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Efficacy of Frankincese on Rats Suffering from Chronic kidney Disease

Ahmed A. Ameen, Hany G. El-Masry and Fardous M. Mohamed,

Nutrition and Food Science Department, Faculty of Home Economics, Helwan University

Abstract

Frankincense (Gum Olibanum), made from resins of Burseraceae family, grows in Somalia, India and Yemen. Many years ago the oldest doctors used this plant for treatment of many diseases.The main target of this study was to investigate the effect of different levels of Frankincense on rats suffering from chronic renal failure. The experiment was carried out using 35 male albino rats (Sprague-Dawley strain). The rats were randomly divided into two main groups; the first main group (7 rats) fed on basal diet as a negative control group. The second main group (28 rats) fed on diet containing 0.7% adenine (adenine diet) for 4 weeks to induce chronic renal failure. After this period, the rats in the second main group were divided into four subgroups, the first subgroup was fed on basal diet as a positive control group.

The other subgroups (2-4) were fed on basal diets supplemented with three levels from frankincense (1%, 2%, and 3%), respectively. Twenty four hours after the experimental period (4 weeks), blood samples were taken for biochemical analyses.The results indicated that using the three levels from frankincense improved the mean values of uric acid, creatinine, Aspartate Amine Transferase (AST), Alanine Amine Transferase (ALT),total cholesterol, total lipids, and triglycerides in serum by usingthe tested diets.The study recommend retesting the use of frankincense on patient with chronic kidney disease.

Key words: Frankincense,Chronic kidney disease,Adenine, Rats,Basal diet.

Introduction

Chronic kidney disease (CKD) is progressive loss in kidney function over a period of months or years ***(Eknoyanet al., 2004).*** If kidneys get worse,metabolic wastes can build to high levels in blood.That may develop complications like high blood pressure, anemia, weak bones, poor nutritional health and nerve damage.Impaired kidney function increases risk of having heart and blood vessel disease. These problems may happen slowly over a long period of time. Chronic kidney disease may be caused by diabetes mellitus, high blood pressure and other disorders ***(Rahmanet al., 1998 and Martínez-Castelaoet al., 2014).***

Frankincense (Boswellia Species) is a French word, meaning "pure incense". It is popularly known as Indian olibanum, salaiguggal, loban, or kundur***(Afsharypuor and Rahmany, 2005).*** Frankincense is secreted by trees of the Boswellia species which are tropical deciduous trees and usually grow as small trees or shrubs with limited natural growing range ***(Safayhiet al., 1997).***

Since ancient times, frankincense has been used in Africa and in many countries such as China, India, and the Middle East countries for the prevention and treatment of various illnesses, especially chronic inflammatory diseases In the Indian traditional medicine, frankincense **(salaiguggal)** has been used as an anti-inflammatory, anti-arthritic, anti-proliferative, and analgesic agent for the treatment of related diseases. In Traditional Chinese Medicine; frankincense is

commonly used as a remedy for improving the blood circulation and in relieving pain in leprosy, gonorrhea, and cancer patients ***(Zhao et al., 2003).***

Mahe al.,(2011) studied the effect of frankincense on chronic kidney disease. Theyreported significant reduction in serum creatinine as well as a decrease in blood urea nitrogen. Soit helps in reducing and treating chronic renal failure and can be used as an alternative medicine for various diseases***(Yousef, 2011).***

Materials and Methods

Diet content:

Frankincense, Casein, all vitamins, minerals, cellulose and choline bitartratewere obtained from Elgomhoria Pharmaceutical Company,Cairo, Egypt.

Adenine:

Adenine (obtained from Elgomhoria Pharmaceutical Company, Cairo, Egypt)was used to induce chronic kidney disease, and used in concentration of 0.7% in the basaldietfor 4 weeks. ***(Yokozawaet al., 1986).***

Experimental animals:

Adult male Sprague-Dawley rats (n=35) which weighing (200±10g) purchased from Farm of experimental animals in Helwan, Egypt.The animals were housed under hygienic conditions at a room temperature of 25±2°C with relative humidity of 40–70% and on 12 hrs light/12 hrs dark cycles in thebiological studies Lab of Faculty of Home Economics. Basal diet and water were allowed ad libitum to all groups.

