Acta Alimentaria 51 (2022) 3, 437–447
DOI: 10.1556/066.2022.00081

AKADÉMIAI KIADÓ

Protective effects of green tea on blood and liver of rats fed with high fructose diet

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ORIGINAL RESEARCH PAPER

Received: April 18, 2022 • Accepted: June 10, 2022
Published online: July 4, 2022

ABSTRACT

This study was designed to investigate the effects of green tea on lipid profile, liver tissue damage, and oxidative stress in rats fed a diet including high fructose. Sprague-Dawley rats were randomly divided into four groups: Control (C), Fructose (F), Green Tea (GT), and F+GT. F and F+GT groups were given 20% fructose in the drinking water for eight weeks. Green tea (2 mg kg^{-1}) was administrated to GT and F+GT groups by oral gavage for eight weeks. Biochemical parameters in serum and oxidative stress markers in the liver were analysed. The liver sections were stained with haematoxylin-eosin. As of the 3rd week of the experiment, the body weight of rats in the F group showed a statistically significant increase in comparison with the F+GT group. The serum glucose and triglyceride levels of the F+GT group significantly decreased when compared with the F group. The fructose-induced degenerative changes in the liver were reduced with green tea. Green tea may serve a protective role against hyperlipidaemia and liver injury in rats fed a high fructose diet.

KEYWORDS

Camellia sinensis, fructose, green tea, liver, oxidative stress

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1. INTRODUCTION

Due to its high sweetness and low cost, the commercial use of fructose has increased considerably in recent days. The use of high-fructose corn syrup as a sweetener has become important in food production. Fructose, also known as fruit sugar, is a monosaccharide, which is found in vegetables and fruits or as a molecular compound of sucrose (Tappy et al., 2010). The high-fructose diet affects glucose and lipid metabolisms in rats resulting in various metabolic disorders including insulin resistance, impaired glucose tolerance, hypertriglyceridaemia, and hepatic fat accumulation (Tappy et al., 2010; Abdelrahman et al., 2018; Shi et al., 2021). Researchers have reported that high fructose consumption impairs the balance between oxidants and antioxidants. For this reason, the fructose-induced insulin resistance and the effects of several antioxidant compounds drew the attention of many researchers (Bagul et al., 2012; Feillet-Coudray et al., 2019; Villeda-González et al., 2020).

Green tea (GT) is produced from the leaves of a plant called *Camellia sinensis*. GT and its major components, catechins, have been indicated to be beneficial for health due to antioxidative, anti-carcinogenic, anti-inflammatory, apoptotic, anti-obesity, hypoglycaemic, hypocholesterolaemic, antimicrobial, and anti-aging activities (Perrier-Robert, 2004; Yang et al., 2018). Also, the lipid-lowering effect of GT has been well documented in animal models of hyperlipidaemia (Yang et al., 2018). It was observed in a study conducted on women that GT reduced the serum cholesterol levels and provided protection from the low-density lipoprotein (LDL) oxidation (Wu et al., 2012).

Additionally, GT consumption has been reported to elevate the serum superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), and catalase (CAT) enzyme activities (Bhardwaj and Khanna, 2012). It has been also demonstrated that green tea is effective in cellular protection against reactive oxygen species (ROS) (Skrzydlewska et al., 2002; Prasanth et al., 2019). Therefore, in the current study, we investigated the effects of green tea on oxidative stress and hyperlipidaemia in the liver of the rats maintained with a high-fructose diet. Furthermore, fructose-induced liver damage was investigated in rats.

2. MATERIALS AND METHODS

The present study was carried out with the Approval of the Bezmialem Vakif University Animal Research Ethics Committee. All animals were placed in polycarbonate cages in a way to ensure that there was only one rat in each cage. They were fed a standard rat pellet diet (Table 1), provided with tap water *ad libitum*, and maintained under standard laboratory conditions of a natural photoperiod of a 12-h light-dark cycle at room temperature ±21 °C.

2.1. Grouping of animals

The adult male Sprague Dawley rats (8–10 weeks) were randomly divided into four groups.

Control (C) group (n = 8): The rats in this group were given drinking tap water during the experiment.

