

Review Article



# Tea and coffee consumption impact on the non-alcoholic fatty liver disease: a systematic review and meta-analysis

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## Abstract

**Introduction:** Non-alcoholic fatty liver disease (NAFLD) is diagnosed when  $\geq 5$ –10% of hepatocytes display macroscopic steatosis in the absence of other etiologies of liver disease. Consumption of coffee or tea or both may decrease the risk of NAFLD, as recommended by studies of liver enzymes.

**Methods:** The required data was collected from different databases such as EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, and Web of Science as well as the database inception to July 2021. In addition, pooled mean difference and 95% confidence intervals (CIs) were considered in the random effects model.

**Results:** Of the total collected 218 articles, 8 met our inclusion criteria to be involved in the meta-analysis. Four studies assessed green tea and one study assessed sour tea consumption in NAFLD patients. Three studies assessed coffee use. All studies have shown an inverse correlation of coffee intake with elevated serum enzyme levels. Based on the meta-analysis outcome, the mean alanine aminotransferase (ALT) in the intervention group was measured as 12.50 points less than that of the control group. The mean aspartate aminotransferase (AST) of the intervention group was 9.23 points lower than that of the control group ( $P$  value  $< 0.001$ ).

**Conclusion:** There is increasing evidence that steadily revealed an opposite relationship between the consumption amount of green tea and coffee and the risk of liver diseases. This meta-analysis supports the protective role of the mentioned beverages in patients suffering from NAFLD.

## Introduction

Non-alcoholic fatty liver disease (NAFLD) is used to define a condition in which excess fat builds up in the liver in the lack of extreme alcohol consumption, viral infection, or any other specific etiology of liver disease.<sup>1,2</sup> It is the most prevalent liver disease common among western industrialized countries with the prevalence rates of 6%–35% around the global.<sup>3,4</sup> NAFLD is diagnosed as the presence of high amount of liver enzymes namely alanine aminotransferase ( $[ALT] > 31$  mg/dL and 41 mg/dL) and aspartate aminotransferase ( $[AST] > 31$  mg/dL and 47 mg/dL) among women and men, respectively.<sup>5–7</sup> There is minor confirmation to support the efficiency of drugs such as pentoxifylline, pioglitazone, vitamin E, and metformin in improve the histological features of NAFLD.<sup>8,9</sup> In order to control NAFLD, lifestyle modification is highly recommended that includes diet

control, weight loss, limited energy intake, and adequate physical activities.<sup>10</sup>

The herbal medicine has been demonstrated to treat NAFLD with good efficacy in previous studies.<sup>11</sup> Recent data suggests that consumption of coffee and tea may have health benefits in a number of medical ailments.<sup>12</sup> Coffee consumption plays a significant role in decreasing the rate of different chronic diseases such as type II diabetes as well as cardiovascular and neurodegenerative strokes.<sup>13,14</sup> According to the obtained results, regular coffee consumption could significantly decrease the serum concentrations of liver enzymes including ALT, AST, and  $\gamma$ -glutamyltransferase (GGT).<sup>15</sup> Routine coffee drinking notably lessens the NAFLD risk over time.<sup>16</sup> The results of the umbrella review exhibited that the previous systematic reviews and meta-analyses described a connection between coffee consumption and

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a decrease in the incidence of NAFLD.<sup>17</sup> Furthermore, the outcomes displayed that, coffee consumption had the useful influence of decreasing the degree of liver fibrosis amongst patients with NAFLD.<sup>17</sup> The correlation between coffee consumption and incidence and prevalence of NAFLD, and also risk of liver fibrosis was quantitatively evaluated in another meta-analysis.<sup>18</sup> The results showed that increased coffee consumption was considerably related to a decreased liver fibrosis risk. Nevertheless, there was no correlation between coffee consumption and incidence or prevalence of NAFLD.<sup>18</sup>

Increased green tea (*Camellia sinensis*) consumption would also significantly decrease the chance of liver diseases.<sup>19</sup> Green tea reduces hepatic steatosis by decreasing hepatic insulin resistance which is the main mechanism in NAFLD pathogenesis.<sup>20</sup> To some extent, it prevents reactive oxygen species (ROS) formation, increases the pro-oxidant enzyme activities, and reduces various inflammatory cytokines.<sup>20</sup> The meta-analysis of data from four studies comprising 234 subjects showed major effects of green tea supplementation in varying serum ALT and AST levels.<sup>21</sup> Drinking coffee and tea would considerably improve the hepatic steatosis and fibrosis levels and decrease the cirrhosis, hence less risk of hepatocellular carcinoma.<sup>22-24</sup>

Several studies have confirmed the hepatoprotective

effect of drinking coffee and green tea on the NAFLD. In this regard, the current research presented a thorough and comprehensive review of the previous studies as well as the meta-analysis to confirm this possible correlation in the present study.

