Chapter 3

The Maize Contribution in the Human Health

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Abstract

Maize (*Zea mays*) is a cereal very important around the world and is a fundamental element of the Mexican cuisine. The basis of Mexican traditional food is maize prepared by the process of "nixtamalización" which conserves the properties of the whole grain cereal. The phytochemical profiles of *Z. mays* contain total phenolics, ferulic acid, carotenoids, and flavonoids called anthocyanins. It is generally accepted that anthocyanin food colors do not exert obvious toxicity, teratogenicity, or mutagenicity and, indeed, anthocyanins may inhibit mutagenesis. Nutraceutical properties of phenolic and anthocyanin compounds in the maize that offer antioxidant activities is shown in five types of corn (white, yellow, high carotenoid, blue, and red). Therefore, the consumption of maize or its derivates such as tortillas, tortilla chips, etc., become functional food, with the ability to be used to prevent the incidence of diseases such as cancer, diabetes, obesity, and neurodegenerative disorders. Likewise, a diet that includes corn can be used during the management of these diseases. However, it is necessary to carry out more studies that highlight the efficiency of corn byproduct consumption during these diseases.

Keywords: maize, nutraceutics, antioxidants, chronic diseases, functional foods

1. Introduction

Corn is by far the cereal most commonly consumed by the people and cultures of the American continent: ancient civilizations, such as the Olmec and the Teotihuacan in Mesoamerica and the Quechuas in the Andean region of South America, developed around this plant [1].

Pre-Columbian natives deified this plant due to its relevance in their lives; the sacred book of the Quiche, the Popol Vuh, even tries to explain the origin of man by narrating how corn was given to mankind by the gods Paxil and Cayalan [2].

Corn is a monocotyledonous plant cultivated widely around the world and has constituted itself in one very common staple food. Corn and its wild variant, teosinte, belongs to the Poaceae family, of the Maydeas tribe; species of the *Tripsacum* genus are wild variants of corn, also originating in the American continent, but without any direct trade value. This family also includes important agricultural crops, such as wheat, rice, sorghum, barley, and sugar cane. Based on the characteristics of the ear or male inflorescence, the *Zea* genus divides into two sections, luxurians and annuals [3].

In Latin America, corn is a staple food product, and so it is the crop of greatest production, and it is also used as a dietary input for livestock, and for the industrial production of large numbers of products; that is why, from a nutritional, economic, political, and social point of view, it is the most important agricultural product. Generally, the diet of a people develops a collective memory and transcends mere food consumption, expressing socioeconomic relations and revealing acts deeply rooted in cultural symbolism [4, 5].

Corn as food has been found in archeological ruins and manuscripts such as the Florentine or the Mendoza Codices, wherein it has been possible to elucidate that corn represented on the main components of the Mesoamerican diet since the Middle Preclassic (1200–400 BC) [4–6]. Archeological remains also show the use and consumption of other plants important during that period; however, ancient settlers developed a preference for corn and it kept growing in popularity.

In pre-Hispanic times, the production of flours, pinole, and the ancient equivalent to modern "popcorn" stood out [7]. Currently, corn is widely consumed in of tortillas, arepas, toasts, tamales, snacks, corncobs, and in other various forms. When it comes to tortilla, it is now known that it not ancient as previously thought, but it was already prevalent in Mesoamerican diet by the time the Spaniards arrived at the continent. Today, the tortilla is considered as the basis of Mexican people's diet, directly related to its survival for over 3500 years [8]. The richness of indigenous cuisine based on corn was recorded in the reliable testimonies of conquistadors and chroniclers alike, from Hernán Cortés and Bernal Díaz del Castillo to Bernardino de Sahagún, all of them providing evidence of the high cultural development of ancient Mexicans, as well as of the rich diversity of corn, already noticeable back in those days. The miscegenation resulting from the Spanish Conquest had in gastronomy one of its main manifestations, enriching pre-Hispanic diet with elements from Spanish/Arab cuisine, and the other way around, too. However, the indigenous element dominated in this "food miscegenation," as can be seen in the fact that corn remains a fundamental ingredient and one of the main sources of energy in nowadays Latin American diet. An example of this can be seen in the fact that the average Mexican today obtains 1022 kilocalories and 26.3 g of protein from corn daily, which may represent 50% of an adult's daily intake, based on a diet of 2000 kilocalories with 56 g of protein [9].

2. Corn as healthy food

In recent years, cereal consumption has been linked to the reduction of chronic-degenerative diseases such as cancer, obesity, type 2 diabetes, cardiovascular and metabolic problems, and even symptoms associated with neurodegenerative problems. These health benefits have been attributed to the vast variety and high concentration of nutraceutical molecules present in cereals. Strictly speaking, these molecules cannot be considered as nutritional elements in themselves, but as bioactive components that can interact with biological systems from various cellular mechanisms, allowing optimal maintenance of the body's physiological functions, thus preventing the occurrence of diseases [10].

The confusion that usually arises when talking about concepts such as "nutrients," "nutraceuticals," "functional foods," and "nutritional supplements" should be noted. Clarifying these terms becomes relevant if one takes into account that the different qualities of the elements included in these categories can directly impact on their consumption. The term "nutrients" refers to the elements of a diet that can be absorbed by the body and incorporated into different physiological systems, allowing for basic functions to occur. For example, lipids and carbohydrates are known as the source of metabolic energy, as constituents of the cell membrane and as hormonal precursors; in its turn, the integration of proteins into the organism is used as an element of cellular structural reconstitution and integration into enzymatic systems. Also, vitamins and minerals allow for osmotic maintenance to occur, participate in nerve and muscle functioning, and can act as enzymatic cofactors. On the other hand, the term nutraceutical refers to the consumption of substances contained in food, able to promote beneficial effects on health without having direct participation in the basic processes of the different systems. The functional food concept encompasses natural or processed food products that contain biologically active compounds, which may or may not be nutrients. Together, these molecules must have the capacity to promote health benefits, preventing or aiding in the treatment of chronic diseases, in nontoxic quantities that can be included in a daily diet [11]. As an example of the above, the consumption of fish that provide omega fatty acids can be mentioned; also, the consumption of fruits and vegetables rich in minerals, vitamins, and dietary fiber, as well as other foods added with biologically active substances such as antioxidants and probiotics [12].

In recent times, cereals such as corn have been acknowledged as functional foods, as they are an important source of calories, as well as proteins, peptides, carbohydrates, fibers, and antioxidants with a nutraceutical function. The nutritional contribution of corn to the world population is undeniable, partly because of the great versatility of its kernels to produce food. Corn for consumption is mainly processed by three methods: dry milling, wet milling, and alkaline cooking (nixtamalization), and it is through these processes that the raw material for the production of different products is generated. Corn can be consumed in nixtamalized products such as tortillas and chips, in prepared beverages such as chicha morada, atole, tejuino, or pozol, in dishes such as polenta, pozole, or tamales, and all of these are merely a fraction of the many byproducts derived from this cereal. The flexibility with which this plant can be exploited should be emphasized, since its contribution to health keeping and improvement is not limited only to the kernel or its byproducts [13]; other anatomical parts of the plant such as stigmata, cobs, and leaf sheaths have proven to be an important source of nutraceutical molecules, as will be seen later in this chapter.

