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Anti-diabetic Properties of *Chenopodium quinoa* on Human Health; An Update and Future Prospects

AUTHORS DETAIL

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INTRODUCTION

There are many disorders which acutely affect human being and are prevalent across the world. Among these, diabetes mellitus occurs abundantly in the developing countries. Diabetes is a chronic condition that occurs when there are raised levels of glucose in the blood because the body cannot produce any or enough of the hormone insulin or use insulin effectively. According to International Diabetes Federation (IDF), in Pakistan every 4th person is affected with diabetes. It is generally classified as type-1, type-2, and gestational diabetes. The occurrence of type-2 diabetes is much more than the type-1 and gestational diabetes (Atkinson et al. 2014). Due to numerous side effects of allopathic treatment, scientists are now moving toward botanicals showing good efficacy. Qunioa (*Chenopodium quinoa* wild) is crop belongs to the Amaranthaceae family; sub family Chenopodioideae and considered as pseudocereal. Its edible seeds are gluten free containing various minerals (P, K, and Mg) and vitamins (Vitamin B1, B2, B3, B6, C and E) which are effective against numerous diseases. Raw uncooked quinoa consists of 13% water, 64% carbohydrates, 14% proteins, and 6% fat. The saponins (glycosides) protection on seed make it unpalatable but protect it against many biotic factors including insect and birds which harshly affect the potential yield (James 2009). Qunioa can be effectively used against many diseases such as cancer, cardiovascular diseases, and diabetes mellitus. The anti-diabetic effects of quinoa are due to the presence of various chemicals which lowered the blood glucose level. It also releases many phytochemicals which help in making an efficient diet for diabetic patients (Graf et al. 2014). This chapter broadly discusses the anti-diabetic impact of quinoa on human health.

Diabetes Mellitus

Diabetes is an autoimmune disease, in which β-cells of the pancreatic islet are attacked by the host immune system, leading to impaired growth and function. Regarding the possible causes of Type-1 Diabetes Mellitus (T1D), in 70-90% of diabetic cases, autoimmunity is the prominent cause of damaging β-cells (Atkinson et al. 2014). Diabetes is mainly divided into two types including type-1 and type-2 diabetes mellitus (T2D) in which T2D (not dependent on insulin) depends on the existence of autoreactive antibodies leading to the damage of β-cells. T2D is considered as an epidemic in multiple countries, especially in developing countries, and one of the major causes of death. Nowadays it has become a major global health concern (Bommer et al. 2018). According to hygiene hypothesis, good hygiene may contribute to the occurrence of diabetes. A precise estimation done by International Diabetes Federation (IDF) in 2021, 536.6 million individuals are suffering from diabetes and this value is expected to extend by 46%, reaching 783.2 million by the year 2045 (Sun Hong et al. 2021). In diabetes, body is unable to differentiate between the invading pathogen and body own cells leading to the attack on the body cells by immune system (Arif et al. 2004). A chronic helminth infection may decrease the occurrence of diabetes due to immune shift indicating an alternative way to control diabetes mellitus (Klement et al. 2008; Hubner et al. 2012).

Mechanism of T1D Development

Typically, after taking the meal, along with insulin production, glucose is also produced in the body which causes an increase in the biotransformation of sugar molecules that are deposited in muscles and fat tissues. Without dependence on insulin, glucose is provided to the brain by the liver during fasting conditions. On the other side, insulin inhibits glucagon secretion in response to which serum fatty acids are produced in low concentrations resulting in decreased production of glucose by the liver (Kangralkar et al. 2010).

Blood hyperglycemia results due to insulin resistance or low assembling of insulin in the blood that hampers the process of glucose uptake in tissue. Because of impaired assembling

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of glucose in the blood, the process of gluconeogenesis and glycogenesis initiates which resulted in fat breakdown and it directed toward diabetic ketoacidosis. Hyperglycemic coma is due to the rising level of glucose in the blood. Less assembling of insulin in the blood may result in the destruction of pancreatic β-cells due to different causes, named as T1DM (Type-1 Diabetes Mellitus). Principal factors which cause the destruction of β-cells are environment, autoimmunity, and a genetic disorder. Because of insulin resistance, there is impeded regulation of insulin which causes another condition called Type-2 Diabetes Mellitus (T2D) (Asmat et al. 2016). Mechanism of glucose management in Liver and pancreas Asis shown in Fig. 1.

