Contents of summary

Part 1 Basics

Chapter 10. Synthetic Collagen

Kazuki C. KURODA, KOIDE Takaki (Department of Chemistry and Biochemistry, School of Advanced Science and Engineering, Waseda University)

Chapter 11. Digestion and Absorption of Collagen and Its Derivatives

SATO Kenji (Marine Biological Function, Division of Applied Biosciences, Graduate School of Agriculture, Kyoto University)

SHIGEMURA Yasutaka (Department of Food & Nutritional Science, Tokyo Kasei University)

Chapter 12. Mammalian Collagen

TANAKA Keisuke, HATTORI Shunji (Nippi Research Institute of Biomatrix)

Chapter 13. Fish and Shellfish Collagen

ISHIHARA Kenji (National Research Institute of Fisheries Science, Fisheries Research and Education Agency of Japan)

HIRAOKA Yoshinobu (Ehime Institute of Invention)

Chapter 14. Lower animal Collagen

ARAI Katsuhiko (Scleroprotein and Leather Research Institute, Faculty of Agriculture, Tokyo University of Agriculture and Technology)

Part 2 Application

Chapter 15. Application of Collagen, Overview

NOMURA Yoshihiro (Scleroprotein and Leather Research Institute, Faculty of Agriculture, Tokyo University of Agriculture and Technology)

Chapter 16. Leather and Leather Goods

YOSHIMURA Keijia (Japan Leather and Leather Goods Industries Association)

Chapter 17. Animal Glue and Industrial Gelatin

DOI Masahiro (Asahi Gelatine Industrial Co., Ltd)

Chapter 18. Inkstick and Classical Animal Glue

UDAKA Kentaro (Independent Administrative Institution National Institutes for Cultural Heritage, Tokyo National Research Institute for Cultural Properties)

Chapter 19. Foods Using Collagen
SUZUKI Satoshi (Nippi, incorporated Fuji Factory)

Chapter 20. Functional Food
KOIZUMI Seiko, MATSUSHITA Aya, DAIMON Mona, HIMENO Ai (Research and Development Center, Nitta Gelatin Inc.)

Chapter 21. Collagen in the Cosmetic Field
AMANO Satoshi (Shiseido Global Innovation Center)

Chapter 22. Characteristics and Applications of Medical Collagen Products
FUJIMOTO Ichiro (Koken Research Center, Koken Co., Ltd.)

Chapter 1. Definition

NISHIYAMA Toshio (Tokyo University of Agriculture and Technology)

Collagens are animal-specific proteins and do not exist in plants. They have not been identified in almost all unicellular organisms. It has still been investigated what multicellular animals are the first to acquire collagens. The tissues of the most ancient animals, Ctenophora and Porifera, were investigated on type IV collagen expression and basement membrane formation, since in recent researches type IV collagen revealed as the evolutionarily most ancient member of the vertebrate collagen family. The results revealed that type IV collagen played a critical role in the transition of unicellular organisms to multicellular animals. These reports suggest that collagen is a key protein that enabled the evolution of animals.

Collagens are the most abundant proteins in mammals including human (around 30% of total protein mass). They were thought as proteins responsible for structural formation and maintenance. Recent research progress has revealed that they play important roles in biological functions such as cell adhesion, proliferation, differentiation, signal transduction, morphogenesis, and wound healing. The collagen superfamily comprises 28 types numbered with Roman numerals (type I collagen to type XXVIII collagen) that contain at least one triple-helical domain. Each collagen consists of three polypeptide chains, called α chains, numbered with Arabic numerals. The three α chains that form the triple helical part of the molecule are composed of repeating peptide triplets of glycine (Gly)-Xaa-Yaa. Xaa is often proline and Yaa is frequently 4-hydroxyproline. The collagens are classified to several families by function and domain homology.

