ACS FOOD SCIENCE & TECHNOLOGY

pubs.acs.org/acsfoodscitech Review

# Recent Advances in Collagen and Collagen-Based Packaging Materials: A Review

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Cite This: ACS Food Sci. Technol. 2025, 5, 1767−1784 Read Online





**ABSTRACT:** Collagen is a vital structural protein found in the extracellular matrix of mammalian skin, bones, muscles, and various other tissues. It is extensively utilized in the food industry due to its distinct biochemical, structural, and physicochemical properties. These attributes enhance the elasticity, texture, and stability of a wide range of food products while also improving their nutritional and health benefits. This review examines the sources, structures, extraction techniques, and physicochemical characteristics of collagen molecules. Furthermore, it investigates methods for producing collagen-based composites, films, coatings, and electrospun fibers. The review also highlights the potential applications of collagen in active and intelligent packaging, as well as its use in the formulation of food additives and materials for food preservation. The objective is to provide a comprehensive overview of collagen and its derivatives in relation to food safety while addressing the challenges and opportunities for developing sustainable, active materials within the food industry.

**KEYWORDS:** *Collagen, Physicochemical properties, Industrial applications, Food processing, Active packaging, Packaging material*

## 1. INTRODUCTION

Food loss and waste occur at every stage of the supply chain, from production to the consumer. Globally, approximately 1.3 billion tons of food, valued at over $1 trillion, are either wasted or lost.[1−3] As a key solution for transporting, distributing, and preserving food until it is consumed, functional food packaging plays a vital role. However, increasing concerns about environmental waste, carbon emissions, consumer demand for ready-to-eat foods with extended shelf lives, and the sustainability of fossil fuel resources have prompted a rise in scientific efforts to develop alternatives to traditional food packaging materials.[4−6] In response to environmental issues and the declining availability of petroleum-based polymers, the food packaging industry is steadily shifting toward biopolymers and biobased plastics sourced from renewable materials.[7−9]

Biomaterials derived from natural resources are promising candidates for numerous practical applications due to their inherent biodegradability, flexibility, and biocompatibility.[4,5,10] Collagen, one of these biopolymer materials, is a promising biomaterial that has been used for a long time in various functional applications. About 25−35% of all animal proteins are made up of these structural proteins, and they are most prevalent in vertebrates.[11] However, inadequate consumption of collagen from animal byproducts can increase disposal costs and reduce revenue opportunities. In 2020, the global collagen market was valued at over $4.7 billion. The healthcare sector (∼48%) and the food and beverage industry (∼32%) together represented around 80% of the demand for collagen and its derivatives. Furthermore, the global collagen market is projected to grow to $7 billion by 2027.[12]

In addition, collagen, a multifunctional protein, is easy to process, has high porosity, low biodegradability, low immunogenicity, excellent biocompatibility, high moisture absorption ability, and has a unique ability to interact with other synthetic polymer materials. It has large-scale extractability, penetration into lipid-free interfaces, and foaming, emulsifying, gelling, and film-forming properties.[13] All these features make collagen a key material suitable for edible coatings and packaging materials or for various food processing, biomedical, pharmaceutical, and cosmetics applications.[11,13,14]

Additionally, collagen films have high mechanical strength due to their special triple helical structure and film-forming ability.[15] For instance, collagen films produced from a 10 mg/mL collagen solution exhibit a tensile strength of 120 MPa, which is similar to or exceeds that of κ-carrageenan films (22 MPa at 10 mg/mL) and gelatin films (60 MPa at 40 mg/mL).[16,17] In addition, collagen has an isoelectric point of approximately pH 7, which improves the water resistance of collagen films. Because of these beneficial properties, collagen is now often utilized in sausage production rather than plastic or natural casings, making it possible to use more palatable collagen casings.[14,18,19] Certain collagen peptides, such as collagen hydrolysates, have special biological properties and

Received: November 5, 2024
Revised: April 11, 2025
Accepted: April 11, 2025
Published: April 21, 2025

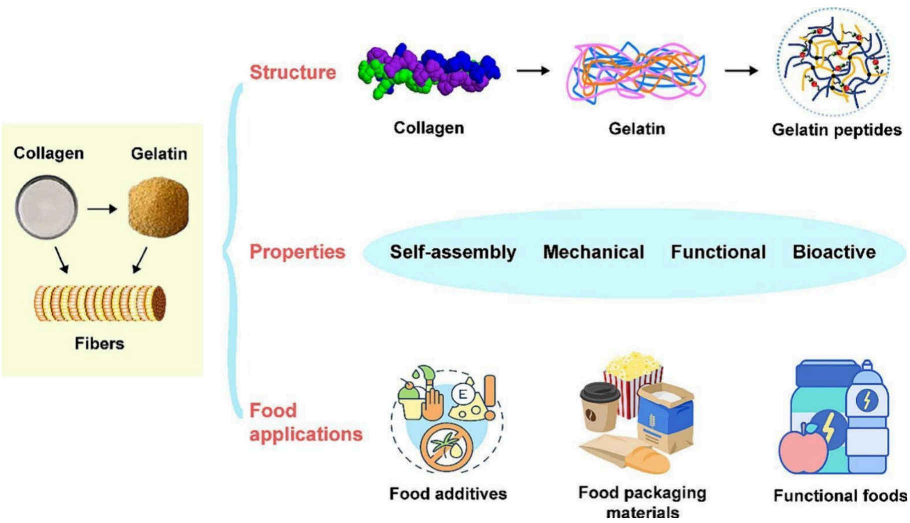


**Figure 1.** Structure properties and uses of collagen for food safety purposes. Reproduced with permission from Ahmad et al.[25] Copyright 2024 International Journal of Biological Macromolecules.

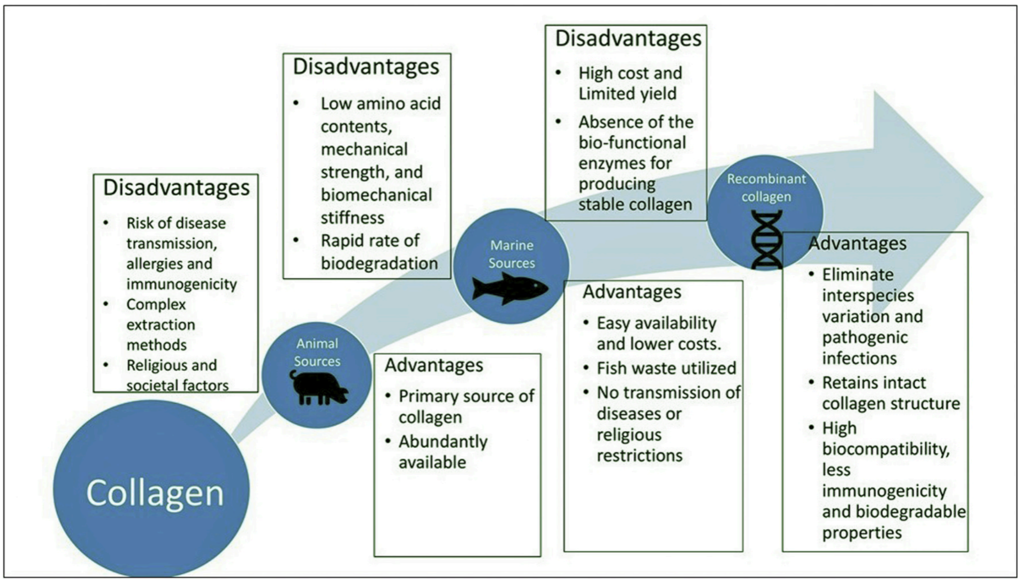


**Figure 2.** Sources of collagen and their features. Reproduced with permission from Gajbhiye and Wairkar.[40] Copyright 2022 Biomaterials Advances.

have a high potential for use in functional food development and quality improvement of processed foods.[13]

Furthermore, due to the chemical compliance of collagen, synthetic active fillers can be incorporated to significantly improve physicochemical performance and provide new functionality, including antioxidant and antibacterial properties.[11] Recently, Zheng et al. (2023) developed a collagen and gallic acid-grafted chitosan film incorporating $\varepsilon$-polylysine for active pork packaging.[20] This film demonstrated excellent antibacterial, antioxidant, and barrier properties, effectively prolonging the shelf life of the pork by 5 days. Similarly, another study reported that collagen films infused with cinnamon essential oil extended the shelf life of pork by over 4 days.[21] In addition to their food preservation properties, collagen-based composite films have extensive applications in food safety evaluation.[22]

Understanding the key characteristics, fundamental structure, and application potential of collagen and its derivatives is essential for utilizing collagen in food safety contexts. Researchers are exploring ways to modify its function and combine it with other natural or synthetic polymers and bioactive compounds to address these challenges, according to one study. Many reviews have emphasized the potential applications of collagen, both in biological and nonmedical fields.[11,23,24] There are limited review articles that address the significance of collagen and its derivatives from the perspective of food packaging and safety. Thus, this study focuses on current research surrounding the composition, properties, and potential applications of collagen and its derivatives in food packaging and preservation (Figure 1).

