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Review Article

Bioactive Peptides from Indonesian High-Protein Fermented Foods: A Promising Source of Functional Compounds

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Abstract

Bioactive peptides (BPs) are short protein fragments with significant physiological functions, including antioxidant, antihypertensive, antimicrobial, and antidiabetic activities. These compounds are commonly released during fermentation, making high-protein fermented foods (HPFF) a promising source of natural health-promoting agents. Indonesia, with its rich biodiversity and long-standing tradition of fermentation, offers a unique variety of traditional HPFF. However, the potential of these indigenous products as BP sources remains underexplored and poorly represented in the global literature. This review aims to examine Indonesian traditional HPFF as a source of BPs, categorize them based on raw material, and highlight their functional and health-related properties. A literature review was conducted using publications from Scopus, PubMed, ProQuest, Google Scholar, and SINTA (2000–2023). The search applied Boolean strategies and the PEO (Population, Exposure, Outcome) framework to identify relevant studies on fermented foods, bioactive peptides, and their biological activities. Indonesian HPFF including *tempeh, rusip, dangke, pekasam*, and *cangkuk* contain BPs with diverse bioactivities. *Tempeh* shows antidiabetic and antihypertensive potential; *rusip* exhibits antioxidant and cholesterol-lowering effects; *dangke* and *cangkuk* demonstrate antimicrobial and ACE-inhibitory activities. These functional properties are influenced by substrate type (e.g., legumes, fish, milk), microbial composition (lactic acid bacteria, *Bacillus* spp., yeasts), and fermentation conditions. Notably, certain Indonesian HPFF exhibit multi-functional peptides with synergistic health effects, suggesting significant therapeutic promise. This review bridges a critical knowledge gap by consolidating evidence on BPs from Indonesian HPFF. It provides a foundation for future investigations into peptide bioactivity, supports functional food innovation, and highlights the global relevance of Indonesia's fermentation heritage in health science and sustainable nutrition.

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1. Introduction

Bioactive peptides (BPs) are short protein fragments with molecular weights below 6 kDa that can positively influence health by acting as antioxidants, ACE inhibitors, antidiabetic agents, and antimicrobials (Sharma *et al*., 2011; Walther and Sieber, 2011; Khan *et al*., 2018). These peptides are typically generated through enzymatic hydrolysis or fermentation processes. Fermentation, in particular, is a traditional bioprocess used for centuries to improve food safety, nutrition, and shelf life (Tamang *et al*., 2016; Leonard *et al*., 2021), while simultaneously enabling the release of BPs through proteolysis by microbial enzymes (Girgih *et al*., 2014; Chakrabarti *et al*., 2018; Najafian and Babji, 2014). Indonesia is home to a rich variety of high-protein fermented foods (HPFF), including those made from legumes, fish, meat, and milk, many of which are prepared using traditional methods and indigenous microbial communities (Romulo and Surya, 2021; Prihanto *et al*., 2024). Several of these foods have shown promising health-related functions, such as antioxidant and antihypertensive activity in *rusip* (Rinto *et al*., 2019; Kurnianto *et al*., 2023; Olalere *et al*., 2023), antidiabetic activity in *tempeh* (Tamam *et al*., 2019), and antimicrobial activity in *dangke* (Sasmita *et al*., 2023). However, these findings are fragmented, mostly published in local journals, and lack systematic global synthesis. Despite their potential, the role of Indonesian HPFF as a significant source of BPs remains underrepresented in the international scientific discourse, which hinders their recognition and utilization in functional food development and global health strategies.

Recent advances in food biochemistry and functional nutrition have underscored the role of BPs as bioactive components derived from various food matrices. Several studies have identified and characterized BPs in milk (Tonolo *et al*., 2020), fermented meat (Wang *et al*., 2022), fish (Kurnianto *et al*., 2025a; Najafian and Babji, 2019), legumes (Zhao *et al*., 2024), and mixed fermented foods (Chourasia *et al*., 2023; Girgih *et al*., 2014). These peptides exert ACE-inhibitory (Rendon-Rosales *et al*., 2019), antioxidant (Ohata *et al*., 2016), antidiabetic (Kurnianto *et al*., 2025a; Yan *et al*., 2019), and immunomodulatory activities (Oyama *et al*., 2017). The fermentation process itself has been shown to influence peptide release depending on microbial strains and fermentation parameters (Guo *et al*., 2023). Indonesian fermented foods such as *tempeh*, *rusip*, *dangke*, *cangkuk*, and *pekasam* have been reported to contain functional peptides (Tamam *et al*., 2019; Sitanggang *et al*., 2020; Rinto *et al*., 2021; Sasmita *et al*., 2023), yet most of these findings remain isolated or published in national databases with limited international exposure. While global reviews on BPs have gained traction, very few focus specifically on the rich diversity of fermented foods from Southeast Asia particularly Indonesia and their contribution to bioactive peptide science.

Although many BPs have been isolated from globally recognized fermented foods, the presence, diversity, and functional roles of BPs in Indonesian traditional HPFF remain rarely studied, under-reported, and poorly understood. The molecular mechanisms underlying their bioactivities and their potential applications in functional food development remain unclear. This review is the first comprehensive synthesis focusing on the potential of Indonesian traditional HPFF as sources of BPs. It categorizes the fermented products based on substrate type milk, meat, fish, and legumes and discusses their associated peptide functions, offering new insight into region-specific food biochemistry. The findings are expected to advance knowledge in food and marine biotechnology by identifying novel BP-rich fermented foods, especially those derived from fish-based substrates. This review will also enhance global awareness of Indonesian fermented foods as functional health-promoting ingredients and support the development of sustainable, culturally rooted functional food products for public health, fisheries, and aquaculture industries.

State the specific objective(s) of your study. If applicable, briefly indicate the main outcomes or findings, especially if they provide a novel contribution to knowledge or application in fisheries and marine sciences.

This review aims to critically analyze and summarize the diversity, sources, and functional properties of bioactive peptides derived from Indonesian traditional HPFF. It highlights the mechanisms of peptide generation through fermentation and discusses the bioactivities relevant to human health. The expected outcome is to establish a scientific foundation that supports future bioprospecting, peptide purification, and nutraceutical application of these indigenous foods, especially within marine and aquaculture-based food systems.

2. Materials and Methods

2.1 Materials

2.1.1 The equipment

This review was conducted entirely as desk-based research and did not employ laboratory apparatus. Computing equipment comprised a workstation-class laptop/desktop (Windows 10 or later, ≥16 GB RAM, multi-core CPU) used for literature screening, data extraction, and figure generation, with stable broadband internet for database queries and full-text retrieval. All computations and figure preparation were performed on this hardware environment.

2.1.2 The materials

Software environments included Microsoft Office 2016 (Microsoft Corporation, Redmond, USA) for document management and figure preparation, with SmartArt in Microsoft Word for conceptual schematics and Microsoft Excel for compact plots and tables. Mendeley Desktop (Mendeley/Elsevier, UK) was used for reference management and citation formatting. A large-language-model assistant (Grammarly) was used solely to refine English expression and summarize author-generated text; all scientific content was verified by the authors, who accept full responsibility for accuracy and integrity.

2.1.3 Ethical approval

This study does not require ethical approval because it does not use experimental animals.

2.2 Methods

2.2.1 Review design, registration, and research question

Following PRISMA 2020 guidance, we designed a systematic literature review to consolidate empirical evidence on the potential of Indonesian HPFF as bioactive peptide sources. We asked: What is the diversity, source, and functional property of bioactive peptides derived from Indonesian traditional HPFF? How can we support the future bioprospecting, purification of peptides, and nutraceutical applications of these indigenous foods, particularly in marine and aquaculture-based food systems?

2.2.2 Information sources and search strategy

We searched Google Scholar, Scopus, ProQuest, PubMed, and SINTA (Science and Technology Index Indonesia) complemented by backward and forward citation chasing from included studies. Searches covered all available years from 2000 to 2023 (Asia/Jakarta). The search strategy applied the PEO (Population, Exposure, Outcome) approach in which populations, including "traditional food sources", exposure, including "fermentation, and outcome, including "biological activity of bioactive peptides. Boolean search operators were used in combinations of main and alternative keywords across selected databases. The main search string included "traditional food" OR "fermented food" OR "traditional fermented food") AND ("bioactive peptides" OR "bioactive peptide source" OR "food source of bioactive peptides") AND ("biological activity of bioactive peptides" OR "bioactivity of bioactive peptides"). To enhance relevance and precision, more specific search terms were also utilized, such as the names of traditional fermented foods *dangke, dadiah, urutan, bebontot, buntilan, bekamal, cangkuk, tauco, tempeh, oncom, gembus,* soy sauce, *terasi, rusip, bekasam, joruk, bakasang, ina sua, budu, cincalok,* and *chao teri* combined with terms related to biological activities, including antihypertensive, antimicrobial, antioxidant, anti-inflammatory, antidiabetic, and anti-cholesterol. Search results were exported and screened for duplication.