Diabetic victims are always at threat with several hurdles ranging from macrovascular to microvascular glitches. Stroke and coronary heart disease are embodied in macrovascular barriers while nephropathy, retinopathy, and neuropathy are included in microvascular complications. The hazard of macrovascular deterioration is more in aged people than in microvascular complications. It is assessed that by 2035, 600 million individuals are to be treated with diabetes and this autoimmune disease is rising extensively around the globe (Berbudi et al. 2016).

Quinoa (*Chenopodium quinoa* wild)

Quinoa, a member of Amaranthaceae family, is an indigenous crop that shows resemblance to cereal crops and primitively grown in the Andean region of South America, including Ecuador, Chile, Peru, Bolivia, and Colombia. From 3000–4000 years, this magnificent crop has been cultivated for livestock feed and for the consumption of human beings (Vega-Galvez et al. 2010). It was considered the principal meal of the Inca civilization. The dominantly spoken language of the Incas was Quechua. Therefore, citizens of the Incas called quinoa; chisaya mama "mother of all the seeds,", because quinoa food was represented together with potato and maize and considered as a chief dietic element. Therefore, it is known as "Inca gold" because of its marvelous healing and beneficial properties. While, in current years quinoa is introduced in different continents and countries of the world including Japan, North America, Europe, China and Australia. Due to present situations, quinoa is restricted to South America only. Hence, quinoa was re-introduced for its nutritional and agronomic attributes (Hussain et al. 2021). It is herbaceous annual plant grown specifically for edible seeds. In comparison with other cereal crops, it contains a high amount of dietary fiber, protein, dietary minerals, vitamin B, and a low level of glycemic index that reduces the gluten concentration making it a beneficial crop for diabetic patients (González Martín et al. 2014). It is considered as a pseudo-cereal crop and has similar characteristics to the amaranth and spinach families (Fuentes et al. 2009). The genus of quinoa is Chenopodium, and around 250 species have been identified all over the world. United Nations declared the international year of quinoa in 2013 to highlight its tremendous potential (Tang et al. 2015b). The acclimatized species of genus *Chenopodium* are categorized into two parts based on crossing relationships, pericarp and perianth morphology (Adolf et al. 2012).

Morphological Characteristics

Quinoa is monoecious annual plant, with an erect stem and alternate leaves colored due to pigments like betacyanin. In India, several varieties are sown, and reliable growth is expressed by plants up to a height of 1.5m, habitually, with large leaf sizes and a large number of branches. The lower and upper leaves have rhomboids and lanceolate shapes, respectively (Gomez and Pando 2015). Petiole and lamina are the components of leaves; petioles are grooved, long and tenuous. The length of the petiole fluctuates sometimes within the same plant and depends on the variety. The leaf blade of a plant shows polymorphism within the same plant; for instance, it can be triangular, wavy, flat, or diamond-shaped (Christensen et al. 2007). The quinoa plant is associated with intense branching and deep root system, which plays a significant role in plant stability on the ground and allows the plant to suffer under drought conditions. The stem of the quinoa plant is woody in nature, erected and ramified.

The inflorescence of quinoa is commonly called panicle, comprising of secondary and tertiary branches along with pedicels holding glomeruli. The length and the diameter of the panicle ranges from 30 to 80 cm and 5 to 30 cm respectively and variability in both depends upon types of genotypes and fertility status of the soil. The number of glomeruli per panicle varies between 80 to 120, while the range of seeds per panicle is up to 3000 (Mujica et al. 2001). Quinoa fruits have ellipsoidal, spherical, and conical shapes and the pericarp of fruit varies in color from yellow to greyish with magenta. Due to the small size of fruits, the weight falls in the range of 1.9 to 4.3g per 1000 seed weight (Kozioł 1992). The embryo, perisperm and episperm are three vital components of seeds (Prego et al. 1998).

