

A study on the functional properties of bioactive peptides derived from snakehead fish (*Channa striata*)

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Abstract. Bioactive peptides are short chains of amino acids that have positive effects on health. Snakehead fish (*Channa striata*) is rich in protein, essential amino acids, and micronutrients that are beneficial for health. This species is widely found in Indonesian waters, including swamps, rivers, and lakes, and has been utilized in pharmaceuticals. The method used in this article involved reviewing national and international journals focusing on snakehead fish and various hydrolysis methods. Literature sources were obtained from platforms such as ScienceDirect, Google Scholar, Pubmed, and Elsevier. The bioactive peptide compounds discussed were derived from different organs of the snakehead fish. The results revealed that snakehead fish protein hydrolysate inhibited angiotensin-converting enzyme (ACE) with an IC₅₀ value of 0.076 μmol/L. Additionally, snakehead fish *head soup* demonstrated antioxidants properties, confirmed through a DPPH test with an IC₅₀ value of 1.39 mM. The identified peptide sequences were PGMLGGSPGGLGGSP and SDGSNIHFPN. Several studies have shown that snakehead fish extract accelerates the wound healing process in both animal models and post-operative patients. The active components involved in this process were arachidonic acid and glycine. Furthermore, skin mucus, intestinal mucus, gill extract, and blood from snakehead fish have been found to inhibit the growth of bacteria such as *Aeromonas hydrophila*, *Pseudomonas aeruginosa*, *Vibrio anguillarum*, *Vibrio fischeri*, *Salmonella enteritidis*, and *Escherichia coli*. The hydrolysis of snakehead fish skin collagen demonstrated an HMG-CoA reductase inhibitory activity of 25%. In conclusion, bioactive peptides derived from various protein precursors of snakehead fish exhibit antihypertensive, antioxidant, wound healing, antimicrobial, and anti-cholesterol properties.

1. Introduction

The snakehead fish (*Channa striata*) is a freshwater species with high economic value and is widely recognized in Southeast Asia. In Indonesia, it is known by various names, including *haruan*, *gabus*, *toman*, *bakok*, *cursing*, and *rutiang*. Its distribution extends across most of Asia, particularly in countries such as Iran, Korea, China, Pakistan, and India. In Southeast Asia, snakehead fish are commonly found in Vietnam, Thailand, Laos, Malaysia, and Cambodia. Snakehead fish belong to the family Chanidae or Ophiocephalidae, with *Channa striata* as their scientific name [1]. In Indonesia, four commonly consumed species include *Channa striata*, *Channa micropeltes*, *Channa lucius*, and *Channa pleurothalmus* [2]. Some smaller species of snakehead fish are popular as ornamental fish, while others are valued for their medicinal properties.

Channa striata is a predatory species with an impressive ability to survive the dry season by burrowing into mud in lakes, canals, and swamps. This fish possesses a labyrinth organ that allows it to breathe air directly. Morphologically, it has an elongated body, a rounded tail, and a broad, flat head resembling that of a snake, which gives it the name “snakehead fish”. The top and sides of its head are

covered with scales, and it has a large mouth with small teeth on the roof. The eyes of the snakehead fish are positioned on the anterior part of the head. Additionally, its dorsal fin is longer than both the anal and pectoral fins [1].

Snakehead fish is rich in essential nutrients, particularly protein and essential amino acids in significant amount, making it a potential source of bioactive peptides. Its main components include protein (19-23%), fat (5.7 %), ash (1.8%), moisture content (83.5%), essential amino acids (leucine, lysine, phenylalanine, and valine), as well as micronutrients such as potassium (K), calcium (Ca), and sodium (Na) [3]. The protein content of snakehead fish is higher than that of most freshwater fish. Beyond its role as a food source, snakehead fish also has applications in the nutraceutical field. Snakehead fish extract has been found to aid in wound healing and alleviate postoperative pain, particularly after childbirth. Several amino acids, including glycine, glutamine, and arginine, play a crucial role in this process [4]. Snakehead fish provides a complete amino acid profile, offering various health benefits [5]. Amino acids are essential for metabolic processes in the human body.

