

The Role Of Probiotics In Skin Aging

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ABSTRACT

Background: The process of skin aging is a complex biological phenomenon consisting of two components, referred to as intrinsic and extrinsic aging, respectively. There are currently several studies that research probiotics as alternative therapeutic options for aging skin.

Content: Skin aging in an individual is a combination of intrinsic and extrinsic skin aging. Intrinsic skin aging is a natural process that occurs with age, influenced by ethnicity, gender, gene, hormone, etc, while the extrinsic skin aging is influenced by environmental factors, such as life style, pollution, and especially ultraviolet radiation (photoaging). Probiotics are defined as live microorganisms that when administered in adequate amounts confer a health benefit to the host. Major probiotic mechanisms of action include enhancement of the epithelial barrier, increased adhesion to intestinal mucosa, and concomitant inhibition of pathogen adhesion, competitive exclusion of pathogenic microorganisms, production of anti-microorganism substances and modulation of the immune system.

Conclusion: Aging is a natural process that we cannot avoid, so probiotics are an alternative therapy to slow down the skin aging process, both intrinsic and extrinsic. Probiotics can decrease MMP (matrix metalloproteinases) level, which is one of the factors that play a role in skin aging.

Keywords : Probiotic, *Lactobacillus*, Skin aging, Healthy lifestyle.

BACKGROUND

The process of skin aging is a complex biological phenomenon consisting of two components, referred to as intrinsic and extrinsic aging, respectively. The age of elderly more than 65 years old in 2050 will be doubled in developing countries.¹

There is an increasing incidence of chronic diseases including skin diseases, which cause the most frequent complaints in the elderly population. Based on data from the Central Bureau of Statistics, the life expectancy in 2020-2035 is 71 years. Along with developments in all fields, elderly people need to pay attention to appearance, this is different from ancient times. It is hoped that the elderly can become successful aging, not only getting old physically, but also mentally and socially healthy, including being happy and satisfied with themselves, which can be achieved in one way, namely, building individual self-confidence through prevention. and treatment of aging skin.^{2,3}

Various ingredients and methods for prevention and treatment are mentioned in the reference, the use of sunscreens is useful for protecting the skin from UV (ultra violet), for a wider range of treatments such as topical therapy, chemical peels, botulinum toxin, filler injection, microdermabrasion, laser, cosmetic surgery, it takes time to get its repair on average more than 2

weeks, depending on the therapy used, and requires continuous repetition of therapy, besides that it requires a lot of money to do the therapy.⁴

Various methods are available for the prevention and treatment of skin aging, starting from the use of photoprotector ingredients, at a minimum, patients should be advised to use sunscreen every day, topical retinoids every night, and topical antioxidants every day. Completing a routine skin care regimen with the use of alpha hydroxy acid (AHA), growth factors, heparin sulfate, stem cells. 4 to more aggressive therapies such as chemical peels, microdermabrasion, botox injections, filler injections, to laser therapy. Several references have stated that the use of probiotics has also been a benefit for health problems, one of which is skin health.⁵

Probiotics is a term that refers to microorganisms that provide benefits to humans and animals. These microorganisms The health benefits of probiotics have been established by several animal and human studies and the scientific literature shows that the clinical use of probiotics is extensive and open to on going evaluation, mechanism of action of probiotics is also observed to slow or inhibit the skin aging process contributing to the balance of gut microbes and also plays an important role in maintaining health. Therefore, the use of probiotics is expected to be an alternative therapy that can be used to prevent skin aging.⁶

CONTENT

Skin aging

Aging is a process that is often considered a natural process that cannot be avoided even though various ways and interventions to live longer have been taken. Humans are born, grow and develop until a certain time limit, then start the aging process. Aging is a process of gradual and progressive decline in the physiological function of the body resulting in the loss of the ability to grow and develop and increase in weakness, signs of aging become visible over time, and skin changes are the first signs of the aging process. changes in skin aging, namely from a combination of intrinsic (gene mutations, cellular metabolism, hormones) and extrinsic (eg, chemicals, toxins, pollutants, ultraviolet / UV, and ionizing radiation). Exogenous or extrinsic aging affects most sun exposed areas of the body, while endogenous or intrinsic changes in the characteristics of aging skin are particularly noticeable in areas of the skin that are protected from the sun.⁷

