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EXPERIMENTAL STUDY

The protective effect of N-acetylcysteine against acrylamide toxicity in liver and small and large intestine tissues

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Abstract: The aim of this study was to investigate the protective effects of N-acetylcysteine against acrylamide toxicity in liver and small and large intestine tissues in rats**.**
The rats were divided into four groups. Acrylamide administration increased MDA levels in all tissues significantly ($p < 0.05$). But acrylamide+NAC administration decreased MDA levels significantly as compared to the acrylamide group, and lowered it to a level close to the control group values ($p < 0.05$). GSH levels in liver and small intestine tissues reduced significantly in the acrylamide group ($p < 0.05$). But acrylamide+NAC administration increased GSH levels significantly in all tissues. Whereas GST activity decreased significantly in the acrylamide group in liver and small intestine tissues as compared to the other groups ($p < 0.05$), the GST activity increased significantly in the acrylamide+NAC group in all tissues as compared to the acrylamide group ($p < 0.05$). Liver histopathology showed that the liver epithelial cells were damaged significantly in the acrylamide group. Small intestine histopathology showed that the intestinal villous epithelial cells were damaged significantly in the acrylamide group.
Our results indicate that a high level of acrylamide causes oxidative damage in liver and small and large intestine tissues, while N-acetylcysteine administration in a pharmacological dose shows to have an antioxidant effect in preventing this damage *(Tab. 2, Fig. 2, Ref. 66)*. Text in PDF *www.elis.sk.*
Key words: acrylamide, N-acetylcysteine, oxidative stress, liver, small and large intestine.

Introduction

Acrylamide (ACR) is an unsaturated amide compound containing a double bond that may react with nucleophiles (1). It was first synthesized in United States in 1950s and used in several industrial fields such as textile, paper and cosmetics. ACR is neurotoxic, genotoxic and highly carcinogenic to humans and animals (2, 3). The experimental research shows that administering acrylamide in certain doses and periods may have toxic and carcinogenic effects on animals and humans (2–5). It has been proven that cooking foods at high temperature leads to high level of acrylamide to form and this fact has been an important milestone for studies related to acrylamide (6, 7). Acrylamide in food occurs at 120 °C or higher temperatures as a result of Maillard reaction between monosaccharides such as fructose or glucose and amino acids such as asparagine (7). The studies show that acrylamide is absorbed in a very rapid and effective manner by means of gastrointestinal system (8, 9).

Oxidative stress is a condition that spoils the oxidant/antioxidant balance in favor of oxidants as a result of a significant increase in reactive oxygen species (ROS) in cells and a decrease in antioxidant levels. Oxidative damage occurs in cellular structural macromolecules such as lipid, protein, carbohydrate and DNA, because free oxygen radicals cannot be detoxified in an adequate manner (10). It has been proven that oxidative stress plays an active role in atherosclerosis, inflammation, diabetes, pathogenesis of ischemia/reperfusion injury, gene mutation, carcinogenesis and damage caused by xenobiotics in tissues (11).

Malondialdehyde (MDA) is the most studied parameter as an indicator of lipid peroxidation in many diseases. MDA is both a biomarker of lipid oxidation and one of the potential causes of cancer. MDA is carcinogenic and was first described as a result of administration topically in rats in 1972 (12). Voitkun and Zhitkovich reported that MDA created cruciate bonds with DNA and proteins. This potential of MDA with genotoxic activities may cause both mutations and cancer (13). *In vitro* studies have shown that ACR decreases the glutathione (GSH) content (14). However, the changes in antioxidant structures following exposure to ACR have not been clarified yet. In a study about the effects of ACR on nerve tissues and antioxidant system, it was observed that while MDA level significantly increased, GSH level significantly decreased (15). Smoking is one of the most striking risk factors for lipid peroxidation. As free radicals occur while smoking (16, 17), plasma MDA level increases (18–20). Similarly, Gonenc et al. observed that plasma MDA levels were significantly high in breast and lung cancers (21). Recently, the studies related to smokers show that acrylamide occurs while the tobacco is burnt at a very

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high temperature and acrylamide is taken into the body together with the smoke. The scientists have interpreted this finding in such a manner that acrylamide may play an active role in lung cancer frequently developing in smokers (22, 23).