## 2. SOURCES OF COLLAGEN

The primary sources of high-quality commercial collagen include bovine bones, hides, pig skin, and various other mammalian byproducts.[11] China produces more than 49 million tons of pork annually, of which 8 million tons are


https://doi.org/10.1021/acsfoodscitech.4c00938
ACS Food Sci. Technol. 2025, 5, 1767−1784

**Table 1. Sources, Methods, Yield, and Extraction Conditions of Seafood-Based Collagen**

| Source | Origin | Time (h) | Yield (%) | Techniques | References |
|---|---|---|---|---|---|
| *Acipenser schrenckii* (Amur sturgeon) | Cartilage | 48 | 27.04% to 02.18% | Acid-soluble collagen and salt solubilization collagen | 41 |
| *Thunnus albacares* (Yellowfin tuna) | Skin | 24 | 3.18% | Acid soluble collagen | 42 |
| Sole fish (*Aseraggodes umbratilis*) | Skin | 32 | 19.2% | Acid soluble collagen | 43 |
| *Lutjanus sp.* (Red snapper) | Skin | 48 | 41% (dry) and 9.7% (wet) | Acid soluble collagen | 44 |
| *Chanos chanos* (Milk fish) | Scales | 61.3 | 0.73% | Acid soluble collagen | 45 |
| *Nibea japonica* (Giant croaker) | Skin | 8.67 | 84.8% | Pepsin soluble collagen | 46 |
| *Acaudina leucoprocta* (Sea cucumber) | Body wall | 144 | 43.9% | Pepsin soluble collagen | 47 |
| *Acromitus hardenbergi* (Jelly fish) | Oral arm and bell | 48 and 144 | 0.29%, 0.39% and 0.09%, 0.16% | Pepsin soluble collagen and acid soluble collagen | 48 |
| *Rhopilema esculentum* (Jellyfish) | Mesoglea | 72 | 0.12% | Acid soluble collagen | 49 |
| *Sciaenops ocellatus* (Red drum fish) | Scales | 8 | 4.32% | Pepsin soluble collagen | 50 |
| *Oreochromis sp.* (Tilapia) | Scales | 01 | 49.42% | Extrusion-hydro-extraction | 51 |
| *Evenchelys macrura* (Marine eel fish) | Skin | 72 | 80.0% | Pepsin soluble collagen | 52 |
| *Cyprinus carpio* (Carp) | Scales, bones, and skin | 96 and 72 | 1.35% and 41.3% | Acid soluble collagen | 53 |
| *Carcharhinus albimarginatus* (Silvertip shark) | Head bone and skeletal | 96 and 96 | 7.10% and 8.99% | Pepsin soluble collagen | 54 |

bones, 7 million tons are skin, and 5 million tons are intestines.[13] Collagen is the most prevalent protein found in livestock processing byproducts with high protein content. Therefore, extracting collagen from these byproducts would offer the potential to produce valuable protein resources from animal slaughter. For instance, type I collagen sourced from bovine is typically extracted from the Achilles tendon, although skin and bones are also used as source materials.[26,27] Collagen type III derived from bovine is exclusively extracted from the skin for research purposes; however, alternative tissue sources exist.[27] Overall, bovine collagen is characterized by advantageous traits such as low immunogenicity and biocompatibility. It is generally well tolerated in vivo and does not trigger an immune response in most people, except for those with significant collagen allergies.[28,29]

Collagen can also be extracted from a range of marine organisms, including fish (*Pisces*), jellyfish (*Cnidaria*), sponges (*Porifera*), mollusks such as octopus and cuttlefish, as well as various species of echinoderms.[11] In the past ten years, extensive research has focused on type I collagen sourced from marine environments, particularly collagen derived from fish. This type of collagen is advantageous because it poses a low risk of disease transmission and contains a high amount of untapped collagen suitable for the food industry. Effective extraction methods have utilized fish scales, bones, skin, and various tissues from invertebrates to obtain collagen from marine animals.[30,31] Figure 2 illustrates the sources of collagen along with their advantages and disadvantages. Fish processing byproducts can serve as a cost-effective source of collagen in the fisheries sector. In the processing industry, roughly 25% of a fish's total weight is utilized, leaving about 75% classified as waste.[32] Scales, bones, and skin represent approximately 30% of this waste and are suitable for collagen extraction due to their significant collagen content. Converting waste into collagen could help address environmental issues related to fish byproducts while also generating additional value, thereby enhancing the profitability of the fish processing industry.[33,34] Table 1 presents the sources and conditions employed for collagen extraction.

Genetically modified bacteria are another source of collagen production.[27] However, this process produces less collagen, which increases manufacturing costs.[11] The most commonly utilized transgenic organism for recombinant expression systems to produce proteins is *Escherichia coli* due to the extensive study conducted on its genomic composition and the consequences of functionalization. *E. coli* is an ideal platform for producing recombinant proteins on an industrial scale due to its rapid growth rate in culture.[27] Naturally, *E. coli* produces a collagen-like protein that features a C-terminal trimerization domain characterized by repetitions of the Gly-X-Y sequence. However, it does not undergo proline hydroxylation, a modification that is typical of human collagen.[35] Collagen produced by *E. coli* and similar bacterial cultures is especially suitable for mechanical applications due to existing challenges related to amino acid sequences and hydroxylation levels.[27]

Additionally, several plant species have shown favorable results in the expression of recombinant human collagen (rhCOL) type I. The P4H genes were successfully introduced into both tobacco (*Nicotiana tabacum*) and maize (*Zea mays*) plants, resulting in plant cells that are capable of producing homotrimer helices of collagen I.[27,36,37] Moreover, post-translationally modified heterotrimeric collagen has been generated by expressing the $\alpha$ and $\beta$ strands of collagen I in a transgenic tobacco plant that has been transformed with genes encoding the enzymes $P_4H$ and lysyl hydroxylase 3 ($LH_3$).[38] Research has indicated that in vivo wounds treated with rhCOL type I produced from a tobacco recombinant system led to a significantly faster wound closure compared to flowable gels derived from animal collagen.[39]

## 3. STRUCTURE OF COLLAGEN

Collagen is a fibrous structural protein and the most prevalent protein in animals. Approximately 30% of the protein content in the human body consists of collagen, primarily located in connective tissues.[55] The structure of collagen, a heteropolymer, is rigid due to its highly organized nature and staggered triple helix arrangement.[56] Fibril-forming collagen has a molecular weight of around 290 kDa, and to date, 29 different types of collagen have been identified and categorized based on their structural characteristics.[55] Collagen exists in several types based on its source, with the most common being types I, II, III, and IV. Notably, type I collagen accounts for over 90% of the total collagen found in the body.[57,58] Type I collagen is mainly present in connective tissues such as skin, tendons,


https://doi.org/10.1021/acsfoodscitech.4c00938
ACS Food Sci. Technol. 2025, 5, 1767−1784

ligaments, and bones. Type II collagen is predominantly located in cartilage, type III in cardiovascular tissues, and type IV in the basement membrane.[59]

The collagen biopolymer features a trimeric structure made up of three polypeptide alpha chains. Its configuration primarily consists of a left-handed triple helix and is notably abundant in three specific amino acid residues: glycine, proline, and hydroxyproline.[57] The peptide chain features repeating units of Gly-X-Y, where X and Y represent nonspecific amino acids, with proline and hydroxyproline being the most frequently occurring.[55,60] The triple helix structure of collagen forms microfibrils via covalent bonding, which then aggregate to create fiber bundles.[61] The fundamental structure of collagen is illustrated schematically in Figure 3a, while Figure 3b depicts the chemical structures of its major components. In the collagen architecture, glycine is crucial for creating a rigid framework that contributes to the formation of tropocollagen. The shape of packed collagen fibrils is believed to be hexagonal and may be sheets or microfibrils. Microscopic evidence shows that the collagen structure is made up of elongated fibrils.[56,62]

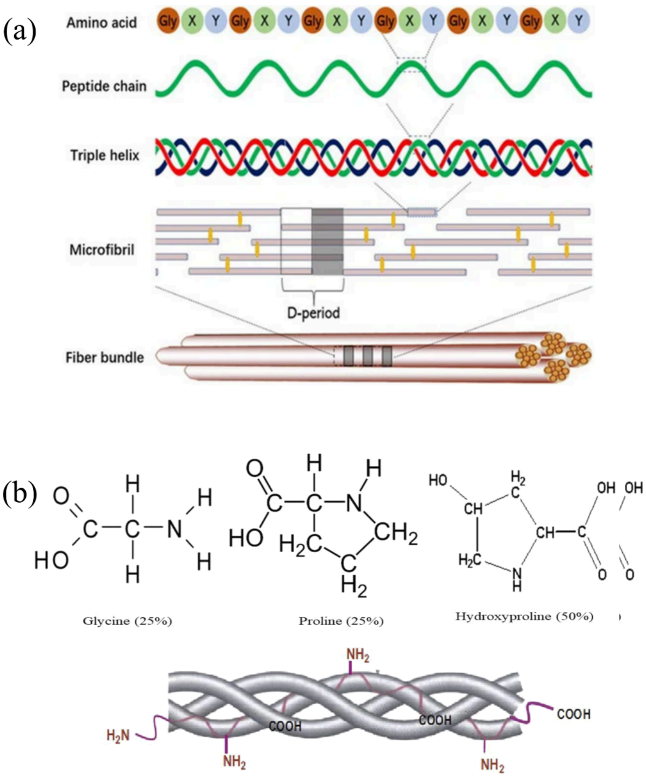


**Figure 3.** (a) Structure of collagen. Reproduced with permission from He et al.[65] Copyright 2021 Applied Sciences. (b) Chemical structures of the collagen main constituents. Reproduced with permission from Tomoaia and Pasca.[67] Copyright 2015 Clujul Medical.

