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Jellyfish collagen: A promising and sustainable marine biomaterial with emerging applications in food, cosmetics, and biomedical— A review

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ABSTRACT

In recent years, consumer awareness of the benefits of collagen has driven a steady increase in demand for collagen-based products. However, mammalian collagen poses health risks and may not be suitable for individuals due to religious reasons. As a result, marine collagen has emerged as a safer and more promising alternative, gaining significant attention. Jellyfish collagen, in particular, has shown potential as a transformative marine biomaterial with applications in food, supplements, cosmetics, medicine, and biomedical materials. It offers several advantages, including antioxidant properties, anti-inflammatory effects, and immunomodulatory activities. Despite its potential, jellyfish collagen products are still scarce in the market. This review examines the extraction and characterization of jellyfish collagen, its physicochemical properties, and the opportunities and challenges in utilizing this marine collagen. Finally, it explores the potential commercial value and future product development to enhance human health.

1. Introduction

Collagen, the most prevalent and widely distributed structural protein in the human body, can primarily be found in the skin, cartilage, tendons, cornea, and various other tissues, accounting for 25–35 % of the body's total protein content (Chen et al., 2019a; Lechner et al., 2014; Subhan et al., 2021). Collagen plays a crucial role in maintaining and supporting cellular, tissue, and organ functions and in repairing tissue damage (Ganesan et al., 2019). Therefore, collagen has garnered significant interest in the fields of food, cosmetic, and pharmaceutical science for its potential as a functional component in foods and nutraceuticals, biomedical materials, and skin grafts (Ahmad et al., 2016; Alcock et al., 2019; Mearns-Spragg et al., 2020). As illustrated in Table 1, collagen products have garnered significant attention from numerous companies and industries. The worldwide market for collagen is expected to exceed $18.7 billion by 2030, driven by the growing demand for this product in the health and cosmetic sectors (Grand View Research, 2025).

While mammalian-derived collagen dominates commercial production, its utilization faces constraints: zoonotic disease risks (bovine spongiform encephalopathy (BSE), transmissible spongiform encephalopathy (TSE), foot-and-mouth disease (FMD), mad cow disease (MCD), and avian influenza (AI), religious prohibitions, and immunogenic complications (Aamodt et al., 2016; Cao et al., 2022; Chen et al., 2019b; Coppola et al., 2020; Felician et al., 2018). These limitations have accelerated exploration of alternative sources, with jellyfish collagen emerging as a promising candidate exhibiting superior bio-compatibility (Ranasinghe et al., 2022), enhanced fibroblast proliferation efficacy (Zhao et al., 2023), and ecological synergy by mitigating jellyfish bloom-induced marine damage (Bonaccorsi et al., 2020). Unlike recombinant collagen from microbial systems plagued by low yields and costly post-translational modifications, jellyfish collagen combines cost-efficiency with reduced immunogenicity, leveraging abundant biomass from climate-driven population explosions.

The jellyfish harvest season is brief. Moreover, jellyfish have a high water content, are prone to autolysis, and require a traditional processing technique that involves salting and drying, as shown in Fig. 1. However, if jellyfish are utilized for collagen production, their economic market value can be significantly enhanced. This study aims to elucidate the potential of jellyfish collagen as a promising and sustainable marine

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Table 1
Commercial collagen products.

Company	Sources of collagen	Product type	Application fields	Country
Acmetea	Fish	Collagen powder	Food/Health supplements/ Beauty	France
Amway	Fish	Collagen peptide drink	Food/Health supplements	America
Meiji	Fish	Collagen powder	Food/Health supplements/ Beauty	Japan
GNC	Fish and bovine	Capsules, tablet, powder	Food/Health supplements/ Beauty	America
Neocell	Fish	Capsule, tablet, powder	Food/Health supplements/ Beauty	America
Gelita	Bovine hide, bone, pigskin, and fish	Collagen powder, functional fudge	Food/Health supplements/ Beauty	Germany
Rousselot	Fish,pigs and cows	Collagen powder, functional fudge, hemostatic material	Food/Health supplements /Biomedicine/ pharmacy.	France
Vida glow	Fish	Collagen powder,oral liquid	Food/Health supplements/ Beauty	Australia
Youtheory	Fish	Collagen Powder, tablet	Food/Health supplements/ Beauty	America
Nature's Bounty	Pigs and cows	Functional fudge,capsule	Food/Health supplements/ Beauty	America
Vital Proteins	Cows,fish	Collagen powder	Food/Health supplements	America
Shiseido	Fish	Oral liquid	Food/Health supplements/ Beauty	Japan
Giant biogene	Recombinant collagen	Essence, emulsion, mask, cream, repair dressing	Cosmetics	China
Jellagen	*Rhizostoma pulmo*	Medical grade collagen	Collagen biomaterial supply and medical equipment product development	Britain
KollaJell	*Cannonball jellyfish*	Capsule	Food/Health supplements/ Beauty	America

(Sources: Product composition specifications from official manufacturer websites. Accessed 19 June 2025.)

biomaterial (Balikci et al., 2024). We systematically investigate its molecular architecture, revealing species-specific polymorphisms that discuss existing taxonomic controversies in source identification. A comparative analysis evaluates extraction methods' efficiency and sustainability alongside novel functional enhancement strategies. Furthermore, this work further investigates transformative applications of jellyfish collagen at the convergence of food science innovation, biomedical engineering breakthroughs, and advanced cosmeceutical technologies.

2. Jellyfish collagen

2.1. Molecular characteristics and taxonomic controversies of jellyfish collagen

Collagen, the most abundant protein in animal tissues, is essential for supporting cell proliferation, migration, and differentiation (Hung et al., 2019; Smith et al., 2023). It is composed of three α-peptide chains, arranged as homotrimers or heterotrimers, featuring repeating sequences of G-X-Y, where G represents glycine, X is often proline, and Y is typically hydroxyproline. These chains self-assemble into a right-handed triple-helix, with glycine located in the center and proline and hydroxyproline positioned on the outer surface (Fig. 2) (Beck et al., 1998; Carvalho et al., 2018; Cheng et al., 2017; Sherman et al., 2015). The triple-helix structure is stabilized by hydrogen bonds and electrostatic interactions, contributing to collagen's rod-like structure and the formation of collagen fibrils through a staggered arrangement (Yang et al., 2023). While 28 types of collagen have been identified in mammals, the collagen derived from jellyfish shares similarities with these mammalian collagens, but also exhibits unique characteristics due to its marine invertebrate origins. Studies on jellyfish collagen have demonstrated a conserved triple-helical structure, with differences observed in amino acid composition and thermal stability compared to mammalian collagens (Smith et al., 2023).

