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The Benefits of *Brassica* Vegetables on Human Health

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Abstract

Brassica or Cruciferous vegetables are the most important genus of the *Brassicaceae* family and consist of thirty-seven different species. *Brassica* vegetables contain low fat, high vitamin, mineral and fibre as well as various phytochemicals. Hydrolysis of glucosinolates in plant tissues is mediated by β-thioglucosidase (myrosinase) enzyme released from plant cells. Hydrolytic products of glucosinolates prevent oxidative stress, induce detoxification enzymes, stimulate the immune system, reduce cancer risk, inhibit malign transformation and carcinogenic mutations in addition to reduce the proliferation of cancer cells. Adequate and balanced nutrition for adults is recommended to consume *Brassica* vegetables at least 5 servings in a week. This paper aims to investigate the health effects of *Brassica* vegetables.

Keywords: *Brassica* Vegetables; Glucosinolates; Isothiocyanates; Sulphoraphane

Introduction

Brassica is the most important genus of the *Brassicaceae* family and consists of 37 different species. This genus comprises six interrelated species, three diploids (*B. Nigra, B. Oleracea and B. Rapa*) and three Amphidiploids (*B. Carinata, B. Juncea and B. Napus*) species.

This genus is categorized as oilseeds, fodder, spices and vegetable plants using buds, inflorescences, leaves, roots and seeds of plants. *B. oleracea* and *B. rapa* contain the majority of *Brassica* plants and they have many options from all species of edible forms. In *B.oleracea* there are vegetables such as kale, collards, cabbage, savoy cabbage, Brussel sprouts, cauliflower, broccoli, kohlrabi and Chinese kale, while in B. Rapa includes turnip, Chinese cabbage, pak choi, komatsuna [1,2]. Other *Brassica* species include mustard greens, Chinese broccoli, Japanese mustard (mizu-na), gai-lohn, horseradish, wasabi, daikon, arugula, watercress and radish [2-4].

Brassica vegetables are rich in sulphur-containing compounds which are responsible for the rich glucosinolate content, the pungent smells and the spicy flavour [3]. According to data from Food and Agriculture Organization (FAO) production of *Brassica* vegetables in the world covers a total of approximately 139 million tons -33.5 million tonnes of cauliflower and broccoli, and 105.7 million tonnes of cabbage and other *Brassicas*-. China is the biggest *Brassica* vegetables producer in the world and constitutes over half of all *Brassica* vegetables production in the world [5].

Characteristic Composition of *Brassica* Vegetables

Nowadays, consumers are demanding products that are rich in nutrients for optimal health benefits. In this respect, the popularity of *Brassica* products is increasing because of their nutritional value, anticancer, antioxidant and anti-inflammatory properties [1].

The components of *Brassica* vegetable depend on many factors such as diversity, harvest period, processing and cooking conditions and environment where they grow. These vegetables contain low fat, high vitamin, mineral and fibre, as well as useful phytochemicals [1,6,7]. In addition, this vegetable group contains well known antioxidants such as vitamins C and E, carotenoids and antioxidant enzymes such as catalase, superoxide dismutase (SOD) and peroxidase, which are found in fresh vegetables. Moreover, these vegetables contain sulphur-containing glucosinolates, anthocyanins, flavonoids, terpenes, S-methyl cysteine sulfoxide, coumarins and other small compounds, which are useful plant metabolites [8].

Vitamin and Mineral Contents

In general, *Brassica* vegetables have high vitamin and mineral content. *Brassica* vegetables are rich in vitamins C and E and carotenoids, which have the potential to prevent and treat malignant and degenerative diseases[9,10]. Also, in *Brassica* products, there is a high amount of folate that reduces vascular disease, cancer and neural tube defect risk [11].

Brassica vegetables contain calcium in the range of 22 mg-150 mg/100g. Since oxalic and phytic acids that bind calcium are found in low levels in these vegetables, the bioavailability of calcium is high [1,12]. Among green leafy vegetables, the Kale is an important mineral source that accumulates high levels of P, S, Cl, Ca, Fe, Sr and K [9]. At the same time, they also contain a high level of potassium, an important mineral that plays an important role in different metabolic processes [1]. Broccoli accumulates most of selenium found in the soil, which can greatly enhance the health promoting properties [6]. Cabbage comprises potentially useful amounts of copper, zinc, iron and a number of other important minerals and trace elements. *Brassica* can be grown under hydroponic conditions, leading to high levels of nutritionally important minerals such as Cr, Fe, Mn, Se and Zn [9]. Heavy metals have the potential to accumulate by cruciferous species (Radish, Juncea) [13].

The energy and nutrient content of 100 grams of some edible *Brassica* vegetables are given in Table 1.

	Broccoli	Brussels sprouts	Cabbage	Cauliflower	Kale	Turnip	Mustard Greens
Water (g)	89.3	86	92.18	92.07	84.04	91.87	90.7
Energy (kkal)	34	43	25	25	49	28	27
Protein (g)	2.82	3.38	1.28	1.92	4.28	1.17	2.86
Total fat (g)	0.37	0.3	0.1	0.28	0.93	0.13	0.42
Carbohydrate (g)	6.64	8.95	5.8	4.97	8.75	6.43	4.67
Fibre (g)	2.6	3.8	2.5	2	3.6	1.8	3.2
Sugar (g)	1.7	2.2	3.2	1.91	2.26	3.8	1.32
Minerals							
Calcium (mg)	47	42	40	22	150	30	115
Iron (mg)	0.73	1.4	0.47	0.42	1.47	0.3	1.64
Magnesium (mg)	21	23	12	15	47	11	32
Phosphorus (mg)	66	69	26	44	92	27	58
Potassium (mg)	316	389	170	299	491	191	384
Sodium (mg)	33	25	18	30	38	67	20
Zinc (mg)	0.41	0.42	0.18	0.27	0.56	0.27	0.25
Selenium (µg)	2.5	1.6	0.3	0.6	0.9	0.7	0.9
Vitamins							
C (mg)	89.2	85	36.6	48.2	120	21	70
Thiamine (mg)	0.071	0.139	0.061	0.05	0.11	0.04	0.08
Riboflavin (mg)	0.117	0.09	0.04	0.06	0.13	0.03	0.11
Niacin (mg)	0.639	0.745	0.234	0.507	1	0.4	0.8
B_6 (mg)	0.175	0.219	0.124	0.184	0.271	0.09	0.18
Folate (µg)	63	61	43	57	141	15	12
A (IU)	623	754	98	0	9990	0	3024
E (mg)	0.78	0.88	0.15	0.08	1.54	0.03	2.01
K (µg)	101.6	177	76	15.5	704.8	0.1	257.5

