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L-Carnitine Reduces Blood Pressure and Oxidative Stress in Salt Loaded-Uninephrectomized Hypertensive Rats

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ABSTRACT

The aim of the present study was to investigate the hemodynamic and antioxidant actions of L-carnitine in salt-loaded, uninephrectomized (UNx) hypertensive rats. Twenty-four male albino rats were randomly divided into three groups. Group 1 rats underwent sham operations without performing nephrectomy, group 2 included uninephrectomized salt-loaded hypertensive rats, and in group 3 UNx salt-loaded rats were treated with L-carnitine (5 g/kg) in the diet. Statistical analysis revealed that systolic blood pressure (SBP), malondialdehyde (MDA), uric acid, urea, total protein, albumin and red distribution width (RDW) were significantly increased, while RBC count was reduced in 4% salt-loaded UNx hypertensive rats. Interestingly, L-carnitine markedly reduced SBP, MDA, serum albumin and RDW compared with 4% salt-loaded UNx hypertensive rats. This finding suggested that L-carnitine reduced the elevated SBP induced by Unx-4% NaCl rats, besides its antioxidant action through reduction of lipid peroxidation level.

Key words: Uninephrectomized salt-loaded hypertension, L-carnitine, hemodynamic, malondialdehyde, rats

INTRODUCTION

Hypertension is considered among the most common global leading cause of death. It could result in several complications such as cardiovascular diseases, cerebrovascular events and kidney failure. Several models have been proposed for induction of hypertension in experimental animals. Salt-loaded uni-nephrectomy (UNx) is among the experimentally induced models which cause hypertension, kidney injury, glomerulosclerosis, proteinuria, and tubulointerstitial damage (Wang *et al.*, 2020). The combination of UNx and NaCl loaded diet for up to 3-4 weeks has been confirmed as a model of hypertension induction in rats (Puyó *et al.*, 2021).

It has also been revealed that UNx could upregulate release of renin via stimulation of renal renin-angiotensin-aldosterone system and decline renal perfusion pressure. Therefore, it could lead to lack of adequate response of contralateral kidney against the elevated BP with pressure natriuresis, which might be due to angiotensin II elevation. Hence, it stimulates aldosterone secretion and renal vasoconstriction (Ames *et al.*, 2019). Furthermore, high NaCl diet intake causes chronically expansion in extracellular volume that leads to elevation of blood pressure and induction of cardiac output (Balafa and Kalaitzidis, 2021).

It has been found that a high salt intake drives oxidative stress. In a study on salt loaded hypertensive rats, it has been recorded that Ang II stimulates the action of nicotinamide-adenine dinucleotide phosphate oxides (NADPH) in renal cortical (Vrankova *et al.*, 2019), and medullary cells, and produces superoxide anion (Kuczeriszka and Wasowicz, 2022), which reduces nitric oxide synthase (NOS) bioactivity (Carlstrom and Montenegro, 2019).

L-carnitine (betahydroxy trimethyl butyric acid) is a tiny, water-soluble compound (molecular weight, 162 D) which was originally discovered in 1905. It's major function is transporting fatty acid in mitochondria and modulating toxic acyl-coenzyme A (acyl-CoA) level in the mitochondrial matrix (Longo *et al.*, 2016). Exogenous L-carnitine reduces the accumulation of acyl-CoA because of unavailability of natural esterase enzyme for removing accumulated acyl-CoA (Kepka *et al.*, 2020). L-carnitine intake in hemodialysis subjects improved their lipid metabolism

variables, red blood cell parameters and antioxidant status (Yang *et al.*, 2014), in addition to its anti-inflammatory action via reducing inflammatory biomarkers (Khalatbari-Soltani and Tabibi, 2015). The beneficial actions of L-carnitine supplementation have been revealed to reduce the clinical outcomes in coronary conditions such as angina pectoris, cardiomyopathy, and congestive heart failure (Mosawi, 2021). Furthermore, L-carnitine has been reported to play a major role in protecting the balance of the antioxidant status in an experimental contrast-induced nephropathy rat model (Boyacioglu *et al.*, 2014). The main purposes of the present investigation was to find out the role of L-carnitine as antioxidant and hypotensive agent in salt loaded uninephrectomized rats.