GSH is a tripeptide and takes charge in the antioxidant defense system of the cell. The active group of glutathione is thiol (-SH) group in cysteine residue. It is synthesized in all organs, especially in the liver, and is present in all mammalian cells (24). While GSH present in mammalian cells is in millimolar concentration (0.5–10 mM), this ratio of plasma is in micromolar concentration. While the majority of total GSH (85–90 %) is present in the cytosol, the remaining thereof (10–15 %) is present in the mitochondria and other organelles. It has been observed under some circumstances that the level of GSH in mitochondria reaches the level of GSH in the cytosol (25). Total glutathione is present as free or combined to proteins (15 %). Free glutathione is generally present in a reduced form and is transformed into an oxidized form during oxidative stress. The most crucial organs ensuring the GSH circulation permanency between organs are the liver and kidney. However, it is also partially provided by spleen, lens, erythrocyte and leukocytes (26). When irreversible cell damage occurs, GSH content in the cell loses its permanency. Measuring the GSH at different values in tissue samples is an important parameter for understanding several pathological conditions (27). GSH basically serves as an inhibitor against ROS. It has been determined that a decrease in GSH level in humans has a vital role in pathophysiology of many diseases including cancer, neurodegenerative and cardiovascular diseases (27–29).

Glutathione S-Transferase (GST) enzyme systems are the enzymes of Phase II metabolism, which are vital in eliminating or altering the endogenic toxins occurring in the cells because of xenobiotics (30). GST ensures the conjugation of different compounds with GSH and thus can use many carcinogenic compounds, environmental contaminants, drugs and many other compounds as substrates. GST enzyme is a dimer comprising two sub-units carrying one bonding area for xenobiotics and GSH (31). It was observed in a study conducted by Srivastava et al. that when the rats were exposed to ACR for ten days, GST activity decreased significantly in all areas of the brain (32). It has been observed in the studies conducted recently that Pi-izoenzyme of GST plays a vital role in tumorigenesis of the lung and is the izoenzyme present mostly in the human lung (33). It has also been observed in a study that GST Pi1 synthesis has increased significantly in the human lung fibroblasts in order to inhibit the cytotoxic effect of smoking (34).

N-acetylcysteine (NAC) is a molecule precursor of GSH. It has an antioxidant effect, and eliminates the hydrogen peroxide (H_2O_2), hydroxyl radicals and hypochlorite acid as *in vitro* (35). The studies have shown that NAC acts as both antioxidant and pro-oxidant in accordance with the dose and time applied. While it protects the rats against oxidative damage when administered in low doses, it may cause lung damage and deaths when applied in high doses (36, 37).

This study investigates the possible toxicity of acrylamide on liver and small and large intestine tissues and the protective role of NAC against this toxicity.

Material and methods

Experimental animals

In the research, 40 male Wistar rats obtained from Experimental Research Unit of Inonu University, Faculty of Medicine, weighting approximately 225–250 grams were used. The experimental protocol was evaluated and approved by the Ethics Review Committee of Inonu University, Faculty of Medicine. The rats were equally divided into four groups as Group 1 (Control; n = 10), Group 2 (Acrylamide; n = 10), Group 3 (NAC; n = 10) and Group 4 (Acrylamide + NAC; n = 10). The rats were maintained in rooms at temperature of 21 °C and moisture of 55–60 % and 12-hour light (08:00–20:00)/dark cycle. The experimental animals were fed *ad libitum*.

Experimental design

Group 1 (n = 10): Control Group (C): 1 mL normal saline was administered with gavage per day.

Group 2 (n = 10): Acrylamide Group (25 mg/kg/day): Acrylamide was dissolved in normal saline, and 1 mL solution was daily administered to each rat with gavage (4, 38–40).

Group 3 (n = 10): N-acetylcysteine Group (250 mg/kg/day): N-acetylcysteine was dissolved in normal saline, and 1 mL solution was administered to each rat daily with gavage (36, 37).

