European Journal of Biological Sciences 2 (3): 46-54, 2010
ISSN 2079-2085

Effect of Regular Drinking of Boiled, Filtered or Turkish Coffee and Its Impact on some Biochemical Parameters Relevant to Atherogenicity and the Functions of the Kidney and the Liver in Rat Model

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Abstract: The effects of three different preparations of coffee beverages on some biochemical parameters of atherogenicity, kidney and liver functions as well as histopathological structure of aorta, kidney and liver were studied. Four groups of rats were used; group (1) kept as a control group, groups (2), (3) and (4) orally received 1.5 ml/100 g body weight of boiled, filtered and Turkish coffee beverages, respectively. The obtained results revealed that administration of boiled and Turkish coffee induced significant increase in atherogenic index represented by the increase in total lipids, triglycerides, total cholesterol, LDL-C and VLDL-C, as well as the significant increase in serum concentrations of uric acid, urea nitrogen, creatinine, AST, ALT, total and direct bilirubin, as compared to the control rats. Hisopathological study showed that boiled coffee induced perivascular leucocytic infiltration in aorta; hypertrophy and vacuolations of endothelial lining glomerular tufts and epithelial lining in renal tubules; and congestion of central vein and hepatic sinusoids. Turkish coffee produced perivascular hemorrhage in aorta; granularity of the cytoplasm in renal tubular epithelium; and congestion of central vein and hepatic sinusoids in liver. It was concluded that regular drinking of boiled and Turkish coffees may be amongst the risk factors for cardiovascular diseases as well as liver and kidney dysfunctions.

Key words: Coffee Beverage · Rats · Liver Functions · Kidney Function · Lipid Profile

INTRODUCTION

Coffee is one of the most commonly consumed beverages worldwide. There are two main types of coffee beans: *Coffea Arabica* (Arabica) and *Coffea Canephora* (Robusta). These two types of coffee beans are used for brewing coffee. *Coffea arabica* is the second-largest worldwide commodity [1]. It contains many of the most important constituents known to be present within functional foods including flavonoids, caffeic acid and ferrulic acid [2]. Additional the biological active components including nicotinic acid, trigonelline, quinolinic acid, tannic acid, pyrogallic acid and caffeine [3], coffee contains carbohydrates, lipids, nitrogenous and phenolic compounds, vitamins, minerals, alkaloids, cafestol, kahweol and chlorogenic acids [4].

Regular coffee consumption has been associated with some adverse effects on various biological markers of coronary heart disease (CHD) risk, including plasma homocysteine [5], insulin resistance [6] and blood pressure [7]. Other study showed conflicting results that may be attributed to distinct habits associated to the coffee consumption in each population, making difficult to differentiate coffee effects from other dietetic and environmental factors effects [8]. Epidemiologic studies indicated that drinking large amounts of coffee significantly reduces the incidence of type 2 diabetes [9]. The acute effects of coffee consumption can be firstly different with long-term habitual consumption. The second physiological effects may be depending on the type of coffee consumed. The third effect may have beneficial effects on other biological pathways implicated

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in the development of CHD that could compensate for any adverse effects. The fourth, risk markers may not causally affect the development of CHD, or their effects may be too modest for any increase caused by coffee consumption to translate into a substantial increase in disease risk [10]. Cafestol and kahweol are fat-soluble diterpenes in coffee beans and presented in commercially important blends of arabica and robusta coffee. The two diterpenes, cafestol is responsible for more than 80% of the effect on serum lipids [11]. Therefore, the purpose of the present study was to evaluate the effect of regular drinking of boiled, filtered and Turkish coffee beverages on some biomarker parameters of atherogenicity, kidney and liver functions as well as histopathological examination of aorta, kidney and liver.

MATERIALS AND METHODS

Preparation of Coffee Beverages: Roasted coffee beans *(Coffee arabica)* were purchased from the local market, Cairo, Egypt. The Three different preparations of coffee beverages such as boiled, filtered and Turkish were prepared by using 10 g powdered of coffee beans per 10 ml of distilled water. Boiled and filtered coffee beverages were prepared at 100°C for 5 minutes, filter paper was used for filtration process to obtain filtered coffee beverage. Turkish coffee beverage was prepared at 70°C.

