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Preparation and Antioxidant Applications of Grape Seed Peptides: A Review

Grape seeds are a major byproduct of the wine industry, with enormous annual global production that has long remained underutilized. Containing approximately 8%-15% protein, grape seeds represent a potential high-quality plant protein resource. Converting grape seed protein into bioactive peptides—particularly those with significant antioxidant activity—via bioenzymatic hydrolysis is a key pathway for achieving their high-value utilization. This paper provides a systematic review of grape seed peptide preparation processes, their antioxidant mechanisms of action, and their application prospects in the food and health sectors.

I. Preparation Process of Grape Seed Peptides

The preparation of grape seed peptides is a multi-step systematic process, primarily involving raw material pretreatment, protein extraction, enzymatic conversion, and product separation and purification.

1. Raw Material Pretreatment

Grape seeds are encased in a hard, woody seed coat and contain components such as oils and tannins, necessitating pretreatment. First, the grape seeds must be washed and dried. Subsequently, approximately 12%-18% of the oils are removed via pressing or solvent extraction, yielding defatted grape seed meal. This step enhances subsequent protein extraction efficiency and prevents oil oxidation from compromising product quality. The defatted seed meal undergoes ultrafine grinding to disrupt cellular structures and increase specific surface area, facilitating protein dissolution.

2. Protein Extraction

Efficient protein extraction from defatted meal forms the foundation for peptide preparation. The alkaline solubilization-acid precipitation method is currently the most widely used. This method exploits the property of grape seed protein to dissolve under alkaline conditions and precipitate near its isoelectric point. Typical process conditions involve dispersing the pulverized seed meal in an alkaline solution (pH 9.0–11.0), stirring and extracting at 50–60°C for 1–2 hours, with a solid-to-liquid ratio typically maintained between 1:10 and 1:15. After extraction, centrifuge to collect the supernatant. Adjust the pH to the isoelectric point of grape seed protein using hydrochloric acid to precipitate the protein. Following washing, neutralization, and drying, grape seed protein isolate powder is obtained, with a protein extraction rate exceeding 70%.

3. Enzymatic Hydrolysis Process

Enzymatic hydrolysis is the core step for directionally cleaving macromolecular proteins into small-molecule bioactive peptides. Process optimization primarily focuses on protease selection and enzymatic hydrolysis parameter control.

Protease Selection: Different proteases yield distinct peptide mixtures with varying sequences and activities due to their specific cleavage sites. Basic proteases are widely used for their high hydrolysis efficiency and lower cost. Composite enzyme hydrolysis is an effective strategy to enhance activity. For example, deep hydrolysis with alkaline proteases followed by modification with flavor proteases can further cleave terminal hydrophobic amino acids, improving product flavor and reducing bitterness while boosting activity.

Parameter Optimization: Enzymatic hydrolysis efficiency is influenced by multiple factors including temperature, pH, enzyme dosage, substrate concentration, and time. Through experimental design methods like response surface analysis, mathematical models can be established to identify optimal process conditions. Studies indicate that for grape seed protein, hydrolysis at pH 8.5–9.0, 50–55°C, and an enzyme-to-substrate ratio of 3–5% for 3–5 hours typically yields high hydrolysate degree and antioxidant activity.

4. Separation and Purification

After enzyme inactivation and centrifugation of the hydrolysate, a crude polypeptide solution is obtained. Membrane separation technology is commonly employed to further enrich active components. Ultrafiltration membranes with different molecular weight cut-offs are selected for fractionation based on the molecular weight range of the target polypeptide. Extensive research confirms that grape seed peptide fractions with molecular weights below 3 kDa, particularly those under 1 kDa, typically exhibit stronger antioxidant activity. For research or high-value products, gel chromatography or preparative liquid chromatography can be employed for further purification and structural characterization of individual bioactive peptides.

II. Antioxidant Mechanism of Grape Seed Peptides

The antioxidant activity of grape seed peptides is not achieved through a single pathway. Its mechanisms primarily include direct scavenging of free radicals, chelation of metal ions, and indirect enhancement of the body's own antioxidant defense capabilities.

