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Role of Skin Microbiome Related Aging: A Systematic Review

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Abstract: The ageing process of the skin is complex and impacted by both internal and external causes. As the skin's antioxidant system deteriorates with age, a well-known hypothesis of ageing holds that oxidative damage causes cellular senescence or apoptosis. The complex ecosystem that is the human microbiota is made up of bacteria, fungi, and viruses, among other microorganisms. Both innate and adaptive immune responses depend on the gut and skin microbiota's ability to modulate the immune system, manage inflammation, and protect against invasive infections. Throughout life, the human microbiome may change and be impacted by a variety of disruptions. "Microbial dysbiosis," a change in the gut microbiota, is connected to the effects of a number of illnesses, including ageing. An innovative synthesis of the "genome-microbiome-exposome," the skin interactome has a major impact on skin health and ageing. In order to protect, prevent, and postpone skin ageing while preserving good skin conditions, future initiatives should concentrate on reducing the negative effects of factors that affect the skin interactome.

Keywords: *Skin microbiome, Aging, Immunological Response.*

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I. INTRODUCTION

The change from a younger to an older, usually less healthy, organism is known as ageing. Although the socially accepted definition of "old" or "aged" is 60 to 70 years old, ageing occurs continually throughout life. All organ systems experience a reduction in structure and function as a result of biological ageing, which is a cellular and molecular process. The ageing process is greatly influenced by genetic factors. A species' lifespan is determined by its genetic makeup, which also helps to explain why members of particular lineages typically live longer and in better health than others. In light of our current understanding of science, it is therefore generally accepted that ageing is ubiquitous, unavoidable, and irreversible. By changing extrinsic factors, such as physical activity, diet, rest, exposure to the environment, and illnesses, ageing can be accelerated or delayed. Through common molecular mechanisms that result in damage accumulation and a diminished ability of cells to repair themselves, these variables impact the ageing process. The accumulation of abnormal proteins, oxidative stress, mitochondrial dysfunction, cellular senescence, genetic and epigenetic changes, and other factors are the main causes of ageing that are currently understood (Lemoine 2021).

Being our body's greatest interface, the skin ages in a complex way due to a combination of internal and external influences. Chronological skin ageing is one of the intrinsic variables. It refers to a sequence of physiological changes in the skin that are unavoidable and occur over time. These changes are caused by hormones, heredity, and cellular metabolic changes, such as metabolites from the gut and skin microbiota. These changes reflect soft tissue changes, including decreased collagen production, decreased cholesterol, skin thinning, and loss of subcutaneous fat. Dryness, pallor, fine wrinkles, and increased laxity are all signs of intrinsically aged skin. An inverted triangle morphology, which is the result of the interaction of recession, resorption of face bone, and soft tissue changes, characterises facial ageing. On the other hand, extrinsic ageing, or photoaging, includes structural and functional changes brought on by various environmental factors, among which ultraviolet radiation (UV) is the primary one. Tobacco usage, food practices, exposure to chemicals, trauma, and air pollution are other external concerns. Significant wrinkles, looseness, roughness, increased fragility, and many telangiectasias are all signs of skin ageing caused by external sources. Moreover, darkening and uneven pigmentation are signs of depigmentation in photodamaged skin. Solar elastosis, a decreased number of fibroblasts, and a decreased amount of extracellular matrix are among the histological features (Makrantonaki, Bekou, and Zouboulis 2012; Tobin 2017).

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There is additional evidence that the skin microbiota plays a role in the ageing process of the skin. diverse age groups have diverse skin microbiomes, according to a number of research. To clarify the relationship between ageing and the skin microbiota, more investigation is required. New findings about the skin microbiota and how it interacts with the immune system will be examined in this evidence-based review (Nurkolis et al. 2024). Our goal was to provide physicians with an overview of current treatment options by thoroughly reviewing all relevant studies in the literature, including those that examined the relationships between the skin microbiota and skin ageing. The development of innovative treatment approaches that target the skin microbiota requires a thorough investigation of these topics.

