



Bioactive Peptides Isolated from Different Sources and Their Inherent Properties

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Abstract

Bioactive peptides are short sequences of amino acids that are generally inactive or less active within parent proteins but can exert specific physiological effects when released through enzymatic hydrolysis, gastrointestinal digestion, fermentation, food processing, or other proteolytic processes. Increasing evidence has established food proteins and other natural protein sources as reservoirs of peptides with antioxidant, antihypertensive, antimicrobial, anti-inflammatory, antidiabetic, immunomodulatory, antithrombotic and mineral-binding activities. This review summarizes the major sources of bioactive peptides, including dairy products, meat and poultry, eggs, fish and marine organisms, cereals, legumes, oilseeds, microorganisms and food-processing by-products. Particular emphasis is placed on the inherent properties that influence biological activity, including peptide length, molecular weight, amino-acid composition, hydrophobicity, charge, sequence, terminal residues, structural conformation, resistance to gastrointestinal digestion and intestinal absorption. Dairy proteins such as caseins and whey proteins are important reservoirs of multifunctional peptides, while marine organisms provide structurally diverse peptides with distinctive stability and pharmacological properties. Plant-derived peptides, especially those from soybean, legumes and cereals, have attracted attention because of their antioxidant and cardiometabolic activities. Modern approaches involving ultrafiltration, chromatography, mass spectrometry, peptidomics, bioinformatics and in-silico prediction are accelerating peptide discovery. However, the translation of in-vitro activity into clinically meaningful effects remains constrained by gastrointestinal stability, bioavailability, purification cost, sequence confirmation, safety and insufficient human trials. Future research should therefore integrate sustainable source utilization, structure–activity relationship studies, advanced delivery systems and rigorous clinical validation.

Keywords: Bioactive peptides; food proteins; peptide isolation; antioxidant peptides; antihypertensive peptides; antimicrobial peptides; marine peptides; plant peptides; dairy peptides; structure–activity relationship; bioavailability; functional foods.



1. Introduction

Proteins have traditionally been regarded primarily as sources of amino acids for nutrition. However, research during recent decades has demonstrated that many proteins also contain short amino-acid sequences capable of producing specific biological effects after their release from parent proteins. These sequences are known as **bioactive peptides (BAPs)**. They may occur naturally in foods or be generated during digestion, fermentation, enzymatic hydrolysis and food processing. A commonly used description places many food-derived bioactive peptides in the range of approximately 2–20 amino acids, although naturally occurring bioactive peptides can extend beyond this range.

Bioactive peptides are receiving considerable attention because they combine nutritional origin with biological functionality. Reported activities include inhibition of angiotensin-converting enzyme (ACE), antioxidant activity, antimicrobial activity, anti-inflammatory effects, modulation of glucose metabolism, immunomodulation, cholesterol-lowering effects, mineral binding and antithrombotic activity.

The source protein is a major determinant of the peptides that can ultimately be generated. Dairy proteins contain numerous encrypted peptide sequences; cereal and legume proteins contain peptides with cardiometabolic and antioxidant potential; eggs provide peptides with ACE-inhibitory, antioxidant and antimicrobial activities; while marine organisms provide unusually diverse peptide structures and activities.

The biological effect of a peptide is not determined simply by its presence. Its **amino-acid sequence, molecular size, charge, hydrophobicity, conformation, terminal residues and resistance to proteolysis** can strongly influence its activity. Consequently, the study of bioactive peptides has developed from simple protein hydrolysis toward sophisticated isolation, structural characterization and structure–activity relationship studies.

2. Major Sources of Bioactive Peptides

2.1 Dairy and Milk Proteins

Milk is one of the most extensively studied sources of bioactive peptides. Major precursor proteins include **caseins, β -lactoglobulin, α -lactalbumin, lactoferrin and other whey proteins**. Bioactive sequences can be released through gastrointestinal digestion, fermentation by lactic acid bacteria, or treatment with proteolytic enzymes.



