State of Knowledge on Amaranth Grain: A Comprehensive Review

Article *in* Journal of Food Science · April 2012

DOI: 10.1111/j.1750-3841.2012.02645.x · Source: PubMed

2 authors:

Valeria Caselato
Federal University of Rio de Janeiro

Jaime Amaya-Farfan
University of Campinas

State of Knowledge on Amaranth Grain: A Comprehensive Review

Valéria Maria Caselato-Sousa and Jaime Amaya-Farfán

Abstract: Amaranth grain is a highly nutritional pseudocereal with a superior amount of proteins when compared to true cereals. It is a reasonably well-balanced food with functional properties that have been shown to provide medicinal benefits. The health benefits attributed include decreasing plasma cholesterol levels, stimulating the immune system, exerting an antitumor activity, reducing blood glucose levels and improving conditions of hypertension and anemia. In addition, it has been reported to possess anti-allergic and antioxidant activities. The present article provides a comprehensive overview of amaranth grain that focuses on recent research reporting its use in the clinical practice and its possible benefits to human health.

Keywords: amaranth, clinical studies, functional food, humans, nutritive value

Introduction: Amaranth, An Unusually Nutritious Grain

Amaranth (*Amaranthus* spp.) has been consumed throughout history, including by the Inca, Maya and Aztec civilizations, where it was used as a staple food. Recently, an increased interest in amaranth appeared in the 1980s, when the United States National Academy of Sciences performed research on the grain and described its high nutritional value and agronomic potential (Monteros and others 1998; Ulbricht and others 2009).

Given the growing acceptance of amaranth in countries where its consumption has not been traditional because of the general consumer interest in grains with medicinal properties, literature reviews on amaranth have been published recently focusing on aspects such as the adaptation to traditional cuisines (Dixit and others 2011), or the nutraceutical properties of this non-conventional grain (Huerta-Ocampo and de la Rosa 2009). The present is a more comprehensive review that attempts to bring somewhat diverging studies on amaranth grain into a new perspective, with a special focus on its ability to modulate the metabolism and inhibit or delay pathological processes both *in vitro* and in animals and/or humans.

There are about 60 different amaranth species, but not all are found in daily menus. Leaves of the young *Amaranthus blitus*, *Amaranthus tricolor*, *Amaranthus cruentus*, *Amaranthus dubius*, *Amaranthus edulis,* and *Amaranthus hypochondriacus* plants are used in salads and soups. The grains of *Amaranthus caudatus*, *Amaranthus hypochodriacus, Amaranthus cruentus, Amaranthus hybridus,* and *Amaranthus mantegazzianus* are made into breads, cakes, cookies, confectionary and soups, whereas such species as *Amaranthus retroflexus*, *Amaranthus. viridis* and *Amaranthus. spinosus*, are not safe for consumption by either humans or livestock.

Whether from the botanical or from the nutrient composition standpoints, this grain shares characteristics of both a cereal and a leguminous seed. Because its protein content and its amino acid composition are somewhere in between those of a cereal and a bean, it could be nutritionally considered as a natural mixture of rice and beans (Amaya-Farfan and others 2005).

Amaranth has a high soluble fiber content (4.2%; Early and Early 1987) and a reported protein concentration between either 12.5% and 17.6%, according to Teutonico and Knorr (1985), or between 16.09% and 18.19%, according to Becker and others (1981). Its methionine contents are around 15.8 mg/g total protein, whereas its lysine levels are about 55.8 mg/g total protein (Table 1 and 2; USDA, Release 24, 2010). The high lysine and methionine concentrations support the high nutritional quality of the grain, especially when compared to other grains in which those amino acids are present at limited levels (Teutonico and Knorr 1985; Bressani 1989). Although this pseudocereal shares the same classes of storage proteins with other grains, Kadoshnnikov and others (2008) have shown that in the ontogenesis of amaranth the proportions of globulins and albumins are reduced, whereas those of glutelins and gliadins are increased. Nevertheless, a low content of storage proteins (42% of the total) has been observed by these authors to occur in amaranth, compared to the high proportions found in wheat and other cereals.

Concerning fiber, the amaranth grain is considered a good source of insoluble fiber. Marcílio and others (2003), in Brazil, and Escudero and others (2004), in Argentina, reported that from the total dietary fiber in *A. cruentus*, 4.2% is soluble fiber.

Amaranth's lipid content shows great variations, ranging between 1.9% and 9.7% depending on the species and the genotype. The fatty acids palmitic (19%), oleic (26%), and linoleic (47%) appear in higher amounts, and the linolenic fatty acid is also found (1.4% of the total fatty acids; Berger and others 2003). A high content of the unsaturated hydrocarbon squalene is found in amaranth oil, ranging from 2.4% to 8.0% of the ether extract (Bruni and others 2001; Rodas and Bressani 2009; Table 2), or amounting to about 0.5% of the grain (dry basis [db]), and to which the beneficial effect of reducing serum cholesterol levels has been attributed (Miettinem and Vanhanen 1994).

Amaranth has also been recognized because of its high vitamin and mineral contents, such as riboflavin, niacin, ascorbic acid,

MS 20110908 Submitted 7/27/2011, Accepted 1/10/2012. Authors Caselato-Sousa and Amaya-Farfán are with Dept. of Food and Nutrition, Univ. of Campinas, Monteiro Lobato St. 80, Campinas, Brazil. Direct inquiries to author Amaya-Farfán (E-mail: jaf@fea.unicamp.br).

doi: 10.1111/j.1750-3841.2012.02645.x

calcium, and magnesium contents (Singhal and Kulkarni 1988; Table 2).

The grain is processed in various ways for consumption, of which the expanded grain form is perhaps the most popular. Other processes include cooking in water, extruding, toasting, incorporating it into flakes (Bressani and others 1993) or pastas and baking into biscuits (Brenner and Willians 1995; Marcílio and others 2005). In Mexico, *A. cruentus* cultivars are used to manufacture cookies called "Alegria," in which amaranth is used in the form of popcorn (Irving and others 1981). In Asia, the Indian diet finds in amaranth grain a culinary acceptable high protein, high fiber, alternative to wheat, easy to incorporate into the traditional cuisine (Dixit and others 2011). In the last few years, the properties of amaranth in cholesterol reduction, as an anti-oxidant, anticancer, anti-allergic, and antihypertensive agent; and as a food for patients with celiac disease and immunodeficiencies, have been assessed in clinical studies.

Most of these properties are explained by the presence of substances such as lunasin, a peptide with antitumoral effects, or of antihyperlipidemic, antidiabetic, and antihelmintic substances found in methanolic extracts, in addition to those with antidiarrheic, antifungal, and antimalarial properties found in aqueous extracts of the seeds (Huerta-Ocampo and de la Rosa 2011). Specific flavonoids such as rutin and some phenolic acids as gallic acid, *p*-hydroxybenzoic acid and vanillic acid with antioxidant effects also occur in amaranth seeds and sprouts (Table 3) (Pasko and others 2008).

Effect of Processing on the Nutritive Value

Aside from the obvious impact that heat or other processing operations can have on digestibility and the bioavailability of carbohydrates, proteins and amino acids, of pertinent relevance are the possible alterations on the profile of all active substances. Queiroz and others (2009), for example, cooked, popped, toasted, extruded and milled amaranth grain and found that processing reduced the mean total content of phenolics by about 30% (gallic acid equivalent/g of dry residue), whereas toasting was the only process whose ethanolic extract showed a significant decrease in antioxidant activity. Extrusion, toasting or popping were operations that did not change the capacity to inhibit amaranth lipid oxidation.

Other studies have pointed out that antioxidant phenolics in amaranth are likewise affected by heat processing. Total phenolics, antioxidant activity, as measured by 2 chemical methods, and phytic acid contents of 2 Peruvian *A. caudatus* varieties were shown to be significantly decreased after undergoing a low-cost extrusion process (Repo-Carrasco-Valencia and others 2009). The content of total phenolics, phytic acid, and the antioxidant activity decreased in both varieties during the hydrothermal treatment. Of significant importance was the comparative total phenolics retention study by Kunyanga and others (2012), which reported that amaranth grain is particularly susceptible to thermal processing losses, in comparison to such cereals and legumes as finger millet, sunflower seeds and pumpkin seeds, or even groundnuts and field beans. In terms of catechin equivalents, the contents of a Kenyan *A. cruentus* cultivar fell by about 70% after soaking and cooking or roasting.

In terms of fractionation by milling, the report of Marcílio and others (2005) raises the issue that in order to retain the maximum nutritive quality, the flour should not be processed to any degree of refinement because of the unique morphology of the seed. These authors showed that refining of the amaranth flour would result

Table 1–Amino acids content of *Amaranthus spp.* (USDA 2010).