MATERIALS AND METHODS

Twenty-four male albino rats were used for this experiment. The rats weighed between 250 and 300 g and their age ranged between 7 and 10 weeks at the beginning of the experiment. All rats were kept and bred in the animal house belonging to Biology Dept., College of Science, Salahaddin University, Erbil, Iraqi Kurdistan region. Eight animals were kept in each plastic cage during the experimental period, bedded on wooden chips and housed under standard conditions (22±4°C and 12:12 dark/light cycle). The rats were supplemented with standard rat pellets and water *ad libitum*.

The current experiment was designated to investigate the action of L-carnitine on hemodynamic and renal function test variables in unilateral nephrectomized (UNx) salt loaded hypertensive rats. The experimental animals were randomly distributed into three groups, each with eight rats.

Group 1 Sham surgery : The rats of this group were undertaken for sham-operated surgery and received standard laboratory rat foods and water *ad libitum.*

Group 2 UNx +NaCl : The rats underwent left unilateral nephrectomy and were fed on 4% NaCl enriched diet and given tap water *ad libitum* for two months.

Group 3 Unx+ L-carnitine : The rats underwent left unilateral nephrectomy and fed on 4% NaCl enriched diet with L-carnitine (5 g/kg diet) and given tap water *ad libitum* for two months. L-carnitine (CAS Number: 541-15-1) was purchased from Cayman Chemical Company. The dose and duration of L-carnitine treatment were according to Zayed *et al.* (2021).

Ketamine hydrochloride (50 mg/kg B.W.) and xylazine (10 mg/kg B.W.) were injected to studied rats for anesthesia. Clippers were used to remove the ventral fur from the xiphoid process to the sub-umbilical region, and the clean abdominal region was prepped by applying two coatings of iodophor solution and let it to dry. A fenestrated drape was used to drape the area, and an incision in the midline was made applying a sterile scalpel blade (No. 10). After opening of visceral parts, the renal arteries were detected and isolated with two. Iris scissors were used to cut the arteries and ureter near to the hilus ligatures as feasible. The kidney was then removed out of its retroperitoneal area. Then, the visceral contents were gently replaced and sterile 3.0 chromic gut suture and 3.0 Ethilon monofilament nylon suture were used for suturing the incisions. The wound was disinfected with iodophor solution and the rats were placed into warmed recovery cages (Mehrvar et al., 2020).

The heart beat rate and blood pressure of the rats were measured using the tail-cuff method in all groups at the end of the experiment using a power Lab (AD Instruments, power lab 2/25). Rats were placed in a restraint chamber and warmed to an ambient temperature of 37-40°C, which took around 10-15 min, before being fitted with occluding cuffs and pneumatic pulse transducers on their tails. For each rat, five readings were taken, with the highest and lowest, as well as any related with excessive noise or animal movement, being deleted. A mercury column Sphygmomanometer was used as comparison to calibrate the apparatus.

Blood samples were taken by heart puncture into a 5 ml syringe and then divided into chilled tubes, either with ethylene diamine tetra acetic acid EDTA to be used for hematological tests, or without EDTA for biochemical tests.

Red blood cell (RBC), White blood cell (WBC), RBC indices and platelet indices were determined by using an automated hematology analyzer.

Malondialdehyde (MDA) was estimated using spectrophotometer. Briefly, 0.5 ml of 17.5% trichloroacetic acid (TCA) and 0.5 ml of 0.66%

(TBA) were added to a 150 µl serum sample, vortexed, then placed in boiling water for 45-60 min, and let to cool. About 0.5 ml of 70% TCA was added and let for 20 min in room temperature, and then centrifuged at 1000 rpm for 15 min. The supernatant was obtained for spectrophotometer readings at 532 nm (Kumar *et al.,* 2019).

Total protein of sera was estimated using Biuret method, through applying a colorimetric method. The measurement was obtained at 550 nm using a visible spectrophotometer (Biolab, France). The level of albumin was determined in all sera samples using a colorimetric method by obtaining the absorbance at 630 nm using a visible spectrophotometer (Biolob, France). The level of uric acid was measured in all sera samples using uricase method, the absorbance was obtained at 492 nm via applying visible spectrophotometer (Biolab, France).

