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The Effect of Milk Thistle, Green Tea, and Cinnamon Beverages on Liver Enzymes of Operating Room Anesthesia Personnel

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Abstract

Background: Millions of health workers in operating rooms worldwide are exposed to inhaled anesthetics. However, the effects of continuous exposure to inhalational anesthetics are still controversial in many studies.
Objectives: The present study investigated the effects of milk thistle, green tea, and cinnamon consumption on liver enzymes in operating room personnel.
Methods: In this study, we investigated the effects of milk thistle tea, green tea, and cinnamon tea on liver enzymes in operating room staff in a controlled, double-blind study from 2019 to 2020. In two parallel groups, 62 subjects were randomly assigned to ingest the beverages the teas. Milk thistle, green tea, and cinnamon were taken daily for four weeks. During the intervention, all participants were educated about the importance of a balanced diet and physical activity.
Results: The milk thistle, green tea, and cinnamon groups showed a significant statistical difference in reduced levels of AST, ALT, ALP, ALB, GGT, bilirubin, and ESR after four weeks (P value $<$ 0.001).
Conclusions: The results of this study demonstrated that ingesting green tea and cinnamon reduced liver enzymes in surgical personnel. Among the extracts, milk thistle had a greater effect on liver enzymes than the other two extracts. It can be concluded that the prescribed milk thistle extract can be considered a potential intervention to improve liver enzyme levels in surgical personnel to reduce the adverse effects of anesthetics.

Keywords: Liver Enzymes, Milk Thistle, Cinnamon, Green Tea

1. Background

The use of anesthetic drugs dates back to 150 years ago, and these drugs are continued in surgeries (1). Inhalation contact with these substances occurs when anesthetics are used in the operating room (OR), and it can cause genetic damage by destroying the DNA of cells (2). It also increases cancer risk by inhibiting neutrophil apoptosis (3, 4). Other side effects of anesthetics include headache, irritability, neurobehavioral changes, and infertility (5, 6). Allergic asthma and allergic contact dermatitis have also been reported in rare cases (7, 8). On the other hand, these substances can cause physiological injuries, especially liver injuries in operating room personnel (9). Recently, serious liver problems have been reported in patients and staff following these gases as anesthetic retainers (10, 11). According to the World Organization for Occupational Safety and Health (OSHA), more than 250,000 hospital staff in the United States are exposed to these gases and are at risk (12).

Causes of air pollution in operating rooms with anesthetic gasses include leakage of gas from anesthesia machines through the vaporizer, lack of a purge system, some common anesthetic methods, pouring of anesthetics, patient exhalation, inefficiency and closure of the system's gas inlet valves, and use of chip tubes without a cuff (13). The balance between the supply of oxygen to the liver via blood circulation and the liver tissue supplying oxygen to the hepatocytes is an important factor in liver metabolism (14). Inhalation of anesthetic gasses reduces the oxygen available to these cells and decreases liver metabolism (15). It interferes with liver metabolism and even causes ischemia of liver cells (16).

The liver is a very important organ for detoxifying xenobiotics that enter the body from the environment, drugs, alcohol, and food (17). Aminotransferases are among the most important and commonly used enzymes for the diagnosis of liver diseases and include aspartate aminotransferase (AST) and alanine aminotransferase (ALT) (18). AST and ALT are enzymes released by hepatic parenchymal cells, and their elevated serum levels are considered the "gold standard" tests for hepatotoxicity associated with anesthetics (19). Other factors used to diagnose hepatitis include CRP and ESR (20). The CRP test is more sensitive and has a better response index than ESR (21). In acute inflammation, CRP rises more rapidly than ESR and falls more rapidly after recovery (22).

There are various supplements and antioxidants, such as chamomile tea (23), cinnamon (24), mountain tea (25), green tea (26), lemon balm (27), milk thistle (28), etc., which have been reported in various studies to have the ability to reduce several oxidative stress parameters. The use of milk thistle to treat liver problems has a long history, and these effects have been demonstrated in recent years by extensive studies in this field (29). Milk thistle is a potent and direct antioxidant, eliminating toxic free radicals. It increases intracellular glutathione and superoxide dismutase activity and acts as a protective barrier for the liver (30). It inhibits the formation of leukotrienes, increases the activity of the enzyme RNA polymerase in the nucleus, and enhances the regenerative capacity of liver cells by stimulating the synthesis of ribosomal proteins (31). Because of its richness in polyphenolic compounds and flavonoids, green tea is a potent antioxidant compared with vitamins C and E and other foods containing antioxidants (32). Cinnamon contains various phenolic antioxidants such as flavonoids, tannins, coumarins, eugenol, acetyleugenol, cineole, and cinnamaldehyde. Cinnamon's antioxidant activity prevents oxidation of hepatocyte walls in a dose-dependent manner, i.e., its antioxidant activity increases at higher concentrations and decreases with decreasing extract concentrations (33).

2. Objectives

Because non-chemical therapeutic interventions have minor side effects compared to chemical compounds and also considering that there is an increase in operating room staff and people who are exposed to these gases, this study aimed to investigate the effect of these gases on liver function and compare the effect of the consumption of milk thistle, green tea, and cinnamon on the level of liver enzymes in the operating room medical staff in a clinical trial to introduce an effective and low-cost intervention with minimal side effects.

3. Methods

3.1. Ethical Principles

This study involved no additional interventions outside the normal diagnostic-therapeutic process and imposed no financial cost on the patients. The tests were performed with blood samples prepared for other regular tests, and no additional blood samples were taken from the patients. Patients were informed about the study and consented to participate. Patients' information was kept confidential by the research team. The Dezful University of Medical Sciences Ethics Committee monitored this study by approved ethical regulations IR.DUMS.REC.1399.010.

