Chemoprotective effects of garden cress (Lepidium sativum) and its constituents towards 2-amino-3-methyl-imidazo[4,5-f]quinoline (IQ)-induced genotoxic effects and colonic preneoplastic lesions

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The chemoprotective effect of garden cress (GC, Lepidium sativum) and its constituents, glucotropaeolin (GT) and benzylisothiocyanate (BITC), a breakdown product of GT, towards 2-amino-3-methyl-imidazo [4,5-f] quinoline (IQ)-induced genotoxic effects and colonic preneoplastic lesions was investigated in single cell gel electrophoresis (SCGE) assays and in aberrant crypt foci (ACF) experiments, respectively. Pretreatment of F344 rats with either fresh GC juice (0.8 ml), GT (150 mg/kg) or BITC (70 mg/kg) for three consecutive days caused a significant (P < 0.05) reduction in IQ (90 mg/kg, 0.2 ml corn oil/animal)-induced DNA damage in colon and liver cells in the range of 75–92%. Chemical analysis of GC juice showed that BITC does not account for the effects of the juice as its concentration in the juice was found to be 1000-fold lower than the dose required to cause a chemoprotective effect. Parallel to the chemoprotection experiments, the modulation of the activities of cytochrome P4501A2, glutathione-S-transferase (GST) and UDP glucuronosyltransferase (UDPGT) by GC juice, GT and BITC was studied. Whereas GT and BITC did not affect the activity of any of the enzymes significantly, GC juice caused a significant (P < 0.05) increase in the activity of hepatic UDPGT-2. In the ACF assay, IQ was administered by gavage on 10 alternating days in corn oil (dose 100 mg/kg). Five days before and during IQ treatment, subgroups received drinking water which contained 5% cress juice. The total number of IQ-induced aberrant crypts and ACF as well as ACF with crypt multiplicity of ≥4 were reduced significantly (P < 0.05) in the group that received IQ plus GC juice compared with the group that was fed with IQ only. However, crypt multiplicity was not significantly different in these two groups when all ACF with all classes of crypt multiplicity were considered in the analysis. This is the first report on the inhibition of HA-induced DNA damage and preneoplastic lesions by a cruciferous plant. Our findings suggest that the chemoprotective effect of GC is mediated through enhancement of detoxification of IQ by UDPGT.

Introduction

Food-borne heterocyclic aromatic amines (HAs) are implicated as etiologies of human colon cancer (1–4). This situation has stimulated intense efforts to identify dietary substances which protect against their mutagenic and carcinogenic effects. In the last 20 years, ~160 articles have been published on the antigenotoxic and anticarcinogenic effects of dietary substances towards HAs, and >650 different complex mixtures and individual compounds have been studied (5). The most widely used methods to detect protective effects were in vitro tests with bacteria and stable mammalian cell lines. These models reflect the situation in laboratory rodents and humans only partly and misleading results have been obtained in particular with compounds that alter the metabolism of HAs (5). Modulation of the metabolism of DNA-reactive carcinogens is known to be an important strategy for chemoprotection (6).

Cruciferous vegetables contain glucosinolates (GS) from which isothiocyanates (ITCs) are liberated by the enzyme myrosinase. ITCs protect laboratory animals against chemically-induced cancer through inhibition of phase I enzymes and/or induction of glutathione-S-transferase (7–13). Of the different ITCs, the anticarcinogenic effect of benzyl isothiocyanate (BITC) has been intensely studied and was found to be a promising chemopreventive agent towards different classes of environmental carcinogens (7–9). Whereas many common Brassica vegetables contain a mixture of different GSs garden cress (GC, Lepidium sativum) contains only one GS, namely glucotropaeolin (GT, 14), the parent compound from which BITC is formed. Therefore we used GC as a model cruciferous plant in the present study.

We investigated the chemoprotective effects of GC juice, GT and BITC towards 2-amino-3-methyl-imidazo [4,5-f] quinoline (IQ)-induced DNA damage and preneoplastic lesions (aberrant crypt foci, ACF) using the in vivo single cell gel electrophoresis (SCGE) assay and the colonic aberrant crypt foci (ACF) model, respectively. IQ, a carcinogenic HA, has been detected in many types of meat and fish (15). The SCGE assay is a microgel electrophoresis technique that enables detection of DNA damage (double strand breaks, single strand breaks and alkali labile sites) in individual cells from different organs (16). The other endpoint, ACF, are preneoplastic lesions believed to be the earliest morphological alterations during the development of colonic mucosal neoplasia and have been used to study the mechanisms of chemical carcinogenesis in the colon (17–19). In contrast to DNA-adduct measurements which were widely used in chemoprevention studies, SCGE assays enable the detection of genetic damage caused by both the HA and the chemopreventive agents. In this context it is notable that we and others have previously shown that ITCs induce chromosomal mutations and genotoxic effects in their own right at concentrations as low as 1 mg/ml (20–23).