Table 1: Energy and nutrient content of 100 grams of edible *Brassica* vegetables [12]

Phenolic Compounds

The *Brassica* genus contains phenolic compounds, one of the bioactive compounds that have positive effects on human health. These compounds show antioxidant activity by inhibiting the biological activation of carcinogens and by increasing the detoxification of reactive oxygen species (ROS) [14]. Phenolics are classified as simple, having low molecular weight, single aromatic cyclic compounds, large and complex tannins and derivatized polyphenols. 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 nonflavonoids (phenolic acids, hydroxycinnamates, stilbenes and others). Flavonoids and hydroxycinnamic acids are the most common and heterogeneous group of polyphenols in *Brassica* species [8]. In addition, *Brassica* vegetables also contain anthocyanins which cause pigmentation in red cabbage and broccoli sprouts [15].

Glucosinolates (β-thioglycoside-N-hydroxysulfates)

Glucosinolates are an important phytochemical group found in *Brassica* vegetables in quantities of 1,500-2,000 µg/g and especially high in Brussels cabbage, cabbage and broccoli [2,16,17]. Glucosinolate is found in spices such as horseradish and mustard, made

from roots and seeds of *Brassica* vegetables, at concentrations as high as 75,000 µg/g fresh weight [2]. The basic structure of glucosinolates includes β-D-thioglucose group, sulphonated oxime (-C=NOH) group, and variable side chain derived from amino acids. The side chain represented by R comprises aliphatic (alkyl, alkenyl, hydroxyalkenyl, w-methylthioalkyl, w-sulfinyl and w-sulfonylalkyl), aromatic (benzyl) or heterocyclic (indolyl) groups in highly variable structure. A small change in the side chain leads to the formation of different glucosinolates [17]. The general structure of glucosinolates is shown in Figure 1.

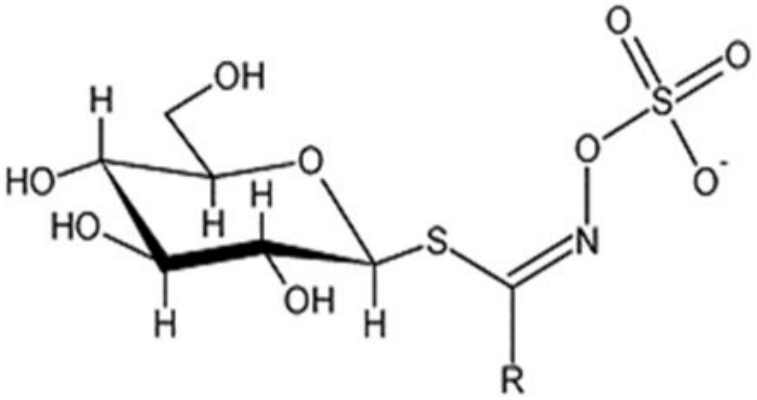

Figure 1: General structure of glucosinolates

Hydrolysis of glucosinolates: Glucosinolates found in plant tissues are not biologically active. Most glucosinolates are chemically and thermally stable whereas hydrolysis products of glucosinolates are biologically active [17]. In raw vegetables, enzymatic hydrolysis occurs only with β-thioglucosidase released when cells are injured by chewing or processing [18]. While cooking vegetables inactivates β-thioglucosidase, glucosinolates are also hydrolysed by microflora in the human intestinal tract and thus can be used biologically in cooked vegetables [2,19].

When the tissue is disrupted, the thioglucosidic bond breaks down, glucose and thiohydrosimate-O-sulphonate (unstable aglycone) are formed by β-thioglucosidase [16,18]. And then, different products can be obtained depending on the reaction conditions (pH) and the structure of glucosinolate. These may be isothiocyanates, nitriles, sulphides, thiocyanates, epithiitriles, oxazolidin-2-thiones and indolyl compounds [17,18] Of the hydrolytic products of glucosinolates, glucoraphanin, gluconasturtiin and glucobrassicin show anticarcinogenic activity. Furthermore, indol-3-carbinol, a metabolite of glucobrasicin, has inhibitory effects on human breast and ovarian cancers (6,20,21].

Approximately 130 different glucosinolates have been identified in the botanical system and glucosinolates have also antioxidant, anticancer, fungicide and bactericidal properties [1,22].

Isothiocyanates

Isothiocyanates are potentially anticarcinogenic phytochemicals that are the result of the metabolism of glucosinolates [23]. Approximately 100 isothiocyanates have been identified but only a few of them are common in the diet and are found in other selected foods as well as *Brassica* vegetables [24]. Isothiocyanates reduce systemic oxidative stress levels, alter cytokine activity depending on inflammatory response, induce apoptosis, inhibit cell cycle progression, inhibit angiogenesis, and also show anti-bacterial, anti-viral and anti-carcinogenic properties [21,25-27]. Two main mechanisms have been proposed for the chemo preventive effect of isothiocyanates. First mechanism is related to the inactivation of the phase I enzyme cytochrome P450s binding with isothiocyanate, as well as the induction of phase II enzymes. The other mechanism involves the induction of apoptosis which causes the deletion of genetically damaged cells and stopping the progression of the cell cycle [7,24,28].

