Health Benefits of Purple Corn (Zea mays L.) Phenolic Compounds

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Health Benefits of Purple Corn (*Zea mays* L.) Phenolic Compounds

Fei Lao, Gregory T. Sigurdson, and M. Mónica Giusti

Abstract: Purple corn (*Zea mays* L.), a grain with one of the deepest shades in the plant kingdom, has caught the attention of the food industry as it could serve as a source for alternatives to synthetic colorants. Also being rich in phenolic compounds with potential health-promoting properties, purple corn is becoming a rising star in the novel ingredients market. Although having been widely advertised as a "healthy" food, the available information on purple corn health benefits has not yet been well reviewed and summarized. In this review, we present compositional information focused on the potential functional phenolic compounds correlated to health-promoting effects. Studies evaluating potential health-benefitting properties, including *in vitro* tests, cell models, animal and human trials, are also discussed. This paper emphasizes research using purple corn, or its extracts, but some other plant sources with similar phenolic composition to purple corn are also mentioned. Dosage and toxicity of purple corn studies are also reviewed. Purple corn phenolic compounds have been shown in numerous studies to have potent antioxidant, anti-inflammatory, antimutagenic, anticarcinogenic, and anti-angiogenesis properties. They were also found to ameliorate lifestyle diseases, such as obesity, diabetes, hyperglycemia, hypertension, and cardiovascular diseases, based on their strong antioxidant power involving biochemical regulation amelioration. With promising evidence from cell and animal studies, this rich source of health-promoting compounds warrants additional attention to better understand its potential contributions to human health.

Keywords: anthocyanins, antioxidants, bioactive compounds, dosage, phenolics

Introduction

Purple corn (*Zea mays* L.), also known as purple maize, is native to the Andes region of what is now Peru. It has been widely cultivated and consumed throughout the Andean region of South America, mainly in Peru, Ecuador, Bolivia, and Argentina. It expresses one of the deepest purple shades found in the plant kingdom. Due to its richness in purple color, purple corn pigments have long been used to color foods and beverages. In South America, purple corn extracts are widely applied in coloring homemade desserts and beverages such as chicha morada and mazamorra morada, a popular drink and dessert prepared from purple corn (FAO 2013). Other countries have also shown interest in using this rich source of pigments to obtain food colorants. According to the United Nations BioTrade Facilitation Program (2011), the average yearly growth of Peruvian purple corn exports value reached 467% from 1998 to 2002, and the price of purple corn almost doubled from $0.75 to $1.36/kg in this 5-y period. In 2002, Peru exported a total value of $24220360 of natural colorants, of which $98000 was contributed solely by purple corn anthocyanin products. Their use as food ingredient and food colorant has been increasing around the world in recent decades, as observed by the increasing importation of purple corn and color products by Germany, France, Italy, Japan, and other countries. The export of Peruvian purple corn business reached $187745641 in 2010. Purple corn color for food use has been recognized by the European Union and Japan under the code of E-163 and under the international numbering system as INS-163iv. The use of the term purple corn color throughout this review refers to commercially produced colorants obtained from purple corn.

For many years, Japan was the main market for purple corn or corn cobs, and this is reflected in the predominance of early research on purple corn originating from Japan or Japanese researchers (Tsuda and others 2003, 2004, 2005, 2006; Sasaki and others 2007; Fukamachi and others 2008; Tsuda 2008). This body of research work has promoted the international purple corn trade, making purple corn a more popular novel ingredient in the food industry. Now researchers around the world are paying more attention to this rich source of phytochemicals. Anthocyanins, the primary pigments in purple corn, have been reported to be associated with the potential to reduce the risk of cardiovascular disease, obesity, diabetes, cancer, and chronic diseases (Konczak and Zhang 2004; He and Giusti 2010). Besides the pigments, other functional phenolic compounds in purple corn have also been reported to have attenuating effects on chronic diseases such as hypertension, diabetes, and cancer (Kim and others 2013; Long and others 2013). In 2013, the phenolic-rich purple corn has been

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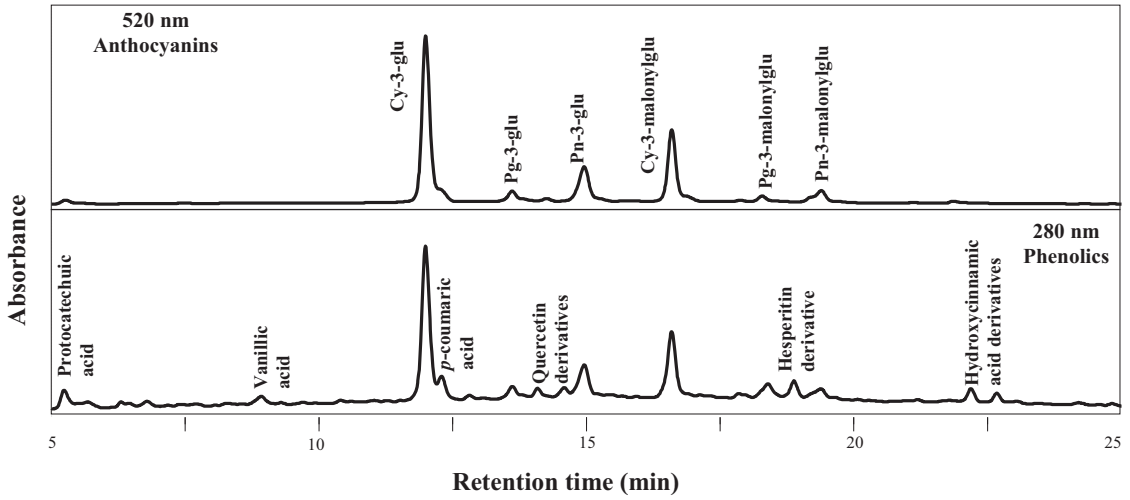


Figure 1—Representative chromatograms of the major anthocyanins and phenolic compounds from combined purple corn (*Zea mays* L.) kernel and cob extracts, identified by comparing to the literature (Pedreschi and Cisneros-Zevallos 2007; Lao and Giusti 2016).

proposed by different commercial companies to have the status of a "superfood" due to its remarkable potential health benefits.

The objective of this paper was to review and summarize the current knowledge of the health benefits of the phenolic compounds of purple corn. This review describes potential functional phenolic compounds previously reported in purple corn. Studies of purple corn phenolics and extracts for health in cell, animal, and human models, and also dosage studies related to purple corn toxicity. The information included describes purple corn ingredients as having desirable nutritional values to meet the requirement for "healthy" food formulations.

Functional Phenolic Compounds in Purple Corn

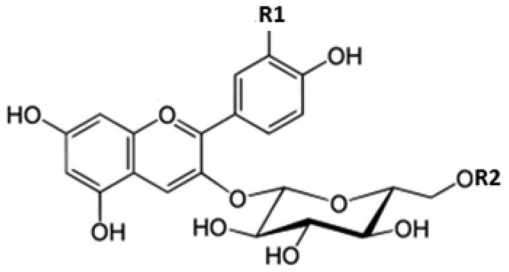
Nutritionally and compositionally, purple corn (*Zea mays* L.) is similar to the more commonly consumed yellow corn as being rich in starch (61% to 78% dry basis, db), nonstarch polysaccharides (about 10% db) (Sinha and others 2011), proteins (6% to 12% db), lipids (3% to 6% db), minerals, and vitamins (Ai and Jane 2016). The macronutrients in corn and their beneficial effects on postprandial glycemic/insulinemic responses, lipid metabolism, colon health, and mineral absorption have been well summarized (Ai and Jane 2016). However, it is the presence of anthocyanins and other phenolic compounds that differentiate purple corn from other conventional corn varieties and make it stand out as a health-promoting food. The typical anthocyanin and phenolic profile of purple corn is shown in Figure 1. The total phenolic content of Andean purple corn, as determined by the Folin-Ciocalteu assay, is about 1756 mg/100 g gallic acid equivalents FW, much higher than the content of well-known phenolic-rich blueberries which contain 138 to 672 mg/100 g FW (Prior and others 1998; Cevallos-Casals and Cisneros-Zevallos 2003). Montilla and others (2011) compared the soluble and bound phenolic compounds in different Bolivian corn cultivars and showed corn with deeper shades tended to contain higher phenolic concentrations. Studies related to purple corn health benefits have therefore been conducted primarily with anthocyanin or phenolic-rich extracts obtained from purple corn; however, studies performed with purple corn juices or powders are also presented in this review. Dose-dependent correlations between the amount of these purple corn functional compounds and certain health-promoting properties were often found.

Anthocyanins

Anthocyanins are a class of water-soluble phenolic compounds which impart the dark purple-red color to purple corn. The anthocyanin content of purple corn ranges from 6.8 to 82.3 mg/g FW depending on which portion of the plant material is evaluated, again much higher than the blueberry (anthocyanin content 1.3 to 3.8 mg/g FW) (Cevallos-Casals and Cisneros-Zevallos 2003; Wu and others 2006; Li and others 2008). The anthocyanin composition of purple corn has been well studied, and 6 major and 17 other minor anthocyanins have been identified (Aoki and others 2002; De Pascual-Teresa and others 2002; Jing and Giusti 2005; González-Paramás and others 2006; Jing and Giusti 2007; Pedreschi and Cisneros-Zevallos 2007; Li and others 2008; González-Manzano and others 2008; Zhao and others 2008; Montilla and others 2011; Žilić and others 2012; Lao and Giusti 2016). The 6 major purple corn anthocyanins include cyanidin-3-glucoside (Cy-3-glu), pelargonidin-3-glucoside (Pg-3-glu), peonidin-3-glucoside (Pn-3-glu), and their malonic acid derivatives attached to the C-6'' position of the glucose moiety (Figure 1 and 2). The minor anthocyanins reported previously include diglucosides of the 3 major anthocyanidins (Žilić and others 2012), dimalonyl attachments to C-6 of the sugar unit of the 3 major anthocyanins (Aoki and others 2002; Jing and Giusti 2007; Jing and others, 2007; Montilla and others, 2011), the major anthocyanidins attached to other sugars such as rutinose (Žilić and others 2012), and the major nonacylated anthocyanins attached to phenolic compounds such as succinic acid and catechin (Gonzalez-Paramas and others 2006; González-Manzano and others 2008; Li and others 2008; Montilla and others 2011). Delphinidin-3-glucoside has also been reported to be in purple corn, but it is rarely detected (Žilić and others 2012).