2.2.3 Eligibility criteria

Articles were excluded if, despite containing the correct keywords, their abstracts and full texts did not address the core research question. The inclusion criteria were: (1) original research articles published in peer-reviewed journals or proceedings; (2) studies focusing on traditional or fermented foods as sources of bioactive peptides; (3) articles that reported at least one type of biological activity (e.g., antihypertensive, antimicrobial, antioxidant, anti-inflammatory, antidiabetic, or anti-cholesterol); and (4) publications written in English or Bahasa. The exclusion criteria included (1) review articles, book chapters, conference abstracts, or non-peer-reviewed publications; (2) studies lacking clear methodology or insufficient data; (3) articles not related to bioactive peptides from traditional or fermented foods; and (4) articles not available in full text. Only articles meeting the inclusion criteria and demonstrating methodological rigor were selected for synthesis.

2.2.4 Study selection and PRISMA flow

From database searching, we identified 1.555 records in total: Scopus (n = 327), Google Scholar (n = 712), Pubmed (n = 106), SINTA (n = 296), and ProQuest (n =114). After deduplication and automated ineligibility filtering, 284 unique records remained for title/abstract screening. We then sought 73 full-text reports relevant to our study; none were unobtainable (n = 0), whereas 14 reports were excluded at this stage for not meeting the scope or eligibility. Consequently, 59 studies were assessed for eligibility. Ultimately, 56 studies met the inclusion criteria and were synthesized in this review. The full selection pathway is depicted in Figure 1 (PRISMA 2020 flow diagram).

2.2.5 Data extraction

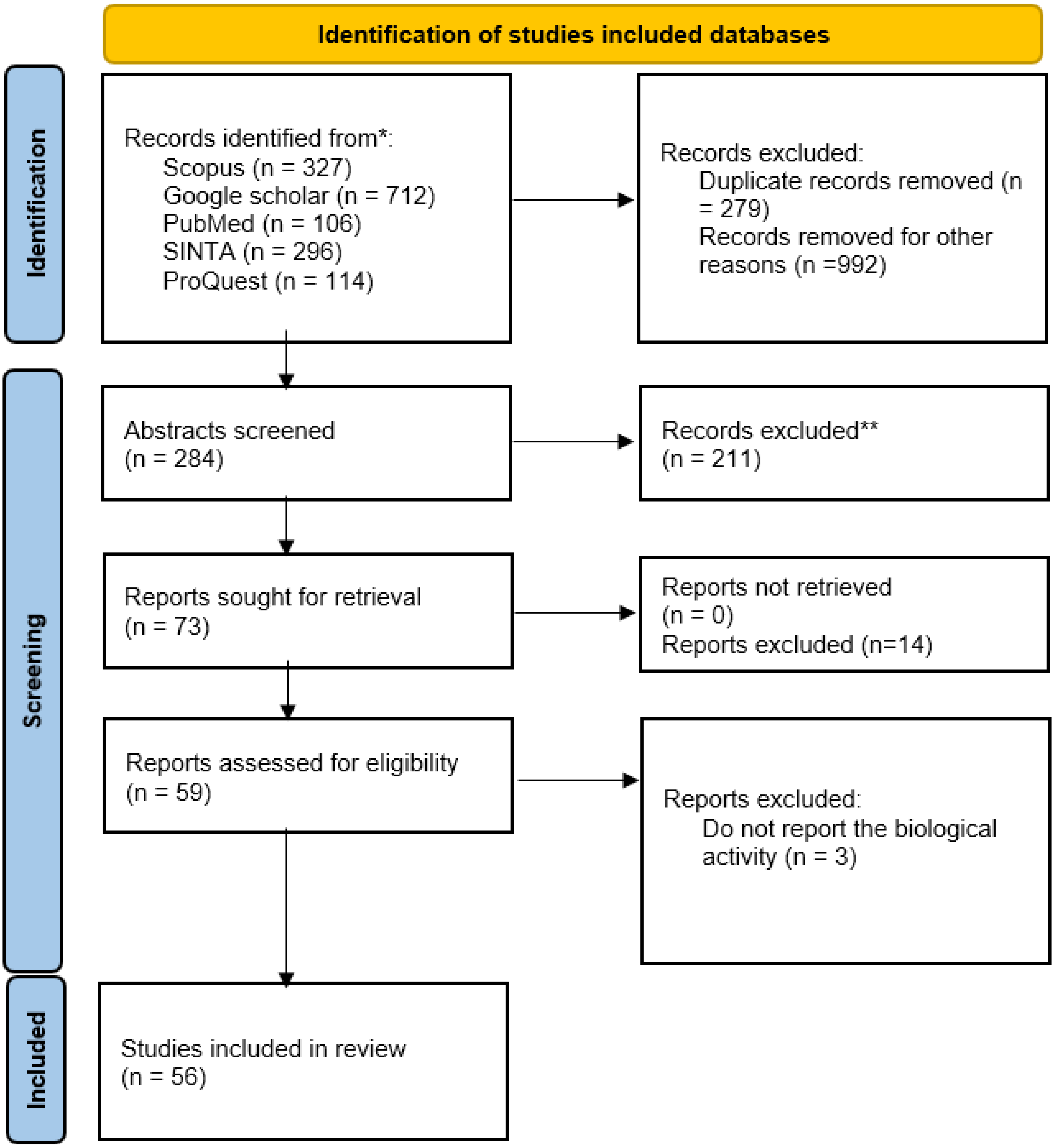

Figure 1. PRISMA 2020 flow diagram for study selection with database yields and screening decisions as described in the text.

The collected articles were analyzed qualitatively through thematic synthesis by two reviewers independently. Key findings related to the types of traditional fermented foods, the processes involved in peptide formation, and the documented bioactivities (e.g., antioxidant, antihypertensive, antimicrobial) were extracted and categorized. The information was integrated to highlight trends, research gaps, and potential applications of BPs derived from traditional fermented foods.

2.3 Analysis Data

The collected articles were analyzed qualitatively through thematic synthesis. Key findings related to the types of traditional fermented foods, the processes involved in peptide formation, and the documented bioactivities (e.g., antioxidant, antihypertensive, antimicrobial) were extracted and categorized. The information was integrated to highlight trends, research gaps, and potential applications of BPs derived from traditional fermented foods. Citations were managed using Mendeley to ensure consistency and traceability of sources.

3. Results and Discussion

3.1 Results

3.1.1 Fermentation as a biocatalytic process for the release of bioactive peptides

Fermentation is an enzymatic hydrolysis method that utilizes proteolytic enzymes produced by microorganisms (Girgih *et al.,* 2014; Chakrabarti *et al.,* 2018). In the context of food, fermentation is known as one of the oldest processing techniques that has been widely applied for various purposes, including increasing shelf life, improving sensory characteristics, and modifying macro components into bioactive compounds (Padhi *et al.,* 2022; Chourasia *et al*., 2023). One important aspect of fermentation is the role of proteolytic microorganisms, either singly or in combination, in hydrolyzing or degrading proteins into peptides. Commonly used microorganisms in this process include lactic acid bacteria (LAB), *Bacillus* spp., yeasts, and molds (Chaudhury *et al*., 2017; Trapsilo *et al*., 2020).

The fermentation process not only modifies the structural integrity of proteins but also facilitates their bioconversion into bioactive peptides (BPs) with specific physiological functions, such as anti-inflammatory, antidiabetic, antioxidant, antimicrobial, and antihypertensive activities (Fitzgerald *et al.,* 2004; El-Fattah *et al*., 2016; Rachman *et al*., 2023). These BPs are commonly present in traditional fermented food products, highlighting the significant role of fermentation in enhancing the functional value of foods. In recent years, growing interest in functional foods enriched with BPs has driven extensive research and innovation efforts (Rutherfurd-Markwick, 2012; Kurnianto *et al.,* 2024). BPs, which are short peptide fragments produced through enzymatic hydrolysis of parent proteins (Abdel-Hamid *et al*., 2017), are particularly abundant in protein-rich food sources (Table 1) (Dziuba and Dziuba, 2014). An overview of the protein bioconversion process during fermentation leading to the formation of BPs in traditional food systems is illustrated in Figure 2.