II. METHODS

Using the PRISMA, we conducted a systematic search of the PubMed, SCOPUS, EuropePMC, ProQuest, and Cochrane Central Databases using the search terms “Skin Microbiome” or “Skin Aging” and “Aging” or “Microbiome.” Duplicate results were eliminated, and the remaining articles were independently screened for relevance by their abstracts with all authors. The full-text of the selected abstract was then carefully read, and those that met our criteria were included in the study.

- *Study Selection*

Cohort prospective, retrospective, and preprinted studies were all included. Every study pertaining to ageing and the skin microbiota was considered.

- *Quality Assessment*

Two writers independently evaluated the studies' quality using the Modified Newcastle-Ottawa Scale (NOS). Each study was given a score between 0 and 9, with a total score of ≥ 7 indicating high quality. By talking with both authors, any disagreements on the quality assessment were settled.

III. RESULTS

315 potentially pertinent papers were found in the first search; 96 of these were promptly eliminated for duplication. 201 papers were eliminated following the initial screening of abstracts and titles. Ten studies were included in this systematic review after eight more papers were eliminated following the full-text review (Figure 1).

In this analysis, all studies were deemed high quality, with no study obtaining fewer than seven stars. The baseline characteristics of the included studies are shown in Table 1. Studies were deemed high quality if they achieved a score of seven stars or more for quality evaluation by NOS (Table 2).

