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Review Article

Quinoa as a multifunctional crop: Therapeutic applications and formulation potential

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Abstract

Quinoa, the antient crop used by the Andean and Inca civilizations, contains a diverse blend of bioactive phytochemicals that have found roles in the mitigation or treatment for a multitude of diseases such as hyperuricemia, hyperlipidemia, multiple types of cancer, celiac disease, diabetes mellitus, anemia, fatty liver disease, osteoporosis, celiac disease, diabetes mellitus, microbial infections, dysbiosis, hyperthyroidism, and ulcerative colitis. Being rich in macro- and micro- nutrients, it is used in a variety of culinary dishes including cereals, Indian kheer, Egyptian kishk, soups, cereals, and many bakery items including bread, cupcakes, and cookies. It is also an effective alternative for patients that cannot digest gluten or individuals on vegetarian diet. Quinoa can be cultivated in harsh environments due to its tolerance to abiotic stresses such as high heat temperature, high salt content in soil, low water conditions, and presence of heavy metals in soil. Novel approaches for using quinoa include treating water contaminated with heavy metals like chromium, cadmium, nickel, arsenic, lead, and wastewater treatment. It has been used to prepare biodegradable films for food packaging, ready-to-eat protein hydrolysates, functional foods and drug delivery systems like composite micelles, microspheres, and nanoparticles. Quinoa can prevent the rancidity of lipids and microbial contamination in packaged food. In future, study on the genetic variants of quinoa, further expansion into its natural constituents, and research or clinical trials for treatment of many diseases can be done.

Keywords: Quinoa, Bioactive, Phytochemicals, Novel Approaches, Vegetarian Diet, Micelles, Nanoparticles.

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Introduction

The annual dicotyledonous plant of the genus Chenopodiaceae, *Chenopodium quinoa Willd* is primarily cultivated in the Andean region of South America. It is a pseudo-grain filled with healthy amounts of proteins, lipids, vitamins, micronutrients (Mg, Fe, Zn, Ca, P and K) and fibers Quinoa is a rich source of multiple biologically active compounds which include ecdysone, polysaccharides, polyphenols, phytoecdysteroids, flavonoids, saponins, and peptides that not only contribute to the nutritional value of a balanced meal but also demonstrate pharmacological activity, with proven action against celiac disease, diabetes mellitus, anemia, microbial infections, ulcerative colitis, fatty liver disease, hyperthyroidism, hyperuricemia, hyper-lipidemia, dysbiosis and inflammation [1, 2]. More than 250 varieties of quinoa seeds are found with varying chemical and nutritional compositions depending upon the genetic diversity and geographic locations [3]. The scope of this study is to provide comprehensive coverage of pharmacological properties, novel products and culinary applications of quinoa.

Clinical trials and animal studies confirm that quinoa metabolites effectively reduce serum triglycerides, LDL cholesterol and total Cholesterol levels in obese and overweight individuals. Quinoa-derived peptides inhibit angiotensin-converting enzyme (ACE) and improve insulin sensitivity by activating the PI3K/AKT signaling pathway, which increases the expression of GLUT-4 in muscle tissue, thereby increasing glucose uptake. They have benefits for diabetic patients due to the low glycemic index [4]. Quinoa is a dense pseudocereal, with high iron content, coupled with vitamin C, phenolic compounds, and flavonoids which enhance non-Heme iron absorption. Quinoa can improve gut microbiota functions and enhance vitamin B6 metabolism [5, 6]. Quinoa demonstrates anticancer potential by their rich content metabolites which increase apoptosis, inhibit proliferations in cancer cell lines and show strong cytotoxic [7]. Quinoa is a functional component in the prevention and management of non-communicable diseases. Incorporating quinoa flour into multigrain bread significantly reduces postprandial glycemic response and improves blood lipid profiles [8]. Quinoa is widely used in the consumer market as gluten-free-snacks, protein-rich cereals, beverages, supplements, pasta and bakery items like bread [9].

In addition to its nutritional and therapeutic significance, recent research has shown a multitude of novel and innovative applications of quinoa in areas such as drug delivery systems. This is largely reflected in the preparation of novel formulations such as nanoparticles, Pickering emulsions (valuable for safely encapsulated and delivering compounds like curcumin and astaxanthin) and phytoremediation (where plants are used to clean up the heavy metals like cadmium, lead, nickel and arsenic) [10, 11]. Additionally, the function of quinoa as halophytes make it suitable for phytodesalination, a process that employs salt-tolerant plants to absorb excess salts from saline soil to offer a suitable solution for soil salinity management and wastewater treatment [12].

Novel quinoa-based products

Nanoparticles

Plant derived silver nanoparticles (AgNPs) have been investigated in the medical field as potential candidates in the treatment of chronic diseases including cancer [13]. Besides their clinical applications, quinoa NPs have demonstrated their use in agriculture as well. Stable AgNPs in the 5–50 nm size range were synthesized for use as bio stimulants in agriculture using an environment-friendly manner by employing saponin extract of quinoa husk as a silver ion reduction agent [14]. A different study used extracts of white quinoa at different concentrations ranging from 5% to 50% w/v to develop novel 7-8 nm iron-oxide NPs [15].

Quinoa based emulsion

Pickering emulsions employ colloidal particles or solid particles as the emulsifiers to stick at the oil-water interface instead of surfactants. They have attracted research interest in recent times owing to their great versatility of applications and stability as opposed to conventional emulsions [16]. A research study prepared a Pickering emulsion through ultrasonic emulsification using quinoa and non-covalent hybrid particles of epigallocatechin-3-gallate. The product limited the oxidation and hydrolysis of lipids in food and pharmaceuticals, preventing the development of undesirable qualities like lousy odor or taste and supplying a foundation for the creation of higher-quality medicine and food delivery systems [17]. Another study prepared a stabilizer for oil-in-water Pickering emulsions through nanoprecipitation using quinoa starch nanoparticles (QSNPs). After being nanomodified, the nanoparticles showed improved oxidative stability, a larger contact angle, and better wettability than QS. Their exceptional freeze-thaw stability allowed them to be manufactured as a re-dispersible dry emulsion using the freeze-drying process [18]. A study used nanoparticles made from quinoa protein as a stabilizer for developing high internal phase emulsions (HIPEs) with an internal phase of 89%. Preparation of nanoparticles using ultrasonication resulted in excellent adsorption and antioxidant activity. These emulsions had better shear thinning and elastic behavior when nanoparticles were exposed to higher ultrasonic density. These HIPEs can potentially replace hydrogenated oils [19].

Quinoa-based hydrogels

Quinoa can be used to produce hydrogels following alkaline protease treatment. These plant-based hydrogels provided the capability for self-assembly, improved rheological properties, and gel hardness, offering themselves as a cost-effective and eco-friendly solution compared to chemically synthesized hydrogels for producing novel plant-based foods.