3.1.2 Bioactive potential of traditional Indonesian fermented foods

Indonesia's rich biodiversity is reflected in its diverse and unique regional cuisines. Traditional foods not only embody regional characteristics, cultural val

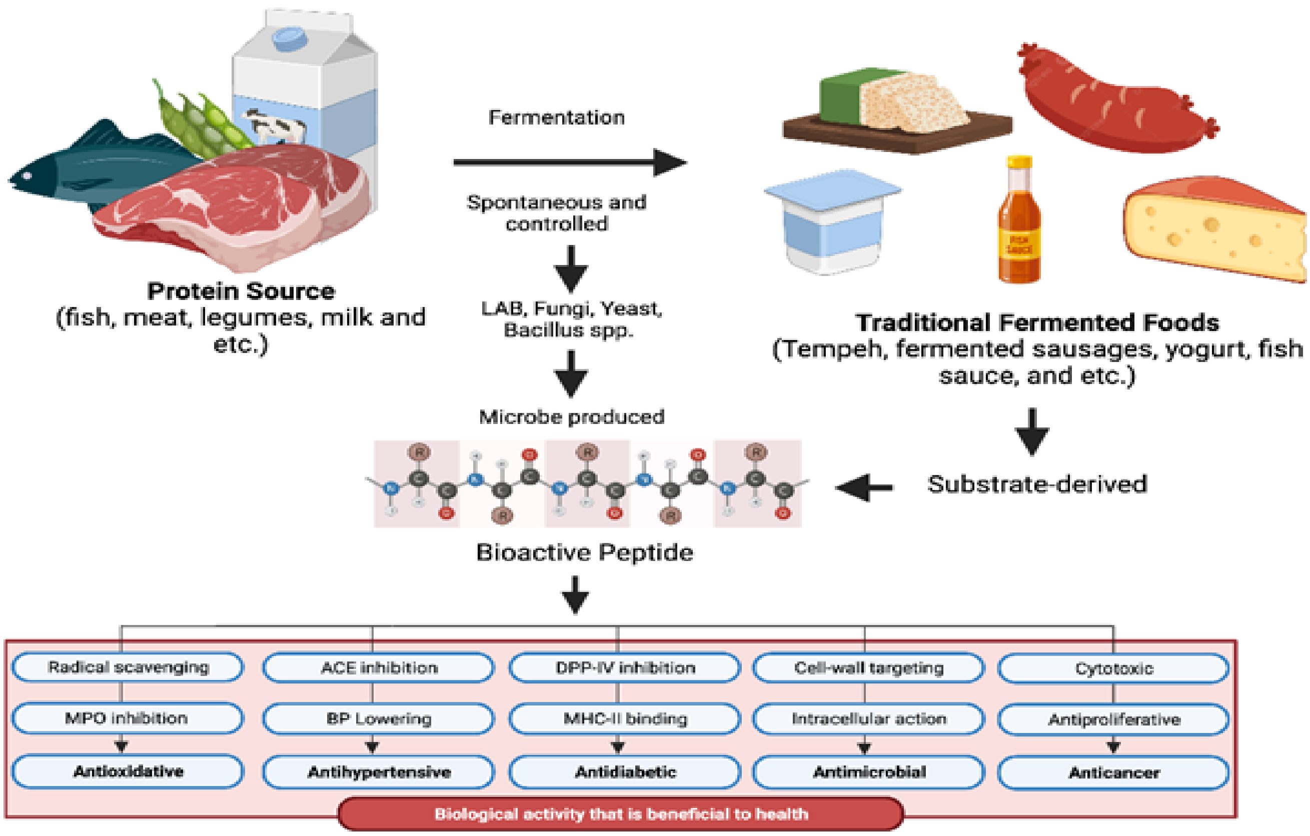

Figure 2. Bioconversion of protein from food sources into peptides with certain functional properties contained in traditional food products through a fermentation process.

Table 1. A type of high protein food which is a source of production of BPs

Foods	Peptide sequences	Bioactivity	Ref.
Cow's Milk	VPP, IPP, LKP, ALPM, PGPIHD, VAGTWY, DN, IPI	Antihypertensive;	(Liu *et al.*, 2015)
	Not specified	Antithrombotic; Hypocholesterolemia	(Rendon-Rosales *et al.*, 2019)
	RELEELNVPGEIVE, YQEPVLGPVRGPFP, EPVLGPVRGPFPIIV, PVLGPVRGPFPIIV, VLGPVRGPFPIIV, LGPVRGPFPIIV, APSFSDIPNPIGSENSEKTTMPLW, SFSDIPNPIGSENSEKTTMPLW, FSDIPNPIGSENSEKTTMPLW, SDIPNPIGSENSEKTTMPLW, DIPNPIGSENSEKTTMPLW, PNPIGSENSEKTTMPLW, PIGSENSEKTTMPLW, IGSENSEKTTMPLW, SENSEKTTMPLW, YQEPVLGPVRGPFPIIV, QEPVLGPVRGPFPIIV	Antihypertensive;	(Ha *et al.*, 2015)
	TVPYMFEN	Antimicrobial	(Hati *et al.*, 2018)
	IPAV	Anti-inflammatory; Antioxidant; Immunomodulatory	(Oyama *et al.*, 2017)
Buffalos Milk	LQDKIHP, VLPVPQK, KIHPFAQTQ, VYPFPGPIPK, FVAPFPE, YPFPGPIPK, LVYPFPGPIPK, LVYPFPGPIPKSLPQN, IKHQGLPQ, YQEPVLGPVRGPFPIIV, LYQEPVLGPVRGPFPIIV	Antioxidant; Antimicrobe	(Taha *et al.*, 2017)
	ACE-inhibitory (FPGPIPK, IPPK, IVPN, and QPPQ) and antioxidant (YPSG, HPFA, and KFQ)	Antihypertensive; Antioxidant	(Abdel-Hamid *et al.*, 2017)
Camel Milk	KDLWDDFKGL dan MPSKPPLL	Antidiabetic	(Mudgil *et al.*, 2019)
Goat Milk	LYQEPVLGPVRGPFPI, YQEPVLGPVRGFPIL, VQSWMHQPPQPLSPT	Hypocholesterolemia	(Mahdi *et al.*, 2018)
Patin Fish	APGHPVPA, GVAAPGHP, LVVAIPAALGHA	Antioxidant	(Najafian and Babji, 2014)
Skipjack Fish	MLVFAV dan DLDLRKDLYA	Antihypertensive; Antioxidant	(Intarasirisawat *et al.*, 2013)
Shrimp	SV, IF, WP	Antihypertensive; Antioxidant	(Kleekayai *et al.*, 2015)
Salmon	GAAEKGVPLF and GVDNPGHPF	Antioxidant	(Vo *et al.*, 2018)
Sardinella	LDDFKL, GTEDELDKY	Antithrombotic	(Jemil *et al.*, 2016)
Soybean	FNKYGR, FPFPRPPHQK, GQSSRPQDRHQK, QRFDQRSPQ, ERQFPFPRPPHQK, GEIPRPRPRPQHPE, EQPRPIPFPRPQPR	Lipopolysaccharide -neutralizing	(Taniguchi *et al.*, 2019)
	Not specified	Antioxidant	(Tonolo *et al.*, 2019)
Pea seed	KEDDEEEEQGEEE	Antihypertensive	(Jakubczyk *et al.*, 2013)
Kidney bean	Not specified	Antioxidant	(Limón *et al.*, 2015)
Maize	LPP, VHLPPP, FNQ, FSQ, LAY, LNPA LSPA, AF, LPN, FYQQ ASY, LVP, FLP, LQP, LSP, LRP	Antihypertensive	(García-Moreno *et al.*, 2015)
	YA, LMCH	Antioxidant	(Tang *et al.*, 2015)
Amaranth	YL, RW, RR, KL, LF, EG GT, HK, RP, HP, PG, GG	Antihypertensive	(Montoya-Rodríguez *et al.*, 2014)
	PYY, RWY, WY, RW PWW, PWR, PW, PWY WYS	Antioxidant	(Montoya-Rodríguez *et al.*, 2014)
	GGV, IVG, VGVL	Antidiabetic	(Soares *et al.*, 2015)

ues, and indigenous culinary traditions but also highlight the connection between local resources, customs, history, and religious beliefs, forming a cohesive social identity (Romulo and Surya, 2021; Surya, 2024; Zannou *et al*., 2022). Beyond their cultural and symbolic significance, traditional foods also play a critical role in promoting tourism, generating economic opportunities, and supporting health and well-being. Among them, fermented foods, particularly high-protein fermented foods (HPFF), have gained increasing scientific and public interest due to their nutritional and functional potential. The diversity of Indonesia's HPFF arises from variations in geography, environment, raw material availability, and local preferences, reflecting both the ecological and cultural richness of the archipelago (Prihanto *et al*., 2024). Examples of Indonesia's HPFF are detailed in Table 2 and Figure 3.

