



Review

Antioxidative peptides from food proteins: A review

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ABSTRACT

Bioactive peptides, as products of hydrolysis of diverse food proteins, are the focus of current research. They exert various biological roles, one of the most crucial of which is the antioxidant activity. Reverse relationship between antioxidant intake and diseases has been approved through plenty of studies. Antioxidant activity of bioactive peptides can be attributed to their radical scavenging, inhibition of lipid peroxidation and metal ion chelation properties of peptides. It also has been proposed that peptide structure and its amino acid sequence can affect its antioxidative properties. This paper reviews bioactive peptides from food sources concerning their antioxidant activities. Additionally, specific characteristics of antioxidative bioactive peptides, enzymatic production, methods to evaluate antioxidant capacity, bioavailability, and safety concerns of peptides are reviewed.

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1. Introduction

Traditionally, dietary protein is regarded as a source of energy and essential amino acids, which are needed for growth and maintenance of physiological functions. Recently, interest has been emerging to identify and characterize bioactive peptides from plant and animal sources. Bioactive peptides are considered specific protein fragments that are inactive within the sequence of the parent protein. After they are released by enzymatic hydrolysis, they may exert various physiological functions. These peptides are in the

size of 2–20 amino acids [61] and molecular masses of less than 6000 Da [91]. The amino acid composition and sequences affect the biopeptide activity [6,74]. Based on their structural properties and their amino acid composition and sequences, these peptides may play various roles, such as opiate-like [88], mineral binding [11], immunomodulatory [23], antimicrobial [58], antioxidative [62], antithrombotic [86], hypocholesterolemic [108] and antihypertensive functions [41]. Moreover, several peptides have been found to possess multifunctional properties [61].

The present paper focuses on the antioxidative bioactive peptides derived from food sources. It describes specific characteristics of antioxidative bioactive peptides. In addition, it presents an overview of issues relevant to bioactive peptides, namely their health effects, enzymatic production, measurement methods of antioxidant activity, bioavailability and safety concerns.

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2. Oxidative stress

Free radicals are generated through normal reactions within the body during respiration in aerobic organisms, particularly vertebrates and humans [16,39]. In addition to the physiological production of oxidants and their secondary reactions, there are other sources for production of oxidants. Oxidation of fats and oils during processing and storage of food products worsen the quality of their lipid content and nutritive values [76]. Consumption of these potentially toxic products can give rise to several diseases [39]. Air pollutants and oxidants in tobacco can also cause some harmful reactions in skin or can be absorbed to blood circulation and exert adverse effects [2,106]. Additionally, UV radiation can stimulate the generation of a variety of oxidants [32,36].

The free radicals, which are physiologically produced, can exert diverse functions like signaling roles and providing defense against infections [27,42,94]. Nevertheless, any excessive amount of reactive radicals can result in cellular damage which, in turn, initiates several diseases including atherosclerosis, arthritis, diabetes and cancer [26,38]. According to the free radical theory of ageing developed by Denham Harman, organisms age when free radicals accumulate in cells and cause harm over time [28]. Generally, reactive species can cause damage in proteins, and mutations in DNA, oxidation of membrane phospholipids [48] and modification in low density lipoproteins (LDL) [1].

Under normal conditions, antioxidant defense systems can remove reactive species through enzymatic (like superoxide dismutase and glutathione peroxidase) and non-enzymatic antioxidants (such as antioxidant vitamins, trace elements, coenzymes and cofactors) [42]. However, in certain circumstances the endogenous defense system fails to protect the body against reactive radicals on its own [43]. This results in oxidative stress, a condition in which the generation of highly reactive molecules such as reactive oxygen species (ROS) and reactive nitrogen species (RNS) exceed their elimination and/or when their elimination is inadequate [55]. In humans, oxidative stress usually plays the role of a promoter rather than an initiator of chronic diseases [78].

This brings about the need for synthetic and natural antioxidants, which can prevent oxidative stress and its deleterious effects. Synthetic antioxidants are cost-effective and efficient but display some toxic and hazardous effects [37]. In the areas of human nutrition and biochemistry, natural antioxidants from food resources have been the focus of growing interest for their potential health benefits with no or little side effects. There has also been an increasing tendency among public to choose natural rather than synthetic antioxidants.