Quinoa protein isolate-gum Arabic conjugates

Spice essential oils have a strong fragrance and are highly hydrophobic. This limits their utility as medication and food preservatives. Using ultrasound-assisted wet heating, conjugates of Arabic gum and quinoa protein isolates were developed to enhance spice essential oils' water solubility and bioactivity in aqueous systems [20]. Additionally, using these conjugates lessened the sensory stimulation that essential oils provided.

Quinoa-based extrusion products

Extrusion is used in cooking, mixing, kneading, and shaping at high temperatures to produce food products for instant consumption. Nutrient content in regular and extruded quinoa products was analyzed using metabolomics extrusion. It showed that processing quinoa in preparation for extruded products effectively enhanced its nutritional profile [21]. A study utilized amylolysis and extrusion techniques in a single stepwise procedure, limiting the loss of polyphenols and improving the digestibility of proteins. The procedure increased the protein digestion rate four-fold faster, reducing the α-amylase concentration to 0.36 g/100 g and non-digested protein content up to 47% at 100 °C when matched with quinoa flour [22]. Another study prepared extrudates of quinoa enriched with goji berry [23].

Novel applications of Quinoa

Phytoremediation

Untreated discharge of industrial waste releases toxic heavy metals into agricultural land. Experiments have been conducted to utilize phytoremediation, a technique that uses plants to lower heavy metal contaminations [24]. A study on quinoa was conducted at the University of Agriculture, Faisalabad, Pakistan. This study exhibited potential for adsorption of heavy metals like Cd, Cr, Pb, and Ni. The levels of these heavy metals allow safe usage of quinoa in food [25]. In a study, quinoa was exposed to Cd and Pb, which decreased plant height, root, shoot, and seed weight. The level of Cd accumulation in seeds prevents its use in food, while Pb accumulation was within permissible limits and can be used in food. The study suggested the use of quinoa for phytoremediation of Cd and Pb [11]. Exposure to Ni caused a decrease in root length, shoot length, chlorophyll biomass, and stomatal conductance with an increase in oxidative stress. The study suggested using quinoa for phytostabilization of soil contaminated with Ni due to the quinoa genotypes' high translocation factor and bioconcentration factor [26]. Quinoa plants exposed to arsenic caused a fall in the growth, stomatal conductance, and grain yield while elevating the oxidative stress. A high concentration of arsenic was retained in roots, showing its phytostabilizing capacity. The study concluded that quinoa exposed to As levels of at least 20 mg per kg was unfit for human consumption [27]. A study reported a high bioaccumulation factor, tolerance index, and translocation factor in quinoa. The study estimated that using biochar made from pomegranate and plum wood reduced the levels of Cd in soil, root, and shoots; thus, it is used to reduce heavy metals in plant organs. However, biochar made from North Forest wood raised the levels of Cd in soil, root, and shoot and, thus, should be avoided [28].

Production of edible films

Quinoa can be used to prepare biocompatible and biodegradable food packaging. In a study, cassava starch films were developed using up to 5% quinoa starch nanocrystals (QSNCs). Compared to movies made without nanoparticles, they had higher tensile strength, water vapor permeability, roughness, water contact angle, and opacity. This suggests the use of QSNCs for food packaging material in the future [29]. Another study prepared edible and biodegradable composite films using Hsian Tsao gum (HG) and quinoa protein (QP). The study concluded that a small addition of HG to QP improved QP films' physical properties, water barrier properties, and antioxidant activity. It also delayed the rancidity of vegetable oil. These biodegradable films demonstrated the ability to prolong the shelf life of foods that degrade quickly, such as meat and vegetable oil [30].

Phyto desalination

Halophytes like quinoa that can tolerate high salt concentration can be used for phytodesalination, a technique for managing high salt content in wastewater. A study probed the impact of various salinity levels on quinoa grown in a hydroponic system. The result estimated that quinoa reduced the levels of Ca, Mg, Na, and Cl by 10%, 7.62%, 5.60%, and 7.01%, respectively, showing the potential for use of quinoa in saline wastewater treatment [31]. A study compared the responses of wheat and quinoa towards exposure to high salt concentrations. The result demonstrated higher Na, Cl, and Mg levels in quinoa and higher absorption efficiency of Na, Cl, and Mg from water in quinoa. Also, the amount and absorption efficiency of Na, Cl, and Mg increased with the increase in salinity. Hence, shows the potential of quinoa to be grown in high-salinity soils and to be used for phytodesalination [32].

Cryopreservation

Quinoa seed extracts (QSE) can reliably be used for preserving genetic material in assisted reproduction. A study used QSE while cryopreserving ram sperm and identified lower levels of hydrogen peroxide (H_2O_2) and malondialdehyde (MDA) and higher contents of total antioxidant capacity (TAC). The post-thawed cryopreserved ram sperm showed downregulated expression of apoptosis-related gene CASP3 while the antioxidant-related genes (GPX1, GABPB1, CAT and

SOD1), were upregulated in all QSE-supplemented samples [33].

3D food printing

The benefit of 3D food printing is that it allows us to control the consistency, texture, and shape of food products. Plant-derived proteins such as quinoa proteins due to their favorable essential amino acid composition can act as potential stabilizers in the formulation of food grade emulsion gels [34]. Food-grade biopolymers such as proteins and polysaccharides can stabilize emulsion gels, making them promising candidates for use as edible inks in 3D food printing. Polysaccharides like sodium alginate, dextran sulfate, fucoidan and inulin can help improve the flexibility of quinoa protein emulsion gel for the 3D printing of functional food [35].

Drug delivery

Micelles

Natural biopolymer-based micellar drug delivery systems offer the benefits of being non-toxic, non-immunogenic, biodegrade-able and biocompatible and allow loading of significant quantities of active ingredients [36]. In a study, the layer-by-layer assembly method was used to prepare composite micelle for quercetin delivery, which is used to treat inflammation. In the composite micelle, Quercetin-hydrolytic quinoa protein (HQP)-epigallocatechin-3-gallate (EGCG) formed the core, while cationic lotus root starch (CLRS) formed the coating shell. Animal studies confirmed the sustained release of drugs from micelle in the colon, lowering the symptoms of ulcerative colitis [37].

Microspheres

Microspheres developed using naturally derived polymers can be used as an effective platform for drug delivery [38]. Microparticles were synthesized using quinoa starch and epichlorohydrin by using inverse emulsion polymerization. The micro particles exhibited good adsorption performance, as confirmed in experiments using methylene blue and some antibiotics [39].

Nanoparticles

Nanoparticles have several key advantages over conventional therapeutics [40]. Quinoa starch nanoparticles loaded with piroxicam were synthesized using a nano-precipitation technique. When compared to the pure drug piroxicam, the piroxicam-loaded nanoparticles were found to have better anti-inflammatory activity, as evident by the *in vitro* dissolution test [41]. Figure 1 shows the attenuation of tumorigenesis and inflammation using nanocarriers loaded with phytochemicals present in quinoa.

