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Cruciferous Vegetables and Cancer Prevention

Rehan Haider[1*] and Asghar Mehdi[2]

[1]Riggs Pharmaceutical, Department of Pharmacy, University of Karachi.*
[2]Head of the Department Pharmacology, Fazaia Ruth Pfau Medical College, Shahrahe Faisal Karachi, Pakistan.

Corresponding Author: Rehan Haider, Riggs Pharmaceutical Department of Pharmacy, University of Karachi

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Abstract

Cancer debris is a major global energy concern, and stop-game plans have gained increasing attention. Cruciferous herbs, a diverse group of vegetables, cauliflower, and kale, have emerged as potential friends in the battle against malignancy. This abstract provides a brief survey of the link between cruciferous vegetables and malignancy, with a focus on the key means and duties of bioactive compounds.

Cruciferous legumes are rich sources of phytochemicals, specifically glucosinolates that are metabolized into bioactive compounds, including, to a degree, isothiocyanates and indole-3-carbinol. These compounds exhibit diverse antagonistic-malignancy characteristics, including the ability to restrain the progress of cancer, encourage apoptosis, prevent angiogenesis, and reduce redness.

Epidemiological studies have shown an inverse connection between cruciferous herb consumption and the risk of different cancers, specifically pleural, colorectal, and prostate cancers. Animal and cell civilization studies have supported mechanistic observations of how cruciferous salad-derived compounds obstruct cancer growth at the microscopic level.

In conclusion, cruciferous fruits are key components of a malignancy-deterrent diet owing to their rich content of bioactive compounds with explained antagonistic-tumor properties. Incorporating these salads into an individual›s routine diet may be a proficient and persuasive approach to lowering cancer risk. Further research is needed to sufficiently decode the precise machines that latent their malignancy-preventive belongings and to authorize optimum abstinence from food guidelines. Despite emphasizing the significance of cruciferous herbs, health campaigns have committed to lowering the global burden of tumors.

Keywords: Cruciferous Produce, Tumor Prevention, Glucosinolates, Isothiocyanates, Bioactive Compounds, Phytochemicals, Community Health and Microscopic Methods.

1. Introduction

Diet, specifically a Western diet, deliberately plays an unfavorable role in the plant structure of carcinogenesis,' as 30% of all cancers are thought to have abstinence from food components [1, 2]. Numerous freed digestive elements have been proven to be mutagenic and are deliberated by many to be synthetic initiators of carcinogenesis, ~while still other dietary components concede the possibility of the present image of promoters of carcinogenesis [3, 4]. Fortunately, for what we must eat, many diets appear to contain a second group of components that can prevent, slow, or even reverse carcinogenesis. Epidemiological studies have recognized that a diet rich in fruits and vegetables is associated with a decreased risk of several different cancers [5, 6]. Furthermore, the benefit from growing digestive consumption of crops and salads is not simply due to the deterioration of the consumption of an unfavorable component to a degree that can be consumed as fat. Studies, particularly judging the effect of cruciferous produce, have demonstrated an opposite relationship between the consumption of cruciferous legumes and malignancy incidence [7, 8]. One meta-study found that even as little as 10 g of crucifers per day can have a meaningful effect on risk. These verdicts have led to a large number of dispassionate and courtroom studies to accept and capture this tumor safeguard effect for the betterment of community health [9, 10].

1.1. Cancer Prevention by Cruciferous Vegetables

Epidemiological Study: In 1982, the National Research Council on Diet, Nutrition, and Cancer established that "there is

enough epidemiological evidence to imply that devouring of cruciferous herbs is guided by a decline in the occurrence of cancer at various sites in humans "A 1996 review of seven companion studies disclosed an inverse union between crucified swallow and stomach malignancy, vegetable and cauliflower ingestion and body part cancer, and between vegetable swallows as well as cancers" [11]. A review of 87 case-control studies determined that 67% characterized an opposite union between crucifers As well as cancer, accompanying vegetable consumption is a preeminent supporter; several studies show this effect.' The authors decided that crucifers decrease the risk of cancer, but this study did not address the relative efficiency of crucifers prepared to accompany different fruits and vegetables. 011 incidence of bladder cancer among 47,909 men revealed an intake of crucifers and no other vegetable type is inversely related to the risk of bladder cancer [12]. Both broccoli and cabbage had significant effects. Taken together, these epidemiological data strongly suggest that a diet rich in broccoli, cabbage, or a mixture of cruciferous vegetables can decrease the risk of breast cancer.

1.2. Laboratory Animal Studies

Many studies on laboratory animals have evaluated the effects of cruciferous vegetables on cancer. By adding powdered, freeze-dried cruciferous plants to the diet of laboratory animals fed with chemical carcinogens. The results of these studies support epidemiological data suggesting that cruciferous vegetables protect against carcinogenesis. For example, broccoli or cabbage was incorporated into the diet of rats that had previously received dimethylbenz anthracene (DMBA), mammary tumor formation was inhibited [13]. "Similarly, the rats were administered 5 or 10% cabbage. After N-methy1nitrosourea, there was a reduction in the incidence of breast cancer sprouts (20%) given in the diet also before, during, and 2 weeks after DMBA administration inhibited mammary gland formation in rats [14, 15]."Aflatoxin-induced hepatocarcinogenesis was reduced in rats by administration of 25% cabbage and dimethylhydrazine-induced tumorigenesis in mice was inhibited by a cabbage diet given only during carcinogen administration" [16, 17]. When mammary tumor cells are placed under the skin of immunodeficient mice, both cabbages reduce the incidence of pulmonary metastases [18]. When each aqueous extract was administered to rats with Brussels sprouts or fed 3 g of Brussels sprouts per day, the occurrence of 8-0x0-guanine in urine as well as the rate of nitropropane-induced oxidative DNA damage was significantly reduced [19]. Many other laboratory studies have supported the results of epidemiological studies. Some characteristics of e-cruciferous vegetables allow them to significantly reduce the risk of cancer

1.3. Chemical Profile of Cruciferous Vegetables

Evidence from epidemiological studies suggests that cruciferous vegetables are better able to protect themselves from cancer than many other fruits or vegetables, leading to the logical proposition that chemoprevention would Cruciferous vegetables are associated with some unique aspects of their biochemistry. Cruciferous the vegetable belongs to the species Bvussicuolerucea, including cabbage and Brussels sprouts, cauliflower, broccoli, cabbage, and cabbage. Cruciferous vegetables contain several relatively unique secondary amino acid metabolites called glucosinolates. While glucosinolates are not considered directly bioactive, many glucosinolate hydrolysis products, particularly isothiocyanates, perform anticarcinogenic activities. Several Glucosinolates give the impression of low to all Brassica, although their relative plethora changes not only across plant subspecies (Table 11.1) but across types inside subspecies (Table 11.2) and in response to growing conditions the Range of glucosinolate content as one of 50 types of cultivated vegetable under the unchanging environments, it's different, nearly having ten of something from 4.0 to 35.6 pmol dry eight [21, 22].