Group 4 (n = 10): Acrylamide (25 mg/kg/day) and N-acetylcysteine (250 mg/kg/day) Group: Acrylamide and N-acetylcysteine were dissolved in normal saline, and 1 mL solution was administered to each rat daily with gavage.

The administrations were continued regularly at the same hours during 21 days. Liver and small and large intestine tissue samples were taken from all decapitated animals at the end of the studies conducted for 21 days. The tissue samples were washed with normal saline and the excessive blood was removed. All tissue samples were divided into two pieces. One of them was placed in formaldehyde solution for routine histopathological examination by light microscopy and the other half was homogenized inside ice for 1–2 minutes at 12000 rpm with a homogenizator (IKA Ultra Turrax T 25 basic, IKA Labotechnik, Staufen, Germany) within 0.1 M Tris-HCl (pH:7.5) buffer. Tissue homogenates were centrifuged for 20 minutes at 4 °C at 5000 rpm. GST activity and GSH, MDA and protein levels of the supernatants were measured. GST activity, GSH, MDA and protein levels were analyzed using spectrophotometric methods.

Biochemical analyses

Reduced glutathione (GSH) analysis

GSH analysis was performed in accordance with Ellman (41) method. The principle of this method is that glutathione reacts with 5,5'-dithiobis 2-nitrobenzoic acid and gives yellow-greenish color. This color is read at spectrophotometer at 410 nm. A 10 % trichloroacetic acid (TCA) solution was added to the supernatants obtained from the liver and small and large intestine samples; they were mixed and centrifuged again at 3000 rpm at 4 °C for 20 minutes, and protein sedimentation was precipitated. The light-colored supernatant samples were used in GSH analysis. Results are ex-

pressed as nmol/g wet tissue. In order to prepare GSH standard, 16 mg GSH was dissolved in 10 mL distilled water by being vortexed. This stock solution was 5mM (5000 µmol/L). By using this stock solution, serial standards of 2500, 1000, 500, 400, 250, 100 and 50 µmol /L were prepared with appropriate dilutions. Distilled water was used as a blank. Standard graphic was plotted based on the recording of absorbance of serial standards at 410 nm.

Malondialdehyde (MDA) analysis

MDA was analyzed in accordance with the method described by Ohkawa et al (42). The main principle of the analysis is based on the fact that MDA in the medium reacts when heated with thiobarbituric acid and creates a pink chromogen. The intensity of pink color is in direct proportion to MDA concentration. The homogenates obtained from liver and small and large intestine tissue samples were used in MDA analysis. Results are expressed as nmol/g wet tissue. Stock solution of 1mmol/L (1000 µmol /L) was prepared in order to obtain MDA standard by taking 17 µL 1,1,3,3 tetramethoxypropane and being completed to 100 mL with ethanol. By using this stock solution, serial standards of 10, 5, 2.5, 1.25 and 0.62 µmol /L were prepared while n-butanol was used as a blank. Standard graphic was plotted based on recording of absorbance at 520 and 535 nm.

Glutathione S-transferase (GST) analysis

GST activity is determined in accordance with the method of Habig et al (43). GST enzyme activity is determined by measuring the enzyme amount catalyzing 1 µmol of S-(2,4 dinitrophenyl)-glutathione occurring in a minute by using GSH and 1-chloro-2,4-dinitrobenzene (CDNB) at 340 nm and 37 °C. The supernatants obtained from the samples of liver and small and large intestine tissues were used for determining the GST activity levels. GST (sigma) was dissolved in normal saline and serial enzyme standards were prepared so as to have 5, 3.75, 2.5, 1.25 and 0.63 units of enzyme activity per mL. Each of these standards was studied like a sample, and absorbance measurements were performed spectrophotometrically. Then, GST standard graphic was plotted and GST activity levels of supernatant samples were measured with this graphic as mU/mg protein.

