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Review

Pharmacological and nutritional activities of potato anthocyanins

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Colored potatoes are due to the accumulation of anthocyanins in the stem tubers. The strong antioxidative activity of potato anthocyanins results from the promotion effects of the anthocyanins on the activities of the antioxidant enzymes and is positively correlated to the anthocyanin content, which derives several important pharmacological actions. Both the antioxidative strength and anti-influenza virus activity of potato anthocyanins are determined by the molecular structures of the anthocyanins and this involves the synergic effects of the anthocyanins and other antioxidants in the tubers. In addition, potato anthocyanins may improve colonic environments. However, so far, the pharmacological and nutritional activities of potato anthocyanins are all verified initially by using model experimental systems and the total anthocyanins of the potatoes with specific colorations, the molecular mechanisms and the universality of the biomedicinal activities of potato anthocyanins are not yet well understood.

Key words: Colored potato, anthocyanin, pharmacological, nutritional activities.

INTRODUCTION

Generally, the skins and/or fleshes of the stem tubers of the ordinarily cultivated varieties of potato (*Solanum tuberosum* L.) are white, yellow, lemon yellow or saffron yellow. Worldwide, the potato cultivars in which the skins and/or fleshes of the stem tubers are red, purple, blue or orange are intuitively denominated colored potatoes (Hayashi et al., 1997; Lewis et al., 1998a; Brown et al., 2003a; Jansen and Flamme, 2006), colorful potatoes (Stelljes, 2001) or pigmented potatoes (Eichhorn and Winterhalter, 2005; Lachman and Hamouz, 2005). Now, lots of colored potato varieties are well known, eg 'Cranberry Red', 'Shetland Black', 'Blaue St. Galler', 'Zhuanxinwu' and the like (Groza et al., 2004; Zhao et al., 2007; Lachman et al., 2009) and many of them are commercially available as specialty potatoes (Sorenson, 1992; Brown et al., 2003a, 2005).

The coloration patterns of the skins and fleshes of colored potatoes are changeable and fascinating. Not all of the colors of the skins are consistent with those of the fleshes (Groza et al., 2004). Colored skins do not definitely imply that the fleshes are colored. However, if the fleshes are colored, the skins are usually colored identically, eg, red, purple or blue colored fleshes are often accompanied by red, purple or blue skins respectively (Brown et al., 2003a; De Jong et al., 2003). Furthermore, the tuber skins of colored potatoes are uniformly colored, but the fleshes may range from partial pigmentation to complete one and different degrees of partial pigmentation result in the colorful streaks, blotches arcs, rings or radiating stars in the fleshes (Brown et al., 2003a; Brown, 2006).

Colored potato colorations originate from the accumulation of anthocyanins in the specific parts of different classes of pigments, that is, carotenoids and anthocyanins (Hayashi et al., 1997; Lewis et al., 1998b; Brown, 2006; Jansen and Flamme, 2006). Carotenoids produce the white, yellow or saffron yellow colors of the skins and/or fleshes (Lewis et al., 1998b; Brown, 2006) and anthocyanins which are derive from six anthocyanidins produce the red, purple, blue or orange colors and different colored potatoes contain different amounts of various kinds of anthocyanins depending on genotypes and locations (Figure 1) (Al-Saikhan et al., 1995; Hung et al., 1997; Lewis et al., 1998a; Rodriguez-Saona et al., 1998; Fossen et al., 2003; Brown et al., 2003b, 2004; Brown, 2005; Eichhorn and Winterhalter,

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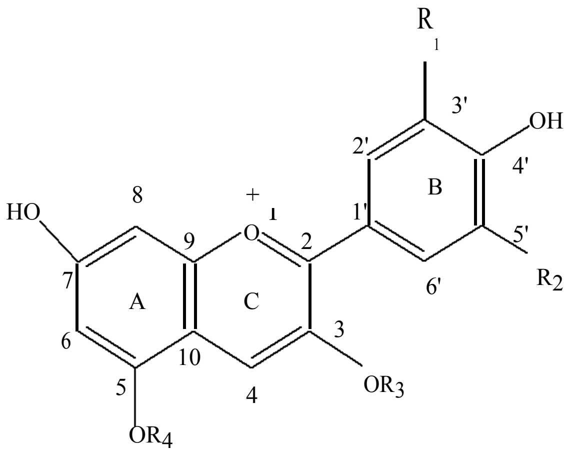


$R_1=R_2=R_3=R_4=H$ pelargonidin
$R_1=OH$ $R_2=R_3=R_4=H$ cyanidin
$R_1=OCH_3$ $R_2=R_3=R_4=H$ peonidin
$R_1=R_2= OH$ $R_3=R_4=H$ delphinidin
$R_1= OCH_3$ $R_2= OH$ $R_3=R_4=H$ petunidin
$R_1= R_2=OCH_3$ $R_3=R_4=H$ malvidin

Figure 1. Anthocyanidins of colored potatoes.

