



Pakistan Journal of Life and Social Sciences

www.pjlss.edu.pk

RESEARCH ARTICLE

Effect of Cinnamon on Renal Functions and Cell Structure of Kidney in Rats

Mahpara Safdar^{1*}, Parvez Iqbal Paracha², Alam Khan², Saleem Khan², Hussain Ali³ and Abdul Aziz⁴

¹Department of Home & Health Sciences, Allama Iqbal Open University, Islamabad, Pakistan

²Department of Human Nutrition, the University of Agriculture, Peshawar, Pakistan

³Small Animals' Section, National Institute of Health, Islamabad, Pakistan

⁴Faculty of Veterinary and Animal Sciences, the University of Poonch, Rawalakot, Azad Kashmir, Pakistan

ARTICLE INFO

Received: Oct 14, 2016

Accepted: Dec 12, 2016

Online: Dec 14, 2016

Keywords

Albino rats

Cinnamon

Histopathology

Kidney function

Safety assessment

ABSTRACT

The present research was conducted to determine the effect of cinnamon intake on functions and cell structure of kidney in rats. For this purpose, 72 adult female albino rats aged 2-3 months, weighing 180-270 gm were divided into three groups as I, II and III, each having 24 rats. Group I was for placebo; whereas, group II and III were offered cinnamon at dose rates of 4mg and 12 mg per day, respectively. The total duration of the experiment was 60 days. Doses were given for first 40 days, then these were stopped and the last 20 days was the follow up period. Six rats from each group were sacrificed at start of the experiment and at days 20, 40 and 60 and blood samples were collected for biochemical analysis and kidneys were removed for observing structural changes. Renal performance parameters including urea, creatinine and electrolytes (sodium, potassium and chlorides) were determined. The changes in cellular structures of kidney were examined microscopically. The results showed that cinnamon intake did not cause any significant changes in blood urea, creatinine and electrolytes and also no structural changes were found in kidneys throughout the experimental period. In conclusion, cinnamon has no adverse effects on the physiology and morphology of normal healthy kidneys, therefore its use is safe for kidneys.

*Corresponding Author:

mahpara.jadoon@gmail.com

INTRODUCTION

Worldwide, herbal products/medicinal plants have gained much importance for their therapeutic properties, having low cost, lesser side effects and easy accessibility. Cinnamon is one of these plants used for the treatment of different ailments. Beneficial use of cinnamon has been studied extensively; however, not enough work has been reported on the side effects of this plant on human health. Therefore, it is important to know both the positive and noxious effects of this therapeutic plant for safe usage.

Cinnamon is mainly produced in Asian countries like Sri Lanka, China, India, Malaysia, Thailand and Vietnam (Chomchalow, 2001). Cinnamon bark is commonly used as a spice. It is one of the spices that can be consumed as such. It is primarily used in cooking as a taste and flavoring material in meat curries and rice dishes. It is used in the preparation

of chocolate, also used in making teas. In Europe, cinnamon and sugar are often used to flavor bread-based dishes, cereals, and fruits. It can also be used in pickling (Kokab and Ahmad, 2011).

In herbal prescriptions, cinnamon is used as a carminative agent. Its use is also associated with cold and debilitated conditions and relieves nausea and vomiting. Because of its mild astringent property, it is predominantly beneficial in infantile diarrhea. External application of cinnamon oil may be helpful for poor circulation, rheumatism and arthritis. If taken internally in the form of powder, pills, tincture and tea, it is helpful for diabetes, impotence, weight loss, and to reduce fever and menstrual problems. Hot drink of cinnamon may help to prevent flu and colds. Cold drink of cinnamon may help stop sweating. The oils of cinnamon leaves, bark and roots add their scent to perfumes (Lawless, 2013).

Cinnamaldehyde increases peripheral blood flow, by its hypotensive and spasmolytic action. Cinnamon oil is a potent antifungal, antibacterial, and uterine stimulant. The cinnamon leaf oil can be used in antiseptics, tonics and in therapies for intestinal gas, colds and hypertension (Dorman and Deans, 2000; Li, 2000).