Sulphoraphane (1-isothiocyanat-(4R)-(methylsulfinyl) butane)

Sulphoraphane is a natural isothiocyanate found in *Brassica* vegetables and is among the most potent bioactive components with antioxidant and anti-tumour properties [28,29]. According to the National Cancer Institute in the US, one of the most promising more than 40 chemopreventive agents including glucosinolate hydrolysis products, such as phenethyl isothiocyanate and indole-3-carbinol, is also sulphoraphane [30].

The concentration of sulphoraphane in broccoli sprouts (1153 mg / 100 g dry weight) is about 10 times greater than mature broccoli (44-171 mg 100 g dry weight). Therefore, broccoli sprouts are recommended as a rich source of sulphoraphane [6]. Sulphoraphane isolated from broccoli extracts as the principal inducer of cell-protective phase II enzymes has been shown to inhibit tumour growth. As broccoli and broccoli sprouts are widely consumed, the extracts obtained from them are seen as a suitable tool for giving sulphoraphane to humans [31]. The metabolic effects of sulphoraphane and its precursor are shown in Figure 2.

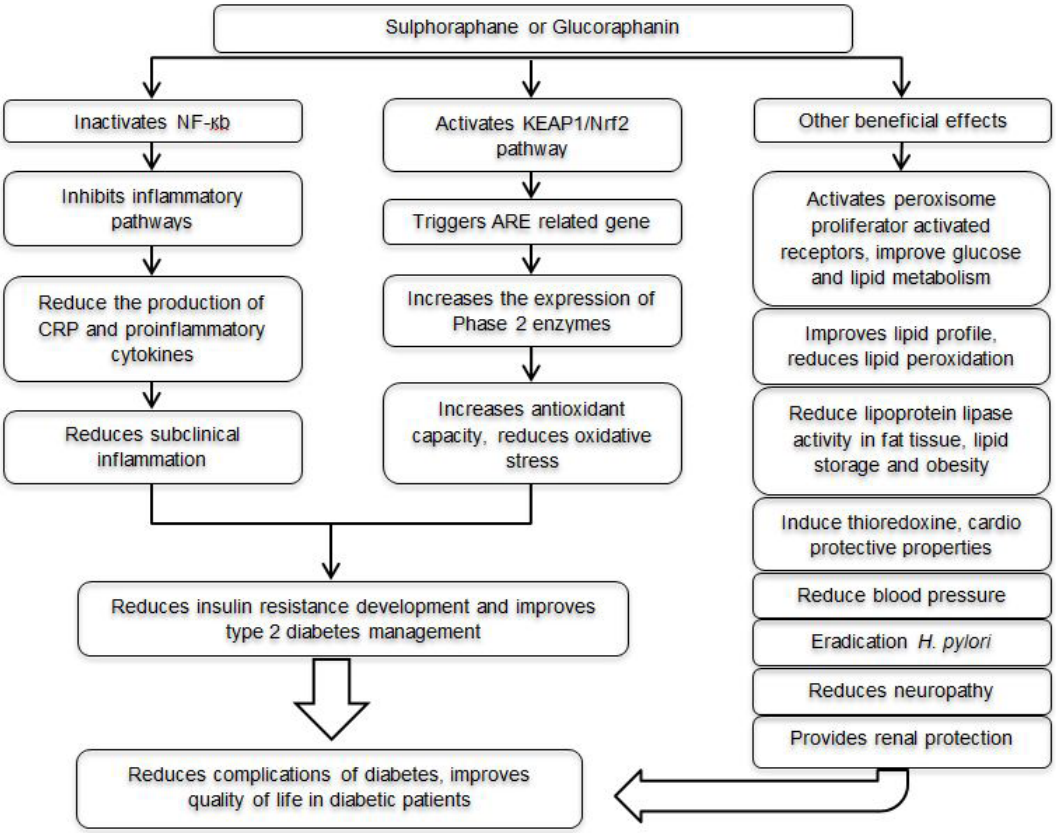

Figure 2: Metabolic effects of sulphoraphane and glucoraphanin

The Impact of Processing and Cooking on Brassica Components

Brassica vegetables are inevitably exposed to various stresses during processing and cooking prior to consumption [32]. Processes such as chopping and cooking lead to the disintegration of cells. Therefore glucosinolates are hydrolysed and hydrolysis products occur [17]. Cooking affects the content of vitamin C, polyphenols, carotenoids, tocopherols and glucosinolates, and thus affects the antioxidant capacity of *Brassica* vegetables [6]. Glucosinolates are water-soluble compounds and pass through cooking water. As a result of boiling 9, 10 or 15 minutes of different Brassica vegetables, an overall reduction of approximately 36% in total glucosinolate content was observed [33]. Cooking methods in which less water is used can reduce glucosinolate losses. However, some cooking practices, including boiling, steaming and high power microwaves, can inactivate β-thioglucosidase that catalyses glucosinolate hydrolysis. Studies conducted show that the inactivation of β-thioglucosidase in *Brassica* vegetables significantly reduces the bioavailability of isothiocyanates [3,34].

Some investigators found that, there has been an increase in both polyphenol and glucosinolate contents in steamed broccoli compared to fresh broccoli while the method of boiling had an adverse effect on the results. In the same study, steamed broccoli did not affect vitamin C level, while boiling significantly reduced the content of vitamin C. It was also shown that boiled and steamed broccoli caused an increase in β-carotene, lutein and α- and gamma-tocopherols compared to fresh broccoli [35]. In addition, the bioavailability of glucosinolates and related isothiocyanates are enriched by the storage and cooking of Brassica vegetables. Although Brussels cabbage, cauliflower and broccoli cannot be stored for several weeks, many cabbages can be stored for a long time at low temperatures [32]. In a study examining the stability of broccoli, Brussels sprouts, cauliflower and green cabbage glucosinolate content under different storage and cooking conditions, no significant difference was found between room temperature and refrigerated storage. However, a decrease of 9-26% was observed in glucosinolate levels after seven days of storage. A remarkable decrease of 75% was observed in glucosinolate levels after 6 hours storage of shredded vegetables. Although there was no significant loss of glucosinolates in baking in the microwave oven and frying method, it was found that boiling caused the glucosinolates to leak into the cooking water and reduce their level by about 90% [34]. In another study, the contents of intact glucosinolates, total phenolics, vitamin C and minerals in fried and edible portions of freshly harvested broccoli were evaluated. It was found in the study that phenolics and vitamin C were more affected than glucosinolates and minerals during frying [36].

