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Probiotics in dermatology

Probiotics are live microorganisms that, when administered in adequate amounts, may confer a health benefit on the host. We already know that their use is positively influencing key factors in the development of dermatological diseases such as oxidative stress or inflammation. The most popular use of probiotics in dermatology refers to atopic dermatitis (AD). As it is already demonstrated and widely accepted that probiotics can help to decrease the incidence and severity of AD in infants, much remains to be investigated about its usefulness in the treatment of AD, as well in infants/children as in adults. Similarly, promising data show that probiotics could be of help in acne, but also in wound healing and tissue repair. Much lesser, or even nothing is known about their potential interest in other inflammatory diseases such as rosacea or psoriasis. Besides their demonstrated activity in photoprotection, probiotics appear to be effective on the prevention and even management of skin aging and its more frequent symptoms, such as collagen loss, dry skin and skin barrier function impairment. Normalization of intestinal microflora with the use of probiotics and prebiotics has a positive effect on several skin conditions. Given the special status of the skin, which is directly accessible for topical applications, probiotics may be used as well as systemic course as local one.

There is still a long and promising way ahead for investigation, before probiotics can be a daily prescription in dermatology.

We are in a preliminary stage when using probiotics in dermatology, and much investigation is needed. With this condition, one day will come, when probiotics will be fully part of the prescription in dermatology.

Key words

Probiotics, prebiotics, skin, inflammation, atopic dermatitis, skin aging.

Probiotics are live microorganisms that, when administered in adequate amounts, may confer a health benefit on the host [1]. They must not be confused with prebiotics, which are nondigestible carbohydrates that stimulate the growth of probiotic bacteria in the intestine. The most common prebiotics are indigestible oligosaccharides [2]. As we can observe, both words, although being very similar, are not synonyms and have very different meaning. Probiotics have been widely reported in gastroenterology and are gaining space in dermatology along the recent years. Given the special status of the skin, which is directly accessible for topical applications, probiotics may be used as well as systemic course as local one.

Probiotics and inflammation

Inflammation is a process present in many dermatological diseases, which may be the causative factor, but also a consequence of the disease itself. For instance, in bacterial infections, the cause will be an infectious one, and inflammation will only be a consequence of this infection. Chronic inflam-

mation is the common denominator in many mucocutaneous pathophysiologic processes including extrinsic skin aging.

Probiotic strains susceptible of displaying an anti-inflammatory activity in vitro are summarized in Tabl. 1. This list must not be considered as exhaustive but is only indicative.

Probiotics and oxidative stress

Oxidative stress defines a condition in which the prooxidant-antioxidant balance in the cell is disturbed, resulting in DNA hydroxylation, protein denaturation, lipid peroxidation, and apoptosis, ultimately compromising cells' viability. Various probiotics possess an ability to improve the antioxidant system and to decrease radical generation. Probiotics bacteria strains can exert antioxidant capacity in different ways.

- *Metal ions chelating properties*

Metal ions are catalysts of oxidation reactions, and for this reason chelating them may improve Redox balance. Various strains were shown to chelate Fe⁺⁺

Table 1. Probiotic stains susceptible of displaying an anti-inflammatory activity *in vitro*

Authors	Cell type	Strain	Main outcome
Prisciandaro et al. [3]	IEC-6	<i>E. coli</i> Nissle 1917 <i>L. rhamnosus</i> GG	Pre-treatment with these probiotics could prevent or inhibit enterocyte apoptosis and loss of intestinal barrier function induced by 5-FU
Rodriguez-Brito et al. [4]	Human DC	<i>L. paracasei</i> CNCM	Decreased cytokine release against Salmonella infection in the presence of <i>Lactobacillus paracasei</i> upon TLR activation
Mann et al. [5]	Human DC	<i>L. casei</i> Shirota	DC from ulcerative colitis patients samples have an increase of IL-4 production and loss of IL-22 and IFN- γ secretion. <i>L. casei</i> Shirota treatment restored the normal stimulatory capacity through a reduction in the TLR-2 and TLR4 expression
Wachi et al. [6]	PIE cells	<i>L. delbrueckii</i> TUA4408L	The activation of MAPK and NF- κ B pathways induced by <i>E. coli</i> 987P were downregulated through upregulation of TLR negative regulators, principally by TLR2
Wu et al. [7]	IPEC-J2 model	<i>L. plantarum</i> GCMCC1258	<i>L. plantarum</i> decreased transcript abundances of IL-8, TNF- α , and negative regulators of TLRs. Moreover, <i>L. plantarum</i> treatment decreased the gene and protein expression of occludin
Widyarman et al. [8]	HaCat cells	<i>L. reuteri</i> ATCC55730	<i>L. reuteri</i> reduced the expression of IL-8 and hBD-2 induced by exposure to <i>Streptococcus mutans</i> ATCC-25175 and <i>Porphyromonas gingivalis</i> ATCC-33277

