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Quinoa-derived biopeptides with antioxidant activity and their applications in the pharmaceutical and food industries

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Abstract

Bioactive peptides resulting from the hydrolysis of proteins in *Chenopodium quinoa* Willd. play significant roles in the body as they exhibit a range of biological functions relevant to human health. Enzymatic hydrolysis has been identified as a sustainable and efficient method for bioactive peptide extraction, minimizing environmental impact and maximizing yield. The challenge was to review and compare methodologies for obtaining peptides from protein concentrates and hydrolysates with antioxidant capabilities. Peptides and amino acids with functional properties can be used in the food and pharmaceutical industries, demonstrating significant biological activity (e.g., antioxidant and anti-inflammatory). This highlights *Chenopodium quinoa* as a valuable source of bioactives, though further in silico and in vivo studies are necessary to fully characterize and validate their potential.

Keywords: *Chenopodium quinoa* Willd; pseudocereal; antioxidant; hydrolysates; biopeptides.

Practical Application: Bioactive peptides derived from Chenopodium quinoa have promising applications in the food and pharmaceutical industries due to their antioxidant and anti-inflammatory properties. Enzymatic hydrolysis offers a sustainable and efficient method for extracting these compounds while preserving their functionality. These peptides can be incorporated into functional foods and nutraceuticals to enhance human health, particularly in managing oxidative stress and inflammation-related disorders. Additionally, their potential in food preservation by reducing oxidative degradation extends the shelf life of perishable products. The antihypertensive effects of quinoa-derived peptides, particularly their role in ACE inhibition, highlight their relevance in cardiovascular health. Further research, including in silico and in vivo studies, is necessary to fully explore their bioactivity and optimize their integration into industrial applications.

1 INTRODUCTION

Quinoa is emerging as a key crop to address global challenges like climate change, soil degradation, and food scarcity. Its adaptability to adverse conditions and rich nutritional profile make it a valuable alternative for sustainable agriculture. As a pseudocereal packed with essential amino acids, proteins, and bioactive compounds, quinoa is increasingly recognized for its health benefits and versatility in the food and pharmaceutical industries (De Ron et al., 2017; Ruiz et al., 2014). Rich in saponins, phenols, flavonoids (Pereira et al., 2022), and bioactive peptides, quinoa supports health by acting as an antioxidant, an anti-inflammatory, and even an anticancer agent. These bioactive compounds, influenced by genetics and the environment, enhance quinoa's role as a functional food (Ahumada et al., 2016; Daliri et al., 2021; Mudgil et al., 2020; Tang & Tsao, 2017). The enzymatic hydrolysis of quinoa proteins produces bioactive peptides with significant antioxidant and antihypertensive properties, positioning quinoa as a source of nutraceuticals (Mudgil et al., 2020; Tang & Tsao, 2017). Studies have shown that quinoa's protein content ranges from 12% to 23%, comparable to that of eggs and milk, making it a promising alternative protein source. Its bioactive peptides, released through hydrolysis, are particularly effective in addressing non-communicable diseases like hypertension and diabetes (Bravo et al., 2009; Nowak et al., 2016; Anaya-González et al., 2019). However, the variability in bioactive potential across studies underscores the need for further research on peptide structures, activity mechanisms, and their relationship with precursor proteins (Guixing et al., 2023). Quinoa's nutritional value, resilience to harsh environments, and the potential to combat malnutrition worldwide solidify its status as a critical crop for the future. Continuous exploration of quinoa-derived biopeptides and their antioxidant mechanisms could unlock new opportunities to optimize its use as a functional food, enhancing both health and sustainability (Fuentes & Paredes-Gónzalez, 2015).

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2 REVIEW

Quinoa, known for its abundance of health-promoting substances such as proteins, amino acids, and bioactive compounds, has become one of the most widely produced and exported Andean grains (Alandia et al., 2020; Bazile et al., 2016). It is primarily cultivated in the Peruvian highlands, including Puno, Ayacucho, Apurímac, Cuzco, and Junín (Alandia et al., 2021). As global dietary trends shift toward healthier, plant-based sources of protein, quinoa stands out as a valuable alternative due to its high protein content and versatility, placing it alongside cereals and legumes as a primary source of plant-based nutrition. In this context, cereals, after legumes, are the primary source of plant-based proteins. Quinoa plants are not grasses, as they produce grain-like seeds with composition and function similar to true cereals, which is why they are referred to as pseudocereals in terms of their uses (Constantino & García-Rojas, 2022; Matías et al., 2018).