Pharmacological properties of quinoa

Quinoa has received much appreciation in the past few decades due to its presence of bioactive compounds responsible for relieving the symptoms of multiple diseases. The summary of such is given in Table 1 and Figure 2.

Diabetes mellitus

Bioactive quinoa peptides released after digestion inhibit α-glucosidase, dipeptidyl peptidase-4, and α-amylase. These peptides also block the action of enzymes that break down incretin and aid in digesting carbohydrates [42]. In an experiment, diabetes was induced in mice using a high-fat diet and streptozotocin. When quinoa was provided in their diet, the mice showed improved glucolipid metabolism and gut microbiota. The results suggested that quinoa could alleviate hyperglycemia [43, 44]. In another study, diabetic rats fed with diets containing 40% quinoa reduced their blood glucose levels from 236.7 mg/dl to 98.7mg/dl. The histopathological studies of the pancreas of quinoa-fed rats showed no significant finding, but an infiltration of inflammatory cells was seen in rats not given quinoa [45].

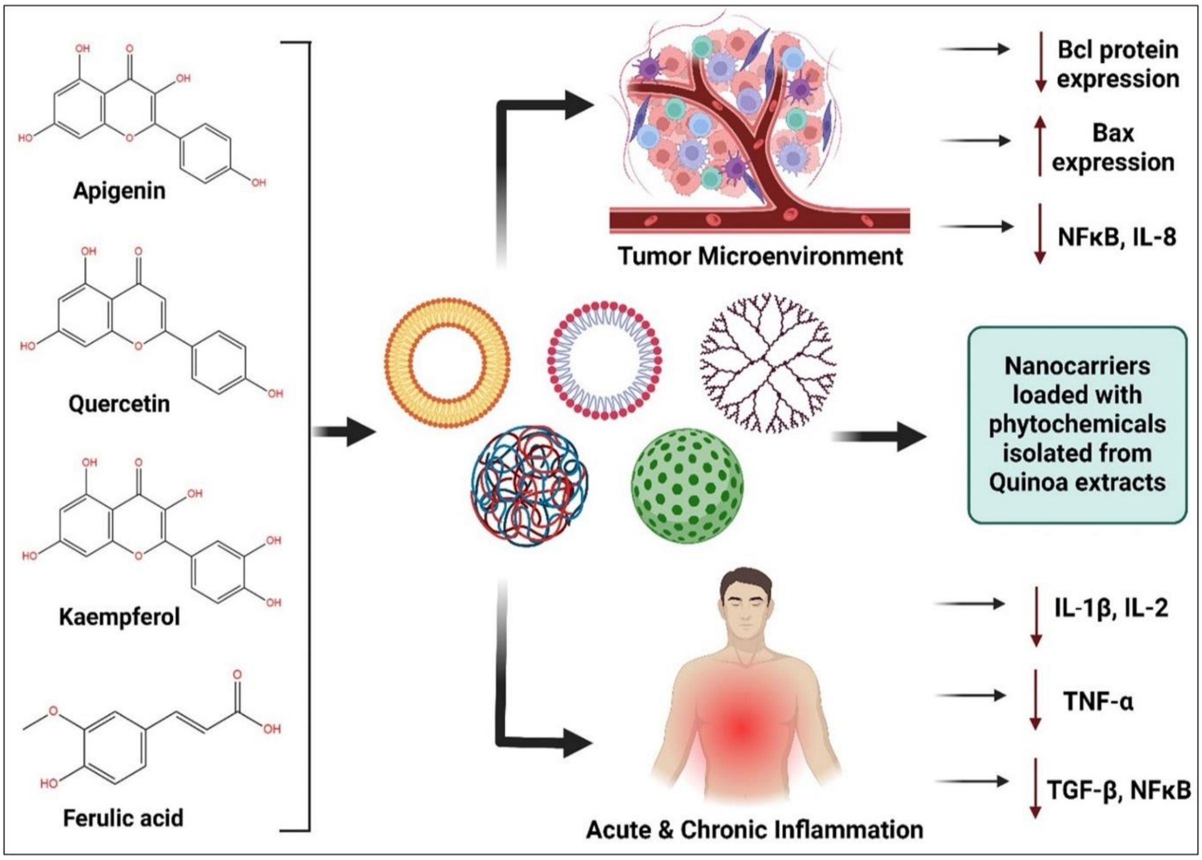

Figure 1: Effect of nanocarriers loaded with phytochemicals extracted from quinoa on cancer and inflammation.

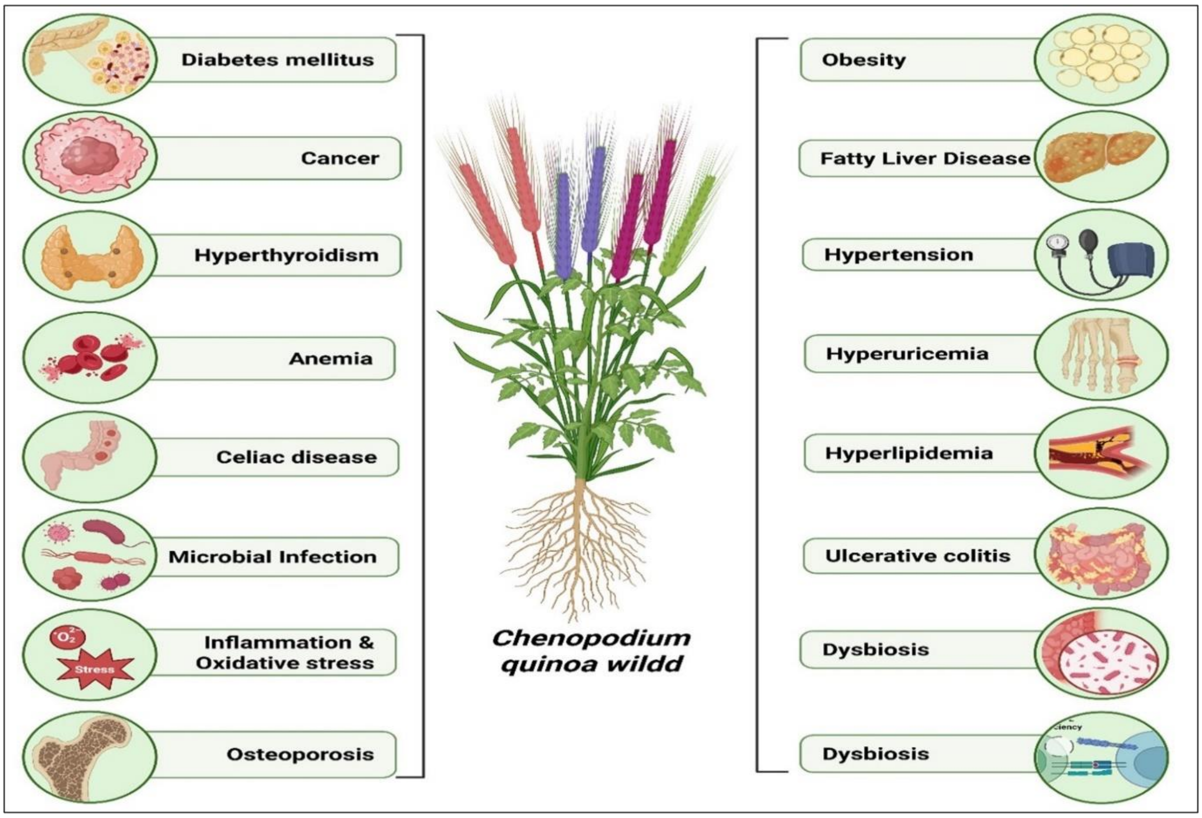

Figure 2: This illustration summarizes the role of Quinoa in the mitigation or treatment of multiple diseases.