Histological determination

Liver and small intestine tissues were taken for examination, the tissue samples were washed with normal saline and the excessive blood was removed. After the tissues had been split into small pieces and embedded in formaldehyde solution, they were cut in the size of 5µm and placed onto the slides. Sections were stained with hematoxylin eosin (H&E); the liver and small intestine tissues were examined using Leica DFC 280 light microscope and leica Q Win Plus Imagine Analysis System (Leica Micros Imaging Solutions Ltd.; Cambridge, U.K.) at x40 magnification for liver tissue and x20 magnification for small intestine tissue.

Tab. 2. GST activity levels of liver and small and large intestine tissues.

Groups	Small intestine	Large intestine	Liver
	GST(mU/ mg Protein)		
C	92.4±18.2	45.6±25.3	150.3±20.3
ACR	47.4±11.9*	29.6±5.6	81.7±16.6*
NAC	115.6±22.7**	45.9±17.3*	181.1±52.3**
ACR-NAC	74.4±10.0***	40.5±12.6**	130.6±9.5***

GST values of tissues are mU/ mg Protein. In terms of small intestine and liver GST activity; it was found that there was a statistically significant difference ($p < 0.05$) between the groups of *C / ACR, **ACR/ NAC and ***ACR / ACR-NAC. In terms of large intestine GST activity; it was found that GST activity decreased when compared with C / ACR, but this decrease was not statistically significant. On the other hand, there was a statistically significant difference ($p < 0.05$) between the groups of **ACR/NAC and ***ACR /ACR-NAC.

Statistical analysis

Statistical analyses were performed via SPSS program (SPSS for Windows version 11.0). All the results were expressed as mean ± standard deviation (mean ± SD). The fact whether the data showed normal distribution was determined by means of Shapiro Wilk test and it was found that the data did not show normal distribution ($p < 0.05$). Therefore, Mann-Whitney U test was used in the comparison of the groups. The value ($p < 0.05$) was accepted as statistically significant.

Results

Biochemical results

Tables 1 and 2 present the tissue levels of MDA, GSH and GST activity. It was found that acrylamide administration increased MDA levels in all tissues significantly in the ACR group as compared to the other groups ($p < 0.05$), while Acrylamide and N-acetylcysteine administration decreased the MDA levels significantly in ACR-NAC group when compared to ACR group (Tab. 1).

Acrylamide administration decreased the GSH levels significantly ($p < 0.05$) in liver and small intestine tissues in ACR

Tab. 1. MDA and GSH values in liver and small and large intestine tissues.

GROUPS	Small Intestine		Large Intestine		Liver	
	MDA	GSH	MDA	GSH	MDA	GSH
C	188±52	781±100	195±37	465±91	453±481	239±200
ACR	328±60*	468±61*	312±29*	302±56	726±74*	672±91*
NAC	168±26**	920±127**	177±31**	704±229*	371±51**	1315±177**
ACR-NAC	221±18***	663±164***	205±60***	639±206**	523±68***	1183±136***

MDA and GSH values are nmol/g wet tissue. In terms of small intestine GSH and MDA levels; it was found that there was a statistically significant difference ($p < 0.05$) between the groups of *C / ACR, **ACR/ NAC, ***ACR / ACR-NAC. In terms of large intestine GSH levels; there were statistically significant differences between the groups of *NAC/ACR and ** ACR-NAC/ACR. In terms of large intestine MDA levels; there were statistically significant differences among the groups of *C / ACR, **ACR/ NAC and ***ACR / ACR-NAC ($p < 0.05$). It was also found that there were statistically significant differences ($p < 0.05$) among the groups of * C / ACR, **NAC/ACR and ***ACR-NAC / ACR in terms of liver GSH and MDA levels.

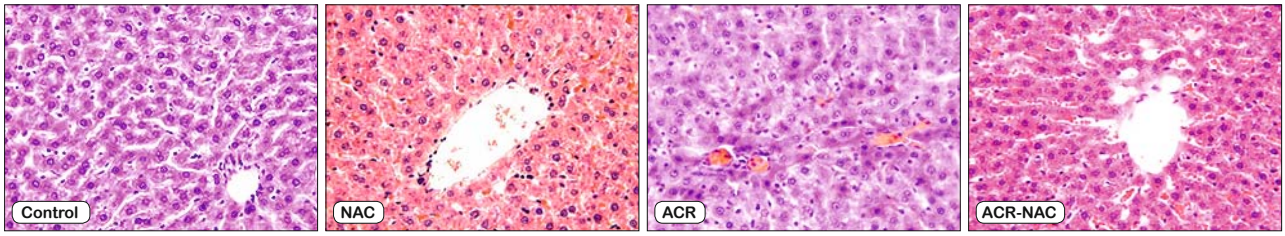

Fig. 1. Liver Histopathology results (H&E x40).

