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Botanical, phytochemical and pharmacological properties of quinoa medicinal plant (*Chenopodium quinoa* Willd.); A review

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ABSTRACT

Background & Aim: Climatic and geographical conditions of Iran and some factors such as climate change, water limitation and the existence of soils with salinity limitation, the cultivation of medicinal plants compatible with such conditions is one of the most important strategies. Quinoa (*Chenopodium quinoa* Willd) is a valuable medicinal plant and will also contribute to community health. Quinoa has been cultivated in the Andes for about 5,000 years. The largest area under quinoa cultivation in Bolivia is 100,000 ha. In this review, the botany, traditional uses, phytochemical and pharmacological properties of quinoa are discussed.

Experimental: In the current review keywords including quinoa and medicinal properties were searched in scientific websites such as Science Direct, PubMed and Google Scholar to compile the botanical and medicinal properties of quinoa (*Chenopodium quinoa* Willd.).

Results: According to the literature review, quinoa protein is 8-22% with proper quality and balance of essential amino acids (lysine, methionine and thyronine). The amount of essential amino acids in quinoa is higher than the daily requirement set by the World Food Organization and the World Health Organization for each person. Compared to other grains, quinoa is high in alpha tocopherols (vitamin E), riboflavin, thiamine and vitamin C, and has 10 times more folic acid. Quinoa seeds are a safe, gluten-free alternative to cereal grains among celiac patients.

Recommended applications/ industries: Quinoa with a high amount of biochemical components and pharmacological effects can be used as a valuable herbal drug. It also provides a gluten-free diet, which is beneficial for celiac patients. Its cultivation for industrial and pharmaceutical purposes can help to improve the production of anti-oxidant, anti-diabetic, anti-inflammatory, anti-celiac and anti-cancer drugs in Iran.

1.Introduction

Recently the use of plant products instead of chemical materials is one of the most important needs of modern civilization in terms of human health (Ruwali and Negi, 2019; Mirzaei *et al.*, 2020). Medicinal plants are a precious and world-famous heritage that has brought enormous wealth to the world. Over the past decades, there has been a wide range of herbal remedies that have led to rapid growth in demand for herbal medicines and of course medicinal plants in the world (Omidi *et al.*, 2015).

Today diabetes, obesity, and other metabolic disorders have reached global epidemic proportions (Nguyen and Lau, 2012; Zimmet *et al.*, 2014). Furthermore, the median age of the world's population is estimated to increase from 26.6 in 2000 to 31.1 in

2050, likely resulting in a mounting prevalence of age-related disorders such as cardiovascular diseases, osteoporosis and frailty (Lunenfeld and Stratton, 2013).

As a strategy to combat metabolic diseases through affordable, integrative strategies, food can play a stronger role in disease treatment and prevention. Food products that confer specific beneficial health effects, termed "functional foods" in 1984, have made their presence all over the world. The effects of functional foods range from improvement of general well-being to reduction of disease risk to the treatment of illness. Functional foods can include conventional foods with specific health-beneficial properties, or foods containing enhanced levels of a particular functional nutrient as a result of natural enrichment, fortification, or processing (Bigliardi and Galati, 2013).

Quinoa (*Chenopodium quinoa will*.) is a pseudocereal food crop that has provided nutrition and sustenance to Andean indigenous cultures for thousands of years and now plays an increasing role in human diets worldwide. Quinoa has been promoted as an alternative agricultural crop due to its stress-tolerant characteristics and marketed as a "superfood" for its nutritious qualities. A plethora of research has recently emerged on quinoa's chemical constituents and therapeutic properties, depicting the crop as an important resource for functional food development (Salehi and Dehghani, 2018). Nevertheless, modern innovation is necessary to further understand and advance the role that quinoa can play in human health. Quinoa production must also meet demand through sustainable agricultural strategies to promote global access to its health benefits. The objectives of this study were to conduct a comprehensive and up-to-date review of the nutritional and health value of quinoa (*Chenopodium quinoa* Willd.) and sustainability for food security and development while outlining recent advancements associated with its use in foods, botanical supplements, and pharmaceuticals (Salehi and Dehghani, 2018).