Preparation of Basal Diet: Basal diet constituents were purchased from El-Gomhorya Company, Cairo, Egypt. The basal diet (AIN-93M) was prepared according to Reeves *et al.* [12]. Diet was formulated to meet recommended nutrients levels for rats.

Experimental Design: Forty adult male albino rats, Sprague Dawley strain, weighing 190±5g, were obtained from the Laboratory Animal Colony, Helwan, Egypt. Rats were fed on the basal diet and water was provided *ad libitum.* Rats were maintained under standard conditions of humidity (50-60%), temperature (20-25°C) and light (12-h light: 12-h dark cycle) for one week before starting the experimental for acclimatization. After acclimatization period (one week), rats were divided into four groups of equal number and weight (ten rats each) as follows:

Group (1): Kept as a control group, fed on the basal diet and orally given saline solution (1.5 ml/ 100g of body weight) by stomach tube for 6 weeks.

Group (2): Fed on the basal diet and orally given boiled coffee beverage (1.5 ml/ 100g of body weight) by stomach tube for 6 weeks.

Group (3): Fed on the basal diet and orally given filtered coffee beverage (1.5 ml/ 100g of body weight) by stomach tube.

Group (4): Fed on the basal diet and orally given Turkish coffee beverage (1.5 ml/ 100g of body weight) by stomach tube.

Determination of Body Weight Gain: Body weight gain (BWG) was evaluated at the end of experimental period using the following formulas:

Body weight gain = final body weight-initial body weight

Biochemical Analysis of Serum: At the end of the experimental period (six weeks), animals were fasted 12 hours (except from water) then sacrificed. Blood samples were collected by cardiac puncture into dry clean centrifuge tubes. For serum separation, blood samples were left at room temperature to clot and then centrifuged for 10 minutes at 3000 rpm. For biochemical analysis of serum, kits were purchased from the Gamma Trade Company for Pharmaceutical and Chemicals, Dokki, Egypt.

Determination of Serum Glucose: Fresh serum was used to determine glucose concentration based on colorimetric enzymatic methods using Spectrophotometer DU7400 adjusted at 500 nm [13].

Determination of Lipid Profile and Lipoprotein Cholesterols: Total lipids (TL), triglyceride (TG) and high-density lipoprotein cholesterol (HDL-C) were estimated by enzymatic colorimetric method [14]. Serum total cholesterol (TC) was determined by the spectrophotometric enzymatic colorimetric method [15]. LDL-cholesterol was derived by Friedwald and Fredrickson formula [16]. Very low-density lipoprotein cholesterols (VLDL-C) were determined using the following equations:

VLDL-c (mg/ dL) = TG/5

Determination of Atherogenic Index: Atherogenic index (AI) was calculated using the following equations as described by Dobiasova and Frohlich [17]:

Log (TG/HDL-C).

Determination of Kidney Functions: Serum concentrations of urea nitrogen and uric acid were determined by enzymatic colorimetric method and creatinine was determined using colorimetric kinetic [18].

Determination of Liver Functions: Serum levels of asprtate aminotransaminase (AST), alanine aminotransferase (ALT) were analyzed enzymaticaly. Serum concentrations of total and direct bilirubin were determined using colorimetric method [18].

Histopathological Examination: Aorta, kidneys and liver of the scarified rats were taken, washed with saline solution and immersed in 10% formalin solution. The fixed specimens were trimmed, washed and dehydrated in ascending grades of alcohol. Specimens then cleared in xylol, embedded in paraffin, sectioned at 4-6 microns thickness and stained with Heamtoxylin and Eosin stain for examination.

Statistical Analysis: Results were expressed as mean±SE. All data from the experiment were examined statistically by one-way analysis of variance with computerized SPSS package program (SPSS 6.00 software for Windows) by ANOVA test. A *P* value <0.05 was considered statistically significant.

RESULTS

Body Weight Gain and Serum Glucose Level: Data in table 1 illustrated that control rats given orally saline solution had significant increase in body weight gain (BWG) (34.10±0.80 g) at p<0.05 as compared to those given orally boiled, filtered or Turkish coffee beverages (26.10±0.70, 25.50±0.70 and 25.60±0.70g, respectively). Oral administration of boiled, filtered and Turkish coffee beverages caused significant decrease in serum levels of glucose (166.60±0.50, 170.40±0.40 and 166.80±0.40 mg/dl, respectively) as compared to the control group (184.60±0.50). There were no significant changes in BWG values and serum glucose levels between groups given orally boiled, filtered and Turkish coffee beverages.