The classification of jellyfish collagen remains a topic of debate in the scientific community. Jellyfish collagen is typically categorized as Type I and Type II collagen based on conventional nomenclature systems. For example, research by Cheng et al. (2017) identified collagen from jellyfish mesoglea as resembling rat tail type I collagen, showing that pepsin-soluble and acid-soluble collagens from jellyfish exhibit similar characteristics to Type I collagen. In contrast, Carvalho et al. (2022) found that jellyfish collagen from *Rhizostoma pulmo* displayed a triple-helical structure similar to Type II collagen. Despite these observations, discrepancies in collagen sequence conservation between mammals and marine invertebrates have led some researchers to question the applicability of traditional collagen classifications for jellyfish. Smith et al. (2023) suggested that the unique features of jellyfish collagen, such as differences in amino acid composition and cell-adhesion properties, warrant a new classification system, proposing Arabic numerals to replace Roman numerals in jellyfish collagen classification. Additionally, companies like Jellagen Ltd. have introduced the term "Type 0" for jellyfish collagen, reflecting the growing interest in

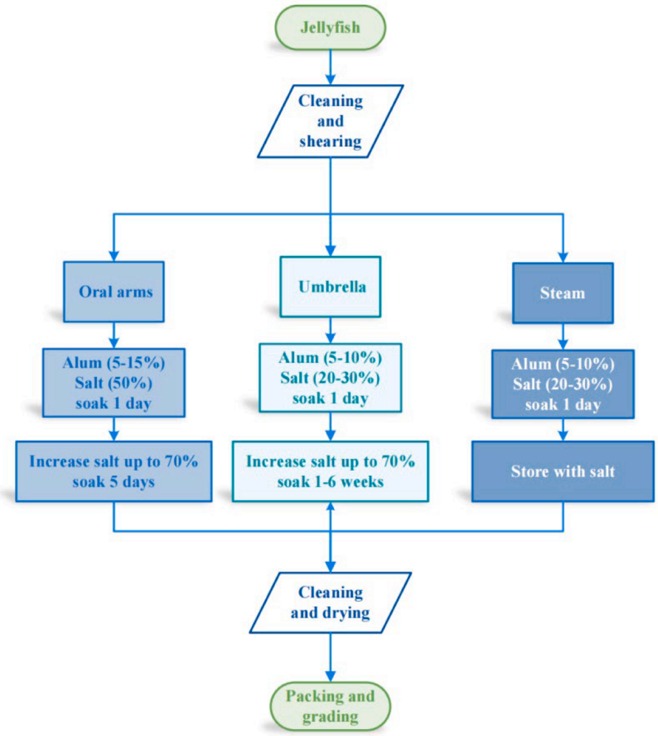

Fig. 1. The procedure of salted jellyfish processing.

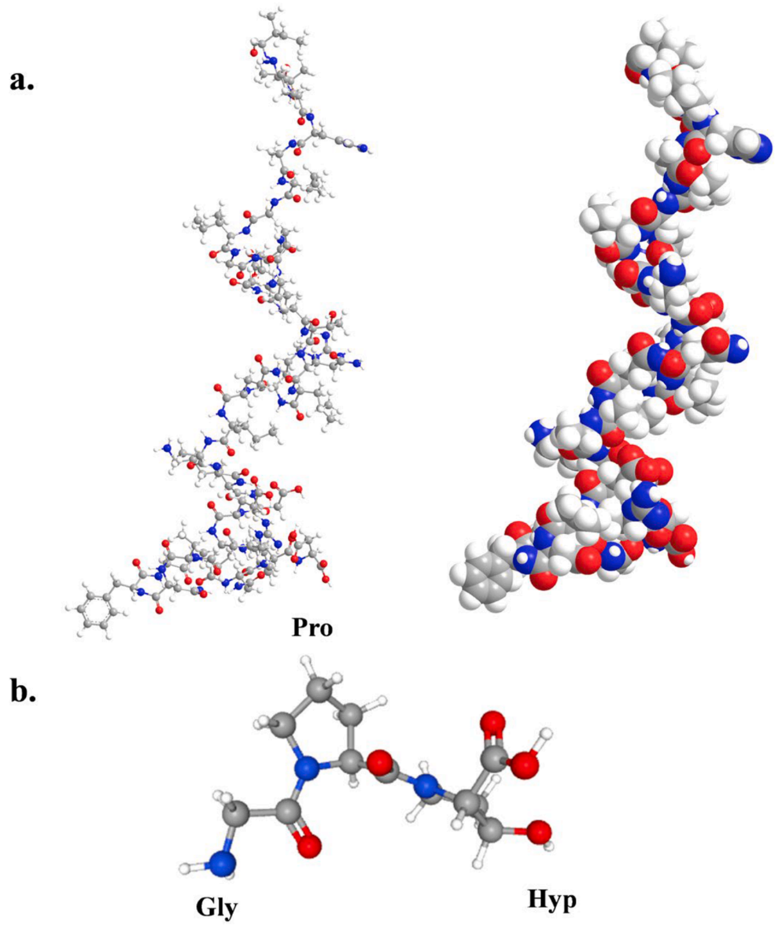

Fig. 2. (a) Triple-helical structure of collagen. (b) Region containing the Gly-X-Y motif.

establishing distinct categorizations for this collagen source.

2.2. The properties and unique characteristics of jellyfish

Emerging approximately 600 million years ago on the evolutionary tree of life, jellyfish exhibit physiological simplicity and exceptionally low immunogenicity (Flaig et al., 2020). Jellyfish collagen demonstrates homology with mammalian types I, II, III, V, and IX collagen, yet it represents a sustainable source characterized by batch-to-batch production consistency and cost-effectiveness compared to mammalian-derived materials (e.g., rat tails and bovine tissues) (Flaig et al., 2020; Paradiso et al., 2019). Relative to mammalian and other marine collagens, jellyfish collagen exhibits reduced toughness and contains minimal non-collagenous impurities, thereby eliminating the need for alkaline pretreatment during processing. This enables the design of more economical and environmentally sustainable protocols for jellyfish collagen production (Chiarelli et al., 2023b).

