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Review

Bio-protective effects of glucosinolates – A review

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ABSTRACT

Glucosinolates are an important and unique class of secondary plant products containing β-D-thioglucose and sulphonated oxime moieties. These include thioglucosides, characterized by side chain with varying aliphatic, aromatic and heteroaromatic carbon skeletons. Glucosinolates get converted into various degradation products (isothiocyanates, thiocyanates, indoles etc.), when vegetables containing them are cut or chewed because during this process they come in contact with the enzyme myrosinase which hydrolyses them. Though the available literature emphasizes the drawbacks of this class of compounds, but the potential benefits that might emerge from their biological activities have been ignored. These compounds possess diverse biological activities including protection against various pathogens and weeds in case of plants and as potent anticarcinogens. The enormous importance of this group of compounds cannot be overlooked and detailed insight into their role in diverse fields and the mechanisms operating behind them is required. The present review focuses on the beneficial bioactivities of glucosinolates such as antifungal, antibacterial, bioherbicidal, antioxidant, antimutagenic and anticarcinogenic etc. along with their experimental evidence and mode of action. These phytochemicals deserve proper position in therapeutic armamentarium. Clinical studies with these biomolecules are required to be accelerated to validate their affect *in vivo*.

1. Introduction

The majority of the research articles that have appeared in the last few decades, regarding glucosinolates (GSLs) and their hydrolytic products in cruciferous plants, generally emphasize the drawbacks of this class of compounds, such as their toxicity and antinutritive properties in animals. Much less has been written about their advantages that might emerge from their biological activities and medicinal uses. The potentially beneficial activities of GSLs and their enzymatic hydrolysis products are antifungal, antibacterial, bioherbicidal, biopesticidal, antioxidant, antimutagenic and anticarcinogenic. In this review an attempt has been made to gather and compile the otherwise scattered information along with their experimental evidence on the beneficial properties of GSLs.

GSLs, organic anions containing β-D-thioglucose and sulphonated oxime moieties, are an important and unique class of secondary plant products found in the seeds, roots, stems and leaves of plants. They are reported to be present in 16 families of dicotyledonous angiosperms, mainly in the Brassicaceae (Fahey, Zalcmann, & Talalay, 2001). GSLs include approximately 100 identified naturally occurring thioglucosides with a common structure, characterized by side chain (R) with varying aliphatic, aromatic and heteroaromatic carbon skeletons, all presumably derived from amino acids by a long chain lengthening process and hydroxylation or oxidation (Table 1) (Hansen, Møller, Sørensen, & de Trejo, 1995). Plants possessing GSLs also contain an enzyme, thioglucoside glucohydrolase, EC 3.2.3.1 (myrosinase). When GSLs and myrosinase come in contact with each other in the presence of water, the enzyme immediately causes the hydrolysis of the parent GSL. The hydrolysis products consist of an aglycone moiety, glucose and sulphate. The aglycone moiety is unstable and rearranges to form isothiocyanates (ITCs), thiocyanates, nitriles, oxazolidinethiones and epithionitriles depending upon the structure of the GSL and the reaction conditions (Fig. 1). Some of the characteristic and interesting properties, attributed to above compounds, are discussed in this review.

2. Biocidal activity

Reports on biocidal activity of plant extracts have been appearing in the literature since the last century. The role of GSLs and their enzymatic hydrolysis products, in addition to being responsible for characteristic pungent flavor, also shows antifungal and antibacterial activities (Chew, 1988; Drobnica et al., 1967). In plant cells GSLs are kept separated from endogenous myrosinase.

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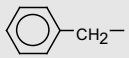
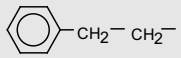
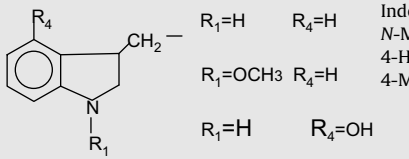
Table 1
List of glucosinolates found in different *Brassica* vegetables. (Adapted from Hansen et al., 1995).

No.	Structure of R-group	Semisystematic names of R-groups	Trivial names	*Brassica* spp. (+ present; − absent)				
				Cabbage	Brussels sprouts	Cauliflower	Broccoli	Chinese cabbage
1	CH_2=CH–CH_2–	Allyl	Sinigrin	+	+	+	+	−
2	CH_2=CH–CH_2–CH_2–	But-3-enyl	Gluconapin	+	+	+	+	+
3	CH_2=CH–CH_2–CH_2–CH_2–	Pent-4-enyl	Glucobrassicanapin	−	−	+	+	+
4	CH_2=CH-CH-CH_2-	(2R)-2-Hydroxybut-3-enyl	Progoitrin	+	+	+	+	+
5	CH_3-S-CH_2-CH_2-CH_2- (OH)	3-Methylthiopropyl	Glucoibervirin	+	−	+	−	−
6	CH_3–S–CH_2–CH_2–CH_2·CH_2–	4-Methylthiobutyl	Glucoerucin	+	+	+	+	−
7	CH_3–SO–CH_2–CH_2–CH_2–	3-Methylsulphinylpropyl	Glucoiberin	+	+	+	+	−
8	CH_3–SO–CH_2–CH_2–CH_2–CH_2–	4-Methylsulphinylbutyl	Glucoraphanin	+	+	+	+	+
9	CH_3–SO–CH_2–CH_2–CH_2–CH_2–CH_2–	5-Methylsulphinylpentyl	Glucoalyssin	−	−	−	−	+
10	CH_3–SO_2–CH_2–CH_2–CH_2–CH_2–	4-Methylsulphonylbutyl	Glucoerysolin	+	−	−	−	−
11		Benzyl	Glucotropaeolin	+	−	−	−	−
12		Phenethyl	Gluconasturtiin	+	+	−	+	+
13		Indol-3-ylmethyl	Glucobrassicin	+	+	+	+	+
14		*N*-Methoxyindol-3-ylmethyl	Neoglucobrassicin	+	+	+	+	+
15		4-Hydroxyindol-3-ylmethyl	4-Hydroxyglucobrassicin	+	+	+	+	+
16		4-Methoxyindol-3-ylmethyl	4-Methoxyglucobrassicin	+	+	+	+	+

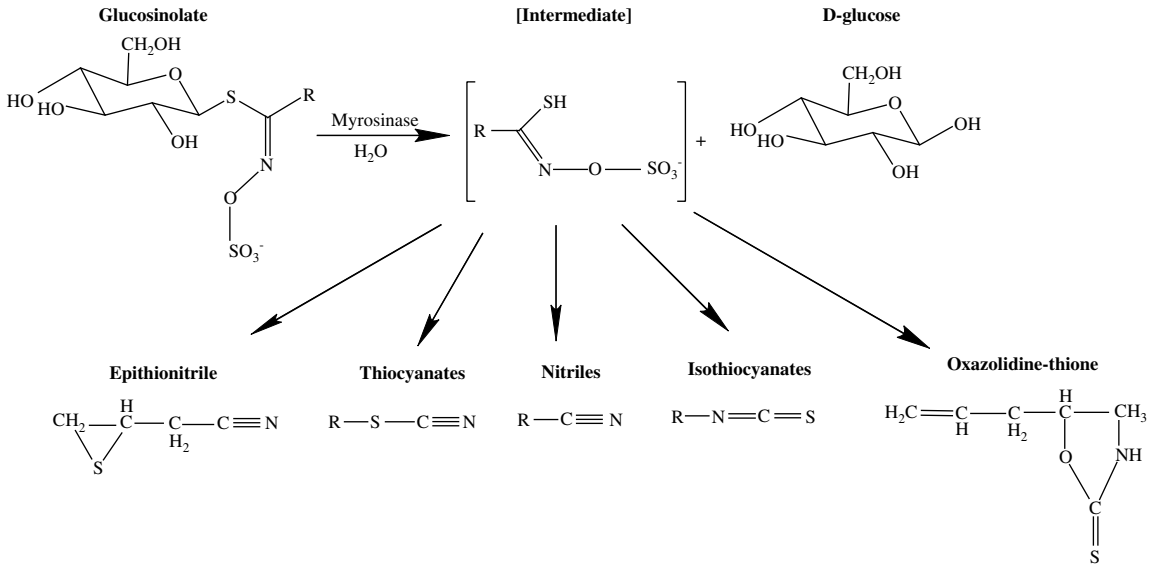


Fig. 1. Hydrolysis of glucosinolates by the enzyme myrosinase and their different hydrolysis products. (Adapted from Rask et al., 2000.)

As a result of mechanical wound or pathogen attack, the GSLs and enzyme come into contact and produces a number of hydrolytic products, *in situ*. This GSL–myrosinase system is present at different concentrations in all Cruciferae organs and plays an important defensive role. Biocidal effect of cruciferous tissues on other microorganisms has been attributed mainly to volatile degradation products of GSLs released from their plants (Brown, Morra, McCaffrey, Auld, & Williams, 1991). GSL degradation products exhibit biocidal activity against various pathogens like fungi, bacteria and various other insects and pests.

2.1. Fungicidal activities

Angus (1994), Chan and Close (1987), Gamliel and Stapleton (1993) and Vierheilig and Ocampo (1990) demonstrated that members of family Brassicaceae have the ability to control the growth of phytopathogenic fungi. Walker, Morell, and Foster (1937) observed the antifungal activity of mustard oils and of cruciferous plant extracts containing allyl and phenethyl isothiocyanates, which was confirmed by Hooker, Walker, and Smith (1943). In addition, Greenhalgh and Mitchell (1976), Gamliel and Stapleton (1993) reported that isothiocyanates released from cabbage tissues are toxic towards *Peronospora parasitica*, *Pythium ultimum* and *Sclerotium rolfsii*. Later on in 1994, Angus reported that volatile compounds from macerated *Brassica* root tissue inhibited the fungal pathogen of wheat, *Gaeumannomyces graminis*. Mari, Iori, Leoni, and Marchi (1993, 1996) reported the protective effect of enzymatic hydrolysis products during shelf life of fruits against some post harvest pathogenic fungi.

Eleven GSLs and their enzymatic hydrolysis products were tested *in vitro* against *Fusarium culmorum* (Manici, Lazzeri, & Palmieri, 1997). The results showed that native GSLs showed no fungitoxic activity whereas their hydrolytic products, in particular sulphate side chain ITCs mainly from glucoiberin, glucoerucin, glucoheirolin and glucotropaeolin, inhibited fungal growth of *Rhizoctonia solani*, *Sclerotinia sclerotiorum*, *Diaporthe phaseolorum* and *Pythium irregulare* with different inhibitory responses depending upon the chemical nature of the hydrolytic products. Smith, Sarwar, Wong and Kirkegaard (1999) reported that incorporation of canola root residues caused reduction in the infection of wheat seedlings by several root fungal pathogens.

