Chapter

Current Advances Research in Nutraceutical Compounds of Legumes, Pseudocereals and Cereals

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Abstract

The increase of the Western-type diet and life-style, with high content of highly processed fats, salt and sugar, as well as sedentary life, is directly linked to an increasing incidence of chronic diseases such as diabetes and obesity, cancer, cardiovascular diseases or stroke, and inflammatory-related diseases, which are a great challenge in global health and are usually associated with negative effects of globalization: rapid urbanization, diet and increased sedentary life worldwide. This has brought new interest and increased research into plant-based diets. In this context, the implementation in the diet of legumes, cereals and pseudo-cereals, due to their nutraceutical properties, which is interesting as well as advisable. These foods, in addition of having a high nutritional value themselves, have synergistic properties as part of a balanced diet. For example, most legumes are rich in lysine which is scarce in cereals, and these are rich in sulphur amino acids, such as methionine, while these amino acids are scarce in legumes and are of great importance for the central nervous system development. These foods or part of a food, due to their qualities, and that they provide health benefits can be classified as nutraceuticals. In addition, due to their health benefits beyond nutritional properties, can be classified as functional foods, promoting prevention and treatment for the above mentioned diseases, among others. This double function is due mainly to the proteins and the presence of various secondary metabolites and bioactive compounds in these foods of plant (grain and seed) origin. Last discovered knowledge and research features will be described in the present book chapter.

Keywords: functional food, nutraceutical benefits, legumes, pseudo-cereals, anti-inflammatory properties, cancer, diabetes mellitus

1. Introduction

Legumes are a main source of edible seeds and a major source of food for a significant worldwide population. They are a relevant sources of plant rich quality proteins (20–50% of seed content) with nutraceutical and health benefit properties on human health helping to prevent diseases such as diabetes, digestive tract diseases, cardiovascular diseases, overweight, obesity, cancer, etc. Legume seeds are also integrated of fiber, carbohydrates, amino acids, micronutrients as several vitamins and minerals. Anti-nutritional compounds have been found in legumes, which may be toxic when consumed raw, while playing a positive role when processed and treated. Despite of the wide germplasm of legume, there are many underutilized food legume seeds with potential to be a source of nutraceutical food [1].

On the other hand, cereals are essential foods providing key nutrients to many countries worldwide. They are frequently consumed removing a large fraction of the whole gain (40%, mainly bran and germ), however and despite of this fact, wheat-based processed foods contains a large part of components with health benefits such as phytosterols/stanols, carotenoids, polyphenols, dietary fibers such as β-glucan and arabinoxylan, carbohydrates such as resistant starch and oligosaccharides (galacto- and fructo-oligosaccharides), vitamins, selenium and folate. They contain phytoestrogens and antioxidants required molecules promoting health benefits. Cereals are also implemented as fermentable substrates promoting probiotic microorganisms' growth. These macromolecules contribute to reduce the risk of major chronic diseases in humans, such as cardiovascular diseases, Parkinson's disease, as well as cancer risk, reduces the rate of cholesterol and fat absorption, lowering blood pressure, and gastrointestinal health. Among the factors affecting the bioactive macromolecules content of cereal as important food ingredients, it can be included the genetics, growing and storage conditions, post-harvest treatments, food formulation and processing.

Therefore, pseudocereals grains, belonging to dicotyledonous plant species, are growing in interest for human diets because their excellent nutritional and nutraceutical value. Pseudocereals are a good source of fiber, proteins, starch, minerals, vitamins, and phytochemicals such as saponins, polyphenols, phytosterols, phytosteroids, and betalains with potential health benefits [2].

Pseudocereals are considered very healthy grains because their content in several bioactive components with high nutraceutical potential. Among these, it encompasses essential amino acids mainly arginine, methionine, lysine, tryptophan, and sulphur-containing amino acids in large amounts. They are also source of polyphenols, saponins, fagopyritols, phytosterols, and essential minerals. However, pseudocereals contain anti-nutrients like phytates and tannins, which can be decreased by processing treatments as soaking, puffing, germination, fermentation, and cooking to also improve their organoleptic characteristics. These treatments improve the nutritional value of pseudocereals by decreasing anti-nutrients amount, while increasing the availability of nutrients. An advantage of pseudocereals is their uses in food for persons suffering from celiac disease due to the absence of gluten in their grains, and in general its great potential to be utilized for the development of functional foods [1, 2].