2005; Lachman and Hamouz, 2005; Reyes et al., 2005; Jansen and Flamme, 2006; Andre et al., 2007; Zhang et al., 2009).

At present, colored potatoes have attracted special interests in many countries due to their colorful appeals and excellent tastes (Sorenson, 1992; Johnson, 1995; Brown, 2005) . The key question is that, besides improving the overall appearance and taste of stem tubers and being nutritious, potato anthocyanins have been proved to hold much anti-illness and anti-aging functionality (Hung et al., 1997; Stelljes, 2001). However, up till now, no comprehensive report concerning the healthy benefits of potato anthocyanins has been published. Consequently, this review attempts to systematically sum up the recent research advances in the understanding of the pharmacological and nutritional activities of the total anthocyanins of special colored potato varieties with specific coloration patterns.

POTATO ANTHOCYANINS HOLD STRONG ANTIOXIDATIVE ACTIVITY

Intensity of the antioxidative activity of potato anthocyanins

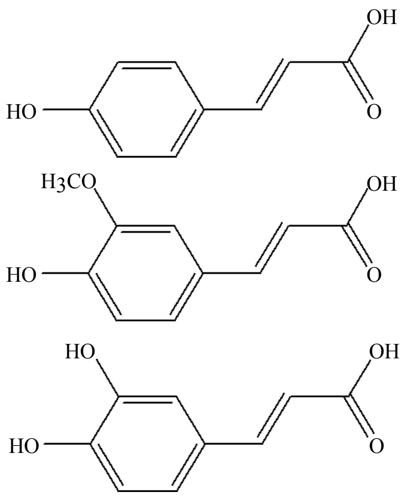
The excellent antioxidative activity of colored potato anthocyanins is mainly displayed by the total anthocyanins of red or purple-fleshed potatoes. Oxygen radical absorbance capacity (ORAC) and ferrous reducing ability of plasma (FRAP) revealed that the antioxidant levels in red or purple-fleshed potatoes were two to three times higher than white/ yellow-fleshed potatoes (Brown et al., 2003; Brown, 2004; Lachman and Hamouz, 2005); the anthocyanins of purple-fleshed potato ‘Inca Purple’ and red-fleshed potato ‘Inca Red’ were shown to possess strong antioxidative activities (Ishii et al., 1996). Regarding this fact, potato anthocyanins are proposed to protect humans against injuries due to oxidants and free radicals (Hung et al., 1997) and thereby providing various health benefits, such as preservation of cardiovascular health, preventing cancers, retarding macular degeneration of the retina and other aging-related deseases (Brown, 2004).

Biochemical and molecular mechanisms of the antioxidative activity of potato anthocyanins

The antioxidative activity of potato anthocyanins may be due to the fact that the anthocyanins can increase the antioxidant enzyme activities in the anthocyanin consumers, such as superoxide dismutase (SOD) and glutathione peroxidase (GSH- Px) . Han et al. (2006a) found that the petanin from “two purple potato varieties” had antioxidant functions attributed to its oxygen free radical scavenging activity and inhibition of linoleic acid oxidation. It improved the antioxidant potentials in rats by enhancing hepatic Mn- SOD, Cu/Zn-SOD and GSH-Px mRNA expression. Han et al. (2007a) further discovered that the purple potato flake diet modulated the antioxidant enzyme, that is hepatic glutathione reductase and glutathione S-transferase and the oxidative status in the serum and liver of the rats fed with a high-cholesterol diet. Han et al. (2007b) also proved that red potato flakes (RPF) significantly decreased the serum thiobarbituric acid reactive substance (TBARS) levels and increased hepatic SOD mRNA level in rats, suggesting that it might improve the endogenous antioxidant system by enhancing hepatic SOD mRNA.

