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ORIGINAL ARTICLE

Frankincense Administration Antagonizes Adenine-induced Chronic Renal Failure in Rats

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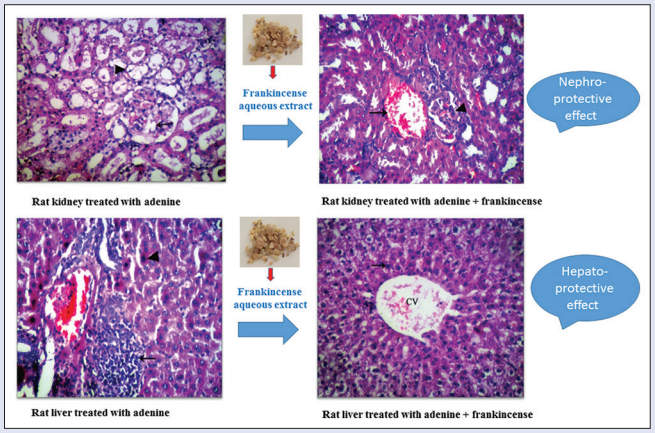
ABSTRACT

Background: Chronic renal failure (CRF) treatment through kidney transplantation or dialysis is restricted because of economic and medical resources deficiency. Thus, demand for using dietary supplements that can delete or ameliorate uremia or even to delay the need for dialysis is rising. **Objectives:** This study is the first one conducted to evaluate the efficacy of frankincense aqueous extract on CRF induced by adenine in rats. **Materials and Methods:** Forty male Sprague-Dawley rats were divided into four equal groups: control, frankincense, adenine, and frankincense + adenine. Kidney function tests, liver function tests, minerals' levels, antioxidant status, and histopathological alterations were investigated. **Results:** Results showed significant increases in relative kidney weight, serum level of urea, creatinine, blood urea nitrogen (BUN), uric acid, phosphorous, cholesterol, total bilirubin, alanine aminotransferase (ALT), and aspartate aminotransferase (AST) in adenine group, as well as significant decreases in body weight, calcium, total protein, and albumin. Significant elevation was also demonstrated in lipid peroxidation marker associated with depletion in activities of superoxide dismutase (SOD) and catalase in tissues of kidney and liver. In addition, there were marked histopathological changes of kidney and liver. **Conclusion:** Study results demonstrated that co-administration of frankincense aqueous extract with adenine is an effective way to reduce the signs of adenine-induced CRF and have returned them to almost completely normal levels.

Key words: Aqueous extract, chronic kidney disease, kidney, liver, oxidative stress

SUMMARY

- Rats treated with adenine showed kidney and liver pathological alterations on both biochemical and histological levels
- Co-administration of frankincense aqueous extract with adenine effectively reduced the signs of adenine-induced CRF and returned them to almost completely normal levels
- Frankincense aqueous extract is a potent nephroprotective and hepatoprotective agent in CRF induced by adenine in rat model.



Abbreviations used: CRF: Chronic renal failure; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; SOD: Superoxide dismutase; CKD: Chronic kidney disease; ROS: Reactive oxygen species; MDA: Malondialdehyde; H and E: Hematoxylin and eosin; BUN: Blood urea nitrogen; PTH: Parathyroid hormone.

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INTRODUCTION

Chronic kidney disease (CKD) has become a globally important health issue.[1] Many different reasons underlay behind CKD including excessive accumulation of body fat,[2] diabetes mellitus,[3,4] exposure to toxic materials,[5-8] and tumors.[9-11] If CKD is not treated, kidney function is progressively lost with time.[12] About 90 uremic solutes were considered as uremic toxins that would increase morbidity in CKD.[13] Besides affecting kidney itself, circulated uremic toxins exhibit lethal outcomes such as hypertension, cardiovascular diseases, neurological impairment, and bone disorders.[14] Therefore, effective removal of uremic compounds improves treatment outcomes and survival in patients with renal failure.[15] Serum urea appears earlier than other nitrogenous wastes with serum creatinine, uric acid, and phosphorous are the most common uremic toxin biomarkers for assessment of kidney failure.[16] Oxidative stress is one of the main effects of uremic toxin retention in the development and progression of CKD.[17] Reactive oxygen species (ROS), if not normally regulated by antioxidants such as catalase and superoxide dismutase (SOD), can influence cell function and can damage proteins, lipids, and nucleic acids. Progression of CKD to advanced stages is associated with a significant increase in the generation of ROS.[4,18] CKD treatment through kidney transplantation or dialysis is restricted because of economic and medical resources deficiency. Thus, demand for using dietary supplements that can delete or ameliorate uremia or even to delay the need for dialysis is rising.