Nutritional Profile

Quinoa grains are an excellent source of indigestible compounds with biological and antioxidant properties (Pellegrini et al. 2018). The nutritional profile of quinoa varies significantly among genotypes and has been categorized into two group; the group A is polyunsaturated fatty acids and phytochemicals present in high amount, and group B consists of long-chain fatty acids and linolenic acid in high concentrations (Nowak et al. 2016; Chen et al. 2019). Quinoa grains have high nutritional value consisting of protein (10–18%), starch (32–60%), fats (4.4–8.8%), ash content (2.4–3.7%) with P and K being the primary ash sources and a fiber

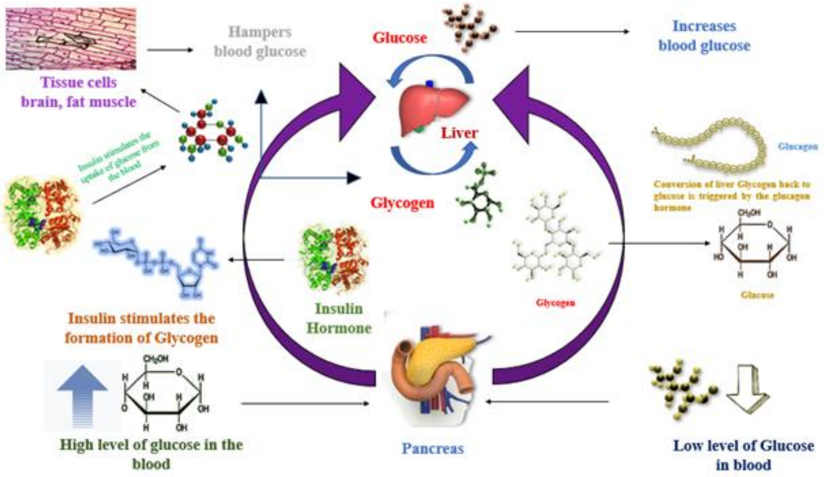

Fig. 1: Mechanism of glucose management in Liver and pancreas.

Table 1: The quinoa's general nutritional profile and comparison to the nutritional profiles of other foods (University of Sydney 2014; USDA 2015).

Food	Carbohydrates(g)	Fiber (g)	Lipids (g)	Proteins (g)	Energy (kcals)	Glycemic index (GI)
Rice	28.59	0.3	0.21	2.38	130	75-89
Corn	20.98	2.4	1.5	3.41	96	60
Wheat	25.12	4.23	0.66	3.6	113	48
Quinoa	21.3	2.8	1.92	4.4	120	35-53

(1.1–13.4%) (Navruz-Varli and Sanlier 2016; Romano et al. 2020). Quinoa grain is a raw material with a high carbohydrate content made up of starch and low sugar content. Due to high nutritional value of quinoa, it is a complete food, mainly due to good quality protein and minerals such as Mg Ca, Fe, Mn, P, Zn, and Cu (Vega-Galvez et al. 2010). It can be used as "functional food" and diminishes the risks related to many diseases. The presence of minerals, vitamins, fiber, antioxidants, fatty acids and plant hormones in quinoa dominates its functional properties that subsidize the nutritional aspects of humans (Repo-Carrasco-Valencia et al. 2011). Comparison of nutritional composition of cooked quinoa to other common cereals is summarized in Table 1.

Biochemical Configuration

Proteins

As proved from previous studies, quinoa is rich in protein and the dietic proteins originate from its grains provide all types of cardinal amino acids. The protein content in quinoa ranges from 12 to 23% (Comino et al. 2013; Fotschki et al. 2020). It is considered as a perfect food as it contains all essential amino acids i.e., histidine, tryptophan, leucine, isoleucine, lysine, phenylalanine, methionine, tyrosine, threonine, and valine (Maradini-Filho 2017). The percentage of globulins and albumins in the grains of quinoa are about 37% and 35%, respectively (Miranda et al. 2012). On quality basis, quinoa proteins are comparable to the protein (casein) present in the milk. An 11S-type protein globulin with a quaternary structure is one of the proteins found in quinoa consisting of a variable content of asparagine, aspartic acid, serine, glycine, leucine, arginine, and glutamine–glutamic acid. By comparing with the total composition of quinoa seed protein, it has approximately low sulfur-containing amino acids. Cysteine, arginine and histidine are the amino acid comprising another protein known as 2S-type albumin (Filho et al. 2017).