This chapter discuss current research advances in nutraceutical properties and key research knowledge on health-promoting aspects of seed bioactive components found in legumes, cereals and pseudocereals, for increasing awareness among the population of the research focus across the beneficial health effects, and disease prevention activities.

2. Legumes

2.1 Antioxidants and anti-inflammatory compounds

Diseases such as obesity, cardiovascular problems, diabetes, inflammation and cancer are related to oxidative stress (OS). When cellular systems are not capable of efficiently eliminating the reactive species produced of oxygen (ROS) and nitrogen (RNS). These produce alterations throughout oxidative processes in different biomolecules such as proteins, lipids and nucleic acids. This can lead to cell death or produce mutations at the DNA level that contribute to the generation of cancer [3].

Legumes, especially the seed coat, are rich in antioxidant compounds. These can terminate oxidative reaction chains by eliminating free radicals and the inhibition of other oxidative reactions [4]. Among the antioxidant compounds present in legumes, flavonoids should be highlighted. The antioxidant capacity of flavonoids is due to the large number of hydroxyl substitutions, which has a direct effect on their ability to donate hydrogen atoms and eliminate free radicals from the environment [5].

Recently, it has been found that conglutins β1, β3 and β6, main types of reserve proteins in *Lupinus angustifolius* seeds, present antioxidant activity, among other health benefits [6], are capable of reducing the expression of pro-inflammatory cytokines IL- 1β, IL-2, IL-6, IL-8, IL-12, IL-17, TNF-α and IFNγ, in addition to decreasing the levels of NF-κB, NO and iNOS, which can make its consumption adequate in the treatment of certain pathologies. In pancreatic cells, these conglutins also reduce the expression levels of chemotactic factors as CCR2 and CCL5, improving the inflammatory state by inhibiting the recruitment and migration of immune cells [7].

2.2 Cancer fighting seeds components

As part of the cancer development, progression, and metastasis, proteolysis process plays an important role. Proteolysis is involved in the degradation of the extracellular matrix causing changes in cellular adhesion, migration, invasion, as well as chemical modification of the cellular environment, including the production of growth factors [4]. Protease inhibitors (PIs) present in the protein fraction of seeds of certain beans as *Phaseolus acutifolius* affect the proliferation and metastasis in fibroblasts, and also affect cell survival and proliferation, inducing partially restoration of the adhesion patterns of the transformed fibroblasts. Other PIs from *Phaseolus vulgaris* seeds inhibit the proliferation of MCF-7 breast cancer cells showing a slight inhibition of the proliferation of hepatoma HepG2 cells and WRL68 embryonic liver cells [4].

Therefore, ROS and RNS generated during carcinogenesis modify gene expression, regulate signals of transduction pathways and modulate protein function, while promoting the activation of enzymes related to angiogenesis [3]. Phytic acid, present in legume seeds exhibits antioxidant function that can regulate proliferation and apoptosis. These processes can be identified by changes in biomarkers of colon cancer cells, suppressing the expression and activity of key regulatory factors of the AKT/mTOR pathway, AKT1 kinase and p70S6K1 [3].

Therefore, it has been found that the main flavonoids present in *P. vulgaris*, quercetin and kaempferol are able to decrease the risk of lung cancer [8]. Quercetin-3-O-glucoside, present in black beans, also reduces the expression of lipogenic proteins helping to improve cardiovascular disease [5]. On the other hand, the flavonoid genistein inhibits carcinogenic cells, being useful against breast and prostate cancers [8].

Extraction samples with ethanol from *Phaseolus angularis* seeds can inhibit the release of prostaglandin E2 and nitric oxide in macrophages induced by lipopolysaccharides (LPS) in a dose-dependent manner, with inhibition of the nuclear factor NF-κB and response of the activating protein AP-1 [4]. Extracts obtained from *Phaseolus calcaratus* prevent nitric oxide production and release, iNOS and COX-2 genes expression, and TNF-α and IL-6 proteins secretion almost totally in LPS-stimulated cells. Furthermore, phenolic compounds with antioxidant potential against DPPH and hydroxyl radicals exhibit anti-inflammatory potential in LPS-stimulated macrophages through down-regulation of ERK/p38 and NF-κB-mediated signalling pathways [4].

2.3 Metabolic syndrome: diabetes, obesity and cardiovascular diseases

Patients diagnosed with diabetes, persistent hyperglycaemia increases the generation of free radicals, which initiates lipid peroxidation and proteins oxidation, altering the structure of the membrane, which in turn leads and promote other complications such as insulin resistance [9].