Keywords: collagen, triple helix, α chain, collagen super family, evolution

Chapter 2. Collagen Family of Proteins

MIZUNO Kazunori (Nippi Research Institute of Biomatrix)

Collagen super family proteins in vertebrates are classified as 28 types of collagen. In addition, some other proteins have collagen triple helical structure. In this chapter, vertebrate collagen has shortly been reviewed in terms of structure, function, and localization. The function of the most abundant type of collagen, type I, is still largely unknown. Collagen family of proteins functions not only as the structural scaffold of cells but also as the regulators of cell differentiation and growth. Each of collagen superfamily members is responsible for maintaining the structure and function of the organism through a variety of functions.

Keywords: fibrillar collagen, FACIT, transmembrane collagen, ficolin, collectin

Chapter 3. The Structure and Physical Properties of Collagen

NOMURA Yoshihiro (Scleroprotein and Leather Research Institute, Faculty of Agriculture, Tokyo University of Agriculture and Technology)
K. L. Goh (Newcastle University in Singapore)

Study on the structure of collagen has been carried out from X-ray diffraction images of biological samples that is a structural protein with a clear molecular orientation without crystallization. In 1955, Ramachandran and Karha proposed the triple helix model of tropocollagen. Then, in 1961, Rich and Crick proposed a new collagen structural model of 10/3-helix. Okuyama showed the 7/3-helix collagen model from structural model from structural analysis using a synthetic peptide of $(Pro\text{-}Hyp\text{-}Gly)_9$. The study on the physical properties of collagen was summarized in the keynote lecture by Goh of the International Union of Leather Technologists and Chemists Societies (IULTCS) in 2019. This session describes the biosynthesis, hierarchical structure, three-dimensional structure and physical properties of collagen.

Keywords: structure, collagen triple helix model, physical properties

Chapter 4. Diverse Biological Functions of the Collagen Family

MIYATA Shinji (Scleroprotein and Leather Research Institute, Faculty of Agriculture, Tokyo University of Agriculture and Technology)

Collagens are the most abundant proteins in vertebrates. 28 different collagen types have been identified so far. Its abundance, tissue distribution, and function can vary widely among collagen types. All collagen members share a common structural feature, the presence of at least one triple-helical domain, which corresponds to a number of $(Gly\text{-}X\text{-}Y)_n$ repeats (X being frequently proline and Y hydroxyproline) in the amino acid sequence. Depending on the types of collagen, the triple-helices are formed by three identical α chains (homotrimers), or by two or more different α chains (heterotrimers). Some collagens, such as type I collagen, consist entirely of the triple-helical repeats; others contain nonhelical domains in addition to the triple-helical domain. Classical fibril-forming collagens are well-known to play structural roles and contribute to mechanical properties, organization, and shape of tissues. Recent studies have also revealed the functional importance of other collagens that do not form fibers by themselves. The physiological roles of the various types of collagen have been discovered through studies using genetically modified mouse models. Moreover, recent large-scale genome-wide association studies have revealed that the mutations in collagen genes cause a variety of human diseases. In this article, we review the functions of collagen, which have been obtained from studies mainly in mice and humans.

Keywords: collagen super family, non-fibrous collagen, molecular species, genetically modified mice, collagen-related diseases

Chapter 5. Collagen Biosynthesis (1): Overview,

A Molecular Ensemble 2.0: the Complexity of Collagen Biosynthesis in the rER

ISHIKAWA Yoshihiro (Department of Ophthalmology, University of California, San Francisco, School of Medicine)

Collagen is a unique molecule because a very complicated biosynthesis process generates this most abundant protein in humans with a relatively simple structure. This complicated process is carried out by over twenty molecules, including various enzymes and molecular chaperones, and which terms a molecular ensemble. In this review, to understand this sophisticated process, a molecular ensemble is classified into three individual steps 1) translation and post-translational modification, 2) triple helix formation, and 3) transport. Each step includes recent findings and updated information describing an expanded molecular ensemble, which calls a molecular ensemble 2.0.

