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Protective effect of aqueous garlic extract against naphthalene-induced oxidative stress in mice

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Abstract

The aim of this study was to investigate the possible protective effects of aqueous garlic extract (AGE) against naphthalene-induced oxidative changes in liver, kidney, lung and brain of mice. Balb/c mice (25–30 g) of either sex were divided into five groups each comprising 10 animals. Mice received for 30 days: 0.9% NaCl, i.p. (control); corn oil, i.p; AGE in a dose of 125 mg kg^{-1}, i.p.; naphthalene in a dose of 100 mg kg^{-1}, i.p. (dissolved in corn oil); and AGE (in a dose of 125 mg kg^{-1}, i.p.) plus naphthalene (in a dose of 100 mg kg^{-1}, i.p.). After decapitation, liver, kidney, lung and brain tissues were excised. Malondialdehyde (MDA) and glutathione (GSH) levels and myeloperoxidase activity (MPO) were determined in the tissues, while oxidant-induced tissue fibrosis was determined by collagen content. Tissues were also examined microscopically. Serum aspartate aminotransferase, alanine aminotransferase levels and blood urea nitrogen and creatinine concentrations were measured for the evaluation of hepatic and renal function, respectively. MDA and GSH levels were also assayed in serum samples. In the naphthalene-treated group, GSH levels decreased significantly, while MDA levels, MPO activity and collagen content increased in the tissues ($P < 0.01$–0.001), suggesting oxidative organ damage, which was also verified histologically. In the AGE-treated naphthalene group, all of these oxidant responses were reversed significantly ($P < 0.05$–0.01). Hepatic and renal function test parameters, which increased significantly ($P < 0.001$) following naphthalene administration, decreased ($P < 0.05$–0.001) after AGE treatment. The results demonstrate the role of oxidative mechanisms in naphthalene-induced tissue damage. The antioxidant properties of AGE ameliorated oxidative organ injury due to naphthalene toxicity.

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Introduction

The mechanism of toxicity of structurally diverse environmental toxicants, including heavy metals and polyhalogenated and polycyclic hydrocarbons, may comprise a common cascade of events that involve oxidative stress and the production of reactive oxygen species (Bagchi et al 2002). Naphthalene is a bicyclic aromatic hydrocarbon that is widely used in moth repellents, lavatory scent discs and soil fumigants. It is also used in the manufacturing of naphthylamines, anthranilic and phthalic acids, and synthetic resins (Stucker et al 1993; Vuchetich et al 1996). The toxicity induced by naphthalene appears to involve the conversion of naphthalene to naphthoquinone, as well as hydroxylated products including 1-naphthol, 2-naphthol and 1,2-dihydroxynaphthalene (Miller et al 1986; Cho et al 1994), which cause oxidative damage. It has been demonstrated that naphthalene exposure results in elevated levels of serum and liver lipid peroxides (Yamauchi et al 1986), and decreased hepatic selenium-dependent glutathione peroxidase activity (Germansky & Jamall 1998). Naphthalene exposure is associated with the development of haemolytic anaemia in humans and rats. Naphthalene has also been shown to induce oxidative stress as evidenced by hepatic and brain lipid peroxidation, glutathione (GSH) depletion, DNA single strand breaks and membrane microviscosity, and excretion of urinary lipid metabolites in rats (Vuchetich et al 1996). Thus, the toxicity of naphthalene is at least in part related to free radicals and free radical-mediated oxidative stress.

The use of alternative therapies, herbs and supplements is very high among patients attending a variety of care settings (Mansoor 2001; Rahman 2003). Garlic has been used

as a folk remedy for a variety of ailments since ancient times. In various models, it has been found that garlic preparations, including aged garlic, prevented tumour promotion (Dorant et al 1993), cardiovascular diseases (Kleijnen et al 1989), liver damage (Nakagawa et al 1989) and aging (Moriguchi et al 1994), which are considered to be associated with oxygen radicals and lipid peroxidation. The intrinsic antioxidant activity of garlic (Rietz et al 1993), garlic extracts (Numagami et al 1996; Prasad et al 1996) and some garlic constituents (Ide et al 1996; Rabinkov et al 1998) has been widely documented in-vivo (Augusti & Sheela 1996; Iqbal & Athar 1998) and in-vitro (Prasad et al 1996; Rabinkov et al 1998). Garlic extracts increase superoxide dismutase (Geng & Lau 1997), glutathione peroxidase (Wei & Lau 1998), and catalase activity (Wei & Lau 1998) in vascular cells in culture, and *S*-allyl-cysteine sulfoxide (alliin), a garlic compound, prevents the decrease in hepatic superoxide dismutase and catalase activity observed in diabetic rats (Augusti & Sheela 1996). Şener et al (2003a, b) previously demonstrated that aqueous garlic extract (AGE) protects against oxidative tissue damage induced by thermal trauma or ischaemia/reperfusion in rats.