3.2. Sampling

This clinical trial study was performed on anesthesia and operating room staff of the operating theatre of Dr. Ganjavian Hospital in Dezful in 2019, and from among the staff, 64 were selected based on inclusion and exclusion criteria and entered the study. The study subjects were included based on the following inclusion criteria: Age range 24 to 64 years, at least one-year work experience, working at least 6 hours daily in the operating room, no more than three days off in the last 60 days, and not taking any antioxidant supplements. The exclusion criteria included: Consumption of alcohol, smoking or illicit drug use, taking medications that affect the level of liver enzymes, being under general anesthesia as a patient in the last three months, and any allergy to the studied beverages (9, 31).

3.3. Study Data Extraction

Data were extracted using a pre-made form: First author's last name, year of publication, study site, study design, target population, study duration, sex, mean age, and the concentration of cinnamon and other extracts. The exact values of different measurements were not mentioned in the results, and just the mean values have been reported.

3.4. Study Selection

Hematological and biochemical parameters were assessed by taking 5 ml of venous blood from each patient under sterile conditions by a trained laboratory technician in a standard medical diagnostic laboratory. Albumin, bilirubin, ALT, AST, GGT, CRP, ESR, ALP, and PT were measured in all patients.

3.5. Randomization of the Samples

To randomize the samples and make a balance between the study groups, patients were randomly divided into four groups. As such, each patient was placed in one of 4 groups: A (control), B (green tea), C (cinnamon tea), and D (milk thistle). Blocking was done in an 8 randomized block design, and 8 blocks were formed according to the sample population. We anticipated all possible scenarios for the groups. For example, the first block would be AACCDDBB, and the next block, for example, would be ABABDCDC, and the rest would be defined similarly. Due to the large number of blocks, block randomization software was used. The subjects were randomly selected and allocated to the blocks, so ultimately, 16 people were in the green tea group, 16 in the cinnamon tea consumer group, 16 in the milk thistle consumer group, and 16 in the control group. In group D, the brew of a teabag containing 3 grams of crushed milk thistle seeds in 300 mL of boiled water was prepared, and the subjects were asked to consume three same serving portions daily. In group B, the brew a tea bag containing 1 gram of green tea leaves in 300 mL of boiled water was prepared and was consumed three times a day, similar to the previous group. In group C, brew a teabag containing one gram of chopped cinnamon stick in 300 mL of boiled water was prepared and consumed at the same dose three times a day for four weeks, similar to the previous two groups. Control group (A) was also asked not to use medications or traditional compounds that could alter the liver enzyme levels during the study period and to follow their usual nutritional pattern. All tea bags were prepared in pure form and purchased from Isfahan University Jahad Medicinal Plants Research Institute (Jahad University Medicinal Plants Research Institute, Isfahan, Iran).

3.6. Statistical Analysis

Data analysis of the study was performed using STATA version 12 software (STATA Corp, College Station, TX, USA). The effect rate was calculated by Hedges' g26 using the difference between the mean serum levels of liver markers (milk thistle, cinnamon, and green tea compared with control). Data were expressed as mean ± standard error (mean standard error) for continuous variables and percentages for classification variables. The normality of variables was assessed by Kolmogorov-Smirnov or Shapiro-Wilk test. Continuous variables were assessed by one-way analysis of variance (ANOVA), and the Tukey post hoc test performed multiple comparisons. The difference between the two groups was analyzed by *t*-test. A value of $<$ 0.05 was considered significant. Data were analyzed using SPSS 22.0 software (SPSS) (Chicago, IL, USA).

4. Results

4.1. Patient Characteristics

A total of 62 people completed the study. Initially, the two groups had no significant differences in age, sex, education level, and severity of fatty liver disease. Biochemical factors before and after the intervention are shown in Tables 1 - 3 as mean ± SD of biochemical factors. The groups were similar in weight (86.20 ± 12.65 kg and 89.49 ± 13.89 kg in the intervention and control groups) and liver enzymes.

4.2. Evaluation of Biochemical Factors in the Subjects

Using repeated measures analysis of variance, the difference between the group of sagebrush and liver enzymes in the four time periods before the intervention, two weeks after the intervention, and four weeks after the intervention was measured. There was a significant difference in the stage. As can be seen in Table 1, the levels of AST, ALT, ALP, ALB, GGT, bilirubin, and ESR enzyme decreased four weeks after the end of the interventions, and enzymes of the milk thistle group seem to have decreased more after the end of the interventions. In addition, individual differences (P-value $<$ 0.05) were found in AST, ESR, and GGT enzyme levels. AST levels showed that AST decreased in all subjects in the experimental group. GGT, ALT, and ESR levels were sharply decreased in all subjects in the experimental group. The highest decrease among liver enzymes was related to ALT, ALP, albumin, and ESR.

Table 2 shows the trend of changes in the mean of the group that consumed green tea and the control group. As can be seen, the levels of AST, ALT, ALP, ALB, GGT, bilirubin, and ESR decreased four weeks after the end of the intervention, but it seems that in the group that consumed milk thistle, it decreased more after the end of the intervention. Looking closely at the test results, GGT, ALP, albumin, and ESR levels were drastically decreased in all subjects in the experimental group who consumed green tea.

Results of data obtained using analysis of variance and repeated measures, the difference between the enzymes of milk thistle, green tea, cinnamon, and AST, ALT, ALP, ALB, GGT, bilirubin, and ESR were measured in 4 stages, including before entering the study, 2 weeks, and 1 month weeks after the end of the study, and 1 month after the end of the intervention. Considering the level of significance, it can be said that there was a significant difference between the three groups in the three stages. The findings of Tables 1 - 2 show that within-group changes in the experimental group are significant (P-value $<$ 0.05).

