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Bioactive Peptide: Properties and Effect on Human Health

Chetan Chougale, Pallavi Mali and Prajakta Londhepatil
Ph. D. Scholar, Department of Animal Husbandry and Dairy Science
Mahatma Phule Krishi Vidyapeeth Rahuri-413722, Ahmednagar (MH)

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Introduction

Peptides are short strings of amino acids, typically comprising 2–50 amino acids. Amino acids are also the building blocks of proteins, but proteins contain more. Peptides may be easier for the body to absorb than proteins because they are smaller and more broken down than proteins. They can more easily penetrate the skin and intestines, which helps them to enter the bloodstream more quickly. It has a beneficial effect on the body and may positively impact human health. Different bioactive peptides have different properties.

Properties of Bioactive Peptides

1. **Pharmacological Properties of Bioactive Peptides:** The peptide can be regarded as a bioactive medication as long as it maintains its biological characteristics. The amino acid composition of the peptide, the amino acids at its N and C termini, the length of the peptide chain, the charge of the amino acids, and whether they are hydrophobic or hydrophilic all affect the activity of peptide drugs. Some of the pharmacological properties of BAPs are discussed below.
2. **Antioxidant Properties of Bioactive Peptides:** One of the main causes of disease in humans is oxidation. Dairy proteins are the source of compounds with anti-free-radical and anti-fatty acid oxidation capabilities. Phosphorylated peptides with hydrophilic and lipophilic antioxidant activity are also produced during the digestion of casein. Different levels of hydrolysis and antioxidant properties are provided by soy peptides.
3. **Antimicrobial Properties of Bioactive Peptides:** Antimicrobial peptides (AMPs) prevent the growth of microorganisms, including bacteria and fungi. AMPs are polypeptides with varying lengths that consist of linear structures with α helices, cyclic structures with disulphide bridge connections, or cyclic structures with an open end. Additionally, certain amino acid residues—such as proline-, glycine-, or histidine-rich

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peptides—are highly concentrated in AMPs. AMP molecules effectively disrupt the highly negatively charged bacterial cell wall or membrane, seemingly causing cationic and hydrophobic effects. *Porphyromonas gingivalis, Salmonella typhimurium, Escherichia coli, Streptococcus sanguis, Streptococcus mutans,* and *Streptococcus sobrinus* are all effectively inhibited by AMPs generated from casein.

4. **Immunomodulatory Properties of Bioactive Peptides:** Proteins and peptides from sources such as egg, milk, soy, and plant sources exhibit anti-inflammatory properties. Ovotransferrin, an egg white protein, inhibits the proliferation of mouse spleen lymphocytes. Peptides from hydrolysates of rice and soybean proteins can stimulate reactive oxygen species (ROS) and trigger nonspecific immune defence systems.
5. **Cytomodulatory Properties of Bioactive Peptides:** Research studies have shown that cytoplasm-interacting compounds that target cancer cells might have anticancer effects, and the reported BAPs have been confirmed to have the potential to be effective cancer-preventive agents.
6. **Metabolic Effects of Bioactive Peptides:** Metabolic changes can lead to several conditions, such as diabetes, obesity, and hypertension (characterized by elevated triglycerides, dense low-density lipoproteins, and low high-density lipoproteins). Several BAPs are involved in the functional regulation of metabolism. Alpha-glucosidase and dipeptidyl peptidase IV (DPP-IV) are intimately involved in the development of type 2 diabetes (T2D). One of the peptides extracted from egg white shows antidiabetic and α-glucosidase inhibitory properties.

Effects of Bioactive Peptides on Human Health:

Food proteins contain biological molecules called peptides, which have a variety of advantageous and constructive effects. Different peptides that are produced from the processing of proteins are in charge of regulating vital physiological natural processes, most notably the endocrinology of living things. Furthermore, because of these BAPs' strong tissue affinity, specificity, and effectiveness, they can interact with an organism's receptors, enzymes, and certain biomolecules to produce benefits that are beneficial to health. Additionally, a number of studies have demonstrated the therapeutic effects of these peptides in the treatment and management of a number of degenerative and chronic diseases, such as cancer, diabetes, obesity, and hypertension.