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Glycine is necessary for collagen synthesis, the primary protein in connective tissues. Glutamine plays a key role in inflammation and proliferation stages during wound healing, serving as an energy source. Meanwhile, arginine promotes wound healing by modulating immune function and influencing endothelial activity. Additionally, the amino acids in snakehead fish contain arachidonic acid and polyunsaturated fatty acids, which stimulate prostaglandin synthesis, another crucial factor in wound healing [4].

In recent years, research on snakehead fish has expanded, particularly in exploring its bioactive properties. Studies on its protein content various peptide fractionation processes have revealed its potential as an antioxidant [6], antihypertensive [7], and inhibitor of α -amylase and α -glucosidase, which helps regulated blood glucose levels [8]. Additionally, snakehead fish has been found to promote wound healing [9], and exhibit anti-cholesterol [10], antinociceptive [11], anti-inflammatory [12], anti-osteoarthritic [13], anti-microbial [14], and antifungal properties [15].

Bioactive peptides are short chains of amino acids that confer health benefits when consumed. These peptides are naturally derived from food proteins through food processing or digestion. However, since this process is uncontrolled, specific strategies are required to enhance the efficient production of bioactive peptides. One of the most extensively studied approaches is enzymatic hydrolysis using commercial enzymes or enzyme mixtures [16]. Over the past two decades, research on bioactive peptides has grown significantly, leading to the commercial success of several peptide-based products. For instance, collagen-derived peptides have been developed and marketed as skin protectants and joint care supplements [10].

Bioactive peptides are protein molecules consisting of fewer than 20 amino acid residues and provide physiological benefits when digested in the body. These peptides have been shown to reduce the risk of cardiovascular disease, inhibit tumor cell growth, regulate blood pressure, and lower blood glucose levels. Structurally, peptides are similar to proteins as both are composed of amino acids; however, peptides contain fewer amino acid residues than proteins. On average, peptides have a molecular weight of less than 10 kDa, whereas proteins typically have a molecular weight exceeding 10 kDa. Due to their lower molecular weight, peptides are more resistant to enzymatic hydrolysis as they pass through the digestive tract. Additionally, their small size facilitates easier absorption into the bloodstream, allowing efficient transport to various target sites in the body. Conversely, peptides with a higher molecular weight are more susceptible to degradation by digestive enzymes. In most cases, structural degradation reduces or eliminates their bioactivity. However, in some instances, peptide breakdown may result in a more active or easily absorbed as they pass through the

digestive tract [17]. Bioactive peptides function similarly to hormones or drugs, regulating physiological processes by binding to specific receptors on target cells. These peptides can positively influence key biological systems, including the cardiovascular, digestive, endocrine, immune, and nervous systems. Furthermore, they possess potential therapeutic properties, acting as antihypertensive, antioxidant, opioid, antibacterial, antithrombotic, and immunomodulatory agents [18]. Some peptides also exhibit multifunctional characteristics; for instance, certain peptide sequences demonstrate both antioxidant and antihypertensive activity. The bioactivity of a peptide is primarily determined by its amino acid composition and sequence.

Recent research has identified protein hydrolysates and peptides derived from fish and marine organisms as excellent sources of bioactive compounds for combating lifestyle-related metabolic diseases [19]. Fish has long been a staple food in various cultures and is rich in bioactive components, including protein, peptides, omega-3 polyunsaturated fatty acids (n-3 PUFA), minerals, and vitamins [20]. Food-derived proteins and peptides have been increasingly recognized as promising natural agents for the prevention and management of diabetes [21]. This article provides a comprehensive review of studies on the health benefits of snakehead fish (*Channa Striata*).

2. Methods

The approach taken in preparing this article involved collecting national and international journals that explored snakehead fish using different hydrolysis techniques. The literature sources were obtained from various platforms including Science Direct, Google Scholar, Pubmed, and Elsevier. The reviewed bioactive peptide compounds were extracted from different organs of the snakehead fish."