Manici et al. (2000) indicated that ITCs produced by the hydrolysis of thiofunctionalized GSLs such as glucoiberin and glucoerucin are more fungitoxic against *P. irregulare* and *R. solani* than alkenyl GSL hydrolysis products. Dandurand, Mosher, and Knudsen (2000) attempted to control fungal pathogens using *Brassica napus* cv. Dwarf Essex, meal. A 100% reduction of myceliogenic germination of *S. sclerotiorum* was observed. Likewise a number of studies have been conducted to observe the fungicidal activities of GSLs. Table 2 presents fungicidal effect of various GSL hydrolysis products on different fungi. Different GSL hydrolysis products respond differently to the microbial population but ITCs are the major inhibitors of microbial activity (Mayton, Oliver, Vaughn, & Loria, 1996). The toxicity and range of activity also vary with changes in the isothiocyanate R-group. Greater toxicity is often related to increased volatility (Lewis & Papavizas, 1971). Biofungicides may act in different ways. They might work by triggering the plant's defense mechanism, or by producing the toxins that kill the target organism or by producing a defensive barrier around the roots of the host plant and thus preventing the harmful fungi to enter the host and thus protecting it from the detrimental effects of fungi. Kojima and Oawa (1971) tried to elucidate the particular biochemical mechanism of fungicidal activity of several ITCs using three different strains of *Saccharomyces cerevisiae* (yeast). They reported that ITCs act by inhibiting the oxygen uptake by yeast through the uncoupler action of oxidative phosphorylation in mitochondria of yeast i.e. inhibiting the coupling between the electron transport and phosphorylation reactions and thus eventually hindering the ATP synthesis.

2.2. Bactericidal activities

GSL hydrolysis products are potent inhibitors of bacterial activity. Allyl isothiocyanates (AITCs) are used as a preservative in the food industry. Tiedink et al. (1991) reported that the hydrolytic products of alkyl and aryl GSL were cytotoxic to *Salmonella typhimurium*. Primarily, reports regarding bactericidal activity of ITCs were limited to human pathogens. Benzyl isothiocyanate is used as an antibiotic to treat infections of respiratory and urinary tracts (Mennicke, Gorler, Krumbiegel, Lorenz, & Rittmann, 1988). Fenwick, Heaney, and Mullin (1983) and Smelt, Crum, and Teunissen (1989) reported that gram negative bacteria are generally less susceptible than gram positive bacteria to ITCs. Some microorganisms avoid toxicity by degrading the inhibitory compounds.

Table 2
Fungicidal effects of various glucosinolate hydrolysis derived products on different fungi.

Hydrolyzed glucosinolate product	Fungi	Reference
Allyl-ITC	*Aspergillus niger*	Hooker et al., 1943
	Aspergillus alliaceas	
	Colletotrichum circinans	
	Giberella sanbinetti	
	Peronospora parasitica	Greenhalgh & Mitchell, 1976
	Fusarium sambucinum	Mayton et al., 1996
	Peronospora parasitica	
	Sclerotium cepivorum	Smolinska & Horbowicz, 1999
	Bipolaris sorokiniana	Sarwar et al., 1998
	Fusarium graminearum	
	Gaeumannomyces graminis var. *tritici*	
	Rhizoctonia solani	
	Helminthosporium solani	Olivier, Vaughn, Mizubuti, & Loria, 1999
	Verticillium dahliae	
	Sclerotium cepivorum	Smolinska & Horbowicz, 1999
	Fusarium oxysporum var. *radicis* f. sp. *lycopersici*	
	Phytophthora capsici	Chung, Huang, Huang, & Jen, 2003
	Pythium aphanidermatum	
	Rhizoctonia solani	
	Sclerotinia sclerotiorum	
	Sclerotium rolfsii	
Allyl: benzyl: 2-phenylethyl: phenyl isothiocyanates in a ratio of 1:3.5:5.3:9.6	*Alternaria alternata*	Troncoso et al., 2005
Alkenyl aliphatic ITCs (methyl-ITC, propenyl-ITC, butenyl-ITC, pentenyl-ITC) (propenyl-ITC, ethyl-ITC)	*Bipolaris sorokiniana*	Sarwar et al., 1998
	Fusarium graminearum	
	Gaeumannomyces graminis var. *tritici*	
	Rhizoctonia solani	
	Fusarium oxysporum	Smolinska et al., 2003
Benzyl-ITC	*Alternaria tenuis*	Drobnica et al., 1967
	Aspergillus oryzae	
	Cladosporium herbarum	
	Fusarium spp.	
	Rhizopus oryzae	
	Monilinia laxa	Mari et al., 1993
	Mucor piriformis	
	Alternaria alternata	Manici et al., 1997
	Fusarium oxysporum var. *radicis* f. sp. *lycopersici*	Smolinska & Horbowicz, 1999
	Fusarium oxysporum	Smolinska et al., 2003
Butenyl-ITC	*Aspergillus niger*	Hooker et al., 1943
	Aspergillus alliaceas	
	Colletotrichum circinans	
	Giberella sanbinetti	
	Phytophthora capsici	Chung et al., 2003
	Pythium aphanidermatum	
	Rhizoctonia solani	
	Sclerotinia sclerotiorum	
	Sclerotium rolfsii	
Glucoerucin derived-ITC	*Pythium irregulare*	Manici et al., 2000
	Rhizoctonia solani	
Glucoiberin derived-ITC	*Fusarium culmorum*	Manici et al., 1997
	Pythium irregulare	Manici et al., 2000
	Rhizoctonia solani	
Glucoraphanin derived-ITC	*Mucor piriformis*	Mari et al., 1996
	Monilinia laxa	
	Botrytis cinerea	
Glucotropaeolin derived-ITC	*Fusarium culmorum*	Manici et al., 1997
3-Indolylacetonitrile	*Penicillium chrysogenum*	Smissman et al., 1961
3-Methylsulfinylpropyl ITC	*Alternaria alternata*	Manici et al., 1997
Propenyl-ITC	*Colletotrichum circinans*	Hooker et al., 1943
	Aspergillus alliaceas	
	Aspergillus niger	
	Giberella sanbinetti	
	Aphanomyces euteiches	Lewis & Papavizas, 1971
	Leptosphaeria maculans	Mithen, Lewis, & Fenwick, 1986
	Cladosporium cucumerinum	Schreiner & Koide, 1993
	Glomus etunicatum	
	Leptosphaeria maculans	Sexton, Kirkegaard, & Howlett, 1999
Phenylethyl-ITC	*Botrytis cinerea*	Dawson et al., 1993
	Gaeumannomyces graminis	Angus, 1994
	Fusarium oxysporum	Smolinska et al., 2003
Sinalbin (p-Hydroxybenzylglucosinolate) derived-ITC	*Penicillium glaucum*	Fenwick et al., 1983
Sinigrin (prop-2-enylglucosinolate) derived-ITC	*Sclerotinia minor*	Sanchi, Odorizzi, Lazzeri, & Marciano, 2005
	Sclerotinia sclerotium	
5-Vinyloxazolidine-2-thione	*Aphanomyces euteiches* f. sp. *pisi*	Smolinska, Knudsen, et al., 1997;

ITC – isothiocyanate.

Greater toxicity of ITCs is often related to increased volatility (Lewis & Papavizas, 1971).

The toxicity and range of activity of GSL hydrolysis derived products vary with the type of organism e.g. ammonium thiocyanate inhibits bacterial growth in soil but stimulates fungi at concentrations $> 250\ \mu g\ g^{-1}$ (Smith, Dawson, & Wenzel, 1945). *B. napus* seed meal extracts inhibited the growth of *Aphanomyces euteiches* (Smolinska, Knudsen, Morra and Borek, 1997) but slightly enhanced the growth of propionibacterium (Rutkowski, Bielecka, Kornacka, Kozlowska, & Roezniakowa, 1972). Koike and Subbarao (2000) conducted a 2-year study in *Verticillium*-infested field plots. They observed a significant decline in the number of *Verticillium dahliae* microsclerotia in soil treated with broccoli residue. In contrast, soil not treated with broccoli residue experienced five-fold increase in number of microsclerotia.

Bacterial infection with *Helicobacter pylori* is associated with a marked increase in the risk of gastric cancer (Normark, Nilsson, Normark, & Hornef, 2003). Fahey et al. (2002) demonstrated that purified sulforaphane (SFN), hydrolytic product of glucoraphanin, inhibited the growth and killed multiple strains of *H. pylori* in the test tube and in tissue culture, including antibiotic resistant strains. Haristoy, Angioi-Duprez, Duprez, and Lozniewski (2003) reported that SFN administration for 5 days eradicated *H. pylori* from 8 out of 11 xenografts of human gastric tissue implanted in immune-compromised mice. The antibacterial activity of GSL hydrolysis products is presented in Table 3.

There is plethora of literature available regarding the antimicrobial activity of GSLs but information about the mechanisms behind this activity is scarce. Zsolnai (1966) proposed a theory regarding the mechanism of antimicrobial action of GSL degradation products. He suggested that GSL hydrolytic products act by inactivating various intracellular enzymes of the pathogen. They do so by oxidative breakdown of –S–S– bridges present in the enzymes. Obstruction of ATP synthesis in bacterial cells through uncoupler action of oxidative phosphorylation in mitochondria is another mode of action of these compounds (Kojima & Oawa, 1971).

2.3. Effects on insects and other invertebrates

GSL hydrolysis products are bioactive and have the potential to be used as naturally produced pesticides for the control of a number of soil-borne pests such as nematodes, fungi and bacteria (Brown & Morra, 1995, 1997; Kirkegaard et al., 2000; Lazzeri, Tacconi, & Palmieri, 1993; Manici et al., 2000; Sarwar, Kirkegaard, Wong, & Desmarchelier, 1998; Smolinska, Morra, Knudsen, & James, 2003). GSL breakdown products are safer biofumigants in pest control as they are considered to be fully biodegradable and less toxic. Insecticidal activity of several ITCs has been demonstrated, especially for aromatic compounds (Ahman, 1986; Borek, Elberson, McCaffrey, & Morra, 1995; Chew, 1988; Lichtenstein, Morgan, & Mueller, 1964; Lichtenstein, Strong, & Morgan, 1962; Seo & Tang, 1982; Wadleigh & Yu, 1988). Borek et al. (1995) demonstrated that aromatic ITCs are most toxic to the eggs of the black vine weevil (*Otiorhynchus sulcatus*). Matthiessen and Shackleton (2000) reported that methyl-ITCs are toxic to whitefringed weevil larvae (*Naupactus leucoloma*). Organic thiocyanates have been used as insecticides to control weevils in grain and to produce rapid eradication of flying insects such as flies (Beekhuis, 1975; Wood, 1975). Nitriles also possess insecticidal activity e.g. 3-indolylacetonitrile, inhibits growth of insects (Smissman, Beck, & Boots, 1961).

