REVIEW ARTICLE

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Bioactive food derived peptides: a review on correlation between structure of bioactive peptides and their functional properties

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Abstract The presence of bioactive peptides has already been reported in many foods such as milk, fermented products, plant and marine proteins. Bioactive peptides are sequences between 2 and 20 amino acids that can inhibit chronic diseases by modulating and improving physiological functions, so these peptides contribute in holding the consumer health. Also, bioactive peptides can affect pro-health or functional properties of food products. Fractionation of the protein hydrolysate revealed a direct relationship between their structure and functional activity. So, this review focuses on different factors effecting on bioactive peptide structures, biological and functional properties such as antihypertensive, antioxidative, hypocholesterolemic, water-holding capacity, foaming capacity, emulsifying properties and solubility. Also, this review looks at the identified bioactive peptides from food protein sources as potential ingredients of health promoting functional foods.

Keywords Bioactive peptides · Food protein hydrolysis · Functional properties · Human health · Peptides structure

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Introduction

In recent years the number of studies on novel functional ingredients with various food sources especially phenolic compounds, bioactive peptides, etc. increased considerably (Bhat et al. 2015; Gu et al. 2015; Irshad et al. 2015; Karami et al. 2015). Particularly, there is more attention on bioactive peptides due to their nutritional capabilities and health effects. Bioactive peptides are inactive within the sequences of their parent protein, but can be released by enzymatic, chemical and microbial hydrolysis (Di Bernardini et al. 2011; Kim and Wijesekara 2010). By far, the most effective and dependable method to produce peptides with the intended functionalities is enzymatic digestion (Kim and Wijesekara 2010). Bioactive peptides usually contain 2–20 amino acid residues per molecule, but in some cases may consist of more than 20 amino acids, and molecular masses of less than 6000 Da (Sarmadi and Ismail 2010). After digestion, bioactive peptides can be absorbed in intestine and enter the blood stream directly, which ensures their bioavailability in vivo and a physiological effect at the target site (Erdmann et al. 2008). Biologically active peptides have a very important contribution in metabolic regulation and modulation. These peptides can be used as functional food ingredients, or nutraceuticals and pharmaceuticals to improve human health and prevent disease. Some of the reported activities include: anti-hypertension, opioid agonists or antagonists, immunomodulatory, antithrombotic, antioxidant, anti-cancer, and antimicrobial activities, in addition to nutrient utilization (Elias et al. 2008). The replacement of synthetic antioxidants with natural antioxidants, synthetic ACE inhibitors with natural ACE inhibitor or synthetic antimicrobial with natural antimicrobial could have beneficial effects in terms of health implications and functionality in

food systems such as increasing the solubility of emulsions containing oil and water.

The functionality of bioactive peptides can be directly affected by various factors such as process conditions, protein sources, sequence and amino acid composition, molecular weight and charge distribution, pH and certain chemical treatments (de Castro and Sato 2015). Thus, this paper provides an overview from structural aspects on various factors governing functional properties of bioactive peptides (Fig. 1).

Correlation between peptides structure and functional properties

Numerous studies have been exhibited that food-derived bioactive peptides based on their structural properties and their amino acid composition and sequences, possess several physiological functions including antioxidant, antimicrobial, angiotensin-I-converting enzyme (ACE) inhibition activities and when added to food, they can cause good functional properties and can contribute to water holding, texture, gelling, whipping and emulsification properties (Liu et al. 2008). Various factors such as the source of proteins, the protein substrate pretreatment, the type of peptidases, and the hydrolysis conditions, could modify the structure and efficacy of protein hydrolysates and types of peptides produced (Ambigaipalan et al. 2015; Xiong et al. 2013) (Fig. 2). It is obvious that the nature of residues in a peptide affect its activity.

Structural factors governing health promoting properties

Relation between peptides structure and the antioxidant activity

It has been shown that hydrolysates exert higher antioxidant activity than purified peptides (Xiong et al. 2013). Many researches have been conducted to evaluate antioxidant properties of bioactive peptides from plant or animal sources (Girgih et al. 2014). The antioxidant or biological activities can be affected by the peptide structure (Saito et al. 2003) that it can affect by the operational conditions applied to isolate proteins, the source of protein, degree of hydrolysis, type of protease (Wang et al. 2010), molecular weight (MW) of peptides (Li et al. 2008), conditions of the hydrolysis process involved (e.g. peptidases, substrate/peptidases ratio, temperature, pH, reaction time etc.) (Shahidi and Zhong 2008). Ambigaipalan et al. (2015) suggested that the type of peptidases used for hydrolysis affects the antioxidant properties; they claimed their efficacy differences are due to endo versus exo-peptidase. It has been shown that the pretreatment of proteins before enzymatic hydrolysis such as heat (HT), hydrostatic pressure (HP), ultrasound (US), microwave (MW) and pulsed electric field (PEF) treatments improved the release of bioactive peptides from various proteins and functionality of peptides (Uluko et al. 2015). Uluko et al. (2015) revealed that pretreatment using ultrasound has the potential to improve antioxidant capacity of aggregated proteins such as milk protein concentrate during enzymatic hydrolysis with digestive enzymes. Particular structural features of the peptides have been asserted to influence antioxidant capacity. For instance, it has been demonstrated that certain amino acids can display higher antioxidative properties when they are incorporated in