2. Original habitat of quinoa

Quinoa (*Chenopodium quinoa* Willd.) is native to the Andes mountains of Chile, Bolivia and Peru. This crop, has been called 41 vegetable caviar" or Inca rice cultivated in the Andes for about 5,000 years and in the valleys of Bolivia, Ecuador, Peru and chile. Quinua means "mother grain" in the Inca language (Martinez, 2015). This crop was a staple food of the Inca people and remains an important food crop for their descendants, the Quechua and Aymara peoples who live in the rural region (Sepahvand and Sheikh, 2015). The largest area under quinoa cultivation in Bolivia is 100,000 ha (Garcia *et al*., 2015).

Quinoa originates in South America in the foothills of the Andes Mountains and the potato and llama origins of Bolivia, Peru and Chile (Fig.1).

Fig. 1. Main origins of quinoa (*Chenopodium quinoa*) cultivation

Quinoa has been successfully cultivated as a new plant in various parts of Europe such as Europe, North America, Africa, Pakistan, China, UAE and India (FAO, 2013). In recent years, due to the medicinal importance of this plant as well as its economic properties in the production of medicine and the need for scientific researches, it has been cultivated in farms and greenhouses (Fig. 2).

Fig 2. Cultivated quinoa in greenhouse conditions for research purposes (Photo by Nasim Pakbaz. 2018).

3. Botanical and cytotaxonomy of quinoa

The domesticated species of *Chenopodium* are divided into two subsections based on pericarp and perianth morphology, and crossing relationships, the first subsection Cellulata contains diploid allotetraploids ($2n=4x=36$) like *C. quinoa* and *Chenopodium berlandieri* subsp. *neutralize*, C3 and optional halophyte (Adolf *et al.*, 2012). Plant height from 0.5 to 2 m and seed size 2 mm and its seeds are fruit and have genotypes sensitive to day length and ineffective day. The growth period is between 100 and 240 days, depending on the cultivar and climate, high diversity of quinoa due to salinity and drought stress has caused this plant to have a wide adaptation to different climatic conditions. Quinoa is a frequently pollinated plant with a metamorphosis rate of only 10 to 17% (Gomez and Pando, 2015).

Quinoa is a gynomonoecious annual plant with bears alternate leaves and erect stems that are variously coloured due to the presence of betacyanins. The plant shows good growth in India with many cultivars reaching up to 1.5m in height, generally, with a large number of branches and a big leaf size. The leaves exhibit polymorphism; the upper leaves being lanceolate while the lower leaves are rhomboidal. A good-developed, highly ramified tap-root system is present, penetrating as deep as 1.5m below the surface, which protects against drought conditions. Quinoa is a frequently pollinated plant with a metamorphosis rate of only 10 to 17% (Gomez Pando, 2015).

4. Genetic diversity of quinoa

Shrubs of different cultivars of quinoa can observe in the stage between the exit of the panicle and the beginning of flowering in green, purple, mixed and red colours. After physiological maturation, the plant has different colours (Bazile *et al.*, 2015).

The inflorescence is a panicle, 15–70 cm in length and rising from the top of the plant and in lower leaves. It has a principal axis from which the secondary axis arises and is of two types; glomerular and amaranth. An important feature of quinoa is the presence of hermaphrodite and unisexual female flowers (Bazile *et al.*, 2015). The hermaphrodite ones are located at the distal end and five anthers, a superior ovary with two or three stigmatic branches and bear five perianth lobes. Some cultivars show male sterility in some or all-female flowers. The fruit is an achene, comprising several layers, viz. perigonium, pericarp and episperm, from outwards to inside, and maybe conical, cylindrical or ellipsoidal, with saponins concentrated in the pericarp. Seed size and colour are variable, where black is dominant over red and yellow, which in turn are dominant to white seed colour (Bazile *et al.*, 2015) (Fig. 3).

Fig. 3. Variety of panicle colours of different cultivars of quinoa

5. Quinoa physiology

Quinoa can withstand and grow in a wide range of temperatures (−4~38°C) and pH (6.0~8.5), under low rainfall (50 mm/year) and high salinity (40 mS/cm) (Graf *et al.*, 2015). Therefore, quinoa could be a potential nutrient supply for most parts of the world.

