Jordan Journal of Agricultural Sciences, Volume **11**, No.**1** 2015

Glucosinolates and their Important Biological and Anti Cancer Effects: A Review

V. Rameeh *

ABSTRACT

Glucosinolates are sulfur-rich plant metabolites of the family of Brassicace and other fifteen families of dicotyledonous angiosperms including a large number of edible species. At least 130 different glucosinolates have been identified. Following tissue damage, glucosinolates undergo hydrolysis catalysed by the enzyme myrosinase to produce a complex array of products which include volatile isothiocyanates and several compounds with goitrogenic and anti cancer activities. Glucosinolates are considered potential source of sulfur for other metabolic processes under low-sulfur conditions, therefore the breakdown of glucosinolates will be increased under sulfur deficiency. However, the pathway for sulfur mobilization from glucosinolates has not been determined.Glucosinolates and their breakdown products have long been recognized for their fungicidal, bacteriocidal, nematocidal and allelopathic properties and have recently attracted intense research interest because of their cancer chemoprotective attributes. Glucosinolate derivatives stop cancer via destroying cancer cells, and they also suppress genes that create new blood vessels, which support tumor growth and spread. These organic compounds also reduce the carcinogenic effects of many environmental toxins by boosting the expression of detoxifying enzymes.

Keywords: Brassicace, dicotyledonous, mobilisation, myrosinase,sulfur.

INTRODUCTION

Glucosinolates are sulfur- and nitrogen-containing plant secondary metabolites common in the order Capparales, which comprises the *Brassicaceae* family with agriculturally main crops, *Brassica* vegetables, and the model plant *Arabidopsis thaliana*. Glucosinolates are hydrolyzed to different bioactive breakdown products by the endogenous enzyme myrosinase (Bones and Rossiter, 1996; Falk et al., 2007). These breakdown products include isothiocyanates, thiocyanates, oxazolidinethiones and nitriles (Fenwick et al., 1983). Glucosinolates can be divided into three classes based on the structure of different amino acid precursors(Table 1): 1. Aliphatic glucosinolates derived from methionine, isoleucine, leucine or valine, 2. aromatic glucosinolates derived from phenylalanine or tyrosine, and 3. indole glucosinolates derived from tryptophan (Fig. 1). The biosynthesis of glucosinolates involves three phases: (*i*) amino acid chain elongation, in which additional methylene groups are inserted into the side chain, (*ii*) change of the aminoacidmoiety to the glucosinolate core structure, (*iii*) and following side chain modifications (Wittstock and Halkier, 2002). More than 130 glucosinolates have been identified. Their structural diversity arises from side chain elongation of the amino acid precursors prior to make up the glucosinolate core

* Agriculture and Natural Resources Research Center of Mazandran, Sari, Iran.
vrameeh@yahoo.com
Received on 16/7/2013 and Accepted for Publication on 27/1/2014.

structure and from a spacious range of secondary modifications viz. oxidation, desaturation, hydroxylation, methoxylation, sulfation and glucosylation (Wittstock and Halkier, 2002; Halkier and Gershenzon, 2006). The chemical nature of hydrolysis products depends mostly on the structure of the glucosinolate side chain, plant species and response conditions (Bones and Rossiter, 1996; Rask *et al.,* 2000). Glucosinolates and their hydrolysis products are often studied as plant defense system in opposition to insects, herbivores and certain microbial pathogens. Besides, they serve as attractants to specialist insects feeding on crucifers (Wittstock *et al.,* 2004). Mostly volatile hydrolysis products are responsible for trait taste and smell of cruciferous vegetables. In a number of *Brassica* vegetables for instance cauliflower, Brussels sprouts, cabbage and broccoli, glucosinolate degradation products, especially isothiocyanates have been shown to have anticarcinogenic properties (Fahey *et al.,* 2001). However, the presence of degradation products is not always beneficial. For instance, the amount of rape meal that can be used in animal food supplement is limited due to the goitrogenic effect of 5-vinyloxazolidine- 2-thione, the spontaneous cyclization product of 2-hydroxy-3-butenyl glucosinolate which accounts for up to 80% of total glucosinolates in rapeseed (Chens, 2001).

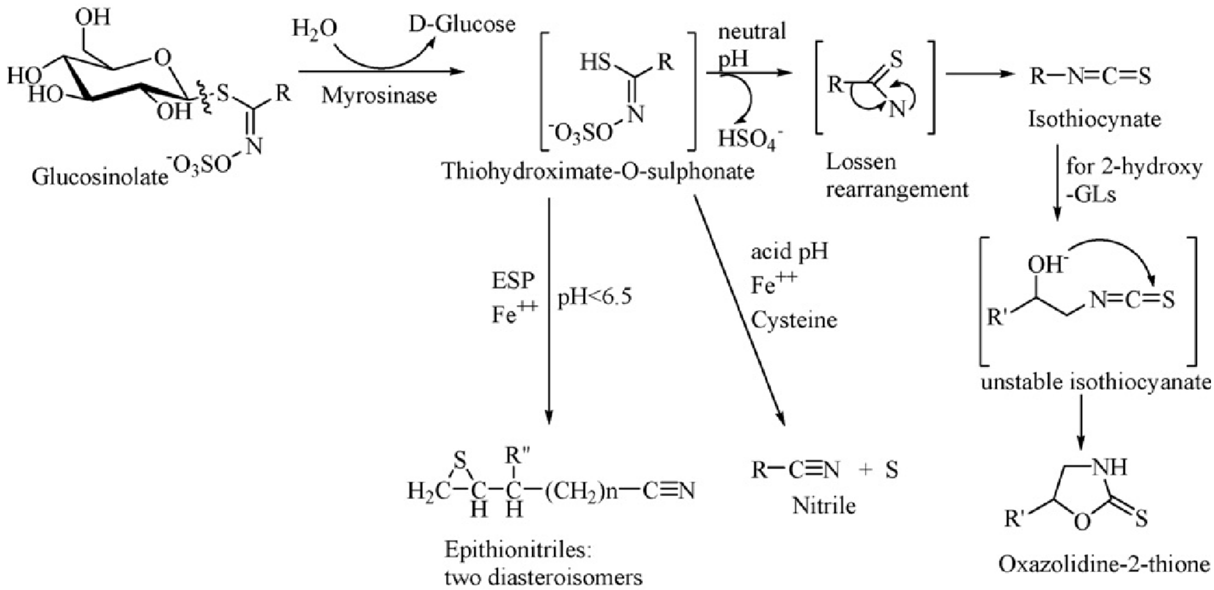


Fig. 1. Schematic pathways of enzymatic hydrolysis of glucosinolate(Tripathi and Mishra, 2007).