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Frankincense is a gum resin of *Boswellia* plant species that grow in Somalia, India, and Yemen. It possesses an anti-inflammatory activity, so it is commonly used in folk medicine in India, Africa, and Western Europe to treat many inflammatory diseases.[19] Frankincense gum, from different species, contains about 60% lipophilic resin (the mixtures of terpenes), 10% volatile oil, and 30% hydrophilic gums (mixture of polysaccharides). Lipophilic resin portion is composed of pentacyclic triterpenic acids, with the major compounds 11-keto-β-boswellic acid and 3-acetyl-11-keto-β-boswellic acid, tetracyclic triterpenic acids, and diterpenes. Gum hydrophilic portion is consisting of pentose and hexose sugar with some oxidizing and digestive enzymes. It also contains polysaccharides containing galactose, arabinose, and 4-methylglucuronic acid. Volatile oil contains pinene, phellandrene, and α-thujene.[20,21] Specifically, 1,8-cineole (eucalyptol), 1-octanol, L-menthol, 3-cyclohexen-1-ol, octanoic acid, thymol, and carvacrol were reported as the chief active components in *B. sacra* water extract.[22] To the best of our knowledge, only two studies in the literature, Mahmoud *et al.*[23] and Moreillon *et al.*,[24] were concerned with studying the effect of frankincense extract on kidney diseases, but these studies used lipophilic portion. Hence, our study aims to evaluate the efficacy of the aqueous extract of frankincense on chronic adenine-induced renal failure in the rat model.

MATERIALS AND METHODS

Preparation of aqueous extract of frankincense

Dried Somalian frankincense (*B. sacra*) bought from a Saudi Arabian local source was grinded to obtain fine powder and stored in airtight plastic containers at 5°C until needed. Frankincense extract was made by soaking 20 g of powder in 100 mL of boiling distilled water for 1 h, settled for 24 h, and then filtered to give 20% w/v extract.

Chemicals and kits

Adenine (Sigma Chemicals, St. Louis, MO, USA), creatinine, urea and uric acid kits (Diamond Diagnostics, USA), albumin, total bilirubin, total protein, total cholesterol, calcium, phosphorous, sodium and magnesium kits (BIOMED, Cairo, Egypt), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) kits (ELITech Clinical Systems, France), and malondialdehyde (MDA), SOD, and catalase kits (Biodiagnostic Company, Dokki, Giza, Egypt) were used.

Animals

Male Sprague-Dawley rats, initially weighing 180–200 g, obtained from Institute of Serum and Vaccines Research, Cairo, Egypt, were housed for about 10 days before used in the experiment under standard conditions (temperature of 25°C, 50%–60% humidity, and a 12/12 h light/dark cycle) consistent with the criteria outlined in the "Guide for the Care and Use of Laboratory Animals" published by the National Institute of Health. Food and water *ad libitum* were permitted. This was approved by the Animal House of Biochemistry, Chemistry Department, Faculty of Science, Damietta University, Egypt.

Induction of chronic renal failure

Chronic renal failure (CRF) was induced according to Al Za'abi *et al.*[25] by daily injection of adenine (i.p) at a dose of 50 mg/kg for successive 28 days.

Experimental design

Rats were grouped randomly into four groups of ten rats for each. Control group fed on a standard diet and received the respective vehicles. Frankincense group received 1 mL of fresh frankincense extract (20% w/v) two times daily for 28 days by gastric intubation. Adenine group received 50 mg/kg bw/day adenine (i.p) for 28 days daily. Frankincense + adenine group received 1 mL of fresh frankincense extract (20% w/v) two times daily in concomitant with 50 mg/kg bw/day adenine (i.p) for 28 days. Body weights were recorded daily. On the 29th day, fasted animals were sacrificed under anesthesia. Sera were routinely separated and stored. Weighed kidney and liver, obtained after decapitation, were washed in saline. One part of each was fixed in 10% formalin for routine hematoxylin and eosin (H and E) staining technique, while the other part was homogenized and stored at −20°C for lipid peroxidation and antioxidant enzyme activities' assays.