Phytochemical bases of the antioxidative activity of potato anthocyanins

Content of the anthocyanins: Colored potatoes contain the antioxidant compounds found in common potatoes, eg polyphenols, ascorbic acid, carotenoids, tocopherols, lipoic acid and selenium (Hejtmánková et al., 2009). Furthermore, colored potatoes contain more than twice high levels of phenolic acids compared to yellow or white fleshed potatoes (Brown, 2005; Wegener et al., 2009). However, the antioxidative activity of potato anthocyanins expresses obvious quantitative effects, being directly reflected by the fact that potatoes with higher anthocyanins levels hold a much stronger antioxidative potential (Brown, 2006). A significantly positive correlation between the antioxidative potential of the potatoes and the total concentration of the anthocyanins has been revealed (Brown et al., 2003a, 2005; Brown, 2006). Reyes et al. (2005) found that a strong positive



p-coumaric acid

ferulic acid

caffeic acid

Figure 2. Phenolic acids acylating potato anthocyanins.

correlation of antioxidant activity not only with anthocyanins content but also with total phenolic compounds present in the purple and red-fleshed potatoes. Hejtmánková et al. (2009) further proved that, for eight varieties of colored potatoes such as ‘Salad Blue’, ‘Shetland Black’, ‘Blue Congo’ and so on, the best positive correlation was observed between antioxidant activity and the total anthocyanin content. As a rule, the higher the anthocyanin content the deeper the stem tuber color and the stronger the antioxidative activity of colored potatoes (Brown et al., 2003b).

Molecular structures of the anthocyanins: Numerous recent investigations have indicated that the antioxidative strength of potato anthocyanins is simultaneouly determined by three structural factors of the anthocyanin molecules, that is hydroxylation degree, acylation and glycosylation patterns (Ishii et al., 1996). Firstly, the antioxidative activity is positively related with the number of the free hydroxyl groups of the anthocyanin molecules, especially those of anthocyanidins, which implies that petunidin has greater antioxidative effects in comparison with malvidin, peonidin or pelargonidin, respectively (Figure 1) (Wang et al., 1997; Hamouz et al., 1999; Lachman et al., 2000; Han et al., 2006a). Secondly, there are three kinds of phenolic acids acylating potato anthocyanins, and, according to the frequency of occurrence from high to low, they are p-coumaric acid (that is cinnamic acid derivate), ferulic acid and caffeic acid (Figure 2) (Naito et al., 1998; Rodríguez-Saona et al., 1998; Eichhorn and Winterhalter, 2005; Lachman and Hamouz, 2005; Zhang et al., 2009). However, the frequent acylation of potato anthocyanins was found to be the one with cinnamic acids, which improves the total antioxidative effectiveness of the anthocyanins greatly (De Souza and De Giovani, 2004; Garcia- Alonso et al., 2004). Finally, the anthocyanins which endue the colored potato tubers with antioxidative properties were confirmed mainly to be the glycosides of peonidin, petunidin, malvidin and so forth (Figure 1) (Brown, 2004; Lachman and Hamouz, 2005). It was found that the glycosidic substitutions at the C_3 or C_5 position of the anthocyanidins reduce the antioxidant activity of the anthocyanins (Wang et al., 1997; De Souza and De Giovani, 2004; Garcia-Alonso et al., 2004).

Synergic effects of the anthocyanins and other antioxidants: Hamouz et al. (1999) and Lachman et al. (2000) thought that the total antioxidative activity of potato anthocyanins was determined both by the content of anthocyanins and that of other phenolic acids and mainly by the isomers of chlorogenic acids. Generally, the antioxidative activities of the natural anthocyanin extracts of colored potatoes are much higher than the pure individual anthocyanin compounds, indicating that the synergic effects of the mixture of the anthocyanins and other antioxidants contained in potato tubers are involved in the antioxidative activity (De Souza and De Giovani, 2004; Garcia-Alonso et al., 2004; Lachman et al., 2009; Wegener et al., 2009).

POTATO ANTHOCYANINS POSSESS IMPORTANT PHARMACOLOGICAL ACTIONS

Anticancer

The research results of recent years have tentatively shown that potato anthocyanins display potential activities to combat four kinds of cancers with different and not well understood mechanisms.

Firstly, potato anthocyanins can inhibit the growth of the cell line of human erythrocyte leukemia. Anthocyanins of purple-peeled and purple-fleshed potato ‘Yunshite 035’ and red-peeled and red-fleshed potato ‘Yunshite 038’ were observed to markedly inhibit the growth of the cell line K562 of human erythrocyte leukemia, suggesting the possibility that they could be exploited as a kind of new natural antileukemic agents (Xie et al., 2003, 2004).