3. Results and Discussion

3.1 Bioactive peptide extraction and fractionation methods

Recent research trends have increasingly focused on obtaining bioactive peptides from natural food sources through enzymatic process. Enzymatic hydrolysis provides the advantage of being controllable and free from organic solvents or toxic chemicals. Employing appropriate methods is essential to ensure the successful extraction of the desired bioactive peptides. The extraction process, which includes fractionation, identification, and characterization, plays a crucial role in the discovery of bioactive peptides. According to Sitanggang et al [22], bioactive peptides can be separated using an enzymatic membrane reactor. Ma et al [23] successfully extracted bioactive peptides from snakehead fish with antihypertensive properties using a *bioaffinity ultrafiltration coupled method* with LC-Orbitrap-MS/MS for peptide separation. Meanwhile, Budiari et al [19] reported that ultrafiltration of

fractions <3 kDa from snakehead fish fillets using distilled water as a solvent resulted in the highest ACE inhibitory activity per μg protein (7.85% ACE inhibition per μg protein). Additionally, Zhang et al [6] identified antioxidant peptides from snakehead fish soup through an ultrafiltration separation system utilizing Amicon Ultra-15 centrifugal filters with molecular weight cut-off (MWC) of 10 kDa and 3 kDa, followed by Reversed-Phase High Performance Liquid Chromatography (RP-HPLC).

3.2 Health benefits of bioactive peptides from snakehead fish (*Channa striata*)

3.2.1 Antihypertensive

Hypertension is a degenerative disease that commonly affects humans due to an unbalanced lifestyle and poor dietary habits. It is a major contributing factor to the development of cardiovascular diseases, including heart failure, stroke, and coronary heart disease. Hypertension is characterized by a systolic blood pressure exceeding 140 mmHg and/or diastolic blood pressure above 90 mmHg. Generally, it is defined as blood pressure surpassing 140/90 mmHg, and is considered critical when it exceeds 180/120 mmHg [24]. According to the World Health Organization (WHO) in 2013, hypertension was responsible for 45% of deaths related to heart disease and 50% of deaths caused by stroke.

Several studies have indicated that nearly all parts of the snakehead fish can be hydrolyzed to produce antihypertensive peptides. The primary targets of these peptides are renin and angiotensin-converting enzymes (ACE). A peptide derived from snakehead fish muscle protein, obtained through enzymatic hydrolysis under high hydrostatic pressure, has shown potential as a natural ACE inhibitor. The long-chain peptide sequence AIGTGKTASPQQAQE exhibited significant inhibitory activity, with an IC_{50} value of $0.076\mu\text{mol/L}$ [7]. ACE plays a crucial role in blood pressure regulation by facilitating the conversion of angiotensin I into angiotensin II, a hormone that constricts blood vessels and elevates blood pressure. Rahman et al [25], reported that several fish-derived peptides exhibited antihypertensive properties by affectively inhibiting ACE activity, with stronger effects compared to other naturally occurring peptides [26]. Additionally, peptides obtained from enzymatically hydrolyzed fish muscle have demonstrated anticoagulant and antiplatelet properties in vitro, highlighting their ability to inhibit coagulation factors in the intrinsic coagulation pathway [27]. Chi *et al.* [7] identified 12 unique peptides in snakehead fish, including those with a net charge (such as Glu and lys) and hydrophobic peptides (such as Val and Pro). Similarly, Berlian et al [28] found that hydrolysis of snakehead fish albumin using the alcalase enzyme produced peptides with the highest ACE inhibitory activity, particularly in fractions with molecular sizes <3 kDa ($56.65 \pm 2.32\%$, $\text{IC}_{50}=36.93\mu\text{g/mL}$). According to Ghaseem et al. [29], bioactive peptides isolated from hydrolyzed snakehead

fish myofibrillar protein also demonstrated significant ACE inhibitory activity.

Table 1. Snakehead fish bioactive peptides as antihypertensives.

