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REVIEW ARTICLE

Evaluation of Bioactive Compounds in Nutrition Physiology

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ABSTRACT: Many peptides released from animal or plant proteins in vitro or in vivo have therapeutic functions in humans beyond bioactivity and adequate nutrition. Different health effects have been attributed to foodborne peptides, including antimicrobial properties, blood pressure lowering (ACE inhibitor) effects, cholesterol lowering ability, antithrombotic and antioxidant activities, increased mineral absorption, immunomodulatory effects and opioid activities. For this reason, nutritional counseling practices deal with these issues. Specific protein fractions with therapeutic effects on body function and health are termed biological peptides and have been shown to have a direct positive effect on health. Angiotensin I-converting enzyme (ACE) is a carboxy-dipeptidyl metalloproteinase associated with the renin-angiotensin system that regulates the production of angiotensin II from vasoconstrictor angiotensin-I and peripheral blood pressure that catalyzes the inactivation of vasodilator bradykinin. For this reason, the ACE inhibitor substance in the diet may inhibit hypertension by inhibiting the renin-angiotensin system. Milk proteins are now the main source of bioactive peptides. Such peptides are seen as natural and non-effective alternatives to drugs in the treatment of hypertension. The natural consumption of biological peptides will not be expected to cause side effects of synthetically produced drugs used to control hypertension. Therefore, it can be used as a powerful functional food additive and the ACE inhibitor is a natural and healthy alternative to drugs.

Keywords: Bioactive peptides, ACE inhibitors, Antihypertensive effect

INTRODUCTION

The role of proteins as physiologically active components in the diet is increasingly recognized. Naturally, most of the proteins that appear in raw foodstuffs apply physiological effects directly or in vitro or in vivo on enzymatic hydrolysis. In recent years, it has come to the conclusion that dietary proteins are rich in biologically active peptide sources. Physiologically active peptides are known to be produced from various food proteins during gastrointestinal digestion and during fermentation of foodstuffs with lactic acid bacteria (Korhonen & Pihlanto, 2006).

Bioactive peptides

By definition, "nutrient-derived bioactive peptides" refers to peptides of different plant or animal origin that may have regulatory functions in the human system beyond normal and adequate nutrition (Hartmann & Meisel, 2007). It is also defined as specific protein fractions with bioactive peptides, body functions and health-improving effects. Bioactive peptides inactive in the main protein sequence, hydrolysis with digestive enzymes from precursor proteins; fermentation through proteolytic starter cultures; It occurs during proteolysis by enzymes originating from plants or microorganisms (Koçak & Şanlı, 2016). Peptides that are inactive in the content of foods are activated by the hydrolysis of proteins. Peptides that become bioactive have regulatory effects through hormone functions (Tez & Aksay, 2010). Once bioactive peptides are taken with food or produced in the intestine, they are again absorbed by the intestinal target parts and reach the peripheral organs (Gür, Güzel, Öncül, Yıldırım, & Yıldırım, 2010). Bioactive peptides can bioactivity in the small and large intestine by getting rid of food proteins along the intestine. However, it is known that most of the food proteins are destroyed during passage through the small intestine and microbial activity occurs mainly in the large intestine, so that release by the microbial enzymes during digestion is given to the proteins reaching this region of the intestine (Möller, Scholz-Ahrens, Roos, & Schrezenmeir, 2008).

Bioactive peptides generally contain 3 to 20 amino acid residues and their bioactivity is based on the amino acid composition and location in the peptide-forming amino acid sequence. These peptides are not active in the sequences of the parent proteins but can be released by enzymatic hydrolysis by proteolytic enzymes during gastrointestinal digestion, by safe bacteria such as lactobacilli during fermentation or food processing. To create a positive health effect, bioactive peptides must cross the GI barrier and live an enzyme degradation (Mora, Aristoy, & Toldrá, 2016).