Vitamins

Folic acid and vitamins B and E are assembled in the embryo of quinoa. It is a much more reliable source of these vitamins (Basantes-Morales et al. 2019). In comparison to other cereals, the grains of quinoa consist of a large amount of riboflavin, vitamin C, thiamine, and folic acid. After the consumption of 100g of quinoa, an adult can easily meet his dietary necessities. 80% of the dietary requirements of children and 40% of the cellulase, protease, and hemi cellulase requirements are fulfilled after consuming 100g of quinoa grains (Mohyuddin et al. 2019). Beta-carotene, which is a precursor of vitamin A, weighs 0.39 mg per 100g of quinoa; tocopherols/vitamin E range from 3.7 to 6.0 mg per 100g, riboflavin/vitamin B2 weighs 0.39 mg; niacin/vitamin B3 weighs 1.06 mg per 100g, pyridoxine/vitamin B6 weighs 0.20 mg per 100g; pantothenic acid/vitamin B5 is 0.61 mg per 100 g, folic acid/vitamin B9 23.5 to 78.1 mg per 100 g, ascorbic acid/vitamin C 4.0 to 16.4 mg per 100 g (Tang et al. 2015a). Amounts of different Vitamins present in per 100g of Raw and polished quinoa seeds are shown in Table 2.

Table 2: The content of certain vitamins in quinoa seeds (mg/100g dry basis) (Ruales and Nair 1993).

Vitamins	Raw whole Quinoa	Polished and washed quinoa
Riboflavin	0.2	0.2
Vitamin C	16.4	19.2
Vitamin A	0.2	0.2
Folic Acid	78.1	66.3
Tocopherols		
γ-tocopherols	5.3	4.9
α-tocotrienols	ND	ND
δ-tocopherols	0.3	0.3
β-tocotrienols	0.3	0.3
α-tocopherols	2.6	2.4
β-tocopherols	0.2	0.2
γ-tocotrienols	0.01	0.01

Table 3: Mineral composition of Quinoa seed (Nowak et al. 2016).

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

Table 4: Carbohydrate content in grains of quinoa (Jan et al. 2019)

Quinoa Genotypes	Carbohydrates (%)
INIA-415 Pasankalla	67
Ccoito	68.1
03-21-1181	69.8
Witulla	69.5
Salcedo INIA	70
03-21-0093	Not detectable
Huaripongo	67.8
Commercial 2	59.4
Commercial 1	63.6
Roja de Copotaque	70.8

Minerals

Quinoa grain contain high concentration of Fe, Cu, Zn, Mg and Ca as compared to other cereals, including wheat, oats, triticale, rice and barley (Filho et al. 2017). The percentages of Ca, Fe and Zn in quinoa grains are 39.43%, 49.04% and 20.25%, respectively (Darwish et al., 2020). Cu (2 to 51 mg/kg), Zn (28 to 48 mg/kg), P (1400 to 5300 mg/kg), Mg (260 to 5020 mg/kg), K (75 to 12000 mg/kg), Ca (275 to 1487 mg/kg) and Fe (14 to 168 mg/kg) are the micronutrient found in quinoa grains. Therefore, for a balanced human diet, micronutrients in quinoa are in ample quantities (Vega-Galvez et al. 2010). Amounts of minerals present in quinoa seeds are enlisted Table 3.

Carbohydrate

The amount of carbohydrates is directly linked with many metabolic processes like protein glycosylation and plays a pivotal role in the nutritional aspects. Seeds of quinoa exhibit some beneficial characteristics like lowering the free fatty acids resulted in reducing hypoglycemic effects. The concentration of gluten is negligible in quinoa grain as compared to wheat, oat etc. that make it a prominent cereal (Hussain et al. 2021). As reported by Jancurová et al. (2009), a remarkable number of carbohydrates in the range of 67–74% of total dry matter are present in quinoa, and nearly 11% of amylose content is present. Concurrently, some distinct carbohydrates are also cataloged, including crude fiber (2.5–3.9%), pentosans (2.9–3.6%), monosaccharides (2%), and disaccharides (2.3%) (Valencia-Chamorro et al. 2003). The starch present in quinoa is described by its high digestibility and solubility. Up to 58.1–64.2% of the dry matter of quinoa is composed of starch, and the concentration of amylose is also low (around 10%), although the concentration fluctuates between 3% to 20%. Around 90% of quinoa starch is made by amylopectin. Quinoa's gelling point is adequately lower under cold temperature storage. Its seeds are characterized by their creamy nature and smooth texture (Vega-Galvez et al. 2010). In comparison, sucrose is present in a substantial quantity (Schoenlechner, 2017). The carbohydrate composition of different genotypes is enlisted in Table 4.

