ISSN 2616-5910 Vol. 6, Issue 1: 117-129, DOI: 10.25236/AJALS.2025.060117

Research Progress and Application Prospects of Sea Cucumber Peptides

Yuan Gao[a] ,Chunming Dong[b,*]

College of Marine Environmental Sciences, Tianjin University of Science and Technology, Tianjin 300457, China
[a]792127931@qq.com, [b]mingchundongjy@tust.edu.cn
**Corresponding author*

Abstract: *Sea cucumber peptides are an important marine biological resource, and their peptide components not only have rich nutritional value, but also exhibit various biological activities, such as antioxidant, anti-inflammatory, anti-tumor, blood pressure lowering, immune regulation, etc. These characteristics make it play a significant role in delaying aging, improving metabolism, and enhancing immunity, providing a theoretical basis for its application in food and health products. Therefore, in-depth research on the structure, function, and mechanism of action of sea cucumber peptides is of great significance for developing new health products and promoting the sustainable utilization of marine biological resources. This article reviews the way to prepare, structural identification, biological activity and mechanism of action, current application status in different fields, challenges and solutions faced by sea cucumber peptides in market applications, and future prospects of sea cucumber peptides. It provides a solid theoretical basis for achieving efficient utilization of sea cucumber peptides through technological innovation, expanding application scenarios, and strengthening safety research in the future.*

Keywords: *Sea cucumber peptide; Preparation technology; Biological activity; Application prospect*

1. Introduction

With the increasing demand for health and nutrition, sea cucumber peptides are receiving more and more attention due to their high biological activity and good absorption. Sea cucumber peptides have a lower molecular weight and are more easily absorbed and utilized by the human body, thereby increasing their application value in health products and functional foods. With the development of biotechnology, the extraction, separation, and purification technology of sea cucumber peptides continues to advance, making their application prospects in the pharmaceutical, cosmetics, and food industries even broader.

In recent years, sea cucumber peptides extracted from sea cucumbers have become a research hotspot due to their unique biological activity. Sea cucumber peptide is a small molecule peptide obtained by enzymatic hydrolysis of sea cucumber collagen and other components. It has various biological activities such as antioxidant, hypotensive, anti fatigue, anti-tumor, anti-inflammatory, and promotion of collagen production. Research has shown that sea cucumber peptides exert their anti-tumor and immune regulatory effects by regulating cellular signaling pathways such as PI3K/AKT, ERK1/2/p38 MAPK/NF - κ B)In addition, sea cucumber peptides have shown promising application prospects in the field of cosmetics, such as improving skin texture, repairing skin barriers, and antioxidation [2].

According to the 2023 China Fisheries Yearbook, the total industry chain output value of China's sea cucumber industry has reached 120.8 billion yuan. In addition, the "2023 China Sea Cucumber Food Consumption Market Research Report" released by iMedia Consulting shows that the market size of the entire sea cucumber industry chain in China will be 132.6 billion yuan in 2023, and it is expected to reach 163.66 billion yuan by 2026[91]. This indicates that the overall market for sea cucumber industry is growing rapidly. Although the sales revenue of sea cucumber peptides was not directly mentioned, it can be inferred that with the expansion of the sea cucumber industry and the increasing demand for health supplements from consumers, sea cucumber peptides, as a deep processed product of sea cucumbers, have great market potential. Especially after the epidemic, consumers' demand for high-end tonics has increased, further promoting the development of the sea cucumber peptide market [90].

ISSN 2616-5910 Vol. 6, Issue 1: 117-129, DOI: 10.25236/AJALS.2025.060117

Refer to sales data from other industries for comparison. For example, in 2015, the sales of the top three leading companies in the global peptide market all exceeded $40 billion [92], indicating the enormous market potential of peptide products. Although sea cucumber peptides belong to a specific niche market, their market prospects cannot be ignored. The sales situation is shown in Fig.1

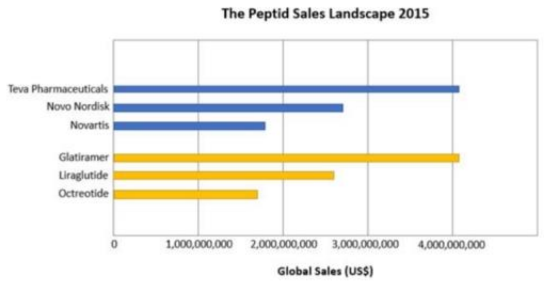

Figure 1: The diagram shows sales for the top three leading companies on the global peptide market 2015 (in blue) and the peptide top sellers 2015 (in yellow)
The diagram does not include insulin products and peptide vaccines[92]

2. Preparation Technology of Sea Cucumber Peptides

2.1. Enzymatic Hydrolysis Method

Enzymatic hydrolysis is a technique that uses enzymatic catalysis to hydrolyze large protein molecules into small peptides. The principle is to use proteases (such as trypsin, neutral protease, alkaline protease, etc.) to specifically cleave peptide bonds in proteins, thereby generating sea cucumber peptides with specific biological activities. Commonly used proteases include alkaline protease, neutral protease, trypsin, flavor protease, papain, bromelain, and pepsin [9]. These enzymes exhibit different hydrolysis efficiencies and product characteristics under different pH, temperature, and time conditions [10].

The type of enzyme has a significant impact on the yield and activity of sea cucumber peptides. For example, alkaline proteases have shown the highest degree of hydrolysis and antioxidant activity in some studies, while neutral proteases have been shown to be the best choice in multiple experiments [10-12]. In addition, the combination of different enzymes may also improve hydrolysis efficiency and product diversity [9].

The enzymatic hydrolysis conditions (such as temperature, pH value, time, enzyme dosage, etc.) also have a significant impact on the yield and activity of sea cucumber peptides. Research has shown that optimizing enzymatic hydrolysis conditions (such as temperature of 55 ℃, pH 8.0, enzyme dosage of 0.79%, and enzymatic hydrolysis time of 3.93 h) can significantly improve the degree of hydrolysis and the antioxidant activity of the products [13-14]. In addition, new technologies such as microwave-assisted enzymatic hydrolysis are also considered feasible methods to improve hydrolysis efficiency [9].

The advantage of enzymatic hydrolysis is that its mild conditions (such as room temperature or low temperature) can retain more bioactive components, and the product has good solubility and bioavailability [9]. However, enzymatic hydrolysis also has certain limitations, such as high cost, difficulty in fully meeting product purity requirements, and strong dependence on certain enzymes [9]. Therefore, future research should further optimize the enzymatic hydrolysis process, improve the purity and activity of the products, to meet the needs of different application fields.

2.2. Other Preparation Methods

2.2.1. Chemical Hydrolysis Method

Principle: Chemical hydrolysis (Note: The term may be inaccurate; it is more appropriately called "enzymatic hydrolysis" in this context) refers to the process of hydrolyzing sea cucumber protein using exogenous enzymes, such as trypsin, alkaline protease, and neutral protease, to break down the protein into amino acids and small peptides. This method relies on the catalytic activity of enzymes. By controlling parameters including temperature, pH value, enzyme dosage, and reaction time, hydrolysis efficiency can be improved[21-23].

