

Effect of Lead Intoxication and Fresh Camel Milk Treatment on Kidney Functions Indices in Albino Rats

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ABSTRACT

Aims: The unique characters of camel's milk make it used extensively in the field of medicine as antidiabetic, anti-microbial, and hepatoprotective agent. The few of studies demonstrating the protective effect of camel's milk against nephrotoxicity compound was the main reason beyond the conduction of the current experiment which aimed to investigate the protective effects of camel's milk against lead induced nephrotoxicity.

Methodology: Therefore, eighteen male albino rats were divided into three groups of six, The first was a control group, the second received orally lead acetate in water as (2ml saline containing 5 mg/Kg body weight of lead acetate) and the third received the same lead acetate dose and supplemented with 2ml of camel milk, the experiment lasted for three weeks. At the end of the experiment period, blood samples were collected for biochemical analysis.

Results: The present findings revealed that, exposure of animals to lead acetate caused a significant increase ($p < 0.05$) in the activities of uric acid and creatinine compared with the control group. Camel milk seemed to offer a marked improvement of both uric acid and creatinine compared with lead acetate group. The kidney parameters were recorded towards the normal values significantly.

Conclusion: The present study concluded that camel milk treatment may play a protective role against lead effect on kidney in albino rats. These protective effects were in the form of improving of kidney blood biochemical parameters of intoxicated albino rats.

Keywords: Camel Milk, Lead, Uric Acid, Creatinine, Urea.

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INTRODUCTION

The kidney is responsible for detoxification of the most of components that exist in the body. Lead is considered a heavy metal toxic chemical agent, if ingested or inhaled, lead and its compounds as lead acetate are poisonous to all living being.¹ Exposure to Lead inform severe changes in renal and endocrine systems.² A group of scientists, revealed that lead toxicity increased as the dose increased and high dose of lead caused toxicity in both liver and kidney.³ Other group of researcher stated that lead's effects on kidney damage are thought to play a major role in its effect on blood pressure.⁴ Since, kidney is the organ through which the excess salt and fluids are excreted. Consequently, impairment of ability of kidney to efficiently excrete salts and fluids can result in the rise in blood volume and, hence blood pressure.⁴

Ekong and colleagues reviewed, that lead contributed to kidney damage at concentration below 5 $\mu\text{g/dL}$ of Blood lead level (BLL), and 4.2 $\mu\text{g/dL}$ was strongly associated with chronic kidney disease.⁵ However, lead's effects on kidney damage are thought to play a major role in its effect on blood pressure. Classically, renal insufficiency is found in acute lead toxicity and is accompanied by abdominal pain, cognitive defects, peripheral neuropathy, arthralgias, anemia with basophilic stippling, and high PbBs $> 80 \mu\text{g/dL}$.⁶ Chronic nephropathy, which may progress to kidney failure, is the classic renal manifestation of lead toxicity. It appears to result from long-term, relatively high-dose exposure to lead that the cells lining the proximal tubules appear to be the tissue in the kidney most highly sensitive to lead.⁷ The evolution of lead nephropathy is usually silent. The central event appears to be

the progressive destruction of tubular cells and their replacement by fibrosis.⁸ In other studies, significant correlations exist between PbBs <10 µg/dL and elevations in serum creatinine; serum creatinine increased 0.14 mg/dL for every 10-fold increase in blood lead.⁹ In a longitudinal study of people with diabetes and hypertension, participants with high blood and bone lead levels were more likely to experience a decline in renal function.¹⁰ Elevated blood lead levels were linked to reduced glomerular filtration rates (an indicator of reduced kidney function).¹¹ Literature data on the effects of acute Pb exposure triggering oxidative stress in the kidney of animals are rare. The administration of lead acetate showed a significant ($p < 0.05$) increase in urea and creatinine concentration compared with other groups.¹² An extensive work to study the severe effects of lead toxicity toward the kidneys has been well-documented.¹³