To shed light on the possible mechanism of protection of GC and its constituents towards IQ-induced genotoxic effects,
we measured the activities of hepatic cytochrome P4501A2 and UDP-glucuronosyltransferase (UDPGT) and hepatic and colonic glutathione-S-transferase (GST) in rats that were treated with GC juice, GT or BITC for three consecutive days. Whereas cytochrome P4501A2 is involved in the metabolic activation of HAs, UDPGT and GST lead to their detoxification (24–26). Furthermore, we also compared the effect of standard and high-fat-fiber free diet on the activities of hepatic UDPGT, GST and P4501A2.

Materials and methods

Preparation of garden cress juice

In all experiments, we used the same batch of garden cress seeds (Austrosaat, Viena, Austria). The plants were cultivated in a green house under standard conditions (day–night cycle 16/8 h, humidity 50–60%, 22–26°C). Eight days after seeding, the young plants were chopped and crude juice was prepared freshly every day with a juice maker apparatus (Elin T3232) just before administration.

Chemical analysis of garden cress

The GT content of GC was analysed by HPLC using sinigrin as a standard (27). The BITC content in GC juice was determined by gas chromatography following headspace solid-phase microextraction (28). A 75 mm carboxenpoly- (dimethylsiloxane)-coated silica fiber (Supelco, St Louis, MO) was exposed to the headspace of the sample, after addition of allyl isothiocyanate (Sigma, St Louis, MO) as an internal standard. Thermal desorption of the analytes to the headspace of the sample, after addition of allyl isothiocyanate (Sigma, St Louis, MO) as an internal standard. Thermal desorption of the analytes into the fiber coating and their subsequent gas chromatography separation were carried out using a Carlo Erba model HRGC 530 chromatograph equipped with a flame ionisation detector. Samples were desorbed at 250°C in the splitless injection port and separation was achieved on a CP-Sil 8CB capillary column (25 m × 0.53 mm i.d.; film thickness, 2 mm, Chrompack) with nitrogen as the carrier gas. Data were collected and peaks integrated using a Shimadzu model C-R6A integrator. Identification was based on the identity of the retention time with that of the authentic standard (Sigma, St Louis, MO); it was confirmed by gas chromatography-mass spectrometry analysis on a Fisons model 800 gas chromatography coupled to a quadrupole Fisons MD 800 mass spectrometer.

Animals and cell isolation

All experiments were carried out with male Fischer 344 rats with a body weight of 250±18 g. The animals were kept under controlled conditions (24 ± 1°C, humidity 50 ± 5%, 12 h light cycle).

For the SCGE assay, each treatment group consisted of three animals. 2-amino-3-methylimidazo[4,5-f]quinoline (IQ), Toronto Research Chemicals, Toronto, Ontario) GT and BITC (both Sigma St Louis, MO) were administered orally by gavage in 0.2 ml corn oil (Knorr Ges.mBH, Wels, Austria) per rat. Negative controls were treated with corn oil only. The treatment schedule was as follows: the animals were gavaged either with garden cress juice (0.8 ml/animal), BITC (70 mg/kg, Sigma, St Louis, MO), or the solvent over three consecutive days and received a single dose of IQ by gavage (90 mg/kg in 0.2 ml corn oil/animal) 24 h later. The doses of BITC and GT were chosen on the basis of previous chemoprevention studies by Huber et al. (29) and Wattenberg et al. (30), respectively. After 4 h of exposure to IQ, the animals were killed and the cells isolated. Liver cells were isolated by a two-step in situ perfusion technique with collagenase (31) while colon cells were isolated as described by Brendler et al. (32) with protease K (Sigma, St Louis, MO). Cell viability was determined with the trypan blue method (33).

Single cell gel electrophoresis assay

Phosphate buffered saline, electrophoresis and neutralization buffer and ethidium bromide stain were composed as described by Singh et al. (34). All components were purchased from Merck (Darmstadt, Germany). Agarose coated slides were made with 1.5% normal melting agarose (Gibco, Paisley, UK) according to the protocol of Klade et al. (35).