Protein precursor	Peptide sequence/Peptide size/ IC_{50}	Bioactivity	Ref
Myofibrillar protein hydrolysate	VPAAPPK ($\text{IC}_{50}=0.45\mu\text{M}$) and NGTWFEPP ($\text{IC}_{50}=0.63\mu\text{M}$)	ACE inhibitors	[29]
Sarcoplasmic protein hydrolysate	LYPPP ($\text{IC}_{50}=1.3\mu\text{M}$) and YSMYPP ($\text{IC}_{50}=2.8\mu\text{M}$)	ACE inhibitors	[30]
Fish fillet extract	96.18% ACE inhibition at an extract concentration of 50 mg/ml	ACE inhibitors	[3]
Skin hydrolysate collagen	13.32% ACE inhibition per μg protein	ACE inhibitors	[31]
Fish fillet extract	7.85% ACE inhibition per μg protein, <3 kDa	ACE inhibitors	[19]
Fish albumin	$\text{IC}_{50}=36.93\mu\text{g/mL}$	ACE inhibitors	[28]
Fish protein hydrolysate	AIGTGKTASPQQAQE ($\text{IC}_{50}=0.076\mu\text{mol/L}$)	ACE inhibitors	[7]

3.2.2 Antioxidant

Excessive accumulation of Reactive Oxygen Species (ROS) around cells can be detrimental. ROS induced cellular damage is a key contributor to the development of diabetes. Under diabetic conditions, chronic hyperglycemia stimulates excessive ROS production in mitochondria, particularly in the endothelium of both large and small blood vessels [32].

Overproduction of ROS, especially superoxide anions, can lead to increased oxidative stress. Oxidative stress occurs when elevated ROS levels surpass the body's defense mechanisms and endogenous antioxidants. Antioxidants play a crucial role in reducing atherosclerosis in cardiovascular disease and mitigating vascular endothelial dysfunction. Their primary function is to neutralize free radicals by preventing and repairing cell damage caused by ROS [33]. Several studies have highlighted the antioxidant properties of snakehead fish protein hydrolysate. An in-vitro study by Radzak et al [34], demonstrated that Snakehead fish fillet exhibit antioxidant activity, as assessed through total phenolic content (TPC), ferric reducing antioxidant power (FRAP), and radical scavenging assays using 2,2-diphenyl-picrylhydrazyl (DPPH) and 2,2'-azino-Bis (3-ethylbenzthiazoline-6-sulphonic acid)

(ABTS). The results indicated high levels of TPC (12799±237.90 mg GAE/100g dry weight), FRAP (1250±0.617 mg FeSO₄/1mg dry weight), DPPH (0.2804±0.035 µg/ml; EC₅₀) and ABTS (4687±0.67 µg/ml; EC₅₀) [34].

Table 2. Snakehead fish bioactive peptides as antioxidants

Protein precursor	Peptide sequences	Method	Bioactivity	Ref
Fish fillet extract	-	FRAP (0.789 µmol Fe(II)/g dry extract)	Antioxidant	[3]
Skin hydrolysate collagen	-	DPPH (73.22% inhibition/50µg protein)	Antioxidant	[31]
Fish skin hydrolysate	-	DPPH radical scavenging (10.75% - 20.77%)	Antioxidant	[35]
Fish skin collagen hydrolysate	-	DPPH Inhibition (48.89%)	Antioxidant	[33]
Fish soup	PGML GGSP GLLG GSP and SDGS NIHFP N	DPPH radical scavenging activity (IC ₅₀ = 1.39 mM) and Fe ²⁺ chelating ability (IC ₅₀ = 4.60 mM)	Antioxidant	[6]
Fish head	-	DPPH (50,70% ABTS (66,67%) FRAP (1,35%) µM Tr/mg)	Antioxidant	[36]
Fish extract	-	DPPH (IC ₅₀ = 0.23 mg protein/ml), FRAP	Antioxidant	[37]

