



Antioxidant Effects of Green-Tea on biochemical and Histopathological Changes of liver in Male Rats Poisoned by Malathion Insecticide

Rahim Raoofi¹, Hossein Kargar Jahromi^{2*}, Zahra Kargar Jahromi², Hassan Ali Abedi³, Hadi Sameni⁴ and Morteza Pourahmad^{2,4,5}

¹Department of Infection Diseases, Faculty Member of Medicine, Jahrom University of Medical Science, Jahrom, Iran.

²Zoonoses Research Center, Jahrom University of Medical Sciences, Jahrom, Iran

³Department of Physiology, Jahrom University of Medical Sciences, Jahrom, Iran

⁴Research Center for Noncommunicable Diseases, Faculty of Medicine, Jahrom University of Medical Sciences, Jahrom, Iran.

⁵Infectious diseases and tropical medicine research center, Isfahan University of medical sciences, Isfahan, IR Iran

Corresponding Email: hossein.kargarjahromy@yahoo.com

ABSTRACT

Malathion is an organophosphate pesticide which is widely used in agriculture, veterinary and industries. Oxidative stress has been identified as one of Malathion's main molecular mechanisms of action in plasma, liver, pancreas, muscles and the brain. Green tea (*Camellia sinensis*), which is the most common drink across the world after water, has many antioxidant properties. The purpose of this research is to investigate the effects of Malathion on the liver and the preventive effects of green tea on Malathion-induced poisoning. Seventy-two Wistar male rats were randomly divided into the control, the sham, and the experimental groups (receiving respectively 40 mg/kg of Malathion; 100, 200, and 400 mg/kg of green tea; and 100, 200, and 400 mg/kg of Malathion and green tea respectively). All injections were performed intraperitoneally for 14 consecutive days. On the 15th day, blood samples were taken from the hearts of the rats to measure serum level of hepatic enzymes, and their liver tissues were removed to be studied. To do the statistical analysis One-way ANOVA test and Duncan's test at the 5% significance level were used. aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), Malondialdehyde (MDA) and Total Oxidation Capacity (TOC) concentrations in the treatment groups with Malathion and green tea extract at 100, 200, and 400 mg/kg doses showed a significant decline compared to the Malathion group ($p < 0.05$), while Total Antioxidant Capacity (TAC) level showed a significant increase with various doses of green tea and Malathion compared to the Malathion group ($p < 0.05$). Green tea, probably due to its strong antioxidant properties, could improve the destructive effects of Malathion on the rat liver.

Keywords: Green tea, Malathion, liver, rat

INTRODUCTION

Nowadays, more chemical pesticides and herbicides are used in agriculture for controlling pests and weeds. These chemicals, including Malathion or Carbofos, cause problems for mammals and other living organisms [1].

Malathion is one of the organophosphates that are used as insecticides, pesticides and also as anthelmintics in veterinary medicine [2]. The most important and conspicuous effects of organophosphates that cause poisoning are their capabilities in inhibiting the vital cholinesterase in the nervous systems of animals [3]. Through inhibiting this enzyme, organophosphates cause accumulation of acetylcholine at the synapses, which leads to constant stimulation [4]. Moreover, they can occupy the sites of nicotine receptors, leading to muscle contraction and adrenaline secretion [5].

Studies have shown that toxic effects of certain organophosphates are not limited to inhibit cholinesterase but that, following the cholinergic crisis [increased acetylcholine], changes such as, damaged cell membranes, the production of free radicals, and disruptions in the antioxidant system of the body are observed [6]. The lipophilic nature of Malathion causes it to react with the unsaturated fatty acids in cell membranes, thereby changing the structure of these membranes [7].

In general, the main functions of the liver include detoxification, elimination of metabolic waste products, and participates in general metabolism of the body [8]. The complex metabolic hepatocytes contain large quantities of enzymes. When the liver is damaged, these enzymes leak into the plasma and, therefore, they can be useful in diagnosing and determining liver damages. Aminotransferases are the most sensitive and most widely used enzymes in the diagnosis of liver damages [9].

Aspartate aminotransferase AST [also known as SGOT] is a microsomal enzyme found in large quantities in the liver. It is released into the blood when liver tissues are destroyed, and its concentration is determined as a marker of hepatic cells [9].