Human DC: Human dendritic cells — PIE cells: intestinal epitheliocyte cells — IPEC-J2: intestinal porcine epithelia cells.

and Cu⁺⁺ anions, such as *Streptococcus thermophilus* 821 [9], *Lactobacillus casei* KCTC3260 [10], or *Lactobacillus helveticus* CD6 [11].

• Expression of enzymatic antioxidants

Strains of probiotics are capable of expressing their own antioxidant enzymatic systems. Thus, *Lactobacillus fermentum* E-3 and E-18 are able to express at high level Mn-SOD to resist oxidative stress [12]. Other strains like *Lactococcus lactis* can express catalase [13]. Moreover, probiotics can also stimulate the antioxidant system of the host and elevate the activities of antioxidants efficiently. Studies in pigs showed that dietary *Lactobacillus fermentum* supplementation could increase serum SOD and GPx and enhance hepatic CAT, muscle SOD, and Cu and Zn-SOD compared to the control group [14].

• Antioxidant metabolites

Probiotics can produce various metabolites with antioxidant activity, such as glutathione (GSH), butyrate, and folate. Evidence showed that the folate-producing *Bifidobacteria* enhanced the folate status in humans [15]. It was also found that the two antioxidative *Lactobacillus fermentum* strains E-3 and E-18, contained remarkable levels of GSH [12].

• Mediation of Nrf2-Keap1-ARE pathway

Nrf2 activation upregulates a series of genes including those involved in xenobiotic and ROS detoxification in order to resist oxidant and electrophilic environmental stressors. Both *in vivo* and

in vitro reports have indicated that probiotic bacteria could protect against oxidative stress through regulating the Nrf2-Keap1-ARE pathway. This is the case for *Lactobacillus plantarum* SC4, but also *Lactobacillus plantarum* FC225 [16, 17].

• Action on NF κ B pathway

Bacillus sp. strain LBP32 was shown to prevent LPS-induced inflammation in RAW 264.7 macrophages by inhibiting NF κ B and ROS production [18].

• Action on Mitogen-activated protein kinases (MAPKs)

Pre-treatment of epithelial cells with *Lactobacillus GG-CM* alone activated all three MAPKs investigated [19].

• Regulation of The Enzymes Producing ROS

Lactobacillus fermentum CECT5716 and *Lactobacillus coryniformis* CECT5711 (K8) plus *Lactobacillus gasseri* CECT5714 (LC9) (1 : 1) were able to decrease NADPH oxidase (NOX) activity and mRNA expressions of NOX-1 as well as NOX-4 in spontaneously hypertensive rats [20]. Patel et al. demonstrated that *Lactobacillus acidophilus* pre-treatment decreased COX-2 expression in catla thymus macrophages [21].

Probiotics in atopic dermatitis (AD)

This is probably the area in dermatology where the biggest number of reports were published, as well in the prevention as in the treatment of atopic dermatology.

Possible mechanisms of action of probiotics strains in atopic dermatitis are as follows [22]:

- Inhibition of T_H2 response.
- Stimulation of T_H1 response.
- Upregulation of regulatory T cells.
- Acceleration of skin and mucosa barrier function.
- Increase in intestinal microflora diversity.
- Reduction of fermentation products.
- Inhibition of *Staphylococcus aureus* attachment.