Phytosterol β-sitosterol, rich among legume lipids, has antioxidant activity and acts as a ROS scavenger facilitating the membrane stabilization. Rats with induced type 2 diabetes showed decrease in the levels of insulin receptors (IR) and glucose transporters GLUT-4. In addition, administration of β-sitosterol resulted in a restoration of the levels of these above membrane proteins, which improved glycaemic control [9]. β-Sitosterol is structurally similar to cholesterol, thus its administration allowed inhibition of intestinal cholesterol absorption while acting as an antioxidant and chemopreventive potential for the appearance of colon cancer [9].

The hydroethanolic extract of *Lupinus mutabilis* seeds, rich in sparteine, palmitic acid, linoleic acid, oleic acid, lupanin, oxilupanin and 11,12-dehydrolupanin, has also been observed to have positive effects in rats with type 2 diabetes by enhancing insulin release. These effect is dependent on the L-type calcium channel, protein kinase A and C systems, and G protein-coupled exocytosis and is partially mediated by K-ATP channels [10].

Soybeans contains isoflavonoids with estrogen-like activity because they have agonist and antagonist receptors activity. Since estrogen has antidiabetic effects by increasing insulin secretion, decreasing insulin resistance and increasing pancreatic β cell mass, these isoflavonoids could have positive effects in individuals with type 2 diabetes [11].

Protease inhibitors regulate the hydrolytic action of proteolytic enzymes. The balance action between proteases and PI is required for a suitable cellular homeostasis, thus when unbalanced, pathological progressions such as cancer are likely to develop [4]. Inhibitors of carbohydrate hydrolases such as α-amylase and α-glucosidases, present in the seeds of numerous legumes, represent a route to lower glucose levels after meals (postprandial glycaemia), both in patients with type 1 and type 2 diabetes. 2 [4, 12]. α-Amylase acts on the α-1,4 glycosidic bonds of starch, which is one of the main sources of postprandial glucose, while intestinal α-glucosidases act on different oligomers of glucose. The peptides present in legume seeds inhibit the degradation of these carbohydrates by shifting the binding site of the substrate in the enzyme and shifting it from the active center [12]. Furthermore, bioactive peptides have been found in soybean germinated seeds that have inhibitory activity of dipeptidyl peptidase 4 (DPP-IV), a serine protease capable of degrading incretins, gastric inhibitory polypeptide (GIP) and glucagon-like peptide type 1 (GLP-1). These incretins are secreted after meals and stimulate insulin secretion, thus the protease inhibitors of these incretins present in soy represent another treatment for patients with diabetes [12]. On the other hand, legumes are a rich source of amino acids, among which arginine stands out. Arginine has proven to be useful in reducing insulin resistance, which is why the intake of legumes is thus equally recommended in diabetic individuals [8]. In this regard, L-homoarginine, especially notable in *Lathyrus sativus* L. provides benefits in individuals with cardiovascular diseases [1].

Interestingly, *Lupinus angustifolius* seed conglutins β1, β3, and β6 are capable of acting positively against diabetes [13]. This activity is mediated by its antioxidant and regulatory activities by (i) increased cellular glucose uptake, (ii) positive regulation of IRS-1, GLUT-4 and increased protein synthesis of p85-PI3K, (iii) activation of IRS-Q/PI-3-KINASE, which activates other components of the signalling cascade, (iv) reduction of oxidative stress reducing the level of protein carbonylation and increasing glutathione levels GSH and decreasing the antioxidant activity of SOD and catalase enzymes, (v) reduction in NO production levels, (vi) increased glucose catabolism, increasing the expression of, among others, hexokinase and decreasing that of GSK3β [6, 14]. Furthermore, the already described anti-inflammatory activity of these conglutins β could also help in the treatment of diabetes by reducing the inflammation of the pancreatic islets [7]. In the same way, it has been found that γ conglutins of the same species have similar activities [15].

Bioactive peptides such as Lunasin, a 43 amino acid peptide, is found in soybeans, barley, rice and wheat, and is capable of lowering cholesterol levels and increasing levels of LDL receptor production, as well as exhibiting anti-inflammatory properties. Interestingly, lupine conglutins exhibit similar cardiovascular protective activities by decreasing LDL levels and increasing their receptors in hepatoma lines in rats [16].

2.4 Anti-nematode agents

Gastrointestinal infections by nematodes are currently a problem due to the development of resistance to anthelmintic drugs [2]. The consumption of legumes, rich in tannins and flavonoids (such as flavanols) has been related to resistance to these infections in ruminants, due to the activity of these compounds against nematodes. Particularly, the proportion of prodelphinidin/procyanidins are related to the anthelmintic activity of legumes, as well as their consumption acting indirectly to the potential of the individual's immune system fighting against parasites [2].

