

Camel's Milk Protects against Aluminum Chloride-Induced Toxicity in the Liver and Kidney of White Albino Rats

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Abstract: Problem statement: Aluminum chloride (AlCl_3) is commonly used in daily life but it can be potentially toxic. Therefore, the present study was carried out to investigate the protective effects of camel's milk against aluminum-induced biochemical alterations and oxidative stress in the liver and kidney of white albino rats. **Approach:** White albino male rats (230-250 g) were divided into three groups of 10 rats: a control group treated with normal saline, the AlCl_3 -treated group and the camel's milk- AlCl_3 -treated group. The AlCl_3 treated group received 0.5 mg kg^{-1} of AlCl_3 orally. The camel's milk- AlCl_3 -treated group was fed 1 mL of fresh camel's milk 10 minutes prior to the administration of oral AlCl_3 . All rats were treated every day for 30 days. Liver and kidney biochemical serum parameters were analyzed. Lipid peroxidation, as determined by the tissue concentrations of thiobarbituric acid reactive substances (TBARS) and hydrogen peroxide (HP), and the oxidative stress status, as measured by glutathione (GSH), superoxide dismutase (SOD) and catalase (CAT) activity, were evaluated in the kidney and liver of treated rats. **Results:** Data showed that the oral administration of AlCl_3 resulted in statistically significant increases in the serum levels of urea, creatinine, bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), cholesterol and triglycerides; the total amount of protein and albumin were also significantly decreased. However, these parameters were within normal levels in the rats given camel's milk prior to AlCl_3 . Additionally, oral administration of AlCl_3 induced lipid peroxidation in the liver and kidney, which was indicated by a significant increase in lipid peroxidation biomarkers (TBARS and HP) and a significant decrease in the activities of GSH, SOD and CAT. In all rats treated with camel's milk before being given AlCl_3 , lipid peroxidation and oxidative stress parameters were within normal levels. **Conclusion:** Treatment with camel's milk prior to AlCl_3 exposure alleviates AlCl_3 -associated hazards and protects the kidney and liver from AlCl_3 toxicity.

Key words: Aluminum chloride, camel's milk, kidney, liver, rats, toxicity

INTRODUCTION

Aluminum, which is the most abundant metal and comprises about 8% of the Earth's crust, is found in combination with oxygen, silicon, fluorine and other elements in the soil, rocks, clays and gems^[1]. It has no known biological function^[2]. Presently, aluminum utensils are widely used throughout the world, especially in developing countries^[3]. The use of such tools may increase an individual's aluminum exposure, particularly when these are used with salty, acidic or alkaline foods^[4].

Additionally, aluminum and its salts are commonly used in daily life as it was believed that it was non-toxic and was quickly excreted in the urine. However, this element can negatively impact human health^[5].

Aluminum chloride (AlCl_3) can be found in food products and in drinking water derived from both natural sources and treatment methods^[6]. The primary sources of aluminum exposure are corn, yellow cheese, salt, herbs, spices, tea, cosmetics, cookware, utensils and containers. Furthermore, it is widely used in food additives and toothpaste^[7]. Aluminum compounds are widely used in medicines, e.g., antacids, phosphate binders, buffered aspirins, vaccines and injectable allergens^[8-10]. Environmental pollution with different aluminum-containing compounds, especially industrial waste water, exposes people to higher than normal levels of aluminum^[11]. Particulate matter distributed by cement-producing factories contains a high amount of aluminum and populations residing near these facilities are exposed to this pollution^[12].

Aluminum is potentially toxic to humans. The Agency for Toxic Substances and Disease Registry (ATSDR)^[13] reported that aluminum is distributed mainly in the bone, liver, testis, kidneys and brain. In patients on dialysis^[14] or on long-term total parenteral nutrition^[15], this metal accumulates in different organs. The toxicological effects of aluminum in humans include encephalopathy^[14], bone disease^[16], anemia^[17] and skeletal system disease^[18]. Furthermore, aluminum is possibly a contributing factor in the development of Alzheimer's disease^[19]. However, this remains contradictory^[18,20].

