Iranian Journal of Applied Animal Science

A Review on Bioactive Peptides and Their Potential Health Benefits and Applications in Poultry

Review Article

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Received on: 1 Jan 2024
Revised on: 15 May 2024
Accepted on: 8 Jul 2024
Online Published on: Sep 2024

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Online version is available on: www.ijas.ir

ABSTRACT

Bioactive peptides are short chains of amino acids with specific biological activities, sourced from proteins in various natural sources such as food, animal tissues, and microbial cultures. They offer potential health benefits including antioxidant, antihypertensive, antimicrobial, and immunomodulatory activities. Researchers are exploring their potential applications in medicine alternatives to pharmaceutical drugs and antibiotics, as well as in the food industry as substitutes for synthetic additives. Bioactive peptides can be derived from a diverse array of natural sources including milk, eggs, fish, plants, and microbial proteins, making them a promising area of research. In poultry nutrition, bioactive peptides have demonstrated remarkable benefits. They exhibit antimicrobial activity, which contributes to better gut health and reduced risk of infections. Additionally, they can enhance growth performance by improving nutrient absorption and utilization, and may play a role in alleviating stress in poultry, leading to improved overall health and performance. Various studies have highlighted the positive effects of bioactive peptides derived from different sources such as soybean, cottonseed, and canola meal on broiler growth, feed conversion ratio, and health indicators. The potential of bioactive peptides as functional nutrients in poultry nutrition and health management is indeed promising.

KEY WORDS bioactive peptides, growth performance, gut health, immunomodulatory, poultry.

INTRODUCTION

Bioactive peptides are short chains of amino acids, usually comprising 2-20 amino acids that exhibit specific biological activities and have the ability to impact physiological functions in the body. These peptides can be derived from various natural sources such as proteins found in food, animal tissues, or microbial cultures, and they have been studied for their potential health benefits, including antioxidant, antihypertensive, antimicrobial, and immunomodulatory activities. Some commercial bioactive peptide products are used in dietary supplements, functional foods, or pharmaceuticals. Various forms of fermented foods, such as milk and soy, have been consumed for their health benefits since ancient times. These foods contain bioactive peptides, which have a rich history dating back to ancient civilizations. However, the modern understanding of bioactive peptides began to emerge in the mid-20th century as researchers started to isolate and identify specific peptides with biological activities. One of the landmark discoveries in the history of bioactive peptides is the identification of opioid peptides in the 1970s (Hughes, 1975; Goldstein *et al*. 1979; Minamino *et al*. 1980). These peptides, including endorphins and enkephalins, were found to have painrelieving properties and played a crucial role in understanding the body's endogenous opioid system (Pert and Snyder, 1973). Another pivotal moment came with the discovery of angiotensin-converting enzyme (ACE) inhibitory peptides in the 1980s (Crantz *et al.* 1980). These peptides were found to have potential benefits for managing hypertension and cardiovascular health (Meisel, 1997; Hartmann and Meisel, 2007; Hernndez-Ledesma and Hsieh, 2013).

Bioactive peptides have been considered as substitutes for various compounds in the field of medicine, food, and nutrition. They have been studied for their potential to replace traditional drug therapies, synthetic additives in food, and supplements due to their potential health benefits. In medicine, bioactive peptides have been researched as potential substitutes for conventional pharmaceutical drugs due to their perceived lower toxicity and potentially fewer side effects (Bruno *et al.* 2013). Thy have also been investigated for their potential to replace certain antibiotics due to the rise of antibiotic resistance. These peptides can exhibit antibacterial, antifungal, and antiviral activities, making them promising candidates for combating microbial infections (Xuan *et al.* 2023). They can disrupt microbial cell membranes, inhibit microbial growth, and modulate the immune system to enhance host defense (Wang *et al.* 2016). In the food and nutrition industry, bioactive peptides have been considered as substitutes for synthetic additives, such as preservatives and flavor enhancers, due to their natural origin and perceived health-promoting properties (Najafian, 2023).

Proteins derived from sources such as milk, eggs, fish, and soybean have been used to produce bioactive peptides due to their potential health benefits (Akbarian *et al.* 2022). Peptides extracted from marine sources, such as fish collagen or shellfish by-products, have also been studied for their bioactivity (Harnedy and FitzGerald, 2012). By-products from animals, such as skin, bones, and connective tissues, can be used as sources of proteins for bioactive peptide production (López-Pedrouso *et al.* 2023). Certain plant proteins, including those from sources like rice, wheat, and legumes, have been investigated as potential sources of bioactive peptides (Garcés-Rimón *et al.* 2022). Certain microbial proteins derived from sources like bacteria and fungi have also been explored for their potential to yield bioactive peptides (Parvez *et al.* 2024).