Estimation of serum biochemical parameters

Serum urea, creatinine, blood urea nitrogen (BUN), uric acid, calcium, phosphorous, sodium, magnesium, total bilirubin, total cholesterol, total protein, albumin, ALT, and AST were assayed according to the instructions provided by the used kits.

Estimation of tissue biochemical parameters

Renal and liver lipid peroxidation product, MDA, as an oxidative stress index in addition to antioxidant enzymes SOD and catalase were assayed according to kits instructions.

Statistical analysis

Data were analyzed using statistical Package for the Social Sciences, version 17 (SPSS Software, SPSS Inc., Chicago, USA) and expressed as mean ± standard deviation (SD). For data with Gaussian distribution, statistical analysis was performed using analysis of variance (One Way ANOVA) followed by Bonferroni multiple comparisons test. For parameters with non-Gaussian distribution, Kruskal–Wallis test was employed followed by Dunnett's test for multiple comparisons. Differences were considered significant at $P < 0.05$.

RESULTS

As shown in Table 1, adenine induced significant weight loss starting from the 3rd week of administration, but by the end of the 4th week, kidney weights were significantly increased (data not shown). Co-administration of frankincense and adenine exhibited a significant increase in body weight and decreased relative kidney weight compared with adenine group.

Results of serum biochemical tests are shown in Table 2. Adenine significantly increased serum urea, creatinine, BUN, uric acid, AST, ALT, total bilirubin, total cholesterol, and phosphorous levels. While it significantly decreased sodium, calcium, albumin, and total protein levels compared with control group. However, compared to adenine group, co-administration of frankincense and adenine reversed all these changes significantly toward normal. About healthy rats administered frankincense compared to healthy control rats, they exhibited slight but significant increases in urea, BUN, magnesium, ALT, and AST levels with significant decrease in albumin level.

Concerning lipid peroxidation and antioxidant status, administration of adenine resulted in a significant elevation in MDA either in kidney or in liver tissue. This elevation was accompanied with significant reductions in SOD and catalase activities. While, co-administration of frankincense and adenine resulted in a significant reduction in MDA concentration either in kidney or in liver tissue compared to adenine group. This reduction was accompanied with significant increases in SOD and catalase activities. Regarding healthy rats administered frankincense extract, they showed a significant elevation in renal MDA accompanied by compensatory significant elevation in renal SOD

Table 1: Body weight (g) changes of rats in different groups throughout the experimental period

Groups	Day 0	1st week	2nd week	3rd week	4th week
Control	178.1±7.8	186.60±8.26	192.20±6.77	209.40±8.56	221.60±8.28
Adenine	203.3±9.2	190.62±6.54	186.13±6.51	163.50±4.9***	153.6±5.441***
Frankincense + adenine	203.7±10.13	184.4±4.68$	174±4.24$$$	177±3.27$$$	193.9±4.95$$$
Frankincense	193±3.74	190.4±4.35	189±3.33	195±4.55	209.6±4.92

Data are expressed as mean±SD. *n*=10 rats in each group. ***P<0.001 versus normal control group. $,$$$$P$<0.05, P<0.001 respectively versus adenine group. SD: Standard deviation

