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# Allicin and Probiotics: Double-edged sword for the management of Striae distensae

Reena Gupta [a,1], Bhupinder Kapoor [a,*,1], Ritam Bandopadhyay [b], Monica Gulati [a,c], Pooja Rani [a], Rajpal Singh Kochhar [d]

[a] School of Pharmaceutical Sciences, Lovely Professional University, Phagwara, 144411, Punjab, India
[b] Indegene Limited, Bengaluru, 560025, India
[c] Faculty of Health, Australian Research Centre in Complementary and Integrative Medicine, University of Technology Sydney, NSW, 2007, Australia
[d] Jagsonpal Pharmaceuticals Ltd., New Delhi, 110049, India

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ABSTRACT

Striae distensae (SD), commonly known as Stretch marks or striae, are one of the most common benign dermal lesions frequently seen in females that often cause a significant physical and psychological impact. A number of treatment modalities ranging from topicals to invasive approaches are commercially available, however, none of the available options is capable of complete eradication of SD. As effectiveness of most of the available topical formulations for SD is attributed to the combined effects of their antioxidant, anti-inflammatory and proliferative effects, allicin and probiotic based topical formulations are hypothesized to be effective in treatment and prevention of SD. Both allicin and probiotics are able to reduce the inflammatory response via suppression of transcription factor i.e., nuclear factor (NF)-κB, and pro-inflammatory cytokines and chemokines levels. Moreover, the antioxidant effect of allicin and probiotics is considered to decrease the reactive oxygen species induced fragmentation of collagen. Also, the effects of allicin on the collagen and elastin tissue as well as beneficial effects of probiotics and their metabolites on skin elasticity and skin hydration are expected to provide multiple target approach for the management of SD. Altogether, a combination formulation containing both allicin and probiotics is considered to be novel approach for the prevention and management of SD.

## 1. Introduction

### 1.1. Striae distensae

Striae distensae (SD), frequently known as stretch marks or striae, are common, aesthetically undesirable dermal lesions or linear scars associated with stretching of the dermis [1,2]. Although the condition is not considered as a medical emergency, striae are frequently connected with emotional and psychological distress due to its disfiguring damage, especially in the women and certain professionals [3]. Despite of long existence in the medical literature, i.e., first described by Troisier and Menetrier in 1889 [4], the exact aetiology of SD is still unknown [5]. It is believed to result from a number of physiological and pathological conditions, including, but not limited to, pregnancy, growth spurts, rapid body weight change, corticosteroids use, hypercortisolism like Cushing's syndrome, genetic disorders such as Marfan syndrome or certain surgical interventions such as breast augmentation [6,7]. SD is commonly seen during pregnancy, affecting more than 90 % of women, in which case, it is nomenclatured as Striae gravidarum [8]. The risk of SD in women is two-times higher than in men, with an overall prevalence varying from 11 % to 88 % [3,9].

The pathogenesis of SD is thought to be multifactorial in origin, mechanical stress on connective tissues being the key factor along with a combination of genetic factors, and hormonal factors [10]. The changes in extracellular matrix components, including fibrillin, elastin, collagen, and fibronectin that provide skin resistance to tension and elasticity are the primary pathological features of SD [11]. Histological alterations include thinning of the epidermis with loss of dermal papillae and rete ridges, separation of collagen bundles, failure of collagen fibrils to form bundles, as well as disruption of elastic fibres and inability of tropoelastin (soluble elastin)- rich fibrils to form elastic fibres [12]. Clinically, there are two stages of SD as per the appearance: striae rubrae and striae

* Corresponding author.
*E-mail address:* bhupipharma@gmail.com (B. Kapoor).
[1] Contributed equally.

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albae. The initial/acute stage (striae rubrae) is characterized by almost normal epidermis, oedematous dermis with initial erythematous, red/-purple, flat or sometimes slightly convex lesions, aligned perpendicular to the direction of skin tension, and can be symptomatic, which on aging (chronic stage; striae albae), become faded due to hypopigmentation and appear thin, wrinkled, and atrophic with blunting of rete ridges (Fig. 1A) [13,14]. Anatomically, these lesions most often appear on the buttocks, lower back, thighs, calves, breast/chest, abdomen, upper arm, and knees (Fig. 1B) [13].