Reports indicate that elevated temperatures can lead to the denaturation of collagen, potentially resulting in the loss of its triple helix structure. Even changes in pH and ionic strength can have profound effects on collagen structure[63−65] due to the hydrogen bonds and hydrophobic forces of collagen, which can cause it to break down in solvents, abnormal pH and unfamiliar temperatures.[65,66]

## 4. COLLAGEN EXTRACTION METHODS

As illustrated in Figure 4, collagen extraction techniques are categorized into established and novel methods. The process of extracting collagen entails eliminating all noncollagenous materials from the raw material to yield pure collagen. This recovery process includes pretreatment, extraction, and purification stages. For skin extraction, the material is washed in cold water for several days and then cut into small, manageable pieces measuring 1 $cm^2$.[68] Pretreatment aims to disrupt the covalent cross-links that exist between collagen molecules, as these cross-links contribute to the structural and mechanical properties of tissues and organs in vivo. It is known that these cross-links degrade very slowly, even in boiling water. Consequently, various mild chemical treatments, including dilute acids and alkalis, are employed to partially hydrolyze collagen and sever these cross-links while preserving the integrity of the collagen chains.[69]

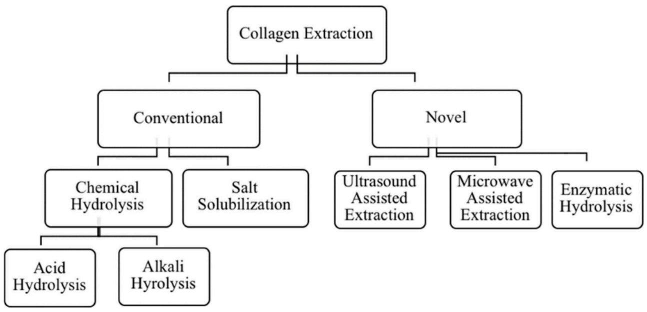


**Figure 4.** Collagen extraction methods. Reproduced with permission from Senadheera et al.[70] Copyright 2020 Marine Drugs.

Additionally, enzymatic methods can be used for pretreatment. To pretreat the skin, simply soak it in a dilute acid or alkali at a controlled temperature. Acid pretreatment is ideal for delicate skins that lack intertwined fibers, such as those found in pork or fish skin. Alkalis, such as sodium hydroxide (NaOH) and calcium hydroxide [$Ca(OH)_2$], are effective for extracting collagen from thicker materials. The thickness of the material influences the duration of the pretreatment. Treatment with NaOH causes significant skin swelling, facilitating deeper diffusion of the alkali into the tissue matrix. The alkali helps hydrolyze unwanted components, including noncollagenous proteins, lipids, pigments, and other organic substances.

Additionally, processing factors such as temperature, duration, and alkali concentration play a critical role in extraction efficiency.[69] Sodium hydroxide (NaOH) concentrations ranging from 0.05 to 0.10 kmol $m^{-3}$ preserve acid-soluble collagen and the native structure; however, higher concentrations can lead to considerable loss or degradation. Depending on the skin's origin or characteristics, skin-specific pretreatment such as soaking, fleshing, waxing, or cutting may be required. Further steps in the process may involve mechanical slicing, the use of alcohol to dissolve fats, heating, application of detergents and solvents, rinsing with hot water, and desalting through chelating agents like ethylene diamine tetraacetic acid (EDTA).[68]

Chemical hydrolysis using acids, alkalis, or salt dissolution is a widely used technique for extracting collagen. Ultrasound, microwaves, and enzymes can aid in the extraction process. Extraction temperatures are typically kept low, around 4 °C, to minimize collagen degradation. Extraction techniques can be


https://doi.org/10.1021/acsfoodscitech.4c00938
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**Table 2. Factors Affecting Collagen Self-Assembly**

| Factors | Effects | References |
|---|---|---|
| Collagen source | The speed at which nucleation occurs in collagen derived from grass carp scale was found to be faster than that in both tilapia skin and bovine dermal-derived collagens. | 74 |
| Extraction method | At temperatures ranging from 4 to 37 °C, extracting collagen at a lower temperature was found to be advantageous in preserving its natural structure and enhancing its self-assembly capability. | 75 |
| Concentration | When the concentration of collagen was increased from 0.01 mg/mL to 2.0 mg/mL, it was observed that the diameter of the fibrils formed also increased. | 76 |
| Temperature | Within the temperature range of 20 to 37 °C, it was observed that higher temperatures could expedite the process of collagen self-assembly. | 77 |
| pH | When the pH level was low (≤6.6), collagen fibrils of varying sizes were produced. As the pH level increased (6.9−9.2), the fibrils became more uniform in size. | 78 |
| Ionic strength | When the concentration of NaCl was increased from 65 mM to 160 mM, it was observed that the lag time in collagen fibril formation increased, and the degree of fibril formation decreased. | 79 |
| Amino acid composition | The addition of lysine was found to increase the size or number of self-assembled collagen fibers, while the inclusion of glutamic acid restricted collagen self-assembly to a higher-order structure. | 80 |
| Molecular chirality | The rate of collagen self-assembly was observed to be faster in the presence of D-glutamic acid compared to L-glutamic acid. However, treatment with L-glutamic acid resulted in the formation of collagen fibrils with a larger diameter. | 77 |
| Ultrasonic treatment | Exposing collagen to ultrasonic treatment was found to increase the rate of collagen fibril formation, reduce the diameter of the fibrils, and increase the size of network pores. | 81 |

customized to achieve specific yields and the desired characteristics of the final product, including polypeptide chain length, solubility, viscosity, thermal stability, emulsifying capacity, and water retention. Several factors affect the quality of the extracted collagen, including the pretreatment process, storage conditions of the hides, as well as the type, age, and gender of the animals (Table 2).[70] The breed and age of poultry can influence the properties of collagen, and variations in collagen structure, such as the hydroxyproline content, can impact the extraction process.

Collagen is usually extracted from the skin using acids or alkalis to disrupt the bonds. Both inorganic and organic acids are applicable, with organic acids like acetic, chloroacetic, citric, and lactic acid proving to be more effective in collagen extraction than their inorganic counterparts.[68] Acetic acid is particularly common in collagen extraction. The application of organic acids results in greater extraction yields and effectively dissolves un-cross-linked collagen. Typically, extraction with acetic acid is conducted at a concentration of 0.5 kmol $m^{-3}$, with a contact duration ranging from 24 to 72 h, accompanied by continuous stirring.[71] Collagen can be extracted through alkaline hydrolysis using substances such as sodium hydroxide, potassium hydroxide, calcium oxide, calcium hydroxide, or sodium carbonate. However, alkaline conditions may hydrolyze collagen fibrils and potentially degrade certain amino acids. This method is primarily employed for extracting collagen from leather processing waste.

Additionally, a collagen-based flame retardant has been developed from collagen derived through alkaline extraction of cowhide. The use of salts for collagen extraction is less prevalent, but neutral salt solutions like citrate, phosphate, sodium chloride, and Tris-HCl have shown effectiveness. Collagen type I is soluble at concentrations below 1.0 kmol $m^{-3}$, but it precipitates when salt concentrations exceed 1.0 kmol $m^{-3}$, necessitating careful control during extraction compared to acid or alkaline hydrolysis.[70] Enzymatic hydrolysis has been developed to overcome some limitations of traditional extraction methods, providing enhanced selectivity and reducing damage to collagen. This approach is less corrosive, requires less energy, and produces less waste compared to chemical extraction techniques.

Additionally, hybrid methods that combine enzymes and chemicals have been documented. Proteolytic enzymes, including pepsin, trypsin, and papain, are commonly utilized for collagen extraction, with animal-derived pepsin being the most prevalent. These enzymes can originate from animal, plant, or microbial sources. Treatment with pepsin enhances the acid solubility of collagen, while papain allows for effective control over the hydrolysis degree.[72] Ultrasound technology (with frequencies of 20 kHz or higher) enhances the yield of collagen extraction while significantly decreasing the extraction duration. The application of ultrasound generates intense turbulence and accelerates chemical reactions within liquids. In studies involving the acid extraction of collagen from sea bass skin, the integrity of the ultrasonically extracted collagen structure remained intact.