Depending on the sequence of amino acids, these peptides may exhibit a variety of activities including mineral binding, immunomodulatory, antimicrobial, antioxidant, antithrombotic, hypocholesterolemic and antihypertensive effects.

Examples of bioactive peptides obtained from grains;

- Antioxidant activity: sardine oil, soya, milk (casein and B-lactoglobulin) egg whites
- Antithrombotic: milk (casein, lactoferrin)
- Hypocholesterolemic: soy, milk (B-lactoglobulin)
- Hypotriglyceridemic: blood

• **Antiobesity:** soy, milk (casein)

Bioactive peptides are obtained by hydrolysis or fermentation from the abovementioned animal and vegetable materials such as milk and dairy products, eggs, soy bean, blood, gelatin, meat and fish (Şimşek & Kılıç, 2016). The most commonly used method is enzymatic hydrolysis. Pepsin, trypsin and chymotrypsin enzymes are used for enzymatic hydrolysis (Gür *et al.*, 2010).

Bioactive peptides can be used as ingredients for functional foods or nutraceuticals due to their potency and safety profile. However, milk proteins are now the main source of diverse bio-functional peptides and it has been proven that daily intake of milk and dairy products is physiologically important for both newborns and adults (Erdmann, Cheung, & Schröder, 2008).

ACE inhibitors

In recent years, some food proteins have been identified as sources of angiotensin I-converting enzyme (ACE) inhibitor peptides and are currently the best known class of bioactive peptides. (Erdmann *et al.*, 2008) ACE is the most common dipeptidyl carboxypeptidase, which is bound to membranes in mammals, usually in vascular endothelial cells (Mora *et al.*, 2016).

The angiotensin I-converting enzyme (ACE) catalyzes the conversion of angiotensin I to the potent vasoconstrictor angiotensin II and plays an important physiological role in regulating blood pressure and fluid and salt balance in mammals (Hartmann & Meisel, 2007). ACE also inactivates the antihypertensive vasodilator bradykinin (Mora *et al.*, 2016).

ACE inhibitors reduce the breakdown of bradykinin, a potent vasodilator, by raising the level of renin in the plasma to a great extent. In this way, the whole of the cardiovascular system undergoes arterial vasodilatation due to the decrease of angiotensin II levels, reducing total peripheral vascular resistance and reducing blood pressure. ACE inhibitors inhibit the formation of hypertension by blocking the effect of the enzyme by binding competitively to ACE. Especially in the C-terminal region, it has been determined that there are strong antihypertensive effects of peptides containing amino acids of proline, lysine and arginine (Erdmann *et al.*, 2008; Kim & Wijesekara, 2010).

Hypertension or high blood pressure is one of the major independent risk factors for cardiovascular disease, which is a leading cause of morbidity and mortality. The pathogenesis of hypertension has shown that angiotensin converting enzyme plays an important physiological role in the regulation of blood pressure (Yu, Zhang, & Zhang, 2016). Therefore, ACE inhibitory substances in foods, inhibiting the renin-angiotensin system, when absorbed into the bloodstream from the intestine, can suppress hypertension (Okamoto *et al.*, 1995).

Many side effects, such as hypotension, elevated potassium levels, decreased renal function, cough, angioedema, edema, skin rashes, and fetal abnormalities have been associated with synthetic ACE inhibitor drugs (Anderson & Moore, 2004). However, these peptides will not be expected to naturally cause consumption, problems associated with synthetically produced drugs used to control hypertension, such as coughs in serum lipid metabolism, and the like (Sciences, Milchwissenschaft, Chemie, Fitzgerald, & Meisel, 2018).