There is no gold standard treatment available for the management of SD, and generally, a multifactorial approach is adopted [3]. The treatment aims at reducing the erythema, stimulating collagen and elastin production and/or increasing pigmentation [15,16]. The available treatment modalities range from topicals and acid peel treatments to more invasive methods such as laser therapy (Fig. 1C). Other approaches like radiofrequency techniques, phototherapy, microdermabrasion, and collagen injections have also been used with variable success. Despite the availability of different varieties of therapies, no single therapy has been reported to completely eradicate the lesions in SD [17].

A large number of commercially available topical agents claim to have prophylactic and/or therapeutic effect in SD; but little evidence is available for their effectiveness. Topical treatment intends to provide improvement in texture and pigmentation with least possible side effects [13]. A number of preparations enriched with natural ingredients like olive oil [18,19], coconut oil [20], bitter almond oil [21], ximenia oil [22], and argan oil [23] have been reported to prevent the striae during pregnancy. Trofolastin$^{R}$, a marketed formulation containing *Centella asiatica* extract, collagen elastin hydrolysates and alpha-tocopherol, reported absolute prevention in women with a history of striae during puberty. The protective effect is attributed to asiaticoside, the active principle of *C. asiatica*, that stimulate fibroblastic activity, synthesis of collagen and fibronectin, and glucocorticoids inhibitory activity [24]. Two proprietary creams of hyaluronic acid i.e., Alphastria cream and Verum cream, combined with various vitamins and fatty acids, were shown to significantly lower the incidence of SD in pregnancy in two different studies [25,26]. A silicone-based cream with synthetic recombinant human growth factors, hyaluronic acid, and vitamin C was reported to improve overall appearance and texture of SD [27]. In a double-blind placebo-controlled study, a cream containing the hydroxyprolisilane C, rose hip oil, *C. asiatica* triterpenes, and vitamin E was found to be effective in reducing severity and incidence of SD during pregnancy [28]. Tropical oil formulation containing mixture of plant extracts such as calendula, lavender, rosemary, chamomile and PurCellin oil™ along with vitamins A and E was found to be safe and effective in treating striae and xerosis [29]. A 15-min massage with almond oil is reported to reduce the development of striae in primiparous women, however, the effect was found to be negligible in women who merely applied almond oil only [21], suggesting the positive impact of massage with moisturiser on skin elasticity. Tretinoin (retinoic acid) increases tissue collagen I levels through stimulation of fibroblasts [30,31], and was found to be effective in management of SD in a number of studies [30–34]. The treatment, however, was often associated with common side effects such as erythema, and scaling of the skin [32–34]. In addition to these studies, few clinical trials on the topical efficacy of tretinoin (NCT05461755, NCT01027793), *C. asiatica* (NCT02601105), cocoa butter (NCT00114660), and olive oil (NCT04489901) are ongoing.

Success of therapies for SD has been reported to be from mild to moderate, and generally without any evidence from rigorous and well-designed controlled trials. Moreover, topical treatment modalities are mainly used as an adjunctive treatment, and the procedural therapies are still believed to be the most effective for SD management [3].

