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THE BENEFICIAL EFFECTS OF *BRASSICA* VEGETABLES ON HUMAN HEALTH

KORZYSTNY WPŁYW WARZYW KAPUSTNYCH NA ZDROWIE CZŁOWIEKA

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ABSTRACT

The products of plant origin are a rich source of biologically active substances, both nutritive and referred as anti-nutritive. A large group of these compounds are substances with antioxidant activity that fights against free radicals. In the family of *Brassicaceae* vegetables, *Brassica*, is the largest and most widely consumed a group of plants in Europe and all over the world. They are characterized by different levels of nutrients. However because of their large and frequent consumption, they may become a significant source of nutrients and bioactive compounds in the daily diet.

The beneficial effects of *Brassica* vegetables on human health have been somewhat linked to phytochemicals. They prevent oxidative stress, induce detoxification enzymes, stimulate immune system, decrease the risk of cancers, inhibit malignant transformation and carcinogenic mutations, as well as, reduce proliferation of cancer cells.

Brassica vegetables contain a lot of valuable metabolites, which are effective in chemoprevention of cancer, what has been already documented by numerous studies. Due to the presence of vitamins C and E, carotenoids and antioxidant enzymes such as catalase, superoxide dismutase (SOD) and peroxidase, these vegetables are considerable source of antioxidants, and due to the presence of polyphenols and the sulfur-organic compounds exert also antimutagenic action. Moreover, these vegetables are also rich in glucosinolates, which are unstable compounds and undergo degradation into biologically active indoles and isothiocyanates under the influence of enzyme presented in plant tissues- myrosynase. These substances through the induction of enzymatic systems I and II phase of xenobiotics metabolism may affect the elimination or neutralization of carcinogenic and mutagenic factors, and consequently inhibit DNA methylation and cancer development. Despite many healthy benefits upon eating of cruciferous vegetables, it has been also seen a negative impact of their certain ingredients on the human body.

STRESZCZENIE

Żywność pochodzenia roślinnego jest bogatym źródłem substancji biologicznie aktywnych, zarówno odżywczych, jak i określanych mianem nieodżywczych. Liczną grupę wśród tych związków stanowią substancje o działaniu przeciwutleniającym, zwalczającym aktywność wolnych rodników. W rodzinie krzyżowych, warzywa kapustne, są największą i równocześnie najpowszechniej spożywaną grupą roślin w Europie i nieomal na całym świecie. Charakteryzują się one zróżnicowanym poziomem składników odżywczych. W związku z tym, że są spożywane z dużą częstotliwością, mogą stać się istotnym źródłem składników odżywczych i bioaktywnych w codziennej diecie człowieka.

Korzystny wpływ warzyw kapustnych na zdrowie człowieka związany jest z obecnością w nich substancji aktywnych, które mogą działać na różnych i uzupełniających się poziomach poprzez zapobieganie stresowi oksydacyjnemu, stymulowanie układu odpornościowego, zmniejszanie ryzyka nowotworów, jak również hamowanie już zainicjowanej zmiany nowotworowej i rakotwórczych mutacji oraz ograniczenie rozprzestrzeniania się komórek rakowych. Warzywa kapustne zawierają wiele cennych metabolitów, których skuteczność w chemoprewencji nowotworowej została udokumentowana licznymi badaniami. Dzięki obecności witaminy C i E, karotenoidów i enzymów antyoksydacyjnych, takich jak: katalaza, dysmutaza ponadtlenkowa (SOD) i peroksydaza są źródłem cennych przeciwutleniaczy, a ze względu na obecność polifenoli oraz związków siarkoorganicznych mają również działanie przeciwmutagenne. Co więcej, warzywa te są również bogate w glukozynolany, które są związkami niestabilnymi, podlegającymi rozkładowi do biologicznie aktywnych izotiocyjania-

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nów i indoli pod wpływem obecnego w tkankach roślinnych enzymu mirozynazy. Substancje te poprzez indukcję układów enzymatycznych I i II fazy metabolizmu ksenobiotyków mogą wpływać na wydalanie bądź neutralizowanie czynników kancerogennych i mutagennych, a w konsekwencji hamować metylację DNA i rozwój nowotworów. Pomimo wielu prozdrowotnych korzyści płynących ze spożywania warzyw krzyżowych, zaobserwowano również negatywny wpływ niektórych składników na ludzki organizm.