Chopping or beating of herbs or even autolysis of harvested salads all the while depository, glucosinolates have taken over the hydrolyzing catalyst myrosinase or thioglucoside gluco hydrolase (EC. 3.2.3.1.), which are situated, except for glucosinolates. The amount of hydrolysis is determined by the level of glucose in the blood, sulfate ions, and a doubtful thione compound (Figure 1). The throne in between can be reshuffled to form isothiocyanate, nitrile, or thiocyanate. Depending on the specific environment, such as pH, temperature, vicinity of iron, and hydration. 1° Major glucosinolates and their bioactive hydrolysis devices from average classic herbs are listed in Table 11.3. There are resources of news applicable to the allure and bioactivity of glucosinolate hydrolysis commodities. Crucifers have an extreme texture content, with approximately 30% of their dry matter accompanying the aerial part, and the plant is nearly 70–90% water by pressure, contingent upon the fabric. Crucifers are also rich in vitamins, including several carotenoids (p-carotene, lutein, and zeaxanthin) and vitamins C, E, and K" in addition to sterols [23]. In the case of products and salads usually destroyed in Sweden, fruits, vegetables, and cauliflower had the highest sterol content (-50 mg/100 g) [24]. These possessions are joined to a better or secondary range by many different fruits and vegetables and are therefore improbably expected to be the main reason for the cruciferous distinguishing anticancer powers effect, even though they grant permission to play a theatrical role, improving the effects of glucosinolate hydrolysis. Crucifers hold almost extreme concentrations of S-methyl cysteine sulfoxide that can Decay, indicating a degree of release of explosive sulfur compounds such as thiols, dimethyl disulfide, and dimethyl trisulfide.

TABLE 11.1
Mean Glucosinolate Content (μmol/g dry mass) in the Edible Tissues of *Brassica oleracea*

Glucosinolates Group	Form	Broccoli	Brussels Sprouts	Cabbage	Cauliflower	Kale
Aliphatics	Sinigrin	0.1	8.9	7.8	9.3	10.4
	Gluconapin	1.0	6.9	0.7	0.3	1.0
	Glucobrassicanapin	0.3	0.5	0.2	0.1	0.1
	Progoitrin	1.0	2.4	0.2	0.3	0.6
	Epiprogoitrin	—	—	—	—	—
	Napoleiferin	0.7	0.4	—	0.2	—
	Glucoiberin	0.1	—	—	—	—
	Glucoraphanin	7.1	1.0	0.1	0.5	1.0
	Glucoalysin	0.2	0.1	—	—	—
Phenyl	Gluconasturtiin	0.4	0.5	0.3	0.4	0.4
Indoles	Glucobrassicin	1.1	3.2	0.9	1.3	1.2
	4-OH Glucobrassicin	0.2	0.6	0.3		0.1
	4-CH_2OH Glucobrassicin	0.4	0.4	0.3		0.2
	Neoglucobrassicin	0.2	0.2	0.2	0.2	0.1
Total		12.8	25.1	10.9	15.1	15.0

Table 11.1: Mean Glucosinolate Content (μMOL/G DRY MASS) in the Edible Tissues of Brassica Oleracea

These compounds guide stuffy odors all the while broiling and off-flavoring [25]. The calorie limit has proven to change detoxification enzymes and reduce the risk of malignancy [26]. Therefore, augmenting discounted consumption due to the lack of palatability concedes the possibility of a confounding effect in anticancer studies. Although control and exploratory mammals devour the unchanging burden of meat by way of the extreme fiber content of cruciferous salads, control, and exploratory diets must be equalized in terms of calories and vitamins, especially when mammals receive 20 or even 30% of their diet as plant powder [27].

TABLE 11.2
Glucosinolate Content (μmol/g dry weight) of Selected Accessions of Broccoli

	Aliphatics					Indoles			Phenyl
Accession	Sinigrin	Progoitrin	Glucoraphanin	Residual	Total	Glucobrassicin	Residual	Total	Gluconasturtiin
Brigidier	0.0	0.9	21.7	3.8	26.3	1.2	1.0	2.2	0.7
Eu 8-1	0.1	7.9	9.6	3.3	20.9	1.3	1.0	2.3	0.6
Florette	0.0	0.3	8.7	1.5	10.4	1.0	0.5	1.6	0.6
Majestic	0.0	0.1	16.0	3.0	19.1	0.3	0.4	0.7	0.2
Peto no.7	0.1	7.2	5.9	18.3	31.4	1.2	2.4	3.6	0.6
Pirate F1	0.0	0.5	10.7	1.9	13.0	2.8	1.3	4.1	0.6
Shogun	0.8	2.6	11.9	3.3	18.7	2.4	3.8	6.2	0.9
VI 158 DH I.S.	6.0	5.3	9.4	10.5	31.2	1.3	0.6	1.9	0.5
Wintergarden	0.0	0.5	17.5	0.9	18.9	1.6	0.9	2.5	0.5
Zeus	0.0	0.1	2.9	0.8	3.8	1.1	1.3	2.3	0.3

Table 11.2: Glucosinolate Content (μmol/g dry weight) of Selected Accessions of Broccoli

TABLE 11.3
Major Glucosinolates and Bioactive Hydrolysis Products in *Brassica oleracea*

Major Glucosinolates	Bioactive Hydrolysis Products
Glucobrassicin	Indole-3-carbinol
Gluconasturtiin	Phenylethyl isothiocyanate
Glucoraphanin	Sulforaphane
Progoitrin	Crambene
Sinigrin	Allyl isothiocyanate
Glucotropaeolin	Benzyl isothiocyanate

Table 11.3: Major Glucosinates and Bioactive Hydrolysis Products in Brassica Oleracea

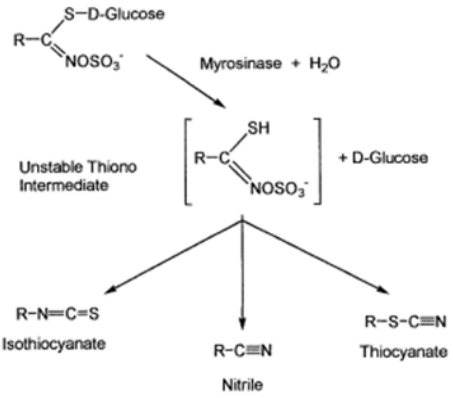

Figure 11: I Myrosinase-Dependent Hydrolysis of Glucosinolates

1.4. Mechanisms of Chemoprevention

In pivotal studies planned to determine the mechanism of cancer prevention by isothiocyanates, Watten Berg treated rats with a single dose of benzyl isothiocyanate either 24, 4, or 2 hours before, respectively. 4 hours after administration of the carcinogen DMBA [28]. He found no effect on tumor incidence when benzyl Isothiocyanate was administered 24 hours before or 4 hours after exposure to the carcinogen. Treatment with benzyl isothiocyanate 4 hours before carcinogen exposure was significantly less effective than that 2 hours before carcinogen exposure, which reduced the incidence of mammary tumors by 77%. This response indicated that even a single dose of benzyl isothiocyanate could prevent initiation in a narrow window of time. Interestingly, when he administered benzyl isothiocyanate in the diet starting 1 week after DMBA treatment, there were fewer advanced breast tumors [29]. He interpreted this as a sign of protection against the role of benzyl isothiocyanate in promotion Since these early studies, it has become increasingly clear that the anticarcinogenic effects of isothiocyanates are unlikely to be due to a single mechanism or even limited to a single stage of carcinogenesis. While numerous studies support the role of isothiocyanates as anti-carcinogens, it is not yet clear to what extent they are responsible for the anticarcinogenic effect of whole vegetables or whether other bioactive components play an equally effective role.

1.5. Induction of Detoxification

It is believed that the main mechanism of chemoprevention using cruciferous vegetables is through the upregulation of detoxification enzymes, leading to the reduced initiation of chemically induced carcinogenesis which was first proposed 25 years ago and has undergone many refinements [30, 31]. But remains essentially unchanged. Clinical studies have clearly shown that ingestion of cooked cabbage and Brussels sprouts daily for 10 days significantly increases drug clearance in healthy college students and that this effect is reversible on a diet without cruciferous vegetables [32]. “Similarly, 500 g of broccoli for 12 days significantly increased the cytochrome P450 (CYP) 1A2-dependent metabolism of caffeine, although it did not alter the CYP2El-dependent metabolism of chlorzoxazone [33]. A diet containing 300 g of cooked Brussels sprouts daily for 3 weeks elevated serum glutathione transferase class a 1.4-fold [34].” Taken together, these data suggest that dietary Cruciferous vegetables can also increase the levels of detoxification enzymes in humans. Rodent feeding studies confirm this effects of whole cruciferous vegetables show that specific detoxification enzymes are regulated by dietary cruciferous plants [35-37].