2.5 Health benefits of anti-nutritional compounds of legumes

Despite the large number of health-beneficial compounds present in legumes, their seeds also contain a fair number of anti-nutritional components. These compounds can be inactivated through food preparation [4]. There are also numerous studies using germplasm resources searching for varieties with low amount of these components, and to be implemented in the diet [1]. These anti-nutritional properties usually are visible in non-balanced diets, even in certain concentrations are beneficial.

Lectins proteins or glycoproteins included in their structure include at least one non-catalytic domain with the ability to bind mono and oligosaccharides [4]. Among their negative properties, they can cause atrophy of the pancreas and interfere with the absorption of nutrients by binding to the intestinal epithelium. However, they are recommended in certain disorders, such as diabetes, obesity, and cancer [4]. *P. vulgaris* is rich in the lectin called phytohemagglutinin. Seed extracts have been shown to reduce postprandial blood glucose in rats in a similar way to metformin, the first choice drug for the type 2 diabetes treatment. The mechanism of action involves binding of phytohemagglutinin to epithelial cells gastric cells and the membrane of the cuticular border of the small and large intestine, which causes the secretion of cholecystokinin and glucagon-like peptides, two hormones that play an important role in digestive processes and the central control of appetite [4]. Lectins also have negative effect on the appearance of appetite and promoting secretion of cholecystokinin and glucagon-like peptides. In addition, lectins bind to membrane or intercellular receptors affecting cell cycle disruption and induction of apoptosis, inhibition of telomerase activity, and inhibiting angiogenesis.

L-Dopa, an amino acid precursor of the neurotransmitters dopamine, norepinephrine, and adrenaline, is present in high quantities in legumes such as *Mucuna pruriens* and *Vicia faba*. This compound is useful in the treatment of Parkinson's [17], as a chronic and progressive process caused by neuronal degeneration in the substantia nigra, leading to a decrease in dopamine values, which in turn decreases the individual's ability to control movements or feelings. L-Dopa would have the property of restoring neurotransmission [17]. Intestinally, L-Dopa and dopamine, both function as prolactin inhibitors (hormone that decrease the sexual desire), thus composition of *Mucuna pruriens* is used in some regions as an aphrodisiac [17].

β-ODAP or β-oxalyldiaminopropionic acid is a glutamate analogue and the cause of neurolathyrism produced after a high intake (more than 30% of the caloric intake) of *Lathyrus sativus* prolonged for a long time. However, a balanced diet could have positive effects in individuals with Alzheimer's [1], since β-ODAP has an activating effect on protein kinase C, which is involved in the memory processes, thus the balanced intake of *Lathyrus sativus* could be recommended in these individuals. On the other hand, β-ODAP has properties as wound healing agent, being useful to tamponade haemorrhages [1].

2.6 Nutritionally fortified food based in legumes

In recent years, research has focused on the development of derivatives of highly consumed products, such as bread or milk, produced by adding legume seed extracts allowing exploiting their nutraceutical potential [18–20].

Bread produced from sprouted lentil extracts added to wheat flour is a rich source of lysine, a scarce amino acid in cereals. Additionally, this added extract increase up to 100% in phenolic acids (quercetin and isorhamnetin) to common bread [18].

Vegetable milk substitutes are an ideal vehicle for the introduction of essential nutrients and nutraceuticals in the human diet because it can be fortified with bioactive ingredients of different plants. In this context, milk substitutes obtained from legumes can be easily fortified with micronutrients such as vitamin B12, vitamin D, calcium and omega-3, scarce in legumes [19].

Mayonnaise preparation replacing the egg yolk with proteins of vegetable origin, such as chickpeas, beans and lupine, would be an easy way to integrate phenolic acids, α-amylases and glucosidases in this food, turning this condiment into a food with antioxidant, antihypertensive and antidiabetic properties [20].

3. Pseudocereals

Pseudocereals have attracted great attention in the last 20 years for their nutritional properties. They content large quantities of fiber high quality protein (that includes essential amino acids rich in sulphur), and starch. They are a good source of iron, zinc and calcium, vitamins, saponins, phytosterols, polyphenols, phytosteroids, and betalains. Pseudocereals have higher content of lysine, methionine and cysteine compared to common cereals, mainly deficient in lysine and secondarily deficient in threonine and tryptophan [21]. The groups of bioactive components in pseudocereal grains include saponins, phenolic compounds, phytosterols, phytoecdysteroids, polysaccharides, betalains, and bioactive proteins and peptides [21].