Secondly, potato anthocyanins can hold back the proliferation of stomach cancer cells by inducing their apoptosis. Hayashi et al. (2006) found that the anthocyanins of red-fleshed potato ‘Inca Red’ and purple-fleshed potato ‘Inca Purple’ induced apoptosis in cultured human stomach cancer KATO cells. because they resulted in the appearance of the apoptotic bodies and DNA fragmentations. On the other hand, feeding with steamed red and purple potato suppressed the proliferation of mouse stomach cancer by 46.2 and 38.5%, respectively and feeding with a 1% solution of the red or purple potato anthocyanins with standard food by 47.6 and 38.1%, respectively, indicating their efficacy against stomach cancer (Hayashi et al., 2006).

Thirdly, potato anthocyanins are cytotoxic to prostate cancer cells. Reddivari et al. (2007) found that the anthocyanin fractions (AF) of colored potato 'CO112F2-2' showed potent antiproliferative properties and increased the cyclin-dependent kinase inhibitor p27 levels in both PC-3 (androgen independent) and LNCaP (androgen dependent) prostate cancer cells. The AF induced caspase-independent apoptosis (CIA) in PC-3 cells and both caspase-dependent and independent apoptosis in LNCaP cells. Reddivari et al. (2007) presumed that the cytotoxic activities of AF in the cancer cells were possibly caused by the activation of CIA.

Finally, potato anthocyanins may hold the activity to combat breast cancer. The results reported by Thompson et al. (2009) indicated that, for the rats' breast cancer induced by 1-methyl-1-nitrosourea, the anthocyanins of a red potato variety 'Mountain Rose' led to a reduction not only in cancer incidence but also in cancer multiplicity and the great inhibition of carcinogenesis might be related to the synergic effects of the anthocyanins and other antioxidants, eg chlorogenic acid derivatives.

Hepatoprotective

So far, only the anthocyanins of purple and red colored potatoes have been verified to be provided with hepatoprotective activity. Han et al. (2006b) certified that, purple potato extract (PPE), that is purple colored potato anthocyanins, had hepatoprotective effects against D-galactosamine (GalN)-induced hepatotoxicity because it inhibited the GalN-induced alterations of the tumor necrosis factor (TNF-), lactate dehydrogenase (LDH), alanine aminotransferase (ALT) and asparate aminotranferase (AST) levels in rat serum and it probably suppressed the changes of thiobarbituric acid-reactive substance (TBARS) and glutathione (GSH) levels in rat liver and lipid peroxidation and/or inflammation in rats. On the other hand, Han et al. (2006c) also proved that red potato extract (RPE) decreased GalN which induced an increase in AST, ALT and LDH activities in rat serum, and the purified extract from RPE also showed an antioxidant property against linoleic acid oxidation. As a consequence, RPE also has a protective effect against GalN-induced hepatotoxicity in rats, acting by inhibiting intracellular GSH depletion.

Antivirus

Anti-influenza virus activity of red-fleshed potato anthocyanins: Up till now, only the anthocyanins of one red-fleshed potato variety were observed to hold antiviral capacity. As a case study, Hayashi et al. (2003) found that the anthocyanins of red-fleshed potato tetraploid 'Inca Red' inactivated both influenza virus A (IVA) and B (IVB) and the IC50 is 48 and 54 g/mL, respectively.

Chemical bases of the antiviral activity of the red-fleshed potato anthocyanins: The main anthocyanin of potato 'Inca Red' was identified as pelanin {pelargonidin-3-O-[6-O-(4-O-*p*-coumaroyl- -L-rhamnopyranosyl) - -D-glucopyranosyl]-5-O- -D-glucopyranoside} (Naito et al., 1998). Hayashi et al. (2003) found that, in comparison with the red-fleshed potato anthocyanins, the antiviral activities of pelanin against IVA and IVB were lower and those of pelargonidin extracted from the red flowers of *Hyacinthus orientalis* were higher, those of pelargonidin 3-*p*-coumaroylglucose, 5-glucose and pelargonidin 3-*p*-coumaroylglucose, 5- malonylglucose from the same red flowers were slightly weak. As a result, Hayashi et al. (2003) presumed that the anti-influenza virus activity of the red-fleshed potato anthocyanins is strongly correlated with the molecular structures of anthocyanins and may originate from the additive or synergistic effects of the anthocyanins and other coexisting constituents in the tuber.