ISSN 2616-5910 Vol. 6, Issue 1: 117-129, DOI: 10.25236/AJALS.2025.060117

Chemical hydrolysis is commonly used to prepare sea cucumber peptides, especially after optimizing hydrolysis conditions, which can significantly improve hydrolysis degree and peptide yield [21] [23-24].

For example, using alkaline protease at 54 ℃ and pH 9.0 can increase the hydrolysis degree of sea cucumber viscera to 67.19% [23].By using ultrafiltration and nanofiltration techniques, peptides and oligopeptides in the hydrolysate can be separated and graded, further improving the purity and antioxidant activity of the products [25-26].

Advantages: Easy to operate, easy to control reaction conditions. The molecular weight distribution of the product can be flexibly controlled by adjusting the enzyme type and reaction parameters [21-22]. The product exhibits high antioxidant activity, especially in the small molecular weight range [26-27].

Disadvantage: Requires exogenous enzymes, high cost. The enzymatic hydrolysis process may produce a significant amount of impurities, which require further purification [23] [25].

High requirements for equipment and strict operating conditions [21-22].

2.2.2. Self Dissolution Method

Principle: The autolysis method utilizes proteases (such as protease B, L, etc.) produced by sea cucumbers themselves to promote autolysis of their body walls and intestines under specific conditions (such as temperature, pH, light, etc.), thereby releasing proteins and peptides. This method does not require external enzymes and relies on the physiological mechanism of sea cucumber itself [28-29].

Application: The autolysis method is commonly used to prepare sea cucumber intestinal peptides, with a hydrolysis degree of up to 38.8% to 57.8% [24] [27] [29]. For example, at 48.3 ℃ pH 4.43、 Under the conditions of a feed to liquid ratio of 1:3 and an autolysis time of 4 hours, the TCA soluble oligopeptide content of sea cucumber intestine autolysis was the highest [30]. Sea cucumber peptides prepared by autolysis method exhibit high antioxidant activity, especially in the small molecular weight range [27-29].

Advantages: No need for exogenous enzymes, lower cost. The product has natural sources and high safety. Under autolysis conditions, the antioxidant activity of sea cucumber peptides is strong, especially in the small molecular weight range [27-29].

Disadvantages: The autolysis process is influenced by various factors, such as temperature pH、 The difficulty of controlling lighting and other factors is relatively high [28-29]. Long autolysis time may lead to a decrease in the quality of sea cucumber and affect subsequent processing [27-28]. The product may contain a significant amount of impurities and requires further purification [23] [25].

Chemical hydrolysis and autolysis have their own advantages and disadvantages, and are suitable for different application scenarios. The chemical hydrolysis method is flexible and highly controllable, but the cost is relatively high; The autolysis method has low cost and high safety, but the control conditions are difficult. Both can effectively prepare sea cucumber peptides with antioxidant activity, providing multiple technical pathways for deep processing of sea cucumbers [24] [28-29].

2.3. Research progress and prospects of preparation technology

The current research progress in preparation technology is mainly reflected in the following aspects: Development of new preparation methods: In recent years, new preparation methods such as single-phase solution freeze-drying technology, novel O/W emulsification technology（as shown in Fig.2）, cross flow mixing technology, and continuous flow reaction technology have been invented, providing new paths for industrial production. In addition, bottom up nano preparation technology has achieved continuous production, significantly improving production efficiency and product quality [31]. It’s shown in Fig.3

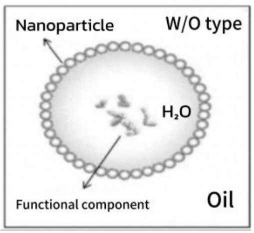

Figure 2: New emulsification technology Pickering lotion

ISSN 2616-5910 Vol. 6, Issue 1: 117-129, DOI: 10.25236/AJALS.2025.060117

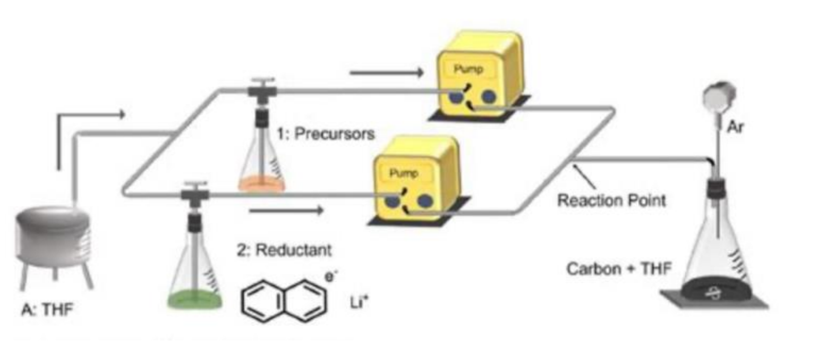

Figure 3: Method for synthesizing nanoparticles in continuous flow reactor - Kexin Microfluidics

Breakthrough in industrial preparation technology: The invention of continuous flow process, combined with linearly scalable equipment, effectively solves the technical threshold problem in industrial production. Meanwhile, by combining four key processes, the preparation of all nanomedicines has been achieved [31] .The process flow is shown in Fig.4

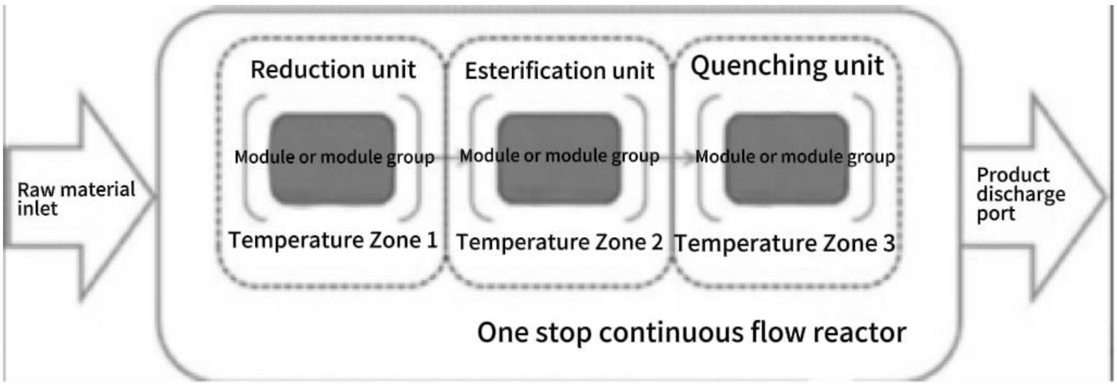

Figure 4: Production method of continuous flow synthesis process for tert butyl peroxy-2-ethylhexyl carbonate with infinite amplification effect

Development of multi method coupling technology: In the preparation of bioactive peptides, the combination of multiple separation methods (such as ultrafiltration gel filtration chromatography ion exchange chromatography) has been widely used, which not only improves the purity, but also saves time and cost [34].