Relation of *Brassica* Vegetables With Health

Phytochemicals in *Brassica* vegetables may show different effects that prevents oxidative stresses, induces detoxification enzymes, stimulates the immune system, reduces the proliferation of cancer cells and inhibits malignant transformation and carcinogenic mutations [37]. They protect human body against ROS that cause DNA damage, modulation of gene expression, base modification,

and body lipid and protein oxidation. Members of the *Brassicaceae* family are known for their anticarcinogenic and genetic material protective effects. However, many of the species of this family accumulate high amounts of metals, which is an undesirable feature. Radish (*Raphanus sativus L.*) has shown to accumulate metals in roots to a higher extent than others members of *Brassicaceae* [38,39]. They also play an important role in the etiopathology of many diseases such as vasospasm, atherosclerosis, cancers, heart attack, stroke and liver damage [8].

Goitrogenic Effect

The degradation products of glucosinolates may exhibit toxic and antinutritional effects in animals. The negative effects of these on thyroid metabolism are extensively studied [40]. *Brassica* vegetables contain thioglycosides metabolized to thiocyanates. These compounds inhibit iodine transport and the incorporation of iodine into thyroglobulin, thereby increasing the proliferation of TSH secretion and thyroid cells. Therefore it was found that these substances cause thyroid carcinomas [41,42]. Although they have different mechanisms of action, both thiocyanate ions and oxazolidin-2-thiones which are formed from glucosinolates having an aliphatic side chain containing the beta-hydroxyl group are goitrogenic [41]. The thiocyanate ions are in competition with iodine, therefore, goitrogenic effects are alleviated by increasing the level of iodine in the diet. In a study of 293 women diagnosed with thyroid cancer in Malaysia a positive relationship was found between consumption of *Brassica* vegetables and cancer of the thyroid. In Malaysian women, a group with mild iodine deficiency, high consumption of *Brassica* vegetables was found to contribute to the explanation of the incidence of high thyroid cancer in this group [42]. There is little epidemiological evidence that the goitrogenic effects of glucosinolate degradation products are an important cause of human disease. For this reason, increased interest in the anticarcinogenic properties of glucosinolates degradation products raises important questions about the negative and beneficial effects of *Brassica* vegetables on nutrition [32].

Antioxidant Effects

Brassica vegetables serve as antioxidants and contain high levels of vitamins that act as protective compounds against various degenerative diseases [6]. Isothiocyanates from *Brassica* vegetables also catalyse the incorporation of glutathione to form a substrate for glutathione S-transferase (GST), a family of phase II enzymes, involved in the detoxification of carcinogens, environmental toxins, and oxidative stress products [10]. The induction of the phase II detoxification response promotes nuclear factor erythroid-derived 2-like 2 (Nrf2)-kelch-like ECH-associated protein 1 (Keap 1) interactions and degradation of mitogen-activated protein kinase activation. Keap 1 is a cytoplasmic protein necessary for the regulation of Nrf2 activity. In sum, Nrf2 modulates gene expression through antioxidant response element (ARE) [43,44]. Targets associated with ARE include NAD(P)H:quinone oxidoreductase 1 (NQO1), heme oxygenase-1 (HO-1) and a-glutamyl cysteine ligase (βGCL)[22].

Anti-inflammatory Effects

Inflammation increases cellular proliferation, inhibits apoptosis and increases the risk of developing cancer [3]. Bioactive substances found in *Brassica* vegetables can reduce inflammation by activating detoxification enzymes, clearing free radicals and inducing immune functions [45]. Isothiocyanates slow down the activity of many inflammation mechanisms. Among reported anti-cancer features, sulphoraphane was also found to reduce the secretion of inflammatory signalling molecules by white blood cells and to reduce the DNA binding of nuclear factor kappa B (NF-κB), a pro-inflammatory transcription factor [3,46].

Because of its anti-inflammatory and antibacterial properties, one of the *Brassica* vegetables, cabbage is widely used in traditional medicine to relieve symptoms associated with gastrointestinal disorders and also in the treatment of small incisions, wounds and mastitis [8].

Cancer Protective Effects

The World Cancer Research Fund points out that diets being rich in *Brassica* vegetables protect human body especially from colon, rectum and thyroid cancers. In addition, when consumed in high quantities as part of the diet with other vegetables, Brassica vegetables usually have protective effects against cancer in other regions [47]. This effect is also attributed to the compounds resulting from the hydrolysis [17]. The ability of *Brassica* vegetable components to change biotransformation enzyme expression. Also, its activities play an important role in cancer prevention. Biotransformation enzymes classified as phase I or activation enzymes (cytochrome P-450 and flavin-dependent monooxygenases) and phase II or detoxification enzymes (GSTs, UDP-glucuronosyltransferases, sulfotransferases, N-acetyltransferases) can detoxify compounds that can damage DNA by playing an important role in the regulation of the toxic, mutagenic and neoplastic effects of chemical carcinogens [2,4,25].

Phase I enzymes include oxidation, reduction and hydrolysis reactions which make the compounds more hydrophilic and thus make them accessible for detoxification [4]. As a result, these enzymes can be converted into procarcinogens. Phase II enzymes catalyse various reactions that provide broad protection against electrophiles and oxidants, collectively by conjugation or other metabolic pathways, thereby converting reactive compounds into readily removable stable metabolites [7]. In addition to their role in metabolizing carcinogens, Biotransformation enzymes can also metabolize endogenous compounds such as steroid hormones. Thus, by altering hormone exposure, it can indirectly affect the promotion and progression of premalignant and malignant tissues [2,7].