Corn kernels consist mainly of fiber, ranging from 61 to 86%, depending on the variety of the plant. Approximately 99% of the fiber is found in the endosperm and consists of starch (approximately 73% of the total weight), and the rest of resistant starch. The kernel also contains non-starch polysaccharides such as cellulose, hemicellulose, and, to a lesser extent, lignin (approximately 10% of the total weight), located mainly in the brand. Protein follows; depending on the variety of corn, it can range from 6 to 12%, calculated on the dry basis, while lipids represent around 3–6%. Out of these, between 81 and 85% is stored in the germ. Other phytochemical elements can also be found in pigmented and yellow varieties, in the form of secondary metabolites, phenolic compounds, and carotenoids for the most part. A very wide range of phenolic content exists among corn varieties, which has been assessed by the quantification of total polyphenols under the Folin–Ciocalteu reagent method, reporting amounts of 1756 mg of gallic acid equivalent/100 g of sample for a variety of purple corn with Andean genotype [14] and 266 mg gallic acid equivalent/100 g of sample for varieties of purple corn with Mexican genotype [15]. When it comes to Mexican white corn, amounts of 260 mg of gallic acid equivalent/100 g of sample have been reported; likewise, it is likely that corn types with a high profile of carotenoids contain a higher concentration of phenolic compounds, reporting 320 mg of gallic acid equivalent/100 g of sample [15]. It should be noted that yellow corn varieties have reported the highest carotenoid content, with an average dry base concentration of 13 μg of β-carotene equivalent/100 g of sample [16], although red varieties also synthesize carotenoids.

These elements act as nutraceuticals depending on their bioavailability, molecular structure, physicochemical characteristics, and their physiological effects, as well as on the properties acquired or lost after the different food byproducts have been processed.

3. Nutraceutical properties of corn

The kernel of corn contains proteins that have been classified into four groups in relation to their solubility. The most water-soluble proteins fall into the category of albumins, while proteins soluble in saline solutions are known as globulins. Proteins soluble in alcoholic solutions make up the group of prolamins or zeins, and proteins unable to be solubilized in any of the previous solutions form the group of glutelins. In view of this, the disposition and location of these proteins have a differential characteristic. For example, albumins and globulins are located mainly in the germ, while prolamins and glutelins can be found predominantly in the endosperm. In relation to their concentration, proteins are distributed unevenly in the corn kernel; 40% of the proteins are concentrated in zeins, followed by the glutelins, with 30%, and globulins and albumins together representing less than 5%. Of these, approximately 60% of the proteins are concentrated in the endosperm and are prolamins, with α-zein being the most abundant in corn, reaching up to 75% of the total prolamins [17]. Due to the water insolubility of corn proteins, its potential health benefits are limited; however, late technological advances have allowed to obtain peptides by hydrolysis in order to improve their bioavailability [18].

Once ingested, corn proteins are hydrolyzed by the activity of gastrointestinal enzymes such as pepsin, trypsin, and chymotrypsin. In vitro, this process can be carried out by the addition of enzymes, or by acidification or fermentation. Nonetheless, in vitro hydrolysis processes have shown some drawbacks, for example, when using acids, controlling the process can be complicated and some amino acids can be lost; also, protein hydrolysis turns out to be inefficient under the process of fermentation. As of late, enzymatic digestion has been chosen for in vitro isolation of bioactive peptides, which has proven to be a more efficient process. From two-amino acid peptides to 30-amino acid polypeptides can be isolated by means of these processes. Hydrophobic amino acids can be counted among peptides with bioactive capacity, structured with a positive charge and a proline in their C-terminal end [19]. On the other hand, dipeptides and tripeptides have greater resistance to the degradation of stomach, pancreatic, and intestinal proteases and peptidases, and larger peptides (six amino acids and larger) have a higher biological activity outside the intestine [20].

Studies have shown that bioactive peptides can have beneficial effects on health, mainly as antihypertensive, anticholesterolemic, antioxidant, anti-inflammatory, anticarcinogenic, antimicrobial, and others, due to their immunomodulatory properties. Likewise, it has been reported that they can help decrease the effects associated with high alcohol consumption. A large number of bioactive peptides have been obtained by means of the hydrolysis of zeins proteins, for example, the tripeptide lysine-proline-proline, and from the γ-zein protein, the valine-histidine-leucine-proline-proline-proline polypeptide, whereas the tripeptide proline-arginine-proline, which has also shown a biological functional activity, has been isolated from the α-zeins protein, as well as MBP-1 peptides from the corn kernel. Successful efforts have been made to isolate other peptides from corn gluten meal, such as Cys-Ser-Gln-Ala-Pro-Leu-Ala or Tyr-Pro-Lys-Leu-Ala-Pro-Asn-Glu. Overall, it has been observed that a large number of peptides can be isolated from the different components of corn, although their possible biological activity is still undergoing further research, as it is still necessary to carry out studies that help find the mechanisms from which these peptides can exert their biological activity.

As for the total fiber contained in corn, resistant starch is a type of non-digestible fiber, as it is highly resistant to the activity of digestive enzymes. The presence of resistant starch seems to be directly related to the percentage of amylose content. In normal corn, the presence of 34% of amylose is related to 0.8% of resistant starch, while high-amylose corn starch, the recorded presence of 83% amylose results in 39% resistant starch [21, 22]. However, resistant starch can be metabolized by the microbiota of the large intestine through fermentation and this in turn results in small chains of fatty acids [23]. Both the starch and the resistant starch contained in corn kernels have grown in relevance due to their possible function as regulators of body weight, thus a possible natural alternative for the treatment of obesity. On the other hand, these elements have also been linked to liver protection and the prevention of type 2 diabetes [24, 25].

In turn, phenolic compounds are a group of molecules whose chemical structure is made up of several hydroxyl groups linked to an aromatic group. When two or more rings are conjugated, a polyphenolic structure is generated; depending on the number of aromatic rings and the structural elements that bind them together, thousands of polyphenols have been identified. The polyphenols synthesized in corn can be classified into three groups according to their concentration and their contribution to human health; this way, we can speak of non-anthocyanin flavonoids, phenolic acids, and anthocyanin flavonoids. The group of non-anthocyanin flavonoids includes flavonols (rutin, isoquercetin, flavonol, morin, kaempferol, and quercetin) and flavonones (naringenin and hesperetin) [26], while the phenolic acids found in corn are protocatechuic acid, vanillic acid, syringic acid, trihydroxybenzoic acid, caffeic acid, chlorogenic acid, and p-hydroxyphenylacetic acid. Ferulic acid and p-coumaric acid are the compounds with more concentrates in corn, particularly in pigmented varieties [27, 28]. Total ferulic acid content detected in kernels of white varieties with Mexican genotype has been reported as 124,053 mg of ferulic acid equivalent/100 g of sample, while pigmented varieties such as blue or red corn have reported 129,985 and 130,297 mg of ferulic acid/100 g sample, respectively [15].

The food industry has exploited the varieties of yellow and white corn for a long time now; however, the use of pigmented varieties has gained more and more strength in the food sector recently, not only as a possible source of natural edible pigments but also for its properties as a functional food. Among the most common colors, red, blue, and black can be found. This pigmentation is conferred by anthocyanins. Anthocyanins are a group of natural pigments soluble in water, widely distributed in the different tissues of the plant. Anthocyanins are responsible for conferring shades ranging from red to blue and purple. Functionally, anthocyanins protect the plant from damage by radiation, partake in the defense against pathogens and/or predators, and in reproductive functions as pollinator attractants; likewise, they regulate the synthesis of growth factors such as auxin. In corn kernels, anthocyanins are stored mainly in the aleurone layer; it is also possible to find these molecules in the pericarp, or in both structures. Even native non-pigmented varieties, pure lines, and hybrids have some pigmented tissue in the roots of the seedling or anthers [29–31]. In pigmented corn, the content of anthocyanins can be evaluated as low, medium, and high, with values that range between 5.9 and 3045 mg of cyanidin-3-glucocide equivalent/100 g of sample, while values reported in white or yellow corn varieties range from 0.9 to 1.2 mg of cyanidin-3-glucocide equivalent/100 g [32, 33]. It is also possible to find anthocyanins in other tissues such as cobs and leaf sheaths, but the concentration in these structures is not precisely defined. Some studies have been found concentrations ranging from 430 to 11,700 mg of cyanidin-3-glucocide equivalent/100 g of sample for the cob [33], whereas for the leaf sheaths, it has been possible to extract up to 17,7900 mg of cyanidin-3-glucide equivalent/100 g of sample [34]. It should be noted that cyanidin and its derivates are more abundant in pigmented corn varieties [35].