Another study demonstrated the hypo-glycemic activity of quinoa peptides in pregnant mice and identified 11 peptides with anti-dipeptidyl peptidase-4 activity [46]. Quinoa components, including phytosteroids, phenolics, polysaccharides, and peptides, have reduced adiposity, dyslipidemia, and hyperglycemia in rat models [47]. Quinoa supplementation in an 8-week clinical trial involving obese women with type 2 diabetes mellitus reduced HbA1c, lipid content, BMI, and weight while improving the antioxidant capability [48]. Quinoa consumption in pre-diabetic individuals improved postprandial blood glucose levels, thereby delaying the progression of the disease [49]. A study shows that red quinoa polysaccharides (RQP) inhibited α-amylase and α-glucosidase in-vitro, suggesting a role in postprandial glucose regulation. In diabetic mice, RQP improved blood glucose levels, lipid metabolism, antioxidant status, and short-chain fatty acid production. Gut microbiome analysis revealed RQP reduced diabetes-associated bacterial taxa while promoting beneficial genera like Akkermansia. These microbial shifts correlated with metabolic improvements, highlighting RQP's potential as a functional food ingredient for type 2 diabetes management via gut microbiota modulation and metabolic regulation [50]. The dipeptidyl peptidase IV (DPP-IV) inhibitory peptides within quinoa have potential as natural therapeutics for treating type 2 diabetes. Controlled malting parameters such as temperature, humidity, and duration can significantly impact peptide production and bioactivity. Optimally malted quinoa exhibited a maximum DPP-IV inhibition of 45.02% (±10.28) and peptide concentrations up to 4.07 μmol/L, strongly depend on malting conditions [51]. Another study result demonstrated that quinoa consumption significantly improved metabolic control in individuals with impaired glucose tolerance (IGT), outperforming conventional dietary methods. Over 12 weeks, quinoa intake reduced post-meal glucose spikes by 28.4% and decreased HbA1c by 0.9%. It also enhanced insulin sensitivity, lowering HOMA-IR by 2.1 points, while favorably modulating lipid profiles with a 15.2% reduction in LDL and an 8.7% increase in HDL cholesterol. These combined effects highlight quinoa's potential as a multifunctional dietary intervention for managing IGT and preventing progression to type 2 diabetes. Further research is needed to determine optimal dosing and explore interactions with other antidiabetic foods [52].

Obesity

Quinoa consumption during an 8-week trial reduced the weight of obese rats previously provided with a high-fat diet, by regulating the PPAR-α/γ signaling pathway in the liver [53]. Quinoa was shown to improve the conditions linked to diabetes mellitus type 2 and obesity in rat models [54]. The insoluble dietary fiber extract lowered the body weight and improved the lipid profile in obese rats [55].

Fatty liver disease

Levels of hepatic enzymes (AST, ALT, and ALP) were lowered in obese rats by using insoluble dietary fiber extract. This had a beneficial impact on liver injury, as evidenced by the analysis of liver tissue. Also, some genes that influence fatty acid degradation were affected by quinoa dietary fiber [55]. Consumption of quinoa seed with 10% psyllium husk in obese rats improved lipid profile and liver and renal functions [56]. Quinoa-rich meals in rats with fatty liver disease positively impacted hepatomegaly, splenomegaly, and hepatic steatosis. Thus, it was postulated that quinoa can be added to patients' diets to prevent non-alcoholic fatty liver disease [57]. Red quinoa bran fed mice with alcohol-induced fatty liver disease reduced lipid droplet accumulation in the liver and prevented liver damage by raising the superoxide dismutase/catalase anti-oxidative system and suppressing the expression of acetyl-CoA carboxylase [58]. Liver injury in Wistar rats triggered by carbon tetrachloride was attenuated by administering an ethanolic extract of Quinoa seeds [59].

Hypertension

Bioactive peptides that inhibit ACE in red quinoa hydrolysate were given to spontaneously hypertensive rats. The results demonstrated a fall in systolic blood pressure in rats [60]. Another experiment found no significant difference between captopril-treated rats and quinoa-treated rats in decreasing systolic and diastolic blood pressure [39]. A study investigated the anti-hypertensive and anti-diabetic activity of bioactive peptides in a beverage fermented using lactic acid bacteria. The study found that LAHMIVAGA and VAHPVF had α-glucosidase and ACE inhibitory activities [61]. Another research study found dual ACE inhibitory and antioxidant activity of novel peptide RGQVIYVL in quinoa bran albumin, while [62] identified the ACE inhibiting peptides, namely NIFRPFAPEL and AALEAPRILNL in quinoa broth fermented with lactic acid yeast and bacteria [63].

Hyperlipidemia/Hypercholesterolemia

Quinoa polysaccharide can improve high fat diet induced hyperlipidemia in mice [64]. Obese rats fed with quinoa bran dietary fiber had improved triglyceride, cholesterol, and low-density lipoprotein-cholesterol [65]. Supplementation of quinoa saponin was found to lower serum lipids along with inflammation, liver injury and body weight [66]. Hyperlipidemic mice when given monascus-fermented quinoa in doses of 1600 mg $kg^{-1}d^{-1}$ significantly lowered the levels of LDL cholesterol, triglycerides, total cholesterol, and resulted in weight loss. This occurred by regulating amino acid levels by affecting different metabolic pathways such as tryptophan, tyrosine, and phenylalanine metabolism. This led to a marked decrease in serum lipid levels in mice with hyperlipidemia induced by high fat diet [43]. Apart from murine models, a study shows that serum triglyceride in obese women was reduced by consuming 50 g and 100 g quinoa daily [67].

Celiac disease

Patients with celiac disease must avoid gluten. Even though gluten-free food is available on the market, it is not rich in nutrients like vitamin D, B6, B12, folate, Fe, Ca, Zn, and Cu. Pseudocereals like quinoa are a better option because they are gluten-free and rich in nutrients [68]. 10% gliadin solution was administered to mice to induce celiac disease in a study. These mice were provided with a diet comprising quinoa and chia. Several parameters, including weight reduction, lipid profile, and liver and kidney function, reflected promising outcomes and confirmed the usefulness of quinoa for celiac disease patients [69].

