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POTENTIAL ANTICANCER PROPERTIES OF BERRIES FROM ORGANIC PRODUCTION – A REVIEW

Summary

Berries belong to the best dietary sources of bioactive compounds, mainly phenolic compounds (phenolic acids, flavonoids including anthocyanins and flavonols, tannins) and vitamin C (ascorbic acid). These compounds, either individually or combined, are responsible for various health benefits of berries, in that protective effects to lower the risk of various cancers. Over the last 25 years, a significant number of research studies have compared the contents of phenolics and vitamins, nutritionally relevant minerals, toxic metals, pesticide residues and macronutrients in crops from organic and non-organic production systems. The most recent meta-analysis summarizing the results of 343 peer-reviewed studies comparing plant food from organic and conventional production concluded that organic products are, on average, characterized by significantly higher concentrations of various antioxidants (i.e. phenolic compounds) and much lower incidence of pesticide residues than their conventional comparators. This finding suggests that berries from organic production may have a grater health effects than non-organic ones. In this paper research on anticancer properties of berries and their bioactive compounds is reviewed.
***Key words**: berries, organic farming, flavonoids, phenolic acids, anticancer properties*

POTENCJALNE WŁAŚCIWOŚCI PRZECIWNOWOTWOROWE OWOCÓW JAGODOWYCH Z UPRAW EKOLOGICZNYCH – PRZEGLĄD BADAŃ

Streszczenie

Owoce jagodowe należą do najlepszych dietetycznych źródeł związków bioaktywnych, a w szczególności związków fenolowych (kwasów fenolowych, flawonoidów, w tym antocyjanów i flawonoli, garbników) i witaminy C (kwasu askorbinowego). Składniki te, pojedynczo lub współdziałając, są odpowiedzialne za różnorodne korzyści zdrowotne wynikające ze spożywania tych owoców, w tym działanie ochronne mające na celu zmniejszenie ryzyka zachorowań na choroby nowotworowe. W ciągu ostatnich 25 lat w wielu badaniach naukowych porównywano zawartość związków fenolowych i witamin, składników mineralnych, metali toksycznych, pozostałości pestycydów i makroelementów w płodach pochodzących z ekologicznych i konwencjonalnych systemów produkcji. Z najnowszej metaanalizy podsumowującej wyniki 343 recenzowanych prac porównujących żywność pochodzenia roślinnego z produkcji ekologicznej i konwencjonalnej wynika, że produkty ekologiczne charakteryzują się średnio znacznie wyższymi zawartościami różnych przeciwutleniaczy (np. związków fenolowych) i znacznie niższą częstotliwością występowania pozostałości pestycydów niż ich konwencjonalne odpowiedniki. To odkrycie pozwala przypuszczać, że owoce jagodowe z upraw ekologicznych mogą mieć większy wpływ na zdrowie człowieka niż owoce z upraw konwencjonalnych. W artykule dokonano przeglądu badań dotyczących właściwości przeciwnowotworowych owoców jagodowych i ich składników bioaktywnych.
***Słowa kluczowe**: owoce jagodowe, uprawa ekologiczna, flawonoidy, kwasy fenolowe, właściwości przeciwnowotworowe*

1. Introduction

There is strong scientific evidence for health benefits associated with increased consumption of crops rich in phenolics and other plant secondary metabolites with antioxidant activity (e.g. carotenoids and vitamins C and E) [4, 21]. These active compounds in foods are involved in the binding of mutagens, inhibition of metabolic activation of pro-mutagens, removing free radicals, inhibition of cancer cell proliferation, intensification of the processes of DNA repair and induction of cancer cells apoptosis. They may also affect the differentiation of cells, exhibit cytotoxic and cytostatic activity against tumour and regulate the immune system [18]. Fruits are the main source of antioxidants with anticancer activity in our diet and among them berries are the richest in this respect [15]. The berry fruits group, whose one common feature is type of the fruit, includes numerous species such as gooseberry, cranberry, bilberry, black chokeberry, raspberry, blackberry, strawberry and wild strawberry. In Poland the most important berries are: strawberry (*Fragaria×ananassa* Duchesne), raspberry (*Rubus idaeus* L.) and blueberry (*Vaccinium corymbosum* L.) [11]. From the nutritional point of view berry fruits play an important role in human nutrition. They contain a lot of bioactive compounds, in that well known antioxidants like flavonoids and phenolic acids. Colour of berry fruits is one of the most important appearance attributes. It is being caused by the accumulation of anthocyanins in flesh and skin of fruits [10, 16]). Phenolics are the only putative defensive molecules ubiquitous in higher plants. They have played a central role in theories of plant-herbivore interactions [25]. Their function and working in plants are very huge and not to the end well known [8-9]. For human health polyphenols are mostly used as antioxidant agents and protect body cells against oxidation. They are a powerful antioxidants as well take part in many metabolic proc-