Lipid Profile and Lipoprotein Cholesterols: Results in table 2 revealed that rats given orally boiled and Turkish coffee beverages had significant increase in serum levels of TL, TG and TC at p<0.05 as compared to the control rats. Oral administration of filtered coffee beverage caused no significant decrease in serum levels of TL, TG and TC (701.44±5.55, 86.09±1.72 and 173.26±2.13mg/dl, respectively) at p<0.05 as compared to the control rats (704.14±5.26, 90.10±0.73 and 177.42±2.80mg/dl, respectively). Oral administration of boiled coffee induced significant increase in serum levels of TL, TG and TL as compared to those given orally filtered and Turkish coffee beverages.

Tabulated results in table 3 revealed that oral administration of boiled and Turkish coffee beverages caused significant increase in serum levels of LDL-C and VLDL-C and significant decrease in serum level of HDL-C at p<0.05 as well as significant increase in atherogenic index as compared to the control group. Filtered coffee beverage extract induced no significant decrease in the above-mentioned parameters as compared to the control rats. Rats given orally boiled coffee beverage had significant increase in serum levels of LDL-C and VLDL-C as well as atherogenic index value as compared to those given orally filtered and Turkish coffee beverages.

Kidney Functions: Data in table 4 indicated that oral administration of boiled, filtered and Turkish coffee beverages caused significant increase in serum levels of uric acid and urea nitrogen at p<0.05 as compared to

Table 1: Body weight gain and serum glucose level in rats.

		Parameters as Mean± SE	
Groups		Body weight gain (g)	Serum glucose level (mg/dl)
Control group		34.10±0.80 a	184.60±0.50 a
Oral administration of coffee beverage prepared by:	Boiled coffee	26.10±0.70 b	166.60±0.50 b
Filtered coffee		25.50±0.70 b	170.40±0.40 b
	Turkish coffee	25.60±0.70 b	166.80±0.40 b

Means in each column with different superscript letters differ significantly at P <0.05. A uses harmonic mean sample size = 10 rats.

Table 2: Serum levels of total lipid, triglycerides and total cholesterol in rats

		Parameters as Mean± SE		
Groups		Total lipid (mg/dL)	Triglycerides (mg/dL)	Total cholesterol (mg/dL)
Control group		704.14±5.26 c	90.10±0.73 c	177.42±2.80 c
Oral administration of coffee beverage prepared by:	Boiled coffee	1007.28±4.57 a	140.90±1.82 a	286.31±1.80 a
	Filtered coffee	701.44±5.55 c	86.09±1.72 c	173.26±2.13 c
	Turkish coffee	935.72±3.87 b	119.60±1.18 b	202.78±2.47 b

Means in each column with different superscript letters differ significantly at P <0.05. A uses harmonic mean sample size = 10 rats.

Table 3: Serum levels of LDL-C, HDL-C and VLDL-C as well as atherogenic index in rats

		Parameters as Mean± SE			
Groups		LDL-C (mg/dL)	HDL-C (mg/dL)	VLDL-C (mg/dL)	Atherogenic index
Control group		115.12±1.54 c	44.28±0.31 a	18.02±0.15 c	0.31±0.003 c
Oral administration of coffee beverage prepared by:	Boiled coffee	221.30±1.78 a	36.65±0.60 c	28.06±0.34 a	0.59±0.005 a
	Filtered coffee	112.50±2.27 c	43.52±0.54 a	17.22±0.34 c	0.30±0.001 c
	Turkish coffee	138.99±2.40 b	39.88±0.23 b	23.92±0.79 b	0.47±0.007 b

Means in each column with different superscript letters differ significantly at P <0.05. A uses harmonic mean sample size = 10 rats.

Table 4: Serum levels of uric acid, urea nitrogen and creatinine in rats

		Parameters as Mean± SE		
Groups		Uric acid (mg/dL)	Urea nitrogen (mg/dL)	Creatinine (mg/dL)
Control group		2.79±0.08 c	20.41±0.38 c	0.29±0.01 c
Oral administration of coffee beverage prepared by:	Boiled coffee	3.83±0.05 a	28.06±0.53 a	0.38±0.01 a
	Filtered coffee	3.21±0.09 b	23.86±1.19 b	0.30±0.01 bc
	Turkish coffee	3.41±0.09 b	24.27±0.36 b	0.32±0.01 b

Means in each column with different superscript letters differ significantly at P <0.05. A uses harmonic mean sample size = 10 rats.