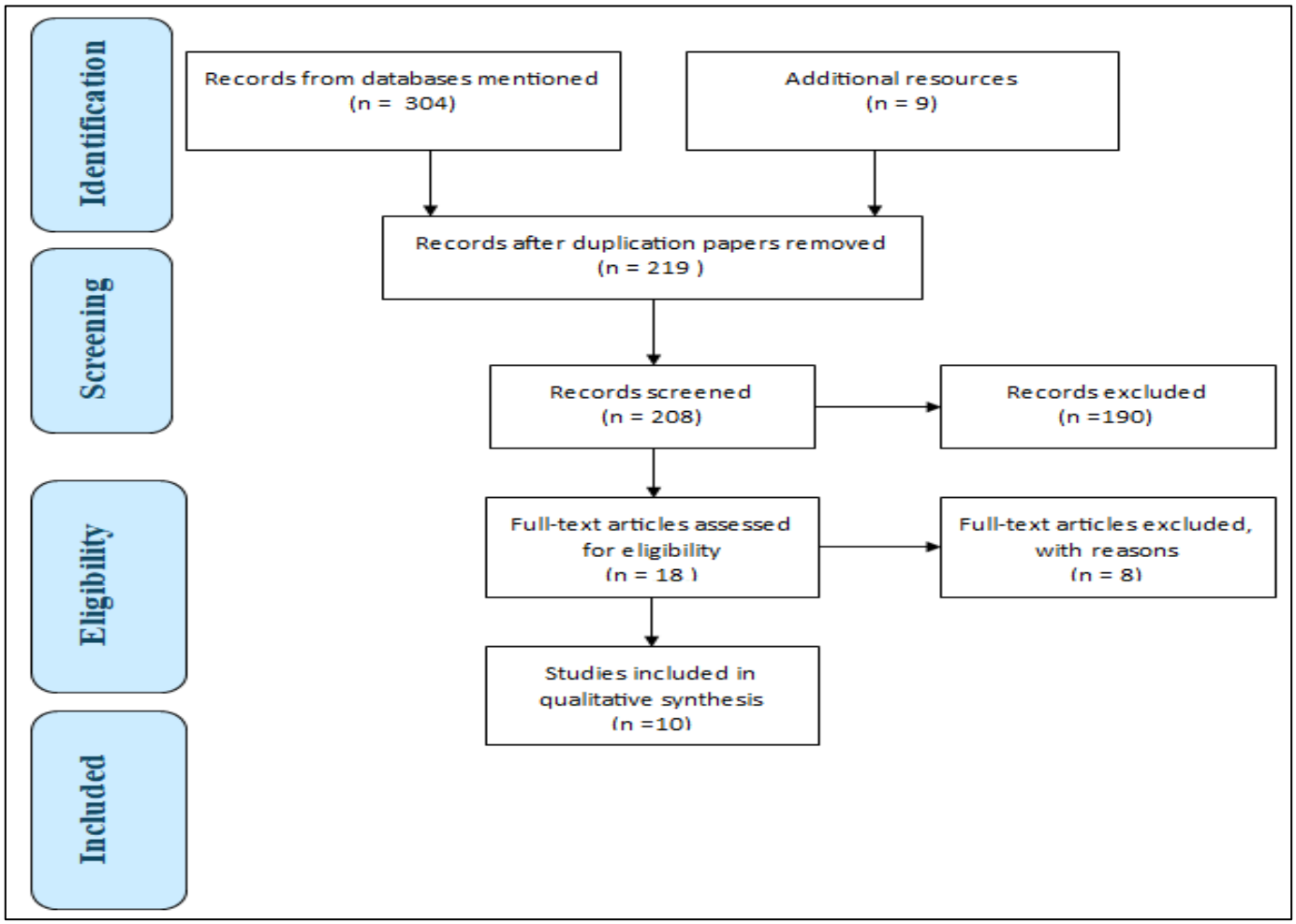

Fig 1. PRISMA Flow Diagram Mentioned in this Study.

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Table 1. Characteristics of the Included Studies

Author and Year	Study Design	Country	Quality Score	Analysis Method	Sample	Result of Study
Li et al 2020(Li et al. 2020)	Cross sectional	USA	8	RNA sequencing	Skin swab	Nine microbial communities (Cyanobacteria, Staphylococcus, Cutibacterium, Lactobacillus, Corynebacterium, Streptococcus, Neisseria, Candida, and Malassezia) and 18 pathways, including antibiotic biosynthesis, have the potential to influence skin ageing, implying that skin microbiomes may play critical roles in skin ageing by modulating immune responses, UV light resistance, and the biosynthesis and metabolism of age-related compounds.
Kim et al 2019(H.-J. Kim et al. 2019)	Cross sectional	China	8	RNA sequencing	Skin swab	The younger group had higher levels of inferred metagenomic functional pathways associated with replication and repair, whereas the older group had higher levels of metabolism-related pathways associated with biodegradation.
Hillebrand et al 2021(Hillebrand et al. 2021)	Cross sectional	Canada	8	RNA sequencing	Skin swab	Over the course of the two-year study, the diversity and composition of the facial skin microbiota in the population under investigation showed very little change. The composition, diversity, and relative abundance of some species, however, varied significantly from year to year for some participants, and these changes were associated with changes in follicular porphyrins and stratum corneum barrier function.
Juge et al 2018(Jugé et al. 2018)	Case control	France	8	RNA sequencing	Skin swab	An examination of the taxonomic composition showed that the older skin had more Proteobacteria and fewer Actinobacteria. Aged skin showed a significant decrease in Propionibacterium relative abundance and a significant increase in Corynebacterium at the genus level.
Dimitriu et al 2019(Dimitriu et al. 2019)	Cross sectional	Canada	8	RNA sequencing	Skin swab dan epitel oral	Compared to V1-V3, V4 primers detect Finegoldia and Peptoniphilus better. The Peptostreptococcaceae family may influence host-microbe interactions; they are affected by skin creams and illustrate dysbiotic conditions in immunocompromised people.
Suzuki et al 2020(Suzuki et al. 2020)	Cross sectional	Japan	8	RNA sequencing	Skin swab	Higher α-diversity was seen in the meibum microbiome, particularly among younger subjects. Nearly 30% of older adults had a low-diversity Corynebacterium sp. or Neisseriaceae microbiome.
Kim et al 2021(G. Kim et al. 2021)	Kohort	Korea	8	RNA sequencing, WGS	Skin sterilized tape	The application of Streptococcal culture supernatant to human skin improved elasticity, hydration, and desquamation. Gene Ontology showed spermidine and glycogen production pathway intersections. Streptococcus spermidine increased collagen and lipid synthesis in aged cells to restore skin architecture and barrier function.