Collagen is regarded as an ideal biomaterial for tissue engineering due to its excellent biocompatibility and its ability to promote cell migration, cell-matrix interactions, and tissue regeneration (Ahmed et al., 2020; Felician et al., 2018). Among collagen sources, jellyfish collagen has emerged as a highly promising candidate material, with unique advantages attributed to its lower impurity content (Chiarelli et al., 2023b). Research has demonstrated that, compared to bovine collagen, jellyfish collagen supports higher viability of osteoblasts and fibroblasts, induces a long-term anti-inflammatory macrophage response *in vivo*, and functions effectively as a nanocarrier for growth factors to aid cartilage regeneration (Ahmed et al., 2021).

Furthermore, jellyfish collagen exhibits lower immunogenicity and inflammatory responses, along with reduced levels of biotoxins, when compared to mammalian and other marine-derived collagens (Chiarelli et al., 2023b). Supporting the above claims, the findings of Song et al. (2006) indicate that jellyfish collagen is non-cytotoxic and promotes significantly higher cell viability than other natural biomaterials, including bovine collagen, gelatin, hyaluronic acid, and dextran. Additionally, the immunogenic response elicited by jellyfish collagen scaffolds was found to be comparable to that induced by bovine collagen or gelatin. Research by Flaig et al. (2020) further corroborates the lower immunogenicity of jellyfish collagen, showing that its overall immune response is weaker than that provoked by porcine pericardium matrix. These ongoing research efforts underscore the distinct properties and significant advantages inherent to jellyfish collagen.

3. Green extraction and efficient modification strategies of jellyfish collagen

3.1. Collagen extraction innovations: Comparative advances

Recent advancements in collagen extraction techniques have led to various innovative methods, each with distinct advantages for enhancing yield and quality. The different extraction methods successfully used to extract collagen from various jellyfish species are presented in Table 2. Organic and inorganic acids, particularly acetic acid, have proven to be effective in breaking down the links between collagen molecules, as they alter the electrostatic properties of collagen, making it more soluble and easier to extract (Wang et al., 2008). Organic acids, in particular, are more efficient than inorganic acids because they solubilize non-crosslinked collagen and break inter-strand crosslinks,

Table 2
Extraction of jellyfish collagen.

Jellyfish species	Country	Collagen extraction method	Collagen yield	Reference
Rhizostoma pulmo	Turkey	Pepsin-soluble collagen extraction	93.5 %, dry wt.	(Yıldız et al., 2024)
Aurelia aurita	Turkey	Acid-soluble collagen extraction	0.01 %, wet wt.	(Balikci et al., 2024)
Rhizostoma pulmo	India	Acid-enzyme extraction	47 %, lyophilized	(James et al., 2023)
Aurelia aurita	Japan	pH-based extraction	Data unavailable	(Sumiyoshi et al., 2020)
Rhopilema esculentum	China	Acid-soluble collagen extraction	Data unavailable	(Sudirman et al., 2023)
Acromitus hardenbergi	Malaysia	Acid-soluble collagen extraction	0.16 g, wet wt.	(Khong et al., 2018)
Acromitus hardenbergi	Malaysia	Pepsin-soluble collagen extraction	0.39 g, wet wt.	(Khong et al., 2018)
Acromitus hardenbergi	Malaysia	Acid-soluble collagen extraction aided by physical treatment	40.2 %, dry wt.	(Khong et al., 2018)
Rhopilema esculentum	China	Acid-soluble collagen extraction	0.12 % wet wt.	(Cheng et al., 2017)
Rhopilema esculentum	China	Pepsin-soluble collagen extraction	0.28 % wet wt.	(Cheng et al., 2017)

providing a higher soluble yield (Senadheera et al., 2020). In contrast, alkali-soluble collagen extraction, which typically uses strong alkaline solutions like sodium hydroxide or potassium hydroxide, dissolves collagen by swelling raw materials and degrading non-collagenous components. While this method results in a large yield, it can lead to the loss of amino acids like serine, cysteine, and histidine, making it less commonly used in recent years (Senadheera et al., 2020).

Enzyme-mediated collagen extraction, using enzymes such as pepsin, offers another powerful approach. This technique is especially advantageous because it allows for specific cleavage of collagen cross-links without causing excessive structural damage. The mild reaction conditions result in higher collagen yields and minimal loss of functional groups (Amirrah et al., 2022). In industrial applications, enzyme-based extractions are often combined with acid or alkali treatments to optimize the process.

While techniques for extracting collagen from jellyfish have not been fully standardized, research has successfully applied methods used for other species. Notably, studies have employed acid and pepsin treatments, as well as combined physical, acid, and enzyme-assisted methods, to extract collagen from jellyfish species like *Cyanea nozakii* and *Acromitus hardenbergi* (Khong et al., 2018; Zhang et al., 2014). These innovative approaches have shown improvements in extraction efficiency, with physical treatment methods proving particularly effective. As shown in Fig. 3, the general procedure for harvesting jellyfish collagen involves cleaning, pretreating the tissue with acidic or alkaline solutions, and then applying either acid, alkali, enzymatic, or combined hydrolysis techniques to extract and purify the collagen (Chiarelli et al., 2023a). These advancements highlight the ongoing progress in collagen extraction, providing more efficient and targeted methods for different sources.

3.2. Modification mechanisms and performance regulation

Owing to lower content of proline and hydroxyproline, jellyfish collagen exhibits a lower degree of cross-linking than mammalian collagen, which greatly limits its application. However, to initiate cross-linking, jellyfish collagen can be modified through various methods, including physical, chemical, and enzymatic treatments (Leonard et al., 2024). Physical cross-linking techniques are employed to enhance the properties of collagen without using chemical reagents, thereby avoiding the potential toxicity associated with chemical additives. The two primary physical methods used for inducing collagen cross-linking are temperature manipulation and ultraviolet (UV) irradiation. Xu et al. (2020) discovered that collagen gels generated through UV exposure at low temperatures exhibit enhanced thermal stability, mechanical strength, and the ability to promote cell growth. Meanwhile, chemical cross-linking has the potential to significantly alter the intrinsic properties of collagen. This technique involves the formation of covalent bonds between the amino groups of collagen, which stabilizes the triple helix structure of collagen while simultaneously enhancing its mechanical properties and thermal stability. The most commonly employed chemical cross-linking methods include glutaraldehyde (GA) treatment, genipin treatment, 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide / N-hydroxysuccinimide (EDC/NHS) coupling, Schiff base reaction, double aldehyde starch (DAS) treatment, and chitosan treatment. For example, Tian et al. (2016) examined the rheological properties of