INTRODUCTION

Chemoprevention is a method in which natural or artificial agents are used in order to turn around, diminish, or avoid the formation of a chronic–degenerative illness. Consequently, chemoprevention is aimed to retard the creation of the disease as well as decline its incidence. Chemopreventive components could stop the promotion and succession of cancer or could target the initiation phase of carcinogenesis [19].

To understand the key mechanism underlying the metabolic regulation, the flow of information and metabolites has to be considered at all levels of the organism, starting from the molecular and cellular level onto the levels of the organs' interaction. Human nutrition and metabolism may serve as the paradigm for the complex influence of the genome with its environment. Nutrigenomics allows to explain better the homeostatic control mechanism and identify regulation in the early phases of diet-related diseases [12]. It was found that the metabolism of nutrients may vary and ultimately result in different health status depending on the genotype of an individual [11]. Nutrigenomics trends towards individualize/personalize food and nutrition, and ultimately individual strategies to preserve health.

The knowledge about nutrient-gene interaction is rapidly increasing in different medical areas, e.g. metabolic diseases, cardiovascular diseases, cancer etc., and it could be the key to understanding the pathology and the progression of polygenic, metabolic and non-metabolic disorders [17].

CHARACTERISATION OF THE *BRASSICACEAE* FAMILY

The *Brassicaceae* is a plant family of enormous economic importance, containing about 340 genera and 3700 species [47]. These vegetables are among the most important vegetables consumed in Europe and all over the world owing to their availability at local markets, cheapness and consumer preference [26, 28, 33, 34, 42]. The genus *Brassica* is the most important within the tribe Brassiceae, which includes some crops and species of great worldwide economic importance such as *Brassica oleracea* L., *Brassica napus* L. and *Brassica rapa* L. The major vegetable species is *B. oleracea*, which includes vegetable, such as kale, red and white cabbage, broccoli, Brussels sprouts, cauliflower and others; *B. rapa* includes vegetable forms, such as turnip, Chinese cabbage and pak choi, along with forage and oilseed types; *B. napus* crops are mainly used like oilseed (rapeseed), although forage and vegetable types like leaf rape and nabicol are also included. Lastly, the mustard group which is formed by three species, *B. carinata*, *B. nigra* and *B. juncea* [5].

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They are characterized by differential levels of many nutrients. However because of their large and frequent consumption, they may become a significant source of nutrients and bioactive compounds in the daily diet [46]. Additionally, these seasonal vegetables may be stored raw for long periods of time and hence could be available throughout the all year [6, 43]. This group of vegetables contains well-known antioxidants, such as vitamins C, E, carotenoids and antioxidant enzymes such as catalase, superoxide dismutase (SOD) and peroxidase, which are found in fresh vegetables [46, 52].

What's more, these vegetables are also rich in beneficial plant's metabolites, which include sulfur containing glucosinolates, anthocyanins, flavonoids, terpenes, S-methylcysteine sulfoxide, coumarins and other minor compounds [46].

The beneficial effects of *Brassica* vegetables on human health have been somewhat linked to phytochemicals. These are "phenolic compounds" that refers to a large number of compounds isolated from plants. Phenolics are classified into simple, low molecular-weight, single aromatic-ringed compounds to large and complex tannins and derived polyphenols [5, 8, 48]. They are categorized on the basis of the number and arrangement of carbon atoms in flavonoids (flavonols, flavones, flavan-3-ols, anthocyanidins, flavanones, isoflavones and others) and non-flavonoids (phenolic acids, hydroxycinnamates, stilbenes and others) and are mostly coupled to sugars and organic acids [5, 8]. Flavonoids and the hydroxycinnamic acids are the most prevailing and heterogeneous group of polyphenols in *Brassica* species [5].

Phytochemicals from *Brassica* vegetables may act on different and complementary levels. They prevent oxidative stress, induce detoxification enzymes, stimulate immune system, decrease the risk of cancers, inhibit malignant transformation and carcinogenic mutations, as well as, reduce proliferation of cancer cells [3, 20, 26, 35, 36].

