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Potential role of collagen and its supplements in treatment of skin ageing

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Abstract

Skin ageing is a complex phenomenon that results in alterations to the physiological functioning of the skin as well as very noticeable phenotypic changes. Particularly, hyaluronic acid, collagen, and elastin fibres experience structural and functional alterations as they age. Collagen is a fibrillar protein that mostly builds the skin, joints, and bones of the mortal body's conjunctive and connective tissues. Because of its connective component in natural structures, this patch is among the most prevalent in a wide variety of living species. because of its power, cornucopia, and direct correlation with the ageing of the skin. The purpose of this study was to illustrate the role that collagen plays in skin ageing and its origins. This composition discusses the two types of skin aging—natural and foreign—as well as the various factors that affect them, such as sunlight, genetic mutation, artificial pollution, and so on. It also discusses how the ageing process works and the subsequent miracles that occur during this phase. Subsequent research has examined the relevance of collagen and its many sources in relation to the ageing process of skin.

Introduction

The process of skin ageing is substantially intricate yet still poorly understood. One way to think of ageing is as the build-up of many harmful alterations in cells and tissues. These alterations have the potential to quickly deteriorate natural processes, raise the risk of illnesses, and ultimately cause death. There is currently no cohesive idea linking the several geriatric models that have been developed thus far. With ageing and related hormonal and beneficial fluctuations, skin, like many other organs, experiences harmful alterations. The face, neck, forearms, and backs of the hands are among the body parts that are frequently exposed to the sun and show outward indications of ageing more quickly than other parts of the body. Skin has two essential purposes. First and foremost, skin acts as a barrier, guarding against bacterial, chemical, and physical infiltration into the body as well as preventing dehumidification due to evaporative water loss. Second, the skin facilitates thermoregulation by controlling the eccrine sweat glands and the skin-hosted vasculature. In addition to mediating the sense of touch, skin is involved in social communication, hormone production, and vulnerable surveillance. As we age, these functions are all impacted. Generally speaking,

photoaged skin exhibits variations in structure and function earlier and more strongly than chronologically aged skin. Presumably, photoaging is an accretive process, and in older individuals, it manifests itself more severely. Even though the skin protection factor (SPF) system has been successfully used in topical products, the public still needs to be convinced of the dangers of sun exposure. The most prominent effects of sun exposure are wrinkles and unwanted saturation, which are telltale signs of print-aging. In general, photoaged skin has rough wrinkles, a rough texture, "broken" blood vessel appearance (telangiectasia), and uneven brown patch saturation (lentigines). Oxidative damage accumulating in apkins and cells is also seen during the ageing process. The reason for this is a disruption in the equilibrium between the natural antioxidant defences and the byproduct of reactive oxygen species (ROS). In the skin, free radical damage can beget deterioration of the stratum corneum and probative connective towel, performing in dropped pliantness and adaptability.

Figure 1: Functions of the skin that decline with age

Many experimental and randomised controlled studies have been conducted in the past 20 years to assess the benefits of collagen on skin health. The primary structural protein in the vibrant connective tissues like skin and bone is collagen. In animals, it comprises around 25% of their total protein content. Collagen makes up to 80% of the dry weight of mature skin. Fibroblasts create collagen fibres, which are organised to resemble facial skin. Collagen's amino acid sequence is only created by alternating repetitions of tripeptides comprising glycine, proline, and hydroxyl proline, despite the fact that its tertiary structure is quite complicated and takes the shape of a coiled coil structures.

Sourced from animal sources such as pig skin, cow bone, and fish scales, the collagen utilised in the research is almost entirely hydrolyzed. Collagen hydrolysates (CH) are created when the molecular bonds in collagen molecules are hydrolyzed as a result of various physical, chemical, and natural degradation processes that the molecules undergo. Hydrolyzed collagen has a reduced antigenic particularity in contrast to its intact form. Skin integrity and appearance can be disfigured as a result of a variety of environmental, hormonal, chronological, and photoaging variables. A decrease in the colour of metabolic conditioning linked to modifications in the quantity and calibre of dermal collagen and elastin, alterations in the structure of the skin, and common signs of ageing can be observed. Skin ageing results in the loss of the connective tissue. Skin tone and suppleness are lost as a result. Additionally, throughout this process, wrinkles and the deepening of facial crimps—two of the most recognised indicators of ageing skin—develop. Sufficient intake of vital nutrients plays a fundamental role in maintaining the health and function of skin. Fibroblasts create collagen fibres, which are organised to resemble facial skin. This keeps the skin from being ripped by overstretching and provides it a high tensile strength. As we age, the dermis experiences morphological, physical, and chemical changes. All things considered, many of the skin's abilities are known to deteriorate with age. Nutrient supplements to benefit ageing skin have been developed as a result of ongoing research into the effects of orally delivered biologically active composites (such as antioxidants and collagen) on skin function. Certain beneficial elements containing antioxidant packages may act in a circular manner on the skin through secondary messengers, or during digestion they may travel through the intestinal hedge, pass through the gastrointestinal tract, and also (via the blood sluice) reach the various body tissues, including the skin, possibly in an active form. These bioactive composites are transported to all skin chambers and can be replenished by the blood on a continual basis.

Skin ageing

Multifaceted changes in skin physiology and, most obviously, phenotypic alterations result from the multifactorial wonder that is skin ageing. Specifically, hyaluronic acid, collagen, and elastin filaments experience structural and functional alterations as we age. Although it is the main external cause among a number of internal and environmental factors, the sun is not the sole aetiological element in skin ageing.

