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Quinoa (*Chenopodium quinoa* Willd), from Nutritional Value to Potential Health Benefits: An Integrative Review

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Abstract

Chenopodium quinoa Willd, known as quinoa, has been cultivated and consumed by humans for the last 5,000-7,000 years. Quinoa was important to pre-Columbian Andean civilizations, as the Incas considered it a gift from their gods. Quinoa has potential health benefits and exceptional nutritional value: a high concentration of protein (all essential amino acids highly bioavailable), unsaturated fatty acids, a low glycemic index; vitamins, minerals and other beneficial compounds; it is also gluten-free; furthermore, quinoa is a sustainable food, as plants exhibit a carbon and water food print that is between 30 and 60 times lower than that of beef. Quinoa is easy to cook, has versatility in preparation, and could be cultivated in different environments. For these reasons, quinoa, previously considered a food of low social prestige, is now the focus of attention of many countries worldwide. However, few studies exist on quinoa or quinoa compounds, *in vitro*, *in vivo* and clinical trials, for assessing its potential clinical applications supported by strong scientific evidence; thus, there is a need for well-designed clinical trials and increased scientific research in this field.

Keywords: Quinoa; Glycemic index; Gluten free; Essential amino acids; Healthy food

Abbreviations

20E: 20-Hydroxyecdysone; ACE: Angiotensin I Converting Enzyme; Ca: Calcium; Cx43: Connexin 43; DPPH: Ferric Thiocyanate and 1,1-Diphenyl-2-Picrylhydrazyl; Fe: Iron; GI: Glycemic Index; HbA1c: Hemoglobin A1c; HF: High Fat Diet; HF20E: High Fat Diet+20-Hydroxyecdysone; HFQ: High Fat Diet+Quinoa; IgE: Immunoglobulin E; K: Potassium; kcals: Kilocalories; Mg: Magnesium; MTT: 3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide; NASA: National Aeronautics and Space Administration; P: Phosphorus; PAI-1: Plasminogen Activator Inhibitor-1; PEPCK: Phosphoenolpyruvate Carboxykinase

Introduction

Quinoa is a grain with exceptional nutritional value; it has been cultivated for the last 5,000-7,000 years in the Andean region of Bolivia and Peru. 2013 was declared by the United Nations as the International Year of Quinoa as recognition of its significant potential [1-4].

Quinoa has high concentrations of protein, all essential amino acids, unsaturated fatty acids, and a low glycemic index (GI); it also contains vitamins, minerals and other beneficial compounds, and is gluten-free by nature. Quinoa is easy to cook and has versatility in preparation [1-4].

In this article, we present an extensive review of quinoa, starting with its history, analyzing its botanical characteristics, and covering its nutritional profile. In addition, we offer a critical comparison with other grains and describe quinoa culinary applications and uses. We also provide an updated review of the scientific information available on quinoa or quinoa compound properties through *in vivo*, *in vitro* and clinical studies, in order to evaluate its potential translational applications.

History

Quinoa has been cultivated for thousands of years in the Andean region of Bolivia and Peru [5,6]. It is known by different local names, or simply quinoa or quinua (quinua is in Quechua) [4]. This plant was called "the mother grain" by the Incas and was considered a gift from their gods, used even for treating medical issues. Traditionally, quinoa seeds were roasted and cooked, added to soups, used as a cereal, and even fermented into beer or chichi (traditional drink of the Andes) [4,7,8].

After the Spanish conquest of South America, the colonists looked down on quinoa as a peasant food or food of the Indians; consequently, quinoa has been considered a food of low social prestige. In addition, the Catholic Church actively suppressed its cultivation after discovering that quinoa was used as a sacred drink (Mudai) during indigenous religious ceremonies. Thus, quinoa remained only where Europeans could not reach and replace it with other grains [4].

Botanical description and cultivation

The botanical name of quinoa is *Chenopodium quinoa* Willd and belongs to the Goosefoot family "Chenopodiaceae", which includes: Swiss chard (*Beta sp.*), spinach (*Spinacia oleracea*) and Lamb's quarters

(*Chenopodium album*). Quinoa is a dicot plant that can grow from 1 to 3m high; it is considered a pseudo-cereal, not a true grain but rather a fruit. The seeds are round and flat, about 1.5-4.0 mm in diameter and their color varies from white to grey and black, with tones of yellow, rose, red, purple and violet (Figure 1). Quinoa has demonstrated a strong tolerance to salty, acid or alkaline soils, in both cold (-5°C) or hot climates (up to 35°C) [4,5].