Table 2: Serum kidney and liver function tests in all studied rat groups

Tests	Frankincense	Control	Adenine	Frankincense + adenine
Creatinine (mg/dL)	0.62±0.04	0.63±0.08	1.05±0.107***	0.69±0.11$$$
Urea (mg/dL)	31.96±4.46**	26.63±2.21	113.3±12.7***	34.04±4.72***,$$$
BUN (mg/dL)	14.92±2.08**	12.42±1.04	52.93±5.95***	15.88±2.19$$$
Uric acid (mg/dL)	1.99±0.58	2.14±0.40	4.17±0.46***	2.16±0.34$$$
Sodium (mmol/L)	124.4±1.70	128.5±4.38	110.7±3.40***	126.3±1.98$$$
Phosphorus (mg/dL)	3.73±0.39	3.66±0.33	7.01±0.62***	4.44±0.30*,$$$
Calcium (mg/dL)	9.76±1.32	9.97±0.24	6.57±0.39***	10.29±0.73$$$
Magnesium (mg/dL)	1.63±0.13***	1.26±0.06	2.14±0.23***	1.76±0.06***,$$$
ALT (IU/L)	31.12±4.98*	24.66±6.43	55.7±1.64***	30.47±3.28$$$
AST (IU/L)	87.44±6.53***	75.81±4.73	190.35±19.48***	89.45±14.65$$$
Albumin (g/dL)	3.03±0.49**	3.79±0.48	2.1±0.26***	3.046±0.34$$$
Total protein (g/dL)	5.5±0.25	6.37±1.65	4.77±0.50***	6.07±0.75$$$
Total bilirubin (mg/dL)	0.13±0.07	0.125±0.08	0.69±0.16***	0.14±0.05$$$
Cholesterol (mg/dL)	89.8±9.325	79.69±16.62	115.58±9.03***	84.9±13.97$$$

Data are expressed as mean±SD. *n*=10 rats in each group. *,**,***P<0.05, P<0.01, P<0.001 respectively versus normal control group. $$$$P$<0.001 versus adenine group. BUN: Blood urea nitrogen; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; SD: Standard deviation

Table 3: Malondialdehyde, superoxide dismutase and catalase levels in kidney and liver tissues of rats in different groups

Biomarkers		Frankincense	Control	Adenine	Frankincense + adenine
MDA (nmol/g tissue)	Renal	277.4±22.5**	215.34±54.72	366.86±31.03***	230.07±19.4*,$$$
	Hepatic	180.12±32.94	148.60±38.57	447.04±86.34***	180.08±86.99$$$
SOD (U/g tissue)	Renal	2123±115.05***	1468.40±390.19	952.25±181.71***	1831±288*,$$$
	Hepatic	1818.4±156.6	1877.98±74.36	613.74±187.52***	1886±123.6$$$
Catalase (K unit/g tissue)	Renal	2.25±0.19***	2.73±0.11	1.595±0.19***	2.41±0.15***,$$$
	Hepatic	1.49±0.34	1.65±0.08	1.29±0.04	2.22±0.18***,$$$

Data are expressed as mean±SD. *n*=10 rats in each group. *,**,***P<0.05, P<0.01, P<0.001 respectively versus normal control group. $$$$P$<0.001 versus adenine group. MDA: Malondialdehyde; SOD: Superoxide dismutase; SD: Standard deviation

activity with significant decrease in renal catalase activity compared to healthy control [Table 3].

Histological signs for severe renal and hepatic tissue damage were noticed in rats administered adenine. Their kidney showed congestion and necrosis of renal glomeruli, besides degenerative changes and necrosis of normal renal tubular epithelium lining renal tubules. Their liver showed lymphohistiocytic infiltration in hepatic tissue and coagulative necrosis of hepatocytes. Rats administered adenine in conjunction with frankincense showed normal liver tissue architecture whereas showed proliferation of mesangial cells in renal glomeruli with congestion in the interstitial capillaries. It is worthy to state that healthy rats administered frankincense extract showed normal architectures of both kidney and liver [Figure 1].

DISCUSSION

In the current study, healthy rats treated with 20% frankincense water extract for consecutive 28 days displayed some significant abnormal changes on the biochemical level. These biochemical changes are somewhat minor compared to those caused by disease induction "adenine-induced CRF" [Tables 2 and 3] and have not lived up enough to cause any detected histopathological change in both liver and kidney tissue sections as evidenced through the normal renal and hepatic architectures shown in Figure 1Kb and Lb. These findings indicate that administration of frankincense water extract to healthy rats is not absolutely safe. Accordingly, traditional administration of frankincense water extract as a protective agent for healthy individuals is not entirely harmless. However, if it was taken to cope with a serious disease like individuals with CKD "as in our animal model" these minor adverse effects may be tolerated or may be canceled through adding one or more protective supplements. Yousef[26] reported that frankincense water extract (5%) is not completely safe; it showed abnormal changes in healthy rats on both levels biochemical in sera and histological in liver and kidney tissues. In 2012, Singh *et al.*[27] concluded that frankincense suspended in corn oil is fairly safe in rat. Asad and Alhomoud[22] concluded that frankincense water extract has proulcerogenic action.