Recent studies have shown that many high-protein fermented foods (HPFF), particularly those originating from traditional Indonesian practices, are rich sources of bioactive peptides (BPs) small protein fragments released during fermentation that possess specific physiological functions. These peptides have been associated with a wide range of health-promoting activities, including antioxidant, antihypertensive, antimicrobial, antidiabetic, and immunomodulatory effects (Rutherfurd-Markwick, 2012; Abdel-Hamid *et al*., 2017). As interest in functional foods continues to rise, the exploration of BPs from traditional fermented products has gained momentum, not only in research but also in industrial innovation. Evidence of the biological activities derived from Indonesian HPFF is summarized in Table 3, emphasizing their functional potential and supporting their development as bioac

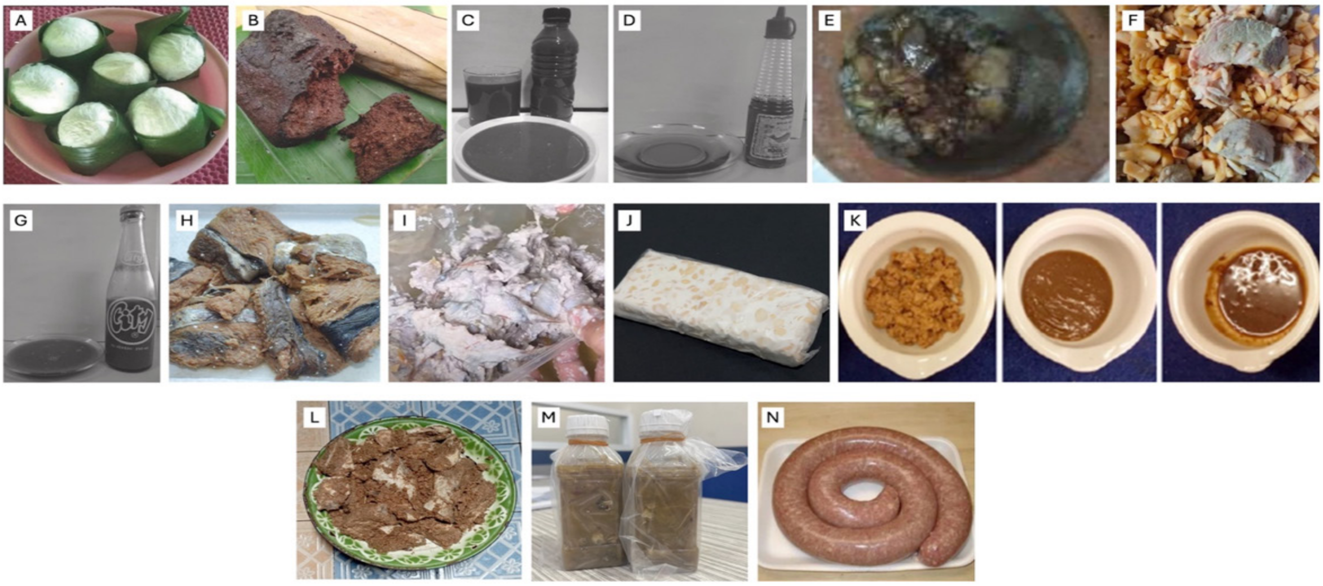

Figure 3. Traditional fermented foods from Indonesia that have the potential as sources of BPs with various biological activities; A) dangke, B) terasi, C) bakasang, D) fish Sauce, E) bekamal, F) cangkuk, G) joruk, H) ina sua, I) bekasam, J) tempeh, K) tauco, L) pekasam, M) rusip, and N) urutan.

Table 2. Indonesian traditional high-protein fermented foods as a sources of BPs

Fermented food	Origins	Culinary application and serving of food	Ref.
Milk-based			
Dangke	Enrekang, South Sulawesi	Yoghurt-like drink or as a side dish. Served with rice and chili sauce, especially when welcoming guests.	(Sa'pang *et al*., 2023)
Dadih	Minangkabau, West Sumatera	As a side dish, eaten with rice, *sambalado* (chili), and sliced onion. Served on important occasions among the Minangkabau.	(Maulid and Ciptandi, 2023)
Meat-based			
Urutan	Bali	Sausages-like food. Often prepared in the *Galungan* Day festival.	(Antara *et al*., 2002)

Table 2. Indonesian traditional high-protein fermented foods as a sources of BPs

Fermented food	Origins	Culinary application and serving of food	Ref.
Bebontot or *buntilan*	Bali	Sausages-like food. Often prepared for religious ceremonies and festivals	(Mulyani *et al*., 2022)
Bekamal	*Osing* people, Banyuwangi	Eaten with rice in a bamboo container as *bekamal* rice. Often prepared on the day of Eid al-Adha or the Feast of Sacrifice.	(Khirzin *et al*., 2023)
Cangkuk	Sorolangun district, Jambi Province	Originally prepared for special occasions like Ramadan and family celebrations	(Mirdhayati and Zain, 2020)
Fish-based			
Terasi	Cham and Mon peoples of Indochina	Often added to chili sauce to make *sambal terasi*, which is widely used in Indonesian dishes	(Herlina and Setiarto 2024a)
Rusip	Bangka Belitung	Commonly used as a condiment for chili sauce and can be consumed either cooked or raw as a side dish	(Baehaki *et al*., 2024)
Bekasam	South Sumatra	Usually served with rice and often served at festivals, religious events and weddings, it is also given as a durable gift to tourists.	(Setiarto and Herlina, 2024)
Joruk	Ogan Komering South Sumatra	As a condiment or side dish.	(Koesoemawardani *et al*., 2021)
Bakasang	Banda Island, Maluku	Commonly used daily as a seasoning and flavoring agent for various dishes	(Wenno *et al*., 2016)
Ina sua	Teon Nila Serua, Central Maluku	It is usually eaten with rice, cassava, sweet potatoes, or traditional ingredients such as *sageru*. It is also eaten during traditional ceremonies such as Christmas and birthdays.	(Persulessy *et al*., 2020)
Budu	West Sumatra	Consumed raw and as a side dish with meals.	(Marlida *et al*., 2023)
Cincalok or *ronto*	Riau and West Kalimantan	Typically consumed with rice or cooked with the addition of various spices such as shallots, garlic and other herbs and spices.	(Murwani *et al*., 2024)
Chao teri	South Sulawesi	Commonly consumed as a side dish, often preserved with mango pickles and stone banana, or used as a flavor enhancer.	(Syahriati *et al*., 2021)
Legume-based			
Tauco	Cianjur, West Java	Use to season many dishes.	(Herlina *et al*., 2022)
Tempeh	Central Java	Commonly used in cuisine and on festive occasions. Sometimes served at important social gatherings such as *kenduri* or *selamatan*, where it is considered a sacred offering in thanksgiving ceremonies.	(Romulo and Surya, 2021)
Gembus	Central Java	Commonly used in cuisine.	(Fajri *et al*., 2024)
Oncom	West Java	Commonly used in cuisine.	(Surya and Romulo, 2023)

