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Review

Functional significance of bioactive peptides derived from soybean

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ABSTRACT

Biologically active peptides play an important role in metabolic regulation and modulation. Several studies have shown that during gastrointestinal digestion, food processing and microbial proteolysis of various animals and plant proteins, small peptides can be released which possess biofunctional properties. These peptides are to prove potential health-enhancing nutraceutical for food and pharmaceutical applications. The beneficial health effects of bioactive peptides may be several like antihypertensive, antioxidative, antiobesity, immunomodulatory, antidiabetic, hypocholesterolemic and anticancer. Soybeans, one of the most abundant plant sources of dietary protein, contain 36–56% of protein. Recent studies showed that soy milk, an aqueous extract of soybean, and its fermented product have great biological properties and are a good source of bioactive peptides. This review focuses on bioactive peptides derived from soybean; we illustrate their production and biofunctional attributes.

Contents

1. Introduction

Bioactive peptides are specific protein fragments that have a positive impact on body functions and may ultimately influence health. Mellander was the first to describe food derived bioactive peptides by reporting that ingestion of casein-derived phosphorylated peptides led to enhanced vitamin D-independent calcification in rachitic neonates [76]. Since then, multitudinous peptides with various bioactivities have been identified. More than 1500 different bioactive peptides have been reported in a database named 'Biopep' [22], as well as database BioPD (bioactive polypeptide database) has also reported more than 1250 peptide with different functional significance. Bioactivities of peptides, encrypted in proteins, are latent until, once they released from their parental protein, they may act as physiological modulators with hormone-like activity. Majority of natural processes within the body are signaled or modulated by the interaction of specific amino acid sequences, either in the form of peptides or fragments of proteins, so they hold future promise for a wide range of therapeutic applications [26]. Bioactive peptides, depending upon their amino acid sequence, may

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Table 1
Examples of biofunctional peptides derived from soybean.

Bioactivity	Peptides	Reference
Anticancer	X-Met-Leu-Pro-Ser-Try-Ser-Pro-Try	[50]
Hypotensive	Tyr-Val-Val-Phe-Lys and Ile-Pro-Pro-Gly-Val-Pro-Try-Trp-Thr	[54]
Anticancer (Lunasin)	SKWQHQQDSCRKQKQGVNLTPCEKHIMEKIQGRGDDDDDDDDD	[28]
Hypocholesteromic	LPYPR	[116]
Antihypertensive	HHL	[97]
Antihypertensive	PGTAVFK	[52]
ACE inhibitory peptide	Val-Ala-His-Ile-Asn-Val-Gly-Lys and Tyr-Val-Trp-Lys	[37]
Phagocytosis stimulatory peptide	His-Cys-Gln-Arg-Pro-Arg and Gln-Arg-Pro-Arg	[116]

influence the major body systems such as cardiovascular, digestive, nervous and immune. The bioactive peptides sequence size, vary from two to twenty amino acid residues, but some peptides (Lunasin 43 amino acid) have long chain of amino acid. Most of the bioactive peptides exhibit specific biofuctional attribute such as lunasin having anticancer properties, but some peptides have found with multifunctional properties, caseinophosphopeptides, milk derived peptide, having mineral binding as well as cytomodulatory effects and inhibit cancer cell growth or stimulate the activity of immunocompetent cells and neonatal intestinal cells [74].