Table 1. Mean Liver Enzymes with Consumption of Milk Thistle Wort at Different Stages of Intervention

Variables	Milk Thistle				Statistical Test, P-Value
	Before	Two Weeks	Four Weeks	One Month	
AST (U/dL)					0.001
Intervention group	45.75 ± 13.2	42 ± 12.49	38.62 ± 12.41	37.87 ± 12.67	
Control	38.12 ± 8.17	40.84 ± 12.01	38.62 ± 7.39	39.12 ± 7.885	
ALT (U/dL)					0.001
Intervention group	61.5 ± 21.81	55.75 ± 21.29	51.87 ± 21.68	51.12 ± 22.51	
Control	49.75 ± 7.86	49.12 ± 7.43	49.87 ± 7.31	50.87 ± 7.95	
ALP (U/dL)					0.001
Intervention group	215.12 ± 38.57	203.25 ± 32.96	192.62 ± 31.44	191.12 ± 29.53	
Control	266.87 ± 103.82	265.25 ± 99.69	265 ± 98.61	270.35 ± 106.11	
ALB (U/dL)					0.001
Intervention group	4.7 ± 0.34	4.56 ± 0.39	4.45 ± 0.37	4.49 ± 0.34	
Control	4.91 ± 0.18	4.97 ± 0.13	5.01 ± 0.14	4.96 ± 0.1.	
GGT (U/dL)					0.001
Intervention group	34.55 ± 27.78	28.7 ± 22.63	25.4 ± 19.32	24.65 ± 18.75	
Control	24.81 ± 9.15	26.63 ± 9.94	27.02 ± 9.25	27.45 ± 8.98	
Bilirubin (mg/dL)					0.001
Intervention group	0.55 ± 0.26	0.45 ± 0.21	0.4 ± 0.17	0.37 ± 0.17	
Control	0.6 ± 0.14	0.6 ± 0.13	0.58 ± 0.13	0.61 ± 0.13	
ESR (mm/hr)					0.001
Intervention group	9.25 ± 4.8	8.5 ± 3.61	7.5 ± 3.05	7.37 ± 2.82	
Control	9.5 ± 2.36	10.62 ± 1.45	11.5 ± 1.15	11.25 ± 1.98	

Abbreviations: AST, Aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; ALB, albumin; GGT, gamma-glutamyl transpeptidase; ESR, erythrocyte sedimentation rate.

As shown in Table 3, the intensity of the decrease in AST, ALT, ALP, ALB, GGT, bilirubin, and ESR enzyme in the four measurements was much higher in the experimental group than in the control group. ALT, ALP, bilirubin, albumin, and ESR levels were significantly decreased in all subjects in the experimental group who consumed cinnamon, and the increase in this enzyme was more marked in the control group.

5. Discussion

Waste anesthetic gases (WAG) present in the OR environment create various occupational hazards, one of the most important being liver dysfunction (34). This study aimed to investigate the effect of milk thistle, green tea, and cinnamon consumption enzyme levels in operating room personnel. A marked increase in the number of days of extract consumption was associated with a decrease in liver enzymes. Biochemical findings were similar to previous studies and confirmed the hepatic protective role of the extracts in all four groups. In our study, there were no statistically significant differences between all four groups regarding weight and body mass index. Regarding fatty liver, overweight and the importance of the role of body mass index (BMI) have been demonstrated in many studies (35-37).

In the present study, we investigated the effects of milk thistle, green tea, and cinnamon administration on surgical personnel liver function tests. Thistle milk, green tea, and cinnamon significantly restored elevated liver enzyme levels. These observations may be due to the presence of natural liver-protective bioactive compounds in milk thistle extract, green tea, and cinnamon, which have the ability to reduce free radical-induced liver damage. This indicates that these compounds help regenerate liver cells, improve liver structure and function, prevent liver damage, and prevent further damage to the liver parenchyma. The most common

Table 2. Mean Liver Enzymes with Green Tea Consumption Wort at Different Intervention Stages

Variables	Green Tea				Statistical Test, P-Value
	Before	Two Weeks	Four Weeks	One Month	
AST (U/dL)					0.001
Intervention group	41.87 ± 12.96	40.5 ± 12.84	38.87 ± 13.56	38.75 ± 13.92	
Control	38.12 ± 8.17	40.84 ± 12.01	38.62 ± 7.39	39.12 ± 7.885	
ALT (U/dL)					0.001
Intervention group	53.12 ± 20.02	51.25 ± 19.76	49 ± 19.86	48.75 ± 20.05	
Control	49.75 ± 7.86	49.12 ± 7.43	49.87 ± 7.31	50.87 ± 7.95	
ALP (U/dL)					0.001
Intervention group	273.37 ± 100.66	250.12 ± 85.06	241.5 ± 80.71	242 ± 80.54	
Control	266.87 ± 103.82	265.25 ± 99.69	265 ± 98.61	270.35 ± 106.11	
ALB (U/dL)					0.001
Intervention group	4.91 ± 0.3	4.83 ± 0.33	4.73 ± 0.32	4.73 ± 0.32	
Control	4.91 ± 0.18	4.97 ± 0.13	5.01 ± 0.14	4.96 ± 0.1.	
GGT (U/dL)					0.001
Intervention group	46.03 ± 32.24	43.62 ± 29.78	41.08 ± 27.88	40.96 ± 27.60	
Control	24.81 ± 9.15	26.63 ± 9.94	27.02 ± 9.25	27.45 ± 8.98	
Bilirubin (mg/dL)					0.001
Intervention group	0.57 ± 0.26	0.47 ± 0.23	0.45 ± 0.22	0.45 ± 0.22	
Control	0.6 ± 0.14	0.6 ± 0.13	0.58 ± 0.13	0.61 ± 0.13	
ESR (mm/hr)					0.001
Intervention group	9.5 ± 4.5	8.75 ± 4.05	8.12 ± 3.7	7.87 ± 3.4	
Control	9.5 ± 2.36	10.62 ± 1.45	11.5 ± 1.15	11.25 ± 1.98	