Intrinsic ageing

Growing older causes natural ageing, which is typified by fine wrinkles and thinning skin. This is the inevitable type of ageing. Dermal shrinkage and decreased collagen, elastin, and hyaluronic acid viscosity are the main characteristics of naturally ageing skin. The three most significant natural growth variables are race, gender, and hereditary variability. The long-lived proteins collagen and elastin are suited to the molecular ageing process of nature. As a result, they gradually sustain damage that impairs their capacity to function properly. The following elements are scattered among a number of theories regarding natural skin ageing. The cellular ageing process known as Hayflick-Limit is accompanied by telomere shortening, mitochondrial DNA alterations, oxidative stress, hereditary mutations, and the loss of several hormone conditions. Reactive oxygen species (ROS), which mostly originate from oxidative cell metabolism, are said to be a key factor in both print and chronological ageing, according to the free revolutionary thesis of ageing. After more investigation, it is currently thought that telomeres—the technological structures assembled at the ends of eukaryotic chromosomes—play a crucial role in the ageing process that occurs naturally at the cellular level. While telomere length shortens with age, intact telomeres are essential for prolonging cell life. Telomeric corrosion is now considered the basis for one of the currently popular theories on ageing, a hand for measuring geriatric, and a kind of internal geriatric watch. About 85–90% of all fatal tumours contain telomerase, the cellular reverse transcriptase enzyme that lengthens or stabilises telomeres; nevertheless, it is missing from many physical apkins. Notably, the epidermis is one of the several regeneration apkins that expresses telomerase. One of the main processes of cellular ageing in the skin may be the spontaneous, gradual shortening of telomeres. Because of aerobic cellular metabolism, telomeres and other components of cells also experience low-grade oxidative damage, which adds to the ageing process. Hormonal shifts dramatically affect the ageing process of the skin. A byproduct of gonad coitus hormones, the pituitary and adrenal glands used to gradually deteriorate starting in the mid-1920s. Dermal structural alterations are in fact more severe in skin that is both innately ageing and photoaged (constantly exposed to sunlight). Areas of the skin shielded from the sun often exhibit characteristics of natural aging. Naturally aged skin typically presents with a somewhat weathered appearance, marked by wrinkles resembling those found on cigarette paper, diminished hair follicles, sweat glands, and

sebaceous glands. Atrophic changes in the skin, such as localized loss of pigmentation, thinning of the epidermis, freckles, and imitation scars, are evident in individuals with skin types I and II, who may also be prone to benign or non-malignant skin cancers. Those with skin types III and IV often display pronounced wrinkles, deep furrows, coarse texture, and widespread, irreversible darkening of the skin. The rate of epidermal turnover decreases by more than 50% by the eighth decade of life, contributing to epidermal thinning, particularly in the stratum spinosum, which can range from 10% to 50%.

Table 1: Table showing types of cutaneous ageing

AGING TYPE	**DETERMINING FACTOR**
Chronological	Passage of time
Genetic	Inherited diseases (e.g.- premature aging syndrome)
Photoaging	UV and Infrared radiation
Behavioural	Diet, tobacco, alcohol abuse, drug addiction
Catabolic	Chronic debilitating diseases (eg- infections, cancers)
Endocrine	Dysfunction or aging of hormone systems
Gravitational	Gravitational force

Intrinsic skin ageing factors

Race: The topmost effect of race on ageing is primarily related to differences in saturation. High situations of saturation are defensive with regard to the accretive goods of print ageing, showing little cutaneous difference. *Anatomical variation*: huge variations in some skin parameters have been observed with respect to the body point studied. The drop in epidermal consistence with ageing was set up to be lower at the tabernacle than at the volar forearm, which may be the effect of accretive print ageing. It's generally assumed that aged skin is naturally less doused, less elastic, more passable

and more susceptible to vexation, because of a supposedly less complete functional hedge.

Extrinsic ageing

Premature skin ageing or photo ageing are synonyms for extrinsic skin ageing

Preventing premature skin aging from external sources is largely achievable. Factors originating externally, such as smoking, airborne pollutants, infrared radiation, ozone, and inadequate nutrition, particularly solar exposure, are the primary contributors to premature skin aging. Solar exposure, particularly to UV light, is the predominant cause, responsible for approximately 80% of facial skin aging. UV radiation's detrimental effects stem from its absorption by chromophores in the skin, leading to subsequent chemical reactions. Photoaged skin typically presents with a rough texture, loss of elasticity, prominent wrinkles, visible blood vessels (telangiectasia), and uneven pigmentation with brown spots (lentigines). Both UVA and UVB radiation contribute to these effects, playing roles in skin aging and the development of skin cancer. The presence of sunburn cells, also known as UV-induced apoptotic cells, has long served as an indicator of skin damage caused by sun exposure. UV-induced apoptosis involves caspase-3, with heightened levels of this enzyme serving as reliable markers of cellular apoptosis. The apoptotic pathway activation also entails caspase-7. Mast cells and macrophages are present in diminished numbers in photoaged skin and are presumed contributors to its causal mechanism. Telomeres do not appear to hold a pivotal role in extrinsic aging. The shortening of telomeres was not correlated with photoaging, as there was no notable distinction in telomere length between sun-exposed and sun-protected regions. In a recent study examining telomere length across 76 epidermal samples from sun-protected areas, 24 epidermal samples from sun-exposed areas, and 60 dermal samples, comparisons unveiled shorter telomere lengths in the epidermis. The natural aging process was evidenced by the reduction in telomere length observed in both the epidermis and dermis with advancing age. However, in this study, telomere shortening was not associated with photoaging. Extrinsically aged skin experiences a decline and reorganization of collagen fibers, alongside the accumulation of disorganized elastin proteins within the dermis, a phenomenon known as elastosis. The decrease in collagen fibers reduces the mechanical support provided by fibroblasts, resulting in diminished resilience. Among external factors, nutrition plays a crucial role in aging and age-related conditions. Specifically, an imbalanced diet characterized by