Glucosinolates and the sulfur budget

Brassica species require a high amount of sulfur. It has been proposed that glucosinolates may act as a sulfurstorage pool which can be mobilized through hydrolysis by myrosinases (Schnug and Ceynowa, 1990). Glucosinolates also contain nitrogen and the glucosinolate-myrosinase system can be considered to be a sink for both nutrients. It was expected that fertilizers would have an influence on this system in *Brassica* crops (Rask *et al.,* 2000). Zhao

et al. showed a clear influence of both nitrogen and sulfur supply on glucosinolates in *B. napus* (Mailer, 1989). Their results suggest an increase in nitrogen supply favors the hydrolysis step converting 3-butenyl to (2*R*)-2- ydroxy-3-butenyl glucosinolates. Aliphatic glucosinolates show a greater sensitivity to sulfur deficiency than indole glucosinolates due to the already sulfur containing precursor methionine. Several studies showed that increased sulfur availability increased the glucosinolate content (Underhill *et al.,* 1980; Kaur *et al.,* 1990)*,* whereas a decreased sulfur supply resulted in a decrease of free sulfate and glucosinolates while at the same timemyrosinase activity increased *(65, 67).*The concentration of whole sulfur in plant tissues has been reported to be 0.5 to 1.5% of the dry weight of the plant (Blake- Kalff *et al.,* 1998, 2000). The primary inorganic form weight and that sulfur atoms comprise 15–20% of the molecular masses of all glucosinolates. Given the somewhat high amount of sulfur present in glucosinolates, changes in sulfur provide can be expected to have a main effect on glucosinolate content. Remarkably, members of the glucosinolate-containing Brassicaceae appear to need higher amounts of sulfur than plants of non-glucosinolate families, and display sulfur deficiency indications, such as chlorosis, inhibited growth, and delayed maturity at higher levels of sulfur supply than other plants (Walker and Booth, 2003). It was shown that crucifers possess 1.1– 1.7% sulfur per gram dry weight in their seeds, while cereals have a sulfur content of 0.18–0.19% (Marschner, 1995). In vegetative tissue with adequate sulfur supply, the typical weight ratio of organic sulfur to organic nitrogen is 0.025 for legumes, 0.032 for cereals, and 0.055 for *Brassica* spp. (Dijkshoorn and Van Wijk, 1967). The high sulfur content of Brassicaceae may reflect their production of specialised sulfur-containing metabolites, such as glucosinolates and defensins. Under natural conditions, the high amounts of sulfur required by Brassicaceae may be supplied by the complement of soil microorganisms related with their roots, which oxidise elemental sulfur to sulfate, thiosulfate, and tetrathionate (Grayston and Germida, 1991; Vong *et al.,* 2002).

Different types of glucosinolates

Glucosinolates are categorized into three classes based on their precursor amino acids and side chain variations. Arvind *et al.,* (2012) suggested that these three classes of glucosinolates are independently biosynthesized and adjusted by different sets of gene families from separate amino acids. Each class is briefly discussed below.

1. Aliphatic glucosinolates

Aliphatic glucosinolates are the major group of glucosinolates in *Brassica* species, contributing about 90% of the total glucosinolate content of the plant (Table 1). Glucosinolates are constitutively biosynthesized *de novo* in cruciferous plants, although their degradation is highly regulated by spatial and temporal division of glucosinolates and myrosinases within the plant based on environmental and biotic stresses. Hydrolysis of glucosinolates makes a large number of biologically active compounds that have a variety of functions. The most common hydrolysis products of aliphatic glucosinolates in many cruciferous species are isothiocyanates that are formed by the rearrangement of aglycone with carbon oxime adjacent to the nitrogen at neutral pH while at acidic pH, nitriles are the predominant products (Fahey *et al.,* 2001). These unstable compounds are cyclised to a class of substances responsible for goiter in animals (Griffiths *et al.,* 1998). By contrast, sulforaphane is one of the derivatives of glucoraphanin, an aliphatic glucosinolate that has several valuable properties for humans and animals. It is known as an inducer of phase II enzymes such as glutathione transferases and quinone reductases of the xenobiotic pathway in human prostate cells (Zhang *et al.,* 1992; Faulkner *et al.,* 1998). The phase II enzymes are maintained the detoxification of electrophilic carcinogens that can make to mutations in DNA and cause different kinds of cancers (Mithen *et al.,* 2000). Enhanced using up cruciferous vegetables appears to decrease the risk of cancers (Nestle, 1997; Talalay 2000; Brooks et al., 2001). The sulforaphane content of these vegetables could be a leading factor in the reduction. Another less documented health benefit of sulforaphane is the embarrassment of *Helicobacter pylori*, a pathogen of peptic ulcers and gastric cancer (Fahey *et al.,* 2002). Sulforaphane also protects human retinal cells against severe oxidative stresses (Gao et al., 2001). Isothiocyanates and other breakdown products of glucosinolates play important roles as repellents of certain insects and pests (Rask *et al.,* 2000; Agrawal and Kurashige, 2003; Barth and Jander, 2006; Benderoth *et al.,* 2006). Leaves of the mutant *myb28myb29* in *Arabidopsis* with low aliphatic glucosinolate content, when fed to the lepidopteran insect *Mamestra brassicae,* enhanced larval weight by 2.6 fold (Beekwilder *et al.,* 2008). Glucosinolates may have specific repulsive or anti-nutritional effects on specific classes of insects and microorganisms. Some *in vitro* studies demonstrated that glucosinolate degradation products, isothiocyanates and nitriles, inhibited fungal and bacterial pathogen growth (Brader *et al.,* 2006; Tierens *et al.,* 2001). In *Arabidopsis,* over expression of *CYP79D2* from cassava increased accumulation of isopropyl and methylpropyl aliphatic glucosinolates and transformed plants showed enhanced resistance against a bacterial soft-rot disease (Brader *et al.,* 2006). Birch *et al.,* (1992) reported that biotic stresses such as pest damage in *Brassica* species alters glucosinolate profiles in roots, stems, leaves and flowers. This suggests that a phytoanticipin property of glucosinolates is involved in the plant defence mechanisms of *Brassica*. Glucosinolates and their breakdown products have many biological functions, with a few compounds acting as biopesticides, biofungicides and soil fumigants, while others play roles in appeal of pollinators and supply oviposition cues to definite insects. The attraction of specialized insects could be due to the glucosinolate-sequestering phenomenon of some insects including harlequin bugs, sawflies, and some homoptera including aphids (Bridges *et al.,* 2002; Mewis *et al.,* 2002).