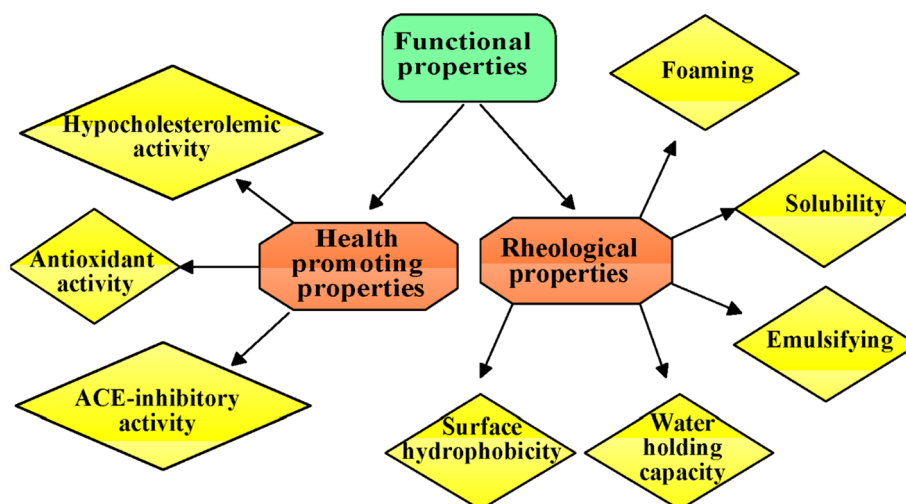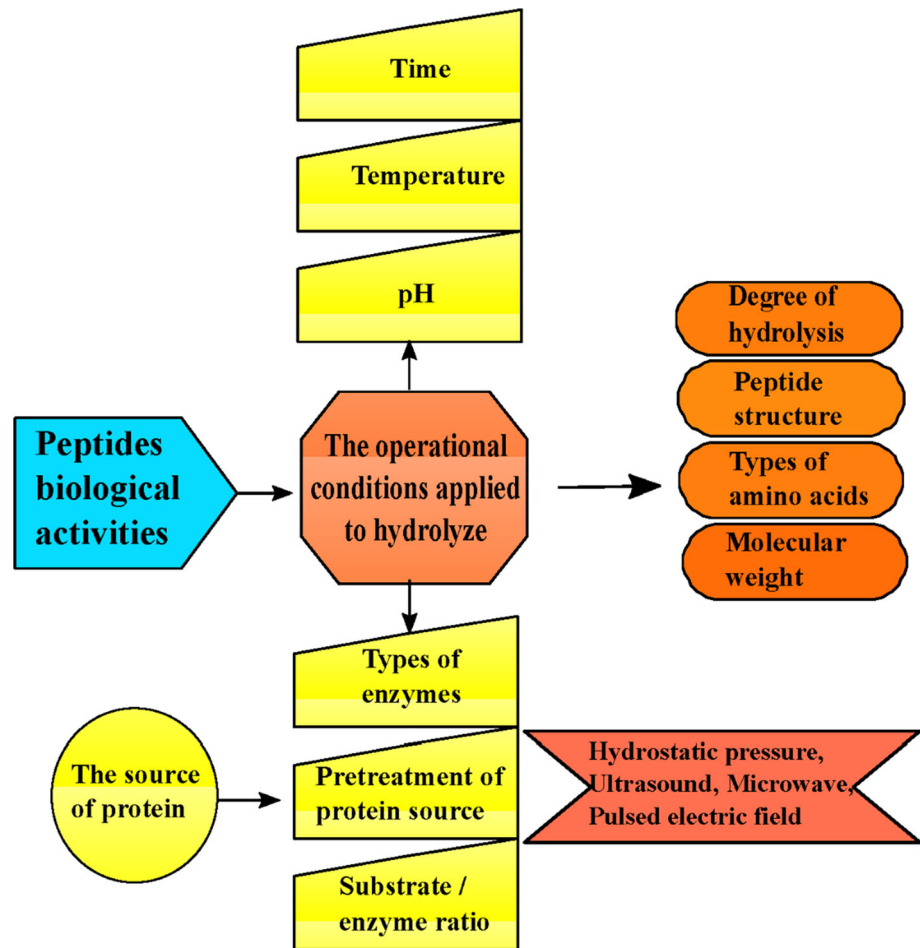Fig. 1 Functional properties of bioactive peptides and hydrolysates