Milk-derived peptides have been associated with antihypertensive, antimicrobial, antioxidant, immunomodulatory, antithrombotic, opioid-like, mineral-binding and metabolic activities. Casein-derived peptides, particularly phosphopeptides, can participate in mineral binding, whereas several whey-derived sequences have demonstrated antioxidant and ACE-inhibitory activity.

Fermentation is particularly important because lactic acid bacteria possess proteolytic systems capable of releasing encrypted peptide sequences. Thus, fermented dairy products can act not merely as foods but also as matrices in which peptide generation occurs.

2.2 Meat and Poultry Proteins

Meat from cattle, pigs, poultry and other terrestrial animals contains proteins that can generate bioactive peptides. Muscle proteins such as myosin, actin and related structural proteins can serve as precursors.

Reported activities include antioxidant, ACE-inhibitory, antimicrobial and anti-inflammatory effects. Enzymatic hydrolysis with proteases such as pepsin, trypsin, alcalase and thermolysin has frequently been employed to produce peptide-rich hydrolysates.

The composition of meat proteins makes them particularly interesting for the production of peptides containing hydrophobic amino acids. Such residues may contribute to antioxidant activity or interactions with enzyme targets, although the relationship is sequence-dependent and cannot be generalized to every peptide.

2.3 Egg Proteins

Egg proteins are another important source. Both **egg white and egg yolk proteins** contain encrypted bioactive sequences. Ovalbumin, ovotransferrin, lysozyme and other proteins have been investigated as peptide precursors.

Egg-derived peptides have been reported to possess ACE-inhibitory, antioxidant, antimicrobial, anti-inflammatory, antidiabetic and mineral-binding activities.

Gastrointestinal digestion is particularly relevant because egg proteins can generate peptides during normal digestion. This makes eggs a useful model for studying the difference between activity observed in an isolated peptide and activity potentially generated following consumption of the intact food.

2.4 Fish and Marine Organisms



Marine resources constitute one of the most chemically diverse reservoirs of bioactive peptides. Sources include **fish, shellfish, mollusks, crustaceans, algae, sponges, marine microorganisms and marine invertebrates**. Marine by-products such as skin, bones and viscera are increasingly investigated as sustainable sources of peptide precursors.

Marine peptides may demonstrate antioxidant, antihypertensive, antimicrobial, anti-inflammatory, antidiabetic, anticoagulant and anticancer activities.

An important characteristic of some marine peptides is their structural diversity. Unlike conventional linear food peptides, marine natural-product peptides can include cyclic structures, unusual residues and post-translational modifications. These features can influence resistance to proteolysis and biological activity.

Fish-processing by-products are particularly attractive because skin and bones contain collagen and gelatin that can be converted into peptide-rich hydrolysates. This approach simultaneously adds value to waste streams and provides potentially useful functional ingredients.

2.5 Cereals and Legumes Plant proteins are increasingly recognized as important peptide sources. Major examples include **soybean, pea, chickpea, lentil, peanut, rice, wheat, oats, maize and other cereal or legume proteins**.

Cereal- and legume-derived peptides have demonstrated antioxidant, antihypertensive, antidiabetic, anti-inflammatory and other biological activities. However, the evidence base is still less mature than that for some dairy-derived peptides, and many studies have investigated hydrolysates without identifying the exact active sequences.

Soybean is particularly well studied. Soy peptides have been associated with ACE inhibition, antioxidant activity, antimicrobial effects, immunomodulation and hypocholesterolemic effects.

The sustainability of plant proteins further increases their importance for future functional-food development.

2.6 Microbial Sources

Microorganisms, including **bacteria, fungi, yeast, microalgae and cyanobacteria**, can produce peptides either as part of their own metabolism or through proteolysis of food proteins.



Bacterial peptides such as bacteriocins are especially important examples of antimicrobial peptides. Marine microorganisms are also being explored for structurally novel compounds with antimicrobial, antioxidant, antiviral, anticancer and other pharmacological activities.