Table 5: Serum levels of AST, ALT and total and direct bilirubin in rats

		Parameters as Mean± SE			
Groups		AST (U/L)	ALT (U/L)	Bilirubin (mg/dL)	Direct bilirubin (mg/dL)
Control group		69.38±0.70 c	29.18±0.45 c	0.29±0.004 c	0.39±0.01 c
Oral administration of coffee beverage prepared by:	Boiled coffee	82.64±0.77 a	41.68±0.55 a	0.38±0.01 a	0.51±0.01 a
	Filtered coffee	70.85±0.70 c	30.46±0.36 c	0.30±0.004 c	0.39±0.01 c
	Turkish coffee	76.14±1.09 b	36.66±0.84 b	0.33±0.01 b	0.44±0.01 b

Means in each column with different superscript letters differ significantly at P <0.05. A uses harmonic mean sample size = 10 rats.

the control rats. Oral administration of boiled and Turkish coffee beverages caused significant increase in serum levels of creatinine (0.38±0.01 and 0.32±0.01mg/dl, respectively) as compared to the control rats (0.29±0.01mg/dl). Rats given orally filtered coffee beverage had no significant increase in serum level of creatinine (0.30±0.01mg/dl) at p<0.05 as compared to the control rats (0.29±0.01mg/dl). Rats given orally boiled coffee had the higher serum concentrations of uric acid, urea nitrogen and creatinine, which were significant increase as compared to those given orally filtered and Turkish coffee beverages.

Liver Functions: Results in table 5 revealed that rats given orally boiled and Turkish coffee beverages had significant increase in serum levels of AST, ALT, total and direct bilirubin as compared to the control rats. Oral administration of filtered coffee beverage caused no significant changes in serum concentrations of AST, ALT, total and direct bilirubin as compared to the control group. Oral administration of boiled coffee beverage induced significant increase in serum levels of the above-mentioned biomarkers as compared to filter and Turkish coffee beverages.

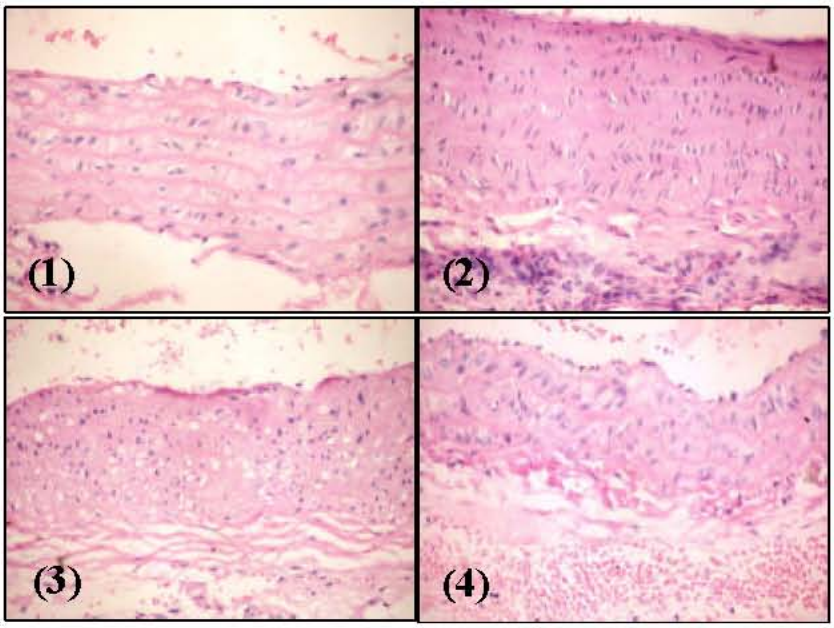

Fig. 1: Aorta of control rats showing no histopathological changes (H and E x 200).
Fig. 2: Aorta of rats given orally boiled beverage showing perivascular leucocytic cells infiltration (H and E x 200).
Fig. 3: Aorta of rats given orally boiled beverage showing marked vacuolations of tunica media (H and E x 200).
Fig. 4: Aorta of rats given orally Turkish coffee beverage showing perivascular hemorrhage (H and E x 200).