2. Indole glucosinolates

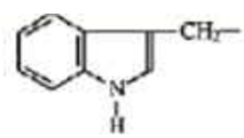
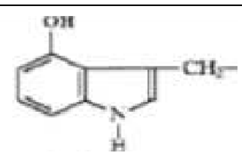
Indole glucosinolates in cruciferous plants are obtained from tryptophan and possess variable R group side chains(Table 1). The moderately high content of indole glucosinolates in the model plant *Arabidopsis* has improved our awareness of the biosynthesis, transportation and functional properties of this group of glucosinolates (Petersen *et al.,* 2002; Brown *et al.,* 2003). Side chain alteration in indole glucosinolates take places through hydroxylations and methoxylations catalysed by several enzymes. Indole glucosinolate types and contents in different organs of the plant are strongly affected by environmental effects. Four main indole glucosinolates have been detected in most *Brassica* species including glucobrassicin, neoglucobrassicin, 4-methoxyglucobrassicin and 4-hydroxyglucobrassicin. Similar to aliphatic glucosinolates, breakdown products of indole glucosinolates have multiple biological functions. Indole-3-carbinol derived from glucobrassicin has strong anticarcinogenic activity (Hrncirik *et al.,* 2001). The indole glucosinolate derived compound 4-methoxyglucobrassicin has strong insect restriction activity (Kim and Jander, 2007; De Vos *et al.,* 2008). Osbourn, (1996) reported antimicrobial activities of indole glucosinolates and their breakdown products in *Brassica* species. Several studies suggest that there is a metabolic association between indole glucosinolates and the plant hormone indole-3-acetic acid (IAA). In the consecutive reactions, indole glucosinolates are degraded into indole acetonitrile (IAN), which is then hydrolyzed by nitrilases into IAA . In clubroot infected *Brassica* roots, indole glucosinolate-based induction of IAA was detected to be responsible for gall formation. The IAA production from indole glucosinolates during gall formation is related to a signalling cascade of IAA and cytokinin complex (Ugajin *et al.,* 2003). Structural similarity data indicates that the indole alkaloid, brassinin, and possibly other cruciferous phytoalexins are derived from glucobrassicin. Studies in rapeseed, mustard and *Arabidopsis* have suggested that methyl jasmonate and wounding induce the biosynthesis of particular indole glucosinolates (Bodnaryk 1992; Brader *et al.,* 2006).

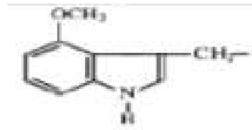
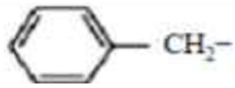
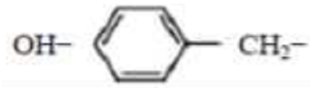
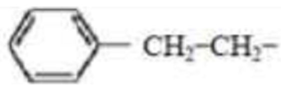
3. Aromatic glucosinolates

The third class of glucosinolates in cruciferous species is aromatic or benzylic glucosinolates,

Yielded from the aromatic parental amino acids phenylalanine and tyrosine(Table 1). Very limited information is available about aromatic glucosinolates at qualitative or quantitative levels. Aromatic glucosinolates are biosynthesized independently from other glucosinolates, which is apparently due to participation of different amino acid precursors in the biosynthesis of the different classes of glucosinolates (Kliebenstein *et al.,* 2001a). Cloning and functional characterization of the *CYP79A* gene of *Arabidopsis* suggests that cytochrome P450-dependent monooxygenase catalyzes the reaction from phenylalanine to phenylacetaldoxime in aromatic glucosinolate biosynthesis (Wittstock and Halkier, 2000). Five aromatic glucosinolates have been recognized in *Brassicaceae*: glucotropaeolin, glucosinalbin, gluconasturtiin, glucobarbarin and glucomalcomiin. The distinctive aroma and spiciness of condiment *Brassica* plant parts, such as the leaves and seeds of white (*Sinapis alba*) and black (*B. nigra*) mustards, is due to the presence of these aromatic glucosinolates (Kliebenstein *et al.,* 2001a).

Table 1. Chemical structures of different classes of glucosinolates in Brassica species.