The highest ALT and AST concentrations are observed in extensive liver necrosis, acute viral hepatitis A and B, hypoxia in liver tissues, and in pronounced liver damage caused by drugs, poisons, and pesticides [10].

Alkaline phosphatase [ALP] is found in most tissues and its concentration increases in people with liver diseases. It is a glycoprotein attached to cell membranes, is found at its highest concentrations in the sinusoids and the central vein endothelium, and the portal system, and at low concentrations in bile ducts [11, 12]. ALP concentration increases along the bile ducts, in hepatitis and cirrhosis, and in lipid sedimentation and accumulation in the liver [10].

Malondialdehyde [MDA] is one of the most frequently used indicators of lipid peroxidation and liver damage [13]. Measurement of serum total antioxidant capacity [TAC] level provides an integrated index, as opposed to one based on simple summation of measurable antioxidants [14], this capacity has a reverse correlation with TOC [15].

Green tea [*Camellia sinensis*] is the most common drink in the world after water, especially in East Asia [China and Japan] and has many antioxidant properties [16].

Leaves of tea trees are the main economically important part of this plant. They contain cellulose compounds, gums, dextrin, pectin, fats and wax, starch, sugars, gallic acid, oxalic acid, quercetin, proteins, fiber, minerals, tannin, caffeine, thein, aromatic substances, and diastase [17]. Moreover, green tea contains polyphenolic substances including the catechins of epigallocatechins-3-gallate [ECGC], epigallocatechin [ECG], epicatechin-3-gallate [ECG], and epicatechin [EC] [18, 19, and 20].

The protective effects of green tea on body tissues may be due to its antioxidant properties [21]. Catechins are the most effective substance in green tea, and ECGC [a very strong and effective antioxidant that plays a major role in preventing various diseases] is the most important catechin [22].

Green tea is known as an anti-inflammatory, anti-cancer, anti-cholesterol, anti-diabetic, anti-mutation, antimicrobial, anti-stroke, and antioxidative material. Furthermore, the bioactive compounds in green tea [catechins and caffeine] stimulate the sympathetic nervous system, thereby, enhance body heat production and lipid oxidation, and thus exert their anti-obesity effects [23, 24, and 25].

Considering what was said above, this research is an attempt to study the effects of Malathion on the liver; also to examine the effects of green tea extract in preventing poisoning induced by Malathion.

MATERIALS AND METHODS

Extract Preparation Method

Firstly, green tea leaves were ground and soaked in 80% ethanol for 24 hours. Then the solution was filtered and extraction performed in a vacuum. The obtained extract was soluble in distilled water (26, 27).

Animals and Their Grouping

All ethical points regarding the treatment of laboratory animals were observed in this research. Wistar male rats with a mean weight of 180-200g were used. They were kept for a week in the animal breeding laboratory room of Jahrom University of Medical Sciences to be adapted to the environment. During the research, the rats were kept under 12 h light/12 h dark conditions at 20-25 C°, and had free access to food and water. Every day at 10 a.m., Malathion was injected intraperitoneally into the rats at 40 mg/kg using insulin syringes (1). Immediately after the injections, the rats were given green tea extract by gavage. Both Malathion and green tea extract were soluble in distilled water.

The rats were randomly divided into nine 8-membered groups. The control group did not receive any substance, the sham group received 0.2cc distilled water injection intraperitoneally and 1ml distilled water by gavage. The experimental group 1 received Malathion injection intraperitoneally at 40 mg/kg/day for two weeks. The experimental groups 2, 3, and 4, were given the minimum, average, and maximum dose of green tea extract (100, 200, and 400 mg /kg/day, respectively) for two weeks by gavage. The experimental groups 5, 6, and 7 were injected intraperitoneally with Malathion at 2 mg/kg/day and were given green tea extract at 100, 200, and 400 mg/kg /day, respectively, by gavage for two weeks.