Amino acids	Unit	Value per 100 g
Tryptophan	g	0.181
Threonine	g	0.558
Isoleucine	g	0.582
Leucine	g	0.879
Lysine	g	0.747
Methionine	g	0.226
Cystine	g	0.191
Phenylalanine	g	0.542
Tyrosine	g	0.329
Valine	g	0.679
Arginine	g	1.060
Histidine	g	0.389
Alanine	g	0.799
Aspartic acid	g	1.261
Glutamic acid	g	2.259
Glycine	g	1.636
Proline	g	0.698
Serine	g	1.148

Table 2–Nutritional content of the *Amaranthus spp*. (USDA 2010).

Nutrient	Unit	Value per 100 g
Water	g	11.29
Energy	kcal	371
Energy	kJ	1554
Protein	g	13.56
Total lipid (fat)	g	7.02
Ash	g	2.88
Carbohydrate, by difference	g	65.25
Fiber, total dietary	g	6.7
Sugars, total	g	1.69
Starch	g	57.27
Calcium, Ca	mg	159
Iron, Fe	mg	7.61
Magnesium, Mg	mg	248
Phosphorus, P	mg	557
Potassium, K	mg	508
Zinco, Zn	mg	2.87
Manganese, Mn	mg	3.333
Vitamin C, total ascorbic acid	mg	4.2
Thiamin	mg	0.116
Riboflavin	mg	0.200
Niacin	mg	0.923
Folate, total	μg	82
Vitamin E (alpha-tocopherol)	mg	1.19
Vitamin B6	mg	0.591
Fatty acids, total saturated	g	1.459
Fatty acids, total monounsaturated	g	1.685
Fatty acids, total polyunsaturated	g	2.778
Fatty acids, 18:3 n-3 c,c,c (ALA)	g	0.042
Phytosterols	mg	24
Squalene in amaranth oil[a]	%	2.4*to*8.00

[a](Bruni and others, 2001; Rodas and Bressani, 2009

Table 3–Phenolic acid and flavonoids content of the seeds and sprouts of 2 cultivars of *Amaranth cruentus* (mg/kg dry weight; Pasko and others 2008).

Nutrient	Seeds	Sprouts
Phenolic acids		
Gallic acid	400 to 440	350 to 370
p-Hydroxybenzoic acid	8.5 to 20.7	n.d.
Vanillic acid	n.d. to 15.5	n.d.
p-Coumaric acid	n.d. to 3.5	4.4 to 42.4
Syringic acid	n.d.	3.7 to 6.3
Flavonoids		
Rutin	n.d.	300 to 690

n.d. = not detected.

in a drastic loss of protein and indispensable amino acids; as the degree of extraction approached 40%, the protein content of the flour was diminished to about 4%, unlike what was observed with the other pseudocereal quinoa.

Hypocholesterolemic Activity

A summary of the *in vitro* and biological assays is presented in Table 4. Several hypotheses have been proposed to explain one of amaranth's most cited abilities, which is the modulation of the serum cholesterol levels. One of such hypotheses cited the content of unsaturated fatty acids (Chaturvedi and others 1993; Chavez-Jauregui and others 2000). Concurrently, the amount of total and soluble fiber has also been mentioned (Danz and Lupton 1992; Grajeta 1997; Plate and Arêas 2002; Mendonça and others 2009), and possibly that the amino acid profile of its protein (Berger and others 2003) may as well be involved in the mechanism. The presence of phytochemicals as tocotrienols (Lehmann 1996; Qureshi and others 1996), phytosterols (Berger and others 2003; Martirosyan and others 2007), and tocopherols and squalene (Lehmann 1996; Qureshi and others 1996; Shin and others 2004; Gonor and others 2006b; Kulakova and others 2006; Martirosyan and others 2007), have undoubtedly been proposed projecting a rather complex scenario, but that also suggests the participation of a set of components of different chemical nature.

Danz and Lupton (1992) reported that amaranth consumption by the rat had a cholesterol lowering effect in the serum, similar to that of a soluble fiber, but also behaving like a poorly fermentable fiber in the colon. Meanwhile, Chaturvedi and others (1993) used the rat model to show that the hypocholesterolemic effect of an amaranth diet was able to reduce total cholesterol by 50% compared to the control diet containing casein. Those authors hypothesized that the unsaturated fatty acid content of amaranth could have promoted the observed effect.

Among the remaining doubts, for instance, is that researches suggesting that amaranth reduces serum cholesterol through some function of squalene cannot explain the mechanism through which this triterpenoid may act. Squalene, while serving as a substrate for HMG-CoA reductase (3-hydroxy-3-methylglutaryl Co-A), should promote, rather than inhibit, cholesterol biosynthesis in the liver. Although no direct evidence was found in favor of the role of squalene, Sawada and others (2002) have suggested that the cholesterol biosynthetic pathway can be quite complex and that inhibitors may cause either hypo- or hypercholesterolemia.

Qureshi and others (1996), however, studied the effect of supplementing the diet with amaranth for 6 wk on cholesterol biosynthesis in chickens. The total and low-density lipoprotein (LDL) cholesterol values decreased significantly in groups fed with amaranth, but the high-density lipoprotein-C (HDL-c) concentrations remained unchanged. The cholesterol 7 alpha-hydroxylase enzyme activity was 10% to 18% higher in the experimental group compared to the control group, whereas the HMG-CoA reductase activity in the liver was 9% lower. This study suggests that the inhibition of HMG-CoA reductase, which results in lower cholesterol levels, was due to the presence of some potent inhibitors of cholesterol synthesis other than amaranth's tocotrienols and squalene.

In turn, Lehmann (1996) stated that the decrease in cholesterol would be associated with some soluble component in the lipid fraction of the amaranth, suggesting that squalene and tocotrienols are responsible for the decrease. On the other hand, Grajeta (1997) also observed a significant reduction in blood and liver cholesterol concentrations in rats fed with whole and defatted amaranth flour and attributed the hypocholesterolemic effect to the soluble fraction of dietetic fibers present in the flours.

Later, Grajeta (1999), through a complex experimental design, observed the effect of whole amaranth and oat bran in the blood and liver of 60 male Buffalo rats. The results showed that the amaranth and oat bran were responsible for a significant decrease in the total blood and liver cholesterol levels of rats, and that the oat bran provided a larger decrease compared to amaranth. The 2 intervention products did not show any effect on blood HDL-c levels, but the amaranth caused the triacylglycerol level to decrease in the liver.

Among the diversity of attempts carried out to show the cholesterol lowering power of amaranth, *in vitro* assays and animal models like rats, hamsters, rabbits, and chickens have been used, besides intervention trials in humans (Table 3). The experiments have tested the different fractions of the grain and used either hypercholesterolemic animals or diets, for the most part. Plate and Arêas (2002) showed that hypercholesterolemic rabbits fed with an extruded defatted (*A. caudatus*) amaranth flour showed a reduction of LDL- and total cholesterol levels by 50%, whereas amaranth oil was not as efficient as the extruded amaranth.

In a study conducted by Berger and others (2003) with hamsters, a diet containing 20% of *A. cruentus* grains and totaling 5% amaranth oil decreased the non-HDL cholesterol level. In this study, the authors suggested that amaranth phytosterols and the protein showed some hypocholesterolemic effect, eliminating the possibility that the composition of fatty acids, tocopherols, and tocotrienols would be responsible for the observed effect.

In another study, Czerwinski and others (2004) utilized rats fed with a diet containing cholesterol to compare the effect of oat and amaranth ingestion, aiming at determining whether the pseudocereal could be used as a replacement for allergic individuals to improve blood lipid levels. Although both the bran and the whole grain showed a positive effect, the authors suggested that amaranth had the additional advantage of being free from known allergens, so it could be used as a replacement for cereals by hypercholesterolemic patients who are allergic to classical cereals.

The effect of a protein concentrate from *A. cruentus* on the amount of lipid in the blood and liver of Wistar rats was studied by Escudero and others (2005). No significant differences were observed in total cholesterol serum levels, but a decrease in LDL-c levels and an increase in HDL-c levels was observed, and the triacylglycerol levels of the experimental group were lower compared to the control group. The results demonstrated that the amaranth protein concentrate has a hypotriacylglycerolemic effect, affecting the lipid metabolism in the liver and increasing the indicators of antioxidant protection in Wistar rats.

Shin and others (2004) made some interesting observations on the effect of amaranth grain, oil and squalene in an experiment in which rats were fed with a semipurified diet containing 1% cholesterol for 4 wk, and amaranth grain or amaranth oil, which were substituted in experimental groups. Both the amaranth grain and the amaranth oil decreased the total blood and liver cholesterol levels and the triacylglycerol concentrations. The fecal cholesterol excretion and bile acid excretion were increased in the amaranth oil group, but only the bile acid excretion was increased in the amaranth group. In another experiment, the rats were fed with a cholesterol diet and salt (control), amaranth squalene or shark squalene for 7 d. The interesting feature of this experiment was that, whereas the amaranth squalene demonstrated a hypolipidemic effect in the blood and liver, an increase in fecal and bile acid

Table 4–*In vitro*, animal and clinical trials testing *Amaranthus spp*.