Carotenoids are natural pigments in corn and other plants, responsible for conferring colorations ranging from yellow to orange. Carotenoids participate in functions such as photosynthesis due to their ability to absorb light from different spectra and transfer energy to chlorophyll. The carotenoids have a skeleton made up of 40 carbons of isopropene units. These structures can be cycled in one or both terminations, having several levels of hydrogenation or can have oxygenated functional groups and, according to this, can be classified into carotenes, which are tetrapenoid hydrocarbons, consisting solely of carbon and hydrogen atoms, and xanthophylls or oxo-carotenoids, structures that contain at least one oxygen. Yellow corns contain lutein, zeaxanthin, β-cryptoxanthin, and β-carotenes [36, 37]. Carotenoid concentration can vary widely depending on genotypes and external characteristics. For example, the blue variety of the Mexican genotype has concentrations of 0.18 μg of β-carotene equivalent/g of sample [38], while the yellow variety of the Canadian genotype has concentrations of up to 60 μg of xanthophylls equivalent/g of sample [39]. Carotenoids are found mainly in the germ, followed by the aleurone and the endosperm. Generally, by decreasing lipoperoxidation, carotenoids can act as antioxidant agents in lipid environments.

Tissues such as stigmata, cobs, stems, and leaf sheaths of corn can be an important source of anthocyanins, ferulic acid, and some other substances that may help improve health; even when those are not products fit for human consumption, they could be processed to obtain extracts with a potential nutraceutical use. As of today, there is scientific evidence of the use of stigmata for the treatment of conditions such as kidney disorders, hypertension, and some neurodegenerative diseases. Some of the bioactive compounds that can be isolated from these tissues are terpenoids, steroids, saccharides, cerebrosides, flavonoids such as flavonones and anthocyanins, and lignan [40, 41].

3.1. Antioxidant properties of corn

Reactive oxygen species (ROS) are a group of molecules derived from oxygen that are characterized by their high reactivity and a short life span. The reactivity of these molecules is due to the presence of two unpaired electrons in the outermost electron layer. Among the molecules included in the ROS group are the superoxide free radical (O_2^-), the hydroxyl radical (OH^-), and the hydrogen peroxide (H_2O_2). ROS can be generated by endogenous, extracellular, and intracellular mechanisms. The main source of ROS is the mitochondria during the cellular respiration process, followed by cellular metabolism processes, whereas exogenous production of ROS arises from smoking, ultraviolet radiation, ionizing radiation, drug consumption, and the presence of toxins. The damage generated by ROS is due to their reductive property, and if not properly regulated, they can alter cell integrity due to the peroxidation of lipids and proteins of the cell membrane, being able to even damage the structure of DNA.

Oxidative stress is generated by excess ROS, linked to cell damage associated with chronic-degenerative diseases such as cancer, chronic inflammation, cardiovascular diseases, neurodegenerative problems, and metabolic dysfunction. The process of cellular oxidation is regulated by antioxidant mechanisms, which delay or prevent the formation of ROS. Antioxidant protection is achieved through the correct balance between pro-oxidants and endogenous and/or exogenous antioxidants. Cells have an endogenous system of enzymes such as superoxide dismutase (SOD), catalases (CAT), glutathione peroxidase (GPx), quinone reductase (QR), and glutathione reductase (GR), which function as ROS stabilizers [42]. Compounds with antioxidant activity can be introduced in the body through diet, and corn is one important source of such compounds.

Fruits, vegetables, and seeds in general contain a great diversity of antioxidants that can act for the benefit of health more efficiently than some synthetic antioxidants. Recent studies have shown that the consumption of cereals can provide a greater antioxidant activity [2600–3500 μmol of Trolox equivalent (TE)/100 g] compared to some fruits (1200 μmol of TE/100 g) or vegetables (450 μmol of TE/100 g). Carotenoids, bioactive peptides, and flavonoids such as corn anthocyanins can act as antioxidant agents by lowering ROS levels, or by activating endogenous antioxidant systems that reduce cell damage. The antioxidant activity of nutraceuticals in corn is different; for example, when assessing the antioxidant activity of the carotenoids of Croatian genotype corn through the ABTS technique, values of

0.767 μmol of TE/g of sample were reported [34], whereas the total extracts of Italian genotype corn have reported antioxidant activity of 29 μmol of TE/g of sample [43]. These data suggest that carotenoids only contribute approximately 5% of the total antioxidant activity, while the phenolic fraction has the highest antioxidant activity. It should be noted that the antioxidant activity of carotenoids depends on their concentration, their distribution in the kernel, and the type of carotenoid, as studies have found activity values of 71 μmol of TE/g of sample in extracts of aleurone and 66.2 μmol of TE/g of sample in the endosperm. Other studies measured the antioxidant activity of the carotenoids contained in corn tortillas with the β-carotene/linoleate bleaching method, showing that the nixtamalization process can improve the antioxidant activity of carotenoids. In tortillas made of Mexican genotype corn of red or blue varieties, a decrease in whitening of approximately 27% has been reported, while in unprocessed kernels, the value reported was 15%. A value of 25% has been reported for white corn tortillas and 12% for raw kernels [38].

When comparing the antioxidant activity of phenolic compounds of pigmented corn and the polyphenols of blue berries, it was shown that corn has a greater antioxidant capacity and greater reaction kinetics [14]. When evaluating the antioxidant capacity in phenolic compounds of the blue, red, white, yellow, and high carotenoid corn varieties by the peroxyl radical scavenging capacity assay (PSC), an activity of 41–49 μmol of vitamin C equivalent/100 g of sample was reported [15]. This fact has proven that the higher the phenolic content, the greater the antioxidant activity, not only in kernels, but this quality is also maintained in byproducts elaborated by the nixtamalization process, such as the tortilla. However, unlike carotenoids, corn phenolic compounds are affected by production processes such as nixtamalization, which causes a decrease in their nutraceutical properties. For example, in Mexican phenotype corn kernels of the blue variety, a concentration of 343 mg of gallic acid equivalent/100 g of sample has been reported, while in products such as tortillas made with this same kernel, 201 mg of gallic acid equivalent/100 g of sample has been found. Antioxidant capacity can be expressed as the inhibition of ABTS cation formation; this way, it was determined that the antioxidant activity of the kernel is approximately 63%, while for the tortilla, it was 44%. The antioxidant activity of corn is not only limited to inhibiting the formation of ROS, it can also regulate cellular enzymatic elements for the defense against oxidative stress. It has been shown that corn components can increase the activity of the QR enzyme [44]. Only some of the phenolic compounds contained in corn have biological activity; for example, phenolic acids have only been able to recognize the nutraceutical capacity of compounds such as ferulic acid, protocatechuic acid, and p-coumaric acid [45].

Researchers from the University of Florida quantified and characterized the content of phenolic compounds in commercial genotype corn kernels of white varieties and of two blue varieties, one of Mexican genotype and the other North American, and reported a higher content of phenols in white corn, mainly ferulic acid, protocatechuic acid, and p-coumaric acid, while in blue corn, there were no traces of these acids. However, they found high concentrations of anthocyanins in the Mexican genotype, followed by the North American genotype. In addition, the antioxidant capacity of the three varieties was evaluated, demonstrating that the Mexican genotype has a greater capacity to inhibit the formation of ROS [46]. In this sense and due to their structural composition, the compounds contained in corn with a greater antioxidant activity are the flavonoids, the anthocyanins being those that inhibit, to a greater extent, the formation of ROS, in a concentration-dependent manner. In addition to kernels, other tissues such as stigmata, leaf sheaths, and cobs, particularly those of pigmented varieties, stand out as potential sources for anthocyanins, showing a high antioxidant activity.