Adenine-induced CRF model provides valuable information about the pathomechanism of various complications associated with a persistent uremic state. It produced metabolic abnormalities in rats resembling CRF complications in humans,[28,29] and it is employed as a disease model for assessment of drug efficiency.[30]

To the best of our knowledge, this is the first study concerning the effects of aqueous extract of frankincense on kidney and liver organs in CKD induced by adenine. In our study, rats receiving adenine showed weight loss with an increase in kidney weight. These results were in accordance with Al Za'abi *et al.* and Törmänen *et al.* study[25,29] and parallel findings

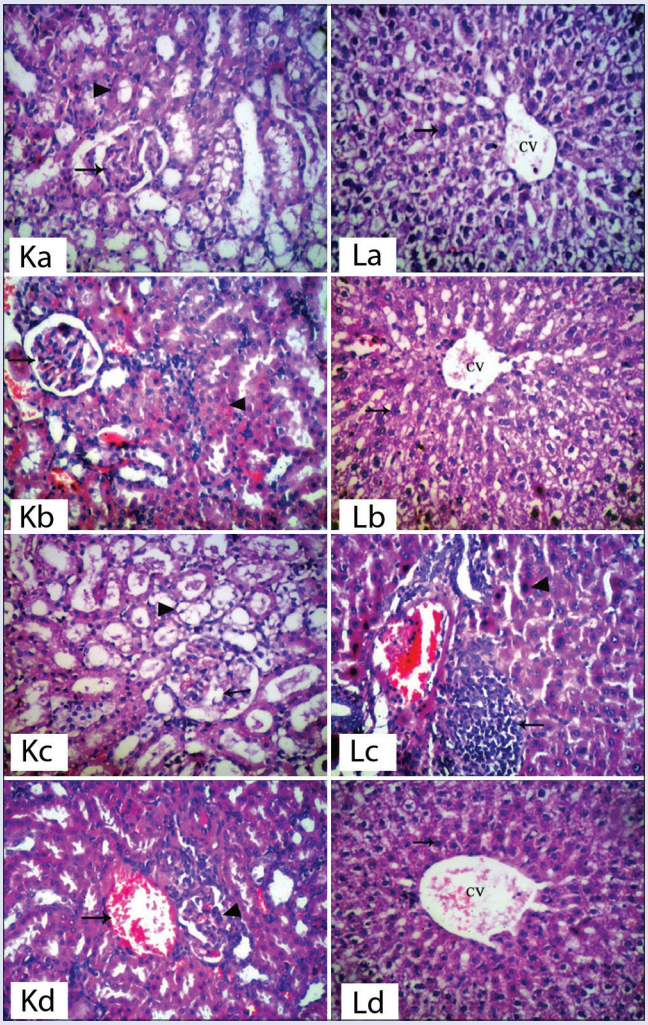

Figure 1: Kidney (K; left) and liver (L; right) histopathology (H and E, ×100). (Ka) normal control rat kidney showing normal renal glomeruli (arrow), and normal renal tubules lined by normal renal tubular epithelium (arrowhead), (Kb) normal control rat kidney treated with frankincense showing normal renal glomeruli (arrow), and normal renal tubules lined by normal renal tubular epithelium (arrowhead), (Kc) adenine-positive control rat kidney showing congestion and necrosis of the renal glomeruli (arrow), beside degenerative changes and necrosis of the normal renal tubular epithelium lining renal tubules (arrowhead), (Kd) adenine rat kidney treated with frankincense showing proliferation of the mesangial cells in the renal glomeruli (arrowhead) with congestion in interstitial capillaries (arrowhead). (La) normal control rat liver showing normal hepatocytes (arrow) and normal radial arrangement around central vein (CV), (Lb) normal control rat liver treated with frankincense showing normal hepatocytes (arrow) and normal radial arrangement around CV, (Lc) adenine positive control rat liver showing lymphohistiocytic infiltration in hepatic tissue (arrow) and coagulative necrosis of hepatocytes (arrowhead), (Ld) adenine rat liver treated with frankincense showing normal hepatocytes (arrow), and normal radial arrangement around CV

observed in CKD patients.[31] In addition to loss of appetite,[32] these changes could be also attributed to the accumulation of uremic toxins which lead to inflammation and activation of protein catabolic pathways that result in protein degradation.[31]

Adenine as one of purines is metabolized to uric acid, by xanthine oxidase, increasing circulated uric acid concentrations. In our model and in harmony with Johnson *et al.*,[33] raised uric acid induced glomerular hypertension and renal disease as noted by the congestion and necrosis of the renal glomeruli alongside degenerative changes and necrosis of the normal renal tubular epithelium lining renal tubules [Figure 1Kc].

