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Poultry Waste: From Waste to Wealth

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Waste from poultry industry has been accounted as the predominant biomass material waste all around the world. Poultry waste product usually comes from feet, bones, residual meat, blood, feather and internal organs. The increment in poultry export due to demand of poultry production from several countries has contributed to the addition of poultry by-product. The by-product from poultry processing plant can be turned into something that has some added values such as gelatin hydrolysate and protein hydrolysate. Partial hydrolysis of collagen which is the major protein in cartilages, skins and bones can produce a soluble protein compound known as gelatin. It has numerous usages in food and pharmaceutical industries for example as gelling binder, stabilizing substances and production of capsules. Besides that, gelatin derived from different sources other than bovine and porcine, for example poultry and fish has getting more attention nowadays due to several issues. Gelatin hydrolysate a bioactive peptide that can involve in various functions of the organism physiologically for example antihypertensive, antioxidant and anticancer effects. This bioactive peptide can be produced by using enzymatic digestion process on gelatin. This review presents about the potential utilization of gelatin and gelatin hydrolysate by using enzymatic proteolysis from poultry especially poultry by-product and poultry feet specifically as an alternative to the available sources that already exist in the industry.

Keywords: poultry, gelatin, gelatin hydrolysates, bioactive peptides

Poultry industry

The exports of beef, pork, lamb, poultry and eggs in United States are equal to 10.1 billion pounds with total value of 9.8 million dollar in September 2018. Broiler has appeared as the highest percent of total export within the amount. Besides that, the amount or broiler export in 2018 has increased by five percent compared to 2017, from 265.6 million pounds on 2017 to 584.6 million pounds on 2018 (USDA, 2018). United States is the world's biggest poultry producer and 18 percent of its poultry production is exported. USDA predicted that in 10 years, the demand for poultry will increase with 34 percent of the global poultry exports come from United States (Olaoye, 2018). The demand for the poultry production is likely to come from the United States, Brazil, the EU, the Russian Federation, India, Thailand and Mexico (FOA, 2017). Besides that, China's economy has undergone an expanding change of livestock farming where the end number of poultry stocks and hogs at the end of 2013 has reached 5.71 and 0.47 billion respectively with 11.9 and 0.72 billion poultry and hog were slaughtered. China has been as the ranked first meat producer in the world for 20 years (Li et al., 2016).

Poultry by-product

The steady expanding of poultry industry has caused a higher waste generated from the processing plants and manufacturing. The by-products from the processing plant consist of the large amount of waste such as dead on arrival, feathers, bones and viscera (Brandelli et al., 2015). Improper management of these waste disposal can contribute to loss of valuable biological resources like enzymes, lipids and protein, environmental problem and diseases (Lasekan et al., 2012). There are lots of usage of poultry by-products such as calcium, collagen and gelatin sources, fertilizer, source of energy, lining components for soil and source of energy. Furthermore, poultry by-products can be transformed into poultry by-product meal, feather meal and hydrolysed feather meal (Mishra et al., 2015). Huge amount of solid by-products come from chicken processing plant for example viscera, legs, heads, feather and bone. These materials can be changed to many functional molecules for example chicken bone can be processed into collagen hydrolysate, meanwhile head, feet and blood can be turned into protein hydrolyste, enzyme and lipid while keratin hydrolysate can be produced from chicken feather (Lasekan et al., 2012).

Feathers from poultry industry has become a serious problem for the environment since the keratins are very difficult to decompose by common protein. The keratin from the feather can be degraded by Microsporum fulvum IBRL SD3 to produce protein that has future utilization for production of animal food and consists of vital amino acid (Darah et al., 2013). Besides that, chicken feather fibre has been formulated as thermoplastics with another material such as different plasticizers in collaboration of production of eco-friendly product from poultry waste (Ullah and Wu, 2013). Raw chicken and lamb bone can be used to remove fluoride from aqueous solution efficiently (Ismail and AbdelKareem, 2015).