6. Biochemical composition of quinoa

6.1. Protein

Several studies have affirmed the high quality of protein in quinoa. Quinoa protein is a complete protein that provides all kinds of essential amino acids (Table 1) (Comino *et al.*, 2013). The storage proteins of quinoa consist mostly of globulin and albumin, with little to no presence of prolamins (Zevallos *et al.*, 2012; Biesiekierski *et al.*, 2013). The protein content of quinoa ranges from 12% to 23%, of which the major protein components are globulins (37%) and albumins (35%) (Dakhili *et al.*, 2019; Filho *et al.*, 2017). Among them, the globulin 11S-type protein, chenopodium, is an oligomeric protein with a quaternary structure (Filho *et al.*, 2017; Graf *et al.*, 2015). The other quinoa protein is 2S-type albumin composed of a high amount of cysteine, arginine, and histidine (Filho *et al.*, 2017).

Table 1. The essential amino acid (mg/g protein) in quinoa (Nowak *et al.*, 2016)

Amino Acids	Amount (g/100g protein)
Isoleucine	4.0
Leucine	6.8
Lysine	5.1
Phenylalanine	4.6
Tyrosine	3.8
Cystine	2.4
Methionine	2.2
Threonine	3.7
Tryptophan	1.2
Valine	4.8

6.2. Peptides

Bioactive peptides are defined as protein fragments with biological activities, including antioxidant, antimicrobial, immunomodulatory, and antihypertensive activities, which are beneficial to health (Sánchez and Vázquez, 2017; Sarmadi and Ismail, 2010). Over the last few years, more attention has been given to the bioactive peptides in quinoa. Some studies have already identified and confirmed the bioactive peptide sequences in quinoa (Hernández-Ledesma, 2019).

6.3. Carbohydrate and fibre

Quinoa starch is characterized by high solubility and digestibility. Starch makes up 58.1–64.2% of the dry matter of quinoa, amylose content in quinoa starch is usually low (~10%) but can vary between 3% and 20%, In contrast, amylopectin makes up around 90% of quinoa starch (Schoenlechner, 2017). According to Lamothe *et al*. (2015), quinoa contains 10% of total dietary fibre. Fibre is the carbohydrate fraction that is resistant to enzymatic digestion and absorption in the small intestine, and which usually undergoes full or partial fermentation in the large intestine. Dietary fibre can promote satiety, reduce cholesterol and lipid absorption, modulate postprandial insulin response, improve intestinal microbiota, and reduce the risk and severity of gastrointestinal infection and inflammation (Brownawell *et al.*, 2012; De Carvalho *et al.*, 2014).

6.4. Lipids

The lipid composition of quinoa is considered to be favourable to human health. The lipid content of quinoa was reported from 5.3% to 14.5%, characterized by a high degree of unsaturation ranging from 70% to 89.4% (Gordillo-Bastidas *et al.*, 2016). A recent study found that quinoa seed oil contains 89.4% unsaturated fatty acids and 54.2% to 58.3% polyunsaturated fatty acids (PUFAs). PUFAs are mostly 18:2n-6 and 18:3n-3, with an omega-6/omega-3 ratio of 6/1, which is generally more favourable than that of other plant oils (Tang *et al.*, 2015a).

6.5. Vitamins

Quinoa can be a good source of some vitamins, documented vitamins in quinoa include vitamin A precursor β-carotene (0.39 mg/100 g), thiamin/vitamin B1 (0.4 mg/100 g), riboflavin/vitamin B2 (0.39 mg/100 g), niacin/vitamin B3 (1.06 mg/100 g), panthothenic acid/vitamin B5 (0.61 mg/100 g), pyridoxine/vitamin B6 (0.20 mg/100 g), folic acid/vitamin B9 (23.5 to 78.1 mg/100 g), ascorbic acid/vitamin C (4.0 to 16.4 mg/100 g), and tocopherols/vitamin E (3.7 to 6.0 mg/100 g) (Vega-Galvez *et al.*, 2010; Tang *et al.*, 2015a).

6.6. Minerals

Minerals content in quinoa is given in Table 2. The grain contains much more calcium, magnesium, iron, copper, and zinc than many kinds of cereal such as wheat, barley, oats, rye, triticale, and rice (Filho *et al.*, 2017). Germination can further increase the iron, calcium, and zinc content of quinoa by 39.43%, 49.04%, and 20.25%, respectively (Darwish *et al.*, 2020). The micronutrients calcium (275 to 1487 mg/kg), copper (2 to 51 mg/kg), iron (14 to 168 mg/kg), magnesium (260 to 5020 mg/kg), phosphorus (1400 to 5300 mg/kg), potassium (75 to 12000 mg/kg), and zinc (28 to 48 mg/kg) are present in sufficient quantities in quinoa to maintain a balanced human diet (Vega-Galvez *et al.*, 2010).