Other phenolics

Phenolic compounds are nonpolymeric phytochemical compounds that contain at least 1 phenolic hydroxyl group in their structures. In this review, other phenolics in purple corn refer to all phenolic compounds except anthocyanins. Phenolic acids and



Anthocyanins	R1	R2
Cyanidin-3-glucoside	OH	H
Pelargonidin-3-glucoside	H	H
Peonidin-3-glucoside	OCH_3	H
Cyanidin-3-(6"-malonylglucoside)	OH	$COCH_2COOH$
Pelargonidin-3- (6"-malonylglucoside)	H	$COCH_2COOH$
Peonidin-3 (6"-malonylglucoside)	OCH_3	$COCH_2COOH$

Figure 2–Chemical structures of 6 major anthocyanins in purple corn (*Zea mays* L.).

flavonoids are the major 2 subclasses of other phenolics reported to be found in purple corn. As shown in Figure 1, a variety of phenolics other than anthocyanins can be detected in a crude purple corn extract. These compounds have been widely reported to contribute potential health-promoting properties to animal and human cells. Anthocyanins are also phenolic compounds that belong to the flavonoid family. However due to their high concentration in purple corn and the major role they are believed to contribute to the health-promoting properties of dark colored plants, they are discussed separately in this review.

Phenolic acids. Phenolic acids in purple corn are usually recovered with organic solvents such as alcohol and acetone (Moore and others 2005; Žilić and others 2012) and identified by HPLC-MS (Pedreschi and Cisneros-Zevallos 2006, 2007; Ramos-Escudero and others 2012a; Žilić and others 2012). The *p*-coumaric acid and ferulic acid contents for dark-hued Bolivian purple corn were 607.5 and 154.2 mg/100 g DW respectively, much higher than yellow cultivars reported to contain 366.7 and 132.9 mg/100 g DW, respectively (Montilla and others 2011). The phenolic acid contents of purple corn were found to vary between cultivars. A more recent study showed ferulic acid to be the most abundant phenolic acid (39.9 mg/kg DW for native and 33.3 mg/kg DW for hybrid maize), followed by diferulic and coumaric acids in Mexico purple corn (Urias-Lugo and others 2015). Most of the phenolic acids are in conjugated or bound forms in purple corn; just a small portion is in free soluble form that can be easily extracted without hydrolysis treatment (Montilla and others 2011; Žilić and others 2012). Currently, more than 9 different phenolic acids have been reported to be found in purple corn. Shown in Figure 3, they included protocatechuic acid, vanillic acid, syringic acid, 2,4,6-trihydroxybenzoic acid, *p*-coumaric acid (also called *p*-hydroxycinnamic acid), caffeic acid, ferulic acid, chlorogenic acid, and *p*-hydroxyphenyl acetic acid, and also their derivatives (Montilla and others 2011; Ramos-Escudero and others 2012a; Žilić and others 2012; Kim and others 2013).

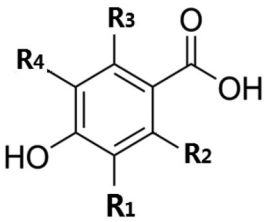
Nonanthocyanin flavonoids. In addition to phenolic acids, other functional compounds found in purple corn include flavonoids. The total flavonoids content in purple corn ranged from 307.42 to 337.51 mg/kg DW, while the yellow-hued corn contained less at 248.64 to 281.20 mg/kg DW (Žilić and others 2012). Similar to phenolic acids, flavonoids in purple corn are recovered by organic solvent mixtures (Moore and others 2005; Žilić and others 2012). Total flavonoids content in purple corn was determined by forming a flavonoid-aluminum complex and measuring absorbance after alkaline treatment (Jia and others 1999; Žilić and others 2012). Rutin, hirsutrin, morin, kaempferol, quercetin, naringenin, hesperitin, and their derivatives are the most commonly reported flavonoids recovered from purple maize (Pedreschi and Cisneros-Zevallos 2007; Ramos-Escudero and others 2012a; Kim and others 2013). The chemical structures of these flavonoids are shown in Figure 4.

Health Benefits of Purple Corn Phenolic Compounds

Interest on the health benefits of purple corn anthocyanins and other phenolics has been increasing over the last several decades. There is a large body of evidence suggesting that these compounds may help reduce the incidence of a variety of chronic diseases. However, it is clear that not all anthocyanins or all phenolics are equal in their potential health-promoting properties. Therefore, in this review, it is specified whether the purple corn health-promoting properties were evaluated as purple corn phenolic compounds mixtures, phenolic-rich extract without pigments, purified anthocyanins, or individual anthocyanins.

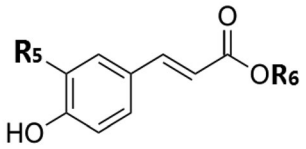
Antioxidant properties

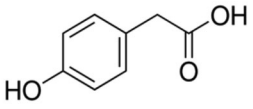
The free radical-involved chain reaction is the generally accepted mechanism for degenerative oxidation in living tissue (Wang and Stoner 2008). Antioxidant capability often refers to the ability to scavenge reactive oxygen radicals: superoxide, singlet oxygen, peroxide, hydrogen peroxide, and hydroxyl radicals (Wang and Stoner 2008). It is thus believed that antioxidants can provide health protection to oxidative degradation/damage in biological systems (Halliwell and others 1992). The antioxidant property of purple corn has been comprehensively evaluated in various free



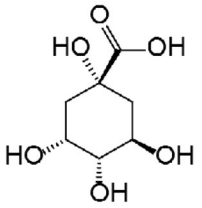
Name	R1	R2	R3	R4
Protocatechuic acid	OH	H	H	H
Vanillic acid	OCH_3	H	H	H
Syringic acid	OCH_3	H	H	OCH_3
2,4,6-trihydroxy-benzoic acid	H	OH	OH	H

Name	R5	R6
p-coumaric acid	H	H
Ferulic acid	OCH_3	H
Caffeic acid	OH	H
Chlorogenic acid	OH	Quinic acid





p-hydroxyphenyl acetic acid



Quinic acid

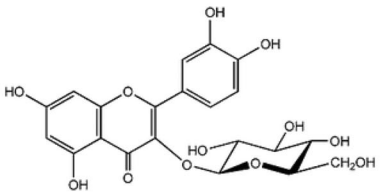
Figure 3–Chemical structures of typical phenolic acids in purple corn (*Zea mays* L.).

radical-scavenging assays, cellular studies *in vitro*, and animal studies *in vivo*.

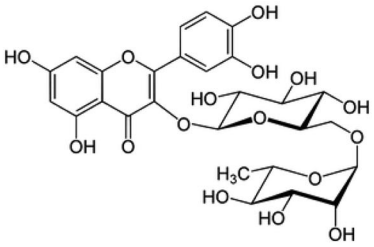
Free radical-scavenging assays (*in vitro*). The free radical tests used to evaluate the antioxidant capabilities of purple corn phenolics include DPPH (2,2-diphenyl-1-picrylhydrazyl), ABTS (2,2'-azino-bis-(3-ethylbenzylthiazoline-6-sulfonic acid), APPH (2,2'-azo-bis-(2-amidinopropane) dihydrochloride), ORAC (oxygen radical absorbance capacity), FRAP (ferric reducing antioxidant power), and deoxyribose assay and nitric oxide scavenging assays (Cevallos-Casals and Cisneros-Zevallos 2003; Del Pozo-Insfran and others 2006; Pedreschi and Cisneros-Zevallos 2006; Lopez-Martinez and others 2009; Lee and others 2010; Lopez-Martinez and others 2011; Ramos-Escudero and others 2012b; Duangkhamchan and Siriamornpun 2015; Vayupharp and Laksanalamai 2015). Consistent between studies, various purple corn extracts exhibited positive antioxidant capability in all assays throughout the years. Overall, the antioxidant activity of purple corn is highly correlated with the amounts of bioactive compounds such as polyphenols, flavonoids, flavanols, and anthocyanins, which can also be impacted by methodology, genotype, and growing location (Ramos-Escudero and others 2012a, b; Khampas and others 2015). Pedreschi and Cisneros-Zevallos (2006) concluded that the antioxidant activities for purple corn anthocyanins (1.019 ± 0.05 μg Trolox equivlent/μg) were higher than those of the other phenolic compounds (0.838 ± 0.11 μg Trolox equivlent/μg). In another study, these 2 portions showed no significant differences in the ABTS reducing power test (Lopez-Martinez and others 2009). It could not be denied that both purple corn anthocyanins and other phenolic compounds were shown to be great antioxidants, and some variation of their antioxidant power should be expected between different studies. The DPPH assay was used to better understand why purple corn showed relatively high antioxidant activity compared to other fruits and vegetables. Purple corn phenolics exhibited higher antioxidant capability and faster reaction kinetics than the same amount of blueberry phenolics, suggesting purple corn phenolics to have a larger number of active hydroxyl groups and more favorable configurations to allow for better interactions with the free radicals (Cevallos-Casals and Cisneros-Zevallos 2003).

The free radical-scavenging capability of purple corn was also found to remain high after industrial processing (Del Pozo-Insfran and others 2006; Lopez-Martinez and others 2011). The antioxidant properties of cooked purple corn kernels, tortillas, and chips were investigated using the ABTS, APPH, and ORAC methods. For both Mexico and America genotypes, anthocyanin losses were similar with average losses of 37%, 54%, and 75% when processed into nixtamal, tortillas, and chips, respectively; their average antioxidant capability losses were 28% after nixtamalization, 37% when processed to tortillas, and 55% when processed into chips (Del Pozo-Insfran and others 2006). The decreased antioxidant response might be associated with losing bioactive phenolic compounds during the alkaline and thermal processing.