The present study was designed to determine the possible protective effects of AGE against naphthalene-induced oxidative damage in the kidney, liver, lung and brain of mice by using biochemical approaches, such as the measurement of malondialdehyde (MDA) and GSH levels and myeloperoxidase (MPO) levels, as well as by the histological analysis of tissue injury.

Materials and Methods

Animals

Balb/c mice (25–30 g) of either sex were housed in a room at a mean constant temperature of $22 \pm 2^{\circ}C$, 50–60% relative humidity, 12-h light/dark cycle, and had free access to standard pellet chow and water. The mice were maintained under these conditions for at least 1 week before the experiments. The study was approved by the Marmara University School of Medicine Animal Care and Use Committee (23.02.2004-86.2003.mar.)

Experimental groups

Mice were used in this study because of the differences in naphthalene toxicity between rats and mice, as reflected by the ability of naphthalene to more severely deplete nonprotein sulfhydryls in mouse tissues as compared with rat tissue (O'Brien et al 1985).

Balb/c mice of either sex were divided into five groups each comprising 10 animals. Mice received for 30 days: 0.9% NaCl, i.p. (control); corn oil, i.p.; AGE in a dose of $125\,mg\,kg^{-1}$, i.p.; naphthalene in a dose of $100\,mg\,kg^{-1}$, i.p. (dissolved in corn oil); and AGE (in a dose of $125\,mg\,kg^{-1}$, i.p.) plus naphthalene (in a dose of $100\,mg\,kg^{-1}$, i.p.; mice in this group received two injections per day).

After 30 days of treatment, mice were killed by decapitation, trunk blood was collected and serum and tissue (liver, kidney, lung and brain) samples were stored at $-70^{\circ}C$. GSH (a key antioxidant) and MDA (an end product of lipid peroxidation) levels were measured in these samples. Tissue-associated MPO activity, as indirect evidence of neutrophil infiltration, was measured in all tissue samples, while oxidant-induced tissue fibrosis was determined by tissue collagen content. For histological analysis, samples of the tissues were fixed in 10% buffered *p*-formaldehyde and prepared for routine paraffin embedding.

Biochemical analysis

Serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels, and blood urea nitrogen (BUN) and creatinine concentrations were determined to assess hepatic and renal function, respectively.

GSH and MDA assays

Tissue samples were homogenized with ice-cold trichloracetic acid (1 g tissue in 10 mL 10% TCA) in an Ultra Turrax tissue homogenizer. GSH measurements were performed using a modification of the Ellman procedure (Beutler 1975). Briefly, after centrifugation at 1200 *g* for 10 min, 0.5 mL of supernatant was added to 2 mL of 0.3 mol/l $Na_2HPO_4.2H_2O$ solution. A 0.2-mL solution of dithiobisnitrobenzoate ($0.4\,mg\,mL^{-1}$ 1% sodium citrate) was added and the absorbance at 412 nm was measured immediately after mixing. GSH levels were calculated using an extinction coefficient of $13\,600\,M^{-1}\,cm^{-1}$. The results are expressed as μmol GSH $(g\ tissue)^{-1}$. The MDA levels were assayed for products of lipid peroxidation by monitoring thiobarbituric acid reactive substance formation as described previously (Beuge & Aust 1978). Lipid peroxidation was expressed in terms of MDA equivalents using an extinction coefficient of $1.56 \times 10^5\,M^{-1}\,cm^{-1}$ and the results are expressed as nmol MDA $(g\ tissue)^{-1}$.