Poultry waste as a source of gelatin

Meat industry has produced wastes from animal such as structural proteins like elastin, keratin and collagen, which are the dominant parts of hard tissues, bones and organs that are insoluble and hard to degrade. Since these by-products have abundant resources of protein, it can be extracted and hydrolyzed before being processed into functional constituents (Brandelli et al., 2015). Skin, tendons, cartilage and bones are the main sources of collagen (Schmidt et al., 2016). In multicellular organism, collagen is found in various forms in tissue. Due to its wide range of industrial applications, collagen has been considered as one of the most useful biomaterial (Lafarga and Hayes, 2014).

Kaewdang et al., (2014) and Wang et al., (2014) has described the process of extracting collagen from various animals for example birds and fish but it is usually derived from slaughter by-product (Schmidt et al., 2016). Collagen extraction from fish has been done in several species for example Japanese sturgeon (*Acipenser schrenckii*) (Liang et al., 2014), bladder of yellow fin Tuna (*Thunnus albacares*) (Kaewdang et al. 2014) and skin of clown featherback (*Chitala ornata*) (Kittiphattanabawon et al., 2015) but marine collagen has some limitation in applications because they have low denaturation temperature (Subhan et al., 2015). Besides that, the limitation of fish gelatin in food and pharmaceutical industries is its strong odor (Chakka et al., 2016). Several studies have also been performed on poultry by-products such as chicken feet (Hashim et al., 2014), duck feet (Kuan et al., 2016), and chicken skin (Munasinghe et al., 2015).

Collagen from bones, connective tissue and skins of animals including poultry and fish can be treated with enzyme, alkali and acid in order to produce gelatin (GMIA, 2013). The extraction method for collagen that was frequently used are based on the solubility of collagen in acidic solutions with added enzymes, acidic solutions and neutral saline solutions (Schmidt et al. 2016). Partial hydrolysis of collagen can produce gelatin that is a soluble protein compound (Kuan et al. 2016). Hydrolysis collagen with acid will produce type A gelatin that has isoelectric point that ranged from pH 7 to pH 9, meanwhile type B gelatin has an isoelectric point that ranges from pH 4.6 to pH 5.2 due to alkaline processing (GMIA, 2013). Lee et al., (2012) stated that gelatin contains 20 types of amino acid that important for human. The most popular production sources of gelatin mainly come from cattle bones (23.1%), bovine hide (29.4%) and porcine skin (46%), and it contains three peptides that are predominantly composed of proline, glycine, and hydroxyproline (Kuan et al., 2016). Besides that, the usage of gelatin derived from bones and skin of fish and poultry in the food industry can reduce the possibility of Bovine Spongiform Encephalopathy Infection (Hanani et al., 2014).

Poultry feet has a numerous amount of protein and mineral which located on skin, muscle, bone and collagen (Putra and Basori, 2014). Almeida and Lannes (2013) stated that 2.7% of chicken feet is fat while 85% of chicken feet is made of protein which is mainly collagen. Chicken feet produces double collagen composition compare to commercial gelatin and the analysis result between chicken feet gelatin and meat gelatin are not significantly different (Almeida and Lannes, 2013). Meanwhile, duck feet which has complex parts of bones and tendons has been a popular choice for collagen and gelatin resources (Kim et al., 2016). Table 1 compares the composition of amino acid residues between four different sources of gelatin such as duck (Abedinia et al., 2017), chicken (Rafieian and Keramat, 2015), quail (Yousefi et al., 2016) and bovine (Kuan et al., 2016). The main amino acid that was detected in all sources are proline followed by glycine and hydroxyproline. Duck feet gelatin has the highest value proline and hydroxyproline content while chicken deboner residue gelatin has the highest value of proline. Meanwhile, there is only a low level of tyrosine and histidine in this four different type of sources. Bovine gelatin has the lowest value of tyrosine followed by duck feet gelatin and quail feet collagen. On the other hand, chicken deboner residue gelatin has no trace of histidine and bovine gelatin has the lowest value of this amino acid compared to other two different source.

Poultry waste as a source of gelatin hydrolysate

Hydrolysates are made of 2-20 amino acids and it is obtained by hydrolysis which is the process of decomposing protein into smaller peptide chain. This process is vital for producing amino acid sources for physiological functions in the human body (Halim et al., 2016). Peptides has potentially enhanced bioactivity and it can be produced by an established method named enzymatic hydrolysis (Karamac et al., 2014). Hydrolysates from enzymatic production has a significant capability as a functional ingredients in food products (Nasri et al., 2013; Elavarasan et al., 2014).