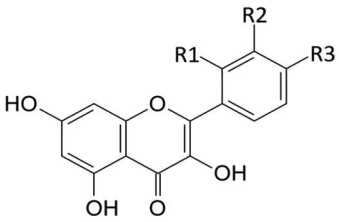
Cellular and animal studies (*ex vivo*). The effect of purple corn extracts on cellular antioxidant response in mouse organs was investigated by treatment with added H_2O_2 to isolated mouse kidney, liver, and brain *ex vivo* (Ramos-Escudero and others 2012b). The presence of malondialdehyde (MDA) in these organs served as an indicator of cell membrane oxidative injury after applying



Hirsutrin



Rutin



Name	R1	R2	R3
Kaempferol	H	H	OH
Quercetin	H	OH	OH
Morin	OH	H	OH
Naringenin	H	H	OH
Hesperitin	H	OH	OCH_3

Figure 4–Chemical structures of typical flavonoids in purple corn (*Zea mays* L.).

H_2O_2. When the organs showed low MDA levels and were treated with purple corn extracts, the levels of antioxidant enzymes superoxide dismutase (SOD), catalase, and total peroxidase in the organs were increased (Ramos-Escudero and others 2012b). These enzymes are believed to have the capability to eliminate reactive oxygen species and prevent oxidative damage to cells. The results of this study suggested that certain functional compounds in purple corn extract could penetrate cell membranes and participate in stimulating antioxidant enzyme secretions to reduce oxidative damage to cells caused by free radicals (Ramos-Escudero and others 2012b).

Cellular and animal studies (*in vivo*). Another study demonstrated the protective effect of purple corn diets against oxidative damage in rat livers and kidneys *in vivo* (Zhang and others 2014). In this work, oxidative stress was induced by addition of fluoride to the rats' drinking water (Zhang and others 2014). Swollen cells and vague cell boundaries were signs of high oxidative stress and were observed in the fluoride alone treated rats. These rats also had high MDA levels in serum and liver tissue (Zhang and others 2014). However, the cells of rats treated with fluoride and the purple corn-rich diet showed fewer swollen cells and significantly lower MDA levels (Zhang and others 2014). The antioxidant enzymes (SOD and glutathione peroxidase) levels for purple corn-treated rats were also significantly higher than the fluoride alone treated group (Zhang and others 2014). These results suggested that purple corn in the diet may alleviate fluoride-induced oxidative damage by elevating the antioxidant capability in livers and kidneys of rats (Zhang and others 2014).

The antioxidant capability of purple corn extract was also evaluated *in vivo* with healthy rats. The cell histology of purple corn color-fed rats presented no significant difference to that of the rats fed a regular diet (Yokohira and others 2008). However, the serum of rats fed with purple corn color presented strong antioxidant power in potential antioxidant tests *in vivo*, and microarray analyses showed purple corn color could induce RNA expression of P450 (cytochrome) oxidoreductase, phosphatidylinositol 3-kinase, and phospholipase A2 (Yokohira and others 2008). The authors thus suggested that purple corn may be effective as antioxidants *in vivo* and may have chemopreventive potential against liver preneoplastic lesion development (Yokohira and others 2008).

Anti-inflammatory activities

Inflammation is thought to play a role in promoting some kinds of cancer in animals and humans (Kwon and others 2007). Anti-inflammatory refers to the property of reducing or inhibiting inflammation. It has been revealed that purple corn pigments can debilitate high-glucose-induced mesangial inflammation, expansion, and hyperplasia by disturbing the inflammatory action of interleukin-8 (IL-8) (Li and others 2012a). When the renal mesangial cells of db/db mice were exposed to high-glucose to induce diabetes, the production of IL-8, a chemokine that is linked to inflammatory processes in glomeruli, was markedly elevated (Li and others 2012a). In contrast, cells that received purple corn anthocyanin-rich extract treatments showed mitigation of IL-8 secretion in a dose-dependent manner (Li and others 2012a). Another study has also demonstrated that purple corn pigments antagonized diabetic kidney problems through control of the IL-8-Tyk2-STAT-signaling pathway (Kang and others 2012).

Cyanidin-3-glucoside (C3G) is the most abundant anthocyanin throughout the plant kingdom as well as in in purple corn (Kong and others 2003; Lao and Giusti 2016). Numerous research studies have shown that C3G has strong anti-inflammatory properties, although not all sources of C3G were purple corn (Reddy and others 2005; Min and others 2010; Serra and others 2013;). Cyclooxygenase (COX) is a well-known inflammatory protein whose abnormal up-regulation is commonly found in many cancers (Martin and others 2003; Wang and Stoner 2008). C3G from *Prunus cerasus* exhibited strong anti-inflammatory property by efficiently inhibiting COX-1 and COX-2 enzyme activity (Reddy and others 2005). Additionally, Tsuda and others (2002) demonstrated C3G may play a role in the prevention of the NO-mediated inflammatory diseases. C3G was found to suppress zymosan-induced

inflammatory response in rats when orally administered; the elevations of inflammatory markers such as peritoneal exudate NOx, tumor necrosis factor (TNF), and others were significantly suppressed by the administration of C3G (Tsuda and others 2002). In a lipopolysaccharide-induced inflammation study using RAW 264.7 cells, C3G from black rice and its metabolites suppressed the production of the proinflammatory cytokines: TNF-α, interleukin-1β (IL-1β), 2 inflammatory mediators, NO, and prostaglandin E2 (PGE2), and also the gene expression of nitric oxide synthase (iNOS) and COX-2 (Min and others 2010). In addition, in an *in vivo* study with carrageenan-induced inflammation BALB/c mice, C3G from black rice was demonstrated to have a significant effect on inhibiting the leukocyte numbers and the levels of TNF-α, PGE2, and protein in the exudates of the air pouch in carrageenan-treated mice, as well as COX-2 expression and nuclear factor-kappa B activation (Min and others 2010). Another study on cytokine-induced inflammatory response in HT-29 human intestinal cells showed that C3G presented higher anti-inflammation efficiency than 5-aminosalicylic acid, a well-established anti-inflammatory drug, in reducing NO, PGE2, IL-8 production, and iNOS and COX-2 expressions (Serra and others 2013).

Anti-mutagenic properties

A mutagen is an agent that induces changes to genetic materials, usually DNA, and thus increases the frequency of mutations. An anti-mutagen refers to an agent with the capability of reducing the rate of mutation. Anthocyanins and phenolic acids are well-known anti-mutagenic agents as evidenced through several studies with many fruits and vegetables (Yoshimoto and others 2001; Santos-Cervantes and others 2007). The antimutagenic properties of purple corn have been examined using the Ames test. Anthocyanin-rich water fractions (WF) and phenolics-rich ethyl acetate fractions (EAF) from purple corn both showed dose-dependent anti-mutagenic activity against the food mutagen Trp-P-1 (Pedreschi and Cisneros-Zevallos 2006). The purple corn phenolics fraction (EAF) was found to be a more potent antimutagen than the anthocyanin-rich fraction (WF) having a lower IC50 value of 95.2±10.95 μg of chlorogenic acid equivalent/plate compared to 321.7±21.36, respectively (Pedreschi and Cisneros-Zevallos 2006). This study also revealed that the predominant mechanism of anti-mutagenic behavior of purple corn anthocyanins was a blocking effect on the S-9 Mix activation system of the mutagen; whereas for the purple corn phenolics, a dual mechanism involved both the blocking of the S-9 Mix and also a scavenging action on Trp-P-1 electrophiles (Pedreschi and Cisneros-Zevallos 2006). In typical food processing procedures, such as the nixtamalization process in masa and tortilla production, some pigments are lost; however, processed purple corn still presented anti-mutagenic activity against 2-aminoanthracene-induced mutagenicity in the Ames test (Mendoza-Díaz and others 2012). Thus, consuming processed purple corn may still have a beneficial anti-mutagenic effect in humans.

Anticarcinogenic and anticancer properties

A carcinogen is a substance, radionuclide, or radiation that has the ability to damage the genome or to disrupt of cellular metabolic processes and thus to exacerbate cancer or its propagation (Poirier 2004). Anticarcinogenic refers to the property of inhibiting or preventing the activity of a carcinogen or the development of carcinoma.

Skin cancer. Skin cancer is the most commonly diagnosed cancer in the United States; however, the number of skin cancer patients is difficult to estimate because some types of cancer are not required to be reported to cancer registries (American Cancer Society 2015). It has been estimated that in 2006, 3.5 million cases were diagnosed among 2.2 million people of nonmelanoma skin cancers (American Cancer Society 2015). Pomegranate fruit extract, rich in pelargonidin-3-glucoside and cyanidin-3-glucoside, has been reported to modulate MAPK and NF-B pathways and to inhibit 12-O-tetradecanoylphorbol-13-acetate-induced skin tumorigenesis in CD-1 mice. Skin tumor incidence was reduced 70% at week 16, and tumor multiplicity was reduced 64% at week 30 for the mice treated with pomegranate fruit extract (Afaq and others 2005). From these findings, it may be inferred that purple corn, also abundant in these 2 pigments, may exhibit potential protective effects against skin cancer.

In related work, anthocyanins from several sources, including purple corn, were incorporated into lipstick formulations and evaluated for potential biologically active properties. In *in* vitro assays, all formulations showed increased UV absorption, free DPPH radical-quenching, and inhibition of melanin production by tyrosinase (Westfall 2015). Moreover, the pigments were found to penetrate into the stratum corneum both *in vitro* and *in vivo* in humans, suggesting further potential protective effects against dermal carcinogenesis (Westfall 2015).