Glucosinolate name	Trivial name	R side chain	Chemical structure
Alipathic 3C	Sinigrin	2-Propenyl	CH2=CH-CH2-
Alipathic 4C	Gluconapin	3-Butenyl	CH2=CH-CH2-CH2-
Alipathic 5C	Glucoalyssin	5-Methylsulfinylpentyl	CH3SO-CH2-CH2- CH2-CH2-CH2-
Alipathic 6C	Glucolesquerellin	6-Methylthiohexyl	CH3S- CH2-CH2- CH2-CH2-(CH2)2-
Alipathic 7C	Glucoarabrshirsutain	7-Methylthioheptyl	CH3S- CH2-CH2- CH2-CH2-(CH2)3-
Indole	Glucobrassicin	3-Indolylmethyl	
Indole	4-Hydroxyglucobrassicin	4-Methyoxy-3-indolylmethyl	

Glucosinolate name	Trivial name	R side chain	Chemical structure
Indole	**Neoglucobrassicin**	**N-Methoxy-3-indolylmethyl**	
Aromatic	**Glucotropacolin**	**Benzyl**	
Aromatic	**Glucosinalbin**	**p-Hydroxybenzyl**	
Aromatic	**Gluconasturtiin**	**2-Phenethyl**	

Biological effects of dietary glucosinolates

Glucosinolate themselves are biologically inactive molecules, but Gls degradation products are biologically active and known for their diversified biological effects. Negative effects of glucosinolates on animals are relative to its concentration in diet. Isothiocyanates are responsible for bitterness (Mithen *et al.,* 2000), whereas nitriles exert health-degrading influence (Tanii *et al.,* 2004). Thiocyanates, thiourea and oxazolidithione may disrupt iodine availability to thyroid thus affecting thyroid function (Wallig *et al.,* 2002). Other adverse effects of glucosinolate metabolites are goitrogenecity (Burel *et al.,* 2000c; Wallig *et al.,* 2002), mutagenecity, hepatotoxicity and nephrotoxicity (Tanii *et al.,* 2004). The negative influence of dietary glucosinolate on animal growth and production may be related to the drastic endocrine disturbance induced by antinutritional factor (Ahlin *et al.,* 1994). The reduced intake of Gls containing diets is due to the presence of sinigrin and progoitrin, these both glucosinolates are associated with bitter taste. Progoitrin produces more profound bitter taste compared to sinigrin. Although, progoitrin is a non-bitter glucosinolates, but is degraded by myrosinase or by heat treatment to the extremely bitter compound goitrin. Therefore, contribution of progoitrin to taste and bitterness vary by its degradation product goitrin, depending on the processing conditions. Gluconapin is also a bitter glucosinolates but its impact on intake is related to its content. Reduced intake often causes growth depression on diets containing high glucosinolate rapeseed meal. The degree of adverse effect of dietary Gls depends on the level and compositions of glucosinolates and their breakdown products. Different animal species have varying glucosinolate tolerance capabilities. Mortality is often reported with high glucosinolates diets in pig, rat and rabbits(Mithen *et al.,* 2000).

Anticancer Benefits

Epidemiological studies have long suggested that an inverse relationship exists between the consumption of *Brassica* vegetables and generation of cancer. Bioassays and feeding studies revealed that several indolyl and isothiocyanate products present anticarcinogenic properties (Zhang *et al.,* 1992). In food-bearing plants, glucosinolates act as natural pesticides and are accumulated in the plant's cells, ready to be released upon tissue damage. Similarly, when consumed by humans, the action of chewing releases the glucosinolates into the body, where they are transformed into bioactive compounds considerd to have anticancer properties. These anticancer compounds operate on several fronts including triggering the body's own detoxification systems (Wallig *et al.,* 2002), slowing cancer cell growth (Tanii *et al.,* 2004) and supporting DNA repair (Burel *et al.,* 2000c). Researchers have found lower levels of these compounds in people with lung cancer than in those who are cancer-free (Burel *et al.,* 2000c; Wallig *et al.,* 2002).The major dietary source of glucosinolates is cruciferous vegetables, the curing properties of which have been extolled for ages. The results of earlier study (Nestle, 1997) showed that cabbage paste, when rubbed on animals, can prevent tumor development. Top glucosinolate sources maintain up cabbage, Brussels sprouts, broccoli, cauliflower, broccoli sprouts, kale and red cabbage (Jeffery and Araya, 2009).

Genetical effects of glucosinolates for reducing of the risk of cancer

Glucosinolates directly affect the function and expression of genes, this is know as the epigenetic effect which means it prepares both wide-raging and long-lasting changes to the gene's function. Human research reveals higher dietary eats of glucosinolates are related to a reduction in the risk of most common cancers. For prostate cancer, the risk is cut by 32 percent and the derivatives of the glucosinolates abundant in broccoli sprouts help prevent stomach cancer by killing the H. pylori bacteria (Cartea and Velasco, 2008; Jeffery and Araya, 2009). Some of the more common cruciferous vegetables to eat are, broccoli and broccoli sprouts, arugula, bok choy, Brussels sprouts, cauliflower, collard greens, horseradish, kale, kohlarabi, parsnips, radishes rutabaga, turnips, watercress and wasabi (Mithen *et al.,* 2000).

Glucosinolates stop "hormone-dependent" cancer cell growth

Indole-3 carbinol is the most widely studied components of cruciferous vegetables; studies have shown that it fights cancers of the breast, prostate, reproductive tract, colon and blood cancers. In cancers of the reproductive tract, indole-3 carbinol prevents the development of tumors by benefiting important ratios of estrogen metabolites.Both sulforaphane and indole-3-carbinol decrease the amount of cancer stimulating estrogen, and this has been shown to help in thyroid as well as breast cancer. Phenethyl isothiocyanate is a natural metabolite of glucosinolates that has been found to down-regulate androgen receptors – minimizing stimulation of prostate cancer by testosterone.Diindolylmethane (DIM) is produced in the body fat, following the ingestion of glucosinolates derived from cruciferous vegetables. DIM helps prevent the growth of estrogen-dependent tumors such as those of the breast and reproductive tract (Fahey *et al.,* 2001).

