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## Food-Derived Bioactive Peptides: From Generation and Identification to Therapeutic and Functional Applications

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### Abstract

Food-derived bioactive peptides have emerged as an important class of naturally occurring compounds with significant potential for promoting human health and preventing chronic diseases. These peptides are encrypted within the primary structure of food proteins and are released through enzymatic hydrolysis, microbial fermentation, food processing, or gastrointestinal digestion. Owing to their structural diversity and multifunctional properties, bioactive peptides have attracted increasing attention from researchers and the food, nutraceutical, and pharmaceutical industries. This review provides a comprehensive overview of the current knowledge on food-derived bioactive peptides, covering their major dietary sources, production strategies, purification methods, and advanced analytical approaches for peptide identification and characterization. Recent developments in high-resolution mass spectrometry, bioinformatics, Artificial Intelligence (AI), and in silico prediction tools have substantially accelerated the discovery and functional evaluation of novel bioactive peptides. The biological activities of food-derived peptides, including antioxidant, antihypertensive, antimicrobial, anti-inflammatory, immunomodulatory, antidiabetic, anticancer, and several emerging health-promoting effects, are critically discussed with emphasis on their underlying molecular mechanisms. Furthermore, current and prospective applications of these peptides in functional foods, nutraceuticals, pharmaceuticals, food preservation, and cosmetic products are highlighted. Despite considerable scientific progress, several challenges remain regarding peptide stability, gastrointestinal bioavailability, large-scale production, and clinical validation. Future advances in biotechnology, precision fermentation, synthetic biology, AI-assisted peptide discovery, and innovative delivery systems are expected to facilitate the translation of food-derived bioactive peptides from laboratory research to commercial and therapeutic applications. Food-derived bioactive peptides represent a rapidly expanding research field with substantial potential for developing sustainable functional ingredients and next-generation health-promoting products.

**Keywords:** Bioactive peptides, Food proteins, Enzymatic hydrolysis, Functional foods, Nutraceuticals, Peptide identification, Biological activities.

## 1 | Introduction

Proteins are among the most abundant and essential biomolecules found in food sources, serving not only as fundamental nutritional components but also as precursors of a wide range of biologically active molecules [1–4]. In recent decades, increasing attention has been directed toward the discovery and utilization of

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bioactive peptides derived from food proteins due to their potential health-promoting properties and applications in pharmaceutical, nutraceutical, and functional food industries [5]. Food-derived bioactive peptides are specific protein fragments, generally consisting of 2-50 amino acids, that exhibit physiological activities beyond their basic nutritional value [6]. These peptides can be released from parent proteins through enzymatic hydrolysis, microbial fermentation, gastrointestinal digestion, or advanced biotechnological approaches. Once generated, bioactive peptides may interact with specific molecular targets and regulate various physiological processes, making them promising candidates for the development of functional ingredients and health-related products [3].

The increasing prevalence of chronic diseases, including cardiovascular disorders, diabetes, obesity, cancer, and inflammatory diseases, has stimulated global interest in naturally derived compounds with preventive and therapeutic potential. Although synthetic drugs remain essential for disease management, concerns regarding adverse effects, drug resistance, and long-term safety have encouraged researchers to explore alternative bioactive molecules from natural sources. Among these natural compounds, food-derived peptides have attracted considerable attention because of their diverse biological activities, high nutritional compatibility, and potential for integration into daily diets [7]. Unlike many plant secondary metabolites and synthetic compounds, bioactive peptides originate from commonly consumed food proteins, which provides advantages in terms of safety, availability, and consumer acceptance. A wide variety of food sources have been investigated as reservoirs of bioactive peptides [6–8]. Animal-derived proteins, particularly milk proteins, represent one of the most extensively studied sources due to their high nutritional quality and rich amino acid composition. Milk-derived peptides obtained from casein and whey proteins have demonstrated numerous biological functions, including Angiotensin-Converting Enzyme (ACE) inhibitory activity, antioxidant effects, antimicrobial properties, and immunomodulatory functions. In addition, marine resources such as fish, shellfish, and other aquatic organisms have emerged as valuable sources of bioactive peptides, particularly collagen-derived peptides with applications in skin health, tissue regeneration, and anti-aging products. Meat proteins have also been recognized as potential sources of functional peptides, including sequences with antioxidant and antihypertensive activities [9].

Plant-derived proteins have gained increasing attention as sustainable and environmentally friendly alternatives for peptide production. Legumes, cereals, oilseeds, and other plant-based materials contain proteins that can be converted into bioactive peptide fractions. Soybean, pea, wheat, rice, and chickpea proteins have been widely studied due to their abundance, nutritional value, and potential health benefits. The growing demand for plant-based functional foods and sustainable production systems has further accelerated research into plant-derived bioactive peptides [10]. The generation of bioactive peptides from food proteins involves several approaches, including enzymatic hydrolysis, microbial fermentation, chemical methods, and emerging biotechnological strategies. Among these methods, enzymatic hydrolysis using proteolytic enzymes such as alcalase, pepsin, trypsin, chymotrypsin, papain, and flavourzyme is one of the most commonly applied techniques because of its efficiency and ability to produce peptide fractions with controlled biological properties. Fermentation using beneficial microorganisms, particularly lactic acid bacteria, represents another promising approach due to its natural processing characteristics and potential contribution to peptide release during food production. Recent advances in biotechnology, including recombinant technologies, computational prediction, and precision fermentation, have opened new possibilities for improving peptide production, optimizing yields, and designing peptides with specific biological functions [11], [12]. Following production, the identification and characterization of bioactive peptides are critical steps for understanding their structure-function relationships and biological mechanisms. Advanced analytical technologies, including High-Performance Liquid Chromatography (HPLC), Liquid Chromatography Coupled with Tandem Mass Spectrometry (LC-MS/MS), Matrix-Assisted Laser Desorption/Ionization Time-Of-Flight Mass Spectrometry (MALDI-TOF-MS), and Nuclear Magnetic Resonance (NMR) spectroscopy, have significantly improved the discovery and characterization of peptide sequences. Furthermore, bioinformatics tools, molecular docking approaches, and AI-based prediction platforms are increasingly being used to identify potential bioactive peptide candidates, predict their interactions with biological targets, and accelerate the

discovery process. Food-derived bioactive peptides exhibit a broad range of biological activities, which determine their potential applications in health and industry. One of the most extensively studied activities is antioxidant activity, where peptides contribute to the reduction of oxidative stress by scavenging Reactive Oxygen Species (ROS) and regulating antioxidant defense pathways. Oxidative stress is associated with the development of numerous chronic diseases; therefore, antioxidant peptides have attracted attention as natural alternatives for maintaining cellular health [13–15]. Antihypertensive peptides, particularly those capable of inhibiting ACE activity, have also been widely investigated due to their potential role in regulating blood pressure and cardiovascular health. Several peptide sequences derived from milk, fish, and plant proteins have demonstrated promising ACE inhibitory effects in vitro and in vivo studies. In addition to antioxidant and antihypertensive properties, food-derived peptides have shown significant anti-inflammatory, antimicrobial, antidiabetic, anticancer, and immunomodulatory activities. Anti-inflammatory peptides may regulate inflammatory signaling pathways, including Nuclear Factor Kappa B (NF- $\kappa$ B)-mediated pathways and cytokine production. Antimicrobial Peptides (AMPs) can disrupt microbial membranes and inhibit pathogen growth, offering potential applications in food preservation and therapeutic development [1]. Furthermore, peptides capable of modulating glucose metabolism and inhibiting enzymes associated with carbohydrate digestion have been explored as potential strategies for diabetes management. The ability of certain peptides to influence cancer-related pathways has also encouraged further investigation into their potential as complementary therapeutic agents. Despite the promising biological activities of food-derived bioactive peptides, several challenges limit their widespread commercial application. These challenges include low bioavailability, susceptibility to gastrointestinal degradation, difficulties in large-scale production, purification costs, and variations in peptide activity depending on food source and processing conditions. Improving peptide stability, enhancing absorption, and developing effective delivery systems are therefore important areas of current research [16]. Recent developments in nanotechnology, encapsulation strategies, and targeted delivery systems may provide innovative solutions to overcome these limitations and increase the practical applications of bioactive peptides. The increasing demand for natural health-promoting compounds has positioned food-derived bioactive peptides as important components of next-generation functional foods, nutraceuticals, pharmaceuticals, and cosmetic products. Their multifunctional properties, combined with advances in biotechnology and analytical techniques, continue to expand their potential applications across multiple industries. However, a comprehensive understanding of their production, structural characteristics, biological mechanisms, and industrial utilization is necessary to facilitate their successful translation from laboratory research to commercial products [1], [9], [16].

This review aims to provide an overview of recent advances in food-derived bioactive peptides, focusing on their generation strategies, identification and characterization methods, biological functions, and functional applications. Particular emphasis is placed on current technologies for peptide production, mechanisms underlying their health-promoting effects, and future perspectives for their utilization in pharmaceutical, food, and related industries.

## 2 | Sources of Food-Derived Bioactive Peptides

Food-derived bioactive peptides can be obtained from a wide range of protein-rich sources, including animal, plant, marine, and emerging alternative resources. The biological potential of these peptides is strongly influenced by the amino acid composition, primary protein structure, molecular size, peptide sequence, and processing conditions applied during their release. Proteins that contain specific amino acid sequences with biological activity are considered precursor proteins, and these encrypted peptide sequences can be released through enzymatic hydrolysis, fermentation, or gastrointestinal digestion [14]. The diversity of food protein sources provides a broad platform for the discovery of peptides with different physiological functions, including antioxidant, antihypertensive, antimicrobial, anti-inflammatory, antidiabetic, immunomodulatory, and anticancer activities. The selection of appropriate protein sources is a critical factor in the development of bioactive peptides because the quantity, quality, and functional properties of the released peptides depend largely on the characteristics of the parent proteins. Generally, animal-derived proteins have received

considerable attention due to their high protein content and balanced amino acid profiles, whereas plant-derived proteins have become increasingly important because of sustainability, availability, and growing consumer demand for plant-based products. In addition, marine organisms and alternative protein sources represent promising reservoirs of novel peptide sequences with unique biological properties [17].

## **2.1 | Animal-Derived Sources**

### **2.1.1 | Milk and dairy proteins**

Milk proteins represent one of the most extensively studied sources of food-derived bioactive peptides due to their high nutritional value and abundance of biologically active sequences. Approximately 80% of milk proteins consist of caseins, while whey proteins account for approximately 20% of total milk protein content. Both fractions contain encrypted peptide sequences that can be released through enzymatic hydrolysis or microbial fermentation. Caseins, including  $\alpha$ -casein,  $\beta$ -casein, and  $\kappa$ -casein, have been widely investigated as precursors of multifunctional peptides. Several casein-derived peptides have demonstrated antihypertensive activity through inhibition of ACE, which plays an important role in blood pressure regulation. These peptides, often referred to as casein-derived ACE inhibitory peptides or casokinins, have attracted attention as potential natural alternatives for supporting cardiovascular health. Whey proteins, including  $\beta$ -lactoglobulin,  $\alpha$ -lactalbumin, immunoglobulins, and lactoferrin, are also important sources of bioactive peptides. Whey-derived peptides have been associated with antioxidant, antimicrobial, immunomodulatory, and metabolic regulatory activities. For example, lactoferrin-derived peptides have demonstrated antimicrobial effects against various microorganisms, while peptides derived from  $\beta$ -lactoglobulin have shown antioxidant and ACE inhibitory properties. The extensive study of dairy-derived peptides has contributed to their incorporation into functional foods, dietary supplements, and nutraceutical formulations. However, factors such as processing conditions, digestion stability, and potential allergenicity remain important considerations for their commercial application [1], [2], [18].