## Materials and Methods

### Data sources and search strategy

We carried out a systematic search from 1990 to July 2021 in different databases including PubMed, Scopus, Web of Science, Google Scholar, Cochrane Library, ProQuest, and EMBASE. The search strategy was a combination of MeSH, Emtree terms and free-text such as tea, coffee, liver disease, liver fibrosis, nonalcoholic fatty liver disease, and hepatic failure. We excluded studies without sufficient statistics or adequate data. [Supplementary file 1](#) presents the following search strategy of the different databases.

### Study selection

All recognized citations were collected and imported into EndNote X9. Subsequently, the duplicate citations were excluded. At that time, two reviewers carefully checked the titles and abstracts individually. Full texts of the selected studies were saved and evaluated comprehensively. [Figure 1](#) displays the study selection process details of the Preferred Reporting Items for Systematic review and

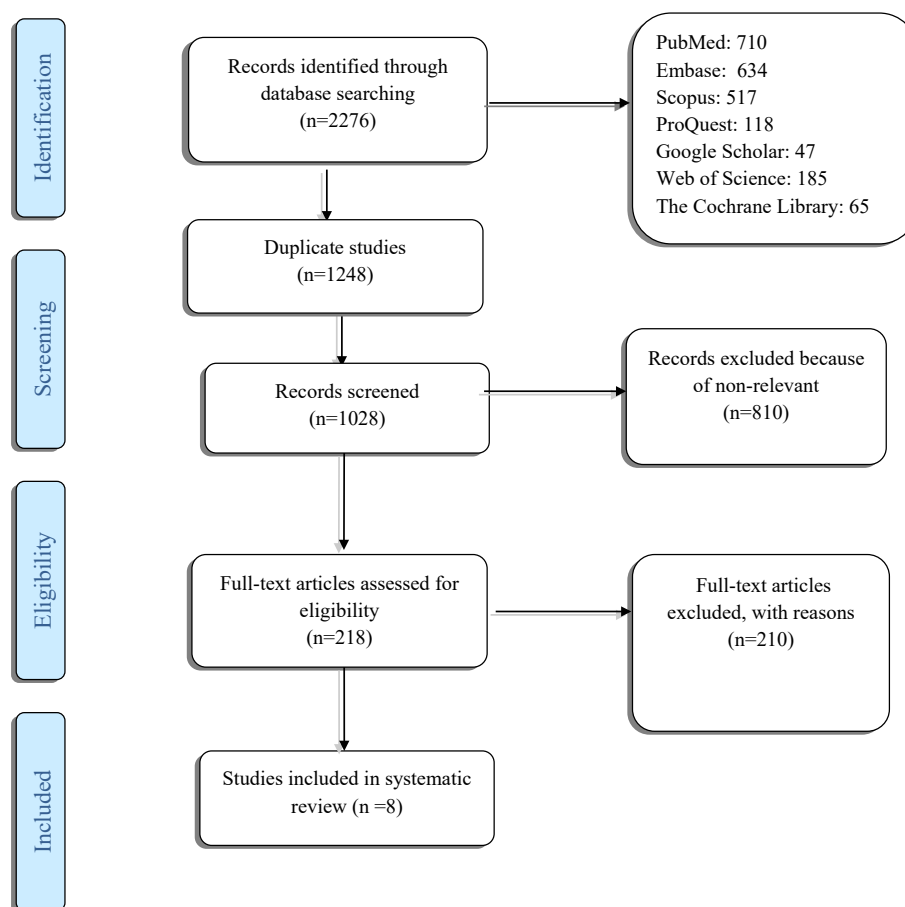


Figure 1. Search and selection process of systematic review

Meta-Analyses (PRISMA) checklist.

### **Inclusion criteria**

All randomized controlled trials (RCTs) studies involved patients with NAFLD, who sought control the disease with coffee and/or tea consumption were included.

### **Exclusion criteria**

All retrospective studies; studies with no access to full-text; withdrawn trials.

