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Comparative Review of Anti-Inflammatory Bioactive Peptides from *Moringa oleifera*, *Pisum sativum*, and *Glycine max:* Production, Mechanisms and Therapeutic Potential

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Abstract: Bioactive peptides derived from plant proteins have attracted increasing scientific interest because of their anti-inflammatory, antioxidant, antihypertensive, and immunomodulatory properties. Among plant protein sources, *Moringa oleifera*, pea (*Pisum sativum*), and soybean (*Glycine max*) are recognized as important reservoirs of functional peptides generated through enzymatic hydrolysis, fermentation, or gastrointestinal digestion. This review critically compares anti-inflammatory peptides derived from moringa, pea, and soybean with emphasis on protein composition, peptide production methods, structural characteristics, molecular mechanisms, and evidence from in vitro and in vivo studies. Soybean peptides remain the most extensively characterized, because of well-studied compounds such as lunasin,soymorphins, glycinin-derived peptides, and β-conglycinin hydrolysates. Pea peptides have demonstrated promising antioxidant-mediated anti-inflammatory activity through modulation of oxidative stress and cytokine signaling pathways, whereas moringa-derived peptides remain comparatively underexplored despite increasing evidence of anti-inflammatory and antioxidant potential. Current evidence suggests that these peptides regulate inflammatory responses through inhibition of nuclear factor-kappa B (NF-κB), suppression of cyclooxygenase-2 (COX-2), reduction of inducible nitric oxide synthase (iNOS), modulation of mitogen-activated protein kinase (MAPK) signaling, and regulation of oxidative stress pathways such as Nrf2/Keap1. However, significant variation in extraction techniques, peptide purification, experimental models, and peptide characterization limits direct comparison across studies. This review highlights current advances, mechanistic insights, translational limitations, and future opportunities for the development of plant-derived anti-inflammatory peptide therapeutics and nutraceuticals.

Keywords: *Bioactive Peptides, Anti-Inflammatory Activity, Moringa Peptides, Pea Peptides, Soybean Peptides, NF-Kb, Cytokines, Nutraceuticals.*

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I. INTRODUCTION

Non-communicable diseases (NCDs) remain the leading cause of mortality worldwide and are responsible for approximately 74% of global deaths. Cardiovascular diseases, cancers, chronic respiratory diseases, and diabetes collectively account for millions of deaths annually and are strongly associated with chronic inflammatory processes (World Health Organization (WHO) , 2024).

Inflammation is a complex biological response that protects the body against infection, injury, and harmful stimuli. While acute inflammation is essential for tissue repair and immune defense, persistent or unresolved inflammation contributes significantly to the development of chronic disorders such as cardiovascular disease, rheumatoid arthritis, inflammatory bowel disease, obesity, type 2 diabetes mellitus, neuro-degenerative diseases, and cancer (Xu et al., 2024). Chronic activation of inflammatory pathways results in excessive production of pro-inflammatory cytokines, reactive oxygen species (ROS), nitric oxide (NO), cyclooxygenase-2 (COX-2), and inducible nitric oxide synthase (iNOS), thereby promoting tissue injury and disease progression.

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Conventional anti-inflammatory therapies, including non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids, are effective in controlling inflammation; however, their long-term use is frequently associated with adverse effects such as gastrointestinal ulceration, renal dysfunction, cardiovascular complications, immunosuppression, and metabolic disturbances (Bindu et al., 2020). Consequently, there is growing interest in identifying safer natural compounds capable of modulating inflammatory pathways with fewer side effects.

Among these compounds, food-derived bioactive peptides have emerged as promising therapeutic and nutraceutical candidates. These peptides are specific amino acid sequences encrypted within parent proteins and released through enzymatic hydrolysis, microbial fermentation, food processing, or gastrointestinal digestion. Depending on their molecular weight, amino acid composition, hydrophobicity, and structural characteristics, bioactive peptides can exhibit antioxidant, antimicrobial, antihypertensive, immunomodulatory, anticancer, and anti-inflammatory activities (Udenigwe & Aluko, 2012; Singh et al., 2014).

Plant proteins are particularly attractive substrates for peptide production because they are sustainable, economically accessible, and generally associated with a lower environmental impact than animal-derived proteins (Aguilar-Toalá et al., 2022). Among plant protein sources, *Moringa oleifera*, pea *(Pisum sativum*), and soybean (*Glycine max)* are considerable due to their high protein content, favorable amino acid profiles, and ability to generate biologically active peptides with anti-inflammatory potential.

Soybean proteins are the most extensively studied source of plant-derived anti-inflammatory peptides. Peptides such as lunasin and soymorphins have exhibited the ability to inhibit nuclear factor-kappa B (NF-κB) signaling, suppress pro-inflammatory cytokine production, and attenuate oxidative stress (Chatterjee et al., 2018; Hernández-Ledesma et al., 2008). Pea proteins have also shown promising antioxidant and anti-inflammatory activities following enzymatic hydrolysis (Ndiaye et al., 2011). In contrast, bioactive peptides derived from Moringa oleifera remain comparatively underexplored despite emerging evidence of antioxidant, immunomodulatory, and anti-inflammatory properties (Avilés-Gaxiola et al., 2021; Fernández-Tomé et al., 2019).

This review provides a comprehensive comparative evaluation of anti-inflammatory peptides derived from *Moringa oleifera*, *Pisum sativum*, and *Glycine max*, focusing on protein composition, peptide production methods, structural characteristics, molecular mechanisms, biological activities, and translational potential. By critically comparing these three important plant protein sources, this review aims to identify current advances, existing limitations, and future opportunities for the development of peptide-based nutraceuticals and therapeutic agents.

II. LITERATURE SEARCH STRATEGY

This review was conducted using a comprehensive search of peer-reviewed literature from PubMed, Scopus, Web of Science, and Google Scholar. Keywords included "*Moringa oleifera* peptides", "pea protein peptides", "soybean bioactive peptides", "anti-inflammatory peptides", "NF-κB", "Nrf2", "JAK/STAT", "MAPK signaling", and "plant-derived bioactive peptides". Publications from 2012 to 2026 were considered. Studies were included if they reported peptide isolation, characterization, anti-inflammatory activity, molecular mechanisms, or translational applications. Studies focused exclusively on crude extracts without peptide characterization were used only as supportive evidence and were clearly distinguished from peptide-specific investigations.

- *Protein Composition, Hydrolysis Characteristics, and Fermentation of Moringa, Pea, and Soybean Proteins*

Protein composition strongly influences peptide yield, amino acid profile, hydrolysis efficiency, and the biological activity of derived peptides. Among plant protein sources, *Moringa oleifera*, pea *(Pisum sativum*), and soybean *(Glycine max)* have attracted increasing attention for bioactive peptide production because of their high protein contents and favorable amino acid compositions.

Moringa oleifera, commonly known as the "miracle tree," possesses considerable nutritional and medicinal value. The leaves and seeds contain approximately 20–35% protein on a dry-weight basis, depending on cultivar, agronomic conditions, maturity stage, and processing method (Busani et al., 2011; Islam et al., 2021). Moringa proteins contain all essential amino acids and are particularly rich in glutamic acid, aspartic acid, leucine, arginine, lysine, alanine, valine, phenylalanine, and proline (Jiarui et al., 2023). These amino acids contribute significantly to the generation of bioactive peptides because hydrophobic residues such as leucine, valine, phenylalanine, alanine, and proline enhance radical scavenging activity and membrane interactions, whereas positively charged residues such as lysine and arginine facilitate interactions with inflammatory mediators and cellular signaling pathways.

The major storage proteins in moringa seeds are globulins and albumins, which serve as suitable substrates for proteolytic enzymes. Alcalase is the enzyme mostly used for moringa protein hydrolysis because of its broad substrate specificity. Typical hydrolysis conditions reported for moringa protein isolates include pH 8.0–9.0, temperatures of 50–55℃, enzyme-to-substrate (E:S) ratios of 1–3% (w/w), and hydrolysis times of 2–4 h. Under these conditions, degrees of hydrolysis generally range from 15–30%, yielding peptides predominantly below 5 kDa that exhibit antioxidant and anti-inflammatory activities. Increased DH generally produces smaller peptides with improved intestinal absorption; however, excessive hydrolysis may degrade functional peptide sequences and reduce biological activity.