Taking Blood Samples and Carry out Biochemical Investigations

Malathion significantly increased aspartate transaminase (AST), alanine transaminase (ALT), and alkaline phosphatase (ALP) On the last day of the research, the rats were weighed; blood samples were taken directly from their hearts using 5 cc syringes (after the rats were anesthetized with diethyl ether); the samples were centrifuged at 3000 rpm for 15 minutes, and the sera were collected and kept in a freezer at -20 C°. To measure biochemical factors including alanine transaminase (ALT), aspartate transaminase (AST), and alkaline phosphatase (ALP), biochemical assessment kits (made in Iran) using the colorimetric method (28) and an autoanalyzer machine (Selectera XL model made in Holland) were applied. The level of Malondialdehyde (MAD) was evaluated by ELISA method (Biospes Italy) and the levels of total antioxidant capacity (TAC) and total oxidant capacity (TOC) were also measured by ELISA (LDN Italy) (29).

Tissue Studies

To perform a histological scrutiny, after 14 days of treatment, the rats were anesthetized on the 15th day using the standard method, and their liver tissues were quickly removed and put in containers with 10% formalin. The tissues were taken out of the solution after 48 hours, and, following tissue passage, 5µ thick paraffin-embedded tissue sections were prepared in the form of serial arrays. Ten cross-sections including five sections were selected from each liver; and stained employing the H&E and PAS methods, and studied using a light microscope. Fifty microscopic fields (magnification 10× 40) were randomly selected to study the hepatic pathological changes including disruption in the radial orientation of hepatocytes, polycythemia, varicocele, necrosis of hepatocytes, Kupffer cell aggregation, infiltration of inflammatory cells, and changes in the portal space.

Statistical analysis

One-way ANOVA was used for statistical analysis of the data. Where statistical differences between the groups were significant, Duncan's test was used to determine the differences between the means. SPSS 21 was employed for statistical calculations; the selected level of significance was $p < 0.05$. The data were calculated and compared in the form of Mean ± SEM in the section on results.

RESULTS

MDA, TOC and TAC:

The groups of 100, 200 and 400 mg/kg doses of the green tea extract significantly reduced MAD and TOC and increased TAC levels compared to the Malathion group ($p < 0.05$) (Table 1). Malathion increased MAD and TOC concentrations and reduced TAC level significantly compared to the control and sham groups ($p < 0.05$) (Table 1,2),

while the Malathion plus the green tea extract at 100, 200, and 400 mg/kg all significantly decreased MAD and TOC and increased TAC level compared to the Malathion group ($p < 0.05$) (Table 1,3).

liver Enzymes

The groups of 200 and 400 mg/kg doses of the green tea extract significantly reduced AST and ALP concentration compared to the control and sham groups ($p < 0.05$) (Table 4,5), but ALT level significantly reduced only at 200 mg/kg dose of the green tea extract compared to the control and the sham ($p < 0.05$) (Table 4,5). Malathion significantly increased AST, ALT and ALP concentrations compared to the control and sham groups ($p < 0.05$) (Table 4,6) while the treatments of Malathion plus the green tea extract at 100, 200, and 400 mg/kg all significantly reduced AST, ALT and ALP concentrations compared to the Malathion group ($p < 0.05$) (Table 6).

Pathological results

Microscopic examination of rat liver tissues in the control group revealed that they were healthy and normal (normal lobular structure, normal central vein and sinusoids and Kupffer cells, normal distribution of glycogen, no lymphocytic infiltration, and no polycythemia).

In the sham group and the 100, 200, and 400 mg/kg doses of the green tea extract, the tissues appeared relatively healthy and showed no special pathological changes.

In the Malathion group, extensive hepatocyte necrosis, degenerative changes, proliferation and activation of Kupffer cells (in aggregated or scattered forms), and infiltration and proliferation of inflammatory cells around the portal and central vein spaces of the centrilobular region and in the sinusoidal space were observed. So was formed of fibrous bridges between the liver lobules, polycythemia and blood congestion in the sinusoids, and cellular ballooning. In this group, progressive liver fibrosis had taken place as evidenced by the presence of collagen fibers in hepatic parenchyma, around the central vein in the centrilobular region, and in the portal space.

In the treatments of Malathion plus 100, 200, and 400 mg/kg of the extract, the destructive effects of Malathion decreased. The above-mentioned changes were of average intensity in the 100; of very slight intensity in the 200; and of slight intensity at the 400 mg/kg dose of the extract.