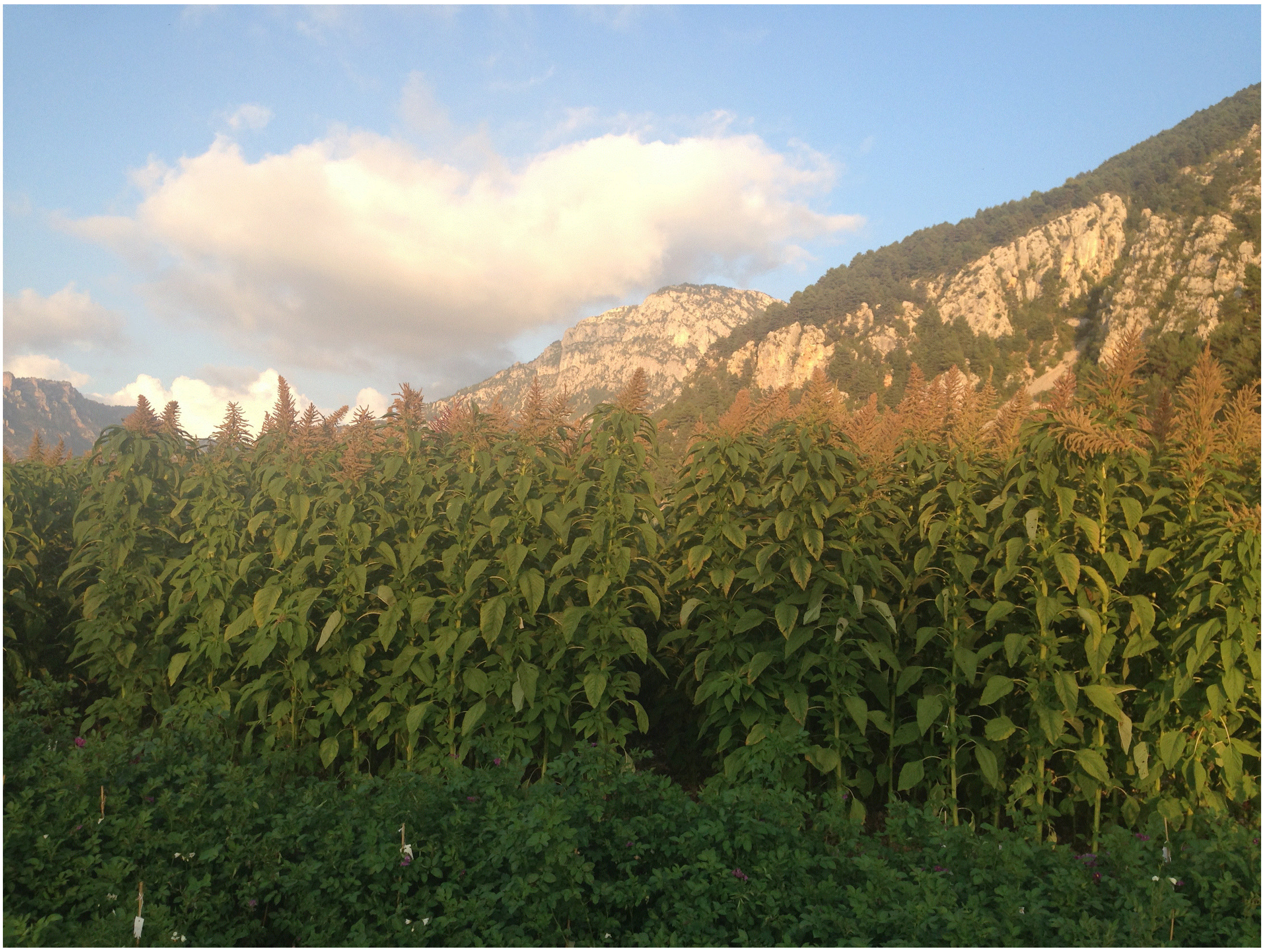

Figure 1: Quinoa plant, Quinoa is a pseudo-cereal. Its seeds can be different colors; its leaves are shaped like a goose's foot.

Quinoa is distributed worldwide and includes 250 varieties. Its classification is based on the color of the plant and fruits, or on plant morphology [4,5]. This grain has been authorized to be sown in Europe, North America, Asia and Africa. In Europe the project "Quinoa: a multipurpose crop for the European Community" was approved in 1993 [4].

Nutritional profile

The effects of globalization and urbanization have influenced dietary patterns and lifestyle behaviors among population groups throughout the world. Traditional food patterns rich in complex carbohydrates, micronutrients, fiber and phytochemicals are being replaced with diets high in animal fats and refined carbohydrates and oils, a situation that has made a direct impact on the prevalence of certain chronic diseases [9]. For this reason, many researchers devote their efforts to analyzing food or food components that may prove to be healthy for human consumption [5]; one example is the work of the HEALTHGRAIN Consortium, which, of note, has included quinoa in its list of healthy grains [10].

Quinoa is considered one of the best vegetal protein sources, as its protein levels are similar to those found in milk and higher than those present in cereals such as wheat, rice and maize. Quinoa also has been used by the National Aeronautics and Space Administration (NASA) due to its versatility in meeting the needs of humans during space missions [3,4,7,11,12].

Protein

Proteins and amino acids are major biological macromolecules that serve as structural constituents and as catalysts for enzymatic reactions, energy sources and protein synthesis in the body [13,14].