1. Direct Radical Scavenging

This represents its most fundamental antioxidant mechanism. Certain amino acid residues in grape seed peptides—such as histidine, tyrosine, tryptophan, methionine, and cysteine—can donate hydrogen atoms or electrons to directly neutralize reactive oxygen species (ROS) and reactive nitrogen species (RNS). These free radicals—including hydroxyl radicals, superoxide anion radicals, hydrogen peroxide, and peroxynitrite—are key factors causing lipid peroxidation, protein denaturation, and DNA damage.

Research indicates that grape seed peptides with specific sequences, particularly short peptides rich in the aforementioned amino acids, exhibit potent free radical scavenging capabilities.

2. Metal Ion Chelation

Transition metal ions such as iron and copper can catalyze the Fenton reaction to generate large quantities of hydroxyl radicals. The side-chain groups of certain amino acids in grape seed peptides can coordinate with these metal ions to form stable chelates, thereby interrupting the chain reaction of radical formation. Peptide sequences rich in glutamic acid, aspartic acid, histidine, and cysteine typically exhibit potent metal ion chelation capabilities.

3. Activation of Endogenous Antioxidant Defense Systems

Recent studies indicate that certain bioactive peptides not only exert direct effects but also modulate cellular signaling pathways to upregulate the expression of endogenous antioxidant enzymes. For example, specific grape seed peptides may activate the Nrf2 signaling pathway, promoting the synthesis of key intracellular antioxidant enzymes such as glutathione peroxidase, superoxide dismutase, and catalase, thereby systematically enhancing cellular antioxidant stress resistance.

III. Functional Applications and Prospects

Based on its distinct antioxidant activity, grape seed peptides demonstrate application potential across multiple fields.

1. Functional Foods and Special Dietary Foods

As a natural antioxidant and nutritional supplement, it can be added to beverages, dairy products, baked goods, and nutrition bars to delay food oxidation, enhance product stability, and provide health benefits. It can also be developed into health foods that assist in antioxidant protection and delay aging.

2. Cosmetics and Personal Care Products

Their antioxidant activity makes them suitable for anti-aging skincare formulations, helping reduce collagen degradation, loss of elasticity, and wrinkle formation caused by oxidative stress. Their natural origin also aligns with market demand for green cosmetic ingredients.

3. Animal Feed Additives

As a green, safe additive, they enhance antioxidant levels in farmed animals, improve meat quality, and reduce oxidative stress, offering potential as a partial replacement for chemically synthesized antioxidants.

IV. Challenges and Outlook

Despite promising prospects, the industrialization of grape seed peptides still faces several challenges:

1. Cost and Scalability: Controlling costs throughout the entire process—from raw material collection and stable supply to enzymatic hydrolysis and separation—is crucial for determining market competitiveness.

2. Activity Stability: Maintaining long-term stability of antioxidant activity during processing and storage of peptide products remains a technical challenge.

3. Structure-Activity Relationships and Standardization: Current understanding of the precise amino acid sequences with strongest antioxidant activity and their mechanisms is limited. Establishing quality standards based on specific active peptide segments represents a future development direction.

Future research will increasingly focus on leveraging proteomics and bioinformatics technologies to predict and screen high-activity peptides, enabling targeted enzymatic hydrolysis. Additionally, in-depth cellular and animal studies will validate their in vivo antioxidant efficacy and safety, propelling grape seed peptides from laboratory research toward large-scale production and application.

V. Conclusion

The development of grape seed peptides exemplifies the successful transformation of agricultural processing byproducts into high-value bioactive compounds. Through systematic preparation techniques, the antioxidant potential within grape seed proteins can be efficiently unlocked. Its multi-mechanism antioxidant action provides a scientific foundation for applications across food, health supplements, and cosmetics. With advancing research and technological progress, grape seed peptides hold promise as a significant natural antioxidant resource, achieving a win-win outcome for resource recycling and the development of the health industry.