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Pea protein contains approximately 20–30% protein and is composed predominantly of globulin storage proteins including legumin (11S globulin), vicilin (7S globulin), and convicilin (Stone et al., 2014). Legumin and vicilin account for approximately 50–80% of total pea protein. Structurally, legumin consists of acidic and basic subunits linked by disulfide bonds, whereas vicilin lacks these linkages and is therefore more susceptible to enzymatic hydrolysis. This structural difference significantly affects peptide release and hydrolysis efficiency.

Pea proteins are rich in lysine, leucine, valine, and arginine but contain lower concentrations of sulfur-containing amino acids such as methionine (Harasym et al., 2025). Alcalase-mediated hydrolysis of pea protein is typically conducted under alkaline conditions (pH 8.0–8.5) at temperatures of 50–55℃, with enzyme-to-substrate ratios of approximately 1–2% and hydrolysis times ranging from 2–4 h. These conditions commonly generate hydrolysates with varying degrees of hydrolysis (DH), depending on enzyme loading and substrate characteristics. Recent evidence indicates that intermediate hydrolysis (DH 10–20%) produces the highest antioxidant activity, whereas extended hydrolysis (DH >20%) enhances ACE-inhibitory activity through the generation of low-molecular-weight peptides (<3 kDa). Such peptides exhibit improved gastrointestinal stability, absorption, and bioavailability (Aluko et al., 2015; Filippo et al., 2025).

Soybean possesses the highest protein concentration among the three plant sources, typically containing 35–40% protein (Singh et al., 2014). Soy proteins are dominated by glycinin (11S globulin) and β-conglycinin (7S globulin), which together account for approximately 70–90% of the total seed protein. Glycinin consists of acidic and basic polypeptides linked by disulfide bonds, whereas β-conglycinin is composed of α′, α, and β subunits that differ in structure, functionality, and digestibility. The abundance of hydrophobic amino acids within these storage proteins makes soybean an excellent substrate for the generation of bioactive peptides with antioxidant, antihypertensive, and anti-inflammatory activities (Fan et al., 2025; Nongonierma & Fitzgerald, 2016; Yi et al., 2020).

Soy protein hydrolysis has been extensively optimized using Alcalase, Flavourzyme, Protamex, pepsin, and other proteases. Among these, Alcalase consistently produces the highest DH. Typical hydrolysis conditions include pH 8.0, temperature 50℃, E:S ratios of 0.5–3.5%, and hydrolysis times ranging from 1–8 h. Under these conditions, DH values between 10 and 25% are commonly achieved (Sheng ma et al., 2013). Sequential hydrolysis with Alcalase followed by Flavourzyme at pH 7.0 and 50℃ for approximately 2h can further increase DH to about 24%, while simultaneously reducing bitterness through exopeptidase activity.

The degree of hydrolysis is a critical parameter affecting peptide functionality and bioavailability. DH represents the percentage of peptide bonds cleaved during enzymatic digestion. Generally, increasing DH decreases peptide molecular weight and improves solubility, digestibility, and intestinal absorption. Peptides below 3 kDa typically demonstrate high bioavailability because they can be absorbed via peptide transporters such as PepT1. However, very high DH values may generate excessive free amino acids and short peptide fragments that exhibit reduced biological activity. Consequently, many studies identify a moderate DH range (approximately 15–25%) as optimal for balancing peptide release, bioactivity, and sensory quality (Dent et al., 2023).

Beyond enzymatic hydrolysis, fermentation has emerged as an effective strategy for generating bioactive peptides from plant proteins. During fermentation, microbial proteases released by bacteria, yeasts, or fungi hydrolyze storage proteins into smaller peptides while simultaneously improving digestibility and reducing antinutritional factors. Common microorganisms include Lactobacillus plantarum, Lactobacillus casei, Bacillus subtilis, and Aspergillus oryzae. Fermentation often generates peptides that differ from those produced by commercial enzymes because microbial proteases possess unique cleavage specificities.

In soybean, fermentation by Bacillus subtilis during natto production extensively hydrolyzes glycinin and β-conglycinin, producing low-molecular-weight peptides with antioxidant, antihypertensive, anti-inflammatory, and immunomodulatory properties (Rizwan et al., 2023). Similarly, lactic acid fermentation of soybean proteins increases peptide release, improves digestibility, and enhances antioxidant activity (Fadlillah et al., 2025). Fermentation also reduces allergenic proteins and antinutritional compounds, thereby improving bioavailability and functional performance (Lim et al., 2022). Comparable benefits have been reported for fermented pea proteins, where lactic acid bacteria increase protein digestibility and peptide yield(Al-Qaisi et al., 2024). Fermentation studies involving moringa proteins remain relatively limited but have shown improved antioxidant activity and increased liberation of small peptides following microbial treatment (Shi et al., 2021).

Soybean provides the greatest quantitative advantage for peptide production because of its high protein content and abundance of storage globulins (Ketnawa & Ogawa, 2021). Pea protein exhibits excellent hydrolysis flexibility owing to the susceptibility of vicilin to proteolytic cleavage (Boukid et al., 2021), while moringa offers a unique combination of complete amino acid composition and high levels of arginine, leucine, phenylalanine, and proline that favor the generation of bioactive peptides (Su & Chen, 2020). The ultimate biological activity of peptides derived from these sources depends not only on protein content but also on amino acid sequence, molecular weight, hydrophobicity, charge distribution, degree of hydrolysis, gastrointestinal stability, and bioavailability (Ketnawa & Ogawa, 2021).

- *Comparative Amino Acid Evidence*

Comparatively, moringa appears particularly rich in arginine, lysine, leucine, and aromatic amino acids relative

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to many plant proteins (Su & Chen, 2020,), which may explain the potent biological activity observed in some moringa-derived peptides. Pea protein is characterized by high lysine, leucine, and arginine but comparatively lower methionine(Boukid et al., 2021; Pinckaers et al., 2024,), making it favorable for anti-inflammatory peptide production but limited in sulfur-containing antioxidant peptide diversity. Soybean contains the most balanced amino acid profile overall and generally contains higher total protein content together with substantial amounts of leucine, lysine, arginine, glutamic acid, and sulfur amino acids (Chéreau et al., 2016), thereby supporting greater peptide diversity and hydrolysis efficiency. Moringa provides highly bioactive peptide sequences despite lower protein abundance, pea offers superior digestibility and efficient hydrolysis, whereas soybean provides the greatest overall peptide-generating capacity because of its quantitative and qualitative amino acid advantages.

Table 1 Comparative Amino Acid Profile of Moringa Leaf, Pea, and Soybean Proteins (g/100 g Protein)
Data Compiled from Islam et al. (2021), Nosworthy et al. (2017), and Stefan et al. (2018).

Amino Acid	Moringa Leaf Protein	Pea Protein	Soybean Protein
Essential Amino Acids			
Histidine	2.2	2.4	2.6
Isoleucine	4.8	4.1	4.7
Leucine	9.2	7.3	7.7
Lysine	5.6	7.0	6.4
Methionine	1.8	0.9	1.3
Phenylalanine	6.2	5.0	5.0
Threonine	4.2	3.7	4.0
Tryptophan	1.4	0.9	1.4
Valine	5.4	4.3	5.3
Non-Essential Amino Acids			
Alanine	6.3	4.2	4.8
Arginine	7.4	8.7	7.2
Aspartic Acid	8.5	11.5	11.6
Glutamic Acid	10.7	17.2	19.0
Glycine	5.3	4.1	4.5
Proline	2.9	4.0	5.3
Serine	4.1	4.8	5.8
Tyrosine	4.0	3.2	3.7
Cysteine	0.6	1.0	1.9

Values are expressed as g amino acid/100 g protein and compiled from published compositional analyses of Moringa leaf, pea, and soybean proteins (Islam et al., 2021; Nosworthy et al., 2017; Stefan et al., 2018).