3.2.3 Wound healing

Snakehead fish contains essential amino acids and fatty acids, which play a crucial role in the wound healing process. Wound healing is a complex biological process involving a series of reactions and interactions between cells and mediators. The skin comprises an intricate network of pro-inflammatory cells that actively participate in wound repair. According to Mat Jais et al [15], the mucus and muscles of snakehead fish are rich in glycine and arachidonic acid, the two compounds that accelerate wound healing through collagen synthesis and re-epithelialization in damaged tissue. Snakehead fish extract contains albumin,

arachidonic acid, glycine, arginine, glutamine, zinc (Zn), and copper (Cu), all of which have been reported to facilitate wound healing and alleviate pain following surgery, trauma, or childbirth [38]. Polyunsaturated fatty acids also contribute to the wound healing process by regulating prostaglandin synthesis [15]. A study by Udayanti and Noviyani [39] demonstrated that administering snakehead fish extract to diabetes mellitus patients in the intervention group effectively accelerated wound healing. Additionally, the wound healing properties of snakehead fish extract have been found to enhance the tensile strength of postoperative wounds [40], showing superior results compared to conventional cetrimide cream. Furthermore, snakehead fish extract have been shown to increase fibroblasts proliferation in the wound healing process of Wistar rat mucosa, with the optimal concentration being 100% [41]. This extract also promotes mesenchymal cells proliferation and maintains sufficient cell viability, making it a potential biochemical agent and healing promoter not only for skin wounds but also for other organ tissues.

Table 3. Snakehead fish bioactive peptides for wound healing

Protein precursor	Bioactive components/amino acids	Biological activity	Ref
Fish extract	Arachidonic acid, glycine	Wound healing	[38]
Mucus (slime) and roe (eggs) fish cork	Oleic (C18:1) 21.25%), linoleic acid (C18:2) 22.47% found in Mucus Arachidic acid (C20:0) 22.16% found in eggs, arachidonic acid (C20:4n-6)	Wound healing	[15]
Fish fillet extract	Lysine (5.49 mg/g), glycine (2.41 mg/g), aspartic acid (2.93 mg/g), glutamic acid (1.13 mg/g)	Wound healing	[3]
protein isolate	Striatin (DLBS0333), 5'-GCACAGAGGCUGAAG UUA	Wound healing	[9]
Fish mucus	Histones H2A and H4 (fragments)	Wound healing	[42]

3.2.4 Antimicrobial

Snakehead fish has demonstrated potential as an antimicrobial agent against certain pathogenic bacteria. Research on commonly used antibiotics is continuously evolving to identify new antimicrobial agents capable of combating infections while addressing resistance issues and minimizing side effects. According to Dhanaraj et al [43], the skin mucus and intestinal mucus of snakehead fish exhibit inhibitory effects against the growth of *Aeromonas hydrophila*, *Pseudomonas aeruginosa*, *Vibrio anguillarum*, *Vibrio fischeri* bacteria. A study by Kumar et al [44], reported that extracts from the gills and blood of snakehead fish possess antimicrobials properties against *Salmonella enteritidis* and *Escherichia coli* bacteria. Zawawi et al

[45] found that the antibacterial activity of snakehead fish extract against *Pseudomonas* spp. and *Escherichia coli* exhibited inhibitory values of 400 mg/mL and 500 mg/mL, respectively, with minimum bactericidal concentration (MBC) values ranging between 650 mg/mL and 550 mg/mL. However, despite initial cytotoxic, the result suggested that snakehead fish extract could enhance cell viability and proliferation at higher concentrations. Additionally, Kong *et al* [14] successfully isolated lactic acid bacteria (LAB) from the intestines of snakehead fish. Two LAB isolates were identified as *Enterococcus faecalis* (Genbank: MT102745.1) and *Lactococcus lactis* (Genbank: MT102746.1), both of which were confirmed as non-pathogenic probiotic strains. These LAB strains hold promise as potential candidates for the development of functional micro-ecological feeds.