Table 1. Effects of Various Doses of Green tea extract and Malathion on Liver Markers in Studied Rats

Parameter/Group	TAC IU/ml	TOC IU/ml	MDA Nmol/L
Control	1.5488 ± .04198 d	.1650 ± .00327 c	.1212 ± .00441 a
Sham	1.5687 ± .04715 d	.1700 ± .00378 c	.1250 ± .00567 a
Green tea extract at 100 mg/kg	3.0512 ± .10631 f	.1250 ± .00463 bc	.1150 ± .00463 a
Green tea extract at 200 mg/kg	3.6962 ± .09032 g	.0937 ± .00532 ab	.1062 ± .00680 a
Green tea extract at 400 mg/kg	5.8400 ± .09177 h	.0638 ± .00324 a	.0575 ± .00453 a
Malathion	.4088 ± .02199 a	1.7588 ± .03383 g	3.2663 ± .06450 e
Malathion + green tea extract at 100 mg/kg	.7213 ± .02409 b	1.4838 ± .01936 f	2.9075 ± .03807 d
Malathion + green tea extract at 200 mg/kg	1.0762 ± .03737 c	1.2612 ± .02287 e	2.4350 ± .03822 c
Malathion + Green tea extract at 400 mg/kg	2.3538 ± .06522 e	.9312 ± .02930 d	2.0275 ± .02871 b
P-value	<0.0001	<0.0001	<0.0001

Abbreviations: IU/L, Internation Unit Per Liter; MDA, Malondialdehyde; TAC, Total Antioxidation Capacity; and TOC, Total oxidation Capacity.

Table 2. Effects of Various Doses of Green tea extract on Liver Markers in Studied Rats

Parameter/Group	TAC IU/ml	TOC IU/ml	MDA Nmol/L
Control	1.5488 ± .04198 a	.1650 ± .00327 d	.1212 ± .00441 bc
Sham	1.5687 ± .04715 a	.1700 ± .00378 d	.1250 ± .00567 c
Green tea extract at 100 mg/kg	3.0512 ± .10631 b	.1250 ± .00463 c	.1150 ± .00463 bc
Green tea extract at 200 mg/kg	3.6962 ± .09032 c	.0937 ± .00532 b	.1062 ± .00680 b
Green tea extract at 400 mg/kg	5.8400 ± .09177 d	.0638 ± .00324 a	.0575 ± .00453 a
P-value	<0.0001	<0.0001	<0.0001

Abbreviations: IU/L, Internation Unit Per Liter; MDA, Malondialdehyde; TAC, Total Antioxidation Capacity; and TOC, Total oxidation Capacity.

Table 3. Effects of Various Doses of Green tea extract with Malathion on Liver Markers in Studied Rats

Parameter/Group	TAC IU/ml	TOC IU/ml	MDA Nmol/L
Control	1.5488 ± .04198 d	.1650 ± .00327 a	.1212 ± .00441 a
Sham	1.5687 ± .04715 d	.1700 ± .00378 a	.1250 ± .00567 a
Malathion	.4088 ± .02199 a	1.7588 ± .03383 e	3.2663 ± .06450 e
Malathion + green tea extract at 100 mg/kg	.7213 ± .02409 b	1.4838 ± .01936 d	2.9075 ± .03807 d
Malathion + green tea extract at 200 mg/kg	1.0762 ± .03737 c	1.2612 ± .02287 c	2.4350 ± .03822 c
Malathion + Green tea extract at 400 mg/kg	2.3538 ± .06522 e	.9312 ± .02930 b	2.0275 ± .02871 b
P-value	<0.0001	<0.0001	<0.0001

Abbreviations: IU/L, Internation Unit Per Liter; MDA, Malondialdehyde; TAC, Total Antioxidation Capacity; and TOC, Total oxidation Capacity.