Innovation in Materials Science: In the field of new materials, research directions include high-strength and high conductivity copper alloys, special layered composite materials, high-performance special steels, etc., emphasizing the relationship between material composition, microstructure, and properties, and developing new technologies for short process, near final shape, efficient, and low-cost preparation and forming processing [33].

Continuous progress in pharmaceutical technology: In terms of drug synthesis and formulation development, new drug synthesis methods, targeted delivery systems（as shown in Fig.5）, drug stability research, and other advancements have been made, driving innovation in drug formulations [37].

ISSN 2616-5910 Vol. 6, Issue 1: 117-129, DOI: 10.25236/AJALS.2025.060117

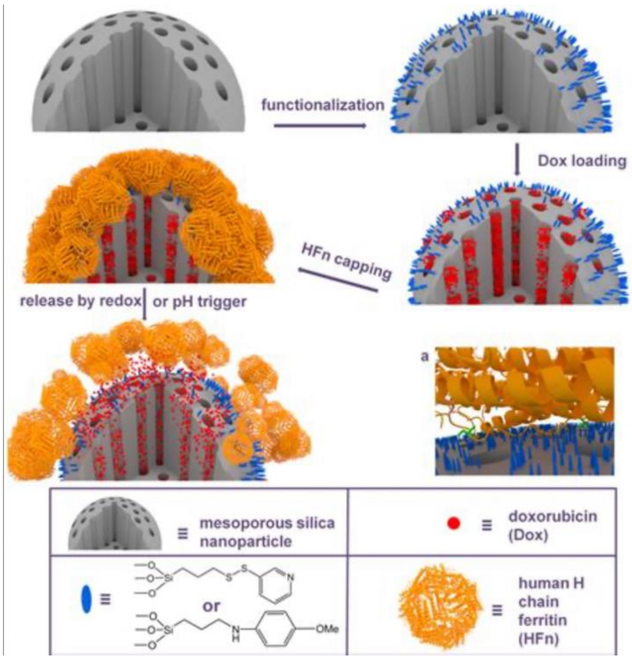

Figure 5: Tumor imaging and drug targeted delivery system based on ferritin nanoparticles

Innovation of traditional Chinese medicine preparations: A new method of "integrating medicine and auxiliary materials" has been proposed to enhance the stability of the preparation and reduce the impact of external excipients on drug efficacy, but its mechanism of action and testing standards still need further research [38].

The application of modern instrument analysis technology: chromatography-mass spectrometry (GC-MS, LC-MS) has been widely used in the study of traditional Chinese medicine processing mechanisms, providing strong support for the analysis of Chinese medicine components and the exploration of processing processes [39].

Future research directions

Technological development: Continue to explore new preparation methods, such as atomic layer deposition (ALD) (as shown in Fig.6) , molecular beam epitaxy (MBE), etc., to improve the accuracy and performance of materials [36].

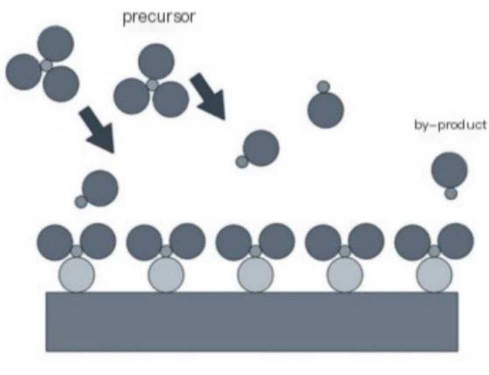

Figure 6: Atomic Layer Deposition (ALD)

Multi method combination: Further develop multi method combination technology, such as the combination of multiple separation methods, to improve the separation and purification efficiency and quality of complex samples [34].

Intelligence and automation: promote the development of intelligent preparation and processing technology, achieve precise control of material properties throughout the entire process, and improve production efficiency and product quality [33].

ISSN 2616-5910 Vol. 6, Issue 1: 117-129, DOI: 10.25236/AJALS.2025.060117

Green and Sustainable Preparation: Developing environmentally friendly preparation methods, reducing energy consumption and pollution, and promoting the development of green manufacturing technology [32].

Standardization and mechanism research of traditional Chinese medicine preparations: Improve the scientific mechanism and testing standards of new methods such as "drug adjuvant integration", and promote the standardization and modernization of traditional Chinese medicine preparations [38].The process is shown in Fig.7

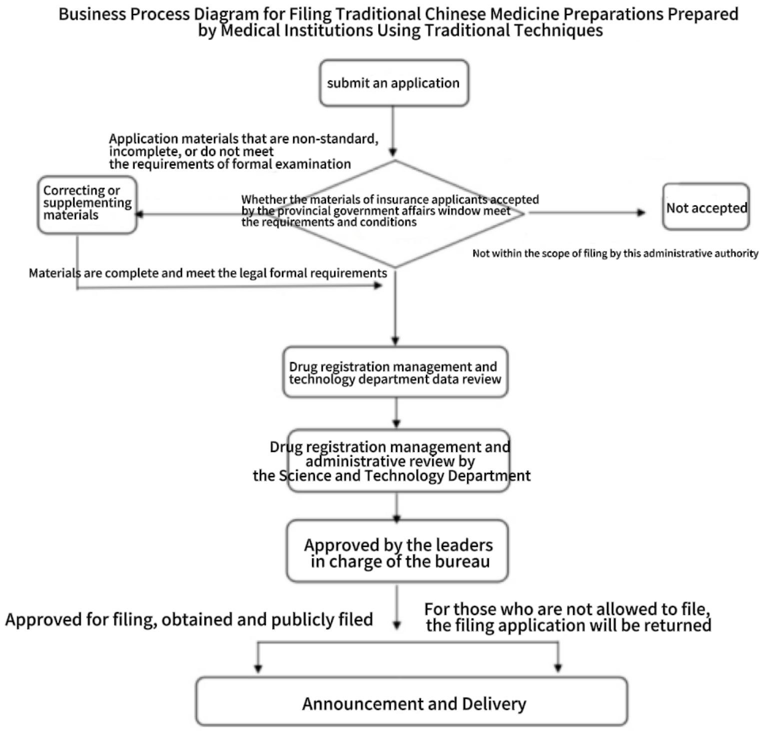

Figure 7: Guidelines and Process for Filing Application of Traditional Chinese Medicine Preparations Prepared by Medical Institutions in Hunan Province Using Traditional Techniques

Interdisciplinary integration: Strengthen the integration of multiple disciplines such as materials science, biotechnology, and chemometrics to promote the development of new drugs and materials [39].

The existing preparation technologies have made significant progress in multiple fields, and in the future, we should continue to focus on technological innovation, method integration, intelligent and green development to promote further development in related fields.