### **2.1.2 | Meat and poultry proteins**

Meat proteins represent another valuable source of bioactive peptides. Skeletal muscle proteins, including myosin, actin, and sarcoplasmic proteins, contain peptide sequences that can exhibit biological functions after hydrolysis. Processing methods such as enzymatic treatment and fermentation can release peptides with antioxidant, antihypertensive, and antimicrobial activities. Collagen, a major structural protein in animal connective tissues, has received particular attention as a source of functional peptides. Collagen-derived peptides, especially those obtained from bovine, porcine, and poultry sources, are rich in glycine, proline, and hydroxyproline. These peptides have been widely studied for their beneficial effects on skin health, collagen synthesis stimulation, joint protection, and anti-aging applications. Due to these properties, collagen peptides have become important ingredients in cosmetic products, functional beverages, and nutritional supplements.

Poultry-derived proteins and by-products from meat processing have also been explored as sustainable sources of bioactive peptides. The utilization of these underused protein resources contributes to waste reduction and supports the development of value-added products [19].

### **2.1.3 | Marine protein sources**

Marine organisms represent a highly diverse and promising source of bioactive peptides. Fish proteins, seafood processing by-products, marine collagen, and other aquatic resources contain numerous peptide sequences with potential health-promoting effects. Fish-derived peptides have demonstrated various biological activities, including antioxidant, ACE inhibitory, antimicrobial, and anti-inflammatory effects. Fish skin, scales, bones, and connective tissues, which are often considered processing waste, are particularly rich in collagen and gelatin proteins. The conversion of these by-products into bioactive peptides provides both environmental and economic benefits by improving resource utilization. Marine-derived collagen peptides have gained considerable interest in the cosmetic and biomedical industries due to their potential roles in skin hydration, elasticity improvement, and tissue regeneration. In addition, peptides obtained from marine

organisms may possess unique amino acid compositions that contribute to their enhanced biological activity compared with terrestrial protein sources [2].

## **2.2 | Plant-Derived Sources**

Plant proteins have emerged as important and sustainable sources of bioactive peptides due to their availability, lower environmental impact, and increasing consumer preference for plant-based nutrition. Although plant proteins may differ from animal proteins in amino acid composition and digestibility, many plant-derived peptides exhibit significant biological activities [18].

### **2.2.1 | Legume-based proteins**

Legumes, including soybean, pea, chickpea, lentil, and beans, are among the most extensively studied plant sources of bioactive peptides. These crops contain high levels of storage proteins, such as globulins and albumins, which serve as precursors for peptide generation. Soybean proteins, particularly glycinin and  $\beta$ -conglycinin, have been widely investigated due to their ability to produce peptides with antioxidant, ACE inhibitory, antidiabetic, and cholesterol-regulating properties. Soy-derived peptides have attracted attention for applications in functional foods and health-promoting formulations. Pea protein has recently gained popularity as a sustainable alternative protein source. Pea-derived peptides have demonstrated antioxidant and antihypertensive activities, while also showing potential applications in plant-based functional foods. Similarly, chickpea and lentil proteins contain bioactive sequences associated with metabolic regulation and oxidative stress reduction [20].

### **2.2.2 | Cereal-derived proteins**

Cereals such as wheat, rice, maize, oat, and barley represent abundant sources of plant proteins with potential bioactive properties. Although cereal proteins generally contain lower protein concentrations compared with legumes, they possess unique peptide sequences that may provide beneficial physiological effects. Wheat gluten proteins have been investigated as sources of antioxidants and AMPs. Rice proteins have attracted attention due to their hypoallergenic characteristics and potential health benefits. Oat-derived peptides have also demonstrated antioxidant and cholesterol-lowering activities, making them attractive candidates for functional food development. The utilization of cereal-derived peptides may contribute to the development of affordable and widely accessible functional ingredients, particularly in regions where cereal crops are major dietary components [2].

### **2.2.3 | Oilseed proteins**

Oilseed crops, including hemp, flaxseed, sesame, sunflower, and rapeseed, have recently received attention as alternative protein sources. These materials contain valuable proteins that can be converted into bioactive peptide fractions. Hemp protein-derived peptides have demonstrated antioxidant and ACE inhibitory activities, while flaxseed peptides have been associated with antioxidant and metabolic regulatory effects. The recovery of bioactive peptides from oilseed processing residues also provides an opportunity for sustainable utilization of agricultural by-products [21].

## **2.3 | Emerging and Alternative Sources of Bioactive Peptides**

The increasing demand for sustainable protein production has encouraged researchers to explore unconventional sources of bioactive peptides. Algae, microorganisms, and insect proteins represent emerging resources with considerable potential [17].

### **2.3.1 | Algae-derived peptides**

Microalgae and marine algae contain proteins with unique amino acid compositions and bioactive potential. Algae-derived peptides have demonstrated antioxidant, antimicrobial, antihypertensive, and anti-inflammatory activities. Their rapid growth, minimal land requirements, and environmental sustainability make algae attractive candidates for future peptide production [16].

### 2.3.2 | Microbial and fermentation-derived peptides

Microorganisms, including bacteria and fungi, can produce peptides either directly or through fermentation processes. Lactic Acid Bacteria (LAB) used in fermented foods can generate bioactive peptides by hydrolyzing food proteins during fermentation. These microbial processes not only improve nutritional properties but may also enhance the functional characteristics of food products [9].

### 2.3.3 | Insect-derived peptides

Insect proteins have recently emerged as sustainable alternatives due to their high protein content, efficient conversion of feed into biomass, and lower environmental impact. Hydrolysates obtained from insect proteins have shown antioxidant, antimicrobial, and anti-inflammatory properties. Although regulatory and consumer acceptance challenges remain, insect-derived peptides represent a promising area for future research. Considering the remarkable diversity of food protein resources, bioactive peptides can be generated from numerous animal, plant, marine, microbial, and insect-derived proteins. These sources differ considerably in their precursor proteins, peptide composition, reported biological activities, and potential industrial applications. A comprehensive summary of the major food sources of bioactive peptides and their associated biological functions is presented in *Table 1*. Although all protein sources provide valuable bioactive peptides, they differ substantially in terms of protein composition, peptide yield, sustainability, processing requirements, and commercial applicability. These similarities and differences are summarized and compared in *Table 2*, providing an overview of the strengths and limitations of each source for future peptide production and industrial utilization [15].

**Table 1. Major food sources of bioactive peptides, precursor proteins, reported activities, and potential applications.**

| Food Source                    | Main Protein Precursors                                                                                                        | Representative Bioactive Peptides/Peptide Fractions                               | Reported Biological Activities                                                  | Potential Applications                                                       |
|--------------------------------|--------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|---------------------------------------------------------------------------------|------------------------------------------------------------------------------|
| Milk                           | Casein ( $\alpha$ -, $\beta$ -, $\kappa$ -casein), whey proteins ( $\beta$ -lactoglobulin, $\alpha$ -lactalbumin, lactoferrin) | Casein-derived peptides (casokinins), whey-derived peptides, lactoferrin peptides | ACE inhibitory, antioxidant, antimicrobial, immunomodulatory, anti-inflammatory | Functional dairy products, cardiovascular health supplements, nutraceuticals |
| Whey proteins                  | $\beta$ -lactoglobulin, $\alpha$ -lactalbumin                                                                                  | Whey protein hydrolysates, lactoferrin-derived peptides                           | Antioxidant, antihypertensive, immune regulation                                | Sports nutrition, functional beverages, dietary supplements                  |
| Meat proteins                  | Myosin, actin, sarcoplasmic proteins                                                                                           | Muscle protein-derived peptide fractions                                          | Antioxidant, ACE inhibitory, antimicrobial                                      | Functional foods, health-promoting ingredients                               |
| Collagen                       | Collagen and gelatin proteins                                                                                                  | Collagen peptides, hydroxyproline-rich peptides                                   | Skin health improvement, antioxidant, anti-aging, tissue regeneration           | Cosmetics, nutraceuticals, joint health supplements                          |
| Fish and marine organisms      | Fish muscle proteins, collagen, gelatin                                                                                        | Marine-derived peptide fractions                                                  | Antioxidant, ACE inhibitory, antimicrobial, anti-inflammatory                   | Marine nutraceuticals, functional foods, biomedical applications             |
| Soybean                        | Glycinin, $\beta$ -conglycinin                                                                                                 | Soy protein-derived peptides                                                      | Antioxidant, ACE inhibitory, antidiabetic, cholesterol regulation               | Plant-based functional foods, metabolic health products                      |
| Pea                            | Legumin, vicilin                                                                                                               | Pea protein hydrolysates and peptides                                             | Antioxidant, antihypertensive, anti-inflammatory                                | Plant-based foods, protein supplements                                       |
| Chickpea                       | Globulins, albumins                                                                                                            | Chickpea-derived peptides                                                         | Antioxidant, ACE inhibitory, glucose regulation                                 | Functional foods, nutraceutical formulations                                 |
| Lentil and beans               | Storage globulins                                                                                                              | Legume-derived peptide fractions                                                  | Antioxidant, antimicrobial, metabolic regulation                                | Health foods and dietary supplements                                         |
| Wheat                          | Gluten proteins, gliadins, glutenins                                                                                           | Wheat protein-derived peptides                                                    | Antioxidant, antimicrobial, ACE inhibitory                                      | Functional cereal products                                                   |
| Rice                           | Rice glutelin, albumin, globulin                                                                                               | Rice-derived peptides                                                             | Antioxidant, anti-inflammatory, hypoallergenic potential                        | Functional foods, specialized nutrition                                      |
| Oat                            | Oat globulins and avenins                                                                                                      | Oat protein-derived peptides                                                      | Antioxidant, cholesterol-lowering effects                                       | Heart-health foods                                                           |
| Hemp seed                      | Hemp storage proteins                                                                                                          | Hemp protein-derived peptides                                                     | Antioxidant, ACE inhibitory                                                     | Sustainable protein products                                                 |
| Flaxseed                       | Flaxseed proteins                                                                                                              | Flaxseed-derived peptides                                                         | Antioxidant, metabolic regulation                                               | Functional foods, nutraceuticals                                             |
| Algae                          | Algal proteins                                                                                                                 | Algae-derived peptide fractions                                                   | Antioxidant, antimicrobial, anti-inflammatory                                   | Sustainable nutraceuticals                                                   |
| Microbial fermentation sources | Food proteins modified by microorganisms                                                                                       | Fermentation-generated peptides                                                   | Antioxidant, antimicrobial, immunomodulatory                                    | Fermented foods, probiotics-associated products                              |
| Insect proteins                | Insect muscle and storage proteins                                                                                             | Insect protein hydrolysates                                                       | Antioxidant, antimicrobial, anti-inflammatory                                   | Future sustainable protein ingredients                                       |