Nowadays, milk, fish, meat, eggs, soybeans, corn, wheat, and algae as many food types, there are hundreds ACE inhibitor peptides identified in many protein hydrolysates (Mora *et al.*, 2016). Because of this direct link between ACE and hypertension, many drugs with inhibitors such as captopril, enalapril, alasepril and lisinopril have been shifted to finding natural and reliable investigations due to many side effects such as a cough, various skin problems, angioneurotic edema, to prevent ACE activity. In vitro and in vivo studies have been carried out on the ACE inhibition effect of proteins obtained from milk and dairy products, vegetable proteins such as soybean, pea, lentil and other sea products from algae (Gao, Chang, Li, & Cao, 2002; Kim & Wijesekara, 2010; Wu, Liao, & Udenigwe, 2017).

In a study, it was found that mice fed with ACE inhibitor-rich foods suppressed spontaneous hypertension. In vivo studies in patients with hypertension nutraceutically, foods with ACE inhibitor peptides may have an antihypertensive effect (Pihlanto, Virtanen, & Korhonen, 2010; Seppo, Jauhainen, Poussa, & Korpela, 2003).

Antihypertensive peptides derived from dairy products

Fermented milky foods are a physiologically important peptide source that provides energy and nutrients as well as positive effects on the body's functions (Pihlanto, 2006; Tirelli, De Noni, & Resmini, 2000).

Although animal and vegetable proteins contain bioactive sequences, milk proteins are shown as the main source of bioactive peptides. Milk proteins, casein and whey proteins are a good bioactive peptide source that can positively affect body function and ultimately affect health (Rasika *et al.*, 2015). In addition, casein and whey are rich in ACE inhibitors (Ra, Ege, & Fak, 2013). Among the different bioactive peptides, ACE inhibitor peptides are the most thoroughly studied group. A number of ACE-inhibitor peptides have been identified from different fermented milk products such as yoghurt (Rasika *et al.*, 2015).

Bioactive peptides derived from milk and dairy products have been reported to have various health benefits such as anticarcinogenic, weight management, antithrombotic, antioxidative, immunomodulatory and antihypertensive properties (Pihlanto, 2006; Tirelli *et al.*, 2000).

Meat-derived antihypertensive peptides

Meat proteins are hydrolyzed by proteolytic enzymes during fermentation and storage, thus producing bioactive peptides from fermented meat products (Arihara, 2006). The amount of bioactive peptides increases during ripening and storage of the meat after cutting (Şimşek & Kılıç, 2016). Bioactive peptides have been isolated from digestive enzymes such as pepsin, trypsin and chymotrypsin in meat products. Several proteases from bacterial, animal and plant sources have also been used to produce bioactive peptides from meat sources (Ryan, Ross, Bolton, Fitzgerald, & Stanton, 2011).

First, during fermentation of meat products, meat proteins are separated by peptides by endogenous enzymes. Protein degradation is not greatly affected by bacteria, as most bacteroids that develop in fermented meat products have poor proteolytic activity. Among the bioactive peptides derived from meat proteins, ACE inhibitor peptides are the most studied (Arihara, 2006).

Other foods antihypertensive peptides

In a study with pea, it was found that increasing the temperature from 25 °C to 50 °C led to an increase in ACE inhibitor and antioxidant activity (Siow & Gan, 2013). Many bioactive peptides have been identified in fermented soy products that show ACE inhibitors, antithrombotic, surfactant and antioxidant

properties (Gibbs, Zougman, Masse, & Mulligan, 2004). Presence of ACE inhibitor peptides in corn produced by fermentation with maize wheat or rice bacteria and lactic acid bacteria has been detected (Kancabaş & Karakaya, 2013). During fermentation of fermented soybean product Douchi, traditionally produced in China, the change in ACE inhibitory activity was investigated and activity increased over the two week fermentation period, but decreased over time (Wang, Li, Cheng, Yin, & Li, 2013).

CONCLUSIONS

Within the group of bioactive peptides, antihypertensive peptides (ACE inhibitor) the ability to test their function in vitro on humans and animals and to test them in different foods. These peptides can be used as powerful functional food additives and provide a natural and healthy alternative to ACE inhibitor drugs.

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CONFLICTS OF INTEREST

“The authors declare no conflict of interest”.

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