Microbial fermentation has an additional advantage: it can be controlled and scaled more readily than harvesting certain natural marine or animal sources.

3. Isolation and Production of Bioactive Peptides

The production of bioactive peptides normally involves several stages:

Protein source → pretreatment → hydrolysis/fermentation → fractionation → purification → activity screening → sequence identification → structural confirmation

Enzymatic hydrolysis is among the most widely used methods because it can be controlled with respect to enzyme type, substrate concentration, pH, temperature and hydrolysis time. Common enzymes include pepsin, trypsin, chymotrypsin, alcalase, thermolysin and flavourzyme. Fermentation provides another route and may generate peptides that differ from those produced by a single commercial enzyme.

After hydrolysis, **ultrafiltration** is often used to separate fractions according to molecular weight. The resulting fractions can be screened for biological activity.

Further purification can involve:

- Ion-exchange chromatography
- Size-exclusion chromatography
- Reverse-phase high-performance liquid chromatography
- Solid-phase extraction
- Affinity chromatography
- Multidimensional liquid chromatography

Classical marine peptide isolation commonly combines gel filtration, ion exchange and reverse-phase HPLC with activity-guided assays.

Mass spectrometry, particularly LC-MS/MS, has become central to peptide identification. Peptidomics and bioinformatics now permit thousands of peptide sequences to be screened computationally before experimental validation.



A major challenge is that purification at laboratory scale does not necessarily translate into economical industrial production. Downstream purification remains one of the major bottlenecks for commercial development.

4. Inherent Physicochemical Properties of Bioactive Peptides

4.1 Molecular Weight and Peptide Length

Molecular size can strongly influence activity, transport and digestion. Many food-derived bioactive peptides are relatively small, often below 3 kDa. Low molecular-weight fractions frequently demonstrate substantial biological activity, although molecular weight alone cannot predict activity.

Small peptides may have improved intestinal transport compared with larger protein fragments, but their stability and sequence must also be considered.

4.2 Amino-Acid Composition

Amino-acid composition is one of the most important determinants of peptide function.

Hydrophobic amino acids such as **Leu, Ile, Val, Phe, Trp, Tyr and Pro** can influence membrane interaction, enzyme binding and antioxidant behavior. Aromatic amino acids can participate in radical-scavenging reactions, while positively charged residues such as Lys and Arg may facilitate interactions with negatively charged microbial membranes.

However, a peptide's activity is determined by the **specific sequence and spatial arrangement**, rather than merely by the total number of hydrophobic or charged residues.

4.3 Hydrophobicity

Hydrophobicity is especially relevant to antimicrobial peptides. Hydrophobic residues can facilitate interaction with lipid membranes, while positively charged residues can promote electrostatic attraction to negatively charged microbial surfaces.

For ACE-inhibitory peptides, hydrophobic residues near specific terminal positions have frequently been associated with increased activity.

4.4 Net Charge

Net charge influences solubility, membrane binding and receptor interactions. Cationic peptides are often particularly effective against microbial membranes because bacterial surfaces generally possess substantial negative charge.

Charge also affects chromatographic purification and peptide behavior in biological fluids.



4.5 Structural Conformation

Bioactive peptides can be linear, cyclic or adopt α -helical, β -sheet, turn or disordered conformations. Marine natural-product peptides can display especially complex structures. Conformation determines whether functional residues are exposed to the biological target. Consequently, two peptides with similar amino-acid composition can have substantially different activities.

5. Major Biological Activities

5.1 Antihypertensive Activity

Antihypertensive peptides are among the most extensively studied food-derived peptides. The major mechanism involves **ACE inhibition**. ACE participates in the renin-angiotensin system and contributes to the formation of angiotensin II. Inhibition of ACE can therefore influence vascular tone and blood pressure.

Some peptides may additionally inhibit renin or influence nitric oxide-related vascular mechanisms. Plant, dairy, animal and marine proteins can all provide antihypertensive peptides.