Publication (reference)	Subjects	N	Amaranth	Duration	Aim	Results	Comments
Whittaker and Ologunde (1990)	Male Sprague–Dawley rats	40	*A. caudatus* cereal	7 d	To compare iron bioavailability in Nigerian grain amaranth cereal fortified by 2 iron compounds.	The iron-fortified cereal had good Fe absorption and showed a significant increase in final Hb or hemoglobin gain.	An iron-fortified cereal would be useful to combat protein-calorie malnutrition and iron deficiency anemia.
Ologunde and others (1991)	Male Sprague Dawley rats	40	*A. caudatus* flour	7 d	To evaluate the iron bioavailability in fortified and unfortified grain amaranth seed flour and $FeSO_4$ fortified casein diet as control.	The relative biological value of unfortified cereal was 40% of control suggesting low iron absorption from the amaranth cereal.	The iron fortificant of choice was ferrous fumarate.
Chatuverdi and others (1993)	Adult male Wistar rats	24	*A. esculentus* seeds	80 d	To study the effect of amaranth seed flour on serum and tissue lipid profile in hypercholesterolemic rats.	Feeding with amaranth seed showed a definite hypocholesterolemic effect.	Effect can be attributed to the preponderance of unsaturated fatty acids.
Ologunde and others (1994)	Male Sprague–Dawley rats	40	*A. caudatus* flour	7 d	To evaluate the iron (Fe) bioavailability to the amaranth cereal.	Amaranth cereal can be considered an ideal food vehicle for iron fortification.	Native phytate and tannin in the grain have no effect on fortified iron.
Tosi and others (1996)	Member sensory panel	10	*A. cruentus* flour	–	To develop the formulation for producing cookies with whole amaranth flour.	The cookies can be labeled "gluten free." The protein level of the cookies was high and nutritional value increased.	
Qureshi and others (1996)	Female chicken	60	*A. hypochondriacus and cruentus* popped, milled and their oils	–	To compare the effects of variously processed amaranth varieties and their oily fraction.	The inhibition of HMG-CoA reductase, which resulted in lower cholesterol levels.	The presence of some potent inhibitors of cholesterol synthesis other than amaranth's tocotrienols and squalene.
Grajeta (1997)	Male Buffalo rats	60	*A. cruentus* seeds			The triacylglycerol level in the liver decreased by 10%.	
Chaturvedi and others (1997)	Humans	6	*A. esculentus* popped and roasted	3 h	To investigate the effect of differently processed (popped and roasted) grain amaranth products on postprandial glycemia in noninsulin dependent diabetic subjects.	The 25:75 combination of amaranth and wheat, wheat and rice can be considered low GI food, 50:50 grain amaranth and wheat medium GI food and popped amaranth and milk combination high GI food.	Due to the starch high digestibility, isolated ingestion of amaranth grains is not recommended to diabetic patients.
Grajeta (1999)	Male Buffalo rats	60	*A. cruentus* seeds	28 d	To examine the hypolipemic effect of amaranth and oat bran in rats depending on the kind of fat in diet.	The diets containing amaranth with lard did not decrease the concentration of these lipids.	Effect can be due the soluble fraction of dietetic fibers present in the flours.
Yu and others (2001)	Human colon cancer cell	–	Amaranth lectin from *A. caudatus*	8 d	To investigate the proliferative effects of the other 2 known dietary Tf-binding lectins: jacalin and amaranth lectin.	The dietary TF-binding lectins can have marked effects on the proliferation of human malignant gastro-intestinal epithelial cells and hence may play a role in intestinal cancer development.	The biological effects of dietary lectins cannot be predicted solely from their carbohydrate binding properties.
Klimczak and others (2002)	*In vitro*	–	*A. caudatus, A. paniculatus* and their ethanolic seed extracts.	–	To investigate the antioxidant activity of ethanolic extracts of amaranth seeds.	The ethanolic extracts of the amaranth seeds showed appreciable antioxidant activity in our model system b-carotene and linoleate.	Amaranth seeds could be a potential source of natural antioxidants.

(*Continued*)

Table 4–Continued

Publication (reference)	Subjects	N	Amaranth	Duration	Aim	Results	Comments
Plate and Arêas (2002)	Male rabbits	18	*A. caudatus* extruded and its oil	21 d	To evaluate the cholesterol-lowering effect of extruded amaranth and amaranth oil in hypercholesterolemic rabbits.	The extrused amaranth reduced LDL-c and total cholesterol levels.	Effect may be due to unsaturated fatty acid composition.
Berger and others (2003)	Hamsters		*A. cruentus* seeds and its oil	4 wk	To verify the hypocholesterolemic effect in rats.	Amaranth affected absorption of cholesterol and bile acids, cholesterol lipoprotein distribution, hepatic cholesterol content, and cholesterol biosynthesis.	Amaranth grain and oil did not affect these pathways identically.
Hibi and others (2003)	*In vitro* and female OVA-TCR Tg mice		*A. hypochondriacus*	14 d	To study the effects of amaranth grain on cytokine and IgE production using *in vitro* helper T cell development and IgE production assays and an animal model of an orally-induced, allergen-specific IgE response.	The amaranth grain and its extract inhibited antigen-specific IgE production through augmenting Th1 cytokine responses *in vivo* and *in vitro*.	It may prove to be a useful tool in the treatment of allergic disease.
Czerwinski and others (2004)	Male Wistar rats	60	*A. hypochondriacus*	32 d	To compare oatmeal with equal in nutritional values 2 allergy-free amaranth meals.	Oat and amaranth meals positively affect plasma lipid profile in rats fed cholesterol-containing diets.	The positive influence can be related to the bioactive components and antioxidant activities.
Shin and others (2004)	Rats	24	Amaranth grain, oil and squalene.	4 wk	To examine the hypocholesterolemic effect of amaranth grain, oil, and squalene.	The cholesterol-lowering effect of amaranth squalene may increase fecal elimination of steroids and interfere with cholesterol absorption.	The different sources of squalene (plant compared with animal) may affect cholesterol metabolism differently.
Escudero and others (2005)	Male Wistar rats	16	Protein concentrate from *A. cruentus*	28 d	To study the effect of protein concentrate from *A. cruentus* on the lipid content in serum and liver tissue of rats.	The protein concentrate from *A. cruentus* has a hypotriglycerideic effect, affects the metabolism of liver lipids, and increases parameters of antioxidant protection in rats.	The protein concentrate from *A. cruentus* can contribute as a supplement in the diet to prevent cardiovascular diseases.
Guerra-Matias and Arêas (2005)	Women	11	*A. cruentus* extruded	7 d	To investigate the starch digestibility of an extruded amaranth product.	The amaranth snack causes high glycemic and insulinemic responses.	The extruded amaranth is recommended for patients with celiac disease and athetes.
Conforti and others (2005)	*In vitro*	–	*A. caudatus* seeds	–	To investigate 2 varieties of *A. caudatus* seeds for their biological activities, antioxidant and antidiabetic, and oil, squalene, and phenolic contents.	The isolated squalene and ethyl acetate extracts showed potent antioxidant activity. The extracts showed antidiabetic activity through α-amylase inhibition.	Seeds of both investigated varieties were found to possess very different levels of squalene.
Marcílio and others (2005)	*Member sensory panel*	39	*A. cruentus* flour		To develop a process for manufacturing gluten-free cookies from amaranth flour as a certified gluten-free, nutritious alternative for celiac patients.	The amaranth showed potential for the manufacture of high nutritive value biscuit products, not only for the gluten-sensitive consumer but also for the common consumer.	The sensorial analysis was conducted with consumers nonceliac patients.