an abundance of refined carbohydrates has been linked to obesity and related metabolic disorders, which in turn correlate with diabetes and skin ailments. Conversely, a well-rounded, nutritious diet supports skin health and optimal functioning. Several studies have highlighted the association between skin aging and dietary carbohydrate intake. Currently, the primary defense against the formation of sunburn cells is sun avoidance and the application of sunscreens, which also offer protection against thymine dimer formation. A lesser degree of UV-induced skin damage is thought to be correlated with fewer sunburn cells. Oxidative damage builds up in cells and tissues as a result of an imbalance between the body's natural antioxidant defences and the formation of reactive oxygen species (ROS). This condition is known as ageing. These free radicals can cause the stratum corneum and underlying connective tissue to deteriorate within the skin, which will ultimately result in less flexibility and suppleness. Damage from the sun increases the creation of ROS, which aids in the development of skin cancer as well as photoaging, which is characterised by wrinkles, rough skin, loss of firmness, and uneven pigmentation. UVA and UVB-activated enzymes are essential to the pathophysiology of photoaging because they initiate proteolytic processes that break down collagen and elastin fibres. Histologically, photoaged skin has solar elastosis, which is characterised by a build-up of degraded dermal elastic tissue. This elastotic substance is made up of hyaluronic acid and other glycosaminoglycans, fibrillin, and elastin.

Table 2: Difference between intrinsic and extrinsic skin aging factors

INTRINSIC FACTORS	**EXTRINSIC FACTORS**
Increased catabolic state (wounds, burns)	Photoaging/UV exposure/blue light exposure)
Insufficient antioxidant protection (genetic variation aka polymorphism)	Environmental intoxication (industrial pollution, smoking, detergents)
Insufficient melanin production (genetic polymorphism) = increased susceptibility to UV aging.	Prolonged inflammation (chronic infection, auto immune disease, inflammatory conditions)

Insufficient detoxification function (genetic polymorphism) = higher vulnerability to toxic substances.	Poor diet (alcohol, food additives, insufficient water intake, saturated fats, etc.)
Sexual hormones deficiencies.	Lack of sleep (inverse day night sleep cycle, poor sleep quality)
Impaired energy metabolism.	Stress (physical, intellectual, exams, emotional etc)

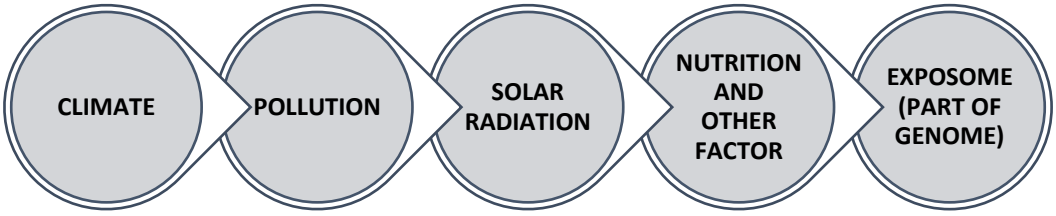

Figure 2: Extrinsic skin aging factors

Mechanism of dermal aging

The dermis experiences major alterations when one ages. One of the main components of ECM, collagen, becomes coarsely dispersed and broken, and its overall quantity decreases. As the dermis gradually atrophys, wrinkles and decreased suppleness are common signs of ageing skin. A decrease in the amount of extracellular matrix (ECM), namely collagen in the dermis, is thought to be one of the primary causes of dermal atrophy. The most effective antiaging strategies focus on and try to stop this process. Dermal ageing is also associated with structural alterations in collagen and other extracellular matrix proteins. Skin aging is a multifaceted process driven by a combination of intrinsic and extrinsic factors that culminate in structural and functional changes over time. Intrinsic aging, determined by genetic factors and chronological age, involves gradual declines in cellular function, including reduced collagen and elastin production, impaired tissue repair, and hormonal fluctuations. Extrinsic aging, on the other hand, results from external influences such as prolonged exposure to ultraviolet

(UV) radiation, pollution, unhealthy lifestyle habits, and repetitive facial expressions. UV radiation accelerates collagen degradation and elastin breakdown, leading to the formation of wrinkles, sagging, and uneven pigmentation. Oxidative stress, generated by both intrinsic and extrinsic factors, damages cellular components and contributes to inflammation, collagen loss, and impaired skin function. Additionally, glycation, where sugar molecules bind to proteins like collagen, stiffens the skin and increases susceptibility to wrinkles. The cumulative effects of these mechanisms result in visible signs of aging, including wrinkles, sagging, loss of elasticity, and uneven skin tone, highlighting the complex nature of skin aging and the importance of holistic approaches to its prevention and management.