Many aliphatic glucosinolate hydrolysis products upregulate several phases of IT detoxification enzymes, including quinone reductase and glutathione-S-transferases. Indole-3-carbinol, derived from indolyl glucosinolate glucobrassicin, upregulates both these phase 11 enzymes and CYPIA112 phase-I cytochrome P450 enzymes. Some concerns have been raised about the safety of CYPI A1 induction, as it not only detoxifies several xenobiotics but also activates several pre-carcinogens, including many polycyclic hydrocarbons [38]. For this reason, it is suggested that mono-functional inducers that only increase phase I1 enzymes may be more effective as chemopreventive agents than indoles, called bifunctional because they can induce both phase I and phase I1 enzymes [39]. “This is an interesting hypothesis, given that animal studies evaluating the anticarcinogenic properties of indole-3-carbohydrate have mixed results. Alternatively, the beneficial effects of indole-3-carbinol on IT-phase metabolism may overcome any adverse effects associated with the stimulation of phase I enzymes.

All Brassica vegetables contain glucobrassicin, the original glucosinolate indole-3-carbinol, and epidemiological and laboratory animal studies have shown that whole vegetables are protective against cancer. If indole-3-carbinol causes both harmful and anticarcinogenic responses in vivo, then other components found in whole vegetables or modifications of indole metabolism in vegetables appear to be capable of neutralizing harmful effects [40]. Designing compounds as mono- or bifunctional inducers is useful when considering the mechanism of detoxification enzyme induction. At the molecular level, glucosinolate hydrolysis products regulate at least two response elements in detoxification enzyme genes: (I) bifunctional inducers interact with a xenobiotics response element (XRE), also called an aryl. The hydrocarbon response element (AhRE) and two monofunctional inducers interact with the antioxidant response element (ARE). The XRE is located in the DNA regulatory region of genes for several proteins, including CYPIAIl2, quinone reductase, and glutathione transferase.

They ARE is located in the regulatory regions of the quinone reductase and glutathione gene transferase Ya2, but not CYP1A1/2 [41]. The gene sequences for these phases of IT enzymes thus contain regulatory regions with both XREs and AREs, while gene sequences for CYPI A112 are lacking They are not and cannot be stimulated by monofunctional inductors. In addition, the regulatory sequence in the gene for γ-glutamyl cysteinyl synthase, the rate-limiting step in glutathione synthesis, contains several ARE sequences, but no XRE has been identified [42]. The classification of molecules that upregulate enzymes as mono-functional or bifunctional inducing agents is therefore more precisely based on whether ARE (mono-functional) or XRE (bifunctional) is triggered, as is the case for describing a whole range of interactions between glucosinolate hydrolysis products and the entire CYP family of enzymes. Although the regulatory regions of several other genes were found to contain one or both of these DNA sequences, no exhaustive search was performed.

1.6. Inhibition of Activation

A large number of pre-carcinogens are bioactivated to the ultimate carcinogen by CYP-dependent oxidation.’ It has been proposed that glucosinolate breakdown products may protect against the initiation of cancer not only by inducing phase 11 detoxification enzymes but also by inhibiting CYP-dependent activation of precarinogens [42]. The anticarcinogenic action of isothiocyanates against nitrosamines has been proposed to be due to the inhibition of the bioactivation of nitrosamines. A CYP2El-dependent activity both phenyl ethyl isothiocyanate (PEITC) 4s and sulforaphane”

have been found to inhibit the phase I enzyme CYP2El [44]. When a group of aryl alkyl isothiocyanates was evaluated as an inhibitor of DNA adduct formation, several were found to be more effective than PEITC, and sulfonamide was found to inhibit the phase I enzyme CYP2El [45, 46]. When a group of aryl alkyl isothiocyanates was evaluated as inhibitors of DNA adduct formation, several were found to be more effective than PEITC, and their ability to inhibit tumorigenesis correlated well with their inhibitory effects on the formation of DNA adducts. This suggested to the authors that the most likely mechanism is via Inhibition of CYP-dependent bioactivation" Very recently, it was shown that benzyl isothiocyanate destroys CYP2El during metabolism [47].

This type of "suicidal" inhibition is much more effective in vivo than competitive inhibitors and would be expected to substantially inhibit CYP2EI metabolism, even at very low levels. In addition to this inhibitory effect on CYP2E1, the ability of benzyl isothiocyanate to activate phase I1 enzymes could be an effective anticarcinogenic compound [48]. Whether all isothiocyanates inhibit CYP2E1 equally remains to be seen, or whether benzyl isothiocyanate itself causes CYP2El destruction. When other enzymatic activities were examined, PEITC, but not sulforaphane or allyl isothiocyanate, was found to inhibit rat microsomal CYPIA112 and CYP2B112 in addition to CYP2E1 [49].

This study did not evaluate the mechanism; therefore, the type of inhibition could not be determined to determine whether it would likely have an effect in vivo. In an interim study in rats, PEITC was found to cause significant loss of CYPIAII2 and CYP3A activity in addition to severe loss of CYP2EI activity." In contrast to an in vitro study that reported acute inhibition of CYP2B enzyme activity, PEITC was found to induce CYP2B enzymes. These data show that not only do products of glucosinolate hydrolysis have numerous effects on CYP enzymes, but these results may differ substantially between in vitro and in vivo effects, between acute, subacute, and chronic effects. It is important to choose models that accurately reflect the conditions expected when eating cruciferous vegetables intermittently, as most consumers do. It would be helpful to know if one should include cruciferous vegetables in their daily diet to obtain some benefit, or should they include them every few days is sufficient to maintain this effect. Other drug-metabolizing enzymes that have been reported to inhibit glucose hydrolysis products include flavin monooxygenases and aldehyde dehydrogenases [50, 51]. However, the possible role of their inhibition in cancer prevention has not been evaluated.

1.7. Inhibition of Cell Proliferation and Apoptosis

Another mechanism by which cancer can be prevented is through the reduction or inhibition of the growth of cells that have been transformed into a malignant state. The idea that cancer cell proliferation can be preferentially inhibited is the basis for attempts to identify compounds that slow or stop tumor growth. To test the hypothesis that glucosinolates may work in this way, cells in culture were treated with native glucosinolates, and their effects on cell number and the cell cycle were analyzed. In general, the original glucosinolates had little or no effect on the cells in the culture until toxic levels were reached. In one study, nine glucosinolates from Brassica seeds did not affect the growth of K562 erythroleukemic cells. In contrast, after myrosinase-dependent hydrolysis, most glucosinolate hydrolysis products inhibited proliferation. Unfortunately, many common glucosinolates in cruciferous foods, including glucobrassicin, gluconasturtin, and glucoraphanin, were not evaluated in this study using the human undifferentiated colon cancer cell line HT29, the original glucosinolate [52].