Moringa protein contains the highest leucine concentration (9.2 g/100 g protein), which may favor generation of bioactive peptides involved in metabolic regulation.

Pea protein is particularly rich in arginine and lysine, amino acids associated with immune modulation and nitric oxide synthesis.

Soybean protein has the highest glutamic acid content and a balanced essential amino acid profile, contributing to its superior digestibility and peptide yield during enzymatic hydrolysis.

Methionine and cysteine remain limiting sulfur-containing amino acids in these plant proteins, although levels vary significantly among sources(Makkar, 2017).

The abundance of hydrophobic amino acids (Leu, Ile, Val, Phe) in soybean and Moringa contributes to the formation of anti-inflammatory and antioxidant peptides after hydrolysis.

Table 2 Functional Amino Acid Groups Relevant to Anti-Inflammatory Peptide Generation from Moringa, Pea, and Soybean Proteins

Amino Acid Group	Moringa (%)	Pea (%)	Soybean (%)	Biological Significance
Hydrophobic amino acids (Ala + Val + Leu + Ile + Met + Pro + Phe + Gly)	40.7	31.8	35.2	Promote interaction with cell membranes and inflammatory signaling proteins; frequently found in antioxidant and NF-κB inhibitory peptides
Aromatic amino acids (Phe + Tyr + Trp)	11.6	9.1	10.1	Enhance radical scavenging, electron donation, and ROS neutralization
Positively charged amino acids (Arg + Lys + His)	15.2	18.1	16.2	Important for immunomodulation, macrophage interaction, and nitric oxide regulation
Sulfur-containing amino acids (Met	2.4	1.3	3.2	Precursors of glutathione synthesis and cellular

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+ Cys)				antioxidant defense
Branched-chain amino acids (BCAAs) (Leu + Ile + Val)	19.4	13.7	17.7	Contribute to immune regulation, protein synthesis, and peptide bioactivity
Acidic amino acids (Asp + Glu)	19.2	28.7	30.6	Influence peptide solubility, metal chelation, and antioxidant activity
Basic amino acids (Arg + Lys + His)	15.2	18.1	16.2	Facilitate interaction with negatively charged biological membranes and inflammatory mediators

Percentages were calculated from amino acid profile data reported by Islam et al. (2021), Nosworthy et al. (2017), and Stefan et al. (2018). Functional roles are based on established structure–activity relationships of food-derived bioactive peptides(Guha & Majumder, 2018).

The abundance of hydrophobic, aromatic, basic, and branched-chain amino acids in Moringa, pea, and soybean proteins suggests a strong potential for generating anti-inflammatory peptides. These amino acid groups are frequently associated with antioxidant activity, NF-κB inhibition, cytokine modulation, and enhanced peptide–membrane interactions (Rivera-Jiménez et al., 2022).

- *Formula Used for Calculating Functional Amino Acid Groups*

The percentage of each amino acid group was calculated as:

Amino Acid Group (%)= (∑Selected Amino Acids ∑Total Amino Acids) ×100\{Amino Acid Group (\%)}=\frac{\sum \text{Selected Amino Acids}}{\sum \text{Total Amino Acids}}\times100Amino Acid Group (%)=∑Total Amino A cids∑Selected Amino Acids×100

Where the selected amino acids correspond to the amino acid group of interest.

Table 3 Classification of Functional Amino Acid Groups Used in the Evaluation of Bioactive Peptides

Amino Acid Group(Karlin et al., 2002, p. 334)	**Formula**
Hydrophobic amino acids	Ala + Val + Leu + Ile + Met + Pro + Phe + Gly
Aromatic amino acids	Phe + Tyr + Trp
Positively charged amino acids	Arg + Lys + His
Sulfur-containing amino acids	Met + Cys
Branched-chain amino acids (BCAAs)	Leu + Ile + Val
Acidic amino acids	Asp + Glu
Basic amino acids	Arg + Lys + His

- *Example Calculation (Moringa Hydrophobic Amino Acids)*

Using the amino acid values from Table 1(Stadtlander & Becker, 2017, p. 49):

Ala (6.3) + Val (5.4) + Leu (9.2) + Ile (4.8) + Met (1.8) + Pro (2.9) + Phe (6.2) + Gly (5.3)
= 41.9 g/100 g protein

If the total quantified amino acids equal 103.0 g/100 g protein:

41.9103.0×100=40.7%\frac{41.9}{103.0}\times100=40.7\%103.041.9×100=40.7%

- *Methodology Statement for the Table*

✓ *Method:*

Amino acid group percentages were calculated from the amino acid composition data of Moringa leaf, pea, and soybean proteins reported by Islam et al. (2021), Nosworthy et al. (2017), and Stefan et al. (2018). Amino acids were grouped according to their physicochemical properties and known contributions to bioactive peptide functionality. Hydrophobic, aromatic, sulfur-containing, branched-chain, acidic, and basic amino acid categories were defined following the structure-activity relationship approach commonly used in bioactive peptide research (Udenigwe & Aluko, 2012; Nongonierma & FitzGerald, 2015; Chakrabarti et al., 2018). Percentages were expressed relative to the total quantified amino acids in each protein source.

Hydrophobic amino acids constituted the largest functional amino acid fraction in Moringa protein (40.7%), followed by soybean (35.2%) and pea protein (31.8%). These residues are particularly important because hydrophobic peptide sequences exhibit enhanced interactions with cellular membranes and inflammatory signaling proteins, thereby contributing to antioxidant and anti-inflammatory activities. Soybean protein contained the highest proportion of sulfur-containing amino acids (3.2%), which may favor glutathione biosynthesis and redox regulation. Pea protein exhibited the highest content of positively charged amino acids (18.1%), particularly arginine, suggesting potential immunomodulatory benefits through nitric oxide-dependent mechanisms (Islam et al., 2021).

➢ *Extraction and Hydrolysis Methods of Moringa oleifera, Pea, and Soybean Proteins*

Bioactive peptide production involves two major steps: protein extraction (or concentration) and enzymatic hydrolysis. Protein extraction is essential because it determines substrate purity, protein recovery, digestibility,

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and the efficiency of subsequent hydrolysis. Following extraction, enzymatic hydrolysis cleaves proteins into smaller peptide fragments with specific biological functions, including antioxidant, anti-inflammatory, antihypertensive, and immunomodulatory activities. Importantly, the choice of proteolytic enzyme is decisive because enzymes differ in substrate specificity, cleavage patterns, and optimal reaction conditions, thereby influencing peptide sequence, molecular weight distribution, and final biological activity (Görgüç et al., 2020; Tadesse & Emire, 2020).

➢ *Protein Extraction Methods*

Before hydrolysis, proteins from moringa, pea, and soybean are isolated or enriched to improve extraction efficiency and increase the availability of hydrolyzable protein fractions (Anyiam et al., 2025). Several extraction methods have been utilized, although their suitability differs according to protein source, structural characteristics, lipid content, and peptide application (Asen et al., 2023).

Table 4 Common Protein Extraction and Concentration Methods Used for Moringa, Pea, and Soybean Proteins

Method	Principle	Major Applications	Advantages	Limitations
Alkaline extraction	Protein solubilization at alkaline pH followed by precipitation (usually near isoelectric point)	Soybean, pea, moringa leaves and seeds, legumes	High protein recovery, inexpensive, scalable	Possible protein denaturation and amino acid modification at high pH
Ultrafiltration	Membrane separation based on molecular size and molecular weight cut-off	Protein concentration and peptide fractionation	Preserves protein functionality, high purity, selective separation	High equipment cost and membrane fouling
Solvent extraction	Organic solvents remove lipids before protein recovery	Oil-rich seeds (e.g., soybean, moringa seed meals)	Efficient defatting improves protein concentration	Risk of solvent residues and protein denaturation

Adapted from studies on plant protein extraction and fractionation technologies (Moure et al., 2006; Stone et al., 2015; Lam et al., 2018; Leone et al., 2016).