esses [7, 13]. As was reported by the authors of an extensive, recently published meta-analysis, many of antioxidants are found in higher concentrations in organic compared to non-organic fruit and vegetables. At the same time organic crops are characterized by significantly lower concentrations of cadmium and lower incidence of pesticide residues (in case of fruit even 7 times lower) than their conventional comparators [1]. On the basis of the above statements one could expect beneficial health impacts (i.e. potent anticancer properties) of berries, especially those produced according to organic farming standards. However, the available research addressing the health impact of organic vs. non-organic products is very limited and there are no studies using berries as a study object. This paper aimed mainly to present research on anticancer properties of berries and bioactive compounds they contain.

2. Berry bioactive compounds and their anticancer effect

Berries contain two major groups of phenolic compounds: flavonoids, in that mainly flavonols and anthocyanins, and phenolic acids, in that a very strong antioxidant - ellagic acid [12]. Results of *in vitro* studies indicate that vitamins and certain phytochemical antioxidants are effective against e.g. human colorectal, breast and stomach cancer cells. In the Faria et al. [6] study a human breast cancer cell line, treated with catechin or procyanidin fractions obtained from a grape seed extract, were used to evaluate the effect of these compounds on cell viability and proliferation. The results showed that some procyanidin fractions (30 microg/mL) as well as catechin (60 microg/mL) were able to decrease cell viability and proliferation. Authors have noticed that the procyanidin fractions that exhibited higher antioxidant activity were the same to affect cell viability and proliferation. In the other study [14] polyphenol-rich berry extracts were screened for their antiproliferative effectiveness using human cervical cancer (HeLa) cells grown in microtiter plates. The results showed the strongest effects of strawberry, arctic bramble, cloudberry and lingonberry extracts, which contained 25-40 microg/mL of phenols. These extracts were also effective against human colon cancer (CaCo-2) cells, but in this case the cell cultures were more sensitive to low concentrations and conversely less sensitive to higher concentrations of extracts. The berries extracts share common polyphenol constituents, especially the ellagitannins, which have been shown to act as effective antiproliferative agents. At the same time the antiproliferative activity of lingonberry was linked predominantly to procyanidins. Zhang et al. [23] examined strawberry crude extracts and purified compounds (e.g. cyanidin-3-glucoside, pelargonidin, kaempferol, quercetin, ellagic acid). These substances were evaluated for antioxidant and human cancer cell antiproliferative activities. Crude extracts (250 µg/mL) and pure compounds (100 µg/mL) inhibited the growth of human oral (CAL-27, KB), colon (HT29, HCT-116), and prostate (LNCaP, DU145) cancer cells with different sensitivities observed between cell lines. The described results confirm the bioactivity of berry fruit phenolics and their potential impact on human health. Thomasseta et al. [19] reported that the consumption of products rich in anthocyanins reduces a risk of colon cancer, due to their antioxidant and anti-inflammatory properties. In their study, patients with colorectal cancer and liver metastases received different doses of standardized extract of blueberries (0.5, 1.0 or 2.0 grams of anthocyanins) 7 days before the scheduled operation. The results showed a reduction of cancer cell proliferation, increased apoptotic index in epithelial cells, as well as a slight decrease in the plasma concentration of insulin-like growth factor 1. The most preferred effects were observed with a daily dose of anthocyanins, which corresponds to approximately 370 g of fresh blueberries [19]. Other authors [20] conducted a study on the anticancer effects of resveratrol (found in red grapes, blueberries, strawberries, raspberries and blackberries). Authors stated that resveratrol (100-150 microM) suppressed cell proliferation by inhibiting insulin like growth factor-1 and also enhanced apoptosis by activating tumour suppressor p53 protein in human colon cancer cells (HT-29 and SW480). De Castro and Teodoro [3] in their review concluded that many of the berry phenolic compounds show anticancer activities and exert their effects through one of the aforementioned mechanisms. It is expected that the effects of polyphenols on cell cycle, cell growth and proliferation, as well as induction of apoptosis in cancer cells, will provide clues for the prediction of novel agents that may be useful in cancer chemoprevention or chemotherapy, therefore, more information is needed with regards to the possible role of plants in cancer prevention and therapy.