Saponins are steroid or triterpenoid glycosides predominantly found in seeds. The saponin fraction present in quinoa and including 3-O-β-D-glucopyranosyl oleanolic acid, has been shown to exhibit anti-inflammatory activity in murine macrophages induced by lipopolysaccharides by inhibiting the production of nitric oxide (NO), tumor necrosis factor (TNF)-α, and interleukin IL-6 [22].

Quinoa saponins have also shown *in vitro* antiobesic effects by inhibiting the accumulation of triglycerides in adipocytes and suppressing adipogenesis [21]. Furthermore, it has been observed that they are capable of inhibiting the expression of PPARγ, C/EBPα and SREBP1c, which act as transcription factors during adipocyte differentiation [23].

Saponins have membranolytic activity. The aglycone group of the saponins structure has affinity with the lipid region of the cell membrane, generating disturbance in the fluidity and permeability of the cell membrane. The membranolytic activity of quinoa saponins on cells of the small intestine can cause an increase in the permeability of the mucosa, which would promote an increase in the rate of exfoliation of intestinal cells, which is associated with an increase in the loss of cholesterol by secretion faecal bile acids and neutral steroids, given the ability of saponins to bind to cholesterol these bile acids [23].

Quinoa extract inhibits the formation of the GSSG dimer and favours the GSH form through the activation of Glutathione-S-transferase (GST) by the action of H_2O_2. Thus, the quinoa extract acts as a reducing agent for disulphide bridges [23]. These activities are directly linked to surfactant and antioxidant properties, and were most of the diseases associated to oxidative stress are characterized by a decrease in GSH or the GSH/GSSG ratio.

Phenolic compounds found in Pseudocereal flours have revealed a wide variety content of flavonoids (anthocyanins, isoflavonoids, flavonols, flavones, flavanones, and flavonoids), phenolic acids and derivatives of tyrosol.

In this regard, squalene is an inhibitor of mRNA expression of 3-hydroxy-3-methylglutaryl coenzyme A, a key reductase enzyme in cholesterol biosynthesis [23]. Rutin, a glucoside flavonoid with numerous pharmacological activities present in buckwheat including its seed [24] shows many benefits such as its anticarcinogenic capacity in numerous types of cancer, neuroprotective and cardioprotective activities, including antihypertensive and anticoagulant effects [25]. Cinnamic acids (hydroxycinnamic acid, hydroxybenzoic acid, caffeic acid and chlorogenic acids), coumarins and isocoumarins contains in pseudocereals have shown high antioxidant activity. Chia seeds are abundant in caffeic acid and chlorogenic acid, which antioxidant activity has been proven *in vitro* but not *in vivo* assessment. However, the effect of caffeic acid on health is controversial since its consumption has also been linked to cancer [26].

Anti-aging agents found in pseudocereals have been proposed as promising bioactive molecules with protective effect against skin aging due to their ability to scavenge free radicals, chelate metal ions, and inhibit collagenase activity in the skin [21].

Phytoecdysteroids with antioxidant capacity, have an anti-obesity effect, assuming a significant reduction in fat mass that is attributed to greater carbohydrate oxidation and fecal lipid excretion in rats [21].

Polysaccharides (carbohydrates) made up of galacturonic acid and glucose monosaccharides contained in quinoa seeds exhibit radical scavenging effects, macrophage proliferation-promoting properties, suppression of NO production, and cytotoxic activity against MCF-7 breast cancer cells [21]. In addition, buckwheat polysaccharides facilitate the secretion of several cellular factors, including TNF-α, NO, IL-2, and IL-1β in macrophages, and show potential for the treatment of leukaemia [21]. ***Phagopyritols*** have antioxidant, anti-inflammatory and antidiabetic activity. Buckwheat phagopyritols significantly suppress increased blood glucose, decreased lipid levels, and improved insulin resistance *in vivo* in an insulin-resistant mouse model. Furthermore, these carbohydrates enhanced glucose uptake in both normal and insulin resistant HepG2 cells [21].

Consumption of ***D-phagemine*** induces a reduction in postprandial blood glucose concentration by inhibiting intestinal disaccharidases. In addition, it achieves the reduction of weight gain, inflammation and impaired glucose tolerance, most probably by influencing the intestinal microbiota. D-phagomin stimulates the diversity of the gut microbiota by increasing bacteroids populations in healthy rats and mitigates the age-related decline in the supposedly beneficial *Lactobacillus* and *Bifidobacterium* populations. In addition, the ability of D-phagemine to counteract sucrose-induced steatosis and hypertension, is due presumably by reducing postprandial hepatic fructose levels [21].

