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Review Article

Anthocyanins and digestive system cancers

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ABSTRACT

The international community suffers from spread digestive system cancers. Hence, our goal was evaluation of anthocyanins efficiency in digestive system cancers improvement. As the result, researchers have declared that anthocyanins have a protective role in digestive system cancers. Also, due to health anthocyanins properties, the useful results were obtained to promote and improve the health of communities. It is suggested that using anthocyanin in the pharmaceutical companies and pay more attention to its effects. Due to anthocyanins in plant crops by proper planning and training in using of plants materials containing these substances, it can be attempt to fight against deadly diseases.

Keywords: Anthocyanin, digestive system, cancer, plant crops

INTRODUCTION

The international community suffers from uncontrolled spread of cancers, and these problems lead to increased mortality around the world. The treatment can increase longevity and quality of life. It should be noted that one of the

most important causes of morbidity and mortality in the world is cancer. In the first place, prevention of these diseases is a priority for all communities, that they arguably have direct relationship with life style and proper nutrition [1-4]. In the area of treatment and prevention of these diseases, attention to safe ways is necessary; one of these ways is treatment via anthocyanins. Anthocyanins is one group of flavonoids, the first anthocyanin crystalline was prepared in 1930 by Scott-Moncrieff. Anthocyanins are widely distributed among purple and blue vegetables and fruits which have been indicated to have various protective properties due to their antioxidant properties [5, 6]. They also found in cereals, legumes and roots. These pigments are generally connected by fruits. In addition, berry fruits are rich sources of dietary anthocyanin [7-10]. In this mini review, we investigated anthocyanins activities in improvement and protection of digestive system cancers.

Anthocyanins usefulness in digestive system cancers:

Lazzè *et. al* stated in their paper the effects of anthocyanins in induction of apoptosis and cell cycle perturbations in various human cell lines that anthocyanin has good and notable impact on the cancer cells in colon [11]. Yi *et. al* indicated in their paper inhibitory effects and apoptosis induction ability of blueberries phenolic compounds on the colon cancer cell proliferation. Findings of this research suggested that blueberry intake daily can decrease cancer risk of colon. Also they suggested that the efficient levels of dosage are close to the explained range of anthocyanin concentrations in plasma of rat .Caco-2 and HT-29 cell growth was remarkably inhibited by (>50%) by the fractions of anthocyanin at concentrations from 15 to 50 µg/ml. Anthocyanin fractions also resulted in 2 to 7 times enhances in fragmentation of DNA, showing the induction of apoptosis [12]. Bermúdez-Soto *et. al* stated in their paper tumor inhibitor up-regulation of carcinoembryonic antigen-related cell adherence molecule 1 in human colon cancer Caco-2 cells following duplicate exposure to dietary levels of a juice of polyphenol-enrich chokeberry that anthocyanin it is a remarkable factor in improvement of human colon cancer [13]. Thoppil *et. al* explained anthocyanins of black currant have chemopreventive activities [14]. Lea *et. al* illustrated inhibitory efficacy of induction and development on the colon cancer via peach and plum phenolic compounds. Inhibitory effects of growth were observed in SW1116, Caco-2, NCM460 and HT29 cells. In Caco-2 cells there was evidence for increased differentiation by increased acting of dipeptidyl peptidase and alkaline phosphatase. Also they stated that