### **Interventions**

Tea and coffee.

### **Types of comparisons**

The quantitative component of this review was considered placebo, and other conventional controls.

### **Types of outcomes**

Primarily, our objective was to assess the impact of drinking coffee and/or tea in NAFLD patients. Liver enzymes levels including ALT and AST was included for NAFLD evaluation and monitoring. The primary outcome was the efficacy of consumption of coffee and/or tea on serum levels of liver enzymes in NAFLD patients.

Table 1 presents PICOS criteria for exclusion and inclusion of studies.

### **Assessment of methodological quality**

The articles were reviewed for assessing selection bias, detection bias, performance bias, reporting bias, and attrition bias, an assessment was separately performed by two authors in terms of the Cochrane handbook.<sup>24</sup> Disagreements between reviewers were solved by discussion till agreement was acquired.

### **Data extraction**

The obtained data comprised the name of the first author, country, publication year, and type of study, sample size, sex, age, type of liver disease, follow-up, tea dosage and duration, cups of coffee per day, outcome.

### **Statistical analysis**

The pooled measure, i.e., the inverse variance-weighted mean of the MD logarithm with 95% CI, was used in this study to find out the relationship between the tea and coffee consumption and liver diseases. Between-study heterogeneity was quantitatively evaluated by Cochrane (Q) and I<sup>2</sup> index. The value more than 50% for this index, represents the higher heterogeneity. All analyses were achieved by Comprehensive Meta-Analysis software version 2.0. In all analyses,  $P < 0.05$  was found significant in terms of statistics.

### **Results**

In the first phase, 2276 articles were collected from

databases, and after eliminating the duplicated items, 1028 articles were remained. Then, the articles were assessed in terms of the inclusion. Considering non-relevance to this review, 810 were then excluded based on the abstract and title. Ultimately, out of 218 articles, 8 epidemiological studies with 405 participants with the age range of 40–60 years were incorporated in the employed meta-analysis, as shown in Table 1.<sup>21,25-31</sup>

### **Effectiveness of green and sour tea with regard to liver enzyme function**

In the study by Sakata et al,<sup>25</sup> 17 patients diagnosed with NAFLD drank green tea with high- and low-density catechins or a placebo for 12 weeks. According to the results from this randomized double-blind study, 12 weeks of consumption of 700 mL green tea per day comprising  $> 1$  g catechin increased the liver fat content and inflammation through decreasing oxidative stress in NAFLD patients.<sup>25</sup> Pezeshki et al. in their placebo-controlled, double-blind, and randomized clinical trial<sup>21</sup> remarked that green tea extract supplementation (500 mg GTE tablet per day) could decrease liver enzymes in 80 participants of 20 to 50 years old diagnosed with NAFLD after 12 weeks. Prescription of GTE is recommended as a new treatment method for enhancing serum levels in liver enzymes among NAFLD patients.<sup>21</sup> Tabatabaee et al conducted another double-blind randomized clinical trial.<sup>26</sup> The difference between the patients with NAFLD in the intervention group who consumed 550 mg of green tea tablets on a daily basis and those in the control group after three months was principally detected in the levels of liver enzyme, anthropometrics, and metabolic indicators.<sup>26</sup> Results of a study in 40 overweight, non-diabetic and dyslipidemic patients with NAFLD, who took the GTE 500 mg capsule two times a day for twelve weeks, revealed that GTE considerably contribute to an increase in the body weight, BMI, lipid profile, ALT, AST, and inflammatory markers (hs-CRP, adiponectin). Moreover, GTE caused a 67.5% regression of fatty liver alterations in compared with placebo which is 25%.<sup>27</sup> These results appeared to be consistent with those obtained by Sakata et al<sup>25</sup> and Fukuzawa et al,<sup>32</sup> which indicated that GTE could decrease the levels of liver enzyme and similarly improve the BMI, lipid profile, and oxidative stress and inflammation markers in subjects with NAFLD for 12 weeks. Furthermore, sour tea supplementation effectively increased the serum liver enzymes in the patients under study.<sup>28</sup> The levels of triglyceride, AST, and ALT in participants who took 450 mg capsule of sour tea per day for eight weeks were significantly reduced, compared to the placebo level.<sup>28</sup>

### **Effectiveness of coffee on liver enzymes**

Supplementation of green coffee extract (GCE) could be beneficial in controlling NAFLD risks factors. Hosseinabadi et al carried out a randomized, double-blind,