Preparation of basal diet:

Basal diet was prepared according to AIN-93 ***Reeves et al.,(1993).*** It consists of 14 % protein, 10 % sucrose, 4.0% corn oil, 2.5% choline chloride, 1% vitamin mixture, 3.5 % salt mixture, L-cysteine 1.89/kg diet and 5% fibers. The remainder was corn starch up to 100 %.

Experiment and grouping of rats:

Rats were randomly distributed into 5 equal groups, each 7 rats. Group (1) (Negative control) was fed on basal diet. Groups from (2) to (5) were fed the basal diet and received 0.7 % adenine in the basal diet daily for 4 weeks.After this period. Frankincense added as a supplementation/ Kg diet.Group (2) was kept as (Positive control; Group (3) received 1% Frankincense/kg diet; Group (4) received 2% Frankincense/kg dietand Group (5)received3% Frankincense/kg diet. At the end of the experiment (4 weeks) rats were scarified and blood samples were collected and used for serum separation, Serum samples were used for estimation of uric acid, creatinine AST,ALT,ALP and total lipid profile.

Biological Parameters:-

Body weight (BWG) and feed intake (FI) were calculated at intervals. (BWG) and feed efficiency ratio (FER) were calculated according to ***(Chapman et al., 1959).***

Serum Analyses:

Were conducted according to the corresponding reference as follow:Serum uric acid (***Fossatiet al., 1980),*** creatinine ***(Young,2001),***serum cholesterol ***(Allainet al., (1974),*** Triglyceride (***Fossati and prencipel, 1982),*** serum total lipids ***(Zoellner and Kirsch., 1962 and Frings and Dunn, 1970),*** Alanine aminotransferase**,** Aspartate aminotransferase and Alkaline phosphatase according to ***(Young,2001).***

Statistical Analysis:

Data were presented as means± SE. Differences between means in different groups were tested for significance using a one-way analysis of variance (ANOVA) followed by Duncan's multiple range tests. Differences were considered significant at probability level P<0.05 according to***Snedecor and Cochran (1986)*** using computerized SPSS program.

Results and Discussion

Data recorded in (Table 1) showed that the mean value±SE of Body Weight Gain (BWG), Feed Intake (FI) and Feed Efficiency Ratio (FER) decreased significantly in the control positive group,these parameters increased significantly(P<0.05) in the frankincense supplemented group compared with the positive control group.The best result of FIwas observed in the group 5 (9 g) which is close to the negative control (10.20 g). BWG and FER in the group treated with (2%) Frankincense showed a non-significant changecompared to the negative control group while the FER in group 5 showed higher value than the negative control.Frankincense supplementation has a greater enhancementof weight gain, food and fluid intake, in rats. This increase FER of the diet which presented for each group. The weight gain was increased when the fluid intake and solid food consumption increased, that may be a result of increasing feed intake whenever the rising the concentration of frankincense that may help and increase the bioavailability of the diet.

As shown in (Table 2),the mean value ±SE of serum uric acid and creatinine of the positive control group fed on adenine diet increased significantly p<0.05, as compared to the negative control group fed on basal diet. On giving frankincense the level of creatinine and uric acid decreasedwith the best result in the group treated with (3%) Frankincense with non-significant change compared to the negative control group.