Intrinsic aging, reactive oxygen species (ROS) are produced by oxidative metabolism of cells. Exposure to solar radiation also increases the production of ROS and causes damage to DNA, protein, and lipids and reduces antioxidants in the skin..^{1,9}

Extrinsic aging, especially caused by UV rays, will also cause an increase in ROS in the dermis. Increased ROS also increases activator protein-1 (AP-1) regulation, then inhibits transforming growth factor (TGF- β), thus inhibiting collagen synthesis.^{10,11}

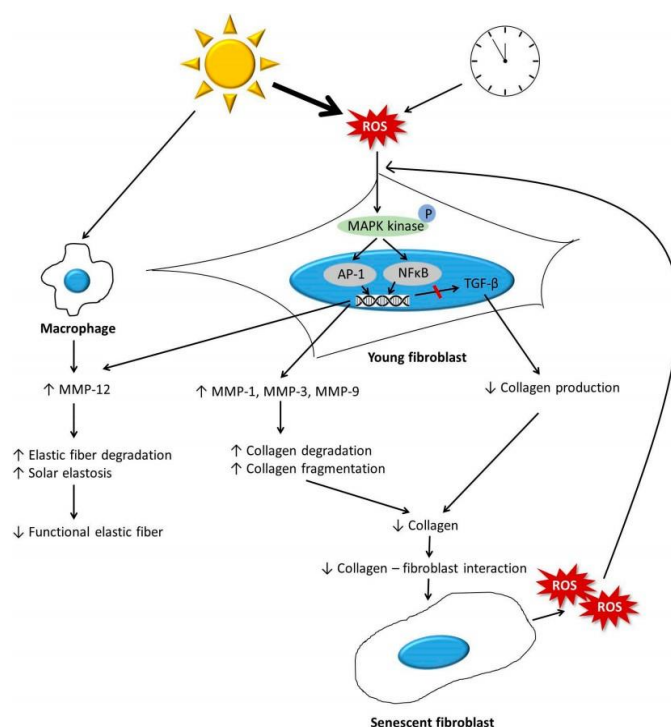


Figure 1. Schematic illustration showing the changes in fibroblasts, collagen, and elastic fibers in the dermal aging process.¹²

Clinical manifestation

Intrinsic and extrinsic skin aging processes have different etiologies and changes in both biological, biochemical and molecular mechanisms but both exert harmful effects on the connective tissue of the skin. These changes can be seen clinically and histopathologically.⁹

Table 1. Clinical features of intrinsic and extrinsic skin aging¹

INTRINSIC AGING	EXTRINSIC AGING
- Xerosis - Pallor - Fine wrinkles - Decreased elasticity - Fragili	- Xerosis - Multiple telangiectases - Deep wrinkles - Decreased elasticity - Fragility - Dyspigmentation

Table 2. Typical histologic of intrinsic and extrinsic skin aging¹

INTRINSIC AGING	EXTRINSIC AGING
- Epidermal thinning - Loss of rete ridges - Decreased number of collagen and elastin fibers	- Solar elastosis - Reduced number of fibroblasts - Reduced amount of extracellular matrix

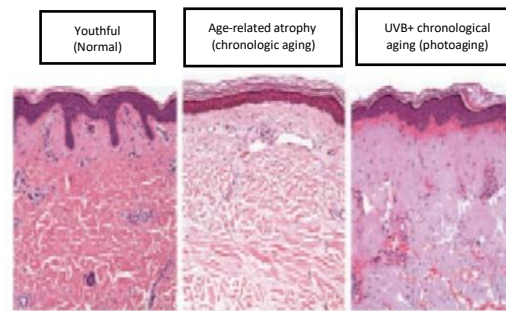


Figure 3. Histopathological features of normal skin, intrinsic aging, extrinsic aging¹⁵