Camel's milk is different from other ruminant milk; it is low in cholesterol, sugar and protein but high in minerals (sodium, potassium, iron, copper, zinc and magnesium), vitamins A, B2, C and E, and contains a high concentration of insulin^[21]. It has no allergic properties and can be consumed by lactase-deficient individuals and those with a weakened immune system.

In fact, this milk is believed to have medicinal properties. In Sahara, fresh butter made from camel's milk is often used as a base for medicines. Other products also developed with camel's milk include cosmetics or pharmaceuticals. A series of metabolic and autoimmune diseases are successfully being treated with camel's milk. Furthermore in India, camel's milk is used therapeutically to treat dropsy, jaundice, problems of the spleen, tuberculosis, asthma, anemia, piles and diabetes^[22]. A beneficial effect of raw camel's milk has been observed in chronic pulmonary tuberculosis patients^[23]. Also, in repeated trials, a 30-35% reduction in the daily insulin dose required by patients with type 1 diabetes was observed in response to treatment with raw camel's milk^[24].

To the best of our knowledge, the therapeutic effect of camel's milk against AlCl₃-induced toxicity has not been examined. Therefore, in the current study, we evaluated the protective effects of camel's milk against AlCl₃ toxicity in the liver and kidney.

MATERIALS AND METHODS

Camel's milk samples: Daily milk samples were collected early in the morning from camel farm in the Abha area (Southeastern Saudi Arabia). Milk was collected from camels by hand milking as normally practiced by the farmers. The samples were collected in sterile screw bottles and kept in cool boxes until transported to the laboratory.

Chemicals: AlCl₃ was purchased from Aldrich Chemical company (Milwaukee, WI, USA).

Determination of AlCl₃ daily dose: In 1989, the FAO/WHO Expert Committee on Food Additives reported that the daily intake of aluminum in children was between 2 and 6 mg, and in adults, it varied between 6 and 14 mg^[25-27]. Therefore, the daily intake of aluminum in an adult with a mean body weight 70 kg is between 0.1 and 0.2 mg kg⁻¹ body weight. According to the guidelines published by the Drugs Institute^[28], established from animal studies, the dosage for rodents should be 4- to 10-fold higher than a human dose. In our study, rats received a daily oral dose of 0.5 mg AlCl₃ [AlCl₃ × 6 H₂O]/kg of body weight. This dose was a 6-fold excess over the minimum dose and 2.8-fold over the maximum dose and, on average, 4-fold higher than the human dose.

Experimental design: White albino male rats (230-250 g) were supplied by the animal house at the medical school of King Khalid University. The rats were housed in standard plastic cages (10 rats/cage) in an environmentally controlled room with a constant temperature of 25-27°C and 12 h light/dark cycle. The rats were fed a "standard lab diet" and given *ad libitum* access to food and water. The Physiology Department committee of King Khalid University approved the design of the experiments, and the protocol follows their guidelines. Three groups of 10 rats were used for the experiments. All treatments were given, using a gavage needle, everyday for 30 days. The groups were treated as follows: Group 1, the Control group, received a daily dose of 1 mL normal saline; Group 2, the AlCl₃-treated group, received 1 mL dose of a solution containing 0.5 mg kg⁻¹ body weight of AlCl₃ orally daily; Group 3, the Camel's milk-AlCl₃ treated group, was treated daily with an oral dose of 1 mL camel's milk followed 10 min later by oral administration of 1 mL AlCl₃ (0.5 mg kg⁻¹) solution.

Collection of blood serum: At the end of day 30, the animals were subjected to over-night fasting before being sacrificed by cervical dislocation and blood samples were collected directly into tubes and were centrifuged at 3000 rpm for 10 min to obtain serum.

Preparation of liver and kidney homogenate: The liver and kidney were quickly removed, washed in ice-cold, isotonic saline and blotted individually on ash-free filter paper. The tissues were then homogenized separately in 0.1 M Tris-HCl buffer, pH 7.4, using a Potter-Elvehjem homogenizer at 4°C and a diluting

factor of four. The crude tissue homogenate was then centrifuged at 9,000 rpm for 15 min in a cold centrifuge. The supernatant was collected and kept at 20°C until used for estimating lipid peroxidation, as determined by plasma concentration of thiobarbituric acid reactive substances (TBARS) and hydrogen peroxide (HP) levels, and the oxidative stress status, as measured by glutathione (GSH), superoxide dismutase (SOD) and catalase (CAT) activity.