Abbreviations: AST, Aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; ALB, albumin; GGT, gamma-glutamyl transpeptidase; ESR, erythrocyte sedimentation rate.

laboratory tests for liver disease are ALT, AST, and ALP. Numerous studies have found an association between markers of liver dysfunction, cardiovascular disease or mortality from vascular and nonvascular causes, and the risk of developing T2 diabetes after controlling for important risk factors. Therefore, studying liver enzymes may play an important role in the prognosis and prevention of chronic diseases. Recently, much attention has been paid to the effect of cinnamon on liver enzymes and fatty liver.

Many experimental and clinical investigations have confirmed the hepatoprotective effect of extracts and their active components. Milk thistle (*Silybum marianum*) has many benefits, including antioxidant, anti-inflammatory, liver protection, and neuroprotective effects. A marked reduction in the plasma levels of liver enzymes such as ALT, AST, and ALP by silymarin has been repeatedly reported (38-40). The mild to moderate increase in serum aminotransferases (ALT and AST) that were initially found in our subjects indicates that the most common abnormality in patients was nonalcoholic fatty liver disease (NAFLD) (41). Their serum levels decreased significantly after diet and treatment with silymarin. Consistent with our study, in a study conducted by Solhi et al. to investigate the effect of silymarin in the treatment of nonalcoholic steatopathy as a clinical trial in 64 nonalcoholic staphylococcal patients in 6 months, the levels of liver enzymes AST and ALT were higher than normal. The results showed that a daily intake of 210 mg oral silymarin for a period of 8 weeks caused a significant decrease (P value $>$ 0.05) in the levels of these enzymes in the intervention group (42). In a study by Dongiovanni et al., silymarin showed beneficial effects as a supportive treatment in most forms of liver disease, including cirrhosis and alcohol abuse-induced liver injury. Clinical studies in cirrhotic patients also demonstrated a significant reduction in deaths due to liver diseases by silymarin (43). Silymarin intake

Table 3. Mean Liver Enzymes with Consumption of Cinnamon Wort at Different Stages of the Intervention

Variables	Cinnamon				Statistical Test, P-Value
	Before	Two Weeks	Four Weeks	One Month	
AST (U/dL)					0.001
Intervention group	44 ± 14.79	43 ± 14.34	42.12 ± 13.56	42.37 ± 13.26	
Control	38.12 ± 8.17	40.84 ± 12.01	38.62 ± 7.39	39.12 ± 7.885	
ALT (U/dL)					0.001
Intervention group	51.12 ± 14.23	49.5 ± 14.48	48.25 ± 14.25	48.25 ± 13.75	
Control	49.75 ± 7.86	49.12 ± 7.43	49.87 ± 7.31	50.87 ± 7.95	
ALP (U/dL)					0.001
Intervention group	231.25 ± 94.52	225.5 ± 92.19	220.37 ± 91.84	219.62 ± 91.35	
Control	266.87 ± 103.82	265.25 ± 99.69	265 ± 98.61	270.35 ± 106.11	
ALB (U/dL)					0.001
Intervention group	5.01 ± 0.3	4.96 ± 0.25	4.91 ± 0.23	4.92 ± 0.26	
Control	4.91 ± 0.18	4.97 ± 0.13	5.01 ± 0.14	4.96 ± 0.1.	
GGT (U/dL)					0.001
Intervention group	21.23 ± 10.85	21.23 ± 10.85	20.58 ± 10.53	20.06 ± 10.44	
Control	24.81 ± 9.15	26.63 ± 9.94	27.02 ± 9.25	27.45 ± 8.98	
Bilirubin (mg/dL)					0.001
Intervention group	0.57 ± 0.14	0.53 ± 0.15	0.52 ± 0.12	0.50 ± 0.13	
Control	0.6 ± 0.14	0.6 ± 0.13	0.58 ± 0.13	0.61 ± 0.13	
ESR (mm/hr)					0.001
Intervention group	10 ± 5.26	9 ± 4.22	8.37 ± 3.61	7.87 ± 2.6	
Control	9.5 ± 2.36	10.62 ± 1.45	11.5 ± 1.15	11.25 ± 1.98	

Abbreviations: AST, Aspartate Aminotransferase; ALT, Alanine Aminotransferase; ALP, Alkaline Phosphatase; ALB, albumin; GGT, Gamma-Glutamyl Trans peptidase; ESR, erythrocyte sedimentation rate.

has also been demonstrated to significantly improve liver histopathological and structural abnormalities in liver diseases of various causes (44, 45). Much attention has been paid to silymarin's antioxidant and anti-inflammatory properties, but despite extensive studies, its exact function has not been fully elucidated. (46). It appears to do so in several ways, including direct free radical scavenging activity, inhibition of reactive radical species formation, and restoration of mitochondrial function (47, 48). In addition, its potent anti-inflammatory property is due to its inhibitory effect on the major transcription factor NF-kB, which has been mentioned in many studies (38, 46, 49, 50).