(*Continued*)

Table 4–Continued

Publication (reference)	Subjects	N	Amaranth	Duration	Aim	Results	Comments
Gonor and others (2006a)	Humans	125	Amaranth squalene	3 mo	To investigate the influence of a diet supplemented with amaranth oil on dynamic of antioxidant and immune status in patients with ischemic heart disease and hyperlipoproteinemia.	The antiatherosclerotic diet with 600 mg squalene promoted the most positive changes of immune status.	The consumption of 200–400 mg of squalene/D produced the greatest improvement of immune status.
Kim and others (2006a)	Male Sprague–Dawley rats	24	*A. esculentus* seeds and its oil	3 wk	To investigate the effect of amaranth on serum glucose and the lipid profile in diabetic rats.	Amaranth seeds and oil supplement reverted the antioxidant enzyme activities to near normal values and increased the hepatic lipid peroxide product and decreased the glutathione content.	The amaranth seeds and oil may be beneficial for correcting hyperglycemia and preventing diabetic complications.
Kim and others (2006b)	Male Sprague–Dawley rats	24	*A. esculentus* seeds and its oil	3 wk	To investigate the effect of amaranth on serum glucose and the lipid profile in diabetic rats.	Amaranth seeds and oil supplementation improve the glucose and lipid metabolism in streptozotocin induced diabetic rats.	It is suggested that the mechanism is interference with intestinal cholesterol and bile acid absorption, leading to an increase in fecal neutral sterol and bile acid excretion.
Gonor and others (2006b)	Humans	125	Amaranth squalene	3 mo	To investigate the influence of a diet supplemented with amaranth oil on dynamic of lipid profile and composition of fatty acids of erythrocytes in patients with ischemic heart disease and hyperlipoproteidemia.	The antiatherosclerotic diet with 600 mg squalene promoted positive changes in serum cholesterol, TG levels and FA composition of erythrocyte membranes.	
Kulakova and others (2006)	Rats		Amaranth oil	28 d	To study the hypocholesterolemic effect of amaranth oil.	The decrease of cholesterol lever in rat blood was not accompanied by its increasing in a liver	An increase in sterols in liver composition of rats.
Martirosyan and others (2007)	Humans	125	Amaranth oil	3 wk	To investigate the effects of amaranth oil in patients sufferring from coronary heart disease and hypertension with obesity.	Amaranth oil decreases the amount of total cholesterol, triglycerides, LDL and VLDL significantly	The dose of amaranth oil is 18 mL/d.
Capriles and others (2008)	*In vitro*	–	*A. cruentus* seeds	–	To compare *in vitro* starch digestibility of processed amaranth seeds and white bread.	The amaranth is a high glycemic food. Rapidly digestible starch contents, hydrolysis index, and predicted glycemic index were significantly increased by popping, roasting, and flaking processes.	Cooked, popped, and extruded amaranth seeds had starch digestibility similar to white bread.
Silva-Sánchez and others (2008)	*In vitro*	–	*A. hypochondriacus*	–	To investigate the presence, characterization, and the anticarcinogenic properties of the peptide lunasin in amaranth seeds.	The amaranth seed proteins could be an alternative. source of lunasin or lunasin-like isoforms.	The amaranth seeds are a potential source of other bioactive peptides with biological functions that could be beneficial to antihypertensive activity.

(*Continued*)

Table 4–Continued

Publication (reference)	Subjects	N	Amaranth	Duration	Aim	Results	Comments
Mendonça and others (2009)	Golden Syrian Hamsters	42	Amaranth protein isolate from *A. cruentus*	4 wk	To evaluate the hypocholesterolemic effect of amaranth protein in hypercholesterolemic hamsters.	The total plasma cholesterol concentration in animals fed on diets containing amaranth protein isolate were 27%, being the non-HDL fractions the most affected.	The amaranth protein has a metabolic effect on endogenous cholesterol metabolism.
Tiengo and others (2009)	*In vitro*	–	*A. cruentus*	–	To characterize and evaluate the activity of the angiotensin converting enzyme inhibitor of the amaranth protein concentrate and of hydrolysates produced with Alcalase.	The alcalase-hydrolyzed protein showed the highest inhibiting activity before and after *in vitro* digestion.	
Tovar-Pérez and others (2009)	*In vitro*	–	*A. hypochondriacus*	–	To obtain ACE-inhibitory peptide fractions produced by alcalase treatment of albumin 1 and globulin of amaranth.	Amaranth proteins are good raw material for production of ACE-inhibitory peptides.	The globulin peptide fraction may have one of the most active naturally-occurring ACE-inhibitory peptides.
Vecchi and Añon (2009)	*In vitro*	–	*A. hypochondriacus*	–	To provide experimental evidence for the presence of antihypertensive peptides in globulin 11S.	The occurrence of 2 tetrapeptides, ALEP and VIKP, was experimentally observed through an *in vitro* evaluation of ACE inhibition.	It was a fist time that a peptide docking approach was used to find ACE inhibitory peptides from a food protein source.
Pasko and others (2009)	Male Wistar rats	36	*A. cruentus* seeds	5 wk	To assess the influence of fructose addition (31%) and addition of amaranth seeds to fodder on the antioxidant status in selected rats' tissues and plasma.	Amaranth seeds can act as a moderate protective agent against fructose-induced changes in rats by reducing lipid peroxidation and by enhancing the antioxidant capacity.	Amaranth sprouts may be used in the diet because they are good sources of anthocyanins and phenolic compounds.
Kabiri and others (2010)	Male New Zealand Rabbits	25	*A. caudatus* extract	60 d	To find out the antiatherosclerosis effect of *A. caudatus* L. on rabbits, and was compared with lovastatin.	*A. caudatus* extract significantly decreased the cholesterol, LDL-C, triglycerides, oxidized LDL (Ox-LDL), apo-lipoprotein B (apoB), CRP, atherogenic index (AI) and HDL-C and apo-lipoprotein A (apoA) increased.	*Amaranthus caudatus* was more effective than lovastatin.
Barrio and Añon (2010)	Human tumor cells	–	*A. mantegazzianus* isolated protein	–	To investigate the potential antitumor properties of *A. mantegazzianus* protein isolate and to elucidate the possible mechanism of action.	The *A. mantegazzianus* protein isolate exhibited potential antitumor properties and propose a putative mechanism of action.	
Pasko and others (2011)	*In vitro*	–	*A. cruentus* seeds	–	To show the nutritional value of amaranth sprouts as a good source of antioxidants.	The sprouts have a higher antioxidant activity than seeds, which may be a result of difference in the content of polyphenols, anthocyanins, and other compounds.	The amaranth seeds and sprouts showed relatively high antioxidant activity.
Betim (2008)	Male Wistar rats	48	*A. cruentus* seeds	6 wk	To verify the hypocholesterolemic effect of 35% of amaranth protein in normolipidemic rats fed.	The amaranth decreased in LDL cholesterol without going beyond the normal limits or adversely affecting the HDL cholesterol level	The moderate and chronic consumption, as a replacement of standard protein, may have a prophylactic effect.

cholesterol excretion and inhibition of the HMG-CoA reductase activity, these effects were not observed with the shark squalene.

Concerning the effect of the oil fraction and squalene on amaranth's hypolipidemic properties, Gonor and others (2006b) studied the influence of a diet containing the oil on the lipid profiles and the erythrocyte fatty acid profiles of cardiac ischemia patients. The diets supplied squalene amounts of 100, 200, 400, and 600 mg/d, and the diet containing 600 mg showed significant positive changes in the cholesterol and triacylglycerol levels as well as in the composition of fatty acids of erythrocyte membranes.

The cholesterol-lowering effect of the amaranth oil fraction in rats was also investigated by Kulakova and others (2006). The authors confirmed that there was a decrease in blood cholesterol levels without observing an increase in liver cholesterol. An increase in liver sterols was observed, but it was thought to occur due to the presence of squalene in the amaranth oil. Such property of the oil was confirmed by Martirosyan and others (2007), while testing the properties of amaranth against coronary heart disease and hypertension, helping to reduce blood pressure. Its beneficial action was the highest when using an 18-mL amaranth oil dosage per day. The hydrocarbon squalene and phytosterols were suggested to be involved in this mechanism. Although most studies have been conducted with animals and/or hypercholesterolemic diets, Betim (2008) have found that if normolipidemic Wistar rats are chronically fed with normolipidemic diets in which 35% of the protein is replaced with the standard diet (AIN 93-G), they respond with a decrease in LDL cholesterol without going beyond the normal limits or adversely affecting the HDL cholesterol level. The authors conclude that moderate and chronic consumption, as a replacement of standard protein, may have a prophylactic effect.

Just as in the case of the protein concentrate, Mendonça and others (2009) attested that the amaranth protein isolate can also reduce the total and LDL cholesterol levels in hamsters. Although the mechanism involved was not described, an attempt was made to partially explain the mechanism by the lysine/arginine ratio.

Regardless of whichever the putative anticholesterolemic or antidyslipidemic factors may be, Kabiri and others (2010) have reported that an aqueous extract of *A. caudatus* is capable of significantly reducing the atherogenic index and injuries of cholesterol-fed atherosclerotic rabbits.

New insights seem to be emerging concerning the elusive role of squalene, or another associated substance present in the amaranth grain, which apparently has an inhibiting effect on squalene biosynthesis. This is the squalene monooxygenase enzyme, which has been identified as a key regulatory site, and whose inhibition ultimately results in a decrease of the synthesis of cholesterol (Belter and others 2011). If diminishing the activity of squalene monooxynase can help regulate the synthesis of cholesterol, then it is possible that an inhibitor, or inhibitors whether direct or indirect, are being coextracted with several of the amaranth seed fractions, including squalene itself. Should this new view be proven correct, it would also explain the intriguing observation made by Shin and others (2004) that the "squalene" from amaranth is not equivalent to shark squalene. It should be pointed out that when squalene was purified for analytical purposes, the substance was not assayed biologically (Rodas and Bressani 2009).