Daily doses of 1, 3 and 6g cinnamon improved fasting blood glucose and lipid profile (Khan et al., 2003). They gave the 3 doses of cinnamon for 40 days and didn't report any adverse effect of cinnamon on human. They argued that people had been using cinnamon for centuries as a spice in food preparations signifying that consumption of cinnamon for longer time was safe. But the regular use of cinnamon for longer duration must be verified by well-designed experimental trials. The present study has been aimed to determine whether cinnamon is safe or not for physiology and morphology of normal healthy kidneys.

Kidneys excrete and retain substances as per need of the body. They also play a role in electrolyte balance. The toxic effect of cinnamon for long time on kidneys could be seen by changes in the kidney functions. The effect of cinnamon on kidney can be determined by the values of blood urea, creatinine, and electrolytes (sodium, potassium and chloride) in addition to histological examination of kidneys.

Urea is formed as a waste product in the breakdown of proteins. An elevated blood urea level indicates that the kidneys may not be functioning properly. Its level may be elevated by gastrointestinal hemorrhage, greater protein breakdown, dehydration and with drugs e.g., glucocorticoids (Sharma et al., 2014). Creatinine is a derivative of muscle metabolism. The serum concentration of creatinine is the most commonly used and generally established measure of kidney function in clinical practice.

Electrolytes maintain a healthy water and acid/base (pH) balance and are typically measured as part of a renal profile which includes sodium (Na^+), potassium (K^+) and chloride (Cl^-). Maximum amount of sodium is found in the extracellular fluid (ECF) and helps to regulate the volume of water in the body. Potassium is predominantly found in the intracellular fluid (ICF) and in fluid part of the blood or plasma in a small quantity. Chloride moves in and out of the cells and helps to maintain electrically neutral environment. The level of chloride usually reflects that of sodium (Bossingham et al., 2005).

The incidence of acute renal failure (ARF) is increasing as a common problem having severe consequences, unsatisfactory treatment regimes, and a huge economic burden to society (Van Biesen et al., 2006; Uchino et al., 2005; Schrier et al., 2004). Acute renal failure may be classified as pre renal, intrinsic renal and post renal failure. In pre renal failure, structurally normal kidneys give functional response to hypoperfusion. The intrinsic

renal failure involves structural damage to the renal parenchyma. The post renal failure involves the urinary tract obstruction. The term acute kidney injury (AKI) has been proposed to reflect the entire spectrum of the condition (Berl, 2005). The outcome of acute change in serum creatinine level, regardless of underlying biology or etiology, is frequently used in clinical trials as both efficacy and safety end points (Coca et al., 2016).

The normal functioning of the kidney is linked with its normal morphology. In this study, the effect of cinnamon on physiology and morphology of kidney was evaluated in rat's model. How does cinnamon effect kidney functions will help to sightsee the safety of its use, for different ailments.

MATERIALS AND METHODS

The effect of cinnamon on cell structure and functions of kidney in rats was studied in the department of Human Nutrition, the University of Agriculture, Peshawar and National Institute of Health (NIH), Islamabad, Pakistan. The facilities of National Veterinary Laboratory (NVL), Islamabad were utilized for biochemical analyses and preparation of slides for histological examination of kidney tissues. The slides were examined by a qualified and experienced histopathologist from the City Medical Laboratory, Peshawar, Pakistan.

Cinnamon for the experimental trial

The bark of cinnamon variety, *Cinnamomum cassia*, was purchased from Khalid Commercial Store, Peshawar, Pakistan. The variety was certified by expert of forest department, Peshawar. *Cinnamomum cassia* was used in this trial for knowing the ill effect of cinnamon because previously its beneficial effect on type 2 diabetes was reported (Khan et al 2003). The bark was finely ground and was stored in an air tight bottle for use during the experimental period.

Experimental animals and research protocol

Rats were used in this experiment and the experimental trial was conducted in the National Institute of Health (NIH), Islamabad, Pakistan. Adult 72 female albino rats were obtained from the Animal Division of NIH. The weight of these rats ranged from 180-270 gm with the age ranging from 2-3 months.

The rats were divided into three groups (I, II and III), each group was having 24 rats. Group I was assigned for placebo and groups II and III were assigned for 4 mg and 12 mg cinnamon per day, respectively. The placebo group was given drinking tap water by drenching as was done in the cinnamon groups for administration of cinnamon. Placebo rats were kept on similar conditions as that of cinnamon rats. All the three groups were kept on standard rat diet known as Chow.