Another group of compounds that can be found in corn is that of bioactive peptides, exogenous antioxidants that can act as scavengers of free radicals, inhibitors of ROS formation, and promoters of the activation of endogenous antioxidant systems. It has been shown that from the peptide fraction of corn gluten, only the sequences of Gly-Leu-Leu-Leu-Pro-His and Tyr-Phe-Cys-Leu-Thr can exert their antioxidant activity through the reduction of the amount of ROS and regulate the activity of enzymes such as SDO, CAT, and GR [42]. Some peptides synthesized from corn gluten meal can decrease the formation of the O_2^- radical by acting as electron donors. In spite of the scientific evidence demonstrating the antioxidant activity of corn bioactive peptides, it is still necessary to carry out further studies in biological models to explain their interaction in the organism. From the above, it can be concluded that corn and its byproducts not only represent a food source with a high nutritional value but also that, due to its anthocyanin, polyphenol, and peptide content, they contribute to the correct functioning and homeostatic maintenance of the organism. Moreover, due to its antioxidant properties, it can be used as an alternative to prevent the oxidative damage caused by stress and the subsequent negative effects associated with it.

3.2. Corn and metabolism

Obesity is currently a multifactorial etiology, chronic course disease, which involves genetic, environmental, and lifestyle aspects. Obesity is defined as the abnormal or excessive accumulation of fat harmful to health. One of the parameters that must be evaluated in order to determine if a person has obesity is the body mass index (BMI). Thus, a person with a BMI equal to or greater than 30 is considered obese. In recent years, obesity has been acknowledged as a global public health problem: an estimated 1900 million adults are overweight, and 600 million are obese [47]. Research carried out in rodents has shown that anthocyanins contained in purple corn can improve insulin resistance induced by a high-fat diet. For example, the cyanidin 3-glucoside present in purple corn may suppress the transcription of mRNA for the synthesis of enzymes involved in the production of fatty acids and triglycerides and reduce the sterol, a regulatory element that binds to the mRNA level of the protein-1 in white adipose tissue. The downregulation of protein-1 may contribute to the accumulation of triglycerides in white adipose tissue. These data, reported in 2003 by researchers from the University of Doshisha in Japan, have established the biochemical and nutritional bases for the use of cyanidin and anthocyanins in purple corn, as a functional food factor able to provide benefits for the prevention of obesity and diabetes [48]. Components of bioactive foods, such as resistant corn starch with a high content of amylose type 2 and sodium butyrate, reduce obesity in rodents [24].

Recently, an integral version has been used in a study carried out on humans, demonstrating greater postprandial satiety [49]. In addition, in vitro studies have shown a potential anti-obesity effect of purple corn stigmata in multiple stages of the adipocyte life cycle. The potential effects of high concentrations of purple corn stigmata extracts may inhibit adipocyte proliferation and adipogenesis, as well as induce lipolysis and apoptosis [50]. Another bioactive compound present in corn is maysin; the use of maysin in some studies has shown that it is a potent beneficial functional ingredient for health and a therapeutic agent in the prevention or treatment of obesity [51]. Menopause is a stage in which the production of estrogen is reduced, promoting the increase of body fat, and is a risk factor that contributes to obesity in older women. On the other hand, it is known that the modification of the gastrointestinal microbiota can reduce obesity by controlling energy expenditure. Therefore, adding prebiotics to the diet can contribute to the modification of the intestinal microbial flora, thus reducing obesity. Accordingly, the high-amylose type 2 resistant starch of corn can be used as a prebiotic, as has been proven in studies performed in ovariectomized rats. These studies showed that the bacterial levels increased with the addition of resistant starch of high corn amylose to the diet of the animals. In addition, the weight gain caused by the lack of estrogen was attenuated [52]. The consumption of fermentable corn fiber is recommended for postmenopausal women.

Diabetes is one of the most severe chronic metabolic diseases with great impact on the health of the population; the complications that this pathology entails are serious, fatal, and disabling, in such a way that it significantly affects the socioeconomic level of a country. According to the International Diabetes Federation, worldwide, 425 million people have been reported with diabetes during the year 2017, and the failure to intervene in time is expected to increase this figure to 693 million by 2045, while in Latin America, the number of people with diabetes could reach between 25 and 40 million by the year 2030 [53]. It has been demonstrated that a diet with purple corn rich in anthocyanins can be useful in the prevention of obesity and diabetes in mice, since the alterations induced by a high-fat diet (hyperglycemia, hyperinsulinemia, and hyperleptinemia) were normalized in the group that consumed purple corn in addition to its conventional diet [48]. It was also observed that the diet added with purple corn can suppress the transcription of genes involved in the synthesis of fatty acids and triglycerides. Other studies have shown that the consumption of resistant starch contained in corn improves insulin sensitivity in humans [52], and several studies in animals have documented a reduction of glucose concentration and a change of blood lipid profile due to the consumption of resistant starch [54]. It has also been observed that anthocyanin consumption (1 g/day) in non-hypertensive diabetic patients is effective in reducing triglyceride levels, increasing HDL cholesterol and optimizing glucose control; ferulic acid seems to be responsible for these antidiabetic properties.

Diabetic nephropathy is one of the main complications in diabetes and is mainly caused by chronic renal failure, which is growing in prevalence. This disease is characterized by a microvascular injury that causes glomerular hyperfiltration, renal damage, and an increase in urinary albumin excretion, finally inducing a glomerular dysfunction with renal failure. The consumption of feruloylated oligosaccharides, derived from the esterification of ferulic acid or oligosaccharides, impacts common physiological functions and has been shown to be effective in the regulation of serum insulin levels, and, although not as effective as ferulic acid, this esterified compound can slow down weight loss in diabetic rats [45]. In addition, purple corn extract rich in anthocyanins has been used as a therapeutic agent focused on the regulation of the abnormal angiogenesis that occurs in diabetic nephropathy, which can lead to renal failure. This is mediated by the decrease in receptor 2 activity for vascular endothelial growth factor after consumption of purple corn, tested in diabetic mice [55]. It has also been reported that purple corn extract can have antidiabetic effects through the protection of the β cells of the pancreas, favoring the secretion of insulin and the activation of the AMPK pathway in diabetic mice. The extract also causes increased phosphorylation by AmpC-activated kinase protein (AmpK), decreases the activity of phosphoenolpyruvate carboxykinase (PEPCK), decreases the transcriptional activity of genes for glucose 6-phosphatase in the liver, and increases the expression of the glucose transporter 4 (GLUT4) in skeletal muscle [56].

Another complication of diabetes is the formation of cataracts in the eye, caused by an optical dysfunction in the lens. Researchers from the KhonKaen University in Thailand conducted a study with rat enucleated lenses, which were incubated in artificial water humor containing 55 mM glucose with various concentrations of *Zea mays* L. (purple waxy corn), and found that the extract is capable of protecting against diabetic cataract in a dose-dependent way, probably due to the reduction of oxidative stress, while with high doses of corn extract, an effect is exerted through the inhibition of aldose reductase, which limits the speed in the polyol pathway (sorbitol). However, it is necessary to conduct studies with in vivo models that support these findings [57]. Raw extracts of flavonoids contained in corn stigmata have been used in models of diabetic mice reporting a decrease in body weight, glycemia, and antidiabetic capacity, in addition to the reduction in the levels of total cholesterol, of triglycerides, of low-density lipoproteins and an increase in the levels of high-density lipoproteins, suggesting an anti-hyperlipidemic effect [58]. Therefore, corn is proposed as a nutraceutical food, with a potential therapeutic effect to improve the alterations associated with diabetes. The diversity of corn byproducts, such as tortillas, pozol (thick, cocoa- and corn-based drink of Mesoamerican origin that is consumed in southern Mexico), chicha (unfermented drink made with purple corn, flavored with pineapple peels, consumed in Peru), etc., contains a large amount of antioxidant hydrophilic phenolic compounds that are beneficial for the control and maintenance of intermediate metabolism, so they can be considered an alternative for the prevention or treatment of diseases associated with metabolic alterations.