Immune System Influence

Gonor and others (2006b) investigated the influence of a diet containing either amaranth oil or squalene on the antioxidant activity and the immune state of 125 patients (ages between 33 and 74 y) with cardiac ischemia and hyperlipoproteinemia over 3 mo. Different amounts of squalene were used in the diet (100, 200, 400, 600 mg/day), and upon comparison, the responses of the groups showed that the diet containing 600 mg of squalene provided a positive effect in the immune state, whereas the diets containing 200 to 400 mg promoted an antioxidant effect.

More recently, authors have reported both positive and negative effects of squalene on the immune system. Whereas Escrich and others (2011) have hypothesized that the chemopreventive effect of extra virgin olive oil on breast cancer may be due at least in part to squalene and phenolic antioxidants, Tritto and others (2009) and Montagnani and others (2011) have attributed an autoimmune reaction of some individuals to a squalene-based adjuvant used in flu vaccines. Although a mechanism for the possible role of squalene on immunomodulation is not yet at reach, it is apparent that the lipid molecule can in fact influence the immune system most likely by altering the immune cell membrane. Tritto and others (2009), for instance, have suggested that in the case of vaccine adjuvants, squalene may activate the protein complex NLPR3/inflammasome, which is required for the correct processing of a number of pro-inflammatory cytokines, including IL1β.

Antitumor Effect

Diet is considered a risk factor for several chronic diseases, including cancer. In an estimated period of 10 to 30 y, normal cells may be transformed in clinically detectable tumors, and the diet may promote or inhibit the development of the disease (Bennink and Om 1998).

Yu and others (2001) also investigated the proliferative effects of diets with 2 lectins that can bind a tumor factor (TF-binding lectin): jacalin (*Artocarpus integrifolia*) and amaranth lectin (*A. caudatus*). Increased Thomsen-Friedenreich antigen (TF-antigen, Gal-beta1–3GalNAc-alpha) expression is a common characteristic of epithelial malignancy and premalignancy. The results showed that the diets containing the TF-binding lectins may be markers of proliferation of malignant gastro-intestinal epithelial cells and that it may have a role in diagnosing intestinal cancer.

Barrio and Añon (2010) studied the antitumor properties of the *A. mantegazzianus* isolated protein (MPI) and elucidated the possible mechanism of action. The study was conducted with 4 different tumor cells: MC3T3E1, UMR106, Caco-2, and TC7. MPI showed an antiproliferative effect on the 4 cell lines with different potentials. MPI inhibits cell adhesion and induces apoptosis and necrosis in the malignant cell UMR 106, and the authors concluded that *A. mantegazzianus* grains show an antitumor potential.

Action on Blood Glucose Levels

The action of amaranth on the levels of blood glucose seems to be somewhat controversial. Although some investigators report that the consumption of either the grain or the oil may protect against insulin deficiency, others assert that the high glycemic index (GI) of the starch is a liability to diabetic patients. Conforti and others (2005) detected antidiabetic activity in 2 varieties of *A. caudatus* seeds using an *in vitro* assay consisting of the inhibition of α-amylase, which acts in the digestion of starch and reduces the absorption of glucose. Using streptozotocin-induced diabetic rats, Kim and others (2006a,b) investigated the effect of amaranth oil and grain supplementation (*A. esculentus* L.) on blood glucose and the lipid profile. The rats were divided into 4 groups: normal control, diabetic control, diabetic group supplemented with amaranth grain, and diabetic group supplemented with amaranth oil for 3 wk. The results showed a decrease in blood glucose and an increase in serum insulin levels.

On the other hand, earlier studies have found that because of the high digestibility of its starch, amaranth grain may not be suitable for diabetics. Chaturvedi and others (1997) studied the effect of amaranth, wheat and grain preparations in the GI of noninsulin-dependent diabetic patients. *A. esculentum* L. was used in the form of "popcorn" (popped) and was prepared with different proportions of wheat flour to create unleavened bread (chapattis). In the amaranth–wheat combination, a GI of 91.7 was observed for a proportion of 50:50 and a GI of 105.7 was observed for a proportion of 25:75. For a combination of popped amaranth and unsweetened milk, a GI of 136.2 was observed. They concluded that due to the high starch digestibility, the isolated ingestion of amaranth grains should not be recommended to diabetic patients.

High GI foods promote hyperglycemia and hyperinsulinemia. A diet with a high GI shows lower satiety, which may result in excess food ingestion, favors an increase in body weight, changes lipid profile and insulin secretion and favors the development of cardiovascular diseases and diabetes mellitus (Jenkins and others 2002). The consumption of high GI foods may also lead to a sequence of hormonal actions that limit the postprandial availability of metabolic fuel, leading to hunger and excess food ingestion. The ingestion of low GI foods, therefore, may lower the secretion of proteolytic counter-regulatory hormones such as cortisol, growth hormone, and glucagon, stimulating protein synthesis (Ludwig and others 1999).

The possible influence of extrusion on starch digestibility and GI has been investigated (Guerra-Matias and Arêas 2005) by comparing an extruded amaranth product to white bread in 11 women and observed that the amaranth provided women with a GI value of 107 and an insulin curve consistent with stimulation of insulin production. The authors have thus concluded that extrusion of the amaranth flour causes a high glycemic and insulin response, and that patients who chose amaranth to manage their celiac disease should plan their diets to ensure the adequate control of blood glucose.

Furthering the above study, Capriles and others (2008), have compared the *in vitro* digestibility of the starch of amaranth seeds and white bread. Raw seeds resulted in rapidly digestible starch content of 30.7% db and a predicted GI of 87.2. The cooked, extruded and popped preparation forms were digested similar to white bread (92.4; 91.2; and 101.3, respectively), and the seeds in the form of either flakes and toasted showed a higher GI (106 and 105.8, respectively). Cooking and extrusion did not alter the digestibility of the seed content. No differences were observed in the digestibility of popped, flake and toasted amaranth. The authors concluded that amaranth is a high GI food, probably due to the small size of its starch granules, the low content of resistant starch (<1%) and its tendency to completely lose the crystalline and granular structure of the starch during the heat treatment processes.

Oxidative stress has a role in the complications of diabetes, which suggests that the production of oxidants increases as a function of glucose metabolism or free fatty acid metabolism through multiple pathways. Oxidative stress may accelerate the basic process of various pathologies (Venugopal and others 2002; Kuroki and others 2003).

Effect on Liver Function

Besides the effects cited on the blood glucose levels, the work of Kim and other (2006a,b) also reported that feeding rats with either the whole grain or its oil resulted in an improvement (decrease) in the animals' AST (aspartate aminotransferase) and ALT (alanine aminotransferase) enzymes, which are liver function markers. Moreover, there was a reduction in TBARS levels (thiobarbituric acid reactive substances, lipid peroxidation and oxidative stress indexes) in the liver cytosol. Considering that the fecal excretion of cholesterol, triacylglycerols, and bile acids of the diabetic animals that consumed amaranth grain and amaranth oil was likewise substantially increased, it is understood that the actions of this grain on the general metabolism can be rather extensive.

Effect on Hypertension

The renin–angiotensin system is a biochemical system that helps control blood pressure. As angiotensinogen is released in response to a drop in blood pressure, sodium depletion or a reduction in plasma volume, the decapeptide angiotensin I is produced (Ondetti and Cushman 1982), followed by the cleavage of the dipeptide His-Leu by the angiotensin-converting enzyme (ACE) to form angiotensin II, a potent vasoconstrictor (Li and others 2004).

A series of reports by several researchers attest to the existence of several proteins capable of generating peptides that can inhibit the function of ACE. Silva-Sánchez and others (2008) investigated the presence of the peptide lunasin in amaranth grains, characterized it and studied its anticarcinogenic properties. The authors concluded that amaranth grains may be a potential source of several bioactive peptides with relevant actions on cancer and hypertension.

Tiengo and others (2009) evaluated the ACE-inhibiting activity and the binding capacity of bile acids of defatted amaranth flour and its *in vitro* products. The alcalase-hydrolyzed protein showed the highest inhibiting activity before and after *in vitro* digestion, suggesting that alcalase releases peptides that are not affected by gastrointestinal enzymes.

Tovar-Pérez and others (2009) studied fractions of peptides that inhibit ACE obtained from albumin 1 and the globulin of amaranth grains (*A. hypochondriacus*) by alcalase hydrolysis. The inhibitory activity against ACE of the albumin 1 products after 15 h of hydrolysis was 40%, and from globulin 35%, after 18 h of hydrolysis.

Vecchi and Añon (2009), in turn, have gathered evidence supporting the presence of antihypertensive peptides also in globulin 11S, one of the most important constituents of the *A. hypochondriacus* grain. A three-dimensional model of globulin 11S was built, and the antihypertensive peptides were mapped through a computational method. The occurrence of 2 tetrapeptides, ALEP and VIKP, was experimentally observed through an *in vitro* evaluation of ACE inhibition, with values of 6.32 mM and 175 μM, respectively.