Additionally, while enzyme treatments can enhance both the yield and purity of collagen, the combination of ultrasound further reduces extraction time. By optimizing the treatment parameters tailored to specific collagen sources, it is possible to minimize structural damage to collagen. Moreover, ultrasound-assisted methods can be conducted safely and cost-effectively, lessening the reliance on corrosive chemicals.[73]

Crude collagen extracts often contain various salts and noncollagenous proteins. To purify collagen, a series of steps, including filtration and centrifugation, are employed. The salting-out process, which involves adding high concentrations of salt, can lead to the precipitation of both target and unwanted proteins. Factors such as temperature, pH, ionic strength, and the type of salt used influence the salting-out behavior of collagen. Due to its lower solubility compared to contaminating proteins, careful selection of salting-out conditions is essential to minimize the coprecipitation of unwanted proteins. The salting-out capacity of ions can be assessed using the lyotropic series, which indicates that anions are generally more effective than cations. Neutral salts derived from strong anions and cations are particularly effective at precipitating collagen, with sodium chloride being commonly utilized. While ammonium sulfate is also effective, it is not considered neutral; hence, neutral salts are favored in biomedical applications to prevent unwanted ionic effects on pH. To precipitate collagen, a neutral salt is added to the collagen solution, the pH is adjusted to 7, and the solution is allowed to sit for 4 to 12 h. The collagen precipitate is then separated by centrifugation.[68] The recovered collagen precipitate can undergo additional salting-out processes for further purification, typically using a refrigerated centrifuge set at 4 °C. Dialysis is conducted to remove the salt. The precipitated


https://doi.org/10.1021/acsfoodscitech.4c00938
ACS Food Sci. Technol. 2025, 5, 1767−1784

collagen is placed in a dialysis bag and dialyzed against an acidic solution or deionized water. Various dialysis techniques, which can be single- or multistage, are employed and may take between 4 and 10 days to remove salts effectively. Additionally, purification methods can be customized to isolate collagen within specific molecular weight ranges through techniques such as membrane filtration and chromatographic separation. It is worth noting that dialysis is often the most time-consuming step in the entire collagen extraction process, accounting for nearly 50% of the total duration.[12]

## 5. PROPERTIES OF COLLAGEN

Collagen's properties are influenced by various factors, including the animal species, the age of the animal, and its growth performance. The amino acid sequence of collagen exhibits significant variability, especially in the content of proline and hydroxyproline, which varies depending on the source.[55] Collagen is an extracellular matrix that provides structure to cells. Collagen has high mechanical strength, giving skin flexibility and strength, which also helps with organ development.[49] Moreover, it is also a well-known fact that the presence of collagen in the skin provides a defense mechanism by preventing the absorption of unwanted substances such as pathogens and toxins.[49,56,57] Collagen also helps preserve the structural integrity of cells, participates in many biological functions of cells, and also plays an important role in bone healing.[58]

The origin of mammalian-based collagen is limited and is mainly produced in cattle and pigs, making it a major concern for a variety of diseases.[59] As highlighted in the Sources section, collagen can be sourced from various terrestrial animals, including birds. However, recent outbreaks of diseases such as bovine spongiform encephalopathy and transmissible spongiform encephalopathy have raised significant concerns regarding the safety of using collagen derived from these animals.[60,61] Recently, aquatic collagen has gained considerable interest in collagen extraction and production. In this regard, fish and seafood have been found to be excellent sources of collagen and gelatin, which is broken down collagen. Marine collagen sources are one of the easiest and safest options, as terrestrial animal sources are very complex, and the extraction process is time-consuming, complicated, and has low yields.[49] Marine-based collagen has a low molecular weight and is, therefore, highly absorbable. It is metabolically suitable, low in toxins and, most importantly, environmentally friendly. Recently, low molecular weight collagen isolated from marine sources has found important applications in cosmetics and food applications.[62]

The self-assembly ability of collagen is a unique property that leads to the formation of fibrils, which can be hierarchically assembled into larger fiber bundles throughout a variety of tissues and organs.[13] Under physiologically similar temperature and pH conditions, collagen molecules can self-assemble into fibrils that exhibit characteristic D periodicity in vitro. The structure of these in vitro-formed fibrils closely resembles that of fibrils assembled in vivo. Additionally, collagen can self-assemble into various products, such as gels or sponges, by altering environmental conditions. These self-assembled structures possess a unique multilayered organization that significantly enhances their physical and biological properties.[77] The self-assembly of collagen in vitro occurs through a nucleation−growth mechanism characterized by a lag phase, a growth phase, and a linear plateau phase. Several factors influence this assembly process, including the source of collagen, extraction methods, and the concentration of collagen molecules. External factors such as temperature, pH, ionic conditions, amino acid composition, molecular chirality, sulfonated chitosan, phytic acid, and sonication also play significant roles. These factors modulate driving forces such as hydrogen bonding, hydrophobic interactions, and electrostatic interactions, leading to variations in the dynamics, structure, and properties of the self-assembled structures. For instance, increased temperature enhances the hydrophobic effect, thereby promoting the self-assembly process, while pH levels closer to the isoelectric point facilitate faster interactions between collagen molecules.[13]

The formation of collagen gel is a continuous process that involves collagen self-assembly, fibril formation, and entanglement. Changes in temperature, pH, or ionic conditions[82] can trigger this process. Gels are formed through an elastic network comprised of collagen fibers, which generally measure around 100 nm in diameter and exhibit a structure akin to that of natural collagen fibers. By manipulating the conditions that trigger the collagen sol−gel transition, it is possible to affect the density and dimensions of the aggregates formed by collagen fibrils.[83] For instance, chloride ions can decrease intermolecular repulsion, leading to the creation of densely packed collagen fibril aggregates that feature D periodic structures. The pH level also influences both the diameter of the fibrils and the quantity of collagen gels; elevated pH levels tend to produce larger fibril diameters and increased pore space. Additional factors impacting the architecture of collagen gel networks include temperature and the size and quantity of microfibrils generated during the nucleation phase.[84,85] Collagen gels consist of intertwined fibrils that confer mechanical strength and viscoelastic properties. The mechanical characteristics of these gels are influenced by their fundamental hierarchical structure and can differ based on the collagen source and the manufacturing process used.[13] Typically, natural collagen gels exhibit limited mechanical properties, rendering them inadequate for various applications. To enhance these properties, various physical, chemical, and enzymatic cross-linking techniques have been developed. However, many of these methods involve potentially harmful substances. Recently, self-compression technology has been introduced as a nontoxic approach to increase the density of collagen fibrils and enhance the mechanical attributes of collagen gels.[86]

## 6. APPLICATIONS OF COLLAGEN IN THE FOOD INDUSTRY

### 6.1. Collagen-Based Composite Materials.

Collagen-based composite materials, such as films, membranes, coatings, and fibers, are extensively used across various industries, including food and packaging, owing to their biodegradability and biocompatibility. These collagen-based tissues are fundamentally structured as a hierarchical arrangement of triple-helical collagen molecules that polymerize to form collagen fibrils. Fibrils serve as the fundamental building blocks of collagen fibers, connected by covalent or noncovalent bonds. This unique structure endows natural collagen with considerable mechanical strength and flexibility.[87] However, the dissociation and extraction process destroys secondary and covalent bonds, disrupting the hierarchical structure of collagen and impairing the intrinsic mechanical properties and heat resistance of collagen materials.[88,89]


https://doi.org/10.1021/acsfoodscitech.4c00938
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To tackle this issue, enhancing collagen by mixing exogenous polymers (either biobased or synthetic) and fillers (organic or inorganic) has garnered significant interest among researchers for improving the mechanical properties of collagen-based composites and boosting their barrier properties.[90−92] For example, Zhao et al. (2023) reported that the addition of celluloses in different geometries (i.e., rod-like cellulose nanocrystalline (CNC), long-chain cellulose nanofiber (CNF), and microscopic cellulosic fines (CF)) increased the water resistance and thermostability of all cellulose/collagen films. Also, the mechanical strength of the films was improved as the concentration of cellulose increased. At a cellulose percentage of 10 wt %, the tensile strength of CNF/collagen (124 MPa) and CF/collagen (113 MPa) composites was significantly higher than that of pristine collagen (90 MPa).[90] Besides, cross-linking has been proven to be an effective strategy for improving the properties of collagen materials.[93,94]

Collagen cross-linking can occur via weak bond interactions, including hydrogen bonds, van der Waals forces, electrostatic interactions, ionic bonds, and hydrophobic interactions, as well as through the formation of chemical bonds such as disulfide bonds and covalent bonds.[95] Cross-linking methods are generally classified into three main categories: physical, chemical, and biological enzymatic approaches. Physical cross-linking involves modifying collagen through various techniques, either individually or in combination, such as ultraviolet light exposure, $\lambda$ radiation, severe dehydration, vacuum cooling, and heating.[94,96] These treatments facilitate the formation of cross-linked structures by enhancing the intermolecular interactions between the carboxylic and amine group residuals in collagen macromolecular chains. While physical treatments can avoid the use of exogenous toxic chemicals, low uniformity and degree of cross-linking are issues.[97] Compared to physical treatment, chemical cross-linking achieves a more uniform and extensive degree of cross-linking in collagen. As the most widely used cross-linking approach, cross-linking agents promote covalent bond formation by establishing interfibrillar connections between collagen fibers. Frequently used chemical cross-linking agents comprise glutaraldehyde, dialdehyde starch, chitosan derivatives, sodium alginate, genipin, and 1-ethyl-3-(3 dimethyl aminopropyl)carbodiimide/N-hydroxysuccinimide (EDC/NHS).[98,99] Glutaraldehyde is recognized as a very effective cross-linker, but residual molecules are associated with cytotoxicity.