3. Inhibition of growth of various cancer cell lines by berry fruit extracts

The growth of various cancer cell lines (e.g. stomach, prostate, colon, cervical and breast) was found to be strongly inhibited by berries [2]. Authors have reported in the review that berry extracts inhibit the growth of cultured cancer cells and certain berries (e.g. blueberry, blackberry, blackcurrant and raspberry) are considerably more effective than other fruits. They have concluded that berry extracts can inhibit the initiation, progression, and invasiveness of colon cancer cells, but the challenge is to increase an understanding of the mechanisms involved [2]. According to Zhang et al. [24] black raspberries and their bioactive components represent promising candidates for future phytochemical-based mechanistic pathway-targeted cancer prevention strategies. In the *in vitro* study authors stated that the black raspberry ethanol extract significantly inhibited the growth of human cervical cancer cells in a dose-dependent and time-dependent manner to a maximum of 54%, 52% and 67%, respectively inhibiting proliferation and regulating apoptosis. Somasagara et al. [7] investigated the anticancer activity of the methanolic extract of strawberries in leukaemia and breast cancer cell lines *ex vivo*, and its cancer therapeutic and chemopreventive potential in mice models. The results suggested that extract of strawberry fruits can induce cytotoxicity in cancer cells, irrespective of origin, in a concentration- and time-dependent manner. Treatment of mice bearing breast adenocarcinoma with extract blocked the proliferation by activating apoptosis of tumour cells in a time-dependent manner and resulted in extended life span, and did not result in any side effects [17]. Wang et al. [22] tested fruit extracts of three strawberry species for the ability to inhibit proliferation of human lung epithelial cancer cells (A549). At the species level, *F. virginiana* fruit extract inhibited the proliferation of A549 cells to a significantly greater extent (34% inhibition) than the extracts from fruit of either *F. chiloensis* (26%) or *F. x ananassa* (25%). The results also suggest that strawberries can inhibit A549 cell population growth. In the study correlations between levels of antioxidant capacity, antioxidant enzyme activity, non-enzyme components, and antiproliferative activities of strawberry genotypes were positive and

high (Wang et al. 2007). In the Diaconeasa et al. [5] study an antiproliferative potential of anthocyanin-rich fractions obtained from commercially available blueberry and blackcurrant juices on three tumour cell lines (B16F10 - murine melanoma, A2780 - ovarian cancer and HeLa - cervical cancer) was evaluated. Authors have determined individual anthocyanins concentrations and antioxidant activity of the juices. For biological testing, the juices were purified in order to obtain fractions rich in anthocyanins. The antiproliferative potential of anthocyanin-rich fractions was found to be associated with anthocyanins' antioxidant potential.

4. Conclusion

The results of both *in vivo* and *in vitro* studies on various cancer cell cultures presented in the article have suggested that bioactive compounds of berries possess anticancer effects, thus have an influence on human health. Dietary intake of berries with high content of phenolic compounds and high antioxidant activity could have a potential to reduce risk of cancer and other diseases known to be induced by oxidative stress. Based on many research results organic products are, on average, characterized by significantly higher concentrations of various antioxidants (i.e. phenolic compounds) and much lower incidence of pesticide residues than their conventional comparators. This finding suggests that berries from organic production may have a grater health effects than non-organic ones.

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