Mammary and prostate carcinogenesis. An estimated 234190 (231840 for women) new cases of breast cancer and 220800 new cases of prostate cancer are expected to occur in the United States during 2015 (American Cancer Society 2015). Breast cancer for women and prostate cancer for men are the most frequently diagnosed cancers aside from skin cancer (American Cancer Society 2015). The anticarcinogenic property of purple corn on mammary and prostate carcinogenesis has been evaluated *in vitro* and *in vivo* (Fukamachi and others 2008; Long and others 2013). Purple corn color demonstrated significant inhibition activity on 7,12-dimethylbenz[α]anthracene-induced mammary carcinogenesis development in human c-Ha-ras proto-oncogene transgenic (Hras128) rats in a dose-dependent manner, supported by the incidence of middle-sized (0.5 to 2.0 g) mammary tumors being significantly decreased in purple corn color-fed rats (Fukamachi and others 2008). The number and incidence of small-sized (<0.5 g) mammary tumors was not suppressed by purple corn color, indicating it was not able to inhibit the emergence of mammary tumors in these rats (Fukamachi and others 2008). *In vitro*, purple corn color was found to inhibit cancer cell viability and induce apoptosis in mammary tumor cells derived from Hras128 rat mammary carcinomas (Fukamachi and others 2008). At the molecular level, purple corn activated caspase-3, a key protease associated with DNA fragmentation and apoptosis, and reduced Ras protein levels in tumor cells (Fukamachi and others 2008). A similar study also showed that C3G could inhibit the growth of HS578T, a human breast carcinoma cell line, in a dose-dependent manner (Chen and others 2005). Anti-proliferative effect of Mexican purple corn phenolics has also been reported in human hormone-dependent mammary (MCF7) and prostate (PC3) cancer cell lines (Urias-Lugo and others 2015).

Long and others (2013) showed the proliferation androgen-dependent prostate cancer in the cell line LNCaP was inhibited by purple corn color through limiting the expression of Cyclin D1 and inhibiting the G1 stage of the cell cycle. In this research, male TRAP transgenic rats for adenocarcinoma of the prostate gland that consumed purple corn pigments showed lower percentages

of adenocarcinoma and higher percentages of low-grade prostatic intraepithelial neoplasia. These findings suggested that purple corn color could retard prostate cancer progression (Long and others 2013).

Colon cancer. Colorectal cancer is the third most common cancer in both men and women. It is estimated in 2015 that about 93090 cases of colon cancer will be diagnosed, and 49700 colorectal cancer-related deaths will occur (American Cancer Society 2015). The benefits of consuming purple corn on colon cancer development have been studied by researchers internationally (Hagiwara and others 2001; Reddy and others 2005; Jing and others 2008; Zhao and others 2009). In a study with male F344/DuCrj rats, purple corn color (5% dietary level) showed significant reduction of colorectal carcinogenesis induced by 1,2-dimethylhydrazine (DMH) and 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP) (Hagiwara and others 2001). Fewer incidences of macroscopic colon nodules and lower average number of aberrant crypt foci were observed in rats fed with purple corn color and receiving PhIP, suggesting purple corn color exerted protective effects against PhIP-induced promotion of colon tumor development (Hagiwara and others 2001). The anti-carcinogenic effects of purple corn color were not accompanied by any evidence of adverse effects (Hagiwara and others 2001). Subsequent *in vitro* cell studies also supported the findings of the *in vivo* study.

Jing and others (2008) measured the inhibition colon cancer cell growth using the human colorectal adenocarcinoma (HT29) cell line with different anthocyanin rich-extracts from purple corn, chokeberry, bilberry, purple carrot, grape, radish, and elderberry. All anthocyanins from this study suppressed the proliferation of HT29 cells. The GI_{50} for Peruvian purple corn anthocyanins was around 14 μg of C3G equiv/mL which was a much lower concentration than pigments from other sources, suggesting purple corn pigments were potent anticolon cancer agents (Jing and others 2008). A similar study also showed Chinese purple corn had antiproliferative capacity against HT29 cells in a dose-dependent manner (Zhao and others 2009). C3G from *Prunus cerasus*, also found in purple corn, showed a dose-dependent growth-inhibition effect to HCT-116 colon tumor cells (Reddy and others 2005). The antiproliferative effect of purple corn has also been recently reported on another colon cancer cell, Caco2. The cell viability of the Caco2 cells was less than 30% compared to the nontreated cells with just 5 mg/mL purple corn phenolics (Urias-Lugo and others 2015). It is important to note that anthocyanin-rich materials have been found to potently inhibit the proliferation of HT29 colon cancer cell lines, but did not present inhibition to the growth of nontumorigenic colonic NCM460 cells (Zhao and others 2004).

The *in vivo* anticarcinogenic effects of purple corn after industrial processing to create tortillas have been investigated in a more recent study (Reynoso-Camacho and others 2015). Four different colored Mexican corn tortilla powders were fed in 27% w/w to male Sprague–Dawley rats treated with 1,2-dimethylhydrazine (DMH) to induce colon carcinogenesis; results clearly demonstrated the protective effect of corn tortilla consumption on the incidence of adenocarcinomas (Reynoso-Camacho and others 2015). White and purple corn tortilla-fed rats developed 77.5% fewer tumors, whereas yellow and red corn tortilla-fed groups developed 55% fewer adenocarcinomas than the DMH control group (Reynoso-Camacho and others 2015). Reduction of colon carcinogenesis by purple corn was thought to be a result of the inhibition of cecal β-glucuronidase activity by induction of detoxifying enzymes (GST and NQO1) in the liver and colon and also the modulation of key proliferative proteins (K-ras and β-catenin) (Reynoso-Camacho and others 2015).

Liver carcinogenesis. An estimated 35660 new cases of liver cancer and 23000 associated deaths are expected to occur in the U.S. during 2015 (American Cancer Society 2015). Many cases in recent decades have been attributed to chronic diseases like diabetes or obesity, for which anthocyanins and polyphenolic compounds have shown promise in amelioration (American Cancer Society 2015). Yokohira and others (2008) investigated the chemopreventative effect of purple corn color on diethylnitrosamine-initiated hepatocarcinogenesis in F344 male rats.

Purple corn color might have modifying effects on mRNA markers concerning liver carcinogenesis development, as suggested by the increasing gene expression ratio for cyp 2c, 2e1, 3a1, and 3a2, phospholipase C, and delta 4 in rat serum (Yokohira and others 2008). The antiproliferative impact of Mexican purple corn phenolics on liver cancer was recently studied with the cell line HepG2 (Urias-Lugo and others 2015). Their results showed a reduction of cell viability that had a strong correlation with the concentration of C3G and its malonic acid acylated derivative (Urias-Lugo and others 2015).

Lung cancer. Lung cancer accounts for more deaths than any other cancer in both genders, accounting for about 27% of all cancer deaths (American Cancer Society 2015). Cyanidin-3-glucoside (C3G), the predominant anthocyanin in purple corn, has been shown to be capable of inhibiting the development of lung tumor cells in mice. This pigment inhibited proliferation of a human lung carcinoma cell line A549 *in vitro*, reduced the size of tumor xenograft growth, and inhibited metastasis *in vivo* (Ding and others 2006). In a mechanistic study it was indicated that C3G could inhibit migration and invasion of A549 tumor cells (Ding and others 2006). Similarly, it was demonstrated that C3G inhibited the migration and invasion of Lewis lung carcinoma cells both *in vitro* and *in vivo* in C57BL/6 male mice (Chen and others 2005). Moreover, C3G isolated from *Prunus cerasus* also showed a dose-dependent growth inhibition effect on NCl-H460 lung tumor cells (Reddy and others 2005).

Antiangiogenesis

Angiogenesis is the process of forming new blood vessels from the existing vascular network and plays a critical factor in tumor growth and metastasis (Huang and others 2006). The antiangiogenesis effect of anthocyanin-rich purple corn extract under hyperglycemic conditions has been investigated in human endothelial cells *ex vivo* and in db/db mice *in vivo* (Kang and others 2013). *Ex vivo*, purple corn extract decreased endothelial expression of vascular endothelial growth factor (VEGF), one of the most potent angiogenesis-activating agents (Wang and Stoner 2008; Kang and others 2013). The extract also attenuated both hypoxia inducible factor (HIF)-1a, endothelial marker of platelet endothelial cell adhesion molecule-1, and integrin b3 induced by the hyperglycemic growth conditions (Kang and others 2013). Similar findings were encountered *in vivo* with mice models treated with 10 mg/kg PCE for 8 wk. Glomerular angiogenesis in the kidney was alleviated due to attenuation of the induction of VEGF and HIF-1a, and mesangial and endothelial induction of angiopoietin proteins was diminished under hyperglycemic conditions (Kang and others 2013). Thus, the authors concluded purple corn extract could be served as a potent therapeutic agent for abnormal angiogenesis (Kang and others 2013).

Amelioration of lifestyle diseases: obesity, diabetes, hyperglycemia, and associated diseases

Obesity can be defined as the accumulation of excess adipose tissue resulting from various metabolic disorders; it is also a strong risk factor for type 2 diabetes, hyperglycemia, hypertension, hyperlipidemia, and various cardiovascular diseases (Lew and Garfinkel 1979; Tsuda and others 2003; Kahn and others 2006). Purple corn has been shown in several studies to have beneficial effects on ameliorating these lifestyle diseases.

A series of experiments have been conducted focusing on the effects of purple corn anthocyanins on the prevention of metabolic syndrome (Tsuda 2008). Purple corn color was shown to prevent obesity in male C57BL/6 mice that were fed a high-fat diet of 300 g lard/kg (Tsuda and others 2003). The mice in the high-fat diet group had significantly higher body weight than those in the control group, the group fed purple corn color alone, and the combined high fat and purple corn color-fed group after 5 wk (Tsuda and others 2003). The adipocytes of the high-fat group were much larger and looser than those of the other groups, but no hypertrophy of adipocytes were found to occur in high-fat and purple corn color-fed mice (Tsuda and others 2003). Interestingly, this study was designed so the energy intake of the mice was standardized between treatment groups, and thus the suppression of weight gain was not due to reduction of dietary fat digestion or energy intake (Tsuda and others 2003; Tsuda 2008). The study examined several parameters such as lipid, glucose, insulin concentrations, and lipogenic enzymes, and it was concluded that purple corn color down-regulated mRNA levels of enzymes included in lipid synthesis and reduced SREBP-1 mRNA levels in white adipose tissue (Tsuda and others 2003).