In the present study, adenine induced chronic kidney disease that led to a significant increase in kidney parameters (uric acid and creatinine) as compared to the negative control group. A similar result was reported by***Adachi et al.,(1998)*** who reported that adenine-rich diets increase uric acid and Creatinine by decreasing the excretion of these substances, because excretion of nitrogenous compounds is suppressed by renal occlusion due to 2,8-dihydroxyadenine (DHA).Treatment of chronic renal failure with Frankincense improved kidney functions in this study compared to the control positive group. In this respect ***Alam et al.,(2011)*** showed that treatment of rats with Oleo-gum-resin of Boswelliaserrata (Kundur) prevented the rise in serum uric acid and serum creatinine***(Yousef, 2011).***

Co-administration of Kundur as antioxidant, vitamin E and selenium was found protective against nephrotoxicity. It has also been reported that the essential oils of Kundur (B. serrata) demonstrated antioxidant activity comparable with α-tocopherol (vitamin E) and butylated hydroxyl toluene (BHT). The reno-protective activity shown by Kundur during study, may be attributed to the chemical constituents of Kundur having anti-oxidative potential**(*Alam et al., 2011).***

Data recorded in (Table 3) showed that the mean value±SE of Serum Alkaline phosphatase(ALP), Alanine Amine Transferase(ALT) and Aspartate Amine Transferase(AST)of the positive control group fed on adenine diet increased significantly p<0.05, as compared to the negative control group fed on basal diet. On adding frankincensein the diet these parameters improvedthe best result in the group treated with (3%) Frankincense, where the levels of liver enzyme became significantlylower than the positive control group and close to the negative control group.

In the present study, adenine induced chronic kidney disease led to a significant increase in liver enzymes (serum Aspartate Amine Transferase (AST), Alanine Amine Transferase (ALT) as compared to negative cntrol group. A similar result was reported by ***(Sakata et al.,2000)*** who reported that adenosine significantly decreased the reperfusion-induced increase in serum levels of aspartate aminotransferase and alanine aminotransferase and Alkaline phosphatase by suppressing the activation of neutrophils and oxidative stress.

Treatment with Boswelliaserrataat different doses inducea significant reduction in serum alanine (ALT) and aspartate amino transferase (AST) activities, the same author demonstrated that Boswellia serrata possess partial positive hepatoprotective effect ***(Majano et al., 2004). Pandey et al., (2005)***reported that Boswellia serrata oleo gum decreased the production of nitric oxide. It is shown that those components that are reducing the production of NO in the liver tissue possess liver protective effect. ***Jyothi et al., (2006)*** reported that Boswellia serrata, through reduction of NO generation, can protect the liver function.

As demonstrated in (Table 4), the mean value±SE of serum LDL,VLDL,Cholesterol and triglycerides of the positive control group fed on adenine diet increased significantly ($p<0.05$), as compared to the negative control group fed on basal diet. While there was a significant decrease in the serum of HDL when compared to the negative control group.The best result was observed in the groups treated with any of the three levels from Frankincense with non-significant change compared with the negative control group.

In the present study, adenine induced chronic kidney disease led to a significant increase in total cholesterol, LDL-C,VLDL-C and triglycerides and accompanied by significant decrease in serum HDL as compared to basal diet group. A similar result reported that chronic renal failure is often associated with dyslipoproteinemia, high levels of cholesterol and triglycerides as well as a decrease in polyunsaturated fatty acids. Each of these abnormalities has been identified as independent risk factors of atherosclerosis ***(Hokanson and Austin,1996).***

Morever,***Trevisan et al.,(2006)*** who reported that Experimental and clinical studies have suggested a correlation between the progression of renal disease and dyslipidemia. High cholesterol and triglyceride plasma levels have been demonstrated to be independent risk factors for progression of renal disease in humans. There are data that oxidative stress and insulin resistance may mediate the lipid-induced renal damage. In the animal model, lipid-lowering agents seem to ameliorate glomerular damage, preventing glomerulosclerosis and interstitial fibrosis.