Glucobrassicin was shown to have no effect (100 PM), while the hydrolysis products di-indolyl methane (0 PM) and sulforaphane (8 PM) reduced cell viability by approximately 50% [53]. An important consideration in evaluating the cytotoxicity of tumor cells is whether the tumor cells are selectively more sensitive than untransformed cells. In one study, a canine breast cancer cell line was found to be more sensitive to the cytotoxic effects of cruciferous nitrile crambene (in the presence of selenium) than untransformed primary canine mammary cells [54]. Showed that human colon cancer cell lines are more sensitive to sulforaphane (CaCo2 cells) or allyl isothiocyanate (HT29 cells) during proliferation than after confluence, when cells become differentiated and more closely resemble normal, untransformed cells Gamet-Payrastre et al [55]. linked the antiproliferative effects of diindolylmethane and sulforaphane in HT29 cells to cell cycle arrest in GO/G1, which prevents re-entry into the cell cycle and DNA synthesis. Other studies have implicated cell cycle arrest. Studies reported in HeLa cells that allyl isothiocyanate, benzyl isothiocyanate, and PEITC all caused cell cycle arrest at G2/M [56]. Similarly, a study on HepC2 cells showed G2/M arrest after treatment with nitrile crambene (A.S. Keck, personal communication). Some isothiocyanates may arrest growth on GOIGI, whereas others cause G2lM arrest. However, differences have been reported this may also be due to differences between the studies, including the experimental design and cell type. It would be interesting to evaluate these compounds in a single system that allows direct comparison of the cell cycle and proliferation effects.

Tumor formation and growth can be controlled by reducing cell proliferation through cell cycle arrest, increased apoptosis, and programmed cell death. Oral administration of glucosinolate sinigrin induced apoptosis and significantly reduced the formation of aberrant crypt deposits in the colons of rats exposed to dimethylhydrazine [57]. The authors suggested that apoptotic deletion of damaged stem cells in sinigrin-treated rats could account for the reduced generation of aberrant crypts. In addition to this in vivo study, they were found to cause isothiocyanates apoptosis in vitro. In a mechanistic study, reported that isothiocyanates cause apoptosis in HeLa cells [58]. This isothiocyanate-induced apoptosis is associated with an increase in caspase 3, a proteolytic enzyme involved in the programmed cell death pathway. Interestingly, not only caspase 3 was increased before apoptosis, but caspase 3 inhibitors were able to inhibit apoptosis in the presence of isothiocyanate, suggesting that isothiocyanate-dependent apoptosis is mediated by caspase 3. C-Jun N-terminal kinase (JNK), which lies upstream of caspase 3

in the apoptotic cascade, is also activated by isothiocyanates [59]. When JNK activation was blocked, isothiocyanate-induced apoptosis was also suppressed, suggesting that JNK plays a role in mediating isothiocyanate-induced apoptosis." In the work of another group of researchers, PEITC was found to induce apoptosis via a p53-dependent pathway, leading these authors to suggest that PEITC-dependent activation of JNK may increase p53 phosphorylation [60]. In addition, overexpression of Bcl-2, which typically opposes Bax, was found to suppress PEITC-induced activation and block PEITC-induced JNK apoptosis. Together, these data support the hypothesis that by activating JNK PEITC can lead to the destruction of tumor cells by apoptosis via p-53, Bax, and caspase 3. Studies of this nature, which continue to monitor upstream effects, add greatly to our knowledge of how isothiocyanates affect tumor growth and programmed cell death. There may be other cell cycle stages where isothiocyanates affect apoptosis, and molecular studies can help elucidate the complex interactions between these signaling molecules.

1.8. Development of Cancer Preventive Means from Circular Vegetables

A large amount of information has been accumulated on the anticancer activity of isothiocyanates derived from the hydrolysis of glucosinolates [61, 62]. The majority of the work has focused on just a few, including indole-3-carbinol, PEITC, sulforaphane, and benzyl isothiocyanate. Scattered studies have shown protection against other indolyl compounds, such as brassinin, which was shown to protect against mammary carcinoma and skin tumors in mice given DMBA [63]. Isothiocyanate is effective in the fight against colon carcinogenesis [64]. There was a range of structure-activity studies of aryl alkyl and alkyl isothiocyanates that were compared for their ability to protect against the development of carcinoma. Several synthetic secondary isothiocyanates are more effective than PEITC [65].

Increasing chain length, leading to increased efficacy in preventing NNK-induced tumorigenicity [66]. However, when a similar series of compounds was evaluated for anticarcinogenesis in two models of carcinogenicity, no consistent order of efficacy was observed for both models.47 Interestingly, efficacy was correlated with inhibition of DNA-adduct formation across both models. Seems it unlikely that research has identified a "magic bullet," natural or synthetic, with the ability to extinguish all cancers. Two glucosinolate breakdown products, PEITC, and indole-3-carbinol, have been developed as prophylactic drugs. These purified compounds may eventually be routinely administered to individuals at high risk of cancer. In another study, researchers used the strong isothiocyanate sulforaphane as a starting point for the development of synthetic anticarcinogenic agents. The bioactivity of non-glucosinolate components has not been extensively studied.

1.9. Phenyl Ethyl Isothiocyanate

Watercress is a particularly good source of gluconasturtin, the parent glucosinolate of PETTC.Feeding watercress to smokers blocked the metabolic activation of 4-(methylnitrosamino)-1-(3-pyridine1)-l-butanone (NNK), a major carcinogen in tobacco [67]. In evaluating the effect of PEITC on NNK bioactivation in rats, PEITC (1 mmol/kg rat) was found to have an inhibitory effect on CYP2E1, effectively blocking the bioactivation of NNK.4s Also, PEITC induced a series of phase I1 enzymes, which could then clear any bioactivated products formed." Recent studies have shown that PEITC inhibits NNK lung carcinogenesis when administered earlier or during NNK administration [68] .Thus, PEITC not only inhibits NNK-induced lung tumorigenesis in rats and mice but also alters NNK metabolism in rodents in the same way that feeding watercress alters urinary metabolites in smokers. These data support the proposal that PEITC or vegetables rich in PEITC could be used as chemopreventive agents in smokers to delay or prevent lung cancer.

When administration of PEITC to rats was initiated one week after NNK, no anti-tumorigenic effect was observed even when administered continuously for 15 weeks [69]. This observation suggests that although PEITC can block initiation, it is unable to suppress proliferation. One study stated that when PEITC and benzyl isothiocyanate were administered post-initiation to rats that received the bladder carcinogen diethyl nitrosamine, there was a significant increase in papillary hyperplasia and carcinoma compared with rats administered the carcinogen alone. In addition, were papillomas and carcinomas present in several rats given isothiocyanates and no carcinogens [70]. The authors concluded that these isothiocyanates are strong promoters of bladder carcinogenesis and even have some outright carcinogenic potential, both initiating and promoting tumor growth.

Although this information comes from only one study, compared to the many studies it suggests, the positive benefit from PEITC serves as a good warning that information regarding toxicity and carcinogenicity is required before purified plant secondary metabolites are used as drugs, regardless of the quality of food of plant origin B Indole-3-Carbinol There are more reports on indole-3-carbinol, its chemistry, toxicology, and potential efficacy as an anticarcinogenic agent than any other glucosinolate hydrolysis product [71, 72]. In animal studies, Indole-3-carbinol was found to inhibit the development of tumors in the fore stomach [73, 74]. "Stomach, mammary gland, uterus, T0ngue and liver of rodents and in the liver of trout" when administered before or during exposure to a carcinogen [75-79]. Because of the many positive anti-initiation studies in laboratory experiments, indole-3-carbinol, like PEITC, has been added to clinical evaluation as an anticarcinogen in individuals at a high risk of cancer. Evaluating clinical trials found long-term treatment with indole-3-carbinol in patients with recurrent respiratory papilloma Of the 18 patients given oral indole-3-carbinol, six showed cessation of papilloma growth, and six showed significantly reduced papilloma growth. No side effects were reported more than 8 months of treatment [80]. A breast cancer prevention study is underway at Strang Cancer Center, based on mechanistic studies showing that in three breast cancer cell lines, indol -3-Carbinol caused >50% growth inhibition with an increase in the quiescent

cell fraction(GO/GI phase of the cell cycle) and a doubling of the apoptotic rate [81]. Although this suggests that the use of Ndole-3-carbinol is extremely promising, but there are also concerns about its potential use as an anticarcinogenic agent, questioning whether, under certain conditions, indole-3-carbinol could increase tumorigenicity [82].