**Table 1.** Main characteristics of the studies included in the meta-analysis of the impact of the coffee and tea consumption in NAFLD patients

References	Mean age	Sample size	Intervention				ALT				AST			
			Intervention		Placebo		Before		After		Before		After	
			Intervention	Placebo	Intervention	Placebo	Intervention	Placebo	Intervention	Placebo	Intervention	Placebo	Intervention	Placebo
1 <sup>27</sup>	41.4	41.13	21	23	Cap GCE200 mg BD	43.85±25.82	36.56±19.19	44.52±30.08	37.04±19.99	35.71 (22.63)	30.00 (9.39)	32.66 (16.74)	32.13 (11.14)	
2 <sup>29</sup>	45.68	44.17	25	23	caffeine200 mg cap OD	-0.12(-4.4 to 4.13;P = 0.79)							- 0.43 (- 5.19 to 4.34; P = 0.87)	
3 <sup>24</sup>	41	39.5	21	24	Green tea tab550mg	32.41±29.43	31.16±21.33	-12.17±19.17	3.5±21.85	25.36±16.83	23.72±12.52	6.78±13.42	0.22±14.63	
4 <sup>22</sup>	47.1	54.2	7	5	Green tea containing 1,080 mg/700 ml	101±95	94±50	42.1±11.3%	3.1±7.8%	120±57	110±58			
5 <sup>28</sup>	41.36	44.5	22	22	GCBE 1 gram/day	33.04 ±4.28	33.63 4.42+	26.04 3.30+	34.04+± 4.81	36.77 ±11.10	37.13 ±9.84	36.00 ±11.13	36.77 ±9.96	
6 <sup>23</sup>			35	36	Cap GTE 500mg OD	44.59±22.93	43.62±23.85	31.38±18.43	37.88±22.92	30.14±13.21	29.69±13.42	22.89±9.32	26.62±12.7	
7 <sup>25</sup>	25	28	40	40	Cap GTE 500mgBD	70.4±15.8	74±16.3	52.8±12.2	72±5.4	65.8±12.4	62.4±12.3	44.3±8.5	59±9.5	
8 <sup>26</sup>	43.3	42.8	30	31	Sour tea	35.16 ± 18.5	40.4 ± 22.3	30.53 ± 13.4	41.6 ± 21.1	45.5 ± 13.4	48.4 ± 6.9	39.8 ± 12.7	48.1 ± 7.8	

ALT, alanine aminotransferase; AST, aspartate aminotransferase; B.D, 2 times a day; GCBE, green coffee bean extract; GCE, green coffee extract; GTE, green tea extract; NAFLD, Non-alcoholic fatty liver disease; OD, once a day.

and controlled clinical trial on 48 patients of 20 to 60 years old suffering from NAFLD who were randomly selected to receive a routine dose of 400 mg GCE (2×300 mg) or placebo for 8 weeks.<sup>29</sup> Results showed that alterations in AST and ALT serums between the two groups were negligible at the end of the study.<sup>29</sup> Although the serum ALT in NAFLD patients in the study of Shahmohammadi et al was improved followed by supplementing GCE with the dose of 1 g/day for eight weeks compared to that in the placebo group, serum AST alterations through the study were not statistically different between these two groups.<sup>30</sup> According to the findings of Mansour et al, six-month supplementation with main coffee components namely caffeine and/or chlorogenic acid (200mg/d) did not improve the hepatic enzymes (ALT, AST, and GGT) in patients with NAFLD.<sup>31</sup>

**Meta-analysis**

**Effectiveness of green tea, sour tea and coffee on alanine aminotransferase**

In 8 studies, mean ALT was reported in both control and intervention groups. Difference between studies was considerable (Q-value = 54.54 df = 7, I<sup>2</sup> = 87.16, P value < 0.001). Based on the meta-analysis results, the mean ALT in the intervention group was 12.50 points lower than that in the control group. Figure 2 showed the forest diagram obtained by combining the results using meta-analysis (pooled mean difference = -12.5, 95% CI = (- 17.77 to -7.23), P value < 0.001).