Glucosinolate-myrosinase system effect on plant-insect/herbivore and plant/pathogen interactions

Glucosinolates and their hydrolysis products clearly play a role as mediators in plant-insect interactions. The role of the glucosinolate-myrosinase system consequently differs, i.e. glucosinolates can serve as general poison and deterrent for generalists while at the same time they can attract and stimulate feeding and egg laying of insects which are specialists on cruciferous plants. Several studies have reported that glucosinolates exhibit growth inhibition or feeding deterrence to a wide range of general herbivores such as birds, slugs and generalist insects (Giamoustaris, 1995; Giamoustaris and Mithen, 1996). It was also found that plants respond to herbivore or insect damage by ystematically accumulating higher levels of glucosinolates and thus presumably increasing their resistance (Martin and Müller, 2006). In a field experiment using lines of *Brassica napus* which differed in their glucosinolate content, Giamoustaris and Mithen (1995) found that increasing levels of glucosinolates resulted in a decrease of damage by generalist herbivores. The opposite was true for *Brassicaceae* specialists. Furthermore, it was found that a decrease in the side chain length of aliphatic glucosinolates and in the extent of hydroxylation increased the feeding amount by *Psylliodes chrysocephala,* suggesting that this *Brassicaceae* specialist is more responsive to particular types of glucosinolates than to the others (Giamoustaris, 1995).

It has been recognized and accepted that glucosinolates serve as cues for feeding and oviposition of many insect herbivores which have become specialists on glucosinolate-containing plant (Mewis *et al.,* 2002; , Miles *et al.,* 2005). Volatile hydrolysis products may serve as a signal for attraction from a distance, whereas intact glucosinolates might act as contact cues for feeding or oviposition stimulation. Behavioralexperiments were confirmed by electrophysiological investigations in which receptor organs or cells responded directly to glucosinolates or their hydrolysis products (Rojas, 1999; Miles *et al.,* 2005). Volatiles produced by glucosinolates can also attract natural enemies of herbivores such as parasitoids and provide indirect protection of the plant. Herbivores that specialize on glucosinolate-containing plants have a mechanism to overcome the toxicity of glucosinolates and their hydrolysis products. For instance, *Plutella xylostella* possesses its own sulfatase gut enzyme that removes the sulfate moiety from the glucosinolate structure. The resulting desulfoglucosinolate does not serve as a substrate for myrosinase anymore and passes through the insect's digestive tract (Ratzka *et al.,* 2002). *Pieris rape* uses nitrile-specifying protein to direct hydrolysis toward nitriles which are less toxic than the usually produced isothiocyanates (Miles *et al.,* 2005).

The role of glucosinolates in defense against pathogens is less clear than that for herbivores. There are many reports demonstrating the toxicity of glucosinolate hydrolysis products to bacteria and fungi *in vitro* (Mari *et al.,* 2002; Smolinskau and James, 2003), but only a few *in vivo* studies were able to correlate glucosinolates with pathogen resistance *(91). Brassica* crops were recognized as »break crops« due to glucosinolates and their hydrolysis products which show inhibitory effects on soil borne pathogens (Angus, *et al.,* 1994; Manici *et al.,* 1997). The hydrolysis products of indole glucosinolates were demonstrated to stimulate growth of certain ectomycrorrhizal species. When the relative antifungal activity of several isothiocyanate breakdown products from different glucosinolates was compared, it was found that aromatic isothiocyanates were more toxic than aliphatic ones and that the fungal toxicity of aliphatic isothiocyanates decreased with increasing length of the side chain (Manici *et al.,* 1997; Sarwar and Kirkegaard, 1998). Tiernes et al. studied the antimicrobial role of crude aqueous extracts from *Arabidopsis*. In one of the fractions, 4-methylsulphinylbutyl isothiocyanate was identified as a major compound with a broad spectrum of antimicrobial activity. A wide range of the fungi and bacteria tested showed 50% inhibition *in vitro* at a concentration lower than 350 ìM of 4- methylsulphinylbutyl isothiocyanate (Tierens *et al., 2001*). When they tested the resistance of an *ArabidopsisMAM1*mutant which after damage exhibits a lower amount of 4-methylsulphinylbutyl isothiocyanate, only *Fusarium oxysporum* was found to be significantly more aggressive than on wild-type plants, suggesting that glucosinolate-derived isothiocyanates might playa role in the protection of *Arabidopsis* against particular pathogens. Development of clubroot disease of the *Brassicaceae*, caused by the obligate biotrophic *Plasmodiphora brassicae*, was related to an increase of auxin and cytokinins resulting in increased cell division and cell elongation (Ludwig-Müller *et al.,* 1993,1999).

REFERENCES

Agrawal A. A., Kurashige N.S. 2003. A role for isothiocyanates in plant resistance against the specialist herbivore ***Pieris rapae***. ***J. Chem. Ecol***. 29: 1403-1415.

Ahlin K.A., Emmanuelson M., Wiktorsson H.1994. Rapeseed products from double low cultivars as feed for dairy cow: effects of long term feeding on thyroid function, fertility and animal health. ***Acta Vet. Scand***. 35, 37–53.

Angus J.F., Gardner P.A., Kirkegaard J.A., Desmarchelier J.M. 1994. Biofumigation – isothiocyanates released from *Brassica* roots inhibit growth of the take-all fungus. ***Plant Soil*** *162*: 107–112.

Arvind H. H., Li G., Zelmer C. D., McVetty P. B.E., Asif M., Goyal A. 2012. Molecular Genetics of Glucosinolate Biosynthesis in Brassicas: Genetic Manipulation and Application Aspects, Crop Plant, Dr Aakash Goyal (Ed.), ISBN: 978-953-51-0527-5, InTech, Available from: http://www.intechopen.com/books/crop-plant/molecular-genetics-of-glucosinolate-biosynthesis-in-brassicas.