Anti-Anemic Effect

The causes of anemia may be due to a number of situations, including chronic infections; hereditary blood problems; or the lack of one or more essential nutrients necessary for the formation of hemoglobin, such as iron, folic acid, B12, B6 and C vitamins, and proteins. Iron deficiency is the most common kind of anemia (Queiroz and Torres 2000), and amaranth grain may be used as an interventional carrier to fight the deficiency.

Whittaker and Ologunde (1990) evaluated the biological availability of iron in a cereal of amaranth grains in weaned male Sprague–Dawley rats induced to anemia. The amaranth cereal was fortified with 3 iron compound sources, ferric, sodium EDTA-chelate (NaFeEDTA), ferrous fumarate ($FeC_4H_2O_4$), and ferrous sulfate heptahydrate ($FeSO_4 \cdot 7H_2O$), and was compared to cereal from amaranth grains without iron fortification. Body weight, hemoglobin concentration, percentage of hematocrit and the relative biological value (RBV) were evaluated. The normal weight gain and high RBV showed good absorption of the nutrients in unfortified cereal from amaranth grains; however, the groups of animals that received iron-fortified cereal showed a significant increase in hemoglobin and hemoglobin gain compared to the group fed with unfortified cereal.

In another study, Ologunde and others (1991) observed the biological availability of fortified amaranth grains in weaned male Sprague–Dawley rats compared to unfortified amaranth grains, and using casein with ferrous sulfate ($FeSO_4$) as a control group. The compounds used were NaFeEDTA, $FeC_4H_2O_4$ and $FeSO_4$. Iron ingestion, increases in hemoglobin, the availability of binding capacity of iron, and serum iron and non-heme iron levels in the liver and the RBV were determined. The RBV were 0.40, 1.55, 1.75, 1.67, and 1.00 for animals that received NaFeEDTA, $FeC_4H_2O_4$ and $FeSO_4$ and casein with $FeSO_4$, respectively. The RBV of the nonfortified cereal was 40%, suggesting that the amaranth without fortification had a low contribution. The authors concluded that amaranth is an ideal cereal to be used in iron fortification and that the most appropriate form of iron is $FeC_4H_2O_4$.

The iron biological availability in ironfortified and nonfortified amaranth flour using a $FeSO_4$-fortified casein control diet was later reevaluated by Ologunde and others (1994). The flour of amaranth grains was fortified with NaFeEDTA, $FeC_4H_2O_4$, and $FeSO_4$. Weaned Sprague–Dawley male rats were used. Iron ingestion, iron gain in hemoglobin, iron availability, total iron binding capacity, iron serum, nonheme iron in the liver, volume of red cells and RBV were observed. The results were similar to those of the previous study (Ologunde and others 1991).

Antioxidant Activity

Antioxidant activity has been reported in several of the various fractions of amaranth. The *in vitro* antioxidant activity of 2 amaranth grain species, *A. caudatus* and *A. paniculatus,* in a model system of β-carotene/linoleic acid was reported by Klimczak and others (2002). These authors estimated the content of phenolic compounds by the Folin–Ciocalteu method as being 39.17 mg/100 g in *A. caudatus* and 56.22 mg/100 g in *A. Paniculatus.*

The biological antioxidant properties, and the amount of oil, squalene and phenolic compounds have also been determined in two *A. caudatus* grain varieties (Oscar Blanco and Victor Red) by Conforti and others (2005). The antioxidant activity was evaluated using a lipid peroxidation assay, The varieties showed different squalene amounts; however, the antioxidant activity did not show significant statistical differences. Nevertheless, a methanolic extract of both varieties displayed antidiabetic activity, showing 50.5% for *A. caudatus* var. Oscar Blanco and 28% for *A. caudatus* var. Victor Red at a concentration of 25 mg/ml.

The phenolic and flavonoid compositions of two *A. cruentus* cultivars were determined by Pasko and others (2008; Table 4). Later, the same group investigated the antioxidant capacity, the amount of phenolic compounds and the content of anthocyanins in *A. cruentus* grains and sprouts. These authors found that at 4 d of germination the seeds significantly increased, not only in the total contents of phenolics and anthocyanins, but also in their antioxidant capacity, as measured by ferric reducing ability of plasma (FRAP), antioxidant capacity by 2,2'-azino-bis(3-ethylbenzothiozoline-6-sulphonic acid (ABTS) and Diphenylpicrylhydrazyl. From these results the authors concluded that although the grains contained a considerable amounts of phenolic compounds, and that the sprouts became a significant source of the flavonoid rutin, thus contributing to the substantially greater levels of antioxidant activity of the sprouts (Pasko and others 2009).

Pasko and others (2011) further evaluated the effect of amaranth grains on oxidative stress in the plasma, heart, kidney, and pancreas of rats. Fructose was administered to induce oxidative stress, which was manifested through an increase of malondialdehyde and a decrease of enzyme antioxidant capacity in the plasma and selected tissues. The ingestion of amaranth grains (310 and 155 g/kg of diet) restored the activity of a number of enzymes and influenced the oxidative stress through the decrease of malondialdehyde, the increase of ferric ion reduction capacity in the plasma (FRAP) and the activity of antioxidant enzymes (erythrocyte superoxide dismutase—eSOD, catalase—CAT, and glutathione peroxidase—GPx1). The results showed that amaranth grains may have a moderate, dose-dependent protective effect against the changes promoted by the fructose-induced oxidative stress in rats through the reduction of lipid peroxidation and increased antioxidant capacity of the tissues.

Celiac Disease

Celiac disease is manifested as an enteropathy of sensitivity to gluten in genetically predisposed individuals. It is characterized by constant injuries of intestinal mucosa caused by gluten ingestion, and the mucosa can completely recover due to the total elimination of gluten from the diet (Molberg and others 2000). The gluten prolamins (gliadin, secalin, and hordein) are associated with injuries of the intestinal mucosa (Sdepanian and others 1999; Valder and others 2002). The only known therapy for patients diagnosed with celiac disease consists of the withdrawal of dietary products that contain gluten.

Therefore, the most sensible strategy is to develop a variety of nutritious foods, such as those derived from amaranth grain. In fact, amaranth has been used for some time by patients with celiac disease because it does not cause allergic reactions for the intestinal mucosa Thompson (2001). Tosi and others (1996) produced gluten-free cookies from whole amaranth flour, cornstarch, eggs, margarine, sugar, baking soda, potassium bitartrate, and butylhydroxytoluene. The cookie showed a high content of protein (5.7 g/100 g) and dietary fiber (1.1 g/100 g) satisfactorily comparing with commercially available traditional cookies without gluten.

Meanwhile, Marcílio and others (2005) used the surface-response methodology for the development of nutritious cookies for celiac disease patients, with amaranth flour which was proven to be gluten free. The cookie with the lowest amaranth flour content met the highest acceptance rating in a sensory analysis trial that was conducted with nonceliac consumers.

From a tolerability study of 40 amaranth varieties, using both SDS-PAGE-immunoblotting and ELISA, it has been established that their binding affinities for both specific anti-gliadin antibodies and human IgAs are quite similar, most of them being in a range below 20 μg/g, as measured by ELISA (Ballabio and others 2011).

Anti-Allergic Action

Research has suggested that the amaranth grain has may be used in the development of nonallergenic food products, with an added potential for use in fighting allergies.

Hibi and others (2003) discovered that some components of the *A. hypochodriacus* grain can inhibit the production of IgE and increase the cytokine Th1 synthesis, both *in vitro* and *in vivo*, as a result of suppressing the cascade of allergenicity for specific antigens. *In vitro*, the studies showed that the soluble water fraction of the amaranth grain promotes the development of helper cells T type 1 (Th1) phenotype, whereas the amaranth extract suppresses the production of IgE, which inhibits the allergic cascade. In *in vivo* studies, mice were fed with amaranth flour and defatted grain soluble extract, and a nonallergenic potential was observed, which may be applied in allergic diseases such as asthma and atopic dermatitis.

Conclusion

Although the great majority of the research about the beneficial functions and actions of amaranth has been conducted in experimental animal models, there are compounds in the grain with potentially beneficial medicinal properties present in the various fractions. Because one of the basic principles of functional foods is the functionality of bioactive substances through multiple metabolic paths, the beneficial health effects of amaranth are likely due to the joint presence of all of them, as found in the whole grain. Future research should be directed to epidemiologic studies and towards consolidating the mechanisms of action, especially in the human body. Nevertheless, it is also desirable to conduct research aimed at determining the minimum amount of amaranth that should be consumed through the diet in order to produce the expected effects. Caution has been recommended, however, concerning the potential effects of the elevated GI associated to the highly digestible starch present in both popped and extruded forms of the grain.

Conflicts of Interest

The authors have no conflicts of interest to declare.

Acknowledgments

The authors are grateful to CNPq (Brazilian Natl. Council for Research and Dept.) for the grant to author Valéria Maria Caselato-Sousa.