Probiotics

Probiotics is a term that refers to microorganisms that provide benefits to humans and animals. These microorganisms contribute to the balance of intestinal microbes. According to the Food and Agriculture Organization (FAO) and the World Health Organization (WHO) probiotics are microorganisms that live in the host body in sufficient quantities, which will provide health benefits. Probiotics is a term that refers to microorganisms that provide benefits to humans and animals. These microorganisms contribute to equilibrium. The microorganisms in probiotics consist mostly of strains of the genera *Lactobacillus* and *Bifidobacterium*, but strains of *Bacillus*, *Pediococcus* and some yeasts have also been found as suitable candidates for probiotics to be found in dairy and non-dairy products.¹⁶

"Prebiotic " refers to the selective fermentation of substances which causes changes in the specific composition and / or activity of microorganisms in the gastrointestinal tract, thereby benefiting the health of the host. Prebiotics are defined as food ingredients that cannot be digested by the digestive tract and have a positive effect on the microflora, namely selectively stimulating bacterial growth in the colon, especially *Lactobacilli* and *Bifidobacteria*. "Synbiotic " is a product that contains both probiotics and prebiotics, so that the components of each of these become mutually supportive and can be beneficial for health. Examples of synbiotics are *oligofructose* and *bifidobacteria*.¹⁷

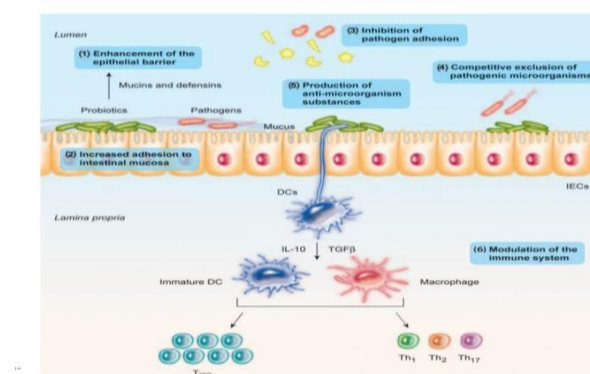


Figure 3. Mechanism of action probiotics¹⁹

The role of probiotics in aging skin

Aging of the skin is generally associated with increased wrinkles, sagging skin, and increased skin laxity, but when considering the causes these claims are changing, and it is important to distinguish between the effects of biological aging (intrinsic aging) and environmental factors, such as sun exposure (extrinsic aging). Generally, photoaging molecular changes are considered as augmentation and amplification of molecular changes associated with chronological skin aging. Skin aging is also characterized by increased pH, oxidative stress, and MMPs activity.^{5,21}

Probiotics and skin aging-associated microflora changes, The normal microflora of the skin is composed of a limited number of microbial types, mainly gram positive species. A number of physiological conditions such as hydration, pH, O₂, and growth substrates are the major factors in determining the limited number of microbial species that colonize human skin. Cutaneous microflora defends the skin against premature aging, inflammation, and dehydration and is involved in competitive exclusion of pathogens and increases the acidic nature of the skin, thereby making it even more inhospitable to many pathogens.⁶

Probiotics and skin aging-associated pH changes, normal skin pH is somewhat acidic and in the range of 4.2–5.6 and has been attributed largely to endogenous agents including the Na⁺/H⁺ antiporter, NHE1, and one or more secretory phospholipase/s A₂ (sPLA₂) enzymes, which hydrolyses membrane phospholipids, thereby generating free fatty acids (FFAs) that contribute to the acidification of the stratum corneum. Recently, a decreased NHE1 expression that accounts for the pH abnormality in moderately aged epidermis in mice and human has been reported. The reduced NHE1 expression could account the impairment of lipid processing and epidermal barrier homeostasis in aged skin even if further studies will be required to delineate whether altered sPLA₂ activity also contributes to the functional abnormalities in moderately aged epidermis.⁶

Probiotics and skin aging-associated altered stratum corneum lipid composition, in the stratum corneum, the ceramides play an important role in barrier function and water holding of the normal stratum corneum. stratum corneum dysfunction associated with aging may result from ceramide deficiency. The existence of sphingomyelinase activity in microorganism in probiotics, there is an increase in the function of ceramides in the stratum corneum, so that there is an improvement in barrier function and elasticity of the stratum corneum.⁶