Table 3. Biological activity of Indonesian traditional fermented food

Source	Products	Protein substrate	Method process	Biological activity	Peptide sequences	Ref.
Milk	*Dadih*	Buffalo Milk	Controlled fermentation (*Lactobacillus, Streptococcus, Leuconostoc, Lactococcus*)	Antihypertensive	-	(Chalid *et al.*, 2018)
	Dadih	Buffalo Milk	Uncontrolled fermentation	Antioxidant	-	(Kusumaningtyas and Utami, 2020)
	Dadih	Buffalo Milk	Uncontrolled fermentation	Antioxidant Antimicrobial	-	(Chalid and Hartiningsih, 2013)
	Dadih	Buffalo Milk	Uncontrolled fermentation	Antioxidant	-	(Chalid *et al.*, 2021)
	Dadih	Buffalo Milk	Uncontrolled fermentation	Antimicrobial	-	(Soenarno *et al.*, 2013)
	Dangke	Cow Milk	Controlled fermentation (*L. plantarum*)	Antimicrobial	-	(Maruddin *et al.*, 2018)
	Dangke	Cow Milk	Uncontrolled fermentation	Antimicrobial	-	(Soenarno *et al.*, 2013)
Meat	*Cangkuk*	Buffalo meat	Uncontrolled fermentation	Antihypertensive	-	(Mirdhayati and Zain, 2020)
	Bebontot	Chicken meat	Uncontrolled fermentation	Antioxidant	-	(Okarini *et al.*, 2019)
Fish	*Joruk*	*Rastrelliger kanagurta*	Uncontrolled fermentation	Antioxidant	-	(Anggrahini *et al.*, 2020)
			Uncontrolled fermentation	Antihypertensive	-	(Agustiari *et al.*, 2019)
	Bakasang	*Katsuwonus pelamis*	Controlled fermentation (*L. casei, L. farciminis* and *L. plantarum*)	Antihypertensive	ALPHA, FQP, DMIPAQK, IKP, LYP, SKVPP, IY	(Nurmahdi *et al.*, 2017; Wenno *et al.*, 2016)
	Bekasam	*Chanos chanos*	Uncontrolled fermentation	Antihypertensive	-	(Wikandari *et al.*, 2011)
			Controlled fermentation (*L. plantarum B1765*)	Antihypertensive	-	(Wikandari and Yuanita, 2016)
		Rasbora argyrotenia	Controlled fermentation (*L. acidophilus*)	Hypocholes-terolemia	KGENYNTG, VTPNLRPKA, AEVVAFLNK, EAIEAIADTMKK	(Rinto and Oktaviani, 2017)
			Controlled fermentation (*L. acidophillus*)	Antioxidant	-	(Rinto *et al.*, 2023)
	Pekasam	*Oreochromis niloticus*	Uncontrolled fermentation	Anti-adherence, antimicrobial	-	(Putri *et al.*, 2021)
		Loma fish	Controlled fermentation (*L. plantarum* IFRPD P15)	Antioxidant	AIPPHPYP, IAEVFLITDPK	(Najafian and Babji, 2018)
	Budu	*Ilisha melastoma*	Uncontrolled fermentation	Antioxidant	LDDPVFIH, VAAGRTDAGVH	(Najafian and Babji, 2019)
	Rusip	*Stolephorus* sp.	Uncontrolled fermentation	Antihypertensive	-	(Rinto *et al.*, 2021; Rinto *et al.*, 2019)
			Uncontrolled fermentation	Antioxidant, anti-cholesterol	-	
		Stolephorus sp.	Uncontrolled fermentation	Anti-diabetic	-	(Kurnianto *et al.*, 2025)

Table 3. Biological activity of Indonesian traditional fermented food

Source	Products	Protein substrate	Method process	Biological activity	Peptide sequences	Ref.
	Shrimp paste	Shrimp	Uncontrolled fermentation	Antioxidant, antihypertensive	WP, SV, IF	(Kleekayai *et al.*, 2015)
Legume	*Tempeh gembus*	Soybean	Uncontrolled fermentation	Antioxidant	-	(Agustina *et al.*, 2018)
	Tempeh	Soybean	Controlled fermentation (*R. microsporus*)	Antihypertensiv, antithrombotic, antioxidant, surface tension	-	(Gibbs *et al.*, 2004)
			Controlled fermentation (*R. microsporus*)	Antioxidant	-	(Watanabe *et al.*, 2006)
			In silico Fermentation Simulation	Antihypertensiv, Antidiabetic	LLF, VVF, RHK, VH, AHK,	(Tamam *et al.*, 2021)
			Controlled fermentation (*R. oligosporus*)	Antihypertensiv, Antidiabetic, Antioxidative and antitumor	VH ALEP GP	(Tamam *et al.*, 2019)
			Controlled fermentation (*R. oligosporus*)	Antioxidant Antihypertensiv, and antidiabetic	IGDLLK, PIEVPAK IGEPGVGK, PLVLYKRVE, KEADGSLVWKQSLQK, QDEDEDEDKPRPSR, IGEPGVGK, QLERRKKVDDGIH, RVDEVRKPTIQINP, VSVQMQVSEGV, WDSEGGIGALEK	(Sitanggang *et al.*, 2020)
	Tempe benguk	*Canavalia ensiformis*	Controlled fermentation (*R. oligosporus*)	Antihypertensive	DLGKAPIN, GKGRFVYG, PFMRWR, DKDHAEI, LAHLYEPS, KIKHPEVK, and LLRDTCK	(Puspitojat *et al.*, 2019)
	Tempeh Koro kratok	*Mucuna pruriens*	Controlled fermentation (*R. oligosporus*)	Antihypertensive	-	(Rizkaprilisa and Hapsari, 2022)
		Phaseolus lunatus	Controlled fermentation (*R. oligosporus*)	Antihypertensive	-	(Rizkaprilisa and Hapsari, 2022)
	Tauco	Soybean	Controlled fermentation (step 1 (*Koji*): *Geobacillus, Weissella, Bacillus, Staphylococcus, Streptococcus;* step 2 (Moromi): *Pediococcus, Weissella, Enterococcus, Staphylococcus, Geobacillus*)	Antioxidant, antimicrobial, antihypertensive, antidiabetic	-	(Herlina and Setiarto, 2025)

tive-rich foods with both local and global significance (Dziuba and Dziuba, 2014).

3.2 Discussion

3.2.1 Fermentation-derived functional peptides

Fermentation is also the most widespread food processing technique and has been localized, shaped by geographic, environmental, and cultural factors, as well as the availability of raw materials (Prihanto *et al*., 2024; Zannou *et al*., 2022). These influences have led to a rich diversity of fermented foods worldwide, each reflecting local traditions and ecological adaptations. In Indonesia, for example, *tempeh*, a fermented soybean product, has served as an affordable protein source, particularly in Java and Bali, where it functions as a meat substitute (Ahnan-Winarno *et al*., 2021; Romulo and Surya, 2021). In eastern Indonesia, the high availability of fish led to the development of *Ina sua*, a fermented fish product from Maluku created to address protein deficiency during periods of limited fishing activity (Persulessy *et al*., 2020). In Sumatera, *dadih* (or *dadiah*), a fermented buffalo milk product with a yogurt-like texture, emerged from the Minangkabau people's reliance on buffaloes for agriculture, transportation, and sugar production (Herlina and Setiarto, 2024b).

Beyond its nutritional and cultural value, fermentation contributes fermentation also contributes to the development of flavor and the generation of BPs (Trapsilo *et al*., 2020). BPs are specific short protein fragments (typically 2–20 amino acids, <6 kDa) that exhibit health-promoting properties (Sarmadi and Ismail, 2010; Hernández-Ledesma *et al*., 2014). These peptides are released from their parent proteins through hydrolysis processes, either enzymatically (e.g., digestion, *in vitro* enzymatic treatment, and microbial fermentation) or non-enzymatically (e.g., heating or acid hydrolysis) (Abdel-Hamid *et al*., 2017). While non-enzymatic methods are cost-effective, they may disrupt protein structures and generate unwanted by-products such as lysinoalanine, thereby reducing biological activity (Ulug *et al*., 2021). According to McKerchar *et al.* (2023), lysinoalanine is a compound formed during protein hydrolysis that can reduce the nutritional value of food and has safety implications for humans. These safety implications arise due to suspected toxicity, although the mechanism is not well understood and the effects depend on the source, dose, duration, and species involved (Friedman, 2008).

The growing scientific interest in BPs is reflected in the BIOPEP-UWM database, which has cataloged over 4,000 BP sequences to date (Minkiewicz *et al*., 2019). These peptides have been associated with a wide range of bioactivities, including antihypertensive, antioxidant, antidiabetic, antimicrobial, cholesterol-lowering, and immunomodulatory effects (Zou *et al*., 2016; Khan *et al*., 2018; Chalamaiah *et al*., 2019; Yan *et al*., 2019). Their functionality is strongly influenced by structural characteristics, such as amino acid sequence, chain length, molecular weight, net charge, and the position of residues at the N- and C-terminal ends (Karami and Akbari-adergani, 2019). Specific structural attributes of BPs, such as the sequence of constituent amino acids, contribute to distinct biological activities (Fitzgerald *et al*., 2004; Rachman *et al*., 2023). For instance, hydrophobic peptides demonstrate superior antioxidant potential by interacting more effectively with hydrophobic targets on cell membranes (Zou *et al*., 2016; Himaya *et al*., 2012). In contrast, the antimicrobial activity of peptides is largely governed by molecular weight, hydrophobicity, and cationic charge, which allow them to disrupt the integrity of negatively charged bacterial membranes (Lei *et al*., 2019; Kurnianto *et al*., 2022). For ACE-inhibitory activity, short-chain peptides such as di- and tripeptides are more effective due to their enhanced ability to cross intestinal epithelial cells and resist degradation during gastrointestinal digestion (Shen and Matsui, 2019).