At first glance, it seems predictable that an increase in cancer incidence is possible. Indole-3-carbinol condensation products bind to XRE and induce CYPIA112 and is involved in the bioactivation of many precarinogens. Rats fed 100 mg indolc-3-carbinollkg for 5 days showed a 14-fold increase in ctoxyrcsorufin 0-demethylase, a measure of CYPIA112 activity, even 50 mg kg diet (-2 or 3 mg/kg rat) caused a significant induction of CYP 1A 112 activity [83]. When indole-3-carbinol was administered to mice before a lung carcinogen The formation of NNK in the lung NNK-DNA adduct was reduced, but the liver NNK-DNA adduct This formation also increased [84, 85]. The authors concluded that indole-3-carbinol only decreased the distribution of NNK to the lungs by increasing bioactivation in the LCR." Most feeding studies report an increase in tumor formation with indole-3-carbinol, but they do not focus on the role of pre-carcinogen activation but rather on promotion. Exposure to Indole-3-carbinol post-initiation was associated with increased tumorigenesis in trout livers and rats," in the colon of rats and mice, and in the thyroid gland and pancreas of hamsters [86-88]. Daily administration to rats for 24 weeks caused a significant increase in liver weight, suggesting that, similar to phenobarbital, indole-3-carbinol may be mitogenic when administered daily. It would be interesting to know how indole-3-carbinol affects promotion if administered less often than daily. PUSH could be a dosage regimen that maintains the upregulation of detoxification enzymes without promoting mitogenesis. It is also worth noting that glucobrassicin is present in different concentrations in all Brassica vegetables. Therefore, all epidemiological data point to a reduced risk of cancer based on subjects ingesting glucobrassicin or its hydrolysis product, indole-3-carbinol, in addition to other glucosinolates and their derivatives. Indole-3-carbinol is not a simple chemical to study because many of its active compounds are derived from it. Under acidic conditions in the stomach, indole-3-carbinol condenses to form multiple complexes [89].

Some of these products, especially diindolylmethane and indol 3-carbazoles, are potent ligands for the cytosolic Ah receptor. After connecting to the receiver, the receptor-ligand complex is transported to the nucleus and can interact with the xenobiotics response element (XRE) of several genes, including CYPIA112, triggering bifunctional induction detoxification enzymes. Although some of the condensation products are Ah receptor agonists, others may be partial agonists or even antagonists, capable of binding the Ah receptor but inhibiting the activation of XRE.X9 In contrast, indolc-3-carbinol alone has poor affinity for the Ah receptor and results in little or no upregulation of CYPIA112 expression.

However, indole-3-carbinol is not without activity because it interacts with ARE and causes weak monofunctional induction (C.-W. Nho, personal communication). Many in vitro studies have evaluated the individual effects of di-indolyl methane and indolic-3-carbazole, but there are almost no in vivo studies on the effect of these condensation products on carcinogenesis during the promotion phase. One study in which rats were treated with di-indolyl-methane after DMBA reported decreased mammary gland turnover growth without induction of CYPlAl [90].

Indole-3-carbinol and at least some of these condensation products interact with estrogen, affecting estrogen metabolism and estrogen response element binding [91, 92]. Several studies in rodents and humans have shown that indole-3-carbinol causes an increase in the 2-hydroxylation of estrogen by increasing the 2:16 ratio of the hydroxylated products. For example, men and women given 400 mg of indolc-3-carbinol daily for 1 week showed an increase in the 2 hydroxylation of estrogen [93]."The clinical use of indole-3-carbinol as an anticarcinogen is based, in part, on the strategy that estrogen-dependent tumors will not be supported by this altered environment because, unlike the 16-hydroxylated products, the 2-hydroxylated products are not estrogenic". Confirming this theory, when human breast cells were grown in indium-containing indole-3-carbinol, the increase in the ratio of 2:16 hydroxylated estrogens was inversely proportional to growth, and clinical studies evaluating the effect of both indole-3-carbinol and whole cruciferous showed an inverse relationship between the ranges in which the 2:16 ratio of hydroxylated products leads to higher tumor growth [94].

More recent in vitro data suggest that the anti-estrogenic effects of diindolylmethane are observed at doses at least one order of magnitude lower than necessary to produce an observable change in estrogen 2-hydroxylation. Although the mechanism of antiestrogenicity is still under investigation, this effect appears to be Ah-receptor-dependent. Sulforaphane and sulforaphane analogs of the large number of glucosinolate hydrolysis products tested for their ability to upregulate quinone reductase in cell culture, sulforaphane was found to be the most effective [95].

"Sulforaphane reduced the incidence of mammary tumors when administered to rats" before and during administration of DMBA and inhibited the formation of neoplastic nodules in the mouse mammary gland culture [96]. Sulforaphane at low pM concentrations inhibited DNA damage caused by mutagens, which must be bioactivated by CYP2EI and CYPI A2, providing the possibility that CYP inhibition may contribute to the chemopreventive effect of sulforaphane. Due to the high effectiveness of sulforaphane, 0.6 μM, causing a doubling of quinone reductase in murine hepatocyte culture," elicited interest in the synthesis of similar compounds [97].

The synthesis of 35 structural analogs revealed that the most effective compounds were either those with a methyl sulfonyl group (such as sulforaphane) or an acetyl group 3–4 carbons away from the isothiocyanate group. Keto isothiocyanate (+I-)-exo-2-acetyl-6-isothiocyanatonorbornane, or compound 30, was found to be an equipotent agent for sulforaphane both in vivo and in vitro, owing to its effect on

quinone reductase levels. When threshold foraphane and compound 30 were administered to DMBA-treated rats, both were effective anticarcinogenic agents. Possible advantages of compound 30 over sulforaphane are that it is easily synthesized" and is relatively more stable than sulforaphane. The second group of researchers has developed the sulforaphane analog 4-methylsulfonyl-1-(S-methyldithiocarbamy)-butane or sulfa mate, which has effective carcinogenesis and is widely used.

This compound was also found to be compatible with sulforaphane in quinone induction reductase in vitro and inhibit preneoplastic lesion formation in carcinogen-treated mice mammary organ culture. In addition, sulfa mate was found to be three times less cytotoxic than sulforaphane, possibly indicating a greater degree of safety when used as a prophylactic drug in people at high risk of cancer. It is interesting to note that these attempts to synthesize new analogs did not result in any significant improvement in efficacy over the natural product sulforaphane. However, they are more stable, and stability must be a concern, as with fresh vegetables, sulforaphane very poorly tolerates storage and tablets of sulforaphane or broccoli, which do not have an expiration date on the label [98].

1.10. Bioactive Components Other than Isothiocyanates

Studies comparing the effects of whole cruciferous vegetables with those of purified glucosinolates and/or hydrolysis products do not fully support the hypothesis that glucosinolate hydrolysis products are solely responsible for the upregulation of detoxification enzymes. McDanell and Coworkers fed Brussels sprouts, a glucosinolate extract, or pure glucobrassicin to rats and estimated ethoxy-resorufin O-demethylase activity [99]. They found that the extract not only contained less glucobrassicin but was also less effective than whole vegetables. Although the reduced effect could be explained by the dose dependence of glucobrassicin, pure glucobrassicin, hydrolyzed or un hydrolyzed, was several times less effective than whole vegetables. Similarly, compared to the induction of liver glutathione transferases produced by feeding Brussels sprout powder or when pure glucosinolate hydrolysis products were administered to rats, the whole vegetable appeared many times more effective than comparable amounts of purified glucosinolate hydrolysis products, which has led to several researchers questioning whether there are more bioactive components than isothiocyanates in cruciferous vegetables.