Bioactive peptides synthesis

Bioactive peptides can be produced through various methods, including enzymatic hydrolysis of proteins, microbial fermentation, and chemical synthesis.

1. Enzymatic hydrolysis

Proteins from various sources, such as milk, eggs, or plants, can be treated with specific enzymes to break them down into smaller peptide fragments. These enzymatic reactions can be controlled to produce peptides with desired bioactive properties. Here's a comprehensive explanation of how bioactive peptides are produced via enzymatic hydrolysis:

1.1. Enzyme selection: Enzymatic hydrolysis begins with the selection of specific enzymes that can target the protein source to produce bioactive peptides. Enzymes such as proteases, including trypsin, pepsin, and papain, are commonly used due to their ability to cleave peptide bonds within proteins (Adler-Nissen, 1986).

1.2. Protein substrate preparation: The protein source, which could be derived from animal, plant, or marine origins, is prepared by grinding or homogenizing it to increase the surface area for enzymatic action. The protein substrate is then suspended in an appropriate buffer solution to create an optimal environment for enzymatic activity (Toldrá, 2010).

1.3. Enzymatic reaction: The protein substrate is mixed with the selected enzyme in a controlled environment, typically at a specific temperature and pH, to initiate the enzymatic reaction. The enzyme catalyzes the hydrolysis of peptide bonds within the proteins, leading to the release of smaller peptides and amino acids (Hartmann and Meisel, 2007).

1.4. Peptide isolation and purification: Following enzymatic hydrolysis, the mixture is subjected to various separation and purification techniques, such as ultrafiltration, chromatography, or precipitation, to isolate and purify the bioactive peptides from the protein fragments and other components of the reaction mixture (Klompong *et al.* 2007).

1.5. Bioactivity assessment: The isolated peptides are then characterized to evaluate their bioactive properties, such as antioxidant, antihypertensive, antimicrobial, or immunomodulatory activities, using various *in vitro* and *in vivo* assays (Udenigwe and Aluko, 2011).

2. Fermentation

Bioactive peptides can be produced through fermentation, a process that utilizes microorganisms such as bacteria, yeast, or fungi to convert raw materials into bioactive compounds. Certain microorganisms can produce bioactive peptides as a byproduct of their metabolic processes. For example, lactic acid bacteria are known to produce bioactive peptides during fermentation of milk proteins (Rizwan *et al.* 2023). This production method offers several advantages, including cost-effectiveness, scalability, and the potential for targeted synthesis of specific peptides with desired bioactive properties.

During fermentation, microorganisms are cultured in a controlled environment with suitable growth conditions, such as temperature, pH, and nutrient availability. The microorganisms are introduced to a substrate containing precursor proteins or polypeptides, such as whey protein, soy protein, or other plant or animal-derived protein sources. As the microorganisms grow and metabolize the substrate, they enzymatically break down the precursor proteins into smaller peptide fragments. These peptide fragments are then released into the surrounding medium as byproducts of microbial metabolism. Some of these peptides exhibit bioactive properties, such as antioxidant, antihypertensive, antimicrobial, or immunomodulatory activities. The production of bioactive peptides via fermentation is influenced by various factors, including the type of microorganism used, the composition of the substrate, and the fermentation conditions. Optimization of these parameters is crucial for maximizing the yield and bioactivity of the resulting peptides (Daliri *et al.* 2018; Minkiewicz *et al.* 2019).

3. Chemical synthesis

Bioactive peptides can also be chemically synthesized by joining individual amino acids together in a specific sequence using solid-phase peptide synthesis or solution-phase peptide synthesis methods (Jeske *et al.* 2018). Producing bioactive peptides via chemical synthesis involves several steps (Akbarian *et al.* 2022).

3.1. Designing the Peptide Sequence: The first step is to design the amino acid sequence of the bioactive peptide. This is based on the desired biological activity and target molecule, and often involves computer-assisted design to optimize the peptide's properties.