The level of serum urea was measured by using a colorimetric method and the absorbance was obtaind at 600 nm using visible spectrophotometer from Biolab, France. The level of serum copper (cu^{+2}) was measured by using a colorimetric method and absorbance was obtained at 580 nm by using a visible spectrophotometer (Randox).

All of the obtained data were presented as means and standard error and the data analysis was performed applying GraphPad prism Version 9. One-way analysis of variance was used for testing the significance for comparing among the treatments and Turkey's test was applied as post hoc test. $P > 0.05$ was considered as significant difference.

RESULTS AND DISCUSSION

SBP was significantly increased in 4% salt-loaded uninephrectomized hypertensive rats (132.1±0.986 mm Hg) compared with the sham group (114.4±0.996 mm Hg). On the other hand, L-carnitine supplementation caused a marked decrease in SBP from (132.1±0.986 mm Hg) to (119.2±1.016 mm Hg; Fig. 1a). Meanwhile, non-significant changes were observed among all the treated groups regarding the heart rate (HR; Fig. 1b). In the present study, experimental hypertension was produced by unilateral nephrectomy (UNx) along with 4% NaCl enriched diets for eight weeks. The elevated arterial pressure led to increased blood flow

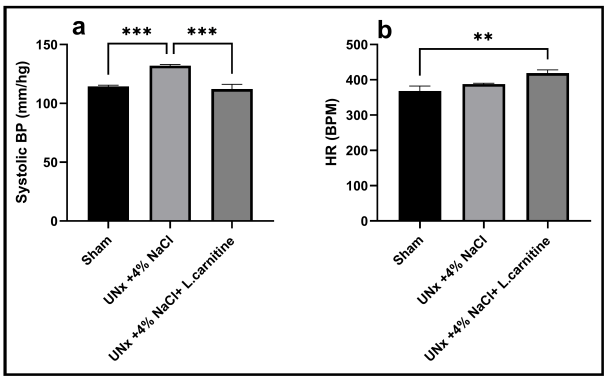

Fig. 1. Effect of L-carnitine on (a) Systolic blood pressure (SBP) and (b) Heart rate (HR) in 4% salt-loaded, uninephrectomized hypertensive male albino rats.

via the kidneys, which declined the ratio of renin secretion to a significant lower level. Low levels of plasma renin activity were found frequently in essential hypertension (HT), the state known as low-renin essential HT (LREH; De Silva and Faraci, 2023). In LREH, the aldosterone plasma level was normal (De Silva and Faraci, 2023). The increased SBP in Unx-salt-loaded rats may be due to the decreased nitric oxide synthase enzyme activity in rats induced with salt-sensitive hypertension (Kim *et al.,* 2019). Moreover, elevated production of superoxide by NADPH oxidase was recorded in aortic rings of NaCl induced hypertensive experimental animals (García-Redondo *et al.*, 2016).

The study showed that L-carnitine administration (5 g/kg) for eight weeks significantly reduced SBP as compared to UNx-salt loaded rats, which could be explained via reduction of plasma Ang II concentration. The possible mechanism of reduction might be due to the stimulatory role of L-carnitine in NO production (Wang *et al.,* 2018).

Statistical analysis revealed that MDA was significantly increased in 4% salt loaded uninephrectomized hypertensive rats (8.728±1.055 µmol/l) compared with the sham group (4.743±0.456 µmol/l). Supplementation with 5 g/kg of L-carnitine caused significant reductionin the MDA (4.512±0.184 µmol/l) compared to the model group (Fig. 2b). The current results showed a higher level of MDA as a marker of lipid peroxidation in UNx-salt-loaded rats. Moreover, significant correlation existed between excess sodium intake and MDA in salt sensitive hypertensive rats (Basta *et al.*, 2022). The findings revealed that oral L-