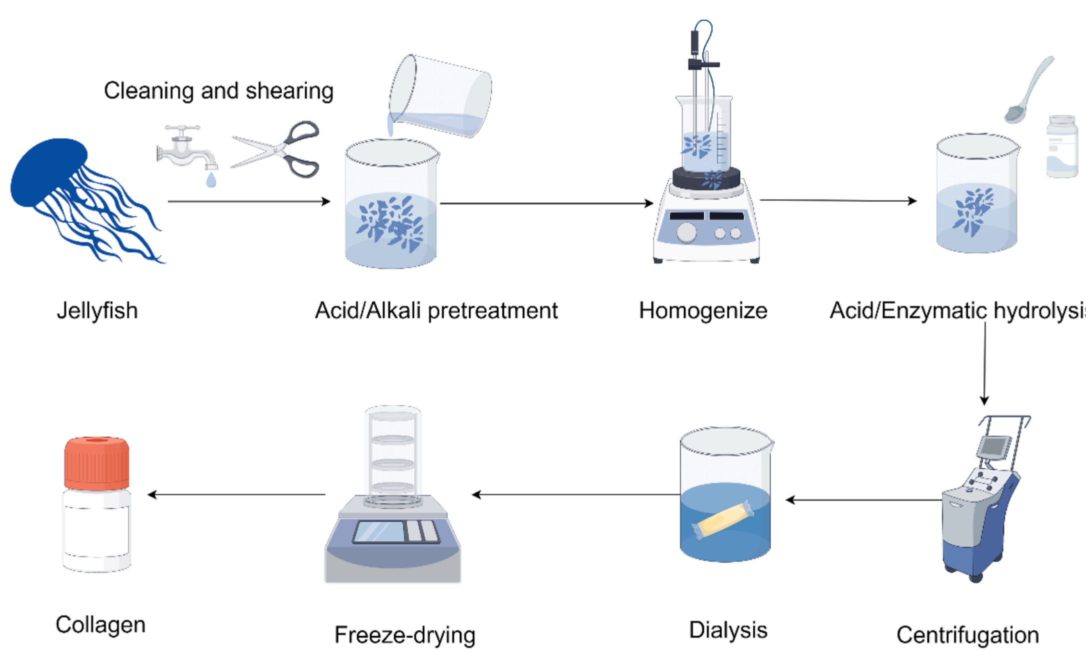

Fig. 3. Process used for the extraction of jellyfish collagen.

glutaraldehyde-crosslinked collagen solutions, revealing that these solutions exhibit greater resistance to deformation.

A primary advantage of enzymatic modification lies in the mild reaction conditions coupled with the ability of enzyme reagents to catalyze reactions with high efficiency. Two types of proteases are commonly employed for the modification of collagen. The first type (e.g., polyphenol oxidase) is capable of catalyzing the generation of reactive groups from low-molecular-weight cross-linking compounds, thereby facilitating direct cross-linking reactions with side-chain groups on protein molecules. In contrast, the other type of protease catalyzes the formation of cross-linking interactions with side-chain groups. For instance, the enzyme glutamine transglutaminase is widely utilized to enhance the structure of collagen. Chen et al. (2005) examined the effect of microbial transglutaminases (MTGases) as cross-linking agents on collagen matrices derived from porcine type I collagen. They found that MTGase induced cross-linking, increasing the viscosity and tensile strength of the collagen solutions. These established modification techniques can also be applied to jellyfish collagen.

4. Translational development: Applications, safety and interdisciplinary convergence

The unique physicochemical properties of jellyfish collagen have expanded its applications across the food industry, cosmetics industry, and biomedical sector (Fig. 4). Jellyfish collagen is gaining increasing attention as a promising alternative to mammalian collagen. The following sections discuss some potential applications for jellyfish collagen.

4.1. Food innovation

4.1.1. Smart packaging

In modern times, food packaging has emerged as a significant concern for both food producers and consumers due to its impact on food quality and the environment. Research focused on sustainable and eco-friendly food packaging materials is gaining momentum (Xiao et al., 2021b). New food-safe films and coatings are being developed as alternatives to traditional plastic packaging (Bakar et al., 2024).

Collagen, with its diverse functional properties (including foaming, film-forming, antibacterial, antioxidant, and biodegradable activities), holds promise as an excellent food packaging material. The unique characteristics of collagen-based packaging can improve the preservation of food, extend its shelf life, and enhance its sensory appeal (Tang et al., 2022). Collagen is commonly used in food packaging materials. For instance, collagen sausage casings are increasingly being employed for sausage production due to their low cost, uniform size, ease of production, process control, and strong compatibility with meat fillings. Interestingly, Azaza et al. (2023) developed composite packaging films by utilizing blue crab chitosan and bluefin tuna collagen. Here, the incorporation of bluefin tuna collagen significantly enhanced the antioxidant properties of the films, and the composite films were effective in preserving shrimp. Meanwhile, T. Zheng et al. (2023a) combined phenolic shell-binding polysaccharides with collagen to enhance the antioxidant and antibacterial properties of collagen membranes.

Although it is widely believed that pure collagen and peppermint films possess distinct waterproof and mechanical properties, findings also show that their performance can be enhanced by incorporating active substances and combining them with other bio-polymers. Hou et al. (2023) prepared novel tilapia collagen films with better mechanical properties and antimicrobial activity by adding transglutaminase (TGase) as a cross-linking agent and lysozyme as an antimicrobial agent. These films were found to have value as protein-based edible films.

Collagen films have also garnered considerable interest in the area of intelligent food packaging. Since the deterioration of protein-rich foods such as meat and aquatic products can lead to pH elevations, T. T. Zheng et al. (2023b) combined bovine collagen with chitosan to develop a film with an antibacterial matrix for smart pH colorimetric films, which could be utilized to assess the freshness of pork. In recent years, the integration of Pickering emulsions into collagen-based films has emerged as an innovative hydrophobic modification technique, showcasing significant potential for introducing new functionalities and enhancing the properties of packaging materials. Pickering emulsions are highly effective at transporting hydrophobic bioactive components and essential oils, improving their compatibility with hydrophilic matrices and thus enhancing the physical properties of packaging films. Ran et al. (2024) incorporated cinnamon essential oil-based Pickering