To better understand the mechanism of how purple corn color functions to prevent obesity, the Tsuda and others (2004, 2005, 2006) tested the impact of the major anthocyanin and related anthocyanidin of purple corn, cyanidin-3-glucoside (C3G), and cyanidin (Cy) on adipocyte functionality. Research has shown C3G and Cy could increase the secretion of adipocytokines, a group of bioactive molecules involved in lipid regulation. They have also been found to enhance adipocyte-specific gene expression (such as lipoprotein lipase, adipocyte fatty acid binding protein 2, uncoupling protein 2, and peroxisome proliferator-activated receptor γ) at least 2-fold in isolated adipocytes from rats fed 2 g/kg anthocyanin diets (Tsuda and others 2004). Then they further examined the detailed gene expression changes due to C3G and Cy treatment using microassay analysis (Tsuda and others 2005). Isolated rat adipocytes treated with 100 μM C3G or Cy for 24 h showed up-regulation of 633 or 427 genes, respectively, related to lipid metabolism and signal transduction (Tsuda and others 2005). With the same treatments on human adipocyte cells, there was significant up-regulation of adiponectin expression, down-regulation of plasminogen activator inhibitor-1 and interleukin-6, and induction of some of lipid metabolism-related genes in both the C3G and Cy treatment groups (Tsuda and others 2006). These results suggest purple corn anthocyanins have unique therapeutic advantages responsible for the regulation of the adipocyte function and possibly in preventing lifestyle disease such as obesity and diabetes.

Lifestyle diseases are often accompanied by other complications and diseases, such as diabetes and neuropathy. A Korean group has worked on the inhibition of diabetes-associated glomerular angiogenesis by purple corn anthocyanins in cell lines and in animal models (Kang and others 2012, 2013; Li and others 2012a,b). Purple corn anthocyanins were shown to dampen high-glucose-induced mesanginal fibrosis inflammation *in vitro*, and these pigments could play a renoprotective role in diabetic nephropathy (Li and others 2012a). This group also demonstrated that purple corn anthocyanins could inhibit diabetes-associated glomerular monocyte activation and macrophage infiltration as well as retard diabetes-associated glomerulosclerosis through disturbing the mesanginal IL-8-Tyk-STAT signal pathway in db/db mice (Kang and others 2012; Li and others 2012b). Moreover, their research showed anthocyanin-rich purple corn extract inhibited diabetes-associated glomerular angiogenesis by attenuating the induction of VEGF and HIF-1α (Kang and others 2013). These studies suggested purple corn anthocyanins may be a potent therapeutic agent for diabetes and hypertension related kidney failure (Kang and others 2012, 2013; Li and others 2012a,b).

Additional research has provided experimental support that purple corn anthocyanins may help ameliorate diabetes, hyperglycemia, and hypertension through inhibition of the enzymes that play critical roles in carbohydrate and lipid metabolisms (Kim and others 2013; Ranilla and others 2009). In an *in vitro* study, purple corn was shown to have potent α-glucosidase inhibitory capabilities in a dose-dependent manner due to its richness in protocatechuic acid. This finding suggested its potential antihypertension and antidiabetic activities (Ranilla and others 2009). Hirsutrin, another phenolic compound found in purple corn, showed potent inhibition of aldose reductase activity (Kim and others 2013). It also inhibited galactitol formation in rat lens and erythrocytes when under high-galactose osmotic stress (Kim and others 2013). These findings implicated that hirsutrin may be useful against complications associated with diabetes.

Other phenolic compounds in purple corn, like anthocyanins, were found to exhibit antidiabetic health properties. They enhanced insulin secretion in hamster pancreatic beta cells (HIT-T15) and also protected the cells from death in culture (Hong and others 2013). *In vivo,* similar activities were found in db/db mice accompanied by lowered blood glucose levels (Hong and others 2013). In this study, purple corn anthocyanins did not demonstrate negative effects to the insulin-secreting pancreatic cells, unlike the commonly used diabetes drug sulfonylurea, which has been reported to accelerate the gradual deterioration of beta cell functionality and induce cell death (Del Guerra and others 2005; Maedler and others 2005; Hong and others 2013).

A more recent study has demonstrated purple corn extracts to have preventive effects on diabetic cataract formation on enucleated rat lenses incubated in 55 mM glucose (Thiraphatthanavong and others 2014). Results showed purple corn extract could help decrease lens opacity by lowering oxidative stress or suppressing aldose reductase, the rate-limiting enzyme in the polyol pathway (Thiraphatthanavong and others 2014).

An extract of purple rice which is similar to purple corn extracts, being abundant in C3G, was reported to suppress blood glucose increases in healthy male Wistar rats and in humans (Shimoda and others 2015). In the human study, 5 males and 3 females were fed a 200 g rice ball containing placebo after 11 h of fasting. Blood samples were collected at 0, 30, 60, 90, and 120 min, and their blood glucose levels were measured (Shimoda and others 2015). One week later, the same subjects were fed a 200-g rice ball, now containing 25 mg of purple rice extract (Shimoda and others 2015). A significant suppression of blood glucose levels at 30 and 90 min was observed when fed the purple rice extract, compared to the placebo treatment (Shimoda and others 2015). The authors also studied the mechanism of carbohydrate

absorption suppression by purple rice extract *in vitro* using 3 carbohydrate digestive enzymes. The results of this evaluation confirmed that the suppression of carbohydrate absorption was achieved by inhibitory effects on α-glucosidase, α-amylase, and aldose reductase activities (Shimoda and others 2015). It could be postulated that purple corn extract, having a similar phenolic profile as purple rice, may also suppress the acute increase in blood glucose after meals.

Blood pressure regulation

Blood pressure is a symptom of many chronic diseases and also plays an important role in overall health. The effects of purple corn on blood pressure regulation have been studied in both animal models and humans. In a study in which spontaneously hypertensive rats were intragastrically administrated purple corn color at a dose of 7.4 mg anthocyanin/kg body weight twice daily for 5 wk, a significant inhibition of an increase in systolic blood pressure was observed after just 8 d (Toyoshi and Kohda 2004). Similarly, another study feeding spontaneously hypertensive rats with purple corn color rich in anthocyanins for 15 wk and found that the systolic blood pressures of the purple corn color-fed rats were significantly lower than those of the control groups (Shindo and others, 2007). The findings of these studies suggest that purple corn pigments had anti-hypertensive effects on hypertensive animals.

The benefits of purple corn extract on blood pressure of mild-to-moderate hypertensive Peruvians was investigated on a small scale ($n = 30$) (Finkel and others 2013). This study showed that in a short period of time (3 wk) purple corn extract had a beneficial effect on reducing systolic and diastolic blood pressure (from139/88 to 132/81 mm Hg) in early-stage hypertension patients, regardless of age, gender, body mass index, or initial average blood pressure reading (Finkel and others 2013). Although the mechanism of blood pressure regulation by purple corn is still not clear, the observed effects of purple corn suggest a great potential for the application of this plant as food supplements and medications.

Heart health

Phenolic compounds, including anthocyanins, have been reported to also have beneficial effects on cardiovascular health (He and Giusti 2010; Wallace 2011). Results of 1 study led to the suggestion that these beneficial properties of phenolic compounds might be due to their capability to inhibit hexanal formation in human low-density lipoproteins and also by inhibition of hydroperoxide formation in lecithin liposomes (Heinonen and others 1998). In the previously mentioned study in which spontaneously hypertensive rats were fed purple corn color for 15 wk, it was shown that the heart rate of the rats (averaging 365 beats/min) was also significantly lower than that of the control rats (385 beats/min in average) (Shindo and others 2007). In another study, broiler chickens fed a diet enriched with purple corn exhibited significantly lower heart weights and abdominal fats compared to chickens fed conventional yellow corn diets; an inverse relationship was found to occur between heart weight and percentage of purple corn in diet, such that heart weight continued to decrease as dietary purple corn increased (Amnueysit and others 2010). These findings further suggest purple corn cultivars may have added heart health benefits compared to yellow corn varieties.

Toxicity Evaluations

In addition to evaluation of all the potential health-benefit properties, the toxicity of purple corn must also be evaluated for any routine or medicinal use. Purple corn pigment-rich extracts have been evaluated toxicologically by different research studies, including 2 major ones conducted in China and Japan. The Chinese research team conducted an evaluation of acute oral toxicity on Wistar rats by gavage feeding purple corn pigment solutions at levels up to 21.5 g/kg bw (Zhou and others 2007). Solutions of purple corn pigments were prepared by first spray-drying extracts obtained by soaking plant materials in 60% to 70% acidic ethanol at 50 to 60 °C and then dissolving the powder in distilled water (Zhou and others 2007). No rats showed any observable symptoms of toxicity or death during the study; therefore, the authors concluded that the oral LD50 for purple corn pigment-rich extract in rats was greater than 21.5 g/kg bw (Zhou and others 2007). In addition, the purple corn extracts presented no significant difference ($P > 0.05$) to the negative control groups in the results of mice marrow micronucleus tests and sperm aberration tests (Zhou and others 2007). According to Chinese toxicity grading standards, the purple corn pigments tested were considered to do no harm and likely have great potential to be developed as a food additive or "healthy" food material (Zhou and others 2007).

