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Research Article

Construction of a Nanostructured Stabilization System for Sea Cucumber Lipids and Their Precise Intestinal Release Mechanism

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Abstract: The annual output of sea cucumber processing by-products in China exceeds 100,000 tons, which are rich in functional lipids such as cerebrosides and EPA/DHA, making them a valuable resource for high-value utilization. However, disadvantages such as the easy oxidation of sea cucumber lipids, intolerance in the gastrointestinal tract, and lack of targeting seriously affect their efficacy. Using sea cucumber processing by-products as raw materials, this paper starts from three aspects: nanostructured stabilization construction, targeted intestinal delivery, and precise release mechanisms. It elaborates on the green and highly efficient preparation of sea cucumber lipids, the triple stabilization system of protein self-assembly, liposomes, and hydrogels, and the pH-enzyme dual-responsive precise release pathway. It reveals the structure-activity relationship and in vivo transport laws, providing a theoretical basis and technical route for the high-value utilization of sea cucumber functional lipids and the creation of novel special dietary foods.

Keywords: Sea cucumber processing; By-products; Sea cucumber lipids; Nanostructured stabilization; Intestinal targeting

Introduction

Sea cucumber is the mariculture species with the largest single output value in China, with an annual yield of over 290,000 tons and an output value exceeding 130 billion yuan. Its processing by-products account for a relatively

high proportion and are rich in highly active substances such as polysaccharides, polypeptides, and lipids, which possess important health benefits including uric acid reduction, anti-Helicobacter pylori effects, and cognitive improvement. Currently, most sea cucumber processing by-products are discarded, causing both a waste of resources and pressure on the environment. Functional lipids are easily degraded by gastric acid and pepsin after oral administration, resulting in low bioavailability, which necessitates solutions for stabilization and targeted delivery. Nano-delivery systems can significantly improve the stability and intestinal absorption rate of lipid active substances. From the perspective of the high-value utilization of marine resources and the strategy of building a strong marine nation, this paper mainly focuses on the research of nanostructured stabilization of sea cucumber lipids and their precise intestinal release, providing new ideas for the resource utilization of sea cucumber by-products and the development of high-end functional products.

1 Highly Efficient Preparation and Structural-Functional Characterization of Sea Cucumber Functional Lipids

1.1 Green, Highly Efficient, and Precise Preparation Technology for Lipids from Sea Cucumber Processing By-products

The components of sea cucumber processing by-products (intestines, eggs, and blanching liquid) are complex, with polysaccharides, proteins, and lipids mixed together. Traditional solvent extraction methods face issues such as low extraction rates, solvent residues, and the destruction of activity. This paper utilizes low-carbon physical coupling highly efficient bioprocessing intelligent technology, aqueous methods combined with fluid extraction technology, and supercritical CO_2 extraction combined technology to achieve the highly efficient separation of lipids and the retention of their components. The raw materials undergo pretreatments of drying, crushing, and desalination to reduce the impact of salt ions on extraction efficiency and system stability. Supercritical CO_2 extraction achieves the selective dissolution of lipids under mild conditions, without employing high-temperature oxidation or leaving organic solvent residues. Coupling molecular distillation, gradient separation, and composite adsorbent decolorization and deodorization simultaneously improves purity and sensory quality. The lipid extraction rate of this method is over 15% higher than traditional methods, and the retention rates of active components such as EPA, DHA, and cerebrosides are all greater than 90%, laying a solid foundation for subsequent stabilization construction.

1.2 Structural Analysis and Structure-Activity Relationship Characterization of Sea Cucumber Active Lipids

The lipids of sea cucumbers are mainly phospholipids, glycolipids, unsaturated fatty acids, and cerebrosides, whose structures affect their function and stability. GC-MS, UPLC-Q-TOF, nuclear magnetic resonance, and mass

spectrometry hyphenated techniques are used to analyze the fatty acid composition, phospholipid types, and the polar head structure of cerebrosides. Molecular simulations, molecular docking, and cell models are utilized to determine the relationship between structure and anti-oxidation, anti-digestion, and targeted recognition. Studies show that sea cucumber lipids contain a large amount of n-3 polyunsaturated fatty acids and special branched-chain lipids, possessing strong membrane affinity and physiological activity. However, unsaturated bonds are easily degraded by oxidation and are readily destroyed in environments with gastric acid and bile salts, thereby losing activity. From the structure-activity relationship, it can be concluded that a higher degree of unsaturation corresponds to a higher oxidative sensitivity of the lipids; the polar head affects gastrointestinal stability and intestinal epithelial affinity, thus providing accurate information for the design of stabilization carriers and targeted modifications.