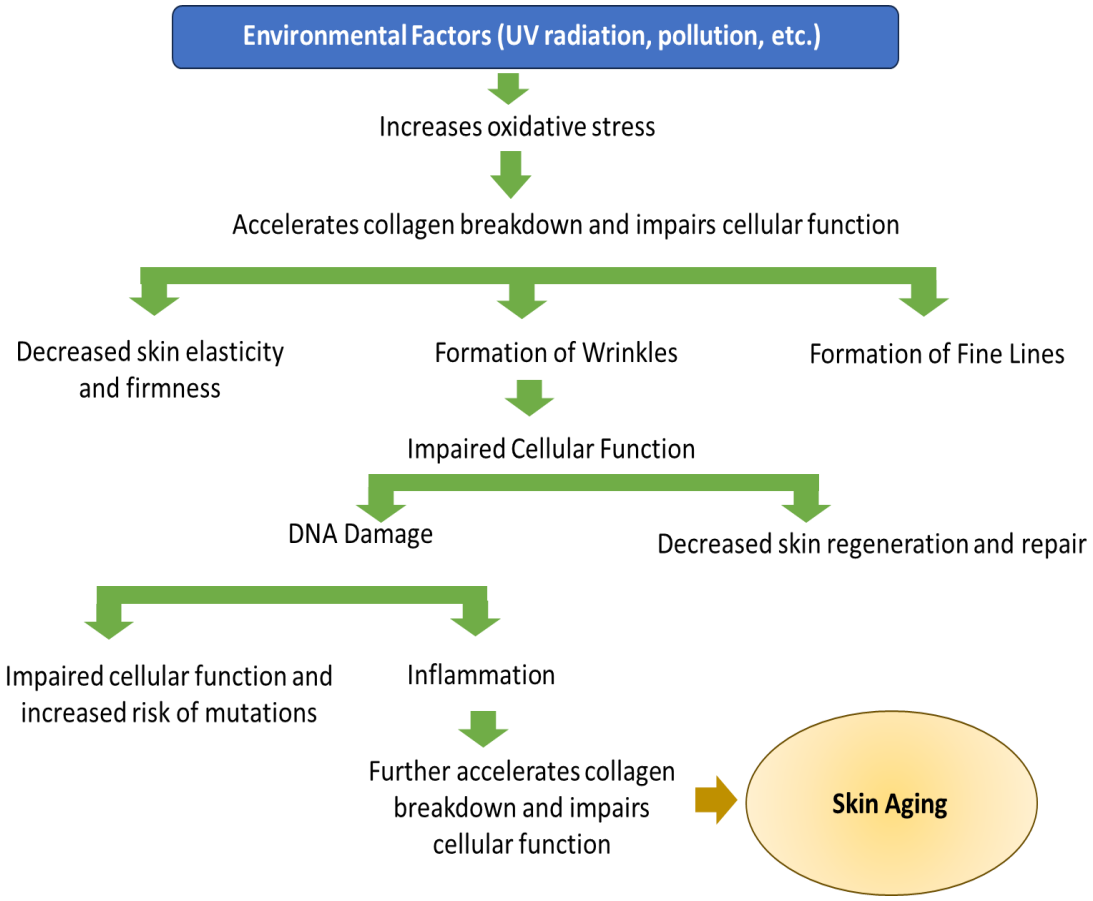

Figure 3: Mechanism of dermal ageing

Composition of the Dermis

Extracellular matrix (ECM), an acellular component, makes up the majority of the dermis, in contrast to the epidermis, which is made up of thick keratinocytes. With

collagen fibres making up over 75% of the skin's dry weight, the extracellular matrix (ECM) gives the skin its flexibility and tensile strength. Eighty to ninety percent of the collagen content in human skin is made up of type I collagen, eight to twelve percent is made up of type III collagen, and less than five percent is made up of type V collagen. Deeper within the dermis, collagen bundles expand. The amorphous proteoglycans (PGs) and glycosaminoglycans (GAGs), which envelop and support the fibrous and cellular matrix elements in the dermis, are further constituents of the extracellular matrix (ECM). They only make up 0.2% of the dermis' dry weight, but they are crucial for controlling the moisture and compressibility of the layer since they can absorb water up to 1000 times their capacity. Immune cells such as mast cells, histiocytes, and dermal dendrocytes, as well as endothelial cells and skin appendages, are additional cellular constituents of the dermis. Dermal resident cells, or fibroblasts, are descended from mesenchymal cells. They are in charge of producing and degrading amorphous and fibrous ECM proteins. Deciphering their role and how they interact with the environment is essential to understanding the molecular processes behind skin ageing.

Changes in Dermal Components with Aging

Collagen

The primary alterations observed in aged skin revolve around quantitative and structural shifts in collagen fibers. In aged skin, collagen fibrils appear fragmented and unevenly dispersed. Previous research has highlighted that elevated collagen degradation and diminished collagen synthesis contribute to this disrupted collagen balance, resulting in an overall deficiency of collagen. Consequently, this phenomenon manifests clinically as skin wrinkling and reduced elasticity, characteristics observed in both naturally aging skin and skin affected by photoaging.

Increased Matrix Metalloproteinase (MMP) Levels

Matrix metalloproteinases (MMPs) are a group of widely distributed endopeptidases that have the ability to break down proteins in the extracellular matrix (ECM). MMPs can be classified into five main categories, namely:

Collagenases (MMP-1, MMP-8, and MMP-13)

Gelatinases (MMP-2 and MMP-9)

Stromelysins (MMP-3, MMP-10, and MMP-11)

Matrilysins (MMP-7 and MMP-26)

Membrane-type (MT) MMPs (MMP-14, MMP-15, and MMP-16)

The breakdown of collagen fibres, which are mostly type I and III in human skin, is one of these processes that MMP-1 significantly contributes to starting. It is interesting to note that there is not always a direct correlation between the rise in MMP levels in aged skin and the rise in natural MMP inhibitor levels. Skin that is photoaged or naturally ageing may have lower levels of tissue inhibitor of metalloproteinase-1 (TIMP-1), which can cause an imbalance that speeds up the breakdown of collagen in the dermis of the skin and causes ageing of the skin. An important factor in the increase of MMP levels in aged skin is reactive oxygen species (ROS). Many things can cause reactive oxygen species (ROS), such as UV light and pro-oxidants that are created during metabolism. Nuclear factor-κB (NF-κB) is a key regulatory factor that is activated by ROS and mediates responses to UV radiation and photoaging. Oxidative damage is particularly severe in photoaged skin, which may explain the presence of more pronounced aging signs such as deep wrinkles. In natural aging, dermal fibroblasts are the primary source of MMPs, while in photoaging, epidermal keratinocytes also contribute to the production of MMPs. This dual mechanism underscores the complex interplay of various factors contributing to skin aging processes. The disruption of collagen, the acceleration of skin ageing, and the appearance of ageing characteristics such as deep wrinkles are caused by the dysregulation of MMPs, the decrease in TIMP-1 levels, and the influence of ROS in both photoaged and natural skin.

Altered signaling of Transforming Growth Factor-β (TGF-β) in the process of aging

TGF-β regulates collagen homeostasis in human dermal fibroblasts through the Smad pathway, which affects both collagen product and decline. Thus, TGF-β/Smad signalling directly upregulates the expression of ECM genes such as versican, fibronectin, décorin, and collagens. The Smad signalling network, in contrast, upregulates TIMPs and downregulates MMPs. The findings indicate that the TGF-β/Smad signalling system plays a crucial role in preserving the mechanical and structural integrity of dermal connective tissues by preventing ECM decline and boosting ECM product. In ageing skin, decreased TGF-β signalling leads to lowered conflation of neo collagen and a decrease in net collagen quantum in the dermis. AP-1, persuaded by ROS, suppresses the TGF-β signalling pathway in dermal fibroblasts.