According to the Codex Alimentarius (2019), quinoa's protein content must meet a minimum standard of 10.0 g/100 g, though studies indicate a wider range from 12 to 22.1%, with an average protein content of 14.6% (Abugoch James, 2009; Gonzalez et al., 2012; Lutz & Bascuñan-Godoy, 2017; Repo-Carrasco et al., 2003). One issue in assessing quinoa's protein content is the variability in the nitrogen-to-protein conversion factor, with some using 5.7 and others using 6.25, and the latter is currently accepted for quinoa. This discrepancy can affect the reported protein values, making it essential to standardize methodologies for more accurate comparisons. Research into the composition of 10 quinoa varieties from diverse geographical locations, with varying agricultural practices (e.g., fertilization and irrigation), found an average protein content of 16.6 g/100 g (Covarrubias et al., 2020). This highlights the impact of environmental and cultivation factors on quinoa's nutritional profile. Several advanced techniques are employed for the characterization and quantification of quinoa proteins, each contributing to a more detailed understanding of their nutritional and functional properties.

2.1 Electrophoresis of protein fractions

The protein fractions in quinoa were separated using sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE), following Laemmli's (1970) method with Brilliant Blue R-250 for staining. Molecular weights were estimated with a broad range of dual-color markers (BIO-RAD). Barba de la Rosa et al. (2009) highlighted the importance of delipidation for improving the protein fraction analysis in quinoa, particularly in the kañihua variety. Quinoa's primary protein components are albumins and globulins, making up 35–37%. The globulin fraction, classified as 11S with a molecular weight of 300–350 kDa, consists of six acid–base polypeptide pairs linked by disulfide bonds. The albumin fraction is highly soluble in water and belongs to the 2S type, while prolamins and glutelins are present in smaller amounts (Vilcacundo et al., 2017).

2.2 Quinoa protein concentrates

According to the Food and Agriculture Organization (FAO, 2018), a protein is considered biologically complete if it contains all essential amino acids in the proper proportions, as compared to a reference protein. Quinoa has a protein content ranging from 12 to 23%, and it is considered a high-quality protein due to the presence of essential amino acids. The primary proteins in quinoa are albumins and globulins. The functional properties of these proteins are defined not only by their nutritional value but also by their technological benefits in food processing (Morales et al., 2020). Various processes have been developed to isolate proteins from quinoa, resulting in protein concentrates with over 70% protein content. These concentrates maintain a protein profile similar to the original material to avoid undesirable changes during processing (Elsohaimy et al., 2015). Protein concentrates are commonly used in industrial food production, enhancing the amino acid profile and overall protein quality. They also provide several functional benefits (Figure 1), such as stabilization, improved viscosity, desirable texture, and enhanced water or oil absorption (Morales et al., 2020).

Protein concentrate evaluation. Quinoa's protein content is 14.15%, and its concentrate has higher levels (70.10% total protein). The protein extraction process, done in an acidic medium, maintains the protein types, mainly albumins (66 kDa) and globulins (55 kDa). Notable globulins identified include 7S (4–92 kDa) and 11S (4–37 kDa) (Barba de la Rosa et al., 2009; Tapia et al., 2017).

2.3 Quinoa protein hydrolysates

Hydrolysates, obtained through enzymatic hydrolysis using plant, animal, or microbial enzyme, are increasingly utilized in the food industry to improve nutritional value. Bioactive peptides from food sources offer a natural alternative to synthetic drugs, exhibiting properties such as antimicrobial,