Fractionation using C18 showed activity resided within a fraction comprising anthocyanins but further fractionation using LH-20 suggested that most of the activity was in a fraction comprising polyphenols other than anthocyanins. It was concluded that multiple phenolic molecules of peach and plum can influence differentiation and growth in cancer cells of human colon [15]. McDougall *et. al* indicated different anti-proliferative efficacy of berry extracts against colonic and cervical cancer cell lines, *in vitro*, that anthocyanin has an important efficacy on the colon cancer. Thus, the lingonberry was affected by procyanidins [16]. Liu *et. al* stated extract of bog bilberry (Vaccinium uliginosum L.) decreases cultured cell viability of 3T3-L1, Hep-G2, and Caco-2, affects progression of cycle cell, and has variable results on membrane permeability that Anthocyanins have an anti-proliferative role in colorectal cancer [17]. Holtung *et. al* explained processing efficacy of black currant pressresidue on proliferation of cell and polyphenol composition that anthocyanins have a remarkable anti-proliferative efficacy in cancer. As well as, extracts obtained at lower temperatures indicated a low inhibition of Caco-2 cell proliferation than extracts obtained at higher temperatures. It should be noted that extracts obtained at higher temperatures showed a greatest inhibition of these cells proliferation .This matter can be due to the complex polyphenols decomposition at higher temperatures, making them more available to the cells [18]. Wang *et. al* illustrated antioxidant extracts repressive efficacy from various potatoes on the cancer cells of human colon and liver proliferation that extracts of antioxidant from 5 potato lines were tested for content of anthocyanin, acting of total phenolic, and chlorogenic acid. Analysis indicated that Mexican wild species S. pinnatisectum has a notable antioxidant activity, content of chlorogenic, and phenolic acid. They also stated that the colon cancer proliferation and cancer cells of liver were remarkably inhibited by antioxidant extracts of potato. The remarkable anti-proliferative actions were found in extracts of pinnatisectum. There was a remarkable difference in cancer cells inhibition ($P < 0.01$) among the 3 polyphenols: malvidin chloride, chlorogenic acid and pelargonidin chloride, stating that chlorogenic acid was an important agent in the anti-proliferation of colon cancer, and liver cancer cells [19]. Bao *et. al* explained that anthocyanin rich extracts have useful, and protective effects on liver cells via antioxidative activity [20]. Chatthongpisut *et. al* stated that purple rice cooked antioxidant and anti-proliferative activities via various ways on cancer cells of human colon that anthocyanins is an anti-proliferative factors [21]. D'evoli *et. al* indicated antioxidant anthocyanins effects of red

chicory (Cichorium intybus L. cultivar) for intestinal health that these findings indicated that the total red chicory leaf can demonstrate a well fount of phytochemicals in whole anthocyanins. Also the capability of these phytochemicals to use effects of cytoprotective and antioxidant in differentiated cells of Caco-2 and effects of anti-proliferative in undifferentiated cells of Caco-2. Importantly, compared with red chicory total leaf extracts, the red part of leaf extracts had a remarkably greatest amount of anthocyanins. The identical extracts effectively corresponded to an increment of anti-proliferative activities, cytoprotective and anti-oxidant. They also stated that these findings demonstrated the red part of the leaf of Treviso red chicory via a good amount of antioxidant anthocyanins could be used for supplements of new food production to ameliorate intestinal health [22]. Bishayee *et. al* illustrated that anthocyanin-rich black currant skin extract has chemopreventive actions against inflammation-driven cancer of liver [23]. Tarozzi *et. al* stated effects of organically and non-organically grown red oranges antioxidant in systems of culture cell that findings indicated that organic red oranges have a remarkably phytochemical compounds such as phenolic, ascorbic acid and AnthocyaninsIt should be noted that they also advised that more researches are essential to confirm the organic agronomy actions is possible to augment the antioxidant activity in other vegetables and fruits [24]. Elisia *et. al* explained anthocyanin protection efficacy against cytotoxicity and peroxyl radical (AAPH)-induced oxidative damage in Caco-2 cells that findings demonstrated that the antioxidant acting of anthocyanins mainly ascribed to cyanidin-3-O-glucoside and usual to blackberry, are efficient in inhibition peroxyl radical induced apoptosis in cells of Caco-2 [25]. Bornsek *et. al* stated anthocyanins action of bilberry and blueberry as strong intracellular antioxidants on the cells of mammalian that anthocyanins have intracellular antioxidant actions if used at lower concentrations (<1 μg/l), there with presenting a long favorable for their protection of health [26]. Lim *et. al* indicated anthocyanin-enriched purple-fleshed sweet potato, P40, role in Prevention of colonic and rectal cancer that findings demonstrated that usage a purple sweet potato, P40, can reduce cancer of colon and rectum via inducing arrest of cell cycle, apoptotic mechanisms and anti-proliferative effects [27]. Taverniti *et. al* stated efficacy of immuno modulatory of wild blueberry anthocyanin-rich extract in human intestinal cells of Caco-2 that intestinal inflammation is a crucial procedure for the maintenance of gastrointestinal functioning. Nonetheless, prolonged or abnormal inflammatory reactions can create the chronic degenerative diseases, usually treated by means