Table 2. Mineral content in quinoa based on the average of 15cultivars (Nowak *et al.*, 2016)

Minerals	Amount
Ca (%)	0.19
P (%)	0.47
Mg (%)	0.26
K (%)	0.87
Na (ppm)	115
Fe (ppm)	205
Cu (ppm)	67
Mn (ppm)	128
Zn (ppm)	50
Minerals	Amount

6.7. Saponins

Quinoa’s outer seed coat (pericarp) is rich in bitter saponins. Saponins are comprised of asteroidal or triterpenoidaglycone (mainly oleanolic acid, hederagenin, phytolaccagenic acid and organic acid), with one or more sugar moieties (Yendo *et al.*, 2010). Saponins are secondary metabolites with a strong bitter taste, which can present in the outer coat (pericarp) of quinoa grains (Alvarez- Jubete *et al.*, 2010; El Hazzam *et al.*, 2020). Quinoa saponins are a mixture of triterpene glycosides mainly derived from hederagenin (HD), phytolaccagenic acid (PA), oleanolic acid (OA), organic acid, and 3β,23,30-trihydroxyolean-12-en-28-oic acid (Hernández- Ledesma, 2019). Among them, HD, PA, and OA are the major aglycones of quinoa saponins (Lim *et al.*, 2020).

6.8. Phenolics

According to the number of benzene rings contained, it can be classified into simpler phenolic acids and more complex polyphenols. In quinoa seed, phenolic acids, including vanillic, protocatechuic, ferulic, caffeic, P-coumaric, 4-hydroxybenzoic, and 8,5′-ferulic acids and their derivatives, have been identified (Hernández-Ledesma, 2019). Phenolics also possess a range of biological activities due to their effects on cell signalling and metabolism, including anti-inflammatory, anticancer, antidiabetic, anti-obesity, and cardioprotective effects (Kelly, 2011; Jeong *et al.*, 2012). Numbers of studies reported that germination significantly increased the total phenolic content in quinoa (Al-Qabba *et al.*, 2020; Bhinder *et al.*, 2021; Darwish *et al.*, 2020; Ujiroghene *et al.*, 2019).