Microgel electrophoresis was performed as described by Singh et al. (36). Briefly, 10 000 cells suspended in 90 μl of low melting point agarose (0.5%) were transferred to a slide precoated with normal melting agarose and covered with a cover glass. After allowing the low melting agarose to solidify by putting the slide on a cooled metal plate for 2 min, the cover glass was carefully removed and the slides submerged into a lysis solution for 24 h. Subsequent to alkaline treatment (pH 13, 20 min) and electrophoresis (300 mA, 25 V, 20 min, Biometra Standard Power Pack P25), the slides were removed from the electrophoresis chamber, washed twice with neutralization buffer and stained with ethidium bromide. DNA migration was determined by measuring the comet tail lengths of the indicator cells using a fluorescence microscope (Nikon EFD-3, 125-fold magnification) connected to a monitor with a specific macro for the NIH public domain image analysis program (37). From each organ, three slides were prepared and from each slide 50 cells were analyzed.

Measurement of enzyme activity

For enzyme measurements, groups of six animals received identical amounts of the putative modifiers as in the SCGE experiments over three days. One day after the last feeding with the protective agents, livers and colons were removed for enzyme determination. In an additional experiment, we compared the effects of standard AIN 76 diet and a modified, high-fat and fiber-free, AIN 76 diet (both SDS, Witham, UK) on the activities of hepatic P4501A2, GST and UDPGT. Liver and colon microsomes were prepared according to Ryan et al. (38) and Strobel et al. (39), respectively, and microsomal protein concentrations were measured according to the method of Bradford (40). The effect of garden cress juice, BITC and GT on hepatic P4501A2 was studied by measuring methoxyresorufin O-demethylase (MROD) activities according to Labet et al. (41) at an excitation of 550 nm and an emission wavelength of 585 nm. The activity of cytosolic GST in hepatic and colonic tissues was determined spectrophotometrically (λ, 340 nm) with 1-chloro-2,4-dinitrobenzene (Sigma, St Louis, MO) as a substrate (42). UDPGT activities were measured with two substrates. Chloramphenicol (Sigma, St Louis, MO) was used to measure predominantly the GT2 isozyme by the radiometric method of Young and Lietmann (43) with slight modifications (44); 4-methylumbelliferone (Sigma, St Louis, MO) was used to analyse preferentially the GT1 isozyme as described by Lilienblum et al. (45). All measurements were carried out in duplicate.

Aberrent crypt foci assay

Each experimental group consisted of eight rats. During the entire experiment, the animals were fed with a modified (high-fat and fiber-free) AIN 76 diet (SDS, Witham, UK), which was composed as described by McIntosh et al. (46). Five days before and during IQ treatment, subgroups received drinking water which contained 5% cress juice. The juice was prepared freshly every day. IQ was given by gavage on 10 alternating days in corn oil (dose 100 mg/kg, 0.2 ml corn oil/animal). As a positive control, azoxymethane (AOM, 30 mg/kg, Sigma, St Louis, MO) was used. 16 weeks after the last IQ administration, the animals were killed and their colons removed, cleaned with Ringer solution (Sigma, St Louis, MO), and fixed in 10% buffered formaldehyde. Colonos were stained with methylene blue (0.2%) and the number of aberrant crypts and ACF was evaluated at 60× magnification (47).

Statistical analysis

For SCGE assays, the distribution pattern of the tail length in the different treatment groups was analysed as suggested by Tice et al. (48) and fitted with a y-distribution. From each slide, the medians of the tail length were calculated; means ± standard deviation and statistics were computed using results from three animals per group. Comparisons of groups of animals were done by ANOVA based on the means of three slides. Post hoc comparisons between experimental groups against control animals were done by Dunnett’s test. Induction of ACF and activities of cytochrome P4501A2, GST and UDPGT were analyzed with a two-sided Dunnett’s test after significant effects were obtained with ANOVA. For all tests, P ≤ 0.05 was considered significant.

Results

The GT and BITC contents of garden cress were found to be 80 mg/g and 28 mg/l, respectively and no detectable amount of GT was found 3 h after the preparation of the juice.