**Table 2. Comparison of major protein sources for bioactive peptide production.**

| Source Category   | Advantages                                                                     | Limitations                                                            |
|-------------------|--------------------------------------------------------------------------------|------------------------------------------------------------------------|
| Animal proteins   | High-quality proteins, well-characterized peptides, strong biological evidence | Allergenicity, sustainability concerns, religious/cultural limitations |
| Marine proteins   | High peptide diversity, utilization of processing waste, unique bioactivities  | Seasonal availability, purification challenges                         |
| Plant proteins    | Sustainable, abundant, low environmental impact                                | Lower digestibility, possible antinutritional factors                  |
| Microbial sources | Controlled production, scalable fermentation                                   | Optimization requirements, regulatory considerations                   |
| Insect proteins   | High sustainability and protein yield                                          | Consumer acceptance and regulatory challenges                          |

### 3 | Generation and Production Strategies of Food-Derived Bioactive Peptides

The biological activities of food-derived peptides are not only determined by their amino acid sequence and molecular structure but are also significantly influenced by the methods employed for their generation. In their native protein structures, bioactive peptide sequences are generally inactive and remain encrypted within larger protein molecules. These peptides are released only after specific peptide bonds are cleaved through enzymatic, microbial, chemical, or physiological processes. Therefore, selecting an appropriate production strategy is essential for maximizing peptide yield, preserving biological activity, and ensuring the feasibility of industrial applications. Several approaches have been developed for producing bioactive peptides from food proteins, among which enzymatic hydrolysis and microbial fermentation are the most widely employed owing to their high specificity, mild processing conditions, and compatibility with food applications. In recent years, emerging biotechnological techniques including recombinant technologies, precision fermentation, enzyme engineering, and computationally assisted peptide design have further expanded the possibilities for producing novel peptides with enhanced bioactivities. Each production strategy possesses unique advantages and limitations with respect to peptide yield, selectivity, production cost, scalability, and industrial implementation. The currently available strategies for producing food-derived bioactive peptides vary considerably in terms of production principles, processing conditions, scalability, and the biological properties of the resulting peptides [22]. A comparative overview of conventional and emerging production technologies is presented in *Table 3*.

**Table 3. Comparison of conventional and emerging production strategies for food-derived bioactive peptides.**

| Production Strategy                  | Principle                                                                                                     | Advantages                                                                                                            | Limitations                                                                                                 | Typical Food Sources                                 | Representative Bioactivities                                                                  |
|--------------------------------------|---------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------|------------------------------------------------------|-----------------------------------------------------------------------------------------------|
| Enzymatic hydrolysis                 | Proteolytic enzymes cleave peptide bonds under controlled conditions to release encrypted bioactive peptides. | High specificity, mild reaction conditions, high peptide quality, suitable for food applications, scalable production | High enzyme cost, peptide bitterness, optimization required for each substrate                              | Milk, fish, soybean, pea, egg, meat, cereal proteins | Antioxidant, ACE inhibitory, antimicrobial, anti-inflammatory, antidiabetic, immunomodulatory |
| Microbial fermentation               | Proteases produced by microorganisms hydrolyze food proteins during fermentation.                             | Natural process, improved nutritional value, probiotic benefits, environmentally friendly                             | Long processing time, strain-dependent variability, lower process control                                   | Dairy products, soy, cereals, legumes, meat products | Antioxidant, antihypertensive, antimicrobial, cholesterol-lowering, immunomodulatory          |
| Chemical hydrolysis                  | Acidic or alkaline reagents hydrolyze peptide bonds.                                                          | Rapid process, inexpensive reagents, simple equipment                                                                 | Non-specific cleavage, amino acid degradation, environmental concerns, not suitable for food-grade peptides | Fish proteins, meat by-products, plant proteins      | Limited due to harsh conditions; mainly industrial hydrolysates                               |
| Simulated gastrointestinal digestion | Sequential digestion using pepsin, pancreatin and intestinal enzymes.                                         | Mimics physiological digestion, useful for bioavailability studies; screening tool                                    | Low yield, time-consuming, difficult to scale up                                                            | Milk, soy, fish, meat proteins                       | ACE inhibitory, antioxidant, opioid-like peptides, mineral-binding peptides                   |
| Precision fermentation               | Genetically engineered microorganisms synthesize target proteins or peptides.                                 | Highly controlled production, sustainable, scalable, high purity                                                      | High development cost, regulatory challenges                                                                | Recombinant microbial systems                        | Custom-designed bioactive peptides with diverse biological functions                          |

Table 3. Continued.

| Production Strategy        | Principle                                                                              | Advantages                                                       | Limitations                                                   | Typical Food Sources                                | Representative Bioactivities                                                                 |
|----------------------------|----------------------------------------------------------------------------------------|------------------------------------------------------------------|---------------------------------------------------------------|-----------------------------------------------------|----------------------------------------------------------------------------------------------|
| Recombinant expression     | Target proteins are expressed in microbial or eukaryotic hosts before peptide release. | High purity, reproducibility, sequence-specific production       | Complex downstream processing; expensive production           | <i>E. coli</i> , yeast, insect cells, plant systems | Therapeutic peptides, AMPs, anticancer peptides                                              |
| Enzyme engineering         | Modified proteases improve catalytic activity and substrate specificity.               | Higher efficiency, reduced reaction time, improved peptide yield | Requires advanced biotechnology, high development cost        | Engineered proteases                                | Improved production of high-value bioactive peptides                                         |
| AI-assisted peptide design | Computational prediction identifies peptide sequences with desired bioactivities.      | Rapid screening, reduced experimental workload, cost-effective   | Requires experimental validation, depends on database quality | In silico peptide libraries                         | Rational design of antioxidant, ACE inhibitory, antimicrobial and anti-inflammatory peptides |

### 3.1 | Enzymatic Hydrolysis

Enzymatic hydrolysis is the most extensively applied method for producing food-derived bioactive peptides because it provides high substrate specificity while preserving the nutritional quality of proteins. During hydrolysis, proteolytic enzymes cleave peptide bonds at specific amino acid residues, releasing peptides with defined molecular weights and biological activities. Compared with chemical hydrolysis, enzymatic hydrolysis operates under relatively mild conditions, minimizing amino acid degradation, undesirable side reactions, and the formation of toxic by-products. Consequently, this approach has become the preferred strategy for producing bioactive peptides intended for food, pharmaceutical, and nutraceutical applications. The selection of proteolytic enzymes is one of the most critical factors influencing peptide production. Both animal-derived digestive enzymes and microbial proteases are commonly employed depending on the desired peptide profile. Among commercial enzymes, Alcalase has been widely used because of its broad substrate specificity and high hydrolytic efficiency. Trypsin preferentially cleaves peptide bonds adjacent to lysine and arginine residues, whereas pepsin primarily hydrolyzes peptide bonds associated with aromatic amino acids under acidic conditions. Papain, Bromelain, Flavourzyme, Neutrase, and Protamex have also been extensively utilized either individually or in combination to improve peptide diversity and biological activity [15].

The physicochemical properties of the hydrolysis process substantially influence both peptide composition and functionality. Factors including enzyme-to-substrate ratio, temperature, pH, hydrolysis time, substrate concentration, and degree of hydrolysis collectively determine peptide yield, molecular weight distribution, and biological efficacy. Excessive hydrolysis may generate very small peptides or free amino acids, which can reduce certain biological activities, whereas insufficient hydrolysis may fail to release the desired bioactive sequences. Therefore, optimization of hydrolysis conditions is essential for maximizing functional performance.

Enzymatic hydrolysis has been successfully applied to numerous food proteins, including milk caseins, whey proteins, fish collagen, soybean proteins, pea proteins, cereal proteins, and egg proteins. Depending on the parent protein and enzyme combination, hydrolysates may exhibit antioxidant, antihypertensive, antimicrobial, anti-inflammatory, antidiabetic, or immunomodulatory properties. Advances in response surface methodology, AI-assisted optimization, and computational enzyme selection have further improved the efficiency of enzymatic peptide production while reducing production costs. Despite its numerous advantages, enzymatic hydrolysis also presents several challenges. Commercial enzymes can be expensive, enzyme recovery is often difficult, and large-scale industrial processes require careful optimization to ensure reproducibility and economic feasibility. Moreover, controlling peptide bitterness, which frequently results from extensive protein hydrolysis, remains an important challenge for the incorporation of peptide hydrolysates into functional foods. The characteristics of proteolytic enzymes largely determine peptide yield, molecular weight distribution, and biological activity [23]. The major commercial proteases commonly used for bioactive peptide production are summarized in Table 4.

**Table 4. Major proteolytic enzymes used for bioactive peptide production: Cleavage specificity, optimal conditions, and representative applications.**

| Major Applications                                                     | Representative Protein Substrates   | Optimum Temperature (°C) | Optimum pH | Cleavage Specificity                              | Type / Source                                        | Enzyme      |
|------------------------------------------------------------------------|-------------------------------------|--------------------------|------------|---------------------------------------------------|------------------------------------------------------|-------------|
| High-yield peptide production; antioxidant and ACE inhibitory peptides | Milk, soy, fish, pea, meat proteins | 50-60                    | 8.0-9.5    | Broad specificity; hydrophobic amino acids        | Serine endopeptidase (Bacillus licheniformis)        | Alcalase    |
| Antihypertensive and AMPs                                              | Milk, soy, egg, fish proteins       | 37                       | 7.5-8.5    | Cleaves after Lys and Arg residues                | Pancreatic serine protease                           | Trypsin     |
| Simulated gastrointestinal digestion; antioxidant peptides             | Milk, fish, meat proteins           | 37                       | 1.5-2.5    | Cleaves near aromatic amino acids (Phe, Tyr, Trp) | Gastric aspartic protease                            | Pepsin      |
| Antioxidant and anti-inflammatory peptides                             | Soy, meat, fish proteins            | 50-65                    | 6.0-7.0    | Broad specificity                                 | Cysteine protease (Carica papaya)                    | Papain      |
| Anti-inflammatory and AMPs                                             | Fish, meat, soy proteins            | 45-60                    | 5.5-7.0    | Broad specificity                                 | Cysteine protease (Ananas comosus)                   | Bromelain   |
| Bitterness reduction; peptide production                               | Soy, fish, wheat proteins           | 45-55                    | 6.0-7.0    | Broad specificity                                 | Mixed endo-/exopeptidases (Aspergillus oryzae)       | Flavourzyme |
| Production of ACE inhibitory peptides                                  | Milk, plant proteins                | 45-55                    | 6.0-7.5    | Broad specificity                                 | Neutral metalloprotease (Bacillus amyloliquefaciens) | Neutrase    |
| Production of antioxidant and AMPs                                     | Fish, soy, meat proteins            | 50-60                    | 6.5-8.0    | Hydrophobic amino acids                           | Mixed bacterial proteases (Bacillus spp.)            | Protamex    |

### 3.2 | Microbial Fermentation

Microbial fermentation represents another important strategy for producing bioactive peptides and has been widely employed in the manufacture of fermented dairy products, meat products, soy-based foods, and cereal-derived foods. During fermentation, microorganisms synthesize extracellular and intracellular proteases capable of hydrolyzing food proteins and releasing biologically active peptide sequences. Unlike direct enzymatic hydrolysis, fermentation simultaneously enhances food preservation, improves sensory characteristics, and increases nutritional value. LAB, including species of *Lactobacillus*, *Lactococcus*, *Streptococcus*, and *Bifidobacterium*, are the most extensively studied microorganisms for peptide production. Their highly efficient proteolytic systems enable the degradation of complex proteins into short peptides with various physiological functions. Numerous studies have reported ACE inhibitory, antioxidant, antimicrobial, immunomodulatory, and anti-inflammatory peptides generated during the fermentation of milk, soy, cereals, and legumes. Compared with enzymatic hydrolysis, microbial fermentation is generally considered a more natural process and is highly compatible with clean-label food production. Nevertheless, peptide production depends strongly on microbial strain selection, fermentation conditions, substrate composition, and incubation time, making process optimization essential for obtaining reproducible results [24].