The capacity of GSLs and their degradation products to keep nematodes in soil under control has also been reported by various workers. Winkler and Otto (1980) reported that rotational plantings of mustard in strawberries checked the spread of nematode, *Pratylenchus penetrans*. Johnson, Golden, Auld, and Sumner (1992) demonstrated that incorporating the rapeseed tissue as green manure in soil reduced the populations of *Meloidogyne incognita* and *Meloidogyne javanica*. Table 4 includes the insecticidal and nematicidal activity of GSL hydrolysis products.

GSLs get broken down in soil to their biologically active compounds so plant tissues containing these compounds are incorporated into soil for controlling soil-borne pests. Different mechanisms have been proposed for their mode of action against pests. They work either by inactivating the thiol group of essential enzymes of the pest or by alkylating the nucleophilic groups of biopolymers like DNA or as uncouplers they affect the respiration of pest and eventually lead to their death (Tsao, Peterson, & Coats, 2002). Uncouplers kill pests by enhancing the respiration and not by inhibiting normal electron transport of the respiratory chain. Respiratory control is lost due to uncoupling between the respiratory chain and phosphorylation, the electron transport along the respiratory chain occurs at full pace without producing ATP.

Table 3
Bactericidal effects of various hydrolysis products of glucosinolates on different bacterial pathogens.

Hydrolyzed glucosinolate product	Bacteria	Reference
Allyl-ITC	*Bacillus cereus* IFO-13494	Isshiki, Tokuoka, Mori, & Chiba, 1992
	Bacillus subtilis IFO-13722	
	Escherichia coli JCM-1649	
	Pseudomonas aeruginosa IFO-13275	
	Salmonella enteritidis JCM-1891	
	Staphylococcus aureus IFO-12732	
	Vibrio parahaemolyticus IFO-12711	
	Pseudomonas corrugate	Delaquis & Sholberg, 1997
	Escherichia coli 0157:H7	Lin, Kim, Du, & Wei, 2000
	Listeria monocytogenes	
	Escherichia coli 0157:H7	Park, Taormina, & Beuchat, 2000
	Escherichia coli 0157:H7	Nadarajah, Han, & Holley, 2005
4-hydroxybenzyl-ITC	*Gluconobacter* spp.	Ekanayake et al., 2006
Methyl-ITC	*Escherichia coli* 0157:H7	Lin et al., 2000
	Listeria monocytogenes	
4-(Methylsulfinyl)butyl isothiocyanate	*Helicobacter pylori*	Fahey et al., 2002 Haristoy et al., 2003 Haristoy, Fahey, Scholtus, & Lozeniewski, 2005
Phenyl-ITC	Nitrifying bacteria	Bending & Lincoln, 2000
Oxazolidinethiones	*Propionic* bacteria	Rutkowski et al., 1972
	Phoma lingam	Schnug & Ceynowa, 1990

ITC – isothiocyanate.

Respiration is accelerated which needs more ATP as source of energy and at the same time ATP production is blocked. This causes exhaustion of stored energy sources which finally leads to death of the pest.

3. Bioherbicidal potential

GSLs may represent a viable source of allelochemical control for variety of weeds. Germination bioassays were conducted by Brown and Morra (1995) with *Lactuca sativa* seeds in the presence of defatted meal of *B. napus*. Only tissues containing GSLs produced volatiles which inhibited germination. The results suggested that this type of control may contribute to reduction in synthetic pesticide usage, if weed seeds are targeted. This effect recently had been referred to as biofumigation. Biofumigation potential of *Brassica* spp. in terms of effect of environment and ontogeny on GSL production, and *in vitro* toxicity of ITCs to soil-borne fungal pathogen have been described by Sarwar and Kirkegaard (1998) and Sarwar et al. (1998).

Some species of the *Brassica* family show potential for use as green manure (incorporating green plant material into the soil) crops (Al-Khatib, Libbey, & Boydston, 1997; Buhler, Kohler, & Foster, 2001; Krishnan, Holshauser, & Nissen, 1998). Norsworthy, Brandenberger, Burgos, and Riley (2005) reported the potential of Brassicaceae green manures as weed suppressants in *Vigna unguiculata*. Petersen, Belz, Walker, and Hurle (2001) analyzed the allelopathic potential of ITCs released by turnip–rape mulch (*Brassica rapa–B. napus*). They reported that ITCs were strong suppressants of germination of *Sonchus asper* (L.) Hill (spiny sowthistle), *Matricaria inodora* L. (scentless mayweed), *Amaranthus hybridus* L. (smooth pigweed), *Echinochloa crusgalli* (L.) Beauv. (barnyard grass), *Alopecurus myosuroides* Huds. (black grass) and *Triticum aestivum* L. (wheat). Vaughn, Palmquist, Duval, and Berhow (2006) also analyzed defatted seedmeals from fifteen GSL-containing plant species for bioherbicidal activity. They reported that at 0.1% rate, seedmeals of *Brassica juncea* (Brown mustard), *Lunaria annua* (Money plant) and *Thlaspi arvense* (Field Pennycress) inhibited the germination of *T. aestivum*, while at 1% rate, eight of the seedmeals were completely inhibitory for *Senna obtusifolia*. Bioherbicidal activity of different plant/plant parts containing GSL hydrolysis products is presented in Table 5.

The exact mechanisms of weed control by ITCs are not known, however evidence suggests that they inhibit seed germination by interfering with protein synthesis and processes involved in the formation of phosphorylated sugars or inhibition of plant enzyme activity (Leblova-Svobodova & Kostir, 1962). To take advantage of these compounds in weed suppression and to protect the crop from their germination inhibiting effects, a complete knowledge of biochemical mechanism involved in suppression and target weed is required as they act in host specific manner.

4. Antioxidant activity

Vitamin C, Vitamin E and carotenoids are direct antioxidants as they neutralize free radicals before they can harm cells. GSLs and their hydrolysis products are considered as indirect antioxidants,

Table 4
Effects of hydrolyzed glucosinolate product and *Brassica* plant materials on insects and nematodes.

Hydrolyzed glucosinolate product/*Brassica* plant material	Pest	Type of pest	Reference
Allyl-ITC	*Cyclocephala* spp.	Insect	Noble, Harvey, & Sams, 2002
	Musca domestica	Insect	Tsao et al., 2002
	Rhyzopertha dominica		
Allyl-isocyanate	*Musca domestica*	Insect	Tsao et al., 2002
	Rhyzopertha dominica		
Allyl-thiocyanate	*Musca domestica*	Insect	Tsao et al., 2002
	Rhyzopertha dominica		
Benzyl-ITC	*Otiorhynchus sulcatus*	Insect	Borek et al., 1995
Biomass of *Brassica oleracea* var. *botrytis*	*Tylenchulus semipenetrans*	Nematode	Zasada & Ferris, 2003
Biomass of *Brassica hirta* and *Brassica oleracea*	*Meloidogyne javanica*	Nematode	Zasada & Ferris, 2004
Biomass of *Brassica juncea*	*Tylenchulus semipenetrans*	Nematode	Zasada & Ferris, 2004
Brassica napus seed meal	*Heterodera glycines*	Nematode	Bhardwaj, Hamama, Porter, & Reese, 1996
	Limonius infuscatus	Insect	Brown et al., 1991
Brassica napus tissue	*Meloidogyne chitwoodi*	Nematode	Mojtahedi, Santo, Hang, & Wilson, 1991
	Meloidogyne incognita	Nematode	Johnson et al., 1992
	Meloidogyne javanica		
Methyl-ITC	*Limonius* spp.	Insect	Beekhuis, 1975
	Naupactus leucoloma	Insect	Matthiessen & Shackleton, 2000
Phenyl-ITC	*Otiorhynchus sulcatus*	Insect	Borek et al., 1995
Phenylethyl-ITC	*Drosophila melanogaster*	Insect	Lichtenstein et al., 1964
	Musa domestica		
	Otiorhynchus sulcatus	Insect	Borek et al., 1995
	Globodera rostochiensis	Nematode	Serra et al., 2002
Propenyl-ITC	*Diabrotica undecimpunctata howardi*	Insect	Landis & Gould, 1988
	Limonius californicus	Insect	Lehman, 1942
	Limonius canus		
	Limonius californicus	Insect	Williams, Morra, Brown, & McCaffrey, 1993
Thiocyanate	*Limonius* spp.	Insect	McCaffrey, Williams, Borek, Brown, & Morra, 1995

ITC – isothiocyanate.

as they do not neutralize free radicals directly, but rather by modulating the activity of xenobiotic metabolizing enzymes (phase I and phase II enzymes, that trigger the long lasting antioxidant activity. Phase I enzymes (cytochrome P450 enzymes) generally increase the reactivity of fat soluble compounds and as a consequence of this process, some reactive molecules are produced which may be more toxic than parent molecule. While phase II enzymes (glutathione-S-transferase, aldehyde reductase, S-methyl transferase, *N*-acetyltransferase etc.) increase water solubility and promote the excretion of these metabolites from the body. Hence inhibition of phase I and induction of phase II enzymes are necessary for the protection of cells against DNA damage by carcinogens and reactive oxygen species. The genes for the phase II enzymes contain a specific sequence of DNA called antioxidant response element (ARE). GSL hydrolytic products have been shown to increase the activity of phase II enzymes by increasing the transcription of genes that contain ARE. This action is mediated by nuclear factor-erythroid 2 p45 related factor-2, which binds to ARE and regulate the transcriptional induction of phase II enzymes (Holst & Williamson, 2004).

