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A Review of the Sources, Mechanisms of Action, and Application Prospects of Antioxidant Peptides

Antioxidant peptides are a class of short amino acid sequences derived from proteins through enzymatic hydrolysis, fermentation, or chemical modification. They exhibit biological activities such as scavenging free radicals, inhibiting lipid peroxidation, and regulating the body's redox balance. Compared to synthetic antioxidants, they offer superior biocompatibility, absorbability, and safety, demonstrating broad application potential in food, health supplements, cosmetics, and pharmaceutical fields. This paper provides a systematic review of the primary sources, mechanisms of action, preparation strategies, and application prospects of antioxidant peptides across various industries.

I. Primary Sources of Antioxidant Peptides

Antioxidant peptides are widely present in natural biological resources and are primarily obtained through the following pathways:

1. Plant Sources

This is one of the most extensively researched and applied sources. Many plant proteins release peptide fragments with antioxidant activity after enzymatic hydrolysis.

Grains and Legumes: Multiple antioxidant peptides have been identified in hydrolysates of soybeans, corn, rice, black beans, peas, and other sources. For instance, black bean peptides have demonstrated potent free radical scavenging capacity in studies.

Oilseed Byproducts: Processing residues like peanut meal, rapeseed meal, and grape seed meal are rich in protein, serving as cost-effective, high-quality sources for antioxidant peptide extraction.

Other Plants: Protein components from certain edible fungi, algae, and traditional Chinese medicinal herbs also represent potential antioxidant peptide sources.

2. Animal Sources

Animal tissues, dairy products, and aquatic processing byproducts contain abundant active peptide precursor proteins.

Dairy proteins: Enzymatically hydrolyzed casein and whey proteins represent one of the most extensively studied sources of antioxidant peptides, with active peptide segments like those derived from β-lactoglobulin widely validated.

Aquatic byproducts: Collagen and myofibrillar proteins from processing waste like fish skin, scales, bones, and shellfish viscera yield highly active antioxidant peptides upon enzymatic hydrolysis. Marine-derived antioxidant peptides have become a research hotspot due to their unique amino acid composition and structure.

Livestock and Poultry Byproducts: Blood, bones, and dander are also rich in proteins suitable for developing bioactive peptides.

3. Microbial Sources

Peptides with antioxidant activity can also be obtained through microbial fermentation or direct enzymatic hydrolysis of microbial cell proteins.

II. Mechanism of Action of Antioxidant Peptides

The antioxidant activity of peptides is not achieved through a single pathway; their mechanism of action constitutes a multi-tiered defense system:

1. Direct Radical Scavenging

This represents the most fundamental mechanism. Certain amino acid residues within peptides can directly donate hydrogen atoms or electrons to neutralize reactive oxygen species (ROS) and reactive nitrogen species (RNS).

Key amino acids: The side-chain groups of histidine, tyrosine, tryptophan, methionine, cysteine, and phenylalanine serve as primary active sites. For instance, the imidazole group of histidine and the phenolic hydroxyl group of tyrosine exhibit strong hydrogen-donating capabilities.

Targets: Hydroxyl radicals, superoxide anions, hydrogen peroxide, peroxynitrite, etc.

2. Metal Ion Chelation

Transition metal ions serve as crucial mediators in catalyzing radical generation. Certain groups within peptides can coordinate with iron ions, copper ions, and others to form stable chelates, thereby blocking radical-generating chain reactions like the Fenton reaction. Peptides rich in glutamic acid, aspartic acid, histidine, and cysteine typically exhibit strong chelating capabilities.

3. Activation of Endogenous Antioxidant Defense Systems

Recent studies indicate that certain antioxidant peptides not only exert direct effects but also modulate cellular signaling pathways to upregulate the expression of endogenous antioxidant enzymes.

Key Pathways: Primarily involve the Nrf2/ARE signaling pathway. Peptides with specific sequences activate Nrf2, facilitating its translocation into the nucleus to initiate transcription of multiple downstream phase II detoxification enzymes and antioxidant enzymes.

Upset enzymes: Include glutathione peroxidase, superoxide dismutase, catalase, heme oxygenase-1, etc., thereby systematically enhancing cellular antioxidant stress resistance.

4. Inhibition of lipid peroxidation chain reactions

Certain highly hydrophobic peptides can insert into cell membranes or lipoproteins, protecting biological membranes from oxidative damage by directly scavenging lipid radicals or blocking radical chain propagation.

III. Preparation and Optimization Strategies for Antioxidant Peptides

The efficient preparation of highly active antioxidant peptides is central to industrialization, with the primary technical approaches outlined below:

1. Enzymatic Hydrolysis

This represents the most mainstream, safe, and controllable preparation method.