of pharmaceutical interventions. Dietary interventions for the prevention of inflammation or abnormal inflammatory reactions are a safer way to pharmacotherapy. Anthocyanins and other polyphenols have been reported to display anti-inflammatory activity. Three bioactive fractions (anthocyanin, phenolic, and water-soluble fractions) were exploited from a powder of wild blueberry .The model of Caco-2 cells was applied to test the immuno modulatory efficacy of the above fractions. The anthocyanin-rich fraction decreased the activation of NF-κB, induced by IL-1β in intestinal epithelial cells of Caco-2. Notably, concentrations of 50 and 100 μg/ml reduced NF-κB activation by 68.9 and 85.2%, respectively. These introductory results provide more support for the food bioactive role as dietary anti-inflammatory factors [28]. Hayashi *et. al* demonstrated apoptosis induction in cultured cells of human stomach cancer by anthocyanins of potato and its inhibitory efficacy on development of stomach cancer in mice that anthocyanins have an ability of apoptosis in cultured human cancer of stomach KATO III cells. They also stated that feeding with steamed purple potato and red potato alone, suppressed by 38.5% and 46.2%, respectively, the development of mouse stomach cancer as compared with the feeding via Irish Cobbler. Feeding via a 1% solution of purple or red potato anthocyanin with standard food suppressed by %38.1% and 47.6, respectively, development of mouse stomach cancer. Thus, eating of potatoes containing great contents of anthocyanin to maintain the presence of potato anthocyanin in the stomach is recommended as a feasible way for protection persons from cancer of stomach [29]. Stoner *et. al* indicated that anthocyanins are capable in inhibiting tumor progress in esophageal tissue [30]. Wang *et. al* demonstrated that anthocyanins in *Rubus occidentalis* are inhibitor of inflammation, cell proliferation and angiogenesis in papillomatous and preneoplastic esophageal tissues and also they are inducers of apoptosis in papillomatous and preneoplastic tissues of esophagus [31]. Charepalli *et. al* explained suppressor activity of anthocyanins for colon tumorigenesis through deletion of colon cancer stem cells that anthocyanins can reduce colon cancer stem cells number [32]. Bishayee *et. al* stated that anthocyanin-rich black currant skin extract can be as chemopreventive factors for liver cancer [33]. Table 1 presents briefly the anthocyanins activities.

Table 1: Anthocyanins activities

Scholars	***Conditions***	**Anthocyanins Activities**
Lazzè *et. al* (2004)	*In vitro*	Have good and notable impact on the cancer cells in colon
Yi *et. al* (2005)	*In vitro*	Reducers colon cancer risk