Synthetic antioxidants are shown to be more effective than natural antioxidants. As an example, the radical-scavenging IC_{50} values for the soybean hydrolysates were higher than those of Trolox or Vitamin C [33]. And yet, natural antioxidants can be equally effective if a higher dose is applied.

3. Antioxidative peptides from food proteins

Several peptides from protein ingredients have been found to possess antioxidant capacity, and their biological activity has been widely studied since the effect was first reported by Marcuse [54]. Antioxidant peptides contain of 5–16 amino acid residues [7]. Antioxidative peptides from foods are considered to be safe and healthy compounds with low molecular weight, low cost, high activity, easy absorption. They have some advantages in comparison to enzymatic antioxidants; that is, with simpler structure they have more stability in different situation and no hazardous immunoreaction. What is more, they present nutritional and functional properties beside their antioxidant activity [30,104]. Studies

that investigate health effects of bioactive peptides apply them in two different forms: either as hydrolysates of precursor proteins or as bioactive peptides. Hydrolysate is a mixture that is mainly composed of peptides and amino acids which are produced through protein hydrolysis by enzyme, acid or alkali treatment or fermentation. When proteolysis of proteins is induced by endogenous proteases, the term “autolysate” is usually used rather than “hydrolysate”. Bioactive peptides, on the other hand, are several linked amino acids purified from hydrolysates.

Vioque et al. [96] have categorized hydrolysates into three main groups based on their degree of hydrolysis (DH) that determine their application: (1) hydrolysates with low DH and improved functional features, (2) hydrolysates with various DHs (generally used as flavorings), and (3) hydrolysates with broad DH (mostly used as nutritional supplements and in special medical diets).

It seems that in the area of nutritional sciences application of non-purified protein hydrolysate can have certain benefits over those of purified peptides since the absorption of oligopeptides can be increased in the presence of sugar and amino acids [70]. Further, it has been shown that hydrolysate exerts higher antioxidant activity than purified peptides [5].

Various studies have been conducted to investigate antioxidant properties of hydrolysates or bioactive peptides from plant or animal sources like peanut kernels [35], rice bran [77], sun flower protein [60], alfalfa leaf protein [104], corn gluten meal [50], frog skin [75], yam [65], egg-yolk protein [81], milk-kefir and soymilk-kefir [51], medicinal mushroom [97], mackerel [103], curry leaves [68], cotton leafworm [95], casein [90], algae protein waste [85] and buckwheat protein [92]. Table 1 presents a list of studies on the antioxidant activities as well as structural properties of peptides and hydrolysates.

The exact mechanism underlying the antioxidant activity of peptides has not fully been understood, yet various studies have displayed that they are inhibitors of lipid peroxidation [64,75,103], scavengers of free radicals [64,75,76] and chelators of transition metal ions [76]. In addition, it has been reported that antioxidative peptides keep cells safe from damage by ROS through the induction of genes. As it has been found that dipeptide Met-Tyr from sardine muscle prevent oxidative stress by stimulating expression of heme oxygenase-1 (HO-1) and ferritin (antioxidant defense proteins) in endothelial cells [15]. Moreover, results from a study revealed that leaf protein is capable of enhancing the activities of glutathione peroxidase (GSH-Px) and superoxide dismutase (SOD) and reducing malondialdehyde (MDA) concentration *in vivo* [18].

Antioxidative properties of the peptides are more related to their composition, structure, and hydrophobicity [6]. Tyr, Trp, Met, Lys, Cys, and His are examples of amino acids that cause antioxidant activity [98]. Amino acids with aromatic residues can donate protons to electron deficient radicals. This property improves the radical-scavenging properties of the amino acid residues [76]. It is proposed that the antioxidative activity of His-containing peptides is in relation with the hydrogen-donating, lipid peroxyl radical trapping and/or the metal ion-chelating ability of the imidazole group [4,76]. On the other hand, SH group in cysteine has an independently crucial antioxidant action due to its direct interaction with radicals [75].