5.2 Antioxidant Activity

Oxidative stress is associated with the generation of reactive oxygen and nitrogen species. Antioxidant peptides may neutralize radicals, chelate transition metals or interact with oxidative pathways.

Histidine-, tyrosine-, tryptophan-, methionine- and cysteine-containing sequences may have antioxidant potential, depending on their position and surrounding residues.

5.3 Antimicrobial Activity

Antimicrobial peptides can act through membrane disruption, pore formation, membrane depolarization or intracellular interference.

Their activity often depends on a combination of positive charge and hydrophobicity. Food-derived antimicrobial peptides are being studied as potential natural preservatives, although activity against target organisms and sensory effects must be carefully evaluated.

5.4 Anti-inflammatory Activity



Some peptides can modulate inflammatory signaling pathways. Reported mechanisms include effects on NF- κ B, MAPK, PI3K/Akt and other pathways. Recent literature also emphasizes the importance of digestion and bioavailability when assessing anti-inflammatory peptide effects.

5.5 Antidiabetic and Metabolic Effects

Certain peptides inhibit enzymes involved in glucose metabolism, including DPP-IV and α -glucosidase. Other peptides may influence insulin signaling or oxidative stress.

Milk-derived peptides are particularly well represented in studies of DPP-IV inhibition and metabolic regulation.

5.6 Immunomodulatory and Mineral-Binding Activities

Certain milk phosphopeptides can bind minerals and potentially influence mineral availability.

Other peptides interact with immune cells or inflammatory pathways.

These properties demonstrate that bioactive peptides should not be considered a single functional class; rather, they represent a broad group of molecules with distinct molecular targets.

6. Structure–Activity Relationships

A central principle in peptide research is that **biological activity is sequence-dependent**.

For example, ACE-inhibitory activity can be affected by residues near the C-terminal region. Hydrophobic and aromatic residues frequently occur in active sequences, but individual positional effects are important.

For antimicrobial peptides, a balance between positive charge and hydrophobicity can promote membrane interaction.

For antioxidant peptides, aromatic or sulfur-containing residues can contribute to radical scavenging, whereas acidic residues may contribute to metal chelation.

Therefore:

Sequence → conformation → target interaction → biological response

This relationship explains why hydrolysate activity cannot automatically be attributed to every peptide within the hydrolysate.

7. Bioavailability and Gastrointestinal Stability

One of the biggest scientific challenges is the difference between **in-vitro activity and activity in the human body**.



A peptide may show excellent ACE inhibition in a test tube but be rapidly degraded by gastrointestinal proteases. Conversely, gastrointestinal digestion can sometimes generate the active peptide from an inactive precursor.

Important factors include:

1. Resistance to pepsin and pancreatic enzymes
2. Intestinal epithelial transport
3. Stability in blood plasma
4. Metabolic degradation
5. Ability to reach the biological target
6. Dose required to produce an effect

Recent research increasingly incorporates simulated gastrointestinal digestion, Caco-2 transport studies, ex-vivo assays and animal models rather than relying exclusively on enzyme assays.\

8. Comparative Overview of Major Sources

Source	Important precursor proteins/materials	Major reported activities
Milk/dairy	Caseins, whey proteins, lactoferrin	ACE inhibition, antioxidant, antimicrobial, immunomodulatory, mineral binding
Meat/poultry	Myosin, actin and muscle proteins	Antioxidant, antihypertensive, antimicrobial
Egg	Ovalbumin, ovotransferrin, lysozyme	ACE inhibition, antioxidant, antimicrobial, anti-inflammatory
Fish	Muscle proteins, collagen	Antioxidant, ACE inhibition, antimicrobial
Marine organisms	Fish, shellfish, algae, sponges, invertebrates	Antioxidant, antimicrobial, anti-inflammatory, anticancer, anticoagulant
Soybean	Glycinin, β -conglycinin	Antioxidant, antihypertensive, hypocholesterolemic, immunomodulatory
Cereals	Gluten and storage proteins	Antioxidant, antihypertensive, antidiabetic
Legumes	Globulins and storage proteins	Antioxidant, antihypertensive, anti-inflammatory
Microorganisms	Microbial proteins and secreted peptides	Antimicrobial, antioxidant and pharmacological activities