A 90-d subchronic oral toxicity study of purple corn color, containing 26.4% anthocyanins, 57.7% other polyphenols, and 10% citric acid, was conducted in Japan using F344 rats (Nabae and others 2008). The no-observed-adverse-effectlevel (NOAEL) was determined to be 5.0% dietary purple corn color for both sexes (male: 3542 mg/kg bw/d, female: 3849 mg/kg bw/d) under the conditions of this experiment (Nabae and others 2008).

Recommended Dosage Levels

In addition to the rather high consumption levels for potential toxicity, the health benefitting potential of purple corn is furthered by the low dosages needed to obtain some health benefits from purple corn extracts. In a variety of studies, mostly at the level of milligrams of purple corn anthocyanins/kg body weight, the dosages of purple corn applied in health-benefit studies involving humans and animals, are shown in Table 1. To summarize, most health-benefit studies conducted with mice used dosages of purple corn anthocyanins around 10 mg/kg bw (Kang and others 2012, 2013; Li and others 2012a; Hong and others 2013). Studies conducted with rats used dosages of purple corn color ranging from 0.2% to 1.0% of the total diet or 7.4 mg/(kg bw) anthocyanin equivalent (Tsuda and others 2003; Yokohira and others 2008; Long and others 2013. In a human study involving slightly hypertensive patients, a daily capsule of 300 mg purple corn extract was prescribed (Finkel and others 2013). Each capsule contained 6% total anthocyanins (18 mg), 15% other phenolic compounds (45 mg), and 76.6% carbohydrates with negligible amounts of fats and proteins. No adverse reactions were reported (Finkel and others 2013).

To date, there is no recommended dosage of purple corn anthocyanin consumption for human health benefits. Despite the accumulating evidence that strongly suggests that these compounds may be beneficial to human health, additional studies must still be conducted to further add to these findings. Anthocyanin consumption in the U.S. has been estimated to be about 12.5 mg/d/person and previously had been reported to be as high as 200 mg/d/person (Wu and others 2006). The dosage of 0.01% purple corn color in daily diet as used in the experiments by Yokohira and others (2008), which approximately corresponds to current estimated average human daily intake of anthocyanins, did not show significant beneficial effects. The level of purple corn color required to achieve beneficial impact was 1% in a rat diet, which

Table 1–The dosages of purple corn anthocyanins and other phenolics applied to animals and humans in health-benefit studies.

Function	Target disease and/or organ	Purple corn source	Subjects	Dose tested in study showing health benefits	Reference
Anticancer	Cancer; Colon	Japanese purple corn color (PCC) powders, 21.5% anthocyanins	F344/DuCrj rats, 6-wk old, male	5% PCC in daily diet	(Hagiwara and others 2001)
Anticarcinogenic	Cancer; Colon	Mexican purple corn, processed to tortilla powers (PCT), 13.03 ± 0.55 mg/100g ACN, 138.14 ± 2.95 mg/100g phenolics	Sprague–Dawley rats, 4–5 wk, male	27 % PCT/BW (w/w)	(Reynoso-Camacho and others 2015)
Anticarcinogenesis	Cancer; Prostate	Japanese purple corn color (PCC) powders, 20.9% anthocyanins	TRAP rats with a Sprague–Dawley genetic background, 6-w-old, male	0.1% and 1% PCC in daily diet (25 and 267 mg PCC/rat/d)	(Long and others 2013)
Anticarcinogenesis	Cancer; Mammary	Japanese purple corn color (PCC) powders, 33.7% anthocyanins	c-Ha-ras transgenic and nontransgenic rats, female	1% PCC in daily diet	(Fukamachi and others 2008)
Anticarcinogenesis Antioxidant	Cancer; Liver	Japanese purple corn color (PCC) powders, 33.7% anthocyanins	F344 rats, 4-wk-old, male	1% PCC in daily diet (correspond to 168.5 mg anthocyanins/kg BW/ d in humans.)	(Yokohira and others 2008)
Antioxidant	Cancer; Liver and kidney	Chinese maize purple plant pigments (MPPP), 57.95% anthocyanins	Wistar rats, male and female	1% PCC in daily diet	(Zhang and others 2014)
Anti-inflammatory	Diabetes glomerulosclerosis; Kidney	Korean purple corn kernel phenolic-rich extract (PCE)	db/db mice and their nondiabetic db/m littermates, Adult, male	10 mg PCE /kg BW daily	(Li and others 2012a, Kang and others 2012)
Anti-angiogenesis	Diabetic nephropathy; Kidney	Korean purple corn kernel anthocyanin-rich extract (PCE)	db/db mice and their nondiabetic db/m littermates, 8-wk-old, male	10 mg PCE/kg BW daily	(Kang and others 2013)
Antidiabetic Antihyperglycemic	Diabetes; pancreatic beta cell	Peruvian purple corn anthocyanin powders (PCA), 10% anthocyanins	C57BL/KsJ *db/db* mice, 6-wk-old, male	10 mg PCA /kg BW daily	(Hong and others 2013)
Blood pressure regulation	Hypertension	Japanese Purple corn color (PCC), 26% anthocyanin	spontaneously hypertensive rats	56.7 mg PCC/kg BW/d	(Toyoshi and Kohda 2004)
Blood pressure and heart rate regulation	Hypertension	Japanese Purple corn color (PCC), 26% anthocyanins	spontaneously hypertensive rats, 3-wk-old, male	1% PCC in diet	(Shindo and others 2007)
Blood pressure regulation	Hypertension	Peruvian purple corn extract (PCE), process to capsule which contained 300mg PCE, 18mg anthocyanin, 45mg phenolics,	Phase-I hypertension humans, 21–70 years old, male and female	1 capsule	(Finkel and others 2013)
Obesity prevention	Obesity	Cy and C3G standard, purity>99%	Wistar rats, 7-wk-old, male	2 g C3G /kg diet, rats had free access to the diet	(Tsuda and others 2004)
Obesity prevention	Obesity	C3G purified from purple corn, purity>95%	Wistar rats, 8-wk-old, male	0.2% C3G in daily diet	(Tsuda and others 2003)

corresponded to 500 mg/kg body weight/d in humans or 168.5 mg anthocyanin/kg bodyweight/d in humans based on the FAO/WHO Joint Expert Committee on Food Additives (Yokohira and others 2008). Considering these values and those from clinical trials on blood pressure control using purple corn anthocyanin consumption rates of 18 mg/d/person, it could be reasonable to speculate that the typical average levels of purple corn anthocyanin daily consumption would do no harm and have additional potential for beneficial health effects (Finkel and others 2013). More research is still required to make consumption dosage recommendations.

Conclusion and Perspective

The functional properties of purple corn have been increasingly studied and have become more popular in recent decades. Although the use of purple corn has been traced back to hundreds of years ago in South America, it is now gaining popularity in the worldwide market due to its deep color and potential health-promoting properties. Currently, more than 20 bioactive phenolic compounds, including phenolic acids, anthocyanins, and other flavonoids, have been reported to be found in purple corn (*Zea* may L.). These phenolic compounds, as presented in this review, have been shown in numerous *in vivo* and *in vitro* studies to have

potent health-benefitting capabilities. Some include antioxidant, anti-inflammatory, anti-mutagenic, anti-carcinogenic, anti-cancer, anti-angiogenesis properties, which can help to ameliorate lifestyle diseases such as obesity, diabetes, hyperglycemia, hypertension, and cardiovascular diseases. These beneficial properties are in large proportions attributed to the strong antioxidant capabilities of purple corn phenolic compounds, as well as their anti-inflammatory properties.

Importantly, these health-benefitting properties still remain at satisfactorily high levels even after undergoing food industry processing. Research has shown that the no-observed-adverse-effect-level (NOAEL) of purple corn color was at least 5.0% of the diet in rats (~3.5 g/kg bw/d) (Nabae and others 2008); and for hypertension patients, daily consumption of only 300 mg purple corn extracts (~18 mg anthocyanins) for 3 wk allowed for beneficial blood pressure reduction (Finkel and others 2013). Most current studies on health benefits of purple corn were conducted with anthocyanins or phenolic compound mixtures. Studies of individual anthocyanin or other isolated phenolic compounds are still in high demand, especially to better understand the potential contribution of the individual components. The most effective functional phenolic compound in purple corn has not yet been identified, and it is still unknown whether the health-benefitting effects are the result of a synergistic relationship of combined components. As only a relatively small dosage of purple corn functional compounds may achieve beneficial effects, this rich source of health-promoting compounds warrants additional study to clarify its mechanisms of action and to better understand its potential contributions to human health.

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Disclaimer

The views expressed in this manuscript are those of the authors and do not necessarily reflect the position or policy of Alicorp S.A.A. (Lima, Peru).

References

Afaq F, Saleem M, Krueger CG, Reed JD, Mukhtar H. 2005. Anthocyanin and hydrolyzable tannin-rich pomegranate fruit extract modulates MAPK and NF-κB pathways and inhibits skin tumorigenesis in CD-1 mice. Intl J Cancer 113:423–33.

Ai Y, Jane J. 2016. Macronutrients in corn and human nutrition. Compr Rev Food Sci Food Saf 15:581–98.

American Cancer Society. 2015. Cancer facts & figures 2015. doi:10.3322/caac.21254

Amnueysit P, Tatakul T, Chalermsan N, Amnueysit K. 2010. Effexts of purple field corn anthocyanins on broiler heart weight. Asian J Food Agro-Industry 3:319–27.

Aoki H, Kuze N, Kato Y. 2002. Anthocyanins isolated from purple corn (*Zea mays* L.). Foods Food Ingredients J Japan 199:41–5.

Cevallos-Casals BA, Cisneros-Zevallos L. 2003. Stoichiometric and kinetic studies of phenolic antioxidants from Andean purple corn and red-fleshed sweetpotato. J Agric Food Chem 51:3313–9.

Chen P-N, Chu S-C, Chiou H-L, Chiang C-L, Yang S-F, Hsieh Y-S. 2005. Cyanidin 3-glucoside and peonidin 3-glucoside inhibit tumor cell growth and induce apoptosis in vitro and suppress tumor growth in vivo. Nutr Cancer 53:232–43.