It has long been known that elevations of serum urea, creatinine, and BUN concentrations are indicators of impaired kidney function. Results of our present study revealed that adenine induces serum urea, creatinine, and BUN elevations as a result of impaired urea and creatinine renal excretion indicating glomerular filtration rate decline, i.e., renal failure. These data are in consistency with other studies.[29,34,35]

In the current study, rats treated only with adenine exhibited hyperphosphatemia with hypocalcemia. Hyperphosphatemia and hypocalcemia have been identified as regular complications in CKD as a result of kidney failure.[36,37] With deteriorating renal function, phosphate excretion is impaired, and as a result, serum phosphate levels rise, and consequently, serum calcium levels fall as serum calcium is inversely regulated in relation to serum phosphate levels. High serum phosphate levels contribute to acidosis and encourage more hypocalcemia by reacting with bioavailable calcium forming $CaHPO_4$. Hypoproteinemia with hypoalbuminemia documented in the present study results may also aid in hypocalcemia as they lead to a decrease in the protein-bound calcium decreasing total calcium. Besides, impaired renal function results in suppression of renal Vitamin D activation and, consequently, lowering in calcitriol production, i.e., there is no or at least too little increase in calcium absorption in the intestine, and there is a loss of calcitriol effect on parathyroid hormone (PTH) actions on bone and kidney to raise plasma Ca level.

Hyponatremia and hypermagnesemia are other common features due to deterioration in kidney function seen after CRF induction by adenine in the current study. It was reported earlier that CKD can result in both elevation of circulated magnesium[38,39] that can cause some cardiovascular disorders and can reduce PTH secretion which produces hypocalcemia[40] and drop of circulated sodium that may cause cardiac arrhythmia through its effect on the membrane potentials of cardiocytes.[41] Hyponatremia may be attributed mainly to increased sodium loss and/or to adrenocortical insufficiency due to inhibited renal tubular reabsorption of sodium. Hypermagnesemia may be attributed to decreased urinary excretion of excess magnesium through kidneys that does not work properly.

As far as we know, this is the first study concerning the effect of frankincense on the liver in adenine-induced CKD. It has long been known that extensive renal damage resulting in end-stage renal failure would also result in hepatic dysfunction due to increase of pro-inflammatory cytokines and free radicals mediated by the generation of uremic toxins.[42,43] Present study data are supportive to these reports; rats with CRF induced by adenine showed evidences for both dyslipidemia and hepatic dysfunction. They suffered from hypercholesterolemia, high serum aminotransferases (ALT and AST), hyperbilirubinemia, and hypoalbuminemia with hypoproteinemia. These data are also in agreement with Boon *et al.*[44] and Yang *et al.*[45] Hypercholesterolemia, a risk factor for coronary heart diseases, may due to oxidative modification, carbamylation of apolipoproteins, and elevation of 3-hydroxy-3-methylglutaryl coenzyme A reductase as a result of hypoalbuminemia.[46,47] High serum aminotransferases may due to cellular infiltration. More elevated AST than ALT may be attributed to more release of mitochondrial AST and reduced AST clearance related to aggressive liver damage.[48,49] Hyperbilirubinemia could be attributed to chronic hemolysis;[50] shortened lifespan of red blood cells due to loss of cell membrane integrity[51] mediated by the action of free radicals and to accumulation of uremic toxins in the blood.[52] Hypoalbuminemia and hypoproteinemia could be attributed

to leakage of albumin in urine[53] and to lowering in albumin synthesis by the liver.[54]

In the current study, obtained data of adenine group revealed high elevations in levels of MDA and great fall in antioxidant enzyme activities of SOD and catalase in homogenate of renal and liver tissues indicating oxidative stress state. This identifies free radical-induced injury with an overall decrease in cellular function. These results are confirmatory to Ali *et al.*[55] and Chang *et al.*,[56] who reported that adenine significantly increased oxidative stress markers and decreased the activities of antioxidant enzymes in renal tissue.