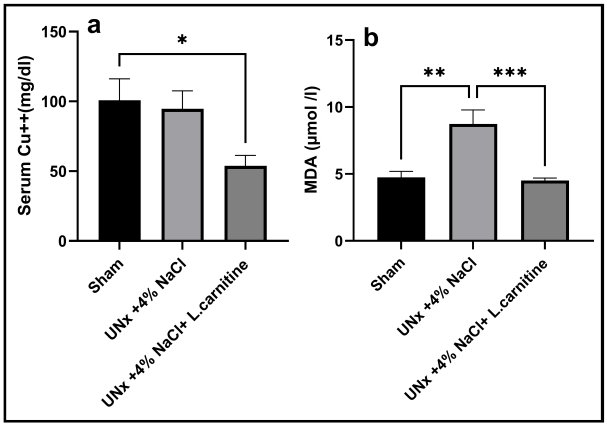

Fig. 2. Effect of L-carnitine on (a) Serum copper (Cu++) and (b) Malondialdehyde (MDA) in 4% salt-loaded, uninephrectomized hypertensive male albino rats.

carnitine administration decreased the serum MDA level. Originally, the reducing influence of L-carnitine administration on plasma MDA was previously suggested in high fructose-fed insulin resistant rats (Hussein *et al.*, 2014) and in some other clinical trials related to hypertension (Lee *et al.*, 2015). The reduced serum MDA by L-carnitine might be due to the stimulation of fatty acid transport into mitochondria for energy production, thereby lowering the availability of lipids for peroxidation. In addition to its antioxidant impact, especially through improving glutathione status (ElGendy and Abbas, 2014). However, the estimation of MDA in serum without having data of MDA within the target tissues was regarded as one of the limitations of the present study.

Serum Cu^{++} was not significantly decreased in 4% salt-loaded uninephrectomized hypertensive rats (94.68±12.83 mg/dl) compared with the sham group (100.8±15.34 mg/dl). However, supplementation with L-carnitine caused a marked decrease in the serum Cu^{++} (53.84±7.431 mg/dl; Fig. 2a). A significant decrease was detected in serum copper in 4% Unx-salt-loaded rats administered with 5 g/kg of L-carnitine. No data were available about the reducing action of L-carnitine administration on the serum copper level in hypertensive experimental models.

Unilateral nephrectomy (UNx) and 4% NaCl intake for eight weeks significantly increased the concentration of serum total protein mean values (5.376±0.261 g/dl) when compared with sham-operated surgery (4.515±0.214). Serum concentration of total protein did not change significantly by dietary intake 5 g/kg L-carnitine (4.810±0.112 g/dl) when compared with the UNx-4% NaCl group (Fig. 3b). Serum total protein and albumin were markedly increased in 4% Unx-salt-loaded rats. There were no reports explaining how this elevation occurred. A possible mechanism was that Unx-salt-loading increased oxidative stress. Consequently, hepatocyte membrane damaged, as a result of tissue injury might cause this elevation.

Serum albumin mean values were significantly increased upon unilateral nephrectomy (UNx) and 4% NaCl intake (4.184±0.097 g/dl) when compared with sham-operated surgery (3.219±0.122 g/dl). L-carnitine did not restore the serum albumin level (Fig. 3a).

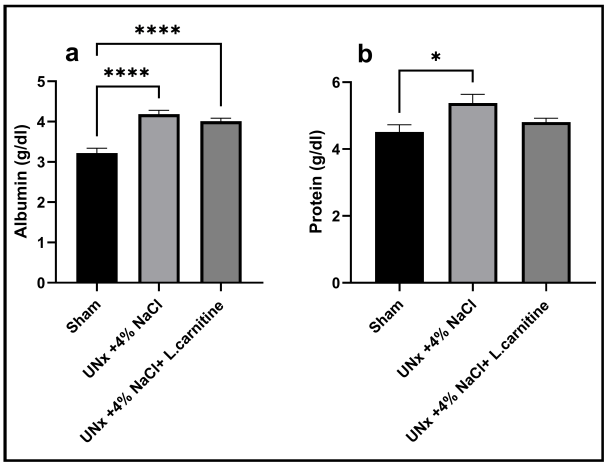

Fig. 3. Effect of L-carnitine on (a) Serum albumin and (b) Serum total protein in 4% salt-loaded, uninephrectomized hypertensive male albino rats.