The most described uses of camel's milk are as drug against several disorders as autoimmune diseases, jaundice, tuberculosis, asthma, anemia, piles and diabetes.¹⁴ and antimicrobial activities of camel's milk proteins were also investigated.¹⁵ In other hand, camel's milk has antitoxic effect against cadmium chloride^{16,17}, CCl₄¹⁸, Paracetamol¹⁹, Aluminum chloride.²⁰ Although, Khan and Alzohairy studied the protective effect of camel's milk against toxic agents induced hepatotoxicity, biochemical parameters such as Kidney biomarkers and lipoprotein profiles were not fully investigated.¹⁸ Therefore, in the present study, we investigated the protective effects of camel's milk against lead- induced nephrotoxicity in rats by assaying kidney functions; urea, uric acid and creatinine.

MATERIALS AND METHODS

Animals

This study was approval by Libyan Academy ethics review committee. Eighteen male Wister Albino rats (150-250 g body weight) were obtained from Biotechnology Research Center (BTRC), Twisha, Tripoli, Libya, and housed in the National Medical Research Center (NMRC), Al Zawiyah, Libya. The rats were kept in a controlled environment of 50-60% humidity at 25 °C with 12-hr light/dark period, and were treated gently. A standard rodent pellets consisting of a mixture of protein, fat, fibre, and ash were used to feed the rats. Diet and water supply were ad libitum. The rats were randomly distributed into three group, each of six animals, the experiment was carried out for three weeks.

Camel Milk

Camel's milk samples were collected in early morning daily from Camel's farm in Tajoura area (east of Tripoli city). Full milk is milked from camels by hand milking as normally practiced by the

farmers. Collected milk in bottles kept in cool boxes until transported to the laboratory.

Lead Acetate

The lead acetate (analytical grade purity) was purchased from Sigma-Aldrich (St. Louis, MO, USA).

Experimental Design Groups

Control Group: was under same room conditions, drank only water ad libitum.

Lead Acetate Group: Given a daily 2 mL dose of a normal saline contains 5 mg/kg body weight of lead acetate orally.

Lead Acetate + Camel Milk Group: Given a daily 2 ml dose of camel milk contains 5 mg/kg body weight of lead acetate orally.

On day 21, rats were anaesthetized with ketamine hydrochloride (10 mg/Kg). Blood samples were collected through open chest method, rats been euthanized immediately after blood collection. Serum collection plastic tubes (Additive clot activator and silicone coated interior, 10.0 ml volume) were used, these tubes supplied from BD Vacutainer®. The resultant serum was collected and stored at -80°C until analysed. Serum Uric acid, urea and creatinine concentration were determined using a standard kit (SEAC, Italy) by means of a UV spectrophotometer (SEAC, Italy). The data are expressed as mean \pm standard error ($n = 6$), n represents the number of Wister albino rat. Statistical analysis was performed student's t -test was used after (21), and $P < 0.05$ were considered statistically significant.

RESULTS

The daily observations showed no external or behaviour changes recorded during experiment with all groups eating and drinking similar amounts. The values of serum uric acid, creatinine and urea levels in group control, lead acetate-camel milk were presented in (Table 1). The results indicated that uric acid levels no significantly changes ($P > 0.01$) between control group, and lead acetate treatment groups (3.130 ± 0.248) and (2.725 ± 0.244) respectively. Administration of camel's milk concurrent with lead acetate resulted in a significant ($p < 0.05$) decrease (1.762 ± 0.258) compared with lead acetate group (Figure 1). There were no statistical ($p > 0.01$) differences in serum creatinine concentration between lead acetate and control group (2.756 ± 0.362 and 3.08 ± 0.246) respectively. However, the addition of camel milk to lead acetate gave lower values in comparison to lead acetate group (Figure 2). The results regarding the serum urea concentration were not significantly ($p > 0.01$) difference between the three treatment groups (42 ± 1.06 , 42.14 ± 3.94 and 39.45 ± 1.43) respectively for control, lead acetate and lead acetate - camel milk groups (Figure 3).

