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From Chlorella to Oral Liquid: Development and Application Prospects of High-Value Bioactive Peptides

Chlorella, a single-celled green algae with a protein content exceeding 50%, serves not only as a premium sustainable protein source but also as a "molecular treasure trove" rich in bioactive peptides. Compared to consuming algae powder directly, specific peptide fragments obtained through targeted enzymatic hydrolysis and separation from chlorella protein using modern biotechnology exhibit more precise and potent physiological regulatory functions. Formulating these highly active peptides into oral liquids serves as a crucial delivery format for convenient and efficient application. This paper aims to systematically review the core biological activities of chlorella peptides, the advantages of oral liquid formulations, and their current research progress and future potential within the broader health industry.

I. Resource Base and Core Technology: From Algal Powder to High-Activity Peptides

The preparation of chlorella peptides is a prerequisite for their high-value applications, integrating resource assessment, bioconversion, and

precision separation technologies throughout the process.

1. Superior Resource Endowment

Chlorella exhibits rapid growth and relatively simple cultivation requirements. Its safety as a food ingredient has been certified by regulatory bodies such as the U.S. FDA, establishing both resource and regulatory foundations for large-scale production. Its protein not only boasts high content but also exhibits a balanced amino acid profile, making it an ideal substrate for bioactive peptide synthesis.

2. Targeted Enzymatic Hydrolysis and Bioactive Enrichment

The key to obtaining high-activity peptides lies in adopting an "activity-directed" preparation strategy. Research indicates that using enzymes such as trypsin and alkaline protease to hydrolyze chlorella protein at optimal pH and temperature efficiently releases peptide segments with specific functions. The complex mixture produced by enzymatic hydrolysis requires preliminary fractionation by molecular weight using ultrafiltration technology. For instance, studies commonly separate hydrolysate into fractions below 1 kDa, 1–3 kDa, and 3–10 kDa, as peptides within distinct molecular weight ranges often exhibit markedly different biological activities.

3. Sequence Identification and Structural Optimization

For ultra-high-activity target fractions, chromatography coupled with mass spectrometry can be employed for purification and sequence

identification. For instance, a pentapeptide with the amino acid sequence LVAKA has been identified in chlorella, demonstrating potent angiotensin-converting enzyme inhibitory potential. Structural optimization strategies—such as alanine scanning, site-directed mutagenesis, or D-amino acid substitution—based on known active peptide templates can significantly enhance both activity and stability. D-amino acid modifications substantially improve peptide stability in the digestive tract, which is critical for oral applications.

II. Core Bioactivity and Mechanism of Action

Chlorella peptides exert their effects not through a single pathway, but rather through their diverse sequence structures, which enable synergistic regulation at multiple key physiological junctures.

1. Oral Health Applications

In the field of oral health, chlorella peptides (such as 3-10 kDa and 1-3 kDa fractions) demonstrate dual benefits. Their core mechanism lies in effectively inhibiting the growth of periodontal pathogens (e.g., Porphyromonas gingivalis) and, more critically, disrupting bacterial biofilm formation to block the stable colonization of dental plaque at its source. Simultaneously, these peptides significantly reduce the release of pro-inflammatory factors like interleukin-1β and tumor necrosis factor-α by suppressing TLR4-mediated inflammatory responses, thereby alleviating gingival inflammation. This provides scientific rationale for

their application in products such as antimicrobial oral gels and health lozenges.

2. Cardiovascular Health Applications

For cardiovascular health, researchers have identified specific angiotensin-converting enzyme (ACE) inhibitory peptides from chlorella, such as LVAKA and its optimized LRAKA sequence. These peptides act like “molecular keys,” competitively or non-competitively inserting into the active site of ACE to block its conversion of angiotensin I into the potent vasoconstrictor angiotensin II. This helps dilate blood vessels and regulate blood pressure, making chlorella peptides a promising raw material for developing functional foods or health supplements with blood pressure-lowering support.