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Kim et al 2020(M. Kim et al. 2020)	Cross sectional	Korea	8	RNA sequencing	Skin swab	Age affected the commensal microbiota on the forehead and hands, including Streptococcus, Staphylococcus, Cutibacterium, and Corynebacterium, which colonise and maintain skin health. Alpha diversity indices on forehead skin increased significantly with age.
Wu et al 2020(Wu et al. 2020)	Cross sectional	China	8	RNA sequencing	Skin swab	The anatomical location dominated Sardinian bacterial and fungal dispersion and interaction. Skin bacterial and fungal populations differed structurally by age.
Russo et al 2023 (Russo et al. 2023)	Cohort	Italy	8	Next generation sequencing	Skin swab	The functionality and linkages of microbiota with host genetic factors may influence two aging-related host processes, namely ROS damage repair and collagen metabolism. LTB4 (latent transforming growth factor beta binding protein 4) is a crucial regulator of transforming growth factor beta (TGFB1, TGFB2, and TGFB3), which governs TGF-beta activation by preserving it in a latent state during extracellular storage. It forms extracellular matrix fibres, mostly collagen and glycosaminoglycans, mostly proteoglycans, which help the matrix recoil after transient stretching.

IV. DISCUSSION

Wrinkles, pigmentary anomalies, and laxity accompany skin ageing. Intrinsic and extrinsic factors can accelerate skin ageing. Immunosenescence, cellular metabolism, and hormonal oscillations contribute to age-related physiological and skin architectural changes. Pollution, cumulative UV exposure, and smoking also alter skin structure. These physiological changes alter the skin microbiota, reducing sebum production. In numerous skin locations, including the cheek, forehead, and forearm, Cutibacterium spp. colonisation decreased with age, likely due to decreased sebaceous gland activity. Prevotella, Rothia, and Veillonella were overrepresented. Due to decreased moisture and sebum production, archaea in the skin microbiome increase with age. Cosmetic medicines contain purified metabolites from anti-aging microorganisms. Novel therapeutics for age-related dermatological disorders may target regulators of skin microbiome homeostasis across age cohorts (Boxberger et al. 2021; Chambers and Vukmanovic-Stejic 2020).

Numerous studies found that nonlesional zones without skin ageing had a more diverse microbiome. In a case–control study of European women, Jugé et al. found that aged skin had more Proteobacteria and Corynebacterium and less Actinobacteria and Propionibacterium. Korean and Chinese women of various ages showed similar results. Li et al. used nested polymerase chain reaction-denaturing gradient gel electrophoresis to show that ageing alters the skin microbiome qualitatively and quantitatively in a case–control study. The resident skin microbiome includes bacteria, fungi, and archaea, whose interactions produce different skin effects (Jugé et al. 2018; Li et al. 2020).

Genetics, gender, pollution, solar exposure, and climate, and lifestyle factors (exercise, stress, sleep, nutrition, and skincare regimen) cause age-related skin changes. Sebum, perspiration, and immunological activity decrease with age, changing skin surface physiology like lipid composition, sebum production, and pH. Dryness, collagen fragmentation, and decreased collagen and elastin levels result from these factors, which may also affect skin ecology and the skin microbiome. Dimitriu et al. used 16s rRNA gene amplicon sequencing to study 495 North American individuals' bacterial microbiomes across four skin sites and the oral mucosa. Demographics, lifestyle, physiology, and ageing affect skin microbiota, while ethnicity most strongly correlates with oral microbiomes (Dimitriu et al. 2019; M. Kim et al. 2020).

V. CONCLUSIONS

This study suggests bacteria and functional pathways important for future skin ageing prevention research, which may help us understand age-related skin microbiome features.

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