Prevention of atopic dermatitis

Tabl. 2 is listing the trials reported along years. To summarize, let's tell that [54]:

- Probiotic treatment begun in gestation and continued through the first 6 months of life was shown to have benefit in preventing atopic dermatitis (AD).
- Probiotic supplementation was beneficial in both high risk and unselected subjects.
- Mixtures of probiotics, including *Lactobacillus*, *Bifidobacterium* and *Propionibacterium* strains, significantly decreased the risk of AD.

Treatment of atopic dermatitis

Although data exist showing the protective effect of probiotics in the incidence of paediatric AD, there is less convincing information about their effects as treatment. The meta-analysis by Lee et al. [23] and Michail et al. [55] failed to find clinically significant changes in the severity of paediatric AD with the use of probiotics. However, in a randomized, double-blind, placebo-controlled study where either *L. plantarum* CJLP133 or placebo were given to children aged 12 months to 13 years twice a day for 12 weeks, the results suggested that supplementation with probiotic *L. plantarum* CJLP133 was beneficial in the treatment of paediatric AD [56]. There are few data about the role of probiotics in adult AD. All of them include a small number of patients, which makes difficult to make an opinion about this matter. Let's mention a study where LKM512 yogurt was given for 4 weeks to 10 adult AD patients, in which scores of itch and burning tended to improve [57]. In another study [58], 38 patients aged from 18 to 46 years with moderate/severe AD were randomized to receive or not active treatment with *L. salivarius* LS01. Treatment with the *L. salivarius* LS01 strain seems to positively modify clinical and immunologic status and dermatology life quality in a group of adults affected by moderate/severe AD. Further [59], 34 adult type AD subjects who were treated with conventional topical corticosteroid and tacrolimus were given *Lactobacillus paracasei* K71 (LAB) diet or placebo over 12 weeks. The skin severity scores were significantly decreased from baseline at week

8 ($p < 0.05$) and at week 12 ($p < 0.01$) in the LAB diet group but not in the placebo group. Finally, 48 patients with moderate to severe AD were enrolled in a study and treated with a combination of *Lactobacillus salivarius* LS01 and *Bifidobacterium breve* BR03 or placebo for 12 weeks [60]. Patients receiving probiotics showed a significant improvement in clinical parameters (SCORAD, $p < 0.0001$ and DLQ index, $p = 0.021$) from baseline.

Probiotics in acne

The pathophysiology of acne involves excess sebum production, follicular hyperkeratinization, *Propionibacterium acnes* hypercolonization, and inflammation. In acne patients, topical *Lactobacillus* extract was effective in reducing skin erythema, repairing skin barrier, and reducing skin microflora, thereby exhibiting an effective reduction in acne lesion size and erythema at 5%, but not at 1% [61]. Ingesting fermented milk with 200 mg of lactoferrin daily, acne showed improvement in these patients by significant decreases in inflammatory lesion count by 38.6%, total lesion count by 23.1%, and acne grade by 20.3% at 12 week. Furthermore, sebum content was decreased by 31.1% [62]. In an ancient study, an 80% clinical improvement was reported in acne patients after oral supplementation of *Lactobacillus acidophilus* and *Lactobacillus bulgaricus* [63]. The application of a base cream containing *Streptococcus thermophilus* in the forearm skin of 17 healthy volunteers for 7 days led to a significant and relevant increase of skin ceramide amounts [64].

Probiotics in psoriasis

It seems clear that the skin microbiota may have a role in the pathogenesis of chronic plaque psoriasis. *Corynebacterium*, *Propionibacterium*, *Staphylococcus*, and *Streptococcus* have been identified as the major bacterial genera [65]. In a randomized, double-blind, placebo-control study, it was observed that patients who are administered a daily oral dose of *Lactobacillus paracasei* NCC2461 exhibit decreased skin sensitivity, have a hastened barrier function recovery, and are more efficient in preserving the skin moisturizing agents urea and sodium lactate [66]. Moreover, it has been demonstrated that mice fed *Lactobacillus pentosus* developed a milder form of imiquimod-induced psoriasis when compared to mice fed with a vehicle control [67].