Keywords: endoplasmic reticulum (ER), protein biosynthesis, protein folding, protein trafficking, quality control

Chapter 6. Collagen Biosynthesis (2): Post-translational Modifications

TAGA Yuki (Nippi Research Institute of Biomatrix)

Collagen extensively receives a series of highly organized enzymatic post-translational modifications, including prolyl hydroxylation and lysyl hydroxylation/glycosylation. These collagen-specific post-translational modifications play various roles in the structure and function of collagen, such as stabilization of collagen triple helix, regulation of cross-link formation, and contribution to interaction of collagen with cells. The importance of collagen post-translational modifications is evidenced from the fact that abnormalities of specific modification enzymes lead to severe connective tissue diseases. However, there are several minor modifications whose function is still unclear. In this chapter, I review studies about the enzymatic post-translational modifications determining the quality of collagen and also introduce chemical modifications (glycation and carbamylation), which accumulate in tissue collagen with aging and certain diseases.

Keywords: post-translational modification, hydroxylation, glycosylation, glycation, carbamylation

Chapter 7. Collagen Biosynthesis (3) Collagen Cross-linking

YAMAUCHI Mitsuo, TERAJIMA Masahiko (Division, Oral and Craniofacial Health Sciences University of North Carolina at Chapel Hill)

The main functions of connective tissues, i.e. providing support, form and connectivity, highly depend on the physicochemical properties of fibrillar collagens, especially its major component, type I collagen. During the biosynthesis, type I collagen undergoes various intra- and extracellular post-translational modifications, and the molecules are packed into a fibril and stabilized by covalent intra- and intermolecular cross-linking. Cross-linking is initiated by the conversion of the lysine and hydroxylysine residues in the amino- and carboxy-termini of the molecule i.e. telopeptides, to aldehydes by the action of lysyl oxidases. Then, the aldehydes can trigger a series of condensation reactions with the adjacent amino acids to form bi-, tri- and tetra-valent cross-links. The quantity, type and maturation of cross-linking vary depending on tissues, aging and pathological state. Recently, the regulatory mechanisms of lysine modifications relevant to cross-linking and how abnormal cross-linking is associated with various pathologies such as fibrosis, osteogenesis imperfecta and cancer development/metastasis have been gradually deciphered. In this chapter, we will overview the basics of collagen cross-linking and recent advancement in this field.

Keywords: cross-link, post-translational modification, lysyl hydroxylase, chaperone, cancer

Chapter 8. Collagen Degradation and Matrix Metalloproteinase

INADA Masaki (Department of Biotechnology and Life Science, Tokyo University of Agriculture and Technology)

Collagen is a major component of extracellular matrix (ECM) and is broadly present in skin, cartilage, skeleton, and various organs. Therefore, its production and degradation are strictly regulated to maintain tissue structures and homeostasis. Type I collagen is mainly produced in hypodermis, tendons, ligaments, and bones. Type II and X collagens are produced in cartilages, and type-IV collagen consists of basement membranes of epithelial tissues.

Matrix metalloproteinases (MMPs) are the family of ECM-degrading enzymes including collagenases such as MMP-1, MMP-8, and MMP-13. In addition, MMP-2, membrane-type MMPs (MT-MMPs), and a serine protease of cathepsin K are also collagen-degrading enzymes. These enzymes have been shown to express during organ formation, tissue destruction, and wound healing, and many molecular biologists have investigated this topic all over the world.

During 1980s to 1990s, the initial studies of the enzymatic activities of collagenases were studied using purified recombinant proteins. In 2000s, the gene recombination technique was used in mice to evaluate the phenotype, and these were inserted gene mutation in the active site of MMPs, MMPs gene transgenic mice, and gene knockout mice.

Collagen degradation has been shown to play a role in different pathological conditions, including osteochondral-bone destruction, inflammatory diseases, cancer invasion, neo-angiogenesis in which all of them were associated with enzymatic activities of MMPs for tissue destruction. In this review, we summarize the knowledge of type I collagen degradation by collagen-degrading MMPs and describe the research transition of the techniques.