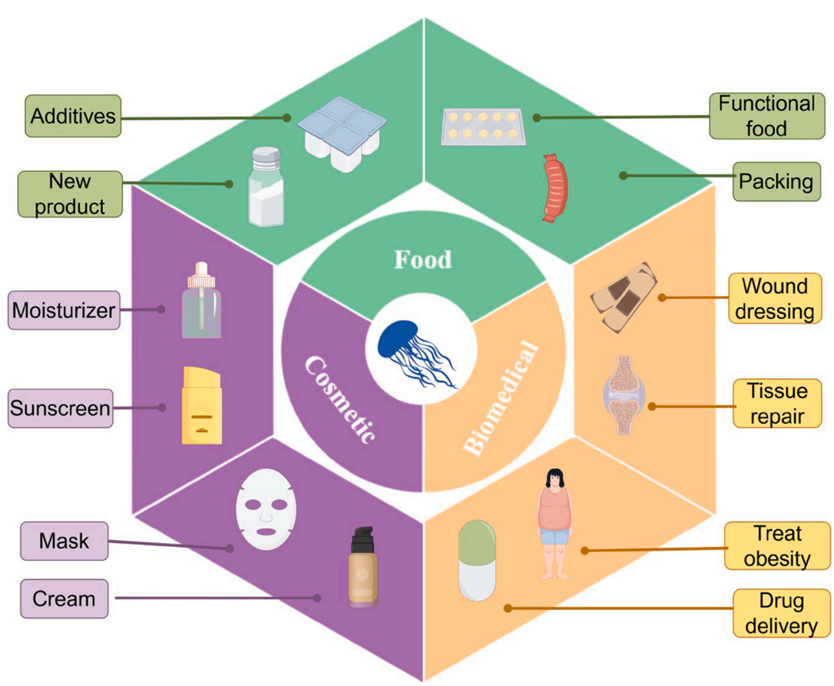

Fig. 4. Applications of jellyfish collagen.

emulsions into collagen to develop reactive packaging films with antimicrobial and antioxidant activities. Moreover, they added oxidized mulberry extracts for pH sensitization, which conferred the films with smart preservation properties and enabled the monitoring of food freshness. Therefore, functionalized collagen films hold great promise in the domain of intelligent food packaging.

Current food packaging materials typically use collagen sourced from pigs, cattle, fish, and other animals. However, research on the utilization of jellyfish collagen in food packaging is rather limited. In the future, modified jellyfish collagen could demonstrate significant potential in this area.

4.1.2. 3D printed food

New technologies, including 3D printing, are gaining attention in the food industry for their potential to customize nutritional content and modify food texture. By altering the structure of food, such as the internal filling rate and pattern, these innovations aim to cater to specific consumer needs, including those of the elderly with swallowing difficulties (Carranza et al., 2023). Extrusion-based 3D printing, the dominant method in the food industry, leverages computer-aided design (CAD) to precisely fabricate intricate geometries, textures, and multi-component structures. A critical challenge lies in developing edible "inks" with tailored rheological properties to ensure printability and structural fidelity. Here, collagen-stabilized emulsions are proving indispensable. Recent advances highlight collagen's dual role as a nutritional enhancer and functional emulsifier. For instance, Lu et al. (2024) engineered a 3D-printable surimi gel ink by incorporating transglutaminase-modified collagen peptides and fish oil. Increasing collagen peptide content reduced emulsion droplet size and improved homogeneity, while simultaneously enhancing localized viscoelasticity and thixotropic recovery—key attributes for layer-by-layer deposition. Similarly, Zhu et al. (2020) demonstrated that acid-soluble bovine collagen could stabilize Pickering emulsions with gel-like consistency, where elevated collagen concentrations boosted both elastic (G') and viscous (G") moduli, directly translating to better shape retention in printed constructs.

The intersection of emulsion science and additive manufacturing opens avenues for nutrient delivery systems. Ma et al. (2024) synthesized a collagen-Lycium barbarum flavonoid hybrid emulsifier that not only stabilized lutein-enriched emulsions but also enhanced their oxidative and digestive stability—a breakthrough for printing bioactive-fortified foods. Despite these innovations, jellyfish collagen emulsions remain underexplored. Consumer demand for nutritionally optimized, visually appealing foods drives this field forward. By tuning emulsion rheology through collagen modification, researchers are overcoming limitations in resolution and material versatility, paving the way for next-generation 3D-printed foods that marry gastronomy with precision nutrition.

4.1.3. Jellyfish collagen-based functional foods

Functional foods are attracting increasing attention due to their potential to prevent diet-related illnesses and promote the physical and emotional well-being of consumers. Marine products are valued for their high protein content, high levels of essential amino acids, and beneficial biological properties, including antioxidation. Hence, they are highly sought-after as functional foods.

One area in which functional foods can have potential applications is hypertension control. Hypertension is a prevalent lifestyle-related disease. Angiotensin-converting enzyme (ACE) plays a key role in regulating blood pressure, and inhibiting ACE activity can help in attenuating elevations in blood pressure (Sarmadi et al., 2011; Zhuang et al., 2012). Zhuang et al. (2012). successfully produced an ACE inhibitory peptide by enzymatically breaking down collagen sourced from jellyfish (*Rhopilema esculentum*) using an alkaline enzyme. Meanwhile, Barzideh et al. (2014) isolated collagen from banded jellyfish (*Chrysaora sp.*) and then extracted a physiologically active peptide, which subsequently demonstrated robust antioxidant and ACE-inhibitory properties. These findings suggest that jellyfish collagen has potential as a source of functional ingredients and drugs for hypertension management. In line with these findings, Morishige et al. (2011) investigated the immunomodulatory effects of jellyfish collagen extract in mice and found that its consumption could bolster immune responses in the mice without triggering allergic reactions. This immunostimulatory nature of jellyfish collagen extract renders it suitable as a type of functional food.

4.2. Biomedical revolution

Jellyfish collagen has become increasingly popular in the field of biomedicine because of its favorable characteristics, including its biocompatibility, biodegradability, and bioinductivity. Additionally, jellyfish collagen has also been found to show biological activities such as antioxidant and anti-inflammatory effects. It can promote tissue regeneration in the bones and skin while also enhancing tendon elasticity. A summary of the potential applications of jellyfish collagen in the field of biomedicine is shown in Table 3.

4.2.1. 3D biological printing

Collagen, a key structural protein in the extracellular matrix (ECM) of nearly all human tissues, has emerged as a highly promising biomaterial for 3D bioprinting due to its intrinsic biocompatibility, mechanical support functions, and role in mediating cell adhesion and signaling (Debnath et al., 2025). However, the inherent challenges of processing native collagen—particularly the difficulty in controlling its thermal gelation—have limited its utility in fabricating complex scaffolds. To overcome these limitations, Feinberg's team at Carnegie Mellon University pioneered the freeform reversible embedding of suspended hydrogels (FRESH) technique, enabling precise 3D bioprinting of

Table 3
Potential biomedical applications of jellyfish collagen.