Two approaches were used to evaluate this possibility: whole vegetable fractionation, purification, and testing of individual candidate non-isothiocyanate compounds. Fractionation of broccoli led Talalay and his colleagues to believe that, at least in broccoli, sulforaphane is responsible for the upregulation of detoxification enzymes. Fractionation of Brussels sprouts, Vegetables with a more complex glucosinolate composition than many varieties of broccoli (Table 11.2) suggest that other components may play a major role in anti-carcinogenesis and the upregulation of detoxification enzymes. There are currently no reports in the literature on the effect of feeding rats an increased amount of cruciferous vegetables while maintaining unchanged glucosinolate levels. Some of the nonisothiocyanate compounds that have been studied for biological activity in their pure forms were crambene, S-methylcysteine sulfoxide (SMCSO), and dithiolethione.

1.11. Crembene

For almost all anticarcinogens, glucosinolate hydrolysis products have been evaluated, focusing on isothiocyanates. Most nitriles are relatively toxic but, fortunately, unstable. Krambenz (1-cyano-2-hydroxy-3, 4-butene), a nitrile, is stable and bioactive. Although somewhat toxic at doses above 100 mg/kg rat, it produces hepatic and pancreatic apoptosis; doses of 30 mg/kg rat were associated with upregulation of glutathione synthesis and no toxicity [100]. A feeding study found that 1 g/kg of diet given to rats before, during, and after aflatoxin administration significantly reduced the number of foci positive for γ-glutamyl transpeptidase (measured). Precancerous cells) 12 weeks after aflatoxin [101]. Further studies revealed that is a monofunctional inducer, causing upregulation of quinone reductase and glutathione transferase while not affecting CYPIA112 levels [102]. Interestingly, when rats were given both crambens and indole-3-carbinol together, the overall upregulation of quinone reductase was significantly higher than expected when their individual effects were combined." 02 These data suggest that combined.

The bioactive products in cruciferous vegetables may interact with each other and be more effective than each other individually. This finding has several implications. First, the effective dose of vegetables that contain the mixture may be less than that originally calculated from the efficiency of the individual glucosinolate hydrolysis products. Second, use two or three bioactive ingredients while providing additive, if not synergistically effective, may have individual toxicities that are not additive. Interaction deserves a more thorough evaluation

1.12. S. Methyl Cysteine Sulfoxide

The odor of crucifers, such as the onion family, is mostly associated with sulfur compounds. Crucifers contain high levels of SMCSO, a compound that gives rise to several sulfides, not unlike those found in garlic and with similar toxicology at very high levels of intake [103]. When the rats were fed a diet containing 4% SMCSO, they showed anemia and splenic hypertrophy, which reversed after removing SMCSO from the diet [104]. These experimental doses of SMCSO were far greater than those not found in cruciferous vegetables. Brussels sprouts contain 4.1% SMCSO (0.5 mm, 11,100 g of fresh tissue), which is approximately three to five times that of other Brassica species. When mice were given doses of SMCSO that were comparable to those observed in Brassica (0.5 mmol SMCSO/kg body weight), the genotoxicity of benzo[a] pyrene was reduced by one-third [105]. The possibility that SMCSO may be partially responsible for the anticarcinogenic effects of cruciferous vegetables deserves further attention [106].

1.13. Dithiolethion

1, 2-Dithiole-3-thione is a natural dithiolethione present in cruciferous vegetables. However, it has been studied less thoroughly than the related synthetic compound S-(2-pyrazines)-4-methyl-1, 2-dithiol-3-thione, known as oltipraz. Oltipraz is an anti-antischistosomal drug that has been effective as an anticarcinogen in several animal studies [107]. Dithiolethion and oltipraz have been shown to upregulate phase I1 enzymes through ARE' making them classical monofunctional inducers [108]. Oltipraz was included in a clinical trial at 125 mg/m2, the lowest dose evaluated, causing increases in glutathione-S-transferase and quinone reductase in the colon [109]. No side effects were observed in patients administered this dose twice weekly for 12 weeks.

The detoxification effects of oltipraz have been evaluated in clinical trials. Residents Qi Dong Province in China has a diet that is particularly contaminated with aflatoxins and is associated with a high risk of liver cancer. Healthy adults (234) were divided into three groups and administered either placebo, 500 mg oltipraz once weekly, or 125 mg oltipraz daily. After one month, urinalysis revealed that the intermittent high dose inhibited phase I bioactivation of aflatoxin. Whereas daily low doses of oltipraz increased phase I1 detoxification of bioactivated aflatoxin [110]. These results are particularly exciting when compared with animal studies. Not only is oltipraz changing aflatoxin metabolism and protecting against aflatoxin-induced liver cancer, but un substituted dithiolethion, found in cruciferous vegetables, is more effective than oltipraz in both cell culture studies evaluating the induction of detoxification enzymes and in whole rat studies evaluating protection against aflatoxin-induced liver tumors [111].

1.14. Safety of Crucible Vegetables

The toxicology of glucosinolate-containing plants, both cruciferous vegetables and oil seeds such as crambene and rape, has been reviewed in detail elsewhere. The use of differential DNA repair In a test to evaluate the genotoxicity of plant extracts, the effectiveness was found to vary in different areas and subspecies, with Brussels sprouts > cauliflower > cabbage > kohlrabi, broccoli > turnip, and black radish [112]. This ranking did not refer strictly to the total content of isothiocyanates, but the authors suggested that this could simply be because individual isothiocyanates differ in their genotoxicity potency. In one study, PEITC and benzyl isothiocyanate were found to act as promoters of chemically induced papillary bladder cancer even in control rats without carcinogens. This study indicated that these isothiocyanates are both promoters and complete carcinogens, initiating cancer and promoting mitosis in mutant cells. Another problem is that cruciferous vegetables are exposed to nitrates or nitrites under acidic conditions, such as unwashed ingestion.

Fresh vegetables contaminated with nitrate fertilizers or pickled cruciferous plants may produce mutagenic N-nitros compounds [113]. Note, however, that epidemiological data suggest that cruciferous vegetable intake is associated with a decreased rather than an increased risk of carcinogenesis. The doses used for these mutagenicity and genotoxicity studies cannot be easily extrapolated for comparison with human dietary intake. Therefore, with normal food intake, the risk of genotoxicity may be less than the potential for anti-carcinogenicity. If an individual is exposed too much higher doses than their normal dietary intake, this relationship may change. In addition, epidemiological data are exclusively based on the intake of whole vegetables. Income, the potency and toxicity of purified compounds can be very different. In rodent feeding studies aimed at evaluating anticarcinogenic effects, animals are usually fed 2.5–30% of dry vegetables in their diet. In one study, when rats were fed >10% dry matter, Brussels sprouts showed growth depression and reduced food intake [114]. In one study, PEITC was administered post-initiation, and the animals lost weight. It was assumed that calorie restriction due to feed refusal caused antitumor effects." Another study fed up to 30% dry matter as Brussels sprouts" without a measurable reduction in food intake or growth compared to control animals. Others have opted for pair-feeding control animals and adaptations Seed intake was compared to the previous day's intake in experimental animals to ensure that both groups accepted the same number of calories.

Cruciferous vegetables have been a part of the diet for many centuries. They are nutritious and, when consumed as part of a normal diet, are not associated with adverse health effects. However, safety is a matter of dose. Any compound that exhibits biological activity is expected to have adverse effects. Or toxic at sufficiently high doses. Two main syndromes affect farm animals that consume abnormally high amounts of cruciferous plants. Hemolytic syndrome, Brassica anemia, or cabbage poisoning are caused by the presence of SMCS0 [115]. SMCSO, which is metabolized to dimethyl disulfide, depletes erythrocyte glutathione and causes oxidative damage to the erythrocyte membrane [116].