3.2. Solid-Phase Peptide Synthesis (SPPS): The most common method for chemical synthesis of peptides is solid-phase peptide synthesis. In SPPS, the peptide chain is built on a solid support (*e.g.*, resin) attached to a solid-phase synthesis apparatus. Amino acids are sequentially added to the growing peptide chain, starting from the C-terminus to the N-terminus, and protected by various protective groups.

3.3. Chemical Activation and Coupling: Each amino acid is activated for coupling with the next using coupling reagents such as carbodiimides. This forms the peptide bond and extends the peptide chain.

3.4. Deprotection and Cleavage: After the peptide chain is completed, the peptide is cleaved from the solid support and the protective groups are removed to yield the crude peptide.

3.5. Purification and Characterization: Following synthesis, the crude peptide is purified using techniques such as high-performance liquid chromatography (HPLC). The purified peptide is then characterized using analytical techniques such as mass spectrometry and high-resolution chromatography to confirm its identity and purity.

3.6. Modification and Cyclization (if needed): Depending on the specific bioactivity desired, the peptide may undergo further modification or cyclization to enhance its stability, bioavailability, or targeting ability.

Among these methods, enzymatic hydrolysis and microbial fermentation are more prevalent for large-scale production due to their efficiency and ability to produce a wide variety of bioactive peptides with potential health benefits. However, the prevalence of a particular production method may vary depending on the specific peptide being targeted and advances in biotechnology. The cost of bioactive peptide production can vary depending on the specific method used, the scale of production, and other factors. However, generally speaking, microbial fermentation methods are often considered more cost-effective compared to chemical synthesis or extraction from natural sources. Microbial fermentation can be an attractive option for cost-effective bioactive peptide production because it can be carried out using relatively simple equipment and can benefit from the rapid growth of microorganisms to produce a high yield of peptides. Lactobacillales, which are a large group of beneficial bacteria in nature are used to produce bioactive peptides. *Lactococcus lactis*, *Lactobacillus helveticus*, and *Lactobacillus delbrueckii* are now well known for this procedure (Akbarian *et al.* 2022).

Bioactive peptides application in poultry

Bioactive peptides, have been shown to have several beneficial effects on poultry. Bioactive peptides have been found to exhibit antimicrobial activity, which can help in controlling pathogens in the gastrointestinal tract of poultry, thereby promoting gut health and reducing the risk of infections. Some bioactive peptides have demonstrated the ability to enhance growth performance in poultry by improving nutrient absorption, utilization, and metabolism, leading to better feed efficiency and growth rates (Sholikin *et al.* 2021a). These effects highlight the potential of bioactive peptides as functional ingredients in poultry nutrition and health management (Mohammadrezaei *et al.* 2021).

When it comes to broilers, bioactive peptides can have several effects on their performance, including improved growth, feed utilization, and overall health. Bioactive peptides have been shown to promote improved growth in broilers by enhancing nutrient absorption and utilization, stimulating metabolic processes, and supporting muscle development. This ultimately leads to increased body weight and better feed conversion ratios. Abdollahi *et al.* (2017) and Abdollahi *et al.* (2018) found that consistently adding 6 g/kg of soybean bioactive peptide (SBP) to broilers diet improved feed conversion ratio (FCR). In another study, continuous supplementation of 6 g/kg of bioactive peptides from cottonseed (BPC) in broiler diets led to positive effects on growth performance, bursa of Fabricius relative weight, antibodies against sheep red blood cells (SRBC) and newcastle disease virus (NDV) antigens, and total antioxidant activity of serum (Landy *et al*. 2020).

Karimzadeh *et al.* (2017) assessed the impact of canola meal peptides (CMP) on the growth, blood metabolites, and antioxidant activities in broiler chickens. The broiler chickens were given basal diets supplemented with 0, 100, 150, 200, or 250 mg CMP/kg. The study found that as the CMP supplementation in the basal diet increased, there was a linear increase in body weight gain and a quadratic decrease in feed conversion ratio from day 0 to day 42. Additionally, the supplementation of the basal diet with CMP led to a linear increase in serum lysozyme and superoxide dismutase activities and immunoglobulin M concentrations at day 42. Furthermore, serum cholesterol and triglyceride concentrations decreased both linearly and quadratically, while total protein increased linearly and quadratically, and P and Ca increased linearly as dietary CMP supplementation increased from 0 to 250 mg/kg at both day 21 and day 42. These findings suggest that the inclusion of CMP in the diet can enhance the performance, blood metabolites, and antioxidant activities in broiler chickens.

