Biotica Research Today

Vol 3:3 165/168

2021

Food Derived Peptides – Role in Human Health

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Open Access

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Keywords

ACE inhibitory peptides, Bioactive properties, Peptides, Protein hydrolysates

How to cite this article?

Vinoth *et al.*, 2021. Food Derived Peptides – Role in Human Health. Biotica Research Today 3(3): 165-168.

Abstract

Food proteins have long been recognized for their nutritional and functional properties. On the other hand, the functional properties of proteins relate to their contribution to the physiochemical and sensory properties of foods. Nowadays, a considerable amount of research has also focused on bioactive peptides which are present in foods, and researchers are trying to utilize such peptides as functional food ingredients aimed at health maintenance. Several bioactive peptides such as antioxidant, antihypertensive, antiproliferative, antimicrobial, neuroactive, hormonal and mineral binding were isolated from the fishes and shellfishes. The process flow of bioactive peptides includes purification and filtration methods and the peptide sequence was identified. The commercial application were also reported and discussed by many researches. Although the efficacies of these peptides were wide range, the safety and conditions of usage are yet to be proven.

Introduction

It has been defined as specific protein fragments that have a positive impact on body functions and conditions and may ultimately influence health. Bioactive peptides have been defined as peptides with hormone- or drug like activity that eventually modulate physiological function through binding interactions to specific receptors on target cells leading to induction of physiological responses (Murray and Fitzgerald, 2007). These are proteins synthesized in the cell in the form of large pre pro peptides, which are then cleaved and modified to give active products. Interestingly, within the protein sequence, the peptides are inactive and thus must be released to exert an effect. Usually bioactive peptides are 2–20 amino acid residues in length, although, some have been reported to be more than 20.

History of Bioactive Peptide Discovery

The first food-derived bioactive peptide was identified in casein phosphorylated peptides enhanced vitamin D-independent bone calcification in rachitic infants (Mellander, 1950). However, interest in this field has increased considerably in the last two decades, with the majority of research focusing on the identification of bioactive peptides from milk proteins.

Classification

Based on the functional properties, bioactive peptides are classified in to several types.

Article History

Received in 11th March 2021

Received in revised form 17th March 2021

Accepted in final form 18th March 2021

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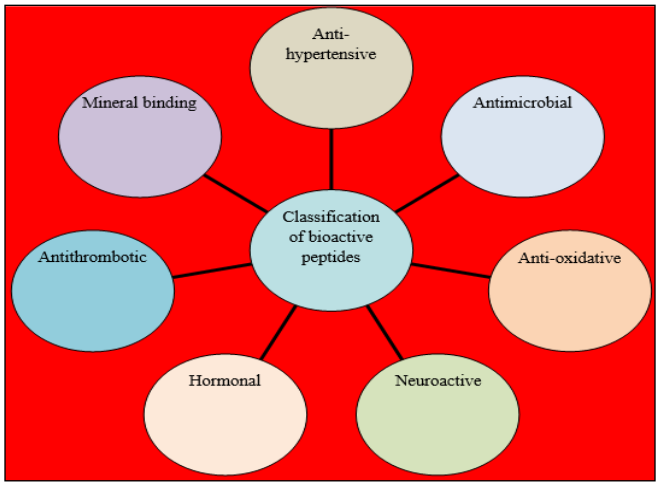

Figure 1: Graphical representation of different types of bioactive peptides

Antihypertensive Peptides

Antihypertensive peptides may contribute to the lowering of blood pressure through inhibition of enzymes including ACE or endothelin converting enzyme (ECE). ACE inhibitory peptides were first discovered in snake venom and since then numerous synthetic ACE inhibitors have been produced, with Captopril being the most common. Captopril and other synthetic ACE inhibitors are known to exert various side-effects such as coughing, taste disturbances and skin rashes. These side effects, coupled with the fact that hypertension affects one third of the Western worlds' population and is a known risk factor for stroke and cardiovascular disease, has contributed to the ongoing search for food derived antihypertensive peptides for exploitation as antihypertensive agents in functional foods and nutraceuticals.