### 3.3 | Emerging Production Technologies

Rapid advances in biotechnology have introduced innovative approaches for producing bioactive peptides beyond conventional hydrolysis and fermentation. Precision fermentation, synthetic biology, recombinant DNA technology, and enzyme engineering have enabled the controlled production of specific peptide sequences with improved efficiency and consistency. Precision fermentation utilizes genetically optimized microorganisms capable of producing target proteins or peptide precursors under highly controlled conditions. Recombinant expression systems have also been investigated to generate peptide-rich proteins that can subsequently undergo enzymatic processing. Meanwhile, enzyme engineering has improved the catalytic performance, stability, and substrate specificity of proteolytic enzymes, thereby enhancing peptide yield and reducing processing time. In parallel, bioinformatics, molecular docking, and AI have become

valuable tools for predicting bioactive peptide sequences before experimental validation. These computational approaches significantly reduce screening time, facilitate enzyme selection, and accelerate the discovery of novel peptides with desired biological properties. As computational biology continues to evolve, AI-assisted peptide design is expected to play an increasingly important role in the development of next-generation functional ingredients [20].

### 3.4 | Factors Influencing Peptide Production

Regardless of the production method employed, the quantity and biological activity of released peptides are strongly affected by multiple processing parameters. The intrinsic characteristics of the parent protein, including amino acid composition, tertiary structure, and accessibility of peptide bonds, largely determine the potential for generating bioactive sequences. Likewise, processing conditions directly influence peptide size, stability, and functionality. Among the operational variables, pH and temperature are particularly important because they regulate enzyme activity and protein denaturation. Hydrolysis duration and enzyme concentration determine the degree of hydrolysis and consequently the molecular weight distribution of the resulting peptides. In addition, pretreatment methods such as ultrasound, high-pressure processing, microwave-assisted processing, and pulsed electric fields have recently been explored to improve protein accessibility and enhance enzymatic efficiency. No single production strategy is universally applicable to all protein sources. Instead, the selection of an appropriate method should consider the characteristics of the raw material, the targeted biological activity, production cost, scalability, and intended industrial application. Continuous integration of conventional processing technologies with modern biotechnological and computational approaches is expected to further improve the sustainable production of food-derived bioactive peptides and facilitate their commercialization in functional foods, nutraceuticals, and pharmaceutical products [25].

The overall workflow for the production and characterization of food-derived bioactive peptides involves a series of interconnected steps, including protein source selection, pretreatment, peptide generation, purification, analytical identification, biological evaluation, and subsequent industrial utilization. A schematic overview of this integrated process is presented in *Fig 1*.

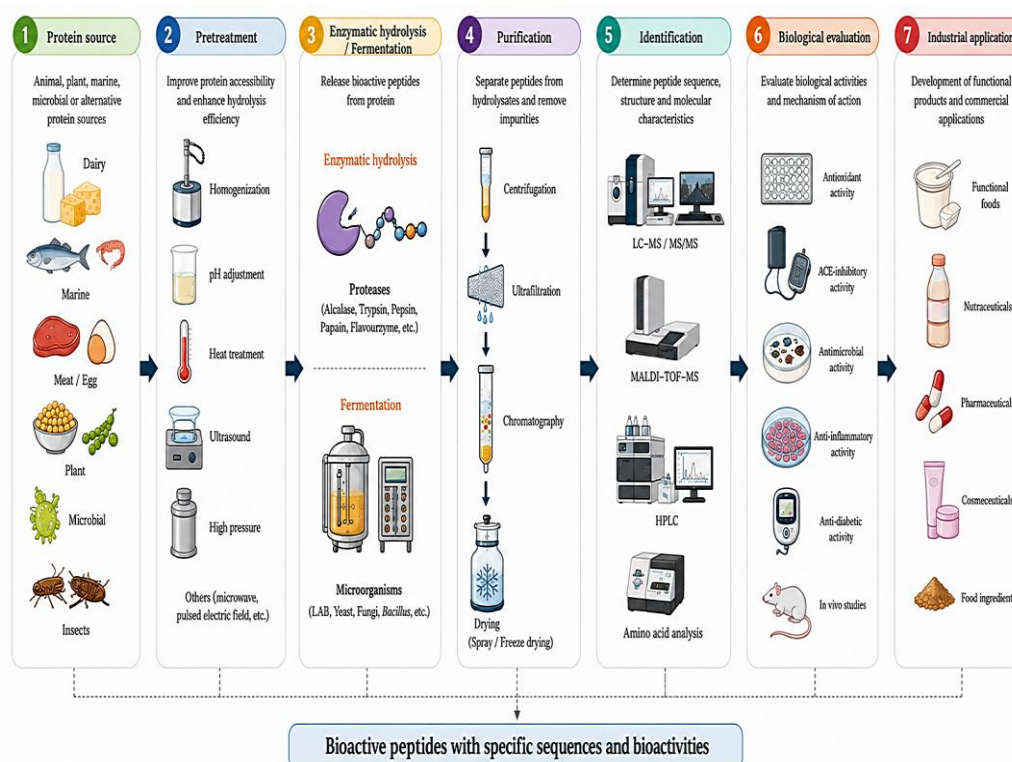


Fig. 1. Schematic overview of the generation, purification, identification, and application of food-derived bioactive peptides.

## 4 | Identification and Characterization of Food-Derived Bioactive Peptides

The successful application of food-derived bioactive peptides in functional foods, nutraceuticals, and pharmaceutical products depends not only on efficient production but also on accurate identification and comprehensive characterization. Following peptide generation through enzymatic hydrolysis, microbial fermentation, or gastrointestinal digestion, complex peptide mixtures must be separated, purified, identified, and evaluated to determine their biological potential. Recent advances in analytical chemistry, mass spectrometry, bioinformatics, and computational biology have significantly accelerated the discovery and characterization of novel bioactive peptides while improving analytical accuracy and throughput [26]. *Fig 2* summarizes the integrated workflow commonly employed for the identification and characterization of food-derived bioactive peptides from protein hydrolysates to biological validation.

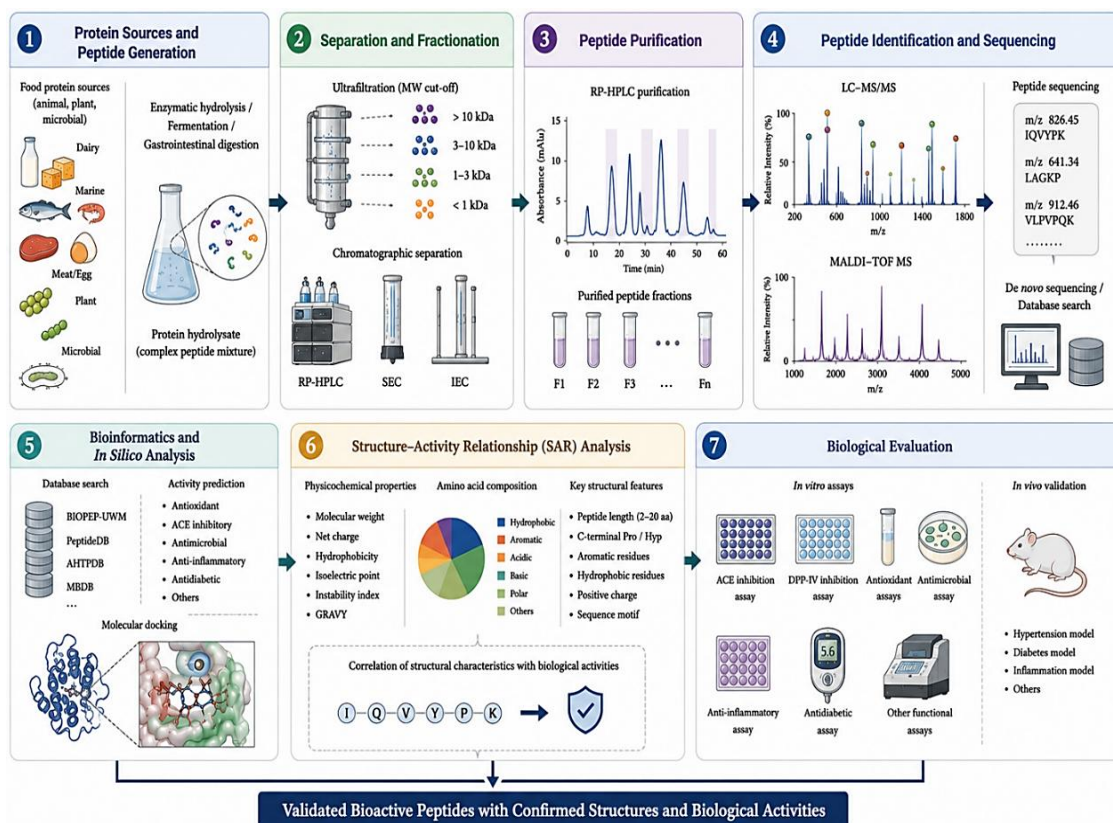


Fig 2. General workflow for the identification and characterization of food-derived bioactive peptides

## 4.1 | Peptide Separation and Purification

The initial hydrolysates obtained from protein sources generally contain highly complex mixtures of peptides with different molecular weights, charges, hydrophobicities, and biological activities. Consequently, purification is an essential step to isolate peptide fractions with specific functional properties before structural characterization and biological evaluation. Membrane-based separation technologies, particularly ultrafiltration, are widely employed as preliminary purification methods because they efficiently fractionate peptides according to molecular weight while maintaining biological activity. Membrane filtration also offers advantages such as simplicity, scalability, low chemical consumption, and compatibility with industrial production. Chromatographic techniques are subsequently applied to achieve higher purification efficiency. Size-exclusion chromatography separates peptides based on molecular size, whereas ion-exchange chromatography utilizes differences in peptide charge. Reverse-Phase High-Performance Liquid Chromatography (RP-HPLC) remains the most frequently used purification technique owing to its excellent separation efficiency, reproducibility, and compatibility with downstream mass spectrometric analysis. In many studies, combinations of ultrafiltration and RP-HPLC are employed to obtain highly purified peptide fractions for structural identification [25].