Sulphoraphane and several isothiocyanates from glucosinolate degradation products affect the initiation and progress of carcinogenesis. Approximately 3 or 5 servings of broccoli or cauliflower per week seem to be cancer preventive, but no therapeutically effective concentrations have been evaluated in clinical trials. It was found that 100 mg of glucoraphanin or 10 mg of purified sulphoraphane per day is well tolerated by humans [48].

Liver Cancer: Liver cancer is the fifth most common cancer in men, the 9th most common cancer type in women and one of the leading causes of cancer deaths worldwide and metastasis has been found to be associated with poor prognosis in humans [26,2749,50]. It is estimated that the incidence of the disease will increase by 50% in 2020 [37]. This type of cancer can relatively be prevented by diet, lifestyle modification and fighting against infections [49].

It was shown that sinigrin, one of the major glucosinolate components found in the seeds of B. nigra and other *Brassicaceae* families, significantly inhibits the proliferation of liver tumour cells via a p53-dependent pathway [50]. In another study, 4-methylthiobutyl isothiocyanate, obtained by enzymatic hydrolysis of glucoerucin isolated from rocket plant species or by metabolic reduction of sulphoraphane of isothiocyanate, was shown to selectively induce cytotoxicity on tumour-initiating cells via a p53-independent mechanism, although no apoptosis or necrosis was observed when applied on normal liver cells [26].

In other study of mice fed with broccoli, low hepatic triglyceride and non-alcoholic fatty liver disease scores were found. At the same time, it was found that the activation of hepatic macrophages was suppressed, liver damage was reduced, and the onset and progression of hepatic neoplasm was slowed down [49]. In another study, it was argued that when applied to rats throughout the initiation and developmental stages of the hepatocarcinogenesis model, cabbage and Kale extracts inhibited ex vivo induced DNA damage [37]. Also, the antioxidant properties of volatile fatty acids extracted from white cabbage extract showed hepatoprotective effect [14].

In a case-control study involving 217 liver cancer cases in Shanghai, the relationship between urinary levels of isothiocyanates and the risk of liver cancer was investigated and it was found that most of the findings in the stratified analysis were inversely correlated but not statistically significant [27]. It has been found that 1-methoxy-3 indolylmethyl alcohol, one of the metabolites of neoglucobrassin, from hydrolytic products of glucosinolates, forms DNA adducts in the liver of mice and this metabolite is genotoxic carcinogen. However, there is no real reason to give up the consumption of *Brassica* vegetables, it was concluded that the benefits of consuming these foods in normal dietary amounts can suppress the side effects of some metabolites [16].

Gastric cancer: Although the incidence of gastric cancer has decreased greatly in many parts of the world, this malignancy is the fifth most common cancer incidence worldwide and one of the second leading causes of death [21]. In a panel organised by the World Cancer Research Fund and the American Institute for Cancer Research, it was said that vegetable consumption 'probably' reduce stomach cancer risk [51]. In a meta-analysis investigating the association between *Brassica* vegetable consumption and gastric cancer risk, the results of prospective trials were found to be statistically significant while *Brassica* vegetable intake had significant results in case control studies. High *Brassica* vegetable intake was found to be inversely proportional to the risk of gastric cancer in humans [21].

Colorectal Cancer: Colon cancer is the third most common cause of cancer-related deaths in the United States [6]. There was a negative relationship between colon cancer risk and consumption of *Brassica* vegetables in eight case control studies; no relationship was found in three and only one positive relationship was found. In five case control studies investigating the relationship between Brassica vegetable consumption and rectal cancer risk, a reduction in cancer risk is observed when high *Brassica* vegetable intake and low intake are compared [10]. In another clinical study, consumption of 250 g/day of broccoli and 250 g/day of Brussels sprouts was found to significantly increase excretion of a potentially carcinogenic 2-amino-1-methyl-6-phenylimidazo [4,5-b] pyridine (PhIP) presented in well cooked meat. It was shown that high consumption of *Brassica* vegetables can reduce the risk of colorectal cancer by increasing the elimination of PhIP and diet-related heterocyclic amine carcinogens [52]. In a multi-centre study, the risk of colorectal cancer was found to be less in the group with the highest consumption of broccoli according to the food frequency questionnaire [53]. In the light of present evidence, it is not possible to conclude that the consumption of *Brassica* vegetables is related to the risk of colorectal cancer [10].

Lung cancer: Lung cancer arises as a result of genetic lesions caused by exposure to smoking or ROS, bacterial, viral infections, oestrogens, and is the leading cause of death worldwide [24,25,28,54]. In many patients with lung cancer, the diseased area cannot be removed because of distant metastases or advanced lesions [24]. Therefore, to reduce the incidence of lung cancer, protective dietary habits are an alternative approach [54]. In a study, the effects of various phytochemical agents on lung cells, GSTP1 and NQO1 inducers of phase II enzymes were investigated in humans. GSTP1 mRNA levels slightly increased after bronchial epithelial cells were exposed to broccoli sprouts, while NQO1 mRNA levels were found to be higher when sulphoraphane was exposed. NQO1 protein expression increased by 11.8 fold in sulphoraphane -treated bronchial epithelial cells [7]. In a study investigating the effects of glucocinolates on cytochrome P450 and phase II enzyme activities in lung cells, glucosinolates at a concentration of 1 μM isolated from *Brassica* vegetables were incubated for 24 hours with cut rat liver slices. As a result, it was found that glucosinolates can modulate basic enzymes (cytochrome P450 and phase II enzymes) in pulmonary carcinogen metabolism, and thus *Brassica* vegetables can show chemo preventive activity in the lung [54].