Physiological and biochemical serum parameter analyses: Creatinine, urea, albumin, protein, bilirubin, cholesterol and triglyceride levels were evaluated as described previously by other groups^[29-34]. Additionally, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) were assayed using commercial kits (Quimica Clinica Aplicada SA Spain). The activity of serum lactate dehydrogenase (LDH) was determined using the method described by Martinek^[35].

Estimation of lipid peroxidation and oxidative stress parameters in tissue homogenate:

Estimation of TBARS: The concentration of TBARS in the liver and kidney homogenate was determined using the method described by Okhawa^[36]. In brief, the reaction mixture contained 0.1 mL tissue homogenate, 0.2 mL sodium dodecyl sulfate, 1.5 mL acetic acid and 1.5 mL aqueous solution of TBA. The pH of 20% acetic acid was pre-adjusted with 1 M NaOH to 3.5. The mixture was made up to 4 mL with distilled water and heated at 95°C for 1 h, in a water bath. After cooling, 1 mL of distilled water and 5 mL of a mixture of n-butanol and pyridine (15:1) were added and this was shaken vigorously using a vortex mixer. The absorbance of the upper organic layer was read at 532 nm. The values were expressed as mM/100 g of tissues.

Estimation of HP: The estimation of HP was done using the method described by Jiang^[37], in which 0.1 mL tissue homogenate (supernatant) was treated with 0.9 mL FOX reagent (88 mg butylated hydroxytoluene, 7.6 mg xylenol orange and 9.8 mg ammonium iron sulfate added to 90 mL methanol and 10 mL 250 mM sulfuric acid) and incubated at 37°C for 30 min. The color development was read at 560 nm. HP levels were expressed as mM/100 g of tissues.

Estimation of GSH: The GSH content of the liver and kidney homogenate was measured at 412 nm using the method described by Sedlak and Lindsay^[38]. The homogenate was precipitated with 50% trichloroacetic acid and then centrifuged at 1000 rpm for 5 min. The

reaction mixture contained 0.5 mL of supernatant, 2.0 mL of Tris-EDT A buffer (0.2 M; pH 8.9) and 0.1 mL of 0.01 M 5,5'-dithio-bis-2-nitrobenzoic acid. The solution was kept at room temperature for 5 min and then read at 412 nm on the spectrophotometer. The values were expressed as mg/100 g of tissues.

Estimation of CAT activity: CAT activity was assayed using a commercially available Catalase Activity Assay Kit (Biovision, K773-100), according to the manufacture's instruction.

Estimation of SOD activity: The activity of hepatic SOD was assayed using a commercially available SOD Activity Assay Kit (Biovision, K335-100), according to the manufacture's instruction.

Statistical analysis: Data are given as the mean \pm SD. Student's t-test was used to determine if the difference observed among various treatment groups at individual time points was significant.

RESULTS

Oral administration of AlCl₃ for 1 month resulted in statistically significant increases in urea, creatinine and bilirubin and decrease in both the total protein and albumin concentrations when compared to the serum from saline-treated rats (Table 1). However, the oral administration of camel's milk prior to treatment with AlCl₃ maintained these parameters within normal levels.

Furthermore, the levels of cholesterol and triglycerides in the serum of AlCl₃-treated were significantly higher than in the control-treated animals (Table 2). Administration of camel's milk prior to AlCl₃ resulted in a highly significant reduction to near normal levels for serum lipid profiles when compared to AlCl₃ treated rats (Table 2).

Evaluation serum levels of AST, ALT, ALP and LDH demonstrated that there was a highly significant increase in the activities of all enzymes in the serum of rats treated with AlCl₃ compared to control rats, while rats treated with camel's milk and AlCl₃ showed normal activities of these enzymes (Table 3). There was a significant increase in the TBARS and HP levels in the liver and kidneys of the AlCl₃-treated rats (Table 4). In contrast, oral administration of camel's milk and AlCl₃ resulted in normal levels. Additionally, the levels of enzymatic (SOD, CAT) and non-enzymatic (GSH) components of the oxidative system in the liver and the kidneys of experimental rats were also impacted by AlCl₃ exposure.