Hyperthyroidism

Hyperthyroidism refers to excess thyroid hormone release by the thyroid gland [69]. A study found the concentration of thyroid hormones to be significantly reduced in quinoa-fed diabetic rats [45]. Similarly, another study recorded decreased thyroxine and triiodothyronine in quinoa-fed rats with hepatic injury [59].

Cancer

Bioactive peptides in quinoa were shown to have anti-tumor activities. A Summary of such studies is given in Table 1.

Colorectal cancer

A study tested quinoa protein hydrolysates in mice with colorectal cancer, demonstrating the reduction in hallmarks of colorectal cancer along with improvement in microbiota dysbiosis and a rise in short-chain fatty acids in the colon [70]. Another study found that quinoa bran terpenoids inhibited the growth of colorectal cancer cells DLD-1 and HCT-8, upregulated the apoptotic proteins activated-caspase-3, 8, 9 and BAX while inhibiting the anti-apoptotic protein BCL-2 in nude mice [71]. Similarly, a study evaluated the activity of 3 peptides, HYNPYFPG, NWFPLPR, and FHPFPR, in colon cancer Caco-2 cells. These peptides inhibited the activity of HDAC1 while regulating the expression of cancer-related genes NFκB, IL-6, IL-8, Bcl-2, and caspase3 [72]. A study testified the therapeutic action of cetuximab on EGF receptor in colorectal cancer by conjugating it with quinoa (type 1 ribosome-inactivating protein present in quinoa), rendering optimistic results [73]. The chemo sensitivity of 5 Fluorouracil (5-FU) can be enhanced using quinoa protein hydrolysate (QPH) obtained from simulated digestion of quinoa grains. This was demonstrated in an in-vivo experiment where the tumor size in the 5-FU+QPH group decreases to 94.49 ± 13.05 mm^3 from 145.90 ± 13.35 mm^3 which was greater than in the in the 5-FU group [74].

Table 1: Summary of studies done on the anti-neoplastic potential of Quinoa.

Cancer Type	**Quinoa Compound(s)/ Formulation**	**Experimental Model**	**Mechanism/ Outcome**	**Reference**
Colorectal Cancer	Quinoa protein hydrolysates	CRC-induced mice	Alleviated cancer hallmarks, improved gut dysbiosis, increased colonic SCFAs	[70]
	Bran-derived terpenoids	DLD-1 and HCT-8 xenografts in nude mice	Induced apoptosis (increased caspase-3, 8, 9, BAX; decreased BCL-2)	[71]
	Peptides: HYNPYFPG, NWFPLPR, FHPFPR	Caco-2 colon cancer cells	Inhibited HDAC1, modulated NF-κB, IL-6, IL-8, BCL-2, caspase-3	[72]
	Quinoa RIP–cetuximab conjugate	EGFR-targeted colorectal cancer	Enhanced cetuximab efficacy via type 1 RIP delivery	[73]
	Quinoa protein hydrolysate (QPH) + 5-FU	In vivo CRC mouse model	Reduced tumor volume (94.49 ± 13.05 mm^3 vs. 145.90 ± 13.35 mm^3 with 5-FU alone)	[74]
Brain Cancer	Whole quinoa extract	C6 rat glioma cells	IC_{50} = 50 ppb (MTT assay), inhibited cell migration (wound healing assay)	[75]
Breast Cancer	Quinoa saponins	MCF-7 and MDA-MB231 cell lines	Tumor suppressive effect in vitro	[76]
	Chitosan–TPP crosslinked quinoa saponin nanoparticles	MC-F7 cells at pH 6	IC_{50} = 4.5 mg/mL, enhanced cytotoxicity in acidic tumor microenvironment	[77]
	Quinoa oil nanoemulsions	DMBA-induced breast cancer in murine model	Modulated tissue architecture, activated anti-oncogenes, reduced oxidative stress	[78]
Lung Cancer	Whole quinoa extract	A549 lung carcinoma cells	Increased BAX, decreased BCL-2 expression, inhibited proliferation and induced apoptosis	[79]

Brain cancer

A study stated that quinoa suppressed glioma cell metastasis in the rat C6 glioma cell lines. The MTT test determined the IC50 value of the quinoa as 50 ppb while the wound test demonstrated that metastasis was inhibited in the glioma cells while it was continued in the control group [75].

Breast cancer

A research study exhibited the tumor-suppressing action of quinoa saponins on breast cancer cell lines MCF-7 and MDA-MB23 [76]. Another study made stable quinoa saponin NPs by using chitosan and pentasodium tripolyphosphate as cross-linking agents that showed cytotoxic action against MC-F7 cells at pH 6 and 3 mg/ml concentration. The IC50 value came out to be 4.5mg/ml [77]. Similarly, a murine model with breast cancer triggered by 7, 12-dimethylbenz (a) anthracene (DMBA) was used to evaluate the anticancer effects of quinoa oil nano-emulsions. These nano-emulsions influenced tissue architecture, anti-oncogene expressions, and oxidative stress markers to show anticancer activity against breast cancer [78].

Lung cancer

A study demonstrated quinoa's anti-proliferative and anti-apoptotic effect on the A549 lung cancer cell line. Also, causing increased BAX expression levels while decreasing the expression of BCL2 [79].

Dysbiosis

The phytochemical constituents present in quinoa seeds can promote probiotic bacteria while inhibiting harmful pathogens. These bioactive compounds contribute to promoting production of Short-chain fatty acids (SCFAs) and lowering intestinal pH [80]. In a study, quinoa protein/ protein hydrolysate was tested in a colon cancer mice model. The findings reflected an auspicious improvement in gut microbiota dysbiosis, lowering the number of harmful bacteria and raising the number of probiotic bacteria [70]. Quinoa polysaccharide can influence gut microbiota by lowering the ratio of Bacteroides and Firmicutes, and the overall abundances of Proteobacteria [64].

Hyperuricemia

Quinoa bran saponins, mainly hederagenin, and oleanolic acid, reduced BUN, uric acid, and creatinine levels, lowering renal damage and inflammation in hyperuricemic mice. The underlying mechanism can be postulated as the decreased expression of uric acid transport-related genes and by inhibiting the PI3K/AKT/NFκB signaling pathway [81]. Hyperuricemic rats given a combination of quinoa and Nigella sativa seeds lowered oxidative stress and improved renal function [82]. Similarly, a diet with quinoa and chia seeds reduced uric acid and creatinine previously elevated due to celiac disease [69].