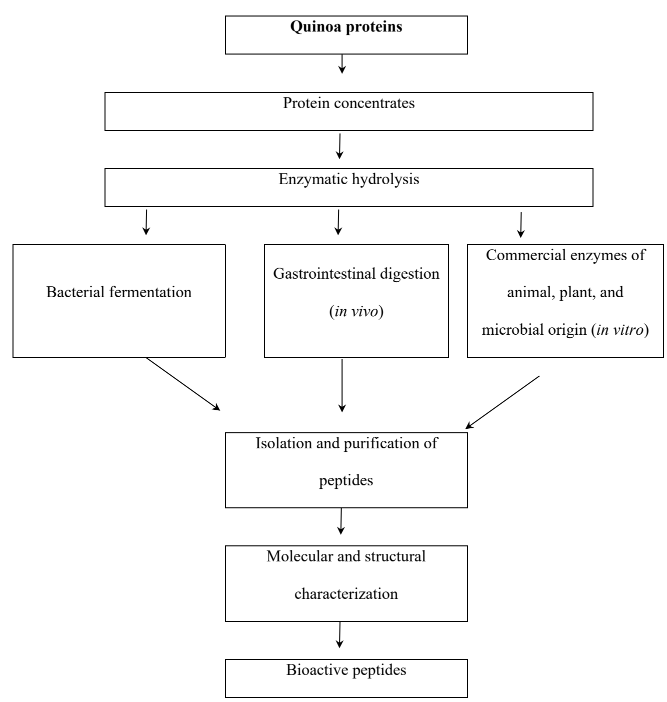

Figure 1. Concept map of the bioactive peptide separation process from quinoa protein.

antihypertensive, antioxidant, and anticancer effects (Agyei & Danquah, 2011; Zheng et al., 2019). Although therapeutic peptides are generally safe with fewer side effects than small-molecule drugs, their high production costs and the lack of large-scale commercial processes limit their widespread use (Agyei & Danquah, 2011). In quinoa, albumin contains peptides that inhibit angiotensin-converting enzyme-I (ACE), which is crucial in managing hypertension, a major risk factor for cardiovascular diseases (Montone et al., 2018; Zheng et al., 2019).

2.3.1 Protein hydrolysate electrophoresis method

Electrophoresis has been instrumental in characterizing the polypeptides comprising quinoa protein concentrates. The most commonly used technique is the one described by Laemmli (1970). The proteins of *Chenopodium quinoa* were characterized by SDS-PAGE electrophoresis. Regarding the pH variation, the results showed that the fractions were similar, with a range of 14–70 kDa, mainly composed of albumins and globulins, which are storage proteins. The proteins were fully hydrolyzed at pH levels of 1.2, 2.0, and 3.2. Gastric hydrolysis resulted in similar effects using pepsin at pH 4.5 and 5.5. After duodenal hydrolysis, complete protein fragmentation was observed (Toapanta, 2016).

The study by Barba de la Rosa et al. (2009) emphasized the importance of delipidation for qualitative analysis of protein fractions, as this process enhances electrophoretic resolution and improves the identification of polypeptide bands. Their research, which focused on Chenopodium pallidicaule Aellen ('kañihua') variety Cupi-Sayhua seeds, demonstrated significant progress in electrophoretic quality when delipidation was applied prior to SDS-PAGE analysis. This finding highlights the relevance of sample preparation in achieving accurate protein characterization."

2.3.2 Evidence of the presence of bioactive peptides

Ochoa (2017) conducted enzymatic hydrolysis on kañihua protein concentrates, producing biopeptides with antiradical and antihypertensive properties. The best hydrolysis (42.82%) was achieved after 240 min using Alcalase and Neutrase, with the Alcalase/Neutrase combination yielding the best results (IC50 of 0.12 mg protein/mL and 42.19% hydrolysis). In this stage, it achieved an average ABTS+ of 2.12 µmol TE/mg of protein. Investigation of the stability conditions of the hydrolysate in the gastrointestinal medium (in vitro) showed an IC50 of 0.07 mg/mL of protein at the end of the test, confirming the stability of the protein fractions (Vilcacundo et al., 2018). The hydrolysate showed significant antioxidant activity and stability in an in vitro gastrointestinal medium. In quinoa hydrolysate characterization, protein levels varied, with levels of 77.81 and 50.75% for bitter and black quinoa, respectively, and an average of 65.52% for Alcalase-treated hydrolysates. Other studies reported protein contents of 99.3 and 85.53% in hydrolysates from *Lupinus mutabilis* and Glycine max, respectively. Factors such as thermal processes, saponin release, and enzyme use affect hydrolysis rates, and fiber, ash, and fat remain in the final products (Díaz, 2016; Elsohaimy et al., 2015; Valencia-Chamorro, 2016).