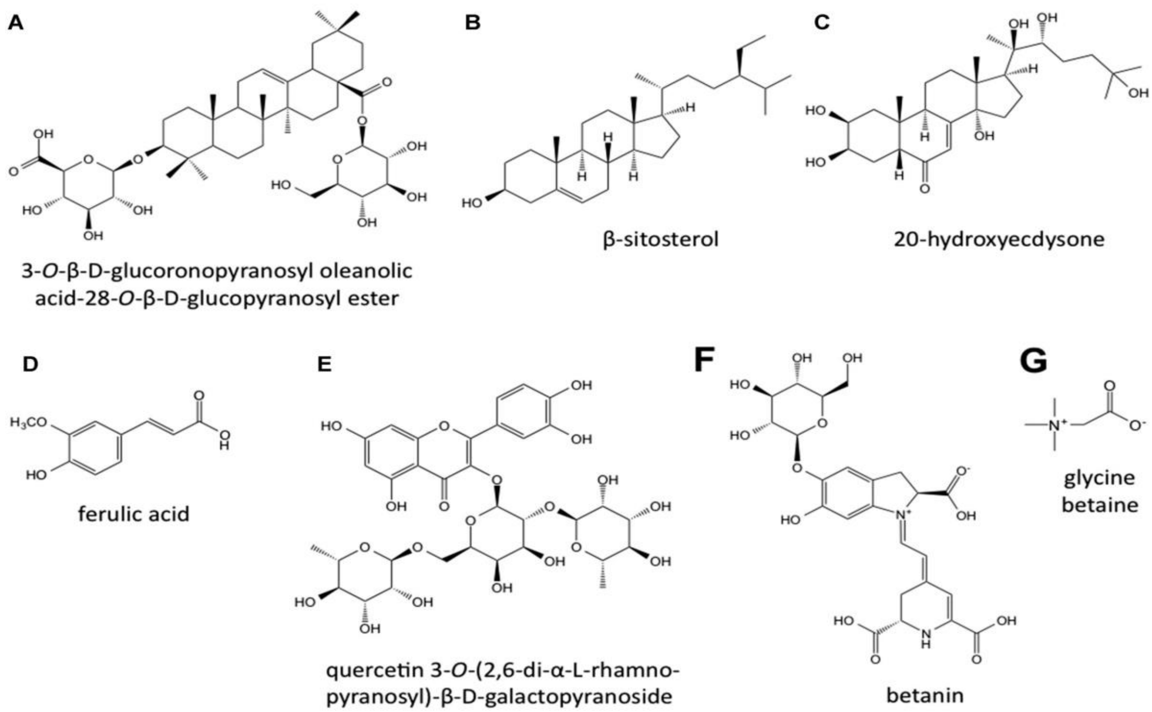

Fig. 4. Major pharmacologically active secondary metabolites are present in quinoa seeds. A: triterpenesaponin, B: phytosterol, C: phytoecdysteroid, D: phenolic acid, E: flavonol glycoside, F: betalain, G: glycine betaine. (Graf *et al.*, 2015)

7. Pharmacological properties and nutritional value of quinoa

Quinoa has many medicinal, health and nutritional values. Gluten-free quality of quinoa benefit several at-risk consumer populations, including the elderly, children, high-performance athletes, lactose-intolerant consumers, osteoporosis-prone women, and people with anaemia, diabetes, dyslipidemia, obesity, or celiac disease (Vega-Galvez *et al.*, 2010).

The beneficial effects for the quinoa-treated group were attributed to the complete essential amino acid profile of the quinoa-formulated baby food, as well as its high digestibility (95.3%), which was higher than that of 5 commercially available infant foods derived from milk and soy. Other studies on quinoa protein quality also support the same view that quinoa protein is an ideal amino acid source that can meet the requirements for adults (Dakhili *et al.*, 2019; Gordillo-

Bastidas *et al.*, 2016; Graf *et al.*, 2015; Nowak *et al.*, 2016).

The use of quinoa seeds as a safe, gluten-free alternative to cereal grains was evaluated in a human clinical trial among celiac patients. The study found that gastrointestinal parameters improved following the quinoa diet and decreases observed in total cholesterol, triglycerides, LDL and HDL, (Zevallos *et al.*, 2014).

In a prospective, double-blind human clinical trial among postmenopausal women with excess weight, quinoa flake consumption (25 g/d for 4 weeks) modulated metabolic parameters posttreatment compared to baseline (De Carvalho *et al.*, 2014).

Clinical studies suggest that the major cholesterol-lowering and antioxidant components of quinoa were proteins, fibre, vitamins (tocopherols and carotenoids), minerals (iron, zinc, magnesium), saponins, phytosterols, phytoecdysteroids, and phenolics (Farinazzi-Machado *et al.*, 2012). However, other quinoa phytochemicals, such as polyunsaturated fatty acids and betalains, may also play an important role (Vega-Galvez *et al.*, 2010).

The amount of essential amino acids in quinoa is higher than the daily requirement set by the World Food Organization and the World Health Organization for each person (FAO, 2013).

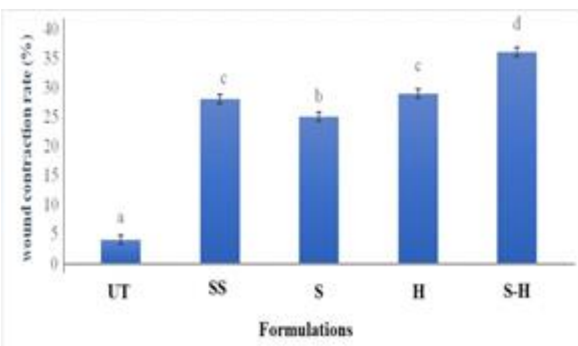

Fig. 5. Percent wound contraction of mice treated with UT, SS, S, H and H-S after 7 days. H=honey, S=shea butter, H-S=honey-shea butter emulsion, SS=silver sulfadiazine, UT=untreated. Each bar denotes mean± standard deviation (n=6). Bars with different lower-case superscript are significantly different at ($p<0.05$).