Anemia

In a study, 7.5% quinoa and 7.5% spirulina were administered in mice with iron deficiency anemia and a rise was recorded in serum hemoglobin and hematocrit, post administration. In another experiment, a group of rats with iron-deficiency anemia were provided with 5-10% quinoa seeds or sprouts in diet. This resulted an increase in the number of red blood cells, platelets, and ferritin [83]. Another study recorded an increase in hematocrit of anemic rats supplemented with quinoa flour from 29.3% to 53.8% in twelve weeks [84].

Ulcerative colitis

Quinoa can be used for the prevention of ulcerative colitis. A study examined the effect of soluble dietary fiber of quinoa bran on ulcerative colitis in 4 weeks' mice model. The result showed downregulated TNF-α and IL-1, reduced apoptosis in colonic cells, upregulated tight junction proteins and an increased volume of gut microbiota with reduction of symptoms [85]. Ulcerative colitis induced by dextran sulfate sodium in mice was ameliorated using oral administration of quinoa protein which inhibited the phosphorylation of NF-κB and IκB-α in colon tissue and lowered the levels of TLR4 in a study. this resulted in a reduction in intestinal barrier injury, inflammatory factor release, colonic shortening as well as weight loss, mitigation in bloody stools, abdominal pain and diarrhea [84].

Microbial infection

Quinoa peptides isolated through enzymatic hydrolysis exhibited bacterio-static and bactericidal activity against *Streptococcus pyogenes* (a gram-positive bacterium) and *Escherichia coli* (a gram-negative bacterium). These peptides could also be employed as preservatives in food packaging [86]. The saponin content in quinoa husk caused leakage of the cytoplasmic material by damaging the cell wall of foodborne pathogenic bacteria [87]. Figure 3 illustrates the antimicrobial spectrum of quinoa.

Inflammation and oxidative stress

In an experiment, quinoa-rich meals given to mice with liver damage prevented the fall in the activities of glutathione peroxidase and superoxide dismutase while causing an increase in malondialdehyde. TGF-β, TNF-α, IL-10 and leptin were reduced to levels comparable to those of the control group (having no liver injury) [57]. Another study measured the DPPH radical scavenging activity as 0.29 mg TE/g and ABTS radical cation as 4.38 mg TE/g in quinoa-fed diabetic rats [45]. After the administration of quinoa, the upregulation of genes involved in oxidative stress, inflammation, autophagy, and apoptosis due to insulin resistance was reduced to similar levels as in the control group [88].

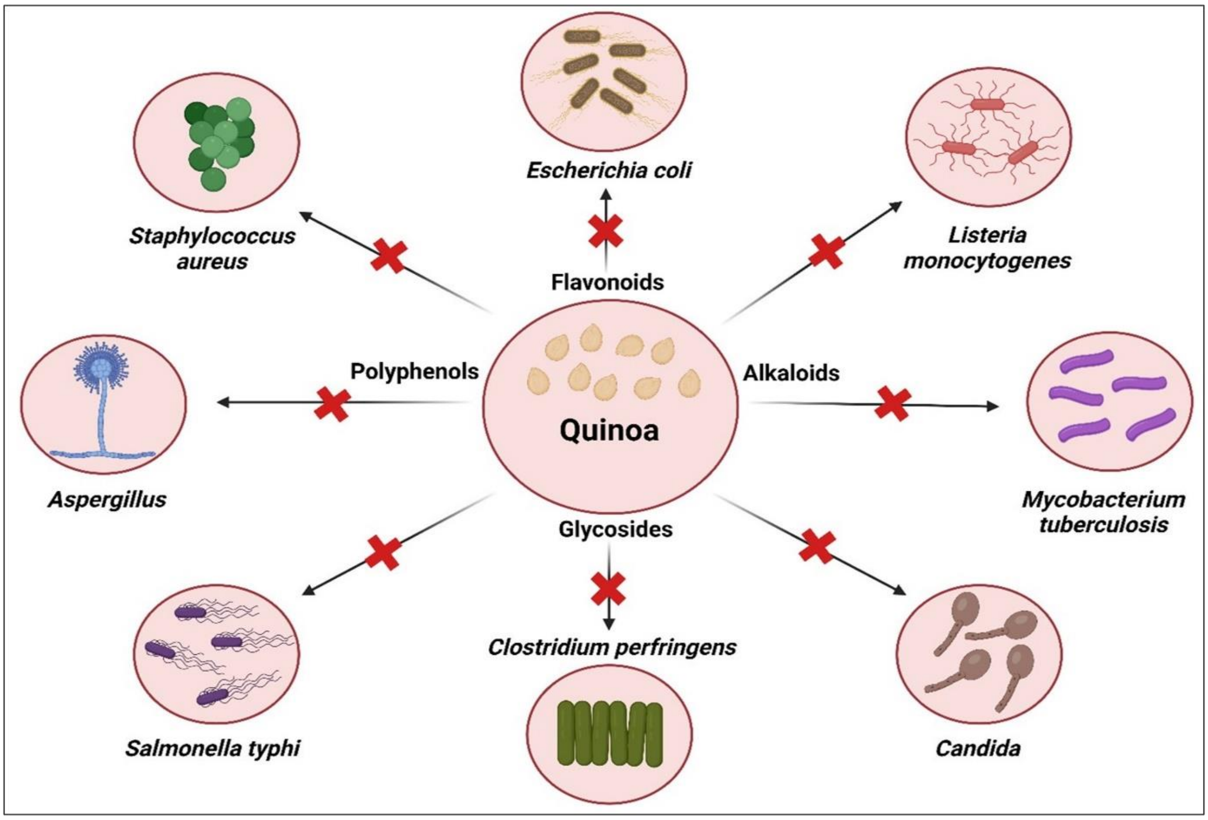

Figure 3: An illustration of the antimicrobial spectrum of quinoa.

Quinoa protein and its hydrolysate (QPH) were found to activate the Nrf2/HO-1 signaling pathway, which plays a pivotal role in protecting cells against oxidative stress. Notably, QPH showed additional benefits by improving mitochondrial function and energy metabolism through regulation of critical signaling pathways such as the PGC-1α/NRF1/TFAM pathway involved in mitochondrial biogenesis, and the G6Pase/PEPCK pathway essential for gluconeogenesis. These results as demonstrated in a study highlight the potential of quinoa-derived proteins as valuable functional ingredients for developing sports nutrition products and anti-fatigue supplements, offering a natural approach to enhance physical performance and recovery [89].

Osteoporosis

In an experiment, dietary quinoa supplementation led to significant improvements in biochemical indicators of bone health in ovariectomized (OVX) mice with postmenopausal osteoporosis (PMO) effectively preventing trabecular microstructure deterioration and bone density loss and in a study. Quinoa enhanced the expression of tight junction proteins, strengthening gut barrier function and lowering intestinal permeability. Additionally, shifts in gut microbiota composition, including a 38% increase in Firmicutes and a 25% decrease in Bacteroidetes were seen. The bone-protective effects of quinoa involve the modulation of key biological pathways such as the restoration of estrogen-related signaling, regulation of bile acid metabolism, activation of benzoate degradation pathways, and stimulation of NOD-like receptor signaling. The study showed strong associations between certain gut microbial species, particularly Lactobacillus species, and bone formation markers, reinforcing the concept of the gut-bone axis [90]. In another study, the combination of Fructus Ligustri Lucidi (FLL) and quinoa alleviated the compromised bone microarchitecture and bone density in OVX mice. This combination also improved intestinal flora function and diversity [91].