Fiber

Quinoa is considered as a chief source of fiber. Fiber content is not markedly affected by the abrading and washing of quinoa with the purpose of eliminating the saponins (Ranhotra et al. 1993). In quinoa the content of dietary fiber is equivalent to legume grains and cereals, but as compared to buckwheat, low dietary content is present in quinoa (Alvarez-Jubete et al. 2009). As reported by Lamothe et al. (2015), the total dietary fiber present in quinoa is 10%. Fiber is a fraction of carbohydrates that are resistant to absorption in the small intestine and enzymatic digestion, but in the large intestine, it normally undergoes partial or full fermentation. Fiber can improve the intestinal microbiota, low cholesterol, reduce the risk of gastrointestinal infections and inflammation (Brownawell et al. 2012; De Carvalho et al. 2014).

Lipids

Quinoa contains 5.3%–14.5% lipids and the lipid content of quinoa is distinguished by a high degree of unsaturation with the range of 70% to 89.4% (Gordillo-Bastidas et al. 2016). Lipid is usually located in embryo of quinoa and the range of fat content is also quite high (5–10%) (Prego et al. 1998). About 25% of the total lipids are characterized by polar lipids, mainly phospholipids such as choline and lysophosphatidic ethanolamine (Benito et al. 2018). The stability of the oil is particularly dependent on natural antioxidants that exist in high quantities including α - tocopherols (69-75 mg/100 g of oil) and γ-tocopherols (76-

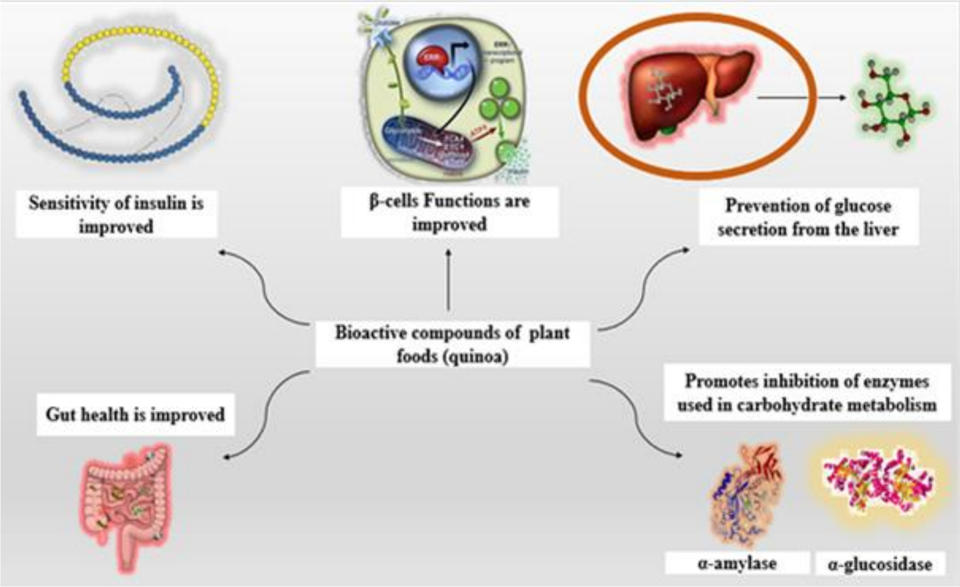

Fig. 2: Functions of bioactive compounds found in *Chenopodium Quinoa.*

Table 5: Functions and biological activities of chemical contents lie in *Chenopodium quinoa.*

Compound	Bioactivity	Plant parts	References
Chlorogenic acid	Anti-diabetic	Seeds & leaves	Tang et al. 2016
20-Hydroxyecdysone S	Anti-diabetic	Seeds	Foucault et al. 2012
Betaine, choline	Anti-diabetic	Seeds	(Olthof and Verhoef 2005)
β-Sitosterol	Anti-diabetic	Seeds	Ahamed et al. 1998

93 mg/100 g of oil) (Kozioł 1992). A contemporary study indicates that 89.4% unsaturated fatty acids are found in quinoa seed oil containing 54.2% to 58.3% polyunsaturated fatty acids (Tang et al. 2015a). Quinoa seed is considered as the primary source of several essential fatty acids, including omega-6 and omega-3. Different phytosterols are also present in quinoa, mainly squalene (Graf et al. 2015).