Regarding renal function tests, unilateral nephrectomy (UNx) and 4% NaCl treatment significantly elevated both serum uric acid and serum urea concentrations, with mean values of 1.364±0.191 and 41.81±3.495 mg/dl, respectively, whereas L-carnitine significantly restored the level of serum urea (35.34±1.601; Fig. 4a and b). The results revealed that a considerable increase in plasma urea and uric acid levels was reported in Unx-salt rats, and this may be due to kidney damage caused by the oxidative stress. Uninephrectomized rats treated with salt diet showed a marked decrease in RBC as compared with the sham group. Unx-salt-loaded caused mineralocorticoid receptor activation that led to an increase of tissue oxidative stress and vascular

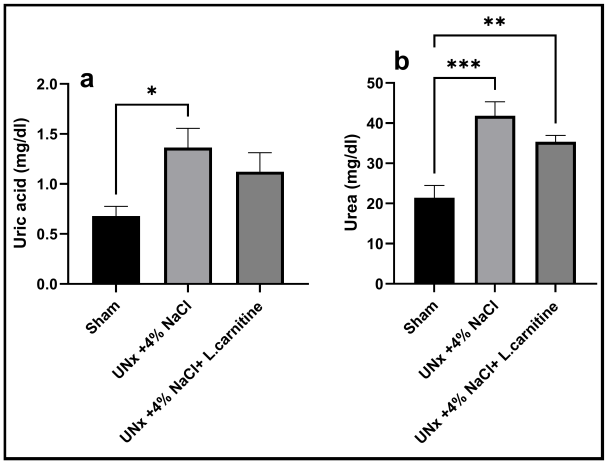

Fig. 4. Effect of L-carnitine on renal function variables in 4% salt-loaded, uninephrectomized hypertensive male albino rats. (a) Significant elevation of uric acid was found in hypertensive model group, while (b). The elevated serum urea in hypertensive rats was significantly restored by L-carnitine treatment.

inflammation, which in turn increased IL-6 and TNF-α protein production by peripheral blood mononuclear cells and monocytes (Zhou et al., 2022).

The red blood cell count was significantly decreased (P<0.05) in 4% salt loaded uninephrectomized hypertensive rats (6.010±0.128 million/mm^3) compared with the sham group (6.625±0.200 million/mm^3). L-carnitine did not yield any significant change in the RBC count (6.091±0.068 10 12/l; Table 1). MCV, MCH and RDWa were all significantly increased in 4% salt loaded uninephrectomized hypertensive rats (59.31±0.749 fl), (18.88±0.268 pg) and (33.45±1.137 fl), respectively, and supplementation with L-carnitine caused reduction in all of these compared to the model group. There was no statistical difference in HB, PCV, MCHC, or RDW among the studied groups.

Normal rats chow with 4% NaCl and UNx treatment did not change significantly the WBC count of UNx rats (5.333±0.559 10^9/l) when compared with sham-operated surgery, while the WBC count was significantly decreased (P<0.01) by dietary intake of L-carnitine (3.085±0.23510^9/l; Table 2). There was no statistical difference in platelet (PLT) and platelet indices (PCT, MPV and PDW) among the studied groups. It was demonstrated that there was a strong association between high RDWa and the risk of adverse outcomes in patients with cardiovascular disease. Although RDWa was found to be higher in patients with coronary artery disease (Fava *et al.*, 2019), oxidative stress was also suggested to be another indicator of the prognostic value of RDWa (Vukicevic *et al.*, 2021).

Table 1. Effects of L-carnitine on RBC and RBC indices in uninephrectomized and 4% NaCl treated hypertensive rats

RBC related variables	Sham	UNx+4% NaCl	UNx+4%NaCl +L.carnitine
*RBC (10^{12}/l)	6.625±0.200^b	6.010±0.128^a	6.091±0.068^a
HB (g/dl)	11.433±0.450^a	11.35±0.283^a	10.84±0.275^a
PCV (%)	36.85±1.198^a	35.68±0.898^a	34.42±0.474^a
*MCV (fl)	55.16±1.117^a	59.31±0.749^b	56.52±0.216^a
*MCH (pg)	17.15±0.269^a	18.88±0.268^b	17.81±0.377^a
MCHC (g/dl)	31.13±0.665^a	31.88±0.562^a	31.51±0.655^a
RDW (%)	9.900±0.267^a	9.766±0.332^a	9.500±0.113^a
**RDWa (fl)	30.05±0.472^a	33.45±1.137^b	30.60±0.182^a

The same superscripts in a col. mean no statistical differences.