## 4.2 | Structural Identification of Bioactive Peptides

Following purification, peptide sequences must be accurately identified to establish structure–activity relationships. Among the available analytical techniques, mass spectrometry has become the cornerstone of peptide identification due to its exceptional sensitivity, specificity, and ability to analyze complex peptide mixtures. LC-MS/MS is currently regarded as the gold standard for peptide sequencing. The combination of chromatographic separation with high-resolution mass spectrometry enables precise determination of peptide molecular weights and amino acid sequences, even in highly complex food matrices. MALDI-TOF MS is another widely used technique that provides rapid molecular mass determination and peptide fingerprinting with minimal sample preparation. In addition to mass spectrometry, amino acid composition analysis, Edman degradation, and NMR spectroscopy may be employed for detailed structural characterization of selected

peptides. Although these techniques are generally less suitable for high-throughput analysis, they provide valuable information regarding peptide conformation, structural stability, and molecular interactions [26].

### 4.3 | Bioinformatics and in Silico Approaches

The rapid development of bioinformatics has transformed the discovery of food-derived bioactive peptides. Instead of relying solely on experimental screening, researchers increasingly utilize computational approaches to predict peptide sequences with desired biological activities before laboratory validation. Several specialized databases containing experimentally validated bioactive peptides facilitate sequence comparison and functional prediction. Machine Learning (ML) algorithms and Quantitative Structure-Activity Relationship (QSAR) models are increasingly employed to identify peptide characteristics associated with antioxidant, antihypertensive, antimicrobial, anti-inflammatory, and antidiabetic activities. Molecular docking simulations further enable researchers to investigate interactions between peptides and biological targets, including ACE, Dipeptidyl Peptidase-IV (DPP-IV), cyclooxygenase enzymes, and inflammatory mediators. AI has recently emerged as a powerful tool for peptide discovery by integrating protein sequence information, enzymatic cleavage prediction, structural modeling, and biological activity prediction. These computational strategies substantially reduce experimental workload, shorten development time, and improve the efficiency of identifying promising peptide candidates [27].

### 4.4 | Structure-Activity Relationships

The biological functions of food-derived peptides are closely associated with their structural characteristics. Peptide length, molecular weight, amino acid composition, sequence arrangement, hydrophobicity, net charge, and three-dimensional conformation collectively determine biological activity. Short peptides consisting of two to twenty amino acid residues generally exhibit superior gastrointestinal absorption and higher bioavailability than larger peptides. Hydrophobic amino acids such as leucine, isoleucine, valine, phenylalanine, and tryptophan often contribute to antioxidant and antimicrobial activities by facilitating interactions with lipid membranes and free radicals. Positively charged amino acids, including lysine and arginine, are commonly associated with antimicrobial activity because they promote electrostatic interactions with negatively charged bacterial membranes. Similarly, the presence of proline residues at the C-terminal region frequently enhances ACE inhibitory activity, while aromatic amino acids contribute to radical scavenging capacity through hydrogen donation and electron transfer mechanisms. Understanding these structure-activity relationships is fundamental for the rational design of functional peptides with enhanced efficacy and improved stability. The integration of advanced purification techniques, high-resolution analytical platforms, and computational prediction tools has substantially accelerated the identification of food-derived bioactive peptides. These multidisciplinary approaches provide the scientific foundation for elucidating peptide mechanisms of action and facilitate the development of novel functional ingredients for food, nutraceutical, and pharmaceutical applications. A variety of analytical techniques have been developed for the separation, purification, identification, and structural characterization of food-derived bioactive peptides [25]. The principles, applications, advantages, and limitations of the major analytical methods are summarized in *Table 5*.

**Table 5. Comparison of analytical techniques used for the identification and characterization of food-derived bioactive peptides.**

| Limitations                      | Advantages                                 | Main application               | Principle                              | Technique                           |
|----------------------------------|--------------------------------------------|--------------------------------|----------------------------------------|-------------------------------------|
| Limited resolution               | Rapid, inexpensive, scalable               | Initial fractionation          | Separation based on molecular weight   | Ultrafiltration                     |
| Lower separation efficiency      | Mild conditions, reproducible              | Peptide purification           | Separation according to molecular size | Size-exclusion chromatography (SEC) |
| Time-consuming                   | High selectivity                           | Peptide purification           | Separation based on charge             | Ion-exchange chromatography (IEC)   |
| Expensive instrumentation        | High resolution, excellent reproducibility | Final purification             | Separation based on hydrophobicity     | RP-HPLC                             |
| High operating cost              | High sensitivity and accuracy              | Peptide identification         | Mass analysis and peptide sequencing   | LC-MS/MS                            |
| Limited quantitative capability  | Rapid analysis                             | Molecular weight determination | Laser desorption ionization            | MALDI-TOF MS                        |
| Only suitable for short peptides | High sequence accuracy                     | Sequence confirmation          | Sequential amino acid identification   | Edman degradation                   |
| High sample requirement          | Detailed structural information            | Three-dimensional structure    | Structural characterization            | NMR spectroscopy                    |
| Requires experimental validation | Fast and cost-effective                    | Mechanism prediction           | Computational interaction analysis     | Molecular docking                   |

## 5 | Biological Functions and Mechanisms of Action of Food-Derived Bioactive Peptides

Food-derived bioactive peptides have attracted considerable attention due to their broad spectrum of physiological activities and their potential applications in disease prevention and health promotion. Unlike intact dietary proteins, these peptides exert specific biological effects after being released through enzymatic hydrolysis, microbial fermentation, food processing, or gastrointestinal digestion. Their biological efficacy is primarily determined by amino acid composition, peptide sequence, molecular weight, hydrophobicity, and resistance to gastrointestinal degradation. Moreover, peptide bioavailability, tissue distribution, and interactions with cellular receptors collectively influence their functional performance in vivo [25]. A growing body of evidence has demonstrated that food-derived bioactive peptides exhibit multiple biological properties, including antioxidant, antihypertensive, antimicrobial, anti-inflammatory, immunomodulatory, antidiabetic, and anticancer activities. These multifunctional peptides interact with diverse molecular targets involved in oxidative stress, inflammation, metabolic regulation, and immune responses. As a result, they have emerged as promising natural ingredients for functional foods, nutraceuticals, and pharmaceutical formulations. Understanding the molecular mechanisms underlying these biological activities is essential for optimizing peptide production, improving bioavailability, and facilitating clinical translation [28].

### 5.1 | Antioxidant Activity

Oxidative stress is recognized as one of the major contributors to aging and the development of chronic diseases, including cardiovascular disorders, diabetes mellitus, neurodegenerative diseases, and cancer. Excessive production of ROS and Reactive Nitrogen Species (RNS) disrupts the cellular redox balance, resulting in lipid peroxidation, protein oxidation, DNA damage, and mitochondrial dysfunction. Consequently, considerable attention has been devoted to identifying natural antioxidant compounds capable of reducing oxidative damage while minimizing the adverse effects associated with synthetic antioxidants. Food-derived bioactive peptides have emerged as effective natural antioxidants because of their ability to scavenge free radicals, chelate transition metal ions, inhibit lipid oxidation, and regulate endogenous antioxidant defense systems. Their antioxidant capacity is closely associated with structural characteristics, particularly amino acid composition and peptide sequence. Peptides containing hydrophobic amino acids such as valine, leucine, isoleucine, phenylalanine, and tryptophan generally exhibit enhanced radical scavenging activity by interacting with lipid-soluble radicals. Likewise, aromatic amino acids including tyrosine, tryptophan, and phenylalanine readily donate electrons or hydrogen atoms to neutralize ROS. Histidine-containing peptides also contribute to antioxidant activity through proton donation and transition metal chelation [29].

Beyond direct radical scavenging, bioactive peptides modulate intracellular antioxidant signaling pathways. Numerous studies have demonstrated that antioxidant peptides activate the Nuclear Factor Erythroid 2-related Factor 2 (Nrf2) signaling pathway, leading to increased expression of antioxidant enzymes such as Superoxide Dismutase (SOD), Catalase (CAT), Glutathione Peroxidase (GPx), and Heme Oxygenase-1 (HO-1). Activation of these endogenous defense mechanisms enhances cellular resistance to oxidative stress while maintaining redox homeostasis. In addition, several peptides suppress excessive ROS generation by improving mitochondrial function and reducing oxidative damage to cellular macromolecules. Antioxidant peptides have been successfully isolated from numerous food sources, including milk proteins, fish collagen, egg proteins, soybean, pea, rice, wheat, marine organisms, and edible insects. Peptides with relatively low molecular weights, generally below 3 kDa, frequently exhibit superior antioxidant activity due to their improved solubility, diffusion capacity, and cellular uptake. Recent investigations have also demonstrated synergistic antioxidant effects when peptide mixtures are combined with natural polyphenols or vitamins, suggesting promising opportunities for developing multifunctional functional foods. Despite encouraging experimental findings, several challenges remain before antioxidant peptides can be fully utilized in commercial applications. Their stability during food processing, resistance to gastrointestinal digestion, absorption efficiency, and long-term efficacy in humans require further investigation through well-designed clinical studies. Nevertheless, antioxidant peptides continue to represent one of the most extensively studied classes of food-derived bioactive compounds owing to their safety, natural origin, and broad therapeutic potential [29].

## 5.2 | Antihypertensive Activity

Hypertension remains one of the leading risk factors for cardiovascular diseases and premature mortality worldwide. Persistent elevation of blood pressure significantly increases the incidence of stroke, heart failure, myocardial infarction, and chronic kidney disease. Although pharmacological antihypertensive agents effectively reduce blood pressure, long-term medication may cause adverse effects, prompting increasing interest in naturally occurring compounds capable of supporting cardiovascular health. Among food-derived bioactive peptides, antihypertensive peptides have received particular attention because of their ability to inhibit ACE, a key component of the renin–angiotensin system. ACE catalyzes the conversion of angiotensin I into the potent vasoconstrictor angiotensin II while simultaneously degrading bradykinin, an endogenous vasodilator. Inhibition of ACE therefore reduces angiotensin II formation, promotes vasodilation, decreases vascular resistance, and ultimately lowers blood pressure. The ACE inhibitory activity of peptides depends strongly on their structural characteristics.

Short peptides composed of two to twelve amino acid residues generally exhibit the highest inhibitory potency [30]. The presence of hydrophobic or aromatic amino acids, particularly proline, phenylalanine, tyrosine, tryptophan, leucine, and valine at the C-terminal region, has been associated with enhanced binding affinity toward the active site of ACE. Molecular docking studies have further demonstrated that hydrogen bonding, hydrophobic interactions, and electrostatic forces collectively determine peptide enzyme interactions and inhibitory efficiency. Milk proteins remain the most extensively investigated sources of antihypertensive peptides, with numerous ACE inhibitory sequences identified from casein and whey proteins. In addition, bioactive peptides exhibiting antihypertensive activity have been isolated from fish proteins, marine collagen, soybean, pea, rice bran, egg proteins, meat proteins, and fermented foods. Fermentation with lactic acid bacteria has proven particularly effective in generating potent ACE inhibitory peptides through microbial proteolysis. Besides ACE inhibition, several food-derived peptides regulate blood pressure through complementary mechanisms. Some peptides enhance endothelial nitric oxide production, thereby improving vascular relaxation and endothelial function. Others exhibit antioxidant and anti-inflammatory activities that indirectly contribute to cardiovascular protection by reducing vascular oxidative stress and chronic inflammation. These multifunctional mechanisms suggest that antihypertensive peptides may provide broader cardiovascular benefits than conventional single-target therapies. Although numerous *in vitro* and animal studies have confirmed the antihypertensive potential of food-derived peptides, clinical translation remains

challenging. Factors including gastrointestinal stability, intestinal absorption, metabolic degradation, dosage optimization, and interindividual variability influence the effectiveness of orally administered peptides. Consequently, future research should emphasize human clinical trials, advanced delivery systems, and peptide formulation strategies to improve bioavailability and maximize therapeutic efficacy [31].