In the present study, a significant increase in liver biochemical markers was observed in the control group. However, the groups treated with green tea extract showed liver protective activity by restoring the altered serum levels of liver biochemical markers. In addition, total protein and albumin were reduced in the control group, while green tea extract restored total protein and albumin to an almost normal range. In this study, the group that consumed green tea significantly decreased AST and ALT levels after four weeks (P-value $<$ 0.001). Based on these results, it can be claimed that green tea has a beneficial effect on improving liver enzyme levels in the operating room medical staff. But in the results of Sakata et al., who evaluated the laboratory parameters, liver, and histology, they observed that ALT decreased after consuming 100 mg of green tea three times a day for 12 weeks, while AST and ALP levels remained unchanged (51). The difference between the results of Sakata et al. 's study and our study is probably in the dosage of green tea.

Recently, the beneficial effects of cinnamon on fatty liver and liver enzymes have been of great interest (52-54). In a study conducted by Sheybani Asl et al. (55), The effect of cinnamon and licorice extract from *Cichorium intybus* L. on the parameters of liver function in patients with NAFLD was investigated. The results demonstrated that in addition to HDL and cholesterol, other factors such as AST, ALT, ALP, FBS, and TG were somewhat improved by injection of the extracts, and interestingly, the reduction of ALT and AST was significant. In conclusion, according to the data of the present study, ingesting cinnamon had no significant effects on liver enzymes in adults and anesthesia personnel in the operating room. However, at doses up to 1500 mg/day in studies conducted for 12 weeks and in studies conducted for both sexes, the effect of cinnamon on the levels of ALT was significant (56, 57).

The results of this study demonstrated that the levels of AST, ALT, ALP, ALB, GGT, bilirubin, and ESR decreased four weeks after the end of the interventions, and it seems that the milk thistle group showed a further decrease after the end of the interventions. In addition, individual differences (P value $<$ 0.05) were found in enzyme levels and AST, ESR, and GGT. GGT, ALT, and ESR levels decreased sharply in all subjects in the experimental groups. The greatest decrease in liver enzymes was found in ALT, ALP, albumin, and ESR, indicating that the intake of milk thistle, green tea, and cinnamon positively affect liver enzymes in surgical personnel. Long-term consumption of green tea promotes weight loss, which may attenuate its beneficial effect in treating NAFLD. It would be feasible that further studies should be conducted before recommending this tea as a treatment. In conclusion, the results show that all extracts reduced AST, ALT, ALP, ALB, GGT, bilirubin, and ESR. Still, milk thistle herb can significantly reduce ALT, ESR, and GGT and also improve liver parameters. In addition, silymarin is well tolerated and appears to have no side effects when taken for at least four weeks. However, long-term studies with silymarin may be needed.

5.1. Conclusions

Milk thistle consumption significantly improved surgical personnel's liver metabolic, chemical, and inflammatory parameters. It can be argued that milk thistle extract can improve serum levels of liver enzymes in surgical personnel and mitigate the toxic effects of anesthetics.

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Footnotes

Authors' Contribution: Study concept and design: Vahid Kheirandish and Farhad Nanaei; analysis and interpretation of data: Neda Shakerian, and; drafting of the manuscript: Maysam Mard-Soltani; critical revision of the manuscript for important intellectual content: Vahid Kheirandish, Faraz Mojab, and Maysam Mard-Soltani; statistical analysis: Neda Shakerian.

Clinical Trial Registration Code: The level of liver enzymes of the personnel was measured in four stages including before the start of the intervention, two weeks after the start of the intervention, one month after the start of the intervention and one month after the end of the intervention.

Conflict of Interests: Kheirandish reported receiving research grants, honoraria, and consulting fees for speaking only from Dezful University of Medical Sciences. The authors declare that they have no known competing financial interests or personal relationships that could have influenced the work reported in this article to the participants.

Data Reproducibility: The data presented in this study are uploaded during submission as a supplementary file and are openly available for readers upon request.

Ethical Approval: IR.DUMS.REC.1399.010.

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Informed Consent: Informed consent was obtained from all participants.

References

1. Aun AG, Golim MA, Nogueira FR, Souza KM, Arruda NM, Braz JRC, et al. Monitoring early cell damage in physicians who are occupationally exposed to inhalational anesthetics. *Mutat Res - Fundam Mol Mech Mutagen*. 2018;**812**:5–9. [PubMed ID: 30388507]. https://doi.org/10.1016/j.mrfmmm.2018.10.002.
2. Braz MG, Carvalho LIM, Chen CO, Blumberg JB, Souza KM, Arruda NM, et al. High concentrations of waste anesthetic gases induce genetic damage and inflammation in physicians exposed for three years: A cross-sectional study. *Indoor Air*. 2020;**30**(3):512–20. [PubMed ID: 31930534]. https://doi.org/10.1111/ina.12643.
3. Xu Y, Jiang W, Xie S, Xue F, Zhu X. The role of inhaled anesthetics in tumorigenesis and tumor immunity. *Cancer Manag Res*. 2020;**12**:1601–9. [PubMed ID: 32184663]. [PubMed Central ID: PMC7061426]. https://doi.org/10.2147/CMAR.S244280.
4. Jiao B, Yang C, Huang NN, Yang N, Wei J, Xu H. Relationship between volatile anesthetics and tumor progression: Unveiling the mystery. *Curr Med Sci*. 2018;**38**(6):962–7. [PubMed ID: 30536056]. https://doi.org/10.1007/s11596-018-1970-6.
5. Ogunyemi D. Reproductive system. *The Handbook of Wellness Medicine*. 2020. p. 116–34. https://doi.org/10.1017/9781108650182.011.