Measurement of MPO activity

Tissue MPO activity was assessed by measuring the H_2O_2-dependent oxidation of *o*-dianizidine 2HCl. One unit of enzyme activity was defined as the amount of MPO present that caused a change in absorbance of 1.0 units min^{-1} at 460 nm and 37°C, and is expressed in units $(g\ tissue)^{-1}$ (Hillegas et al 1990).

Tissue collagen measurement

Tissue samples were cut with a razor blade and immediately fixed in 10% formalin in 0.1 M phosphate buffer (pH; 7.2) in paraffin, and sections approximately 15 μm thick were obtained. The evaluation of collagen content was based on the method of Lopez de Leon & Rojkind (1985), which is based on selective binding of the dyes Sirius Red and Fast Green FCF to collagen and non-collagenous components, respectively. Both dyes were eluted readily and simultaneously by using 0.1 M NaOH/methanol (1:1, v/v). Finally, the absorbance at 540 and 605 nm was used to determine the amount of collagen and protein, respectively.

Histological preparation and analysis

Samples of liver, lung, kidney and brain tissue were fixed in 10% formaldehyde and processed routinely for embedding in paraffin. Paraffin sections were stained with haematoxylin and eosin and examined under a light microscope. Microscopic scoring was done by experienced histologists, unaware of which treatment the animal was subjected to. The histological score of an organ was calculated as the sum of the scores (0 to 3) given for each criterion, using the semiquantitative scale outlined in Table 1 (Özveri et al 2001). The maximum score calculated was 12 for the liver, lung and kidney, and 9 for the brain.

Statistical analysis

Statistical analysis was carried out using GraphPad Prism 3.0 (GraphPad Software; San Diego, CA, USA). Groups of data were compared using analysis of variance followed by Tukey's multiple comparison tests. Values of $P < 0.05$ were regarded as significant. All data are expressed as means ± s.d.

Table 1 Criteria for the microscopic scoring of tissue damage

Tissue	Appearance
Liver	Vasocongestion
	Vacuolization of hepatocytes and pyknotic hepatocyte nuclei
	Enlargement of sinusoids
	Kupffer cell infiltration
Kidney	Degeneration of Bowman space and glomeruli
	Degeneration of proximal and distal tubules
	Vascular congestion and interstitial oedema
	Leukocyte infiltration
Lung	Vascular congestion and interstitial oedema
	Alveolar haemorrhage
	Interalveolar septal fusion
	Inflammatory cell infiltration
Brain	Degeneration of neurons
	Vasocongestion
	Oedema

Scores for each criterion were: 0, none; 1, mild; 2, moderate, 3, severe. At least five microscopic areas were examined to score each specimen.

Results

Hepatic and renal function

Serum AST and ALT levels were determined to measure hepatic function, while BUN and serum creatinine concentrations were used for the assessment of renal function. AST and ALT levels were significantly increased in the naphthalene group ($P < 0.05$ and $P < 0.001$, respectively). Treatment with AGE caused a significant reduction in both AST and ALT levels ($P < 0.01$ and $P < 0.05$, respectively; Table 2). BUN and creatinine levels, which were significantly increased in the naphthalene group ($P < 0.01$), were reversed to control levels by AGE treatment ($P < 0.01$ and $P < 0.05$, respectively; Table 2).

Tissue and serum GSH and MDA levels

The mean GSH levels of liver, kidney, lung and brain samples in the naphthalene-treated group were significantly lower compared with the control group ($P < 0.01$–0.001; Figure 1). In the AGE-treated naphthalene group, GSH levels were restored in all tissues ($P < 0.05$–0.001), whereas AGE and corn oil treatment alone had no significant effect. Similarly, the decrease in serum GSH levels due to chronic naphthalene administration ($P < 0.01$) was significantly reversed by AGE treatment ($P < 0.05$; Table 2).

The mean level of MDA, a major degradation product of lipid peroxidation, was increased in all tissues after naphthalene administration compared with the control group ($P < 0.01$–0.001; Figure 2). In the AGE-treated naphthalene group, there was a marked decrease in MDA levels compared with the naphthalene group ($P < 0.05$–0.001), whereas AGE and corn oil alone had no effect. Moreover, the serum MDA level, which was higher in the naphthalene group compared with the control group ($P < 0.001$), was also reversed by AGE treatment ($P < 0.001$; Table 2).

