



Effects of the Mixture of *Cynara cardunculus* var *scolymus* and *Cinnamomum zeylanicum* on Hepatic Enzymes Activity and Lipid Profiles in Patients with Non-alcoholic Fatty Liver Disease

**Razieh Yosef Poor¹, Mohammad Abdollahi², Ali Akbar Malekird^{1,2*},
Esmaeil Movahednia³, Sara Mostafalou² and Zeynab Sheybani Asl¹**

¹Department of Biology, Payame Noor University, Tehran, Iran.

²Toxicology and Diseases Group, The Institute of Pharmaceutical Sciences (TIPS), and Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran.

³Faculty of Medicine, Shahrekord University of Medical Science, Shahrekord, Iran.

Authors' contributions

This work was carried out in collaboration between all authors. Authors RYP and ZSA participated in design of the study and carried out biochemical testes. Author MA conceived and supervised entire study and edited the manuscript. Author AAM participated in design of the study and carried out the study, performed statistical analysis and drafted the manuscript. Author EM participated in design of the study and carried out clinical test. All authors read and approved the final manuscript.

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ABSTRACT

Objective: Nonalcoholic fatty liver disease (NAFLD) is rapidly going to be one of the most common metabolic diseases which can negatively affect the liver function and needs to be more explored within the context of new and efficient therapies. The aim of this study was to determine the benefit of *Cynara cardunculus* var *scolymus* and *Cinnamomum zeylanicum* mixture infusion (1.5 and 0.25 g/100 mL and twice/day) on patients with NAFLD.

*Corresponding author: E-mail: Mohammad.Abdollahi@UToronto.Ca; Mohammad@TUMS.Ac.Ir;

Methods: The study was designed as a before-after clinical trial and performed on 20 patients having NAFLD. They were asked to use the mixture of extracts prepared in special bags twice a day for 30 days. Before and after using the mixture, Liver markers of NAFLD including alanin aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphates (ALP), cholesterol (chol), triglycerides (TG), high-density lipoprotein (HDL) and low-density lipoprotein (LDL) and also, fatty liver ultrasonographic grading were measured.

Results: Treatment with mixture of extracts in patients with NAFLD resulted in a significant decrease in ALT, AST, and ALP. Also there was a significant improvement in lipid profile of the patients given by decreased TG, Chol, and LDL and increased HDL in serum. Moreover, a significant decrease in grade of sonographic examination was showed. No significant linear correlation was found between age, BMI and gender one way side and biochemical parameters and liver enzymes.

Conclusion: Taken together, it is concluded that the mixture of *Cynara cardunculus var scolymus*, *Cinnamomum zeylanicum* can have beneficial effects on hepatic function and lipid profiles of patients with NAFLD.

Keywords: *Cinnamomum zeylanicum*; *Cynara cardunculus var scolymus*; elevated liver enzymes; lipid type; nonalcoholic fatty liver disease.

1. INTRODUCTION

As the sedentary lifestyle has caused a high rate of metabolic complications like obesity and type 2 diabetes, increasing prevalence of one related disorder manifested by fat deposition in the liver is becoming a global public health issue. Non-alcoholic fatty liver disease (NAFLD) has been reported to be prevalent ranging from 9 to 36.9% worldwide and this percent is rising. It can lead to the progressive disease, non-alcoholic steatohepatitis (NASH), which considered the major cause of cirrhosis. NAFLD is very similar to a state in which insulin resistance occurs and is mostly associated with type 2 diabetes and metabolic syndrome. In this way, therapeutic measures for insulin resistance like weight loss, thiazolidinediones, and metformin have been applicable due to their beneficial effects, but specific and effective medicines for NAFLD are limited and a large number of medical investigations have focused on exploring new and efficient approaches for treating this widespread disorder [1,2,3].

On the other hand, traditional medicine offers promising strategies for treatment of NAFLD given by potential history of various medicinal plants. There is a strong background on effectiveness of *Cinnamomum zeylanicum* in alleviating diabetes and metabolic syndrome via increased responsiveness to insulin [4,5,6,7,8]. *Cynara cardunculus var scolymus* also known as artichoke has been reported to reinforce hepatic function and lower blood cholesterol via affecting inhibiting the activity of the main enzyme involved in cholesterol biosynthesis, HMG-CoA reductase, in hepatocytes [9,10,11,12].

This study was designed to evaluate the protective effect of *Cynara scolymus* and *Cinnamomum zeylanicum* mixture extract on patients with NAFLD.

2. MATERIALS AND METHODS

2.1 Studies

This prospective cross-sectional study monitored 20 adults aged 21-72 years (9 men and 11 women) randomly selected patients with NAFLD who referred to the interdisciplinary ultrasound department of the clinic of Shahrekord city in the year 2013 for sonographic examination of the abdomen. They were included in this study after being recognized as the second stage of NAFLD without any history of coronary artery disease, diabetes, severe anemia, bleeding diathesis, cancer within the past "5 years", and any condition likely to lead to death within 5 years. Also, none of the patients had suffered from viral hepatitis or autoimmune-related disorders or reported alcohol consumption. The protocol of study was approved by Tehran University of Medical Science in accordance with the Declaration of Helsinki. In this regard all participants were provided with specific written information about the aims of the study before written consents were obtained. Before blood sampling, each individual was completely interviewed by a specialized physician who filled in a structured questionnaire about disease and habit diet. The included subjects were administered *Cynara cardunculus var scolymus* and *Cinnamomum zeylanicum* mixture infusion (1.5 and 0.25 g/100 mL respectively) for 30 days

at 7.5 a.m. and 2 p.m. every day. A supervisor carefully checked to make sure that the volunteers were taking infusion properly. Blood samples were collected from all subjects before using *Cynara cardunculus var scolymus* and *Cinnamomum zeylanicum* infusion and 12 hours after the last dose of 30-day treatment with infusion.