Interaction between Fibroblasts and the ECM

In young skin, fibroblasts adhere closely to the surrounding intact extracellular matrix (ECM), which predominantly consists of type I collagen. This close adherence enables

fibroblasts to exert mechanical forces on the surrounding ECM, facilitating their spreading and maintenance of a normal elongated shape. However, in aged skin, fibroblast attachment becomes compromised due to progressive ECM degradation, resulting in a reduction in fibroblast size, diminished extension, and a collapsed morphology. The decrease in fibroblast size is a critical characteristic of aged fibroblasts and is associated with a decrease in the production of ECM factors. Moreover, the diminished spreading and size of dermal fibroblasts can lead to an increase in mitochondrial reactive oxygen species (ROS) generation, further exacerbating ECM degradation through the upregulation of matrix metalloproteinases (MMPs). Recently, Quin et al. proposed a mechanism by which age-related reductions in fibroblast size activate AP-1, a transcription factor that subsequently induces the production of multiple MMPs observed in aged human skin. Elevated ROS levels in fibroblasts exhibiting aged features may potentially disrupt this pathway.

Changes to other ECM Components

Elastic Fiber Remodeling

Elastic fibres are essential to the skin's pliancy because they allow the skin to be flexible and adaptable. Fibroblasts in the dermis are the main producers of these fibres, which are created from soluble tropoelastin molecules—a precursor to elastin—by lysyl oxidase-assisted cross-linking (LOX). With wide peripheral elastic filaments in the reticular dermis, mostly made of elastin, and vertically stacked fibrillin-rich microfibrils in the papillary dermis, elastic filaments in youthful skin have a well-organized structure. On the other hand, the elastic fibre system undergoes structural changes as it ages. The papillary dermis's fibrillin-rich microfibrils significantly deteriorate with normal skin ageing. Fibulin-5 is involved in this process because it is essential in joining tropoelastin to microfibrils and creating elastic filaments. Fibulin-5 may have a role in the remodelling of elastic fibres that occurs naturally as skin ages, according to available data. The pattern of fibulin-5 localization is entirely disturbed in old skin, whereas in young, healthy skin, it is equally dispersed throughout the dermis along elastic fibres. Photoaging is distinguished from natural ageing by the build-up of jumbled elastic filaments across the dermis—a condition called "solar elastosis." The activation of matrix metalloproteinases (MMPs) is the primary cause of the enhanced breakdown of elastic fibres in photoaging. Interestingly, the more elastic material seen in solar elastosis is not useful; this is because the coarse and twisted filaments do not

contribute to appropriate elasticity. In conclusion, a reduction in the quantity of functional elastic filaments in the skin occurs with age, resulting in functional alterations including pliancy loss and wrinkle development. The buildup of jumbled elastic filaments is a crucial element in photoaging, whereas the breakdown of fibrillin-rich microfibrils plays a role in normal ageing.

Changes in Glycosaminoglycans

Large linear polysaccharides called glycosaminoglycans (GAGs) are important components of the extracellular matrix (ECM). GAGs come in six different forms: hyaluronic acid (HA), heparan sulphate (HS), keratan sulphate (KS), dermatan sulphate (DS), and chondroitin sulphate (CS). Hyaluronic acid (HA) creates supermolecular structures that contribute to improved tissue stiffness when it is crosslinked with matrix proteins such as collagen. Dermal HA, which is plentiful in the papillary dermis, is primarily produced by fibroblasts in the dermis. Dermal HA increases tissue stiffness and imparts cushioning and shock-absorbing qualities through interactions with other ECM proteins, including collagen. While the quantity of HA itself is not considerably different from young skin, naturally aged skin has lower amounts of HA binding proteins (HABPs). Conversely, photoaged skin, particularly in areas impacted by solar elastosis, shows a significant elevation in dermal HA concentration. Despite the fact that UV light increases the synthesis of HA synthase (HAS), aged skin that has been exposed to the sun has far lower HAS mRNA levels than skin that has been sheltered from the sun. This shows that other regulatory mechanisms may be involved in the decrease in HAS expression in skin that has been photodamaged. As with solar elastosis, aberrant protein accumulation may be the cause of the elevated HA seen in photoaged skin. In skin that has been photoaged, both total sulfated GAGs and HA rise, whereas total sulfated GAGs decrease with natural ageing. The area impacted by solar elastosis also exhibits a rise in CS staining.

Changes to Proteoglycans

PGs are a family of monkeyshine conjugated proteins, and are essential for maintaining the mechanical strength of the skin. Several former studies have delved changes to these major PGs in naturally aged skin, with results varying depending on the position, gender of the subjects, and discovery styles. In natural aging, the quantum of elastic filaments is reduced; still, in foreign aging, non-functional, abnormal elastic filaments accumulate in the papillary dermis Changes to the quantum of knaveries and PGs vary

in naturally aged skin, but these factors generally increase with aging, with the exceptions of decorin and biglycan in photoaged skin. Any increase observed in photoaged skin seems to be the result of abnormal accumulation or through compensational recovery responses for accretive damage to the ECM.

The impact of aging on the functions of the skin barrier and thermoregulation

The outermost layer of the skin, known as the epidermis, lacks blood vessels and relies solely on the underlying dermis for nourishment. Comprised mainly of keratinocytes organized in a stratified epithelium, the epidermis houses proliferating keratinocytes in its basal layer, which rest on a basement membrane at the junction between the dermis and epidermis. Keratinocyte maturation involves a loss of proliferative capacity, eventually leading to their transformation into corneocytes. At the outermost layer of the epidermis, the stratum corneum consists of protein-modified corneocytes embedded in a lipid-rich extracellular matrix, forming a water-impermeable barrier that prevents water loss and the entry of foreign substances through the skin. The flattening of the dermal-epidermal junction reduces the contact surface area between the epidermis and dermis, diminishing nutrient exchange and potentially impacting keratinocyte proliferation. This flattening also reduces the epidermis' resistance to shearing forces, making it more vulnerable to damage. However, trans-epidermal water loss, which serves as a measure of stratum corneum integrity, remains unchanged with chronological aging. Furthermore, the aging process affects the skin's ability to regulate body temperature, diminishing heat tolerance. Consequently, older individuals are more susceptible to heat-related illnesses, including potentially fatal heat strokes during periods of elevated temperatures.