Table 2. Effects of L-carnitine on WBC and platelet and platelet indices in ninephrectomized and 4% NaCl treated hypertensive rats

Platelets variables	Sham	UNx+4% NaCl	UNx+4%NaCl +L.carnitine
**WBCs counts (10^9/l)	5.016±0.440^b	5.333±0.559^b	3.085±0.235^a
PLT (10^9/l)	683.6±24.44^a	659.0±37.53^a	679.2±36.42^a
PCT (%)	0.371±0.013^a	0.356±0.019^a	0.362±0.017^a
MPV (Fl)	5.466±0.071^a	5.450±0.042^a	5.371±0.064^a
PDW (Fl)	8.816±0.087^a	8.766±0.042^a	8.700±0.072^a

The same superscripts in a col. mean no statistical differences.

CONCLUSION

This study concluded that L-carnitine reduced the elevated BP induced by Unx-4% NaCl rats, and this could be relevant to its antioxidant properties, because it significantly decreased MDA levels.

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REFERENCES

Ames, M. K., Atkins, C. E. and Pitt, B. (2019). The renin-angiotensin-aldosterone system and its suppression. *J. Vet.Internal Med.* **33**: 363-382.

Balafa, O. and Kalaitzidis, R. G. (2021). Salt sensitivity and hypertension. *J. Hum. Hypertens* **35**: 184-192.

Basta, M., Saleh, S. R., Aly, R. G. and Dief, A. E. (2022). Resveratrol ameliorates the behavioural and molecular changes in rats exposed to uninephrectomy: Role of hippocampal SIRT1, BDNF and AChE. *J. Physiol. Biochem.* **2022**: 01-13.

Boyacioglu, M., Turgut, H., Akgullu, C., Eryilmaz, U., Kum, C. and Onbasili, O. A. (2014). The effect of L-carnitine on oxidative stress responses of experimental contrast-induced nephropathy in rats. *J. Vet. Med. Sci.* **76**: 01-08.

Carlstrom, M. and Montenegro, M. (2019). Therapeutic value of stimulating the nitrate-nitrite-nitric oxide pathway to attenuate oxidative stress and restore nitric oxide bioavailability in cardiorenal disease. *J. Inter. Med.* **285**: 02-18.

De Silva, T. M. and Faraci, F. M. (2023). The DOCA-salt model of hypertension for studies of cerebrovascular function, stroke and brain health. *Neural Repair: Methods and Protocols*. pp. 481-487. Springer.

ElGendy, A. A. and Abbas, A. M. (2014). Effects of warfarin and L-carnitine on hemostatic function and oxidative stress in streptozotocin-induced diabetic rats. *J. Physiol. Biochem.* **70**: 535-546.

Fava, C., Cattazzo, F., Hu, Z.-D., Lippi, G. and Montagnana, M. (2019). The role of red blood cell distribution width (RDW) in cardiovascular risk assessment: Useful or hype? *Ann. Translational Med.* **7**. *doi: 10.21037/atm.2019.09.58*.

García-Redondo, A. B., Aguado, A., Briones, A. M. and Salaices, M. (2016). NADPH oxidases and vascular remodelling in cardiovascular diseases. *Pharmacol. Res.* **114**: 110-120.

Hussein, S. A., Abd El-Hamid, O. M. and Hemdan, H. S. (2014). Protective effect of L-carnitine on metabolic disorders, oxidative stress, antioxidant status and inflammation in a rat model. *Int. J. Biol. Chem.* **8**: 21-36.

Kepka, A., Ochocinska, A., Borzym-Kluczyk, M., Skorupa, E., Stasiewicz-Jarocka, B., Chojnowska, S. and Waszkiewicz, N. (2020). Preventive role of L-carnitine and balanced diet in Alzheimer's disease. *Nutrients* **12**: 1987. *doi:10.3390/ nu12071987*.

Khalatbari-Soltani, S. and Tabibi, H. (2015). Inflammation and L-carnitine therapy in hemodialysis patients: A review. *Clin. Experiment. Nephrol.* **19**: 331-335.

Kim, S., Jo, C. H. and Kim, G. H. (2019). Effects of empagliflozin on nondiabetic salt-sensitive hypertension in uninephrectomized rats. *Hypertension Res.* **42**: 1905-1915.