In a prospective study, the relationship between urinary isothiocyanate levels and lung cancer risk was investigated in non-

smokers. Isothiocyanate levels in urine were not associated with lung cancer risk among non-smokers. However, in the secondary analyses, isothiocy anate levels in the urine were found to be an interaction between the GSTM1 genotype and lung cancer risk [25]. In another study, isothiocyanates were found to exhibit cytotoxicity as dose-dependent in different lung adenocarcinomas (A549) and large cell lung carcinoma (H1299) cells (non-small cell lung cancer cell lines) in p53 status [24]. In a study examining the effect of sulphoraphane on pulmonary carcinogenesis induced by the benzo(a)pyrene [B(a)P], a member of the polycyclic aromatic hydrocarbon family and causing oxidative damage, mice were given sulphoraphane 9 μmol per day of oral body weight. In conclusion, it was shown that sulphoraphane treatment has antioxidant effect by reducing the production of hydrogen peroxide, and it may also protect the cellular integrity and homeostasis against B (a)P *in vivo* [28]. While the effect of *Brassica* vegetable consumption on the risk of lung cancer is evaluated, it should be remembered that the benefits of consuming increasing amounts of *Brassica* vegetables are probably small compared to the benefit of giving up smoking [3].

Breast Cancer: Epidemiological evidence that the consumption of *Brassica* vegetables is negatively related to breast cancer risk is derived from current case control studies. In addition, some reports suggest that the consumption of some *Brassica* vegetables reduces the breast cancer risk (Kim and Park, 2009) [10]. The endogenous oestrogen 17[beta]-oestradiol, 16a-hydroxyestrona (16aOHE1) or 2-hydroxystreone (2OHE1) can be metabolized. In contrast to 2OHE1, 16aOHE1 is more estrogenic and oestrogen in culture has been found to increase sensitive breast cancer cells. Shifting 17β-oestradiol metabolism to 2OHE1 and staying away from 16aOHE1 can reduce the risk of oestrogen sensitive cancer, such as breast cancer [3]. In another study, 2832 breast cancer women aged 50-74 years and 2650 healthy women's diets were compared. It was reported that daily consumption of 1-2 portions of *Brassica* vegetable reduces the risk of breast cancer by 20-40%, possibly by altering the pathway of oestrogen metabolism. On the other hand no relationship between total vegetable and fruit intake and breast cancer risk was found [55]. In another study, the edible portion of cauliflower was shown to contain substances which significantly inhibit the growth of breast cancer cells in both oestrogen receptor-positive and oestrogen receptor-negative individuals [6].

In a study measuring *Brassica* vegetable consumption with urinary isothiocyanate biomarker, excess consumption of *Brassica* vegetables was found to be associated with a significantly reduced risk of breast cancer among Chinese women [56]. In a case-control study of Caucasian women suffering from breast cancer, *Brassica* vegetable consumption, especially broccoli consumption, was negatively associated with breast cancer risk in premenopausal women [57]. These findings suggest that *Brassica* vegetables may play a role in reducing the risk of breast cancer in premenopausal women. Nevertheless, the combined analysis of eight cohort studies reported that there was no association between individual or overall fruit and vegetable intake and breast cancer risk [10].

Prostate cancer: Prostate cancer is the most common solid tumour. Nutritional habits are associated with prostate cancer risk. The most reported finding about diet and prostate cancer is associated with increased risk of fat and high-fat foods. However, developments of the understanding of cellular events leading to cancer and regulation of metabolic and genetic changes leading to cancer suggest that vegetable products may indeed play a role in prostate cancer [2,58].

The induction of *Brassica* vegetables and GST-π in cell culture models is particularly concerned with prostate cancer. GST-π is the predominant GST active in prostate tissue and expression of this gene disappears in the prostate cancer, prostate cancer precursor lesion and prostate intra epithelial neoplasm. Loss of GST-π appears to be an important step in the early development of prostate cancer, and it is thought that upregulation of this gene may somehow provide protection against prostate cancer growth [2]. Feeding animals with broccoli was found to alter biotransformation enzyme levels in peripheral tissues that are far from the absorption points or metabolism points [59].

A population-based case-control study in which consumption of 28 or more portions of vegetables per week was compared with 14 or fewer portions of vegetables per week, it was found that a high level of consumption of vegetables, especially *Brassica* vegetables, reduces the risk of prostate cancer in prostate cancer patients under the age of 65[60]. Similarly, in another case-control study, *Brassica* vegetable consumption was found to reduce the risk of prostate cancer [61]. Taking high amounts of *Brassica* vegetables, including broccoli and cauliflower, can reduce the risk of advanced prostate cancer and especially metastatic prostate cancer [10]. Although glucosinolate hydrolysis products were found to inhibit the growth of cultured prostate cancer cells and induce apoptosis, the results of epidemiological studies of *Brassica* vegetable intake and prostate cancer risk are inconsistent [3].

Pancreatic Cancer: In Japan and the United States, pancreatic cancer is the fifth and fourth cause of cancer-related deaths, respectively. This type of cancer is usually diagnosed at an advanced stage and for this reason its prognosis is very poor [62].

In a cohort study, there is no evidence that there is generally a negative relationship between vegetable intake and pancreatic cancer. However, negative association with consumption of dark green vegetables was observed in high-risk individuals [63]. In another report, among specific subgroups of fruits and vegetables, a nonsignificant inverse correlation was observed between *Brassica* vegetable consumption of three or more servings per week and consuming one serving of *Brassica* vegetable per week. There was a statistically significant lower risk of pancreatic cancer, when people consuming one or more portions of cabbage per week were compared to those who did not consume cabbage at all [64].

In a study investigating the effects of benzyl isothiocyanate (BITC), one of the isothiocyanate family, on radiation sensitivity of human pancreatic cancer cells, two human pancreatic cancer cell lines were treated with BITC and then exposed to X-rays, resulting in an increase in the number of apoptotic cells. It was concluded that BITC has the potential to be a supplement to the existing radiation therapy for pancreatic carcinoma [62].