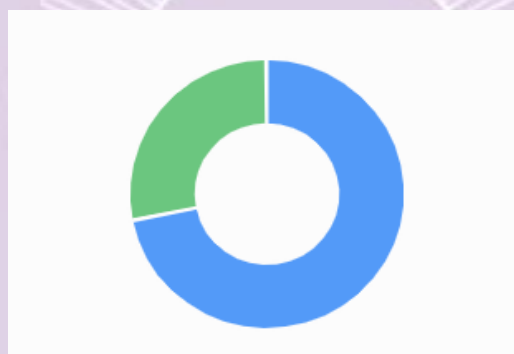
The diversity of these sources is consistent with recent reviews showing that plant and marine matrices constitute a substantial proportion of recent antihypertensive peptide research, while dairy, animal, insect and fungal sources are also being investigated.

9. Graphical Representation of the Evidence Base

A recent systematic review covering **177 studies of food-derived antihypertensive peptides published from January 2020 to January 2025** reported that plant and marine matrices together accounted for approximately **72% of the evidence base**. The remaining approximately 28% represented dairy, terrestrial animal, insect, fungal and other matrices.

Distribution of source groups in a recent antihypertensive-peptide evidence base

Plant and marine matrices together represented approximately 72% of 177 included studies; the remaining 28% represented other source groups.



Other source groups Plant + marine

Based on the 2020–January 2025 systematic review; categories are grouped as reported in that review.

Figure 1. Approximate distribution of the evidence base reported in a recent systematic review.

The values represent percentages of studies, not the biological potency of the source categories.

A second useful way to visualize the field is to consider the major biological functions reported across sources:

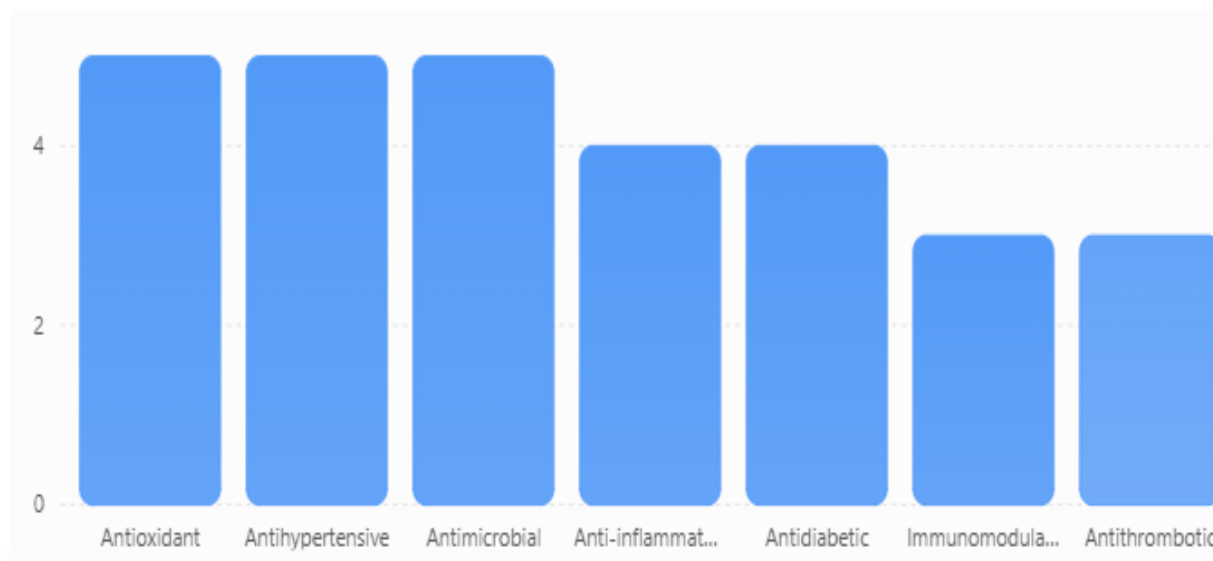
Major biological activities investigated in bioactive-peptide research

Qualitative literature synthesis showing major activity classes rather than a quantitative prevalence estimate.