**Effectiveness of green tea, sour tea and coffee on aspartate aminotransferase**

In 7 studies, the mean AST was reported in both control and intervention groups. Heterogeneity between studies was significant (Q-value = 305.30 df = 6, I<sup>2</sup> = 98.03, P value < 0.001). According to the results of meta-analysis, the mean AST in the intervention group was 9.23 points lower than the control group. Figure 3 showed the forest diagram obtained by combining the results using meta-analysis (pooled mean difference = -9.23, 95% CI = (- 21.35 to -2.89), P value < 0.001).

**Discussion**

This meta-analysis evaluated the association between coffee consumption and green tea drinking and NAFLD based on all published studies. Our results have shown an inverse correlation of coffee intake with elevated serum enzyme levels. Based on the meta-analysis outcome, the mean of ALT in the intervention group was measured as 12.50 points less than that of the control group and the mean of AST in the intervention group was 9.23 points lower than that of the control group. Our outcomes support the protective role of the coffee and green tea in patients suffering from NAFLD.

NAFLD is a highly prevalent chronic liver disease in the developed countries.<sup>33</sup> There is a growing body of

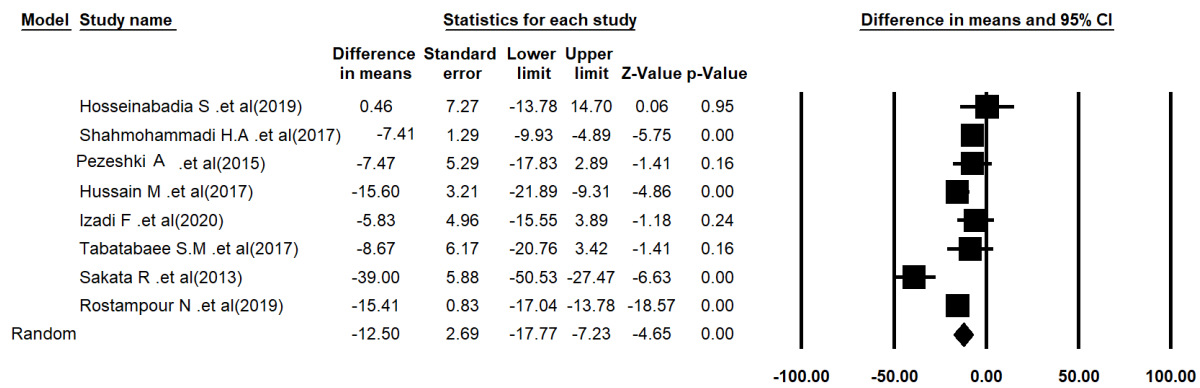


Figure 2. Forest plot of comparison coffee and tea drinking vs. control on ALT levels

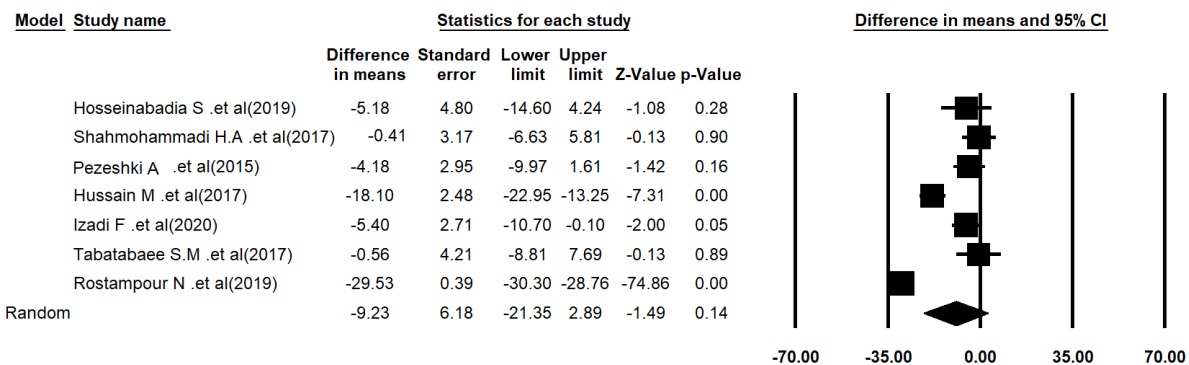


Figure 3. Forest plot of comparison coffee and tea drinking vs. control on AST levels