Barth, C., Jander G. 2006. *Arabidopsis* myrosinases TGG1 and TGG2 have redundant function in glucosinolate breakdown and insect defense. ***Plant J.*** 46: 549-562.

Beekwilder J., Leeuwen W., Dam N.M., Bertossi M., Grandi V., Mizzi L., Soloviev M., Szabados L., Molthoff J.W., Schipper B., Verbocht H., Vos R.C.H., Morandini P., Aarts M.G.M,. Bovy A. 2008. The impact of the absence of aliphatic glucosinolates on insect herbivory in ***Arabidopsis***. ***PLoS One***. 3(4): e2068.

Benderoth M., Textor S., Windsor A.J., Mitchell-Olds T., Gershenzon J., Kroymann J. 2006. Positive selection driving diversification in plant secondary metabolism. ***Proc Natl Acad Sci USA*** 103(24): 9118-9123.

Birch, A.N.E., Griffiths D.W., Hopkins R.J., Smith W.H.M., McKinlay R.G. 1992.

Glucosinolate responses of swede, kale, forage and oilseed rape to root damage by turnip root fly (*Delia floralis*) larvae. ***J Sci Food Agric***. 60: 1-9.

Bodnaryk R.P. 1992. Effects of wounding on glucosinolates in the cotyledons of oilseed rape and mustard. ***Phytochem***. 31: 2671-2677.

Brader G., Mikkelsen M.D., Halkier B.A., Palva E.T. 2006. Altering glucosinolate profiles modulates disease resistance in plants*.* ***Plant J.*** 46: 758-767.

Bridges M., Jines A.M.E., Bones A.M., Hodgson C., Cole R., Bartlet E., Wallsgrove R., Karapapa V.K., Watts N., Rossiter J.T. 2002. Spatial organization of the glucosinolate-myrosinase system in *Brassica* specialist aphids is similar to that of the host plant. ***Proc Biol Sci.*** 269(1487): 187-191.

Brooks J., Paton V., Vidanes G. 2001. Potent induction of phase 2 enzymes in human prostate cells by sulforaphane. ***Cancer Epidemiol Biomarkers Prev***. 10: 949-954.

Blake-Kalff M.M.A., Harrison K.R., Hawkesford M.J., Zhao F.J., McGrath S.P.1998. Distribution of sulfur within oilseed rape leaves in response to sulfur deficiency during vegetative growth. ***Plant Physiology*** 118, 1337–1344.

Blake-Kalff M.M.A., Hawkesford M.J., Zhao F.J., McGrath S.P. 2000. Diagnosing sulfur deficiency in field-grown oilseed rape (*Brassica napus* L.) and wheat (Triticum aestivum L.). ***Plant and Soil*** 225, 95–107.

Bones A.M., Rossiter J.T. 1996.The myrosinase-glucosinolate system, its organisation and biochemistry. ***Physiol Plant*** *97*: 194–208.

Brown P.D., Tokuhisa J.G., Reichelt M., Gershenzon J. 2003. Variation of lucosinolate accumulation among different organs and developmental stages of ***Arabidopsisthaliana***. ***Phytochem***. 62: 471-481.

Burel C., Boujard T., Escaffre A.M., Kaushik S.J., Boeuf G., Mol K.A., Van der Geyten S., Kuhn E.R. 2000c. Dietary low glucosinolate rapeseed meal affect thyroid status and nutrient utilization in rainbow trout (*Oncorhynchus mykiss*). **Brit. J. Nutr**. 83, 653–664.

Cartea M.E., Velasco P. 2008. Glucosinolates in Brassica foods: Bioavailability in food and significance for human health. Phytochemistry Reviews; 7(2): 213-229.

Chens A. 2001.Update on glucosinolate metabolism and transport. ***Plant Physiol Biochem*** *39*: 743–758.

De Vos M., Kriksunov K.L., Jander G. 2008. Indole-3-Acetonitrile production fromindole glucosinolates deters oviposition by *Pieris rapae*. ***Plant Physiol*** 146: 916-926.

Dijkshoorn W.J., VanWijk A.L. 1967. The sulphur requirements of plants as evidenced by the sulphur-nitrogen ratio in the organic matter: a reviewof the published data. **Plant and Soil** 26, 129–157.

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

Fahey J.W., Haristoy X., Dolan P., Kensler T., Scholtus I., Stephenson K., Talalay P., Lozniewski A. 2002. Sulforaphane inhibits extracellular, intracellular, and antibiotic-resistant strains of *Helicobacter pylori* and prevents benzo pyreneinduced stomach ulcers. ***Proc Natl Acad Sci USA***. 99: 7610-7615.

Fahey J.W., Zalcmann A.T., Talalay P. 2001. The chemical diversity and distribution of glucosinolates and isothiocyanates among plants. ***Phytochem***. 56: 5-51.

Falk K.L., Tokuhisa J., Gershenzon J. 2007. The effect of sulphur nutrition on plant glucosinolate content: physiology and molecular mechanisms. ***Plant Biology*** *9:* 573–581.

Faulkner K., Mithen R., Williamson G. 1998. Selective increase of the potential anticarcinogen 4-methylsulphinylbutyl glucosinolate in broccoli. ***Carcinogenesis***. 19: 605-609.

Fenwick G.R., Heaney R.K., Mullin W.J. 1983. Glucosinolates and their breakdown products in food and food plants. ***Crit Rev Food*** *Sci Nutr.* 18: 123-201.

Jeffery E.H., Araya M. 2009. Physiological effects of broccoli consumption. **Phytochemistry Reviews**; 8(1): 283-298.

Gao X., Dinkova-Kostova A., Talalay P. 2001. Powerful and prolonged protection of human retinal pigment epithelial cells, keratinocytes, and mouse leukemia cells against oxidative damage: the indirect antioxidant effects of sulforaphane. ***Proc Natl Acad Sci USA***. 98: 15221-15226.