6. Chen C, Lin L. Alkaloids in diet. *Handbook of Dietary Phytochemicals*. 2020. p. 1–35. https://doi.org/10.1007/978-981-13-1745-3_36-1.
7. de Groot A. Allergic contact dermatitis from topical drugs: An overview. *Dermatitis*. 2021;**32**(4):197–213. [PubMed ID: 34415695]. https://doi.org/10.1097/DER.0000000000000737.
8. Kvisselgaard AD, Mosbech HF, Fransson S, Garvey LH. Risk of immediate-type allergy to local anesthetics is overestimated-results from 5 years of provocation testing in a danish allergy clinic. *J Allergy Clin Immunol Pract*. 2018;**6**(4):1217–23. [PubMed ID: 28988784]. https://doi.org/10.1016/j.jaip.2017.08.010.
9. Gül H. Occupational health and safety in operating rooms. *Healthcare Access*. 2022. https://doi.org/10.5772/intechopen.97223.
10. Greenwood M, Meechan JG. 3 rd, editor. *General medicine and surgery for dental practitioners*. London: Springer nature; 2019. https://doi.org/10.1007/978-3-319-97737-9.
11. Neghab M, Amiri F, Soleimani E, Yousefinejad S, Hassanzadeh J. Toxic responses of the liver and kidneys following occupational exposure to anesthetic gases. *Excli J*. 2020;**19**:418–29. [PubMed ID: 32327960]. [PubMed Central ID: PMC7174577]. https://doi.org/10.17179/excli2019-1911.
12. Pokhrel LR, Grady KD. Risk assessment of occupational exposure to anesthesia Isoflurane in the hospital and veterinary settings. *Sci Total Environ*. 2021;**783**:146894. [PubMed ID: 33865128]. https://doi.org/10.1016/j.scitotenv.2021.146894.
13. Eisenkraft JB, Jaffe MB. Hazards of the anesthesia delivery system. *Anesthesia Equipment*. 2021. p. 489–525. https://doi.org/10.1016/b978-0-323-67279-5.00023-6.
14. Li H, Yu XH, Ou X, Ouyang XP, Tang CK. Hepatic cholesterol transport and its role in non-alcoholic fatty liver disease and atherosclerosis. *Prog Lipid Res*. 2021;**83**:101109. [PubMed ID: 34097928]. https://doi.org/10.1016/j.plipres.2021.101109.
15. Wang PP, Huang X, Yang MW, Fang SY, Hong FF, Yang SL. Effects of non-drug treatment on liver cells apoptosis during hepatic ischemia-reperfusion injury. *Life Sci*. 2021;**275**:119321. [PubMed ID: 33711387]. https://doi.org/10.1016/j.lfs.2021.119321.
16. Maly O, Zajak J, Hyspler R, Turek Z, Astapenko D, Jun D, et al. Inhalation of molecular hydrogen prevents ischemia-reperfusion liver damage during major liver resection. *Ann Transl Med*. 2019;**7**(23):774. [PubMed ID: 32042790]. [PubMed Central ID: PMC6989999]. https://doi.org/10.21037/atm.2019.11.43.
17. Dutta S, Prasad Mishra S, Kumar Sahu A, Mishra K, Kashyap P, Sahu B. Hepatocytes and their role in metabolism. *Drug Metabolism*. 2021. https://doi.org/10.5772/intechopen.99083.
18. Sripongpun P, Kim WR, Mannalithara A, Charu V, Vidovszky A, Asch S, et al. The steatosis-associated fibrosis estimator (SAFE) score: A tool to detect low-risk NAFLD in primary care. *Hepatology*. 2023;**77**(1):256–67. [PubMed ID: 35477908]. [PubMed Central ID: PMC9613815]. https://doi.org/10.1002/hep.32545.
19. Giashuddin S, Alawad M. Histopathological diagnosis of nonalcoholic steatohepatitis (NA SH). *Methods Mol Biol*. 2022;**2455**:1–18. [PubMed ID: 35212981]. https://doi.org/10.1007/978-1-0716-2128-8_1.
20. Gulhar R, Ashraf MA, Jialal I. *Physiology, acute phase reactants*. Treasure Island (FL): StatPearls Publishing; 2018.
21. Wang Y, Li Y, Qiao L, Sun S. Comparison of a comprehensive set of fibrinolytic markers with c-reactive protein and erythrocyte sedimentation rate for the diagnosis of periprosthetic joint infection. *J Arthroplasty*. 2020;**35**(9):2613–8. [PubMed ID: 32461024]. https://doi.org/10.1016/j.arth.2020.04.096.
22. Zhang W, Yuan Y, Zhang S, Jin C, Wu L, Mei H, et al. Erythrocyte sedimentation rate in covid-19 infections. *medRxiv*. 2020. https://doi.org/10.1101/2020.06.25.20139881.
23. Perestrelo BO, Carvalho PM, Souza DN, Carneiro MJ, Cirino JPG, Carvalho PO, et al. Antioxidant effect of chamomile tea on the salivary glands of streptozotocin-induced diabetic rats. *Braz Oral Res*. 2022;**36**. e034. [PubMed ID: 35293499]. https://doi.org/10.1590/1807-3107bor-2022.vol36.0034.