3.2.2 Food as sources of bioactive peptides

Dairy products like milk and cheese are prominent sources of BPs with diverse biological activities, including antihypertensive, antithrombotic, antidiabetic, antioxidant, and antimicrobial properties (Mohanty *et al*., 2016; Pritchard *et al*., 2010; Choi *et al*., 2012; Sanchez and Vazquez, 2017). In Indonesia, traditional fermented foods, deeply rooted in regional culinary heritage, are reported to contain BPs with various biological activities, highlighting their potential as a significant BP source (Chourasia *et al*., 2021; Padhi *et al*., 2022). Animal-derived BPs are primarily sourced from milk, fish, meat, and eggs (Abd-Talib *et al*., 2022; Zambrowicz *et al*., 2015), with milk and its derivatives being the most significant due to their high digestibility (Chai *et al*., 2020). Milk proteins, particularly casein, undergo fermentation catalyzed by LAB, which possess a robust proteolytic system (Elfahri *et al*., 2014). LAB hydrolyze casein into oligopeptides (4–18 amino acids) via extracellular enzymes, followed by further degradation into shorter peptides or amino acids by intracellular enzymes (Elfahri *et al*., 2014). These peptides are subsequently released into the medium. Among the BPs derived from fermented milk, ACE inhibitor peptides are well-documented for their antihypertensive properties (Rendon-Rosales *et al*., 2019).

Various studies show that BPs can be obtained from other animal sources, such as meat and various fish species (Sanchez and Vazquez, 2017). For example, the production of fermented meat sauce from fermented pork, which was produced using *koji* for 24 weeks, was reported to have high antioxidant activity (>90% hydroxyl radical). The identification results showed that a low molecular weight peptide (406.26 Da) and two other unidentified tripeptides were involved with the QYP sequence (Ohata *et al.,* 2016). Yu *et al.* (2020) reported pork sarcoplasmic and myofibrillar proteins fermented using *L. plantarum* CD101 and *S. simulans* NJ201 for four days at 30°C had antioxidant peptide activity, in which a large amount of the activity was due to hydrophobic peptides released from sarcoplasmic proteins during the fermentation process. Another study on sarcoplasmic protein catfish showed high 2,2-diphenyl-1-picrylhydrazyl (DPPH) and 2,2'-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid (ABTS) radical-scavenging activities. The identification results showed the peptides PGHPVPA, GVAAPGHP, and LVVAIPAALGHA, in which hydrophobic (Val), hydrophilic (His and Pro) and acidic (Asp) residues in the peptide sequences are believed to contribute to antioxidant activity (Najafian and Babji, 2014). LDDFKL and GTEDELDKY peptide sequences from sardines were also reported to exhibit antithrombotic activity (Jemil *et al*., 2016).

Apart from animal sources, there is increasing interest in the benefits of BPs derived from plant sources such as cereals and legumes (Chai *et al.*, 2020). Cereals have a relatively high protein content (10 – 15%), so they can be used as a fermentation substrate for the growth of probiotics such as *Lactobacillus* and *Bifidobacterium*. Like cereals, legumes are also the primary substrate for fermented foods in Asian countries (Chi and Cho, 2016). Studies showed that several legume-based fermented foods from Asia have various functional activities such as anticancer, antidiabetic, antitumor, antihypertensive, and antioxidant antiviral (Kumari *et al.*, 2022; Nurkholis *et al.*, 2022). Tamam *et al.* (2021) reported that *tempeh*, which is soybeans fermented by *R. oligosporus,* has health benefits ranging from antihypertension (AV, GL, GF, PL, AP, DM, PAP, DY, IAK, ALEP, VIKP, RIY), antidiabetic (PS, SV, AE, SI, EP, HV, VH, PF, RN, NR, DY and HF), antitumor (EF) and antioxidant (KP, MY). Another study on *natto,* which is soybeans fermented by *B. subtilis,* showed neutralizing and angiogenic LPS activity with identified peptide sequences KFNKYGR, FPFPRPPHQK, GQSSRPQDRHQK, QRFDQRSPQ, ERQFPFPRPPHQK, and EQPRPIPFPRPQRR (Taniguchi *et al*., 2019). Antidiabetic activity by inhibiting the DPP-IV enzyme was also reported in *natto* (Sato *et al*., 2018).

3.2.3 High-protein fermented foods in Indonesia

HPFF in Indonesia are derived from animal and plant-based sources, such as milk, fish, meat, and legumes. Milk and its derivative products are a source of easily digestible protein and the primary source of BPs (Chai *et al.*, 2020; Korhonen, 2009). Notable milk-based HPFFs include *dangke* and *dadiah*, both recognized for their functional potential. *Dangke* is a traditional soft cheese from Enrekang, South Sulawesi, made from buffalo milk and papaya latex, which is produced traditionally by fermentation techniques by the local community (Yusuf *et al.*, 2022; Zakariah *et al.*, 2022). *Dangke* naturally contains a variety of lactic acid bacteria, such as *L. fermentum*, *L. plantarum*, and *L. acidophilus* which play a role in the fermentation process and the formation of various BPs (Nur *et al.*, 2017; Zakariah *et al.*, 2022; Jatmiko *et al.*, 2017). In contrast, *dadih* or *dadiah* is a traditional food from Minangkabau made from buffalo milk which is fermented spontaneously in a bamboo tube (Arnold *et al.*, 2021). *Dadih* is similar to yoghurt, with a smooth and shiny surface, even consistency, creamy colour, pleasant aroma, and sour taste (Surono, 2016). Since it is a product of spontaneous fermentation, various LAB (*Leuconostoc mesenteroides, Lactococcus lactis* subsp. *lactis, Levilactobacillus brevis, Lacticaseibacillus casei, Lactiplantibacillus plantarum* subsp. *plantarum, Enterococcus faecium, Limosilactobacillus fermentum,* and *Lacticaseibacillus rhamnosus*) and yeast (*Saccharomyces cerevisiae, Candida metapsilosis*, and *Kluyveromyces marxianus*) grows during the fermentation process (Wirawati, 2018; Nuraida, 2015; Jatmiko *et al*., 2017).

Fermented meat also contributes to Indonesia's HPFF diversity, though this is not well-known. Examples of these include *urutan*, *bebontot*/*buntilan*, *bekamal*, and *cangkuk*. *Urutan*, a traditional Balinese sausage made from pork, spices, sugar, and salt, undergoes sun-dried fermentation for five days and is associated with the Galungan festival (Antara *et al.*, 2002). *Bebontot or buntilan*, also Balinese, is naturally fermented without added LAB, combining spiced meat wrapped in banana leaves and dried for four to five days (Mulyani *et al.*, 2022). *Bekamal*, a meat preservation method from Banyuwangi dating to the 1400s, involves fermenting finely chopped beef, mutton, or chicken with salt and sugar in clay storage (*kendil*) for 1–3 months (Khirzin *et al*., 2023). Lastly, *cangkuk*, from Sorolangun, Jambi, is a fermented mix of buffalo meat, bamboo shoots, and salt, traditionally prepared for Ramadan and family celebrations (Mirdhayati and Zain, 2020).

Indonesia boasts a variety of traditional HPFF derived from legumes, including *tauco*, *tempeh*, *on-*

com, *gembus*, and soy sauce (Surono, 2016). *Tauco*, a fermented soybean paste introduced by the Hokkien Chinese, is popular in coastal areas like Cianjur, West Java. Known for its umami flavor, it is produced through two fermentation stages: *koji/meju* and *brine/moromi* (Herlina *et al*., 2022). *Tempeh*, native to Central Java, is a fermented soybean product made using *Rhizopus sp.* as a starter culture (Nout and Kiers, 2005; Jeleń *et al*., 2013). Variations of *tempeh* include versions made from other legumes such as *koro kratok* (*Phaseolus lunatus L.*), soy-pulp products, jack beans (*Canavalia ensiformis*), and *Mucuna pruriens*. It holds cultural significance and is often served at important ceremonies like *kenduri* or *selamatan* (Romulo and Surya, 2021). *Gembus*, or *tempeh gembus*, is made from tofu dregs fermented with *Rhizopus sp.* and is widely consumed in Central Java (Fajri *et al*., 2024). Meanwhile, *oncom*, a mold-fermented soy food from West Java, has been integral to Sundanese cuisine for centuries. It exists in two types: red *oncom*, made from soy pulp (*okara*) using *Neurospora sp.*, and black *oncom*, made from peanut press cake using *Rhizopus oligosporus* or *Mucor sp.*, with the types distinguished by the spore color of the molds used (Surya and Romulo, 2023).