Among these techniques, alkaline extraction remains the most widely applied method for plant proteins, particularly soybean and pea proteins, because plant storage proteins exhibit higher solubility under alkaline conditions. In this process, proteins are dissolved at alkaline pH (typically pH 8–11), followed by precipitation near the isoelectric point (approximately pH 4–5), allowing protein recovery as isolates or concentrates (Chandran et al., 2023). The method is attractive due low cost, industrial scalability, and relatively high extraction yield. Soybean and pea proteins are especially suitable for alkaline extraction because their dominant globulins (glycinin, β-conglycinin, legumin, and vicilin) exhibit favorable solubility behavior in alkaline media. Similarly, moringa leaf proteins have been extracted using alkaline-assisted methods to improve protein concentration prior to hydrolysis. However, excessive alkalinity may induce protein denaturation, lysine modification, racemization, or reduced functionality, which can negatively affect peptide quality and bioactivity (Prandi et al., 2022).

A critical comparison reveals that alkaline extraction generally provides higher protein recovery for soybean than for pea or moringa because soybean possesses greater total protein content (35–40%) and abundant storage globulins. Pea proteins are moderately extractable, although extraction efficiency may vary due to vicilin–legumin ratios and cultivar variability. Moringa proteins present additional challenges because the leaf matrix contains polyphenols, fiber, chlorophyll, and antinutritional compounds that may interfere with extraction and reduce protein purity. Consequently, although alkaline extraction is effective across all three plant sources, soybean typically yields the highest protein isolate recovery, while moringa often requires additional clarification or purification steps.

Ultrafiltration is another important technology, particularly for protein concentration and peptide purification after hydrolysis. This membrane-based process separates proteins or peptides according to molecular weight cut-offs, enabling selective enrichment of low-molecular-weight peptides associated with stronger bioactivity and improved gastrointestinal absorption. Compared with alkaline extraction, ultrafiltration offers superior selectivity and minimizes severe chemical modification because no harsh pH treatment is required. In soybean and pea protein systems, ultrafiltration has been employed to obtain concentrated protein fractions and peptide isolates with improved purity and functional properties. However, the method is expensive, energy-intensive, and susceptible to membrane fouling, limiting large-scale implementation in some settings (Hernandez-Ledesma & Hsieh, 2013; Ramakrishnan et al., 2024).

In contrast, solvent extraction is primarily applied to oil-rich materials such as soybean meal and moringa seeds, where lipids are removed prior to protein recovery. Organic solvents, particularly hexane, are frequently used to defat raw materials, thereby improving protein concentration and extraction efficiency. Soybean processing commonly incorporates solvent extraction because high lipid content may hinder efficient protein isolation. Moringa seeds, which are rich in oil, similarly benefit from defatting prior to protein extraction. Pea protein, however, generally requires less solvent treatment because peas contain lower lipid levels than soybean and moringa seeds. Despite improved protein accessibility, solvent extraction has notable disadvantages, including environmental concerns, potential solvent residues, and possible reductions in protein functionality caused by structural alterations during

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processing (Arguelles-Peña et al., 2021; Nwaneri & Johnson, 2025).

➢ *Enzymatic Hydrolysis of Extracted Proteins*

Following extraction, proteins undergo enzymatic hydrolysis to release bioactive peptides. Enzymatic hydrolysis is preferred over chemical hydrolysis because it occurs under milder conditions, provides greater specificity, minimizes amino acid destruction, and enables targeted production of peptides with desirable biological activities (Tadesse & Emire, 2020). Common food-grade proteases include Alcalase, pepsin, trypsin, Flavourzyme, papain, bromelain, and pancreatin, each differing in cleavage specificity and hydrolytic efficiency. For example, Alcalase generally produces shorter hydrophobic peptides with enhanced antioxidant and anti-inflammatory properties, whereas trypsin preferentially cleaves peptide bonds adjacent to lysine and arginine residues, generating peptides with distinct bioactivities (Cheng et al., 2021).

Comparatively, soybean proteins are highly suitable for enzymatic hydrolysis because glycinin and β-conglycinin provide abundant cleavage sites for proteases and yield high peptide recovery(Jara et al., 2018). Pea proteins, particularly vicilin-rich fractions, exhibit greater susceptibility to enzymatic cleavage due to reduced structural rigidity, often resulting in efficient hydrolysis and favorable digestibility(Boukid et al., 2021). Moringa proteins, although lower in total abundance, contain diverse amino acid profiles(Avilés-Gaxiola & Heredia, 2021) capable of generating peptides with promising anti-inflammatory potential(Avilés-Gaxiola et al., 2021). Nevertheless, extraction complexity and matrix interference may reduce hydrolysis efficiency relative to soybean and pea proteins. Therefore, successful bioactive peptide production depends not only on protein quantity but also on extraction strategy, enzyme specificity, protein structure, amino acid composition, and downstream peptide purification.

Table 5 Comparative Production Characteristics of Bioactive Peptides from *Moringa oleifera*, Pea, and Soybean Proteins

Feature	Moringa oleifera	Pea (Pisum sativum)	Soybean (Glycine max)
Protein content of raw material (%)	20–30% (leaves), 30–40% (seeds)(Su & Chen, 2020, p. 54)	20–30%(Pandey et al., 2016, p. 456)	35–40%(Pandey et al., 2016, p. 456)
Typical protein yield after extraction (%)	35–60%	60–80%	70–90%
Typical protein purity of isolates (%)	70–90%	80–90%	85–95%
Major storage proteins	Albumins, globulins	Legumin (11S), vicilin (7S), convicilin	Glycinin (11S), β-conglycinin
Common hydrolytic enzymes	Alcalase®, papain, Flavourzyme®	Alcalase®, trypsin, pancreatin	Alcalase®, Neutrase®, pepsin
Degree of hydrolysis (%)	15–35%	10–30%	15–40%
Major peptide molecular weight	<1–5 kDa	<3 kDa	<1–10 kDa
Common purification methods	Ultrafiltration, ion-exchange chromatography, RP-HPLC	Ultrafiltration, gel filtration chromatography	Ultrafiltration, RP-HPLC, UHPLC-MS/MS
Major bioactivities	Antioxidant, anti-inflammatory, antihypertensive, antimicrobial	Antioxidant, cytokine modulation, antihypertensive	Anti-inflammatory, immunomodulatory, antioxidant, cholesterol-lowering
Representative peptide identification techniques	LC-MS/MS, MALDI-TOF-MS	LC-MS/MS	UHPLC-MS/MS, LC-MS/MS, MALDI-TOF-MS

Adapted from studies on protein extraction and peptide production from Moringa oleifera, pea, and soybean proteins (Aluko, 2015; Avilés-Gaxiola et al., 2018; Lam et al., 2018; León-López et al., 2019; Nongonierma & FitzGerald, 2017; Sánchez & Vázquez, 2017).

The protein content and extraction efficiency of the raw material strongly influence peptide production. Soybean generally provides the highest protein content (35–40%), extraction yield (70–90%), and isolate purity (85–95%), making it one of the most economically viable sources of bioactive peptides. Pea proteins typically yield 60–80% protein recovery with purities reaching 80–90%, while Moringa oleifera proteins often exhibit lower extraction yields (35–60%) because of the presence of fiber, polyphenols, and other interfering compounds that reduce extraction efficiency (Lam et al., 2018; Avilés-Gaxiola et al., 2018).

The choice of enzyme significantly affects peptide production. Alcalase® is the most frequently used protease across all three protein sources due to its broad specificity and high hydrolytic efficiency, producing low-molecular-weight peptides with strong antioxidant and ACE-inhibitory properties. Soybean proteins generally achieve the highest degree of hydrolysis owing to their favorable protein structure and susceptibility to enzymatic cleavage, whereas pea and moringa proteins often require optimization of enzyme concentration and hydrolysis conditions to maximize peptide release (Nongonierma & FitzGerald, 2017; Udenigwe & Aluko, 2012).