literature complying with the protective impacts of coffee consumption against the improvement and progression of liver disease due to numerous reasons.<sup>34</sup> Two meta-analyses evidently showed that patients with preexistent liver disease who drink coffee more than two cups a day are less exposed to fibrosis and cirrhosis incidence, hence lower hepatocellular and carcinoma as well as mortality rates.<sup>35,36</sup> Given that coffee is rich in antioxidants and other constituents, it contributes to enzyme synthesis modification. Numerous researches have highlighted the role of coffee consumption in decreasing the levels of GGT and ALT in the liver and protecting it against liver cell growth caused by alcohol particularly in high-risk subjects.<sup>37</sup> Green tea is rich in polyphenolic catechins that have thermogenic, hypolipidemic, anti-inflammatory, and antioxidant activities that could alleviate the incidence and progression of NAFLD.<sup>38</sup> According to another meta-analysis, a substantial decrease in the liver disease risk (RR=0.68, 95% CI=0.56-0.82,  $P=0.000$ ) was observed among the individuals who drink green tea.<sup>39</sup> This trend covers to an extensive spectrum of liver conditions containing hepatocellular carcinoma, liver cirrhosis, hepatitis, liver steatosis, and chronic liver disease.<sup>39</sup> Data meta-analysis applied to four research works showed substantial effects of green tea supplementation in changing ALT (-12.81 U/L; 95% CI: -18.17 to -7.45) and AST (-10.91 U/L; 95% CI: -19.66 to -2.17) blood

concentrations. In addition, this study highlighted the possible positive impacts of green tea supplementation on the NAFLD.<sup>40</sup> The meta-analysis of 15 RCTs concerning the impact of green tea or green tea catechin on liver enzymes in subjects with NAFLD showed that its consumption affected liver enzymes insignificantly (ALT [SMD=-0.17, CI -0.42 to 0.08,  $p=.19$ ], AST [SMD = -0.07, CI -0.43 to 0.29,  $P = 0.69$ ]).<sup>41</sup> Nevertheless, subgroup analyses indicated that green tea decreased the levels of liver enzymes in patients with NAFLD; however, a small yet notable increase in the liver enzyme levels was detected in healthy individuals.<sup>41</sup>

### Study limitations

Some limitations of this meta-analysis should be considered. The definition of coffee and green tea consumption were different between the involved articles. The applicable data about coffee consumption and tea drinking, including the type of tea used, components, brewing method, and time of drinking, were not evidently stated in the articles. All the articles involved in the meta-analysis are randomized clinical trials displaying only association, but not a fundamental correlation of these beverages as a hepatoprotective agent. All studies included in this analysis possessed a relatively small sample size. The findings may be also limited by the small number of included studies owing to the higher heterogeneity.



## Conclusion

Coffee and tea consumption appears to be positively affecting patients with liver diseases or those exposed to developing liver diseases. Additional research is necessary to approve the findings, and determine the effectiveness of coffee and tea for the primary prevention of liver diseases. Clinical prospective large-scale double-blind studies with higher dosages, longer duration are also required.

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## Authors' Contribution

**Data curation:** Sanam Dolati.

**Formal analysis:** Nafiseh Vahed, Morteza Ghojzadeh.

**Funding acquisition:** Hassan Soleimanpour.

**Investigation:** Sanam Dolati.

**Methodology:** Morteza Ghojzadeh, Mahsa Kangari, Nafiseh Vahed.

**Project administration:** Hassan Soleimanpour.

**Resources:** Hassan Soleimanpour.

**Software:** Morteza Ghojzadeh, Mahsa Kangari, Nafiseh Vahed.

**Supervision:** Hassan Soleimanpour.

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**Visualization:** Zahra Parsian, Hadi Hamishehkar.

**Writing—original draft:** Sanam Dolati, Hassan Soleimanpour.

**Writing—review & editing:** Hassan Soleimanpour, Sanam Dolati.

## Competing Interests

The authors declare that they have no competing interests.

## Ethical Approval

The current study was approved by the Research Ethics Committee of Tabriz University of Medical Science (No: IR.TBZMED.REC.1399.941).

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## Supplementary Files

Supplementary file 1. Search Strategy of databases

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## Study Highlights

### What is current knowledge?

- Several studies have confirmed the hepatoprotective effect of drinking coffee and green tea on the Non-alcoholic fatty liver disease (NAFLD).

### What is new here?

- Based on our meta-analysis outcome, the mean alanine aminotransferase (ALT) in the group which used coffee and green tea was measured as 12.50 points less than that of the control group. The mean aspartate aminotransferase (AST) of the group which used coffee and green tea was 9.23 points lower than that of the control group.

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