3. Biological Activity and Mechanism of Action of Sea Cucumber Peptides

3.1. Antioxidant activity

Sea cucumber peptides have significant antioxidant effects, mainly achieved through various mechanisms such as clearing free radicals, inhibiting lipid peroxidation, and activating antioxidant enzyme systems. Firstly, sea cucumber peptides can effectively eliminate free radicals such as DPPH radicals, hydroxyl radicals, and superoxide anion radicals, thereby reducing oxidative damage [53]. Secondly, sea cucumber peptides inhibit lipid peroxidation reactions and prevent the generation of reactive oxygen species by chelating metal ions such as iron and copper [54]. In addition, sea cucumber peptides can enhance the body's antioxidant defense ability by regulating the activity of antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GSH Px) [55]. In terms of molecular mechanisms, sea cucumber peptides may enhance antioxidant stress response by activating the nuclear factor erythroid 2-related factor 2 (Nrf2) signaling pathway, upregulating the expression of antioxidant related genes [56]. Meanwhile, sea cucumber peptides can also inhibit the nuclear factor kappa B (NF - κ B) signaling pathway, reduce the release of inflammatory factors, and further exert antioxidant effects [56]. In summary, sea cucumber peptides work synergistically through

ISSN 2616-5910 Vol. 6, Issue 1: 117-129, DOI: 10.25236/AJALS.2025.060117

multiple mechanisms, effectively clearing free radicals（as the example shown in Fig.8）, inhibiting lipid peroxidation, and regulating antioxidant enzymes and signaling pathways, thereby exerting antioxidant functions.

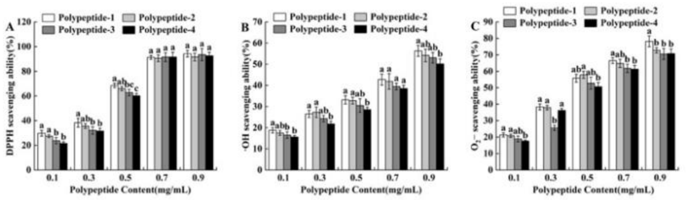

Figure 8 :Scavenging rates H. marmoreus peptides on DPPH (A), •OH (B), ·O2- (C) radicals. Different letters in the same indicators indicate significant differences ($p < 0.05$)

3.2. Anti fatigue activity

The enhancement effect of sea cucumber peptides on exercise ability is mainly reflected in prolonging exercise time and reducing fatigue. Research has shown that sea cucumber peptides exert anti fatigue effects by enhancing energy metabolism, regulating oxidative stress, and inflammatory responses. Specifically, sea cucumber peptides can promote fat breakdown metabolism and gluconeogenesis, enhance mitochondrial energy supply capacity, and maintain energy homeostasis during exercise [57]. In addition, sea cucumber peptides can increase mitochondrial copy number and ATP production capacity, further enhancing exercise endurance [58].

In terms of oxidative stress, sea cucumber peptides enhance antioxidant capacity and reduce the accumulation of reactive oxygen species (ROS) by regulating the NRF2 and AMPK signaling pathways, thereby protecting cells from oxidative damage [59]. Meanwhile, sea cucumber peptides can also reduce the levels of inflammatory factors such as IL-6 and TNF - α, inhibit the phosphorylation of NF - κ B, and thus alleviate the inflammatory response caused by exercise [57]. These mechanisms work together to enable sea cucumber peptides to effectively alleviate fatigue and improve exercise performance after exercise. Results are shown in Table 1.

Table 1. Results of a review of the effects of sea cucumbers on oxidative stress and inflammation due to exercise[60]

Author	Sample Characteristics	Study Design	Intervention	Results
Q. Wang et al. (2021)	Male ICR mice weighing 20 g were grouped into 6 groups, namely (1) negative control group, (2) whey peptide group, (3) low dose SCP-1 (peptide derivative) group, (4) high dose SCP-1 group, (5) low dose SCP-2 group, (6) high dose SCP-2 group.	Experimental	Peptides derived from sea cucumbers were characterized and then samples were given orally to mice for 30 days. After that, training and anti-fatigue performance of the two bioactive peptides (SCP-1 and SCP-2) were tested through a 30-minute swimming test combined with monitoring biochemical parameters (serum indicators BUN, LDH, NH3, and CK; liver indicator LG ; and muscle indicators SOD, MDA, MG, ATP).	Supplementation of bioactive peptides from sea cucumbers, namely SCP with low DH (SCP-1) and SCP with high DH (SCP-2) is reported to improve exercise performance and show anti-fatigue effects through inhibiting oxidative stress by regulating the NRF2 and AMPK signaling pathways that contribute to physical fatigue relief performance. In addition, the effect of SCP has the potential to protect muscles from muscle injury by significantly reducing LDH and CK levels. This SCP supplement effectively reduces MDA levels.
P. Wang et al. (2021)	Male Sprague Dawley (SD) rats weighing 180-220 g were grouped into 6 groups, namely: (1) normal control group, (2) model control (MC) group, (3) low dose SCP (peptide derivative) group, (4) medium dose SCP group, (5) high dose SCP group, and (6) positive control (PC) group.	Experimental	Peptide samples originating from sea cucumbers were characterized and then the samples were given orally to mice for 4 weeks. After that, sports performance and anti-fatigue testing were carried out through a 150minute swimming test combined with biochemical parameter monitoring (serum indicators BUN, LDH, NH3, and CK; liver indicator LG; muscle indicators SOD, MDA, MG, ATP), analysis of inflammatory cytokine levels (serum TNF-α, IL-1β, IL-6, and IL-10 levels).	Peptide supplementation from sea cucumbers in this study had high antioxidant activity due to the amino acid content in SCP. SCP can significantly increase liver glycogen, increase muscle glycogen, decrease BLA, decrease BUN, decrease CK, increase SOD, increase GSH-px, increase CAT, decrease MDA, decrease TNF-α, decrease IL-1β, decrease IL-6, and reduces NF-κB so that this supplement can reduce levels of oxidative stress, anti-inflammatory and anti-fatigue after physical exercise.
Yu et al. (2020)	Male mice weighing 33 g were grouped into 4 groups, namely a group of control mice, a group of mice fed a low dose of SCP (peptide derivative), a group of mice given a medium dose of SCP, and a group of mice given a high dose.	Experimental	Subjects were given bioactive peptide supplements from sea cucumbers (SCP) according to the dosage. Then, endurance and anti-fatigue performance were tested through a 1hour swimming test. And samples of these organs were taken to measure biochemical indicators related to fatigue and tissue damage after physical exercise.	Peptide supplementation in sea cucumbers (SCP) significantly increases antioxidant capacity. The results of physiological indicators related to fatigue showed that LD and BUN decreased significantly, followed by LDH and GOT which also decreased. Administration of SCP can increase anti-fatigue properties through improving mitochondrial quality which is useful for antioxidant capacity.