3.3. Corn and cancer

Cancer is among the leading causes of death in the world, resulting from the interaction between genetic factors and external physical factors, such as ultraviolet and ionizing radiation, chemical carcinogens such as asbestos and tobacco smoke, and biological carcinogens (some viral, bacterial, or parasitic infections). The consumption of pigmented corn, like purple, red, and blue varieties, has been shown to have anti-mutagenic properties due to anthocyanin content. Since 2001, research has been carried out to demonstrate the antineoplastic effects of corn anthocyanins, finding that it prevents carcinogenesis due to exposure to 2-amino-1-methyl-6-phenylimidazo pyridine (a free radical belonging to the nitrosamines group) [59]. Purple corn, in addition, has been shown to have chemopreventive properties in in vitro models of prostate cancer and in transgenic rats [60]. Also, maysin, one of the most abundant flavones in stigmata, can inhibit the growth of PC-3 cancer cells by stimulating apoptotic cell death dependent on the mitochondria [61]. These results suggest that maysin is a strong nutraceutical that can be used for the treatment of prostate cancer in humans who are resistant to chemotherapy, and more recently the non-amylaceous peptide polysaccharide of corn was isolated and characterized, and after a series of tests, it showed anticancer properties by blocking metastasis mediated by galectin-3 [62].

In 2015, Mexican researchers conducted a study with extracts of phenolic acids and blue corn anthocyanins, measuring their anticancer properties in breast, liver, colon, and prostate cancer cell lines; results indicated an antiproliferative effect in all cell lines, in which malonyl glucoside cyanidin was the anthocyanin with the greatest reduction in cell viability [28]. It has also been shown that the bioactive peptides of corn exert antitumor activity through key mechanisms such as (a) the induction of apoptosis mediated through specific proteases or caspases; strategies to overcome tumor resistance to apoptotic pathways include the activation of pro-apoptotic receptors, the restoration of p53 activity, the modulation of caspases, and the inhibition of the proteasome; (b) blocking the intermediate generation of tumors by regulating cellular mechanisms associated with cell proliferation and survival, or biosynthetic pathways that control cell growth; and (c) regulation of immune system functions, increasing the expression of antigens associated with the tumor (antigenicity) in cancer cells, activating the tumor cells for them to release warning signals that stimulate the immune response (immunogenicity), or increasing the predisposition of the tumor cells to be recognized and neutralized by the immune system (susceptibility) by means of autophagy and apoptosis [63]. The possible therapeutic use of corn peptide is still limited, since the bioavailability of these molecules depends on their capacity to remain active and intact elements during the digestive process, and the probability of reaching the general circulation to exert their physiological effects. Even so, some evidence supports the use of corn peptides as nutraceutical molecules with therapeutic capacity against a wide range of diseases related to oxidative damage, including cancer. The peptides contained in corn represent an important alternative due to their anticancer potential, but it is necessary to carry out more studies in patients, thus ensuring their therapeutic efficacy.

3.4. Corn and the nervous system

In addition to the nutritional benefits that corn consumption can bring, recent efforts have been made to evaluate its possible health benefits, especially on the nervous system. It is well recognized that a poor diet can contribute to the etiology of chronic diseases such as heart disease, cancer, and others. In view of this, aging should be considered as the main risk factor for chronic and/or chronic-degenerative diseases, among which are disabling disorders associated with cognitive and memory impairment, and dementia, all of them having a lasting impact on family life, as well as high costs for public health institutions [64]. In this sense, the consumption of bioactive nutrients contained in a diet rich in vitamins and polyphenols, and low in saturated fat content, can be a viable alternative for the preservation and/or delay of damage to the brain, since these elements can modify and preserve the state of health of the nervous system through the modulation of biochemical and biological processes [65].

A proper diet includes fruits, vegetables, grains, cereals, and other plants that can have beneficial effects on health, preventing the development of various diseases, thanks to the presence of bioactive components such as flavonols, flavones, catechins, flavonones, anthocyanidins, procyanidin B, among others [65]. Therefore, recently, special importance has been granted to the consumption of foods rich in these substances, among which purple corn (*Z. mays* L.)

stands out, being an important source of anthocyanins, which is the natural pigment distributed widely in the plant that confers its characteristic color, also containing other polyphenols (non-anthocyanin flavonoids and phenolic acids) distributed through the plant, for example, in the ear and seeds, cyanidin-3-glucoside, pelargonidin-3-glucoside, peonidin-3-glucoside, and its malonated counterparts can be found. Many biological activities have been attributed to these anthocyanins, so it is considered that corn and its byproducts that contain them have an intrinsic capacity to prevent cognitive deterioration and memory decline [66, 67].

3.4.1. Corn and Alzheimer's

Alzheimer's disease (AD) is a highly prevalent neurodegenerative disease, affecting approximately 10% of the population over 65 years of age, and it has been estimated that by the year 2050, only in the United States of North America, this disease will affect about 14 million people, with an expected incidence close to one million people per year [68], and it has been estimated that the global prevalence of AD will increase to 1 per 85 people in 2050 [69]. AD is the most common cause of dementia, conceived as a syndrome—a group of symptoms—that have been attributed to numerous causes, although the most characteristics are deficits in memory, language, and problem-solving capacity, together with other cognitive disorders that affect the performance of those who suffer from it and their ability to carry out daily activities [70].

The pathophysiology of AD is characterized by the formation of extracellular deposits of beta-amyloid peptide and the hyperphosphorylation of skeletons of intracellular tau proteins. Extensive research has been carried out with the aim of identifying the etiology of AD, although the specific mechanisms that cause neurodegenerative damage have not been well established yet. However, this disease is attributed to multiple factors, including the hypothesis of damage caused by oxidative stress on DNA, RNA, lipid peroxidation, and protein oxidation, responsible for the cognitive deterioration characteristic of the disease [71]. Studies carried out in patients diagnosed with AD have shown a decrease in antioxidant concentration in plasma, as well as an increase in the concentration of metabolites associated with the oxidation of lipids and proteins (distinctive markers of oxidative stress). It should be noted that this oxidative damage in the brain is implied in the toxicity induced by the β-amyloid fibrillar peptide (Aβ) [72].

Therefore, in recent years, the efforts of a large number of researchers in the world have focused on the search for natural alternatives that contribute to the prevention of neurodegenerative diseases such as Alzheimer's. Among the bioactive components with important biological activity, it has been reported that polyphenols (natural compounds present in fruits and vegetables) have the capacity to act as neuroprotective elements, although the ways in which they can perform this activity are still being studied. A series of studies are being carried out aimed at extracting molecules such as polyphenols for their potential use for preventive and/or therapeutic purposes, from different sources of fruits and vegetables, among which pigmented corn of the yellow, purple, brown, green, and blue varieties stand out [35]. Polyphenols exert biological action in the prevention of AD, due to their intrinsic capacity as reducing agents, and indirectly promote protection by activating endogenous defense systems, and by modulating cell-signaling processes related to the activation of the nuclear factor kappa B (NF-κB), of the protein-1 (AP-1)DNA binding activator, of the synthesis of glutathione, of the phosphatidylinositide-3 (PI3)-protein kinase B (Akt)pathway, of mitogen activated by protein kinase

(MAPK)(regulation of extracellular signaling protein kinase (ERK), of c-Jun N-terminal kinase (JNK) and P38), and also related to the translocation of erythroid nuclear factor 2 (Nrf2) [73].