1.3 Lipid Activity Evaluation and Key Efficacy Target Verification

A three-level research system encompassing molecular, cellular, and animal levels is constructed to systematically explore various aspects of sea cucumber lipids, such as cognitive function improvement, blood pressure reduction, and anti-fatigue properties, and to identify the rate-limiting steps, namely the two links of intestinal absorption and target organ enrichment. The human intestinal epithelial cell Caco-2 model is used to evaluate transport efficiency, while mouse simulated gastrointestinal digestion and in vivo imaging are used to trace in vivo behaviors. The results indicate that the degradation rate of free sea cucumber lipids in simulated gastric fluid over 2 hours is greater than 40%; they are easily emulsified and inactivated by bile salts in intestinal fluid, resulting in an oral bioavailability of less than 20%. Lipid activity relies on intact intestinal absorption and effective enrichment in target tissues, and it is difficult for natural lipids to break through the gastrointestinal barrier. The above results demonstrate that stabilized protection and precise intestinal administration methods can effectively enhance the bioavailability and efficacy of sea cucumber lipids, pointing a specific direction for the construction of nano-delivery systems.

2 Construction and Performance Optimization of the Nanostructured Stabilization System for Sea Cucumber Lipids

2.1 Construction and Stabilization Mechanism of Protein Self-Assembling Nanocarriers

Using marine-derived proteins as a matrix, sea cucumber lipids are encapsulated and protected by means of self-assembling nanoparticles. Utilizing the amphiphilicity and hydrophobic interaction of proteins, a core-shell structure is formed under mild conditions, encapsulating the lipids within the hydrophobic core. By adjusting

protein concentration, pH value, and ionic strength, the particle size is controlled between 80nm and 150nm, the PDI is less than 0.2, and the Zeta potential is maintained between -25mV and -35mV, thereby increasing dispersibility and improving anti-flocculation. Relying on the dual roles of steric hindrance and the interfacial film, this system completely isolates oxygen, light, and metal ions, significantly slowing down the oxidation rate of lipids. In simulated gastric fluid, the protein shell can resist hydrolysis by pepsin, maintaining the structural stability of the lipids with an oxidative degradation rate of less than 15%. Protein self-assembling carriers possess good biocompatibility, are biodegradable, and have no immunogenicity, making them suitable as stable carriers for sea cucumber lipids.

2.2 Composite Stabilization System of Liposome Encapsulation and Hydrogel Microcapsules

To improve anti-digestibility, a liposome-hydrogel composite delivery system was prepared. Using phospholipids and cholesterol as membrane materials, nanoliposomes are prepared via thin-film hydration and ultrasonication methods to encapsulate sea cucumber lipids, forming the first layer of protection. The liposomes are then dispersed into a natural polysaccharide hydrogel matrix to form a microcapsule structure, creating a dual barrier with pH responsiveness and enzyme responsiveness. The liposome bilayer simulates biological membranes, reducing gastrointestinal rejection and enhancing intestinal epithelial affinity. The hydrogel network delays enzyme penetration and diffusive degradation, achieving sustained release and protective effects. In vitro simulated digestion results show that the release amount of the composite system in gastric fluid after 2 hours is less than 10%; it gradually swells and releases the drug in intestinal fluid, with a lipid integrity rate above 85%. There are no significant changes when stored at 4°C for 3 months, solving the stability problems during the storage and transportation of sea cucumber lipids.

2.3 Key Parameter Optimization and Performance Evaluation of the Stabilization System

Systematic improvement work is carried out concerning four aspects: encapsulation efficiency, stability, anti-digestibility, and release controllability, proceeding from three perspectives: carrier composition, preparation process, and formulation parameters. Determining the optimal ratios of protein, lipid, and polysaccharide, along with homogenization pressure, ultrasonication time, and cross-linking density, yields results of an encapsulation efficiency greater than 85% and a drug loading capacity greater than 10%. Accelerated oxidation experiments, simulated gastrointestinal fluid digestion, particle size measurement, and structural characterization are utilized to demonstrate the stabilization effect. The results show that the nanostructured stabilization system can extend the oxidation induction period of sea cucumber lipids by more than 3 times, and a gastric acid destruction rate of ≤15%

meets the requirements for oral preparations. Furthermore, it can improve the dispersibility, redissolubility, and emulsifiability of lipids, making it suitable for various dosage forms such as powders, liquids, and pastes, providing stable, safe, and highly efficient carrier technology for the development of high-end functional foods.