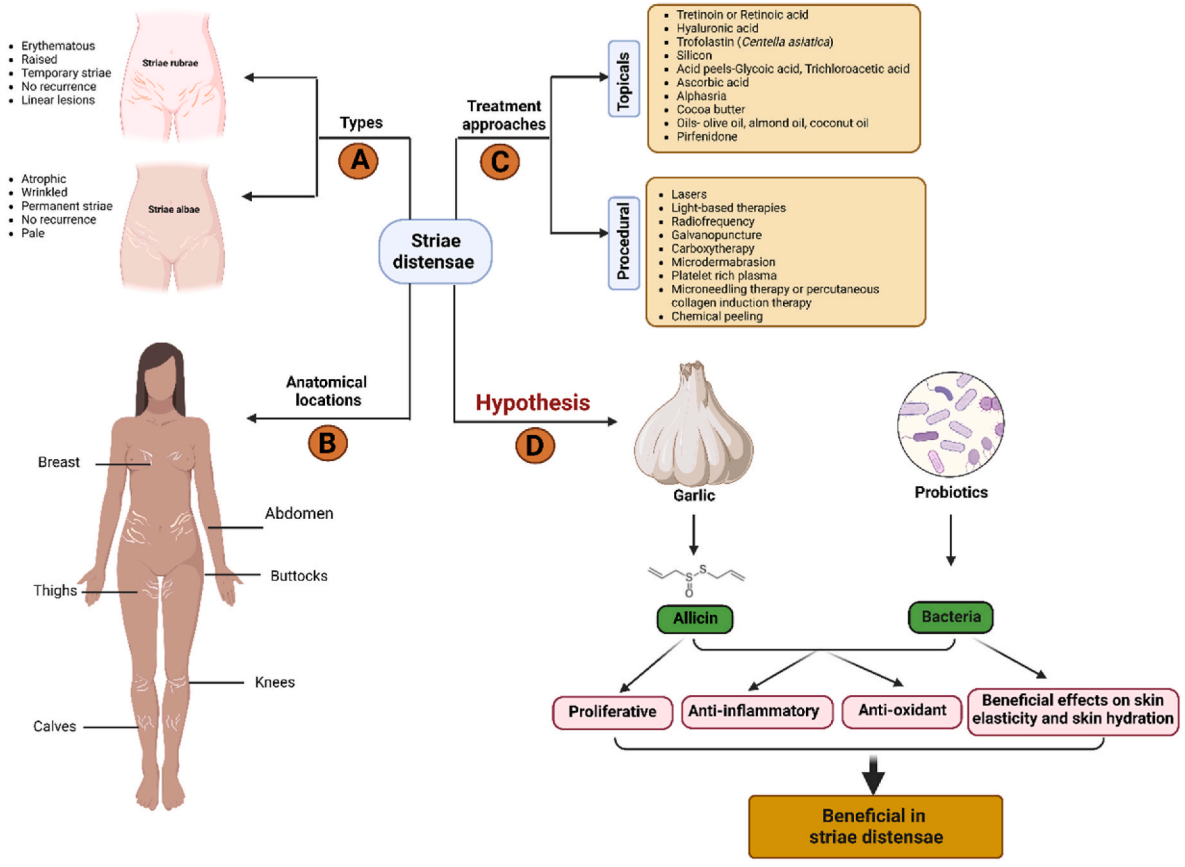


**Fig. 1.** (A) Illustration of striae rubrae and striae albae along with the characteristic features (B) Common anatomical locations affected by striae distensae (C) Topical agents and procedural therapies used for striae distensae (D) Proposed role of allicin and probiotics in management of striae distensae.

However, although minimal, the procedural therapies are still invasive, and may cause discomfort, pain, bleeding, erythema, and pruritis, thus being not univocally suitable for all. Moreover, high cost of treatment, particularly with fractional laser and fractional microneedle radiofrequency is another factor limiting the applications of these approaches [14]. Therefore, there is still a scope to find out more effective, safe, and economical topical treatment for the aesthetically undesirable dermal lesions associated with SD.

### 1.2. Human microbiota

Although more than three centuries have been passed since the first ever report of microorganisms present in gastrointestinal tract of human being by Antonie van Leeuwenhoek [35], the field of microbiome research has evolved rapidly over the past few decades, especially with an advancement in sequencing technology [36,37]. Similar to gut, skin is home to a vast array of microorganisms including bacteria, fungi, and viruses, collectively known as skin microbiota. Along with the gut microbiota, skin microbiota plays a significant role in the protection against invading pathogens, promotion of defense and immune responses, and helps in tissue repair mechanism, all these actions are mediated via mutual or commensal interactions of microbiota with mammalian host cells [38,39]. Dysbiosis of skin and/or gut microbiota is associated with an altered immune response, promoting the development of skin diseases, such as atopic dermatitis, psoriasis, acne vulgaris, dandruff, and even skin cancer [40]. Although, so far, no study has been conducted to assess the correlation of microbiota dysbiosis with SD, the direct relationship of commensal microorganisms and their metabolites with anti-inflammatory and immunomodulatory properties endorsed their role in management of SD, which is reported to be mechanism of action of some of the commercially available products, viz. SilDerm™ and Liforma® stretch mark repair creams [13].