24. Kadhim EM. Review study of antioxidants and the cinnamon oil effects. *Med Sci J Adv Res*. 2021;**2**(1):1–9. https://doi.org/10.46966/msjar.v2i1.12.
25. Zyzelewicz D, Kulbat-Warycha K, Oracz J, Zyzelewicz K. Polyphenols and other bioactive compounds of sideritis plants and their potential biological activity. *Molecules*. 2020;**25**(16). [PubMed ID: 32824863]. [PubMed Central ID: PMC7464829]. https://doi.org/10.3390/molecules25163763.
26. Jayawardana BC, Warnasooriya VB, Thotawattage GH, Dharmasena VAKI, Liyanage R. Black and green tea (Camellia sinensis L.) extracts as natural antioxidants in uncured pork sausages. *J Food Process Preserv*. 2019;**43**(2). https://doi.org/10.1111/jfpp.13870.
27. Ulgen C, Yildirim AB, Sahin G, Turker AU. Do magnetic field applications affect in vitro regeneration, growth, phenolic profiles, antioxidant potential and defense enzyme activities (SOD, CAT and PAL) in lemon balm (Melissa officinalis L.)? *Ind Crops Prod*. 2021;**169**. https://doi.org/10.1016/j.indcrop.2021.113624.
28. Viktorova J, Stranska-Zachariasova M, Fenclova M, Vitek L, Hajslova J, Kren V, et al. Complex evaluation of antioxidant capacity of milk thistle dietary supplements. *Antioxidants (Basel)*. 2019;**8**(8). [PubMed ID: 31426591]. [PubMed Central ID: PMC6720444]. https://doi.org/10.3390/antiox8080317.
29. Khazaei R, Seidavi A, Bouyeh M. A review on the mechanisms of the effect of silymarin in milk thistle (Silybum marianum) on some laboratory animals. *Vet Med Sci*. 2022;**8**(1):289–301. [PubMed ID: 34599793]. [PubMed Central ID: PMC8788984]. https://doi.org/10.1002/vms3.641.
30. Vairetti M, Di Pasqua LG, Cagna M, Richelmi P, Ferrigno A, Berardo C. Changes in glutathione content in liver diseases: An update. *Antioxidants (Basel)*. 2021;**10**(3). [PubMed ID: 33670839]. [PubMed Central ID: PMC7997318]. https://doi.org/10.3390/antiox10030364.
31. Taleb A, Ahmad KA, Ihsan AU, Qu J, Lin N, Hezam K, et al. Antioxidant effects and mechanism of silymarin in oxidative stress induced cardiovascular diseases. *Biomed Pharmacother*. 2018;**102**:689–98. [PubMed ID: 29604588]. https://doi.org/10.1016/j.biopha.2018.03.140.
32. Jakubczyk K, Kochman J, Kwiatkowska A, Kaldunska J, Dec K, Kawczuga D, et al. Antioxidant properties and nutritional composition of matcha green tea. *Foods*. 2020;**9**(4). [PubMed ID: 32290537]. [PubMed Central ID: PMC7231151]. https://doi.org/10.3390/foods9040483.
33. Momtaz S, Hassani S, Khan F, Ziaee M, Abdollahi M. Cinnamon, a promising prospect towards Alzheimer's disease. *Pharmacol Res*. 2018;**130**:241–58. [PubMed ID: 29258915]. https://doi.org/10.1016/j.phrs.2017.12.011.
34. Deng HB, Li FX, Cai YH, Xu SY. Waste anesthetic gas exposure and strategies for solution. *J Anesth*. 2018;**32**(2):269–82. [PubMed ID: 29404778]. https://doi.org/10.1007/s00540-018-2448-1.
35. Sae-Tan S, Grove KA, Lambert JD. Weight control and prevention of metabolic syndrome by green tea. *Pharmacol Res*. 2011;**64**(2):146–54. [PubMed ID: 21193040]. [PubMed Central ID: PMC3123415]. https://doi.org/10.1016/j.phrs.2010.12.013.
36. Mascaro CM, Bouzas C, Tur JA. Association between non-alcoholic fatty liver disease and mediterranean lifestyle: A systematic review. *Nutrients*. 2021;**14**(1). [PubMed ID: 35010923]. [PubMed Central ID: PMC8746321]. https://doi.org/10.3390/nu14010049.
37. Lampignano L, Donghia R, Sila A, Bortone I, Tatoli R, De Nucci S, et al. Mediterranean diet and fatty liver risk in a population of overweight older italians: A propensity score-matched case-cohort study. *Nutrients*. 2022;**14**(2). [PubMed ID: 35057439]. [PubMed Central ID: PMC8779579]. https://doi.org/10.3390/nu14020258.
38. Abenavoli L, Izzo AA, Milic N, Cicala C, Santini A, Capasso R. Milk thistle (Silybum marianum): A concise overview on its chemistry, pharmacological, and nutraceutical uses in liver diseases. *Phytother Res*. 2018;**32**(11):2202–13. [PubMed ID: 30080294]. https://doi.org/10.