Fig. 2 Key factors influencing the peptides biological activities

dipeptides structure (Nagasawa et al. 2001). In contrast, other findings suggested that its structural conformation can reduce the antioxidant activity of the constituent amino acids. In fact, it is stated that peptide conformation is capable of showing both synergistic and antagonistic effects, as far as the antioxidant activity of free amino acids is concerned (Hernández-Ledesma et al. 2005). Chen et al. (1995) stated that substitution of L-Histidine by D-Histidine in a peptide can reduce the antioxidant activity. They reported that the correct positioning of imidazole group is the key factor influencing the antioxidant activity. It has been reported that the antioxidant activity of corn gluten meal hydrolysates was related to the concentration and molecular weight of hydrolysates. Antioxidant activity of peptides with molecular weight 500–1500 Da was stronger than that of peptides above 1500 Da and peptides below 500 Da (Li et al. 2008). Moreover, other factors can influence antioxidant activity of bioactive peptides; it has been stated that the antioxidant activity of a peptide depends on which amino acids are in the sequence and also on the position that they occupy in the sequence. For example, tri-peptides with tryptophan and tyrosine at their C-terminus showed strong radical-scavenging activity, and different combinations of amino acids in tri-peptide chains also showed different antioxidant activities (Cumby et al. 2008). Saito et al. (2003) have reported that any change in the arrangements of amino acid sequence in tripeptides resulted in different antioxidant activities. Mendis et al. (2005) indicated that hydrophobic amino acids present in the peptides structure affect antioxidant activity of a peptide in inhibiting lipid peroxidation, they reported that hydrophobicity property leads to high interactions between the peptide and the fatty acids, concluding in protection against oxidation. Amino acids of tyrosine, tryptophan, methionine, lysine, cysteine, and histidine can cause antioxidant activity (Mundi and Aluko 2014). Antioxidative activity of Histidine -containing peptides has attributed to the hydrogen-donating, lipid peroxyl radical trapping and/or the metal ion-chelating ability of the imidazole group (Rajapakse et al. 2005). SH group in cysteine due to its direct interaction with radicals has an independently crucial antioxidant action (Qian et al. 2008). Amino acids with aromatic residues improve the radical-scavenging properties of the peptides because they can donate protons to electron deficient radicals (Rajapakse et al. 2005). Mundi and Aluko (2014) showed the higher DPPH

inhibitory activity for < 1 and 5–10 kDa peptide fractions due to higher contents of hydrophobic aliphatic (valine, isoleucine and leucine) and hydrophobic aromatic (phenylanaline and tyrosine) amino acid residues in the two fractions, when compared to the 1–3 and 3–5 kDa fractions.

It has reported that hydrolysates categorized into three main groups based on their degree of hydrolysis (DH) that determine their application: 1. hydrolysates with broad DH (mostly used as nutritional supplements and in special medical diets), 2. hydrolysates with various DHs (generally used as flavorings), 3. hydrolysates with low DH and improved functional features (Vioque et al. 2001).

Type of peptidase, as previously mentioned, affect functional properties of peptides. Cumby et al. (2008) suggested canola sample hydrolyzed by Alcalase had similar degrees of hydrolysis (20.6% and 18.9%, respectively) with that hydrolyzed by a combination of Alcalase and Flavourzyme while the hydrolysate prepared with Flavourzyme alone had the lowest degree of hydrolysis (6.33%). This was unexpected as the combination of Alcalase and Flavourzyme was thought to produce a more extensively hydrolyzed product than using one peptidases alone. They reported Flavourzyme hydrolysates of canola protein with a lower DH exhibited higher antioxidant efficiency than hydrolysates produced using Alcalase. Also, they indicated scavenging capacity increased with increasing concentration. The hydrolysates prepared using Flavourzyme had the highest scavenging activity at all concentrations, while similar values were obtained for hydrolysates prepared using Alcalase or the combination of the two peptidases. Table 1 indicates some antioxidant peptides derived from food sources. Ambigaipalan et al. (2015) indicated that hydrolysis condition employed to produce peptides potentially affect antioxidant activities of date's seed protein hydrolysates. Raikos and Dassios (2014) findings indicated that peptides with sequences of tyrosine–glycine–tyrosine–threonine–glycine–alanine and isoleucine–serine–glutamate–leucine–glycine–tryptophan released from human milk after digestion with pepsin and pancreatin could be exhibited high radical scavenging activity, and this property was related to the occurrence of the amino acid tryptophan which can break radical chain reactions thanks to the donation of the hydrogen attached to the nitrogen of its indole ring.

Chen et al. (1995) reported that the antioxidant properties of the isolated peptides from soy varied depending on their structure and the assay systems used because investigation of the inhibition of linoleic acid peroxidation assay showed peptides containing two tyrosine residues had higher antioxidant activity than the corresponding peptides containing two His residues, and tyrosine–(histidine–leucine–arginine)–tyrosine exhibited the highest activity

(Saito et al. 2003). Also amino acids, such as tryptophan, tyrosine, methionine, lysine, histidine–tyrosine–proline, proline, alanine and cysteine, occurred in the sequence of antioxidant peptides are supposed to be responsible for the reported antioxidant activity (Cumby et al. 2008). The antioxidant activity of the two aromatic amino acids tryptophan and phenylalanine has been related to their capacity to act as radical scavengers, and the antioxidant activity of tyrosine is attributed to the special capability of phenolic groups to act as hydrogen donors (Ren et al. 2008). Six antioxidant peptides from the proteolytic hydrolysis of soybean protein have been detected by Chen et al. (1995). They discovered that the active peptides included 5–16 amino acid residues with hydrophobic valine or leucine amino acids at the N-terminal position and proline, histidine or tyrosine in the sequence. Upon comparing the antioxidant capacity of 28 short-chain peptides structurally attributed to leucine–leucine–proline–histidine–histidine, the tripeptide unit proline–histidine–histidine was found to be an active center responsible for the antioxidant activity of soy protein hydrolysate (Shahidi and Zhong 2010). It was hypothesized that histidine-containing peptides can act as metal chelator, active oxygen quencher and hydroxyl radical scavenger, so it affects the antioxidant activity of the protein hydrolysate (Chen et al. 1995).