Immunomodulation

Quinoa-derived protein components can influence immune activity, specifically macrophages. This was evaluated in a study where QPH, at a concentration of 1000 μg/mL, boosted the production of key immune signaling molecules, including IFN-γ and TNF-α, while also promoting the release of IL-10. This pattern suggests that QPH may help maintain a balanced immune response. Additionally, the low-molecular-weight quinoa peptide fraction (QPF) was found to significantly enhance the phagocytic function of spleen macrophages, indicating its potential role in stimulating systemic immune defense mechanisms [92]. Quinoa cereal grains with immunomodulatory properties can contribute to preserving the function of hepatic myeloid cells, such as monocytes and macrophages, which play a central role in regulating the immune environment of the gut-associated lymphoid tissue (GALT). This regulatory action appears to involve their interaction with innate lymphoid cells (ILCs) and regulatory T cells (Tregs), both of which are essential for maintaining immune balance and managing inflammatory responses. The coordinated relationship between these immune players suggests that functional grains could help modulate immune activity in both the liver and intestines, offering a nutritional strategy to support immune system stability [52].

Culinary preparations of quinoa

The number of individuals switching to a vegan/vegetarian diet (that relies on plant-based foods) or a flexitarian diet (that limits meat and processed food) has increased. However, their daily protein requirement is not fulfilled without meat consumption, fueling the search for plant-based foods with high protein content. For individuals with Gluten-related disorders like celiac disease, avoiding gluten is the only effective treatment. This goes for 0.9-2.4% of the population in the US [93]. Since gluten is present in staple crops like wheat, rye, barley, oats, etc., allergic patients are left to consume processed versions of such crops. Also, the need for nutritious food has increased due to the increase in malnourishment and hunger, especially in developing countries. Ancient crops like quinoa that lack gluten and contain rich nutritional content can be beneficial for them. Below are examples of the use of quinoa in culinary preparation. A summary of culinary preparations made using Quinoa is given in Table 2.

Quinoa beverages

Plant-based beverages like coconut milk, almond milk, oat milk, etc., are available for individuals with lactose intolerance or allergies. However, these options contain less protein than cow's milk [94]. A study investigated the addition of oat β-glucan as a stabilizer in the development of plant-based milk from quinoa [95]. Some beverages were developed using three varieties of quinoa sprouts. It was stated that sprouted quinoa contains higher nutritional content with a lower content of saponins [96] . Quinoa milk was prepared in another study using an extraction procedure similar to rice milk. The protein content was roughly half of cow's milk and 5.6 times higher when compared to rice milk. However, the lipid content was lower than in cow's milk [97]. The limitation observed was the bitterness and aroma, for which the study suggested the addition of flavors. One way to overcome the undesired organoleptic properties was fermentation, which in food sciences refers to utilizing microorganisms and their enzymes to achieve desirable quality characteristics [98]. A quinoa-based fermented beverage was prepared in a research study using three bacterial strains [99]. The beverage had no phase separation and was stable throughout the 28-day storage period. However, care must be taken regarding the food processing procedures and finished products due to them being impacted by variations in quinoa genotypes. A similar study used quinoa flour and three lactic acid bacteria strains to produce a yogurt-like beverage. It improves digestibility, antioxidant activity, and protein quality after 20 hours of fermentation. Still, further research is needed to optimize the organoleptic profile and consumer acceptability [100]. A study used quinoa vegetable extract fermented with water kefir grains, yielding functional beverages with enhanced nutritional and probiotic properties. This product exhibited significant improvements in bioactive compound profile compared to conventional substrates, suggesting their potential as innovative functional food alternatives. This resulted in beverages with superior organoleptic qualities and potential health benefits, making this approach particularly valuable for developing plant-based probiotic products [101]. Soy protein can play an important role as a functional additive in improving the stability of quinoa-based milk. When added at a moderate concentration (around 4% w/w of quinoa), it helps maintain the colloidal stability of the milk system. This effect appears to occur through two main mechanisms. First, soy protein can modify the surface hydrophobicity of the system, showing better results than phenolic compounds. Second, it forms stronger interactions with vanillic acid compared to native quinoa proteins. Together, these effects help improve the structural integrity and shelf-life of quinoa milk, making soy protein a useful ingredient for developing plant-based dairy alternatives [102]. Germination and roasting can impact the flavor of quinoa. In a study, different conditions the odor of quinoa and germinated quinoa were examined using sensory evaluation and electronic nose (E-nose). Results shown that roasting germinated quinoa at 160 °C for 15 min obtained best optimal aroma of quinoa. Germination enhanced the floral aromas, whereas roasting mainly generated caramel, cocoa and roasted nut aromas of quinoa. However, germination and roasting lowered the contents of Volatile Organic Compounds (VOCs) [103].

Quinoa pasta

Culinary preparations like pasta will be challenging due to the lack of gluten as we know that gluten provides the structure and viscoelasticity of wheat-based foods like pasta, bread, biscuits and cookies. This is important since the product's texture, look, and taste affect consumer perception. Methods used to enhance the qualities of gluten-free products include the addition of hydrocolloids (e.g., guar gum, xanthan gum, and sodium alginate) and proteins (e.g., casein and egg white) [104]. Pasta prepared with durum semolina and 20% quinoa grain provided more excellent protein, fat, fibers, and minerals with an acceptable sensory score [105]. Another research study developed pasta using chia seed flour and quinoa flour variations. The pasta with 15% chia seed and quinoa yielded the most significant outcomes regarding flavor and cooking [106]. Optimizing processing conditions enables the production of high-value gluten-free quinoa pasta with superior cooking quality, appropriate technical characteristics, and acceptable texture and color for consumers. While gluten removal in baked products often leads to undesirable traits and altered textures/flavors, the primary objective remains developing gluten-free food products that mimic the taste and texture of conventional gluten-containing counter-parts. Furthermore, commonly gluten-free bakery products typically lack adequate protein sources and dietary fiber. Quinoa serves as an excellent source of complete protein and total dietary fiber. In this study, quinoa flour was utilized as a primary ingredient in gluten-free shortbread formulation to enhance its nutritional profile [107].