Conversely, dialdehyde polysaccharide (e.g., starch, cellulose, sodium alginate) demonstrates enhanced biocompatibility, offering a reduced potential for cytotoxic responses.[100,101] EDC/NHS represents a 'zero-length' cross-linking technique that activates collagen molecules, enabling the direct bonding of adjacent fibrils. This method is distinguished by its avoidance of exogenous substances, ensuring biocompatibility and noncytotoxicity.[94] Besides, collagen entanglement can be enhanced by the addition of acids and adjusting the pH values below the isoelectric point.[102] The incorporation of metal ion chelates such as $Ca^{2+}$ and $Fe^{3+}$ into collagen-based films can improve their mechanical and barrier properties, owing to the ions' strong electrostatic interactions with biopolymers.[103] Enzymatic cross-linking, on the other hand, uses enzymes such as lysyl oxidase, transglutaminase, polyphenol oxidase, and peroxidase as catalysts to polymerize collagen via modifying the amino group residuals and forming intra- or intermolecular fibrillar bonds.[95,98,99] Enzymatic cross-linking is notable for its mild reaction conditions, low toxicity, and high catalytic efficiency. Furthermore, the characteristics of collagen-based materials can be improved through a synergistic strategy that integrates various blending and cross-linking methods.

*6.1.1. Collagen-Based Film Manufacturing Methods.* Collagen exhibits exceptional film-forming capabilities and a strong ability to encapsulate bioactive compounds, including antimicrobial and antioxidant agents. However, its mechanical and thermal properties tend to diminish postextraction, which restricts its use in food packaging. To enhance these properties, incorporating exogenous polymers, fillers, and cross-linkers is a common strategy for creating collagen-based composite (edible) films with improved mechanical, barrier, and thermal properties. Various processing techniques have been employed to produce collagen-based composite materials with diverse properties and functionalities, as outlined in Table 3. Solution casting is predominantly utilized in academic research for fabricating collagen-based films, favored for its simplicity and convenience. This method involves dissolving collagen, optionally with exogenous polymers and fillers, in a solvent to create solutions or dispersions, which are subsequently cast and dried to form a film.[88,104,105]

Nevertheless, solution casting methods are difficult to apply for industrial purposes and face challenges in scale-up.[106,107] On the other hand, extrusion technology is particularly suitable for the industrial manufacture of collagen-based materials, including edible films and sausage casings. Typically, the collagen extraction process involves mixing collagen with water and various additives to form a paste. This paste can be further combined with additional exogenous polymers and fillers. The resulting mixture/gel is processed through various extrusion methods.[95] In the coextrusion method applied to sausage casings, both the collagen gel and sausage components are extruded simultaneously through either a rotating cone mechanism or a counter-rotating nozzle system. This rotational action aligns the collagen fibers in a specific direction, enabling the adjustment of the film's strength and elasticity by changing the rotational speeds of the inner and outer cone.[108] Specifically, lower rotational speeds result in films that exhibit higher tensile strength and elasticity because of a more chaotic fiber orientation and enhanced entanglement of the collagen fibers. As the collagen film exits the nozzle, it undergoes precipitation and dehydration in a saline solution (such as saturated sodium chloride), which leads to the formation of a robust collagen network with enhanced tensile strength.[109] Following this, treatments with agents like glutaraldehyde, glyoxal, liquid smoke, sugars, or minerals are applied to facilitate cross-linking and enhance the stability of the film.

Additionally, polyethylene as a synthetic polymer was also blended with hydrolyzed collagen to form packaging materials and reduce the environmental impact of plastics.[110] Polyethylene films incorporating up to 50 wt % of hydrolyzed collagen were processed using the blown extrusion technique, resulting in transparent and flexible films. Notably, the film with 20% collagen exhibited satisfactory thermomechanical properties.[110] Blends of biodegradable thermoplastic polyester, specifically poly(butylene succinate-*co*-adipate) (PBSA), and hydrolyzed collagen were also processed using blow film extrusion and injection molding, incorporating up to 20% weight of collagen.[111,112] In their study, hydrolyzed collagen served as a plasticizer, effectively decreasing the melt viscosity


https://doi.org/10.1021/acsfoodscitech.4c00938
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Table 3. Examples of Collagen-Based Composite Materials and Their Forming Techniques

| Collagen source | Exogenous polymers/fillers | Processing method | Material | Main findings | References |
|---|---|---|---|---|---|
| Hydrolyzed collagen | Poly(butylene succinate-*co*-adipate) | Melting extrusion and injection molding | Film | Blend up to 20 wt % collagen was suitable for injection molding and resulted in films with good tensile properties. | 111, 112 |
| | | | | The secondary structure of the hydrolyzed collagen influenced the rheology, morphology, and mechanical properties of the produced blends. | |
| Pepsin-soluble collagen (Calfskin) | Chitosan, ZnO nanoparticles, mulberry extract | Solution casting | Film | The composite films showed higher barrier, mechanical, and antioxidant properties compared to the collagen counterpart. | 123 |
| Bovine collagen (Cowhide) | Celluloses in different geometries | Solution casting | Film | Cellulose enhanced films' mechanical properties, water resistance, and thermostability. | 90, 104 |
| Bovine collagen (Cowhide) | - | Enzymatic cross-linking and casting | Film | Laccase successfully cross-linked collagen film. | 88, 89 |
| | | | | Co-adding gallotannins enhanced the film's properties | |
| Type I collagen from the bovine tendon | Poly(vinyl alcohol) | Electrospinning | Fiber | Although collagen presented difficulty in spinning, it had good interaction with PVA, creating homogeneous fibers. | 117 |
| | | | | Collagen had a 70% prevalence of the helical structure after the spinning process. | |
| Hydrolyzed collagen | Sodium alginate, glycerol, and nano-$SiO_2$ | Solution casting | Film | The addition of $SiO_2$ led to enhanced thermal stability and mechanical properties. | 105 |
| Bovine collagen (Cowhide) | Carboxymethyl chitosan-amorphous calcium orthophosphate (CMCS-ACP) nanoparticles | Solution casting and socking | Film | Mineralization using CMCS-ACP improved the wet-state mechanical properties of films. | 91 |
| Bovine collagen (Cowhide) | Carboxymethyl cellulose (CMC) and glycerol | Molding and immersing | Film | CMC improved the dry mechanical properties but weakened the wet ones. | 92 |
| | | | | CMC improved the shrinkage stability and thermostability. | |
| Bovine native collagen and bovine telopeptide-poor collagen | Soy protein isolate | Nozzle extrusion and precipitation | Film - sausage casing | Co-gelling proteins are more prone to be incorporated into native collagen. | 109 |
| | | | | The substitution of collagen by co-gelling proteins decreases the tensile strength. | |
| Marine collagen | Graphene oxide and iron oxide nanoparticles | Solution casting | Film | The incorporation of both oxides improved physicochemical properties and decreased the hydrophilicity of the films. | 124 |
| Acid-soluble collagen (bovine Achilles tendon) | Tannic acid-functionalized 2D-clay nanoplatelets | Solution casting | Film | A transparent collagen nanocomposite film was developed. | 125 |
| | | | | The film exhibited reinforced thermal stability, enzymatic resistance, tensile strength, and hydrophobicity. | |
| Type I collagen of bovine skin | Polycaprolactone (PCL) | Electrospinning | Fiber | Collagen/PCL nonwoven had smaller fiber diameters compared to pure PCL. | 120 |
| | | | | FTIR analysis confirmed the interaction between PCL and collagen through hydrogen bonding. | |
| Bovine collagen (Cowhide) | Glutaraldehyde | Chemical cross-linking and casting | Film | Acid cross-linking led to intramolecular cross-linking. | 93 |
| | | | | Basic cross-linking led to intermolecular cross-linking. | |
| | | | | Film properties could be modulated by controlling reaction pH. | |
| Bovine collagen (Cattle skin) from four sources | - | Extrusion and precipitation | Film - sausage casing | The suitability of collagen is partly determined by soluble collagen content. | 126 |
| | | | | Soluble collagen content is associated with dispersions' mechanical and rheological properties. | |
| | | | | Collagen from young cattle skin is a potential source for coextruded sausage casings. | |
| Bovine collagen (Cowhide) | Enzymatically oxidized phenolic acids (EOPA) | Solution casting | Film | EOPA enhanced the film's water vapor permeability, mechanical properties, and thermostability. | 127 |
| | | | | These properties were improved with the increased phenolic hydroxyl number. | |
| Bovine collagen (Cowhide) | Phenolic acid-grafted chitosan | Solution casting | Film | The film's properties were phenolic acid dependent. | 128 |
| | | | | Phenolic acid improved the antioxidant and antimicrobial activities of the films. | |
| Bovine collagen (Cowhide) | Sodium polyacrylate and a metal ion ($CaCl_2$, $FeCl_3$ or $AgNO_3$) | Solution casting | Film | Metal ions improved the mechanical properties, thermal stability, and barrier properties of the composite film. | 103 |
| Hydrolyzed collagen | Polyethylene | Blown extrusion | Film | Transparent, cohesive and flexible film was obtained. | 110 |



https://doi.org/10.1021/acsfoodscitech.4c00938
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**Table 3. continued**

| Collagen source | Exogenous polymers/fillers | Processing method | Material | Main findings | References |
|---|---|---|---|---|---|
| Acid soluble collagen | Zein and gallic acid | Electrospinning | Fiber | Satisfactory thermomechanical properties characterized films containing 20% collagen.<br>The smooth and bead-free submicron fiber was produced.<br>Strong interactions and hydrogen bond formation occurred among the compounds.<br>Gallic acid decreased fibers' hydrophobicity but increased antioxidant activity. | 121 |
| Type I collagen | Poly(lactic-*co*-glycolic acid) (PLGA) | Electrospinning | Fiber | Incorporating collagen in the PLGA matrix promoted an increase in the material's rigidity, showing a 38% and 70% increase in the elastic modulus and tensile strength compared to pure PLGA. | 118 |

in PBSA-based blends. When 5% weight of collagen was added to the PBSA matrix, the elongation at break improved from 1000% to 1200%, while the break stress and Young's modulus remained comparable to those of pure PBSA.[111] Therefore, collagen-based composites emerge as promising options for creating sustainable materials suitable for food and packaging applications.