Probiotics and skin aging-associated oxidative stress, the epidermis of skin possesses an extremely efficient antioxidant activity that is superior to most tissues, and it has been proposed that the reduction in efficiency of this system during aging is an important factor in skin aging. Generation of reactive oxide species (ROS) is thought to play a major role in skin aging. All the biological structures, as human skin, undergo the detrimental action of ROS. The free radical theory of aging proposes that aging results from accumulation of oxidative damage over a lifetime due to excess ROS, which result from aerobic metabolism ROS generation is increased in aged skin and represents a key step in molecular pathways, which eventually lead to increased collagen breakdown. ROS cause damage to lipids, proteins, and DNA and also influence cellular senescence.⁶

Probiotics and skin aging-associated collagen level reduction, the processes associated with intrinsic skin aging are thought to result from a combination of events including decreased proliferative capacity of skin-derived cells, decreased matrix synthesis in the dermis, and increased expression of enzymes that degrade the collagenous matrix. Collagen is one of the main building blocks of human skin, providing much of the skin's strength. Dermal fibroblasts make precursor molecules called procollagen, which is converted into collagen. There are two important regulators of collagen production: transforming growth factor (TGF)- β , a cytokine that promotes collagen production, and activator protein (AP)-1, a transcription factor that inhibits collagen production and up-regulates collagen breakdown by up regulating enzymes called matrix metalloproteinases (MMP). In aged skin, there is elevation of AP-1 as compared to young skin. MMP activity is increased in aged human skin, and is associated with dramatic increased levels of degraded collagen.⁶

Probiotics and skin aging-associated altered immune response, the senescence of the immune system especially affects cell-mediated as well humoral immunity. A decrease has also been

observed in the ratio of mature to immature T lymphocytes and an increase in proinflammatory cytokine and ROS production. Age related alterations in immune function also affect the skin, and may account for the increased susceptibility in the elderly to cutaneous infections and malignancies, and decreased or variable contact hypersensitivity reactions. The association between the composition of the *Bifidobacterium* microbiota and the different level of proinflammatory cytokine TNF α as well as antiinflammatory cytokine TGF β and regulatory cytokine IL-10 has been recently investigated.⁶

Skin aging-associated biochemical, molecular, and cellular changes and possible sites of action of probiotics

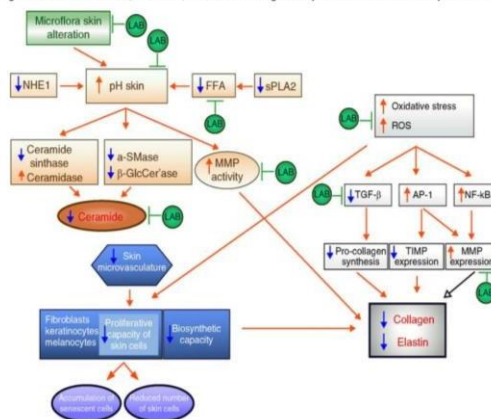


Figure 4. Skin aging-associated biochemical, molecular, and cellular changes and possible sites of action of probiotics⁶

Kim *et al*, who performed on fibroblasts in human skin, with the intervention of giving *L. plantarum* HY7714 1×10^9 CFU / ml (colony forming units / milliliter) compared to placebo, the outcome decreased MMP-1 and MMP-13. Results showed that the administration of *L. plantarum* HY7714 1×10^9 CFU / ml effectively inhibited the expression of MMP-1 in human skin fibroblasts caused by UVB exposure and effectively inhibited MMP-13 in the dermis.²²

Kim *et al*, the hairless rats were 8 for the control group, 8 for the UVB group only and 8 for the treatment group with UVB intervention with *L. plantarum* HY7714 1×10^9 CFU and compared with UVB alone, the outcome seen was a change in wrinkles.²²

Sugimoto *et al*, the hairless mice with the intervention group were exposed to UV + *Bifidobacterium breve* Yakult strain (BBY), compared with the control group, namely the group that was not given UV and the group that was given only UV, the outcome was a change in elasticity. skin, skin surface, elastase activity and levels of IL-1 β .²³