Quinoa oil is equivalent to corn oil, 87% of which is unsaturated fatty acids and mainly contains oleic, linoleic and linolenic (Vega-Galvez *et al.*, 2010).

Quinoa is used in the main homeland as a complete meal as well as in a combination of different foods and diverse products (Salehi and Dehghani, 2018).

Quinoa seeds are a rich source of antioxidants and beneficial nutrients and have the potential to be used in bread, soups, salads and baby food, and are good food for people with small intestinal autoimmune disorders (celiac disease) (Sepahvand and Sheikh, 2015).

The leaves of this plant are used in salads. The seeds of this plant are rich in protein and are the only plant that provides all the essential amino acids in the body (FAO, 2015).

8. Potential health benefits of quinoa

Quinoa has potential health benefits and exceptional nutritional value. Summary of the potential health benefits of quinoa is given in Table 3.

8.1. Diabetes disease

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 fibre 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 (Pasko *et al.*, 2010b).

8.2. Celiac disease

Zevallos et al. (2014) 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 intraepithelial lymphocytes per 100 enterocytes decreased from 30.3 to 29.7 (Zevallos *et al.*, 2014).

8.3. 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 (De Carvalho *et al.*, 2014).

8.4. Homocysteine in plasma

McRae (2013) 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 by 1.23 μmol/L (McRae, 2013).

8.5. 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, higher concentrations of plasma betaine were associated also with lower TG, homocysteine and markers of inflammation (Ross *et al.*, 2011).

Generally, 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 adding 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.

Table 3. Complete summary of the potential health benefits of quinoa compound

Compound	Dose	Model	Effect	Reference
Betaine	2 mM	H2.35 mouse hepatocyte cells	Improves mitochondrial respiration.	(Lee, 2015)
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.	(Gawlik-Dziki *et al.*, 2013)
Quinoa flour	WI	Analysis of quinoa flour	ACE inhibition activity (23.3%), potent free radical-scavenging.	(Asao and Watanabe, 2010)
Saponins	300 μg	Mice	No lethality or local toxicity.	(Verza *et al.*, 2012)
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.	(Foucault *et al.*, 2014; Foucault *et al.*, 2011)
Extract from seeds ofquinoa	2,000 mg/kg	Male Wistar rats	Tendency of decreased food intake, body weight, fat deposition, and blood TG levels.	(Meneguetti *et al.*, 2011)
Quinoa seeds	310 g/kg	Male Wistar rats	Reduction in total cholesterol (26%), LDL (57%), TG (11%), glucose (10%), and malondialdehyde in plasma.	(Pasko *et al.*, 2010a; Pasko *et al.*, 2010b)
Quinoa flakes	25 g	Postmenopausal women who were overweight	Reduction in serum TG, and tendency of decreased total cholesterol and LDL	(De Carvalho *et al.*, 2010)

			and increased glutathione.	
Betaine	4 g	Healthy adults	Decreased plasma homocysteine 1.23 µmol/L.	(McRae, 2013)
Quinoa	50 g	Celiac patients	Good tolerance without any exacerbation of celiac disease. Trend toward improved histological parameters and serum total cholesterol.	(Zevallos *et al.*, 2014)
Low GI diet that includedquinoa	WI	Patients with type 2 diabetes	HbA1c decreased 50% and HDL increased 1.7 mg/dL.	(Jenkins *et al.*, 2008)

9. Conclusion

Quinoa (*Chenopodium quinoa* Willd) has many medicinal and nutritional values and is a medicinal plant beneficial to human health.Its protein is 8-22% with proper quality and balance of essential amino acids. The amount of essential amino acids in quinoa is higher than the daily requirement set by the World Food Organization and the World Health Organization for each person. The use of pseudo cereals 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 addition of quinoa in the diet maybe 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, fibre, complex carbohydrates and other beneficial compounds such as betaine, and maybe used to improve the metabolic risk factor profile and help to control type 2 diabetes. Quinoa may be useful for some other medical complications such as cancer, obesity and dyslipidemia. Furthermore, quinoa, as plant food, is highly sustainable, with a carbon and water footprint that is 30 to 60 times lower than that of beef. Quinoa is considered one of the best leaf-protein concentrate sources and so has the potential as a protein substitute for the food and pharmaceutical industry. 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.

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