2.2 Plant Material

Cynara scolymus and *Cinnamomum zeylanicum* were supplied by Arak Medicinal Plants Company and identified as *Cynara cardunculus var scolymus* and *Cinnamomum Zeylanicum* in Agriculture department of Arak University.

2.3 Infusion Preparation and Protocol

Leaves of *Cynara cardunculus var scolymus* was dried and cleaned and then packed with cinnamon in 1.5 and 0.25 g bags. The subjects were instructed how to prepare the infusion by mixing a total of *Cynara cardunculus var scolymus* and *Cinnamomum zeylanicum* (1.5 and 0.25 g/100 mL and twice/day) infusion in 100 mL 98°C water for 30 minutes [13]. A qualified expert supervised the whole procedure.

2.4 Biochemical Analysis of Serum Parameters

All biochemical serum analyses including alanin amino transferase (ALT), aspartate amino transferase (AST), alkaline phosphates (ALP), cholesterol (Chol), triglycerides (TG), high-density lipoprotein (HDL) and low-density lipoprotein (LDL) were performed in the same laboratory.

2.5 Statistical Analysis

Results are presented as mean \pm SD. Statistical analyses were conducted using SPSS software (version 18). The paired t- test and Wilcoxon Matched-Pairs Signed-Ranks Test analysis were applied to this study and associations between parameters were determined through Pearson correlation analysis. Value of $p < 0.05$ were considered statistically significant.

3. RESULTS

"The mean \pm SD" values of subjects were for age (32.92 \pm 5.41) and BMI (27.59 \pm 2.81) and sex

percentage (Male (45%), Female (55%). As shown in Table 1, after using *Cynara cardunculus var scolymus* and *Cinnamomum zeylanicum* infusion, the activity of ALT, AST, and ALP was decreased significantly. The combination of extracts caused not only a decrease in the serum LDL, TG, and Chol, but an increase in HDL level Table 1. Moreover, analysis by Wilcoxon Matched-Pairs Signed-Ranks Test showed a significant decrease in grade of sonographic examination (1.84 \pm 0.76 before and 0.95 \pm 0.71 after, $p < 0.001$). No significant linear correlation was found between age, body mass index (BMI) and gender one way side and biochemical parameters and liver enzymes.

4. DISCUSSION

The present work studied the protective effects of mixture extract of *Cynara cardunculus var scolymus* and *Cinnamomum zeylanicum* on metabolic profile of hepatic function in related to lipid parameters in NAFLD patients. So, 30 days treatment with extract could reduce not only the level of serum transaminases (ALT and AST) and ALP, but also improved the lipid profile of patients given by decreased blood TG, Chol, and LDL and increased HDL.

In a survey conducted by Clark et al. (2003), elevated level of serum transaminase (ALT and AST) was found common in the US population were strongly in association with obesity and other features of metabolic syndrome implicated on the existence of NAFLD. For this reason, they proposed that elevated serum transaminases could be a valid indicator or predictive of NAFLD if the other chronic liver diseases like alcoholic liver disease, viral hepatitis, and hemochromatosis were excluded [14]. In this way, monitoring the level of serum transaminases along with lipid parameters were considered as diagnostic criteria of NAFLD patients before and after treatment with extracts in this study.

Lowering effect of treatment with mixture extract of *Cynara cardunculus var scolymus* and *Cinnamomum zeylanicum* on serum transaminases ALT and AST was significant and indicated that hepatocellular damages has been decreased and the function of the liver cell has been partially improved. Furthermore, significant decrease in serum ALP presented beneficial effect of the extracts on biliary duct.

Table 1. The effect of aqueous extract of *Cynara cardunculus var scolymus* and *Cinnamomum zeylanicum* on lipid profile and liver biochemical enzymes parameters

Biochemical tests	Before	After	P value
ALT (U/L)	46.42±12.99	35.26±14.04	0.001
AST(U/L)	47±11.70	37.47±11.18	0.001
ALP(IU/L)	266.84±108.07	205.05±77.97	0.000
TG (mg/dl)	286.42±61.43	204.26±59.90	0.000
Chol (mg/dl)	260.74±36.14	214.74±41.35	0.000
LDL (mg/dl)	152.21±30.56	123.82±29.36	0.000
HDL(mg/dl)	38±6.70	43.79±7.34	0.002

On the other hand, observed improvement in lipid profile of the patients indicated that hepato-protection of the extracts could be partially due to their lowering effect on the burden of liver function in lipid metabolism. In this regard, hypolipidemic effect of *Cynara cardunculus var scolymus* has become evident through both reduced cholesterol biosynthesis via inhibiting the activity of HMGCoA-reductase in hepatocytes and increased excretion of fecal bile acids and neutral sterols [9,12]. Miccadei et al. (2008) indicated that *Cynara cardunculus var scolymus* had a marked antioxidative potential that protects hepatocytes from an oxidative stress [15]. Another report showed that in vivo *Cynara cardunculus var scolymus* extract administration may be useful for the prevention of oxidative stress-induced hepatotoxicity [16]. Also *Cynara cardunculus var scolymus* has potent hepatoprotective activity [17]. Regarding our finding, the explanation is that beneficial effects of *Cynara cardunculus var scolymus* due to antioxidative potential.

5. CONCLUSION

In conclusion, the results of this study show that *Cynara cardunculus var scolymus* and *Cinnamomum zeylanicum* extract can be a good candidate for future investigations focusing on treatment of NAFLD.

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images.

ETHICAL APPROVAL

All experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki."

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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