Bladder Cancer: Increased risk of urothelial bladder cancer in humans is associated with GST or NQO1 deficiency [6]. The main place of bladder cancer development is the bladder epithelium. Isothiocyanates present in *Brassica* vegetables are delivered to the bladder epithelium by urinary excretion, where they protect the cells against cancer [65]. It was reported that isothiocyanate extract obtained from broccoli sprouts significantly induces both GST and quinone oxidoreductase in bladder tissues and cells of mice [66]. In a study evaluating the specific role of *Brassica* vegetables or isothiocyanates in the diet against bladder cancer, a cultured broccoli sprout extract showed that human bladder carcinoma cells inhibit growth and almost all of this inhibition results from isothiocyanates [67].

The Health Professionals Follow-up Study also reported a non-significant inverse association between total fruit and vegetable intake and the risk of bladder cancer. However, it was found that consumption of broccoli and cabbage from *Brassica* vegetables was significantly associated with the risk of bladder cancer. These observations suggest that high *Brassica* consumption may reduce the risk of bladder cancer, while other vegetables and fruits may not have significant beneficial effects on this cancer [68]. In the alpha-tocopherol beta-carotene cancer prevention study, Michaud et al found no correlation between consumption of Brassica vegetables and risk of bladder cancer [69]. In a study of 697 newly diagnosed bladder carcinoma patients and a control group, it was shown that isothiocyanates from *Brassica* vegetable consumption are protective against bladder cancer. Isothiocyanate intake was negatively correlated with the risk of bladder cancer and this effect was shown to be stronger in non-smokers than in heavy smokers [70]. In another study, application of freeze-dried broccoli extracts to rats was found to inhibit the development of N-butyl-N- (4-hydroxybutyl) nitrosamine-induced bladder cancer in a significant and dose-dependent manner without causing histological alteration in the bladder [71].

In conclusion, the isothiocyanate extract in *Brassica* vegetables is a potent stimulant of GST and quinone oxidoreductase 1 in the bladder, and is a promising agent to prevent bladder cancer. Furthermore, the major isothiocyanate, sulphoraphane found in broccoli sprouts extracts not only induces enzymes that detoxify carcinogens, but also activates apoptosis and blocks cell cycle progression [6].

Neurological diseases (Neurodegenerative diseases)

While many of the neurodegenerative disorders are hereditary, some are secondary to toxic or metabolic processes. The cause of neurodegeneration is still unknown. It has been suggested that oxidative stress plays a key role in mostly [22]. Since there is no pharmacological treatment to prevent the development of neurodegenerative disorders, dietary intake of antioxidant foods or plant extracts has positive effects on human health [72]. It was reported that glucosinolates present in *Brassica* vegetables and their degradation products, isothiocyanates, prevent some chronic diseases such as cancer, neurodegenerative diseases. Isothiocyanates play an active role in the central nervous system and peripheral nervous system, through mechanisms involving modulation of inflammatory pathways as well as apoptosis and reduction in cell death activation. Specifically, these phytochemicals have been shown to induce NF-κB translocation and thus proinflammatory cytokine production, as well as the production of oxidative species and neuronal apoptotic death pathways [22]. In one study, pre-treatment with sulphoraphane was found to reduce cognitive deficits caused by phencyclidine (PCP) after repeated PCP administration. It was found that when dietary intake of sulphoraphane -rich broccoli sprouts during juvenile and adolescence, sulphoraphane can prevent the onset of psychosis and it was also found to have proinflammatory and therapeutic effects on schizophrenia cognitive impairment [44]. In another study, raw broccoli sprouts juice protected cells against β-amyloid peptide (Aβ)-induced cytotoxicity and apoptosis. This protection was shown to be provided modulation of mitochondrial function, HSP70 gene transcription and expression, and through activation of the Nrf2-ARE signalling pathway. Moreover, broccoli juice was found to increase the activity of antioxidant enzymes such as HO-1, thioredoxin, thioredoxin reductase, NQO1 and also intracellular glutathione content, mRNA levels, through Nrf2 activation. The results of this study indicate that pharmacological activation of the broccoli sprout juice and Nrf2 signalling pathway is a protective and therapeutic strategy for alzheimer diseases [72].

Antidiabetic Effects: Controls of blood sugar is important to prevent or retard diabetic complications that cause the increase of mortality and morbidity and novel therapeutic approaches are looked for / searched for this situation [43,73]. Functional foods and their nutraceutical components might be recent treatment modalities for type 2 diabetes mellitus and preventing its long-term complications [74]. It is thought about diabetic complications are connected with oxidative stress because of disorders in glucose and lipid metabolisms, and increased antioxidant capacity is reported to be effective in reducing diabetic complications [73,75].

Sulphoraphane is a strong activator of Nrf2 and it was found that sulphoraphane prohibits various diabetic complications such as cardiomyopathy, nephropathy, neuropathy and retinopathy by increasing activity of Nrf2 [73,76,77]. In addition, enabled Nrf2 by sulphoraphane suppresses hyperglycaemia–induced oxidative stress and metabolic dysfunction in human microvascular endothelium cells [79].

In diabetic rats, it was reported that cabbage extract, 1 g per body weight, increases the activation of glutathione and SOD and decreases catalase activity in diabetic kidney. As a result, antioxidant and antihyperglycemic properties of red cabbage extract might provide potential therapeutic sources for diabetic treatment [80]. Moreover, it was shown that sulphoraphane ameliorates hyperglycaemia and reduced blood-insulin concentration, protects number of insulin-producing islet, inhibits death of β-cell due to increased oxidative stress or pyogenesis and decreases cell-death induced by cytokines in rat insulinoma cells [81,82].

In a randomized controlled double-blind clinical study, 10 g or 5 g powder of broccoli sprout or placebo for 4 weeks was given to patients with type 2 diabetes separated three groups. As a consequence, it was observed that powder of broccoli sprout decreases serum malondialdehyde and oxidized LDL concentrations of patients, being useful to ameliorate oxidant and antioxidant levels and increases the capacity of total antioxidant [75]. Significant reductions of insulin concentration and HOMA-IR have been reported in another study performed same application [83]. A relation between consumption of citrus and type 2 diabetes was not found in a prospective of meta-analysis study, but it has been found out that there are a contrary relevance between type 2 diabetes and *Brassica* vegetables [84].