2.4 Biological activity of peptides

2.4.1 Methods for evaluating antioxidant capacity

Quinoa protein hydrolysates are being explored for their health benefits, including inhibiting dipeptidyl peptidase IV (DPP-IV) linked to diabetes and exhibiting antioxidant properties through methods like oxygen radical absorbance capacity (ORAC), 2,2′-azino-bis(3-ethylbenzothiazoline)-6-sulfonic acid (ABTS), and ferric reducing antioxidant power (FRAP) (Martínez et al., 2019; Nongonierma et al., 2015). Quinoa's bioactive compounds, including polyphenols, carotenoids, fiber, and oleic acid, contribute to its health benefits (Cao et al., 2020). Excess reactive oxygen species (ROS) from factors like ultraviolet exposure and poor diet can lead to oxidative stress and chronic diseases (Abbasi et al., 2022; Cao et al., 2020; Chirinos et al., 2023). Natural antioxidants, such as peptides, help neutralize reactive oxygen species (ROS) (González-Muñoz et al., 2022). Their efficiency and metal chelation abilities are evaluated through assays such as the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay, ORAC, and total radical-trapping antioxidant parameter (TRAP) (Durand et al., 2021; Esfandi et al., 2019).

2.4.1.1 Detection of antioxidant and ACE inhibitor peptides through in silico approach and peptide synthesis

Computational (*in silico*) and bioinformatics analyses provide a robust framework for predicting bioactive peptides derived from quinoa proteins. However, scaling up production and comprehensively validating their health benefits remain areas requiring further investigation (Guo et al., 2023). Peptides with angiotensin-converting enzyme (ACE)-inhibitory or antioxidant properties were identified using liquid chromatography-tandem mass spectrometry (LC-MS/MS) and cross-referenced against bioactive peptide databases such as *PepBank* (Minkiewicz et al., 2019). Two ACE-inhibitory peptides were subsequently synthesized, achieving over 98% purity, and demonstrated significant antioxidant activity and ACE-inhibition efficacy (Zheng et al., 2019).

2.4.2 Antioxidant activity of biopeptides

2.4.2.1 ABTS radical scavenging activity

Studies on the antioxidant activity of biopeptides have shown that their scavenging effect, measured by the disappearance of the blue color of ABTS+ at 734 nm, is influenced by structural characteristics, such as molecular weight, amino acid composition, sequences, and hydrophobicity (Ren et al., 2014). Glutathione (GSH) was used as a control in these studies (Selamassakul et al., 2018). Additionally, the metal chelating capacity of biopeptides is another method to assess their antioxidant potential (Wan et al., 2017).

2.4.2.2 Peptide extraction

Quinoa peptides are extracted using cellulase and hemicellulase to enhance protein yield, followed by Alcalase and trypsin for hydrolysis. Peptides from quinoa bran albumin (QBAH) showed 24.26% hydrolysis, with strong ACE-inhibitory (62.38%) and antioxidant activities (51.77%) (Zheng et al., 2019). Hydrophobic amino acids like Val, Leu, Tyr, and Phe contribute to high ACE-inhibitory and antioxidant activities. Short peptides (2–12 residues) containing these amino acids are particularly effective (Lee & Hur, 2019; Shazly et al., 2017). Peptides like RGQVIYVL, which is 62.5% hydrophobic, maintain stability and bioactivity during digestion, offering potential health benefits, including antihypertensive effects (Gleeson et al., 2017).