The experimental trial was for 60 days. From the starting day of the experiment i.e. day 0 to day 40,

simple drinking tap water to each rat of placebo (group I), 4 mg cinnamon in drinking water (equal to the volume of placebo drinking water) to each rat of group II and 12mg cinnamon in drinking water (equal to the volume of placebo drinking water) to each rat of group III was administered into the stomach of each rat by using a feeding tube.

From day 41 to day 60, the experimental trial i.e. placebo and cinnamon by drenching was stopped and all the rats of all the three groups were fed only the rat standard diet (Chow). This 20 days (41-60 days) trial on standard diet was to know whether the histological and physiological changes, if happened during the experimental trial, were persisting or recovered.

The selection of 4 mg and 12 mg cinnamon per day was calculated on the basis of a previous human study where 1 and 3g cinnamon per day was given (Khan et al., 2003). The calculation was made on the average body weight of rats to the average body weight of an adult human subject.

Collection of blood sample

At the start of the experiment i.e. day 0, six rats from each group were anesthetized for collection of blood samples for biochemical analyses. This baseline data was used as control for all groups. The placebo group was used as the parallel control at each stage of the trial. Similarly another 6 rats from each group on day 20, 40 and 60 were anesthetized for collection of blood samples for biochemical analyses. About 2-3 ml blood was taken from each rat and centrifuged at 4000 rpm to separate blood serum. The sera were stored in sterilized vials at -20 °C for further biochemical analyses.

Surgical removal of kidney

After collection of blood samples from the anesthetized rats, kidneys of all the six rats from each group were surgically removed at day 0, 20, 40 and 60. The removed kidneys of all the rats were preserved in 10% formalin for histopathological studies.

Determination of kidney functions

Kidney functions were determined by conducting renal function tests (RFT) including blood urea, creatinine, and electrolytes (Na⁺, K⁺ and Cl⁻).

Urea was determined by enzymatic U.V. method of Newman and Price (2001) and AMP diagnostics kit and Creatinine was determined by using the method of Tietz and Andresen (1986) and Crescent diagnostic kit, at Metrolab 1600. Sodium (Na) and potassium (K) were analyzed on Seac Fp 20 flame photometer by the method of Harris (2010). Chloride ion was determined by Metrolab 1600 using the method of Miller (1984) and Pioneer Diagnostics kit.

Assessment of morphology of kidney

The slides of kidney tissues were prepared at National Veterinary Laboratory (NVL), Islamabad, Pakistan by using the standard method of Bancroft and Gamble (2008). The organs (kidneys) were fixed in neutral

buffered 10% formalin. Tissues were trimmed off to a thickness of 4-5mm, then enclosed in labelled tissue cassette and placed in basket of automatic tissue processor. Dehydration process was done using 70%, 90% and absolute alcohol solutions. Next was the clearing process using paraffin wax I and II.

After cooling the paraffin blocks, microtomy (cutting of blocks) was done to a thickness of 5 µm, for exposing the suitable tissue area at slide. For drying purposes, the slides were placed on a hot plate. Pre-staining techniques involved de-paraffinization with xylene I and II. Rehydration was done by processing the slides through decreasing grades of alcohol. Staining was done by dipping the slides in Harris haematoxylin solution. Post staining procedures included dehydration process i.e. dipping the slides in increasing grades of alcohol. The slides were cleared by using xylene I and II and mounting was done with Canada balsam and cover slips were placed. The slides of kidney were microscopically examined with the help of experienced Histopathologist using advance research microscope (OLYMPUS BX51) along with attached camera DP12 for morphological examination and photographs.

Statistical analysis

The collected data were entered to the computer for error checking. The effect of cinnamon by amount of doses and duration of treatment on kidney in rats was assessed by running General Linear Model (GLM). Completely Randomized Design (CRD) was run by using SAS v.9 software (SAS Ins.) for statistical significance of various groups and durations considered in the study at 5% level of probability. All the results were presented as mean ± SE for six replications (Kalender et al., 2012; Sun et al., 2015).

RESULTS AND DISCUSSION

Effect of cinnamon on serum urea

The effect of cinnamon on serum urea levels of rats was determined and the result is given in Table 1.

The urea values on day 0 in Table 1 are the values before the start of placebo or cinnamon. So these urea values were used as control values for the study.