Relation between peptides structure and the ACE-inhibitory activity of peptides

Angiotensin I-converting enzyme (ACE) plays a crucial role in the regulation of blood pressure as it promotes the conversion of angiotensin I to the potent vasoconstrictor angiotensin II as well as inactivates the vasodilator bradykinin. ACE-inhibitory substances are used to decrease the blood pressure of hypertensive patients (Rho et al. 2009). By inhibiting these processes, synthetic ACE inhibitors such as captopril, enalapril, alacepril, lisinopril and ramipril have been widely used for the effective clinical treatment of hypertension and heart failure in humans (Boye et al. 2010). These synthetic drugs, however, have several side effects including diarrhea, coughing, allergies, taste disturbances, skin rashes, impaired renal function, and in some cases excessively low blood pressure, i.e. hypotension (Tenenbaum et al. 2000). Therefore, search for natural ACE inhibitors as alternatives to synthetic ones is one of the great interests for safe and economical using them as pharmaceuticals. Although the effectiveness of the ACE-inhibitory activity may not be as high as those of synthetic drugs, many natural ACE-inhibitory peptides isolated from different food proteins could be applied in the prevention of hypertension and in the initial treatment of mildly hypertensive individuals (Li et al. 2008).

Table 1 Food derived bioactive peptides with antioxidant activity

Protein	Process	Bioactive peptide	References
Royal jelly protein	Protease N	Ala-Leu, Phe-Lys, Phe-Arg, Ile-Arg, Lys-Phe, Lys-Leu, Lys-Tyr, Arg-Tyr, Tyr-Asp,Tyr-Tyr, Leu-Asp-Arg, Lys-Asn-Tyr-Pro	Guo et al. (2009)
Rice	Alcalase	Thr-Gln-Val-Tyr	Li et al. (2007)
Palmaria palmata protein	Corolase PP	Ser-Asp-Ile-Thr-Arg-Pro-Gly-Gly-Asn-Met	Harnedy et al. (2017)
Wheat germ	Bacillus licheniformis alkaline protease	Ile-Val-Tyr	Matsui et al. (1999)
Soy (β-conglycinin)	protease	Leu-Leu-Pro-His-His	Chen et al. (1995)
Egg (egg white)	Pepsin-	Tyr-Ala-Glu-Glu-Arg-Tyr-Pro-Ile-Leu	Davalos et al. (2004)
Corn gluten meal	Alkaline protease and Flavourzyme	Leu-Pro-Phe, Leu-Leu-Pro-Phe, Phe-Leu-Pro-Phe	Zhuang et al. (2013)
Hemp seed protein	Pepsin	Trp-Val-Tyr-Tyr, Pro-Ser-Leu-Pro-Ala	Girgih et al. (2014)
Sweet potato protein green tender	Alcalase	Tyr-Tyr-Ile-Val-Ser	Zhang et al. (2014)
Sorghum	Alcalase	Leu-Asp-Ser-Cys-Lys-Asp-Tyr-Val-Met-Glu	Agrawal et al. (2017)
Sea squirt (*Halocynthia roretzi*) protein	Pepsin	Leu-Glu-Trp, Met-Thr-Thr-Leu, and Tyr-Tyr-Pro-Tyr-Gln-Leu	Kim et al. (2018)
Wheat germ protein	Alcalase	Gly-Asn-Pro-Ile-Pro-Arg-Glu-Pro-Gly-Gln-Val-Pro-Ala-Tyr	Karami et al. (2018)

Cheung et al. (1980) indicated that the ACE inhibitor activity by peptides depended on the affinity of N- or C-terminal amino acid residues for the ACE active site. From this point of view, Matsui et al. (1999) have separated 12 ACE inhibitor peptides from sardine muscle hydrolysate, and displayed that the di-peptide, valine- tyrosine with the IC_{50} value of 5.2 mM, acted as a key ACE inhibitor. It has been reported that most of the ACE inhibitor peptides are short structure peptides with only two to nine amino acids. It is known that di- or tri peptides, especially those with C-terminal proline or hydroxyl proline residues, are generally resistant to degradation by digestive enzymes (Vermeirssen et al. 2004). Moreover, short peptides consisting of two or three amino acids are absorbed more rapidly than free amino acids (Erdmann et al. 2008). Also, findings in spontaneously hypertensive rats (SHR) showed that di-peptides with a C-terminal tyrosine residue caused a slow and prolonged decrease in systolic blood pressure compared to di-peptides with phenylalanine at the C-terminal. In contrast, di-peptides with C-terminal phenylalanine produced a more rapid reduction and a shorter duration of action (Erdmann et al. 2008).

Mundi and Aluko (2014) suggested that peptide fractions with molecular masses less than 1 kDa and 5–10 kDa have higher renin-inhibitory activities that it may be attributed to the increased levels of hydrophobic (valine, Isoleucine and leucine) and aromatic (phenylalanine and tryptophan) amino acids when compared to the 1–3 and 3–5 kDa peptide fractions. It is also well known that smaller size peptides may be more bioactive because of the higher probability for increased rate of intestinal absorption and entry into cells when compared with the bigger size peptides. Udenigwe et al. (2012) stated that nature and position of the amino acid play a major role in enhancing renin inhibition rather than size of peptides. Mundi and Aluko (2014) also reported the peptide fractions of Kidney Bean Protein Hydrolysate (KBH) have higher ACE-inhibitory activity than mung bean hydrolysate prepared with Neutrase. They concluded that the differences in these findings may be attributed by differences in the peptidase type, the concentration of the sample used, as well as the peptidase-to-substrate ratio, all of which could affect the type of peptides produced. Moreover, Matsui and Tanaka (2010) reported that peptides with antioxidant and ACE-inhibitory activities are usually rich in hydrophobic amino