Although milk and milk products are greatly studied as source of bioactive peptides, many bioactive peptides are also found in other animal and plant sources like egg, fish, oyster, cereal (rice, wheat, soybean, buckwheat, barley, and corn), soybean, and radish seeds [64,72,117]. Royal jelly (RJ), a bee product has also been discovered as a good source of ACE-inhibitory peptides [73]. Soybean (*Glycine max*) is economically the most important bean in the world, providing vegetable protein for millions of people and ingredients for hundreds of chemical products and a potential source of bioactive peptides. Soy proteins are abundant and relatively inexpensive source of protein having high nutritional value and excellent functional properties. They are not only the excellent source of dietary protein, but additionally having antihypertensive, anticholesterolemic, antioxidative and anticancer activity. Glycinin and β-conglycinin, accounting for 65–80% of total soy proteins, are the precursor of most of the isolated peptides [113]. β-Conglycinin composed of three subunits (α, α′ and β) which share a large degree of amino acid homologies. On the other hand Glycinin, have five major subunits, G1, G2, G3, G4, and G5. All the essential amino acid those found in animal protein is present in soy proteins. In addition nutritional value of soy protein is around equal to animal protein of high biological value. For example, isolated soy protein has a protein digestibility-corrected amino acid score of 1.0, which is same as that of casein and egg protein. However, soy proteins contain low methionine/glycine and lysine/arginine ratios compared to casein. Soymilk is a suitable food for lactose-intolerant consumers, vegetarians and milk-allergy patients, as it is free of cholesterol, gluten and lactose [19]. Soy milk provides adequate proteins, iron, unsaturated fatty acids and other nutrients but contains low fat, carbohydrates and calcium. It naturally has the same amount of protein as cow's milk. Several bioactive peptides have been isolated, purified and characterized from soy milk with ACE-inhibitory, hypocholestromic, immunomodulatory and anticancer activities (Table 1). Foods containing sufficient soy protein (6.25 g of soy protein per reference amount customarily consumed) are permitted in the United States to carry a health claim on their labels based on evidence that consumption of soy protein can reduce the risk of coronary heart disease (FDA). Aglycin, a natural bioactive peptide isolated from soybean, is stable in digestive enzymes and has an antidiabetic potential. Study demonstrated that oral administration of aglycin can potentially attenuate or prevent hyperglycemia by increasing insulin receptor signaling pathway in the skeletal muscle of streptozotocin/high-fat-diet-induced diabetic mice [66]. Atheroprotective role of bioactive peptides derived from soy protein such as β-conglycinin and glycinin were also studied and suggested their preventing effect through absorption from the intestinal tract [79].

2. Bioactive peptides mechanism of action

Cardiovascular disease (CVD) has been recognized as the biggest cause of death worldwide. The renine–angiotensin system regulates blood pressure and fluid balance, and plays an important role in the physiology of CVDs. Angiotensin converting enzyme (ACE), is a nonspecific dipeptidyl carboxy peptidase, converts the inactive decapeptide angiotensin I by cleaving dipeptide from the C-terminus into the potent vasoconstricting octapeptide angiotensin II in the renin-angiotensin system (RAS). This potent vasoconstrictor is also involved in the release of a sodium-retaining steroid, aldosterone, from the adrenal cortex, which has a tendency to increase blood pressure [80]. ACE is widely distributed in mammalian tissues, predominantly as a membrane-bound ectoenzyme in vascular endothelial cells and also in several other cell types including absorptive epithelial, neuroepithelial, and male germinal cells [98]. ACE is a multifunctional enzyme that also catalyses the degradation of bradykinin, a blood pressure lowering nonapeptide in the kallikrein–kinin system [10,46,48]. Inhibition of ACE is considered to be a useful therapeutic approach in the treatment of hypertension. ACE-inhibitory peptides block the first step in the renin-angiotensin system and interrupt the negative feedback effects of angiotensin II. ACE-inhibitory peptides, derived from different plant and animal sources, when compared with chemosynthetic drugs, can be used as potent alternatives of synthetic drugs because of the increasing interest for safe and economical.

Oxidation reactions within the body during respiration in aerobic organisms; particularly vertebrates and humans can produce free radicals [24], as well as air pollutants and tobacco oxidants can be absorbed to blood circulation and exert adverse effects. In addition, UV radiation can stimulate the generation of a variety of oxidants [39]. Oxidative damage plays a significantly pathological role in human diseases like cancer, emphysema, cirrhosis, atherosclerosis, and arthritis. When the mechanism of antioxidant protection becomes unbalanced by factors such as aging, deterioration of physiological functions may occur, resulting in diseases and accelerating aging. Antioxidant food supplements or bioactive peptides may be used to help the human body and animals to reduce the oxidative damage [115]. Proteins and peptides can inhibit lipid oxidation through multiple pathways including inactivation of reactive oxygen species, scavenging free radicals, chelation of prooxidative transition metals, reduction of hydroperoxides, and contribute to the endogenous antioxidant capacity of foods. Antioxidant activity of protein can be increased by their hydrolysis; peptides have substantially higher antioxidant activity than intact proteins [23].

Dyslipidemia, characterized by the presence of one or more than one abnormal serum lipid concentration (total cholesterol-TC, LDL-C, triglycerides and HDL-C), is a prime risk factor for cardiovascular diseases (CVD). Atherosclerosis is a vascular chronic inflammation in the arterial wall that can lead to clinical manifestations including