes.

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