In addition to the presence of proper amino acids, their correct positioning in peptide sequence plays an important role in antioxidant activity of peptides [76]. Chen et al. [7] designed 28 synthetic peptides following the structure of an antioxidative peptide (Leu-Leu-Pro-His-His) from digestion of a soybean protein, conglycinin [5]. It was revealed that the antioxidant activity of a peptide was more dependent on His-His segment in the Leu-Leu-Pro-His-His domain and its activity was decreased by removing a His residue from the C-terminus. According to the result from the same study, Pro-His-His sequence displayed the greatest antiox-

Table 1

Antioxidant peptides derived from sources.

Source of peptides	Characteristic ^a	Preparation	Activity	Reference
Rice endosperm protein	FRDEHKK and KHDRGDEF	Five different proteases, Neutrase was the most effective	Inhibition of autooxidation, DPPH, superoxide and hydroxyl radical-scavenging activity	[107]
Peanut kernels protein	Molecular weight 3–5 kDa	Different proteases esperase was the most effective	Reducing power, Inhibition of human LDL oxidation, DPPH radical-scavenging and metal-chelating activity	[35]
Algae protein waste	VECYGPNRPQF	Pepsin	Hydroxyl, superoxide, peroxy, DPPH and ABTS radicals scavenging activity, protective effects on DNA and prevention of cellular damage	[85]
Peptide from frog skin	LEEEEEELEGCE	Alcalase, neutrase, pepsin, papain, α -chymotrypsin and trypsin	Inhibition of lipid peroxidation, DPPH, hydroxyl, superoxide, peroxy radical scavenger	[75]
Sunflower protein	Hydrolysate with 37% DH, enriched in certain amino acids, such as histidine and arginine	Pepsin and pancreatin	Copper-chelating activity	[60]
Alfalfa leaf protein	Molecular weight <1000 Da	Alcalase	Reducing power, radical chelating and scavenging activities	[104]
Zein hydrolysate	Contains up to 6.5% free amino acids and the rest short peptides (<500 Da)	Pepsin, pancreatin and alcalase	Radical chelating and scavenging activities	[109]
Corn gluten meal	Peptides fraction of 500–1500 Da, 41.12% hydrophobic amino acids and ~12.7% aromatic amino acids	Alcalase	Lipid peroxidation, reducing power, scavenging activity	[50]
Peanut protein	Not specified	Alcalase	Inhibition of linoleic acid autooxidation, radical-scavenging activity, reducing power, and inhibitor of liver lipid oxidation	[8]
Yam ichyoimo tubers	Not specified	Autolysis and enzymatic digestion (trypsin, pepsin, papain)	Inhibition of linoleic acid oxidation, radical-scavenging activity	[65]
Soy protein fractions	Peptides with molecular weight of <10 kDa	Ultrafiltration and hydrolysis by Flavourzyme	Antioxidant activity in emulsion, radical scavengers, reducing power	[63]

^a Amino acids are presented in single-letter code.**Table 2**

Amino acid compositions and their positioning in relation with peptide antioxidant activity.

Amino acids	Mechanism of action	Examples
Aromatic AAs (Tyr, His, Trp, Phe)	Converting radicals to stable molecules by donating electron, while keeping their own stability via resonance structure Improving the radical-scavenging properties of the amino acids residues [76]	His at N-termini as an effective metal ion chelator [6] His at C-termini as an effective scavenger against various radicals [6] Tripeptides with Trp or Tyr at C-termini as strong radical scavengers but weak peroxynitrite scavengers [82]
Hydrophobic AAs	Enhancing the solubility of peptide in lipid which facilitates accessibility to hydrophobic radical species and to hydrophobic PUFAs [6,75,89], Gly as hydrogen donor [75]	Val or Leu, at the N-termini and Pro, His, or Tyr in the sequences [5] High reactivity of aliphatic groups in Ala, Val, Leu to hydrophobic PUFAs [75] Ala or Leu at the terminus, Gln and a Pro residue in the sequences of peptide from gluten [89]
Acidic and basic AAs	Carboxyl and amino groups in the side chains as chelator of metal ions [90], as hydrogen donor [75]	Asp (acidic amino acid) and His (basic amino acid) residues in peptide purified from fermented mussel sauce [76]
Cysteine	SH group as radical scavenger [72], protecting tissue from oxidative stress, improving the glutathione activity [83]	Tripeptides with Cys as strong scavengers against peroxynitrite radicals [82] In curry leave protein SH group together with other functional groups involved in its antioxidant activity [68]