The protein biological value measures the proportion of protein absorbed from a food which then becomes incorporated into the proteins of the body. Quinoa has a high biological value (73%), similar to that of beef (74%), and higher than those of white rice (56%), wheat (49%) and corn (36%). Quinoa also contains all ten essential amino acids, and its protein content ranges from 12.9 to 16.5% [4,15-17]. Of primary interest is the high lys value, an essential amino acid that is deficient in many grains [16,18]. Quinoa is also high in the essential amino acid met, which is deficient in many legumes [19,20]. According to the daily recommended amounts of amino acids indicated by the Food and Agriculture Organization (FAO) of the United Nations and by the World Health Organization (WHO), quinoa fulfills the amino acid requirements for adults: 180% of histidine (his), 274% of isoleucine (ile), 338% of lysine (lys), 212% of methionine+cysteine (met+cys), 320% of phenylalanine+tyrosine (phe+tyr), 331% of threonine (thr), 228% of tryptophan (trp) and 323% of valine (val) (20). For these reasons, quinoa could represent a valuable source of nutrition, especially for infants and children, and may be used in nutritive foods and beverages [21].

Another feature of note is the high sustainability of plant food consumption due to their low carbon, water and ecological food prints. In this sense, quinoa is an excellent protein source such as beef, but it has a carbon and water food print that is between 30 and 60 times lower in value [22].

Carbohydrates

Carbohydrates are organic compounds comprised of carbon, hydrogen, and oxygen. Carbohydrates act as signaling molecules, energy sources and structural components [14].

Starch, as a carbohydrate, provides the major source of physiological energy in the human diet. The content of starch in quinoa ranges from 58.1% to 64.2% of dry matter, of which 11% is amylose. Moreover, quinoa has a high content of D-xylose and maltose and a low content of glucose and fructose.

100 g of quinoa contains: Glucose 1.70 mg, fructose 0.20 mg, saccharose 2.90 mg and maltose 1.40 mg [4,5,17]. In addition, there are studies that suggest that quinoa polysaccharides have antioxidant properties [23].

Lipids

Lipids are concentrated sources of energy as well as structural components of cell membranes that the body uses for performing a variety of normal functions [2,4]. A higher intake of vegetables is associated with a reduced risk of type 2 diabetes, due to their high unsaturated fat content, which is associated with lower inflammation [24,25].

The quality of lipids is very important. For example, it is known that omega-6 stimulates inflammatory activity in the body, while omega-3 performs anti-inflammatory functions. A lower ratio of omega-6: omega-3 fatty acids are more desirable for reducing the risk of cardiovascular disease, cancer, and inflammatory and autoimmune diseases [2,4,26].

The total lipid content of quinoa is 14.5%, with approximately 70%-89.4% being unsaturated (38.9%-57% of linoleic acid, 24.0%-27.7% of oleic acid and 4% of α-linolenic acid). The unsaturated fatty acid content is protected by vitamin E in this plant. The ratio between omega-6 and omega-3 in quinoa is about 6:1 [2,4].

Fiber

Dietary fiber is the indigestible portion of food derived from plants and has two main components: soluble and insoluble. Soluble fiber dissolves in water, is readily fermented in the colon into gases and physiologically active products, and has prebiotic properties. Insoluble fiber, which does not dissolve in water, is either metabolically inert and provides bulking mass, or it can be prebiotic and metabolically ferment in the large intestine. Bulking fibers absorb water, easing defecation [3,27].

Greater consumption of fiber-rich whole grains is associated with a lower risk of type 2 diabetes [24] and cardiovascular disease [28]. Quinoa is an excellent source of dietary fiber, comprising about 2.6%-10% of the total weight of the grain; about 78% of its fiber content is insoluble and 22% soluble [3,5,17,27,29].

Glycemic index (GI)

The GI is a ranking of carbohydrates on a scale from 0 to 100 according to their impact on blood sugar levels during the 2 h following consumption. Low GI (<55) foods produce gradual rises in blood sugar and insulin levels. Low GI diets have been shown to improve glucose and lipid levels and weight control because they help control appetite [30,31]. Low GI diets also reduce insulin resistance and the risk of cardiovascular diseases, diabetes and some cancers [9,24,32]. It is reported that fasting insulin is lower in individuals with higher dietary fiber intakes [33] and that the ingestion of complex carbohydrates promotes longevity [14]; and also that a high GI diet increases the levels of inflammation biomarkers. In patients with celiac disease, a reduced inflammatory state could provide certain protective mechanisms, thus, following a low GI diet could meliorate this disease [34].

The GI for quinoa ranges 35-53 depending on the cooking time; 150 g of quinoa, cooked, refrigerated and reheated in the microwave for 1.5 min has a GI of 53. Therefore, even when more or less “overcooked”, quinoa maintains a low GI [32].

In Table 1 we present a summary of the nutritional profile of cooked quinoa, in comparison with common cereals (also cooked).