GSL hydrolysis products, especially isothiocyanates have gained attention as potent inducers of phase II enzymes which are important in the detoxification of electrophiles and protection against oxidative stress (Prestera, Zhang, Spencer, Wilezak, & Talalay, 1993). ITCs are powerful electrophiles, because of the reactivity of central carbon atom of the N═C═S group, which reacts readily with sulfur, nitrogen and oxygen-based nucleophiles (Barton & Ollis, 1979). However, there is very less evidence regarding the participation of these compounds in oxidation or reduction reactions like direct-acting antioxidant under physiological conditions. Plumb et al. (1996) examined the free radical scavenging properties of some GSLs from cruciferous vegetables by means of deoxyribose assay, ABTS (2,2′-azino-bis(3-ethylbenzthiazoline-6-sulphonic acid) and bleomycin assay. They reported that GSLs are unlikely to have direct antioxidant activity. Purified GSLs such as p-hydroxybenzyl GSL, but-3-enyl GSL and 3-methylsulfinylpropyl GSL were found to have only weak antioxidant activity in their assay system.

SFN (4-methylsulfinylbutyl isothiocyanate) is considered as the most active phase II enzyme inducer. SFN has been attributed indirect antioxidant activity which would arise from induction of glutathione transferases, quinine reductase and heme oxygenase (Fahey & Talalay, 1999). Kim, Jin, and Ishii (2004) demonstrated that desulfo GSLs have higher antioxidant activity than dimeric 4-mercaptobutyl desulfo GSLs due to the asymmetrical S–S bond as an electron donor. Barillari et al. (2005) reported that glucoerucin and its metabolite erucin are hydroperoxide scavenging antioxidants and thus possess good direct antioxidant activity. Glucoraphasatin, the major GSL of *Raphanus sativus* possesses reducing capacity against H_2O_2 and $ABTS^{*+}$ radical cation.

Hence there is compelling evidence that GSLs can help reducing the damaging effects of free radicals both directly as well as indirectly. A living system cannot escape from free radicals as they are byproducts of normal metabolic processes of body or can be produced through external factors such as pollution, radiation, herbicides or even cigarette smoke. As free radicals are highly unstable due to presence of unpaired electrons in their outer orbital, they can cause damage to parts of cells such as proteins, DNA, amino acids and cell membranes by stealing their electrons through a process called oxidation. Hence these important cellular components loose their ability to function normally and it consequently increases the risk of various diseases. Thus GSLs constitute an important defense mechanism for the body against the damaging effects of these free radicals.

5. Antimutagenic and antiproliferative activity

Chemopreventive agents, on the basis of the mechanism through which they exert anticancer effects, can be divided into two groups: antimutagenic and antiproliferative (Steele, 2003). In concentrations, not dangerous to human and animal health, these compounds also have shown an inhibitory effect against cancer

Table 5
Bioherbicidal activity of glucosinolate containing plants/plant parts.

Source	Weed/plants	Reference
Green manure from *Brassica juncea* and *Sinapis alba*	*Amaranthus palmeri* *Ipomoea hederacea* var. *integriuscula* *Leptochloa filiformis* *Lamium amplexicaule* *Cyperus iria* *Mollugo verticillata*	Norsworthy et al., 2005
Mulch of *Brassica rapa* and *Brassica napus*	*Alopecurus myosuroides* *Amaranthus hybridus* *Echinochloa crusgalli* *Matricaria inodoea* *Sonchus asper* *Triticum aestivum*	Petersen et al., 2001
Root, stem and leaf tissues of *Brassica napus*	*Lactuca sativa*	Brown & Morra, 1995
Seedmeals of *Brassica juncea* *Lunaria annua* *Thlaspi arvense*	*Triticum aestivum*	Vaughn et al., 2006
Seedmeals of *Brassica juncea* *Eruca vesicaria* *Erysimum* sp. *Lepidium sativum* *Lobularia maritime* *Matthiola longipetala*	*Senna obtusifolia*	Vaughn et al., 2006
Sinapis alba	*Capsella-bursa pastoris* *Kochia scoparia* *Setaria viridis*	Al-Khatib et al., 1997

Table 6
Antiproliferative activities of glucosinolate hydrolysis products.

Hydrolyzed glucosinolate products	Antiproliferative activity	References
Allyl-ITC	Inhibition of HL60 ($p53^-$) and human myeloblastic leukemia-1 cells ($p53^+$)	Xu & Thornalley, 2000
	Inhibition of growth of PC-3 human prostate cancer xenografts in mice	Srivastava et al., 2003
	Inhibition of human prostate cancer cell lines LNCaP by causing G2/M arrest and induction of apoptosis	Xiao et al., 2003
	Inhibition of cyclophophamide-induced urotoxicity	Manesh & Kuttan, 2005
Benzyl-ITC	Apoptosis in colon carcinoma cell line HT29 by activation of caspase-3	Kirlin, Cai, DeLong, Patten, & Jones, 1999
	Inhibition of human colon cancer cell lines LS-174 and Caco-2	Bonnesen, Eggleston, & Hayes, 2001
	Inhibition of head and neck squamous cell carcinoma (HNSCC) cells by activation of caspase-3 and PARP cleavage mediated by activation of MAPK	Lui et al., 2003
	Apoptotic induction, cell cycle arrest and inhibition of nuclear factor kappaB activation against human pancreatic cancer cell line BxPC-3	Srivastava & Singh, 2004
	Protective effects against initiation of pancreatic carcinogenesis in hamsters	Kuroiwa et al., 2006
Indole-3-carbinol (in combination with antiestrogen tamoxifen)	Inhibit the growth of the estrogen-dependent human MCF-7 breast cancer cell line	Cover et al., 1999
Indole ethyl-ITC	Antiproliferative and apoptotic effects on neuroblastoma cell lines: SMS-KCNR, SK-N-SH, SH-S454, IMR-32	Singh et al., 2007
4-Methylsulphinylbutyl-ITC	Suppression of human MDA-MB-231 breast cancer cells' activity	Rosea et al., 2005
	Dose-dependent cytotoxicity on human colon adenocarcinoma HT29 cells.	Gamet-Payrastre et al., 2000
	Inhibition of benzo (a) pyrene and 1,6-dinitropyrene-DNA adduct formation in human mammary epithelial cells	Singletary & MacDonald, 2000
	Inhibition of azoxymethane-induced colonic crypt foci in F344 rats	Chung et al., 2000
	Inhibition of human colon cancer cell lines LNCaP	Bonnesen et al., 2001
	Growth inhibition, cell cycle arrest and apoptosis in human T-cell leukemia	Fimognari et al., 2002
	Inhibition of benzo (a) pyrene-induced forestomach cancer in mice	Fahey et al., 2002
	Cell growth arrest and apoptosis in L-1210 leukemia and ME-18 melanoma cells	Misiewicz, Skupinska, & Kasprzycka-Guttman, 2003
	Inhibition of human hepatocellular liver carcinoma cell line HepG2	Kim et al., 2003
	Caspase-mediated apoptosis in cultured PC-3 human prostate cancer cells	Singh et al., 2004
	Induction of medulloblastoma cell apoptosis due to activation of caspases-3 and-9	Gingras et al., 2004
	Inhibition of human prostate carcinoma cell line DU-145	Wang et al., 2004
	Suppression of human MDA-MB-231 breast cancer cells' activity	Rosea et al., 2005
	Protective effects against initiation of pancreatic carcinogenesis in hamsters	Kuroiwa et al., 2006
7-Methylsulphinylheptyl-ITC	Suppression of human MDA-MB-231 breast cancer cells' activity	Rosea et al., 2005
Phenyl-ITC	Inhibition of cyclophophamide-induced urotoxicity	Manesh & Kuttan, 2005
Phenylethyl-ITC	Inhibition of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone-induced DNA adduct formation and tumorigenicity in lungs of F344 rats	Morse et al., 1989
	Inhibition of azoxymethane-induced colonic aberrant crypt foci formation in rats	Zhang et al., 1994
	Inhibition of human prostate cancer cells DU-145 and LNCaP by G_0–G_1 arrest and enhancement of p21 protein	Chiao et al., 2000
	Inhibition of azoxymethane-induced colonic crypt foci in F344 rats	Chung et al., 2000
	Induction of apoptosis in p53-deficient PC-3 human prostate cancer cell line mediated by extracellular signal-regulated kinases	Xiao & Singh, 2002
	Induction of apoptosis in human prostate cancer cell line LNCaP	Chen, Han, Kori, Kong, & Tan, 2002
	Inhibition of urinary bladder tumorigenesis in rats induced by *N*-butyl-*N*-(4-hydroxybutyl) nitrosamine	Nishikawa, Morse, & Chung, 2003
	Inhibition of human colon cancer cell lines HT29 by inhibition of NF-kappaB activity and activation of caspase-3	Jeong, Kim, Hu, & Kong, 2004
	Inhibition of human leukemia HL60 cells by inhibition of protein kinase C	Johnson, Chun, Bittman, & Jarvis, 2004
	Inhibition of human bladder carcinoma and human leukemia cells	Pullar et al., 2004
	4-(Methylnitrosamino)-1(3-pyridyl)-1-butone-induced pulmonary neoplasia in rats	Wu, Kassie, & Mersch-Sundermann, 2005
	Inhibits growth of ovarian cancer cells by inducing apoptosis	Satyan et al., 2006
Phenylbenzyl-ITC	Inhibition of human cervical cancer cell line HeLa by induction of caspase-3 protease activity	Yu, Mandlekar, Harvey, Ucker, & Kong, 1998
Phenylmethyl-ITC	Inhibition of human cervical cancer cell line HeLa by induction of caspase-3 protease activity	Yu et al., 1998

ITC – isothiocyanate.

(Nastruzzi et al., 1996). Dietary GSLs exhibit anticarcinogenicity by blocking formation of endogenous or exogenous carcinogens so preventing initiation of carcinogenesis.

Sedmikova et al. (1999) demonstrated that cauliflower juice treated by high-pressure and freezing showed strong anti-mutagenicity towards 2-amino-3-methyl-3H-imidazo-(4, 5-*f*)-quinoline (IQ). Mandelova and Totusek (2007) reported that administration of broccoli juice treated by high-pressure for 14 days to males of BALB/C mice decreased the mutagenic effects of applied mutagens. These results were in agreement with the similar tests performed on *S. typhimurium* TA 98 with metabolic activation. They reported that SFN and indole-3-carbinol have

antimutagenic properties. High-pressure treatment can be regarded as a method, used for extension of durability, deactivation of microorganisms, maintenance of nutritional value and for preservation of phytochemicals. Shishu, Singla, and Kaur (2003) proved strong antimutagenic abilities of SFN against group of heterocyclic amines, 2-amino-3-methyl-3H-imidazo-(4,5-*f*)-quinoline(IQ), 2-amino-3,4-dimethylimidazo[4,5-*f*]quinoline (MeIQ) and 2-amino-3,8-dimethylimidazo[4,5-*f*]quinoxaline (MeIQx). Murugan, Balakrishnamurthy, and Mathew (2007) investigated the antimutagenic effect of broccoli flower head by the Ames *Salmonella* reverse mutation assay. They reported that ethanol extracts of broccoli flower head at 46 mg/plate suppressed the mutagenic effect induced by the corresponding mutagens on all the tester strains TA 98, TA102 and TA 1535.