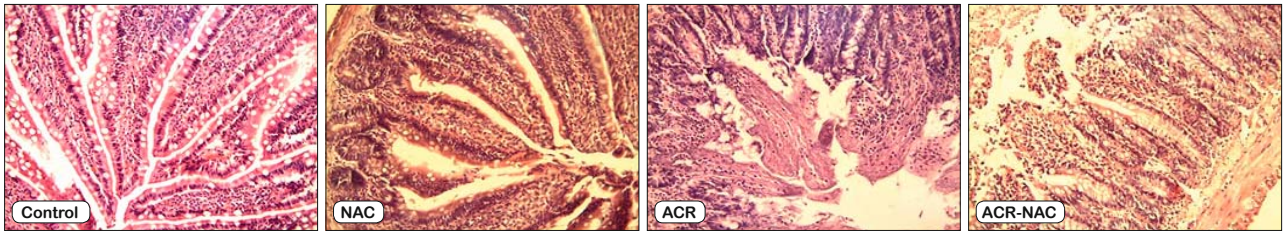

Fig. 2. Histopathology results of small intestine (H&E x20).

group as compared to other groups, but when acrylamide and N-acetylcysteine were administered together, GSH levels increased significantly when compared to ACR group ($p < 0.05$). It was also found that acrylamide administration decreased the large intestine GSH levels in a statistically insignificant manner; however, NAC administration prevented the GSH decrease ($p < 0.05$) (Tab. 1).

Acrylamide administration decreased the level of GST activity significantly in liver and small intestine tissues in ACR group as compared to other groups ($p < 0.05$). However, when acrylamide and N-acetylcysteine were administered together, GST activity increased significantly when compared to ACR group ($p < 0.05$). It was also observed that acrylamide administration decreased the large intestine GST activity, but this decrease was not statistically significant as compared to the control group. When acrylamide and N-acetylcysteine were administered together, GST activity levels increased significantly as compared to ACR group ($p < 0.05$) (Tab. 2).

Histological results

The hepatocytes in the control group had normal appearance, but different-sized vacuoles in the cytoplasm of hepatocytes were observed in ACR group. The cytoplasm of hepatocyte cells was more eosinophilic than in the others. Furthermore, nuclei of eosinophilic-cytoplasm hepatocytes were heterochromatic. The histological appearance of the NAC group was similar to the control group. Although some vacuoles were observed in ACR+NAC group, there were fewer of them than in ACR group. In addition, eosinophilic hepatocyte cells were rarer in ACR+NAC group when compared to ACR group (Fig. 1).

Small intestine tissues, villous structures and single-layered prismatic epithelial tissue in the control group had normal histological appearance. In ACR group however, villous structures were damaged, epithelium covering the villous surface was rubbed off and cell density in lamina propria was decreased. The small intestine in NAC group had normal appearance, but the top sections of villous structures in ACR+NAC group were rubbed off while their lateral surfaces had strong epithelium (Fig. 2).

Discussion

Acrylamide is a xenobiotic which is commonly used in industry and has some genetic risks that have not been cleared yet (44). Acrylamide that is found in foods is basically dangerous to human health. In Maillard reaction, the amino group of asparagine amino acid and carbonyl group of glucose react and acrylamide occurs (45). Acrylamide especially occurs in fried, roasted, grilled or baked foods at a temperature above 120 °C (46). Acrylamide occurs in products such as biscuit or milk pudding because of Maillard reaction occurring when sugar, oil and milk are cooked at high temperature. As a consequence, human health is negatively affected. The structure of some proteins in milk is spoiled because of Maillard reaction and effects toxic to the liver may take place (47).