Alahyaribeik *et al.* (2022) examined how adding mixed feather bioactive peptides (MFBPs) to the water affects the intestinal health, meat quality, and plasma cholesterol levels of broiler chickens.

Peptides with a molecular weight of less than 3 kilo Daltons, produced by the hydrolysis of feather by *Bacillus licheniformis*, were isolated .One group received plain water (control), while the other received water containing 50 mg/L of MFBPs. The results showed that birds receiving MFBPs during the final period exhibited greater body weight gain. The birds received bioactive peptides showed higher villus height and muscle layer thickness in different parts of the intestine, but lower epithelial thickness compared to control birds. Additionally, the MFBPs led to a decrease in serum total cholesterol, triglyceride, and low-density lipoprotein in the broilers. Furthermore, supplementing with MFBPs significantly reduced the amount of malondialdehyde (MDA) in the thigh muscle. They proposed that incorporating MFBPs into the diet of broilers could enhance meat quality, lower cholesterol concentration in the serum, and improve gut health.

Bahadori *et al.* (2022) examined how the use of sesame meal bioactive peptides (SMBP) either alone or in conjunction with a blend of savory and thyme essential oils (STEO) impacted the growth, carcass, jejunal morphology, and cecal microbial composition of broiler chickens. The diets included a standard corn-soybean meal, the standard diet with the addition of 0.5 g/kg of Bacitracin as an antibiotic, 3 g/kg of SMBP, 0.5 g/kg of STEO, and a combination of 3 g/kg of SMBP and 0.5 g/kg of STEO. The findings revealed that incorporating SMBP + STEO into the diet improved body weight gain and feed conversion ratio during the 11 to 24-day period. The dietary treatments did not significantly affect the carcass characteristics and internal organs. In terms of jejunal morphology, birds that received the SMBP + STEO diets exhibited greater villus length (VL) and the ratio of VL to crypt depth (CD), while CD was lower in broilers fed with the SMBP + STEO diet. Additionally, including SMBP in combination with STEO increased the viable count of *Lactobacillus*, while the population of *E. coli* decreased in birds fed with the SMBP + STEO diet. Overall, based on the results of this study, it can be concluded that incorporating dietary SMBP in combination with STEO had positive effects on the growth performance, jejunal morphometric indices, and cecal microbial composition of broiler chickens.

The quality of poultry meat often declines due to fat oxidation during storage, but adding fish waste-derived bioactive peptides to the birds' diet can help improve the meat's resistance to oxidation. Aslam *et al.* (2020) investigated how different levels of fish waste derived bioactive peptides in the broiler's diet affected the antioxidant potential of their breast meat and the quality of nuggets made from that meat. They fed broilers with varying concentrations of bioactive peptides (0, 50, 100, 150, 200, and 250 mg/kg feed). The results showed that the dietary supplementation of bioactive peptides significantly improved the antioxidant status and delayed lipid oxidation in the breast meat compared to the control group. Additionally, the quality parameters of the nuggets were also positively influenced by the bioactive peptides and storage duration. Therefore, incorporating bioactive peptides into the broiler birds' diet can enhance the antioxidant properties and shelf stability of both their breast meat and the nuggets made from it.

Sholikin *et al.* (2021a) in a meta-analysis, examined how different levels of antimicrobial peptides (AMPs) affect various aspects of broiler chicken growth, including performance, digestibility, small intestine structure, and blood serum parameters. The results indicated that increasing the level of AMPs had a quadratic effect on body weight (BW), average daily gain (ADG), and feed conversion ratio (FCR). It also linearly reduced mortality during both the starter and finisher periods. Additionally, there was a linear increase in metabolizable energy. Small intestine morphology in the duodenum, specifically villus height and villus height to crypt depth ratio, showed a linear increase, while crypt depth exhibited a linear decrease. Mucosa thickness in the jejunum was quadratically affected, while crypt depth showed a linear decrease. Categorical analysis revealed that AMPs had a similar impact to antibiotics on broiler performance (BW, ADG, FCR), with a comparable improvement observed in the control group. They suggested that the use of AMPs as effective substitutes for antibiotic growth promoters (AGP), as they can enhance broiler growth performance, digestibility, small intestine morphology, and blood serum parameters throughout all rearing periods. Additionally, the study suggests optimal dietary AMP addition doses of 337 and 359 mg/kg for the starter and finisher phases, respectively.