acids, which enhance absorption and interaction with target enzymes or free radicals. Milk derived bioactive peptides play important roles in human health and nutrition (Sánchez and Vázquez 2017). Some of these peptides have several functional properties, for instance peptides from the sequence 60–70 of β-casein exhibit ACE-inhibitory activities. This sequence is maintained from proteolysis due to its high hydrophobicity and the presence of proline residues (Sharma et al. 2011). Muguerza et al. (2006) have isolated ACE inhibitory peptides (e.g., valine–arginine–tyrosine–leucine) from the enzymatic hydrolysis of milk proteins. Recently three new ACE inhibitory peptides with IC_{50} values ranging from 316 to 354 μmol/L have been determined from goat milk hydrolysate and also exhibited antihypertensive effect in spontaneously hypertensive rats (Erdmann et al. 2008).

Raikos and Dassios (2014) revealed a potent ACE inhibitor in human milk and corresponded to the β-casein fragment f (125–129) with the sequence histidine–leucine–proline–leucine–proline. In this case, it was supposed that the presence of the amino acid proline at the C-terminal end could be crucial in terms of the activity observed (Raikos and Dassios 2014). Table 2 indicates some antihypertensive peptides derived from food sources.

Relation between peptides structure and the hypocholesterolemic activity of peptides

Various studies have shown that several dietary proteins can improve blood lipid profile. To date, hypocholesterolemic properties have been reported for, soy (Hori et al. 2001), whey (Nagaoka et al. 1992) and fish protein (Wergedahl et al. 2004), capable of changing the plasma profile from atherogenic to cardioprotective. In contrast, bovine casein tends to cause species-dependent

hypercholesterolemia and atheromatous plaques in animal studies (Van Der Meer et al. 1988). The exact mechanisms responsible for the hypocholesterolemic effects are not clear, but evidence indicates that the specific amino acid composition in dietary proteins and peptides structure influences the effect of the protein source on plasma cholesterol levels. It has been reported that dietary proteins with low ratios of methionine–glycine and lysine–arginine, such as soy and fish protein, favor a hypocholesterolemic effect. In contrast, bovine casein tends to raise cholesterol levels probably because of its high ratios of methionine–glycine and lysine–arginine (Erdmann et al. 2008).

It has been reported that soy protein hypocholesterolemic effects has received the most attention recently (Erdmann et al. 2008). Several researches suggested a range of possible mechanism of action in soy protein's ability to reduce total plasma cholesterol including induction of LDL receptor expression, enhance of bile acid synthesis and excretion as well as decline in steroid absorption from the intestine. Moreover, changes in the endocrine status such as alteration in the insulin–glucagon ratio and in thyroid hormone concentrations have also been reported (Erdmann et al. 2008). It has also been suggested that soy protein hydrolysates reduce total cholesterol levels more effectively than intact soy protein (Zhang and Beynen 1993). A peptide derived from soy glycinin, leucine–proline–tyrosine–proline–arginine, was discovered to produce serum cholesterol-lowering effects (Yoshikawa et al. 2000). Peptide leucine–proline–tyrosine–proline–arginine is structurally homologous to enterostatin (valine–proline–aspartate–proline–arginine), an endogenous peptide showing hypocholesterolemic and anorectic effects (Takenaka et al. 2003). Peptides isoleucine–alanine–valine–proline–glycine–glutamate–valine–alanine is another glycinin-derived peptide with cholesterol-lowering activity (Pak

Table 2 Food derived bioactive peptides with anti-hypertensive activity

Protein	Process	Bioactive peptide	References
Wheat (gliadin)	Acid protease	Leu-Ala-Pro	Motoi and Kodama (2003)
Fermented soybean	Enzymatic hydrolysis	Leu-Val-Gln-Gly-Ser	Rho et al. (2009)
α_{S1}-Casein	pepsin	Arg-Tyr-Leu-Gly-Tyr and Ala-Tyr-Phe-Tyr-Pro-Glu-Leu	Hernández-Ledesma et al. (2013)
Whey	Trypsin	Tyr-Leu in N terminus	Sharma et al. (2011)
Wakame	Pepsin	Tyr-Asn-Lys-Leu	Suetsuna and Nakano (2000)
Hemp seed protein	Pepsin	Trp-Val-Tyr-Tyr and Pro-Ser-Leu-Pro-Ala	Girgih et al. (2014)
Rapeseed protein	Alcalase	Leu-Tyr and Arg-Ala-Leu-Pro	He et al. (2013)
Peach seed protein	Thermolysin	Leu-Tyr-Ser-Pro-His, Leu-Tyr-Thr-Pro-His and His-Leu-Leu-Pro	Vásquez-Villanueva et al. (2015)
Walnut protein	Pepsin	Tyr-Glu-Pro	Gu et al. (2015)

et al. 2005). It has been reported that both peptides leucine–proline–tyrosine–arginine–proline and isoleucine–alanine–valine–proline–glycine–lutamate–valine–alanine inhibited 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMGR) which is a known key enzyme in cholesterol biosynthesis. Investigations on the structure–activity relationship indicated that the hydrophobic region of both peptides is a required structural element for their biological activity. The maximum length of the hydrophobic sequence was stated to be four amino acids. In addition, the proline residue seems to be a key component and can be located at both the C-terminus and in any other position of the amino acid sequence except the N-terminus (Pak et al. 2005). Table 3 indicates some hypocholesterolemic peptides derived from food sources.