## 2. Hypothesis

The etiological relevance suggests that the SD can be managed by topical drug therapies. The targeted treatment strategies include stimulation of collagen production and fibroblastic activity for improvement of tissue strength, reduction in wrinkling and roughness of skin (to improve texture), improving cell proliferation, exerting anti-inflammatory effect, increasing cell elasticity as well as vascularity, and hyperpigmentation [13,14]. Though a number of therapeutic modalities are available, none has been reported to be effective in complete eradication of SD. We hypothesize that a combination of allicin, and probiotics due to their effects on a number of dermatological parameters can be used in the management of SD.

## 3. Justification of the proposed hypothesis

The available scientific evidences indicate that the efficacy of topical formulations in SD is attributed to their anti-inflammatory [41,42], and antioxidant properties [41]. Two commercially available topical formulations i.e., SilDerm™ and Liforma claimed to be effective in management of SD also contain anti-inflammatory ingredients [13]. Improvement in collagen content by certain phytochemicals is the other mechanism reported to be useful in management of the SD [43,44].

As allicin possesses strong anti-inflammatory [45,46], antioxidant [47], and vascularity induction properties (Fig. 1D) [48], it is likely to be effective in the management of SD. Immunomodulatory property of allicin is attributed to inhibition of transcription factor i.e., nuclear factor (NF)-**κ**B, thereby, inhibiting the transcription of several cytokine genes involved in proinflammatory responses, such as tumor necrosis factor-α (TNF-***α***), interleukin (IL)-1β, IL-6, IL12(p70), and monocyte chemoattractant protein-1 (MCP-1) [45,49]. Topical application of allicin was found to be safe and effective in ameliorating the imiquimod-induced psoriasis-like skin inflammation in mice. Beneficial actions of allicin are attributed to decreased expression of pro-inflammatory cytokines and chemokines, as well as inhibition of TNF-receptor associated factor 6/mitogen-activated protein kinase/NF-κB and signal transducer and activator of transcription 3/NF-κB signalling pathways [50].

Extracellular matrix molecules, such as collagens, are the good targets for oxygen free radicals. In fact, collagen is the only protein susceptible to fragmentation by superoxide anion as demonstrated by the liberation of small 4-hydroxyproline-containing-peptides [51,52]. The anti-oxidant activity, coupled with stimulation of collagen production, are the dual actions of ascorbic acid that are reported to be responsible for its beneficial role in striae [53,54]. Allicin is a natural anti-oxidant that decreases the production of reactive oxygen species (ROS) i.e., superoxide, nitric oxide and hydroxyl radicals [47,55]. The decreased levels of these reactive species are attributed to reduced expression of ROS producing nicotinamide adenine dinucleotide phosphate oxidases, and promoting the cellular scavenger enzymes such as catalase, superoxide dismutase, and glutathione peroxidase and several types of peroxidases [47]. Due to potent anti-oxidant property, allicin is expected to inhibit/reduce the ROS induced fragmentation of collagen, thereby, being a potential molecule for the prophylaxis and treatment of striae. Moreover, anti-oxidant and/or anti-inflammatory properties of active garlic components are also responsible for their antiwrinkle effect [56].