Table 4. Effects of Various Doses of Green tea extract and Malathion on Liver Markers in Studied Rats

Parameter/Group	AST (SGOT) IU/L	ALT (SGPT) IU/L	ALP (ALK) IU/L
Control	141±2.77746 b	71.875±8.17464 b	138.75±2.81419 b
Sham	146.5±2.48567 b	73.625±2.05667 b	144.125±2.07397 b
Green tea extract at 100 mg/kg	128.625±3.3324 b	62.875±2.05667 b	128.625±13.86431 ab
Green tea extract at 200 mg/kg	105±2.54951 a	50.375±2.29469 a	101.5±2.81419 a
Green tea extract at 400 mg/kg	174.125±3.4405 c	64.875±1.30845 b	115.75±3.55788 c
Malathion	333.875±23.03292 e	418.76±3.28110 e	497.5±1.86066 e
Malathion + green tea extract at 100 mg/kg	230.375±3.49968 d	264±8.51627 d	389±2.09591 f
Malathion + green tea extract at 200 mg/kg	172.75±2.74350 c	138.875±6.79285 c	215±3.46281 d
Malathion + Green tea extract at 400 mg/kg	179.25±3.59439 c	140.875±3.59439 c	269±11.99553 e
P-value	<0.0001	<0.0001	<0.0001

Abbreviations: ALT, Alanine Transferase; ALP, Alkaline phosphatase; AST, Aspartate Transferase, IU/L, Internation Unit Per Liter.

Table 5. Effects of Various Doses of Green tea extract on Liver Markers in Studied Rats

Parameter/Group	AST (SGOT) IU/L	ALT (SGPT) IU/L	ALP (ALK) IU/L
Control	141±2.77746 b	71.875±8.17464 b	138.75±2.81419 b
Sham	146.5±2.48567 b	73.625±2.05667 b	144.125±2.07397 b
Green tea extract at 100 mg/kg	128.625±3.3324 b	62.875±2.05667 b	128.625±13.86431 ab
Green tea extract at 200 mg/kg	105±2.54951 a	50.375±2.29469 a	101.5±2.81419 a
Green tea extract at 400 mg/kg	174.125±3.44050 c	64.875±1.30845 b	115.75±3.55788 c
P-value	<0.0001	<0.0001	<0.0001

Abbreviations: ALT, Alanine Transferase; ALP, Alkaline phosphatase; AST, Aspartate Transferase, IU/L, Internation Unit Per Liter.

Table 6. Effects of Various Doses of Green tea extract with Malathion on Liver Markers in Studied Rats

Parameter/Group	AST (SGOT) IU/L	ALT (SGPT) IU/L	ALP (ALK) IU/L
Control	141±2.77746 a	71.875±8.17464 a	138.75±2.81419 a
Sham	146.5±2.48567 a	73.625±2.05667 a	144.125±2.07397 a
Malathion	333.875±23.03292 d	418.76±3.28110 d	497.5±1.86066 c
Malathion + green tea extract at 100 mg/kg	230.375±3.49968 c	264±8.51627 c	389±2.09591 d
Malathion + green tea extract at 200 mg/kg	172.75±2.74350 b	138.875±6.79285 b	215±3.46281 b
Malathion + Green tea extract at 400 mg/kg	179.25±3.59439 b	140.875±3.59439 b	269±11.99553 c
P-value	<0.0001	<0.0001	<0.0001

Abbreviations: ALT, Alanine Transferase; ALP, Alkaline phosphatase; AST, Aspartate Transferase, IU/L, Internation Unit Per Liter.

- Based on Duncan's test, means in each column with at least one letter in common are not significant at the 5% level
- Means are expressed as Mean ± SEM
- P<0.05 was considered statistically significant

DISCUSSION

The present study showed that the injection of Malathion increased serum concentrations of AST, ALT and ALP. The results agree with those found by Jabbar et al. in 1990 and by Kalender et al. in 2010 [30, 31].

Malathion's main mechanism of action is the inhibition of cholinesterase activity [6]. However, it has been proved in recent years that the main mechanism of acute and chronic toxicity of organophosphates is through creating oxidative stress [32]. Recent studies have shown that organophosphates, including Malathion, exert part of their toxicity independently of their cholinesterase activities; for example, oxidative stress is created through increasing free radicals or by weakening the antioxidant system in tissues such as the brain [33] and the liver [34], and in the blood [35]. Studies indicate that reactive oxygen species [ROS] play a role in the toxicity caused by organophosphates, especially Malathion, in humans [36] and in rats [6, 37].

Attachment of free radicals to hepatocyte membranes damages these membranes and causes necrosis, thereby increasing the activities of AST, ALT, and ALP. This causes enzymes that normally are inside cellular cytosols to be released into the blood [38]. Raised serum levels of these enzymes indicate structural damages in cellular membranes in the liver, leading to disrupted function of these membranes, and signify the degree and type of liver damages [38].