Treated chronic renal failure groups with Frankincense improved total cholesterol, total lipids, and triglycerides, as compared non – treated group (control positive group). Asimilar result was reported by***Azadmehr et al.,(2014)*** who reportedsignificant reductions of Cholesterol, LDL and TG levels.In another study, ***Ahangarpour et al.,(2014)***reported that the treatment of Boswelliaserrata caused significant increase in blood HDL levels as well as a remarkable decrease in cholesterol, LDL, triglyceride, VLDL after 6 weeks which is in agreement with our results. ***Pandey et al.,(2005)*** indicated hypocholesterolemic effect of gum resins extract of Boswellia in rats.Recently ***Mehrzadi et al.,(2016)*** showed the efficiency of the use of Boswellia serrate gum resin for control of lipid profile and blood glucose in diabetic patient.

The study concluded that intake of frankincence may help in case of chronic kidney disease, and recommended its trial on patient suffering from chronic kidney disease.

Table 1:

Feed Intake (FI), Body Weight Gain (BWG) and FeedEfficiency Ratio (FER) of rats

Groups	Feed Intake (g/day)	BWG%	FER
G1:Control (-ve)	10.20	11.26 ± 1.92^{b}	0.070 ± 0.011^{b}
G2:Control(+ve)	6.20	-7.06 ± 1.29^{d}	-0.070 ± 0.15^{d}
G3:1%Frankincense	8.12	4.28 ± 0.82^{c}	0.033 ± 0.008^{c}
G4:2%Frankincense	8.70	10.28 ± 0.51^{b}	0.073 ± 0.003^{b}
G5:3%Frankincense	9.00	16.13 ± 2.23^{a}	0.113 ± 0.013^{a}

Mean values are expressed as means ± SE.

Means with different superscript letters in the same column are significantly different at $P< 0.05$.

Table 2:

Effect of Frankincense on kidney functions (Creatinine and Uric Acid)in rats suffering from chronic kidney disease and on treatment

Groups	Creatinine(mg/dl)	Uric Acid (mg/dl)
G1:Control (-ve)	0.606±0.02^{c}	2.30±0.11^{c}
G2:Control(+ve)	1.043±0.05^{a}	3.43±0.16^{a}
G3:1%Frankincense	0.776±0.06^{b}	2.86±0.08^{b}
G4:2%Frankincense	0.640±0.05^{bc}	2.67±0.03^{b}
G5:3%Frankincense	0.586±0.03^{c}	2.54±0.08^{bc}

Mean values are expressed as means ± SE.

Means with different superscript letters in the same column are significantly different atP< 0.05.

Table 3:

Effect of Frankincense on liver functions in rats suffering from chronic kidney disease and on treatment

Groups	AST (µ/L)	ALT (µ/L)	ALP (µ/L)
G1:Control(-ve)	22.90±1.05^{c}	65.86±2.91^{d}	238.20±4.57^{d}
G2:Control (+ve)	46.46±1.97^{a}	94.00±2.20^{a}	316.50±2.17^{a}
G3:1%Frankincense	35.66±4.48^{b}	81.80±2.31^{b}	270.03±5.05^{c}
G4:2%Frankincense	34.86±2.96^{b}	83.66±1.96^{b}	291.90±4.51^{b}
G5:3%Frankincense	31.54±3.32^{bc}	74.63±1.44^{c}	242.60±4.78^{d}

Mean values are expressed as means ± SE.

Means with different superscript letters in thesame column are significantly different at P < 0.05.

Table 4:

Effect of Frankincense on lipid profile in rats suffering from chronic kidney disease and on treatment

Groups	Total Cholesterol(mg/dl)	Triglycerides(mg/dl)	HDL-C(mg/dl)	LDL-C(mg/dl)	VLDL-C(mg/dl)
G1:Control (-ve)	105.00±3.05^{b}	83.83±5.25^{b}	51.00±4.58^{a}	37.23±2.03^{b}	16.76±1.05^{b}
G2:Control (+ve)	125.76±2.82^{a}	108.40±1.22^{a}	34.90±2.22^{b}	69.18±2.59^{a}	21.68±0.24^{a}
G3:1% Frankincense	106.67±4.33^{b}	84.00±3.78^{b}	46.80±2.13^{a}	43.06±6.43^{b}	16.80±0.75^{b}
G4:2% Frankincense	100.33±3.75^{b}	80.66±8.08^{b}	49.23±2.42^{a}	34.96±6.96^{b}	16.13±1.61^{b}
G5:3% Frankincense	98.66±5.48^{b}	73.20±4.77^{b}	54.30±3.53^{a}	29.72±5.34^{b}	14.64±0.95^{b}

Mean values are expressed as means ± SE.