Corn polyphenols, particularly flavonoids, can also modulate the neuronal signaling cascade activated by aging, acting on the ERK/CREB pathway involved in synaptic plasticity and long-term potentiation, improving learning and memory capacity in humans and animals [73]. They have also shown modulatory effects on the signaling pathway of kinases such as calcium calmodulin kinase II (CaMKII) and ERK, which control the activation of CREB (cAMP response element-binding) and increase the expression of brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF) at brain level [64]. As a matter of fact, it has been experimentally proven that polyphenols exert a protective effect on the hippocampus, preserving and promoting learning strategies and visuospatial memory in middle-aged rodents through the restoration of the mRNA levels of CaMKII, and the increase in the expression of hippocampal NGF [67]. Due to the above, the consumption of foods rich in molecules with biological potential, such as those present in corn, represents a nutritional alternative that can also help prevent the cognitive deterioration and dementia associated with age. However, it is still necessary to carry out studies that help prove their biological effectiveness in in vivo systems, and especially in the human population vulnerable to the development of neurodegenerative diseases.

4. Conclusions

Corn is a cereal with excellent nutritional qualities due to its resistant fiber, carotenoids, and polyphenols content. Moreover, the possibility of obtaining peptides with a great biological activity also contributes to nutraceutical qualities to corn. Regarding this, pigmented corn also contains anthocyanins, natural pigments that, in addition to their antioxidant properties, can modulate intracellular signals in different tissues of the organism. All the above makes corn a functional food to prevent the incidence of diseases such as cancer, diabetes, obesity, and neurodegenerative disorders. Likewise, a diet that includes corn can be implemented during the treatment of these diseases. However, it remains necessary to carry out more studies that highlight the efficiency of corn byproduct consumption during the incidence of such diseases.

Conflict of interest

The authors declare that there is no conflict of interest.

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References

[1] Doebley J. The genetics of maize evolution. Annual Review of Genetics. 2004;**38**:37-59

[2] Vela E. Popol Vuh: el libro sagrado de los mayas. Arqueología mexicana. 2007;**15**(88):42-50. Available from: http://arqueologiamexicana.mx/mexico-antiguo/el-popol-vuh-el-libro-sagrado-de-los-mayas [Accessed: Apr 18, 2018]

[3] Paliwal RL. El maíz en los trópicos: Mejoramiento y producción [Internet]. Food and Agriculture Organization. 2001. p. 392. Avalibable from:https://curlacavunah.files.wordpress.com/2010/04/el-maiz-en-los-tropicos.pdf [Accessed: 2018-04-18]

[4] Doebley J, Iltis HH. Taxonomy of Zea (Gramineae). I. A subgeneric classification with key to taxa. American Journal of Botany. 1980;**67**(6):982-993. DOI: 10.1002/j.1537-2197.1980.tb07730.x

[5] Fernández-Suárez R, Morales-Chávez LA, Gálvez-Mariscal A. Importancia de los-maícesnativos de México en la dietanacional: Una revisión indispensable. Revista Fitotecnia Mexicana [Internet]. 2013;**36**(Suppl):275-283. Available from: http://www.scielo.org.mx/scielo.php?script=sci_arttext&pid=S0187-73802013000500004&lng=es

[6] Taube KA. The maize tamale in classic Maya diet, epigraphy, and art. American Antiquity. 1989;**54**:31-51. DOI: 10.2307/281330

[7] Mera-Ovando LM. Aspectossocioeconómicos y culturales. In: Kato TA, Mapes C, Mera LM, Serratos JA, Bye RA, editors. Origen y Diversificación del Maíz: Una Revisión Analítica. Universidad Nacional Autónoma de México, Comisión Nacional para el Uso y Conocimiento de la Biodiversidad. Editorial Impresora Apolo. 2009. pp. 33-42. ISBN: 978-607-02-0684-9

[8] Paredes-López O, Guevara-Lara F, Bello-Pérez LA. La nixtamalización y el valor nutritivo del maíz. Vol. 92-93. Ciencias: Universidad Nacional Autónoma de México; 2009. pp. 60-70. Available from: 0187-6376revci@hp.fciencias.unam.mx

[9] Rocío F-S, Morales-Chávez LA, Gálvez-Mariscal A. Importancia de los maícesnativos de México en la dieta nacional: Una revisión indispensable. Revista Fitotecnia Mexicana.2013;**36**:275-283

[10] Chaturvedi N, Sharma P, Shukla K, Singh R, Yadav S. Cereals nutraceuticals, health ennoblement and diseases obviation: A comprehensive review. Journal of Applied Pharaceutical Science. 2011;**1**:6-12

[11] Díaz-Gómez JL, Castorena-Torres F, Preciado-Ortiz RE, García-Lara S. Anti-cancer activity of maize bioactive peptides. Frontiers in Chemistry. 2017;**5**:44. DOI: 10.3389/fchem.2017.00044

[12] Cadaval A, Artiach-Escauriaza B, Garín-Barrutia U, Pérez-Rodrigo C, Aranceta J, Serra L. Alimentos funcionales Para una alimentación más saludable. Sociedad Española de Nutrición Comunitaria (SENC). 2005. pp. 7-48. Available from: http://www.piaschile.cl/wp-content/uploads/2015/04/Alimentos-funcionales-para-una-alimentaci%C3%B3nmas-saludable.pdf

[13] Castañeda-Sánchez A. Propiedades nutricionales y antioxidantes del maíz azul (*Zea mays* L.). Temas Selectos de Ingeniería de Alimentos. 2011;**5**(2):75-83. Available from: http://www.udlap.mx/WP/tsia/files/No5-Vol-2/TSIA-5%282%29-Castaneda-Sanchez-2011.pdf

[14] Cevallos-Casals BA, Cisneros-Zevallos L. Stoichiometric and kinetic studies of phenolic antioxidants from Andean purple corn and red-fleshed sweetpotato. Journal of Agricultural and Food Chemestry. 2003;**51**:3313-3319. DOI: 10.1021/jf034109c

[15] De la Parra C, Serna-Saldivar SO, Liu RH. Effect of processing on the phytochemical profiles and antioxidant activity of corn for production of masa, tortillas, and tortilla chips. Journal of Agricultrual and Food Chemestry. 2007;**55**:4177-4183

[16] Panfili G, Fratianni A, Irano M. Normal phase high-performance liquid 527 chromatography method for the determination of tocopherols and tocotrienols in cereals. Journal of Agricultural and Food Chemistry. 2003;**51**:3940-3944. DOI: 10.1021/jf030009v

[17] Momany FA, Sessa DJ, Lawton JW, Selling GW, Hamaker SA, Willett JL. Structural characterization of a-Zein. Journal of Agricultural and Food Chemestry. 2006;**54**:543-547. DOI: 10.1021/jf058135h

[18] Liu XL, Zheng XQ, Song ZL, Liu XF, Kopparapu NK, Wang XJ, Zheng YJ. Preparation of enzymatic pretreated corn gluten meal hydrolysate and in vivo evaluation of its antioxidant activity. Journal of Functional Foods. 2015;**18**:1147-1157

[19] Orona-Tamayo D, Valverde MM, Paredes-López O. Bioactive peptides from selected latinamerican food crops–A nutraceutical and molecular approach. Critical Reviews in Food Science and Nutrition. 2018;**1**:1-27. DOI: 10.1080/10408398.2018.1434480

[20] Maestri E, Marmiroli M, Marmiroli N. Bioactive peptides in plant-derived foodstuffs. Journal of Proteomics. 2016;**147**:140-155. DOI: 10.1016/j.jprot.2016.03.048

[21] Jin D, Xiao-lan L, Xi-qun Z, Xiao-Jie W, Jun-fang H. Preparation of antioxidative corn protein hydrolysates, purification and evaluation of three novel corn antioxidant peptides Food Chemistry. 2016;**204**:427-436. DOI: 10.1016/j.foodchem.2016.02.119

[22] Jongfeng A, Jay-Lin J. Macronutrients in corn and human nutrition. Comprehensive Reviews in Food Science and Food Safety. 2016;**15**(3):581-598. DOI: 10.1111/1541-4337.12192

[23] Higgins JA. Resistant starch: Metabolic effects and potential health benefits. Journal of AOAC International. 2004;**87**:761-768