2.5 Effect of agricultural factors on quinoa protein quality

2.5.1 Variety influence

Studies on quinoa varieties in various regions highlight the importance of genotypes in determining agronomic and nutritional performance, especially under challenging conditions. In the Sahara Desert, quinoa's success in arid environments was primarily influenced by the variety, with factors such as seedling height, panicle number, grain protein, saponin content, and maturity being the key indicators (Oustani et al., 2023). In northwestern Europe, a study of 13 quinoa varieties from 2017 to 2019 found that late-maturing varieties yielded less but had higher protein levels, with linoleic, α-linolenic, and oleic acids being the predominant fatty acids (De Bock et al., 2021). Genotypic variation also plays a crucial role in quinoa's nutritional quality. A study analyzing 15 cultivars showed differences in mineral and protein contents and grain viability, reinforcing the need to consider the genetic background in breeding (Granado-Rodríguez et al., 2021). Nutritional and morphological evaluations of quinoa genotypes cultivated in the Czech Republic revealed a protein content range of 13.44–20.01%, positively correlated with the flavonoid mauritianin. Total phenolic content exhibited significant interannual variability, whereas antioxidant activity remained relatively stable. The predominant phenolic compounds identified were the flavonoids miquelianin, rutin, and isoquercetin, with the latter two and N-feruloyl octopamine demonstrating notable stability under fluctuating climatic conditions. Notably, six compounds, including those aforementioned, were detected and quantified in quinoa seeds for the first time. These findings underscore quinoa's adaptability to Central European agroclimatic conditions and its potential as a nutrient-dense crop, providing critical insights for plant breeding programs targeting enhanced nutritional quality (Dostalíková et al., 2023).

2.5.2 Fertilizer use influence

Studies indicate that fertilizers, such as goat manure, can enhance grain yield and protein content in quinoa varieties. Low doses of manure increased monounsaturated and polyunsaturated fatty acids while reducing soluble sugars and trace elements. González et al. (2023) confirmed that manure improves quinoa's nutritional quality. Additionally, nitrogenous fertilizers positively affect quinoa's grain quality and yield, providing valuable insights into plant metabolism (Li et al., 2023). A study on 10 quinoa varieties showed that growth during the rainy season, combined with specific fertilization, resulted in successful yields when plants were grown at 67 plants/ha (Nguyen & Chuyen, 2023).

2.5.3 Irrigation effect

Research on quinoa cultivation under water scarcity highlights its potential as a resilient crop. In Chile (2014–2016), soil water depletion significantly reduced yield but showed a relationship between seed yield and leaf water potential, protein, albumins, and globulins. The "purple" genotype stood out, maintaining performance and protein content under water-limited conditions, particularly in the grain-filling and physiological maturity stages (Valdivia-Cea et al., 2021). Other studies explored irrigation strategies and nitrogen fertilizer application. Controlled plant density increased seed mass and protein content, suggesting quinoa's suitability for crop rotation programs (Wang et al., 2020). Maestro-Gaitán et al. (2023) examined drought-tolerant cultivars and found that the F16 genotype produced larger seeds in the primary panicle but with lower nutritional quality, while F14, F15, and Titicaca genotypes yielded smaller seeds in the secondary panicle, richer in proteins and minerals like iron, calcium, and zinc. Fischer et al. (2017) analyzed controlled irrigation's impact on protein content and bioactive compounds. They observed changes in albumin and globulin levels across treatments and noted a higher extraction of protein fractions from washed seeds, emphasizing protein variability under different irrigation conditions.

2.5.4 Salinization effect

Quinoa shows resilience to challenging conditions, making it a valuable crop for addressing food security and biodiversity conservation. Studies reveal that high soil salinity can reduce plant height by 30% and seed yield by 37%, although the content of essential amino acids remains stable, with a decrease in fatty acid levels (Toderich et al., 2020). Its ability to grow in poor, saline soils underlines its potential in the face of climate change, as it maintains good productivity while offering a high nutritional value (Ruiz et al., 2014). Research on quinoa genotypes highlights differences in stress tolerance. For instance, the A7 genotype shows greater salt tolerance than Vikinga, experiencing less reduction in growth and biomass under salinity stress (Parvez et al., 2020). However, exposure to both salinity and arsenic significantly reduces growth, biomass, and chlorophyll content while increasing oxidative stress. Another study found that quinoa's protein content in saline soils ranges from 13.0 to 16.7%, depending on the variety and fertilization levels (Wu et al., 2016).

2.5.5 Abiotic stress effect

One of the major concerns for agricultural researchers is the tolerance of cultivars to abiotic stress concerning genetic variability and the nutritional content of quinoa. Experiments were conducted to adapt some quinoa varieties to warm and dry climates. It was found that dry soils had detrimental effects on seed production, with a lower percentage of plants. Cultivation after frost dates proved more convenient. Mineral and protein contents in seeds were better in varieties originating from South America (Noulas et al., 2017). Lung'aho et al. (2020) conducted research to assess the adaptability of quinoa in different regions of African countries with varying altitudes, soils, and climatic conditions, such as Ethiopia, Kenya, Uganda, and Zambia. They found that the average protein content of Kancolla, Titicaca, and other varieties ranged from 14 to 17%, with the Kancolla variety cultivated in Ethiopia and Kenya having protein content higher than that obtained in Peru. They concluded by emphasizing the benefits of introducing quinoa cultivation in Africa.