Table 1: Serum biochemistry of rats treated with AlCl₃ or camel's milk + AlCl₃

Parameter	Control	AlCl ₃	Camel's milk + AlCl ₃
Total protein (g dL ⁻¹)	6.24±0.450	4.68±0.310*	7.20±0.36*
Albumin (g dL ⁻¹)	4.25±0.120	3.20±0.168*	5.10±0.19*
Urea (mg dL ⁻¹)	31.60±3.110	52.44±4.10*	31.70±3.65*
Creatinine (mg dL ⁻¹)	0.60±0.028	1.34±0.132*	0.64±0.115*
Bilirubin (mg dL ⁻¹)	0.75±0.011	1.62±0.069*	0.73±0.060*

Note: Values are given as mean ± SD for groups of six animals each. Values are statistically significant, *, p<0.05. AlCl₃-treated rats were compared with control rats; camel's milk + AlCl₃-treated rats were compared with AlCl₃-treated rats

Table 2: Serum lipid profiles of rats treated with AlCl₃ or camel's milk + AlCl₃

Parameter (mg dL ⁻¹)	Control	AlCl ₃	Camel's milk + AlCl ₃
Cholesterol	148.0±4.9	198.6±2.3*	150.0±2.4*
Triglycerides	91.7±3.3	133.5 ± 2.06*	91.8±1.09*

Note: Values are given as mean ± SD for groups of six animals each. Values are statistically significant, *, p<0.05. AlCl₃-treated rats were compared with control rats; camel's milk + AlCl₃-treated rats were compared with AlCl₃-treated rats

Table 3: Changes in the activities of serum AST, ALT, ALP and LDH in rats treated with AlCl₃ or camel's milk + AlCl₃

Parameter (U L ⁻¹)	Control	AlCl ₃	Camel's milk + AlCl ₃
AST	43.4±1.75	67.40±1.37*	44.9±1.63*
ALT	27.0±1.79	65.38±2.12*	29.9±2.09*
ALP	45.0±1.72	78.90±2.03	45.8±2.36*
LDH	734.2±38.1	1160.80±33.7*	762.1±32.8*

Note: Values are given as mean ± SD for groups of six animals each. Values are statistically significant, *, p<0.05. AlCl₃-treated rats were compared with control rats; camel's milk + AlCl₃-treated rats were compared with AlCl₃-treated rats

Table 4: Changes in the levels of TBARS, HP, GSH and the activity of CAT and SOD in the liver and kidney of rats treated with AlCl₃ or camel's milk + AlCl₃

Parameter	Control	AlCl ₃	Camel's milk + AlCl ₃
Liver			
TBARS ^a	0.87±0.058	2.39±0.188*	0.88±0.080*
HP ^b	85.30±2.920	119.20±4.890*	92.30±4.270*
GSH ^c	66.00±1.430	19.40±0.910*	55.72±1.270*
CAT ^d	76.70±1.480	47.80±1.200*	72.70±0.707*
SOD ^e	13.20±0.610	8.50±0.370*	12.80±0.920*
Kidney			
TBARS ^a	0.66±0.040	1.96±0.041*	0.70±0.024*
HP ^b	68.30±2.760	117.20±2.220*	72.50±2.210*
GSH ^c	44.20±1.670	30.20±0.560*	41.10±1.480*
CAT ^d	63.60±2.280	41.80±1.070*	61.10±1.750*
SOD ^e	7.12±0.096	3.15±1.312*	6.80±0.379*

Note: Values are given as mean ± SD for groups of six animals each. Values are statistically significant, *, p<0.05. AlCl₃-treated rats were compared with control rats; camel's milk + AlCl₃-treated rats were compared with AlCl₃-treated rats. ^aTBARS, mM/100 g tissue; ^bHP, mM/100 g tissue; ^cGSH, mg/100 g protein; ^dCAT, U mg⁻¹ protein; ^eSOD, U mg⁻¹ protein

In rats treated with AlCl₃ alone, the activities of these proteins were decreased in comparison to the control group; while the oral administration of camel's milk prior to AlCl₃ treatment resulted in a significant

increase in SOD, CAT and GSH activity compared to the AlCl₃-treated rats.