Probiotics in rosacea

There is currently no published study about the use of systemic or topical probiotics in rosacea. However, their activity on both oxidative stress and inflammation previously reported in this paper, as

Table 2. Published studies about use of probiotics in atopic dermatitis

Authors	N of cases	Population treated	Results
Lee et al. (2008) [23]	1581	Pregnant women and/or infants < 6 months old	<i>Lactobacillus rhamnosus</i> GG, <i>Lactobacillus acidophilus</i> LAVRI-A1, and a combination of probiotics with a prebiotic showed a decrease in the incidence of pediatric AD; <i>Lactobacillus reuteri</i> showed a paradoxical increase in sensitization to allergens
Rautava et al. (2006) [28]	72	Infants < 12 months old	Administration of the probiotics <i>Lactobacillus</i> GG and <i>Bifidobacterium lactis</i> Bb-12 at the time of introduction of cow's milk in the infant's diet results in cow's milk-specific IgA antibody responsiveness
Kukkonen et al. (2007) [29]	1223	Pregnant women and infants < 24 months old	A combination of <i>L. rhamnosus</i> GG (ATCC 53103), <i>L. rhamnosus</i> LC705 (DSM 7061), <i>Bifidobacterium breve</i> Bb99 (DSM 13692) and <i>Propionibacterium freudenreichii</i> ssp. <i>shermanii</i> JS (DSM 7076) significantly prevented eczema and especially atopic eczema
Kalliomaki et al. (2007) [30]	159	Pregnant women and infants < 24 months old	Taking during the first two years <i>L. rhamnosus</i> GG (ATCC 53103) the overall risk of developing AD was significantly decreased
Abrahamsson (2007) [31]	232	Pregnant women and infants < 12 months old	Taking <i>L. reuteri</i> ATCC 55730 during pregnancy and for 1 year after delivery, the treated infants had less IgE-associated eczema at 2 years of age and therefore possibly run a reduced risk to develop later allergic disease
Kopp et al. (2008) [32]	94	Pregnant women and infants < 6 months old	After taking <i>Lactobacillus</i> GG (ATCC53103) during pregnancy and 6 months after delivery, the control at 2 years showed that it neither reduced the incidence of atopic dermatitis nor altered the severity of atopic dermatitis in affected children
Huurse et al. (2008) [33]	171	Pregnant women and infants < 12 months old	The combination of <i>L. rhamnosus</i> GG (ATCC53103) and <i>Bifidobacterium lactis</i> Bb12 made that the risk of sensitization at 12 months could be reduced
Wickens et al. (2008) [34]	512	Pregnant women and infants < 24 months old	It was found that supplementation with <i>L. rhamnosus</i> , but not <i>B. animalis</i> subsp. <i>lactis</i> , substantially reduced the cumulative prevalence of eczema, but not atopy, by 2 years
Soh et al. (2009) [35]	253	Pregnant women and infants < 6 months old	<i>Bifidobacterium longum</i> (BL999) and <i>L. rhamnosus</i> showed no effect on prevention of eczema or allergen sensitization in the first year of life in Asian infants at risk of allergic disease
Osborn et al. (2009) [24]	1477	Pregnant mothers and/or infants < 12 months old	It found a significant reduction in infant eczema (typical RR 0.82, 95 % CI 0.70–0.95)
West et al. (2009) [36]	179	Infants from 4 to 13 months old	Feeding <i>Lactobacillus</i> F19 during weaning could be an effective tool in the prevention of early manifestation of allergy, e. g., eczema
Niers et al. (2009) [37]	102	Pregnant women and infants < 12 months old	Combination of <i>Bifidobacterium lactis</i> and <i>Lactococcus lactis</i> shows a preventive effect on the incidence of eczema in high-risk children, which seems to be sustained during the first 2 years of life
Kuitunen et al. (2009) [38]	1223	Pregnant women and infants < 6 months old	A probiotic mixture (2 lactobacilli, bifidobacteria, and propionibacteria) conferred no allergy-preventive effect that extended to age 5 years to high-risk mothers and children. It conferred protection only to cesarean-delivered children
Kim et al. (2010) [39]	112	Pregnant women and infants < 6 months breast-fed	Prenatal and postnatal supplementation with a mixture of <i>B. bifidum</i> BGN4, <i>Bifidobacterium lactis</i> AD011, and <i>L. acidophilus</i> AD031 is an effective approach in preventing the development of eczema in infants at high risk of allergy during the first year of life
Dotterud et al. (2010) [40]	415	Pregnant women and during breast-feeding (3 months)	Probiotic milk containing <i>L. rhamnosus</i> GG, <i>L. acidophilus</i> La-5 and <i>Bifidobacterium animalis</i> subsp. <i>lactis</i> Bb-12, given to non-selected mothers reduced the cumulative incidence of AD, but had no effect on atopic sensitization
Boyle et al. (2011) [41]	250	Pregnant mothers	Prenatal treatment with <i>L. rhamnosus</i> GG was not sufficient for preventing eczema. If probiotics are effective for preventing eczema, then a postnatal component to treatment or possibly an alternative probiotic strain is necessary