Mechanism of ACE Inhibition

In the rennin-angiotensin system, Angiotensinogen present in the liver has been converted into angiotensin I, by the action of renin which is released from kidney. ACE catalyses the conversion of the inactive form of angiotensin I (Ang I) to the potent vasoconstrictor angiotensin II (Ang II). Additionally, ACE is involved in the deactivation of the hypotensive peptide, bradykinin. This is as a result of ACE cleaving the C-terminal dipeptide from Ang I (His-Leu) and bradykinin. Ang II is a documented potent vasoconstrictor which acts directly on vascular smooth muscle cells. Ang II is also responsible for the expansion of vascular volume via sodium retention and fluid retention. Bradykinin is responsible for uterine and ileal smooth muscle contraction, enhanced vascular permeability, activation of peripheral and C fibers and increases in mucous secretion. Furthermore, bradykinin contributes to vasodilation by advancing the assembly of arachidonic acid metabolites, nitric oxide, and endothelium-derived hyperpolarizing factor in the vascular endothelium. Therefore, ACE inhibitors function by maintaining the balance between the associated vasoconstrictive and salt-retentive attributes of Ang II with the vasodilatory effect of bradykinin. The balance is maintained by decreasing the production of Ang II and reducing the degradation of bradykinin. While synthetic ACE inhibitors, such as Captopril function by directly blocking the action of ACE, ACE inhibitory peptides function by reacting with ACE, thus ACE is unavailable to cleave AngI and prevent the production of the vasoconstrictor Ang II. In the past decade, it has been reported that muscle proteins from animals are a viable source of ACE inhibitory peptides in vitro and may potentially be incorporated into nutraceutical products to exert antihypertensive effects in vivo.

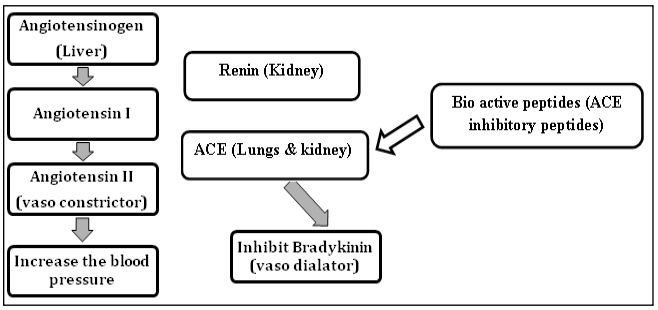

Figure 2: Mechanism of action of ACE inhibitory peptides

Antioxidative Peptides

Antioxidants are known to be beneficial to human health as they may protect the body against molecules known as reactive oxygen species (ROS), which can attack membrane lipids, protein and DNA. This in turn can be a causative factor in many diseases such as cardiovascular disease, diabetes cancer and Alzheimer's disease. Lipid oxidation can cause deterioration of food quality and a reduction in the shelf-life of a food product, while the consumption of foods containing lipid oxidation products has been linked to various diseases, including cancers, diabetes and cardiovascular disease.

The use of natural antioxidants in foodstuffs is appealing because of the potential health risk associated with synthetic antioxidants in vivo. Antioxidant peptides have been found in numerous foodstuffs including milk, wheat, potato and fungi. In the past number of years, a great deal of research has focused on antioxidant peptides sourced from fish, while the research on antioxidant peptides from the hydrolysates of domesticated animal muscle is limited. There are a number of methods available to measure antioxidant potential of various food components based on the ability of potential antioxidants to scavenge ROS, free radicals or prevent oxidation in model systems.

Antimicrobial Peptides

Antimicrobial peptides (AMPs) have been identified in a range of foods to date, with peptides released from milk proteins being the most plentiful source of AMPs.

Indeed, AMPs have been found in a host of different milk proteins including the caseins and lactoferrin. While AMPs from the protein of muscle foods are less well documented, there has been one report of AMPs from a bovine meat source. In this study, the antimicrobial and human cancer cell cytotoxic effects of four previously identified ACE inhibitory peptides, were evaluated. The four peptides GFHI, DFHING, FHG and GLSDGEWQ were assayed for antimicrobial activity against six pathogenic bacteria, three Gram-positive (*Bacillus cereus, Listeria monocytogenes* and *Staphylococcus aureus*) and three Gram-negative (*Salmonella typhimurium, Escherichia coli* and *Pseudomonas aeruginosa*). The peptide GLSDGEWQ inhibited the growth of *S. typhimurium, B. cereus, E. coli* and *L. monocytogenes*. This was the only peptide that inhibited the growth of both Gram-positive and Gram-negative pathogens. GFHI and FHG inhibited the growth of the pathogen *P. aeruginosa*.