Structural factors governing rheological properties

Structural factors affecting on the solubility of peptides

The degradation of proteins to peptides and smaller structures leads to more soluble products (Gbogouri et al. 2004). It has also been reported that hydrolysates have an excellent solubility at high degrees of hydrolysis (Shahidi et al. 1995). The balance of hydrophilic and hydrophobic forces occurred in peptides structure is another crucial influence on solubility increments (Gbogouri et al. 2004). It was said that in addition to polar and ionizable groups of protein hydrolysates, enzymatic hydrolysis affects the molecular size and hydrophobicity and so, these factors switch peptides structure and thereby they leads to change in solubility of peptides (Klompong et al. 2007). The smaller peptides from myofibrillar proteins are expected to have proportionally more polar residues, with the ability to form hydrogen bonds with water and augment solubility (Gbogouri et al. 2004). Concluding, hydrolysates with smaller peptides, i.e. higher DH, were more soluble. The pH affects the charge on the weakly acidic and basic side chain groups

and hydrolysates generally show low solubility at their isoelectric points (Linder et al., 1996). Solubility variations depend on net charge of peptides and surface hydrophobicity in the peptides structure. Solubility increase when pH moves away from pI (Isoelectric point) and surface hydrophobicity promotes the aggregation via hydrophobic interaction (Sorgentini and Wagner 2002).

Structural factors effecting on the emulsifying properties of peptides

The mechanism to generate the emulsion system is attributed to the adsorption of peptides on the surface of freshly formed oil droplets during homogenization and the formation of a protective membrane that inhibits coalescence of the oil droplet (Klompong et al. 2007). Hydrolysates are surface-active materials and promote oil-in-water emulsion because of hydrophilic and hydrophobic groups with their associated charges in their structure (Gbogouri et al. 2004). Klompong et al. (2007) findings regarding protein hydrolysates from yellow stripe trevally (Selaroides leptolepis) meat by Alcalase 2.4L (HA) and Flavourzyme 500L (HF) showed that Emulsifying Activity Index (EAI) and Emulsion Stability Index (ESI) for both HA and HF decreased ($p < 0.05$) with increasing DH. At low DH level (5%), hydrolysates showed strong emulsifying properties. With a limited degree of hydrolysis, the hydrolysates have special emulsifying activity and stability (Kristinsson and Rasco 2000). In the stability of the emulsion, higher contents of peptides with larger molecular weight peptides or more hydrophobic peptides have critical role (Klompong et al. 2007). On the other hand, extreme hydrolysis could cause the loss of emulsifying properties (Gbogouri et al. 2004; Kristinsson and Rasco 2000). The peptides with low molecular weight may not be amphiphilic enough to exhibit proper emulsifying properties (Klompong et al. 2007). Due to their small peptide size, hydrolysates with a higher DH had poorer EAI and ESI. Small peptides show less efficiency in decreasing the interface tension because they cannot unfold and reorient at the interface similar to

Table 3 Some bioactive peptides with hypocholesterolemic activity

Protein	Process	Bioactive peptide	References
β-Lactoglobulin	Trypsin, chymotrypsin	Ile-Ile-Ala-Glu-Lys	Hernández-Ledesma et al. (2013)
β-Lactoglobulin	Trypsin	Ile-Ala-Glu-Lys	Zhong et al. (2007)
Soy	Alcalase	Trp-Gly-Ala-Pro-Ser-Leu, Leu-Pro-Tyr-Pro	Zhong et al. (2007)
Glycinin	Enzymatic hydrolysis	LPYPR, IAVPGEVA	Erdmann et al. (2008)
Brassica carinata protein	Trypsin, chymotrypsin, and carboxypeptidase A	His-Tyr-Val-Ile-Leu-Pro-Met-Lys-Trp(1800–1400 Da)	Pedroche et al. (2007)

large peptides to stabilize emulsions but they migrate rapidly and adsorb at the interface (Gbogouri et al. 2004; Rahali et al. 2000). Apart from peptide size, amphiphilicity of peptides is important for interfacial and emulsifying properties. Rahali et al. (2000) analyzed amino acid sequence at an oil/water interface and concluded that amphiphilic character was more important than peptide length for emulsion properties. The flexibility of protein or peptide structure may also be a vital factor governing the emulsifying properties (Klompong et al. 2007). When considering the effect of pH on EAI and ESI, it depends on peptides solubility. For instance, Klompong et al. (2007) found the lowest EAI and ESI at pH 4, with coincidental decrease in solubility. Since the lowest solubility occurred at pH 4, peptides could not move rapidly to the interface. Moreover, the net charge of peptide might be minimized at pH 4. The higher EAI of hydrolysates accompanied their higher solubility (Mutilangi et al. 1996). Hydrolysates with high solubility can rapidly diffuse and adsorb at the interface. Also, emulsifying properties were influenced by specificity of peptidase. Klompong et al. (2007) suggested at the same DH, hydrolyzed by Flavourzyme (HF) had a better EAI than had hydrolyzed by Alcalase (HA). So, HA showed a higher ESI than did HF. In general, EAI and ESI increased when the pH is moved away from the pH 4. Thus indicating that the sequence and composition of amino acids in peptide between HA and HF might be different, leading to varying charge of the resulting peptides at a particular pH (Klompong et al. 2007).