In this research, serum levels of AST, ALT, and ALP significantly decreased in groups treated with Malathion and different doses of the green tea extract compared to the group treated with Malathion.

Green tea extract has antioxidant and free-radical-scavenging properties [39]. Reduced levels of the mentioned enzymes following green tea extract administration may result from the antioxidant properties of the extract and from the resultant prevention of intracellular enzymes from leaking out of cells due to cellular stabilization or regeneration [40].

Results of numerous studies suggest the protective effects of green tea against various poisons and medicines. Mantal et al. studied male albino rats and found that green tea extract could significantly reduce ALT and AST in rats that received the insecticide Fenitrothion [41]. Chen and his research team concluded that taking green tea extract could significantly reduce ALP, ALT, and AST levels in rats with liver failure induced by leflunomide [42]. In a study conducted by Khorsandi et al. on immature male Balb/C rats, it was found that injecting these rats with green tea extract could improve liver failure caused by taking acetaminophen due to the strong antioxidant effects of the extract [43]. Similar research suggests the inhibitory effects of green tea extract on liver failure caused by nitropropane [44], beta-D-galactosamine [45], and micromycin [46].

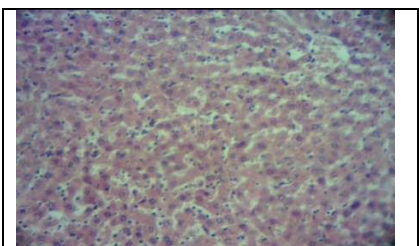
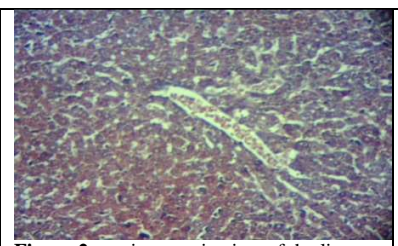
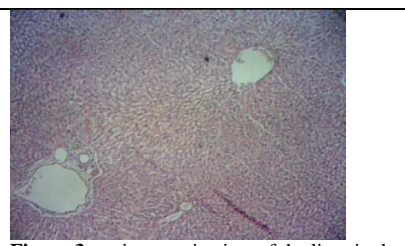


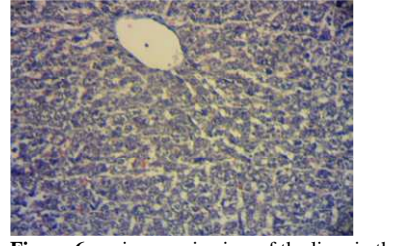

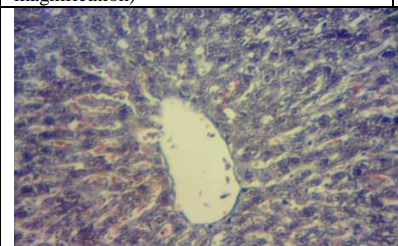

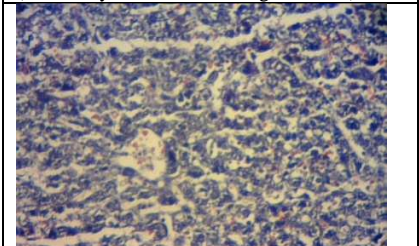
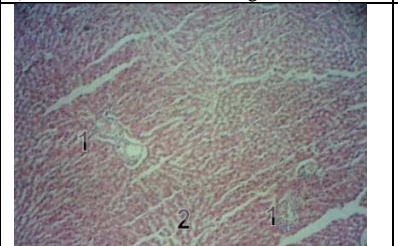
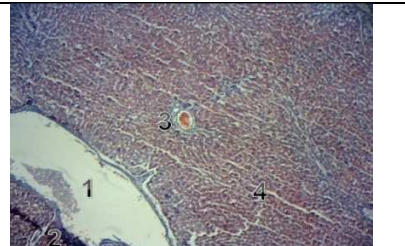
In this study, MDA, TOC and TAC levels