Quinoa cookies

A study explored the sensory properties of quinoa-based bakery products. Quinoa products had a darker color compared to other cereals due to the formation of melanoidins. They were also harder due to their higher protein and fiber content [108]. Also, the expansion during baking was lower due to the lack of gluten [109]. The quinoa breed influences cookie quality. Breeds with higher protein content had lower heights, while breeds with higher water-holding capacity retained more water and decreased cookie diameter [110]. Heat-treated quinoa cookies offered an improved content of phenols, flavonoids, ferulic acid, quercetin, and kaempferol. So, the cooking method is also important. In certain studies, quinoa flour was mixed with other ingredients. Some cookies were prepared using 10% chia and 15% quinoa seed flour. The cookies had a good nutritional profile with acceptable taste and could be stored for 60 days under packaged conditions without deterioration in texture or microbial growth [111].

Quinoa bread

Bread made with quinoa flour has low glycemic index values with good storage stability and, thus, has the potential to be developed as a staple [112]. Quinoa bread offers a higher nutritional content than wheat flour. A study found 12.8 times higher polyphenolic content in bread containing 25% quinoa than in wheat bread [113]. In another research study, the dough of pseudocereals, including quinoa, was fermented, and higher content of ash, protein, TPC, antioxidant activity, and mineral concentrations were found after analysis [114]. Similarly, in another study, taboon (Palestinian flatbread) was prepared with quinoa flour, pretreated to reduce saponin content, and wheat [115]. An issue regarding quinoa bread was its organoleptic traits, which affected the consumer acceptability [116]. Microwave treatment when applied in quinoa flour shows many positive effects, mainly it increases the gas holding capacity when added in gluten-free (GF) dough. Thus, the increase in the bread volume, making it softer mainly increases both physical and sensory qualities of quinoa-enriched GF bread [117].

Quinoa kheer

In a study, kheer (Indian pudding or porridge) was prepared with Kodo millet, quinoa seed, and coconut milk with honey and dates as sweeteners. The best consumer acceptability was seen with the quinoa kheer sample with rice, honey, dates, quinoa, Kodo millet, and coconut milk, in the ratio 80:50:10:5:5 [118].

Quinoa soup

Instant dry mushroom soup prepared with quinoa seed flour showed improved nutritional, physical and sensory characteristics, in comparison to rice flour [119]. Gluten-free tarhana soup can be prepared by replacing wheat flour with quinoa flour. The product had better rheological properties [120].

Table 2: Culinary preparations made using Quinoa.

Culinary Product	Composition / Preparation	Primary Findings	References
Quinoa Beverages	Quinoa milk (sprouted, fermented, with stabilizers like oat β-glucan)	Higher protein than rice milk, lower lipid content than cow's milk, improved stability and digestibility, issues with bitterness and aroma addressed via fermentation	[94, 122]
Quinoa Pasta	Quinoa mixed with durum wheat semolina, chia seed flour	Enhanced protein, fiber, and minerals, acceptable sensory profile, improved cooking quality with chia	[104, 106, 107]
, Quinoa Cookies	Quinoa flour (alone or mixed with chia, heat-treated)	Darker, harder texture, influenced by quinoa breed, improved phenolics and shelf stability	[108, 111]
Quinoa Bread	Quinoa flour or blends (fermented, pretreated)	Low glycemic index, enhanced polyphenols, protein, antioxidant activity, challenges in taste and acceptability	[113, 116]
Quinoa Kheer	Quinoa with Kodo millet, coconut milk, honey, dates	Best acceptability with quinoa-millet blend and natural sweeteners	[118]
Quinoa Soup	Quinoa seed flour in instant mushroom and tarhana soups	Improved nutrition, texture, and sensory characteristics, suitable gluten-free alternative	[119, 120]
Quinoa Kishk	Fermented milk with quinoa seeds	Enhanced protein, fat, fiber, and mineral content	[121]
Quinoa Functional Foods	Quinoa-based products with bioactive compounds	Antioxidant, anti-inflammatory benefits, potential for functional food development	[123]

Quinoa-kisho

Egyptian Kishk is a popular dish from Egypt. It is prepared using fermented milk and whole grains such as rice, corn, wheat, or sorghum. In a research study, Kishk used quinoa seeds to improve their protein, fat, fiber and mineral content [121].

Quinoa functional food

Functional foods offer medical benefits beyond nutritional content. Quinoa can be used to prepare functional due to its diverse bioactive compounds responsible for antioxidant, anti-inflammatory, and other benefits [123].

Conclusion and future perspective

Quinoa was used as a staple crop by the Andean and Inca civilizations centuries ago. Its cultivation had then become limited due to the Spanish colonization. However, quinoa has re-emerged in the past few decades, owing to the rich nutritional content found in it. Quinoa is now available in most countries. The yearly cultivation and amount of research conducted on quinoa have greatly increased. Recently, quinoa has been proposed for use in treating water for high salt content and heavy metals like chromium, cadmium, nickel, arsenic, and lead through phytodesalination and phytoremediation. Also, research has been conducted on the use of novel peptides on cancer cell lines in the hope of treating cancer of the brain, lungs, and colon. Quinoa can be used to make biocompatible and biodegradable films as a green alternative for food packaging. It can be combined with other ingredients to prepare ready-to-eat protein hydrolysates, and functional foods. It has been used to stabilize Pickering emulsion and O/W based emulsion. It can be used to prevent microbial contamination, lipid peroxidation and rancidity in packed food and researched for its preparation of composite micelles, microspheres, nanoparticles used in drug delivery systems.

Studies have identified carbohydrates, protein, lipid, and micronutrient content, but more recently, researchers have studied and isolated bioactive peptides for their use in alleviating certain diseases like celiac disease, hyperglycemia, hypertension, hyperuricemia, liver and kidney injury. Quinoa can be used to make delicious meals like soups, cereals, Indian kheer, Egyptian kishk and bakery items like cookies, bread and cupcakes. Functional foods with health benefits for diseased individuals can be prepared. Quinoa when compared to staple crops like wheat, soy, sorghum, and rice offers better nutritional content. Quinoa can be used to combat hunger and malnourishment in underdeveloped countries due to its nutritional profile and its tolerance to abiotic stresses like low water, high salt content in soil, high heat and temperature conditions, and presence of heavy metals in soil.

In the future, clinical trials can be conducted regarding novel peptides isolated from quinoa responsible for therapeutic applications. The possible allergies and toxicities of quinoa can be estimated. The use of quinoa in industrial wastewater treatment can be further investigated. Since quinoa has spread throughout the world, it can be utilized to prepare the local cuisines of the country. Furthermore, it can be used in the preparation of instant food and marketed products that were previously made using other crops. Research should be done to improve the overall taste, smell and color by the addition of other ingredients. Studies can be done regarding the rising cost and demand of quinoa in the world and predict future trends. Experiments can be conducted studying the contents in different quinoa genotypes giving farmers and researchers the opportunity to choose the genotype that best suits their needs. Further studies on the phytochemical constituents could help us isolate more novel peptides which could be used in improving the symptoms in the diseases on which quinoa has not yet been tested. The impact of growth stimulants, physiological factors, chemicals and PGPR can be tested to provide optimal conditions for growth of quinoa.

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