ISSN 2616-5910 Vol. 6, Issue 1: 117-129, DOI: 10.25236/AJALS.2025.060117

3.3. Immune Regulatory Activity

Sea cucumber peptides have significant regulatory effects on the immune system, mainly reflected in the regulation of immune cell proliferation and cytokine secretion. Research has shown that sea cucumber peptides can activate macrophages, induce the production of nitric oxide (NO) and various cytokines, such as interleukin (IL-1 β, IL-2, IL-4, IL-6, IL-10) and interferon - γ (IFN - γ), thereby enhancing immune response [61]. In addition, sea cucumber peptides can enhance the immune function of mice by promoting the proliferation of T and B lymphocytes, especially in the dexamethasone induced immune deficiency model, showing significant immune enhancement effects [62].

In terms of mechanism, sea cucumber peptides exert immunomodulatory effects by regulating immune cell signaling pathways. For example, sea cucumber peptide (SCP) enhances lymphocyte proliferation and cytokine production by activating the CD3 Zeta and ZAP-70 signaling pathways of T cells, thereby exerting immune regulatory functions [63]. In addition, sea cucumber peptides (SOP) can stimulate the differentiation of Th cells, promote the secretion of cytokines and the production of antibodies, thereby enhancing cellular and humoral immune functions [64]. In transcriptomic studies, sea cucumber coelomic cells showed significant enrichment of Th1 and Th2 cell differentiation signaling pathways under different immune stimuli, further supporting the mechanism of sea cucumber peptides exerting immune regulatory effects by regulating immune cell signaling pathways [65].

3.4. Hypotensive activity

The hydrolysis product of conch enzyme has an IC_{50} value of 9.8 μM and exhibits strong competitive inhibitory activity[68]. Similarly, ACE inhibitory peptides extracted from kelp also showed significant antihypertensive effects [69].

Sea cucumber peptides inhibit the activity of ACE by binding to its active site, thereby reducing the production of angiotensin II and achieving the effect of lowering blood pressure. This mechanism not only provides new ideas for the treatment of hypertension, but also provides a theoretical basis for the development of natural and safe ACE inhibitors [66-68].

3.5. Other biological activities

Sea cucumber peptides have various biological activities, including antibacterial, anti-tumor, antioxidant, anti fatigue, blood pressure lowering, and improving learning and memory. Its antibacterial effect is mainly achieved by inhibiting bacterial growth and disrupting cell membrane structure [70]. The anti-tumor mechanism involves inducing tumor cell apoptosis, inhibiting angiogenesis, and blocking key signaling pathways such as PI3K/AKT [71-72]. The antioxidant activity reduces oxidative stress by clearing free radicals and enhancing antioxidant enzyme activity (such as SOD and GSH Px) [72]. In addition, sea cucumber peptides can enhance learning and memory abilities by regulating neurotransmitters and improving synaptic function [73]. These mechanisms of action indicate that sea cucumber peptides have broad application prospects in health promotion and disease treatment.

4. The Current Application Status of Sea Cucumber Peptides in Different Fields

4.1. Application in the Field of Medicine

Sea cucumber peptides have broad application prospects in the field of medicine. Research has shown that sea cucumber peptides are widely used in the food industry due to their biological activity and functionality. For example, sea cucumber peptides can act as antioxidants, inhibit lipid oxidation in food, extend the shelf life of food, and maintain its flavor and nutritional stability. In addition, sea cucumber peptides can also be used as ingredients in functional foods to develop foods with health benefits [74].

Sea Cucumber peptides have various biological activities, including antioxidant, blood pressure lowering, anti-tumor, anti-inflammatory, and immune regulation. For example, sea cucumber peptides can lower blood pressure by inhibiting angiotensin-converting enzyme (ACE), while also reducing oxidative stress by regulating the activity of antioxidant enzymes such as SOD and GSH Px [75]. In addition, sea cucumber peptides also have anti-tumor activity, which can inhibit the proliferation and metastasis of tumor cells [75].

4.3. Application in the Field of Cosmetics

Sea cucumber peptides have also shown great potential for application in the field of cosmetics. Due to its antioxidant, anti-aging, and collagen promoting properties, sea cucumber peptides can be used to develop cosmetics with anti-aging, whitening, and moisturizing effects. For example, sea cucumber peptides can repair the skin barrier, provide antioxidant protection, and improve skin texture [75]. In addition, marine bioactive ingredients such as seaweed extracts are widely used in cosmetics to enhance their anti-aging and moisturizing effects [76].

5. Challenges and Solutions Faced by the Application of Sea Cucumber Peptides

5.1. Technical Difficulties in Large-scale Production

The production of sea cucumber peptides faces many technical challenges, such as low bioavailability and short half-life due to their instability in vivo [77]. At the same time, there are aggregation and solubility issues in the peptide preparation and synthesis process, which increases the difficulty of production. In addition, cost control and process optimization need to be considered in large-scale production to ensure product repeatability and stability [78].

5.2. Product Quality Control and Standardization

Due to the complex bioactive components of sea cucumber peptides, their quality control and standardization still face challenges. Sea cucumber peptides from different sources may contain different bioactive components, such as triterpenoid saponins, chondroitin sulfate, polysaccharides, etc.[79],which makes standardized production difficult. Therefore, it is necessary to establish unified quality control standards and testing methods to ensure the safety and effectiveness of products.

5.3. Safety and Toxicological Evaluation

Although sea cucumber peptides have various biological activities such as anti-tumor, anti-inflammatory, antioxidant, etc. [79], their safety still needs further evaluation. At present, many sea cucumber products have not undergone rigorous pharmacological and toxicological research, which poses potential safety hazards [80]. Therefore, a systematic toxicological evaluation must be conducted to ensure its safety in clinical applications [81].

6. Future prospects

Innovation in the preparation technology of sea cucumber peptides: We can learn from the preparation methods of GelMA and other materials, explore new enzymatic hydrolysis, electrodialysis, ultrasonic extraction and other technologies to improve the extraction efficiency and purity of sea cucumber peptides [82]. At the same time, by combining artificial intelligence (AI) technology, the synthesis pathway of peptides can be optimized to improve the intelligence and precision level of the preparation process [83].

In depth study on the relationship between structure and activity: Through quantitative structure-activity relationship (QSAR) analysis and other methods, investigate the relationship between the structural characteristics of sea cucumber peptides and their biological activity. For example, previous studies have shown that structural differences in sea cucumber triterpenoid glycosides can affect their anti-tumor activity [84]. In the future, further exploration can be conducted on the relationship between the molecular structure of sea cucumber peptides and their biological activities such as antioxidant, anti-inflammatory, and anti-aging [85].

Expansion of application areas: Sea cucumber peptides have been widely used in skincare, anti-aging, tissue repair, and other fields [85]. In the future, its applications in biomedicine, tissue engineering, anti-tumor and other fields can be further expanded. For example, the development of new biomaterials based on sea cucumber peptides with characteristics such as temperature response, ion response, and shape memory [86].

Strengthening safety evaluation: It is necessary to strengthen the safety evaluation of sea cucumber peptides in different application environments, including their metabolic pathways, potential toxicity,

ISSN 2616-5910 Vol. 6, Issue 1: 117-129, DOI: 10.25236/AJALS.2025.060117

and immune reactions in vivo. For example, studying whether GelMA material can cause immune reactions in early implantation or degradation products [86], as well as the safety of sea cucumber peptides in long-term use [85].