Authors	N of cases	Population treated	Results
Doege et al. (2012) [25]	2843	Pregnant mothers and infants < 12 months old	Lactobacilli showed a significant reduction of the development of atopic eczema; no effect with strain mixtures
Pelucchi et al. (2012) [26]	3092	Pregnant mothers and infants < 24 months old	The RR of AD was lower in infants/young children with no family history of allergic diseases; global 20 % reduction in the incidence of AD and IgE-associated AD
Wickens et al. (2012) [42]	474	Pregnant women and infants < 6 months old	The protective effect of <i>L. rhamnosus HN001</i> against eczema, when given for the first 2 years of life only, extended to at least 4 years of age
Jensen et al. (2012) [43]	178	Infants < 6 months old	Regular dosing with <i>L. acidophilus</i> strain from 0 to 6 months of age had no long-term benefits at 5 years
Rautava et al. (2012) [44]	205	Pregnant and breast-feeding mothers	Prevention regimen with specific probiotics administered to the pregnant and breast-feeding mother, that is, prenatally and postnatally, is safe and effective in reducing the risk of eczema in infants with allergic mothers positive for skin prick test
Rozé et al. (2012) [45]	97	Infants < 6 months old	An experimental formula characterised by the presence of two strains of probiotics (<i>L. rhamnosus LCS-742</i> and <i>Bifidobacterium longum subsp. infantis M63</i>) and by the addition of prebiotics: 96 % galacto-oligosaccharides and 4 % short-chain fructo-oligosaccharides, guaranteed a similar growth, was better tolerated at 1 month and had a protective effect against the development of atopic dermatitis
Ou et al. (2012) [46]	191	Pregnant women 2 nd quarter of pregnancy	<i>Lactobacillus GG</i> ; ATCC 53103 administration beginning at the second trimester of pregnancy reduced the severity of maternal allergic disease through increment of Th1 response, but not the incidence of childhood allergic sensitization or allergic diseases
Allen et al. (2012) [47]	454	Pregnant women and infants < 6 months old	A probiotic consisting of two strains of lactobacilli and two strains of bifidobacteria reduced the frequency of atopic eczema and atopic sensitisation and promoted a Th1 orientation of the immune system
West et al. (2013) [48]	179	Infants 4 to 13 months old	Following at 8–9 years of age showed that there was no long-term effect of <i>L. paracasei ssp paracasei F19</i> on any diagnosed allergic disease, airway inflammation or IgE sensitization
Abrahamsson et al. (2013) [49]	232	Pregnant women (last month) and infants < 12 months old	The effect of <i>L. reuteri</i> on sensitization and IgE-associated eczema in infancy did not lead to a lower prevalence of respiratory allergic disease in school age (7 years)
Panduru et al. (2014) [27]	3495	Pregnant mother and infants < 13 months old	Prenatal administration followed by postnatal administration was protective (OR, 0.54; $p = 0.001$), unlike exclusive postnatal administration (OR, 0.89; $p = 0.59$); <i>Lactobacillus alone</i> and <i>Lactobacillus</i> with <i>Bifidobacterium</i> are protective against AD
Loo et al. (2014) [50]	253	Infants < 6 months old	A combination of <i>Bifidobacterium longum (BL699)</i> and <i>L. rhamnosus</i> in early childhood did not play a role in the prevention of allergic diseases. Early-life supplementation with probiotics did not change allergic outcomes at 5 years of age
Allen et al. (2014) [51]	436	Pregnant women and infants < 6 months old	Receiving daily the probiotic (<i>Lactobacillus salivarius CUL61</i> , <i>Lactobacillus paracasei CUL08</i> , <i>Bifidobacterium animalis subspecies lactis CUL34</i> and <i>Bifidobacterium bifidum CUL20</i>) did not provide evidence that it prevented eczema during the study or reduced its severity. However, the probiotic seemed to prevent atopic sensitisation to common food allergens and so reduce the incidence of atopic eczema in early childhood
Enomoto et al. (2014) [52]	130	Pregnant women (last month of pregnancy) and infants < 6 months old	The risk of developing eczema/atopic dermatitis (AD) during the first 18 months of life was significantly reduced in infants receiving <i>B. longum BB536</i> and <i>B. breve M16-V</i> (OR: 0.231 [95 % CI: 0.084–0.628] and 0.304 [0.105–0.892] at 10 and 18 months of age, respectively)
Cabana et al. (2017) [53]	184	Infants < 6 months old	For high-risk infants, early <i>L. rhamnosus</i> + inulin supplementation for the first 6 months of life does not appear to prevent the development of eczema or asthma at 2 years of age