Keywords: matrix metalloproteinase, collagenase, gelatinase, genetically modified mouse

Chapter 9. Abnormal Collagen Metabolism and Related Diseases

ITOH Yoshifumi (Kennedy Institute of Rheumatology, University of Oxford)

Fibrillar collagens, such as type I collagen, are major components of bone, skin, and interstitial matrix of different organs. The levels of the collagens in the tissue are regulated precisely by the production and the degradation. Once this balance is disrupted and the production of collagens exceeds the degradation, it would result in fibrotic conditions, leading to organ malfunction. On the other hand, if the degradation exceeds production, it causes tissue destruction. When cells migrate within a tissue, regardless of pathological or physiological conditions, fibrillar collagen that acts as a physical barrier needs to be locally degraded. But in the event found in disease conditions including cancer cell invasion and growth or inflammatory arthritis such as rheumatoid arthritis, the cell migration associating fibrillar collagen degradation is highly upregulated. Another type of collagen that can be a physical barrier for cell migration is non-fibrillar type IV collagen. Type IV collagen is a major component of the basement membrane of epithelial and endothelial cells, and it needs to be degraded when epithelial cancer cells grow or invade. Therefore, controlling abnormal collagen metabolism would lead to the discovery of therapeutics for the diseases. In this section, collagen metabolism and the disorders related to abnormal collagen metabolism will be discussed.

Keywords: collagen, collagenase, fibrosis, tissue damage, cell invasion

Chapter 10. Synthetic Collagen

Kazuki C. KURODA, KOIDE Takaki (Department of Chemistry and Biochemistry, School of Advanced Science and Engineering, Waseda University)

In this review, we describe design, synthesis, and applications of synthetic collagens. The so-called synthetic collagens include collagen-mimetic peptides (CMPs) and collagen-like polymeric or supramolecular materials. CMPs are soluble mimics for small parts of natural collagen triple helices. CMPs are generally prepared chemically, and they are utilized in structural and biochemical studies on collagen. In the molecular design of CMPs, providing enough thermal stability to the triple helix is particularly important, and many concepts have been tested for the purpose. The use of appropriately designed CMPs has enabled easy access to the essence of collagen, avoiding difficulty in handling of insoluble and multifaceted natural collagen with huge molecular size. Polymeric or supramolecular materials based on CMP are promising biomaterials for both in vitro and in vivo applications. They are free from contamination of zoonotic pathogens. The synthetic collagen-like materials are not only the surrogates for natural collagen, but also used as artificial extracellular matrices with tunable physical properties and physiological activities.

Keywords: collagen-mimetic peptide (CMP), molecular design, supramolecular material, artificial extracellular material

Chapter 11. Digestion and Absorption of Collagen and Its Derivatives

SATO Kenji (Marine Biological Function, Division of Applied Biosciences, Graduate School of Agriculture, Kyoto University)
SHIGEMURA Yasutaka (Department of Food & Nutritional Science Tokyo Kasei University)

There was limited information on structure and quantity of food-derived collagen peptides in human blood before 2000. In the last two decades, more than 15 collagen di- and tri-peptides have been demonstrated to increase in human peripheral blood after ingestion of gelatin, a denature form of collagen, and its enzymatic hydrolysate, namely collagen peptide. Among the food-derived collagen peptides in human blood, Pro-Hyp and Hyp-Gly are main constituents. Period of ingestion of collagen peptides and molecular weight of collagen peptide for ingestion affect the ratio of Pro-Hyp and Hyp-Gly in human blood. Part of collagen dipeptides is converted to cyclic di-peptide, diketopiperazine, in human body possibly via enzymatic reaction. While Pro-Hyp and Hyp-Gly resist to exo peptidases in blood, Pro-Hyp can be cleaved in the tissue under inflammation, indicating some specific peptidase are induced at inflammatory tissue. Majority of collagen dipeptides are excreted into urine. However, part of Pro-Hyp has been demonstrated to be incorporated into some cells and further metabolized. In the primary cultured mouse skin fibroblasts, Pro-Hyp is specifically incorporated into the fibroblasts expressing mesenchymal stem cell marker, p75NTR, which triggers growth of the fibroblasts attached on collagen fibrils. While target molecule of Pro-Hyp or its metabolites in the cell remains to be elucidated, the food-derived Pro-Hyp and related compounds in cells might be responsible for the beneficial activities upon the ingestion of gelatin and collagen peptide.