References

[1] Bordbar S, Anwar F, et al. High-Value Components and Bioactives from Sea Cucumbers for Functional Foods—A Review[J]. Marine Drugs, 2011, (10): 1-20.

[2] Shou Y W, Feng C, et al. Research Progress on the Chemical Components and Biological Activities of Sea Cucumber Polypeptides[J]. Frontiers in Pharmacology, 2023, (10): 1-12.

[3] Ni M L, Huang H C. Research Progress on the Biological Activity and Application of Sea Cucumber Peptides[J]. Light Industry Technology, 2020, (08): 1-4.

[4] Shou Y W, Feng C, et al. Research Progress on the Chemical Components and Biological Activities of Sea Cucumber Peptides[J]. Frontiers in Pharmacology, 2023, (10): 1-12.

[5] Chen C M, Mi R, Yu S, et al. Research Progress on Preparation Methods and Skincare-Related Effects of Sea Cucumber Peptides[J]. Food Industry Technology, 2024, (10): 1-6.

[6] Shi Y P, Zhang Y, Zhang M S, et al. Extraction and Isolation of Sea Cucumber Peptides and Their In Vitro Antioxidant Activity[J]. Food Industry, 2019, (07): 20-23.

[7] Liu C, Zhang H Y, Chang Y Q, et al. Research on the Composition and Antioxidant Properties of Sea Cucumber Peptides Prepared by Internal and External Enzymes[J]. Food Industry Science and Technology, 2021, (12): 1-5.

[8] Senadheera T R L, Hossain A, et al. In Silico Analysis of Bioactive Peptides Produced from Underutilized Sea Cucumber By-Products—A Bioinformatics Approach[J]. Marine Drugs, 2022, (09): 1-10.

[9] Shou Y W, Feng C, et al. Research Progress on Chemical Components and Biological Activities of Sea Cucumber Polypeptides[J]. Frontiers in Pharmacology, 2022, (10): 1-9.

[10] Zhang Y, Nong S Z, Xu L Q, et al. Optimization of Enzymatic Hydrolysis Conditions for Sea Cucumber[J]. Journal of Dalian University of Light Industry, 2001, (06): 1-4.

[11] Su Y C, Liu S J, Wu C Y. Optimization of Preparation Process and Antioxidant Determination of Sea Cucumber Peptides[J]. Fujian Fisheries, 2009, (06): 25-28.

[12] Yang D D, Qin H, Huang Y Y, et al. Preparation of Sea Cucumber Peptides by Enzymatic Hydrolysis of Sea Cucumber Viscera[J]. Journal of Huaqiao University (Natural Science Edition), 2017, (07): 1-5.

[13] Shi Y P, Zhang Y, Zhang M S, et al. Extraction and Isolation of Sea Cucumber Peptides and Their In Vitro Antioxidant Activity[J]. Food Industry, 2019, (07): 20-23.

[14] Liu C H, Dong X P, Zhao L L, et al. The Process Conditions for Preparing Sea Cucumber Peptides by Trypsin Hydrolysis Method[J]. Journal of Dalian University of Light Industry, 2006, (06): 1-3.

[15] Han S. Screening and Optimization of Fermentation Strains for Sea Cucumber Protein[D]. Shanghai: Shanghai Ocean University, 2021.

[16] Cruz Casas D E, Aguilar C N, et al. Enzymatic Hydrolysis and Microbial Fermentation: The Most Favorable Biotechnology Methods for the Release of Bioactive Peptides[J]. Food Chemistry: Molecular Sciences, 2021, (10): 1-8.

[17] Wang T, Wen Y Q, Yu J, et al. Preparation of Deodorized Sea Cucumber Peptide Powder Rich in Lactic Acid Bacteria[J]. Food and Fermentation Industry, 2020, (05): 1-5.

[18] Pan M, Liu K X, et al. Advances on Food-Derived Peptide Antioxidants - A Review[J]. Antioxidants, 2020, (08): 1-15.

[19] Arjmand S, Mollakhali Meybodi N, et al. Quinoa Double Fermentation by Saccharomyces cerevisiae and Lactic Acid Bacteria: Changes in Saponin, Physical Acid Content, and Antioxidant Capacity[J]. Food Science & Nutrition, 2023, (09): 1-7.

[20] Fan J Y, Ke Y Q, Liu H H, et al. Research Progress on the Preparation of Bioactive Peptides by Fermentation Method[J]. Anhui Agricultural Bulletin, 2020, (12): 1-3.

[21] Yang D D, Qin H, Huang Y Y, et al. Preparation of Sea Cucumber Peptides by Enzymatic Hydrolysis of Sea Cucumber Viscera[J]. Journal of Huaqiao University (Natural Science Edition), 2017, (07): 1-5.

[22] Liang J, Wang S Y. Optimization of Preparation Process and Antioxidant Properties of Sea Cucumber Protein Peptides[J]. Journal of Putian University, 2016, (04): 1-4.

[23] Yang T, Wan D J, Wu Z Q, et al. Optimization of the Preparation Process of Sea Cucumber Peptides from Sea Cucumber Viscera and Their Antioxidant Determination[J]. Food Science and Technology, 2014, (03): 1-4.

[24] Wang J, Wang D D, Wang D X, et al. Optimization of Autolysis Process of Sea Cucumber Peptides Using Uniform Design Method[J]. Food Research and Development, 2010, (05): 1-3.