Fiber present in the pseudocereals is also capable of inhibiting the absorption of cholesterol, while binding to bile acids favours the catabolism of cholesterol or the fermentation of fiber in the colon, promoting short-chain fatty acids that contribute to the reduction of cholesterol synthesis in the liver [23].

Bioactive peptides composition in pseudocereals include different families with multiple health benefits. The main mechanism controlling blood pressure is based on the renin-angiotensin-aldosterone system (RAAS) and angiotensin converting enzyme (ACE) inhibitors. ACE is responsible for the conversion of angiotensin I to angiotensin II, which increases peripheral vascular resistance, and inducing a hypertensive action [16]. Pseudocereals as Amaranth contains a large amount of 11S and 7S globulin proteins with antihypertensive effects. The breakdown of these proteins by the enzymes of the digestive tract gives rise to bioactive peptides that have an antihypertensive activity up to 8 times higher than the unmodified proteins and with a similar effect on lowering blood pressure in rats compared to captopril drug [16].

In addition to antihypertensive activity, the 11S globulins of amaranth contain peptides with antioxidant activity, mainly derived from the acid subunit [16]. Other peptides from amaranth with lectin nature has an inhibitory power against malignant cancer cells. Amaranth protein hydrolysate has the ability to rearrange the cell cytoskeleton in certain osteosarcoma lines, inhibiting cell adhesion and inducing apoptosis and necrosis [21]. These protein hydrolysates have immunomodulatory effects on epithelial cells through the NF-ƙB signalling pathways. Particularly, the SSEDIKE peptide has the ability to attenuate the activation of epithelial cells and inhibit the allergic reaction in mice with food allergies, preventing IgE secretion, and controlling intestinal inflammation by preventing NF-ƙs activation [16]. Amaranth peptides derived from globulin and glutelin have the ability to inactivate enzymes associated with type 2 diabetes, such as α-amylase and DPP-IV [16].

Quinoa peptides originated after gastrointestinal digestion show inhibitory activity against DPP-IV, α-amylase and α-glycosylase, being those released during the duodenal phase and presenting the greatest inhibitory effect. Specifically, three peptides derived from 11S globulin with the capacity to inhibit incretin degradation have been identified [27]. Interestingly, it has been observed that protein fraction of quinoa hydrolysed with alkalase has radical scavenging capacity, and this antioxidant activity increases at the same time as the level of digestion.

Seventeen peptides with antioxidant activity have been identified in quinoa derived from 11S globulin and other proteins, some of the including functional motives such as LWREGM, DKDYPK, and DVYSPEAG, IFQEYI and RELGEWGI [28]. Millet, a 14-mer peptide, SDRLLGPNNQYLPK sequence exhibited antioxidant and chelating capacity. Similarly, seven other bioactive peptides have been found in sorghum with antioxidant capacity [29].

On the other hand, lunasin from amaranth is capable of preventing cancer, since it is able to enter the cell nucleus and inhibit the transformation of fibroblast cancer cells [16]. In quinoa, it has been observed that the fraction of peptides below 5 kDa have greater antioxidant capacity, which peptides in the high kDa range exhibited a greater mass anticancer capacity [28].

Antimicrobial peptides around 4 kDa are also present in buckwheat showing capability of inhibition of the reverse transcriptase activity of HIV-1 *in vitro*. In addition, other buckwheat-derived peptides rich in glycine and cysteine exhibited antifungal activity against *Mycosphaerella arachidicola* and *Fusarium oxysporum*. Other peptides found in buckwheat possess antimicrobial activity against gram-positive and gram-negative bacteria [29].

4. Cereals

Cereal consumption can reduce the risk of diseases such as heart disease, type II diabetes, and cancer [30]. The development of nutritious, safe, affordable and sustainable food products to prevent lifestyle-related diseases is important and desirable, thus, foods rich in fiber, which can reduce the risk of non-communicable diseases, have become even more desired for consumers [5, 30].

Cereals are a great source of protein, vitamins, minerals, fiber, and important bioactive compounds. These bioactive compounds are concentrated in the outer layers of the seed, and phenolic compounds (phenolic acids and flavonoids) are among them one of the most important because of their healthy properties [30].