Sholikin *et al.* (2021b) conducted another meta-analysis to evaluate the impact of antimicrobial peptide (AMP) addition on bacteria levels, immune responses, and antioxidant activity in broilers. The study found that in the starter phase, AMP addition reduced bacteria levels in the ileum (coliform and total aerobic bacteria), caecum (*Clostridium* spp., *Escherichia coli*, *Coliform* and lactic acid bacteria), and excreta (*Clostridium* spp.). Additionally, immune response and antioxidant activity were improved. Similar reductions in bacteria levels and improvements in immune response and antioxidant activity were observed in the finisher phase. In summary, AMP addition effectively decreased pathogenic bacteria and enhanced immune responses and antioxidant activity in broilers.

Salavati *et al.* (2020) assessed the impact of bioactive peptides derived from sesame meal (BPSM) in comparison to mannan-oligosaccharides (MOS) as a prebiotic supplement and avilamycin (as an antibiotic). The results showed that weight gain increased in birds that received MOS and 100 mg/kg BPSM on days 1–11 and 1–32, respectively. The dietary treatments did not affect food consumption in broilers. However, FCR improved in broiler chickens fed 100 mg/kg BPSM supplement. Diets supplemented with antibiotic, MOS, or all graded levels of BPSM decreased the viable cell count of Escherichia coli in the caecum segment of broiler chickens. When considering the intestinal morphometric indices, the villus length was greater in the antibiotic, MOS, 100 or 150 mg/kg BPSM groups compared with the control diet. In conclusion, the positive impact of BPSM supplementation on the performance, gut microbiota, and intestinal morphology was clearly evident in broiler chickens.

With same treatments, Salavati *et al.* (2021) also showed that the dietary BPSM did not significantly affect certain serum parameters like IgG and IgM levels, cholesterol, triglycerides, low-density lipoprotein (LDL), and aspartate aminotransferase (AST) activity. However, the concentration of albumin in the blood increased in broiler chickens fed the diet containing 100 mg/kg BPSM. Furthermore, the addition of 100 mg/kg BPSM and MOS improved the digestibility of crude protein and ether extract in the birds. Additionally, certain vital amino acids' digestibility, such as histidine, methionine, tyrosine, and threonine, showed improvement in birds receiving the BPSM and MOS diets. The body weight gain and food conversion ratio were also enhanced in the birds that received MOS or 100 mg/kg BPSM, respectively. They suggested that BPSM could be beneficial as a dietary supplement for broiler chickens without adversely affecting their immune response and nutrient digestibility.

Landy *et al.* (2020) designed broiler chickens diets to contain 0 (control), 3, 4, 5, and 6 g bioactive peptides from cottonseed (BPC)/kg of diet compared to a control diet supplemented with 50U excessive dietary vitamin E and control diet supplemented with 2 mg lincomycin. Throughout the entire trial, broilers fed with diets containing 5 g BPC/kg showed increased feed intake compared to other groups and broilers fed diets supplemented with 6 g BPC/kg demonstrated significantly better FCR values. Supplementation of 3 g BPC/kg led to increased antibody titres against Newcastle disease virus and sheep red blood cell. Dietary supplementation of vitamin E, antibiotic, and 3, 4, and 5 g BPC/kg led to a significant increase in total antioxidant activity of serum compared to those receiving the basal diet. They suggested that supplementing broiler diets with 6 g BPC/kg could have positive effects on growth performance, immune responses, and total antioxidant activity of serum, offering an alternative to antibiotics in broiler diets.

Mohammadrezaei *et al.* (2021) compared the effects of bioactive peptides from cottonseed meal (CSBP) to zinc bacitracin, an antibiotic growth promoter (AGP), on broiler chickens. The results showed that the 20 g/kg CSBP increased feed intake and FCR, while the antibiotic group had increased body weight and feed intake. Livability, EPEF, and EBI improved in chickens fed the antibiotic and 15 g/kg CSBP supplement. Additionally, including CSBP in broiler diets could improve growth rate and balance gut microbiota, suggesting it as a potential alternative to antibiotics in AGP-free production systems.