Time, pH value, temperature and enzyme concentration are the essential factor that influence the properties of hydrolysate during hydrolysis (Dos Santos et al., 2011; Srichanun et al.,2014).

Table 1: Amino acid composition of duck feet gelatin, chicken deboner residue gelatin, quail feet collagen and bovine gelatin

Amino acid (residues/1000 residues)	Duck Feet Gelatin	Chicken Deboner Residue Gelatin	Quail Feet Collagen	Bovine Gelatin
Reference	Abedinia et al. 2017	Rafieian and Keramat, 2015	Yousefi et al. 2016	Kuan et al. 2016
Alanine	81.28	74.5	92	7.28
Arginine	56.73	65.8	90	8.88
Aspargine		42.8	-	-
Aspartic acid	27.29	-	48	3.75
Cysteine	-	-	-	0.47
Glutamine	-	97.1	-	-
Glutamic acid	55.37	-	95	7.51
Glycine	298.11	29.5	194	38.45
Histidine	7.08	-	9	1.16
Hydroxyproline	107.08	74.7	112	11.28
Isoleucine	11.41	9.9	16	1.66
Leucine	25.10	24.7	36	3.14
Lysine	17.56	32.1	27	3.31
Methionine	14.79	7.5	13	1.69
Phenylalanine	18.41	36.2	28	2.47
Proline	106.83	115.1	135	13.74
Serine	37.57	17.5	28	3.79
Threonine	23.72	13.5	24	2.37
Tyrosine	4.65	7.3	5	0.39
Valine	20.28	21.2	24	2.55

Betty et al., (2014) stated that hydrolysis generated two-end carbonyl and amino groups in order to convert hydrophobic groups. Hydrolysis of animal by-products can produce bioactive peptide that can cause physiological effects such as dipeptidyl peptidase-IV (DPP-IV) inhibitory, angiotensin-I converting enzyme (ACE), and antioxidant activities (Brandelli et al., 2015).

Bioactive peptides is the fragments of amino acid sequence that usually made of 2-20 amino acid residues and exhibit antimicrobial, antioxidant, antihypertensive and immunomodulatory activities (Lopez et al., 2014) (Bah et al., 2016). They usually consist of approximately small number of amino acid, a high concentration of hydrophobic amino acid residues and the appearance of Arginine, Lysine and Proline residues (Li-Chan, 2015). Furthermore, the activities of bioactive peptides are based on the composition of amino acid and its sequence with 3 to 40 amino acid residues. Three-enzyme system is the suitable method to use for sequential enzymatic digestion, in order to obtain functionally active peptides. There are some potential that can assist in human health promotion such as nutraceutical potentials within bioactive peptide in gelatin hydrolysate (Ngo et al., 2012).

As the duck meat utilization increase, the duck by –products such as feet, head, bones, viscera and skin also increase (Lee et al., 2012). Evolving of new industrial science in the duck processing by-products for searching of novel bioactive compounds will turn waste into something beneficial for example opportunities and challenges for the domestic farm. Hence, it has been found that extraction is the first step to isolate natural bioactive compounds from duck processing by-products (Zou et al., 2017). Animal wastes have been used widely in the protein hydrolysates production in food ingredients because it is convenient to extract (Lasekan et al., 2012). About 10-13% of collagen and gelatin which have been described as protein that contain biologically active peptides on their sequence can be found in bones (Aleman et al. 2013). The study of enzymatic hydrolysis on poultry by-product has been done on chicken skin by using Alcalase and combination of Pepsin and Pancreatin (Onuh et al., 2014) and chicken paw (Mokrejs et al. 2017) by using Protamex. Meanwhile, Abedinia et al., (2017) have done extraction on duck feet by using three different treatments such as sodium hydroxide for alkaline treatment, acetic acid for acidic treatment and Pepsin for enzymatic treatment. Lee et al., (2012) have used nine proteases that were Alcalase, Collaganase, Flavourzyme, Neutrase, Protamex, papain, pepsin, trypsin and α-chymotrypin in order to obtain gelatin hydrolysate from duck skin by-products.