Food	Energy (kcals)	Proteins (g)	Essential amino acids (number)	Carbo-hydrates (g)	Lipids (g)	Unsaturated fatty acids (g)	Fiber (g)	GI
Quinoa	120	4.4	10/10	21.3	1.92	1.61	2.8	35-53
Rice (white, medium grain)	130	2.38	9/10	28.59	0.21	0.12	0.3	75-89
Wheat (soft, white)	113	3.6	10/10	25.12	0.66	0.35	4.23	48

Corn (sweet, yellow)	96	3.41	9/10	20.98	1.5	0.98	2.4	60

Table 1: General nutritional profile of quinoa, we observe the overall content of quinoa in comparison with that of other foods [35,36]. *Portion size is 100 g of each cooked food; as a norm, cooked food increases its size 3 times. kcal: Kilocalories, GI: Glycemic index.

Vitamins

Vitamins are compounds essential for the health of humans. Quinoa has many vitamins, with 100 g of this grain containing: 0.4 mg of thiamine, 78.1 mg of folic acid, 1.4 mg of vitamin C, 0.20 mg of vitamin B6, and 0.61 mg of pantothenic acid [4]. Its vitamin E content ranges 37.49-59.82 μg/g. Tocopherol isoforms have also been detected in this seed: γ-tocopherol (47-53 μg/g), α-tocopherol (17-26 μg/g), and β- and δ-tocopherol (<5 μm/g) [2,5].

Minerals

Dietary minerals are essential chemical elements that play a role in regulating electrolyte balance, glucose homeostasis, the transmission of nerve impulses and enzyme cofactors in the body [37].

Calcium, magnesium and potassium in quinoa are found in sufficient quantities and bioavailable forms necessary for maintaining a balanced human diet. Quinoa contains: 874 mg/kg of calcium (Ca) [4,5,38], iron (Fe) 948.5 mg/kg, phosphorus (P) 2735.0 mg/kg-4543.3 mg/kg, potassium (K) 9562.2 mg/kg and magnesium (Mg) 1901.5 mg/kg [3,5,39].

Betaine

Betaine is an essential osmolyte source of methyl groups and finds its source either in diet or in the oxidation of choline. Its metabolism methylates homocysteine into methionine, also producing N,N-dimethylglycine. Mammals use betaine to assist in cell volume regulation, and as a methyl donor for the remethylation of homocysteine into methionine [27,40-42].

Hyperhomocysteinemia makes a person more prone to endothelial cell injury by activating inflammation pathways and is thus a possible risk factor for coronary artery disease. For this reason, betaine consumption could prove beneficial, as it converts homocysteine into methione. Nevertheless, urinary excretion of betaine is minimal, even following a large betaine dose [43,44]. It is generally agreed that most people consume between 100 mg/day and 300 mg/day [5,41,45].

Betaine content of foods: cooked white rice 0 μg/g; cooked oatmeal 139 μg/g; cooked wheat spaghetti 287 μg/g; cooked quinoa approximately 1310 μg/g–2000 μg/g [45].

Polyphenols

Polyphenols are natural organic chemicals with large multiples of phenol structural units. They are commonly found in plant foods and represent the most abundant antioxidants found in the human diet [46].

Quinoa presents at least 23 phenolic compounds. The total phenolic content (mg/kg quinoa) is 466.99, 634.66 and 682.05 for white, red and black quinoa, respectively. The most abundant phenols are ferulic acid and quercetin [1,6,47]. Quinoa contains more phenols than whole cereals, including wheat, barley, millet, rice and buckwheat [11].

Isoflavones

Isoflavones are organic compounds that have a role in influencing sex hormone metabolism and biological activity through intracellular enzymes, protein synthesis, growth factor actions, malignant cell proliferations, differentiation and angiogenesis [48].
In particular, quinoa contains the isoflavones daidzein and genistein; these hormones could be recognized by human estrogen receptors and act as antagonists of vessel contraction and reduce arterial resistance [4].

Carotenoids

Carotenoids are organic pigments found in the chloroplasts and chromoplasts of plants. The function of carotenoids in plants is to protect chlorophyll from photodamage. In humans, they exhibit antioxidant activity [27,49].

The total carotenoid content of white, red and black quinoa seeds are 11.87, 14.97 and 17.61 μg/g, respectively [50,51]. The β-carotene content of quinoa leaves ranges from 4.3 μg/1 g-19.5 μg/1 g [38].

Gluten

Gluten is one of the most abundant components of food (including grains) [52]. Gluten is a composite of the proteins gliadin and glutenin [51].

Celiac disease is an immune-mediated reaction to gluten, characterized by an insufficient T- cell-mediated immune response that causes inflammatory injury to the small intestine [17,52]. Celiac disease patients must consume food with gluten substitutes or gluten-free grains [17,34,51,52].

Several gluten-free foodstuffs contain more salt and fat (saturated fat) but fewer minerals and vitamins than their gluten-containing counterparts. For this reason, quinoa is an excellent gluten-free grain, with a high content of vitamins and minerals that make it a potentially essential part of any healthy, gluten-free diet [7,17,34,53]; also quinoa complies with the Codex Alimentarius nomenclature of gluten-free products (gluten content <20 mg/kg) [51].