POTATO ANTHOCYANINS MAY IMPROVE THE COLONIC ENVIRONMENT

The anthocyanins of red and purple-fleshed potato varieties may hold beneficial effects on colonic environment. The findings based on the effects of various colored potato flakes on the cecal fermentation and fecal bile acid excretions of rats primarily showed that the anthocyanins of red fleshed potato variety (Hokkai No. 91) could significantly increase the cecal lactobacillus count and secondary bile acid excretions and the anthocyanins of purple fleshed potato variety (Hokkai No. 92) could significantly improve the fecal total and secondary bile acid excretions (Han et al., 2008). Thus, potato anthocyanins may be helpful for the improvement of the colonic environment of rats.

FUTURE RESEARCH

Despite the significant research of the pharmacological and nutritional activities of potato anthocyanins over the past few years, three aspects are waiting to be further studied in detail. The first is that, until now, the major interest of the scientists studying the pharmacological and nutritional activities of potato anthocyanins was to investigate the activities of the anthocyanins of special colored potato varieties with specific coloration patterns, mainly the red or purple- skined or fleshed ones. In fact, it is totally unclear whether different colored potatoes definitely have distinct or similar pharmacological or nutritional activities. The general rule which underlies the relationship between the pharmacological or nutritional activity and the colored potato variety remains to be unequivocally established. The second is that many of the pharmacological and nutritional activities of potato anthocyanins were displayed by the total anthocyanins of the potatoes. Nevertheless, a large amount of evidences has indicated that different colored potatoes may contain different contents of various kinds of anthocyanins (Lewis et al., 1998a; Rodriguez-Saona et al., 1998, 1999; Brown et al., 2003b, 2004; Eichhorn and Winterhalter, 2005; Lachman and Hamouz, 2005; Reyes et al., 2005; Jansen and Flamme, 2006; Andre et al., 2007), and, just as discussed above, the specific bioactivities of the anthocyanins are related to the molecular structures of the anthocyanins. So, a more detailed work is clearly needed to determine the definite pharmacological or nutritional activities of the individual anthocyanin of colored potatoes. The third is that many of the pharmacological and nutritional activities of potato anthocyanins were initially understood by using some convenient model experimental systems, eg cell lines and rats. Moreover, the mechanisms of the specific pharmacological or nutritional activities of the anthocyanins are not yet well understood. For example, the interaction of the red-fleshed potato anthocyanins and influenza viruses is not clear at all (Hayashi et al., 2003). Accordingly, a great deal of researches should be conducted to verify the universality and mechanism of the activities of potato anthocyanins in different organisms, especially in human beings.

Holding many pharmacological and nutritional values, potato anthocyanins will play an important role in the industrial development of potatoes. As demonstrated by the gigantic commercial success to date, just because colored potatoes are provided with radiantly beautiful colors and strong antioxidative activity, they have been become one of the peculiar foods which are extraordinarily favored by ordinary food processors and consumers (Brown et al., 2003a, 2003b, 2007; Eichhorn and Winterhalte, 2005; Lachman and Hamouz, 2005). A general opinion is steadily forming which holds that chronic dietary intake of potato anthocyanins as ordinary food and drink has a positive effect on human well-being (Brown, 2006; Lachman et al., 2009) . What is more important is that colored potatoes have been thought to be the good potential sources for natural colorants and antioxidants (Lewis et al., 1998b; Rodriguez-Saona et al., 1998; Reyes and Cisneros-Zevallos, 2003; Reyes et al., 2004). Besides imparting an aesthetic visual effect on foods and drinks, potato anthocyanins are regarded as an important alternative to many unsafe synthetic colorants, meaning that the anthocyanins have potential applications in many industries, that is food, nutraceutical and so on (Francis, 1989; Bridle and Timberlake, 1997). Currently, potato breeders and researchers are attracted to develop new potato varieties with high levels of anthocyanins in order to increase the health and nutritional benefits of potatoes and processed foods made from potatoes (Brown et al., 2003a, 2003b, 2004; Brown, 2005, 2006; Reyes et al., 2005). It is thus evident that potato anthocyanins have turned out to set a new trend in potato industry (Brown et al., 2003a).

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