Antihypertensive activities of gelatin hydrolysate

Hypertension is one of the dominant factors of chronic diseases worldwide. It is also known as a risk component for cardiovascular diseases (CVDs) in developed and developing countries (Ghanbari et al., 2015). Besides that, hypertension has been the high-priority public health challenge that needs critical view with prevention, detention, treatment and control (Bhatt et al., 2014). Hypertension happens when angiotensin-I is produced from angiotensinogen by renin. After that, angiotensin-I will be cleaved to angiotensin-II, which is a potent vasoconstrictor by angiotensin I-converting enzyme (ACE) (Nasri et al., 2013). ACE then acts on the vasodilator kallidin and bradykinin in order to prevent vasodilatory effect. The bioactive peptides activity of inhibition of ACE-I is a beneficial therapeutic approach in pharmalogical treatment of hypertension and important in sustaining normal blood pressure (Lafarga and Hayes, 2014) (Nasri et al., 2013).

The ACE inhibitory peptide is usually made up of small fragments that are composed of 2 to 12 amino acids (Tavano. 2013). Tripeptide residues hold a crucial act as a competitive binding at the ACE active site. Besides that, the hydrophobic, or positively charged, amino acids at C-terminal are usually spotted in the most effective ACE inhibitory peptide (Choonpicharn et al., 2014). ACE inhibitors that are derived naturally from food may not be as powerful as the synthetic drugs, nevertheless they carry no side effects or mild effects compare to the synthetic drugs that have been acknowledge to cause dizziness, dysgeusia, headache, angioedema and cough (Norris and Fitzgerald, 2013; Bah et al., 2013) (Daliri et al., 2016). Anti-hypertensive peptides stop the formation of angiotensin-II by reducing the fluid volume and relaxing the arterial wall hence improving heart function and boosting the rate of oxygen flow to the liver, kidney and heart (Ngo et al., 2012). Aluko (2015) stated that some peptides are managed to regulate the renin-angiotensin system (RAS) as it slow down the activities angiotensin-converting enzymes (ACE) or renin. Besides that, the peptide can also intensify the endothelial nitric oxide synthase (Enos) pathway to surge (NO) levels inside vascular walls and promote vasodilation.

Table 2 shows some studies of the gelatin hydrolysate from poultry sources that have the antihypertensive activity from chicken breast (Sangsawad et al., 2017), chicken skin (Onuh et al., 2015) and chicken collagen (Soladoye et al. 2015). Chicken collagen hydrolysed with Flavourzyme and Neutrase shows a higher IC_{50} value compare to chicken breast hydrolysed with in vitro gastrointestinal digestion. The range IC_{50} value of chicken breast is between 0.37 µM to 11.98 µM while the IC_{50} value of chicken collagen hydrolysed with Flavourzyme and Neutrase is 47.2 µg/ml and 59.7 µg/ml respectively. Chicken skin hydrolysed with Alcalase or combination of Pepsin/Pancreatin shows positive activity in both *in vitro and in vivo* studies.

Antioxidative activities of gelatin hydrolysate

Every biological process that produces energy in living organism will experience production of reactive oxygen species (ROS) and free radicals. Free radicals can cause oxidative damage that will lead to aging and diseases such as atherosclerosis, diabetes, cancer and cirrhosis (Abeyrathne et al., 2018).

Antioxidants are crucial to retard oxidation-induced deterioration in food system and also play an important role in human health by protecting the body from diverse effect causes by excessive free radicals (Wang et al., 2015). Antioxidants manage rancidity development, delay the production of toxic oxidation products, regulate nutritional quality and prolong the shelf-life of products when added to food. Natural antioxidants obtained from edible materials, edible by-products and residual sources have been getting attention due to awareness and limitation of the usage of synthetic antioxidants (Shahidi and Ambigaipalan. 2015).