Jellyfish species	Region	Application(s)	Reference
Nomura jellyfish	Japan	Activates dendritic cells and contributes to improved health.	(Putra et al., 2015)
Catostylus tagi	Europe	Enables the controlled release of therapeutic proteins.	(Calejo et al., 2012)
Rhopilema esculentum	China	Acts as a hemostatic material and for wound healing.	(Cheng et al., 2017)
Moon jellyfish	Japan	Accelerates physiological wound healing.	(Sumiyoshi et al., 2021)
Aurelia aurita	Japan	Accelerates the wound healing process.	(Sumiyoshi et al., 2020)
Rhizostoma pulmo	UK	Can be used in hydrogels for cartilage tissue engineering.	(Carvalho et al., 2022)
Rhopilema esculentum	China	Protects articular cartilage and suppresses the degradation of cartilage.	(Sudirman et al., 2023)
Rhizostoma pulmo	UK	Had great potential in the field of cartilage regeneration.	(Carvalho et al., 2023)
Rhizostoma pulmo	UK	Acts as an alternative injectable medialization laryngoplasty material	(Bowen et al., 2022)
Rhopilema esculentum	China	Widely applicable scaffold for regenerative medicine.	(Zhao et al., 2023)
Rhizostoma pulmo	China	A fully biocompatible cell culture substrate suitable for in vitro cytocompatibility analyses	(Ren et al., 2023)
Rhizostoma pulmo	Tukiye	Inorganic membranes containing jellyfish collagen show excellent properties in wound healing.	(Yıldız et al., 2024)
Aurelia aurita	Marmara Sea	Acts as a suitable source of collagen when biomaterials with high biocompatibility are required.	(Balikci et al., 2024)
Rhizostoma pulmo	India	Is suitable for the development of neuroprotective anti-oxidants.	(James et al., 2023)

collagen-based constructs across multiple scales, from capillaries to entire cardiac organs. Notably, FRESH-printed cardiac tissues embedded with human cardiomyocytes demonstrated synchronized contractions and directional electrical propagation, while micro-computed tomography confirmed their ability to replicate patient-specific anatomical structures (Lee et al., 2019). These advancements underscore collagen's potential in tissue engineering and have catalyzed innovations in bioink development, particularly with alternative collagen sources such as jellyfish-derived collagen. Exhibiting superior biocompatibility, low immunogenicity, and tunable rheological properties, jellyfish collagen has proven compatible with both extrusion-based and light-cured bioprinting platforms. Collaborative efforts between Jellagen and Copner Biotech, supported by SMART Cymru funding, have successfully integrated this material into next-generation bioprinting systems, further advancing its applications in regenerative medicine (Jellagen Ltd., 2022).

4.2.2. 4D biological printing

However, the static nature of traditional 3D-printed structures struggles to meet the biomimetic demands of dynamic physiological environments, driving the emergence of 4D bioprinting. Over the past decade, 4D printing has evolved by introducing time as a fourth dimension. In 2013, Tibbits from MIT's Self-Assembly Laboratory first conceptualized 4D printing, initially defined as "3D printing + time," enabling the fabrication of objects capable of shape-shifting over time. Recent advancements have refined this definition to encompass the creation of 3D structures with stimuli-responsive properties that react to external triggers such as water, heat, pH, light, and electromagnetic fields (Lai et al., 2024). A notable example is the work by. Mainik et al. (2025), who developed a type I collagen methacrylamide ink system to fabricate well-defined 3D microstructures. Their study demonstrated the complete reversibility of temperature-induced collagen self-assembly within printed materials, unveiling novel responsive mechanisms that highlight collagen's potential as a dynamic biomaterial for future applications.

In tissue engineering, 4D bioprinting has found significant utility in bone regeneration. Collagen-based smart composites, such as hydroxyapatite-incorporated scaffolds, enhance osteogenic activity in 4D-printed bone constructs by leveraging bioactive ceramic integration (Hwangbo et al., 2021). Similarly, 4D bioprinting offers promising advances in skin regeneration through dynamic skin substitutes. These grafts adapt their geometry to match wound contours, improving integration and accelerating healing. Douillet et al. (2022) utilized laser-assisted 4D bioprinting to engineer fibroblast- and myofibroblast-laden collagen matrices, which self-organized into dispersed and aggregated cellular patterns after 5 days of in vitro culture. This approach provides a powerful tool to model dynamic skin repair processes and cellular reorganization.

4D bioprinting has made significant strides in creating dynamic tissues, including skin, bone, cartilage, vasculature, and muscle. However, the technology is still in its early stages and faces several challenges, such as limited mechanical strength and unproven long-term degradation safety. Overcoming these obstacles will require innovative approaches, such as genetic engineering to improve collagen properties or the use of machine learning to optimize multi-material printing protocols. Despite these challenges, 4D bioprinting holds transformative potential for fields like biomanufacturing, tissue engineering, regenerative medicine, and personalized therapeutics, offering a promising bridge between static constructs and adaptive biological systems.

4.2.3. Hemostasis and wound healing

Prior studies have shown that collagen is an effective hemostatic agent. Cheng et al. (2017) extracted collagen from the mesoderm of the jellyfish *Rhopilema esculentum Kishinouye* and produced lyophilized jellyfish collagen. Their investigation revealed that blood cells and platelets adhered to and aggregated on the surface of the collagen sponge. This suggests that jellyfish collagen sponges hold promise as hemostatic agents. Moreover, jellyfish collagen is also being explored for its potential in promoting wound healing, because it directly stimulates keratinocyte migration — a process that cannot be achieved with conventional artificial dermal grafts (Sumiyoshi et al., 2021). Research by Sumiyoshi et al. (2021) revealed that the topical application of moon jellyfish collagen on normal skin grafts can mitigate excessive inflammation, suppress scar formation, and expedite the healing process. Moreover, in mouse models of diabetes, the application of jellyfish collagen to wounds has been found to accelerate healing, demonstrating its potential for treating non-healing diabetic skin ulcers.