3 Precise Intestinal Release Mechanism and In Vivo Transport Laws of Sea Cucumber Lipids

3.1 Molecular Basis for Targeted Intestinal Delivery and Carrier Design Strategies

The intestine is the central site for the absorption and functional exertion of sea cucumber lipids, and precise delivery relies on three pathways: pH-responsive, enzyme-responsive, and active targeting. The gastrointestinal pH gradient (stomach 1.5–2.5, small intestine 6.8–7.4, colon 7.0–7.5) provides natural signals for pH-responsive release. Intestine-specific enzymes (lipases, glycosidases) can trigger carrier degradation. This paper uses carriers modified with pH-sensitive phospholipids, polysaccharide matrices, and targeting ligands for targeted enrichment in the small intestine. The carrier is compact in the stomach, while in the small intestine, the increased pH causes the carrier to swell or its membrane to dissociate, and intestinal enzymes degrade the matrix, thereby realizing the directional release of lipids. Combined with the targeted transport properties of ferritin self-assembling carriers, the speed of intestinal epithelial uptake and transmembrane transport is improved, subsequently achieving the goals of site locking, precise release, and highly efficient absorption.

3.2 Kinetics and Regulation Mechanism of Precise Intestinal Release

A three-dimensional evaluation system comprising in vitro simulated digestion, in situ perfusion, and in vivo imaging is established to study the release kinetics and transport pathways of sea cucumber lipid nanocarriers. The dynamic membrane dialysis method is used to study the release laws, fitting first-order or Weibull models to obtain the release rate and complete release time of the carrier in various intestinal segments. A rat in situ intestinal perfusion model is used to detect the absorption rate and effective permeability coefficient. Fluorescent labeling and small animal in vivo imaging are utilized to trace the distribution, transmembrane transport, and target tissue enrichment of the carrier in the intestine. The results show that the stabilized carriers exhibit characteristics of low release in the stomach, high release in the small intestine, and sustained release in the colon; lipids are efficiently absorbed in the jejunum and ileum, and transmembrane transport is primarily accomplished through endocytosis and exocytosis, preventing loss caused by passive diffusion. Release behavior can be precisely controlled by utilizing carrier composition, cross-linking degree, and surface modification, satisfying the release requirements across various efficacy scenarios.

3.3 Improvement of In Vivo Bioavailability and Synergistic Efficacy Mechanism

Nanostructured stabilization and precise intestinal administration significantly improve the bioavailability and efficacy of sea cucumber liposomes. From a pharmacokinetic perspective, the area under the blood concentration-time curve (AUC) of the nano group is 3-5 times higher than that of the free group, with a prolonged half-life and unchanged peak concentration. The enrichment amount of lipids in the brain, liver, and cardiovascular system is significantly increased, which closely aligns with the efficacy of improving cognition and protecting cardiovascular and cerebrovascular systems. Mechanistically, stabilized carriers can reduce gastrointestinal degradation, improve solubility, promote intestinal epithelial absorption, and prolong circulation time, thereby achieving the effects of protection, targeting, release, absorption, and enrichment. Overcoming the barriers to the oral application of sea cucumber lipids provides scientific basis and technical support for the development of high-end functional foods and special dietary products, such as therapeutic diets for improving Alzheimer's disease, functional diets for lowering blood pressure, and functional diets for delaying aging.

Conclusion

This paper establishes a composite nanostructured stabilization system for sea cucumber lipids comprising protein self-assembly, liposomes, and hydrogels, and studies the mechanism of achieving precise intestinal release through dual pH and enzyme responsiveness, overcoming the problems of sea cucumber lipids being prone to oxidation, instability, and low bioavailability. The research can improve the utilization rate of sea cucumber processing by-products, increasing resource utilization by more than 5%, which aligns with the strategies of building a strong marine nation and green, low-carbon development. In the future, further research can be conducted on aspects such as the precise modification of targeting ligands, multi-component co-delivery, industrial process scale-up, and human clinical verification. This will enable sea cucumber functional lipids to be more widely applied in special dietary foods, health foods, and foods for special medical purposes, injecting new vitality into the upgrading of the entire industrial chain of marine biological resources and the construction of a Healthy China.

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