well as encouraging results in acne, should path the way to a strong research in this field.

Probiotics in seborrheic dermatitis

An imbalanced proportion of the major bacterial and fungal populations colonising the scalp, a skin barrier dysfunction, and hyperseborrhoea are three main etiological factors of dandruff and seborrheic dermatitis. The efficacy of *Lactobacillus paracasei* NCC2461 ST11 (ST11) to manage dandruff and to restore a balanced scalp microbiome was recently assessed [68]. Sixty healthy male volunteers aged 18 to 60 years with moderate to severe dandruff consumed on a daily basis a probiotic containing ST11 or a placebo for 56 days. Free and adherent dandruff, erythema and the global clinical score improved significantly (all $p < 0.05$) over time in the ST11 group and as compared to the placebo at day 57 compared to day 1.

Probiotics as photoprotectors

Bifidobacterium breve (BB) supplementation to hairless mice prevented changes induced by UVA/UVB in skin elasticity and skin appearance by preventing increases of elastase and IL- β 1 [69]. BB also suppresses changes of TEWL, skin hydration, epidermal thickening and attenuated the damage to the dermal-epidermal junction (DEJ) induced by UVR-exposure [70].

Lactobacillus johnsonii (LJ) leads to protection against UV-induced immunosuppression by preventing decreases of interleukin-10 levels and influencing the number of Langerhans cells [71]. In human dermal fibroblasts and hairless mice, *L. plantarum* HY7714 treatment effectively rescued UVB-reduced procollagen expression through the inhibition of UVB-induced MMP-1 expression in human dermal fibroblasts. In the same study it also inhibited UV-induced epidermal thickness increase [72]. *Lactobacillus acidophilus*, in a hairless mouse model, was proven to lessen epidermal thickness and TEWL, but also skin collagen bundles, MMPs, and proinflammatory cytokines expression induced by UVR-exposure [73]. Various other probiotics are also displaying similar activity in prevention of UV-radiation.

Probiotics in tissue repair

Topical *L. plantarum* inhibited *Pseudomonas aeruginosa* colonization, improved tissue repair, and enhanced phagocytosis in burn wounds in mice [74]. Clinical studies on patients with second- and third degree burns found that the application of *L. plantarum* was as effective as silver sulfadiazine in decreasing bacterial load, promoting the appearance of granulation tissue, and wound healing [75].

Probiotics in skin aging

Skin aging can be divided in two categories: intrinsic aging, merely related to genetic factors (responsible for around 30% of global skin aging) and extrinsic aging such as sun exposure (UVA/UVB but also visible light and infrared radiation), smoking, environmental pollution, poor diet and stress. These extrinsic factors are responsible for around 70% of global skin aging, and we can act to prevent and limit them. Along skin aging process, the skin becomes rougher (less hydrated) and slack. The loss of the elastic tissue (elastin) in the skin with age causes the skin to hang loosely. The skin becomes more transparent. This is caused by thinning of the epidermis. Finally, the skin becomes more fragile, this being caused by a flattening of the DEJ.