On the starting day of the experiment (day 0), the mean serum urea levels of the rats for placebo and cinnamon groups were 26.67 ± 4.88mg dL⁻¹, 27.17 ± 4.62 mg dL⁻¹ and 29.17 ± 4.19 mg dL⁻¹ respectively. At day 40, their mean serum urea levels were 30.50 ± 4.62 mg dL⁻¹, 30.33 ± 3.79 mg dL⁻¹ and 32.67 ± 1.61 mg dL⁻¹ respectively. The data showed no significant change in the mean serum urea levels for both the cinnamon groups at days 20 and 40 when compared with the mean serum urea values on day 0 of the respective groups and placebos.

Table 1: Effect of Cinnamon on Serum Urea in Rats

Groups ¹ of Rats	Doses of Cinn. (mg day ⁻¹)	Serum Urea (mg dL ⁻¹) ^{2,3}			
		Before Cinn. Intake (only on Chow)	During Cinn. Intake		After Cinn. Intake (only on Chow)
		Day 0	Day 20	Day 40	Day 60
		Mean±SE	Mean±SE	Mean±SE	Mean±SE
Group I	0	26.67 ± 4.88	30.17 ± 3.66	30.50 ± 4.62	33.67 ± 3.36
Group II	4	27.17 ± 4.62	28.83 ± 3.75	30.33 ± 3.79	32.50 ± 2.74
Group III	12	29.17 ± 4.19	33.50 ± 2.42	32.67 ± 1.61	35.0 ± 0.93

1-Each group was having 24 rats; Group I was for Placebo, Group II was for 4mg cinnamon per day and Group III was for 12 mg cinnamon per day; 2-The data given in columns 3, 4, 5 and 6 are the mean of six rats; 3-Means showed non-significant (P>0.05) interaction between groups and durations.

Table 2: Effect of Cinnamon on Serum Creatinine in Rats

Groups ¹ of Rats	Doses of Cinn. (mg day ⁻¹)	Serum Creatinine (mg dL ⁻¹) ^{2,3}			
		Before Cinn. Intake (only on Chow)	During Cinn. Intake		After Cinn. Intake (only on Chow)
		Day 0	Day 20	Day 40	Day 60
		Mean±SE	Mean±SE	Mean±SE	Mean±SE
Group I	0	0.57 ± 0.05	0.68 ± 0.02	0.65 ± 0.08	0.69 ± 0.03
Group II	4	0.58 ± 0.04	0.64 ± 0.03	0.50 ± 0.07	0.61 ± 0.04
Group III	12	0.60 ± 0.04	0.69 ± 0.06	0.57 ± 0.07	0.62 ± 0.06

1-Each group was having 24 rats; Group I was for Placebo, Group II was for 4mg cinnamon per day and Group III was for 12 mg cinnamon per day; 2-The data given in columns 3, 4, 5 and 6 are the mean of six rats; 3-Means showed non-significant (P>0.05) interaction between groups and durations

At day 40 the placebo and cinnamon were stopped for the next 20 days. Then at day 60, the mean serum urea levels of placebo and cinnamon groups were 33.67 ± 3.36 mg dL⁻¹, 32.50 ± 2.74 mg dL⁻¹ and 35.00 ± 0.93 mg dL⁻¹ respectively. There was an overall non-significant (P>0.05) change in the mean serum urea levels of rats of cinnamon groups as compared to the mean serum urea values of the rats of the same groups at the start of the trial and placebo at day 60.

In all the three groups independent of the cinnamon dose, the mean urea concentrations did not change significantly in rats, as given in Table 1. However, a non-significant increasing trend has been observed in all the three groups. Since there were no diet variations over the time and the same isocaloric and isoproteic diet was given to all rats of all the groups, *ad libitum*, therefore this trend could be justified as, with the increasing age, the amount of diet consumed increased and hence the amount of protein thus leading to slightly increasing urea concentrations. Urea levels increase with increasing age and also with increased content of protein in diet (Fouque and Laville, 2009).

The non-significant effect of cinnamon on urea concentration indicated that cinnamon intake is safe for kidney as far as urea is concerned. El-yamani (2011) evaluated the impacts of cinnamon, cardamom and ginger on hyperglycemic rats and reported that cinnamon diet improved the renal function to the maximum when fed to the diabetic rats. Ullah et al. (2013) reported that *C. zeylanicum* significantly attenuated renal functional changes associated with

gentamicin as assessed by urea, creatinine, uric acid, electrolytes and urinary protein.