In Table 2, we present a summary of the principal quinoa compounds.

Vitamins		Minerals		Polyphenols	
Thiamine mg/100 g	0.4	Fe mg/kg	948.5	Total Phenolic Content mg/kg	467-682
Folic acid mg/100 g	78.1	Ca mg/kg	874	Ferulic acid mg/kg	37.5-58.4

Vitamin C mg/100 g	1.4	P mg/kg	2735	Quercetin mg/kg	5.3-13
B6 mg/100 g	0.2	K mg/kg	9562	Isoflavones	
Pantothenic acid mg/100 g	0.61	Mg mg/kg	1903	Daidzein mg/100 g	0.78-2.05
Vitamin E µg/1 g	37.49-59.82			Carotenoids	
Total carotenoids µg/g					11.87-17.61

Table 2: Summary of quinoa compounds. Quinoa contains several vitamins, minerals and antioxidant molecules. Fe: Iron, Ca: Calcium, P: Phosphorus, K: Potassium, Mg: Magnesium.

Anti-nutritional factors

Saponins are natural detergents made of glycosylated secondary metabolites that are utilized by the plant as a predator repellent [54].

Quinoa contains saponins with a bitter taste, which could cause gastric irritation; its content varies between 0.1% and 5%; quinoa could even be classified according to its free saponin content, into either sweet (<0.11%) or bitter quinoa (>0.11%). In addition, there are studies of methods for saponin removal without any significant modification of nutritional value, such as thoroughly washing it in cold water [55].

On the other hand, isolated saponins could also have certain health benefits, such as anti-inflammatory activity [4,5,56-58].

Phytic acid is a saturated cyclic acid and is the principal storage form of phosphorus in many plant tissues. If the content of phytic acid is high in the food, this acid binds minerals, thereby rendering them unavailable for metabolism [27,59]. But, if the phytic acid content is low, it could act as an antioxidant: chelates various metals (for example, suppresses damaging Fe-catalysed redox reactions), inhibits xanthine oxidase, suppresses oxidant damage to the intestinal epithelium, and interferes with the formation of ADP-Fe-oxygen complexes that initiate lipid peroxidation; prevents the formation of carcinogens and blocks the interaction of carcinogens with cells; controls cell division and reduces cell proliferation rate; increases the immune response by enhancing the activity of natural killer cells; may be involved in cellular and nuclear signalling pathways; important source of P; inhibitor for renal stone development; hypoglycaemic (for example, by chelating Ca, an a-amylase cofactor) and cholesterol-lowering (by binding Zn and decreasing Zn:Cu ratio) effects; affects the metabolic and detoxification capacity of the liver; reduces blood glucose and lipid, and hepatic lipid levels; inhibits calcification of cardiovascular system (lower level of Ca in aorta); prevention of platelet aggregation; high affinity for hydroxyapatite; adsorption onto Ca-based crystals; *in vitro* effect on gene expression through chromatin remodelling [27].

The general content of phytic acid in quinoa is low and ranges from 10.5 mg to 13.5 mg, in comparison with corn that contains 720 mg, wheat 390 mg and rice 60 mg [4].

Protease inhibitors are proteins that form very stable complexes with proteolytic enzymes in the body. The content of protease inhibitors in quinoa seeds is <50 ppm, which is very low and does not pose any serious concerns [4].

Allergenicity

Asao and others observed that quinoa consumption did not show a positive reaction against wheat protein antibodies and suggested that quinoa could be ingested by people who have allergies against wheat proteins [11]. However, Astier and others reported a case of anaphylaxis to quinoa in France: a 52 year old man developed a systemic reaction consisting of dysphagia, dysphonia, urticaria and angioedema after the ingestion of quinoa with fish and bread. They tested samples of the ingested food, and only quinoa showed Immunoglobulin E (IgE) reactivity in the patient's serum [60].

Current status in experimental and clinical research

As we have seen above, quinoa has outstanding potential for human nutrition. Therefore, in this section we will provide an updated review of scientific information available on quinoa or quinoa compounds in different models.

In vitro

Betaine: Lee and others tested a betaine pretreatment (2 mM) in H2.35 mouse hepatocyte cells. They observed an increase in cytochrome C oxidase activity and improved mitochondrial respiration (mitochondrial dysfunction is a commonly found in many pathological conditions and ageing) [40].

Polyphenols: Gawlik-Dziki and others cultured AT-2 and MAT-LyLu prostate cancer cells with quinoa leaf extract (rich in ferulic, sinapinic and gallic acid). They observed that cell proliferation was blocked, the expression of Connexin 43 (Cx43) was decreased, and lipid oxidation was prevented, inhibiting lipoxygenase activity. They also concluded that 80% of phenolics are available *in vitro* [61].

Quinoa flour: Extracts from quinoa flour and from that of whole cereals (wheat, barley, millet, rice, buckwheat) were used to evaluate antioxidant potential. The ferric thiocyanate and 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity methods were used; also, the Angiotensin I Converting Enzyme (ACE) inhibitory activity was measured. Quinoa presented higher antioxidant potential and higher ACE inhibition activity (23.3%) in comparison with the same whole cereals. These results suggested that quinoa possesses potent free radical-scavenging compounds [11].