*6.1.2. Collagen-Based Electrospun Fibers.* Electrospinning, known as electrostatic spinning, is a flexible, nonthermal technique used to produce nonwoven materials made up of fibers with diameters ranging from several hundred nanometers to several micrometers.[113] This electrohydrodynamic technique involves dissolving the polymer(s) in a solvent, which can be either pure or blended, to create a spin-dope solution with ideal properties for electrospinning into fibers. Various electrospinning configurations have been explored, including needle spinneret and free-surface designs.[114,115] In standard needle electrospinning, the spin-dope is pumped toward an electrostatically charged spinneret, with the resulting surface charges causing the solution to eject toward a grounded target substrate. During this process, solvent evaporation and Coulombic repulsion facilitate the production of ultrafine, continuous fibers that are arranged into a nonwoven structure. Although a single-needle electrospinner offers limited production rates, utilizing multiple needles can significantly increase throughput; however, this approach adds complexity to the system setup.[114]

In contrast, needle-free electrospinning processes utilize different spin electrode configurations (e.g., wires, cylinders, disks, balls, planar metals, or helical coils) to achieve higher production rates. In this method, a polymer solution is deposited onto a positively charged electrode, forming multiple jets that travel toward a collector substrate positioned between the rotating electrode and the ground electrode.[116] Free-surface electrospinning processes are generally better suited for large-scale commercial production compared to the spinneret method. The electrospinning process and the resulting fiber characteristics are affected by several factors, including processing parameters (such as voltage, the distance between the spinning and collecting electrodes, and the flow rate of the spin dope), solution properties (including surface tension, electrical conductivity, viscosity, and solvent vapor pressure), and environmental conditions (like temperature and relative humidity).[114] Collagen and its composites with synthetic and biopolymers have been successfully electrospuned into ultra-thin fibers with diverse properties (Table 3).

Nonwovens produced from these fibers are characterized by porosity, high surface-to-volume ratio, lightweight and tunable morphology. These materials have extensive applications in wound dressings, tissue engineering, encapsulation, and food packaging.[117−121] Choosing a suitable solvent system for collagen is important because it has a significant impact on the structural properties of collagen. Solvents such as hexafluoro-2-propanol and tetrahydrofuran tend to produce collagen electrospun fibers with a less ordered structure, similar to the properties associated with gelatin, characterized by broken $\alpha$-linkages.[122] These solvents can induce hydrolysis of collagen molecules, destroying the bonds that maintain the triple helical structure and causing denaturation.[120] These changes not only reduce the biological activity of collagen but also impair the tensile properties of collagen nanofibers.[119] Addressing this challenge, Mauricio et al. utilized an acetic acid aqueous solution to produce type I collagen/poly(vinyl


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alcohol) electrospun fibers using a single-needle setup.[117] Remarkably, these fibers retained 70% of their helical structure postspinning and exhibited the same moisture temperature as native collagen. Chakrapani et al. electrospun type I collagen of bovine skin blended with polycaprolactone in acetic acid solution.[120] The fibers had a diameter range of 100−200 nm with an optimum porosity of 60%.

Additionally, Song et al. (2022) developed a collagen/zein composite electrospun nonwoven, infused with garlic acid through a single-needle setup. In their research, collagen and zein were dissolved in a tertiary solvent mixture comprising acetic acid, ethanol, and water, incorporating up to 10 wt % garlic acids into the fibers. This garlic acid-loaded nonwoven demonstrated efficacy in preserving the quality of tilapia muscle and extending its shelf life, highlighting its potential for active food packaging applications.[121]

**6.2. Collagen Used as Food Additives.** In food processing, collagen can be used as an ingredient to improve food quality. For example, collagen fibers work well as emulsifiers in food applications, especially acidic foods.[129,130] Bioactive substances can also be encapsulated in collagen carriers, as evidenced by the excellent antioxidant activity of rosemary extract, which prevents sausage lipid oxidation during storage.[131] Pre-emulsifying wheat grass and collagen in chicken patties instead of pork back fat at acceptable replacement ratios (40% or less) can help minimize cooking losses while maintaining the organoleptic quality of the patties.[132] Collagen can be added to hams and frankfurters as an extender and binder to improve the binding quality (fuzziness and cooking loss) of foods during refrigerated storage and cooking.[133] In the process of preparing chicken ham, collagen can play the role of vegetable protein, improve the texture of the ham and reduce losses due to compression and freezing while maintaining positive organoleptic properties.[134]

**6.3. Collagen for Food Packaging and Preservation Applications.** In food packaging and preservation, collagen is an effective film-forming material that can be used as an alternative to nondegradable plastic packaging materials. Collagen can easily create a stable network that can stretch or contract in response to mechanical activity in a continuous process, making it an excellent material for casings throughout sausage manufacturing.[109,135] Much like natural casings, which are stiff and translucent films derived from an animal's gastrointestinal tract, collagen casings also exhibit unique cooking properties and tenderness when used to encase sausages.[14] Collagen casing prevents direct contact with air and water vapor, which can reduce the amount of gravy oozing from the sausage.[136] The strong mechanical properties and barrier properties of collagen films allow them to be effectively used as edible wrappers for a variety of fudges.

Nevertheless, some application-related problems may arise, such as the collagen film swelling rapidly in water and the possibility of the collagen shell rupturing or detaching from the meat during meat loading or cooking.[19,137,138] Physical (dehydration heat and aging treatment),[132,134] chemical (glutaraldehyde)[135] or enzymatic (transglutaminase)[136] cross-linking methods are achieved through noncovalent linkages between or within collagen molecules. Covalent bond formation can enhance the physicochemical and mechanical properties of collagen casings and films. While chemical or enzymatic cross-linking is a quick and efficient method, it may pose risks to human health.[136,139]

In contrast, physical cross-linking is generally safer and more environmentally friendly; however, it tends to have reduced cross-linking effectiveness and may lead to collagen degeneration.[140] It is possible to get beyond the drawbacks of single cross-linking that were previously described by combining two or more cross-linking techniques. For instance, Chen et al.[19] examined the effects of drying temperature and glutaraldehyde cross-linking on collagen casings and discovered that although the higher drying temperature induced a lower degree of denaturation of collagen, it enhanced the physicochemical and mechanical qualities of the glutaraldehyde-cross-linked casings.

Collagen can also be processed into films that can be cut to the precise dimensions required by consumers. For example, Jiang et al. (2020) cut collagen-chitosan-lemon (C−CCS-LEO) films into 15 cm × 15 cm bags to package 100 g of refrigerated pork, mechanically sealed, and stored at 4 °C for 21 days.[141] Research has demonstrated that C−CS-LEO film exhibits excellent antioxidant and preservative properties, making it suitable as a packaging material for refrigerated pork. Additionally, collagen films significantly enhance the juiciness and reduce shrinkage loss in mesh products, with no discernible negative impact on meat color or lipid oxidation.[142]

Theoretically, wrapping fresh meat or meat products, such as roasts or hams, with collagen film can prevent the elastic net from adhering. During the cooking or smoking process, collagen films can integrate with the meat, allowing the elastic mesh to be easily removed from the final product while enhancing its visual appeal without compromising the surface. Despite the growing body of research on collagen-based films, there is a scarcity of studies specifically examining their application in meat products.[143−145]

*6.3.1. Active Packaging.* New packaging films (CCG/PL) have been developed using collagen, chitosan functionalized with gallic acid (GA), and $\varepsilon$-polylysine ($\varepsilon$-PL) in varying proportions of 2.5%, 5%, and 10% by weight.[20] These films were specifically formulated to prolong the storage life of pork at 4 °C. Fourier transform infrared analysis indicated the formation of hydrogen bonds between collagen and gallic acid (GA), while no significant interactions were observed between the polymers and $\varepsilon$-polylysine ($\varepsilon$-PL). Scanning electron microscopy (SEM) images revealed that the cross sections of the CCG/PL films were dense; however, $\varepsilon$-PL aggregation was noted when the content reached 10% by weight. The CCG/PL films demonstrated effective light-blocking capabilities, with UV light transmittance below 4% within the 200−350 nm range. Compared to the CC film, the DPPH free radical scavenging rate increased significantly by 84.35%, attributed to the synergistic effects of GA and $\varepsilon$-PL in enhancing antioxidant activity. As shown in Figure 5a and 5b, the CCG/PL film containing 5% $\varepsilon$-PL exhibited excellent antimicrobial properties against *S. aureus* and showed good tensile strength (65.34 MPa). When used to wrap pork, the CCG/PL film with 5% $\varepsilon$-PL effectively reduced lipid oxidation and inhibited bacterial growth during storage, leading to an approximate shelf life extension of 5 days compared to pork stored in polyethylene film.