Chemoprotective properties of hydrolysis products of GSLs against chemical carcinogens have been well demonstrated. They block the initiation of tumours in a variety of tissues e.g. liver, bladder, pancreas, colon, small intestine etc. It was reported that the hydrolytic products of methyl sulphinyl GSL are the most potent inducers of phase II enzymes which detoxify carcinogens. Wattenberg (1983) demonstrated, by using animal models, that induction of phase II enzymes directly or indirectly reduces the risk of carcinogenesis. Epidemiological data suggested that dietary intake of cruciferous vegetables may protect against the risk of various types of cancers (Ambrosone et al., 2004; Cohen, Kristal, & Stanfordm, 2000; Verhoeven, Goldbohm, Van Poppel, Verhagen, & Van den Brandt, 1996; Zhang et al., 2000). ITCs have been found to impose significant protection against cancer in animal models induced by a variety of chemical carcinogens (Conaway, Yang, & Chung, 2002; Hecht, 2000; Jiao et al., 1997; Morse et al., 1989 Morse et al., 1991, Stoner et al., 1991; Talalay & Fahey, 2001; Wattenberg, 1977; Yang et al., 2002).

Many studies have indicated that SFN has potent anticancer effects. Zhang, Kensler, Cho, Posner, and Talalay (1994) reported that SFN offered significant protection against 9,10-dimethyl-1,2-benzanthracene-induced mammary tumorigenesis in rats. SFN as well as its *N*-acetylcysteine conjugate, administered during the post-initiation period significantly inhibited azoxymethane-induced colonic aberrant crypt foci formation in rats (Chung, Conaway, Rao, & Reddy, 2000). Singh, Xiao, Lew, Dhir, and Singh (2004) reported that SFN inhibited proliferation of cultured PC-3 human prostate cancer cells by inducing apoptosis. Rosea, Huangb, Ongb, and Whiteman (2005) reported that ITCs (4-methysulfinylbutyl and 7-methylsulphinylheptyl isothiocyanates) derived form *Brassica oleracea* var. *italica* (broccoli) and *Rorippa nasturtium-aquaticum* (watercress) inhibit metalloproteinase 9 (extracellular endopeptidase that selectively degrade the components of various extracellular matrixes) activities and also suppress the invasive potential of human MDA-MB-231 breast cancer cells *in vitro*. Chemoprotective activities of different GSLs are presented in Table 6.

These compounds work against various cancer cells by induction of antioxidant and detoxifying enzymes such as glutathione-S-transferases and UDP-glucuronosyl transferase and by inhibition of carcinogen-activating enzymes such as cytochrome P450 or altering steroid hormone metabolism. Apoptosis induction through various signal transduction pathways is another mode of action of these compounds. SFN-induced apoptosis was associated with upregulation of BAX (promoter of apoptosis), down-regulation of BCL-2 (suppressor of apoptosis) and activation of caspases-3, -9 and -8 (executers of apoptosis). It was observed that SFN-induced apoptosis and cleavage of procaspase-3 and poly (ADP-ribose) polymerase (PARP), substrates for caspases, were blocked upon pretreatment of cells with pan caspase inhibitor z-VADfmk and specific inhibitors of caspase-9 (z-LEHDfmk) and caspase-8 (z-IETDfmk), suggesting involvement of both caspase-9 and caspase-8 pathways in SFN-induced cell death (Singh et al., 2004).

6. Conclusion

GSLs comprise a distinctive group of bioactive compounds possessing wide array of bioactivities. They are not only important to plants as they act as their major defense system but also to humans in many ways. Natural products are in demand nowadays for the control of pathogens due to the detrimental effects of synthetic chemicals and orthodox practices. GSLs, among other natural products, are a preferred choice among farmers for the control of pathogens as they are safer fumigants in pest control. These natural products are considered to be fully biodegradable and are non-toxic, making them eligible contenders for integrated pest management. However the potential of these compounds in agriculture needs to be fully exploited. Earlier research was focused on lowering the GSL content from the plant tissues because of their characteristic property of imparting bitterness but recently their tremendous benefit in agriculture and medicine has encouraged the plant breeders to develop varieties containing increased levels of GSLs.

However, another potential benefit of GSLs as cancer chemopreventive agents deserves further attention. Extensive body of literature demonstrates that this group of compounds acts as potent chemopreventive agents either by enhancing apoptosis in cancer cells, by arresting cell cycle progression etc. Some of these compounds have also shown encouraging results in clinical trials showing their strong potential in drug development against various cancers. However, there are still many areas that need further research to avail the full health benefits of these compounds. Studies should be conducted to explore the potential of these compounds for the prevention of various other diseases. At present, there is a need to further unravel, characterize, patent and commercialize the protective components like glucosinolates from different plants for the benefit of humans and plant health. Biochemical mechanisms and pathways responsible for different activities of GSLs are still not well understood and deserve further exploration.

References

Ahman, I. (1986). Toxicities of host secondary compounds to eggs of the *Brassica* specialist *Dasineura brassicae*. *Journal of Chemical Ecology, 12*, 1481–1488.

Al-Khatib, K., Libbey, C., & Boydston, R. (1997). Weed suppression with *Brassica* green manure crops in green pea. *Weed Science, 45*, 439–445.

Ambrosone, C. B., McCann, S. E., Freudenheim, J. L., Marshall, J. R., Zhang, Y., & Shields, P. G. (2004). Breast cancer risk in premenopausal women is inversely associated with consumption of broccoli, a source of isothiocyanates, but is not modified by GST genotype. *The Journal of Nutrition, 134*, 1134–1138.

Angus, J. F. (1994). Biofumigation: isothiocyanates released from *Brassica* roots inhibit the growth of the take-all fungus. *Plant and Soil, 162*, 107–112.

Barillari, J., Canistro, D., Paolini, M., Ferroni, F., Pedulli, G. F., Iori, R., et al. (2005). Direct antioxidant activity of purified glucoerucin, the dietary secondary metabolite contained in rocket (*Eruca sativa* Mill.) seeds and sprouts. *Journal of Agricultural and Food Chemistry, 53*, 2475–2482.

Barton, D., & Ollis, W. D. (1979). *Comprehensive organic chemistry: The synthesis and reactions of organic compounds*. (pp. 461–477). New York: Pergamon.

Beekhuis, H. A. (1975). Technology and industrial applications. In A. A. Newman (Ed.), *Chemistry and biochemistry of thiocyanic acid and its derivatives* (pp. 222–255). London: Academic Press.

Bending, G. D., & Lincoln, S. D. (2000). Inhibition of soil nitrifying bacteria communities and their activities by glucosinolate hydrolysis products. *Soil Biology & Biochemistry, 32*, 1261–1269.

Bhardwaj, H. L., Hamama, A. A., Porter, D. M., & Reese, P. F., Jr. (1996). Rapeseed meal as a natural pesticide. In J. Janick (Ed.), *Progress in new crops* (pp. 615–619). Arlington, VA: ASHS Press.

Bonnesen, C., Eggleston, I. M., & Hayes, J. D. (2001). Dietary indoles and isothiocyanates that are generated from cruciferous vegetables can both stimulate apoptosis and confer protection against DNA damage in human colon cell lines. *Cancer Research, 61*, 6120–6130.

Borek, V., Elberson, L. R., McCaffrey, J. P., & Morra, M. J. (1995). Toxicity of aliphatic and aromatic isothiocyanates to eggs of the black vine weevil (Coleoptera: Curculionidae). *Journal of Economic Entomology, 88*, 1192–1196.

Brown, P. D., & Morra, M. J. (1995). Hydrolysis products of glucosinolates in *Brassica napus* tissues as inhibitors of seed germination. *Plant and Soil, 181*, 307–316.

Brown, P. D., & Morra, M. J. (1997). Control of soil-borne plant pests using glucosinolate-containing plants. *Advances in Agronomy, 61*, 167–231.

Brown, P. D., Morra, M. J., McCaffrey, J. P., Auld, D. L., & Williams, L., III (1991). Allelochemicals produced during glucosinolate degradation in soil. *Journal of Chemical Ecology, 17*, 2021–2034.

Buhler, D. D., Kohler, K. A., & Foster, M. S. (2001). Corn, soybean, and weed responses to spring-seeded smother plants. *Journal of Sustainable Agriculture, 18*, 63–79.

Chan, M. K. Y., & Close, R. C. (1987). Aphanomyces root rot of peas control by the use of cruciferous amendments. *New Zealand Journal of Agricultural Research, 30*, 225–233.

Chen, Y. R., Han, J., Kori, R., Kong, A. N., & Tan, T. H. (2002). Phenylethyl isothiocyanate induces apoptotic signaling via suppressing phosphatase activity against c-Jun N-terminal kinase. *The Journal of Biological Chemistry, 277*, 39334–39342.

Chew, F. S. (1988). Biological effects of glucosinolates. In H. G. Cutler (Ed.), *Biologically active natural products: Potential use in agriculture* (pp. 155–181). Washington, D.C.: American Chemical Society.

Chiao, J. W., Chung, F., Krzeminski, J., Amin, S., Arshad, R., Ahmed, T., et al. (2000). Modulation of growth of human prostate cancer cells by the *N*-acetylcysteine conjugate of phenethyl isothiocyanate. *International Journal of Oncology, 16*, 1215–1219.

Chung, F. L., Conaway, C. C., Rao, C. V., & Reddy, B. S. (2000). Chemoprevention of colonic aberrant crypt foci in Fischer rats by sulforaphane and phenethyl isothiocyanate. *Carcinogenesis, 21*, 2287–2291.

Chung, W. C., Huang, J. W., Huang, H. C., & Jen, J. F. (2003). Control by *Brassica* seed pomace combined with *Pseudomonas boreopolis*, of damping-off of watermelon caused by *Pythium* sp. *Canadian Journal of Plant Pathology, 25*, 285–294.

Cohen, J. H., Kristal, A. R., & Stanfordm, J. L. (2000). Fruit and vegetable intakes and prostate cancer risk. *Journal of the National Cancer Institute, 92*, 61–68.