Reactive oxygen species (ROS) in the body can cause lipid and protein oxidation, DNA damage, base modification and modulation of gene expression. What is more, they play an important role in etiopathology of many diseases, including: atherosclerosis, vasospasm, cancers, stroke, heart attack and liver injury. Imbalance between ROS and antioxidants causes oxidative stress. Oxidative stress may be caused by antioxidant deficiency in the diets or increased production of free radicals by stress, smoking, environmental contaminations, which immigrate in to the water and food (heavy metals, pesticides, nitrates, nitrites, nitrosamines etc.) [41].

Other threats are substances of mutagenic and carcinogenic properties presented in food products due to improper storage conditions (eg. mycotoxins) or heat treatment (eg. heterocyclic aromatic amines, acrylamide, genotoxic lipid peroxidation products). The presence of antioxidants, and particularly their release during heat treatment, suggest that cabbage can effectively protect other food ingredients against thermooxidative changes [39].

Antioxidants and other bioactive compounds detoxify ROS and prevent damage to cellular macromolecules and organelles through multi-mechanisms [10, 60]. In human body, several mechanisms are known to defend from free radicals (for example antioxidant enzymes), however in some cases there is a need more substances to overcome their impact. Consumption of vegetables including *Brassica* species has been strongly associated with the reduced risk of chronic diseases, such as cardiovascular disease, cancer, diabetes, Alzheimer's disease, cataracts and age-related functional decline [9, 37, 59].

The better part of chronic–degenerative diseases contributes many widespread risk factors and pathogenetic determinants [19, 29]. Additionally, cancer, human atherosclerosis and age-related brain and heart degeneration are mostly related with DNA changes [14, 19, 30]. The formation of cancer is a prolonged and complex process consisting of initiation, promotion and progression [18]. Cruciferous vegetables consumption appears to lower the risk for some kinds of cancers, like renal cancers, prostate and possibly colorectal. The evidence is however not as strong for lung, breast, and oral cancers [55].

Glucosinolates (GLSs) are a major group of natural plant compounds that are mainly presented in *Brassicaceae*. Upon cellular disruption, GLSs are hydrolysed by the myrosinase action to various bioactive breakdown products (isothiocyanates, nitriles, thiocyanates, epithionitriles, and oxazolidines) [4]. It is crucial, especially because such an induction generally takes some time. Therefore, in contrast to antioxidants, which work is "off", the protective effect is extended due to the presence of isothiocyanates [39].

The isothiocyanates (ITCs) occurring in brassica vegetables, have focused particular attention on their potential anti-cancer abilities. Limited studies have been however performed in order to investigate thoroughly the impact of ITCs structure on NF- κB transactivation and anti-inflammatory action [32, 50].

All substances of bioactive properties presented in these vegetables may decrease inflammation for the reason that they may operate on diverse and complementary stages i.e. stimulate detoxification enzymes, scavenge free radicals and induce immune functions [19]. ITCs, presenting in many cruciferous vegetables, indicate interesting chemopreventive activities against numerous chronic–degenerative diseases, together with cancer, cardiovascular diseases, neurodegeneration and diabetes [19].

The *in vivo* studies on the defending capability of ITCs against cardiovascular diseases offer promising results. They also imply that an elevated ingestion of these compounds, instead of giving advantageous effects, may contribute to negative consequences. ITCs have shown protective activity on nervous system in both, *in vitro* and *in vivo* tests of neuronal cell death or neurodegeneration, respectively. They are capable of scavenging the free radicals or enlarge endogenous cellular antioxidant barrier via activation of the Nrf2 transcription factor pathway. Other mechanisms of their action are modulation of signal transduction cascades or effects on gene expression [13, 19, 38].

Constant inflammation plays an essential role in many human illnesses and ITCs slow down the activity of many inflammation mechanisms, restrain cyclooxygenase 2, and permanently inactivate the macrophage migration inhibitory factor [19].