Collagen, the main component of the extracellular matrix, is extensively utilized across various industries. It can be used in its natural fibrous form or after undergoing denaturation. This versatility stems from its numerous functional properties and its capacity to be processed into a wide variety of products, such as gels, porous scaffolds, fibers, films, meshes, and micro/nanoparticles, as noted by Oliveira et al.[146] In this context,


https://doi.org/10.1021/acsfoodscitech.4c00938
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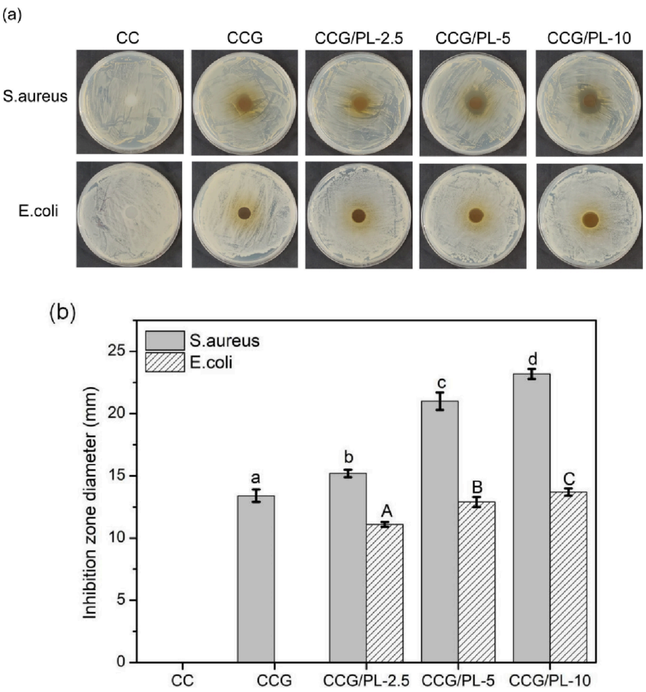


**Figure 5.** Antibacterial activity of collagen/chitosan (CC), collagen/chitosan-g-gallic acid (CCG), collagen/chitosan-g-gallic acid/2.5% ε-polylysine (CCG/PL-2.5), collagen/chitosan-g-gallic acid/5.0% ε-polylysine (CCG/PL-5) and collagen/chitosan-g-gallic acid/10% ε-polylysine (CCG/PL-10) films against *S. aureus* and *E. coli*. Reproduced with permission from Zheng et al.[20] Copyright 2023 Food Hydrocolloids.

gelatin, which is collagen that has been thermally denatured and has a molecular weight ranging from 15 to 250 kDa, exhibits unique rheological properties. It is primarily used in the food industry as a food additive, a microencapsulating agent, and a biodegradable packaging material, as emphasized by Bello et al.[147]

Laccase was utilized to oxidize five distinct phenolic acids. UV−vis and FTIR analyses of the oxidized phenolic acids indicated the formation of quinones, showing an increase in their quantity relative to the number of hydroxyl groups present in the phenolic acids. These quinones were subsequently utilized to modify collagen films.[127] FTIR and X-ray photoelectron spectroscopy confirmed the formation of covalent cross-links between the quinones and the -$NH_2$ groups of collagen molecules. Collagen films cross-linked with quinones demonstrated enhanced physicochemical properties, including decreased water vapor permeability, increased resistance to enzymatic degradation, improved mechanical strength, and enhanced thermal stability. These properties significantly improved with a higher number of phenolic hydroxyl groups in the phenolic acids. Furthermore, the incorporation of phenolic acids conferred antioxidant and antibacterial properties to the collagen films. These results indicate that collagen films cross-linked with laccase-oxidized phenolic acids have promising potential for use in active edible food packaging.[127]

Fish processing byproducts are often regarded as cost-effective resources, commonly used as feed in aquaculture or as agricultural fertilizers. This research focused on extracting type I collagen from discarded fish skin and utilizing it in the production of active food packaging films. Carboxymethyl cellulose (CMC) acted as a cross-linking agent in the collagen films, while root extract (BLRE) served as an antioxidant. The films containing BLRE exhibited outstanding characteristics, including high biodegradability, reduced transparency, and strong UV−vis barrier properties. Additionally, the BLRE-loaded films demonstrated impressive antioxidant activity. When tested with various food simulants, these films released

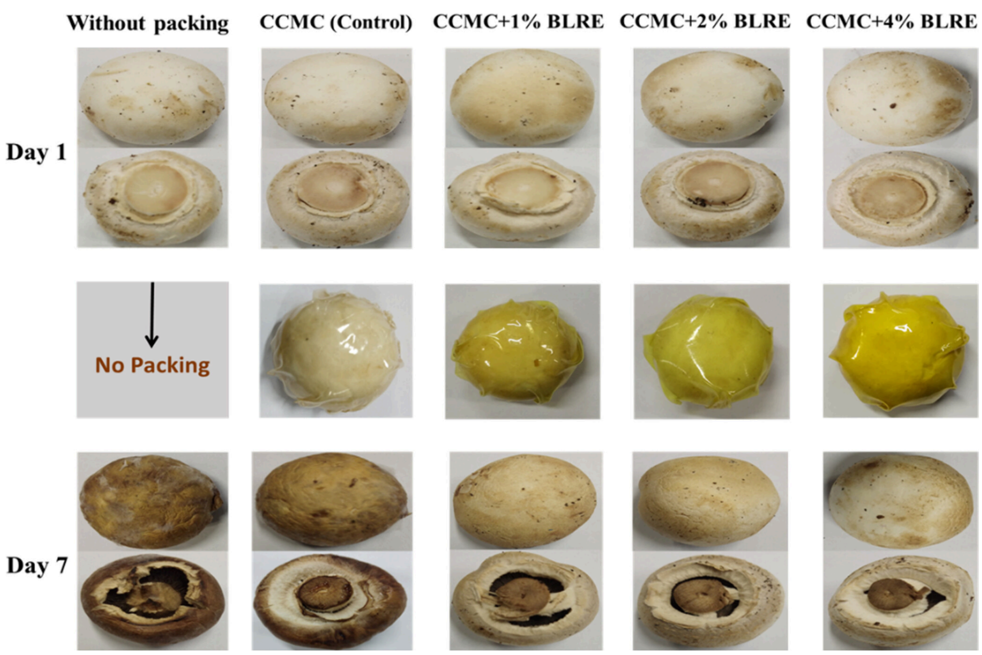


**Figure 6.** Effect of packaging on the quality of mushrooms packaged with collagen/carboxymethyl cellulose-based films for 7 days. CCMC: collagen + carboxymethyl cellulose, CCMC + 1% BLRE: collagen + carboxymethyl cellulose (CMC) + 1% *Berberis lyceum* root extract (BLRE), CCMC + 2% BLRE: collagen + CMC + 2% BLRE, CCMC + 4% BLRE: collagen + CMC + 4% BLRE films. Reproduced with permission from Ahmed et al.[148] Copyright 2022 Journal of Food Processing and Preservation.


https://doi.org/10.1021/acsfoodscitech.4c00938
ACS Food Sci. Technol. 2025, 5, 1767−1784