ROS occur to a certain level during normal physiologic metabolism in full eukaryotic cells. The leading radicals are superoxide anion radical (O_2^{-}), hydrogen peroxide (H_2O_2), hydroxyl radical ($\cdot OH$), singlet oxygen ($^1O_2$) and peroxyl radical ($LOO\cdot$). However, ROS occurring at a certain level during normal metabolism is detoxified by antioxidant systems of the cell and this eliminates the oxidative damage that may occur in the macromolecules of cell (proteins, enzymes, lipids, carbohydrates, DNA and RNA). In other words, there is a balance between the levels of oxidants occurring in the cell under physiologic conditions and total antioxidant capacity. This condition is called oxidant/antioxidant balance (48, 49).

The research using experimental animals, humans and cell cultures has demonstrated that acrylamide administration increases the generation of free oxygen radicals and decreases the GSH and GST activity levels. Therefore, oxidant/antioxidant balance is spoiled, oxidative stress occurs and thereby, oxidative damage occurs in cells (1, 14, 50–52).

One study found that the level of thiobarbituric acid reactive products had increased significantly in the liver samples taken

from the rats administrated with acrylamide in acute dose. It was observed that the increase in lipid peroxidation was due to the decrease in liver GSH levels (53).

In a study wherein rats were administrated with acrylamide in single and repetitive doses, Srivastava indicated that acrylamide decreased the GST and GSH levels in the brain tissue and thus oxidative damage based on acrylamide occurred (14).

Pupel et al (50) discussed the relationship between the GSH level and genotoxic effect of acrylamide. The study found that conjugation with acrylamide in accordance with the high GSH level within the cell decreased the glycidamide generation (acrylamide is metabolized to a chemically reactive epoxide) and prevented the genotoxic damage based on glycidamide in a significant manner. In addition, even low acrylamide (1 mM) in animals administered with GSH synthesis inhibitor caused severe damage to cell DNAs. These results showed that intracellular GSH level had utmost importance in preventing the genotoxic effects based on both acrylamide and glycidamide.

In another study, in which acrylamide was administered to the rats an increase was observed in thiobarbituric acid reagents, GST activity levels and Superoxide Dismutase (SOD) levels in accordance with the dose of acrylamide administered; however, a significant decrease was achieved in GSH levels (54). In our study however, while MDA levels increased significantly in small and large intestine and liver tissues after acrylamide administration, GST activity and GSH levels decreased significantly. In the study conducted by Yousef and El-Demerdash, it was observed that GST activity increased in the tissues following the acrylamide administration. This result was not consistent with our results. We assumed that the inconsistency was due to lower acrylamide doses administered by Yousef and El-Demerdash and owing to a different administration period.

In our study, however, while MDA levels increased in liver and small and large intestine tissues in ACR group as compared to the control group ($p < 0.05$), a statistically significant decrease was observed in GSH and GST levels in ACR group when compared to the control group. These results show that acrylamide causes a significant decrease in antioxidant parameters. Acrylamide especially decreases the GSH and GST activity levels of cells, spoils the oxidant/antioxidant balance against the oxidants and thus leads to oxidative damage in cells (1, 14, 50–52, 55–58).

N-acetylcysteine is a thiol compound (59) which clears the free radicals by reacting with the reactive oxygen radicals (60). In our study, acrylamide administration decreased the GSH level and GST activity in the tissues and increased the MDA level. When NAC was administered together with acrylamide, these results were approximated to that of the control group. NAC shows this effect owing to the increase in GSH level and GST enzyme activity. In a study conducted by Eskiocak et al (61), it was found that N-acetylcysteine decreased lipid peroxidation when taken in pharmacological doses and caused a significant increase in GSH level known to decrease the oxidative stress; these findings are vital in terms of supporting our study.