Hosseinpoor *et al.* (2023) tried to explore how enzymatic or fermentative hydrolysis of canola meal (CM) protein produces bioactive peptides. The peptides obtained from

CM fell within the molecular weight range of 180–500 daltons. The highest quantities of di- and tripeptides were observed in CM pre-treated with protease (15.6%). All treatments resulted in reduced glucosinolate and phytic acid levels in CM compared to the untreated sample. The lowest levels of glucosinolate (15.45 mm/g) and phytic acid, along with the highest crude protein content (42.07%), were also evident in the sample pre-hydrolyzed by protease. The CM hydrolyzed using a commercial protease enzyme showed the highest antioxidant activity. Consumption of 15% CM in the diet reduced the performance of broiler chickens compared to the control group, but the villi length, as an indicator of intestinal morphology, improved in all segments of the small intestine compared to the control group. Additionally, there was no significant difference observed between the different treatments regarding the population of *Lactobacillus* and *Escherichia coli* bacteria.

Liu *et al.* (2022) examined the impact of bioactive peptides obtained from the solid-state fermentation of cottonseed meal on various aspects of yellow-feathered broilers' well-being. The control group received a basic diet, while the three experimental groups were fed diets containing 1%, 2%, and 3% cottonseed meal bioactive peptides (CSBP), replacing an equivalent amount of protein from cottonseed meal in the basic diet. The results showed that dietary supplementation of 2% and 3% CSBP led to increased average daily weight gain, crude protein digestibility, total serum protein, and immunoglobulin (Ig) G levels in the serum. Furthermore, the 3% CSBP diet increased albumin, total antioxidant capacity, spleen weight/body weight ratio, interleukin-6, and IgM, while reducing the feed-to-gain ratio, total cholesterol, urea nitrogen, total superoxide dismutase, glutathione peroxidase, and malondialdehyde levels in the serum. The 2% CSBP diet led to increased PepT1 expression in the duodenum, jejunum, and ileum. Additionally, the 1%, 2%, and 3% CSBP diets increased S6 kinase-polypeptide-1 and inositol-3-hydroxylase expression in the chest and leg muscles. Overall, the inclusion of CSBP in diets proved beneficial in enhancing the growth performance, nutrient digestibility, protein metabolism, antioxidant capacity, and immune function of yellow-feathered broilers. The period of growth is crucial for laying hens as it is a time of rapid growth with accompanying challenges such as unstable digestion, incomplete organ development, and high mortality.

Zhao *et al.* (2022), investigated the impact of small peptides plant active on the growth, immunity, antioxidant capacity, and intestinal health of growing laying hens. The small plant active peptide was a product of Mytech Company (Chengdu, China) with dehulled soybean meal (SBM) and soybean protein concentrate (SPC) as raw materials by combined liquid enzymatic hydrolysis process. The dietary treatments included a corn-soybean meal-based diet supplemented with 0 g/kg, 1.5 g/kg, 3.0 g/kg, 4.5 g/kg, and 6.0 g/kg of small peptides, respectively. The results indicate that adding small peptides significantly increased the growth rate of laying hens, as well as elevated serum immunoglobulins and antioxidant levels, while reducing inflammation parameters. Additionally, small peptide supplementation improved intestinal function by promoting gut development and enhancing gut integrity, barrier function, and the diversity of gut microbiota in growing hens. The most optimal performance was observed among the hens fed the 4.5 g/kg level of small peptides. They suggested that that small peptide supplementation could enhance the economic value of growing hens by boosting growth rate and disease resistance, with the ideal addition amount for Tianfu green shell laying hens being 4.5 g/kg.

CONCLUSION

Studying bioactive peptides is crucial due to their potential to offer a range of health benefits, including antioxidant, antimicrobial, antihypertensive, and anti-inflammatory properties. Research can aid in the discovery and extraction of novel bioactive peptides from natural sources, broadening the scope of their potential uses in pharmaceuticals, functional foods, and nutraceuticals. Furthermore, additional investigation can enhance our comprehension of the mechanisms through which bioactive peptides work, thereby assisting in the development of new therapeutic treatments and dietary approaches.

REFERENCES

Abdollahi M.R., Zaefarian F., Gu Y., Xiao W., Jia J. and Ravindran V. (2017). Influence of soybean bioactive peptides on growth performance, nutrient utilisation, digestive tract development and intestinal histology in broilers. *J. Appl. Anim. Nutr*. **5,** 7-13.

Abdollahi M.R., Zaefarian F., Gu Y., Xiao W., Jia J. and Ravindran V. (2018). Influence of soybean bioactive peptides on performance, foot pad lesions and carcass characteristics in broilers. *J. Appl. Anim. Nutr*. **6,** 3-9.

Adler-Nissen J. (1986). Enzymic Hydrolysis of Food Proteins. Applied Science Publishers, Elsevier, London, United Kingdom.