Due to its anti-inflammatory and antibacterial properties, cabbage has widespread use in traditional medicine, in alleviation of symptoms associated with gastrointestinal disorders (gastritis, peptic and duodenal ulcers, irritable bowel syndrome), as well as, in treatment of minor cuts, wounds and mastitis [51].

Red cabbage has attracted recently much attention because of its physiological functions and applications [45]. Pigmented flavonoids, especially the anthocyanins are thought to be most important kind of flavonoids in plants because of their potent antioxidant activity and other physicochemical and biological properties. The anthocyanins in red cabbage inhibit amyloid β protein--induced neurotoxicity in neuron-like PC12 cells. Red cabbage juice given to female ICR mice via gavage displayed a protective effect on oxidative stress in brain of mice administered i.p. with *N*-methyl-D-aspartate

(NMDA) [25, 40]. Some anthocyanidins i.e. delphinidin and cyaniding, inhibit cyclooxygenase-2 (COX-2) expression, in lipopolysaccharide (LPS)-activated murine macrophage RAW264 and COX-2 which plays an important role in inflammation and cancerogenesis. The red cabbage juice may have anti-inflammatory potential [45]. Considerable consumption of anthocyanins has been shown to have health beneficial influence on a range of disorders, like cancer, aging, neurological diseases, inflammation, diabetes, as well as, bacterial infections [16, 24, 44]. Depending on the kind of plant, anthocyanins may constitute of the greater part of the TPC such as those in the cruciferous cabbage and cauliflower [44].

In addition sulforaphane (SFN), a natural component of cruciferous vegetables (broccoli, Brussels sprouts, etc.), has been demonstrated to possess a variety of defensive effects in models of tissue injury and cancer. Cisplatin (cis-diamminedichloroplatinum II, CIS) is a strong and extensively used chemotherapeutic agent to treat different types of cancers, but its remedial application is limited because of dose-dependent nephrotoxicity. Cell death and inflammation play an important role in the formation and succession of CIS-induced nephropathy. *Guerrero-Beltrán* et al. [23] confirmed that the cisplatin-induced nephropathy is related with activation of different cell death and proinflammatory pathways (p53, JNK, p38α, TNF-α and NF-κB) and malfunction of key prosurvival signaling mechanisms (ERK and p38-β); and these pathological changes can be excluded by a natural, economical, antioxidant/anti-inflammatory ingredient from cruciferous vegetables (e.g., broccoli, Brussels sprouts, etc.), as long as, an innovative approach for preventing this destructive barrier of the chemotherapy.

In the study of *Ferrarini* et al. [18], the extracts of fresh *Brassica* vegetables (broccoli, cauliflower, Brussels sprouts) showed the highest anti-proliferative and antioxidant activities on carcinoma HT-29 cells and no genotoxic activity was detected in the tested samples. The application of cooking methods influenced the anti-proliferative activity of Brassica extracts however did not alter considerably the antioxidant activity presented in the raw vegetables.

Hwang et al. [27] analysed the influence of indole-3-carbinol on *Candida albicans* and reported a significant increase of the reactive oxygen species and hydroxyl radical accumulation. Hence, it was shown that indole-3-carbinol has apoptosis effects, including a production of hydroxyl radicals, cytochrome c release and an activation of metacaspase. Both, hydroxyl radicals and metacaspases triggered apoptosis in *Candida albicans.*

In the paper of *Chiu* et al. [7], a detailed history of dietary practices and food preferences was collected with using of food frequency questionnaire from 348 cases and 470 controls in a population-based case-control study conducted in Nebraska during 1999-2002. The authors observed that higher intake of green, leafy vegetables and cruciferous vegetables are associated with a lower risk of NHL (non-Hodgkin lymphoma). At the same time, *Tang* et al. [54] reported that phenethyl isothiocyanate (PEITC), one of many compounds found in cruciferous vegetables, might exhibit anticancer activity and may become a potent agent against human prostate cancer cells in the future.

In a study by *Zhang* et al. [58], 134,796 Chinese adults participated in 2 population-based prospective cohort studies of the Shanghai Women's and Men's Health Study. Dietary intakes were assessed at baseline through in-person interviews by using validated food-frequency questionnaires. Deaths were ascertained by biennial home visits and linkage with vital statistics registries. The authors reported that cruciferous vegetable consumption is associated with a reduced risk of total and cardiovascular disease mortality.