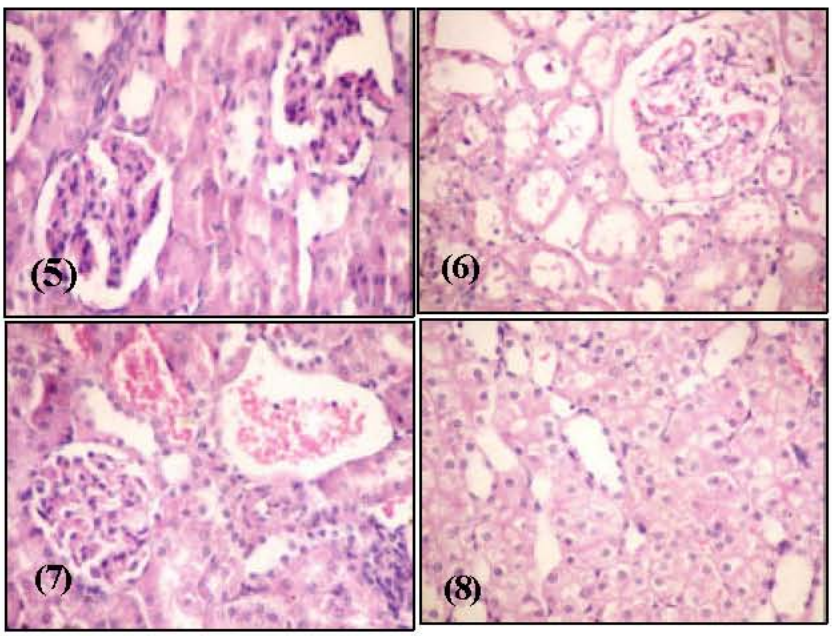

Fig. 5: Kidney of rats from control group showing the normal histological structure of renal parenchyma (H and E x200).
Fig. 6: Kidney of rats given orally boiled coffee beverage showing hypertrophy and vacuolations of endothelial lining glomerular tufts and epithelial lining renal tubules (H and E x 200).
Fig. 7: Kidney of rats given orally filtered coffee beverage showing small focal leucocytic cells aggregation (H and E x 200).
Fig. 8: Kidney of rats given orally Turkish coffee beverage showing granularity of the cytoplasm of renal tubular epithelium (H and E x 200).

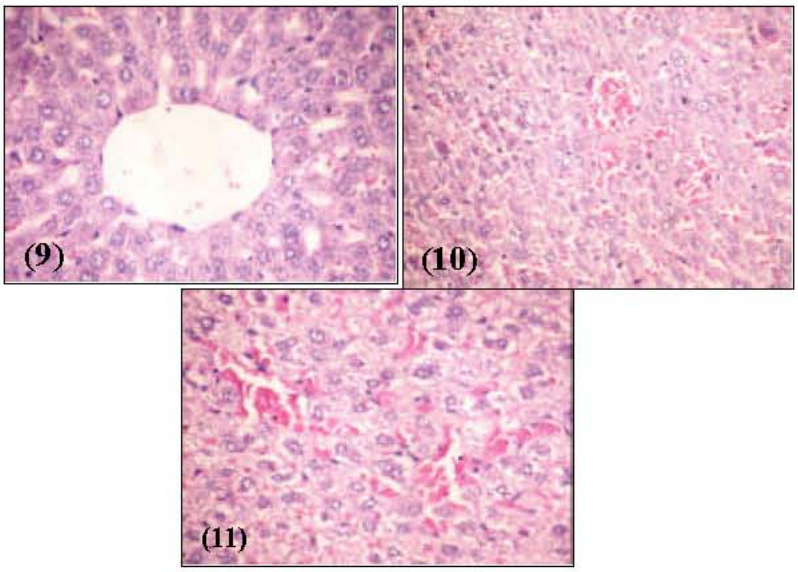

Fig. 9: Liver of control rat showing the normal histological structure of hepatic lobule (H and Ex 200).
Fig. 10: Liver of rats given orally boiled coffee beverage showing congestion of central vein and hepatic sinusoids together with vacuolations (H and Ex 200).
Fig. 11: Liver of rats given orally Turkish coffee beverage showing congestion of central vein and hepatic sinusoids (H and Ex 200).