Effect of cinnamon on serum creatinine

The effect of cinnamon on serum creatinine levels of rats is given in Table 2.

The creatinine values on day 0 in Table 2 are the values before the start of placebo or cinnamon. So these creatinine values were used as control values for the study. On the starting day of the experiment (day 0), the mean serum creatinine levels of the rats for placebo and cinnamon groups were 0.57 ± 0.05 mg dL⁻¹, 0.58 ± 0.04 mg dL⁻¹ and 0.60 ± 0.04 mg dL⁻¹ respectively. When the rats of placebo and cinnamon groups used placebo and cinnamon for 40 days, their mean serum creatinine levels were 0.65 ± 0.08 mg dL⁻¹, 0.50 ± 0.07 mg dL⁻¹ and 0.57 ± 0.07 mg dL⁻¹ respectively. The data showed non-significant (P>0.05) change in the mean serum creatinine levels for group II and III at day 40 when compared with the mean serum creatinine values on day 0 of the respective groups and with the mean serum creatinine values on day 40 of group I (Table 2).

At day 60, the mean serum creatinine levels of placebo and cinnamon groups were 0.69 ± 0.03 mg dL⁻¹, 0.61 ± 0.04 mg dL⁻¹ and 0.62 ± 0.06 mg dL⁻¹ respectively. There was an overall non-significant increase in the mean serum creatinine levels of rats of placebo and dose groups at this duration, as compared to the mean serum values of the rats of the same groups at the start of the experiment. Creatinine excretion is directly related to age (Rowe et al., 1976) and muscle mass (Goldwasser et al., 1997; James et al., 1988).

Table 3: Effect of Cinnamon on Serum Sodium in Rats

Groups ¹ of Rats	Doses of Cinn. (mg day ⁻¹)	Serum Sodium (mmol L ⁻¹) ^{2,3}			
		Before Cinn. Intake (only on Chow)	During Cinn. Intake		After Cinn. Intake (only on Chow)
		Day 0	Day 20	Day 40	Day 60
		Mean±SE	Mean±SE	Mean±SE	Mean±SE
Group I	0	139.53 ± 1.60	139.80 ± 1.67	142.48 ± 2.11	158.47 ± 1.08
Group II	4	138.42 ± 3.25	140.67 ± 2.26	148.77 ± 2.53	157.02 ± 0.75
Group III	12	139.08 ± 1.44	140.30 ± 1.58	146.63 ± 1.13	159.07 ± 0.81

1-Each group was having 24 rats; Group I was for Placebo, Group II was for 4mg cinnamon per day and Group III was for 12 mg cinnamon per day; 2-The data given in columns 3, 4, 5 and 6 are the mean of six rats; 3-Means showed non-significant (P>0.05) interaction between groups and durations.

The non-significant effect of cinnamon on serum creatinine level in Table 2 indicate that there is no adverse effect of cinnamon intake on kidney functions as for as creatinine is concerned. Similar non-significant results with cinnamon treatment were reported by Tang et al. (2008). They concluded that the percentage of water soluble oxalate differed markedly between cinnamon (6%) and turmeric (91%) that seemed to be the primary cause of the greater urinary oxalate excretion/oxalate absorption from turmeric. They found that the ratio of oxalate to creatinine for the turmeric treatment was significantly higher than the corresponding ratios for the control and cinnamon treatments.

Effect of cinnamon on serum sodium

The effect of cinnamon on serum sodium levels of rats was determined and the result is given in Table 3.

On the starting day of the experiment (day 0), the mean serum sodium levels of the rats for placebo and cinnamon groups were 139.53±1.60 mmol L⁻¹, 138.42±3.25 mmol L⁻¹ and 139.08±1.44 mmol L⁻¹ respectively.

After consumption of 4 mg and 12 mg cinnamon per day for 20 and 40 days non-significant changes were observed in the mean serum sodium levels of the rats of both the cinnamon groups at day 20 and 40, when compared with the respective mean serum sodium levels of the rats at day 0 and with that of respective placebo values at the respective days.