4.2.4. Bone and cartilage regeneration

Jellyfish collagen exhibits significant potential in the regeneration of bone and cartilage tissues. Flaig et al. (2020) conducted in vivo investigations to explore the immunoregulatory and bone-healing capabilities of jellyfish collagen scaffolds following their subcutaneous and cranial implantation in Wistar rats. Their findings reveal that jellyfish collagen scaffolds could induce a sustained anti-inflammatory response in macrophages and facilitate angiogenesis at the implantation site, exhibiting remarkable biocompatibility and tissue healing properties. Collagen hydrogels also present a promising option for cartilage repair. Riacci et al. (2021) developed a novel 3D hydrogel by using collagen derived from *Rhizostoma pulmo* jellyfish, and they found that this hydrogel provided an optimal environment for the growth of human chondrocytes. Rastian et al. (2018) conducted a physicochemical and biofunctional analysis of acid-soluble collagen derived from *Catostylus mosaicus* jellyfish collected from Persian Gulf reefs. Their findings demonstrate that jellyfish collagen, when incorporated into mixed agarose biomaterials, could promote osteoblast attachment and growth. These results underscore the potential of jellyfish collagen in the preparation of various biomaterials.

4.2.5. Prevention and treatment of obesity

The global prevalence of obesity has increased in recent years, largely due to changes in dietary patterns and sedentary lifestyles. Obesity significantly contributes to health conditions such as hypertension, diabetes, fatty liver disease, and stroke. The primary treatment options for obesity include dietary restrictions, medication, and surgery (Yao et al., 2018). However, it is challenging to sustain long-term weight loss because of difficulties in following dietary restrictions, side effects from prolonged medication use, and high surgical risks (Derosa et al., 2012). Bariatric surgery carries some risk because it has adverse effects on certain populations, including weight regain, depression and suicidal ideation, increased perinatal morbidity, and a propensity for bone fractures and kidney stones (Liao et al., 2022; Magro et al., 2008). Therefore, there is a pressing need to explore safer approaches for obesity prevention. Ma et al. (2023) studied the effectiveness of *Nemopilema nomurai* peptides (Nomura jellyfish peptides) in reducing lipid levels in 3T3-L1 adipocytes. These peptides exerted anti-adipogenic effects in 3T3-L1 adipocytes and could hinder adipogenesis by reducing energy consumption. Thus, peptides from the Nomura jellyfish could potentially be used in developing drugs for treating obesity in the future. Lv et al. (2022) demonstrated that in mice, the administration of jellyfish (*Nemopilema nomurai*) collagen hydrolysates could prevent obesity, high blood glucose levels, and elevated lipid levels induced by a high-fat diet. Jellyfish collagen hydrolysates mitigated oxidative stress by enhancing glutathione and reducing the levels of reactive oxygen species in the liver. Furthermore, they ameliorated the inflammatory response by downregulating the expression of tumor necrosis factor (TNF)-α, interleukin (IL)-1β, and IL-8 genes in the liver and ileum. Additionally, findings have indicated that collagen hydrolysates could be valuable in reversing the gut dysbiosis triggered by a high-fat diet, further highlighting the potential utility of jellyfish collagen hydrolysates in obesity prevention and treatment.

4.2.6. Drug delivery

Conventional drug delivery methods, such as oral and intravenous administration, are associated with drawbacks such as inadequate drug accumulation at target sites, low bioavailability, premature excretion, and the need for repeated administration (Adepu et al., 2021). These challenges can be addressed by employing smart carrier systems, known as drug delivery systems (DDS), that precisely transport drugs or biomolecules to their target sites (Adepu et al., 2021). Collagen and its derivatives are ideal drug carriers due to their inherently exceptional biocompatibility and biodegradability (Elzoghby et al., 2012). Further, owing to the inherent properties of collagen, its shape and size can be manipulated. Additionally, collagen particles, sponges, hydrogels, and scaffolds can also be fabricated (Chen et al., 2019c). Collagen particles can be readily produced using methods such as emulsification-gel-solvent extraction, and their structure can facilitate drug retention. Drug release can be achieved by breaking down collagen components, resulting in a two-phase release mechanism: an initial burst release of biomolecules from the surface of the particles, followed by a gradual release over an extended period (Tahir et al., 2023).

Calejo et al. (2012) developed a microparticulate protein delivery system by using jellyfish collagen as a polymer matrix. In this system, the proteins maintained their activity during encapsulation and cross-linking, highlighting the potential of jellyfish collagen for the controlled release of therapeutic proteins. In addition, gelatin has also been recognized as a favorable option for DDS because it is easier to chemically modify than collagen. Gelatin also possesses a greater variety of functional groups, allowing for numerous coupling modifications with cross-linkers or targeting ligands (Bhattacharyya et al., 2022; Xiao et al., 2021a). Given the increasing demand for biocompatible protein drug carriers, the development of collagen- and gelatin-based drug carriers and their large-scale production represents a very promising area of biomedical research.

4.3. Cosmetics and sustainable materials

Collagen is a natural humectant and possesses moisturizing, regenerative, and film-forming characteristics. It is extensively utilized as a primary component in numerous cosmetic formulations for skin and hair care. Collagen fillers are also utilized in aesthetic medicine, where the subcutaneous injection of collagen enhances skin quality and density and aids in healing skin imperfections (Sionkowska et al., 2017). During collagen maturation, its water solubility and acidity decrease due to increased cross-linking. Meanwhile, shorter polypeptides and peptides derived from collagen exhibit superior solubility in water, excellent hydrophilicity, and enhanced skin penetration when compared to native collagen. This facilitates their integration into cosmetic formulations and enables them to improve skin characteristics (Al-Nimry et al., 2021). Hydrolyzed collagen is widely employed due to its exceptional compatibility with human cells and high biodegradability and is used in several cosmetic products (Chotphruethipong et al., 2020). Studies have demonstrated that collagen hydrolysates can exert chemotactic effects on skin fibroblasts, aiding in skin regeneration (Sionkowska et al., 2020). To enhance its stability, the collagen used for cosmetic applications can be modified through a controlled cross-linking process. The susceptibility of collagen to high temperatures and enzymatic degradation makes the structural stabilization of collagen necessary (Goegele et al., 2020). It is possible to employ physical, chemical, and biological methods to improve the structure of collagen. Chemical agents that are typically used for collagen cross-linking interact with the amino and carboxyl groups of collagen, creating cross-links (Sionkowska et al., 2020). Sionkowska et al. (2020) discovered that although cross-linked collagen is not commonly used in cosmetic products, it could be suitable for developing cosmetic masks and wound dressings.