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III. ANTI-INFLAMMATORY PEPTIDES DERIVED FROM MORINGA

➢ *Overview of Moringa Proteins and Peptides*

Moringa oleifera is widely recognized for its nutritional and medicinal importance. The plant contains proteins, vitamins, minerals, polyphenols, glucosinolates, and isothiocyanates with biological activities. Although most anti-inflammatory studies on moringa involve crude extracts or phytochemicals rather than purified peptides, study has shown that moringa proteins can generate bioactive peptides with antioxidant and anti-inflammatory properties.

Avilés-Gaxiola et al., (2021) identified several peptides from moringa leaf hydrolysates exhibiting antioxidant and anti-inflammatory potential. These peptides were rich in hydrophobic amino acids such as valine, alanine, and proline, which may enhance radical scavenging activity and membrane interactions.

➢ *Mechanisms of Anti-Inflammatory Activity of Moringa-derived peptides*

Moringa-derived peptides exert anti-inflammatory effects through multiple interconnected mechanisms:

- *JAK--STAT Pathway Inhibition*

According to the study by Hong et al. (2022), *Moringa oleifera* peptide (KETTTIVR) ameliorates colitis by inhibiting JAK-STAT pathway activation via inhibiting phosphorylation of JAK2 and STAT3 in DSS-induced colitis mice.

- *Modulation of Cytokines*

Moringa oleifera peptide (KETTTIVR) treatment in colitis mice demonstrated specific cytokine effects, serum TNF-α, IL-1β, IL-6 and IFN-γ were significantly decreased and IL-10 significantly increased (Hong et al., 2022).

- *NF-κB Pathway Suppression*

Evidence for direct NF-κB inhibition by purified moringa peptides remains limited. Most available studies demonstrating NF-κB suppression have employed crude extracts or phytochemical-rich fractions containing isothiocyanates, flavonoids, and phenolic compounds rather than isolated peptides (Lee et al., 2013).

However, an important limitation within current moringa literature is the frequent inability to distinguish between peptide-mediated effects and effects attributable to phytochemicals such as isothiocyanates, flavonoids, or phenolic compounds.

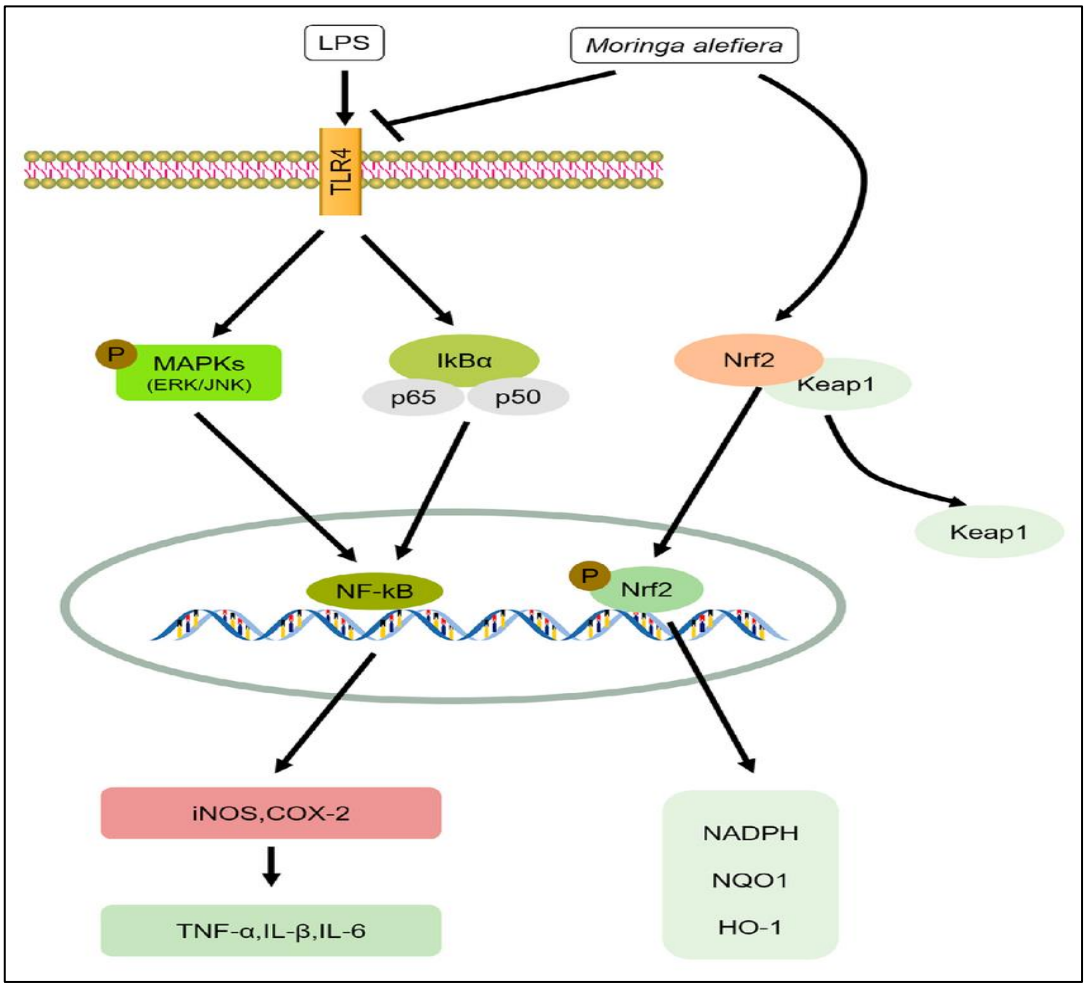

Fig 1 Anti-Inflammatory Signaling Pathways Modulated by Moringa Oleifera-Derived Bioactive Compounds and Peptides. Adapted from (Kou et al., 2018) Nutraceutical/pharmacological potential of *Moringa oleifera*

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Table 6 Anti-Inflammatory Peptides Identified from *Moringa oleifera*

Peptide	Sequence	Source	Anti-inflammatory Evidence
KETTTIVR	KETTTIVR	Moringa leaf hydrolysate	JAK2/STAT3 inhibition
LAYKPPG	LAYKPPG	Moringa leaf hydrolysate	Antioxidant/anti-inflammatory
SDPFNSG	SDPFNSG	Moringa leaf hydrolysate	ROS suppression
AFEGPKR	AFEGPKR	Moringa leaf hydrolysate	Macrophage modulation
AFEGPKR	AFEGPKR	Moringa leaf hydrolysate	Macrophage modulation

- *In Vitro and In Vivo Evidence of the Anti-Inflammatory Activity of Moringa-derived Peptides and Protein-Derived Bioactives*

Most Moringa anti-inflammatory studies utilize macrophage models such as RAW 264.7 murine macrophages stimulated with lipopolysaccharide (LPS). Moringa hydrolysates significantly reduce NO production and inflammatory cytokines in these models.

In vitro studies have provided important evidence supporting the anti-inflammatory potential of Moringa oleifera protein-derived peptides. Most research utilized lipopolysaccharide (LPS)-stimulated RAW 264.7 murine macrophages, a well-established model for evaluating inflammatory responses. Upon LPS stimulation, macrophages produce excessive amounts of nitric oxide (NO), reactive oxygen species (ROS), and pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1β (IL-1β), primarily through activation of the nuclear factor kappa B (NF-κB) signaling pathway. Consequently, suppression of these mediators is considered indicative of anti-inflammatory activity.