At day 60, the mean serum sodium levels of cinnamon groups (when they were not using cinnamon for the last 20 days) were 158.47 ± 1.08 mmol L⁻¹, 157.02 ± 0.75 mmol L⁻¹ and 159.07 ± 0.81 mmol L⁻¹ respectively. There was a non-significant (P>0.05) change in the mean serum sodium levels of rats of cinnamon groups at days 60 as well, as compared to their respective mean serum values of the rats at the start of the experiment and placebo values on day 60.

The mean sodium concentrations non-significantly (P>0.05) changed with cinnamon intake for 40 days. Even when the doses were stopped at day 40, there was still a non-significant (P>0.05) change in sodium concentration at day 60, as shown in Table 3. This

indicates that cinnamon intake did not alter the sodium concentration and is safe for kidney as for as urea (Table 1), creatinine (Table 2) and sodium (Table 3) is concerned.

Effect of Cinnamon on Serum Potassium

The effect of cinnamon on serum potassium levels of rats was determined and the result is given in Table 4.

On the starting day of the experiment (day 0), the mean serum potassium levels of the rats for placebo and cinnamon groups were 5.47 ± 0.17 mmol L⁻¹, 5.42 ± 0.26 mmol L⁻¹ and 5.43 ± 0.10 mmol L⁻¹ respectively. When the rats of placebo and cinnamon groups used placebo and cinnamon for 20 days and 40 days, their mean serum potassium levels were non-significantly (P>0.05) changed when compared with the mean serum potassium values on day 0 of the respective groups and placebo values at respective durations (Table 4).

At day 60, the mean serum potassium levels of placebo and cinnamon groups were 5.48 ± 0.16 mmol L⁻¹, 5.60 ± 0.16 mmol L⁻¹ and 5.62 ± 0.16 mmol L⁻¹ respectively. There was an overall non-significant (P>0.05) change in the mean serum potassium levels of rats of placebo and cinnamon groups at day 60, as compared to their respective mean serum values of the rats of the all the three groups at the start of the experiment.

From Table 4 it is clear that cinnamon did not change the potassium concentration in 40 days similar to placebo. These results suggested that cinnamon has no side effect on kidneys, as for as urea (Table 1), creatinine (Table 2) sodium (Table 3) and potassium (Table 4) concentration is concerned.

Effect of cinnamon on serum chloride

The effect of cinnamon on serum chloride levels of rats was determined and the result is given in Table 5.

The chloride values of the rats for placebo and cinnamon groups on the starting day of the experiment (day 0) were 92.33 ± 1.80 mmol L⁻¹, 91.67 ± 2.56 mmol L⁻¹ and 91.83 ± 3.06 mmol L⁻¹ respectively.

There was a non-significant (P>0.05) change in the mean serum chloride levels of rats of group II and III at days 20, 40 and 60, as compared to its respective mean serum values at the start of the experiment and placebo values on respective days (Table 5).

Table 4: Effect of Cinnamon on Serum Potassium in Rats

Groups ¹ of Rats	Doses of Cinn. (mg day ⁻¹)	Serum Potassium (mmol L ⁻¹) ^{2,3}			
		Before Cinn. Intake (only on Chow)	During Cinn. Intake		After Cinn. Intake (only on Chow)
		Day 0	Day 20	Day 40	Day 60
		Mean±SE	Mean±SE	Mean±SE	Mean±SE
Group I	0	5.47 ± 0.17	5.40 ± 0.22	5.38 ± 0.29	5.48 ± 0.16
Group II	4	5.42 ± 0.26	5.32 ± 0.34	5.40 ± 0.25	5.60 ± 0.16
Group III	12	5.43 ± 0.10	5.43 ± 0.30	5.53 ± 0.19	5.62 ± 0.16

1-Each group was having 24 rats; Group I was for Placebo, Group II was for 4mg cinnamon per day and Group III was for 12 mg cinnamon per day; 2-The data given in columns 3, 4, 5 and 6 are the mean of six rats; 3-Means showed non-significant (P>0.05) interaction between groups and durations.