Giamoustaris A.M. 1995. The effect of modifying the glucosinolate content of leaves of oilseed rape *Brassica napus* ssp *oleifera* on its interaction with specialist and generalist pests. ***Ann Appl Biol*** *126*: 347–363.

Giamoustaris A., Mithen R. 1996. Genetics of aliphatic glucosinolates 4 Side-chain modification in *Brassica oleracea*. ***TheorAppl Genet*** *93*: 1006–1010.

Grayston S.J., Germida J.J. 1991. Sulfur-oxidizing bacteria as plant growth promoting rhizobacteria for canola. Canadian **Journal of Microbiology** 37, 521–529.

Griffiths D.W., Birch A.N.E., Hillman J.R. 1998. Anti-nutritional compounds in the *Brassicaceae* – analysis, biosynthesis, chemistry and dietary effects. ***J Hort Sci Biotech***. 73: 1-18.

Halkier B.A., Gershenzon J. 2006. Biology and biochemistry of glucosinolates. ***Annu Rev Plant Biol*** *57*: 303–333.

Hrncirik K., Valusek J., Velisek J. 2001. Investigation of ascorbigen as a breakdown product of glucobrassicin autolysis in *Brassica* vegetables. ***Eur Food Res Technol.*** 212: 576-581 http://toxicology.usu.edu/endnote/Chemoprevention-CruciferousVeg-NutrCan2001.pdf

http://www.huffingtonpost.com/joel-fuhrman-md/cancer-prevention_b_1624965.html

Kaur S., Gupta S.K., Sukhija P.S., Munshi S.K. 1990. Accumulation of glucosinolates in developing mustard *Brassica juncea* L seeds in response to sulfur application. ***Plant Sci*** *66*: 181–184.

Kim J.H., Jander G. 2007. Myzus persicae (green peach aphid) feeding on *Arabidopsis* induces the formation of a deterrent indole glucosinolates. ***Plant J.*** 49: 1008-1019.

Kliebenstein D.J., Gershenzon J., Mitchell-Olds T. 2001a. Comparative quantitative trait loci mapping of aliphatic, indole and benzylic glucosinolate production in *Arabidopsis thaliana* leaves and seeds. ***Genetics***. 159: 359-370.

Ludwig-Müller J., Bendel U., Thermann P., Ruppel M., Epstein E., Hilgenberg W. 1993. Concentrations of indole- 3-acetic-acid in plants of tolerant and susceptible varieties of chinese-cabbage infected with *Plasmodiophora brassicae* woron. ***New Phytol*** *125*: 763–769.

Ludwig-Müller J., Pieper K., Ruppel M., Cohen J.D., Epstein E., Kiddle G., Bennett R. 1999. Indole glucosinolate and auxin biosynthesis in *Arabidopsis thaliana* L Heynh glucosinolate mutants and the development of clubroot disease. ***Planta*** *208*: 409–419.

Mailer R.J. 1989. Effects of applied sulfur on glucosinolate and oil concentrations in the seeds of rape *Brassica napus* L and turnip rape *Brassica rapa*Lvar silvestris lam briggs. ***Aust J AgricRes*** *40*: 617–624.

Manici L.M., Lazzeri L., Palmieri S. 1997. In vitro fungitoxic activity of some glucosinolates and their enzyme-derived products toward plant pathogenic fungi. ***J Agric Food Chem*** *45*: 2768–2773.

Mari M., Leoni O., Iori R., Cembali T. 2002. Antifungal vapour- phase activity of allyl-isothiocyanate against *Penicillium expansum* on pears. ***Plant Pathol*** *51*: 231–236.

Marschner H. 1995. Mineral Nutrition of Higher Plants, 2nd ed., London: Academic Press.

Martin, N., and C. Müller, 2006. Induction of plant responses by a sequestering insect: relationship of glucosinolate concentration and myrosinase activity. ***Basic Appl Ecol*** *8*: 13–25.

Mewis I.Z., Ulrich C., Schnitzler W.H. 2002. The role of glucosinolates and their hydrolysis products in oviposition and host-plant finding by cabbage webworm, *Hellula undalis*. ***Entomol Exp Appl*** *105*: 129–139.

Miles C.I., Del Campo M.L., Renwick J.A. 2005. Behavioral and chemosensory responses to a host recognition cue by larvae of *Pieris rapae*. ***J Comp Physiol Neuroethol Sens Neural Behav Physiol*** *191*: 147–155.

Mithen R.F., Dekker M., Verkerk R., Rabot S., Johnson I.T. 2000. The nutritional significance, biosynthesis and bioavailability of glucosinolates in human foods. ***J Sci Food Agri.*** 80: 967-984.

Nestle M., 1997. Broccoli sprouts as inducers of carcinogen-detoxifying enzyme systems; clinical, dietary, and policy implications. ***Proc Natl Acad Sci USA***. 94: 11149-11151.

Osbourn A.E. 1996. Performed antimicrobial compounds and plant defense against fungal attack. ***Plant Cell***. 8: 1821-1831.

Petersen B.L., Chen S., Hansen C.H., Olsen C.E., Halkier B.A. 2002. Composition and content of glucosinolates in developing *Arabidopsis thaliana*. ***Planta***. 214: 562-571.

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

Ratzka A., Vogel H., Kliebenstein D.J., Mitchellolds T., Kroymann J. 2002. Disarming the mustard oil bomb. ***Proc Natl Acad Sci U S A*** *99*: 11223–11228.

Rojas J.C. 1999. Electrophysiological and behavioral responses of the cabbage moth to plant volatiles. ***J Chem Ecol*** *25*: 1867–1883.

Sarwar M., Kirkegaard J.A. 1998. Biofumigation potential of brassicas – II Effect of environment and ontogeny on glucosinolate production and implications for screening. ***Plant Soil*** *201*: 91–101.