Before we investigated the chemoprotective effects of GC, GT, and BITC, a dose-response study was carried out on IQ-induced genotoxicity. DNA strand breakage as measured by comet tail length in hepatocytes and colonocytes increased as a function of the IQ dose administered (Figure 1). Whereas a dose level of 45 mg/kg induced a significant effect only in hepatocytes, the two higher doses (90 and 150 mg/kg) induced significant genotoxicity in both organs. Additionally, in experiments in which rats were exposed to IQ for 4 h, 6 h, and 24 h, significant effects were measured after 4 h and 6 h exposure while exposure for 24 h yielded comet tail lengths which were
Chemoprevention by garden cress and its constituents

In subsequent experiments, we studied the chemoprotective effects of GC juice, GT and BITC towards IQ-induced DNA damage in hepatocytes and colonocytes of rats exposed to 90 mg IQ/kg for 4 h. The results of these experiments are summarized in Table I. Pretreatment of the animals with GC juice, GT or BITC prevented IQ-induced DNA damage almost completely. GC juice appeared to be more effective than the pure chemicals. It is also notable that GC juice alone caused a significant reduction in the tail length of background DNA damage compared with untreated (control) animals.

IQ induced an average of 19.75 total aberrant crypts, 8.16 ACF per colon and 2.39 aberrant crypts per focus; the frequency of foci with ≥4 aberrant crypts/animal was 2.27. Administration of a 5% GC juice in the drinking water during IQ treatment resulted in a significant reduction of the total number of aberrant crypts, ACF as well as the number of ACF with a crypt multiplicity of ≥4 (P < 0.05). However, aberrant crypt multiplicity was not significantly different in the two groups when all ACF with different numbers of aberrant crypts were considered in the analysis (Table II). The values of the different parameters for the group of rats treated with GC juice alone were similar to those in the untreated group.

The results of assays for induction of enzyme activities can be summarized as follows (Table III): (i) hepatic P4501A2 activity of animals treated with GC juice, GT or BITC was similar to that of untreated animals. (ii) Neither the pure compounds nor the juice increased the activity of UDPGT-1 and GST significantly. (iii) Garden cress juice increased hepatic UDPGT-2 activity significantly. Attempts to measure UDPGT in the colonic tissue were not successful due to low background activities and strong inter-individual variations (data not shown).

In the experiment in which we compared activities of hepatic P4501A2, UDPGT and GST in rats kept on either standard diet or high-fat and fiber-free diet, similar levels of background enzyme activities were found with both groups (Table IV). Administration of GC juice for three consecutive days increased the activity of UDPGT-2, but not UDPGT-1, GST or P4501A2, in both groups.

**Discussion**

In this study, we used two different experimental models, namely the *in vivo* SCGE assay and colonic ACF experiments, to investigate the chemopreventive effect of GC juice and its constituents towards the genotoxic and carcinogenic potential of IQ, a heterocyclic aromatic amine suspected to be a risk factor for human colon cancer. Moreover, attempts were made to elucidate the mechanisms of protection.

The results of the dose response experiments (Figure 1) show that IQ causes DNA damage in organs of rats which are targets for tumor induction by this compound. This result was not expected *a priori* as HAs gave negative or only marginal effects in other *in vivo* genotoxicity tests such as the bone marrow micronucleus assay and in chromosomal aberration tests (5,49).

Our experiments showed that garden cress juice and its constituents attenuate the genotoxic effects of IQ. At present, a number of reports on antimutagenic effects of breakdown products of glucosinolates towards polycyclic aromatic hydrocarbons and nitrosamines are available. However, data on protective effects towards HAs are scarce and no results from experiments with crude cruciferous plant juices are available. We recently failed to find a DNA-protective effect of phenethyl-ITC towards PhIP when the ITC was administered simultaneously with the amine (12). On the other hand, administration of BITC before treatment with 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP) was reported to reduce PhIP-induced rat colon DNA adducts (29).

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**Table I.** Effect of BITC, GT and GC juice on IQ-induced DNA damage in rat liver and colon cells. The animals (three per group) were orally treated for three consecutive days with GT, BITC or fresh GC juice. 24 h later, IQ suspended in corn oil or corn oil alone was given by gavage. Four hours later, liver and colon cells were isolated and processed as described in materials and methods. From each organ, 150 cells were analyzed.