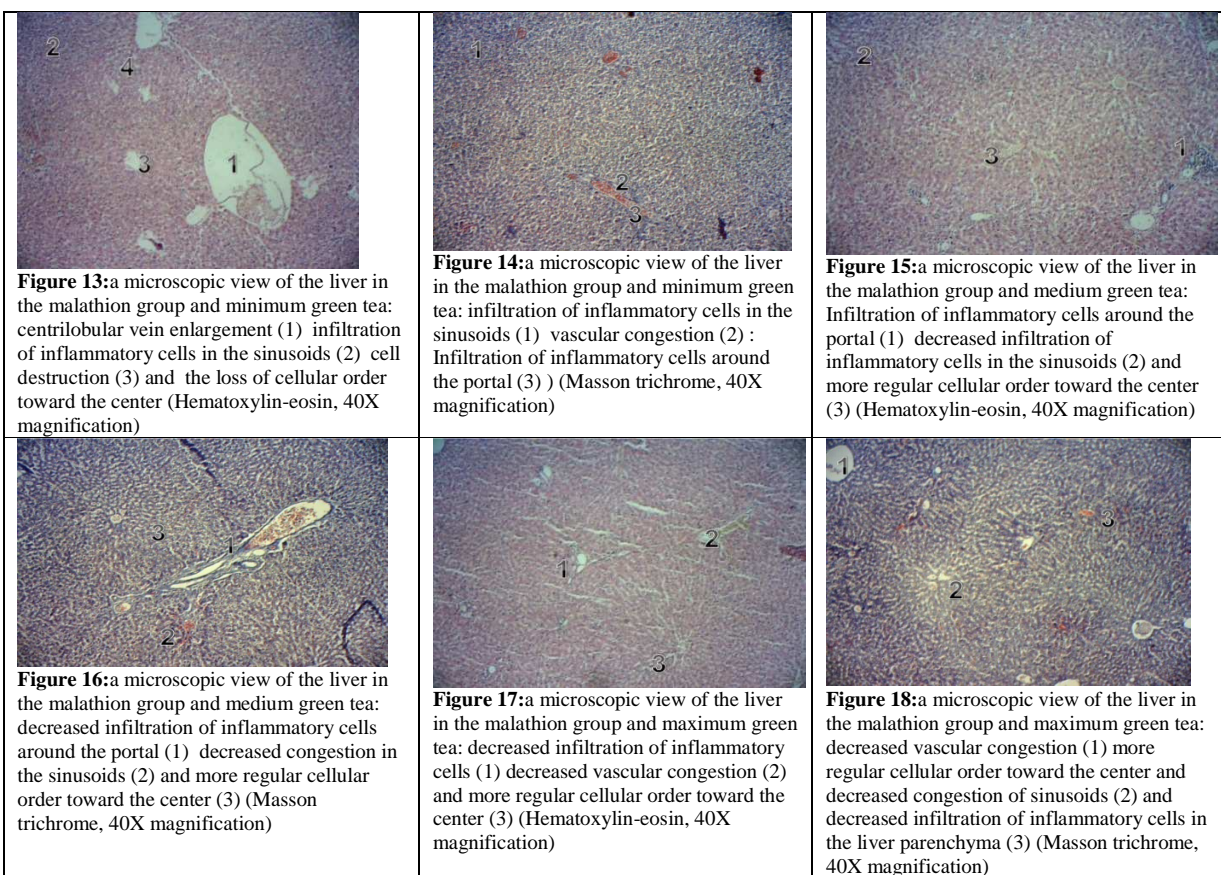
TAC is a biochemical parameter suitable for evaluating the overall antioxidant status of serum and body fluids resulting from antioxidant intake and/ or production, and their consumption by normal or increased levels of ROS production. When the oxidant/antioxidant balance is tilted towards oxidants and oxidative stress arises, there is a significant negative correlation between the TAC and TOC values [29]. MDA, an end product of polyunsaturated fatty acid oxygenation, is also a reliable and commonly used marker of the overall lipid peroxidation level and the presence of oxidative stress [29].

In this study, elevation of TAC and reduction of TOC and MAD levels in groups treated with Malathion and different doses of the green tea extract may be attributed to antioxidant activity of green tea. Haidari et al. showed that Green Tea [*Camellia sinensis*] Supplementation to Diabetic Rats Improves Serum and Hepatic Oxidative Stress Markers [47]. Skrzydlewska *et al.* also demonstrated that dietary supplementation with green tea catechins can improve total antioxidant capacity [TAC] and decrease malondialdehyde [MDA] concentration [48].