Zhuang et al. (2009) examined the antioxidant properties of jellyfish collagen peptides by evaluating their ability to scavenge superoxide anions and hydroxyl radicals as well as their capacity to chelate copper in a linoleic acid emulsion system in vitro. They also explored the ability of jellyfish collagen peptides to inhibit melanin production. Their results indicate that jellyfish collagen peptides possess antioxidant and copper-chelating abilities, making them promising ingredients for skin whitening products. In another study, Kim et al. (2016) extracted collagen from jellyfish and investigated its moisturizing properties. Their findings suggest that jellyfish collagen extracts hold immense potential as cosmetic ingredients with hydrating properties. Currently, the research predominantly focuses on extracting collagen from fish, and there is limited literature on the use of jellyfish collagen in cosmetics. However, the further exploration of jellyfish collagen and its potential in cosmetics is anticipated as research in this area grows.

4.4. Safety assessment of jellyfish collagen

Jellyfish collagen has garnered significant attention due to its potential applications across various fields, including food, medicine and cosmetics. However, its safety profile is a critical consideration requiring comprehensive evaluation. One primary safety concern associated with marine-derived products is the presence of toxic metals and metalloids, which pose health risks upon long-term consumption. Research by Cammiller et al. (2025) demonstrated the absence of detectable toxic metals and metalloids in analyzed jellyfish collagen samples, highlighting its potential safety. Furthermore, none of the analyzed samples exceeded European Union (EU) regulatory limits, and the calculated average daily doses consistently remained below the tolerable daily intakes. This indicates that the consumption of jellyfish collagen at recommended doses is safe.

Beyond chemical safety, the cytotoxicity and biocompatibility of jellyfish collagen have also been extensively investigated. As outlined in Section 2.1, jellyfish collagen typically exhibits excellent biocompatibility and lacks cytotoxicity, forming a foundation for its use in biomedical field. Nevertheless, allergic reactions constitute an essential factor that must be considered when assessing jellyfish collagen's safety. It should be noted that some marine collagens have been reported to elicit allergic reactions (Kalic et al., 2020; Li et al., 2022). As a protein derived from a marine organism, jellyfish collagen may also trigger allergic responses in susceptible individuals. Although specific research on the allergenicity of jellyfish collagen remains relatively limited, existing studies consider the risk of allergic reactions to jellyfish collagen to be relatively low (Chiarelli et al., 2023b).

5. Challenges and prospects in developing jellyfish collagen as a sustainable biomaterial

Jellyfish represent a relatively nascent fishery resource in Western countries, where modern consumers may be unfamiliar with products derived from this organism (Chiarelli et al., 2023b). As an emerging sustainable biomaterial, consumer acceptance poses a significant challenge to the large-scale production and application of jellyfish collagen. Although extraction technologies have advanced in recent years, current marine collagen extraction processes predominantly rely on acid hydrolysis or enzymatic methods—approaches requiring further improvements in efficiency and cost-effectiveness (Table 2). Moreover, most existing research on jellyfish collagen extraction remains confined to laboratory-scale studies, indicating considerable gaps towards scalable industrial production and practical implementation. Additionally, the relatively poor mechanical properties of jellyfish collagen, as noted in Section 2.2, present a significant hurdle for its applications in demanding fields such as tissue engineering. While studies have demonstrated favorable biocompatibility of jellyfish collagen, clinical validation remains insufficient. Prior to widespread adoption, comprehensive toxicity evaluations, allergenic testing, and robust clinical trial data must be generated to substantiate its safety for human applications. Long-term safety profiles also warrant further verification. Crucially, as a novel biomaterial, jellyfish collagen lacks well-defined safety standards and regulatory frameworks, necessitating multidisciplinary breakthroughs to achieve commercialization.

Nevertheless, jellyfish collagen holds substantial promise as a sustainable biomaterial. Advances in green extraction technologies and biotechnology are anticipated to significantly enhance extraction and cost efficiency. Future research is also expected to focus on overcoming its mechanical limitations, particularly through strategies like integrating jellyfish collagen into composite structures with other synthetic or biological materials to enhance performance. Furthermore, establishing rigorous safety standards and clinical validation protocols will facilitate market entry and foster consumer trust. In summary, jellyfish collagen represents a transformative innovation in biomaterials, offering a sustainable, safe, and multifunctional alternative to conventional collagen sources. With escalating global demand for sustainable and biocompatible materials, it is poised to play a pivotal role in advancing tissue engineering, regenerative medicine, and related fields.

6. Conclusion and outlook

Jellyfish collagen exhibits irreplaceable advantages across ecological, functional, and ethical dimensions compared to traditional mammalian collagens. Ecologically, its utilization supports sustainable marine resource management by converting jellyfish blooms—often considered oceanic nuisances—into valuable raw materials. Functionally, its superior biocompatibility and structural adaptability enable diverse applications in regenerative medicine, edible films, and bioactive cosmetics. Ethically, it avoids zoonotic disease transmission risks and cultural-religious restrictions while creating economic opportunities for coastal communities. To fully realize the potential of jellyfish collagen, a phased development strategy could be considered. Initial efforts may focus on establishing high-throughput screening platforms to identify collagen-rich jellyfish species, alongside developing standardized extraction protocols to enhance industrial scalability. Building upon these foundations, future exploratory efforts might explore the integration of synthetic biology and AI-driven molecular design to tailor collagen sequences for specialized applications in extreme environments. Jellyfish collagen provides a blueprint for developing ethically sound, ecologically balanced, and commercially viable biomaterials. To ensure the long-term viability and economic development of the jellyfish collagen industry, it will be crucial to protect marine biodiversity and ensure the sustainable growth and harvest of jellyfish. Future efforts must balance technological innovation with marine conservation strategies to ensure the long-term sustainability of the industry.

Ethical statement

This manuscript serves as a review article and does not address ethical considerations pertaining to human or animal experimentation.

CRediT authorship contribution statement

Bing Hu: Writing – review & editing, Writing – original draft, Methodology, Conceptualization. **Zixin Zong:** Writing – review & editing, Writing – original draft, Software, Methodology, Investigation. **Lingyu Han:** Writing – review & editing, Writing – original draft, Software, Methodology, Investigation. **Jijuan Cao:** Writing – review & editing, Methodology, Conceptualization. **Jixin Yang:** Writing – review & editing, Methodology, Conceptualization. **Qiuyue Zheng:** Writing – review & editing, Validation, Software. **Xiaobo Zhang:** Writing – review & editing, Software, Investigation. **Yu Liu:** Writing – review & editing, Methodology, Conceptualization. **Ziang Yao:** Writing – review & editing, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

No data was used for the research described in the article.

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