Akbarian M., Khani A., Eghbalpour S. and Uversky V.N. (2022). Bioactive peptides: Synthesis, sources, applications, and proposed mechanisms of action. *Int. J. Mol. Sci*. **23,** 1445-1455.

Alahyaribeik S., Nazarpour M., Tabandeh F., Honarbakhsh S. and Sharifi S.D. (2022). Effects of bioactive peptides derived from feather keratin on plasma cholesterol level, lipid oxidation of meat, and performance of broiler chicks. *Trop. Anim. Health Prod*. **54,** 271-279.

Aslam S., Shukat R., Khan M.I. and Shahid M. (2020). Effect of dietary supplementation of bioactive peptides on antioxidant potential of broiler breast meat and physicochemical characteristics of nuggets. *Food Sci. Anim. Resour.* **40,** 55-62.

Bahadori M.M., Rezaeipour V., Abdullahpour R. and Irani M. (2022). Effects of sesame meal bioactive peptides, individually or in combination with a mixture of essential oils, on growth performance, carcass, jejunal morphology, and microbial composition of broiler chickens. *Trop. Anim. Health Prod.* **54,** 235-241.

Bruno B.J., Miller G.D. and Lim C.S. (2013). Basics and recent advances in peptide and protein drug delivery. *Ther. Deliv.* **4,** 1443-1467.

Crantz F.R., Swartz S.L., Hollenberg N.K., Moore T.J., Dluhy R.G. and Williams G.H. (1980). Differences in response to the peptidyldipeptide hydrolase inhibitors SQ 20,881 and SQ 14,225 in normal-renin essential hypertension. *Hypertension.* **2,** 604-609.

Daliri E.B.M., Lee B.H. and Oh D.H. (2018). Current trends and perspectives of bioactive peptides. *Crit. Rev. Food Sci. Nutr.* **58,** 2273-2284.

Garcés-Rimón M., Morales D. and Miguel-Castro M. (2022). Potential role of bioactive proteins and peptides derived from legumes towards metabolic syndrome. *Nutrients.* **14,** 5271-5279.

Goldstein A., Tachibana S., Lowney L.I., Hunkapiller M. and Hood L. (1979). Dynorphin-(1-13), an extraordinarily potent opioid peptide. *Proc. Natl. Acad. Sci.* **76,** 6666-6670.

Harnedy P.A. and FitzGerald R.J. (2012). Bioactive peptides from marine processing waste and shellfish: A review. *J. Funct. Foods.* **4,** 6-24.

Hartmann R. and Meisel H. (2007). Food-derived peptides with biological activity: from research to food applications. *Curr. Opin. Biotechnol.* **18,** 163-169.

Hernández-Ledesma B. and Hsieh C.C. (2013). Bioactive Food Peptides in Health and Disease. BoD–Books on Demand, Norderstedt, Germany.

Hosseinpoor L., Navidshad B., Faseleh Jahromi M., Karimzadeh S., Kalantari Hesari A., Mirzaei Aghjehgheshlagh F. and Heydari A. (2023). The antioxidant properties of bioactive peptides derived from enzymatic hydrolyzed or fermented canola meal and its effects on broiler chickens. *Int. J. Pept. Res. Ther.* **29,** 40-49.

Hughes J. (1975). Isolation of an endogenous compound from the brain with pharmacological properties similar to morphine. *Brain Res.* **88,** 295-308.

Jeske S., Zannini E. and Arendt E.K. (2018). Past, present and future: The strength of plant-based dairy substitutes based on gluten-free raw materials. *Food Res. Int.* **110,** 42-51.

Karimzadeh S., Rezaei M. and Yansari A.T. (2017). Effects of different levels of canola meal peptides on growth performance and blood metabolites in broiler chickens. *Livest. Sci.* **203,** 37-40.

Klompong V., Benjakul S., Kantachote D. and Shahidi F. (2007). Antioxidative activity and functional properties of protein hydrolysate of yellow stripe trevally (*Selaroides leptolepis*) as influenced by the degree of hydrolysis and enzyme type. *Food Chem.* **102,** 1317-1327.

Landy N., Kheiri F. and Faghani M. (2020). Evaluation of cottonseed bioactive peptides on growth performance, carcase traits, immunity, total antioxidant activity of serum and intestinal morphology in broiler chickens. *Italian J. Anim. Sci.* **19,** 1375-1386.