Conaway, C. C., Yang, Y. M., & Chung, F. L. (2002). Isothiocyanates as cancer chemopreventive agents: their biological activities and metabolism in rodents and humans. *Current Drug Metabolism, 3*, 233–255.

Cover, C. M., Hsieh, S. J., Cram, E. J., Hong, C., Riby, J. E., Bjeldanes, L. F., et al. (1999). Indole-3-carbinol and tamoxifen cooperate to arrest the cell cycle of MCF-7 human breast cancer cells. *Cancer Research, 59*, 1244–1251.

Dandurand, L. M., Mosher, R. D., & Knudsen, G. R. (2000). Combined effects of *Brassica napus* seed meal and *Trichoderma harzianum* on two soilborne plant pathogens. *Canadian Journal of Microbiology, 46*, 1051–1057.

Dawson, G. W., Doughty, K. J., Hick, A. J., Pickett, J. A., Pye, B. J., Smart, L. E., et al. (1993). Chemical precursors for studying the effects of glucosinolate catabolites on diseases and pests of oilseed rape (*Brassica napus*) or related plants. *Pesticide Science, 39*, 271–278.

Delaquis, P. J., & Sholberg, P. L. (1997). Antimicrobial activity of gaseous allyl isothiocyanate. *Journal of Food Protection, 60*, 943–947.

Drobnica, L., Zemanova, M., Nemec, P., Antos, K., Kristian, P., Stullerova, A., et al. (1967). Antifungal activity of isothiocyanates and related compounds. I. Naturally occurring isothiocyanates and their analogues. *Applied Microbiology, 15*, 701–709.

Ekanayake, A., Kester, J. J., Li, J. J., Zehentbauer, G. N., Bunke, P. R., & Zent, J. B. (2006). Isogard(tm) a natural anti-microbial agent derived from white mustard seed. *Acta Horticulturae, 709*, 101–108.

Fahey, J. W., Haristoy, X., Dolan, P. M., Fahey, J. W., Haristoy, X., Dolan, P. M., et al. (2002). Sulforaphane inhibits extracellular, intracellular, and antibiotic-resistant strains of *Helicobacter pylori* and prevents benzo[a]pyrene-induced stomach tumors. *Proceedings of the National Academy of Sciences of the United States of America, 99*, 7610–7615.

Fahey, J. W., & Talalay, P. (1999). Antioxidant functions of sulforaphane: a potent inducer of phase II detoxication enzymes. *Food and Chemical Toxicology, 37*, 973–979.

Fahey, J. W., Zalcmann, A. T., & Talalay, P. (2001). The chemical diversity and distribution of glucosinolates and isothiocyanates among plants. *Phytochemistry, 56*, 5–51.

Fenwick, G. R., Heaney, R. K., & Mullin, W. J. (1983). Glucosinolates and their breakdown products in food and food plants. *Critical Reviews in Food Science and Nutrition, 18*, 123–201.

Fimognari, C., Nusse, M., Cesari, R., Iori, R., Cantelli-Forti, G., & Hrelia, P. (2002). Growth inhibition, cell-cycle arrest and apoptosis in human T-cell leukemia by the isothiocyanate sulforaphane. *Carcinogenesis, 23*, 581–586.

Gamet-Payrastre, L., Li, P., Lumeau, S., Cassar, G., Dupont, M., Chevolleau, S., et al. (2000). Sulforaphane, a naturally occurring isothiocyanate, induces cell cycle arrest and apoptosis in HT29 human colon cancer cells. *Cancer Research, 60*, 1426–1433.

Gamliel, A., & Stapleton, J. J. (1993). Characterization of antifungal volatile compounds evolved from solarized soil amended with cabbage residues. *Phytopathology, 83*, 899–905.

Gingras, D., Gendron, M., Boivin, D., Moghrabi, A., Theoret, Y., & Beliveau, R. (2004). Induction of medulloblastoma cell apoptosis by sulforaphane, a dietary anticarcinogen from *Brassica* vegetables. *Cancer Letters, 203*, 35–43.

Greenhalgh, J. R., & Mitchell, N. D. (1976). The involvement of flavour volatiles in the resistance to downy mildew of wild and cultivated forms of *Brassica oleracea*. *The New Phytologist, 77*, 391–398.

Hansen, M., Møller, P., Sørensen, H., & de Trejo, M. C. (1995). Glucosinolates in broccoli stored under controlled atmosphere. *Journal of the American Society for Horticultural Science, 120*, 1069–1074.

Haristoy, X., Angioi-Duprez, K., Duprez, A., & Lozniewski, A. (2003). Efficacy of sulforaphane in eradicating *Helicobacter pylori* human gastric xenografts implanted in nude mice. *Antimicrobial Agents and Chemotherapy, 47*, 3982–3984.

Haristoy, X., Fahey, J. W., Scholtus, I., & Lozeniewski, A. (2005). Evaluation of the antimicrobial effects of several isothiocyanates on *Helicobacter pylori*. *Planta Medica, 71*, 326–330.

Hecht, S. S. (2000). Inhibition of carcinogenesis by isothiocyanates. *Drug Metabolism Reviews, 32*, 395–411.

Holst, B., & Williamson, G. (2004). A critical review of the bioavailability of glucosinolates and related compounds. *Natural Product Reports, 21*, 425–447.

Hooker, W. J., Walker, J. C., & Smith, F. G. (1943). Toxicity of beta-phenethyl isothiocyanate to certain fungi. *American Journal of Botany, 30*, 632–637.

Isshiki, K., Tokuoka, K., Mori, R., & Chiba, S. (1992). Preliminary examination of allyl isothiocyanate vapor for food preservation. *Bioscience, Biotechnology, and Biochemistry, 56*, 1476–1477.

Jeong, W. S., Kim, I. W., Hu, R., & Kong, A. N. (2004). Modulatory properties of various natural chemopreventive agents on the activation of NF-kappaB signaling pathway. *Pharmaceutical Research, 21*, 661–670.

Jiao, D., Smith, T. J., Yang, C. S., Pittman, B., Desai, D., Amin, S., et al. (1997). Chemopreventive activity of thiol conjugates of isothiocyanates for lung tumorigenesis. *Carcinogenesis, 18*, 2143–2147.

Johnson, A. W., Golden, A. M., Auld, D. L., & Sumner, D. R. (1992). Effects of rapeseed and vetch as green manure crops and fallow on nematodes and soil-borne pathogens. *Journal of Nematology, 24*, 117–126.

Johnson, C. R., Chun, J., Bittman, R., & Jarvis, W. D. (2004). Intrinsic cytotoxicity and chemomodulatory actions of novel phenethylisothiocyanate sphingoid base derivatives in HL-60 human promyelocytic leukemia cells. *The Journal of Pharmacology and Experimental Therapeutics, 309*, 452–461.

Kim, B. R., Hu, R., Keum, Y. S., Hebbar, V., Shen, V. G., Nair, S. S., et al. (2003). Effects of glutathione on antioxidant response element-mediated gene expression and apoptosis elicited by sulforaphane. *Cancer Research, 63*, 7520–7525.

Kim, S. J., Jin, S., & Ishii, G. (2004). Isolation and structural elucidation of 4-(β-D-glucopyranosyldisulfanyl) butyl glucosinolate from leaves of rocket salad (*Eruca sativa* L.) and its antioxidative activity. *Bioscience, Biotechnology, and Biochemistry, 68*, 2444–2450.

Kirkegaard, J. A., Sarwar, M., Wong, P. T. W., Mead, A., Howe, G., & Newell, M. (2000). Field studies on the biofumigation of take-all by *Brassica* break crops. *Australian Journal of Agricultural Research, 51*, 445–456.

Kirlin, W. G., Cai, J., DeLong, M. J., Patten, E. J., & Jones, D. P. (1999). Dietary compounds that induce cancer preventive phase 2 enzymes activate apoptosis at comparable doses in HT29 colon carcinoma cells. *The Journal of Nutrition, 129*, 1827–1835.

Koike, S., & Subbarao, K. V. (2000). Broccoli residues can control *Verticillium* wilt of cauliflower. *California Agriculture, 4*, 30–33.

Kojima, M., & Oawa, K. (1971). Studies on the effect of isothiocyanates and their analogues on microorganisms. (I) Effects of isothiocyanates on the oxygen uptake of yeasts. *Journal of Fermentation Technology, 49*, 740–746.

Krishnan, G., Holshauser, D. L., & Nissen, S. J. (1998). Weed control in soybean (*Glycine max*) with green manure crops. *Weed Technology, 12*, 97–102.

Kuroiwa, Y., Nishikawa, A., Kitamura, Y., Kanki, K., Ishii, Y., Umemura, T., et al. (2006). Protective effects of benzyl isothiocyanate and sulforaphane but not resveratrol against initiation of pancreatic carcinogenesis in hamsters. *Cancer Letters, 241*, 275–280.

Landis, D. A., & Gould, F. (1988). Screening for phyto-protectants to guard corn seeds/seedlings from southern corn rootworm feeding injury. *Journal of Entomological Science, 23*, 201–211.

Lazzeri, L., Tacconi, R., & Palmieri, S. (1993). In vitro activity of some glucosinolates and their reaction products toward a population of the nematode *Heterodera schachtii*. *Journal of Agricultural and Food Chemistry, 41*, 825–829.

Leblova-Svobodova, S., & Kostir, J. (1962). Action of isothiocyanates on germinating plants. *Experientia, 18*, 554–555.

Lehman, R. S. (1942). Laboratory tests of organic fumigants for wireworms. *Journal of Economic Entomology, 35*, 659–661.

Lewis, J. A., & Papavizas, G. C. (1971). Effect of sulphur-containing volatile compounds and vapors from cabbage decomposition on *Aphanomyces euteiches*. *Phytopathology, 61*, 208–214.

Lichtenstein, E. P., Morgan, D. G., & Mueller, C. H. (1964). Naturally occurring insecticides in cruciferous crops. *Journal of Agricultural and Food Chemistry, 12*, 158–161.

Lichtenstein, E. P., Strong, F. M., & Morgan, D. G. (1962). Identification of 2-phenylethylisothio-cyanate as an insecticide occurring naturally in the edible part of turnips. *Journal of Agricultural and Food Chemistry, 10*, 30–33.

Lin, C. M., Kim, J., Du, W. X., & Wei, C. I. (2000). Bactericidal activity of isothiocyanate against pathogens on fresh produce. *Journal of Food Protection, 63*, 25–30.