Schnug E., Ceynowa J. 1990. Phytopathological aspects of glucosinolates in oilseed rape. ***J Agron Crop Sci-Z Acker Pflanzenbau*** *165*: 319–328.

Smolinskau M.K, JAMES R.L. 2003. Isothiocyanates produced by *Brassicaceae* species as inhibitors of *Fusarium oxysporum*. ***Plant Dis*** *87*: 407–412.

Talalay P. 2000. Chemoprotection against cancer by induction of phase 2 enzymes. *Bio Factors*. 12: 5-11.

Tanii H., Takayasu T., Higashi T., Leng S., Saojoh K. 2004. Allylnitrile: generation from cruciferous vegetables and behavioral effect on mice of repeated exposure. **Food Chem**. Toxicol. 42, 453–458.

Tierens K., Thomma B.P.H., Brouwer M., Schmidt J., Kistner K., Porzel A., Mauch-Mani B., Cammue B.P.A., Broekaert W.F. 2001. Study of the role of antimicrobial glucosinolate- derived isothiocyanates in resistance of *Arabidopsis* to microbial pathogens. ***Plant Physiol*** *12 5*: 1688–1699.

Tripathi M.K., Mishra A.S. 2007. Glucosinolates in animal nutrition: A review. **Animal Feed Science and Technology** 132: 1–27.

Ugajin T., Takita K., Takahashi H., Muraoka S., Tada T., Mitsui T., Hayakawa T., Ohyama T., Hori H. 2003. Increase in indole 3-acetic acid (IAA) level and nitrilase activity in turnips induced by *Plasmodiophora brassicae* infection. ***Plant Biotech***. 20: 215-220.

Underhill E.W., Chisholm M.D., Steck W. 1980. E-5, Z-7-Dodecadienal, a sex-pheromone component of the western tent caterpillar, *Malacosoma californicum Lepidoptera, Lasiocampidae* ***Can Entomol*** *112*: 629–641.

Vong P.C., Lasserre-Joulin F., Guckert A. 2002. Mobilization of labeled organic sulfur in rhizosphere of rape and barley and in non-rhizosphere soil. **Journal of Plant Nutrition** 25, 2191–2204.

Walker K.C., Booth E.J. 2003. Sulphur nutrition and oilseed quality. **In Sulphur in Plants** (Abrol, Y. P. and Ahmad, A., eds.), Dordrecht: Kluwer Academic Publishers, pp.323–339.

Wallig M.A., Belyea R.L., Tumbleson M.E. 2002. Effect of pelleting on glucosinolates content of Crambe meal. **Anim. Feed Sci. Technol**. 99, 205–214.

Wittstock U., Halkier B.A. 2000. Cytochrome P450 *CYP79A2* from *Arabidopsis thaliana* L. catalyzes the conversion of L-phenyl alanine to phenylacetaldoxime in the biosynthesis of the benzylglucosinolate. ***J Biol Chem***. 275: 14659-14666.

Wittstock U., Halkier B.A. 2002. Glucosinolate research in the *Arabidopsis* era. *Trends Plant Sci 7*: 263–270.

Wittstock U., Agerbirk N., Stauber E.J., Olsen C.E., Hippler M., Itchell-Olds T., Gershenson J. 2004. Successful herbivore ontack due to metabolic diversion of a plant chemical defense. ***Proc Natl Acad SciUSA101***: 4859–4864.

Zhang Y., Talalay P., Cho C.G., Posner G.H. 1992. A major inducer of anticarcinogenic protective enzymes from broccoli: isolation and elucidation of structure. ***Proc Natl Acad Sci USA***. 89: 2399-2403..

مراجعة: الجلاكوسينولات و تأثيراتها البيولوجية ومضادات السرطان المهمة

رميح*

ملخــص

الجلاكوسينولات عبارة عن مواد غنية بالكبريت، ناتجة عن عمليات الأيض في النباتات التي تنتمي إلى العائلة الصليبية، بالإضافة إلى خمس عشر عائلة من مغطاة البذور ذوات الفلقتين والمتضمنة عددا كبيرا من الأصناف القابلة للأكل. تم التعرف على الأقل إلى 130 من الجلاكوسينولات. بعد عملية سحق الأنسجة تتحلل الجلاكوسينولات بوساطة إنزيم مايروسينيز لإنتاج مجموعة معقدة من النواتج التي تتضمن ايزوثيوسينات متطايرة، والعديد من المركبات التي لها اثر في الغدة الدرقية ومعالجة السرطان. يعدُّ أداء الغلوسينوليت أثناء عمليات الأيض ذو علاقة بتركيز الكبريت، حيث وجد أن تكسر الغوسينوليت يزداد عند تناقص تركيز الكبريت، ولكن لم يعرف بعد المسار الذي يسلكه الكبريت مع الجلاكوسينولات. عرفت الجلاكوسينولات والمواد الناتجة من تكسرها بخصائصها التي تساعد في علاج الأمراض الفطرية والبكتيرية والنمياتودا وكذلك خصائص السمية، حديثا تم إجراء العديد من الأبحاث عليها لوجود صفات تساعد في علاج السرطان. حيث إن مشتقات الجلاكوسينولات تعمل على إيقاف تقدم السرطان من خلال تدمير الخلايا السرطانية، وتثبيط الجينات المسؤولة عن إنتاج أوعية جديدة والتي تدعم نمو الورم وانتشاره. كما أن هذه المواد العضوية تعمل على تقليل حدوث السرطانات الناجمة عن السموم البيئية عن طريق زيادة إنتاج الإنزيمات التي تعمل على إزالة السموم.

الكلمات الدالة: العائلة الصليبية، ذوات الفلقتين، الحركية، مايروسينيز، الكبريت.

* مركز البحوث والمصادر الزراعية والطبيعية، ايران.
vrameeh@yahoo.com

تاريخ استلام البحث 2013/7/16 وتاريخ قبوله 2014/1/27.