1002/ptr.6171.
39. Ra S, Shin R, Ri H, Ri J, Ri H, Ri A. Effect of lesimarin against thioacetamide-induced liver cirrhosis in rat. *Braz J Pharm Sci*. 2019;**55**. https://doi.org/10.1590/s2175-97902019000217821.
40. Lamia SS, Emran T, Rikta JK, Chowdhury NI, Sarker M, Jain P, et al. Coenzyme q10 and silymarin reduce ccl(4)-induced oxidative stress and liver and kidney injury in ovariectomized rats-implications for protective therapy in chronic liver and kidney diseases. *Pathophysiology*. 2021;**28**(1):50–63. [PubMed ID: 35366269]. [PubMed Central ID: PMC8830449]. https://doi.org/10.3390/pathophysiology28010005.
41. Kathak RR, Sumon AH, Molla NH, Hasan M, Miah R, Tuba HR, et al. The association between elevated lipid profile and liver enzymes: a study on Bangladeshi adults. *Sci Rep*. 2022;**12**(1):1711. [PubMed ID: 35110625]. [PubMed Central ID: PMC8810783]. https://doi.org/10.1038/s41598-022-05766-y.
42. Solhi H, Ghahremani R, Kazemifar AM, Hoseini Yazdi Z. Silymarin in treatment of non-alcoholic steatohepatitis: A randomized clinical trial. *Caspian J Intern Med*. 2014;**5**(1):9–12. [PubMed ID: 24490006]. [PubMed Central ID: PMC3894463].
43. Dongiovanni P, Paolini E, Corsini A, Sirtori CR, Ruscica M. Nonalcoholic fatty liver disease or metabolic dysfunction-associated fatty liver disease diagnoses and cardiovascular diseases: From epidemiology to drug approaches. *Eur J Clin Invest*. 2021;**51**(7). e13519. [PubMed ID: 33583033]. https://doi.org/10.1111/eci.13519.
44. Khalili A, Fallah P, Hashemi SA, Ahmadian-Attari MM, Jamshidi V, Mazloom R, et al. New mechanistic insights into hepatoprotective activity of milk thistle and chicory quantified extract: The role of hepatic Farnesoid-X activated receptors. *Avicenna J Phytomed*. 2021;**11**(4):367–79. [PubMed ID: 34290968]. [PubMed Central ID: PMC8264225]. https://doi.org/10.22038/ajp.2020.17281.
45. Gillessen A, Schmidt HH. Silymarin as supportive treatment in liver diseases: A narrative review. *Adv Ther*. 2020;**37**(4):1279–301. [PubMed ID: 32065376]. [PubMed Central ID: PMC7140758]. https://doi.org/10.1007/s12325-020-01251-y.
46. Tighe SP, Akhtar D, Iqbal U, Ahmed A. Chronic liver disease and silymarin: A biochemical and clinical review. *J Clin Transl Hepatol*. 2020;**8**(4):454–8. [PubMed ID: 33447529]. [PubMed Central ID: PMC7782115]. https://doi.org/10.14218/JCTH.2020.00012.
47. Kesharwani SS, Jain V, Dey S, Sharma S, Mallya P, Kumar VA. An overview of advanced formulation and nanotechnology-based approaches for solubility and bioavailability enhancement of silymarin. *J Drug Deliv Sci Technol*. 2020;**60**. https://doi.org/10.1016/j.jddst.2020.102021.
48. Kadoglou NPE, Panayiotou C, Vardas M, Balaskas N, Kostomitsopoulos NG, Tsaroucha AK, et al. A comprehensive review of the cardiovascular protective properties of silibinin/silymarin: A new kid on the block. *Pharmaceuticals (Basel)*. 2022;**15**(5). [PubMed ID: 35631363]. [PubMed Central ID: PMC9145573]. https://doi.org/10.3390/ph15050538.
49. Hashem A, Shastri Y, Al Otaibi M, Buchel E, Saleh H, Ahmad R, et al. Expert opinion on the management of non-alcoholic fatty liver disease (nafld) in the middle east with a focus on the use of silymarin. *Gastroenterology Insights*. 2021;**12**(2):155–65. https://doi.org/10.3390/gastroent12020014.
50. Camini FC, Costa DC. Silymarin: not just another antioxidant. *J Basic Clin Physiol Pharmacol*. 2020;**31**(4). [PubMed ID: 32134732]. https://doi.org/10.1515/jbcpp-2019-0206.
51. Sakata R, Nakamura T, Torimura T, Ueno T, Sata M. Green tea with high-density catechins improves liver function and fat infiltration in non-alcoholic fatty liver disease (NAFLD) patients: a double-blind placebo-controlled study. *Int J Mol Med*. 2013;**32**(5):989–94. [PubMed ID: 24065295]. https://doi.org/10.3892/ijmm.2013.1503.
52. Askari F, Rashidkhani B, Hekmatdoost A. Cinnamon may have therapeutic benefits on lipid profile, liver enzymes, insulin resistance, and high-sensitivity C-reactive protein in nonalcoholic fatty liver disease patients. *Nutr Res*. 2014;**34**(2):143–8. [PubMed ID: 24461315]. https://doi.org/10.1016/j.nutres.2013.11.005.
53. Wickenberg J, Lindstedt S, Nilsson J, Hlebowicz J. Cassia cinnamon does not change the insulin sensitivity or the liver enzymes in subjects with impaired glucose tolerance. *Nutr J*. 2014;**13**:96. [PubMed ID: 25249415]. [PubMed Central ID: PMC4180052]. https://doi.org/10.1186/1475-2891-13-96.
54. Rahimlou M, Ahmadnia H, Hekmatdoost A. Dietary supplements and pediatric non-alcoholic fatty liver disease: Present and the future. *World J Hepatol*. 2015;**7**(25):2597–602. [PubMed ID: 26557952]. [PubMed Central ID: PMC4635145]. https://doi.org/10.4254/wjh.v7.i25.2597.
55. Sheybani Asl Z, Malekirad AA, Abdollahi M, Bakhshipour A, Akbari Dastjerdi H, Mostafalou S, et al. Effects of the mixture of cichorium intybus l. And cinnamomum zeylanicum on hepatic enzymes activity and biochemical parameters in patients with nonalcoholic fatty liver disease. *Health*. 2014;**6**(11):1212–7. https://doi.org/10.4236/health.2014.611148.
56. Shekarchizadeh-Esfahani P, Heydarpour F, Izadi F, Jalili C. The effect of cinnamon supplementation on liver enzymes in adults: A systematic review and meta-analysis of randomized controlled trials. *Complement Ther Med*. 2021;**58**:102699. [PubMed ID: 33639251]. https://doi.org/10.1016/j.ctim.2021.102699.
57. Mousavi SM, Jayedi A, Bagheri A, Zargarzadeh N, Wong A, Persad E, et al. What is the influence of cinnamon supplementation on liver enzymes? A systematic review and meta-analysis of randomized controlled trials. *Phytother Res*. 2021;**35**(10):5634–46. [PubMed ID: 34212447]. https://doi.org/10.1002/ptr.7200.