Liu J., Luo Y., Zhang X., Gao Y. and Zhang W. (2022). Effects of bioactive peptides derived from cottonseed meal solid-state fermentation on the growth, metabolism, and immunity of yellow-feathered broilers. *Anim. Sci. J.* **93,** 1-9.

López-Pedrouso M., Zaky A.A., Lorenzo J.M., Camiña M. and Franco D. (2023). A review on bioactive peptides derived from meat and by-products: Extraction methods, biological activities, applications and limitations. *Meat Sci.* **204,** 109278-109288.

Meisel H. (1997). Biochemical properties of bioactive peptides derived from milk proteins: potential nutraceuticals for food and pharmaceutical applications. *Livest. Prod. Sci.* **50,** 125-138.

Minamino N., Kangawa K., Fukuda A., Matsuo H. and Iagarashi M. (1980). A new opioid octapeptide related to dynorphin from porcine hypothalamus. *Biochem. Biophys. Res. Commun.* **95,** 1475-1481.

Minkiewicz P., Iwaniak A. and Darewicz M. (2019). BIOPEP-UWM database of bioactive peptides: Current opportunities. *Int. J. Mol. Sci.* **20,** 5978-5987.

Mohammadrezaei M., Navidshad B., Gheisari A. and Toghyani M. (2021). Cottonseed meal bioactive peptides as an alternative to antibiotic growth promoters in broiler chicks. *Int. J. Pept. Res. Ther.* **27,** 329-340.

Parvez M.A.K., Jubyda F., Ayaz M., Sarker A., Haque N., Khan S., Mou T., Rahman M. and Huq, M. (2024). Microbial and plant-derived bioactive peptides and their applications against foodborne pathogens: Current status and future prospects. *Int. J. Microbiol.* **2024,** 1-29.

Pert C.B. and Snyder S.H. (1973). Opiate receptor: Demonstration in nervous tissue. *Science.* **179,** 1011-1014.

Rizwan D., Masoodi F.A., Wani S.M. and Mir S.A. (2023). Bioactive peptides from fermented foods and their relevance in COVID-19 mitigation. *Food Prod. Proc. Nutr.* **5,** 53-62.

Salavati M.E., Rezaeipour V., Abdullahpour R. and Mousavi S.N. (2021). Bioactive peptides from sesame meal for broiler chickens: Its influence on the serum biochemical metabolites, immunity responses and nutrient digestibility. *Int. J. Pept. Res. Ther.* **27,** 1297-1303.

Salavati M.E., Rezaeipour V., Abdullahpour R. and Mousavi N. (2020). Effects of graded inclusion of bioactive peptides derived from sesame meal on the growth performance, internal organs, gut microbiota and intestinal morphology of broiler chickens. *Int. J. Pept. Res. Ther.* **26,** 1541-1548.

Sholikin M.M., Irawan A., Prihambodo T.R., Qomariyah N., Wahyudi A.T., Nomura J. and Jayanegara A. (2021a). Antimicrobial peptides as an additive in broiler chicken nutrition: a meta-analysis of bird performance, nutrient digestibility and serum metabolites. *J. Anim. Feed Sci*. **30,** 100-110.

Sholikin M.M., Wahyudi A.T., Jayanegara A., Nomura J. and Nahrowi N. (2021b). A meta-analysis of antimicrobial peptide effects on intestinal bacteria, immune response, and antioxidant activity of broilers. *Trop. Anim. Sci. J.* **44,** 188-197.

Toldrá F. (2010). Handbook of Meat Processing. John Wiley & Sons, Blackwell Publishing, New York.

Udenigwe C.C. and Aluko R.E. (2012). Food protein-derived bioactive peptides: production, processing, and potential health benefits. *J. Food Sci*. **77,** 11-24.

Xuan J., Feng W., Wang J., Wang R., Zhang B., Bo L. and Sun L. (2023). Antimicrobial peptides for combating drug-resistant bacterial infections. *Drug. Resist. Updat*. **68,** 1-8.

Wang G., Li X. and Wang Z. (2016). APD3: the antimicrobial peptide database as a tool for research and education. *Nucleic Acids. Res*. **44,** 1087-1093.

Zhao X., Zhang Y., He W., Wei Y., Han S., Xia L. and Cui C. (2022). Effects of small peptide supplementation on growth performance, intestinal barrier of laying hens during the brooding and growing periods. *Front. Immunol*. **13,** 1-10.