Fructose receiving (F) group (n = 8): The rats were given 20% fructose (Merck, 104005) freshly diluted in tap water each day during the experiment.

Table 1. The content of the feed given to all groups

Features	Rat feed
Moisture, % not more than	12.0
Crude fibre, % not more than	7.0
Crude ash, % not more than	8.0
Ash insoluble in HCl, % not more than	2.0
Metabolical energy, kcal kg^{-1}, not less than	2,600
Crude protein, % not less than	23.0
Crude fat, % not less than	6.0

Green tea (GT) group (n = 8): GT extract (2 g kg^{-1}) was obtained by brewing the *C. sinensis* leaves that were collected from Rize/Turkey in 80 °C tap water for 15 min and administered to the rats through gavage every day during the experiment.

F+GT group (n = 8): The animals received 20% fructose and GT extract for 56 consecutive days through gavage.

The daily feed and water consumption of each rat was measured between 9.30 and 10:00 on daily basis. The body weight of the rats in all groups was measured weekly during the experiment.

At the end of the 8-week experimental period, the overnight-fasted rats were sacrificed by collecting blood from their hearts under anesthaesia achieved with ketamine hydrochloride (50 mg kg^{-1}) and xylazine hydrochloride (10 mg kg^{-1}). Liver tissue samples were collected from the animals. Liver weight was measured for the rats in all groups. Then, the liver tissues were embedded in paraffin. The remaining liver tissue samples were stored at –86 °C.

2.2. Biochemical parameters

The levels of serum glucose, total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), very low-density lipoprotein (VLDL), and the liver enzymes alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were measured in all serum samples using the Roche Cobas c501.

The tissue samples were used to prepare 10% homogenates in cold NaCl (0.9%) solution. The homogenates were centrifuged at 4,000 *g* for 10 min at 4 °C. The levels of GSH were detected colorimetrically based on the reaction with 5,5-dithiobis 2-nitrobenzoic acid (DTNB) using the methodology of Beutler et al. (1963). MDA was analysed according to the methods of Ledwozyw et al. (1986). CAT and SOD enzyme activities were quantified using the methods of Aebi (1984) and Sun et al. (1988), respectively. Lowry's method was used for protein determination (Lowry et al., 1951).

2.3. Liver histology

Liver tissue sections were stained with haematoxylin and eosin. The slides were examined and photographed under an Olympus CX31 light microscope equipped with a digital camera using the Olympus DP2-BSW microscope imaging software program. Randomly selected 10 areas were evaluated in each section.

2.4. Statistical analyses

The descriptive statistics of the data were expressed using the mean and standard deviation. Quantitative data were compared between the groups using the Kruskal–Wallis Test. $P < 0.05$ was considered statistically significant. The Mann–Whitney U test was used to examine the differences between the two groups. The statistical analysis was conducted using the SPSS 22.0 software program.

3. RESULTS AND DISCUSSION

The high-fructose intake causes elevated accumulation of hepatic TG, and thus, impairs the lipid and glucose metabolisms. Both human and animal studies have reported that a diet component like fructose leads to fat infiltration and lipid peroxidation in the liver (Tappy et al., 2010; Lim et al., 2010). Figure 1 demonstrates the analysis of the total weekly food intake of the rats. The feed consumption significantly decreased in the F group as compared to the C group at all weeks ($P < 0.05$). However, there was no statistically significant difference between the F and F+GT groups regarding weekly feed consumption ($P > 0.05$). As shown in Fig. 1, weekly liquid consumption of the F group significantly increased as of the 2nd week in comparison with the C group ($P < 0.05$). Again in the same week, the weekly water consumption of the F+GT group significantly decreased as compared to the F group ($P < 0.05$).

The data regarding body weight measurements are indicated in Fig. 1. It was specified that the body weight of the rats significantly decreased in the GT group between the 3rd and 8th weeks when compared to the C group ($P < 0.05$). On the other hand, there was an increase in the F group, but it was not statistically significant. The measurements performed between the 2nd and 8th weeks showed that the body weight of the animals in the F+GT group significantly fell when compared with the F group ($P < 0.05$). We have concluded from this study conducted on rats fed a high-carbohydrate diet for eight weeks that food consumption decreased but water consumption increased in the rats consuming high volume fructose diluted in drinking water. Moreover, high fructose was found to cause an elevation in body weight along with hyperglycaemia.