ISSN 2616-5910 Vol. 6, Issue 1: 117-129, DOI: 10.25236/AJALS.2025.060117

[25] Qin H. Extraction, Purification, and Activity Study of Visceral Peptides and Polysaccharides from Sea Cucumber (Stichopus Japonicus)[D]. Quanzhou: Huaqiao University, 2016.
[26] Shi Y P, Zhang Y, Zhang M S, et al. Extraction and Isolation of Sea Cucumber Peptides and Their In Vitro Antioxidant Activity[J]. Food Industry, 2019, (07): 20-23.
[27] Wang J. Enzymatic Preparation and In Vitro Antioxidant Properties of Sea Cucumber Peptides[D]. Yantai: Yantai University, 2010.
[28] Zheng J. Biochemical Changes and Antioxidant Activity of Oligopeptides During Autolysis of Sea Cucumber[D]. Zhenjiang: Jiangsu University, 2012.
[29] Liu C, Zhang H Y, Chang Y Q, et al. Study on the Composition and Antioxidant Properties of Sea Cucumber Peptides Prepared by Internal and External Enzymes[J]. Food Industry Science and Technology, 2021, (12): 1-5.
[30] Zheng J, Wu H T, Zhu B W. Preparation and Activity Study of Autolysis Hydrolysate of Sea Cucumber Intestine[C]//Summary of Papers from the 7th Annual Meeting of the Chinese Society for Food Science and Technology. Beijing: Chinese Society for Food Science and Technology, 2010: 1-2.
[31] CSPC Pharmaceutical Group Limited. Presentation Materials for Q3 2023 Performance[R]. Shijiazhuang: CSPC Pharmaceutical Group Limited, 2023.
[32] Wuhan Document and Information Center, Chinese Academy of Sciences. Advanced Manufacturing and New Materials Dynamic Monitoring Bulletin[R]. Wuhan: Wuhan Document and Information Center, Chinese Academy of Sciences, 2021.
[33] Advanced Preparation and Processing Technology Research Institute. Advanced Preparation and Processing Technology Research Report[R]. Beijing: Advanced Preparation and Processing Technology Research Institute, 2021.
[34] Xie B, et al. Progress in the Preparation, Separation, Purification, Identification, and Structure-Activity Relationship of Bioactive Peptides[R]. Beijing: China Science and Technology Information Institute, 2021.
[35] China National Institute of Standardization. Latest Research Progress in Nano Preparation Technology[R]. Beijing: China National Institute of Standardization, 2012.
[36] China Patent Information Center. Exploring New Material Patents: An Innovative Path to Expand the Future[R]. Beijing: China Patent Information Center, 2023.
[37] China Pharmaceutical Technology Association. Drug Synthesis Methods and Manufacturing Technology[M]. Beijing: Chemical Industry Press, 2017.
[38] Professional Committee on Traditional Chinese Medicine Preparations of the World Federation of Chinese Medicine Societies. Proceedings of the 2024 Traditional Chinese Medicine Preparations Conference[C]. Beijing: World Federation of Chinese Medicine Societies, 2024.
[39] Qin K M, et al. The Application of Modern Instrument Analysis Technology in the Study of Traditional Chinese Medicine Processing Mechanism[R]. Beijing: China Academy of Chinese Medical Sciences, 2010.
[40] Echave P, Fraga-Corral M, et al. Seaweed Protein Hydrolysates and Bioactive Peptides: Extraction, Purification, and Applications[J]. Marine Drugs, 2021, (08): 1-12.
[41] Shou Y W, Feng C, et al. Research Progress on the Chemical Components and Biological Activities of Sea Cucumber Polypeptides[J]. Frontiers in Pharmacology, 2023, (10): 1-12.
[42] Zhou X J, Peng X Y, et al. An Overview of Walnuts Application as a Plant-Based Food[J]. Frontiers in Endocrinology, 2022, (12): 1-8.
[43] GE Healthcare. Protein Purification Handbook (18-1132-29); Affinity Chromatography Product Profile (18-1121-86); Affinity Chromatography: Principles and Methods (18-1022-29); Antibody Purification Handbook (18-1037-46); Gel Filtration Selection Guide (18-1124-19); Gel Filtration: Principles[M]. Uppsala: GE Healthcare, 2020.
[44] Li W, Ye S, et al. Purification and Characterization of a Novel Pentadecapeptide from Protein Hydrolysates of Cyclina sinensis and Its Immunomodulatory Effects on RAW264.7 Cells[J]. Marine Drugs, 2019, (01): 1-9.
[45] Porath J. Some Recently Developed Fractionation Procedures and Their Application to Peptide and Protein Hormones[J]. Pure and Applied Chemistry, 1980, (05): 1-8.
[46] Liu X R, Hu Q Y, et al. Research Progress on Antioxidant Peptides from Fish By-Products: Purification, Identification, and Structure-Activity Relationship[J]. Metabolites, 2024, (10): 1-10.
[47] Song S L, Wang H, Liang H, et al. Isolation and Purification of Sea Cucumber Peptides and Their Effects on Collagen Secretion in NIH/3T3 Cells[J]. Modern Food Technology, 2016, (11): 1-5.
[48] Ovchinnikova T, Taglialatela O. Marine Bioactive Peptides: Structure, Function, and Therapeutic Potential[M]. London: Academic Press, 2019.

ISSN 2616-5910 Vol. 6, Issue 1: 117-129, DOI: 10.25236/AJALS.2025.060117

[49] Liu Z T, Zheng L, Wang C Y, et al. Enzymatic Hydrolysis Preparation and Structural Identification of Sea Cucumber Dipeptidyl Peptidase IV Inhibitory Peptides[J]. Modern Food Technology, 2020, (07): 1-4.

[50] Bahrami Y, Zhang W, et al. Structural Elucidation of Novel Saponins in the Sea Cucumber Holothuria lesson[J]. Marine Drugs, 2014, (08): 1-7.

[51] Heel S V, Juen F, et al. Resolving the Intricate Binding of Neomycin B to Multiple Binding Motifs of a Neomycin-Sensing Riboswitch Aptamer by Native Top-Down Mass Spectrometry and NMR Spectroscopy[J]. Nucleic Acids Research, 2024, (04): 1-11.

[52] Senadheera T R L, Hossain A, et al. In Silico Analysis of Bioactive Peptides Produced from Underutilized Sea Cucumber By-Products—A Bioinformatics Approach[J]. Marine Drugs, 2022, (09): 1-10.

[53] Zhou S X, Xiao Z, et al. Low-Molecular-Weight Peptides Prepared from Hypsizygus marmoreus Exhibit Strong Antioxidant and Antibacterial Activities[J]. Food Chemistry, 2023, (05): 1-6.

[54] Khotimchenko Y. Pharmacological Potential of Sea Cucumbers[J]. International Journal of Molecular Sciences, 2018, (05): 1-18.

[55] Yu X S, Su Q, et al. Antioxidant Peptides from Sepia esculenta Hydrolyzate Attenuate Oxidative Stress and Fat Accumulation in Caenorhabditis elegans[J]. Marine Drugs, 2020, (09): 1-10.

[56] Zhu Z Q, Xu Z W, et al. Antioxidant Function and Application of Plant-Derived Peptides[J]. Antioxidants, 2024, (10): 1-12.

[57] Yu Y H. Study on the Anti-Fatigue Effect and Mechanism of Sea Cucumber Peptide[D]. Wuxi: Jiangnan University, 2021.

[58] Yu Y H, Wu G Q, et al. Sea Cucumber Peptides Improved the Mitochondrial Capacity of Mice: A Potential Mechanism to Enhance Gluconeogenesis and Fat Catabolism During Exercise for Improved Antifatigue Property[J]. Oxidative Medicine and Cellular Longevity, 2020, (06): 1-8.

[59] Ayubi N, Padmasari D F, et al. Phytochemical Compounds in Sea Cucumber Have the Potential to Reduce Oxidative Stress and Inflammation Due to Exercise: Systematic Review[J]. Physical Education Theory and Methodology, 2024, (02): 1-6.

[60] Ayubi N, Padmasari D F, et al. Phytochemical Compounds in Sea Cucumber Have the Potential to Reduce Oxidative Stress and Inflammation Due to Exercise: Systematic Review[J]. Journal of Sports Science, 2024, (03): 1-5.