Meanwhile, co-administration of frankincense with adenine to rats in the present study attenuated the decrease in body weight as well as decrease in relative kidney weight, which may be attributed to its potential ability to block protein catabolic pathways that cause muscle protein wasting. Frankincense aqueous extract when taken along with adenine was able to cancel serum adenine-induced increase in uric acid and to keep its level within normal. This effect may be due to boswellic acids inhibitory effect on xanthine oxidase activity.[57] Since high serum urea, creatinine, and BUN levels are markers of uremic toxins and consequently of kidney function impairment, dramatic reduction of the former to near normal and normalization of the latter two are appreciated achievements gained by frankincense aqueous extract co-administration. These data are inconsistent with Mahmoud *et al.*[23] Concerning signs of adenine-induced CRF complications, administration of frankincense plus adenine first ameliorated P, Ca, Mg, and Na ionic disturbances, indicating it has a good impact on the severity of kidney diseases. Second, it significantly reduced the level of cholesterol toward control. This improvement may be related to the improvement of hypoalbuminemia as documented in the present study. Finally, it showed amelioration of liver functions indicating that frankincense has hepatoprotective power that can inhibit or at least decrease liver damage. This amelioration represented by improvements in serum levels of aminotransferases, bilirubin, albumin, and total proteins besides decreasing MDA levels in tissue associated with an elevation in the activities of the antioxidant enzymes, SOD and catalase. This might be due to frankincense anti-inflammatory properties, confirmed previously by many authors,[19,58,59] and to its antioxidant properties, which protect against cellular leakage and loss of functional integrity of the cell membrane in hepatocytes. Biggs *et al.*[60] confirmed that frankincense is an important source of triterpenes, monoterpenes, diterpenes, total phenolics, flavonoids, and saponins, suggesting that frankincense has antioxidant properties. Other studies reported that frankincense has hepatoprotective effect on drug-induced liver injury.[61,62]

Liver function improvements documented through the above-mentioned biochemical tests for the frankincense plus adenine group were coincide with their liver histological examination findings. Liver tissue of rats administered adenine alongside frankincense showed complete normal architecture. Meanwhile, histological signs for severe hepatic tissue damage were noticed in liver of rats administered only adenine including lymphohistiocytic infiltration in hepatic tissue with coagulative necrosis of hepatocytes. These findings confirm the ability of frankincense water extract to antagonize adenine action on the liver in our adenine-induced CRF animal model.

Concerning kidney histology, level of improvements in rat kidney tissue for frankincense plus adenine group compared to adenine group was not in the strength of those on the biochemical level documented above. This might be due to that the treatment duration "28 days" may was not enough to achieve satisfying renal tissue repair.

Frankincense water extract contains some active components with antioxidant activities and some with anti-inflammatory activities. L-menthol is well documented to have antioxidant, anti-inflammatory, and analgesic activities. It is able to interact with cellular membranes due to its lipophilicity and to affect ion channels and consequently to affect regulation of Ca^{2+}, Na^{+}, or Cl^{-} ions transfer.[63] *Mentha piperita* leaf essential oil that contains menthol as the chief constituent is a hepato- and renal-protector against CCl_4-induced oxidative actions in rats.[64] Carvacrol and thymol have antioxidant effects.[65] Carvacrol is anti-inflammatory and exhibits protective actions against kidney/liver injuries.[66] 1,8-Cineole possess antioxidant, anti-inflammatory, and pain-relieving activities.[67] In rats, octanoic acid did not show any suppressing effect on liver regeneration after partial hepatectomy.[68] About both 1-octanol and 3-cyclohexen-1-ol, we could not find any paper in the literature concerning their effects on liver or kidney.

CONCLUSION

Aqueous extract of frankincense (*B. sacra*) is a potent nephroprotective and hepatoprotective agent in CRF rat model induced by adenine, as evidenced by improvement of the biochemical and pathological changes, that may mainly attributed to its content of antioxidant active components.

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Conflicts of interest

There are no conflicts of interest.

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