3. Neuroprotection and Cognitive Health Applications

Neuroprotection represents one of the cutting-edge research directions for chlorella peptides. For instance, the peptide segment VECYGPNRPEF has been demonstrated to exhibit multi-target neuroprotective effects. It not only directly scavenges reactive oxygen species (ROS) and enhances the activity of endogenous antioxidant enzymes like superoxide dismutase (SOD), but also suppresses excessive activation of brain microglia, reducing levels of neuroinflammatory factors such as tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6). More significantly, this peptide segment also reduces β-amyloid deposition, a

key pathological feature of Alzheimer's disease. In model organism studies, such peptides demonstrate potential for improving memory and cognitive function, suggesting their value in delaying neurodegeneration and supporting brain health product development.

4. Antioxidant and Metabolic Regulation Applications

Broad antioxidant activity constitutes the fundamental function of chlorella peptides. Comprehensive peptide fractions with molecular weights below 30 kDa typically exhibit strong scavenging capacity against DPPH and ABTS radicals. Beyond direct antioxidant effects, research on peptides from similar algal sources (e.g., spirulina) suggests chlorella peptides may influence glycometabolism and lipid metabolism by regulating core cellular energy pathways like AMPK. This action supports anti-fatigue effects, delays cellular aging, and aids metabolic health, making them suitable for diverse dietary supplement applications.

III. Application Advantages and Industrialization Prospects of Oral Liquid Formulations

Developing chlorella peptides into an oral liquid formulation represents a crucial step in realizing its market value. This dosage form offers significant advantages:

High Bioavailability: The liquid formulation eliminates the need for disintegration and dissolution processes, making it particularly suitable for elderly individuals or those with swallowing difficulties. It enables

relatively rapid absorption and onset of action.

Flavor Masking and Taste Optimization: Chlorella naturally possesses a distinct algal odor. In oral liquids, this can be effectively mitigated by adding natural flavor enhancers, employing microencapsulation technology, or blending with flavor matrices like fruit juices to improve palatability and consumer acceptance.

High Formulation Flexibility: Oral liquids facilitate functional compounding. For instance, peptides with diverse functions—such as blood pressure reduction, antioxidant effects, and fatigue resistance—can be scientifically combined. They may also synergize with vitamins, minerals, or extracts from traditional medicinal foods to develop multifunctional products tailored for specific demographics (e.g., middle-aged/elderly individuals, athletes).

Stable Quality Control: Compared to solid beverages, liquid formulations ensure more consistent distribution of contents, guaranteeing stable active ingredient concentrations in each dose.

Current Challenges and Future Outlook

Despite promising prospects, the industrialization of chlorella peptide oral solutions faces challenges. First, achieving high yields, purity, and cost control for active peptides during large-scale production remains a core technical hurdle. Second, clinical validation of in vivo efficacy is insufficient, requiring more rigorously designed human trials to

substantiate claimed health benefits. Additionally, formulation technologies must address long-term stability of peptides in liquid environments, preventing precipitation and denaturation.

Looking ahead, the field will evolve through these trends:

Rational Design and Precision Synthesis: Integrating bioinformatics and artificial intelligence to predict and design higher-activity peptide sequences, alongside developing efficient, green targeted enzymatic digestion and separation/purification processes.

Deepening Evidence-Based Research: Conducting more cellular, animal, and human clinical studies to elucidate mechanisms of action and establish dose-response relationships, providing robust scientific backing for product claims.

Smart Delivery and Advanced Formulations: Explore advanced delivery systems like liposomes and nanoemulsions to enhance oral bioavailability and targeting of peptides.

Market Segmentation and Personalization: Develop specialized, tailored formulations for distinct segments such as sub-health management, sports nutrition, and senior wellness.

IV.Conclusion

Chlorella Peptide Oral Solution represents a successful approach to transforming premium algal resources into high-value-added health products. Leveraging chlorella's abundant protein resources, modern

biotechnology unlocks peptide segments with multiple bioactivities—including oral health benefits, cardiovascular protection, neuroprotection, and antioxidant properties—and delivers them efficiently through the user-friendly oral solution formulation. Although challenges remain in scaling production, ensuring stability, and conducting clinical validation, the convergence of biotechnology, food science, and clinical nutrition positions Chlorella Peptide Oral Solution to secure a significant position within the vast functional food and dietary supplement market. It not only offers consumers a new natural option for health management but also charts a promising course for deepening the development and enhancing the value of the chlorella industry, fully embodying the sustainable development concept of "seeking health from the ocean and microalgae."