Table 5: Effect of Cinnamon on Serum Chloride in Rats

Groups ¹ of Rats	Doses of Cinn. (mg day ⁻¹)	Serum Chloride (mmol L ⁻¹) ^{2,3}			
		Before Cinn. Intake (only on Chow)	During Cinn. Intake		After Cinn. Intake (only on Chow)
		Day 0	Day 20	Day 40	Day 60
		Mean±SE	Mean±SE	Mean±SE	Mean±SE
Group I	0	92.33 ± 1.80	112.00 ± 2.14	108.33 ± 2.72	110.67 ± 3.72
Group II	4	91.67 ± 2.56	113.17 ± 2.55	106.67 ± 1.82	106.00 ± 2.41
Group III	12	91.83 ± 3.06	105.67 ± 4.54	105.83 ± 1.35	102.33 ± 2.97

1-Each group was having 24 rats; Group I was for Placebo, Group II was for 4mg cinnamon per day and Group III was for 12 mg cinnamon per day; 2-The data given in columns 3, 4, 5 and 6 are the mean of six rats; 3-Means showed non-significant (P>0.05) interaction between groups and durations.

The non-significant change in chloride levels with/without cinnamon intake assures its safety for consumption. Thus cinnamon intake is not injurious for kidney functions as far as the serum concentration of urea (Table 1), creatinine (Table 2), sodium (Table 3), potassium (Table 4) and chloride (Table 5) is concerned.

Effect of cinnamon on morphology of kidney in rats

Morphology of kidney before treatments showed normal glomeruli and tubules. The structures of kidney with and without use of 4mg and 12mg cinnamon per day remained normal showing normal structure of glomeruli and tubules with a few congested blood vessels. These congested blood vessels might be due to ligation of animals. Normal kidney morphology was also observed by Mishra et al. (2010), as they reported that cinnamon protects the kidney by reducing glomerular expansion and decreasing the tubular dilations.

Conclusions

Cinnamon doses 4mg and 12mg in normal adult rats for 40 days did not affect kidney functions and cellular structure. Cinnamon intake did not affect blood urea, creatinine and electrolytes, sodium, potassium and chloride. Morphology of the kidney showed normal structures of the renal tubules and glomeruli. As renal physiology and morphology was not disturbed by the cinnamon doses throughout the experimental period, therefore it may be considered as safe as far as kidney is concerned.

Conflict of interests

The authors declare that there are no conflicts of interests.

Authors' contributions

MS, PIP and AK designed the study. MS performed experimental trials, data analysis and wrote the manuscript. PIP supervised the research. SK, HA and AA participated in all the research activities during the trial. All the authors participated in the write up of this manuscript.

Acknowledgements

We are thankful to (i) Higher Education Commission of Pakistan for financial support of research, (ii) National Institute of Health (NIH) Islamabad, for provision of rats and facilitation for experimental trial (iii) Department of Human Nutrition, Peshawar, for providing this opportunity to the scholar (iv) National Veterinary Lab (NVL) Islamabad, for facilitation in slide preparation and (v) CITI LAB for histopathological studies.

REFERENCES

- Bancroft JD and M Gamble, 2008. Theory and practice of histological techniques. 6th edition. Elsevier publication, Philadelphia, USA, pp: 53-121.
- Berl T, 2005. American society of nephrology renal research report. Journal of the American Society of Nephrology 16: 1886-903
- Bossingham MJ, NS Carnell and WW Campbell, 2005. Water balance, hydration status, and fat-free mass hydration in younger and older adults. The American Journal of Clinical Nutrition 81: 1342-1350.