Additionally, studies have indicated that a high-fructose diet induces an elevation in TC, TG, and blood glucose levels, and green tea is effective in decreasing blood TG in rats with hyperglycaemia resulting from a diet rich in fructose (Shrestha et al., 2009; Ramires et al., 2011). Shrestha et al. (2009) reported that dietary fructose significantly increased plasma glucose in rats fed a diet containing 60% fructose as compared to the control group, but green tea lowered the increased glucose levels in rats. On the contrary, TC concentration was not significantly affected in the green tea group when compared with the fructose group.

Our findings are consistent with the results of previous studies. The data regarding liver weight and biochemical parameters are given in Table 2. During the experiment, the liver weight of the rats receiving fructose was significantly elevated as compared to the rats in the C group ($P < 0.05$). It was also observed that green tea, when applied simultaneously with fructose, has the potential to normalise the elevated liver weight ($P < 0.05$). It was observed when the F and F+GT groups were compared that giving green tea to the rats along with fructose led to a significant fall in the serum glucose levels ($P < 0.05$). On the other hand, no statistically significant difference was observed between the groups regarding the serum TC, HDL, and LDL

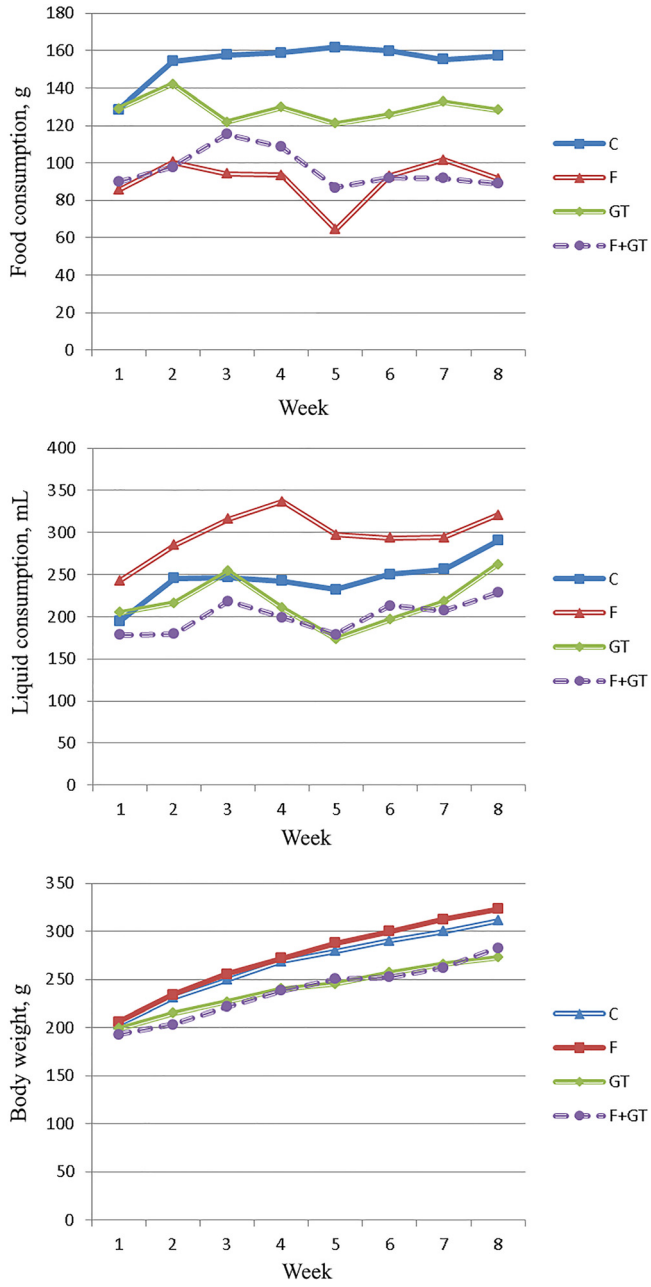

Fig. 1. Food and liquid consumption and body weight of rats fed a high-fructose diet, treated with green tea, on a weekly basis