Neuroactive Peptides

Neuroactive peptides exist in dairy products which play an active role in nervous system; they are known as opioid peptides. Opioid peptides are also having pharmacological similarity to opium (morphine). They are opioid receptor ligands with agonistic or antagonistic activities and are characterized by distinct N-terminal sequences and are called atypical opioid peptides different from that of the typical endogenous opioid peptides. Opioid peptides are short sequences of amino acids that mimic the effect of opiates in the brain. The typical opioid peptides, all originate from three precursor proteins – pro-opiomelanocortin (endorphins), proenkephalin (enkephalin) and prodynorphin (dynorphins). Opioid peptides may be produced by the body itself, for example endorphins, or be absorbed from partially digested food (casomorphins, exorphins and rubiscolins). The effect of these peptides varies, but they all resemble opiates. The opioid food peptides have lengths of typically 4-8 amino acids. The body's own opioids are generally much longer. Brain opioid peptide systems are known to play an important role in motivation, emotion, attachment behavior, the response to stress and pain, and the control of food intake. The human genome contains three homologous genes that are known to code for endogenous opioid peptides. Each gene codes for a large protein that can be processed to yield smaller peptides that have opiate-like activity.

Hormonal Peptides

Peptides such as gastrin, hormone releasing factors (GRFs), and calcitonin gene related peptide (CGRP) identified from marine sources exert complex and multiple physiological effects by serving as hormones by regulating hormonal responses associated with the control of important metabolic, growth and development processes. These peptides purified from cod hydrolysate from heads, stomach, and viscera, shrimp head hydrolysate, cooked sardine head, and gut hydrolysate, and from a cooked siki (*Centroscymnus coelolepsis*) head hydrolysate.

Antithromotic Peptides

Peptides isolated from anchovy sauce were capable of inducing apoptosis in a human lymphoma cell line. The peptide of interest was characterized as being hydrophobic and having a molecular weight of 440.9 Da. Protein hydrolysates from different fish species were investigated for their antiproliferative activity on two human breast cancer cell lines. Hydrolysates of blue whiting, cod, plaice and salmon resulted in the significant inhibition of growth. Recently, the hydrolysate of tuna dark muscle by-product was examined for potential antiproliferative activity by exposure to the human breast cancer cell line. Peptide fractions within the molecular weight range of 400 and 1400 Da exhibited the strongest antiproliferative activity. Peptides separated from bovine k-casein inhibit platelet aggregation and combined with the receptor site, consequently preventing fibrinogen binding with blood platelets. These peptides are released during gastrointestinal digestion and absorbed intact into the blood, which supports the concept that they exert an antithrombotic effect in vivo.

Mineral Binding Peptides

Several phosphopeptides containing the cluster sequence -Ser(P)-Ser(P)-Ser(P)-Glu(E)- Glu(E)- have been identified from whole bovine casein. These sequences provide the peptides with the unique capacity to keep Ca, P and other mineral in a solution at intestinal pH. Several phosphopeptides have been identified from enzymatic digest of milk proteins. The highly anionic character of these peptides renders them resistant to further proteolytic attack, allows them to form soluble complexes with calcium and prevents the formation of insoluble calcium phosphate. The proportion of phosphor-peptides interacting with colloidal calcium phosphate correlates with their relative content of phosphoserine residues. Various phosphopeptide fractions revealed significant differences in their calcium-binding activities, which may be due to variant amino acid composition around the phosphorylated region.

The formation of casein phospho peptide has been observed during in vitro digestion of bovine caseins and specific casein phosphor peptide residues have been identified in the intestinal content of mini pigs after ingestion of a diet containing casein. Casein phosphor peptide can be formed also during cheese ripening due to plasmin and microbial

protease activity during ripening.

Conclusion

Recent studies have shown that bioactive peptides play a vital role in human health & nutrition, and they can be a part of the human diet for several years. More studies should be conducted to further explore the physiological effects of these peptides in humans. Fish-derived bioactive peptides may have great potential for use as nutraceuticals and pharmaceuticals and, and they may be a better substitute for synthetic antioxidants. Bioactive peptides have already found interesting applications as dietary supplements and as pharmaceutical preparations such as tablets, toothpaste, and dental filling material. The efficacy and safe conditions of use of these peptides in animals and in humans remain yet to be proven.

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