Table 1: Effects of exposure to lead acetate, and lead acetate + camel milk on Uric acid, Creatinine, and Urea (mean \pm standard deviation within eighteen male Wister albino rats ($n = 6$ per group))

Parameter	Control	Lead acetate	Lead acetate + camel milk
	Mean \pm SE	Mean \pm SE	Mean \pm SE
Uric acid (mg/dl)	3.130 \pm 0.248	2.725 \pm 0.244	1.762 \pm 0.258*
Creatinine (mg/dl)	3.080 \pm 0.246	2.756 \pm 0.362	1.621 \pm 0.030*
Urea (mg/dl)	42.00 \pm 1.06	42.14 \pm 3.94	39.45 \pm 1.43

*Mean value was significantly different to that at control and lead acetate group ($P < 0.05$), SE = standard error

Fig 1: Shows the effect of lead acetate and lead acetate concurrent with camel milk on Uric acid.
*Significant at ($P < 0.05$), compared with the lead acetate group.

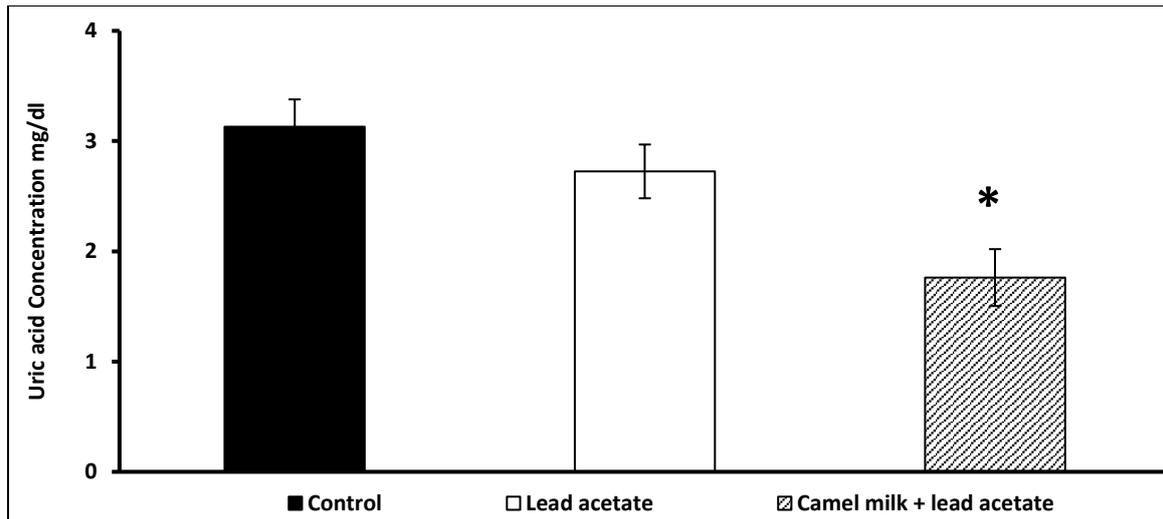


Fig 2: Shows the effect of lead acetate and lead acetate concurrent with camel milk on Creatinine.
*Significant at ($P < 0.05$), compared with the lead acetate group.