Table 2. The liver tissue weight and biochemical parameters of the rats

	C group (n = 8)	F group (n = 8)	GT group (n = 8)	F+GT group (n = 8)	P
Glucose (mg dL^{-1})	177.5 ± 34.3	163.0 ± 17.0	$116.1^{a,b}$ ± 25.0	$129.4^{a,b}$ ± 24.7	*0.001**
TC (mg dL^{-1})	72.0 ± 8.7	79.6 ± 6.3	77.1 ± 5.1	80.0 ± 8.8	0.184
HDL (mg dL^{-1})	60.1 ± 8.3	63.4 ± 7.3	67.3 ± 5.7	67.6 ± 4.6	0.140
LDL (mg dL^{-1})	18.1 ± 4.0	17.4 ± 2.2	19.4 ± 3.7	17.0 ± 4.2	0.548
VLDL (mg dL^{-1})	7.5 ± 1.4	11.0^{a} ± 2.1	6.4^{b} ± 0.5	$9.5^{a,c}$ ± 1.9	*0.000**
TG (mg dL^{-1})	37.0 ± 7.1	55.0^{a} ± 10.5	32.0^{b} ± 3.1	$47.1^{a,c}$ ± 9.4	*0.000**
AST (U L^{-1})	92.1 ± 17.8	76.0^{a} ± 13.0	$140.9^{a,b}$ ± 32.8	$92.6^{b,c}$ ± 17.3	*0.001**
ALT (U L^{-1})	46.4 ± 4.5	35.0^{a} ± 6.6	45.1^{b} ± 6.5	$35.4^{a,c}$ ± 7.0	*0.001**
Liver (g)	7.7 ± 1.4	9.0^{a} ± 0.8	6.4^{b} ± 0.7	7.2^{b} ± 0.7	*0.001**

C: Control group; F: Fructose group; GT: Green tea group; F+GT: Fructose + green tea group.
TC: Total cholesterol; HDL: high density lipoprotein; LDL: low density lipoprotein; VLDL: very low density lipoprotein; TG: triglyceride; AST: aspartate aminotransferase; ALT: alanine aminotransferase.
[a]: $P < 0.05$ versus Control group, [b] $P < 0.01$ versus Fructose group, [c]: $P < 0.001$ versus Green tea group.

levels. The serum VLDL and TG levels of the F group showed a significant elevation as compared to the control rats ($P < 0.05$). Additionally, it was determined that the VLDL and TG parameters showed a non-significant decrease in the F+GT group. The ALT and AST levels lowered in group F as compared to the controls. The AST levels of the rats in the F+GT group approximated the values measured in controls; nevertheless, no change was detected in the ALT levels (Table 2). This study demonstrated that fructose intake significantly elevated the serum TG level but did not influence the TC, HDL, and LDL levels.

It was identified that green tea applied along with a fructose diet lowered the elevated TG level to some extent. The results of another study carried out on rats, which was maintained on a diet containing 60% fructose for nine weeks, were consistent with our results in that the serum glucose and TG levels of the fructose-fed rats increased as compared to the control group, but no alteration was observed in the TC, LDL, and HDL cholesterol levels. On the other hand, the administration of 0.5 and 1% green tea extract along with fructose reduces the TG level (Masterjohn et al., 2013). The studies reported that the serum AST and ALT levels of the animals fed a high-fructose diet showed an increase compared with the controls (Masterjohn et al., 2013; Giriş et al., 2014). Unlike other studies, this study indicated that fructose made a decrease in the AST level while F+GT ensured the decreased AST value reach the AST level of healthy rats. In our study, fructose decreased serum ALT levels and GT did not change it. It indicated that the use of green tea reduced the plasma AST and ALT levels the indicators of hepatic damage in experimental animals (Jadeja et al., 2014). ALT is one of the major liver enzymes and is generally felt to be more active and a more specific indicator of liver damage as compared to AST. In this study, we used green tea brewed for 15 min prior to use and obtained similar results to the studies using green tea extract. Therefore, we believe that extending the brewing time may enhance the protective effect of green tea.