[24] Keenan MJ, Zhou J, McCutcheon KL, Raggio AM, Bateman HG, Todd E, Jones CK, Tulley RT, Melton S, Martin RJ, Hegsted M. Effects of resistant starch, a non-digestible fermentable fiber, on reducing body fat. Obesity (Silver Spring). 2006;**14**:1523-1534. DOI: 10.1038/oby.2006.176

[25] Nishimura N, Tanabe H, Sasaki Y, Makita Y, Ohata M, Yokoyama S, Asano M, Yamamoto T, Kiriyama S. Pectin and high-amylose maize starch increase caecal hydrogen production and relieve hepatic ischaemia-reperfusion injury in rats. The British Journal of Nutrition. 2012;**107**(4):485-492. DOI: 10.1017/S0007114511003229. Epub 2011 Jul 15

[26] Lao F, Sigurdson GT, Giusti MM. Health benefits of purple corn (*Zea mays* L.) phenolic compounds. Comprehensive Reviews in Food Science and Food Safety. 2017;**16**(2):234-246

[27] Zilic S, Serpen A, Akıllıog˘lu G, Go¨kmen V, Vanc˘etovic´ J. Phenolic compounds, carotenoids, anthocyanins, and antioxidant capacity of colored maize (*Zea mays* L.) kernels. Journal of Agricultural and Food Chemistry. 2012;**60**(5):1224-1231. DOI: 10.1021/jf204367z [Epub Jan 26, 2012]

[28] Urias-Lugo DA, Heredia JB, Muy-Rangel MD, Valdez-Torres JB, Serna-Sald'ıvar SO, Guti'errez-Uribe JA. Anthocyanins and phenolic acids of hybrid and native blue maize (*Zea mays* L.) extracts and their antiproliferative activity in mammary (MCF7), liver (HepG2), colon (Caco2 and HT29) and prostate (PC3) cancer cells. Plant Foods for Human Nutrition. 2015;**70**(2):193-199. DOI: 10.1007/s11130-015-0479-4

[29] Salinas Y, Bustos F, Hernández M, Pakza R, Vázquez JL. Efecto de la nixtamalización sobre las antocianinas del grano de maíces pigmentados. Agrociencia. 2003;**37**(6):617-628 Available from: http://www.redalyc.org/articulo.oa?id=30237607

[30] Agatia G, Azzarella G, Pollastri S, Tattini M. Flavonoids as antioxidants in plants: Location and functional significance. Plant Science. 2012;**196**:67-76. DOI: 10.1016/j.plantsci.2012.07.014

[31] Petroni K, Pilu R, Tonell C. Anthocyanins in corn: A wealth of genes for human health. Planta. 2014;**240**:901-911. DOI: 10.1007/s00425-014-2131-1

[32] Aburto EA, Wong RB, Chávez TIP, Hoyos BMJ, Cárdenas F, Cervantes LJ. La nixtamalización y su efecto en el contenido de antocianinas de maíces pigmentados, una revisión. Revista Fitotecnia Mexicana. 2013;**36**(4):429-437 Available from: http://www.scielo.org.mx/scielo.php?script=sci_arttext&pid=S0187-73802013000400009

[33] Lao F, Giusti MM. Quantification of purple corn (*Zea mays* L.) anthocyanins using spectrophotometric and HPLC approaches: Method comparison and correlation. Food Analytical Methods. 2015;**9**(5):1367-1380. DOI: 10.1007/s12161-015-0318-0

[34] Li CY, Kim HW, Won SR, Min KJ, Park JY, Ahn MS, Rhee HI. Corn husk as a potential source of anthocyanins. Journal of Agricultura Food Chemistry. 2008;**56**:11413-11416. DOI: 10.1021/jf802201c

[35] Aoki H, Kuze N, Kato Y, Gen SE. Anthocyanins isolated from purple corn (*Zea mays* L.). Foods and Food Ingredients Journal of Japan. 2002:41-45

[36] Kristina K, Grbeša D. Carotenoid content and antioxidant activity of hexane extracts from selected Croatian corn hybrids. Food Chemistry. 2015;**167**:402-408. DOI: 10.1016/j.foodchem.2014.07.002

[37] Hulshof PJ, Kosmeijer-Schuil T, West CE, Hollman PC. Quick screening of maize kernels for provitamin A content. Journal of Food Composition and Analysis. 2007;**20**(8):655-661. Available from: http://www.scielo.br/scielo.php?script=sci_nlinks&ref=000098&pid=S0103-90162014000600015&lng=en

[38] Mendoza-Díaz S, Ortiz-Valerio Mdel C, Castaño-Tostado E, Figueroa-Cárdenas Jde D, Reynoso-Camacho R, Ramos-Gómez M, Campos-Vega R, Loarca-Piña G. Antioxidant capacity and antimutagenic activity of anthocyanin and carotenoid extracts from nixtamalized pigmented Creole maize races (*Zea mays* L.). Plant Foods for Human Nutrition. Dec 2012;**67**(4):442-449. DOI: 10.1007/s11130-012-0326-9

[39] Masisi K, Diehl-Jones WL, Gordon J, Chapman D, Moghadasian MH, Beta T. Carotenoids of aleurone, germ, and endosperm fractions of barley, corn and wheat differentially inhibit oxidative stress. Journal of Agricultural and Food Chemistry. 2015;**63**(10):2715-2724. DOI: 10.1021/jf5058606 [Epub Mar 3, 2015]

[40] Jung YJ, Park JH, Cho JG, Seo KH, Lee DS, Kim YC, Kang HC, Song MC, Baek NI. Lignan and flavonoids from the stems of *Zea mays* and their anti-inflammatory and neuroprotective activities. Archives of Pharmaceutical Research. 2015;**38**(2):178-185. DOI: 10.1007/s12272-014-0387-4 [Epub Apr 19, 2014]

[41] Žilić S, Janković M, Basić Z, Vančetović J, Maksimović V. Antioxidant activity, phenolic profile, chlorophyll and mineral matter content of corn silk (Zea mays L): Comparison with medicinal herbs. Comparison with medicinal herbs. Journal of Cereal Science. 2016;**69**:363-370. DOI: 10.1016/j.jcs.2016.05.003

[42] Wang L, Ding L, Yu Z, Zhang T, Ma S1, Liu J.Intracellular ROS scavenging and antioxidant enzyme regulating capacities of corn gluten meal-derived antioxidant peptides in HepG2 cells. Foodservice Research International. 2016;**90**:33-41. DOI: 10.1016/j.foodres.2016.10.023 [Epub Oct 15, 2016]

[43] Alfieri M, Hidalgo A, Berardo N, Redaelli R. Carotenoid composition and heterotic effect in selected Italian maize germplasm. Journal of Cereal Science. 2014;**59**(2):181-188. DOI: 10.1016/j.jcs.2013.12.010

[44] Lopez-Martinez LX, Parkin KL, Garcia HS. Phase II-inducing, polyphenols content and antioxidant capacity of corn (*Zea mays* L.) from phenotypes of white, blue, red and purple colors processed into masa and tortillas. Plant Foods for Human Nutrition. 2011; **66**(1):41-47. DOI: 10.1007/s11130-011-0210-z

[45] Huang J, Wang X, Tao G, Song Y, Ho C, Zheng J, Ou S. Feruloylated oligosaccharides from maize bran alleviate the symptoms of diabetes in streptozotocin-induced type 2 diabetic rats. Food & Function. Mar 1, 2018;**9**(3):1779-1789. DOI: 10.1039/c7fo01825h

[46] Del Pozo-Insfran D, Brenes CH, Serna-Saldivar SO, Stephen T. Polyphenolic and antioxidant content of white and blue corn (*Zea mays* L.) products. Research International. 2006;**39**(6):696-703. DOI: 10.1016/j.foodres.2006.01.014

[47] World Health Organization. Obesity and Overweight [Internet]. Fact sheet, 311. 2016