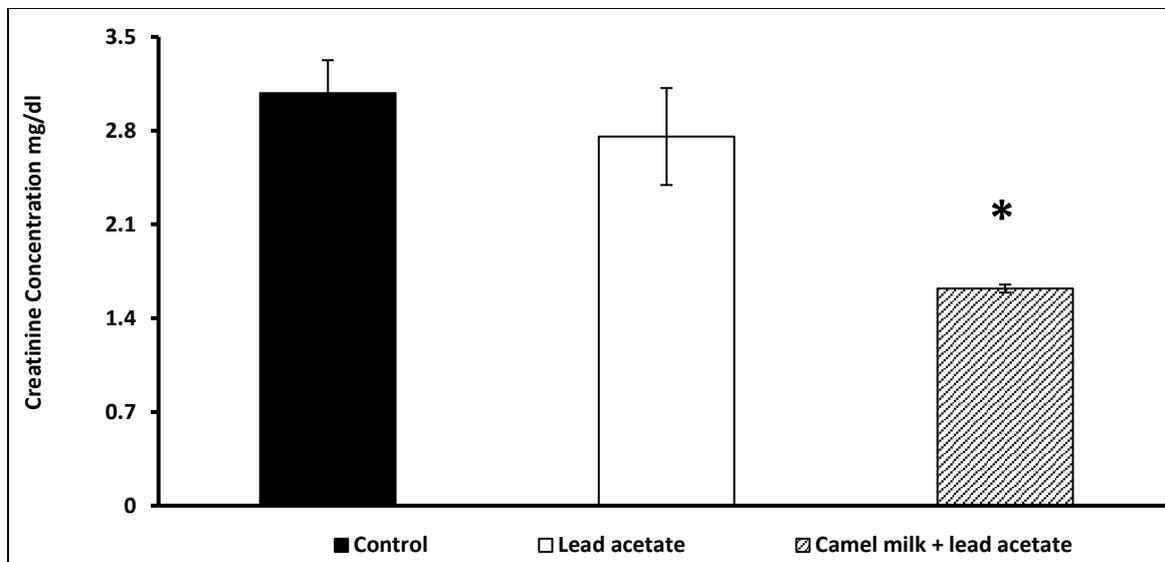
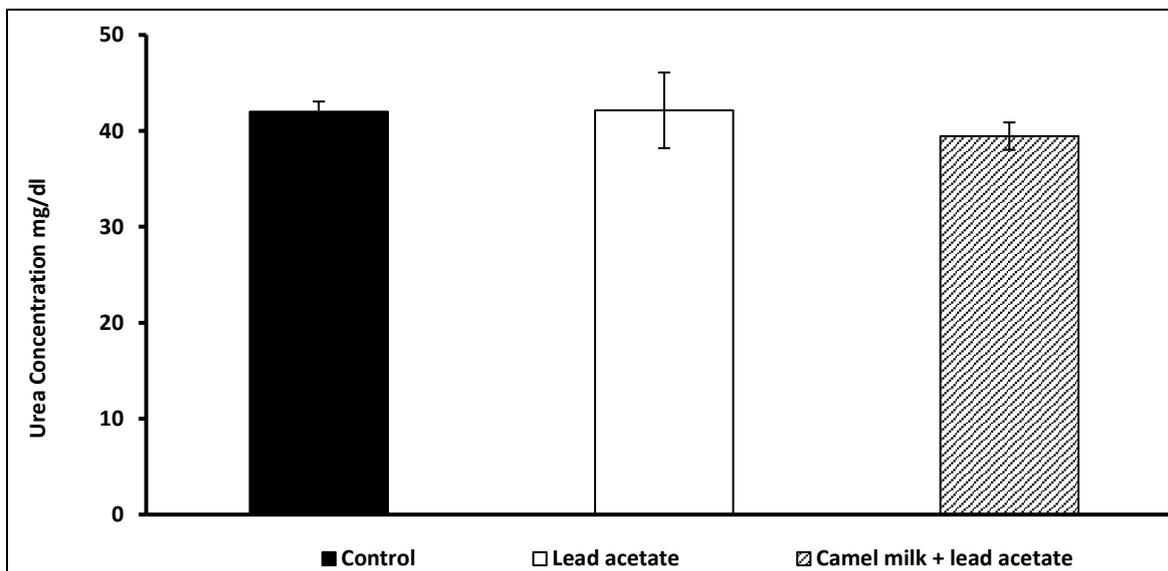


Fig 3: Shows the effect of lead acetate and lead acetate concurrent with camel milk on Urea.