Table 2 Serum malondialdehyde (MDA), glutathione (GSH), alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN) and creatinine levels in the different treatment groups (n = 10 mice per group)

Parameter	Control	Corn oil	Aqueous garlic extract	Naphthalene	Naphthalene + aqueous garlic extract
MDA (nmol mL^{-1})	2.3 ± 0.1	2.2 ± 0.1	2.3 ± 0.2	5.1 ± 0.3***	2.6 ± 0.3^{+++}
GSH (μmol mL^{-1})	26.3 ± 1.6	27. ± 1.9	27.6 ± 1.4	17.8 ± 1.1**	24.6 ± 1.6^{+}
ALT (units L^{-1})	69.3 ± 3.3	64.8 ± 2.6	65.8 ± 2.2	103.8 ± 6.7***	83.0 ± 3.4^{++}
AST (units L^{-1})	168.5 ± 7.4	163.2 ± 7.8	156.8 ± 6.6	206.8 ± 12.8*	157.0 ± 6.2^{+}
BUN (mg dL^{-1})	26.3 ± 1.5	24.7 ± 1.9	22.0 ± 0.9	36.6 ± 2.2**	26.2 ± 1.7^{++}
Creatinine (mg dL^{-1})	0.48 ± 0.03	0.53 ± 0.04	0.46 ± 0.04	0.73 ± 0.05**	0.53 ± 0.04^{+}

Groups of data were compared using analysis of variance followed by Tukey's multiple comparison tests. Data are mean ± s.d. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$, compared with the control group. $^{+}P < 0.05$, $^{++}P < 0.01$, $^{+++}P < 0.001$, compared with the naphthalene-treated group.

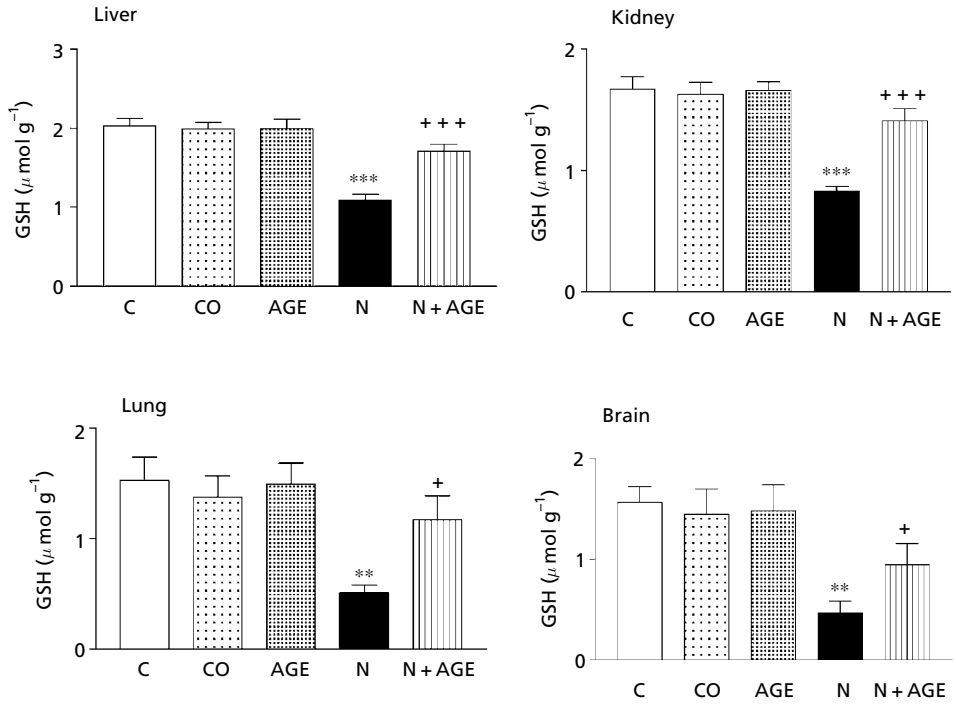

Figure 1 Glutathione (GSH) levels in the liver, kidney, lung and brain tissues of control (C), corn oil (CO), aqueous garlic extract (AGE), naphthalene (N) and N + AGE groups. Each group comprised 10 mice. Groups of data were compared with analysis of variance followed by Tukey's multiple comparison tests. $^{**}P < 0.01$, $^{***}P < 0.001$, compared with the control group. $^{+}P < 0.05$, $^{+++}P < 0.001$, compared with the naphthalene-treated group.