Table 1: Continued

Scholars	*Conditions*	Anthocyanins Activities
Bermúdez-Soto *et. al* (2007)	*In vitro*	Factors in improvement of human colon cancer Caco-2
Thoppil *et. al* (2012)	*In vivo*	Bioactive anthocyanins of black currant have chemopreventive activities against diethylnitrosamine-inflicted hepatocarcinogenesis
Lea *et. al* (2008)	*In vitro*	Influencers growth and differentiation in human colon cancer cells
McDougall *et. al* (2008)	*In vitro*	Anti-proliferative activity
Liu *et. al* (2010)	*In vitro*	Have an anti-proliferative role in colorectal cancer
Holtung *et. al* (2011)	*In vitro*	Higher temperatures indicated a greatest inhibition of Caco-2 cells proliferation than extracts obtained at lower temperatures
Wang *et. al* (2011)	*In vitro*	The anti-proliferation of colon cancer and liver cancer cells
Bao *et. al* (2008)	*In vivo*	Have useful and protective effects on liver cells via antioxidative activity
Chatthongpisut *et. al* (2015)	*In vitro*	Anti-proliferative factors
D'evoli *et. al* (2013)	*In vitro*	Augmenters of antioxidant, cytoprotective, and anti-proliferative activities
Bishayee *et. al* (2013)	*In vivo*	Anthocyanin-rich black currant skin extract has chemopreventive actions against inflammation-driven cancer of liver
Tarozzi *et. al* (2006)	*In vitro*	Antioxidant activity
Elisia *et. al* (2008)	*In vitro*	Inducers apoptosis in cultured Caco-2 cells
Bornsek *et. al* (2012)	*In vitro*	Antioxidant activity
Lim *et. al* (2012)	*In vitro and In vivo*	A protector of colorectal cancer via cell cycle arrest, apoptotic mechanisms and anti-proliferative effects
Taverniti *et. al* (2014)	*In vitro*	A bioactive as potential dietary anti-inflammatory agents
Hayashi *et. al* (2006)	*In vivo*	A feasible way for protection persons from cancer of stomach
Stoner *et. al* (2010)	*In vivo*	A inhibitor of tumor progress in esophageal tissue
Wang *et. al* (2009)	*In vivo*	A inhibitor of inflammation, cell proliferation and angiogenesis in papillomatous and preneoplastic esophageal tissues
Wang *et. al* (2009)	*In vivo*	A inducers of apoptosis in papillomatous and preneoplastic tissues of esophagus
Charepalli *et. al* (2015)	*In vivo*	Suppressor of colon tumorigenesis through deletion of colon cancer stem cells
Bishayee et. al (2011)	*In vivo*	Anthocynins can be as chemopreventive factors for liver cancer

DISCUSSION

Anthocyanin has antioxidant properties *in vitro* and *in vivo*. On the other hand, researchers showed that anthocyanins are able to inhibit the different cancer cells growth and they are chemopreventive factors [33, 34]. Scholars also explained that the anticancer properties of anthocyanins have been widely evaluated *in vitro* studies and some gastrointestinal cancer models of animal and they demonstrated that anthocyanins can improve intestinal health [35, 36]. In another study, it was indicated anthocyanins chemopreventive factors for human colorectal cancer [37]. As well as, *in vitro*

and *in vivo* studies have been reported anthocyanin can protect against cancer of colorectal by inducing cellcycle arrest, apoptotic mechanisms, and anti-proliferative [27]. Anthocyanins are found in many vegetables and fruits; however, sweet potato and processed tomato products. Among the antioxidant effects of anthocyanins, use of these benefits are necessary for health promotion. In the other hand, dietary intakes of sweet potato and its products have an associated with decreased risk of chronic diseases such as cancer, so sweet potato and tomato products are good anti-cancers. Also, data suggested that the promoting effect of anthocyanins on ARE-regulated phase II enzyme expression seems to be a critical point in modulating the immune system against oxidative stress in liver, so anthocyanins can be as a protector of liver cancer [27, 38].

CONCLUSION

As a result, Researchers have declared that anthocyanins have a protective role in digestive system cancers. So it is suggested that using anthocyanin inpharmaceutical products pay more attention to its effects. In herbal medicine, due to anthocyanins in plant crops by proper planning and training in using of plants containing these substances, it can be attempt to fight against deadly diseases. Also, due to health anthocyanins properties, the useful results were obtained to promote health of communities.

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