A study by Avilés-Gaxiola et al. (2021) investigated Moringa oleifera leaf protein hydrolysates (MOLPHs) generated through simulated gastrointestinal digestion(Avilés-Gaxiola et al., 2021). The process produced 14 novel peptide sequences, several of which contained hydrophobic and aromatic amino acids known to contribute to antioxidant and anti-inflammatory activities. When tested in LPS-stimulated RAW 264.7 macrophages, the peptide-rich hydrolysate significantly reduced inflammatory responses without inducing cytotoxicity. At a concentration of 100 µg/mL, nitric oxide production was reduced by approximately 30.5% compared with untreated LPS-stimulated controls, while cell viability remained above 90%, indicating that the observed effects were due to biological activity rather than cellular toxicity (Avilés-Gaxiola et al., 2021).

Beyond nitric oxide inhibition, the hydrolysates exhibited strong antioxidant activity, which is closely linked to anti-inflammatory effects (Avilés-Gaxiola et al., 2021). Excessive ROS generation amplifies inflammatory signaling through activation of NF-κB and mitogen-activated protein kinase (MAPK) pathways. The Moringa-derived peptides effectively scavenged free radicals and reduced intracellular oxidative stress, thereby limiting downstream inflammatory signaling. The authors suggested that the anti-inflammatory activity was mediated by suppression of oxidative stress-induced activation of pro-inflammatory transcription factors and reduction of inducible nitric oxide synthase (iNOS) activity, the enzyme primarily responsible for NO overproduction during inflammation.

Also, Avilés-Gaxiola et al. (2021) isolated several bioactive peptides from alcalase-generated Moringa oleifera leaf protein hydrolysates, including LAYKPPG, SDPFNSG, AFEGPKR, and GGIF. These peptides exhibited potent antioxidant activities in ABTS and ORAC assays and were subsequently evaluated in LPS-activated macrophages. The peptides reduced intracellular oxidative stress and attenuated inflammatory responses by decreasing ROS accumulation and limiting activation of inflammatory signaling pathways. The presence of amino acids such as tyrosine, phenylalanine, proline, glycine, and lysine was proposed to enhance radical-scavenging capacity and contribute to modulation of cellular inflammatory responses.

Although numerous bioactive peptides with antioxidant and anti-inflammatory potential have been identified from Moringa oleifera proteins, direct in vivo studies of purified moringa peptides remain relatively scarce. Most animal studies have evaluated crude extracts, protein hydrolysates, or other protein-derived bioactive compounds rather than isolated peptide sequences. Consequently, the translation of peptide-specific anti-inflammatory effects from in vitro models to whole-animal systems remains an important research gap.

Evidence from animal studies nevertheless supports the anti-inflammatory potential of moringa-derived protein constituents. In a carrageenan-induced paw edema model, aqueous leaf extract of M. oleifera (200 mg/kg body weight) significantly reduced acute inflammation in rats, demonstrating inhibition of paw swelling comparable to standard anti-inflammatory drugs. Similar effects were observed in formaldehyde-induced paw edema and cotton pellet granuloma models, indicating activity against both acute and chronic inflammatory responses. The reduction in edema was associated with suppression of inflammatory mediator production and attenuation of oxidative stress-related tissue damage (Mittal et al., 2017).

Jaja-Chimedza et al. (2017) developed an isothiocyanate-enriched moringa seed extract containing moringa isothiocyanate-1 (MIC-1). In carrageenan-induced rat paw edema, oral administration of the extract reduced paw swelling by approximately 33% at 500 mg/kg, an effect comparable to aspirin (27% inhibition at 300 mg/kg). Molecular analyses demonstrated significant reductions in nitric oxide (NO), inducible nitric oxide synthase (iNOS), interleukin-1β (IL-1β), and interleukin-6 (IL-6), alongside increased expression of antioxidant and cytoprotective enzymes including heme oxygenase-1 (HO-1), glutathione

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S-transferase P1 (GSTP1), and NAD(P)H quinone dehydrogenase 1 (NQO1). These suggest that moringa-derived bioactives suppress inflammation through modulation of NF-κB-dependent pathways and enhancement of endogenous antioxidant defenses (Jaja-Chimedza et al., 2017).

Additionally, Mahdi et al., 2017 studied arthritis models. In complete Freund's adjuvant (CFA)-induced arthritis in rats, oral administration of M. oleifera leaf extract (250–500 mg/kg/day) significantly reduced paw volume, arthritic score, and inflammatory tissue damage. Treatment also decreased oxidative stress markers while improving antioxidant enzyme activities, indicating that suppression of oxidative injury contributes substantially to the anti-inflammatory effects of moringa-derived compounds (Mahdi et al., 2017).

Another protein-derived anti-inflammatory molecule from M. oleifera is the flower trypsin inhibitor (MoFTI), a peptide-rich protein fraction. In mice, intraperitoneal administration of MoFTI (15–30 mg/kg) significantly reduced carrageenan-induced paw edema and lowered cytokine and nitric oxide production during the inflammatory response. These studies show that moringa protein-derived molecules can exert anti-inflammatory activity in vivo through regulation of inflammatory mediator (Patriota et al., 2021).

Animal studies shows that moringa-derived proteins, peptide-rich hydrolysates, and related bioactive compounds can reduce edema formation, suppress pro-inflammatory cytokines (IL-1β, IL-6), decrease nitric oxide production, inhibit NF-κB-mediated signaling, and enhance antioxidant defense systems. Nevertheless, most in vivo evidence is derived from crude extracts or partially purified fractions rather than structurally characterized peptides. Future studies should focus on validating individual peptide sequences in animal models, determining dose-response relationships, assessing bioavailability, and elucidating molecular mechanisms to confirm their therapeutic potential as anti-inflammatory agents.

➢ *Limitations of Current Moringa Peptide Research*

Although several bioactive peptides have been identified from *Moringa oleifera* proteins, peptide-specific anti-inflammatory evidence remains limited compared with soybean and pea proteins. Most published studies have investigated crude extracts, hydrolysates, or phytochemical-rich fractions. Consequently, attribution of observed anti-inflammatory effects to individual peptides remains challenging. Future studies should focus on purification, structural characterization, bioavailability assessment, and validation of individual peptide sequences in animal models and human trials.

IV. ANTI-INFLAMMATORY PEPTIDES DERIVED FROM PEA

➢ *Overview of Pea Protein Composition and Bioactive Peptide Generation*

Pea protein has become increasingly important in functional food and nutraceutical applications due to its sustainability, nutritional quality, and relatively low allergenicity compared with soybean proteins (Boukid et al., 2021). The major storage proteins in pea include legumin and vicilin.

Enzymatic hydrolysis of pea proteins using Alcalase®, trypsin, pancreatin, and Flavourzyme® generates peptides with antioxidant, antihypertensive, and anti-inflammatory properties.

Ndiaye et al. (2012) studied that enzymatic hydrolysates of yellow field pea proteins possessed antioxidant and immunomodulatory activity (Hernandez-Ledesma & Hsieh, 2013). More recently, studies identified small peptides capable of reducing oxidative stress and inflammatory injury (Zhao & Liu, 2023).

➢ *Mechanisms of Anti-inflammatory Pea Peptides Activity*

Pea peptides exert anti-inflammatory activity indirectly through oxidative stress regulation.

Pea-derived peptides commonly:

- Scavenge reactive oxygen species
- Activate Nrf2/Keap1 signaling
- Increase antioxidant enzyme activity
- Reduce lipid peroxidation
- Modulate cytokine production

The Nrf2/Keap1 pathway is an important antioxidant defense system regulating transcription of antioxidant enzymes including superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GSH-Px) (Zhao & Liu, 2023). Activation of this pathway reduces oxidative stress-mediated inflammatory injury.