Antioxidant peptides that come from animal sources have nutritional values and also bioavailability that benefit in human health. Meat by-products and meat muscle are excellent sources for the generation of bioactive peptide by using direct solvent extraction or enzymatic hydrolysis since they have abundant sources of protein (Liu et al., 2016).

DPPH radical scavenging activity and reducing power can be used to detect antioxidant peptides. This is crucial since antioxidant activity may reduce the reactive oxygen species (ROS) and other free radicals in food that may compose oxidative damage to DNA, proteins and lipids (Escudero et al., 2013). Bioactive peptides also exhibited analgesic, antioxidant and anti-inflammatory activity in vitro and in vivo (Chakrabarti et al., 2014). Protein hydrolysate peptides have identical properties to amino acid and proteins except that peptide solubility in aqueous or lipid foods can be manipulated based on the type of enzyme of enzyme used for proteolysis. Furthermore, peptides have a distinguished antioxidant effect compare to amino acid due to its multiple units on a single chain (Aluko, 2015).

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Table 2 : Antihypertensive activities of poultry gelatin hydrolysate

Source	Preparation	Activity *in vitro / in vivo*	Reference
Chicken Breast	Invitro gastrointestinal digestion	IC_{50} value 0.37 µM, 6.35 µM, 11.98µM	Sangsawad et al.,2017
Chicken Skin	Hydrolysis with Alcalase or combination of Pepsin/Pancreatin	IC_{50} 0.36-0.64 mg/ml Decrease blood pressure in SHR (100 mg peptides/kg body weight)	Onuh et al.,2015
Chicken Collagen	Hydrolysis with Flavourzyme and Neutrase	IC_{50} value of Flavourzyme is 47.2 µg/ml and Neutrase is 59.7 µg/ml	Soladoye et al.,2015

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Table 3 shows some studies of the gelatin hydrolysate from poultry sources that exhibit the antioxidant activity. Duck skin, duck meat and chicken skin hydrolysates are tested for their radical scavenging activity while chicken collagen hydrolysate is tested for ORAC-FL assay. Chicken skin hydrolysate are tested for six different type of antioxidant activities whereas duck meat are tested for five different type of antioxidant activities.

Anticancer/anti-proliferative activities of gelatin hydrolysate

A vast amount of deaths all around the world are caused by non-communicable diseases (NCDs) and cancer has been expected as the primary cause of death (WHO 2018) (Bray et al., 2018). In 2018, it had been expected that there were 18.1 million cancer cases reported and 9.6 million deaths causes by cancer. Lung cancer is the most frequent diagnosed cancer and leading cause of death for male meanwhile for female, breast cancer is the real culprit (Bray et al., 2018).

Harris et al., (2013) stated that surgery and chemotherapy which is the most accepted method now have a minor successful percentage and could not suppress the cancer from reappearing. When the chemical agents are designed to attack the cancer that is rapidly growing, it also has the side effect on normal cell (Gaspar et al. 2013).

Anticancer peptides can be trusted as an inventive procedure for the molecurlarly targeted cancer drug discovery and development process. One of the unique mechanism and numerous extraordinary properties of anticancer peptides is, it doesn't impair with normal body physiological function. Thus, the anticancer peptide has become an assuring molecules for anticancer agents (Gaspar et al., 2013; Huang et al., 2015). Pepsin has been recognized as the most capable enzyme in extracting food proteins to produce anticancer peptides. This enzyme only hydrolyzes peptide bond that consist of hydrophobic amino acid especially aromatic acid residues such as tryptophan, phenylalanine, and tyrosine.

The potential mechanism for anticancer peptide is the hydrolysis of the bioactive hydrophobic peptide inside the parent protein that was released during peptide bond split was responsible for suppressing the cancer cell lines, inducing apoptosis and inhibiting cell cycle (Chalamaiah et al., 2018). The activity of anticancer peptide depends on their structural characteristics for example amino acid length, composition, hydrophobicity, sequence and etc. The prime amino acid in anticancer peptides are hydrophobic amino acids for example alanine, proline, leucine, glycine and one or more residues of serine, tryrosine, arginine, glutamic acid, threonine and lysine (Chi et al., 2015; Vital et al., 2014; Wang and Zhang, 2017).