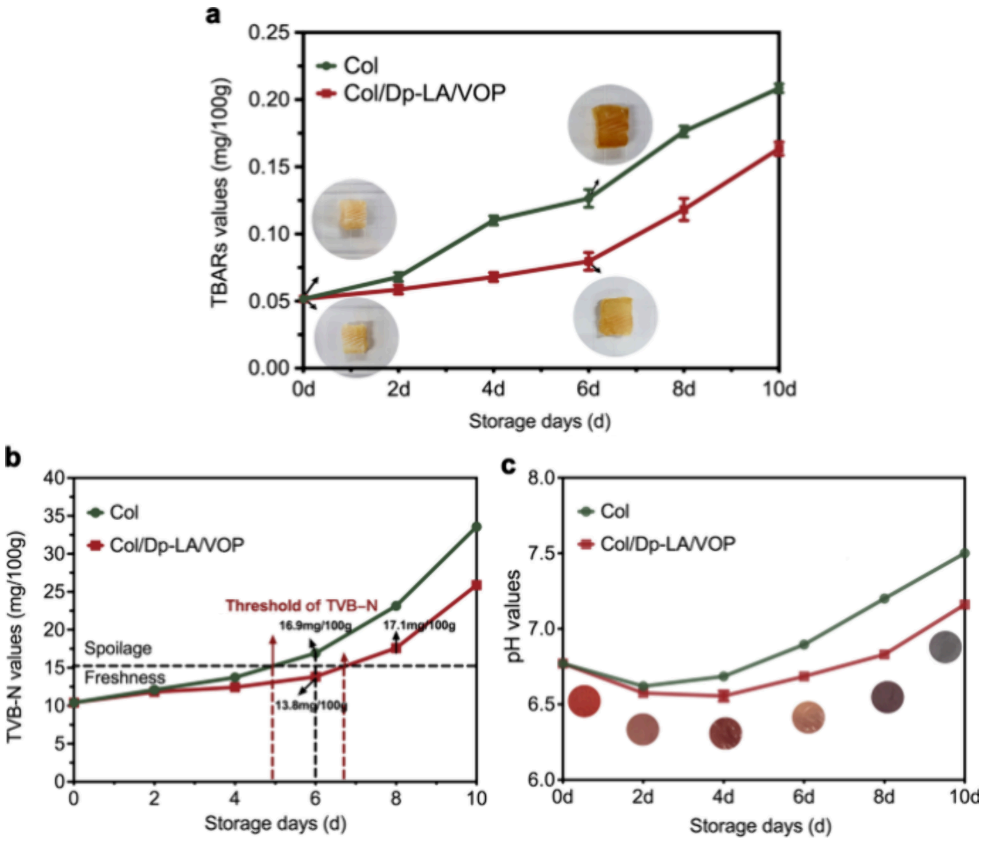


**Figure 7.** (a) The TBAR values and photograph, (b) TVB-N values, and (c) pH values of the fish fillets wrapped in the Col film and Col/Dp-LA/VOP film, respectively, and the color changes of the Col/Dp-LA/VOP film for monitoring the fish freshness at 4 °C for 10 days. Reproduced with permission from Yin et al.[149] Copyright 2023 Collagen and leather.

higher levels of antioxidants in acidic and alcoholic simulants compared to fatty simulants. Furthermore, the films were used for packaging mushrooms, successfully extending their shelf life (Figure 6). As a result, this study advocates for the extraction of collagen from fish waste and its application as eco-friendly materials for food packaging.[148]

*6.3.2. Intelligent Packaging.* Yin and co-workers[149] developed an advanced collagen-based packaging film that possesses both strength and the ability to indicate fish freshness visually. Microscopic analysis using scanning electron microscopy and atomic force microscopy revealed that films produced by combining delphinidin with collagen cross-linked via laccase displayed a denser structure with a rougher surface. In comparison to the pure collagen film, the laccase-catalyzed collagen/delphinidin film (Col/Dp-LA film) demonstrated a significant increase in both dry and wet tensile strengths, with enhancements of 41.74 and 13.13 MPa, respectively. Additionally, Col/Dp-LA films exhibited remarkable antioxidant and barrier properties, as indicated by their ability to scavenge free radicals, effectively transmit light, and resist water vapor transmission.[149] To prepare intelligent collagen-based films, pigment from *Vaccinium oxycoccus* was integrated into Col/Dp-LA films. This addition enabled the films to change color in response to varying pH levels. When used to preserve fish fillets, the film released delphinidin, effectively mitigating oxidative rancidity and extending the shelf life of the fish by 2 days. Notably, as the fish quality declined, the color of the film changed distinctly from purplish-red to gray-blue (Figure 7). These findings indicate that collagen films treated with delphinidin, laccase, and *Vaccinium oxycoccus* pigment have considerable potential for applications in the active and intelligent food packaging industry.[149]

A new type of packaging film referred to as CCG/PL, was developed to preserve pork stored at 4 °C. This packaging material is composed of collagen, chitosan functionalized with gallic acid (GA), and $\varepsilon$-polylysine ($\varepsilon$-PL) in varying proportions of 2.5%, 5%, and 10% by weight.[20] Fourier transform infrared analysis revealed the formation of hydrogen bonds between collagen and gallic acid (GA), while no significant interactions were observed between the polymers and $\varepsilon$-polylysine ($\varepsilon$-PL). SEM images indicated that although the cross-section of the CCG/PL film was dense, $\varepsilon$-PL tended to aggregate when its content reached 10%. These CCG/PL films effectively blocked UV light, exhibiting less than 4% transmittance in the 200−350 nm range. Compared to conventional CC film, the CCG/PL film demonstrated a remarkable 84.35% increase in DPPH free radical scavenging activity, attributed to the combined antioxidant effects of GA and $\varepsilon$-PL. The CCG/PL film containing 5% $\varepsilon$-PL exhibited strong antimicrobial properties against *S. aureus* and showcased good tensile strength (65.34 MPa). When used to wrap pork, this film effectively reduced lipid oxidation and inhibited bacterial growth during storage, resulting in an approximate shelf life extension of 5 days compared to pork stored in traditional polyethylene film.[20]

*6.3.3. Coating.* The shelf life of food can be extended by applying surface coatings. Furthermore, it has been demonstrated that collagen coatings offer meat a barrier against oxygen and water, which lessens rancidity, color degradation, and purging.[150] Liu et al. investigated the quality of fresh red porgy fillets at 4 °C using collagen-chitosan composites coated with pepsin-soluble collagen (PSC) produced from blue shark skin. The greatest results for K value, drip loss and sensory evaluation were obtained by coating with 1% chitosan solution containing 0.8% PSC. Additionally, the shelf life was extended to 10 days compared to the control group (uncoated).[151] Collagen coatings, such as collagen-based films, have been extensively studied,[149] but there are few reports on their use in meat packaging. In contrast, extensive research has been conducted on the use of gelatin, which is derived from the partial hydrolysis of collagen, to preserve and extend the shelf life of meat products.[152−154]

Lima et al. developed an innovative edible coating by mixing collagen and glycerol with galactomannan extracted from the seeds of *Adenanthera pavonina* and *Caesalpinia pulcherrima*.[155] The primary objective was to assess the impact of these coatings on the gas exchange rate when applied to mangoes and apples. The initial phase of the research involved formulating coating solutions with appropriate wettability for each fruit type. These solutions were then analyzed for their mechanical properties, color, opacity, and permeability to $CO_2$, $O_2$, and water vapor.

When mangoes were coated with a solution comprising *A. pavonina* galactomannan (0.5%), collagen (1.5%), and glycerol (1.5%), gas transfer rates were compared to uncoated mangoes. The coated mangoes exhibited a 28% reduction in oxygen consumption and an 11% decrease in carbon dioxide production compared to their uncoated counterparts.[155] Similarly, in the case of apples, a coating solution containing *C. pulcherrima* galactomannan (0.5%) and collagen (1.5%) was applied without glycerol. Apples with the coating showed approximately a 50% reduction in carbon dioxide production and oxygen consumption compared to apples without the coating. These findings indicate that these coatings could serve as effective tools for prolonging the shelf life of mangoes and apples by decreasing the rate of gas exchange in the fruit.[155]

This review discusses collagen derived from animal by-products of food production as a promising and sustainable packaging material for food processing applications. The presence of significant biomolecules in food processing waste from animals has garnered considerable attention from researchers, consumers, and various regulatory agencies. Collagen-based composite films exhibit excellent biological, functional, and mechanical properties. These unique attributes, along with biodegradability, edibility, and bioavailability, have facilitated the widespread use of collagen-based composites in numerous food processing applications. Moreover, several biological characteristics of these composites, including antimicrobial, antioxidant, and anticoagulant activities, have been extensively reviewed.

Given these biological functions, collagen derived from animal byproducts has significant potential for applications in food safety and packaging. However, the current availability of collagen and its derivatives is limited, and standardized protocols for their preparation remain lacking. Further research is needed to determine the optimal method for incorporating collagen and its derivatives as additives into various foods, as well as to investigate their potential interactions with other food ingredients during processing and storage. Additionally, the water resistance of collagen-based coatings or films is inadequate, and these materials may struggle to withstand the mechanical stresses associated with continuous food processing. Therefore, further investigation is necessary to understand the interplay between the mechanical, physicochemical, and functional properties of collagen-based active food packaging materials and the controlled release of active ingredients.

A combinatorial approach is essential because no single polymer can meet all the requirements for a desired practical application. Therefore, the design of collagen-based composite biomaterials should be explored to address the limitations of collagen and create biomaterial composites with all the necessary properties required for food safety applications. The side chains of collagen are rich in amino acid residues, providing numerous opportunities for enzymatic, chemical, and physical modifications. These modifications could help overcome the current limitations associated with collagen-based food packaging. Furthermore, the exact structure−activity relationships and molecular mechanisms of biologically active collagen and its derivatives remain unclear. The lack of clinical efficacy data and the high cost of industrial manufacturing further hinder the development of collagen as a functional food ingredient.

Nevertheless, addressing these challenges is crucial to promoting the application of enhanced collagen and its derivatives in the food sector. Since current development is still in the experimental stage, continued research is essential to ensure long-term safety. Despite these hurdles, the exploration of all known natural sources of collagen, along with the evaluation of synthetic alternatives, has had a significant impact on the collagen market. Consequently, this trend is expected to continue, creating new and promising research opportunities in the food-related sector.

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Complete contact information is available at: https://pubs.acs.org/10.1021/acsfoodscitech.4c00938


https://doi.org/10.1021/acsfoodscitech.4c00938
ACS Food Sci. Technol. 2025, 5, 1767−1784

### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

This research was supported by a grant from the National Research Foundation of Korea (NRF) grant funded by the Korean government (MSIT) (2022R1A2B5B02001422).

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