Table 4. Snakehead fish bioactive peptides as antimicrobials

Source	Inhibition value and type of bacteria	Biological activity	Ref
Skin mucus and intestinal mucus	<ul style="list-style-type: none"> - Skin mucus can inhibit <i>A. hydrophila</i> bacteria (19.5 ± 2mm). <i>P.aeruginosa</i> (28 ± 2.9 mm) and <i>V. anguillarum</i> (24.5 ± 2.4 mm) - Intestinal mucus can inhibit the bacteria <i>A. hydrophila</i> (16 ± 1.4 mm), <i>P. aeruginosa</i> (29 ± 3.2 mm), <i>V. anguillarum</i> (18.3 ± 1.5 mm) and <i>V. fischeri</i> (21.5 ± 1.8 mm). 	Anti bacterial	[43]
Fish gill and blood extract	<ul style="list-style-type: none"> - Gill extract can inhibit <i>Salmonella enteritidis</i> bacteria (60% ACN fraction) - Blood extract can inhibit <i>Escherichia coli</i> bacteria (40% ACN fraction) 	Anti bacterial	[44]
Snakehead fish fillet extract	<ul style="list-style-type: none"> - The inhibitory concentration value of 400-500mg/mL can inhibit <i>Pseudomonas</i> spp and <i>Escherichia coli</i> bacteria 	Anti bacterial	[45]
Isolate LAB from the intestines of snakehead fish	<ul style="list-style-type: none"> - <i>Enterococcus faecalis</i> and <i>Lactococcus lactis</i> with 16S rRNA sequences 	Anti bacterial	[14]

3.2.5 Anti-cholesterol

Research on the potential of snakehead fish as an anti-cholesterol agent remains limited. Anti-cholesterol compounds and antioxidants play a crucial role in preventing cardiovascular disease, which are often caused by arterial plaque formation due to cholesterol oxidation. In recent years, bioactive peptides with anti-cholesterol and antioxidant properties have been explored as alternative therapeutic agents. Anti-cholesterol peptides can be obtained through the hydrolysis of snakehead fish skin. A study by Sinaga *et al.* [33] revealed that collagen extracted from snakehead fish skin exhibited HMG-CoA reductase inhibitory activity comparable to that pravastatin. Peptide hydrolysates derived from snakehead fish skin collagen demonstrated the ability to inhibit the HMG-CoA reductase (HMGR) enzyme, which plays a key role in cholesterol biosynthesis. Virginia *et al* [10] reported that collagen hydrolysates from snakehead fish skin resulted in 25.8% inhibition of HMG-CoA reductase. Additionally, hydrolysis using 50 kDa collagenase from *Bacillus licheniformis* F11.4 showed significant inhibitory activity against HMG-CoA reductase. By inhibiting this enzyme, cholesterol synthesis is reduced, indicating its potential as an anti-cholesterol agent. Furthermore, research by Kong *et al.* [14] investigated the cholesterol-lowering effects of lactic acid bacteria (LAB) isolated from the intestines of snakehead fish. A total of 10 LAB strains were identified, exhibiting cholesterol-lowering capacities ranging from 18.7% to 48.4%. The mechanism of action of bioactive peptides from snakehead fish intestinal isolates resembles that of statin drugs, such as pravastatin, which function by inhibiting HMG-CoA reductase. However, peptides derived from natural sources, such as fish collagen, may serve as promising natural alternatives for cholesterol reduction.

Table 5. Snakehead fish bioactive peptides as anti-cholesterol

Source	Mechanism	Biological activity	Ref.
Hydrolysis of snakehead fish skin collagen	25.8% inhibition of HMG-CoA Reductase	Anti-cholesterol	[10]
Isolate lactic acid bacteria from the intestines of snakehead fish (<i>Channa argus</i>)	Through LAB media (MRS-CHOL medium), isolates can reduce cholesterol by 48.4%	Anti-cholesterol	[14]
Fish skin collagen hydrolysate	50% inhibition of HMG-CoA Reductase	Anti-cholesterol	[33]

4 Conclusion

Snakehead fish is a well-known freshwater species in Southeast Asia, particularly for its medicinal properties. Several studies have demonstrated that

bioactive peptide derived from snakehead fish exhibit various health benefits, including antihypertensive, antioxidants, wound-healing, antimicrobial, and anti-cholesterol activities. Due to these properties, snakehead fish holds significant potential as a source of pharmaceutical compounds, in addition to serving as a nutritious food that supports overall human health.

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Conflict of Interest

The authors declare that they have no known financial conflicts of interest or personal relationships that could have influenced the work presented in this paper.

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