Indonesia, with its rich fisheries resources, has a diverse array of traditional HPFF derived from fish. *Terasi*, a fermented shrimp paste, is a staple in Indonesian households, enhancing the flavor of local dishes, particularly in *sambal terasi*. It is produced by salting, grinding, sun-drying, and fermenting shrimp, a tradition rooted in the Cham and Mon cultures of Indochina (Herlina and Setiarto, 2024a). *Rusip*, from Bangka Belitung, is made from anchovies, salt, and palm sugar, fermented for use as a condiment or side dish, either raw or cooked (Baehaki *et al*., 2024). *Bekasam*, known for its umami flavor, is a fermented freshwater fish product typically fried with shallots, garlic, and chilies, and commonly served at festivals and weddings in South Sumatra (Setiarto and Herlina, 2024). *Joruk*, also from South Sumatra, is made by fermenting *wader* fish (*Rasbora* spp.) with salt, palm sugar, and cooked rice for one to two weeks. Unlike *bekasam*, *joruk* contains palm sugar and rice, highlighting regional variation in fermentation practices (Koesoemawardani *et al*., 2021). *Bakasang*, a fermented skipjack tuna product from Maluku, is prepared with 20% salt and fermented for 7–14 days. It serves as a daily seasoning and staple for the Banda community (Koesoemawardani *et al*., 2021). Similarly, *ina sua*, from Central Maluku, involves fermenting fish in a salt solution and is consumed with rice or traditional staples like cassava and sweet potatoes. It is a crucial food source during fishing downtimes and features prominently in traditional ceremonies (Persulessy *et al*., 2020).

Other Indonesian Traditional HPFF derived from fisheries product called *budu* from West Sumatra. *Budu* is produced through prolonged natural fermentation of marine fish using microbes from the fish and its environment. The process includes salting, sun-drying, and aerobic fermentation, resulting in a flavorful and durable product (Marlida *et al*., 2023). *Cincalok*, from West Kalimantan, is made from small shrimp (*Acetes* sp.) mixed with salt and sugar, then fermented for 3–7 days (Murwani *et al*., 2024; Nurhayati *et al*., 2024). Its umami flavor, derived from free glutamate produced during fermentation, makes it a popular condiment or rice accompaniment (Nofiani and Ardiningsih, 2018). *Chao teri*, from South Sulawesi, is a fermented anchovy dish valued for its thick, pasta-like texture and distinctive sour and salty taste. Like *Cincalok*, its fermentation process enriches both its flavor and nutritional profile, making it a prized element in local culinary traditions (Syahriati *et al*., 2021).

3.2.4 Bioactive peptides in Indonesian traditional fermented food

Dairy products like milk and cheese are prominent sources of BPs with diverse biological activities, including antihypertensive, antithrombotic, antidiabetic, antioxidant, and antimicrobial properties (Mohanty *et al*., 2016; Pritchard *et al*., 2010; Choi *et al*., 2012; Sanchez and Vazquez, 2017). In Indonesia, traditional fermented foods, deeply rooted in regional culinary heritage, are reported to contain BPs with various biological activities, highlighting their potential as a significant BP source (Chourasia *et al*., 2021; Padhi *et al*., 2022). Animal-derived BPs are primarily sourced from milk, fish, and meat (Abd-Talib *et al*., 2022), with milk and its derivatives being the most significant due to their high digestibility (Chai *et al*., 2020). Milk proteins, particularly casein, undergo fermentation catalyzed by LAB, which possess a robust proteolytic system (Elfahri *et al*., 2014). LAB hydrolyze casein into oligopeptides (4–18 amino acids) via extracellular enzymes, followed by further degradation into shorter peptides or amino acids by intracellular enzymes (Elfahri *et al*., 2014). These peptides are subsequently released into the medium. Among the BPs derived from fermented milk, ACE inhibitor peptides are well-documented for their antihypertensive properties (Rendon-Rosales *et al*., 2019).

Dangke and *dadih*, Indonesian traditional fermented dairy products, contain diverse LAB that contribute to BPs formation and functional properties. *Dangke* harbors LAB such as *L. fermentum*, *L. plan-*

tarum, and *L. acidophilus*, in which BPs with reported antidiabetic and antimicrobial activities (Zakariah *et al*., 2022). Sasmita *et al.* (2023) demonstrated that consuming 1.5 g/200 g body weight of *dangke* for 14 days reduced fasting blood glucose by 29%. Additionally, *dangke* exhibits antimicrobial effects against *E. coli* FNCC 0091 and *S. aureus* FNCC 0047, with inhibition zones of 26 mm and 13 mm, respectively (Soenarno *et al*., 2013). Meanwhile, *dadih* undergoes spontaneous fermentation, enriched with LAB such as *L. mesenteroides*, *L. lactis*, *L. brevis*, and *L. rhamnosus*, along with yeast species (*S. cerevisiae*, *C. metapsilosis*, *K. marxianus*) (Nuraida, 2015; Wirawati, 2018). The proteolytic activity of LAB in *dadih* hydrolyzes milk proteins into BPs with ACE inhibitory (87.75%) and antioxidant (86.46%) properties. The peptide fraction below 3 kDa even exhibited ACE inhibition up to 99.3%, highlighting *dadih's* antihypertensive potential (Kusumaningtyas and Utami, 2020). Meanwhile, Fermented meat products like *cangkuk* exhibit antihypertensive activity with ACE inhibition of 36.5–79.6%, influenced by bamboo shoot preparation and its ratio with meat, with the highest inhibition achieved at a 1:0.75 ratio (Mirdhayati and Zain, 2020). Similarly, *bebentot* demonstrates antioxidant activity, with radical scavenging increasing after 120 hours of fermentation and glutamic acid being the predominant amino acid (Okarini *et al*., 2019).

BPs from fermented legume products, particularly tempeh, have been widely studied for their health benefits and functional properties. Proteomic analysis of soy tempeh identified peptides (189.12–573.40 Da) with antihypertensive, antidiabetic, antioxidant, and antitumor activities (Tamam *et al*., 2019). *Koro kratok* tempeh (*Phaseolus lunatus L.*) exhibits ACE inhibitory activity of up to 84.97%, which increases with extended fermentation and peptide fractionation (Handayani *et al*., 2020). Similarly, peptides from *koro benguk* tempeh (*Mucuna pruriens*), particularly those <1 kDa, show ACE inhibition after simulated digestion (Rizkaprilisa and Hapsari, 2022). Another fermented legume product, *tauco*, contains low molecular weight peptides contributing to umami flavor and bioactivities, including antioxidant, antidiabetic, and antihypertensive properties. Peptidomic analysis identified 649 peptides with up to 31 amino acid residues, which accounted for 87.50% of the variation in peptide profiles (Herlina *et al*., 2022). Despite these findings, other traditional fermented products like *oncom* and *gembus* remain underexplored and warrant further investigation for their BP potential.

Traditional fermented fish products in Indonesia have shown potential as sources of BPs with diverse health benefits, though studies remain limited. In fermented fish products, *rusip* exhibits anti-cholesterol shown by 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibition of 16.66–50%, antioxidant (37.90–51.36% ABTS activity), and antihypertensive (ACE inhibition of 63.79–95.76%) properties, mainly attributed to peptides <1 kDa (Rinto *et al*., 2019). The study by Kurnianto *et al.* (2025a) also demonstrated the potential bioactivity of rusip as an antidiabetic through an α-glucosidase (53.8-59.8%) and α-amylase (40.3-46.7%) inhibitory mechanism, as well as reducing fasting blood glucose, HbA1c, and HOMA-IR and improving insulin levels, HOMA-B and QUICKI in STZ-NA-induced diabetes rats. Likewise, *bakasang* achieves ACE inhibition of 68.8% with identified peptide sequences (294.35–801.96 Da) and *in vivo* studies showing reduced MDA levels and iNOS expression in hypertensive rats (Nurmahdi *et al*., 2017). *Bekasam* demonstrates ACE inhibitory (35.67–51.77%) and HMG-CoA reductase inhibitory (85.71–92.86%) activities, linked to peptides <3 kDa (Wikandari *et al*., 2011). The study by Kurnianto *et al.* (2025b) on shrimp paste also demonstrated strong bioactivity, including antioxidant activity (3.90 mg AEAC/g sample by DPPH assay and 8.76 ± 0.22 mg AEAC/g sample by FRAP assay), antidiabetic potential via α-amylase and α-glucosidase inhibition (IC50 of 1.95 and 7.24 mg/mL), and antimicrobial effects against E. coli (32.78 mm) and S. aureus (30.85 mm).