oxidative activity among all tested peptides. Saito et al. [82] have reported that any change in the arrangements of amino acid sequence in tripeptides resulted in different antioxidant activities. Table 2 provides further information regarding the effect of amino acid compositions and their correct positioning in peptide sequences.

Peptide linkage and/or specific structural features of the peptides have been claimed to influence antioxidant capacity. For example, it has been shown that certain amino acids can exert higher antioxidative properties when they are incorporated in dipeptides [66]. In contrast to these findings, other results indicated that peptide bond or its structural conformation can reduce the antioxidant activity of the constituent amino acids. Therefore, apparently peptide conformation behaves as a double-edged sword; i.e., it is capable of showing both synergistic and antagonistic effects, as far as the antioxidant activity of free amino acids is concerned [31].

Moreover, it has been stated that the configuration of peptides can also affect antioxidant activity. Chen et al. [7] found that substitution of L-His by D-His in an antioxidative peptide leads to reduction of the activity. They concluded the correct positioning of imidazole group is the key factor influencing the antioxidant activity.

Apart from what was mentioned above, other factors can influence antioxidant activity of bioactive peptides as well. The antioxidant and biological activities can be affected by the operational conditions applied to isolate proteins, degree of hydrolysis, type of protease [24,73], peptide structure [82] and peptide concentration. The effect of protein concentration on antioxidant activity was reported for peanut protein hydrolysates [8]. In addition, molecular weight (MW) of peptides can influence antioxidant activity. It was found that the antioxidant activity of corn gluten meal hydrolysates was related to the concentration and molecular weight of hydrolysates. Antioxidant activity of peptides of MW 500–1500 Da was stronger than that of peptides above 1500 Da and peptides below 500 Da [50]. However, it has been postulated that the overall antioxidative activity must be ascribed to the integrative effects of these actions rather than to the individual actions of peptides [6].

3.1. Health effects of antioxidative peptides

As mentioned previously, free radicals are involved in initiation or progress of several degenerative diseases. For example, recent evidence suggests that oxidative stress may contribute to type II diabetes by increasing insulin resistance or impairing insulin secretion. Uncontrolled generation of free radicals worsens the development and progression of diabetes and its complications [42]. It also has been suggested that oxidative stress plays a key role in the initiation or progress of cardiovascular complications (like atherosclerotic process and alteration in lipid metabolism) in patients with metabolic syndrome [69].

Therefore, due to the close relationship between oxidative stress and diseases, control of oxidative stress seems to be one of the crucial steps in slowing down the progress of these diseases or preventing their complications. In this regard, a vast number of antioxidants are isolated and identified from natural sources to control oxidative stress. Beside various well-known natural antioxidants like Vitamin C, polyphenols, flavonoids and carotenoids, peptides with antioxidative properties are also the focus of recent research. For instance, ingestion of Douchi (fermented soybean food) extracts to rats had an effect of increasing SOD activities in liver and kidney, catalase (CAT) activity in liver, GSH-Px activity in kidney as well as decreasing serum thiobarbituric acid-reactive substances (TBARS) in liver and kidney. These results were attributed to the peptides and free amino acids components of

Douchi extracts which act as antioxidant [99]. In addition, it has been found that the radical-scavenging capacity of plasma rose while an elevated concentration of MDA in the aorta dropped following an intake of egg white hydrolysates (0.5 g/kg/day of egg white hydrolysates) by spontaneously hypertensive rats (SHR). It has been postulated that egg white hydrolysates may contribute in prevention of oxidative stress by increment of plasma radical-scavenging capacity and inhibition of lipid peroxidation [53]. Pena-Ramos and Xiong have reported that soy protein isolate and its hydrolysates decreased TBARS by 28–65% [73]. In another study, it was shown that the ingestion of soy protein isolate (SPI) or soy peptide to male Wistar rats reduced paraquat (PQ)-induced oxidative stress. Such effects were not observed when amino acid mixture was fed to rats. Additionally, soy protein isolates and soy peptide prevented the elevation of the serum TBARS concentration [93]. Soymilk-kefir has exhibited to have significant antimutagenic and antioxidant activities. It was proposed that fermented soymilk can be considered as a food with preventative roles in mutagenic and oxidative damage [51].