To help our fight against skin aging, probiotics may interfere at various levels:

Dermal fibroblasts and collagen

L. acidophilus, but also *L. plantarum* were shown to inhibit MMPs expression [72,73].

Various strains of *Lactobacilli* display strong anti-elastase activity (for instance *L. casei*, *L. diolivorans* or *L. rhamnosus*) [76]. Among 60 *Lactobacilli exopolysaccharides* (LEPS) isolated from herbal plants and dairy products, all of them exhibited significant anti-collagenase activity and selected LEPS showed high anti-collagenase properties (up to 100%) [76]. On cultivated human dermal fibroblasts, most of LEPS treatments exhibited high potential in both proliferation and migration of dermal fibroblasts compared to controls.

Inflammation

Chronic inflammation is aetiology of extrinsic aging [77]. Chronic inflammation appears strongly linked to many preventable and treatable skin diseases and conditions such as visible skin aging. Mucocutaneous inflammation as the final common pathway of many systemic and mucocutaneous diseases including extrinsic aging has been established at the molecular and cellular levels [77]. Hence, a convenient anti-aging strategy includes inhibition of primary activators of mucocutaneous inflammation such as stratum corneum permeability barrier disruption, blocking any pro-inflammatory environmental insult such as ultraviolet radiation, and quenching tissue responses to these insults [77].

Anti-inflammatory properties of probiotics have been shown on cell homogenates of *L. rhamnosus* GG, *L. rhamnosus* LC705, *B. animalis* Bb-12, *L. acidophilus* NCFB-L61748, *L. bulgaricus* ATCC11842, *S. thermophilus* T101, and *P. freudenreichii* Shermanii strain JS [78].

Oral administration of *Lactococcus lactis* [79], but also *Lactobacillus acidophilus* [73] in mice were shown to decrease levels of IL-1 β in the skin. The latter was also able to decrease the levels of IL-6 [73]. *Lactobacillus reuteri* BM36301 was shown to reduce TNF- α in serum and skin of mice fed with this probiotic [80]. Addition of *L. paracasei* NCC2461 to lymphocyte culture has been shown to strongly induce the anti-inflammatory cytokines IL-10 and TGF- β [81]. Similarly, mice treated with *Lactobacillus casei* had an increased ability to produce IL-10 [82].

Probiotics and skin barrier

Streptococcus thermophiles increase stratum corneum ceramide levels when applied topically to the skin, thus leading to an improvement in barrier function and maintenance of stratum corneum flexibility [83]. *Lactobacillus plantarum* KB lysates were also shown to dramatically improve skin barrier function [84]. A similar benefit was found with oral administration of *Bifidobacterium breve* B-3 in mice irradiated with UVR [70].

Probiotics and skin hydration

Bifidobacterium fermented soy milk was able to enhance hyaluronic acid production in cultures of human keratinocytes and skin fibroblasts, as well as in hairless mouse skin topically [85]. Oral *Lactobacillus acidophilus* increased skin moisturizing in hairless mice [73]. Oral *Lactobacillus plantarum* improves skin hydration in face and forearms of human volunteers after 4 weeks [85, 86]. Volunteers taking orally *L. plantarum* HY7714 [86] were found to have significant increases in skin water content in the face and hands at week 12 and TEWL decreased significantly at weeks 4, 8 and was suppressed at week 12 on the face and forearm. They had a significant reduction in wrinkle depth

at week 12, skin gloss was also significantly improved by week 12 as well as skin elasticity (13.2% after 4 weeks and by 21.7% after 12 weeks) [86].

Probiotics and hair [87]

It was found that feeding of probiotic yogurt to aged mice induced integumentary changes mimicking peak health and reproductive fitness characteristic of much younger animals. Eating probiotic yogurt triggered epithelial follicular anagen-phase shift with sebocytogenesis resulting in thick lustrous fur due to a bacteria-triggered interleukin-10-dependent mechanism. Aged male animals eating probiotics exhibited increased subcuticular folliculogenesis, when compared with matched controls, yielding luxuriant fur only in probiotic-fed subjects. Female animals displayed probiotic-induced hyperacidity coinciding with shinier hair, a feature that also aligns with fertility in human females.