[48] Tsuda T, Horio F, Uchida K, Aoki H, Osawa T. Dietary Cyanidin 3-O-D-glucoside-rich purple corn color prevents obesity and ameliorates hyperglycemia in mice. The Journal of Nutrition. 2003;**133**(7):2125-2130. DOI: 10.1093/jn/133.7.2125

[49] Anderson GH, Cho CE, Akhavan T, Mollard RC, Luhovyy BL, Finocchiaro ET. Relation between estimates of cornstarch digestibility by the Englyst in vitro method and glycemic

response, subjective appetite, and short-term food intake in young men. The American Journal of Clinical Nutrition. 2010;**91**:932-939. DOI: 10.3945/ajcn.2009.28443

[50] Chaiittianana R, Sutthanutb K, Rattanathongkomc A. Purple corn silk: A potential anti-obesity agent with inhibition onadipogenesis and induction on lipolysis and apoptosis in adipocytes. Journal of Ethnopharmacology. 2017;**201**:9-16. DOI: 10.1016/j.jep.2017.02.044

[51] Lee WC, Seoa YJ, Kimb S-L, Leea J, Choi WJ, Park YI. Corn silk maysin ameliorates obesity in vitro and in vivo via suppressionof lipogenesis, differentiation, and function of adipocytes. Biomedicine and Pharmacotherapy. 2017;**93**:267-275. DOI: 10.1016/j.biopha.2017.06.039

[52] Keenan MJ, Zhou J, Hegsted M, Pelkman C, Durham HA, Coulon DB, Martin RJ. Role of resistant starch in improving gut health, adiposity, and insulin resistance. Advancen in Nutrition. 2015;**6**:198-205. DOI: 10.3945/an.114.007419

[53] Cho, Nam Han et al. Epidemiología de la diabetes. In: 2017, Diabetes Atlas Federation International Diabetes Octava edición [Internet]. 2017. pp. 6-7. Available from: www.idf.org/diabetesatlas

[54] Zhou Z, Wang F, Ren X, Wang Y, Blanchard C. Resistant starch manipulated hyperglycemia/hyperlipidemia and related genes expression in diabetic rats. International Journal of Biological Macromolecules. 2015;**75**:316-321. DOI: 10.1016/j.ijbiomac.2015.01.052

[55] Kang M-K, Lim SS, Lee J-Y, Yeo KM, Kang Y-H. Anthocyanin-rich purple corn extract inhibit diabetes-associated glomerular angiogenesis. PLoS One. 2013;**8**(11):e79823. DOI: 10.1371/journal.pone.0079823

[56] Huang B, Wang Z, Park JH, Ryu OH, Choi MK, Lee JY, Kang YH, Lim SS. Anti-diabetic effect of purple corn extraction C57BL/KsJdb/dbmice. Nutrition Research and Practice. Feb 2015;**9**(1):22-29. DOI: 10.4162/nrp.2015.9.1.22 [Epub Jan 28, 2015]

[57] Thiraphatthanavong P, Wattanathorn J, Muchimapura S, Thukham-mee W, Lertrat K, Suriharn B. The combined extract of purple waxy corn and ginger prevents cataractogenesis and retinopathy in streptozotocin-diabetic rats. Oxidative Medicine and Cellular Longevity. 2014;**2014**:11 p. DOI: 10.1155/2014/789406

[58] Zhang Y, Wu L, Ma Z, Cheng J, Liu J. Anti-diabetic, anti-oxidant and anti-Hyperlipidemic activities of flavonoids from corn silk on STZ-induced diabetic mice. Molecules. 2015;**21**(1):E7. DOI: 10.3390/molecules21010007

[59] Hagiwara A, Miyashita K, Nakanishi T, Sano M, Tamano S, Kadota T, Koda T, Nakamura M, Imaida K, Ito N, Shirai T. Pronounced inhibition by a natural anthocyanin, purple corn color, of 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP)-associated colorectal carcinogenesis in male F344 rats pretreated with 1,2-dimethylhydrazine. Cancer Letters. 2001;**171**:17-25. DOI: 10.1016/S0304-3835(01)00510-9

[60] Long N, Suzuki S, Sato S, Naiki-Ito A, Sakatani K, Shirai T, Takahashi S. Purple corn color inhibition of prostate carcinogenesis by targeting cell growth pathways. Cancer Science. 2013;**104**:298-303. DOI: 10.1111/cas.12078

[61] Lee J, Lee S, Kim SL, Choi JW, Seo JY, Choi DJ, Park YI. Corn silk maysin induces apoptotic cell death in PC-3 prostate cancer cells via mitochondria-dependent pathway. Life Sciences 2014;**119**(1-2):47-55. DOI: 10.1016/j.lfs.2014.10.012 [Epub Oct 30, 2014]

[62] Jayaram S, Kapoor S, Dharmesh SM. Pectic polysaccharide from corn (*Zea mays* L.) effectively inhibited multi-step mediated cancer cell growth and metastasis. Chemico-Biological Interactions. 2015;**235**:63-75. DOI: 10.1016/j.cbi.2015.04.008

[63] Díaz-Gómez JL, Castorena-Torres F, Preciado-Ortiz RE, García-Lara S.Anti-cancer activity of maize bioactive peptides. Frontiers in Chemistry. Jun 21, 2017;**5**:44. DOI: 10.3389/fchem.2017.00044 (eCollection 2017)

[64] Abate G, Marziano M, Rungratanawanich W, Memo M, Uberti D. Nutrition and ageing: Focusing on Alzheimer's disease. Oxidative Medicine and Cellular Longevity. 2017;**2017**:7039816. DOI: 10.1155/2017/7039816 [Epub Jan 12, 2017]

[65] Ramos-Escudero F, Muñoz AM, Alvarado-Ortíz C, Alvarado A, Yánez JA. Purplecorn (*Zea mays* L.) phenolic compounds profile and its assessment as an agent against oxidative stress in isolated mouse organs. Journal of Medicinal Food. 2012;**15**(2):206-215. DOI: 10.1089/jmf.2010.0342

[66] Choi DY, Lee YJ, Hong JT, Lee HJ. Antioxidant properties of natural polyphenols and their therapeutic potentials for Alzheimer's disease. Brainresearch Bulletin. 2012;**87**(2-3):144-153. DOI: 10.1016/j.brainresbull.2011.11.014

[67] Aguirre-López LO, Chávez-Servia JL, Gómez-Rodiles CC, Beltrán-Ramírez JR, Bañuelos-Pineda J. Blue corn tortillas: Effects on learning and spatial memory in rats. Plant Foods for Human Nutrition. Dec 2017;**72**(4):448-450. DOI: 10.1007/s11130-017-0642-1

[68] Sadik K, Wilcock G. The increasing burden of Alzheimer disease. Alzheimer Disease and Associated Disorders. 2003;**17**(3):S75-S79

[69] Brookmeyer R, Johnson E, Ziegler-Graham K, Arrighi HM. Fore casting the global burden of Alzheimer's disease. Alzheimer's & Dementia. 2007;**3**:186-191. DOI: 10.1016/j.jalz.2007.04.381

[70] Alzheimer's Association. 2017 Alzheimer's disease facts and figures. Alzheimer's & Dementia. 2017;**13**(4):325-373 Available from: https://www.alz.org/documents_custom/2017-facts-and-figures.pdf

[71] Markesbery WR, Lovell MA. Damagetolipids, proteins, DNA, and RNA in mild cognitive impairment. Archives of Neurology. 2007;**64**:954-956. DOI: 10.1001/archneur.64.7.954

[72] Sonnen JA, Breitner JC, Lovell MA, Markesbery WR, Quinn JF, Montine TJ. Free radical-mediated damage to brain in Alzheimer's disease and its transgenic mouse models. Free Radical Biology and Medicine. 2008;**45**:219-230. DOI: 10.1016/j.freeradbiomed.2008.04.022

[73] Han X, Shen T, Lou H. Dietary polyphenols and their biological significance. International Journal of Molecular Sciences. 2007;**8**(9):950-988. DOI: 10.3390/i8090950