Cereal proteins should be part of a healthy and balanced diet, although they are considered of lower quality compared to proteins from animal products due to their low amino acid profile and low digestibility. The protein content in cereals is determined by genetic and environmental factors, being for example, common wheat (*Triticum aestivum*) a cereal that contain a lower amount of protein than ancient species [30].

Protein quality is determined by the proportion of essential amino acids. The einkorn (old) variety has been shown to have a higher content of essential amino acids (threonine, lysine, valine, methionine, leucine, isoleucine and phenylalanine) compared to modern species, although it is low in lysine and high in glutamic acid [30].

Studying ***the amino acids composition of cereal proteins***, it is possible to find L-theanine that exhibits various health benefits such as anxiolytic and relaxant properties, cognitive and emotional enhancement, neuroprotection, anti-inflammatory, and physiological effects such as lowering blood pressure [31]. Although the presence of this amino acid in the human body is conditioned by its intake, and that L-theanine reacts with free sugars losing its nutraceutical value, it has been determined that the consumption of products wheat-enriched with L-theanine have a beneficial effect on health and well-being, and its enrichment could be carried out by enzymatic modification of wheat flour (gluten trans-amination) [31]. This molecular alteration of wheat flour is used mainly for two purposes: to modify the rheology of the wheat dough, and, conversion of glutamine residues into γ-glutamylamines.

Furthermore, gluten is a very important functional protein, responsible for the viscoelastic property of wheat doughs. It is constituted by two type of proteins, gliadin and glutenin [31, 32]. Gliadin and glutenin are insoluble proteins that have a storage function in the seed [30]. Gluten content in ancient wheats is higher than in modern varieties, in addition of having a higher gliadin/glutenin ratio. On the other hand, although the amount of proteins in millet and wheat is similar, millet does not contain gluten, which is currently important for the diets of people with celiac disease as responsible for the symptoms [30].

Celiac disease is characterized by the loss of absorption villi in the small intestine, which prevents nutrients from being properly absorbed [32]. Thus, peptides rich in proline are not digested and accumulate in the small intestine, which initiates an immune response. These effects are mainly due to the gliadin fractions of gluten, especially α-gliadin and γ -gliadin [30]. Different gluten-free products have been developed based on wheat flours, but problems at a nutritional, organoleptic and technological level persist, in addition to the fact that these foods are generally more expensive [32].

Since the exogenous process that causes celiac disease is well known, a prevention strategy that focuses on reducing gluten toxicity can be carried out as an alternative to a gluten-free diet [32]. Ribeiro et al. [31] have developed a study by which, it is possible to obtain flour rich in L-theanine by transamination of gluten (catalysed by microbial transglutaminase). This transamination would cause the substitution of glutamine by L-theanine in the constituents of gluten rich, which can prevent the immune stimulation that gluten would cause in celiac disease. Alternatively, non-celiac gluten sensitivity is a disorder characterized by intestinal symptoms and extra-intestinal manifestations (headache, fatigue, depression, muscle pain, dermatitis, anaemia, etc.), and its pathogenesis is still not exactly understood, and currently it has been shown that it does not depend solely on gluten, but that high contents of trypsin-amylase inhibitors (ATIs) that can cause gastrointestinal symptoms by stimulating toll-like receptors (TLRs) [30].

Dietary fibers is one of the most important components of cereals, with positive health effects. Dietary fibers are non-starch polysaccharides, such as cellulose, pectin, arabinoxylan, glucan and lignin, which cannot be enzymatically digested in the human digestive tract until reaching the large intestine, where they can be partially digested [33]. Cereals compounds as fiber has shown beneficial for type II diabetes improvement, such in the case of arabinoxylan [33].

Furthermore, beta-glucans are polysaccharides derived from D-glucose molecules linked by beta-glycosidic bonds. It is a part of dietary fibers that are supposed to have a large number of health benefits, including treating some gastrointestinal diseases and supporting the immune system [34]. beta-glucans present in cereals are not digested in the stomach or intestines and have a great ability to form bonds with water, creating sticky gels in the gastrointestinal tract, which results in a delay in gastric evacuation that causes a delay in the action of enzymes that act on starch, obstructing the absorption of digestible carbohydrates. This mechanism causes a reduction in blood glucose as well as insulin secretion, which could contribute to a reduction in the incidence of type II diabetes [34].

Beta-glucans could prevent colorectal cancer, since these act stimulating the immune system by activating macrophages and cytokines production and secretion, among others factors, and binding to immunologically competent cell membrane receptors [34].