We found that the weight of liver tissue in the F group was statistically higher than in the healthy rats. Thus, we suggested that fructose intake may induce the growth of liver tissue, or increased lipidosis volume may cause such an increase in liver tissue weight. On the other hand,

the liver weight of the rats in the F+GT group was observed to be similar to the Control group which may be interpreted as that simultaneous consumption of fructose and green tea may prevent the hepatic damage caused by fructose. In a study presenting similar results to this study, fructose was found to considerably increase the liver weight in the rats on a 60% diet as compared to the control group (Shrestha et al., 2009). Another related study indicated that the liver tissue weight was 40% higher in the rats receiving a 65% high fructose diet than in the controls (Jung et al., 2013). Additionally, another study reported that the liver mass of the fructose-fed rats increases independent of any changes in hepatic lipid, triglyceride, or glycogen (Masterjohn et al., 2013).

Oxidative stress can be prevented through many enzymatic or non-enzymatic antioxidant defence systems. Oxidative stress induced by fructose consumption in rats raises the production of free radicals in many tissues and impairs the balance in antioxidant defence (Sivakumar and Anuradha, 2011). Oxygen radicals are known to induce membrane peroxidation and MDA formation. MDA is an indicator of lipid damage in cells and tissues and the elevation of MDA is an indirect marker of ROS production (Salgueiro et al., 2016). A study investigated potential alterations in the redox setting of the liver induced by long-term fructose consumption in rats, which were maintained for nine weeks on a fructose-enriched diet containing 10% fructose solution instead of drinking water. This study indicated that a fructose-enriched diet led to an increased expression of SOD but did not affect antioxidant enzyme activity, lipid peroxidation, thiol content, and the level of protein oxidation (Nestorov et al., 2014). According to Salgueiro et al. (2016), elevated oxidative stress leads to liver damage. In the present study, the hepatic MDA and GSH levels were increased by fructose but no significant change was observed in enzyme activities.

Liver GSH and MDA levels and hepatic SOD and CAT activities were measured as oxidative stress parameters (Table 3). The GSH levels of the F+GT rats barely increased as compared to the fructose-fed rats. Nonetheless, fructose administration was identified to significantly elevate the MDA level when compared with the healthy controls ($P < 0.05$). However, no statistically significant difference was observed between the F+GT and F groups. Similarly, there was no statistically significant difference between the groups regarding the SOD and CAT activities. We believe that the duration of fructose administration, rather than the dose, is determinative of the hepatic damage. It was determined that the GSH level was barely elevated in the fructose group by GT. Dietary fructose has been reported to produce both pro-oxidative and anti-oxidative effects depending on the experimental conditions, dosage, duration of treatment, and

Table 3. Liver GSH, MDA levels and CAT, SOD activities in all groups

	C group ($n = 8$)	F group ($n = 8$)	GT group ($n = 8$)	F+GT group ($n = 8$)	P
GSH (nmol mg^{-1})	5.26 ± 1.22	6.94[a] ± 1.10	6.16[a] ± 1.05	7.18[a] ± 1.29	0.051
MDA (nmol mg^{-1})	0.13 ± 0.05	0.16[a] ± 0.07	0.20 ± 0.05	0.24[a] ± 0.16	0.068
SOD (U mg^{-1})	1.05 ± 0.09	1.09 ± 0.08	1.14 ± 0.07	1.19 ± 0.11	0.058
CAT (U mg^{-1})	138 ± 52	164 ± 30	177 ± 29	147[a] ± 32	0.206

C: Control group; F: Fructose group; GT: Green tea group; F+GT: Fructose + green tea group.
GSH: Glutathione; MDA: malondialdehyde; SOD: superoxide dismutase; CAT: catalase.
[a]: $P < 0.05$ *versus* Control group.

pathophysiological milieu (Nestorov et al., 2014). The specified dose of GT administered in this study did not have a role in the prevention of fructose-induced oxidative damage, but increasing the dose may provide better protection against oxidative damage.