Collagen

Collagen, a vital structural protein, plays a fundamental role in maintaining the inherent integrity of vertebrates. It serves as a primary component in the bones, muscles, skin, and tendons, providing support for delicate organs. Constituting approximately 25 percent of the body's proteins in mammals, collagen possesses a complex tertiary structure, forming a coiled coil configuration. However, its amino acid sequence is relatively simple, characterized by repeated glycine, proline, and hydroxyproline-containing tripeptides. The term "collagen" encompasses a group of proteins that assemble into right-handed three-polypeptide three-dimensional complexes. This designation applies to all members of the collagen family, which exhibit variations in

tissue distribution, size, and function. The extracellular matrix of connective tissues represents a complex blend of diverse protein families, defining structural integrity and facilitating various physiological functions. Collagens, as trimeric extracellular matrix molecules, are essential for providing structural integrity and performing other functions within the extracellular matrix. Comprising three alpha chains that form the triple helical structure, collagens consist of repeating peptide triads of glycine-X-Y, where X and Y can vary but are often proline and hydroxyproline. The primary role of the extracellular matrix is to confer specific mechanical and biochemical properties to tissues. While resident cells are responsible for its synthesis and maintenance, the extracellular matrix also influences cellular function. Cell-matrix interactions mediated by specific cell receptors and matrix components play a crucial role in cell attachment, migration, isolation, and gene expression regulation. Previously viewed solely as proteins with characteristic molecular structures contributing to extracellular scaffolding, collagens are now recognized for their diverse roles in various tissues and organs. They contribute to tissue stability and maintain structural integrity in connective tissues and parenchymal organs. Recent studies have elucidated the molecular organization of collagen fibers, particularly the presence of D-periodic fibrils containing intermolecular covalent cross-links, which confer high tensile strength and mechanical stability. Collagen types are classified into several subfamilies based on sequence homologies and similarities in structural organization and supramolecular arrangement, including fibril-forming collagens, fibril-associated collagens (FACIT), network-forming collagens, anchoring fibrils, transmembrane collagens, and basement membrane collagens. These collagen types exhibit considerable complexity and diversity in their structure, splice variants, non-helical domains, assembly, and function. Fibril-forming collagens, representing the most abundant and diverse family, constitute approximately 90% of total collagen content.

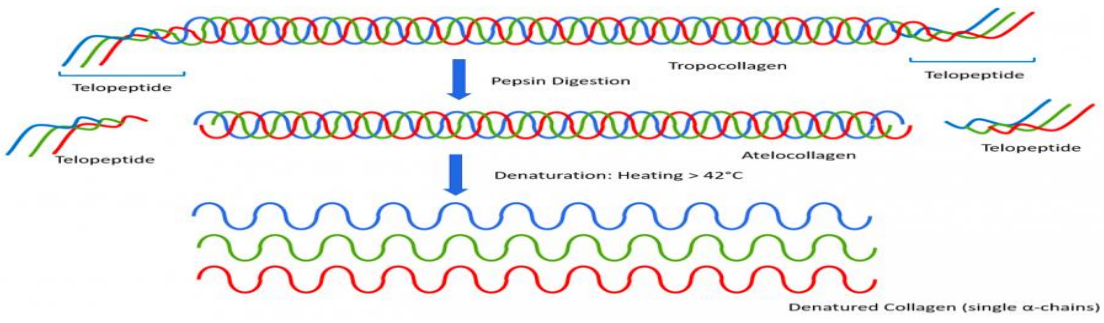

Figure 3: Molecular structure of collagen

Table 3: General classification of collagen types

CLASSIFICATION	***COLLAGEN TYPES***	***SUPRAMOLECULAR STRUCTURE***
Fibril-forming collagen	1,2,3	Straited fibrils
	5,11	straited fibrils, retain N-terminal regulatory domains
	24,27	unknown
FACIT[a]collagen	9,12,14	Associated with fibrils, other interactions
FACIT-like collagen	16,19,21,22	Interfacial regions, basement membrane zone
Network forming collagens		
Basement membrane	4	Chicken wire network with lateral association
Beaded filament-forming	6	Beaded filaments, network
Anchoring fibrils	7	Laterally associated anti-parallel dimers
Hexagonal networks	8,10	Hexagonal lattices
Transmembrane collagens	13,17,23,25 Gliomedins, ectodysplasin	Transmembrane and shed soluble ecto-domains
Multiplexin collagen (Endostatin-15 and-18)	15,18	Basement membranes, cleaved C-terminal domains influence angiogenesis
Other molecules with collagenous domains	26,28	Collagenous domains in primarily non-collagenous molecules
	Acetylcholinesterase, adiponectin, Clq, collectins, surfactant protein, other	

Sources of collagen

There are several sources from which collagen is obtained. Some of them are discussed below:

Natural sources

Collagen, a crucial protein for skin health, can be obtained from various natural sources. One of the primary sources is animal-derived foods such as beef, chicken, fish, and bone broth. These foods contain collagen-rich parts like skin, bones, cartilage, and connective tissues, which are often used to make collagen supplements. Bone broth, in particular, is simmered from animal bones and connective tissues, releasing collagen and other nutrients into the broth. Another source is gelatin, which is derived from collagen by boiling animal tissues. Gelatin is commonly used in cooking and can be found in desserts, gummy candies, and certain dairy products. Additionally, collagen can be obtained from certain plant-based sources. While plants themselves do not contain collagen, some foods contain nutrients that support collagen production in the body. For example, fruits like citrus fruits, strawberries, and kiwi are rich in vitamin C, which is essential for collagen synthesis. Other foods such as soy products, beans, nuts, and seeds contain amino acids like proline and glycine, which are building blocks for collagen production. Furthermore, certain marine sources like fish collagen peptides are becoming increasingly popular. These peptides are extracted from fish skin and scales and are easily absorbed by the body due to their small molecular size. Marine collagen supplements are often promoted for their bioavailability and potential benefits for skin health. Collagen sources can be attained from beast and vegetable sources. From beast sources, the most common are bovine, porcine, mortal collagen, and marine organism similar as scale fish and fish skin.1 bovine collagen is generally used as a temporary cover for extra-oral injuries and also for the becks on the body. It has large operations because of its helpfulness and biocompatibility. Porcine collagen matrices, on the negative, have the eventuality to be useful for grafting of soft apkins. It offers an autogenous transplant using a biocompatible surgical material. Types I and II are derived from the muscle, cartilage, and skin of horses. Funk neck is where types I, II, III, and V originate. Types I and III are arranged from skin, Type IV from muscle tissue, and Type IX in funk embryo sternal cartilage. Marine collagen is a viable natural supply as well. According to reports, it poses little risk of spreading diseases, the FDA has classified it as GRAS (generally recognised as safe), and it is also an inexpensive raw material for products because many body parts that contain it are wasted after being consumed. A broad variety of foods produced from plants and animals, as well as certain marine sources, are considered natural sources of collagen. These foods can help

stimulate the formation of collagen and improve the health of your skin when included in a balanced diet.

Synthetic sources

Although animal-derived (natural) collagen is utilised in many therapeutic procedures, there are concerns about its role in inflammation, batch-to-batch variability, and potential transfection of complaints. Certain artificial sources, such as the substance with a commercial brand, have been established in order to prevent susceptible issues. This is a synthetic protein consisting of 36 amino acids that self-assembles into hydrogels and triadic helix nanofibers; it resembles real collagen and may improve over commercial bloodsuckers or treatments based on naturally derived collagen. Recombinant technology has been used to create a new synthetic collagen source that yields high-quality, adulterant-free collagen that is inferred from beasts. These recombinant collagens have been made mostly in factory cell culture, nonentity cell societies, incentive, and mammalian cells. Synthetic sources of collagen offer alternative avenues for obtaining this crucial protein, especially for individuals seeking non-animal-derived options or those looking for specific collagen types or formulations. One of the primary synthetic sources of collagen is recombinant DNA technology, where collagen genes are inserted into host cells, such as bacteria or yeast, to produce collagen proteins. This method allows for the production of specific collagen types in controlled laboratory settings, offering precise control over purity and quality. Another synthetic approach involves peptide synthesis, where short collagen peptides are chemically synthesized in the laboratory. These synthetic peptides can mimic the structure and function of natural collagen and are often used in cosmetic formulations and skincare products for their potential anti-aging effects. Additionally, synthetic collagen-like materials, such as collagen-mimetic peptides (CMPs) and collagen-mimetic proteins (CMPs), are engineered to replicate the structural properties of collagen. These materials can be tailored to exhibit specific mechanical and biological properties, making them versatile for various applications in tissue engineering, drug delivery, and regenerative medicine. Furthermore, advances in biomaterials science have led to the development of synthetic collagen scaffolds and matrices for tissue engineering and regenerative medicine applications. These scaffolds are designed to provide structural support and promote cell adhesion, proliferation, and differentiation in tissue repair and regeneration processes. Synthetic collagen-based materials offer

advantages such as tunable mechanical properties, controlled degradation rates, and the absence of potential immunogenicity or disease transmission risks associated with animal-derived collagen. In general, collagen derived from synthetic sources has a range of prospects for use in biomedical and cosmetic applications, offering customised solutions to meet individual requirements and preferences. Synthetic collagen products are becoming more and more useful in several domains of research and development, whether it be through peptide synthesis, recombinant DNA technologies, or manufactured materials that resemble collagen.

Marine sources

Marine life is another essential, secure natural supply. Used extensively for this purpose are the bones, skin, fins, scales, and scales of freshwater and saltwater fish, starfish, doormat, bloodsuckers, ocean devil, octopus, squid, cuttlefish, ocean anemone, and prawn. These have several advantages over land-based beast sources, including lower immersion due to low molecular weight, almost nonexistent natural pollutants and poisons, low seditious response, and so on. These marine collagens have a high yield and provide little risk of complaint transfer, making them suitable volition sources. Because of their potential advantages and sustainability over typical animal-derived collagen, marine sources of collagen have drawn interest. Collagen extracted from marine sources, such as fish skin, scales, and bones, offers unique advantages, including high bioavailability and compatibility with human collagen. Marine collagen is typically obtained through a process of hydrolysis, where collagen-rich marine tissues are broken down into smaller peptides for easier absorption by the body. One of the key marine collagen sources is fish collagen, derived from fish skin and scales. Fish collagen peptides are known for their small molecular size, making them highly bioavailable and easily absorbed by the body. Additionally, fish collagen is rich in type I collagen, which is the most abundant collagen type in human skin, making it particularly beneficial for skin health. Marine collagen supplements derived from fish collagen are popular for their potential to support skin elasticity, hydration, and overall youthfulness. Another marine collagen source is derived from shellfish, such as shrimp and crab shells. These shellfish contain chitin, a polysaccharide that can be hydrolyzed to produce collagen-like peptides. While less common than fish collagen, shellfish-derived collagen supplements offer similar benefits for skin, joint, and bone health. In addition to collagen peptides, marine sources also provide other bioactive compounds

that can complement collagen's effects on skin and overall health. For example, marine collagen supplements may contain antioxidants like astaxanthin, omega-3 fatty acids, and minerals like calcium and magnesium, which contribute to skin hydration, elasticity, and anti-inflammatory properties. Furthermore, the use of marine collagen aligns with sustainability efforts, as fish skin, scales, and shells are often byproducts of the seafood industry that would otherwise go to waste. By utilizing these marine resources, collagen manufacturers can reduce environmental impact and promote a more sustainable approach to collagen production. All things considered, marine collagen sources present a viable option for enhancing joint health, skin health, and general wellbeing. In the world of cosmetics and nutritional supplementation, marine collagen supplements are becoming more and more well-liked due to their high absorption, compatibility with human collagen, and sustainable origin.