Structural factors effecting on the foaming properties of peptides

Foam formation is conducted by three factors, including transportation, penetration and reorganization of molecules at the air–water interface. In order to have good foaming, a protein must be capable of migrating rapidly to the air–water interface, unfolding and re-arranging at the interface (Klompong et al. 2007). Foam stability to correlate with the nature of the film and reflects the extent of protein–protein interaction within the matrix (Mutilangi et al. 1996). Authors expressed that flexible protein section by enhancing viscosity of the aqueous phase, protein concentration and film thickness can enhance foam stability (Klompong et al. 2007). Mutilangi et al. (1996) suggested that the foaming capacity of protein was improved by making it more flexible, exposing more hydrophobic residues and increasing capacity to decrease surface tension. For the adsorption at the air–water interface, molecules should contain hydrophobic regions in their structure (Mutilangi et al. 1996).

In general, high molecular weight peptides have direct effect on foam stability of protein hydrolysates (van der

Ven et al. 2002). Hydrophobicity of structurally unfolded proteins has been known in relation to foaming properties (Townsend and Nakai 1983). Excessive hydrolysis may reduce the foaming stability because the more microscopic peptides do not have the strength needed to maintain stable foam (Shahidi et al. 1995). Klompong et al. (2007) stated as DH increased, both hydrolyzed by Alcalase and hydrolyzed by Flavourzyme displayed a lower foaming capacity and foam stability. Shahidi et al. (1995) reported good foaming properties for capelin protein hydrolysates at low DH (12%). Klompong et al. (2007) showed that pH affected the foaming properties of both hydrolyzed by Alcalase and hydrolyzed by Flavourzyme hydrolysates. Foaming capacity was declining at pH 4. The foaming capacity of HA was maximum at pH 6 with a slight decrease at alkaline pH. So, net charge must influence the adsorption of the proteins at the air–water interface. The foaming property was increased when the net charge was enhanced (Sorgentini and Wagner 2002; Townsend and Nakai 1983). The foaming characteristics of proteins reached to minimum at the lowest solubility, so these properties intend to reduce at their isoelectric pH (Klompong et al. 2007). Protein solubility plays an important role to the foaming behavior of protein. The pH of the dispersing medium dramatically influences foaming properties, especially foam stability (Townsend and Nakai 1983). Foam stability depends on the nature of the film and reflects the extent of protein–protein interaction within the matrix (Mutilangi et al. 1996). It has been reported the decreased foam stability at very acidic or alkaline pH may be due to the repulsion of peptides via ionic repulsion. It is known that the size and charge of peptides may be different for hydrolysates produced by different peptidases. Klompong et al. (2007) reported that hydrolysis by Flavourzyme (HF) could form flexible films around the air bubbles because HF most likely contained larger peptides. Kristinsson and Rasco (2000) indicated that fish protein hydrolysates (FPH) can use as emulsifying and emulsion stabilizing ingredients in a variety of products as well as aid in the formation and stabilization of foam-based ones due to the good foaming and emulsifying characteristics.

Structural factors effecting on the water holding capacity property of peptides

Water holding is important factor that influences basic quality characteristics and yield of protein products because it is significant in the determination of mechanical strength, elasticity, plasticity, and flow of food materials and was critical for desirable functions of plant protein materials, such as swelling, wet ability, water holding capacity, gelation and surface properties (Ge et al. 2000). Protein hydrolysates from seal meat were found to improve

Table 4 Studies on structural factors governing rheological properties of peptides and hydrolysates