3.2. Enzymatic production of bioactive peptides

Basically, biologically active peptides can be generated from precursor proteins in multiple ways, including: enzymatic hydrolysis (either by digestive enzymes or enzymes derived from microorganisms and plants) and microbial fermentation [45]. In South East Asian countries such as China, Japan and Korea, fermentation is used widely as the oldest way to preserve food. It is believed that fermentation can increase the nutraceutical value of foods, besides the long storability, possibly due to fragmentation of proteins to bioactive peptide by microbial proteases [76].

Generally, enzymatic hydrolysis is widely applied to upgrade the functional features (like emulsifying properties of the hydrolyzed protein) and nutritional properties of proteins [3,63,105]. For example, enzymatic digestion of β -conglycinin and glycinin has been found to increase its antioxidant activity [82]. This can be due to the fact that upon hydrolysis more active amino acid R groups will be exposed that leads to increased antioxidant activity [56]. It has been reported that additional advantage of hydrolysis can be development of hydrophobicity since proteolysis unfolds the protein chains. In addition, hydrolysis decreases allergenic agents [63]. However, the cleavage of peptide bonds enhances levels of free amino and carboxyl groups resulting in enhanced solubility. Therefore, hydrolysis can increase or decrease the hydrophobicity which mostly depends on the nature of the precursor protein and molecular weight of the generated peptides [3]. Moreover, reportedly hydrolysis leads to production of small bioactive peptides [47,63] and bitterness of peptides of below 1000 Da is much less than fractions with a higher molecular mass [10]. However, it has been reported that extensive hydrolysis could adversely affect functional properties of peptides [47].

Despite the high nutritive value of alfalfa leaf protein, it has limited application due to its poor solubility and negative sensory properties in color, taste and texture [9]. Such limitations can be overcome by application of enzymatic hydrolysis [104].

Protease specificity affects size, amount, composition of free amino acid and peptides and their amino acid sequence which in turn influences the antioxidant activity of the hydrolysates [5,40,103]. In their research, Peña-Ramos and Xiong [73] used different enzymes to produce hydrolysates from native and heated soy protein isolates. They reported that using different enzymes resulted in the formation of a mixture of peptides with different degrees of hydrolysis and accordingly different ranges of antioxidant activity.

In different studies, it has been found that antioxidant activity of alcalase-derived hydrolysates is higher than that of other

Table 3

Possible routes of intact absorption of peptides.

Transportation route	Remarks	Candidates	Reference
Paracellular route	Diffusion through the tight junctions between cells by energy independent passive diffusion process	Large water-soluble peptides	[21]
Passive diffusion	Diffusion through transcellular by energy independent passive diffusion process	Hydrophobic peptides	[110]
Via transporter	Exit of some peptides from the enterocyte into the portal circulation via a peptide transporter located intestinal basolateral membrane	Hydrolysis-resistant small peptides	[20]
Endocytosis	Binding of molecules to the cells and their absorption into cell via vesiculation	Usually large polar peptides	[21,110]
Lymphatic system	Absorption of peptides from interstitial space into the intestinal lymphatic system	Highly lipophilic peptides too large to be absorbed into the portal circulation	[12,80]

hydrolysates [71,75]. It is also reported that peptides produced by alcalase have diverse biological activities, including antioxidant activity [71]. Moreover, in comparison to other proteases, it provides higher yields of antioxidative peptides and develops shorter peptides. The resulting bioactive peptides are more resistant to digestive enzymes [44,71].