- Chomchalow N, 2001. Spice production in Asia-An overview. *Assumption University Journal of Technology*, 5: 1-14.
- Coca SG, A Zabetian, BS Ferket, J Zhou, JM Testani, AX Garg and CR Parikh, 2016. Evaluation of short-term changes in serum creatinine level as a meaningful end point in randomized clinical trials. *Journal of the American Society of Nephrology* 27: 2529-2542
- Dorman H and S Deans, 2000. Antimicrobial agents from plants: antibacterial activity of plant volatile oils. *Journal of Applied Microbiology*, 88: 308-316.
- El-yamani M, 2011. Cinnamon, cardamom and ginger impact as evaluated on hyperglycemic rats. *Journal of Specific Education*, 20: 664-679.
- Fouque D and M Laville, 2009. Low protein diets for chronic kidney disease in non diabetic adults. Published by John Wiley & Sons, Ltd. *Cochrane Database of Systematic Reviews*, Issue 3. Art. No.: CD001892. DOI: 10.1002/14651858.CD001892.pub3.
- Goldwasser P, A Aboul-Magd and M Maru, 1997. Race and creatinine excretion in chronic renal insufficiency. *American Journal of Kidney Diseases*, 30: 16-22.
- Harris DC, 2010. *Quantitative chemical analysis*. 8th edition. W.H. Freeman and Company, Macmillan publishers, USA.
- James GD, JE Sealey, M Alderman, S Ljungman, FB Mueller, MS Pecker and JH Laragh, 1988. A longitudinal study of urinary creatinine and creatinine clearance in normal subjects race, sex, and age differences. *American Journal of Hypertension* 1: 124-131.
- Kalender Y, S Kaya, D Durak, FG Uzun and F Demir, 2012. Protective effects of catechin and quercetin on antioxidant status, lipid peroxidation and testis-histoarchitecture induced by chlorpyrifos in male rats. *Environmental Toxicology and Pharmacology*, 33: 141-148.
- Khan A, M Safdar, MMA Khan, KN Khattak and RA Anderson, 2003. Cinnamon improves glucose and lipids of people with type 2 diabetes. *Diabetes Care*, 26: 3215-3218.
- Kokab S and S Ahmad, 2011. *Developing Herbal Pharmaceutics in Pakistan-II: Distinctiveness of Selected Medicinal Herbs and Uses*. National Resource Division, Pakistan Agriculture Research Council, Islamabad, Pakistan 3: 7-8.
- Lawless J, 2013. *The Encyclopedia of Essential Oils: The Complete Guide to the Use of Aromatic Oils In Aromatherapy, Herbalism, Health, and Well Being*. Conari Press, China, pp: 200-204.
- Li TS, 2000. *Medicinal plants: Culture, utilization and phytopharmacology*. CRC press, USA, pp: 121-123.
- Miller W, 1984. *Chloride*. Kaplan A et al. Clin Chem The CV Mosby Co. St Louis. Toronto, Princeton, Canada, pp: 1059-1062.
- Mishra A, R Bhatti, A Singh and MPS Ishar, 2010. Ameliorative effect of the cinnamon oil from *Cinnamomum zeylanicum* upon early stage diabetic nephropathy. *Planta Medica*, 76: 412-417.
- Newman D and C Price, 2001. Nonprotein nitrogen metabolites. *Tietz Fundamentals of Clinical Chemistry*, 5: 420-425.
- Rowe JW, R Andres, JD Tobin, AH Norris and NW Shock, 1976. The effect of age on creatinine clearance in men: a cross-sectional and longitudinal study. *Journal of Gerontology*, 31: 155-163.
- Schrier RW, W Wang, B Poole and A Mitra, 2004. Acute renal failure: definitions, diagnosis, pathogenesis, and therapy. *Journal of Clinical Investigation*, 114: 5-14.
- Sharma NO, KB Sodavadiya, SM Nigoskar, DV Agnihotri and BK Agrawal, 2014. Association between blood urea level and serum creatinine level in renal insufficiency subjects. *International Journal of Medical and Applied Sciences*, 3: 238-243.
- Sun Y, L Yan, Y Liang, X Li, X Cao and C Lu, 2015. Reduction of epidural scar adhesion by topical application of simvastatin after laminectomy in rats. *European Review for Medical and Pharmacological Sciences*, 19: 3-8.
- Tang M, DE Larson-Meyer and M Liebman, 2008. Effect of cinnamon and turmeric on urinary oxalate excretion, plasma lipids, and plasma glucose in healthy subjects. *The American Journal of Clinical Nutrition*, 87: 1262-1267.
- Tietz NW and BD Andresen, 1986. *Textbook of clinical chemistry*. Saunders Publishers, Philadelphia, USA, pp: 1274-1278.
- Uchino S, JA Kellum, R Bellomo, GS Doig, H Morimatsu, S Morgera and E Macedo, 2005. Acute renal failure in critically ill patients: a multinational, multicenter study. *Journal of the American Medical Association*, 294: 813-818.
- Ullah N, MA Khan, T Khan & W Ahmad, 2013. Bioactive traditional plant *Cinnamomum zeylanicum* successfully combat against nephrotoxic effects of aminoglycosides. *Bangladesh Journal of Pharmacology* 8: 15-21.
- Van Biesen W, R Vanholder and N Lameire, 2006. Defining acute renal failure: RIFLE and beyond. *Clinical Journal of the American Society of Nephrology*, 1: 1314-1319.