<table>
<thead>
<tr>
<th>Group</th>
<th>Dose</th>
<th>Mean ± SD of comet tail length (μm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Liver</td>
</tr>
<tr>
<td>Control</td>
<td>None</td>
<td>6.2 ± 3.5</td>
</tr>
<tr>
<td>GT</td>
<td>150</td>
<td>9.3 ± 5.3</td>
</tr>
<tr>
<td>IQ</td>
<td>100</td>
<td>38.4 ± 19.5b</td>
</tr>
<tr>
<td>IQ + GT</td>
<td>100 IQ + 150 GT</td>
<td>13.7 ± 3.9b</td>
</tr>
<tr>
<td>Control</td>
<td>None</td>
<td>6.2 ± 3.5</td>
</tr>
<tr>
<td>BITC</td>
<td>70</td>
<td>4.7 ± 0.7</td>
</tr>
<tr>
<td>IQ</td>
<td>90</td>
<td>48.1 ± 4.2b</td>
</tr>
<tr>
<td>IQ + BITC</td>
<td>100 IQ + 70 BITC</td>
<td>8.9 ± 1.3c</td>
</tr>
<tr>
<td>Control</td>
<td>None</td>
<td>5.1 ± 3.5</td>
</tr>
<tr>
<td>Cress</td>
<td>2 ml/kg</td>
<td>1.6 ± 0.5</td>
</tr>
<tr>
<td>IQ</td>
<td>90</td>
<td>43.5 ± 28.3</td>
</tr>
<tr>
<td>IQ + cress</td>
<td>90 IQ + 2 ml cress juice/kg</td>
<td>4.6 ± 2.6c</td>
</tr>
</tbody>
</table>

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*a* Unless otherwise specified, numbers give doses in mg/kg body weight.  
*b* Significantly different from the value of the control animals, Dunnett’s test, *P* < 0.05.  
*c* Significantly different from the value of the IQ treated animals, Dunnett’s test, *P* < 0.05.

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Fig. 1. Induction of DNA damage in liver and colon cells of rats treated orally with different doses of IQ. Four hours after treatment, animals were killed and cells isolated from liver and colon. 150 cells were analyzed from each organ. Values are means ± SD of comet tail length of cells from three animals per group. ■ liver; △ colon. Asterisks indicate statistical significance (*P* < 0.05; **P* < 0.01).
ACF assays have been used in a number of chemoprevention studies with HAs. One of the shortcomings of this experimental model is that the foci yield induced by these compounds is very low when standard diets are fed to the animals (50–53). In order to overcome this problem, we used a high-fat and fiber-free diet in combination with multiple IQ treatments. The higher frequency of ACF obtained in this modified model enabled the detection of protective effects of GC juice. In the ACF assay, the parameters that are quantified by topographic evaluation of colonic mucosa are the number and size of ACF and the number of crypts present in each ACF (crypt multiplicity). Feeding of rats with GC juice significantly reduced the total number of IQ-induced aberrant crypts and ACF as well as the number of ACF with a crypt multiplicity of ≥4. However, the average crypt multiplicity did not change in the group fed with GC juice plus IQ compared with the IQ group. The significant reduction in the number of ACF with crypt multiplicity of ≥4 is quite interesting in the light of previous reports in which ACF ≥4-crypts were found to be best correlated with final tumor incidence (50).

To shed light on the possible mechanism of protection of BITC, GT and GC juice against IQ-induced DNA damage, we investigated the levels of cytochrome P4501A2, GST and UDPGT activities in liver and colon tissues of rats fed with either standard diet or high-fat-ber free None 1.20 ± 1.79 0.40 ± 0.54 1.00 ± 1.73 0.20 ± 0.44
Pos. control (AOM) 30 mg/kg 159.50 ± 24.70a 41.00 ± 5.65a 3.89 ± 0.17 a 18.50 ± 3.53a
Garden cress 5% in water 1.66 ± 1.63 0.83 ± 0.75 1.41 ± 1.49 0.14 ± 0.37
IQ 100 mg/kg, 10× 19.75 ± 7.11a 8.16 ± 2.14a 2.39 ± 0.58 2.27 ± 1.91a
Garden cress + IQ 5% in water 11.10 ± 5.04ab 3.90 ± 1.66ab 2.88 ± 0.62 1.00± 0.67ab
IQ 10 × 100 mg/kg

Table II. Effect of GC juice on IQ-induced ACF in rats IQ was administered 10 times on alternate days by gavage. GC juice (5%, v/v) was given 5 days before and during administration of IQ. Data are given as means ± SD of eight animals per group, except for the AOM group which consisted of three animals.

Table III. Effects of garden cress and its constituents on the activities of P4501A2, GST and UDPGT. Activity of P4501A2 was determined by using methoxyresorufin as a substrate. GST, UDPGT-2 and UDPGT-1 were measured by using CDNB, chloramphenicol and 4-methylumbelliferone as substrates, respectively. Values are means ± SD (n = 6). Animals were treated with fresh cress juice, BITC or GT over a three day period and were killed 24 h after the last treatment. All measurements were made in duplicate.