3.3. Methods to evaluate antioxidant activity

Significance of oxidative stress and the preventative roles of antioxidant urge an interest to investigate antioxidant efficacy of food products. Several methods have been developed to assess antioxidant capacity. These methods aid researchers to determine the amount of antioxidant compounds in food products, to evaluate their ability to resist oxidation and the antioxidant activity which may be present inside the organism after ingestion [34,84]. On the basis of the chemical reactions, the assays for measuring antioxidant capacity are classified into two groups: methods based on hydrogen atom transfer (HAT) and methods based on electron transfer (ET) [34]. The majority of HAT-based assays apply a competitive reaction, in which antioxidant and substrate compete for thermally generated peroxy radicals. The oxygen radical absorbance capacity (ORAC), total radical trapping antioxidant parameter (TRAP) and β -carotene bleaching assay are examples of HAT-based assays. ET-based assays measure the capacity of an antioxidant in the reduction of an oxidant, which also acts as the probe for monitoring the reaction and indicator of the reaction endpoint [111]. The Trolox equivalent antioxidant capacity (TEAC), the ferric ion reducing antioxidant power (FRAP) and 2,2-diphenyl-1-picrylhydrazyl radical-scavenging capacity (DPPH) are examples of ET-based assays used frequently to measure antioxidant activity of peptides. Following reaction and electron transfer occur during ET-based assays: Probe (oxidant) + e (from antioxidant) \rightarrow reduced probe + oxidized antioxidant [59].

It seems that the HAT-based reaction is a key step in the radical chain reaction; therefore, it is more relevant to the radical chain-breaking antioxidant capacity [52,59]. However, reducing power of a compound is considered an important and chemically valid parameter. ET-based assay can also present useful information. For example, some water-soluble oxidants such as peroxyxynitrite and hypochlorite are shown to be reduced to harmless species by antioxidants [34].

In addition to aforementioned assays, there are other methods to measure ROS and RNS. These assays include superoxide, hydrogen peroxide, hydroxyl, single oxygen and peroxyxynitrite scavenging assays.

It should be mentioned that, in vitro measurement of antioxidant capacity of compounds cannot be directly related to their capacity in vivo situation since their bioavailability, in vivo reactivity, in vivo stability and storage in tissue are not taken into consideration in these assays. Moreover, they have very little similarity to biological systems. As a result, in vivo evidence is required to support the in vitro based antioxidant efficiency of compounds [34,59]. Biomarkers of lipid and protein peroxidations as well as DNA damage can be assessed to monitor changes in oxidative stress in vivo [101].

Finally, although there are several methods to evaluate antioxidant capacity of food products, none of them can be used as an official standardized method. Therefore, it is suggested that each evaluation be done by various methods of measurement in different oxidation conditions [19].

3.4. Bioavailability of bioactive peptides

Although a good deal of evidence has confirmed the in vitro antioxidant activity of bioactive peptide, it is important but hard to consider a relation between in vitro antioxidant properties and in vivo antioxidant capacity of peptides since they are subject to degradation and modification in the intestine, vascular system and liver. Therefore, it can be implied that the peptides should be able to overcome the barriers and reach their target in an active form.

It has been indicated that a small portion of bioactive peptides can pass the intestine barrier and although it is usually too small to be considered nutritionally important, it can present the biological effects in tissue level [21,22]. Intact absorption of peptides is regarded as a normal physiological process which is different from regular peptide transporter route [21]. Table 3 presents a number of mechanisms for intact absorption of peptides, including: paracellular route, passive diffusion, transport via carrier, endocytosis and lymphatic system.

Peptides and proteins can escape digestion and be absorbed in an intact form through the interstitial space into the intestinal lymphatic system. However, the ability of compounds to enter the intestinal lymphatic system is affected by their permeability via the capillary of the portal circulation and lipid solubility [12]. It has been proposed that drugs transported through gastrointestinal lymphatic system can escape the hepatic metabolism [100].