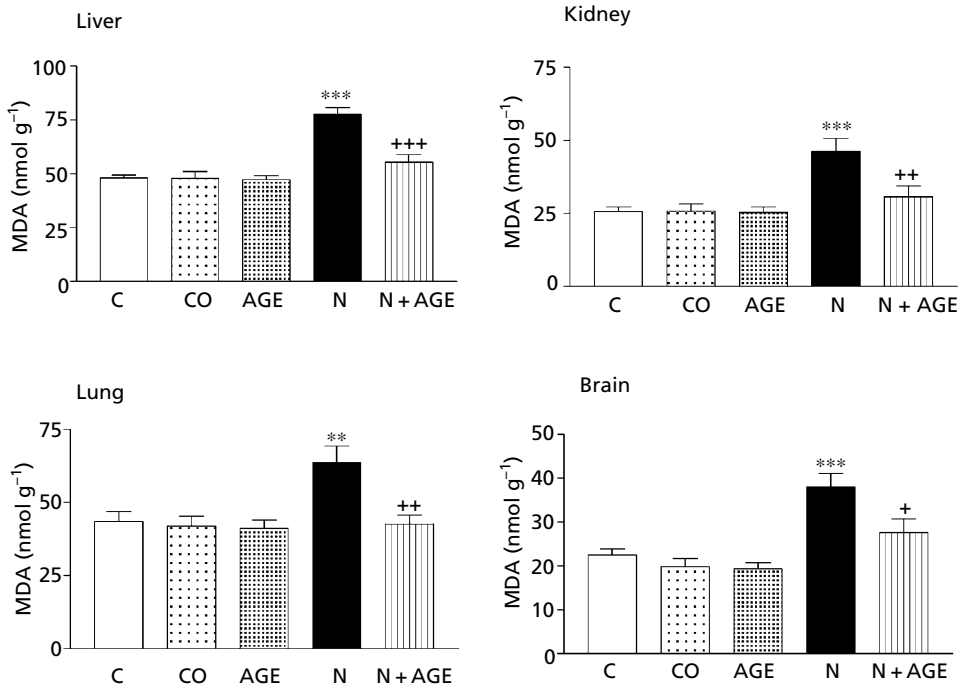

Figure 2 Malondialdehyde (MDA) levels in the liver, kidney, lung and brain tissues of control (C), corn oil (CO), aqueous garlic extract (AGE), naphthalene (N) and N + AGE groups. Each group comprised 10 mice. Groups of data were compared with analysis of variance followed by Tukey's multiple comparison tests. $^{**}P < 0.01$, $^{***}P < 0.001$, compared with the control group. $^{+}P < 0.05$, $^{++}P < 0.01$, $^{+++}P < 0.001$, compared with the naphthalene-treated group.

MPO activity

Chronic naphthalene administration increased MPO activity in the liver, kidney, lung and brain tissue samples compared with those in the control group ($P < 0.05$–0.001) and AGE treatment reversed this effect ($P < 0.05$–0.001). AGE and corn oil treatment alone had no effect on tissue MPO activity in control animals (Figure 3).

Tissue collagen content

As an indicator of the level of fibrotic activity in tissues, the collagen content in all the tissues was markedly increased after naphthalene administration when compared with the control group ($P < 0.01$–0.001; Figure 4). In the AGE-treated naphthalene group, this effect was reversed ($P < 0.05$–0.001), whereas AGE and corn oil alone did not change the collagen content of these tissues in control animals.

Histological examination

Naphthalene-induced cellular damage was found in all tissues as evidenced by structural degeneration, vasocongestion and oedema, accompanied by inflammatory cell infiltration (Table 3). Although AGE treatment did reduce the scores, the differences were not significant.

Discussion

Chronic naphthalene administration resulted in a significant increase in lipid peroxidation in all tissues (liver, kidney, lung and brain), including blood, compared with control animals. It also caused a significant reduction in the tissue and blood GSH content, indicating the utilization of endogenous antioxidants for protection against naphthalene-induced oxidant injury. Moreover, naphthalene caused significant increases in MPO activity in the kidney, liver, lung and brain tissues, indicating that naphthalene exacerbated neutrophil-derived reactive oxygen metabolite production and may be involved in the risk of multiple organ damage. In this study, the renal and hepatic dysfunction (assessed by serum BUN and creatinine concentrations, and ALT and AST levels, respectively) and tissue damage in the chronic naphthalene-treated group seemed to be the consequence of naphthalene-induced oxidative damage.