De Pascual-Teresa S, Santos-Buelga C, Rivas-Gonzalo JC. 2002. LC-MS analysis of anthocyanins from purple corn cob. J Sci Food Agric 82:1003–6.

Del Guerra S, Marselli L, Lupi R, Boggi U, Mosca F, Benzi L, Del Prato S, Marchetti P. 2005. Effects of prolonged in vitro exposure to sulphonylureas on the function and survival of human islets. J Diabetes Complicat 19:60–4.

Del Pozo-Insfran D, Brenes CH, Serna Saldivar SO, Talcott ST. 2006. Polyphenolic and antioxidant content of white and blue corn (*Zea mays* L.) products. Food Res Intl 39:696–703.

Ding M, Feng R, Wang SY, Bowman L, Lu Y, Qian Y, Castranova V, Jiang B-H, Shi X. 2006. Cyanidin-3-glucoside, a natural product derived from blackberry, exhibits chemopreventive and chemotherapeutic activity. J Biol Chem 281:17359–68.

Duangkhamchan W, Siriamornpun S. 2015. Quality attributes and anthocyanin content of rice coated by purple-corn cob extract as affected by coating conditions. Food Bioprod Process 96:171–9.

FAO. 2013. Traditional High-Andean cuisine, 1st ed. Food and Agriculture Organization of the United Nations. Available from: http://www.fao.org/docrep/018/i1466e/i1466e.pdf. Accessed 2014 May 16.

Finkel ML, Sanchez S, Mak T, Granstein J, Lefkowitz A. 2013. Anthocyanin-rich purple corn extract and its effects on the blood pressure of adults. J Evid Based Complement Altern Med 18:237–42.

Fukamachi K, Imada T, Ohshima Y, Xu J, Tsuda H. 2008. Purple corn color suppresses Ras protein level and inhibits 7,12-dimethylbenz[a]anthracene-induced mammary carcinogenesis in the rat. Cancer Sci 99:1841–6.

González-Manzano S, Pérez-Alonso JJ, Salinas-Moreno Y, Mateus N, Silva AMS, de Freitas V, Santos-Buelga C. 2008. Flavanol-anthocyanin pigments in corn: NMR characterisation and presence in different purple corn varieties. J Food Compos Anal 21:521–6.

González-Paramás AM, Lopes da Silva F, Martín-López P, Macz-Pop G, González-Manzano, S, Alcalde-Eon C, Pérez-Alonso JJ, Escribano-Bailón MT, Rivas-Gonzalo, JC, Santos-Buelga, C. 2006. Flavanol–anthocyanin condensed pigments in plant extracts. Food Chem 94:428–36.

Hagiwara A, Miyashita K, Nakanishi T, Sano M, Tamano S, Kadota T, Koda T, Nakamura M, Imaida K, Ito N, Shirai T. 2001. 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 Lett 171:17–25.

Halliwell B, Gutteridge JM, Cross CE. 1992. Free radicals, antioxidants, and human disease: where are we now?. J Lab Clin Med 119:598–620

He J, Giusti MM. 2010. Anthocyanins: natural colorants with health-promoting properties. Annu Rev Food Sci Technol - (new 2010) 1:163–87.

Heinonen IM, Meyer AS, Frankel EN. 1998. Antioxidant activity of berry phenolics on human low-density lipoprotein and liposome oxidation. J Agric Food Chem 46:4107–12.

Hong SH, Heo J, Kim J, Kwon S-O, Yeo K-M, Bakowska-Barczak AM, Kolodziejczyk P, Ryu O-H, Choi M-K, Kang Y-H, Lim SS, Suh H-W, Huh S-O, Lee J-Y. 2013. Antidiabetic and beta cell-protection activities of purple corn anthocyanins. Biomol Ther 21:284–9.

Huang C, Li J, Song L, Zhang D, Tong Q, Ding M, Bowman L, Aziz R, Stoner GD. 2006. Black raspberry extracts inhibit benzo(a)pyrene diol-epoxide-induced activator protein 1 activation and VEGF transcription by targeting the phosphotidylinositol 3-kinase/Akt pathway. Cancer Res 66:581–7.

Jia Z, Tang M, Wu J. 1999. The determination of flavonoid contents in mulberry and their scavenging effects on superoxide radicals. Food Chem 64:555–9.

Jing P, Giusti MM. 2005. Characterization of anthocyanin-rich waste from purple corncobs (*Zea mays* L.) and its application to color milk. J Agric Food Chem 53:8775–81.

Jing P, Giusti MM. 2007. Effects of extraction conditions on improving the yield and quality of an anthocyanin-rich purple corn (*Zea mays* L.) color extract. J Food Sci 72:C363–8.

Jing P, Noriega V, Schwartz SJ, Giusti MM. 2007. Effects of growing conditions on purple corncob (*Zea mays* L.) anthocyanins. J Agric Food Chem 55:8625–9.

Jing P, Bomser JA, Schwartz SJ, He J, Magnuson BA, Giusti MM. 2008. Structure-function relationships of anthocyanins from various anthocyanin-rich extracts on the inhibition of colon cancer cell growth. J Agric Food Chem 56:9391–8.

Kahn SE, Hull RL, Utzschneider KM. 2006. Mechanisms linking obesity to insulin resistance and type 2 diabetes. Nature 444:840–6.

Kang MK, Li J, Kim J-L, Gong J-H, Kwak S-N, Park JHY, Lee J-Y, Lim SS, Kang YH. 2012. Purple corn anthocyanins inhibit diabetes-associated glomerular monocyte activation and macrophage infiltration. AJP Ren Physiol 303:F1060–9.

Kang MK, Lim SS, Lee JY, Yeo KM, Kang YH. 2013. Anthocyanin-rich purple corn extract inhibits diabetes-associated glomerular angiogenesis. PLoS One 8:1–10.

Khampas S, Lertrat K, Lomthaisong K, Simla S, Suriharn B. 2015. Effect of location, genotype and their interactions for anthocyanins and antioxidant activities of purple waxy corn cob. Turkish J F Crop 20:15–23.

Kim TH, Kim JK, Kang Y-H, Lee J-Y, Kang IJ, Lim SS. 2013. Aldose reductase inhibitory activity of compounds from *Zea mays* L. Biomed Res Intl 2013:1–8.

Konczak I, Zhang W. 2004. Anthocyanins - More than nature's colours. J Biomed Biotechnol 2004:239–40.

Kong JM, Chia LS, Goh NK, Chia TF, Brouillard R, 2003. Analysis and biological activities of anthocyanins. Phytochemistry 64: 923–33.

Kwon JY, Lee KW, Hur HJ, Lee HJ. 2007. Peonidin inhibits phorbol-ester-induced COX-2 expression and transformation in JB6 P+ cells by blocking phosphorylation of ERK-1 and -2. Ann N Y Acad Sci 1095:513–20.

Lao F, Giusti MM. 2016. Quantification of purple corn (*Zea mays* L.) anthocyanins using spectrophotometric and HPLC approaches: method comparison and correlation. Food Anal Methods 9:1367–80.

Lee CH, Garcia HS, Parkin KL. 2010. Bioactivities of kernel extracts of 18 strains of maize (*Zea mays*). J Food Sci 75:667–72.

Lew EA, Garfinkel L. 1979. Variations in mortality by weight among 750,000 men and women. J Chronic Dis 32:563–76.

Li CY, Kim HW, Won SR, Min HK, Park KJ, Park JY, Ahn MS, Rhee HI. 2008. Corn husk as a potential source of anthocyanins. J Agric Food Chem 56:11413–6.

Li J, Kang MK, Kim JK, Kim JL, Kang SW, Lim, SS, Kang YH. 2012a. Purple corn anthocyanins retard diabetes-associated glomerulosclerosis in mesangial cells and db/db mice. Eur J Nutr 51:961–73.

Li J, Lim SS, Lee JY, Kim JK, Kang SW, Kim JL, Kang YH. 2012b. Purple corn anthocyanins dampened high-glucose-induced mesangial fibrosis and inflammation: possible renoprotective role in diabetic nephropathy. J Nutr Biochem 23:320–31.

Long N, Suzuki S, Sato S, Naiki-Ito A, Sakatani K, Shirai T, Takahashi, S. 2013. Purple corn color inhibition of prostate carcinogenesis by targeting cell growth pathways. Cancer Sci 104:298–303.

Lopez-Martinez LX, Oliart-Ros RM, Valerio-Alfaro G, Lee CH, Parkin KL, Garcia HS. 2009. Antioxidant activity, phenolic compounds and anthocyanins content of eighteen strains of Mexican maize. LWT - Food Sci Technol 42:1187–92.

Lopez-Martinez LX, Parkin KL, Garcia HS. 2011. 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 Hum Nutr 66:41–7.

Maedler K, Carr RD, Bosco D, Zuellig RA, Berney T, Donath MY. 2005. Sulfonylurea induced beta-cell apoptosis in cultured human islets. J Clin Endocrinol Metab 90:501–6.

Martin S, Giannone G, Andriantsitohaina R, Martinez MC. 2003. Delphinidin, an active compound of red wine, inhibits endothelial cell apoptosis via nitric oxide pathway and regulation of calcium homeostasis. Br J Pharmacol 139:1095–102.

Mendoza-Díaz S, Ortiz-Valerio MDC, Castaño-Tostado E, Figueroa-Cárdenas JDD, Reynoso-Camacho R, Ramos-Gómez M, Campos-Vega R, Loarca-Piña G. 2012. Antioxidant capacity and antimutagenic activity of anthocyanin and carotenoid extracts from nixtamalized pigmented creole maize races (*Zea mays* L.). Plant Foods Hum Nutr 67:442–9.

Min SW, Ryu SN, Kim DH. 2010. Anti-inflammatory effects of black rice, cyanidin-3-O-beta-d-glycoside, and its metabolites, cyanidin and protocatechuic acid. Intl Immunopharmacol 10:959–66.