### 5.3 | Antimicrobial Activity

The rapid emergence of antimicrobial resistance has become one of the most pressing global public health challenges, necessitating the development of novel antimicrobial agents with improved efficacy and lower potential for resistance development. In this context, food-derived bioactive peptides have attracted increasing attention as natural antimicrobial compounds due to their broad-spectrum activity against bacteria, fungi, and certain viruses. Unlike conventional antibiotics that often target specific metabolic pathways, many AMPs exert their effects through multiple mechanisms, thereby reducing the likelihood of microbial resistance. The antimicrobial activity of bioactive peptides is closely associated with their physicochemical properties, including peptide length, net positive charge, hydrophobicity, amphipathicity, and amino acid composition. Most AMPs are relatively short, containing between 10 and 50 amino acid residues, and possess positively charged amino acids such as lysine and arginine. These cationic residues facilitate electrostatic interactions with negatively charged microbial membranes, while hydrophobic amino acids promote membrane insertion and disruption [32]. The primary mechanism of AMPs involves destabilization of microbial cell membranes. Following electrostatic attraction to the cell surface, peptides penetrate the lipid bilayer and induce membrane permeabilization through several proposed models, including the barrel-stave, toroidal pore, and carpet mechanisms. Membrane disruption ultimately results in leakage of intracellular components, loss of membrane integrity, dissipation of ion gradients, and cell death. In addition to membrane-targeting effects, several peptides interfere with intracellular processes by inhibiting DNA and RNA synthesis, protein biosynthesis, enzyme activity, and essential metabolic pathways. Food-derived AMPs have been isolated from numerous protein sources. Milk proteins produce several well-characterized AMPs, including lactoferricin and lactoferrampin, which exhibit potent activity against both Gram-positive and Gram-negative bacteria. Egg-derived peptides such as lysozyme fragments possess bacteriolytic properties through degradation of bacterial cell walls. Fish proteins and marine collagen hydrolysates have also yielded AMPs capable of inhibiting foodborne pathogens and spoilage microorganisms. Furthermore, peptides derived from soybean, wheat, pea, and other plant proteins have demonstrated inhibitory effects against a variety of bacterial and fungal species, highlighting their potential as natural food preservatives [33]. Recent investigations have demonstrated that AMPs may also inhibit biofilm formation, an important virulence factor that contributes to persistent infections and antibiotic resistance. By preventing bacterial adhesion or disrupting mature biofilms, these peptides enhance microbial susceptibility to host immune responses and conventional antimicrobial agents. Such multifunctional properties have increased interest in their incorporation into active food packaging systems, edible coatings, and functional food formulations aimed at improving food safety and shelf life. Despite their considerable potential, several limitations remain regarding the commercial application of AMPs. Factors including susceptibility to enzymatic degradation, reduced activity under complex food matrices, potential cytotoxicity at high concentrations, and production costs continue to restrict large-scale implementation. Consequently, current research focuses on peptide modification, nanoencapsulation, and advanced delivery systems to improve peptide stability, bioavailability, and antimicrobial efficacy [34].

### 5.4 | Anti-Inflammatory and Immunomodulatory Activities

Chronic inflammation is increasingly recognized as a fundamental contributor to the development of numerous non-communicable diseases, including obesity, Type 2 Diabetes (T2DM) mellitus, cardiovascular diseases, neurodegenerative disorders, inflammatory bowel disease, and cancer. Persistent activation of inflammatory signaling pathways results in excessive production of pro-inflammatory cytokines, oxidative stress, and progressive tissue damage. Consequently, naturally occurring anti-inflammatory compounds have become attractive candidates for disease prevention and complementary therapeutic interventions. Food-

derived bioactive peptides have demonstrated remarkable anti-inflammatory properties through modulation of multiple cellular signaling pathways. Among these, inhibition of the NF- $\kappa$ B signaling pathway represents one of the best-characterized mechanisms. Under inflammatory conditions, activation of NF- $\kappa$ B stimulates the transcription of numerous pro-inflammatory mediators, including Tumor Necrosis Factor-Alpha (TNF- $\alpha$ ), Interleukin-1 Beta (IL-1 $\beta$ ), Interleukin-6 (IL-6), Cyclooxygenase-2 (COX-2), and inducible Nitric Oxide Synthase (iNOS). Numerous food-derived peptides suppress NF- $\kappa$ B activation, thereby reducing cytokine production and attenuating inflammatory responses [23].

In addition to NF- $\kappa$ B inhibition, several bioactive peptides regulate Mitogen-Activated Protein Kinase (MAPK) signaling pathways, including Extracellular Signal-Regulated Kinase (ERK), c-Jun N-Terminal Kinase (JNK), and p38 MAPK. Suppression of these signaling cascades contributes to decreased expression of inflammatory mediators while protecting tissues from chronic inflammatory injury. Furthermore, antioxidant peptides frequently exhibit indirect anti-inflammatory effects by reducing intracellular ROS, which serve as important upstream activators of inflammatory signaling pathways. Food-derived peptides also exert significant immunomodulatory activities by regulating both innate and adaptive immune responses. These peptides influence macrophage activation, dendritic cell maturation, natural killer cell function, and lymphocyte proliferation, thereby contributing to immune homeostasis. Several studies have demonstrated that specific peptides promote macrophage polarization toward the anti-inflammatory M2 phenotype while suppressing the pro-inflammatory M1 phenotype [22]. This immunoregulatory function is particularly important for controlling excessive inflammatory responses without inducing generalized immunosuppression. Milk-derived peptides remain among the most extensively investigated immunomodulatory compounds. Casein-derived peptides and lactoferrin-derived peptides have demonstrated the ability to regulate cytokine production, stimulate antibody responses, and enhance mucosal immunity. Likewise, peptides isolated from fish collagen, soy proteins, egg proteins, rice bran, and fermented food products have shown promising anti-inflammatory activities in both cellular and animal models. Increasing evidence also indicates that fermentation-derived peptides generated by lactic acid bacteria possess enhanced immunoregulatory properties owing to their unique peptide profiles. Another emerging area of research involves the interaction between bioactive peptides and the gut Microbiota. Certain peptides promote the growth of beneficial intestinal microorganisms while suppressing pathogenic bacteria, thereby contributing to improved intestinal barrier integrity and immune regulation. Through modulation of host Microbiota interactions, these peptides may exert systemic anti-inflammatory effects extending beyond the gastrointestinal tract [15], [22], [23]. Although substantial experimental evidence supports the anti-inflammatory and immunomodulatory properties of food-derived peptides, translation into clinical practice remains limited. Future investigations should emphasize well-designed human intervention studies, standardized peptide production protocols, pharmacokinetic evaluation, and long-term safety assessment. A deeper understanding of peptide receptor interactions and immune signaling networks will facilitate the development of peptide-based functional foods and therapeutic formulations targeting chronic inflammatory diseases [25].

## 5.5 | Antidiabetic Activity

Diabetes mellitus, particularly T2DM, is one of the fastest-growing metabolic disorders worldwide and is characterized by chronic hyperglycemia resulting from impaired insulin secretion, insulin resistance, or a combination of both. Persistent hyperglycemia is associated with severe complications, including cardiovascular disease, nephropathy, retinopathy, neuropathy, and impaired wound healing. Consequently, considerable attention has been directed toward identifying naturally derived compounds capable of improving glucose homeostasis with minimal adverse effects [23]. Among these, food-derived bioactive peptides have emerged as promising candidates because of their ability to regulate multiple metabolic pathways involved in glucose metabolism. Unlike conventional antidiabetic drugs that generally target a single metabolic pathway, bioactive peptides often exhibit multifunctional mechanisms of action. Their antidiabetic effects include inhibition of carbohydrate-digesting enzymes, modulation of incretin metabolism,

enhancement of insulin signaling, improvement of glucose uptake, attenuation of oxidative stress, and suppression of chronic inflammation. These complementary mechanisms may provide synergistic benefits in the prevention and management of T2DM. One of the best-characterized mechanisms involves inhibition of DPP-IV, a serine protease responsible for the rapid degradation of incretin hormones, particularly Glucagon-Like Peptide-1 (GLP-1) and Glucose-dependent Insulinotropic Polypeptide (GIP). By inhibiting DPP-IV activity, bioactive peptides prolong the half-life of incretin hormones, thereby enhancing glucose-stimulated insulin secretion, suppressing glucagon release, delaying gastric emptying, and improving postprandial glucose regulation. Numerous peptides isolated from milk, fish, soy, oat, rice bran, and egg proteins have demonstrated potent DPP-IV inhibitory activity in both *in vitro* and animal studies. Another important mechanism involves inhibition of digestive enzymes responsible for carbohydrate hydrolysis, including  $\alpha$ -amylase and  $\alpha$ -glucosidase.

Suppression of these enzymes slows the digestion and absorption of dietary carbohydrates, thereby reducing postprandial blood glucose excursions. Several plant-derived peptides, particularly those obtained from soybean, pea, wheat, and rice proteins, have exhibited significant inhibitory effects against these enzymes, suggesting their potential incorporation into functional foods designed for glycemic control. Food-derived peptides have also been shown to improve insulin sensitivity through modulation of intracellular signaling pathways [30]. Activation of the Phosphoinositide 3-Kinase/Protein Kinase B (PI3K/Akt) pathway promotes translocation of Glucose Transporter Type 4 (GLUT4) to the plasma membrane in skeletal muscle and adipose tissues, thereby enhancing glucose uptake. In addition, activation of AMP-Activated Protein Kinase (AMPK) contributes to improved glucose utilization, increased fatty acid oxidation, and reduced hepatic gluconeogenesis. These metabolic effects collectively improve insulin responsiveness and energy homeostasis [34]. Oxidative stress and chronic low-grade inflammation play central roles in the progression of insulin resistance and pancreatic  $\beta$ -cell dysfunction. Consequently, many antioxidants and anti-inflammatory peptides indirectly contribute to improved glycemic control by reducing ROS production, suppressing inflammatory cytokines, and protecting pancreatic  $\beta$ -cells against oxidative damage. Such multifunctionality distinguishes food-derived peptides from conventional glucose-lowering agents and supports their potential application as complementary nutritional interventions. Although numerous experimental studies have demonstrated promising antidiabetic activities, clinical evidence remains relatively limited. Future investigations should focus on improving peptide stability during gastrointestinal digestion, enhancing intestinal absorption through advanced delivery systems, and conducting well-designed human clinical trials to establish effective dosages and long-term therapeutic efficacy [30]. Nevertheless, current evidence strongly supports the potential of food-derived bioactive peptides as valuable functional ingredients for diabetes prevention and metabolic health management.