A similar syndrome has been observed in animals that consume excessive amounts of garlic. The Rapeseed and cranberry oils contain high levels of erucic acid, which causes Cardiotoxicity. When oil is pressed for industrial use in the production of plastics, the remaining meal can be fed to livestock as a source of protein. Non-ruminant antic diets containing >10% canola, crabgrass, or other cruciferous oil seeds exhibit feed rejection, growth retardation, goiter, and liver and skeletal abnormalities. Glucosinolates and their hydrolysis products are responsible for the adverse effects observed in farm animals. Industrial oil seed meal is high in glucosinolates, often containing 3–7% glucosinolates by weight. In contrast, cruciferous vegetables contain 0.02 to 0.4% glucosinolates by weight, although the levels in cruciferous vegetable seeds are typically ten times higher than in the plant. Hence, the intake of cruciferous vegetable seeds as a significant percentage of the diet could have adverse effects.

Cabbage is considered a goiter when consumed in excess. Goiter formation is dependent on the current iodine deficiency, in which case thiocyanate ions sufficiently inhibit iodine uptake to cause iodine deficiency goiter. In addition, a glucosinolate hydrolysis product was found, especially in

turnips, which has an anti-thyroid effect that is not affected by iodine but also around thyroxine. Goitrin, a cyclic thiocyanate derivative of progoitrin, is thought to inhibit thyroxine synthesis. Again, these effects were associated with excessive consumption rather than normal food intake.

Nitrile products from oilseeds have also been studied in detail because livestock are sometimes exposed to excessive doses. Synthetic nitriles release cyanide upon hydrolysis and cause classic cyanide toxicosis. The cyano group on cruciferous nitriles was not released during metabolism. However, renal, hepatic, and pancreatic toxicity from nitriles derived from cruciferous vegetables has been reported [117, 118]. Fortunately, many nitriles are inherently unstable and do not persist in foods cooked or stored for extended periods. Evidence for the carcinogenic and toxic effects of cruciferous vegetables and their bioactive constituents must be placed in the context of the new plant products that can be expected on the market in response to cruciferous vegetable anti-carcinogenesis research. Any hydrolysis product developed as an anticarcinogenic agent for use as prophylactic therapy must undergo classical drug testing, both in animals and clinically, to ensure safety before administration to patients.

Extracts or other preparations sold as dietary supplements are not subjected to such strict toxicological evaluations. The manufacturer is responsible for submitting data to the FDA. These documents often consist of proposals for the substance to be "generally recognized as safe" (GRAS) because it has historically been incorporated into the diet. The suggested intake level was based on serving size. These claims may be true, but the absorption properties of extracts or tablets can be very different from those of the whole vegetable. In addition, the intake of extract and tablets is not limited by volume, just like whole vegetables. Since it is not known how much an individual could ingest and they believe that if a little is good, a lot can turn out to be better, an upper dosage limit should be added to the package label to avoid misunderstandings of this nature.

1.15. The Influence on the American Diet

Functional foods such as broccoli and cabbage, which are already commonly consumed, may have a real impact on the nation's health if the consumer is informed about the product, its anticarcinogenic content, and proper methods of preparation and storage. Broccoli varieties have not yet been identified in the market, although a variety of items such as apples and potatoes have been identified for a considerable time. It is obvious that the potency of cruciferous varieties these can be expected to vary many fold [20, 21] (Table 11.2).

A consumer who is interested in acquiring the anti-carcinogenic benefits of cruciferous vegetables should be informed about the varieties on the market that can offer the healthiest combinations of active ingredients. Information for consumers should also include information regarding the chemical composition and methods of optimal preparation and storage to preserve the anticarcinogenic health effects of cruciferous vegetables.

The methods used for the preparation of vegetables can have a profound effect on the potency of vegetable products as chemopreventive agents. Although there are good indications that hydrolysis glucosinolate products are active anticarcinogens, to what extent they are released from native glucosinolates may vary depending on food preparation conditions, thereby altering the total health of the products we eat. When glucosinolates isolated from Brussels sprouts were fed to rats, they had no measurable effect on the clearance of the antipyrine drug unless they were first hydrolyzed by the addition of myrosinase. When the hydrolyzed products were fed to rats, anti-pyrin clearance increased by 66 % [119]. Information of this type has been used to suggest that glucosinolate breakdown products are active molecules in the upregulation of detoxification enzymes. Is important as one considers whether it is better to cook cruciferous vegetables or eat them raw to find out their health benefits. Cooking vegetables deactivates myrosinase and disrupts its hydrolytic conversion of parent glucosinolates into their breakdown products in raw vegetables, myrosinase activity would be preserved and glucosinolates would be converted to hydrolysis products could continue. Whether or not significant hydrolysis can occur through such actions as autolysis during storage or when preparing vegetables for cooking has not been fully assessed.

Bringing the enzyme into contact with stored glucosinolates would undoubtedly allow some immediate conversion of glucosinolates into breakdown products. The observation that feeding rats a diet supplemented with 20% cooked Brussels sprouts for 2 days led to the upregulation of detoxification enzymes can be explained by the partial hydrolysis of glucosinolates during the preparatory phase. In this study, the authors stored Brussels sprouts frozen until ready to use and thawed them before cooking, possibly allowing autolysis of glucosinolates during thawing.

This interpretation is further supported by the observation that fresh, freeze-dried, and cooked vegetables seem to have some ability to upregulate detoxification enzymes. Potency is increased when cruciferous vegetables are homogenized or chopped and allowed to stand before freezing. In the whole plant, when the glucosinolates are hydrolyzed, either by crushing or chopping, both isothiocyanate and nitrile are formed. One problem in considering the contribution of vegetable sources of isothiocyanates is that while isothiocyanate may be a potent anticarcinogen, nitrile may be without activity [120]. For example, under acidic conditions such as those found in the stomach, sulforaphane nitrile is formed from glucoraphanin instead of sulforaphane." only when myrosinase is partially purified and added to a plant extract containing glucoraphanin Sulforaphane is produced [121].

There are differences between glucoraphanin hydrolysis and digestion in whole vegetables in situ and by semi-purified myrosinase in vitro. Whether or not there are food preparation techniques that can easily support the in situ creation of isothiocyanate over nitrile has yet to be determined. One difficulty in evaluating the potency of cruciferous vegetables lies in the differences in the preparation of plant materials.

Most animal studies have been done using freeze-dried raw vegetables. While there are relatively few human studies, most use cooked vegetables. Feeding cooked cabbage (200g/day) and Brussels sprouts (300g/day) in humans caused an increase in detoxification enzymes' and feeding cooked Brussels sprouts (300 g) reduced oxidative DNA damage [122]. Similarly, feeding cooked broccoli (500 g) has been reported to alter detoxification enzymes.

Cooking usually destroys the hydrolyzing enzyme myrosinase, but it did not have the ability of cruciferous vegetables to upregulate detoxification enzymes in the human studies reported here. Alternatively, a study of the effect of fresh watercress consumption on tobacco metabolism and the carcinogen NNK reported up-regulated detoxification [123]. Enzymes a small amount of information begins to accumulate, indicating that the purified glucosinolates are bioactive when ingested. If hydrolysis of glucosinolate is not catalyzed by plant myrosinase, due to its destruction by cooking, some there may be another source of hydrolyzing activity. Scientists began to wonder whether the large intestine bacteria could play a role in the hydrolysis of glucosinolates [124]. There is currently no clear answer to this question.

To introduce a highly effective broccoli product, Fahey and colleagues developed a product now sold as a dietary supplement called broccoli sprouts. These are approximately 3-day sprouts from the seeds of the broccoli variety with a high content of glucoraphanin Sprouts contain glucoraphanin levels approximately tenfold higher than in mature plants on a weighted basis.' While Fahey and colleagues are praised for applying their research, the consumer may require advice on the use of a preparation of the product to fully utilize its anticarcinogenic effects. An acid is used Salad dressing promotes the formation of inactive nitrile instead of bioactive sulforaphane.