Keywords: collagen peptide, Pro-Hyp, Hyp-Gly, diketopiperazine, fibroblast

Chapter 12. Mammalian Collagen

TANAKA Keisuke, HATTORI Shunji (Nippi Research Institute of Biomatrix)

Collagen is the major protein of the extracellular matrix and is the most abundant protein found in mammals, comprising approximately 30% of the total protein. At present, 28 types of collagen have been identified, and types I, II, and III are the main types of collagen found in connective tissue. Collagen exists in mammalian body as bundles called collagen fibers, and has great tensile strength to maintain the architecture of skin, bone, cartilage, tendon and others. In addition to supporting most tissues, collagen plays a large part in cellular activity through interactions with receptors on the surfaces of cells. Collagen can be extracted and purified from a variety of sources such as species and tissues for many applications in food, cosmetic, pharmaceutical and medical industries. Mammalian collagen (e.g., bovine and porcine collagen) shows high sequence homology to human collagen, and has similar properties to human collagen in terms of its thermal stability and ability of self-assembly into fibrils in vitro. In addition to these advantages, it offers low immunogenicity, good biocompatibility and moderate biodegradability as a biomaterial. Therefore, mammalian collagen can be suitable for medical use.

Keywords: mammal, structural protein, cell function, thermal stability, self-assembly

Chapter 13. Fish and Shellfish Collagen

ISHIHARA Kenji (National Research Institute of Fisheries Science, Fisheries Research and Education Agency of Japan)
HIRAOKA Yoshinobu (Ehime Institute of Invention)

Fish are divided into cyclostomes, cartilaginous fish, and teleosts, all of which have type I collagen as their main collagen. Their collagen molecules are mainly of (α1) 2α2 type, but some teleosts have species with α1α2α3 molecular species. Unlike livestock animals, fish are poikilothermal animals, so the denaturation temperature of their collagen is generally lower than that of livestock-derived collagen. Denaturation temperature is related to the hydroxyproline content in the collagen molecule. Collagen is related to the quality of raw fish meat. A correlation is observed between the collagen content in muscle and the hardness of sashimi. Invertebrate collagen has also been shown to be related to meat water retention and breaking strength. The cnidarian jellyfish are mostly made of collagen, except for water and ash. Echizen jellyfish is a large jellyfish that come to the coast of the Sea of Japan and cause great damage to the fishery. When powder containing mainly collagen was prepared from Echizen jellyfish and administered to rats, the possibility of promoting lipid metabolism was observed. We also introduced a technique for extracting collagen from the backbones of large fish such as cultured yellowtail and skipjack as a collagen raw material. We prepared a peptide with enhanced ACE inhibitory activity using an enzyme. The prepared peptide showed hypotensive activity on spontaneously hypertensive rats and contained a novel peptide having ACE inhibitory activity.

Keywords: fish, invertebrate, denaturation temperature, ACE inhibitory activity

Chapter 14. Lower animal Collagen

Katsuhiko Arai (Scleroprotein and Leather Research Institute, Faculty of Agriculture, Tokyo University of Agriculture and Technology)

As known for connective tissue or extracellular matrix, the original function of collagen molecule is a filler material of the intercellular space and the adhesive bond to tie cells together. A kind of collagen molecule appeared when unicellular organism evolved into a certain multicellular animal, thus collagen-like protein is found even in the lowest animal, a genus of Porifera.

In this section, characteristics of collagen molecules found in the cnidarian belonging to the diploblastic animals in addition to a family of lower triploblastic animals including the mollusks (shell, squid and octopus), the arthropod (shrimp and insect) and the echinoderm (sea cucumber, sea urchin and starfish) will be introduced.