## 5.6 | Anticancer Activity

Cancer remains one of the leading causes of morbidity and mortality worldwide despite substantial advances in diagnosis and treatment. Conventional therapeutic approaches, including chemotherapy and radiotherapy, are frequently associated with severe adverse effects, drug resistance, and limited selectivity toward malignant cells. Consequently, naturally occurring bioactive compounds capable of selectively targeting cancer cells while minimizing toxicity to normal tissues have attracted increasing scientific interest. Food-derived bioactive peptides have recently emerged as promising candidates owing to their diverse anticancer mechanisms and favorable safety profiles [2]. The anticancer activity of bioactive peptides is mediated through multiple molecular pathways that regulate tumor initiation, proliferation, angiogenesis, invasion, metastasis, and programmed cell death. Unlike many conventional chemotherapeutic agents, these peptides often influence several cellular targets simultaneously, thereby reducing the probability of therapeutic resistance. Their relatively small molecular size also facilitates interactions with cellular membranes and intracellular proteins involved in cancer progression. One of the most extensively investigated mechanisms is the induction of apoptosis. Numerous food-derived peptides activate intrinsic mitochondrial apoptotic pathways through modulation of Bcl-2 family proteins, increased mitochondrial membrane permeability, cytochrome c release,

and subsequent activation of Caspase-9 and Caspase-3. Other peptides stimulate the extrinsic apoptotic pathway by activating death receptors located on the cell surface. Through these mechanisms, malignant cells undergo controlled programmed cell death without provoking excessive inflammatory responses [28]. In addition to apoptosis induction, several peptides inhibit uncontrolled cancer cell proliferation by arresting the cell cycle at the G0/G1, S, or G2/M phases. This effect is frequently associated with regulation of cyclins, Cyclin-Dependent Kinases (CDKs), and tumor suppressor proteins such as p53. Cell-cycle arrest prevents DNA replication and mitotic progression, thereby suppressing tumor growth and enhancing the susceptibility of cancer cells to other therapeutic interventions. Tumor angiogenesis represents another critical target of food-derived bioactive peptides. Several studies have demonstrated that specific peptides suppress Vascular Endothelial Growth Factor (VEGF) signaling, thereby inhibiting the formation of new blood vessels required for tumor growth and metastasis. Other peptides reduce cancer cell migration and invasion by regulating Matrix Metalloproteinases (MMPs), Epithelial–Mesenchymal Transition (EMT), and extracellular matrix remodeling. These effects collectively contribute to reduced metastatic potential and improved control of tumor progression. Accumulating evidence also suggests that bioactive peptides modulate intracellular signaling pathways involved in cancer development, including PI3K/Akt, MAPK, Wnt/ $\beta$ -catenin, NF- $\kappa$ B, and mTOR pathways. By regulating these signaling networks, peptides inhibit cellular proliferation, promote apoptosis, suppress inflammation, and reduce oxidative stress within the tumor microenvironment. Moreover, several antioxidant peptides indirectly contribute to cancer prevention by minimizing oxidative DNA damage and maintaining genomic stability.

Anticancer peptides have been identified from a wide variety of food proteins, including milk caseins, whey proteins, fish collagen, marine organisms, soybean, egg proteins, cereals, and edible insects. Marine-derived peptides have attracted particular attention because of their structural diversity and potent biological activities. Although most evidence currently originates from *in vitro* studies and animal models, several peptide candidates have demonstrated encouraging therapeutic potential for future pharmaceutical development [26]. Despite these promising findings, several obstacles continue to limit clinical application. Poor oral bioavailability, rapid enzymatic degradation, insufficient tumor-specific targeting, and large-scale production costs remain major challenges. Recent advances in peptide engineering, nanotechnology-based drug delivery systems, and peptide conjugation strategies are expected to overcome many of these limitations and accelerate the translation of food-derived anticancer peptides into clinical practice. The multifunctional biological activities of food-derived peptides, combined with their relatively low toxicity and natural origin, make them attractive candidates for complementary cancer prevention strategies and the development of next-generation peptide-based therapeutics. Continued interdisciplinary research integrating food science, molecular biology, biotechnology, and clinical medicine will be essential to fully exploit their therapeutic potential [31].

## 5.7 | Other Emerging Biological Activities

Beyond their well-established antioxidant, antihypertensive, antimicrobial, anti-inflammatory, antidiabetic, and anticancer properties, food-derived bioactive peptides have demonstrated a wide range of additional biological activities that further expand their potential applications in functional foods, nutraceuticals, and pharmaceutical products. Advances in peptide discovery, high-throughput screening, and bioinformatics have accelerated the identification of multifunctional peptides capable of simultaneously modulating several physiological processes. These emerging activities highlight the versatility of food-derived peptides and support their development as natural health-promoting ingredients. The diverse biological functions of food-derived bioactive peptides are associated with distinct molecular mechanisms and depend strongly on peptide structure and food origin [23]. A schematic overview of the principal biological activities and their underlying molecular mechanisms is presented in *Fig. 3*, while a comprehensive summary of their representative food sources, mechanisms, and potential health applications is provided in *Table 6*.

### 5.7.1 | Anti-obesity activity

Obesity is a complex metabolic disorder characterized by excessive fat accumulation and chronic low-grade inflammation, which significantly increase the risk of cardiovascular diseases, diabetes mellitus, and certain cancers. Recent studies have demonstrated that several food-derived peptides exhibit anti-obesity effects through multiple mechanisms, including appetite regulation, inhibition of adipogenesis, stimulation of lipolysis, enhancement of fatty acid oxidation, and modulation of energy metabolism. Some peptides regulate the secretion of appetite-related hormones such as leptin, ghrelin, Peptide YY (PYY), and GLP-1, thereby promoting satiety and reducing energy intake. Others inhibit the differentiation of preadipocytes into mature adipocytes by suppressing adipogenic transcription factors, including Peroxisome Proliferator-Activated Receptor Gamma (PPAR $\gamma$ ) and CCAAT/Enhancer-Binding Proteins (C/EBPs). In addition, activation of AMPK by certain peptides enhances lipid oxidation while reducing triglyceride accumulation in adipose tissue. These findings suggest that food-derived peptides may serve as promising dietary components for body weight management and obesity prevention [15], [22–24].

### 5.7.2 | Hypocholesterolemic activity

Dyslipidemia is a major contributor to atherosclerosis and cardiovascular disease. Numerous food-derived peptides have demonstrated cholesterol-lowering properties through regulation of lipid metabolism. Several peptides inhibit intestinal cholesterol absorption, while others increase bile acid excretion or modulate hepatic cholesterol synthesis by influencing the expression of key metabolic enzymes. Bioactive peptides have also been reported to regulate the expression of Low-Density Lipoprotein Receptors (LDLR), enhance reverse cholesterol transport, and improve plasma lipid profiles by reducing total cholesterol, Low-Density Lipoprotein Cholesterol (LDL-C), and triglyceride concentrations while increasing High-Density Lipoprotein Cholesterol (HDL-C). These combined effects contribute to improved cardiovascular health and support the incorporation of peptide-rich ingredients into functional foods targeting lipid disorders [2].

### 5.7.3 | Neuroprotective activity

The increasing prevalence of neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease has stimulated interest in naturally derived neuroprotective compounds. Food-derived bioactive peptides have shown considerable potential to protect neuronal cells through antioxidant, anti-inflammatory, and anti-apoptotic mechanisms. Several peptides reduce neuronal oxidative stress by scavenging ROS and enhancing endogenous antioxidant defenses. Others suppress neuroinflammation by inhibiting microglial activation and decreasing the production of inflammatory cytokines within the central nervous system. In addition, certain peptides inhibit acetylcholinesterase activity, thereby increasing acetylcholine availability and improving cognitive function. Experimental evidence further suggests that some peptides interfere with amyloid- $\beta$  aggregation and tau protein hyperphosphorylation, two pathological hallmarks of Alzheimer's disease. Although these findings remain largely preclinical, they indicate promising opportunities for developing peptide-based strategies for maintaining brain health [26].

### 5.7.4 | Bone health and osteogenic activity

Food-derived peptides have also demonstrated beneficial effects on skeletal health through stimulation of bone formation and inhibition of bone resorption. Calcium-binding phosphopeptides derived from milk caseins enhance calcium solubility and intestinal absorption, thereby improving mineral bioavailability and supporting bone mineralization. Several collagen-derived peptides stimulate osteoblast proliferation, differentiation, and extracellular matrix synthesis while suppressing osteoclast-mediated bone resorption. These effects are mediated through multiple signaling pathways involved in bone remodeling, including Transforming Growth Factor-Beta (TGF- $\beta$ ), Bone Morphogenetic Proteins (BMPs), and Wnt/ $\beta$ -Catenin signaling. Consequently, bioactive peptides have attracted increasing attention as nutritional interventions for osteoporosis prevention and healthy aging [2].

### 5.7.5 | Gut Microbiota modulation

The gut Microbiota plays a fundamental role in nutrient metabolism, immune regulation, and maintenance of intestinal homeostasis. Recent evidence suggests that food-derived peptides may positively influence microbial composition by promoting the growth of beneficial microorganisms while suppressing pathogenic species. Through modulation of microbial diversity and metabolic activity, bioactive peptides contribute to improved intestinal barrier integrity, increased production of short-chain fatty acids, and reduced intestinal inflammation. These changes may indirectly influence systemic metabolic health, immune function, and even neurological processes through the gut-brain axis. The interaction between bioactive peptides and the gut microbiome has therefore emerged as an important research area with significant implications for precision nutrition [29].

### 5.7.6 | Wound healing and tissue regeneration

An emerging application of food-derived bioactive peptides involves tissue repair and regenerative medicine. Several peptides have demonstrated the ability to accelerate wound healing by stimulating fibroblast proliferation, collagen synthesis, angiogenesis, and re-epithelialization. Their antioxidant and anti-inflammatory properties further contribute to an optimal healing environment by reducing oxidative damage and excessive inflammatory responses. Marine collagen peptides have been particularly well investigated for wound healing applications owing to their excellent biocompatibility and regenerative properties. Recent advances in biomaterial engineering have also enabled the incorporation of bioactive peptides into hydrogels, wound dressings, and tissue-engineered scaffolds, expanding their potential clinical applications. Collectively, these emerging biological activities demonstrate that food-derived bioactive peptides possess multifunctional physiological properties extending far beyond their traditionally recognized health benefits [30]. As advances in peptide engineering, omics technologies, computational biology, and precision nutrition continue to accelerate peptide discovery, these naturally occurring compounds are expected to play an increasingly important role in the prevention and management of chronic diseases. Nevertheless, additional studies addressing peptide bioavailability, molecular mechanisms, safety, and long-term clinical efficacy remain essential before their widespread application in healthcare and food industries can be fully realized.