Table 3 : Antioxidant activities of poultry gelatin hydrolysates

Source	Preparation	Activity	Reference
Duck Skin	Solid Phase Peptide Synthesis using ASP48S	Free radical scavenging activity	Lee et al.2013
Duck Meat	Hydrolysis with Protamex	DPPH Scavenging activity Metal Chelating Hydroxyl Radical Scavenging Activity	Wang et al.2015
Chicken Collagen	Hydrolysis with Flavourzyme, Neutrase, Alcalase	ORAC-FL Assay	Soladoye et al.2015
Chicken Skin	Hydrolysis with Alcalase	DPPH Scavenging activity Metal Chelating Hydroxyl Radical Scavenging Activity Reducing Power Assay	Omar and Sarbon, 2016

Table 4: Anticancer/Anti proliferative Activities of Gelatin Hydrolysate

Source	Preparation	Activity	Reference
Ruditapes philippinarum	Hydrolysis with Flavourzyme, Neutrase, Protamex, Alcalase, Papain, Pepsin, α-cymotrypsin, Trypsin	Induced apoptosis on prostate, breast and lung cancer cells	Kim et al.2013
Blood clam	Neutrase	Cytotoxic and changed the morphologies of the PC-3 cells and increased the apoptotic PC-3 cells	Chi et al.2015
Skate cartilage	Alcalase and Trypsin	Exhibited anti-proliferation activity by inducing apoptosis on HeLa cell line	Pan et al.2016
Oyster	Protease from B.cereus SU12	Induced apoptotic changes, cell growth inhibition, and oxidative DNA damage on human colon carcinoma (HT-29) cell lines	Umayaparvathi et al.2014

Hydrophobic amino acids can strengthen the interaction between membrane bilayers of tumor cell and anticancer peptides hence produce particular and stronger cytotoxic activity (Chi et al., 2015; Pan et al., 2016). Besides that, the presence of charged amino acid such as heterocyclic amino acid and glutamic acid, for example proline in the peptide sequence also leads to anticancer properties of peptide (Chi et al., 2015; Kannan et al., 2010).

Kim et al. (2013) stated that anticancer peptides promote cell death using various mechanisms, such as apoptosis, affecting the tubulin-microtubule equilibrium, or inhibiting angiogenesis. As apoptosis normally does not causes inflammatory or immune response, it becomes a better way of cancer cell death during cancer treatments (Kim et al., 2013). Numerous bioactive peptide have exhibit selective cytotoxic activity towards a broad range of cancer cell lines both *in vitro and vivo* (Cicero et al., 2016).

Table 4 shows some studies of the gelatin hydrolysates from various sources that have been proven in exhibiting anticancer or anti-proliferative activities. Ruditapes philippinarum and oyster hydrolysates have the ability to induced apoptosis changes on prostate, breast, lung and colon cancer cells respectively. Blood clam hydrolysates that was hydrolyse with Neutrase has shown the positive activity towards PC-3 cells where it can change the cell morphology and increase the apoptotic of the cell. Pan et al., 2016 study on skate cartilage hydrolysates has shown the exhibition anti- proliferation activity on HeLa cell lines by inducing apoptosis.

CONCLUSION

The most common sources of gelatin come from bovine and porcine. Nevertheless, people keep looking for other alternatives since the Bovine Spongiform Encephalopathy (BSE) outbreak and also, there is also religious prohibited food from bovine and porcine sources. Recently, there has been a lot of study about gelatin extracted from poultry feet for example chicken feet, silky fowl feet and also duck feet. Gelatin extraction process can add the value of by-products animal by turning the waste into something beneficial. Besides that, gelatin hydrolysates exhibit bioactive peptides that can offer the natural remedy for severe health issue such as hypertension and cancer. The amino acid content in the peptide can be used to prevent the oxidation of food which is the major issue of food deterioration. Hence, the study about gelatin hydrolysates from poultry feet can contribute to waste management and production of functional food.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

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AUTHOR CONTRIBUTIONS

FAMZ perform the experiment, analyse the data and wrote the manuscript. NS, NH and AWS supervised, design the experiment and reviewed the manuscript. All authors read and approved the final version.

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