Keywords: Embryo-like animal, Sponge phylum, Porifera, Mollusk, Arthropod, Echinodermata

Chapter 15. Application of Collagen, Overview

NOMURA Yoshihiro (Scleroprotein and Leather Research Institute, Faculty of Agriculture, Tokyo University of Agriculture and Technology)

Collagen, gelatin, glue and hydrolyzed collagen are used as functional materials. Collagen prepared as a by-product of meat products has a long history and is closely related to our lives. This chapter outlines collagen as a functional material.

Keywords: by-product, functional material

Chapter 16. Leather and Leather Goods

YOSHIMURA Keiji (Japan Leather and Leather Goods Industries Association)

Leather has been the most used in considering the use of collagen. The leather derived as a by-product of meat production is processed into leather. The production volume in 2015 was 22.27 billion m^2, which is used for footwear, automobiles, clothing, furniture and gloves. This chapter describes the history of leather and the leather manufacturing process.

Keywords: leather, by-product, history of leather, leather manufacturing process

Chapter 17. Animal Glue and Industrial Gelatin

DOI Masahiro (Asahi Gelatine Industrial Co., Ltd)

In Japan, glue is divided into Japanese glue and Western glue (gelatin). Japanese glue is a product obtained by degreasing and dehairing the skin under relatively mild conditions filtering the solution extracted with warm water and drying. On the other hand, Western glue is a purified gelatin from which impurities have been removed, and is produced in large quantities with the use of bovine bone and hide as a raw material for fixing silver for photography. Animal glue has higher viscosity and adhesiveness. In this chapter, the history and characteristics of the use of animal glue and industrial gelatin are explained.

Keywords: animal glue, industrial gelatin, viscosity, adhesiveness

Chapter 18. Inkstick and Classical Animal Glue

UDAKA Kentaro (Independent Administrative Institution National Institutes for Cultural Heritage, Tokyo National Research Institute for Cultural Properties)

Inkstick (*sumi*/ 墨) is a traditional material that has been widely used for paintings and calligraphies in East Asia throughout the ages. It is a composite material mainly of soot and animal glue. Soot is a pigment that is basically hydrophobic, and can be dispersed in water by the function of animal glue. Depending on these raw materials and the blending conditions, the properties of inksticks vary.

For traditional East Asian paintings, there are various techniques that utilize the interaction of inkstick, water, and the base. Different properties of inkstick affect the appearances of the works.

Soot is mainly composed of carbon. The properties of soot, such as color, texture, diameter of primary particles, aggregate and agglomerate size, and amount and types of surface functional groups, depend on the raw materials and production conditions.

Animal glue is composed mainly of gelatin, and contains a small amount of fat and ash. Gelatin is a polymer formed from several hundreds of amino acid residues, and is an amphoteric surfactant and an adhesive. Molecular weight, components, and physicochemical properties of animal glue depend on the raw materials and production conditions. In addition, reflecting them, applicability and interaction with other materials are also diverse. Animal glue is classified into industrial animal glue (洋膠), domestic animal glue (和膠), and classical animal glue (古典的膠).

Inkstick is a complex research subject involving diverse materials and technologies. In recent years, systematization of these elements has advanced, and the research results are being used in various applications.

Keywords: inkstick, soot, animal glue, cultural properties, dispersion

Chapter 19. Foods Using Collagen

SUZUKI Satoshi (Nippi, incorporated Fuji Factory)

Collagen has been consumed in a variety of forms. This chapter describes features and examples of foods in which collagen, gelatin and collagen peptides are utilized. Edible films have the properties of collagen. Sausage casings and water-soluble gelatin films make up the majority and are in much demand. Collagen used in cooking is mainly based on the gel properties of heat-modified gelatin and is widely used at home and in restaurants, for example, in appetizers and jellies. Gelatin has also developed in Europe as an ingredient in confectionery and desserts. In confectionery making, the physical characteristics of gelatin, such as its high foaming properties and ease of gelation, are used. Very recently, new applications of collagen, especially in Japan, have been used to maintain the shape of prepared foods in convenience stores and other applications, based on the advanced distribution system. It is also expected to be in demand for food for elderly people. Collagen peptides are soluble in cold water, and their demand is growing for use in beverages and other applications due to their low viscosity and non-gelling properties. Among the applications where its chemical properties are exploited are in microcapsules and for removing turbidity in the sake and wine manufacturing process. Collagen is also used as a specific amino acid source and seasoning due to its characteristic amino acid composition. Thus, collagen has been in the diet for a long time, and its properties, nutritional characteristics and composition have been studied for a long time. Even today, the various physicochemical properties of collagen, which are irreplaceable, are still in wide demand as a high-value food material.