In vivo

Saponins: In mice, Verza and others reported that no lethality or local toxicity (local swelling, loss of hair, and piloerection) was observed after administering 300 µg of quinoa saponins [62].

20-hydroxyecdysone: Ecdysteroids are steroid hormones which have been implicated in plant repellence against insects, and in the control of the molting and reproduction processes of arthropods. The main phytoecdysteroid found in plants is 20-hydroxyecdysone (20E). Quinoa contains about 1.9% of 20E. These ecdysteroids have anabolic properties and help in controlling blood glucose levels. Graf and others tested an extract from quinoa seeds in obese mice and observed that fasting blood glucose levels were significantly lower [63].

Moreover, Foucault and others conducted a study on six-week-old male C57BL/6J mice. Mice were fed with a high-fat diet (HF) ad libitum, for 3 weeks. The high-fat diet group was supplemented or not with either quinoa powder (HFQ) or pure 20E (HF20E). The epididymal adipose tissue following treatment was significantly lower in the HFQ and in the HF20E vs. HF group. The HFQ showed a trend of reduced lipid storage capacity in the adipose tissue, increased LPL and PPAR-γ mRNA levels, and reduced expression of Phosphoenolpyruvate carboxykinase (PEPCK) and Plasminogen activator inhibitor-1 (PAI-1) in the adipose tissue, as well as decreased adipocyte hypertrophy [64,65].

Extract from seeds of quinoa: Meneguetti and others analyzed the effects of an extract from quinoa seeds in male Wistar rats assigned randomly to different groups: (1) a sedentary supplemented group, which received 2,000 mg/kg of the extract; (2) a sedentary control group, non-supplemented; (3) an exercise supplemented group with 2,000 mg/kg of the extract; and (4) an exercise control group non-supplemented. Follow-up was performed for 30 days. They observed beneficial effects in both supplemented groups (sedentary and exercise), as these groups showed a tendency of decreased food intake, body weight, fat deposition, and blood triglycerides (TG) levels [15].

Quinoa seeds in lipid profile and glucose levels: Pasko and others conducted a five week study with 24 male Wistar rats divided into different groups: a control group (corn starch); a control group with 31% of its dieting consisting of fructose; a group fed with a diet of quinoa seeds (310 g/kg); and a group fed with a diet of quinoa seeds (310 g/kg) and 31% of fructose. The group fed with quinoa showed significantly reduced serum total cholesterol (26%), LDL (57%), TG (11%) and glucose (10%). Fructose significantly decreased HDL (15%) levels in the control group, but when quinoa seeds were added to the diet, the decrease in HDL levels was inhibited [66]. The same research group analyzed fructose administration effects in the same animal groups, and they reported an increase in oxidative stress (high malondialdehyde) in the control group with 31% of its dieting consisting of fructose. In addition, the co-administration of quinoa seeds (310 g/kg fodder) decreased malondialdehyde in plasma [67].

Clinical studies

Quinoa and serum lipids: A prospective and double-blind study was conducted in overweight, postmenopausal women testing the effects of quinoa flakes vs corn flakes (25 g for 4 weeks). The group that consumed quinoa flakes showed a significant reduction in serum TG, a tendency of reduced total cholesterol and LDL and increased glutathione [68].

Quinoa and celiac disease: Zevallos and others conducted a study in nineteen celiac patients who consumed 50 g/day of quinoa for 6 weeks as part of their usual gluten-free diet. Duodenal biopsies and blood samples were obtained. Quinoa consumption was well-tolerated and did not exacerbate the clinical presentation of celiac disease. The study showed a positive trend toward improved histological parameters (the ratio of villus height to crypt depth improved from slightly below normal values 2.8:1 to normal levels 3:1, surface-enterocyte cell height improved from 28.76 µm to 29.77 µm and the number of intra-epithelial lymphocytes per 100 enterocytes decreased from 30.3 to 29.7 and serum total cholesterol [51].

Betaine and homocysteine in plasma: McRae conducted a meta-analysis of randomized placebo-controlled trials that used betaine supplementation. This analysis included five randomized controlled trials, published between 2002 and 2010. The studies used healthy adult participants who were supplemented with at least 4 g/d of betaine for a period between 6 and 24 weeks. The meta-analysis concluded that betaine supplementation decreased plasma homocysteine 1.23 µmol/L [69].

Betaine and metabolic syndrome: There is a significant negative association between markers of obesity (BMI, percent body fat and waist circumference) and plasma betaine concentrations in human cross-sectional data; in addition, more than 20% of patients with diabetes mellitus excrete abnormal amounts of betaine in their urine (41). Higher concentrations of plasma betaine were associated also with lower non-HDL cholesterol, TG, homocysteine and markers of inflammation [70].