The term probiotics, first ever reported by German Scientist Werner Kollath in 1953 as “active substances that are essential for a healthy development of life” has undergone many transformations, and the globally accepted version as recommended by World Health Organization, and Food and Agriculture Organization of the United Nations is “live microorganisms that, when administered in adequate amounts, confer a health benefit on the host” [57,58]. Probiotic bacteriotherapeutics, particularly consisting of *Lactobacilli* and *Bifidobacterium*, are widely reported to have potential in prevention and treatment of skin diseases including eczema, atopic dermatitis, acne, and psoriasis [59–61]. Although not even a single scientific study investigated the role of probiotics in SD, many commercially available probiotic topical formulations claim to be effective in the management of SD [62–64]. The efficacy of these formulations is assumed to be due to anti-inflammatory and immunomodulatory properties of probiotics that have been proved scientifically in a number of studies [65,66]. The anti-inflammatory action of probiotics is attributed to increased production of interleukin 10 and/or inhibition of lipopolysaccharide-induced production of pro-inflammatory cytokines in macrophages [67]. Another study documented the reduction in inflammatory lesions even after one month of cessation of topical probiotic treatment, indicating the additional immunomodulatory effect, which needs further investigation [61]. Moreover, administration of *Lactococcus lactis* strain H61, *Lactobacillus plantarum* HY7714, and *L. casei* subsp. *casei 327* were reported to increase skin elasticity, and skin hydration, along with the significant reduction in skin wrinkles [68–70]. Lastly, a number of *in vitro* and *in vivo* studies demonstrated the anti-oxidant potential of probiotics [71–73] and their metabolites, technically known as postbiotics [74–76], which is expected to be due to increased activity of anti-oxidative enzymes such as glutathione-S-transferase, glutathione reductase, glutathione peroxidase, superoxide dismutase and catalase, re-establishment of microbiota, as well as decreasing the levels of lipid peroxidation (e.g., malondialdehyde) [77]. The prominent anti-oxidant potential of probiotics and postbiotics is expected to inhibit oxygen-free radical induced fragmentation of collagen [51], thereby, assumed to be effective in the management of SD. All these studies endorsed the direct or indirect correlation of probiotics administration with the management of SD by virtue of their anti-inflammatory, immunomodulatory, and anti-oxidant properties, along with their potential effects on skin elasticity, and skin hydration properties.

The potent anti-inflammatory, immunomodulatory, and anti-oxidant properties of allicin and probiotics combination make them a strong contender for the topical treatment of SD. Moreover, allicin is reported to exhibit dual properties on natural microbiota of body. Li et al., in a

recent publication have reported that allicin increased the abundance of probiotic microbes, such as *Lactobacillus*, *Clostridium* and *Akkermansia*, while it reduced pathogenic microbes, such as *Enterobacter*, *Erysipelatoclostridium* and *Colidextribacter* [78]. Many other recent studies documented the prebiotic effect of allicin. Allicin treatment is reported to stimulate the growth of various microbiota such as *Lactobacilli*, *Bifidobacteria*, and *Bacteroides* [79–81]. Recently, the combination of *Allium sativum* and *Lactobacillus acidophilus* has been used as synbiotics in one of the study [82]. Various scientific studies demonstrated the beneficial role of topical probiotics in dermatological diseases. They have been reported to increase stratum corneum ceramide levels that lend flexibility to skin; produce short chain fatty acids, including butyrate, that regulate the expression of occludin and zona occludens, associated with the improvement of the epithelial barrier integrity thus keeping the skin hydrated and preventing growth of pathogens [83–85].

Therefore, the proposed combination of allicin and probiotics will not only improve the survival/growth rate of bacterial strains used in this combination, but will also stimulate the growth of skin microbiota. Also, the potential beneficial effects of probiotics and their metabolites on skin elasticity and skin hydration are expected to provide multiple target approach for the management of SD. Probiotic bacteriotherapeutics, particularly consisting of *Lactobacilli* and *Bifidobacterium*, are widely reported to have potential in prevention and treatment of various skin. Due to their validated beneficial effects as well as safety profile, we recommend species of these two genera that can be used in combination with allicin for the management of Striae distensae. However, well planned preclinical and clinical studies need to be conducted to prove the hypothesis.

## 4. Conclusions

A number of natural ingredients have been tried by young women to get rid of this cosmeceutical condition of SD with varying success. As effectiveness of most of the available topical formulations is attributed to their antioxidant, anti-inflammatory and proliferative effects, topical formulation containing allicin and probiotics are hypothesized to be effective in treatment and prevention of SD. The effect of allicin on the collagen and elastin tissue is further anticipated to support in the management SD. Moreover, the beneficial effects of both probiotics and postbiotics on skin elasticity and hydration also help in the management of SD. Overall, a combination of allicin and probiotics appears to provide a multiple target approach for the successful management of SD.

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## CRediT authorship contribution statement

**Reena Gupta:** Writing – original draft, Conceptualization. **Bhupinder Kapoor:** Supervision, Resources. **Ritam Bandopadhyay:** Writing – review & editing, Conceptualization. **Monica Gulati:** Writing – review & editing, Supervision. **Pooja Rani:** Conceptualization. **Rajpal Singh Kochhar:** Conceptualization.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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