Li et al. (2016) reported that 30% fructose added to the drinking water of the rats produced hepatic fat accumulation and liver degeneration. Yao et al. (2015) argued that epigallocatechin-3-gallate had a protective activity against acetaminophen-induced liver injury in rats. Black tea extract has been identified to have a preventive effect on cadmium-induced lipid changes and liver cell damage (Mantur et al., 2014). It has been observed in several experiments that the effect of fructose, which induces liver damage, was reduced with the use of brewed green tea. Livers of the rats in all groups were evaluated considering the pycnotic nuclei and vacuolisation in hepatocytes, ruptured endothelium of veins, sinusoidal dilatation, and necrosis criteria. The structure of the liver was normal in the rats selected for the C group. Sinusoidal dilatation and pycnotic nuclei and vacuolisation in hepatocytes were observed in the livers of the rats, which were on a fructose diet. Even though ruptured endothelium of veins was occasionally observed, there was no case of necrosis. It was identified that green tea administration lowered the fructose-induced damage of liver tissue in the rats taking fructose (Fig. 2). It can be therefore concluded that green tea has a protective influence on liver damage.

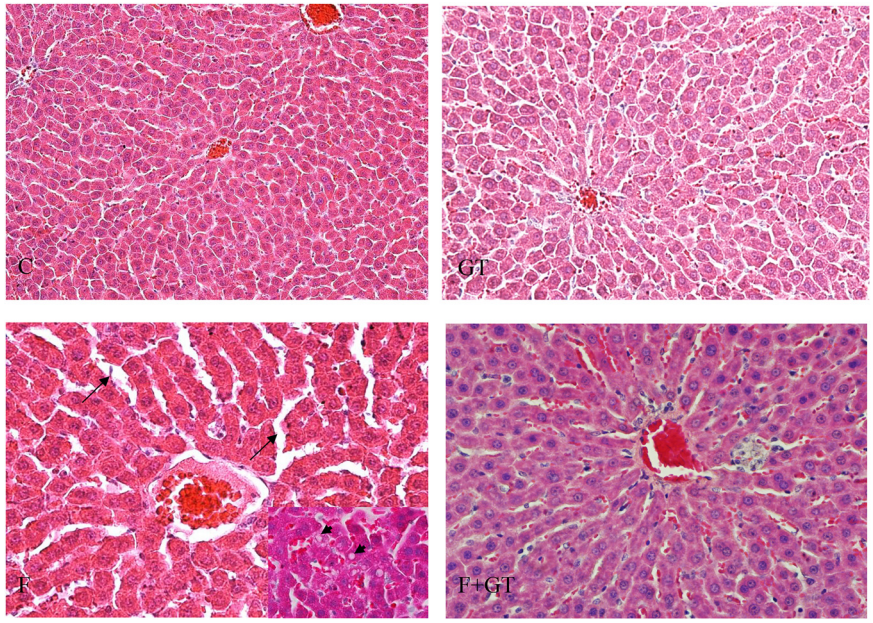

Fig. 2. Hematoxylin-eosin staining of the liver tissue of animals. C – Control and GT – Green tea groups showed the normal histological appearance of the liver, F – Fructose group showed vacuolar degeneration in hepatocytes (arrowheads) and sinusoidal dilation (arrows). Also, this group showed disturbances in the radial arrangement of hepatocytes, F+GT – Fructose + Green tea group showed almost normal tissue morphology. Magnification × 400

4. CONCLUSIONS

Our results indicated that fructose consumption can cause lipid profile disorders and liver damage. Green tea consumed with fructose may be effective in regulating TG and VLDL levels and improving liver damage. On the other hand, a low dose of green tea, which was brewed for 15 min, failed to manage the fructose-induced oxidative stress. The study data may suggest that there is a protective potential of green tea on the liver in rats exposed to high fructose.

ACKNOWLEDGEMENTS

The authors thank Demiroglu Bilim University for the support.

REFERENCES

Abdelrahman, A.M., Al Suleimani, Y.M., Ashique, M., Manoj, P., and Ali, B.H. (2018). Effect of infliximab and tocilizumab on fructose-induced hyperinsulinemia and hypertension in rats. *Biomedicine & Pharmacotherapy*, 105: 182–186.