Quinoa and diabetes: Jenkins and others tested a low GI diet (quinoa included). For 6 months, they performed follow-up on 210 patients divided into 2 groups (high cereal fiber diet or low GI diet). They observed a greater decrease of Hemoglobin A1c (HbA1c) in the low GI diet (-0.50%) and an increase in HDL (1.7 mg/dL) in a statistically significant manner [71].

To summarize the results presented in this section, quinoa emerges as a food of particular interest to celiac patients, as the potential cornerstone of a healthy, gluten-free diet. Furthermore, we hypothesize that including quinoa in the diet could decrease oxidative stress, improve serum lipid profile, help to control body weight and serum glucose, and decrease cardiovascular disease and type 2 diabetes risk factors; quinoa may even prove beneficial in reversing the effects of these diseases. However, until now, very few studies using quinoa or quinoa compounds *in vitro*, *in vivo* or clinical trials have taken place for determining translational applications based on strong scientific evidence.

In Table 3, we provide a complete summary of the potential health benefits of quinoa.

Compound	Dose	Model	Effect	Reference
Betaine	2 mM	H2.35 mouse hepatocyte cells	Improves mitochondrial respiration	[40]
Quinoa leaves extract	WI	AT-2 and MAT-LyLu prostate cancer cells	Cell proliferation was blocked, expression of Cx43 decreased, and lipid oxidation was prevented.	[61]
Quinoa flour	WI	Analysis of quinoa flour	ACE inhibition activity (23.3%), potent free radical-scavenging.	[11]
Saponins	300 µg	Mice	No lethality or local toxicity.	[62]

20-hydroxyecdysone	WI	C57BL/6J mice	Decreased epididymal adipose tissue. Trend of reduced lipid storage capacity in the adipose tissue, increased LPL and P-PARg, reduced expression of PEPCK and PAI-1 in adipose tissue, and also decreased adipocyte hypertrophy.	[64,65]
Extract from seeds of quinoa	2,000 mg/kg	Male Wistar rats	Tendency of decreased food intake, body weight, fat deposition, and blood TG levels.	[15]
Quinoa seeds	310 g/kg	Male Wistar rats	Reduction in total cholesterol (26%), LDL (57%), TG (11%), glucose (10%), and malondialdehyde in plasma.	[66,67]
Quinoa flakes	25 g	Postmenopausal women who were overweight	Reduction in serum TG, and tendency of decreased total cholesterol and LDL and increased glutathione.	[68]
Betaine	4 g	Healthy adults	Decreased plasma homocysteine 1.23 μmol/L.	[69]
Quinoa	50 g	Celiac patients	Good tolerance without any exacerbation of celiac disease. Trend toward improved histological parameters and serum total cholesterol.	[51]
Low GI diet that included quinoa	WI	Patients with type 2 diabetes	HbA1c decreased 50% and HDL increased 1.7 mg/dL.	[71]

Table 3: Potential health benefits of quinoa, we review the effects of quinoa or its components in *in vitro* and *in vivo* studies and in clinical trials. WI: Without information, ACE: Angiotensin I Converting Enzyme, LPL: Lipopolysaccharides, PAI-1: Plasminogen Activator Inhibitor-1, Hb1Ac: Hemoglobin A1c.

Culinary Issues

Quinoa is traditionally cooked as a whole grain similar to rice or milled into flour and made into pasta and breads [8]. This grain can also be processed by extrusion, drum-drying and autoclaving. Quinoa is very versatile in terms of culinary preparation: whole grains, uncooked or roasted flour, small leaves, meal, and instant powder can be prepared in a number of ways. There are numerous recipes available featuring approximately 100 preparations (Figure 2). Commercially available quinoa products exist such as pasta, bread, cookies, muffins, cereal, snacks, drinks, flakes, baby food, and diet supplements; in general, these have approximately 20% quinoa content [5,11,72-80]. The fresh leaves and tender shoots of the plant are eaten raw in salads, or cooked and eaten as a vegetable [1,5,20].

Quinoa cooking times varied from 11.9 to 19.2 min depending on the kind of seed (longer cooking time also correlated with higher protein content). Water uptake ratio varied from 2.5 to 4.0 fold [73].

Organoleptic properties

Organoleptic properties are the aspects of food as experienced by the senses, including taste, sight, smell, and touch. Food texture refers to those qualities of a food that can be felt with the fingers, tongue, palate, or teeth. In addition, the replacement of refined flour by whole grains such as quinoa could produce changes in the organoleptic properties of foods, like darker color due to the presence of bran, and may influence the consumer decisions.

Cooked quinoa normally has a texture described as creamy and smooth but, at the same time, slightly crunchy [79].

Conclusion

The use of pseudocereals such as quinoa represents a promising area of research, as its use could improve the intake of certain macromolecules and phytochemicals that are known to be beneficial to human health. Quinoa is an attractive, gluten-free alternative available to celiac patients, and including quinoa in the diet may prove to be a good strategy for consuming high biological value proteins as well as all bioavailable essential amino acids, something that other grains rarely offer. Quinoa also contains unsaturated lipids, fiber, complex carbohydrates and other beneficial compounds such as betaine, and may be used to improve the metabolic risk factor profile and help control type 2 diabetes. Quinoa may be useful for some other medical complications such as cancer, obesity and dyslipidemia. Furthermore, quinoa, as a plant food, is highly sustainable, with a carbon and water food print that is 30 to 60 times lower than that of beef.