Bioactive peptides derived from pea (*Pisum sativum*) proteins exert anti-inflammatory effects primarily through antioxidant and immunomodulatory mechanisms. The peptide EEHLCFR has been associated with activation of the Nrf2 signaling pathway and scavenging of reactive oxygen species (ROS), thereby enhancing cellular antioxidant defenses. YLVN contributes mainly through direct ROS scavenging, while TFY reduces lipid peroxidation and oxidative damage. The peptide FEGTVFENG exhibits dual functionality by inhibiting angiotensin-converting enzyme (ACE) activity and reducing oxidative stress. In contrast, DLKLP appears to exert a more direct immunomodulatory effect through regulation of pro-inflammatory cytokines, particularly TNF-α and IL-6. Collectively, these peptides converge on the suppression of oxidative stress and inflammatory signaling pathways, leading to attenuation of inflammatory responses (Girgih et al., 2011; Udenigwe & Aluko, 2011).

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➢ *In vitro and In Vivo Anti-Inflammatory Effects of Pea-Derived Peptides and Protein Fractions*

In vitro studies show that pea-derived peptides possess significant anti-inflammatory activity(Liu et al., 2024). Girgih et al. carried out research on enzymatic pea protein hydrolysates (PPH) generated from yellow field pea (*Pisum sativum* L.) proteins and evaluated their effects in LPS/IFN-γ-stimulated RAW 264.7 murine macrophages. Pre-treatment with PPH significantly reduced inflammatory responses without affecting cell viability. Nitric oxide production was decreased by approximately 20%, while secretion of the pro-inflammatory cytokines TNF-α and IL-6 was inhibited by up to 35% and 80%, respectively. The anti-inflammatory effects were accompanied by strong antioxidant activity, suggesting that suppression of oxidative stress contributed to attenuation of macrophage activation. These findings indicate that pea-derived peptides can modulate key inflammatory mediators involved in chronic inflammatory diseases and support their potential application as functional food ingredients with immunomodulatory properties (Girgih et al., 2011).

Compared with soybean-derived bioactive peptides, in vivo studies of anti-inflammatory activity of pea (*Pisum sativum*) peptides remain relatively limited (Rizzello et al., 2016). Nevertheless, animal studies provide evidence that pea protein-derived bioactive fractions can attenuate intestinal and systemic inflammation through modulation of inflammatory cytokines, oxidative stress pathways, and gut barrier function.

Utrilla et al. (2015) evaluated pea seed protein albumin extracts and purified albumin fractions containing bioactive peptides and Bowman–Birk inhibitor (BBI)-related proteins in a dextran sulfate sodium (DSS)-induced colitis mouse model (Utrilla et al., 2015). Oral administration of pea seed extract (15 g/kg/day) or albumin fraction (1.5 g/kg/day) significantly ameliorated intestinal inflammation and reduced histological damage compared with untreated colitic mice. Treatment markedly decreased the colonic expression of several pro-inflammatory mediators, including TNF-α, IL-1β, inducible nitric oxide synthase (iNOS), matrix metalloproteinases (MMPs), adhesion molecules, and toll-like receptors (TLRs). Furthermore, the pea-derived fractions improved epithelial barrier integrity and partially restored the intestinal microbiota composition toward that of healthy animals, demonstrating both anti-inflammatory and gut-protective effects.

The anti-inflammatory activity was attributed mainly to bioactive peptide-containing albumin fractions rich in Bowman–Birk inhibitor-like proteins (Utrilla et al., 2015). These peptides suppress excessive protease activity during intestinal inflammation, thereby reducing activation of NF-κB signaling and downstream cytokine production, and the restoration of epithelial barrier proteins contributed to reduced intestinal permeability and decreased inflammatory cell infiltration.

Pea protein hydrolysates and peptide-rich fractions exert anti-inflammatory effects through multiple mechanisms, including inhibition of NF-κB activation, suppression of Toll-like receptor 4 (TLR4) signaling, reduction of oxidative stress, and modulation of cytokine production (Mishima et al., 2023). Animal studies involving food-derived bioactive peptides consistently show reductions in TNF-α, NF-κB, and TLR4 expression together with improvements in intestinal morphology and immune homeostasis, supporting the therapeutic potential of plant-derived peptides, including those from pea proteins.

The anti-inflammatory benefits of pea peptides appear particularly relevant in inflammatory bowel disease (IBD) models. In DSS-induced colitis, pea protein fractions reduced mucosal injury, preserved crypt architecture, and attenuated inflammatory infiltration of colonic tissues. These effects were accompanied by downregulation of cytokines and inflammatory enzymes while maintaining proteins involved in epithelial barrier function. These suggest that pea peptides may exert both direct immunomodulatory effects and indirect protective effects through preservation of gut integrity.

V. ANTI-INFLAMMATORY PEPTIDES DERIVED FROM SOYBEAN

➢ *Overview of Soybean Bioactive Peptides and Proteins*

Soybean proteins are among the most extensively studied plant protein sources for bioactive peptide production (Liu et al., 2014). The high protein content and favorable amino acid composition of soybean facilitate production of peptides with antioxidant, anti-inflammatory, antihypertensive, and immunomodulatory properties.

Major anti-inflammatory soybean peptides include:

- Lunasin
- Soymorphins
- Glycinin-derived peptides
- β-conglycinin-derived peptides
- Fermented soybean peptides

➢ *Lunasin and Its Mechanisms*

Lunasin is the best-characterized soybean bioactive peptide (Liu et al., 2014). It contains a poly-aspartic acid tail and an RGD (Arg-Gly-Asp) motif associated with integrin binding (Wan et al., 2017).

Lunasin exerts anti-inflammatory activity through:

The multifunctional structure of lunasin contributes substantially to its broad biological activity (Liu et al., 2014).

Lunasin is the best-characterized soybean bioactive peptide. It contains a poly-aspartic acid tail and an RGD (Arg-Gly-Asp) motif associated with integrin binding(Rizzello et al., 201).

Lunasin exerts anti-inflammatory activity through:

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The multifunctional structure of lunasin contributes substantially to its broad biological activity (Liu et al., 2014).

- *In Vitro and In Vivo Evidence on the Anti-Inflammatory Activity of Soybean Peptides*

Soybean peptides have demonstrated anti-inflammatory activity in both cell culture and animal models (Yi et al., 2020). LPS-stimulated RAW264.7 macrophages are frequently used to evaluate cytokine inhibition and inflammatory pathway suppression (Yi et al., 2020).

Kovacs-Nolan et al. (2012) studied the soy-derived peptide VPY in vitro and in vivo in a mouse model of DSS-induced colitis (Kohno, 2017). VPY inhibited the secretion of IL-8 and TNF-α (Kohno, 2017). In mice, VPY treatment reduced DSS-induced colitis symptoms, weight loss, and decreased gene expression of pro-inflammatory cytokines in the colon (Kohno, 2017).

Yi et al. (2020) demonstrated that soybean peptides significantly reduced NO, TNF-α, IL-6, and IL-1β production through inhibition of TLR4-mediated MAPK/JNK and NF-κB signaling pathways (Yi et al., 2020).

Animal studies further show reduction of edema, oxidative tissue injury, intestinal inflammation, and inflammatory cytokines following administration of soybean peptide-rich hydrolysates (Ren et al., 2013)

Soybean peptides are among the most extensively studied plant-derived peptides, with substantial mechanistic and translational evidence (Hu et al., 2023).