Lui, V. W., Wentzel, A. L., Xiao, D., Lew, K. L., Singh, S. V., & Grandis, J. R. (2003). Requirement of a carbon spacer in benzyl isothiocyanate-mediated cytotoxicity and MAPK activation in head and neck squamous cell carcinoma. *Carcinogenesis, 24*, 1705–1712.

McCaffrey, J. P., Williams, L., III, Borek, V., Brown, P. D., & Morra, M. J. (1995). Toxicity of ionic thiocyanate-amended soil to the wireworm, *Limonius californicus* (Coleoptera: Elateridae). *Journal of Economic Entomology, 88*, 793–797.

Mandelova, L., & Totusek, J. (2007). Broccoli juice treated by high pressure: chemoprotective effects of sulforaphane and indole-3-carbinol. *High Pressure Research, 27*, 151–156.

Manesh, C., & Kuttan, G. (2005). Effect of naturally occurring isothiocyanates in the inhibition of cyclophosphamide-induced urotoxicity. *Phytomedicine, 12*, 487–493.

Manici, L. M., Lazzeri, L., Baruzzi, G., Leoni, O., Galletti, S., & Palmieri, S. (2000). Suppressive activity of some glucosinolate enzyme degradation products on *Pythium irregulare* and *Rhizoctonia solani* in sterile soil. *Pest Management Science, 56*, 921–926.

Manici, L. M., Lazzeri, L., & Palmieri, S. (1997). In vitro fungitoxic activity of some glucosinolates and their enzyme-derived products toward plant pathogenic fungi. *Journal of Agricultural and Food Chemistry, 45*, 2768–2773.

Mari, M., Iori, R., Leoni, O., & Marchi, A. (1993). *In vitro* activity of glucosinolate-derived isothiocyanates against post-harvest fruit pathogens. *Annals of Applied Biology, 123*, 155–164.

Mari, M., Iori, R., Leoni, O., & Marchi, A. (1996). Bioassays of glucosinolate-derived isothiocyanates against postharvest pear pathogens. *Plant Pathology, 45*, 753–760.

Matthiessen, J. N., & Shackleton, M. A. (2000). Advantageous attributes of larval whitefringed weevil, *Naupactus leucoloma* (Coleoptera: Curculionidae) for bioassaying soil fumigants, and responses to pure and plant-derived isothiocyanates. *Bulletin of Entomological Research, 90*, 349–355.

Mayton, H. S., Oliver, C., Vaughn, S. F., & Loria, R. (1996). Correlation of fungicidal activity of *Brassica* species with allyl isothiocyanate production in macerated leaf tissue. *Phytopathology, 86*, 267–271.

Mennicke, W. H., Gorler, K., Krumbiegel, G., Lorenz, D., & Rittmann, N. (1988). Studies on the metabolism and excretion of benzyl isothiocyanate in man. *Xenobiotica, 18*, 441–447.

Misiewicz, I., Skupinska, K., & Kasprzycka-Guttman, T. (2003). Sulforaphane and 2-oxohexyl isothiocyanate induce cell growth arrest and apoptosis in L-1210 leukemia and ME-18 melanoma cells. *Oncology Reports, 10*, 2045–2050.

Mithen, R. F., Lewis, B. G., & Fenwick, G. R. (1986). In vitro activity of glucosinolates and their products against *Leptosphaeria maculans*. *Transactions of the British Mycological Society, 87*, 433–440.

Mojtahedi, H., Santo, G. S., Hang, A. N., & Wilson, J. H. (1991). Suppression of root-knot nematode populations with selected rapeseed cultivars as green manure. *Journal of Nematology, 23*, 170–174.

Morse, M. A., Eklind, K. I., Hecht, S. S., Jordan, K. G., Choi, C. I., Desai, D. H., et al. (1991). Structure-activity relationships for inhibition of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone lung tumorigenesis by arylalkyl isothiocyanates in A/J mice. *Cancer Research, 51*, 1846–1850.

Morse, M. A., Wang, C. X., Stoner, G. D., Mandal, S., Conran, P. B., Amin, S. G., et al. (1989). Inhibition of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone-induced DNA adduct formation and tumorigenicity in the lung of F344 rats by dietary phenethyl isothiocyanate. *Cancer Research, 49*, 549–553.

Murugan, S. S., Balakrishnamurthy, P., & Mathew, Y. J. (2007). Antimutagenic effect of broccoli flower head by the Ames *Salmonella* reverse mutation assay. *Phytotherapy Research, 21*, 545–547.

Nadarajah, D., Han, J. H., & Holley, R. A. (2005). Use of mustard flour to inactivate *Escherichia coli* O157:H7 in ground beef under nitrogen flushed packaging. *International Journal of Food Microbiology, 99*, 257–267.

Nastruzzi, C., Cortesi, R., Esposito, E., Menegatti, E., Leoni, O., Iori, R., et al. (1996). In vitro cytotoxic activity of some glucosinolate-derived products generated by myrosinase hydrolysis. *Journal of Agricultural and Food Chemistry, 44*, 1014–1021.

Nishikawa, A., Morse, M. A., & Chung, F. L. (2003). Inhibitory effects of 2-mercaptoethane sulfonate and 6-phenylhexyl isothiocyanate on urinary bladder tumorigenesis in rats induced by *N*-butyl-*N*-(4-hydroxybutyl)nitrosamine. *Cancer Letters, 193*, 11–16.

Noble, R. R. P., Harvey, S. G., & Sams, C. E. (2002). Toxicity of Indian mustard and allyl isothiocyanate to masked chafer beetle larvae. *Plant Health Progress*. doi:10.1094/PHP-2002-0610-01-RS.

Normark, S., Nilsson, C., Normark, B. H., & Hornef, M. W. (2003). Persistent infection with *Helicobacter pylori* and the development of gastric cancer. *Advances in Cancer Research, 90*, 63–89.

Norsworthy, J. K., Brandenberger, L., Burgos, N. R., & Riley, M. (2005). Weed suppression in *Vigna unguiculata* with a spring-seeded Brassicaceae green manure. *Crop Protection, 24*, 441–447.

Olivier, C., Vaughn, S. F., Mizubuti, S. G., & Loria, R. (1999). Variation in allyl isothiocyanate production within *Brassica* species and correlation with fungicidal activity. *Journal of Chemical Ecology, 2*, 2687–2701.

Park, C. M., Taormina, P. J., & Beuchat, L. R. (2000). Efficacy of allyl isothiocyanate in killing enterohemorrhagic *Escherichia coli* O157:H7 on alfalfa seeds. *International Journal of Food Microbiology, 56*, 13–20.

Petersen, J., Belz, R., Walker, F., & Hurle, K. (2001). Weed suppression by release of isothiocyanates from turnip–rape mulch. *Agronomy Journal, 93*, 37–43.

Plumb, G. W., Lambert, N., Chambers, S. J., Wanigatunga, S., Heaney, R. K., Plumb, J. A., et al. (1996). Are whole extracts and purified glucosinolates from cruciferous vegetables antioxidants. *Free Radical Research, 25*, 75–86.

Prestera, T., Zhang, Y., Spencer, S. R., Wilezak, C., & Talalay, P. (1993). The electrophile counterattack response: protection against neoplasia and toxicity. *Advances in Enzyme Regulation, 33*, 281–296.

Pullar, J. M., Thomson, S. J., King, M. J., Turnbull, C. I., Midwinter, R. G., & Hampton, M. B. (2004). The chemopreventive agentphenethyl isothiocyanate sensitizes cells to Fas-mediated apoptosis. *Carcinogenesis, 25*, 765–772.

Rask, L., Andreasson, E., Ekbom, B., Eriksson, S., Pontoppidan, B., & Meijer, J. (2000). Myrosinase: gene family evolution and herbivore defense in Brassicaceae. *Plant Molecular Biology, 42*, 93–113.

Rosea, P., Huangb, Q., Ongb, C. N., & Whiteman, M. (2005). Broccoli and watercress suppress matrix metalloproteinase-9 activity and invasiveness of human MDA-MB-231 breast cancer cells. *Toxicology and Applied Pharmacology, 209*, 105–113.

Rutkowski, A., Bielecka, M., Kornacka, D., Kozlowska, H., & Roezniakowa, B. (1972). Rapeseed meal XX. Influence of toxic compounds of rapeseed meal on the technological properties of propionic acid bacteria. *Journal of Canadian Institute of Food Science and Technology, 5*, 67–71.

Sanchi, S., Odorizzi, S., Lazzeri, L., & Marciano, P. (2005). Effect of *Brassica carinata* seed meal treatment on the *Trichoderma harzianum* t39–*Sclerotinia* species interaction. *Acta Horticulturae, 698*, 287–292.

Sarwar, M., & Kirkegaard, J. A. (1998). Biofumigation potential of brassicas. *Plant and Soil, 201*, 91–101.

Sarwar, M., Kirkegaard, J. A., Wong, P. T. W., & Desmarchelier, J. M. (1998). Biofumigation potential of brassicas. III *In-vitro* toxicity of isothiocyanates to soil-borne fungal pathogens. *Plant and Soil, 201*, 103–112.

Satyan, K. S., Swamy, N., Dizon, D. S., Singh, R., Granai, C. O., & Brard, L. (2006). Phenethyl isothiocyanate (PEITC) inhibits growth of ovarian cancer cells by inducing apoptosis: role of caspase and MAPK activation. *Gynecologic Oncology, 103*, 261–270.

Schnug, E., & Ceynowa, J. (1990). Phytopathological aspects of glucosinolates in oilseed rape. *Journal of Agronomy and Crop Science, 165*, 319–328.

Schreiner, R. P., & Koide, R. T. (1993). Antifungal compounds from the roots of mycotrophic and non-mycotrophic plant species. *The New Phytologist, 123*, 99–105.

Sedmikova, M., Turek, B., Barta, I., Strohalm, J., Smerak, P., Houska, M., et al. (1999). Evaluation of the antimutagenic activity of pressure treated and heat pasteurized cauliflower juice. *Czech Journal of Food Sciences, 17*, 149–152.

Seo, S. T., & Tang, C. S. (1982). Hawaiian fruit flies (Diptera: Tephritidae): toxicity of benzyl isothiocyanate against eggs or 1st instars of three species. *Journal of Economic Entomology, 75*, 1132–1135.

Serra, B., Rosa, E., Iori, R., Barillari, J., Cardoso, A., Abreu, C., et al. (2002). In vitro activity of 2-phenylethyl glucosinolate, and its hydrolysis derivatives on the root-knot nematode *Globodera rostochiensis* (Woll.). *Scientia Horticulturae, 92*, 75–81.