Montilla EC, Hillebrand S, Antezana A, Winterhalter P. 2011. Soluble and bound phenolic compounds in different Bolivian purple corn (Zea mays L.) cultivars. J Agric Food Chem 59:7068–74.

Moore J, Hao Z, Zhou K, Luther M, Costa J, Yu L. 2005. Carotenoid, tocopherol, phenolic acid, and antioxidant properties of Maryland-grown soft wheat. J Agric Food Chem 53:6649–57.

Nabae K, Hayashi SM, Kawabe M, Ichihara T, Hagiwara A, Tamano S, Tsushima Y, Uchida K, Koda T, Nakamura M, Ogawa K, Shirai T. 2008. A 90-day oral toxicity study of purple corn color, a natural food colorant, in F344 rats. Food Chem Toxicol 46:774–80.

Pedreschi R, Cisneros-Zevallos L. 2006. Antimutagenic and antioxidant properties of phenolic fractions from Andean purple corn (*Zea mays* L.). J Agric Food Chem 54:4557–67.

Pedreschi R, Cisneros-Zevallos L. 2007. Phenolic profiles of Andean purple corn (*Zea mays* L.). Food Chem 100:956–63.

Poirier MC. 2004. Chemical-induced DNA damage and human cancer risk. Nat Rev Cancer 4:630–7.

Prior RL, Cao G, Martin A, Sofic E, Mcewen J, Brien CO, Lischner N, Ehlenfeldt M, Kalt W, Krewer G, Mainland CM. 1998. Antioxidant capacity as influenced by total phenolic and anthocyanin content, maturity, and variety of Vaccinium species. J Agric Food Chem 8561:2686–93.

Ramos-Escudero F, González-Miret ML, García-Asuero A. 2012a. Effect of various extractions systems on the antioxidant activity kinetic and color of extracts from purple corn. Vitae 19(1): 41–8. Available from: http://www.scielo.org.co/scielo.php?script=sci_arttext&pid=S0121-40042012000100005&lng=en&nrm=iso. Posted February 21, 2012.

Ramos-Escudero F, Muñoz AM, Alvarado-Ortíz C, Alvarado Á, Yáñez JA. 2012b. Purple corn (*Zea mays* L.) phenolic compounds profile and its assessment as an agent against oxidative stress in isolated mouse organs. J Med Food 15:206–15.

Ranilla LG, Apostolidis E, Genovese MI, Lajolo FM, Shetty K. 2009. Evaluation of indigenous grains from the Peruvian Andean region for antidiabetes and antihypertension potential using in vitro methods. J Med Food 12:704–13.

Reddy MK, Alexander-Lindo RL, Nair MG. 2005. Relative inhibition of lipid peroxidation, cyclooxygenase enzymes, and human tumor cell proliferation by natural food colors. J Agric Food Chem 53:9268–73.

Reynoso-Camacho R, Guerrero-Villanueva G, de Dios Figueroa J, Gallegos-Corona MA, Mendoza S, Loarca-Piña G, Ramos-Gomez M. 2015. Anticarcinogenic effect of corn tortilla against 1,2-dimethylhydrazine (DMH)-induced colon carcinogenesis in Sprague–Dawley rats. Plant Foods Hum Nutr 70:146–52.

Santos-Cervantes ME, Ibarra-Zazueta ME, Loarca-Piña G, Paredes-López O, Delgado-Vargas F. 2007. Antioxidant and antimutagenic activities of Randia echinocarpa fruit. Plant Foods Hum Nutr 62:71–7.

Sasaki R, Nishimura N, Hoshino H, Isa Y, Kadowaki M, Ichi T, Tanaka A, Nishium S, Fukuda I, Ashida H, Horio F, Tsuda T. 2007. Cyanidin 3-glucoside ameliorates hyperglycemia and insulin sensitivity due to downregulation of retinol binding protein 4 expression in diabetic mice. Biochem Pharmacol 74:1619–27.

Serra D, Paixão J, Nunes C, Dinis TCP, Almeida LM. 2013. Cyanidin-3-glucoside suppresses cytokine-induced inflammatory response in human intestinal cells: comparison with 5-aminosalicylic acid. PLoS One 8:1–9.

Shimoda H, Aitani M, Tanaka J, Hitoe S. 2015. Purple rice extract exhibits preventive activities on experimental diabetes models and human subjects. J Rice Res 03:2–5.

Shindo M, Kasai T, Abe A, Kondo Y. 2007. Effects of dietary administration of plant-derived anthocyanin-rich colors to spontaneously hypertensive rats. J Nutr Sci Vitaminol (Tokyo) 53:90–3.

Sinha AK, Kumar V, Makkar HPS, De Boeck G, Becker K. 2011. Non-starch polysaccharides and their role in fish nutrition—a review. Food Chem 127:1409–26.

Thiraphatthanavong P, Wattanathorn J, Muchimapura S, Thukham-mee W, Wannanon P, Tong-un T, Suriharn B, Lertrat K. 2014. Preventive effect of *Zea mays* L. (purple waxy corn) on experimental diabetic cataract. Biomed Res Int 2014:1–8.

Toyoshi T, Kohda T. 2004. Antihypertensive activity of purple corn color in spontaneously hypertensive rats. Foods Food Ingred J Japan 209:671–9. In Japanese.

Tsuda T. 2008. Regulation of adipocyte function by anthocyanins; possibility of preventing the metabolic syndrome. J Agric Food Chem 56:642–6.

Tsuda T, Horio F, Uchida K, Aoki H, Osawa T. 2003. Dietary cyanidin 3-O-beta-D-glucoside-rich purple corn color prevents obesity and ameliorates hyperglycemia in mice. J Nutr 133:2125–30.

Tsuda T, Ueno Y, Aoki H, Koda T, Horio F, Takahashi N, Kawada T, Osawa T. 2004. Anthocyanin enhances adipocytokine secretion and adipocyte-specific gene expression in isolated rat adipocytes. Biochem Biophys Res Commun 316:149–57.

Tsuda T, Ueno Y, Kojo H, Yoshikawa T, Osawa T. 2005. Gene expression profile of isolated rat adipocytes treated with anthocyanins. Biochim Biophys Acta 1733:137–47.

Tsuda T, Ueno Y, Yoshikawa T, Kojo H, Osawa T. 2006. Microarray profiling of gene expression in human adipocytes in response to anthocyanins. Biochem Pharmacol 71:1184–97.

United Nations BioTrade Program. 2011. Sector assessment natural ingredients for cosmetics and pharmaceuticals in Peru. Available from: http://www.biotrade.org/ResourcesNewsAssess/peru-assessment-naturalingredients.pdf. Accessed 2015 September 3.

Urias-Lugo DA, Heredia JB, Muy-Rangel MD, Valdez-Torres JB, Serna-Saldívar SO, Gutiérrez-Uribe JA. 2015. 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 Hum Nutr 70:193–9.

Vayupharp B, Laksanalamai V. 2015. Antioxidant properties and color stability of anthocyanin purified extracts from thai waxy purple corn cob. J Food Nutr Res 3:629–36.

Wallace TC. 2011. Anthocyanins in cardiovascular disease 1. Adv Nutr 2:1–7.

Wang L-S, Stoner GD. 2008. Anthocyanins and their role in cancer prevention. Cancer Lett 269:281–90.

Westfall A. 2015. Evaluation of the efficacy of anthocyanins as biologically active ingredients in lipstick formulations. [Master of Science thesis]. Columbus, OH: The Ohio State University. 118 p. Available from: http://rave.ohiolink.edu/etdc/view?acc_num=osu1429170218

Wu X, Beecher GR, Holden JM, Haytowitz DB, Gebhardt SE, Prior RL. 2006. Concentrations of anthocyanins in common foods in the United States and estimation of normal consumption. J Agric Food Chem 54:4069–75.

Yokohira M, Yamakawa K, Saoo K, Matsuda, Y, Hosokawa K, Hashimoto N, Kuno T, Imaida K. 2008. Antioxidant effects of flavonoids used as food additives (purple corn color, enzymatically modified isoquercitrin, and isoquercitrin) on liver carcinogenesis in a rat medium-term bioassay. J Food Sci 73:561–8.

Yoshimoto M, Okuno S, Yamaguchi M, Yamakawa O. 2001. Antimutagenicity of deacylated anthocyanins in purple-fleshed sweetpotato. Biosci Biotechnol Biochem 65:1652–5.

Zhang Z, Zhou B, Wang H, Wang F, Song Y, Liu S, Xi S. 2014. Maize purple plant pigment protects against fluoride-induced oxidative damage of liver and kidney in rats. Intl J Environ Res Public Health 11:1020–33.

Zhao C, Giusti MM, Malik M, Moyer MP, Magnuson BA. 2004. Effects of commercial anthocyanin-rich on colonic cancer and nontumorigenic colonic cell growth. J Agric Food Chem 52:6122–8.

Zhao X, Corrales M, Zhang C, Hu X, Ma Y, Tauscher B. 2008. Composition and thermal stability of anthocyanins from Chinese purple corn (*Zea mays* L.). J Agric Food Chem 56:10761–6.

Zhao X, Zhang C, Guigas C, Ma Y, Corrales M, Tauscher B, Hu X. 2009. Composition, antimicrobial activity, and antiproliferative capacity of anthocyanin extracts of purple corn (*Zea mays* L.) from China. Eur Food Res Technol 228:759–65.

Zhou B, Wang X, Guo L, Zhang Z, Xu C. 2007. Toxicological assessment on safety of maize purple plant pigment. J Chinese Inst Food Sci Technol 7(6):141–3. In Chinese.

Žilić S, Serpen A, Akıllıoğlu G, Gökmen V, Vančetović J. 2012. Phenolic compounds, carotenoids, anthocyanins, and antioxidant capacity of colored maize (*Zea mays* L.) kernels. J Agric Food Chem 60:1224–31.