Naphthalene exposure is associated with several toxic manifestations in humans and laboratory animals, with the lens of the eye and the lungs being the most sensitive (Stohs et al 2002). In humans, toxicity mostly involves low dose, chronic exposure to naphthalene (O'Brien et al 1985). In mice, 200 mg kg^{-1} intraperitoneal naphthalene administration caused pulmonary damage (O'Brien et al 1985). Koch et al (1976) reported the development of cataracts following exposure to naphthalene. In tests with Chinese hamster ovary cells, naphthalene induced sister chromatid exchanges with and without exogenous metabolic activation. Naphthalene caused an increase in the incidence and severity of olfactory epithelial metaplasia of respiratory epithelium in the nose and chronic inflammation in the lungs of mice (National Toxicology Program 1992).

Naphthalene undergoes extensive microsomal metabolism. The first step in naphthalene metabolism is oxidative

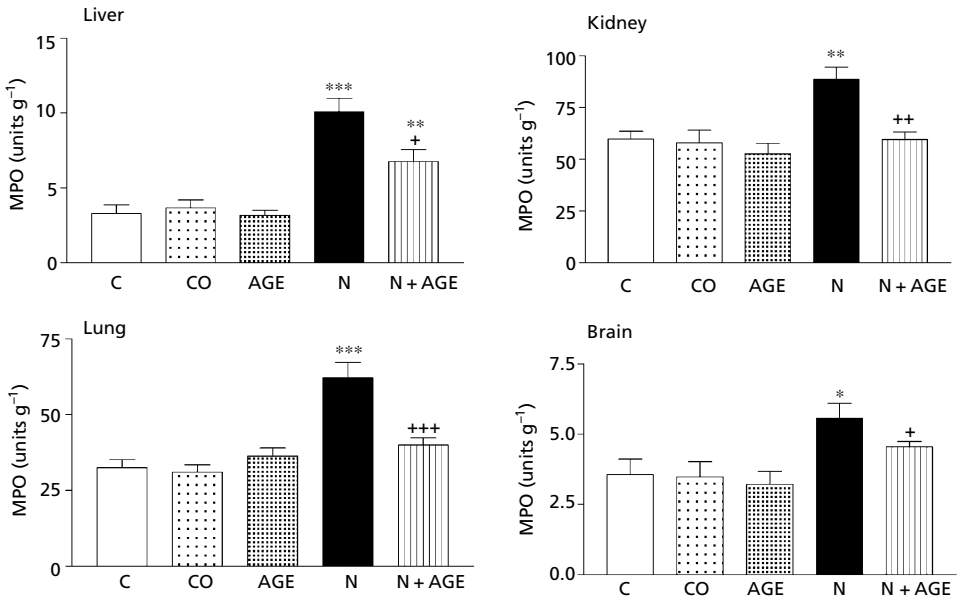

Figure 3 Myeloperoxidase (MPO) activity in the liver, kidney, lung and brain tissues of control (C), corn oil (CO), aqueous garlic extract (AGE), naphthalene (N) and N + AGE groups. Each group comprised 10 mice. Groups of data were compared with analysis of variance followed by Tukey's multiple comparison tests. $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$, compared with the control group. $^{+}P < 0.05$, $^{++}P < 0.01$, $^{+++}P < 0.001$, compared with the naphthalene-treated group.