Peptide or protein hydrolysate	Treatment	Outcome	References
Soy protein peptides	Proteolytic enzymatic (papain) modification of soy protein isolates (SPI), followed by ultrafiltration was used to fractionate of proteins into peptides with controlled molecular size	Soy protein peptides prepared from SPI by papain modification and ultrafiltration had lower molecular weight, higher solubility, and higher emulsifying properties	Wu et al. (1998)
Rice endosperm protein hydrolysates	Controlled enzymatic hydrolysis was used. The optimum degree of hydrolysis (DH) was determined for acid, neutral, and alkaline type proteases	The optimum DH was 6–10% for good emulsifying properties of rice protein, depending on enzyme specificity. High hydrophobic and sulfhydryl disulfide (SH-SS) interactions contributed to protein insolubility even at high DH	Paraman et al. (2007)
Rice bran protein hydrolysate (RBPH)	Rice bran protein (RBP) was hydrolyzed by trypsin and the DH values were set to be 1, 3, and 6%	Emulsions prepared with 3% DH RBP were much more stable than the emulsions prepared with RBPH with other DH values, and this RBP has potential as an emulsifier in the food industry	Zang et al. (2018)
Peanut protein hydrolysate	Peanut protein isolate (PPI) was modified with extrusion pretreatment and papain-induced proteolysis	Extrusion pretreatment conducted at 130 °C enhanced the protease accessibilities of the main constitutive proteins in EPPI (extrudates of PPI), concluding in a remarkable increase in DH and protein solubility for the hydrolysates. Extrusion pretreatment cause to a noticeable enhancement in the emulsification property of hydrolysates	Chen et al. (2018)
Rice glutelin hydrolysate	Rice glutelin was hydrolyzed by trypsin at an optimized enzyme/substrate ratio and the influence of the degree of hydrolysis (DH) on the structure, solubility, rheology, and emulsifying properties of rice glutelin hydrolysate was investigated	Protein hydrolysis changed molecular weight, increased flexibility, altered surface hydrophobicity, and increased solubility. Emulsions prepared with 2% DH rice glutelin were stable over a range of environmental conditions: pH 7–9; NaCl < 100 mM (pH 7); temperatures < 90 °C (pH 7, 0 mM NaCl) studied	Xu et al. (2016)
Soy protein hydrolysate	Soy protein isolate was treated by high-pressure micro-fluidization and pancreatin hydrolysis	Micro fluidization increased the accessibility of some subunits in SPI to pancreatin hydrolysis, resulting in changes in protein solubility (PS), surface hydrophobicity (H_0) for hydrolysates. Emulsion systems formed by control SPI and SPIH (SPI hydrolysates) were unstable because of fast coalescence and bridging flocculation during homogenization, while that formed by MSPIH (micro fluidization pretreated SPIH) with 5.8% DH was more stable and indicated smaller mean droplet size. Compared with SPIH, MSPIH showed a stronger increase in PS and a more moderate change in H_0 during pancreatin hydrolysis, indicating the production of more surface-active soluble peptides, which may explain their markedly improved emulsifying capabilities	Chen et al. (2016)
Acylated rapeseed (*Brassica napus* L.) peptides	A peptide fraction having an average size of 5.6 amino acids has been purified from a rapeseed hydrolyzate, acylated using C_{10}–C_{14} acyl chlorides	Emulsions produced from acylated peptides were more stable to phase separation than those prepared from SDS. The C_{14} acylated peptides were more effective for generating emulsions than the C_{10} and C_{12} derivatives, especially concerning the stability of emulsions against coalescence and phase separation, which was better than SDS and close to BSA	Sánchez-Vioque et al. (2004)

water-holding capacity in meat products (Cumby et al. 2008).

The water holding capacity property is affected by the concentration, pH and by the peptidases employed during the hydrolysis process influencing on peptides structure (Ge et al. 2000). Also, composition of the peptides in each of the fractions may also play an important role. Cumby et al. (2008) reported that Flavourzyme hydrolysate was

most effective in decreasing the drip volume, followed by hydrolysates prepared by combination of Alcalase and Flavourzyme and least effective was the one prepared by Alcalase alone. It is clear that lower-molecular-weight peptides are more effective in holding water than larger-size peptides because smaller fragments of peptides would be more hydrophilic. Also, it has been reported that Flavourzyme has a good tendency to produce low-molecular-weight peptide fragments. Moreover, studies have shown that hydrolysate would cause a better water-holding capacity if hydrolysis via enzyme preserved most of the hydrophilic amino acid residues (Cumby et al. 2008). Also, they stated that canola protein hydrolysates improved water-holding capacity of meat products and also, they indicated hydrolysates prepared using Flavourzyme were superior in terms of their water-holding capacity.

Structural factors effecting on the surface hydrophobicity property of peptides

Since the hydrophobic interactions are the driving forces for manifestation of the physiological functions of peptides, information on the hydrophobic character of bioactive peptides could contribute to further understanding of their mechanism of action. The surface hydrophobic site is partly responsible for formation and maintenance of the spatial structures as well as protein interactions, including binding to cell membranes, protein–protein recognition, and formation of complexes with biologically active compounds (Voronov et al. 2002). When protein is hydrolyzed, protein globular structure may cause alter in as the hydrophobic regions hidden within the native protein are exposed (Mundi and Aluko 2014).

Mundi and Aluko (2014), observed a decrease in the surface hydrophobicity of smaller Kidney Bean Protein Hydrolysate (KBH) prepared by Alcalase hydrolysis compared to the larger peptides. This is probably because there are more oligopeptides available as the size of the membranes increased with larger surface containing the exposed hydrophobic residues. On a similar note Molina Ortiz and Wagner (2002) also reported that smaller chain peptides had less surface hydrophobicity. In contrast, Wang et al. (2007) indicated that permeate with a molecular weight cut-off of 5 kDa had higher surface hydrophobicity than the hydrolysate. Table 4 indicates some recently studies on structural factors governing rheological properties of peptides and hydrolysates.

Conclusion

In this review, we revealed that some types of food proteins-derived bioactive peptides are a potential modulator in the body. Bioactive peptides with various structures show functional activities such as: antioxidant activity, ACE inhibitor activity, hypocholesterolemic activity and also, they were found to improve water-holding capacity, foaming capacity, emulsifying properties and solubility in products. This review stated that biological and functionality aspects of protein hydrolysates were mainly influenced by peptide structure and its amino acid sequence. Thereby, in order to maximize the functionality and biological activities of the protein hydrolysates, the determination of variables that exerts significant impact on hydrolysis processes is necessary. Also, further researches are needed on the safety and quality of the foods containing bioactive peptides and to develop modern techniques to enrich active peptide from food protein and to facilitate the production of these peptides in huge quantities for the market and to stabilize of chemical structures and biological activity of peptides in different food matrices new technique are needed. It is possible that encapsulation improve stability of peptides in various food products and also during their digestion.

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