Sexton, A. C., Kirkegaard, J. A., & Howlett, B. J. (1999). Glucosinolates in *Brassica juncea* and resistance to Australian isolates of *Leptosphaeria maculans*, the blackleg fungus. *Australasian Plant Pathology, 28*, 95–102.

Shishu, Singla, A. K., & Kaur, I. P. (2003). Inhibition of mutagenicity of food-derived heterocyclic amines by sulphoraphane – an isothiocyanate isolated from radish. *Planta Medica, 69*, 184–186.

Singh, A. V., Xiao, D., Lew, K. L., Dhir, R., & Singh, S. V. (2004). Sulforaphane induces caspase-mediated apoptosis in cultured PC-3 human prostate cancer cells and retards growth of PC-3 xenografts in vivo. *Carcinogenesis, 25*, 83–90.

Singh, R. K., Lange, T. S., Kim, K. K., Zou, Y., Lieb, C., Sholler, G. L., et al. (2007). Effect of indole ethyl isothiocyanates on proliferation, apoptosis and MAPK signalling in neuroblastoma cell lines. *Bioorganic & Medicinal Chemistry Letters, 17*, 5846–5852.

Singletary, K., & MacDonald, C. (2000). Inhibition of benzo(a)pyrene- and 1,6-dinitropyrene-DNA adduct formation in human mammary epithelial cells by dibenzoylmethane and sulforaphane. *Cancer Letters, 155*, 47–54.

Smelt, J. H., Crum, S. J. H., & Teunissen, W. (1989). Accelerated transformation of the fumigant methyl isothiocyanate in soil after repeated application of metham-sodium. *Journal of Environmental Science and Health, 24*, 437–455.

Smissman, E. E., Beck, S. D., & Boots, M. R. (1961). Growth inhibition of insects and a fungus by indole-3-acetonitrile. *Science, 133*, 462.

Smith, B. J., Sarwar, M., Wong, P. T. W., & Kirkegaard, J. A. 1999. Suppression of cereal pathogens by canola root tissues in soil. In *Proceedings of the 10th international rapeseed congress*, Australia, pp. 334.

Smith, N. R., Dawson, V. T., & Wenzel, M. E. (1945). The effect of certain herbicides on soil microorg anisms. *Proceedings of the Soil Science Society of America, 10*, 197–201.

Smolinska, U., & Horbowicz, M. (1999). Fungicidal activity of volatiles from selected cruciferous plants against resting propagules of soil-borne fungal pathogens. *Journal of Phytopathology, 147*, 119–124.

Smolinska, U., Knudsen, G. R., Morra, M. J., & Borek, V. (1997). Inhibition of *Aphanomyces euteiches* f. sp. *pisi* by volatiles produced by hydrolysis of *Brassica napus* seed meal. *Plant Disease, 81*, 288–292.

Smolinska, U., Morra, M. J., Knudsen, G. R., & James, R. L. (2003). Isothiocyanates produced by Brassicaceae species as inhibitors of *Fusarium oxysporum*. *Plant Disease, 87*, 407–412.

Srivastava, S. K., & Singh, S. V. (2004). Cell cycle arrest, apoptosis induction and inhibition of nuclear factor kappa B activation in anti-proliferative activity of benzyl isothiocyanate against human pancreatic cancer cells. *Carcinogenesis, 25*, 1701–1709.

Srivastava, S. K., Xiao, D., Lew, K. L., Hershberger, P., Kokkinakis, D. M., Johnson, C. S., et al. (2003). Allyl isothiocyanate, a constituent of cruciferous vegetables, inhibits growth of PC-3 human prostate cancer xenografts in vivo. *Carcinogenesis, 24*, 1665–1670.

Steele, V. E. (2003). Current mechanistic approaches to the chemoprevention of cancer. *Journal of Biochemistry and Molecular Biology, 36*, 78–81.

Stoner, G. D., Morrissey, D. T., Heur, Y. H., Daniel, E. M., Galati, A. J., & Wagner, S. A. (1991). Inhibitory effects of phenethyl isothiocyanate on *N*-

nitrosobenzylmethylamine carcinogenesis in the rat esophagus. *Cancer Research, 51*, 2063–2068.
Talalay, P., & Fahey, J. W. (2001). Phytochemicals from cruciferous plants protect against cancer by modulating carcinogen metabolism. *The Journal of Nutrition, 131*, 3027–3033.
Tiedink, H. G. M., Malingre, C. E., van Broekhoven, L. W., Jongen, W. M. F., Lewis, J., & Fenwick, G. R. (1991). Role of glucosinolates in the formation of *N*-nitroso compounds. *Journal of Agricultural and Food Chemistry, 39*, 922–926.
Troncoso, R., Espinoza, C., Sanchez-Estrada, A., Tiznado, M. E., Hugo, S., & Garcia, H. S. (2005). Analysis of the isothiocyanates present in cabbage leaves extract and their potential application to control *Alternaria* rot in bell peppers. *Food Research International, 38*, 701–708.
Tsao, R., Peterson, C. J., & Coats, J. R. (2002). Glucosinolate breakdown products as insect fumigants and their effect on carbon dioxide emission of insects. *BMC Ecology, 2*, 5.
Vaughn, S., Palmquist, D., Duval, S., & Berhow, M. (2006). Herbicidal activity of glucosinolate-containing seedmeals. *Weed Science, 54*, 743–748.
Verhoeven, D. T., Goldbohm, R. A., Van Poppel, G., Verhagen, H., & Van den Brandt, P. A. (1996). Epidemiological studies on *Brassica* vegetables and cancer risk. *Cancer Epidemiology, Biomarkers & Prevention, 5*, 733–748.
Vierheilig, H., & Ocampo, J. A. (1990). Effect of isothiocyanates on germination of spores of *G. mosseae*. *Soil Biology and Biochemistry, 22*, 1161–1163.
Wadleigh, R. W., & Yu, S. J. (1988). Detoxification of isothiocyanate allelochemicals by gluta-thione transferase in three lepidopterous species. *Journal of Chemical Ecology, 14*, 1279–1288.
Walker, J. C., Morell, S., & Foster, H. H. (1937). Toxicity of mustard oils and related sulfur compounds to certain fungi. *American Journal of Botany, 24*, 536–541.
Wang, L., Liu, D., Ahmed, T., Chung, F. L., Conaway, C., & Chiao, J. W. (2004). Targeting cell cycle machinery as a molecular mechanism of sulforaphane in prostate cancer prevention. *International Journal of Oncology, 24*, 187–192.
Wattenberg, L. W. (1977). Inhibition of carcinogenic effects of polycyclic hydrocarbons by benzyl isothiocyanate and related compounds. *Journal of the National Cancer Institute, 58*, 395–398.
Wattenberg, L. W. (1983). Inhibition of neoplasia by minor dietary constituents. *Cancer Research, 43*, 2448–2453.
Williams, L., III, Morra, M. J., Brown, P. D., & McCaffrey, J. P. (1993). Toxicity of allyl isothiocyanate-amended soil to *Limonius californicus* (Mann.) (Coleoptera: Elateridae) wireworms. *Journal of Chemical Ecology, 19*, 1033–1046.
Winkler, H., & Otto, G. (1980). Replant losses with strawberries and suggestions for their reduction. *Horticultural Abstracts, 50*, 344.
Wood, J. L. (1975). Biochemistry. In A. A. Newman (Ed.), *Chemistry and biochemistry of thiocyanic acid and its derivatives* (pp. 156–221). London: Academic Press.
Wu, X., Kassie, F., & Mersch-Sundermann, V. (2005). Induction of apoptosis in tumor cells by naturally occurring sulfur-containing compounds. *Mutation Research, 589*, 81–102.
Xiao, D., & Singh, S. V. (2002). Phenethyl isothiocyanate-induced apoptosis in p53-deficient PC-3 human prostate cancer cell line is mediated by extracellular signal-regulated kinases. *Cancer Research, 62*, 3615–3619.
Xiao, D., Srivastava, S. K., Lew, K. L., Zeng, Y., Hershberger, P., Johnson, C. S., et al. (2003). Allyl isothiocyanate, a constituent of cruciferous vegetables, inhibits proliferation of human prostate cancer cells by causing G2/M arrest and inducing apoptosis. *Carcinogenesis, 24*, 891–897.
Xu, K., & Thornalley, P. J. (2000). Studies on the mechanism of the inhibition of human leukaemia cell growth by dietary isothiocyanates and their cysteine adducts in vitro. *Biochemical Pharmacology, 60*, 221–231.
Yang, Y. M., Conaway, C. C., Chiao, J. W., Wang, C. X., Amin, S., Whysner, J., et al. (2002). Inhibition of benzo(*a*)pyrene-induced lung tumorigenesis in A/J mice by dietary *N*-acetylcysteine conjugates of benzyl and phenethyl isothiocyanates during the postinitiation phase is associated with activation of mitogen-activated protein kinases and p53 activity and induction of apoptosis. *Cancer Research, 62*, 2–7.
Yu, R., Mandlekar, S., Harvey, K. J., Ucker, D. S., & Kong, A. N. (1998). Chemopreventive isothiocyanates induce apoptosis and caspase-3-like protease activity. *Cancer Research, 58*, 402–408.
Zasada, I. A., & Ferris, H. (2003). Sensitivity of *Meloidogyne javanica* and *Tylenchulus semipenetrans* to isothiocyanates in laboratory assays. *Phytopathology, 93*, 747–750.
Zasada, I. A., & Ferris, H. (2004). Nematode suppression with brassicaceous amendments: application based upon glucosinolate profiles. *Soil Biology and Biochemistry, 36*, 1017–1024.
Zhang, S. M., Hunter, D. J., Rosner, B. A., Giovannucci, E. L., Colditz, G. A., Speizer, F. E., et al. (2000). Intakes of fruits, vegetables, and related nutrients and the risk of non-Hodgkin's lymphoma among women. *Cancer Epidemiology, Biomarkers & Prevention, 9*, 477–485.
Zhang, Y., Kensler, T. W., Cho, C. G., Posner, G. H., & Talalay, P. (1994). Anticarcinogenic activities of sulforaphane and structurally related synthetic norbornyl isothiocyanates. *Proceedings of the National Academy of Sciences of the United States of America, 91*, 3147–3150.
Zsolnai, T. (1966). Antimicrobial effect of thiocyanates and isothiocyanates. *Arztliche Forschung, 16*, 870–876.