Histopathological Examination: Histopathological examination of aorta from control rats revealed no histopathological changes as shown in figure 1. Oral administration of boiled coffee beverage revealed perivascular leucocytic cells infiltration (Figure 2) and other examined sections marked vacuolations of tunica media as shown in figure 3. Aorta of rats given orally filtered coffee beverage showed no histopathological changes. Oral administration of Turkish coffee beverage revealed perivascular hemorrhage as shown in figure 2.

Histopathological examination of the kidney from control rats revealed normal histological structure of renal parenchyma as show in figure 5. Examined kidney of rats given orally boiled coffee beverage showed hypertrophy and vacuolations of endothelial lining glomerular tufts and epithelial lining renal tubules (Figure 6). Meanwhile, kidney of rats given orally filter coffee beverage extract showed small focal leucocytic cells aggregation (Figure 7). Kidney of rats given orally Turkish coffee beverage extract had granularity of the cytoplasm of renal tubular epithelium as shown in figure 8.

Histopathological examination of the livers from control group revealed the normal histological structure of hepatic lobule as shown in figure 9. Oral administrations of boiled coffee beverage showing congestion of central vein and hepatic sinusoids together with vacuolations (Figure 10). Examined sections from group given orally filtered coffee beverage extract revealed apparent normal hepatocytes. Turkish coffee beverage caused congestion of central vein and hepatic sinusoids as shown in figure 11.

DISCUSSIONS

The main objective of the present study was to investigate the biological effects of boiled, filtered and Turkish coffee beverages on some biomarker parameters of atherogenicity, kidney and liver functions as well as histological changes of aorta, kidney and liver.

The present results showed that oral administration of boiled, filtered or Turkish coffee beverages caused significant decreased in body weight and serum glucose levels as compared to the control rats. These results agreed with the ones reported that regular coffee intake was inversely associated to weight gain and increased energy expenditure. Consequently, coffee consumption may decrease diabetes risk by helping to control body weight [19]. Epidemiologic studies [9] indicated that drinking large amounts of coffee reduces the incidence of type 2 diabetes. In another study [3] revealed that coffee consumption improved insulin sensitivity in non-diabetic elderly men and reduced the risk of both type 2 diabetes and impaired glucose tolerance in men and women who drank 5 or more cups per day. Coffee is the main source for caffeine and can influence the insulin sensitivity and the glucose metabolism in a negative way [20]. Previous

studies reported that caffeine promotes lipolysis in rat adipocytes [21] and glucose consumption with an increase in blood epinephrine [22]. Therefore, caffeine may be stimulate and increased the energy spending which lead to a weight reduction [23]. Moreover, the effect of caffeine in improve blood glucose level and glucose homeostasis may be due to the inhibition of adenosine receptors, because adenosine stimulates hepatic glucose production through the activation of A2B adenosine receptors, selective A2B receptor antagonists have hypoglycemic effect in diabetic mice and A1 adenosine receptor antagonism improve glucose tolerance in obese rats. Therefore, the balanced A1 and A2B antagonism may explain the positive affects of caffeine on glucose homeostasis [24]. In addition, Park *et al.* [25] showed that coffee caffeine help on improved diabetic symptoms by enhancing insulin sensitivity and beta cells function through improved insulin / IGF-1 signaling through induction of insulin receptor substrate in mildly diabetic rats. Furthermore, the antidiabetic effect of coffee may be due to chlorogenic acid-derived constituents [26].