In a research conducted by Syrian Hamster Embryo (SHE) culture, some morphological changes were observed in the embryo cells after administering 0.5 M acrylamide for 7 days. When acrylamide and N-acetylcysteinewere were administered together, the morphological changes took place at the lowest level. Adding acrylamide to the embryo culture administered with buthionine sulfoximine (GSH synthesis inhibitor) caused severe morphological changes. It was concluded in the study that acrylamide decreased GSH level; adding buthionine sulfoximine to the culture medium before acrylamide administration decreased the GSH level significantly. When acrylamide and NAC were administered together, the cellular GSH level increased. These results have been interpreted in such a manner that the level of morphological changes is in vital correlation with the cellular GSH levels (51).

In our study, acrylamide in the dose of 25 mg/kg was administered to the rats daily for 21 days. Histopathological examinations performed on small intestine and liver tissues taken from ACR group showed that severe tissue damage based on acrylamide took place. However, histopathological results in ACR+NAC group revealed that NAC decreased significantly the tissue damage based on acrylamide.

While the hepatocytes had normal appearance in the control group, the ACR group showed cell damage in hepatocytes. The histological appearance of NAC group was similar to that of the control group. Although there were some vacuoles and eosinophilic hepatocyte cells in ACR+NAC group, there were fewer of them when compared to ACR group. When the small intestine tissue was observed histopathologically, it was found that villous structures and single-layered prismatic epithelium coating thereof had normal appearance. The villous structures were spoiled in ACR group and enterocytes were rubbed off. While small intestine had normal appearance in NAC group, in ACR+NAC group, the top sections of villous structures were rubbed off, whereas the epithelial tissue of their lateral surfaces was strong. Studies in which acrylamide was added to the cell culture medium, the oxidant parameters increased and cell damage appeared. These findings support our study (55, 56, 61–63).

Contrary to other xenobiotics, acrylamide is dissolved in water very well and thus is distributed to all the tissues in a very rapid manner after being taken orally. Acrylamide is transformed into acrylamide-glutathione complex compound by being conjugated with GST/GSH system in all tissues (esophagus, stomach, small and large intestine) through the gastrointestinal tract and the tissues of the digestive system are protected against the harmful effects of acrylamide. Therefore, some acrylamide in the foods, which is taken orally, is detoxified in the gastrointestinal tract. However, conjugating acrylamide through the digestive system in an effective manner is totally dependent on GST activity and GSH levels of tissues (64). After acrylamide is absorbed from the intestines to the blood stream, it is rapidly distributed to the liver and other tissues. Acrylamide is rapidly cleared off in the blood because its half-life is short. Some of acrylamide taken into the liver is detoxified by being conjugated with GST/GSH system and the remaining acrylamide is oxidized with cytochrome P-450 enzyme system and transformed into glycidamide. Glycidamide is an oxidized form of acrylamide. Catabolism of both acrylamide and glycidamide takes

place in such a manner that glutathione-dependent GST enzyme is catalyzed and excreted from the body via urination. The main excretion metabolite of acrylamide is the structure of N-acetyl-S-(3-Amino-3-oxopropyl)-cysteine (65, 66). In our study, GSH was used in the cells for detoxifying the acrylamide in both digestive system and liver when we administered acrylamide, and a significant decrease was experienced in GSH levels of the tissues. MDA level increased as a result of lipid peroxidation occurring due to the failure to detoxify the acrylamide. Similarly, as GSH was required for the activity of GST enzyme, significant decreases were observed in GST activity in parallel to the decrease in the GSH level of the cells. As NAC is a thiol compound, precursor of GSH, it increased the GSH level in the tissues and thereby also the GST enzyme activity. In this condition, a significant decrease was observed in MDA levels due to lipid peroxidation, i.e. because acrylamide was detoxified in an adequate manner.

When the results of the study are considered together, it has been detected that acrylamide administered at a toxic level increases the MDA levels in liver and small and large intestine tissues and causes cell damage based on oxidative stress; however, administering NAC in a pharmacological dose increases GSH and GST enzyme activities and this is effective in terms of eliminating oxidative damage. Our study reveals that acrylamide taken in toxic dose causes damage to liver and small and large intestine tissues. As it occurs naturally when the food is cooked at high temperature, nutrients with antioxidant property consumed together with foods containing acrylamide may be effective in preventing the possible damage.

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