DISCUSSION

Aluminum is potentially toxic to humans and animals. It is present in many manufactured foods, medicines and, for purification purposes, it is also added to drinking water^[39]. The present study investigated the protective effects of camel's milk against the harmful effects of AlCl₃ on the liver and kidney of white albino rats through the analysis of multiple biochemical serum parameters, lipid peroxidation and oxidative stress in these organs.

Most studies examining the toxic effects of AlCl₃ in animals have administered this compound intraperitoneally or parenterally, which does not represent the main route of human exposure^[40]. Aluminum enters the body via two major routes: pulmonary and oral. Although only a small portion of aluminum is absorbed through the gastrointestinal tract, oral intake is associated with the greatest toxicological implications^[40]. For this reason, our current study evaluated orally administered AlCl₃.

It has been reported that animals exposed to AlCl₃ displayed hepatic necrosis, which was indicated by an increase in serum levels of liver-specific enzymes including AST and ALT^[41-43]. This was attributed to the DNA and/or RNA binding potential of aluminum, which may inhibit the function of important enzymes, such as hexokinase, acids, alkalines, phosphatases and phosphodiesterases^[44]. In our study, liver damage was addressed through biochemical assays. Four separate liver enzymes, including AST and ALT, which, together, are known as transaminases, ALP, which is a cholestatic liver enzyme, and LDH, are reliable indicators of liver function. AST and ALT are critical enzymes for biological processes^[25]. An increase in serum AST and ALT in rats treated with AlCl₃ was in agreement with previous findings demonstrating that AlCl₃ exposure promoted liver necrosis^[39, 41, 42]. AST is released in to the plasma from the injured hepatic cells. Also, an elevated serum level of ALT is indicative of liver disease, as this enzyme is present in large quantities in the liver and increases in the serum following hepatocellular degeneration or destruction. Therefore, increases in the serum level of these enzymes suggests liver damage and alterations in liver function. Because it is a membrane-bound enzyme related to the transport of various metabolites, ALP is a sensitive biomarker of liver disease^[45]. Its activity is

dependent on energy metabolism and processes in the body and a decrease in its activity may indicate impaired cellular energy processing^[46]. AlCl₃-induced increases in ALP activity is in agreement with published results^[44,47]. Also, El-Demerdash^[39] reported that, in mice fed wheat containing an aluminum residue, the activity of these enzymes was also increased. Additionally, the aluminum-induced increase in the ALP may also be due to increased osteoblastic activity, which disrupts bone formation^[47].

LDH is another index of hepatotoxicity. In the serum of AlCl₃-treated rats, there was a significant increase in the LDH level compared to rats given normal saline, which is in agreement with published findings demonstrating that, in rats, hepatic damage by drugs and chemical substances is characterized by increased serum LDH^[48-50]. The increase in total bilirubin in the serum of AlCl₃-treated rats may be the result of decreased liver uptake (conjugation) or increased production from hemolysis^[51]. Our results demonstrated that oral administration of AlCl₃ caused a significant increase in serum cholesterol and triglycerides, which may indicate a loss of membrane integrity, disturbance of lipid metabolism and/or liver dysfunction^[52].

With regards to renal damage, biochemical findings in this study are in agreement with other studies^[11,14,47,53] demonstrating that the oral administration of AlCl₃ resulted in a significant increase in serum urea and creatinine and a substantial decrease in total protein and albumin levels compared to control animals. Collectively, these findings demonstrate that accumulation of aluminum in the kidneys may promote degeneration of renal tubular cells leading to nephrotoxicity^[11,14]. Szilagyi *et al.*^[47] reported that alterations in serum urea may be related to metabolic disturbances secondary to renal dysfunction. Alternatively, Katyal *et al.*^[53] published that the increase in urea serum concentration in aluminum-treated animals may be due to aluminum-mediated changes in liver function; urea is the end product of protein catabolism. Albumin is the most abundant protein in human plasma, representing 55–65% of the total protein. Rate at which albumin is synthesized in the liver depends on protein intake, which is regulated by the plasma albumin level. Most of the albumin filtered through the kidney glomeruli is reabsorbed by proximal tubule cells where lysosomal enzymes degrade the albumin into fragments that are returned to the circulation. The observed decrease in albumin in aluminum-treated rats may be due to changes in protein