The bars are an illustrative synthesis and should not be interpreted as measured frequencies.

Figure 2. Conceptual visualization of major activity areas frequently discussed in the literature. **These values are illustrative and are not quantitative publication counts;** they are included to communicate the breadth of reported functions.

10. Applications



The multifunctionality of bioactive peptides creates opportunities in several sectors.

Functional foods

Peptides can be incorporated into beverages, fermented products, protein hydrolysates and specialized nutritional formulations.

Nutraceuticals

Peptide-rich fractions may be developed as ingredients targeting cardiovascular, metabolic or oxidative-stress-related health outcomes.

Food preservation

Antimicrobial peptides have potential as natural alternatives or complements to conventional preservatives.

Cosmetics

Antioxidant, antimicrobial and collagen-derived peptides have potential applications in skin-care formulations.

Pharmaceuticals

Some highly potent natural peptides provide templates for drug development. Marine natural-product research has demonstrated particularly broad pharmacological potential.



11. Challenges and Future Perspectives

Despite significant progress, several limitations remain.

- ❖ **First, activity confirmation is essential.** Many studies demonstrate activity using purified enzymes or cell systems, but this does not automatically establish human efficacy.
- ❖ **Second, peptide identification remains important.** Hydrolysates may contain hundreds of peptides, and identifying the actual active sequence is necessary for reproducibility.
- ❖ **Third, bioavailability is a major barrier.** Peptides may be degraded before reaching their target.
- ❖ **Fourth, purification can be expensive.** Industrial-scale production requires high recovery, reproducible purity and economically viable downstream processing.
- ❖ **Fifth, safety requires systematic evaluation.** Allergenicity, toxicity, interactions with medications and long-term consumption need consideration before health claims are established.

Future research is likely to combine **proteomics, peptidomics, artificial intelligence, molecular docking, machine learning and targeted experimental validation**. Such approaches can identify promising peptide sequences before extensive laboratory purification. Sustainable production will also become increasingly important. Marine by-products, dairy whey, fish skin, bones and plant-processing residues represent valuable sources that could simultaneously reduce waste and generate high-value ingredients.

12. Conclusion

Bioactive peptides represent a diverse group of naturally derived molecules with substantial potential in food, nutrition, biotechnology and pharmaceutical research. They can be obtained from dairy proteins, meat, eggs, fish, marine organisms, cereals, legumes, oilseeds and microorganisms. Their biological functions include antioxidant, antihypertensive, antimicrobial, anti-inflammatory, antidiabetic, immunomodulatory, antithrombotic and mineral-binding activities.

The biological activity of a peptide is strongly influenced by its **amino-acid sequence, molecular weight, hydrophobicity, charge, terminal residues, structural conformation**



and resistance to digestion. Consequently, the identification of a peptide source alone is insufficient; understanding the relationship between structure and function is essential.

Dairy and plant proteins provide abundant and comparatively accessible peptide reservoirs, while marine organisms provide exceptional structural diversity. Food-processing by-products offer an important opportunity for sustainable peptide production.

The field is moving from simple protein hydrolysis toward integrated workflows involving enzymatic production, chromatographic purification, mass spectrometry, peptidomics, computational prediction, gastrointestinal models and clinical validation. Nevertheless, successful translation requires overcoming limitations in bioavailability, purification, reproducibility, safety and human evidence.

Overall, bioactive peptides can be regarded as **multifunctional molecular components linking food proteins with biological regulation.** Their future development will depend not only on discovering new peptides but also on demonstrating that identified peptides remain stable, bioavailable, safe and biologically effective under physiologically relevant conditions.

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