Keywords: edible films, seasoning, sausage casing, gelatin, collagen peptide

Chaper 20. Functional Food

KOIZUMI Seiko, MATSUSHITA Aya, DAIMON Mona, HIMENO Ai
(Research and Development Center, Nitta Gelatin Inc.)

Collagen, gelatin or collagen peptide (Collagen Hydrolysate, CH) are used in cosmetics, general foods and health foods, etc. depending on their physical properties. These materials are eaten since ancient times and have been confirmed to be safe. Among them, an extensive range of functionality by CH has been reported in many clinical trials. Thus, it has been widely used in "Foods with Function Claims system" since 2015. We would introduce the absorption and metabolism of CH, and function of CH to skin, knee joints, bone, muscle, blood vessels, diabetes, cognitive health, and immunity reported in clinical trials.

Keywords: absorption, metabolism, skin aging, osteoarthritis, osteoporosis

Chaper 21. Collagen in the Cosmetic Field

AMANO Satoshi (Shiseido Global Innovation Center)

In the cosmetics field, collagen is blended in cosmetics and positioned as a material used as a component that enhances the moisturizing effect, and also has the aspect of being an indispensable biopolymer that exists and functions in the skin. In the skin, various types of collagens exist in the epidermis, basement membrane, dermis, and subcutaneous tissue, and work to keep the skin in good condition. However, this collagen also changes due to aging and ultraviolet rays, and causes aging changes such as wrinkles and sagging. Keeping the skin in good condition is one of the important roles of basic skin care. Aging is an important research target in the cosmetics research, and as a result of aging, the internal structure of the skin and its components changes. It is important to propose a practical skin care method by finding out what mechanism and how to control the aging process. In this chapter, while briefly touching on the collagen as a material and the functional component evaluation system related to collagen, the main contents are the elucidation of the mechanism of damage to the epidermis basement membrane during skin aging process using three-dimensional cultured skin models and human skins and its development to a skin care method. Moreover, the damage mechanism of the dermis and the research on its care method were described.

Keywords: basement membrane, dermis, three-dimensional cultured skin models

Chaper 22. Characteristics and Applications of Medical Collagen Products

FUJIMOTO Ichiro (Koken Research Center, Koken Co., Ltd.)

Collagen has many possibilities as a medical device by taking advantage of its advantages as a biological material. It can be molded into a variety of shapes, its biocompatibility, safety, biodegradable is evaluated many collagen medical devices are manufactured and used in the medical field. In particular, atelocollagen was removed telo-peptide region by enzymatic treatment seems to be a useful material as a medical application antigenicity is suppressed.

Currently, medical collagen products used in Japan are products registered and managed as medical devices of highly controlled medical devices. As medical applications for regenerative medicine, skin tissue, periodontal tissue, neural tissue, cartilage tissue, bone tissue, are used in. Other clinical applications, surgical hemostasis, improvement of dry eye, plastic surgery area, have also spread.

In this chapter, technical information such as the situation of medical collagen in general, and relationship with collagen characteristics are included, and the description of medical equipment and the contents of the classification are introduced. In the second half, we introduce regenerative medicine products that use autologous cells or allogenic cells that are recently newly applied in medical applications in combination with collagen and finally explain the possibilities for medical applications of human collagen.

Keywords: medical collagen, medical equipment, Japan Pharmaceutical and Medical Device Act (PMDA), regenerative medicine, biocompatibility