As previously mentioned, data revealed that boiled and Turkish coffee beverages caused significant increase in atherogenic index values represented by the significant increase in total lipids, triglycerides, total cholesterol, LDL-C and VLDL-C, while induced significant decrease in HDL-C. However, there were no significant changes with oral administration of filtered coffee beverage as compared to the control rats. These results were confirmed by histopathological examination of aorta. The present results agreed with previous studies showed that boiled coffee increased serum cholesterol [27] and serum lipid concentrations [28], while filtered coffee did not have such affect. Recently, Hammar *et al.* [29] reported that boiled coffee was associated with hypercholesterolemia and risk of coronary heart disease. These elevations may be attributed to the lipid component of boiled coffee that powerfully raises serum cholesterol, LDL-C levels, as well as triglycerides [30]. Coffee lipid that are responsible for these elevation were cafestol and kahweol, which classified as diterpenes and removed through filtering process due to a general adsorption of coffee lipids onto the filter paper [31]. Unfiltered coffee contains approximately 1-2g of lipids per liter, while lipid levels found in filtered coffee are nearly negligible [32]. The two diterpenes cafestol are responsible for increased serum triglycerides [33] and serum lipids [11]. The mechanism by which boiled and Turkish coffees raise serum lipoprotein cholesterol levels may be attributed to the effect of coffee diterpenes on lipoprotein metabolism through the effects on cholesteryl ester transfer protein (CETP), phospholipids transfer proteins (PLTP) and lecithin cholesterol acyltransferase (LCAT). Therefore, cafestol and kahweol significantly raised the activity of CETP and PLTP, while LCAT activity significantly reduced. CETP catalyses the transfer of cholesterol esters synthesized by LCAT from HDL to LDL and very low-density lipoprotein (VLDL). PLTP can affect the net mass transfer of phospholipids between lipoproteins. While the reduction in LCAT results in a lowering of serum HDL-C [34]. Moreover, Al Kanhal [35] reported that triacylglycerols are the major lipid constituents of the coffee oil along with sterol esters, sterols/triterpene alcohol, hydrocarbons and the hydrolyzed products of triacylglycerols as the minor components. Fatty acid composition of total oil showed the presence of fatty acids of C14, C16, C18 and C20 carbon chains. Palmitic and linoleic acids were the major fatty acids. Pancreatic lipase hydrolysis revealed that the linoleoyl and palmitoyl are esterified at the Sn-2 and Sn-1, 3 positions of triacylglycerols respectively. The presence of high amounts of palmitic acid at Sn-1, 3 positions in coffee oil may be partly responsible for its hypercholesterolemic effects. Recent researches indicated that the diterpenes cafestol and kahweol have a cholesterol-raising effect by lowering the synthesis of cholesterol 7á-and 12á-hydroxylase, which are key enzymes in the biosynthesis of bile acids, being the main path for cholesterol excretion [36].

The present study revealed that oral administration of boiled, filtered or Turkish coffee beverages increased significantly serum levels of uric acid and urea nitrogen. Boiled and Turkish coffee beverages caused significant increase in serum level of creatinine, compared to the control rats. These finding confirmed by the histopathological changes in kidney sections. The present data were in accordance with the ones indicated that coffee caffeine increased uric acid and creatinine levels in serum of rats [24]. Portoles *et al.* [37] reported that coffee consumption increased serum urea and creatinin concentrations. These elevations may be attributed to that coffee caffeine inhibits A2A adenosine receptors, accelerate the development of interstitial inflammation, augments proteinuria and change renal function and structure. Recently, Tofovic *et al.* [38] reported that coffee produced severe tubulointerstitial damage including tubular atrophy, presence of proteinaceous material, tubular dilatation, interstitial inflammation and interstitial fibrosis, as well as increased glomerulosclerosis and adversely affects renal function in rats and these effects may be due to increased the activity of the renin angiotensin system.

The present data recorded that rats given orally Turkish or boiled coffee beverages had significant increase in serum levels of AST, ALT, total and direct bilirubin. These results agreed with previous study [39] demonstrated that cafestol and kahweol affect liver cells, boiled coffee or preparations rich in cafestol and kahweol raise the serum concentration of ALT. These results were observed with boiled and Turkish coffees contains cafestol and kahweol. The elevations in liver enzymes may be related to the effect of coffee on the integrity of liver cells as showed in hisopathological study. These results agreed with the ones study demonstrated that the elevations of liver enzymes may indicated to injury of hepatocytes. ALT is predominantly present in the cytosol of hepatocytes and AST is in the mitochondria. When hepatocytes sustain damage to their membranes ALT is released from the cytosol, whereas when hepatocytes sustain more severe damage AST is released from the mitochondria. Recently, Boekschoten *et al.* [40] reported that Kahweol and cafestol are the component of coffee oil that is responsible for the effect on liver enzyme. The elevations of liver enzyme levels are caused by a switch from consumption of filtered coffee to unfiltered coffee. Bilirubin levels were 38% increased during the follow-up measurement after four weeks compared to baseline. Moreover, Wousten-van der Wouvv *et al.* [33] revealed that long-term consumption of boiled coffee increased serum AST concentration, which excludes extensive damage to liver cells and reduced levels of ã-glutamyl transpeptidase.

In conclusion, the results of our study indicated regular drinking of boiled and Turkish coffees may be amongst the risk factors for cardiovascular diseases as well as liver and kidney dysfunctions.

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