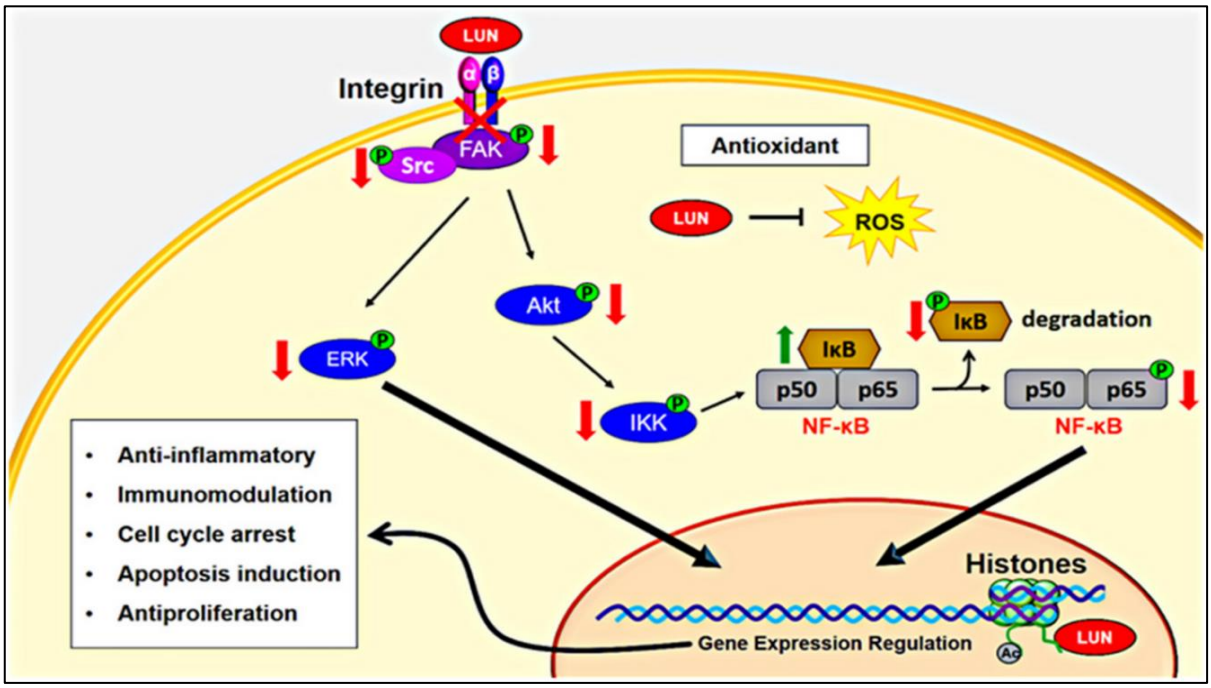

Fig 2 Molecular Mechanism of Lunasin-Mediated Anti-Inflammatory Activity.
Adapted from Abiona (2025), Lunasin: A promising bioactive peptide for the management of inflammatory and chronic disease

The biological activity of peptides is strongly influenced by structural properties, including molecular weight, amino acid composition, hydrophobicity, charge distribution, and conformational stability (Zaky et al., 2022).

Table 7 Comparative Structural Features of Anti-Inflammatory Peptides Derived from Moringa, Pea and Soybean

Feature	Moringa Peptides	Pea Peptides	Soybean Peptides
Typical size	4–44 aa	3–10 aa	3–44 aa
Dominant residues	Glycine, cysteine	Hydrophobic residues	Aspartic acid, arginine
Major motif	Cysteine-rich motifs	Short hydrophobic chains	RGD motif
Main activity	Antioxidant and immunomodulatory	Oxidative stress modulation	Direct anti-inflammatory activity
Bioavailability evidence	Limited	Moderate	Relatively extensive
Mechanistic evidence	Limited	Moderate	Extensive

Small peptides (<3 kDa) generally exhibit improved intestinal absorption and biological activity. Hydrophobic residues often enhance membrane permeability and radical scavenging ability (Gan et al., 2025).

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The RGD motif in Lunasin facilitates integrin interactions, contributing to modulation of inflammatory signaling pathways (Cam & Mejía, 2012). In contrast, many pea peptides exert both antioxidant-mediated effects and regulate transcriptional pathways (Gan et al., 2025).

VI. COMPARATIVE MECHANISMS OF ANTI-INFLAMMATORY ACTION

Despite differences in structure and origin, moringa, pea, and soybean peptides share several overlapping anti-inflammatory mechanisms (Liu et al., 2022).

Common pathways include (Liu et al., 2022):

- NF-κB inhibition
- Reduction of pro-inflammatory cytokines
- Suppression of oxidative stress
- Modulation of nitric oxide production
- Reduction of ROS accumulation

However, mechanistic depth varies substantially among plant sources.

Soybean peptides exhibit comprehensive evidence for direct modulation of inflammatory transcription pathways including NF-κB and MAPK/JNK signaling(Song et al., 2024; Yi et al., 2020).

Pea peptides predominantly act through antioxidant defense systems and oxidative stress reduction (Li et al., 2022; Zhao & Liu, 2023).

Moringa peptides remain comparatively less characterized, and many studied activities may partly derive from non-peptide phytochemicals (Hong et al., 2022; Mbikay, 2012).

Therefore, although soybean peptides currently possess the most comprehensive mechanistic evidence, this does not necessarily imply universal superiority across all inflammatory conditions.

Table 8 Mechanistic Mapping of Moringa, Pea and Soybean Peptides to Major Inflammatory Signaling Pathways.

Peptide/Fraction	NF-κB	Nrf2	JAK/STAT	MAPK
Lunasin	✓ Strong inhibition	Indirect activation	Limited evidence	✓
Soybean PF peptides	✓	✓	Emerging evidence	✓
EEHLCFR	Weak	✓ Strong activation	Not reported	Indirect
FEGTVFENG	Indirect	✓ Strong activation	Not reported	Indirect
Pea hydrolysate	✓	✓	Not reported	✓
Moringa peptide fractions	✓	✓	Limited evidence	✓

Table 9 Comparative Mechanistic Strength of Evidence of Moringa, Pea and Soybean

Source	Cellular Evidence	Animal Evidence	Human Evidence
Soybean	Strong	Strong	Limited
Pea	Moderate	Moderate	Very Limited
Moringa	Limited	Moderate	Absent

VII. TRANSLATIONAL CHALLENGES AND LIMITATIONS

Several challenges limit clinical translation of plant-derived bioactive peptides:

➢ *Gastrointestinal Stability*

Peptides may undergo degradation during digestion, reducing bioavailability and therapeutic efficacy (Amigo & Hernández-Ledesma, 2020).

➢ *Peptide Purification*

Many studies utilize crude hydrolysates rather than purified peptides, making it difficult to identify active sequences (Toldrá et al., 2020).

➢ *Lack of Clinical Studies*

Most available evidence derives from *in vitro* experiments or animal studies. Human clinical trials remain limited (Duffuler et al., 2022).

➢ *Standardization Issues*

Differences in hydrolysis conditions, peptide purification methods, and assay systems complicate cross-study comparisons (Lammi et al., 2019).

➢ *Commercialization Challenges*

Large-scale production, peptide stability, sensory characteristics, regulatory approval, and cost remain important barriers to commercialization (Duffuler et al., 2022).

VIII. FUTURE PERSPECTIVES

➢ *Future Research should Prioritize:*

- Isolation and characterization of novel peptide sequences
- Structure–activity relationship studies
- Molecular docking and computational peptide prediction
- AI-guided peptide discovery
- Nanoencapsulation and delivery systems
- Gastrointestinal stability studies

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- Human clinical trials
- Fermentation optimization
- Recombinant peptide production
- Multi-omics and peptidomics approaches

Advanced analytical techniques such as UHPLC-MS/MS, molecular docking, transcriptomics, and peptidomics are expected to accelerate the discovery of highly potent anti-inflammatory peptides (Mattosinhos et al., 2025).

IX. CONCLUSION

Moringa oleifera, *Pisum sativum*, and *Glycine max* represent promising plant sources of anti-inflammatory peptides with potential applications in functional foods and nutraceuticals. Current evidence indicates that soybean-derived peptides possess the most comprehensive mechanistic and translational support, particularly through modulation of NF-κB, MAPK, and cytokine-mediated inflammatory pathways. Pea-derived peptides exhibit substantial antioxidant-mediated anti-inflammatory effects, primarily through regulation of oxidative stress and activation of Nrf2-dependent defense systems. In contrast, although Moringa oleifera contains promising bioactive proteins and peptides, peptide-specific anti-inflammatory evidence remains limited, and many reported effects stem from phytochemical-rich extracts rather than purified peptides. Future investigations should prioritize peptide purification, structure–activity relationship studies, gastrointestinal stability, bioavailability assessment, and human clinical trials to facilitate the development of peptide-based therapeutic and nutraceutical products.

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