Beta-glucans exhibit different properties, such as solubility, degree of branching, and molecular mass and shape, which may have impact on their biological activity [34]. A diet rich in beta-glucans has a positive effect on health by preventing diabetes, hypercholesterolemia, obesity, cardiovascular diseases, and cancer. Beta-glucans are present in cereals as barley or oats, and have been shown to lower blood cholesterol and glucose, in addition of acting as a major factor in the prevention of obesity and metabolic diseases [34]. These present in cereals are not digested in the stomach or intestines and have a great ability to bind water molecules, forming sticky gels in the gastrointestinal tract, which results in a delay in gastric evacuation and a delay in the action of enzymes that act on starch, obstructing the absorption of digestible carbohydrates. This mechanism causes a reduction in blood glucose as well as insulin secretion, which could contribute to a reduction in the incidence of type II diabetes [34]. They also have a positive effect on lipid metabolism, reducing blood cholesterol (hypocholesterolaemia effect) [34].

In addition, beta-glucans have antioxidant properties by eliminating excess of ROS molecules implicated in diseases. They also have immunostimulatory properties that are beneficial for the prevention of infectious diseases, gastrointestinal cancer, and colorectal cancer, while have prebiotic properties with beneficial effects on the flora of the gastrointestinal tract and prevents diseases of the large intestine and digestive system [34].

Interestingly, recent studies show that the administration of rice bran supplement (RBS) improves sleep *via* histamine H1 receptor (H1R) antagonist. This could represent a breakthrough as a therapeutic agent for insomnia. Furthermore, it has also been observed that H1R antagonists or antihistamines have been used to improve the symptoms of different conditions such as depression, pain, forgetfulness and allergy.

Cereals also contain ***polyphenols*** which are nutraceutical bioactive compounds with antioxidant properties, as well as antimicrobial and immunomodulatory properties [33]. Polyphenols are secondary metabolites synthesized by plants from phenylalanine, and are derived from C6-C3 structures [5]. Ferulic acid is one of the main phenols in wheat. Its content in cereals depends on both the species and the variety, as well as the growing conditions. Phenylpropanoids have beneficial properties for health and those biosynthesized from the aromatic amino acid L-phenylalanine [5]. Its antioxidant capacity is due to the large number of hydroxyl substitutions in each flavonoid molecule, which has an effect on the donor capacity of hydrogen atoms to scavenge free radicals [5]. They are involved in the prevention of cardiovascular diseases, and their metabolism is critical to improve vascular efficiency. The composition of the phenolic compounds is also important, having great effect on the estrogenic activity and the protective efficacy of the flavonoids of *Sorghum bicolour* to prevent colon cancer [5]. Increasing the consumption of fruits and vegetables rich in flavonoids can help control weight, being important with the current global problem of overweight and obesity. Foods high in flavonoids and anthocyanin may be associated with lowering weight gain [5]. Flavonoids improve the function of vitamin C, promoting its absorption and oxidation protection. They also regenerate other antioxidants, such as tocopherols, by donating hydrogen to the tocopheroxyl radical, in a similar way to vitamin C [5].

The bran of cereals is rich in polyphenols, but these are normally eliminated before consumption, and most of the phytochemicals are lost in the development process. Although there is an increase in the consumption of whole cereal (with bran), which is important for polyphenols intake, and therefore their effect, being more effective in terms of health benefits [5].

Therefore, resistant starch (RS) are carbohydrate fractions that persist in the intestine after digestion by pancreatic amylase, reaching the large intestine where it is available for fermentation by the intestinal microbiota [35]. A higher amount of RS in ingested food can prevent or be therapeutic for diseases such as diabetes. RS has different benefits, such as a prebiotic effect, a reduction in the risk of cardiovascular diseases, an improvement in cholesterol metabolism, and a reduction in the risk of colon cancer [35].

5. Conclusion

Legume, cereal and pseudo-cereal seeds are staple food with great importance worldwide for food security, and their seed compounds have demonstrated to be of high interest at nutritional and nutraceutical level due to large number of health benefits and their potential uses as functional foods.

Many seed compounds have been described and their outstanding properties related to health improvement as anti-inflammatory-related diseases as type 2 diabetes, cardiovascular diseases, cancer, among others. Different molecular mechanisms have demonstrated to be implicated in these health benefits, but many other are still to be studies and deeply understand in order to explore effective diagnosis, therapies, and develop treatment based in grain/seed nutraceutical compounds.

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Conflict of interest statement

The authors have declared that no competing interests exist.

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