synthesis and/or metabolism in the liver^[42]. Furthermore, aluminum may promote proteinuria by causing a nephritic syndrome or chronic glomerulonephritis.

It has also been suggested that the toxic effects associated with aluminum are due to the generation of Reactive Oxygen Species (ROS)^[39], which results in the oxidative deterioration of cellular lipids, proteins and DNA^[39,54]. Therefore, aluminum toxicity appears to be mediated, in part, by free-radical generation^[55,56]. A recent study demonstrated that aluminum may alter the activity of a number of tissue antioxidative enzymes, such as xanthine oxidase, GSH, SOD^[55]. Our data support this hypothesis; both TBARS and HP levels were found to be elevated in AlCl₃-treated rats while GSH, SOD and CAT activity were decreased in the liver and kidney. These observations are similar to previously published findings demonstrating that aluminum intake promoted oxidative stress^[57-60]. Although aluminum is not a transition metal, and therefore, cannot initiate peroxidation, many studies have searched for a correlation between aluminum accumulation and oxidative damage in tissues^[60-62]. An *in vitro* study indicated that aluminum greatly accelerates iron-mediated lipid peroxidation^[62]. Another study reported that exposure to aluminum could promote disruptions in the mineral balance, resulting in aluminum ions replacing iron and magnesium, which would then lead to a reduction in Fe²⁺ binding to ferritin^[63]. Free iron ions released from biological complexes by aluminum can catalyze HP decomposition to hydroxyl radicals via Fenton's reaction^[63]. This high hydroxyl radical reactivity could initiate the peroxidation of membrane lipids, causing membrane damage. The primary effects of aluminum on the liver and kidney functions are thought to be mediated via damage to cell membranes. Lipid peroxidation of biological membranes leads to a loss of membrane fluidity, changes in membrane potential, an increase in membrane permeability and alterations in receptor functions^[60]. In the present report, we observed a significant increase in lipid peroxidation after AlCl₃ exposure, as measured in terms of TBARS and HP levels in the liver and kidney of the rats. These results are in agreement with many studies that also demonstrated a significant increase in TBARS and HP in the kidney, liver and the brain of rats after intoxication by aluminum salts^[53,60,63,64]. The increased lipid peroxidation is due to inhibition or a change in the activity of non-enzymatic and enzymatic components of the oxidative system, i.e., GSH, SOD and CAT, in the

liver and kidney. The glutathione peroxidase system consists of several components, one of which is GSH^[65]. GSH, an essential component of oxidative system, serves as a cofactor for glutathione transferase, which helps to remove certain drugs and chemicals, as well as other reactive molecules, from the cells^[65]. Moreover, GSH can interact directly with certain ROS, i.e, hydroxyl radicals, to detoxify them, as well as performing other critical activities in the cell. Thus, GSH is probably the most important antioxidant present in cells^[65]. The enzymatic antioxidant defense system, which includes SODs and CATs, can decompose superoxide and hydrogen peroxide in the cells and are the main defense against oxidative injuries. SOD catalyzes the rapid removal of superoxide radicals, generating H₂O₂. Therefore, SOD works in collaboration with H₂O₂-removing enzymes. CAT is present in the peroxisomes of nearly all aerobic cells and functions to protect the cell from the toxic effects of hydrogen peroxide through catalyzing its decomposition into molecular oxygen and water without the production of free radicals. In the present study, AlCl₃ exposure induced free radicals and it may inhibit the enzymes involved in antioxidant defense, specifically, SOD and CAT. We observed a significant decrease in these enzymes in the kidney and liver of treated rats. Our results are in agreement with Nehru and Anand^[60] who observed a significant decrease in SOD and CAT activity in the brain after aluminum treatment. The decrease in both enzyme activities could be the result of reduced synthesis of these enzymes due to higher intracellular concentrations of aluminum or accumulation of free radicals^[60]. Also Orihuela *et al.*^[66] reported that, at high doses, aluminum is capable of inducing free radicals and decreasing the levels of GSH. Aluminum might also affect GSH synthesis by decreasing glutathione-synthase activity, which would result in reduced GSH levels.