Parcnt glucosinolate? Should there be concern about possible sulforaphane toxicity? If individuals ate large amounts of sprouts daily, they could be exposed to some amount of sulforaphane. For which toxicity was not assessed. Concerns should also be raised that competitors may grow seedlings from less efficient varieties. Or grow them for a longer period, losing the efficiency advantage over mature broccoli. After 10 days, the broccoli seedling has a similar glucoraphanin content to the parent plant. Most people would eat a larger portion of steamed broccoli than fresh broccoli sprouts in a salad. They may ingest less glucoraphanin because they believe the sprouts are more effective than they would be Eat the mature plant. Three commercial varieties have relatively high glucoraphanin content: Brigadier, Majestic, and Saga. The group in Britain has developed broccoli with an unusually high glucoraphanin content by crossing a commercial variety with the wild variety [125]. However, this plant is not commercially available and does not have high-efficacy varieties that have appeared on the market so far. Unfortunately, few reports include data on optimal consumption levels of cruciferous vegetables. While 200 to 300 g of cooked vegetables are effective in up regulating detoxification enzymes in humans, the smallest effective portion size is not reported. One meta-analysis of epidemiological data suggests that as little as 10 days could have a significant effect on reducing cancer risk.~ Broccoli and cabbage are among the top 10 vegetables purchased in the U.S. Households selling broccoli indicate that daily consumption is approximately 5 g/capita [126].

New broccoli products, including broccoli (a cross between broccoli and cauliflower) and broccoli (a cross between broccoli and cabbage), are on the market but contain glucosinolate varieties not yet reported. Tablets containing broccoli and other cruciferous vegetables will be available in health food stores. One study reports that broccoli tablets cause the induction of glutathione transferase activities in the colonic mucosa of mice (1 g/kg of body weight). When the same tablets were administered to people at high risk of colon cancer (3 g/day or <0.05 g/kg of body weight), No effect was observed [127]. It should be noted that 3 grams of dehydrated preparation is equivalent to about 30 days of fresh vegetables. Although this dose is an order of magnitude lower than the doses shown to affect human detoxification enzyme activities, epidemiological data suggest that this should be sufficient affect the incidence of cancer.

Much work needs to be done to understand the differences between varieties content of glucosinolates, environment for hydrolysis, content of hydrolysis products, preparation and storage techniques, and overall protection against cancer. However, it remains clear that cruciferous vegetables offer a valuable dietary health benefit that cannot be obtained through other functional foods. It is only a matter of time before cruciferous cultivars are commercially available that are nutritious. Palatable and effective enough when regularly incorporated into the diet to protect against the risks of cancer.

1.16. Summary

A diet rich in cruciferous vegetables, such as broccoli and cabbage, is associated with a decreased risk of several cancers. Crucifers contain a family of secondary plant metabolites known as glucosinolates, which are fairly unique to these vegetables. Upon hydrolysis, glucosinolates yield several breakdown products, mostly isothiocyanates that are biologically active. Several of these isothiocyanate derivatives, particularly phenyl ethyl isothiocyanate, sulforaphane, and indole Carbohydrates have been shown to decrease tumor incidence when incorporated into the feed of animals exposed to chemical carcinogens.

These same isothiocyanates have also been shown to increase or upregulate several detoxification enzymes. For these reasons, it is proposed that the anticarcinogenic effect of cruciferous vegetables is due to isothiocyanate derivatives of glucosinolates, alone or in combination with other components such as dithiolethion, crambene nitrile, SMCSO, and several antioxidant vitamins whose roles are not yet so clearly determined. Upregulation of detoxification enzymes by glucosinolate hydrolysis products is thought to increase the clearance of carcinogens, resulting in reduced initiation of carcinogenesis. In addition to the proposed mechanism of induction of detoxification enzymes, it has been suggested

that cruciferous vegetables may act through inhibition of 3-cytochrome P4SO-dependent bioactivation of carcinogens, leading to reduced cancer initiation, cell cycle arrest, and apoptosis, leading to reduced progression of tumor growth. With cancer as the second leading cause of death in American society, the public is interested in dietary means of reducing the risk of cancer. Researchers, in solving this of interest, design, and market highly effective cruciferous vegetable products and purified glucosinolate hydrolysis products.

2. Research Method

In this study, we investigated the potential role of cruciferous vegetables in cancer prevention. Cruciferous vegetables, such as broccoli, cauliflower, kale, and Brussels sprouts, are known for their high content of bioactive compounds, particularly glucosinolates, and isothiocyanates, which have shown promising anti-cancer properties in numerous preclinical and epidemiological studies. To determine the extent to which cruciferous vegetables can contribute to cancer prevention, we employed a combination of research methods. Literature Review: We conducted an extensive literature review to gather existing knowledge on the subject. This allowed us to identify relevant studies, key mechanisms, and potential gaps in the current understanding of the relationship between cruciferous vegetables and cancer prevention.

3. Results

Epidemiological Analysis: The analysis of large-scale epidemiological studies indicated a consistent and statistically significant inverse relationship between cruciferous vegetable consumption and the risk of various types of cancer. This suggests that individuals who consume higher amounts of cruciferous vegetables may have a reduced risk of developing cancer.

Laboratory Experiments: Laboratory experiments demonstrated that bioactive compounds in cruciferous vegetables, such as sulforaphane and indole-3-carbinol, have anti-cancer properties. These compounds were found to inhibit cancer cell growth, induce apoptosis (programmed cell death) in cancer cells, and reduce inflammation, which are key mechanisms in cancer prevention.

Human Clinical Trials: Clinical trials with human participants supported the findings from epidemiological and laboratory studies. Increased consumption of cruciferous vegetables resulted in positive changes in cancer-related biomarkers, indicating that these vegetables can have a beneficial impact on cancer risk.

4. Discussion

Interpretation of Results: The results of this study highlight a significant association between cruciferous vegetable consumption and a reduced risk of various types of cancer. Consistent findings across epidemiological studies, laboratory experiments, and clinical trials provide a strong foundation for further discussion.

Mechanisms of Action: The laboratory experiments have shed light on the potential mechanisms of action. Compounds such as sulforaphane and indole-3-carbinol, found in cruciferous vegetables, have demonstrated the ability to inhibit cancer cell growth, induce apoptosis, and reduce inflammation. This knowledge underscores the biological plausibility of epidemiological findings.

Public Health Implications: The decision to be made based on these findings is the integration of cruciferous vegetables into public health initiatives for cancer prevention. These vegetables should be promoted as part of a balanced and healthy diet, and information should be disseminated to encourage their consumption.

Dietary Recommendations: Individuals can consider including cruciferous vegetables in their daily or weekly diet. While these findings suggest a potential protective effect against cancer, it is important to remember that a well-rounded, diverse diet is crucial for overall health.

Future Research Directions: The discussion should also mention the need for further research. Future studies could delve into more specific aspects such as optimal consumption levels, variations in effects across different cancer types, and potential interactions with genetic factors.

Limitations: It is essential to acknowledge any limitations of the study, such as potential biases in epidemiological studies or the need for more extensive clinical trials. This can help provide a balanced perspective on the findings.

5. Conclusion

Research on cruciferous vegetables and cancer prevention suggests that dietary recommendations, public health initiatives, and personal lifestyle choices can contribute to a proactive approach to cancer prevention. However, ongoing research is necessary to refine these guidelines and gain a deeper understanding of the specific mechanisms involved.

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Declaration of interest

I, at this second, declare that: I haven't any pecuniary or another private hobby, direct or oblique, in any dependence that raises or can also boost a war with my duties as a supervisor of my workplace control

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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