Anti-diabetic Nature

Pharmacological Activity of Quinoa

Quinoa contains a variety of bioactive compounds, particularly in its seeds, stems, leaves, and roots. These bioactive compounds have many beneficial biological consequences including antioxidant, anti-inflammatory, anti-diabetic, anti-fungal, anti-microbial and anti-cancer effects (Table 5) (Shah et al. 2022).

Antidiabetic Consequences

Quinoa contains higher levels of bioactive peptides, protein, fiber, tocopherols, and phenolic acids, which are well known for their antidiabetic attributes (Cisneros-Yupanqui et al. 2020). In diabetic patients, HbA1c and BMI levels can be controlled after consumption of quinoa. Furthermore, quinoa aids in the maintenance of blood glucose levels and the improvement of health in people with prediabetes (Abellan et al. 2017). Graf et al. (2014) studied the impact of some compounds such as phytoecdysteroids which are leached by the seeds of quinoa. For the objective, with leaching efficiency being optimized, an 80°C temperature, a 70% ethanol concentration, a period of 4 hours, and a 5 ml/g solvent ratio were used. Quinoa leachate with the compounds and markedly lowered the blood glucose level in mice which were obese and hyperglycemic. In another study by Li et al. (2018), glucose and fat levels were assessed after consumption of quinoa-enriched bread in patients with cardiovascular disorders, and it was unveiled that the glucose levels in the control group were low. Hanan et al. (2019) examined the anti-diabetic and antioxidant activity of quinoa seed powder in diabetic rats. Rats blood and glucose levels were minimized after consumption of quinoa in different concentrations. Furthermore, rats were fed with several concentrations of quinoa seed powder which resulted in the reduced level of thyroid hormones. There are several other plants from which phenolic compounds exhibit in vitro α-glucosidase and α-amylase inhibitory consequences (Hemalatha et al. 2016). Another research which was performed in vitro demonstrated the quinoa polysaccharides inhibitory effects on α -glucosidase and α-amylase (Tan et al. 2020). Peptides located in quinoa might assist in controlling the blood sugar levels as the α-amylase and α-glucosidase dipeptidyl-peptidase-4 (DPP-IV) are influenced by inhibitory effects of quinoa peptides (Nongonierma et al. 2015; Vilcacundo et al. 2017; Guo et al. 2020; Mudgil et al. 2020). For the remedy of diabetes mellitus type-2, DPP-IV inhibitors are efficiently used as they assist to reduce the fasting hyperglycemia by protracting insulin secretion (Green et al. 2006; Kasina and Baradhi 2019). Moreover, it is stated that hypoglycemic potential is also present in the saponins (Marrelli et al. 2016; Ren et al. 2017; Singh et al. 2017). The process of digestion and gastric emptying slow up due to high protein content of quinoa (Cisneros-Yupanqui et al. 2020). Various functions of bioactive compounds found in *Chenopodium Quinoa* are illustrated in Fig. 2.

The hypoglycemic potential of quinoa has been proved in many in-vitro studies (Al-Qabba et al. 2020; Cisneros-Yupanqui et al. 2020; Noratto et al. 2019; Ujiroghene et al. 2019; Ayyash et al. 2018; Hemalatha et al. 2016; Graf et al. 2014). According to Hemalatha et al. (2016), quinoa extract can inhibit the enzymes α-amylase and α-glucosidase. In another study, a low glycemic diet including quinoa was tested in diabetic patients and the results indicated a drop in HbA1c and increase in HDL (1.7 mg/dL) level (Pasko et al. 2010b).

Conclusion

Chenopodium quinoa attains a nutritionally rich profile, including lipids, carbohydrates, proteins, vitamins, and minerals. It is a superfood (gluten-free diet) for humans and is relatively much better than other cereals. It has an exceptional and beneficial composition, including fiber, phenolics, bioactive peptides, proteins, and tocopherols. It is very effective against certain diseases such as cardiovascular issues, celiac disease, and especially against T_2D. Diabetes is inhibited by its enzyme inhibition properties and the production of less glucose, which stabilizes the intensity of the disease. If it is consumed on daily basis, it can overcome diabetes and other diseases more efficiently than a synthetic drug.

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