DISCUSSION

Intoxication by lead has been associated with renal function impairment in several research works.^{22,23} A conclusive opinion not being reached up to now to prove that an excess of lead in the body may cause chronic renal failure, because the renal disease may take a longer time after acute symptoms. Therefore, urinary haemo-biochemistry is one of the important factors to provide an indication of the kidneys function. The increase in the serum of creatinine caused by lead intoxication resulted to renal function impairment could be due to intrinsic renal lesions, decreased perfusion of the kidney obstruction of lower urinary tract or due to deranged metabolic process caused by this metal.²⁴

A large number of papers were reported that exposure to lead acetate induces chronic and as well irreversible lead nephropathy (that is interstitial nephritis). However, studies on the effect of lead in cases of under nutrition are still lacking in the literature.²⁵ Rats treated with lead had the serum urea increased in acute and chronic intrinsic renal disease and when there is decreased effective circulating blood volume with decreased renal perfusion.²⁴ Ghorbe group concluded that oral administration of lead acetate significantly increased in the blood urea and serum creatinine.²⁶ It has been observed in this regards that the urinary volume is markedly increased in lead exposure group, and they stated that the increase of urine might be due to diuretic effect of lead or the high concentration of calcium in plasma, and that urinary pH did not changed as well the specific gravity. The damaging effect of lead exposure on kidneys has also been described by other authors.²⁷ Some works have reported increased serum concentrations of urea indicating reduced Glomerular Filtration Rate (GFR) in cadmium-exposed rats.²⁸

In our study revealed that lead acetate exposure didn't show any significant changes on urea, uric acid, and creatinine (no increase or decrease). However lead acetate with camel milk shows a significant decrease in both uric acid and creatinine ($P < 0.05$).

Therefore, our results may disagree with the previous studies that showed an increase in the values of uric acid and creatinine and it did agree with some. A group of researcher reported a significant decrease in creatinine with to lead acetate treated rats.²⁹ Other researchers, concluded that only (18.7%) of his sample group shows change in urea and that other parameters when exposed to lead shows normal levels, stating that one of the group had reduced creatinine clearance.³⁰ Other heavy metal cadmium reduced creatinine clearance and GFR among older cohorts of women.³¹ Lead was also found to be associated with reduced creatinine clearance.³² Borges and his group, reported that exposure to lead for 65 days didn't shows significant changes in urea and uric acid.³³ Supplementation of diabetic rats with camel milk for 30 days result in significantly reduced kidney function parameters.³⁴

Urea and uric acid are the principal waste products of protein catabolism. They are synthesized in the liver from the ammonia which produced as a result of amino acids de-amination³⁵, while, creatinine is the major waste product of creatine metabolism by muscle. In the kidney, creatinine is distilled by the glomerulus and excreted by the tubules and only free Creatinine appears in the blood serum.³⁶

Al-Shamsi in 2006 stated that the presence of vitamin C significantly reduced the blood urea nitrogen (BUN) levels in diabetic rats.³⁷ It is well confirmed that camel milk has a high

content of vitamins and minerals as well immunoglobulin content. A researchers in their study concluded that camel milk content of vitamin C may reach up to three times higher than dairy milk and about ten times higher in iron.³⁸ Same group also found a high content of unsaturated fatty acids, and vitamin B complex. A previous work done by Camello Safari in 2012 revealed that levels of potassium, magnesium, iron, copper, manganese, sodium and zinc are higher than in cow's milk.³⁹ The beneficial use of camel milk in improving the growth rate and liver function was confirmed lately by the work of Draid in 2016.⁴⁰

CONCLUSION

The ameliorated effect was more obvious with camel milk treatment on uric acid and creatinine approached those of control. The lead acetate treated animals with camel milk reduced the uric acid and creatinine by as much 43% and 47% respectively to the control.

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