Polyphenols, especially catechins, are among the main soluble constituents of green tea extract. Green tea catechins are strong scavengers of superoxide, hydrogen peroxide, and nitric acid is obtained from various chemical materials [49]. Green tea catechins have the antioxidant properties of urate, beta-carotene, vitamin C, vitamin E in protecting cells [50]. Moreover, it has been proved that green tea catechins prevent lipid peroxidation by chemical materials in the liver and kidney of animals [51].

Histopathological findings of this research conform to its biochemical outcomes. In the Malathion group, increased activities of hepatic enzymes were accompanied by extensive tissue damages, including the disintegration of sinusoids, hepatocyte necrosis, degenerative changes, and blood congestion in sinusoids. These destructive effects clearly decreased in groups treated with various doses of green tea extract compared to the Malathion group.

 <p>Figure 1:a microscopic view of the liver in Control Group ,with a natural structure(Hematoxylin-eosin, 40X magnification)</p>	 <p>Figure 2: a microscopic view of the liver in Control Group ,with a natural structure and leukocyte infiltration and congestion cannot be seen (Masson trichrome, 40X magnification)</p>	 <p>Figure 3:a microscopic view of the liver in the second Control Group ,with a natural structure and Central venous congestion cannot be seen (Hematoxylin-eosin, 40X magnification)</p>
 <p>figure 4:a microscopic view of the liver in the second Control Group ,with a natural structure and Collagen fibers cannot be seen (Masson trichrome, 40X magnification)</p>	 <p>Figure 5:a microscopic view of the liver in the positive Control Group (minimum green tea). Its tissues seem relatively healthy, without any certain pathological changes (Hematoxylin-eosin, 40X magnification)</p>	 <p>Figure 6:a microscopic view of the liver in the positive Control Group (minimum green tea). Its tissues seem relatively healthy, without any certain pathological changes (Masson trichrome, 40X magnification)</p>
 <p>Figure 7:a microscopic view of the liver in the positive Control Group (medium green tea). Its tissues seem relatively healthy, without any certain pathological changes (Hematoxylin-eosin, 40X magnification)</p>	 <p>Figure 8:a microscopic view of the liver in the positive Control Group (medium green tea). Its tissues seem relatively healthy, without any certain pathological changes (Masson trichrome, 40X magnification)</p>	 <p>Figure 9:a microscopic view of the liver in the positive Control Group (maximum green tea). Its tissues seem relatively healthy, without any certain pathological changes (Hematoxylin-eosin, 40X magnification)</p>
 <p>Figure 10:a microscopic view of the liver in the positive Control Group (maximum green tea). Its tissues seem relatively healthy, without any certain pathological changes (Masson trichrome, 40X magnification)</p>	 <p>Figure 11:a microscopic view of the liver in the malathion group: Infiltration of inflammatory cells around the portal (1) and the loss of cellular order toward the center (2) (Hematoxylin-eosin, 40X magnification)</p>	 <p>Figure 12:a microscopic view of the liver in the malathion group: centrilobular vein enlargement (1) Infiltration of inflammatory cells and collagen fibers around the centrilobular vein (2) Infiltration of inflammatory cells around the portal (3) and the loss of cellular order toward the center (4) (Masson trichrome, 40X magnification)</p>



Malathion, in the body, is changed to its toxic metabolite Malaxon by the hepatic cytochrome p450 system through oxidative desulfurization [52]. The maximum cytochrome p450 concentration was observed in hepatic cells in the centrilobular region[53]. Results of studies have shown that green tea inhibits cytochrome p450 expression. Therefore, green tea prevents liver tissue from destruction and formation of toxic metabolite of Malathion through inhibiting p450 cytochrome.

CONCLUSION

Based on the results of this study, green tea extract was able to protect rat liver against toxicity resulting from Malathion intake probably because of the extract's antioxidant properties and due to the polyphenols that it contains. Of course, protective effects of green tea extract against Malathion were dose-dependent and, in this research, it was found that the 200 mg/kg dose was more effective in improving hepatic failure caused by Malathion.

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