Aebi, H. (1984). Catalase in vitro. *Methods in Enzymology*, 105: 121–126.

Bagul, P.K., Middela, H., Matapally, S., Padiya, R., Bastia, T., Madhusudana, K., Reddy, B.R., Chakravarty, S., and Banerjee, S.K. (2012). Attenuation of insulin resistance, metabolic syndrome and hepatic oxidative stress by resveratrol in fructose-fed rats. *Pharmacological Research*, 66(3): 260–268.

Beutler, E., Duron, O., and Kelly, B.M. (1963). Improved method for the determination of blood glutathione. *Journal of Laboratory and Clinical Medicine*, 61: 882–888.

Bhardwaj, P. and Khanna, D. (2012). Green tea catechins: Defensive role in cardiovascular disorders. *Chinese Journal of Natural Medicine*, 11(4): 345–353.

Feillet-Coudray, C., Fouret, G., Vigor, C., Bonafos, B., Jover, B., Blachnio-Zabielska, A., Rieusset, J., Casas, F., Gaillet, S., Landrier, J.F., Durand, T., and Coudray C. (2019). Long-term measures of dyslipidemia, inflammation, and oxidative stress in rats fed a high-fat/high-fructose diet. *Lipids*, 54(1): 81–97.

Giriş, M., Abbasoğlu, S.D., Kumral, A., Olgaç, V., Koçak-Toker, N., and Uysal, M. (2014). Effect of carnosine alone or combined with α-tocopherol on hepatic steatosis and oxidative stress in fructose-induced insulin-resistant rats. *Journal of Physiolology and Biochemistry*, 70(2): 385–395.

Jadeja, R., Devkar, R.V., and Nammi, S. (2014). Herbal medicines for the treatment of nonalcoholic fatty acid steatohepatitis: current scenario and future prospects. *Evidence-Based Complementary and Alternative Medicine*, 2014: 648308.

Jung, M.H., Seong, P.N., and Kim, K.H. (2013). Effect of green tea extract microencapsulation on hypertriglyceridemia and cardiovascular tissues in high fructose-fed diet. *Nutrition Research Practice*, 7(5): 366–372.

Ledwozyw, A., Michalak, J., Stepień, A., and Kadziołka, A. (1986). The relationship between plasma triglycerides, cholesterol, total lipids and lipid peroxidation products during human atherosclerosis. *Clinica Chimica Acta*, 155(3): 275–283.

Li, W., Huang, D., Gao, A., and Yang, X. (2016). Stachyose increases absorption and hepatoprotective effect of tea polyphenols in high fructose-fed mice. *Molecular Nutrition & Food Research*, 60(3): 502–510.

Lim, J.S., Mietus-Synder, M., Valente, A., Schwartz, J.M., and Lustig, R.H. (2010). The role of fructose in the pathogenesis of NAFLD and the metabolic syndrome. *Nature Reviews Gastroenterology & Hepatology*, 7: 251–264.

Lowry, O.H., Rosebrough, N.J., Farr, A.L., and Randall, R.J. (1951). Protein measurement with the Folin phenol reagent. *Journal of Biological Chemistry*, 193(1): 265–275.

Mantur, V.S., Somannavar, M.S., Yendigeri, S., Das, K.K., and Goudar, S.S. (2014). Ameliorating effect of black tea extract on cadmium chloride-induced alteration of serum lipid profile and liver histopathology in rats. *Indian Journal of Physiology and Pharmacology*, 58(2): 128–132.

Masterjohn, C., Park, Y., Lee, J., Noh, S.K., Koo, S.I., and Bruno, R.S. (2013). Dietary fructose feeding increases adipose methylglyoxal accumulation in rats in association with low expression and activity of glyoxalase-2. *Nutrients*, 5(8): 3311–3328.

Nestorov, J., Glban, A.M., Mijuskovic, A., Nikolić-Kokić, A., Elaković, I., Veličković, N., and Matić, G (2014). Long-term fructose-enriched diet introduced immediately after weaning does not induce oxidative stress in the rat liver. *Nutrition Research*, 34(7): 646–652.