Riso et al. [49] evaluated the effect of broccoli intake on biomarkers of DNA damage and repair. Twenty-seven young healthy smokers consumed a portion of steamed broccoli (250g/day) or a control diet for 10 days each within a crossover design with a washout period and the blood was collected before and after each period. They observed that broccoli intake was associated with increased protection against $H_{(2)}O_{(2)}$-induced DNA strand breaks and lower levels of oxidised DNA bases in PBMCs (peripheral blood mononuclear cellsfrom smokers). On the other hand, *Badurska-Stankiewicz* et al. [2] analysed the roles of nutritional habits and addictions in the incidence of thyroid carcinoma. Two hundred ninety-seven patients with thyroid carcinoma consumed cruciferous plants significantly more often than healthy subjects ($p = 0.0001$). The authors noted that one of the environmental factors causing the increase of this type of cancer could be overconsumption of cruciferous vegetables.

Jakubikova et al. [31] analysed the anti-myeloma activity of the isothiocyanates, sulforaphane and phenethyl isothiocyanate on a panel of human myeloma cell lines, as well as, on primary myeloma tumor cells. This study showed that isothiocyanates may have therapeutic potent anti-myeloma activities and may enhance the activity of other anti-multiple myeloma agents.

An experiment on healthy adults consuming a *Brassica*-enriched diet vs. vitamin–mineral–fiber supplement exerted a 22% reduction in lipid peroxidation as assessed by urinary F2-isoprostane levels [21]. Urinary mutant excretion has been also enhanced by cruciferous vegetables among subjects exposed to fried meat ($n = 4$ fried meat with cruciferous vegetables; $n = 4$ with fried meat and non-cruciferous vegetables intake daily for 6 weeks) [15].

The study on 200 healthy adults living in China [53] showed that glucoraphanin beverages (broccoli) consumed nightly for 2 weeks, were not associated with lower aflatoxin–DNA adduct formation, but significantly higher excretion of these adducts in subjects, who concurrently demonstrating high urinary dithiocarbamate levels. This paper suggested that cruciferous vegetables exert protective effects in ability of inducing phase I/II enzymes, both NAT and GST. In the study with heavy smokers, it was evidenced a significant reduction in DNA adducts in exfoliated bladder cells after 12 months of a diet rich in cruciferous vegetables [55].

Recently, it has been reported that daily consumption of broccoli sprouts for 2 months (70 g a day of glucoraphanin) can be effective in reducing the oxidative stress induced by *Helicobacter pylori* and may be also helpful in prevention of gastritis in experimental animals and humans [46, 56].

Ayaz et al. [1] found that phenolics extracted from kale leaves (*B. oleracea*), rich in quercetin and kaempferol derivatives, substanially inhibited the growth of the bacteria: *Staphylococcus aureus*, *Enterobacter faecalis*, *Bacillus subtilis* and *Moraxella catarrhalis*. The last is known to be a main respiratory pathogen in humans. What is interesting, isorhamnetin obtained from mustard leaf showed a strong activity in reducing serum glucose levels in people suffering from *Diabetes mellitus* [5, 57]. Experiments performed with the use of animal and human models evidenced that isorhamnetin reveal distinct vasodilator, as well as vascular protective effects in human cardiovascular diseases [5, 8, 22]. Beside these, quercetin, kaempferol and isorhamnetin were shown to possess anti-inflammatory properties on activated macrophages [5, 22].

Brassica vegetables have long been regarded as excellent sources of pharmaceuticals, what could be explained by their structure diversity, as well as, by wide variety of beneficial effects on human health. Many compounds have been isolated from *Brassica* vegetables and further pharmacological studies *in vitro* or *in vivo* have shown that they have a large spectrum of biological activities, including antibacterial, antifungal, antitumor, antimutagenic, antiinflammatory, neuroprotective and antioxidative. In addition to numerous beneficial properties, some components of *Brassica* vegetables (e.g. progoitrin) may exert antinutritive effects on the human body.

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