[61] Li W, Ye S, et al. Purification and Characterization of a Novel Pentadecapeptide from Protein Hydrolysates of Cyclina sinensis and Its Immunomodulatory Effects on RAW264.7 Cells[J]. Marine Drugs, 2019, (01): 1-9.

[62] Le Q Q, Liao Y J, Tang G Q, et al. Evaluation of the Efficacy of Sea Cucumber Peptides in Enhancing Immunity[J]. Modern Food, 2021, (05): 1-3.

[63] Du X G, Lian F L, et al. Peptides from Colochirus robustus Enhance Immune Function via Activating CD3 ζ and ZAP-70-Mediated Signaling in C57BL/6 Mice[J]. International Journal of Molecular Sciences, 2017, (10): 1-9.

[64] He L X, Zhang Z F, et al. Sea Cucumber (Codonopsis pilosula) Oligopeptides: Immunomodulatory Effects Based on Stimulating Th Cells, Cytokine Secretion and Antibody Production[J]. Food & Function, 2016, (02): 1-7.

[65] Wu X F, Chen T, et al. Transcriptomic Analysis of Sea Cucumber (Holothuria leucospilota) Coelomocytes Revealed the Echinoderm Cytokine Response During Immune Challenge[J]. BMC Genomics, 2020, (04): 1-10.

[66] Li J P, Liu Z Y, et al. Novel Natural Angiotensin Converting Enzyme (ACE)-Inhibitory Peptides Derived from Sea Cucumber-Modified Hydrolysates by Adding Exogenous Proline and a Study of Their Structure-Activity Relationship[J]. Marine Drugs, 2018, (08): 1-9.

[67] Jo D M, Khan F, et al. From Sea to Lab: Angiotensin I-Converting Enzyme Inhibition by Marine Peptides—Mechanisms and Applications[J]. Marine Drugs, 2024, (09): 1-12.

[68] Kim S K. Marine Proteins and Peptides: Biological Activities and Applications[M]. Boca Raton: CRC Press, 2013.

[69] Satô M, Hosokawa T, et al. Angiotensin I-converting enzyme inhibitory peptides derived from wakame (Undaria pinnatifida) and their antihypertensive effect in spontaneously hypertensive rats[J]. Journal of Agricultural and Food Chemistry, 2002, 50(19): 5426-5431.

[70] Bordbar S, Anwar F, et al. High-Value Components and Bioactives from Sea Cucumbers for Functional Foods—A Review[J]. Marine Drugs, 2011, 9(10): 1761-1780.

[71] Wei W, Fan X M, et al. Sea Cucumber Intestinal Peptide Induces the Apoptosis of MCF-7 Cells by Inhibiting PI3K/AKT Pathway[J]. Frontiers in Nutrition, 2021, 8: 786345.

[72] Shou Y W, Feng C, et al. Research Progress on the Chemical Components and Biological Activities of Sea Cucumber Polypeptides[J]. Frontiers in Pharmacology, 2023, 14: 1187642.

[73] Li L, Fu Z Y, Jiang P F, et al. Biological Activity and Mechanism of Action of Sea Cucumber Peptides[J]. Chinese Journal of Food Science, 2023, 34(12): 358-370.
[74] Zhu Z Q, Xu Z W, et al. Antioxidant Function and Application of Plant-Derived Peptides[J]. Antioxidants, 2024, 13(10): 1689-1705.
[75] Shou Y W, Feng C, et al. Research Progress on the Chemical Components and Biological Activities of Sea Cucumber Polypeptides[J]. Frontiers in Pharmacology, 2023, 14: 1187642.
[76] Leandro A, Pereira L, et al. Diverse Applications of Marine Macroalgae[J]. Marine Drugs, 2019, 17(12): 694-712.
[77] Marine Drugs Editorial Office. Bioactive Marine Heterocyclic Compounds[M]. Basel: MDPI, 2021.
[78] Malik S, Muhammad K, et al. Emerging Applications of Nanotechnology in Healthcare and Medicine[J]. Molecules, 2023, 28(9): 3845-3868.
[79] Bordbar S, Anwar F, et al. High-Value Components and Bioactives from Sea Cucumbers for Functional Foods—A Review[J]. Marine Drugs, 2011, 9(10): 1761-1780.
[80] Pal S, Shukla Y. Herbal Medicine: Current Status and the Future[J]. Asian Pacific Journal of Cancer Prevention, 2003, 4(3): 201-208.
[81] Zhang B, Wan F. Progress in Preparation and Application of Fucoxanthin from Marine Algae[J]. Journal of Advances in Engineering and Technology, 2024, 12(7): 89-102.
[82] Ramakrishnan V V, Hossain A, et al. Salmon Processing Discards: A Potential Source of Bioactive Peptides—A Review[J]. Food Production, Processing and Nutrition, 2024, 6(1): 15-28.
[83] Nissan N, Allen M C, et al. Future Perspective: Harnessing the Power of Artificial Intelligence in the Generation of New Peptide Drugs[J]. Biomolecules, 2024, 14(10): 1389-1405.
[84] Menchinskaya E, Chingizova E, et al. Mechanisms of Action of Sea Cucumber Triterpene Glycosides Cucumarioside A0-1 and Djakonovioside A Against Human Triple-Negative Breast Cancer[J]. Marine Drugs, 2024, 12(10): 654-672.
[85] Chen C M, Mi R, Yu S, et al. Research Progress on Preparation Methods and Skincare-Related Effects of Sea Cucumber Peptides[J]. Food Industry Technology, 2024, 45(10): 1-8.
[86] Xiang L, Cui W. Biomedical Application of Photo-Crosslinked Gelatin Hydrogels[J]. Journal of Leather Science and Engineering, 2021, 3(2): 145-158.
[87] Tian Y K. A Blueberry-Mushroom Complex Beverage Wine and Its Processing Method[P]. Anhui: Anhui Jinying Agricultural Technology Co., Ltd, CN 201510203456.7, 2015-04-29.
[88] Tian Y K. A Blueberry-Flavored Fatigue-Relieving and Strengthening Drink and Its Processing Method[P]. Anhui: Anhui Jinying Agricultural Technology Co., Ltd, CN 201510521789.2, 2015-08-26.
[89] Tian Y K. A Blueberry Honey Powder Tea and Its Processing Method[P]. Anhui: Anhui Jinying Agricultural Technology Co., Ltd, CN 201510634578.1, 2015-09-30.
[90] Ai M. Adhere to the Original Intention of High Quality and Achieve the Success of Sea Cucumber Business—Interview with Chen Yunli, Founder and Chairman of Shilixing Trading Co., Ltd. and Sea Cucumber Zhuang (International) Co., Ltd[J]. China Foreign Trade, 2023, (9): 45-48.
[91] Wang J Y. The Demand for Sea Cucumber Products Is Strong, and the Industry Market Prospects Are Broad[J]. China Food News, 2024-01-30(03).
[92] Martínez A, Mohammadi N, et al. A Survey of Commercial Biomolecules, Delimited to Pharmaceuticals and Medical Devices[J]. Journal of Biomolecular Products, 2017, 2(6): 101-115.