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a. **Metabolic Effects of Bioactive Peptides:** Obesity is an abnormal condition that involves excessive body fat accumulation and increases the risk of associated health problems. The worldwide prevalence of obesity has almost tripled since 1975, which is an alarming and dreadful sign of human health impairment. Obesity increases the likelihood of diseases such as type 2 diabetes, cardiovascular diseases, obstructive sleep apnoea, osteoarthritis, and depression. BAPs with antioxidant, anti-inflammatory, antimicrobial, and antiviral properties have been used to treat metabolic disorders, such as type 2 diabetes and obesity. Endogenous and BAPs from various sources that contain 20 amino acid residues exhibit anti-obesity properties. Analogues for novel targets such as amylin, leptin, GLP-1 MC4R, neuropeptide Y antagonists, cannabinoid type-1 receptor blockers, MetAP2 inhibitors, lipase inhibitors, and anti-obesity vaccines are currently being studied, and it is predicted that the combined use of two or more classes of drugs involving various pathways might be beneficial. BAPs face several challenges affecting their prolonged use and development, and these challenges mainly include their chemical instability, hydrolysis, and aggregation due to their misfolding, short half-life, elimination, and low permeability through the cell membrane, among other characteristics. However, a peptidomimetic approach involving the editing of naturally occurring peptides is currently being used to develop promising drugs. This approach includes various chemical modifications, L-to-D-form isomerization, and synthetic amino acid substitution. Researchers have aimed to target dipeptidyl peptidase-IV, STAT signalling, and protein–protein interactions for the treatment of arthritis, cardiovascular diseases, antimicrobials, immunomodulators, and peptidomimetics. Due to the limited number of anti-obesity pharmacological drugs, chemists are now looking beyond traditional peptides and working on the development of multifunctional peptides, peptide engineering, and peptide aptamers, among others, via peptidomimetics as modern alternatives for newer design strategies. These BAPs reduce the body weight of the treated animals and exert their anti-obesity activity by inhibiting the expression of the nuclear transcription factor PPARγ.

b. **Cholesterol-Lowering Peptides:** Peptides are known to mediate the cholesterol-lowering effect of food proteins. Lupin peptides alter the transcription factors SREBP2 and HNF1α of cholesterol metabolism. Phenylalanine-proline (FP) is the world's first

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cholesterol-lowering dipeptide, and the cited study provided the first identification of FP as a novel cholesterol-lowering dipeptide. The active dipeptide FP can be identified by evaluations of cholesterol micellar solubility and cholesterol absorption in Caco-2 cells in vitro. However, the FP-containing fraction is not the only fraction with cholesterol-lowering properties. Moreover, FP peptide might not be the only peptide in the fraction with hypocholesterolaemia properties. The oral administration of FP results in significant reductions in the total serum and non-HDL-cholesterol concentrations in hypercholesterolaemia rats fed a high-fat and high-cholesterol diet. NPC1L1 is essential in the absorption of dietary cholesterol, and the mediation of NPC1L1 protein has a therapeutic function against high cholesterol. FP induces a significant decrease in NPC1L1 mRNA expression but does not significantly affect NPC1L1 expression at the protein level. Therefore, it can be speculated that the effect of FP on cholesterol absorption does not involve NPC1L1 expression. ABCA1 mediates HDL cholesterol biogenesis by promoting the efflux of cholesterol and phospholipids to ApoAI22. ABCA1 is widely expressed throughout the body.

c. **Mechanism of Action of Anti-Diabetic Peptides against Type 2 Diabetes:** T2D is a significant common human health problem that is increasing worldwide. The enzymes α-glucosidase and dipeptidyl peptidase IV (DPP-IV) play an important role in the development of T2D. Hence, the reduction or inhibition of their activity might be one of the essential strategies in the management of T2D. Anti-diabetic peptides for T2D and the level of their health impacts. Studies in the field of BAPs have demonstrated that dietary proteins could be a natural source of alpha-glucosidase and DPP-IV inhibitory peptides. Studies have shown that BAPs found in milk and other proteins play a significant role in the management of T2D through many pathways, including by decreasing appetite, regulating the plasma glucose levels, and preventing the synthesis of glucose from proteins in the body. Peptidyl active ingredients could be used to eliminate or decrease the incidence of T2D via the diet and supplementation. Bioactive peptides exhibit antidiabetic effects for type 2 diabetes mellitus based on inhibition against α- amylase, α-glucosidase, sodium glucose co-transporter-2 inhibitors, plasma-based dipeptidyl peptidase-4 (DPP4) inhibitors (an obesity-independent parameter for glycaemic deregulation in type 2 diabetes patients), and

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insulin mimetic (which promote the glucose entry into the tissues, whereas the glucose either be converted into energy or stored for later use), respectively. The schematic diagram indicates the anti-inflammatory activity of bioactive peptides derived from food protein occurs via inhibition of the NF-KB, MAPK, and JAK-STAT pathways. MAPK: mitogen-activated protein kinase; MAP3K: MAPK kinase; NF-κB: nuclear factor-kappa B; TGF-β: transforming growth factor β; TNF-α: tumor necrosis factor α; JAK-STAT: Janus kinase-signal transducer and activator of transcription.

d. Mechanism of Action of Anti-Inflammatory Peptides: Soy, which is also dense in proteins and readily available, has mainly been studied in relation to its antioxidant and anti-inflammatory activities. The BAPs show anti-inflammatory activity via the NF-κB, MAPK, and/or JAK-STAT pathways by inhibiting (1) the phosphorylation of MAPKKK mediated by the interaction of the stimulus (TNFα, IL-1, or LPS) with its receptor (TNFR, IL-1R, or TLR, respectively) and (2) the downstream phosphorylation of MAPK to thus inhibit transcription factors (c-Myc, ATF-2, and c-Jun).

Bioactive peptides, inhibit key enzymes involved in diabetes—DPP IV, α-amylase, and α-glucosidase, which results in the antidiabetic activity mainly by promoting insulin signaling and the AMPK signaling pathway.