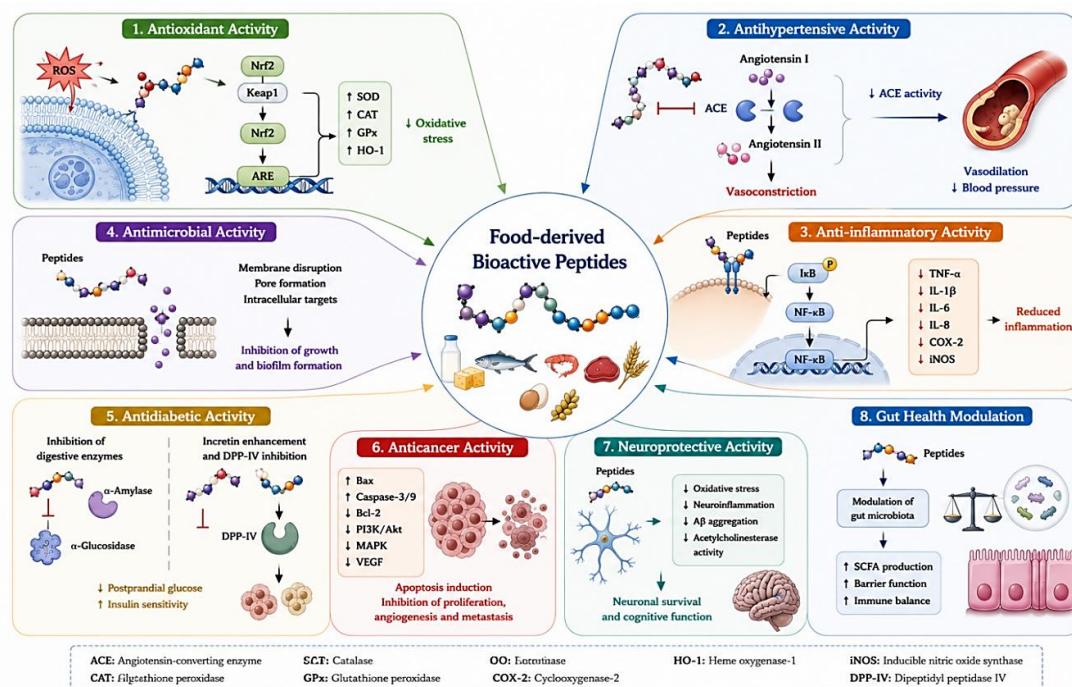


Fig 3. Major biological activities and molecular mechanisms of food-derived bioactive peptides.

**Table 6. Biological activities and mechanisms of food-derived bioactive peptides.**

| Biological Activity       | Main Mechanism                                                 | Representative Sources               | Potential Applications                     |
|---------------------------|----------------------------------------------------------------|--------------------------------------|--------------------------------------------|
| Antioxidant               | ROS scavenging, metal chelation, Nrf2 activation               | Milk, fish, soybean, cereals         | Oxidative stress control, health promotion |
| Antihypertensive          | ACE inhibition, NO regulation                                  | Casein, whey, fish, fermented foods  | Blood pressure management                  |
| Antimicrobial             | Membrane disruption, microbial inhibition                      | Milk, egg, fish, plant proteins      | Food preservation, infection control       |
| Anti-inflammatory         | NF- $\kappa$ B and MAPK regulation, cytokine reduction         | Dairy, marine, plant proteins        | Inflammation control, immune balance       |
| Immunomodulatory          | Regulation of immune cell responses                            | Lactoferrin, casein, fermented foods | Immune enhancement                         |
| Antidiabetic              | DPP-IV, $\alpha$ -amylase and $\alpha$ -glucosidase inhibition | Dairy, soy, rice, oat proteins       | Glucose regulation                         |
| Anticancer                | Apoptosis induction, inhibition of proliferation               | Milk, marine proteins, legumes       | Cancer prevention strategies               |
| Anti-obesity              | AMPK activation, reduced adipogenesis                          | Dairy, soy, marine peptides          | Weight management                          |
| Neuroprotective           | Antioxidant and anti-inflammatory effects                      | Milk, collagen, plant proteins       | Brain health protection                    |
| Bone health               | Calcium binding, osteoblast stimulation                        | Casein phosphopeptides, collagen     | Bone formation support                     |
| Gut Microbiota modulation | Microbial balance improvement                                  | Fermented foods, dairy peptides      | Intestinal health                          |

## 6 | Functional and Therapeutic Applications of Food-Derived Bioactive Peptides

The growing body of evidence regarding the biological activities of food-derived bioactive peptides has accelerated their application in various industrial and biomedical fields. Owing to their multifunctional properties, high biocompatibility, and natural origin, these peptides have emerged as valuable functional ingredients for the development of innovative products in the food, pharmaceutical, cosmetic, and agricultural sectors. Although numerous applications remain at the research stage, recent technological advances have significantly expanded the commercial potential of bioactive peptides. The multifunctional properties of food-derived bioactive peptides have enabled their application in several industrial sectors, including functional foods, pharmaceuticals, cosmetics, and food preservation [29]. The major applications of these peptides are summarized in *Table 7*.

**Table 7. Applications of food-derived bioactive peptides in different industries.**

| Application Area                  | Main Functions                                                 | Examples Of Applications                                                       |
|-----------------------------------|----------------------------------------------------------------|--------------------------------------------------------------------------------|
| Functional foods & nutraceuticals | Antioxidant, antihypertensive, antidiabetic, immune regulation | Peptide-enriched beverages, supplements, fortified foods                       |
| Pharmaceutical applications       | Therapeutic effects against chronic diseases                   | Peptide-based agents for cardiovascular, metabolic, and inflammatory disorders |
| Cosmetic products                 | Antioxidant, collagen stimulation, skin protection             | Anti-aging creams, skin repair formulations                                    |
| Food preservation                 | Antimicrobial and antioxidant activities                       | Edible coatings, active packaging systems                                      |
| Biotechnology and health products | Peptide production and targeted delivery                       | Encapsulation systems, advanced peptide formulations                           |

### 6.1 | Functional Foods and Nutraceuticals

One of the most important applications of food-derived bioactive peptides is their incorporation into functional foods and nutraceutical products. Peptide-enriched dairy products, protein beverages, fermented foods, dietary supplements, and fortified nutritional formulations have been developed to promote cardiovascular health, improve antioxidant capacity, regulate glucose metabolism, and support immune function. The increasing consumer preference for naturally derived health-promoting ingredients has further stimulated the commercialization of peptide-based functional products [31].

### 6.2 | Pharmaceutical Applications

Food-derived peptides have attracted considerable attention as potential therapeutic agents or complementary treatments for chronic diseases. Their antihypertensive, antimicrobial, anti-inflammatory, antidiabetic, and anticancer properties provide opportunities for the development of peptide-based pharmaceuticals with improved safety profiles compared with many synthetic drugs. In addition, advances in nanotechnology and

targeted drug delivery systems have enhanced peptide stability, bioavailability, and therapeutic efficacy, facilitating their translation into clinical applications [32].

### **6.3 | Cosmetic and Personal Care Products**

Bioactive peptides are increasingly incorporated into cosmetic formulations owing to their antioxidant, collagen-stimulating, anti-inflammatory, and skin-protective properties. Marine collagen peptides, milk-derived peptides, and plant-derived peptides have shown promising effects in improving skin hydration, reducing oxidative damage, promoting wound healing, and delaying signs of skin aging. Consequently, peptide-based ingredients have become important components of modern cosmeceutical products [33].

### **6.4 | Food Preservation and Packaging**

Natural antimicrobial and antioxidant peptides have emerged as promising alternatives to synthetic food preservatives. Their incorporation into edible coatings, biodegradable films, and active food packaging materials can inhibit microbial growth, reduce lipid oxidation, and extend the shelf life of food products while maintaining food quality and safety. Such applications also support the growing demand for clean-label and environmentally sustainable food preservation technologies [34].

### **6.5 | Future Industrial Perspectives**

Despite remarkable progress, the large-scale commercialization of food-derived bioactive peptides remains limited by challenges including production cost, peptide stability, gastrointestinal bioavailability, regulatory approval, and standardization of manufacturing processes. Future research should focus on integrating advanced bioprocessing technologies, AI-assisted peptide discovery, precision fermentation, and novel delivery systems to improve production efficiency and clinical effectiveness. These multidisciplinary approaches are expected to accelerate the translation of bioactive peptides from laboratory research to industrial and therapeutic applications [23].

## **7 | Conclusion**

Food-derived bioactive peptides have emerged as one of the most promising classes of natural bioactive compounds owing to their diverse physiological functions and broad application potential across the food, nutraceutical, pharmaceutical, and biomedical industries. This review has highlighted the entire developmental pathway of these peptides, from their occurrence in various food protein sources and production through enzymatic hydrolysis, microbial fermentation, and emerging biotechnological approaches to their identification using advanced analytical techniques and computational tools. Continuous improvements in peptide purification, high-resolution mass spectrometry, bioinformatics, and AI have substantially accelerated the discovery of novel peptide sequences with enhanced biological activities and improved functional properties. A substantial body of evidence demonstrates that food-derived bioactive peptides exert multiple beneficial effects, including antioxidant, antihypertensive, antimicrobial, anti-inflammatory, immunomodulatory, antidiabetic, and anticancer activities, in addition to several emerging functions such as anti-obesity, neuroprotective, hypocholesterolemic, osteogenic, and gut Microbiota-modulating effects. These multifunctional properties are mediated through complex molecular mechanisms involving the regulation of oxidative stress, inflammatory signaling pathways, metabolic homeostasis, immune responses, and cellular survival. Such versatility highlights the significant potential of bioactive peptides as multifunctional ingredients for disease prevention and health promotion [24]. Despite remarkable scientific progress, several challenges continue to limit the widespread commercialization and clinical translation of food-derived bioactive peptides. Variability among protein sources, limited gastrointestinal stability, low oral bioavailability, insufficient clinical evidence, production costs, and regulatory considerations remain major obstacles that require further investigation. Addressing these challenges will require interdisciplinary collaboration among food scientists, biotechnologists, analytical chemists, computational biologists, and clinical researchers to establish standardized production protocols, improve peptide delivery systems, and validate long-term safety

and efficacy in human populations. Future advances in omics technologies, synthetic biology, precision fermentation, enzyme engineering, AI-assisted peptide discovery, and nanotechnology-based delivery systems are expected to significantly accelerate the development of next-generation bioactive peptides with enhanced stability, target specificity, and therapeutic efficacy. As research continues to bridge the gap between laboratory discovery and industrial application, food-derived bioactive peptides are anticipated to play an increasingly important role in the development of sustainable functional foods, personalized nutrition strategies, and innovative therapeutic interventions. These naturally occurring compounds represent a rapidly expanding field with considerable scientific, industrial, and clinical significance, offering promising opportunities for improving human health and supporting the transition toward more sustainable and preventive healthcare approaches [34].

## Authors' Contributions

The author was responsible for all stages of the research and manuscript preparation and approved the final version.

## Data Availability

All data are included in the text.

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## Conflict of Interest

There are no competing interests to declare.

## Consent for Publication

The author confirms consent for the publication of this work

## Ethics Approval and Consent to Participate

This article does not contain any studies with human participants performed by the author.

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