Molecular size and structural properties, such as hydrophobicity, affect the major transport route for peptides [87]. Research findings indicate that peptides with 2–6 amino acids are absorbed more readily in comparison to protein and free amino acids [25]. Roberts et al. [79] reported that small (di- and tripeptides) and large

(10–51 amino acids) peptides can cross the intestinal barrier intact and exhibit their biological functions at the tissue level. However, as the molecular weight of peptides increases, their chance to pass the intestinal barrier decreases. It has been recorded that presence of proline and hydroxyl proline results in peptide resistance to digestive enzymes, especially tripeptides with Pro-Pro at the C-terminal that are resistant to proline-specific peptidases [17].

Moreover, in a study, it was observed that the amount of peptide in human plasma increased dose-dependent manner. It was, thus, proposed that saturation of peptide transporters could affect the amount of peptides entering peripheral blood [57].

Therefore, it can be deduced due to the incomplete bioavailability of peptide following oral ingestion, a peptide with pronounced antioxidant activity in vitro may exert little or no activity in vivo. However, other bypass routes which increase the chance of peptide absorption can diminish the problem. On the contrary, it is possible that in vivo antioxidant activity can be higher than in vitro activity. In such cases, as it has been suggested [14], bioactive peptides may display their biological functions by mechanisms other than what is applied in experiment. In addition, it has been suggested that the strong in vivo activity can be due to increased activity of peptides following their breakdown by gastrointestinal proteases [49].

3.5. Safety concerns of bioactive peptide

Beside all health benefits related to peptides it is necessary to assess their ill effects before they are exploited into consumable products. Limited studies are carried out on evaluation of adverse effects of food-derived bioactive peptides on human health. Although cytotoxic effects of peptides have been reported, such effects include malignant cells. Therefore, they can be recognized as potential anticancer agents [29]. Most allergenic substances from foods and pollens are protein-based compounds. Admittedly, bioactive peptides are products of hydrolysis of proteins and break down of proteins to low molecular weight peptides lessens the allergenic properties during hydrolysis [63]. However, it may happen that some peptides may keep a part of their parent protein allergenic properties [29], which indicates that their hazardous allergenic effects should be taken into consideration. For example, in a study the major peanut allergen, namely Ara h 1, was cleaved to low molecular weight peptides by gastro-duodenal digestion. The produced peptides kept their parent protein allergenic potential [13].

Bioactive peptide are produced from food sources most of which have been consumed by human beings for long with rare adverse effects. However, due to the possibility of presence of any cytotoxic effects of peptides, research needs to carry out on their safety.

4. Conclusions

Bioactive peptides have been known to be a part human diet for several years. With the appearance of chromatographic methods the number of studies on bioactive peptides from animal and plant sources mounted. As the findings of these studies showed, peptides exert regulatory functions besides their nutritional roles. Bioactive peptide can be used as a basic compound of functional foods, nutraceuticals and dietary supplements. Moreover, they have the capability to be used as constituents of pharmaceuticals. Some of bioactive peptides have already been commercialized and are available in the market in countries like Japan.

However, as they display a higher activity than precursor proteins, bioactive peptides may interact with other compounds (like carbohydrates and lipids) in food context [46]. In addition, they may form allergenic or toxic compounds; therefore, there is a need to develop more research on the safety of the foods containing

bioactive peptides. Moreover, there is need to develop modern techniques to enrich active peptide from food protein and to facilitate the production of these peptides in huge amounts for the market. There are few clinical human studies on the health benefits of bioactive peptides; thus, further study should be conducted to explain the physiological importance of these peptides in human.

In the area of food-derived peptide research, peptides from plant origin may offer a better choice. This can be due to the fact that plants are rich sources of pharmacologically and biologically active compounds, the main activity of which is attributed to the antioxidant activity [65]. Next, aromatic plants and herbs contain electron donors that can terminate radical chain reaction. This can hinder rancidity of food lipids and boost consumer acceptance of food products [67,68]. Third, according to Food and Agriculture Organization (FAO), leaf proteins are regarded as rich sources of high quality protein for human consumption, attributable to their abundance in nature, nutritive value, and being free from animal cholesterol [9]. Finally, products with plant-derived bioactive peptides can meet the needs of vegetarians who avoid consuming animal-derived products due to health and/or religious reasons. From such a viewpoint, hydrolysates or bioactive peptides from plant origins can be considered superior to those from animal origins, which necessitate further investigation.

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