Table 4: Marine sources of collagen

SOURCE	**TISSUE**
Fish	skin, bone fins, and scales up to 50%-70%. spp-Baltic cold skin. Black drum and sheepshead seabream collagen type 1.
Marine sponge	Fibrillar collagen source in organic components of sponge. Rich source of collagen1 and 4.
Jelly fish	Has 60% of collagen mostly types4, 5, 2.

Collagen supplements used in ageing

Collagen supplements have surged in popularity as a potential remedy for skin aging, driven by collagen's crucial role in maintaining skin structure, elasticity, and firmness. With age, the body's natural collagen production declines, resulting in the formation of wrinkles, sagging skin, and loss of firmness. Research suggests that collagen supplements may offer benefits for addressing these signs of aging. Studies indicate that oral collagen supplementation can enhance collagen density, skin hydration, and elasticity, potentially reducing the appearance of wrinkles and promoting a more youthful look. However, it's important to acknowledge that research on collagen supplements for skin aging remains limited, and outcomes may vary depending on

individual factors and the specific product used. Before starting any new dietary regimen or supplement, it's advisable to consult with a healthcare professional. Collagen serves as the primary structural protein in connective tissues such as skin and bone, comprising approximately 25% of the body's proteins in mammals. Over the past two decades, numerous experimental and randomized controlled trials have investigated the effects of collagen on skin health. Collagen used in these studies is typically in hydrolyzed form and sourced from animal origins like porcine skin, bovine bone, and fish scales. Through various degradative processes, collagen hydrolysates (CH) are formed, which have lower antigenic specificity compared to complete collagen. Studies have observed changes in skin volume and quality, as well as typical aging symptoms due to alterations in dermal collagen and elastin production. In skin aging, the connective tissue undergoes degradation, resulting in decreased elasticity and tone. Environmental, hormonal, chronological, and photoaging factors contribute to changes in skin appearance and integrity. Adequate nutrition plays a fundamental role in skin function and appearance, prompting researchers to explore the relationship between skin health and nutrition. Intervention studies have suggested potential benefits of orally administered collagen peptides on extracellular matrix molecule production in human fibroblasts. Additionally, there is growing interest in the effects of orally administered biologically active compounds, such as antioxidants, on skin function, leading to the development of nutritional supplements targeting skin health. Research has indicated that the PEPT1 transporter facilitates the absorption of collagen-derived peptides, including proline-hydroxyproline and glycine-proline-hydroxyproline. Because of their large molecular weight, topical collagen-containing treatments may not considerably enhance skin texture; nevertheless, oral collagen bioactive peptide consumption facilitates systemic absorption and distribution to several skin layers. Collagen peptides activate fibroblasts, encouraging the generation of hyaluronic acid, elastin, and collagen—all critical components of healthy, youthful skin.

Future aspects of collagen in skin aging

There are many intriguing directions that collagen may go in the future when it comes to treating skin ageing. First off, new collagen-based treatments have bright futures because to developments in biotechnology and regenerative medicine. In an effort to restore collagen in ageing skin and maybe prevent or reverse age-related symptoms,

researchers are exploring techniques including tissue engineering and stem cell treatment. Furthermore, custom collagen therapies that address specific skin issues might become mainstream as personalised medicine gets acceptance and provide accurate remedies. In contemplating the future aspects of collagen in skin aging, several promising avenues emerge. Firstly, advancements in biotechnology and regenerative medicine offer the potential for novel collagen-based therapies. Researchers are exploring techniques such as tissue engineering and stem cell therapy to regenerate collagen in aged skin, potentially reversing or slowing down the signs of aging. Moreover, with the rise of personalized medicine, tailored collagen treatments could become prevalent, addressing individual skin concerns with precision. Additionally, the integration of artificial intelligence and machine learning in dermatology holds promise for predicting and preventing skin aging. AI algorithms can analyze vast amounts of data, including genetic predispositions, lifestyle factors, and environmental influences, to provide personalized recommendations for collagen preservation and rejuvenation. Furthermore, the skincare industry continues to innovate with collagen-boosting formulations, incorporating advanced delivery systems and bioactive ingredients that stimulate collagen production and inhibit its degradation. From peptides and growth factors to botanical extracts and nanotechnology, future skincare products may offer unprecedented efficacy in maintaining youthful skin. As awareness of environmental factors contributing to collagen depletion grows, there is also a shift towards sustainable practices in skincare. Future formulations may prioritize eco-friendly sourcing of collagen and adopt packaging that minimizes environmental impact, aligning with consumer preferences for ethically conscious products. In conclusion, the future of collagen in combating skin aging is promising, with advancements in biotechnology, personalized medicine, artificial intelligence, and sustainable skincare driving innovation. By harnessing these emerging technologies and practices, the quest for youthful, radiant skin may reach unprecedented heights.

Abbreviations

SPF-Sun protection factor; ROS-Reactive oxygen species; CH-Collagen Hydrolysates; UV-Ultraviolet; ECM-Extracellular matrix; PGs-Proteoglycans; MMP-Matrix metalloproteinase; TGF-Transforming growth factor; LOX-Lysyl oxidase; CS-Chondroitin sulphates; DS-Dermatan sulphate; KS-Keratan sulphate; HS-Heparin

sulphate; HA-Hyaluronic acid; FACIT-Fibril associated collagen; GRAS-Generally rated as safe; PRO-HYP: Proline and hydroxyproline.

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