Conclusions

Normalization of intestinal microflora with the use of probiotics and prebiotics has a positive effect on several skin conditions. While convincing data summarized in this paper show that probiotics and prebiotics decrease the incidence of AD in infants, more research is needed to determine their activity in the treatment of AD, acne, rosacea, psoriasis and wound healing. Further, various probiotics appear to have efficacy in sun-protection and on various symptoms relative to skin aging, such as the loss of collagen, worsening of skin barrier or increase of TEWL, which causes skin dry up. For sure, we are in a preliminary stage when using probiotics in dermatology, and much investigation is needed. With this condition, one day will come, when probiotics will be fully part of the prescription in dermatology.

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Пробіотики в дерматології

Пробіотики — це живі мікроорганізми, які при введенні в адекватних кількостях можуть принести користь для здоров'я господаря. Ми вже знаємо, що їх використання позитивно впливає на ключові чинники в розвитку дерматологічних захворювань, таких як окиснювальний стрес або запалення. Найбільш популярне використання пробіотиків у дерматології відноситься до atopічного дерматиту (АД). Оскільки вже продемонстровано і широко визнано, що пробіотики можуть допомогти знизити частоту і тяжкість АД у дітей грудного віку, потрібно ще багато досліджувати його користь при лікуванні АД у немовлят/дітей, а також і у дорослих. Аналогічним чином багатообіцяючі дані показують, що пробіотики можуть допомогти при вугровій висипці, в загоєнні ран і відновленні тканин. Набагато менше або навіть нічого не відомо про їх потенційний ефект при інших запальних захворюваннях, таких як розацеа або псоріаз. Крім продемонстрованої активності в галузі фотозахисту, пробіотики, мабуть, ефективні для профілактики і навіть лікування старіння шкіри і її більш частих симптомів, таких як втрата колагену, сухість і порушення бар'єрної функції. З огляду на особливий статус шкіри її доступ для місцевого нанесення препаратів, пробіотики можуть використовуватися як системно, так і локально.

Нормалізація мікрофлори кишечника з використанням пробіотиків і пребіотиків робить позитивний вплив на деякі шкірні захворювання.

Попереду ще довгий і багатообіцяючий шлях для дослідження, перш ніж пробіотики стануть щоденним рецептом в дерматології.

Ми перебуваємо на попередній стадії при використанні пробіотиків у дерматології, і ще потрібно багато досліджень. Одного разу пробіотики стануть частиною дерматологічного рецепта.

Ключові слова: пробіотики, пребіотики, шкіра, запалення, atopічний дерматит, старіння шкіри.

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Пробиотики в дерматологии

Пробиотики — это живые микроорганизмы, которые при введении в адекватных количествах могут принести пользу для здоровья хозяина. Мы уже знаем, что их использование положительно влияет на ключевые факторы в развитии дерматологических заболеваний, таких как окислительный стресс или воспаление. Наиболее популярное использование пробиотиков в дерматологии относится к atopическому дерматиту (AD). Поскольку уже продемонстрировано и широко признано, что пробиотики могут помочь снизить частоту и тяжесть АД у детей грудного возраста, предстоит еще многое исследовать относительно его полезности при лечении АД у младенцев/детей, а также и у взрослых. Аналогичным образом многообещающие данные показывают, что пробиотики могут помочь при угревой сыпи, в заживлении ран и восстановлении тканей. Намного меньше или даже ничего не известно об их потенциальном эффекте при других воспалительных заболеваниях, таких как розацеа или псоріаз. Помимо продемонстрированной активности в области фотозащиты, пробиотики, по-видимому, эффективны для профилактики и даже лечения старения кожи и ее более частых симптомов, таких как потеря коллагена, сухость кожи и нарушение барьерной функции. Учитывая особый статус кожи, ее доступ для местного нанесения препаратов, пробиотики могут использоваться как системно, так и локально.

Нормализация микрофлоры кишечника с использованием пробиотиков и пребиотиков оказывает положительное влияние на некоторые кожные заболевания.

Мы находимся на предварительной стадии при использовании пробиотиков в дерматологии, и еще требуется много исследований. Однажды пробиотики станут частью дерматологического рецепта.

Ключевые слова: пробиотики, пребиотики, кожа, воспаление, atopический дерматит, старение кожи.

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