Our results demonstrated that treatment with camel's milk prior to AlCl₃ alleviates AlCl₃-associated hazards and protects the kidneys and liver from AlCl₃ toxicity. The protective effect of camel's milk could be attributed to its antioxidant activity and it may possibly have chelating effects on aluminum. It has been reported that camel's milk contains high levels of vitamins A, B2, C and E and is very rich in magnesium (Mg) and other trace elements^[21]. These vitamins are antioxidants that have been found to be useful in preventing tissue injury caused by toxic agents. Mg protects cells from heavy metals such as aluminum, mercury, lead, cadmium, beryllium and nickel, which explains why re-mineralization is so essential for heavy

metal detoxification and chelating. In fact, Mg deficiency has been associated with production of ROS^[67]. Additionally, Mg protects cells against oxyradical damage and assists in the absorption and metabolism of vitamins B, C and E^[68], which are antioxidants important in cellular protection. Recent evidence suggests that vitamin E enhances glutathione levels and may play a protective role in Mg deficiency-induced cardiac lesions^[68]. Also, it has been reported that Mg is essential for biosynthesis of glutathione because the enzyme, glutathione synthetase, requires γ -glutamyl cysteine, glycine, ATP and Mg ions to form glutathione^[69].

Additionally, camel's milk is rich in zinc (Zn)^[21], which is a trace element essential for living organisms. More than 300 enzymes require Zn for their activity. It also plays an important role in DNA replication, transcription and protein synthesis, influencing cell division and differentiation^[70]. It has been noted that Zn has a relationship with many enzymes in the body and can prevent cell damage through activation of the antioxidant system^[71-73]. Zinc is an essential component of the oxidant defense system and functions at many levels^[74]. One study has shown that a diet deficient in Zn paves the way for cell damage in the rat testis^[75]. Furthermore, Zn deficiency increases lipid peroxidation in various rat tissues, whereas the Zn supplementation corrects this increase^[72,73,76]. Interestingly, a protective effect of Zn has been reported *in vitro* against cadmium toxicity. This is probably due to induction of oxidative stress and apoptosis^[77,78].

Our study demonstrated that treatment of rats with camel's milk prior to AlCl₃ resulted in decreased cholesterol and triglyceride levels in the serum compared to the AlCl₃-intoxicated group. It can be concluded that camel's milk can act in several ways to lower serum cholesterol and triglycerides. First, uptake of cholesterol and triglycerides in the gastrointestinal tract could be inhibited; second, LDL-cholesterol could be eliminated from the blood via the LDL receptor; and finally, the activity of cholesterol-degrading enzymes could be increased.

Another interpretation for the improvement of the evaluated parameters in the present investigation may be due to a decrease in aluminum accumulation in the liver and kidneys in the rats given camel's milk. The possible mechanisms include camel's milk-mediated reduction of the renal uptake of aluminum by competition for a common transporter, which would result in protective activity against aluminum-mediated damage to hepatocytes and renal function. Previously,

we reported that camel's milk alleviates alterations in biochemical parameters and oxidative stress produced in the liver of rats treated with cadmium chloride^[79], which correlates with our current findings.

CONCLUSION

Aluminum has adverse effects on human health. Our results demonstrate that AlCl₃ is capable of inducing marked alterations in biochemical parameters and oxidative damage, and inhibiting the function of antioxidant enzymes. Consequently, attention should be paid to the sources of aluminum in food, water and medical drugs. Camel's milk, administered before AlCl₃ exposure, minimized AlCl₃-associated hazards. Therefore, drinking camel's milk could be beneficial for alleviating aluminum toxicity. Further studies are required, using a human population, to confirm these protective effects.

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