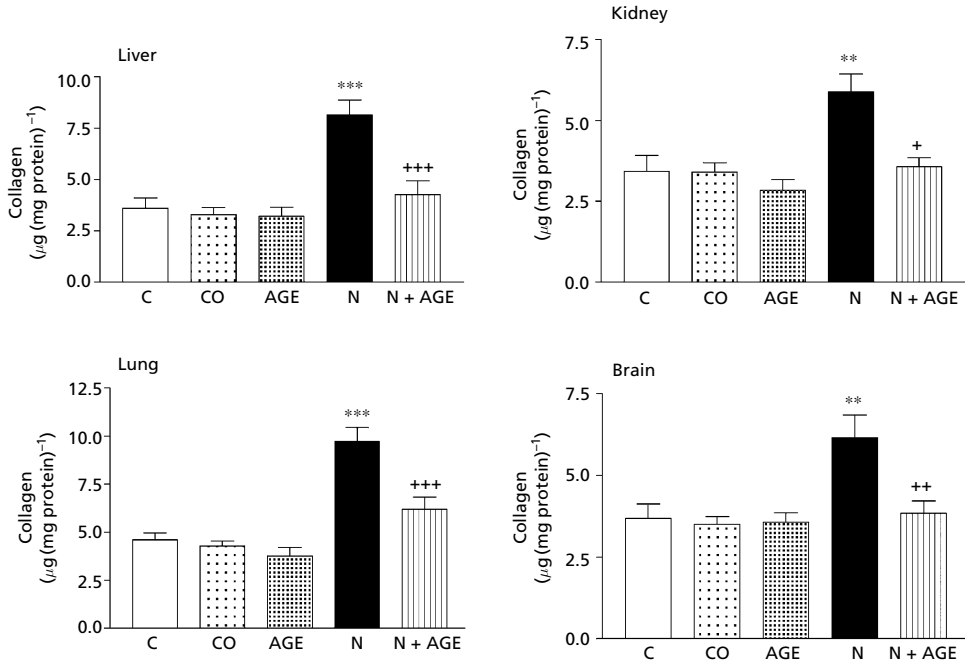

Figure 4 Collagen content in the liver, kidney, lung and brain tissues of control (C), corn oil (CO), aqueous garlic extract (AGE), naphthalene (N) and N + AGE groups. Each group comprised 10 mice. Groups of data were compared with analysis of variance followed by Tukey's multiple comparison tests. $^{**}P < 0.01$, $^{***}P < 0.001$, compared with the control group. $^{+}P < 0.05$, $^{++}P < 0.01$, $^{+++}P < 0.001$, compared with the naphthalene-treated group.

Table 3 Total histological scores of the liver, kidney, lung and brain tissues in the different treatment groups (n = 10 mice per group).

Tissue	Control	Corn oil	Aqueous garlic extract	Naphthalene	Naphthalene + aqueous garlic extract
Liver	0.5 ± 0.5	0.4 ± 0.5	0.3 ± 0.5	11.3 ± 0.8***	5.6 ± 1.4
Kidney	0.3 ± 0.5	0.4 ± 0.5	0.4 ± 0.5	10.8 ± 1.6***	6.8 ± 1.2
Lung	0.4 ± 0.5	0.4 ± 0.5	0.3 ± 0.5	11.8 ± 0.4***	6.3 ± 1.0
Brain	0.2 ± 0.4	0.2 ± 0.4	0. 3 ± 0.5	8.8 ± 0.4***	4.8 ± 1.0

The maximum score was 12 for the liver, kidney and lung, and 9 for the brain. Groups of data were compared with the Kruskal–Wallis test followed by Dunn's test. Data are mean ± s.d. $^{***}P < 0.001$, compared with the control group.

in nature and is catalysed by cytochrome P-450 oxygenases in the microsome, producing an electrophilic arene epoxide intermediate, 1,2-naphthalene oxide (Jerina et al 1970). The epoxides can spontaneously rearrange to form naphthols (predominantly 1-naphthol), which undergo further metabolism to naphthaquinons. Naphthaquinons are directly toxic to mononuclear leukocytes and depleted GSH to 1% of control levels (Wilson et al 1996). As GSH is a key antioxidant, depletion of GSH may cause oxidant damage. Bagchi et al (2001) demonstrated that cultured macrophage J774A.1 cells with naphthalene resulted in a concentration-dependent increase in the production of superoxide anion and hydroxyl radical production. Thus, depletion of GSH and tissue damage may occur not only as a result of metabolism of naphthalene to reactive intermediates, but also to the formation of reactive oxygen species.