Moreover, the anti-nutritional factors in the quinoa grain could easily be inactivated or reduced to safe health levels when appropriate techniques for industrial processing or household preparation of this food are used. As for culinary applications, the replacement of refined flour by whole grains such as quinoa raises several challenges that need to be addressed, including changes in organoleptic properties.

Finally, quinoa could represent a strategic crop used to complement the diet in rural/marginal regions where energy-protein malnutrition affects a greater part of the population in certain developing countries.

In summary, there are few *in vitro* or *in vivo* studies or clinical trials using quinoa or quinoa compounds; there is a justified need for well-designed clinical trials and increased scientific research in this field, in order to determine the most effective translational applications of quinoa based on solid scientific evidence. Quinoa, known as the "mother grain", represents an exotic and healthy rediscovered food in the developed world.

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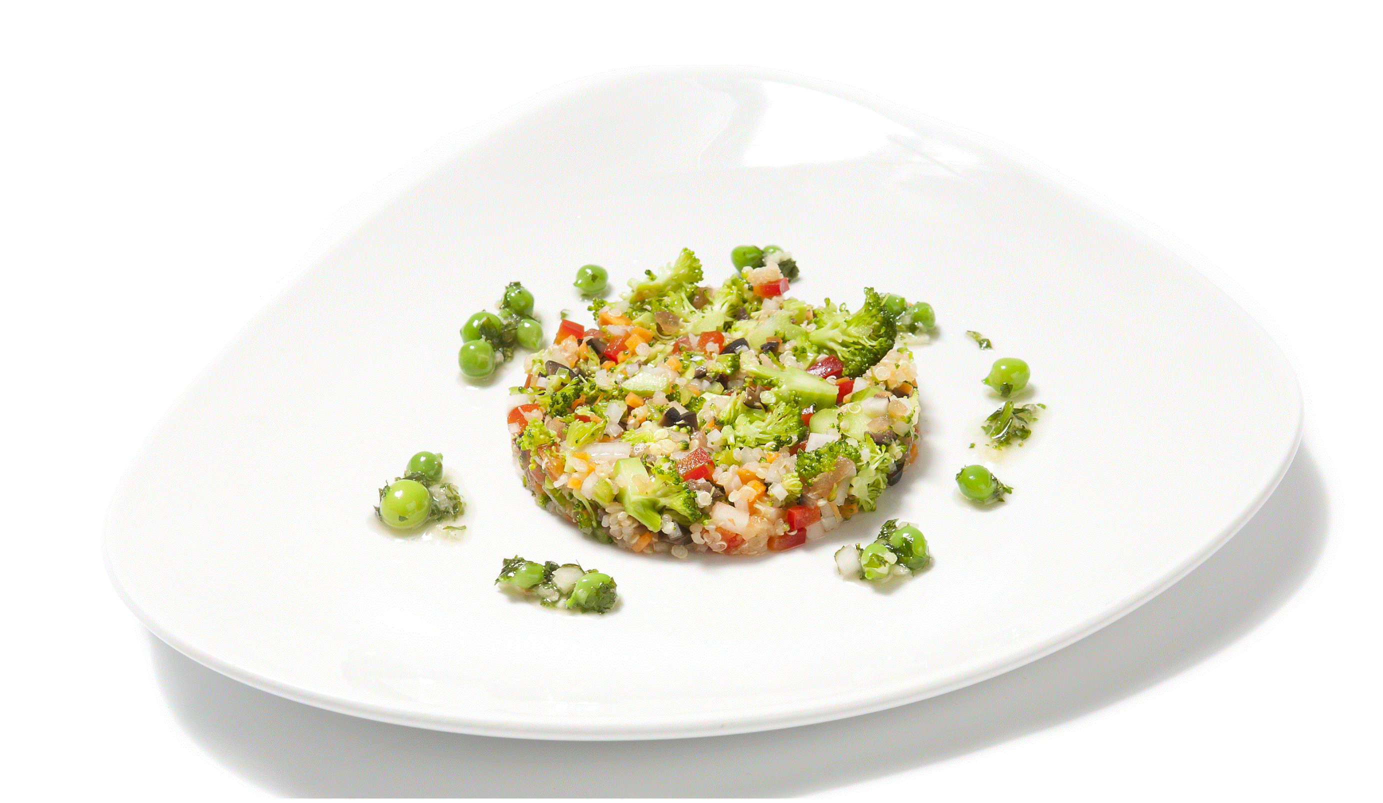

Figure 2: Quinoa salad, quinoa is very versatile in culinary preparation; in this picture quinoa is boiled in water and then mixed with vegetables.

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Potential Conflicts of Interest

The authors (EGB, ER, DADR, TM and RG) have no potential conflicts of interest relevant to this work.

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