Fermentation in fish produces protein fragments such as bioactive peptides whose biological activity depends on structural characteristics such as amino acid sequence and composition, terminal residue type, hydrophobicity, molecular weight, and net charge (Zaky *et al*., 2022; Nirmal *et al*., 2022). Bashir *et al.* (2020) reported that antioxidant peptides from mackerel consist of 10–19 residues with molecular weights of 547–1049 Da. These peptides also exhibit amphiphilic properties (containing both hydrophobic and hydrophilic residues), where the hydrophobic portion plays a role in providing electrons to stabilise DNA, while the hydrophilic portion acts as a proton donor and metal chelator (Yang *et al*., 2020). Gui *et al.* (2022) and Lima *et al.* (2019) reported several types of residues known to enhance antioxidant activity, such as Tyr, Trp, Ala, Pro, Gly, and Arg at the peptide terminal. Similar to antioxidant peptides, antihypertensive peptides have low molecular weights, consist of 7–8 residues, and have hydrophobicity of 10–11 kcal/mol (Tamam *et al*., 2018). Studies on the peptides ALGPQFY, LVPPLA, and LAPPTM from the muscle of Actinopyga lecanora showed that sequences with medium hydrophobicity tend to have the most effective ACE inhibition (Auwal *et al*., 2019). Several residues such as Tyr, Phe, Cys, Trp, Leu, Pro, His, and Arg have been shown to affect hydrophobicity, resulting in increased ACE hydrolysis and ACE receptor binding (Abdelhedi and Nasri 2019; Ketnawa *et al*., 2019).

Unlike antioxidant and antihypertensive peptides, antimicrobial peptides have higher molecular weights, longer residue sequences, and are cationic and highly hydrophobic (Tamam *et al*., 2018; Kurnianto *et al*., 2022; Lei *et al.,* 2019). Studies by Tang *et al.* (2014) and Zhang *et al.* (2019) showed that the antimicrobial properties of the peptide RLFRHAFKAVLRL (from anchovy) and the peptide FAHWPDLGPGSPSVKKHGKVIM (from Japanese eel muscle) have a positive charge of +4 (pI = 12.71) and +2 (pI = 10.30) and contain 61% hydrophobic residues. The hydrophobic nature facilitates electrostatic binding interactions between the peptide and microbial cell membranes, leading to cell damage and death (Liang *et al*., 2020; Mohanty *et al*., 2016). The peptide compound derived from fermented fish is also reported to exhibit antidiabetic activity (Kurnianto *et al*., 2025a). The presence of hydrophobic residues is believed to play a crucial role in this activity (Nongonierma and FitzGerald, 2019). Another study reported that the peptide WGDEHIPGSPYH from silver carp bladder exhibits DPP-IV inhibitory activity, which is likely due to the role of the Trp residue (Hong *et al.,* 2020). Hydrophobic residues such as Leu, Iso, Tyr, Val, and pro at the -N terminal are also suspected to be responsible for the antidiabetic activity observed in sturgeon skin hydrolysates, boar-fish meat, and salmon skin (Harnedy-Rothwell *et al*., 2020; Jin *et al*., 2020; Gui *et al*., 2022). Although many studies have demonstrated the bioactivity of these traditional fish fermented products, the precise mechanisms are required for further investigate their full potential and health benefits. For instance, identifying the specific peptides involved in their bioactivity would provide a deeper understanding of their precise mechanisms.

3.2.5 Future prospect

Food-derived BPs are generally considered to be more "natural." Therefore, consumers' perceptions of acceptance of these BPs tend to be higher. However, using BPs derived from food as oral products also has challenges and consequences, one related to regulating BPs. The regulation includes laws, regulations, and licensing systems that govern product production, import, export, and sale. In the context of the biomedical and food industries, this involves various aspects, such as food, drugs, and other products that impact health and nutrition. Most developed countries have strong regulations ensuring the safety and efficacy of BPs products (Gavrish *et al*., 2008). The novelty and potential health and nutritional roles of these BPs and proteins derived from food hydrolysates are so crucial that researchers must understand and engage with existing regulatory systems to translate findings from the laboratory into the real world.

In-silico exploration of BPs, such as QSAR, BIOPEP-UWM, and peptide Cutter from EXPASY, involves methods regarding the activity and structure of peptides in databases and literature (Kurnianto *et al*., 2023). This method can predict the sequence of peptides that may have any bioactivity, their structural-functional relationships, the specific location of the peptides in the parent protein, and their possible mechanism of action (Holton *et al*., 2013). There is ample data on food-derived BPs and the enzymes required to produce BPs from major proteins. However, most only describe endogenous BPs, which have physiological relevance, not those obtained from food (Minkiewicz *et al*., 2019). In addition, the information available in various databases often involves well-characterized and purified proteolytic enzymes, compared to enzymes used commercially for food processing, which are less specific for the substrate and vary in purity.

After the peptides have been produced, either through conventional or in-silico methods, the next step is to ensure the bioactivity of the peptides. However, unlike synthetic drug molecules, which are single entities, BPs targets isolated from foods are usually mixtures of peptides. Purification of these peptides to 99% purity will not only increase costs to unacceptable levels and decrease yields but will also eliminate any beneficial additive or synergistic effects with other peptides present in the entire hydrolysate. BPs are generally hydrophobic, making them less soluble at higher concentrations. Li-Chan *et al.* (2015) recommended preparing various formulations of several different BPs, each with a low concentration but the same level of bioactivity. Proteins from food sources are often hydrolyzed using proteases such as trypsin, pepsin, chymotrypsin, bromelain, ficain, or papain. Although there are several advantages of using enzymatic hydrolysis, such as the absence of residues of toxic chemicals and organic solvents in the final product, using enzymes on an industrial scale greatly increases production costs. One solution is to use cheaper enzyme sources, such as by-products from the meat industry, such as animal-derived pancreas. The peptide mixture produced during hydrolysis (via *in vitro* enzymatic reactions) depends on the complexity of the starting materials. This causes the purification process to take longer; each peptide may require complex purification protocols.

On the other hand, naturally occurring peptides have many advantages compared to peptides produced by enzymatic hydrolysis because these peptides are considered safe (Agyei *et al*., 2018; Erdmann *et al*., 2008). However, the lack of technology on a larger scale and the very expensive purification techniques are limitations for commercializing the extraction of naturally occurring BPs from foodstuffs (Agyei *et al*., 2018). Thus, research should address the challenges associated with production methods for commercializing food-derived BPs. Most of the BPs cannot maintain their original structure after undergoing enzymatic hydrolysis from gastric and intestinal enzymes so these BPs are difficult to absorb as intact bioactive structures into the blood. Recent studies on orally administered nanoparticles may help direct the future commercialization of novel bioactive nutraceutical peptides by increasing their bioavailability and shelf life. In addition, for medical peptides, especially long-chain peptides, the intravenous injection method is a direct and effective way to prevent BPs from being deactivated in the digestive tract and allow the BPs to show their efficacy or bioactivity efficacy, although safety aspects must be carefully evaluated.

4. Conclusion

Traditional Indonesian HPFF made from raw materials such as meat, fish, milk, and legumes has potential BPs content with various biological activities such as antimicrobial, antioxidant, antidiabetic, and antihypertensive. The BPs is formed from a fermentation process generally done traditionally without specific culture starters. Interest in HPFF original BPs is increasing because it is considered more 'natural' and can improve human health. However, lack of technology on a larger scale, very expensive purification techniques, and unclear regulations cause limitations for commercializing the BPs from HPFF. Further studies are required to investigate the unexplored BPs from traditional HPFF as well as their working mechanism or mode of action of each explored bioactive peptide bioactivity. Understanding their bioactivity can help preserve the existence of these traditional foods by highlighting their role in immunity and health functions.

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Authors' Contributions

All authors have contributed to the final manuscript. The contributions of each author are as follows: Muh, Sal, Sis, and Fat; collected the data, drafted the manuscript, and designed the figures. Had, Ngu, Eko, and Din; devised the main conceptual ideas and provided critical revisions to the article. All authors discussed the results and contributed to the final manuscript. Muh and Din; proofread the manuscript and provided advice.

Conflict of Interest

The authors declare that they have no competing interests.

Declaration of Artificial Intelligence (AI)

The author(s) acknowledge the use of Grammarly for check the grammar and punctuation in preparing this manuscript. All AI-generated content was rigorously reviewed, edited, and validated to ensure accuracy and originality. Full responsibility for the manuscript's final content rests with the author(s).

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