Kuczeriszka, M. and Wasowicz, K. (2022). Animal models of hypertension: The status of nitric oxide and oxidative stress and the role of the renal medulla. *Nitric Oxide* **125**. *doi:10.1016/j.niox.2022.06.003*.

Kumar, N., Rai, A., Reddy, N. D., Shenoy, R. R., Mudgal, J., Bansal, P., Rao, C. M. and Sharma, N. (2019). Improved *in vitro* and *in vivo* hepatoprotective effects of liposomal silymarin in alcohol-induced hepatotoxicity in Wistar rats. *Pharmacol. Rep.* **71**: 703-712.

Lee, B. J., Lin, J. S., Lin, Y. C. and Lin, P.-T. (2015). Antiinflammatory effects of L-carnitine supplementation (1000 mg/d) in coronary artery disease patients. *Nutrition* **31**: 475-479.

Longo, N., Frigeni, M. and Pasquali, M. (2016). Carnitine transport and fatty acid oxidation. *BBA -Mol. Cell Res.* **1863**: 2422-2435.

Mehrvar, S., Foomani, F. H., Shimada, S., Yang, C., Zheleznova, N. N., Mostaghimi, S. and Ranji, M. (2020). The early effects of uninephrectomy on rat kidney metabolic state using optical imaging. *J. Biophotonics* **13**. e202000089.

Mosawi, A. J. (2021). The uses of L-carnitine in cardiology. *Int. J. Biomed. Res.* **1**: *doi: 10.31579/IJBR-2021/006*.

Puyó, A. M., Kouyoumdzian, N. M., Prince, P. D., Robbesaul, G. D., Kim, G., Pandolfo, M.,

Fernández, B. E., Galleano, M. L. and Choi, M. R. (2021). Renal oxidative stress in a model of hypertension induced by saline overload: Role of chloride anion. *J. Hypertension* **39**: e34.

Vrankova, S., Zemancikova, A., Torok, J. and Pechanova, O. (2019). Effect of low dose L-NAME pretreatment on nitric oxide/reactive oxygen species balance and vasoactivity in L-NAME/salt-induced hypertensive rats. *J. Phys. Pharm.* **70**: 535-544.

Vukicevic, P., Klisic, A., Neskovic, V., Babic, L., Mikic, A., Bogavac-Stanojevic, N. and Kotur-Stevuljevic, J. (2021). New markers of platelet activation and reactivity and oxidative stress parameters in patients undergoing coronary artery bypass grafting. *Oxid. Med. Cell. Long.* **2021**. *doi:10.1155/2021/8915253.*

Wang, Q., Ishizawa, K., Li, J., Fujii, W., Nemoto, Y., Yamazaki, O., Tamura, Y., Miura, Y., Nie, X. and Abe, R. (2020). Urinary phosphate-containing nanoparticle contributes to inflammation and kidney injury in a salt-sensitive hypertension rat model. *Comm. Biol.* **3**: 575. *doi:10.1038/s42003-020-01298-1.*

Wang, Z. Y., Liu, Y. Y., Liu, G. H., Lu, H. B. and Mao, C. Y. (2018). L-carnitine and heart disease. *Life Sci.* **194**: 88-97.

Yang, S. K., Xiao, L., Song, P. A., Xu, X., Liu, F. Y. and Sun, L. (2014). Effect of L-carnitine therapy on patients in maintenance hemodialysis: A systematic review and meta-analysis. *J. Nephrol.* **27**: 317-329.

Zayed, E. A., Shoka, A. A. A., El-Shazly, K. A., El-Mosallamy, A., Zayed, A. A. and Abd El-Latif, H. A. (2021). Treatment with omega-3 and L-carnitine improve cardiac and renal complications in metabolic syndrome-induced rats. *Asian J. Cardiol. Res*. pp. 27-37.

Zhou, Q., Li, J., Xiang, Z., Zou, H. and Shao, X. (2022). Amelioration of renal injury by resveratrol in a rat renal transplantation model via activation of the SIRT1/NF-κB signaling pathway. *BioMed Res. International* **2022**. *doi:10.1155/2022/7140961.*