Table IV. Effect of GC juice on the activities of hepatic UDPGT, GST and P4501A2 in rats fed with either standard diet or high-fat-fiber free diet. Activity of P4501A2 was determined by using methoxyresorufin as a substrate. GST, UDPGT-2 and UDPGT-1 were measured by using CDNB chloramphenicol and 4-methylumbelliferone as substrates, respectively. Values are means ± SD (n = 5). Animals were treated with fresh GC juice over a three day period and were killed 24 h after the last treatment. All measurements were made in duplicate.

*Significantly different from the value of the untreated control group, ANOVA + two sided Dunnett’s test, P < 0.05.

#Significantly different from the value of the untreated control group, two sided Dunnett’s test, P < 0.05.
lead to the formation of water-soluble detoxification products (27,51–54). The activity of P4501A2 was not altered by any of the protective substances. On the contrary, it was of great interest that GC juice significantly induced the activity of hepatic UDPGT-2 which might have been responsible for the attenuation of the genotoxicity of IQ in both liver and colon tissues as well as for the reduction ACF frequency in the colon, as the activity of UDPGT enzyme in colonic tissue is very low (55). Although earlier works showed that UDPGT enzymes are induced by xenobiotics (25) and glucosinolate break-down products (56), to our knowledge, this is the first report on the possible association between induction of UDPGT activities and prevention of DNA damage and preneoplastic lesions by HAs. Taken together with previous reports in which glucuronidation reactions were shown to play a key role in the detoxification of HAs in rodents and humans (26,57–60), it is plausible that the observed protective effects of GC juice are due to induction of the activity of UDPGT-2. The effects of GC constituents, BITC and GT, on the level and the pattern of enzyme induction were different from cress juice. While GT induced a moderate induction of GST and UDPGT activities, BITC caused a higher, but statistically non-significant, increase in the activity of colonic GST. The enhancement of GST activity by GT is probably the result of its conversion into BITC by bacterial myrosinase in the digestive tract (61). The induction of GST by BITC, and other ITCs has been reported earlier (10). However, the role of GST in the detoxification of HAs is not as important as it is for other chemicals (26). It is known from earlier investigations that cruciferous plants and their constituents protect against other classes of DNA-reactive carcinogens as well (for review see ref. 61), but their protection is mediated via inhibition of phase I enzymes and/or GST induction. For example, isothiocyanates potently inhibit CYP2E1 (62), an enzyme which plays a crucial role in the metabolic activation of AOM (63). The reduction by Brussels sprouts, sulforaphane and phenethyl isothiocyanate of AOM-induced colonic ACF (64,65), may be related to the inhibition of activation of the carcinogen by these agents.

As described in the Results section, GC juice significantly induced the activity of hepatic UDPGT-2 in rats of both diet groups (high-fat and fiber-free or standard) whereas the levels of hepatic UDPGT-1, GST and P4501A2 were not affected in both groups. The fact that comparable enzyme activities were found in liver tissue of rats from the two diet groups suggests that the higher fecal yield measured upon feeding rats with high-fat and fiber-free diet is not related to changes in the pattern of IQ-metabolism. Rather, since dietary fat and dietary fiber are known to play a promotive (66) and preventive (67) role, respectively, in the development of colon cancer, it is likely that these factors account for the increased ACF frequency observed in rats fed with the high-fat and fiber-free diet.

High performance liquid chromatography and gas chromatography analyses of GC juice for its BITC content revealed a concentration of 28 mg/l BITC. This concentration is three orders of magnitude lower than the amount of BITC required to cause enzyme induction and chemoprotective effects in the present experiment. This finding indicates that compounds other than BITC account for the chemoprotective effect of GC juice. Cruciferous vegetables are known to contain numerous other chemoprotective organosulphur phytochemicals such as dithiolthiones and S-methyl-cysteine sulfoxide (61,68) which may account for the effects of the GC juice seen in the present study.

This is the first report on the chemopreventive effect of GC towards the genotoxic effects of a HA compound. We demonstrated that GC and its constituents induce UDPGT, an enzyme which plays a key role in the detoxification of HAs, and the enhanced activity of this enzyme might be, at least partly, responsible for the observed reduction in IQ-induced genotoxic effects and colonic preneoplastic lesions. The amount of juice required to bring about the changes in the activity of UDPGT was quite small and comparable to the level of GC humans consume in the form of salad.

References


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