Lee *et al*, a number of 110 individuals aged 41-59 years with dry skin and wrinkles, divided into 61 in the group given probiotics and 49 with placebo. The intervention was given a probiotic in powder form containing *L. Plantarum* HY7714 (1×10^{10} CFU) for 12 weeks, compared to the placebo group. for the outcome changes in the water content of the skin, TEWL, wrinkles on the face.²⁴

Gauthier *et al*, healthy women aged > 18 years, given UV exposure. intervention by giving a drinking supplement containing 5×8^{10} (cfu) *Lactobacillus johnsonii* La1 and 7.2 mg carotenoids compared to placebo. The outcome was decreased Langerhans cells, increased factor XIIIa + type I skin dendrocytes, and decreased dermal inflammatory cells.²⁵

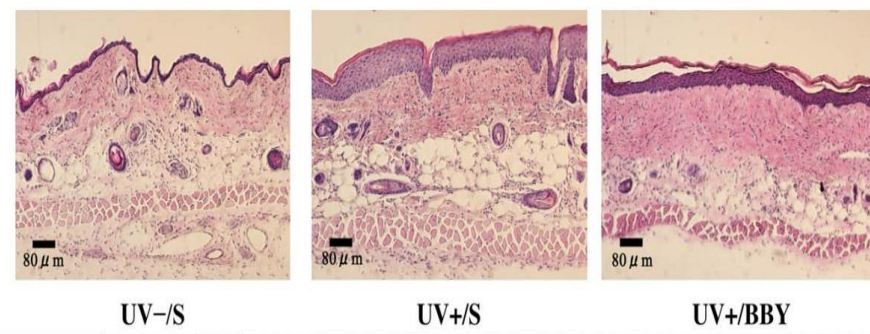


Figure 5.Effect of oral administration of BBY on epidermal thickening effect of oral administration²³

No	Author	Media	P (Population)	I (Intervention)	C (Comparasion)	Result
1	Kim <i>et al</i>	Human	Fibroblasts in human skin	<i>L.plantarum</i> HY7714 1×10^9 CFU / ml	Placebo	<i>L.plantarum</i> HY7714 1×10^9 CFU / ml effectively inhibited expression of MMP-1 in human skin fibroblasts caused by UVB exposure and effectively inhibited MMP-13 in the dermis
2	Kim <i>et al</i>	Animal	hairless rats	UVB+ <i>L.plantarum</i> HY7714 1×10^9 CFU	UVB	- Change in wrinkles - <i>L.Plantarum</i> HY7714 inhibited the number, depth, and area of wrinkles in hairless mice and the data also showed that <i>L. plantarum</i> HY7714 significantly inhibited thickening of the epidermis in hairless mice caused by UVB exposure.
3	Sugimoto <i>et al</i>	Animal	hairless mice	UV+ <i>Bifidobacterium breve</i>	UV	Changes skin, skin surface, elastase

				Yakult strain (BBY).		activity and levels of IL-1 β BBY significantly prevents damage to the elasticity and surface of the skin
4	Lee <i>et al</i>	Human	Individuals aged 41-59 years old	<i>L.Plantarum</i> HY7714(1×10^{10} CFU) for 12 weeks	Placebo	Probiotic group changes in the water content of skin, TEWL, wrinkle on the face. Reduce deep wrinkles at week 12
5	Gauthier <i>et al</i>	Human	healthy women aged > 18 years	5×8^{10} (cfu) <i>Lactobacillus johnsonii</i> La1 and 7.2 mg carotenoids	Placebo	Decreased Langerhans cells, increased factor XIIIa + type I skin dendrocytes, and decreased dermal inflammatory cells

CONCLUSION

Skin aging, along with developments in all fields, the elderly are also expected to become successful aging, one of which is to build self-confidence by preventing and managing skin aging. There have been many therapeutic modalities that have been carried out, and currently there are one of the alternatives to prevent photoaging and skin aging is skin care with probiotics. Early studies in animal models and clinical trials in humans have shown that probiotics can slow both intrinsic and extrinsic aging processes, so, this can be a new thing for the cosmetic dermatology division, that probiotics can restore acidic skin pH, reduce oxidative stress, improve skin barrier function.

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