As a free radical generating system, lipid peroxidation has been suggested to be closely related to oxidant-induced tissue damage, and MDA is a good indicator of the degree of lipid peroxidation (Vuchetich et al 1996; Şener et al 2003a, b). Lipid peroxidation mediated by reactive oxygen species is believed to be an important cause of damage to cell membranes and attention has been focused on the role of reactive oxygen species in mediating the microvascular disturbances that precede tissue damage induced by various chemicals (Reiter et al 2000). In our study, intraperitoneal administration of 100 mg kg^{-1} naphthalene significantly increased lipid peroxidation in liver, lung, kidney and brain tissues of mice, indicating oxidative damage. This increase in lipid peroxidation may partly be due to the free radicals generated by neutrophils. While the MPO and MDA levels were increased, GSH levels were decreased in these tissues.

GSH, the main intracellular non-protein sulfhydryl, plays an important role in the maintenance of cellular proteins and lipids in their functional state, and provides major protection in oxidative injury by participating in the cellular defence systems against oxidative damage (Ross 1988). Several reports indicate that tissue injury, induced by various stimuli, is coupled with GSH depletion (Paller & Patten 1992; Şener et al 2003b, c).

GSH depletion plays a key role in the toxicity of naphthalene and is an effective biomarker. Rao & Pandya (1981) reported increased lipid peroxidation in liver of naphthalene treated rats. Yamauchi et al (1986) demonstrated that naphthalene elevated the serum lipid peroxides, with a concomitant decrease in GSH levels in lenses, suggesting enhanced lipid peroxidation. In another study conducted in rats, naphthalene (750 mg kg^{-1}, i.p.) resulted in enhanced lipid peroxidation in the liver, but not in other tissues, including eye, lung and heart (Germansky & Jamall 1998). The lack of effect of naphthalene on lipid peroxidation in the lung was confirmed by Honda et al (1990) who demonstrated a significant depletion of pulmonary GSH levels but no changes in lipid peroxidation and phospholipid content in the liver. On the other hand, Vuchetich et al (1996) demonstrated that high-dose naphthalene administration to Sprague-Dawley rats resulted in significant increases in lipid peroxidation in the liver and brain after 24 h. Thus, toxicity varies depending on dose, route of administration and species. Since most exposure to naphthalene is of a low dose, chronic nature, we administered naphthalene in a dose of 100 mg kg^{-1} to mice for 30 days. We observed a significant increase in lipid peroxidation in the liver, kidney, lung and brain tissues, while GSH was decreased. Since the roles of oxidative stress, reactive oxygen species and the critical role of GSH in preventing naphthalene toxicity are well documented, agents that have antioxidant properties would be beneficial. The GSH precursor *N*-acetylcysteine and free radical spin trapping agent α-phenyl-*N*-*t*-butylnitrone have been shown to decrease naphthalene-induced cataracts effectively (Wells et al 1989). Since the administration of AGE prevented the tissue and blood GSH depletion, it appears that the protective effect of AGE involves the maintenance of antioxidant capacity in protecting the tissues against oxidative stress.

Besides their direct damaging effects on tissues, free radicals seem to trigger the accumulation of leukocytes in the tissue involved and therefore also cause tissue injury indirectly through activated neutrophils. Activated neutrophils are known to induce tissue injury through the production and release of reactive oxygen metabolites and cytotoxic proteins (e.g. proteases, MPO, lactoferrin) into the extracellular fluid. MPO is an essential enzyme for normal neutrophil function. When neutrophils are stimulated by various stimulants, MPO as well as other tissue-damaging substances are released from the cells. Thus, it is an index of neutrophil infiltration. Since neutrophil infiltration is an important event for acute inflammation, an increase in MPO activity due to naphthalene may cause inflammation and damage in the organs. AGE treatment significantly decreased the enzyme activity and prevented neutrophil infiltration into the damaged tissue. These results suggest that naphthalene-induced oxidative damage involves the interaction of neutrophils and the protective effect of AGE is mediated in part by blocking neutrophil infiltration into the tissues. This may also result in reduced lipid peroxidation and less accumulation of MDA since activation of neutrophils might lead to the generation of oxygen reactive metabolites (Kettle & Winterbourn 1997).

In conclusion, AGE treatment significantly inhibits MDA production with a concomitant replenishment of tissue GSH content, indicating a reduction in lipid peroxidation and cellular injury, which protects the liver, kidney, lung and brain tissues against naphthalene-induced oxidative damage. The results suggest that AGE, with its potent free radical scavenging and antioxidant properties, may be a promising agent against naphthalene toxicity by protecting tissues against oxidative damage. However, as these effects may be species dependent, further studies are required to extend these results to humans.

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