References

Amaya-Farfan J, Marcílio R, Spehar RC. 2005. Should Brazil invest in new crop grains? Seg Alim Nutr 12:47–56.

Ballabio C, Uberti F, Di Lorenzo C, Brandolini A, Penas E, Restani P. 2011. Biochemical and immunochemical characterization of different varieties of amaranth (*Amaranthus* L. ssp.) as a safe ingredient for gluten-free products. J Agric Food Chem 59:12969–74.

Barrio DA, Añón MC. 2010. Potential antitumor properties of a protein isolate obtained from the seeds of *Amaranthus mantegazzianus*. Eur J Nutr 49:73–82.

Becker R, Wheeler EL, Lorens K, Stafford A, Grosjean OK, Betschart AA, Saunders RM. 1981. A composition study of amaranth grain. J Food Sci 46:1175–80.

Belter A, Skupinska M, Giel-Pietranszuk M, Grabarkiewicz T, Rychlewski, L, Barciszewski J. 2011. Squalene monooxygenase, a target for hypercholesterolemic therapy. Biol Chem 392:1053–75.

Bennink MR, Om AS. 1998. Inhibition of colon cancer (CC) by soy phytochemicals but not by soy protein. FASEB J 12:3806.

Berger A, Gremaud R, Baumgartner M, Rein D, Monnard I, Kratky E, Geiger W, Burri J, Dionisi F, Allan M, Lambelet P. 2003. Cholesterol-lowering properties of amaranth grain and oil in hamsters. Intl J Vitam Nutr Res 73:39–47.

Betim CB. 2008. Metabolic Changes Beneficial to Rats Arising from the Consumption of Amaranth Master's Thesis. School of Food Engineering, University of Campinas Library. Available from: http://www.fea.unicamp.br/alimentarium/ver_documento.php?did=583. Accessed February 28, 2012.

Brenner D, Willians JT. 1995. Grain amaranth (*Amaranth* spp). In: Willians JT, editor. Underutilized crops: cereals and pseudocereals. London: Chapman & Hall. p 128–86.

Bressani R. 1989. The proteins of grain amaranth. Food Rev Intl 5:13–38.

Bressani R, de Martell ECM, de Godinez CM. 1993. Protein quality evaluation of amaranth in adult humans. Plant Foods Hum Nutr 43:123–43.

Bruni R, Medici A, Guerrini A, Scalia S, Poli F, Muzzoli M, Sacchetti G. 2001. Wild *Amaranthus caudatus* seed oil, a nutraceutical resource from Ecuadorian flora. J Agric Food Chem 49:5545–60.

Capriles VD, Coelho KD, Guerra-Matias AC, Arêas JAG. 2008. Effects of processing methods on amaranth starch digestibility and predicted glycemic index. J Food Sci 73:H160–4.

Chaturvedi A, Sarojini G, Devi NL. 1993. Hypocholesterolemic effect of amaranth seeds (*Amaranthus esculantus*). Plant Foods Hum Nutr 44:63–70.

Chaturvedi A, Sarojini G, Nirmala GI, Nirmalamma N, Satyanarayana D. 1997. Glycemic index of grain amaranth, wheat and rice in NIDDM subjects. Plant Foods Hum Nutr 50:171–8.

Chavez-Jauregui RN, Silva MEMP, Arêas JAG. 2000. Extrusion cooking process for amaranth. J Food Sci 65:1009–15.

Conforti F, Giancarlo A, Statti A, Loizzo MR, Gianni A, Sacchetti B, Poli F, Menichini F. 2005. In vitro antioxidant effect and inhibition of a alpha-amylase of two varieties of *Amaranthus caudatus* seeds. Biol Pharm Bull 28:1098–102.

Czerwinski J, Bartnikowska E, Leontowicz H, Lange E, Leontowicz M, Katrich E, Trakhtenberg S, Gorinstein S. 2004. Oat (*Avena sativa* L.) and amaranth (Amaranthus hypochondriacus) meals positively affect plasma lipid profile in rats fed cholesterol-containing diets. J Nutr Biochem 15:622–9.

Danz RA, Lupton JR. 1992. Physiological-effects of dietary amaranth (*Amaranthus cruentus*) on rats. Cereal Foods World 37:489–94.

Dixit AA, Azar KMJ, Gardner CD, Palaniappan LP. 2011. Incorporation of whole, ancient grains into a modern Asian Indian diet to reduce the burden of chronic disease Nutr Rev 69:479–88.

Early D, Early JC. 1987.Tranferencia de tecnología indígena para la preparación de la Kiwicha (*Amaranthus*). Primeira parte. El amaranto y su potencial. Boletín 4:8–12.

Escrich E, Solanas M, Moral R, Escrich R. 2011. Modulatory effects and molecular mechanisms of olive oil and other dietary lipids in breast cancer. 17:817–30.

Escudero NL, de Arellano ML, Luco JM, Gimenez MS, Mucciarelli SI. 2004. Comparison of the chemical composition and nutritional value of Amaranthus cruentus flour and its protein concentrate. Plant Foods Hum Nutr 59:15–21.

Escudero NL, Zirulnik F, Gomez NN, Mucciarelli SI, Gimenez MS. 2005. Influence of a protein concentrate from *Amaranthus cruentus* seeds on lipid metabolism. Exp Biol Med 231:50–9.

Gonor KV, Pogozheva AV, Derbeneva SA, Mal'tsev GIu, Trushina EN, Mustafina OK. 2006a. The influence of a diet with including amaranth oil on antioxidant and immune status in patients with ischemic heart disease and hyperlipoproteidemia. Vopr Pitan 75:30–3.

Gonor KV, Pogozheva AV, Kulakova SN, Medvedev FA, Miroshnichenko LA. 2006b. The influence of diet with amaranth oil on lipid metabolism in patients with ischemic heart disease and hyperlipoproteidemia. Vopr Pitan 75(3):17–21.

Grajeta H. 1997. Effects of amaranthus (*Amaranthus cruentus*) seeds on lipid metabolism in rats. Bromatol Chem Toksykol 30:25–30.

Grajeta H. 1999. Effect of amaranth and oat bran on blood serum and liver lipids in rats depending on the kind of dietary fats. Nahrung 43:114–7.

Guerra-Matias A, Arêas JAG. 2005. Glycemic and insulinemic responses in women consuming extruded amaranth (*Amaranthus cruentus* L). Nutr Res 25:815–22.

Hibi M, Hachimura S, Hashizume S, Obata T, Kaminogawa S. 2003. Amaranth grain inhibits antigen-specific IgE production through augmentation of the IFN-gamma response in vivo and in vitro. Cytotechnology 43:33–40.

Huerta-Ocampo JA, de la Rosa APB. 2009. Amaranth: a pseudo-cereal with nutraceutical properties. J Diet Suppl 6:390–417.

Huerta-Ocampo JA, de la Rosa, APB. 2011. Amaranth: a pseudo-cereal with nutraceutical properties. Curr Nutr Food Sci 7:1–9.

Irving DW, Betschart AA, Saunders RM. 1981. Morphological studies on *Amaranthus cruentus*. J Food Sci 46(4):1170–74.

Jenkis DJ, Kendall CW, Augustin LS, Franceschi S, Hamidi M, Marchie A, Jenkis A, Axelsen M. 2002. Glycemic index: overview of implications in health and disease. Am J Clin Nutr 76(1):266S-73S.

Kabiri N, Asgary S, Madani H, Mahzouni P. 2010. Effects of Amaranthus caudatus l. extract and lovastatin on atherosclerosis in hypercholesterolemic rabbits. J Med Plants Res 4: 355–64.

Kadoshnikov SI, Kadoshnikova IG, Kulikov YA, Martirosyan, DM. 2008. Researches of fractional composition of protein of amaranth. Curr Nutr Food Scien 4:196–205.

Kim HK, Kim MJ, Cho HY, Kim EK, Shin DH. 2006a. Antioxidative and antidiabetic effects of amaranth (*Amaranthus esculantus*) in streptozotocin-induced diabetic rats. Cell Biochem Funct 24:195–9.

Kim HK, Mi-Jeong K, Dong-Hoon S. 2006b. Improvement of lipid profile by amaranth *(Amaranthus esculantus)* supplementation in streptozotocin-induced diabetic rats. Ann Nutr Metab 50:277–81.

Klimczak I, Malecka M, Pacholek B. 2002. Antioxidant activity of ethanolic extracts of amaranth seeds. Nahrung 46:184–6.

Kulakova SN, Pozdniakov AL, Korf II, Karagodina ZV, Medvedev FA, Viktorova EV, Gonor KV, Kamysheva IM, Gadzhieva ZM. 2006. Amaranths oil: peculiarities of chemical composition and influence on lipid metabolism by rats. Vopr Pitan 75:36–42.