2.5.6 Selenium and restricted irrigation effect

Sadak and Bakhoum (2022) found that selenium is crucial for plant antioxidant protection, but excessive amounts can reduce productivity. In their study on *Chenopodium quinoa* Willd., they observed that selenium and restricted irrigation caused decreased shoot length, leaf damage, and lower biomass.

2.5.7 Planting period effect

Temel and Yolcu (2020) in Turkey found that planting the Mint Vanilla quinoa variety in late March and harvesting at full bloom resulted in higher plant height, dry biomass, and crude protein yields, as well as improved digestibility. Plants planted later showed lower fiber content. In Vietnam, Nguyen and Chuyen (2023) observed that quinoa grown in the rainy season with proper fertilization (nitrogen, phosphorus, potassium, and organic compost) resulted in good yields. Budakli Carpici et al. (2023) highlighted that planting the Titicaca quinoa variety in May produced better agronomic outcomes in terms of plant size, dry matter yield, and protein content.

2.6 Applications of peptides for pharmaceutical and food purposes

Quinoa proteins, after digestion or processing, release bioactive peptides (small chains of 3–20 amino acids) that can benefit human health by reducing the risk of chronic diseases (Tang & Tsao, 2017). These peptides are part of a growing interest in "nutraceutical" foods, which provide both nutrition and health benefits, supporting optimal bodily functions (Martínez et al., 2019). Advanced techniques like supercritical fluid extraction and enzymatic hydrolysis improve quinoa's nutritional quality, producing highly pure protein hydrolysates and oils suitable for pharmaceutical and nutraceutical use (Olivera-Montenegro et al., 2022). Quinoa also contains bioactive compounds such as phenols, flavonoids, and peptides, particularly in red and black varieties. These compounds have shown antioxidant, antimicrobial, anti-inflammatory, and even anticancer properties while improving insulin sensitivity and reducing fat in mammals without hormonal side effects (Jukka-Pekka et al., 2022). Among its proteins, globulins stand out for their bioactivity. After digestion, globulins can inhibit enzymes linked to hypertension and diabetes, with studies demonstrating significant activity when processed with enzymes like pancreatin or thermolysin (Chirinos et al., 2023; Tavano et al., 2022). Studies have also highlighted the potential of quinoa-derived peptides in reducing blood pressure and managing diabetes. These peptides, isolated through ultrafiltration and chromatography, have shown high antioxidant and enzyme-inhibitory activities. For example, in hypertensive animals, peptides reduced blood pressure comparably to standard drugs like captopril (Cisneros-Yupanqui et al., 2022; González-Muñoz et al., 2022).

Finally, quinoa protein fractions have demonstrated anti-inflammatory and antioxidant potential. Albumins were more effective after digestion, while intact globulins showed higher trypsin-inhibitory activity. These findings underscore quinoa's role as a source of bioactive molecules with applications in preventing age-related diseases and some cancers (Capraro et al., 2021).

In addition to basic nutrients, quinoa contains various bioactive components, with red and black quinoa varieties showing higher levels of phenols and flavonoids and superior radical-scavenging activities. These bioactives have demonstrated insulin-sensitizing, fat-reducing, and fitness-improving activities in mammals without inducing androgenic or estrogenic effects. Many of these bioactives such as isoflavones, carotenoids, phytosterols, tocopherols, polysaccharides, and peptides with antioxidant, antimicrobial, anticancer, and anti-inflammatory properties exhibit beneficial health effects (Jukka-Pekka et al., 2022). While assessing the solubility profiles of quinoa grain proteins, protein fractions, including albumins, globulins, prolamins, and glutelins, were isolated, reflecting their susceptibility to digestion by digestive enzymes like pepsin, trypsin, and chymotrypsin when used separately. Globulins, the major protein fraction, exhibited promising results in additional tests, including amino acid profiling, with some limitations of lysine in relation to FAO standards, and the potential for the release of bioactive peptides after digestion. While pepsin-digested globulins inhibited only 5% of ACE activity after 24 h, the addition of pancreatin resulted in complete inhibition. The antioxidant activity (DPPH) also indicated similar outcomes, with pepsin hydrolysis proving ineffective in releasing antioxidant peptides, whereas hydrolysis by pancreatin was 35 times more effective (Tavano et al., 2022). In their investigation, Abbasi et al. (2022), also, aimed to assess the free radical scavenging activity and the inhibitory effect of bioactive peptides fractionated by SDS-PAGE obtained from quinoa proteins hydrolyzed by Alcalase and trypsin on alpha-glucosidase.