Perrier-Robert, A. (2004). *Book of tea.* Octopus Publishing Co, London, p. 128.

Prasanth, M.I., Sivamaruthi, B.S., Chaiyasut, C., and Tencomnao, T. (2019). A review of the role of green tea (*Camellia sinensis*) in antiphotoaging, stress resistance, neuroprotection, and autophagy. *Nutrients*, 11(2): 474.

Ramirez, F.R., Escalona-Cardoso, G.N., Garduno-Siciliano, L., Galaviz-Hernández, C., and Paniagua-Castro, N. (2011). Antiobesity and hypoglycemic effects of aqueous extract of *Ibervillea sonorae* in mice fed a high-fat diet with fructose. *Journal of Biomedicine and Biotechnology*, 2011: 968984.

Salgueiro, A.C., Folmer, V., Silva, M.P., Mendez, A.S.L., Zemolin, A.P.P., Posser, T., Franco, J.L., Puntel, R.L., and Puntel, G.O. (2016). Effects of *Bauhinia forficata* tea on oxidative stress and liver damage in diabetic mice. *Oxidative Medicine and Cellular Longevity*, 2016: 8902954.

Shi, Y.N., Liu, Y.J., Xie, Z., and Zhang, W.J. (2021). Fructose and metabolic diseases: too much to be good. *Chinese Medical Journal (Engl)*, 134(11): 1276–1285.

Shrestha, S., Ehlers, S.J., Lee, J.Y., Fernandez, M.L., and Koo, S.I. (2009). Dietary green tea extract lowers plasma and hepatic triglycerides and decreases the expression of sterol regulatory element-binding protein-1c mRNA and its responsive genes in fructose-fed, overiectomized rats. *Journal of Nutrition*, 139(4): 640–645.

Sivakumar, A.S. and Anuradha, C.V. (2011). Effect of galangin supplementation on oxidative changes and inflammatory changes in fructose-fed rat liver. *Chemico-Biological Interactions*, 193(2): 141–148.

Skrzydlewska, E., Ostrowska, J., Farbiszewski, R., and Michalak, K. (2002). Protective effect of green tea against lipid peroxidation in the rat liver, blood serum and the brain. *Phytomedicine*, 9(3): 232–238.

Sun, Y., Oberley, L.W., and Li, Y. (1988). A simple method for clinical assay of superoxide dismutase. *Clinical Chemistry*, 34(3): 497–500.

Tappy, L., Le, K.A., Tran, C., and Paquot, N. (2010). Fructose and metabolic diseases: new findings, new questions. *Nutrition*, 26(11–12): 1044–1049.

Villeda-González, J.D., Gómez-Olivares, J.L., Baiza-Gutman, L.A., Manuel-Apolinar, L., Damasio-Santana, L., Millán-Pacheco, C., Ángeles-Mejía, S., Cortés-Ginez, M.C., Cruz-López, M., Vidal-Moreno, C.J., and Díaz-Flores M. (2020). Nicotinamide reduces inflammation and oxidative stress via the cholinergic system in fructose-induced metabolic syndrome in rats. *Life Science*, 250: 117585.

Wu, A.H., Spicer, D., Stanczyk, F.Z., Tseng, C.C., Yang, C.S., and Pike, M.C. (2012). Effect of 2-month controlled green tea intervention on lipoprotein cholesterol, glucose, and hormone levels in healthy postmenopausal women. *Cancer Prevention Research (Phila)*, 5(3): 393–402.

Yang, C.S., Wang, H., and Sheridan, Z.P. (2018). Studies on prevention of obesity, metabolic syndrome, diabetes, cardiovascular diseases and cancer by tea. *Journal of Food and Drug Analysis*, 26(1): 1–13.

Yao, H.T., Yang, Y.C., Chang, C.H., Yang, H.T., and Yin, M.C. (2015). Protective effects of (–)-epigallocatechin-3-gallate against acetaminophen-induced liver injury in rats. *Biomedicine (Taipei)*, 5(3): 15.