Kunyanga CN, Imungi JK, Okoth MW, Biesalski HK, Vadivel V. 2012. Total phenolic content, antioxidant and antidiabetic properties of methanolic extract of raw and traditionally processed Kenyan indigenous food ingredients. LWT—Food Sci Technol 45 (2012):269–76.

Kuroki T, Isshiki K, King GL. 2003. Oxidative stress: the lead or supporting actor in the pathogenesis of diabetic complications. J Am Soc Nephrol 14(3):S216–20.

Lehmann JW. 1996. Case history of grain amaranth as an alternative crop. Cereal Foods World 4:399–410.

Li GH, Le GW, Shi YH, Sundar S. 2004. Angiotensin I-converting enzyme inhibitory peptides derived from food proteins and their physiological and pharmacological effects. Nutr Res 24:469–89.

Ludwig DS, Majzoub JA, Al-Zahrani A, Dallal GE, Blanco I, Roberts SB. 1999. High glycemic index foods, overeating and obesity. Pediatrics 103:26–32.

Marcílio R, Amaya-Farfan J, Ciacco CF, Spehar CF. 2003. Fracionamento do grão de amaranto (*A. cruentus*) brasileiro e suas características composicionais. Cienc Tecnol Alim 23:511–16.

Marcílio R, Amaya-Farfán J, Silva MAAP. 2005. Avaliação da farinha de amaranto na elaboração de biscoito tipo "cookie" para celíacos. Braz J Food Technol 8:175–81.

Martirosyan DM, Miroshnichenko LA, Kulakova SN, Pogojeva AV, Zoloedov V. 2007. Amaranth oil application for coronary heart disease and hypertension. Lipids Health Dis 6:1–12.

Mendonça S, Saldiva PH, Cruz RJ, Arêas JAG. 2009. Amaranth protein presents cholesterol-lowering effect. Food Chem 116:738–42.

Miettinem TA, Vanhanen A. 1994. Serum concentration and metabolism of cholesterol during rapeseed oil and squalene feeding. Am J Clin Nutr 59:356–63.

Molberg O, McAdam SN, Sollid LM. 2000. Role of tissue transglutaminase in celiac disease. J Pediatr Gastroenterol Nutr 30:232–40.

Montagnani S, Tuccori M, Lombardo G, Testi A, Mantarro S, Ruggiero E, Blandizzi C. 2011. Autoimmune hemolytic anemia following MF59-adjuvanted influenza vaccine administration: a report of two cases. Ann Pharmacother 45(1):e8.

Monteros CJ, Nieto CC, Caicedo CV, Rivera MM, Vimos CN. 1998. Iniap alegria primera variedade mejorada de amaranto para la sierra ecuatoriana. In: Producción y procesamiento de quinua en Ecuador. Available from: http://www.idrc.ca. Accessed May 12, 2011.

Ologunde MO, Shepard RL, Afolabi OA, Oke OL. 1991. Bioavailability to rats of iron from fortified grain amaranth flour. Intl J Food Sci Technol 26:493–500.

Ologunde MO, Shepard RL, Afolabi OA, Oke OL. 1994. Bioavailability to rats of iron from fortified grain amaranth. Plant Foods Hum Nutr 45:191–201.
Ondetti MA, Cushman DW. 1982. Enzymes of the renin-angiotensin system and their inhibitors. Ann Rev Biochem 51:283–308.
Pasko P, Barton H, Zagrodzki P, Gorinstein S, Fołta M, Zachwieja S. 2009. Anthocyanins, total polyphenols and antioxidant activity in amaranth and quinoa seeds and sprouts during their growth. Food Chem 115:994–8.
Pasko P, Bartn H, Zagrodizki P, Chlopicka J, Izewska A, Gawlik M, Gawlik M, Gorinstein S. 2011. Effect of amaranth seeds in diet on oxidative status in plasma and selected tissues of high fructose-fed rats. Food Chem 126:85–90.
Pasko P, Sajewicz M, Gorinstein S, Zachwieja Z. 2008. Analysis of selected phenolic acids and flavonoids in *Amaranthus cruentus* and *Chenopodium quinoa* seeds and sprouts by HPLC. Acta Chrom 20:661–72.
Plate AYA, Arêas JAG. 2002. Cholesterol-lowering effect of extruded amaranth *(Amaranthus caudatus L.)* in hypercholesterolemic rabbits. Food Chem 76:1–6.
Queiroz SS, Torres MAA. 2000. Anemia ferropriva na infância. J Pediatr 76:298–304.
Queiroz YS, Soares RAM, Capriles VD, Torres EAFD, Areas JAG. 2009. Effect of processing on the antioxidant activity of amaranth grain. Arch Latinoam Nutr 59:419–24.
Qureshi AA, Lehmann JL, Peterson DM. 1996. Amaranth and its oil inhibit cholesterol biosynthesis in 6-week-old female chickens. J Nutr 128:1972–78.
Repo-Carrasco-Valencia R, Peña J, Callio H, Salminen S. 2009. Dietary fiber and other functional components of two varieties of crude and extruded Kiwicha (*Amaranthus caudatus*). J Cereal Sci 49:219–24.
Rodas B, Bressani R. 2009. The oil, fatty acid and squalene content of varieties of raw and processed amaranth grain. Arch Latinoam Nutr 59:82–7.
Sawada M, Matsuao M, Seki J. 2002. Inhibition of cholesterol synthesis causes both hypercholesterolemia and hypocholesterolemia in hamsters. Biol Pharm Bull 25:1577–82.
Sdepanian VL, Morais MB, Fagundes-Neto U. 1999. Doença celíaca: a evolução dos conhecimentos desde sua centenária descrição original até os dias atuais. Arq Gastroenter 36: 244–57.
Shin DH, Heo HJ, Lee YJ, Kim HK. 2004. Amaranth squalene reduces serum and liver lipid levels in rats fed a cholesterol diet. Br J Biomed Sci 61:11–4.
Silva-Sánchez C, de la Rosa AP, León-Galván MF, de Limen BO, de León-Rodríguez A, de Mejía EG. 2008. Bioactive peptides in amaranth (Amaranthus hypochondriacus) seed. J Agric Food Chem 56:1233–40.
Singhal RS, Kulkarni PR. 1988. Review: amaranths-an underutilized resource. Intl J Food Sci Technol 23:125–39.
Teutonico R, Knorr D. 1985. Amaranth, composition, properties, and applications of a rediscovered food crop. Food Technol 39:49–60.
Thompson T. 2001. Case problem: questions regarding the acceptability of buckwheat, amaranth, quinoa, and oats from a patient with celiac disease. J Am Diet Assoc 101:586–7.
Tiengo A, Faria M, Netto FM. 2009. Characterization and ACE-inhibitory activity of amaranth proteins. J Food Sci 74:H121–6.
Tosi EA, Ciappini MC, Masciarelli R. 1996. Utilizacin de la harina integral de amaranto *(Amaranthus cruentus)* en la fabricacin de galletas para celacos. Alimentaria 33:49–55.
Tovar-Pérez EG, Guerrero-Legarreta I, Farrés-Gonzales A, Soriano-Santos J. 2009. Angiotensin I-converting enzyme-inhibitory peptide fractions from albumin 1 and globulin as obtained of amaranth grain. Food Chem 116:437–44.
Tritto E, Mosca F, De Gregorio E. 2009. Mechanism of action of licensed vaccine adjuvants. Vaccine 27(25–26):3331–4.
Ulbricht C, Abrams T, Conquer J, Costa D, Grims-Serrano JM, Taylor S, Varguese M. 2009. An evidence-based systematic review of amaranth (*Amaranthus spp.*) by the natural standard research collaboration. J Diet Suppl 6:390–417.
United States Department of Agriculture. Nutrient Data Laboratory (USDA). 2010. Available from: http://www.nal.usda.gov/fnic/foodcomp/cgi-bin/measure.pl. Accessed December 26, 2011.
Valder WL, de Ru A, van der Wal Y, Kogy YMC, Benckhinjesen W, Mearin ML, Drijifhout JW, van Veelen P, Koning F. 2002. Specificity of tissue transglutaminase explains cereal toxicity in celiac disease. J Exp Med 195:643–9.
Vecchi B, Añón MC. 2009. ACE inhibitory tetrapeptides from *Amaranthus hypochondriacus* 11S globulin. Phytochemistry 70:864–70.
Venugopal SK, Devaraj S, Yang T, Jialal I. 2002. Alpha-tocopherol decreases superoxide anion release in human monocytes under hyperglycemic conditions via inhibition of protein kinase C-alpha. Diabetes 51:3049–54.
Whittaker P, Ologunde M. 1990. Study of iron bioavailability in a native Nigerian grain amaranth cereal for young children, using a rat model. Cereal Chem 67:505–8.
Yu LG, Milton JD, Fernig DG, Rhodes JM. 2001. Opposite effects on human colon cancer cell proliferation of two dietary Thomsen-Friedenreich antigen-binding lectins. J Cell Physiol 186:282–7.