Cholesterol-Lowering Effects

The development of coronary heart disease due to high cholesterol levels is one of the main causes of death in the world. The general characteristics of cholesterol-lowering foods are absorption site competition and reduced endogenous cholesterol synthesis. Broccoli sprouts was shown to reduce cholesterol and lipid levels in addition to well-known chemo protective effects [20]. In a study in which twelve healthy individuals consumed 100 g fresh broccoli for one week, it was found that after one week total cholesterol and LDL cholesterol decreased and HDL cholesterol increased significantly. It was found that taking only one week of broccoli sprouts improves cholesterol metabolism and reduces oxidative stress markers [85]. In another study, LDL cholesterol levels were examined in 77 men after consuming broccoli-cabbage juice, and in the test group serum LDL-cholesterol levels decreased by 8.5% at 9 weeks. However, there was no reduction in serum LDL-cholesterol levels in the control group [6].

The effects of increased cholesterol formation on cholesterol metabolism of cabbage extract in hepatoma-carrying rats exhibiting hypercholesterolemia were investigated and it has been found that cabbage extract decreased serum cholesterol levels and increased bile acid excretion and cholesterol 7alpha-hydrolase activity in faeces. These results show that cabbage suppresses hypercholesterolemia by increasing cholesterol catabolism in hepatoma developing rats [86]. Red cabbage and Brussels polyphenols lowered the cholesterol concentration in erythrocytes of hypercholesterolemic patients. It was concluded that the polyphenol contents of these compounds directly affect the erythrocyte membranes and that this effect may be related to anthocyanins [87]. In another study, the hypocholesterolemic exchange effects of the addition of broccoli sprouts to the diet of hamsters fed high amounts of cholesterol and fat containing diets were investigated. A freeze-dried broccoli extract containing 2 or 20 μmol of glucoraphanin (BSX, BS10X), glucoraphanin-rich broccoli sprouts extract (GRE), sulphoraphane-rich broccoli sprouts extract (SFE) and simvastatin were administered for 7 weeks. As a result hepatic cholesterol was reduced in all animals with BS10X and SFE treatments. At the same concentration, consumption of glucoraphanin and broccoli sprouts (BS10X) had more pronounced effects on cholesterol homeostasis than GRE [20].

Infections of Helicobacter Pylori

Helicobacter Pylori is highly related to various gastrointestinal diseases such as gastric infection, chronic superficial gastritis, duodenal and gastric ulcer, stomach adenocarcinoma and non-Hodgkin's lymphoma of stomach [88,89]. The reproductive ability in gastric acid of *H. Pylori* depends on its production of urease enzyme. This enzyme is not found in mammalian tissues. Urease inactivates gastric acid through transforming urea of host into ammonia. It showed that sulphoraphane and other isothiocyanates inhibit urease produced by *H. Pylori* [90].

It found out that purified sulphoraphane restrains growth of cancer cells and kills more than more *H. Pylori* strains not excepting strains of antibiotic resistant in test tube. In an animal model, it was provided that given sulphoraphane for 5 days to immune-suppressed mice does away with *H. Pylori* in eight of the eleven xenographies of human gastric tissues implanted these mice [91]. In addition, in a small clinic search, it was found that consumption of glucoraphanin-rich broccoli sprouts, 56 g/d glucoraphanin, for 1 week is connected with *H. Pylori* eradication in only three of nine gastritis patients [92]. It was also reported that daily intake of broccoli sprouts for two months (70 g/d glucoraphanin) might be effective to reduce oxidative stress due to *H. Pylori* and also useful to prevent gastritis in experimental animals and humans [8]. In another study, it was found extract of broccoli sprouts containing sulphoraphane doesn't inhibit density of *H. Pylori* infection; on the other hand it precludes lipid peroxidation in gastric mucosa. A cytoprotective role of sulphoraphane has been stated in gastritis induced by *H. Pylori* [93].

In brief, two mechanisms are proposed that sulphoraphane influences on infection of *H. Pylori*. The first of them is a direct effect of it on *H. Pylori* and this effect helps to decrease gastritis. The second of these is to show indirect effect on host by stimulating cytoprotective responses [88].

Recommended of Intake

Daily consumption of *Brassica* vegetable is 54 g per capita in Germany. The most common intakes of them are white cabbage, cauliflower and red cabbage. Increases in *Brassica* consumption with age was seen although there are little differences between the genders. In other study in Germany, per capita consumption of glucosinolates' amounts has been confirmed as 46 mg in winter and 36 mg in summer. Per capita consumption of glucosinolates' amounts in Finland and Denmark has been found to be 6 mg in winter and 4 mg in summer [17].

Although many associations including the National Cancer Institute suggest daily consumption of fruits and vegetables between 5 and 9 servings, separate proposals have not been made for Brassica vegetables. However, analysis of prospective cohort studies suggests intake of Brassica vegetable serving at least 5 times for adults [3].

Conclusion

Brassica vegetables contain compounds that are rich in sulphur known as glucosinolates. Cutting or chewing these vegetables ends up with generation of bioactive hydrolysis products of glucosinolate such as isothiocyanates and indole-3-carbinol. Glucosinolates is involved in relatively high concentrations in these vegetables, but bioavailability of isothiocyanates might be decreased by cooking, especially boiling and high power microwave baking. Available data reveal that the consumption of vegetables belonging to only *Brassica* family reduces risk of diseases and might narrow the metastasis of tumours in some individuals. In order to increase the bioavailability of isothiocyanates in the diet, care should be taken to the cooking method, especially these vegetables should be steamed and less cooked so that the content of glucosinolate is protected and shredded vegetables should not be stored for a long time.

More consumption of these vegetables was found to be associated with some cancer types as low-risk. Therefore, orders of adequate and balanced nutrition including intake of 5-9 serving fruits and vegetables should be performed.

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