The inhibitory potential of angiotensin-converting enzyme (ACE, linked to anti-hypertensive effects) and dipeptidyl peptidase IV (DPP-IV, associated with anti-diabetic effects) was evaluated for peptides derived from thermolysin-hydrolyzed quinoa globulin using *in silico* and *in vitro* approaches. *In silico* hydrolysis of globulin fractions generated peptides of diverse sizes and sequences, with 25 peptides displaying high bioactivity probability scores (>0.8). Simulated gastrointestinal digestion of these peptides revealed four stable sequences (PR, SPH, IPPG, and SG) with strong predicted bioactivity for ACE and DPP-IV inhibition. *In vitro* validation using thermolysin-hydrolyzed quinoa globulin and protein concentrates corroborated these findings, demonstrating significant IC_{50} values for both ACE and DPP-IV inhibition. These results highlight thermolysin-processed quinoa globulin as a promising source of dual-functional bioactive peptides for managing hypertension and diabetes (Chirinos et al., 2023).

Peptides were obtained from quinoa through electrodialysis and ultrafiltration fractionation, and their antihypertensive and antidiabetic activities were evaluated. Experimental data showed the production of peptides ranging between 0.4 and 1.5 kDa. *In vitro* studies indicated their potential antidiabetic activity. Their *in vivo* antihypertensive effects were investigated in naturally hypertensive experimental animals, and the results showed a decrease in systolic blood pressure in the presence of fractionated peptides, with 100 mg/kg being a dose comparable to captopril (positive control). Further characterization is needed for peptide sequencing and their role in metabolism (González-Muñoz et al., 2022).

After enzymatic hydrolysis of quinoa proteins and using ultrafiltration and chromatography techniques, active fractions were purified and separated. These fractions exhibited higher antioxidant (3,784.9 μmol TE/g) and better ACE-inhibitory activities (IC50, 39.1 μg/mL), representing 2.3- and 7.7-fold increase, respectively, compared to the initial hydrolysate. These results demonstrate the potential of quinoa peptides as functional ingredients in the food industry (Cisneros-Yupanqui et al., 2022). Capraro et al. (2021) investigated the potential effects of quinoa proteins and their purified peptides (using the Osborne method, 1924) on chronic inflammation and oxidative stress. In vitro studies evaluated immunomodulatory, antioxidant, and trypsin-inhibitory activities. Peptides generated by the simulated gastrointestinal digestion of each fraction were also tested for selected bioactivities. None of the peptides induced inflammation in Caco-2 cells, with the protein fractions showing varying degrees of cell protection against interleukin (IL)-1β-induced inflammation. Immunomodulatory and antioxidant activities were greater in the albumin fraction, primarily after hydrolysis. In contrast, globulins exhibited higher trypsin-inhibitory activity in their intact form. These findings lay the groundwork for the utilization of quinoa seeds as a source of anti-inflammatory molecules, outlining their important role in age-related diseases and certain forms of cancer (Table 1).