Protease Selection: Alkaline proteases, flavor proteases, trypsin, pepsin, and others are widely utilized. Different proteases yield mixtures of peptides with varying sequences and activities due to their distinct cleavage site specificities. Composite hydrolysis (e.g., sequential use of alkaline protease followed by flavor protease) often yields products with higher activity or superior flavor.

Process Optimization: Statistical tools like response surface methodology are employed to systematically optimize parameters such as hydrolysis temperature, pH, duration, and enzyme-substrate ratio to maximize target activity.

2. Microbial Fermentation Method

Protein substrates are fermented using microorganisms like lactic acid bacteria, Bacillus species, or fungi. Multiple proteases secreted by microorganisms during growth act synergistically, potentially generating beneficial secondary metabolites that synergize functionally with peptides.

3. Separation, Purification, and Identification

Crude enzymatic hydrolysates are complex mixtures requiring further separation and enrichment.

Separation Techniques: Ultrafiltration is a common fractionation method, rapidly enriching high-activity fractions by molecular weight (e.g., <3 kDa, <1 kDa). Gel filtration and reverse-phase high-performance liquid chromatography are employed for further purification to obtain individual peptide fragments.

Structural Identification: Liquid chromatography-tandem mass spectrometry is used for amino acid sequencing. Chemical synthesis of target peptides followed by activity validation ultimately confirms key active sequences.

4. Stability and Activity Enhancement Strategies

To improve application value, natural peptides are often modified:

Chemical modifications: Acetylation, glycosylation, or incorporation of D-amino acids can enhance stability and protease resistance.

Self-assembly strategies: Designing specific sequences enables self-assembly into nanostructures. Studies indicate that self-assembled antioxidant peptides, by forming ordered nanostructures, can function more effectively at biological interfaces and achieve sustained-release effects.

IV. Application Prospects and Challenges

1. Application Prospects

Functional Foods and Special Dietary Foods: As a natural antioxidant and nutritional fortifier, it is used in beverages, dairy products, baked goods, and health foods for middle-aged and elderly individuals to help combat oxidative stress and delay age-related functional decline.

Cosmetics and Personal Care Products: Applied in anti-aging skincare products to counteract oxidative damage caused by UV rays and pollution, reducing wrinkles and improving elasticity.

Pharmaceuticals and Health Sector: Holds potential for development as adjunctive therapeutic agents to alleviate chronic diseases closely linked to oxidative stress, such as cardiovascular diseases, neurodegenerative disorders, and diabetic complications.

Animal Feed Additives: Serves as a green, safe feed additive to enhance antioxidant levels and disease resistance in farmed animals while improving meat quality.

2. Key Challenges

Cost of Large-Scale Production: Comprehensive cost control throughout the entire process—from raw materials to high-purity active peptides—is critical, particularly during separation and purification.

In Vivo Activity Validation and Stability: In vitro activity does not guarantee in vivo efficacy. The stability of peptides in the digestive system, absorption rates, and actual biological effects in target tissues require more thorough validation through cellular and animal studies.

Structure-Activity Relationships and Standardization: Most products remain mixtures, with unclear quantitative relationships between precise active component sequences/concentrations and product efficacy. Establishing quality standards based on specific bioactive peptides is essential for industry advancement.

Regulatory Compliance and Market Access: As novel food ingredients or cosmetic raw materials, rigorous safety assessments and approval processes must be completed.

V. Future Outlook

Future research will focus more on:

Rational Design and Efficient Screening: Integrating bioinformatics, artificial intelligence, and molecular modeling to predict and design novel antioxidant peptide sequences with ultra-high activity, while establishing high-throughput screening platforms.

Green Sustainable Preparation Technologies: Optimizing enzymatic hydrolysis and fermentation processes, developing efficient, low-energy consumption separation techniques, and deepening utilization of novel protein resources such as marine and insect sources.

In-Depth Mechanism Studies: Systematically elucidating the complex action networks and metabolic fates of antioxidant peptides at molecular, cellular, and whole-animal levels using multi-omics technologies.

Innovative product development: Create precision antioxidant peptide products targeting specific populations and health concerns, while exploring applications in cross-disciplinary fields such as novel delivery systems and medical device coatings.

VI.Conclusion

Antioxidant peptides, derived from abundant natural protein resources, exert antioxidant functions through multi-level mechanisms. Their green and safe characteristics align strongly with the development needs of the health industry. Although challenges remain in large-scale production, standardization, and in vivo efficacy validation, advancing basic research and biotechnological progress hold promise for transitioning antioxidant peptides from laboratory settings to broader market applications. This shift will inject innovative momentum into the food, health, and beauty industries while offering novel preventive and intervention strategies against chronic diseases linked to oxidative stress, yielding significant social and economic value.