3 CURRENT AND FUTURE CHALLENGES

Quinoa protein concentrates are valued for their exceptional nutritional and biological properties, including bioactive compounds like antioxidants, peptides, and oils. These compounds have demonstrated the ability to neutralize free radicals and reduce their harmful effects in vitro. The FAO recognizes quinoa and other pseudocereals for their outstanding functional benefits, such as antibacterial, antitumor, antioxidant, anti-inflammatory, and antihypertensive properties (Bazile & Santivañez, 2015). Biopeptides from plant proteins offer promising applications in the food and pharmaceutical industries, particularly for their radical-scavenging abilities. However, further research is needed to confirm their in vivo antioxidant effects. This study emphasizes the need to explore quinoa's bioactive compounds and suggests using bioinformatics to predict their behavior in metabolic and oxidative processes. Oxidation, such as lipid peroxidation, can reduce food shelf life and affect flavor, which is typically addressed by synthetic antioxidants—though their improper use raises toxicity concerns. Natural alternatives like phenolic compounds, tocopherols, and carotenoids are being explored, with quinoa protein hydrolysates showing promise in retaining antioxidant activities. Studies suggest that hydrolyzed quinoa proteins could offer antihypertensive and antidiabetic benefits (Chirinos et al., 2023). Exploring bioinformatics applications and the structure–activity relationships of biopeptides could lead to new antioxidant compounds and biomarkers for efficacy testing in living organisms (Durand et al., 2021). This approach could advance the development of natural antioxidants.

Table 1. Summary of bioactive peptide research*.

Product	Method	Effect	Reference
Peptides between 0.4 and 1.5 kDa	Electrodialysis with ultrafiltration	Antidiabetic and antihypertensive	González-Muñoz et al., 2022
Peptides between 10 and 3 kDa	Enzymatic hydrolysis, ultrafiltration-chromatography	Antioxidant and ACE inhibitory	Cisneros-Yupanqui et al., 2022
Albumins and globulins	*In vitro* gastrointestinal digestion	Immunomodulatory and antioxidant	Capraro et al., 2021
Bioactive peptides	Pigment extraction	Antioxidant, antimicrobial, anticancer, and anti-inflammatory	Jukka-Pekka et al., 2022
Isolated peptides	LC-MS/MS coupled with nano LC	Peptide sequences	Zheng et al., 2019
Protein hydrolysate	Supercritical fluid extraction of oil	Enhanced nutritional quality, high purity, solvent-free	Olivera-Montenegro et al., 2022
Protein fractions	Electrophoretic profile	Digestive enzyme hydrolysis	Tavano et al., 2022
Bioactive peptides by SDS-PAGE	Fractionation – ultrafiltration, enzymatic hydrolysis	Antioxidant, α-glucosidase inhibitory	Abbasi et al., 2022
Peptides between 0.4 and 1.5 kDa	*In silico* and *in vitro* hydrolyses	Antihypertensive, antidiabetic,and ACE inhibitory	Chirinos et al., 2023
Hydrophobic amino acids	Enzymatic hydrolysis	High content of hydrophobic amino acids	Zheng et al., 2019
Amino acids (valine, isoleucine, leucine, and Gln)	Enzymatic hydrolysis	Branched-chain amino acids	Esfandi et al., 2019

*This table summarizes different methods and effects for bioactive peptides from various sources.

4 CONCLUSIONS

Quinoa protein concentrates, containing 70–80% protein, are rich in albumins and globulins that can be hydrolyzed into peptides and amino acids with functional properties. These bioactive compounds offer significant biological benefits, including antihypertensive, antioxidant, antiglycemic, antitumoral, anti-inflammatory, and antibacterial effects, making quinoa a valuable resource for the food and pharmaceutical industries. Antioxidant peptides derived from quinoa have been widely studied for their role in preventing and managing chronic non-communicable diseases and their use in nutraceuticals. The antioxidant activity of these peptides is closely linked to structural features, such as molecular weight, amino acid composition, sequences, and hydrophobicity. However, further research is needed to fully characterize these bioactive compounds, both through computational (*in silico*) and experimental (*in vivo*) methods. This includes validating their activities using enzymes from natural plant, animal, and microbial sources to deepen the understanding of their health benefits.

4.1 Limitations and recommendations

While quinoa has been traditionally consumed by ancestral populations and is now globally revalued for its nutritional excellence—including protein quality comparable to animal sources—this review highlights gaps in the systematic exploration of scientific databases. A more rigorous selection and curation of specialized databases (e.g., bioactive peptide repositories and ethnopharmacological archives) could enhance the identification of quinoa-derived compounds. Furthermore, although quinoa contains bioactive ingredients of interest for health and medicine (e.g., ACE-inhibitory peptides and antioxidant flavonoids), their therapeutic potential remains understudied *in vivo*. Robust preclinical and clinical trials are essential to validate these compounds' efficacy, safety, and bioavailability, ensuring quinoa's evidence-based application as a functional food.

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