Means with different superscript letters in the same column are significantly different at P < 0.05.

References

Adachi Y.; Sasagawa I.; Tateno T.; Tomaru M.; Kubota Y. and Nakada T. (1998):
Influence of adenineinduced chronic renal failure on testicular function in the rat. Andrologia; 30:115–8.

Afsharypuor S. and Rahmany M. (2005):
Essential oil constituents of two African Olibanums available in Isfahan Commercial Market. Iran J Pharmacol Sci.1:167–70.

Ahangarpour A .; Heidari H .;Fatemeh R.A.; Pakmehr M.; Shahbazian H.; Ahmadi I.; Mombeini Z. and Mehrangiz B.H. (2014):
Effect of Boswellia serrata supplementation on blood lipid, hepatic enzymes and fructosamine levels in type2 diabetic patients, J Diabetes MetabDisord. ,13(1) :13-29.

Alam M.; Javed K. and Jafri M.A. (2011):
Effect of oleo-gum-resin of Boswelliaserrata (Kundur) on renal functions in Albino rats, Indian Journal Of Traditional Knowledge, 10(4) : 736-740.

Allain C.C.; Poon L.S.; Chan,C.S.G.; Richmond W. and Paul C. (1974):
Enzymatic Determination of Total Serum Cholesterol.CLINICAL CHEMISTRY, 20 (4): 1974.

Azadmehr A.; Ziaee A.; Ghanei L.; Huseini H.F.;Hajiaghaee R.;Tavakoli-far B. and Kordafshari G.(2014):
Anti-Oxidant, Anti-hyperglycemic and Anti-Hyperlipidemic Effects of Olibanum Gum in Type 2 Diabetic Patients, Iran J Pharm Res.13(3): 1003–1009.

Chapman D.; Castilla R. and Campbell J.A. (1959):
Evaluation of protein in food. Determination of protein andfeed efficiencyratio. Can. J. Biochem.Physol.; 37:679-686.

Eknoyan G.; Lameire N. and Barsoum R. (2004):
The burden of kidney disease: improving global outcomes. Kidney Int. 66: 1310–14.

Fossati P. and Principe L. (1982):
Serum triglycerides determined calorimetrically with an enzyme that produces hydrogen peroxide. Clinical Chem.; 28, 2077-2080.

Fossati P.,Prencipe L. and Berti G. (1980):
Enzymeticcolometeric method for determination of uric acid in serum. Clin. Chem.; 26(2): 227 – 273.

Frings C.S. and Dunn R.T. (1970):
A calorimetric method for determination of total serum lipids based on the sulfo-vanilin reaction. Am. J.Clin. Path.; 53: 89-91.

Hokanson J.E. and Austin M.A. (1996):
Plasma triglyceride level is a risk factor for cardiovascular disease independent of high-density lipoprotein cholesterol level: a meta-analysis of population based prospective studies. J. Cardiovascular Risk; 3:213-219.

Jyothi Y.; Jagadish V.K.; Asad M. (2006):

Effect of hexane extract of boswelliaserrata oleo-gum resin on cheically induced liver damage. Pak J Pharm Sci , 19: 125–129.

Mahe A.;Javed K. and Jafri M. (2011):

Indian journal of Traditional knowledge. Vol 10(4), pp: 736 –740.

Martínez-Castelao A.;Górriz G. L. and Bover J. (2014):

Consensus document for the detection and management of chronic kidney disease. *Nefrologia. 34 (2): 243–62*.

Majano P.L.; Medin J.; Zubia I.; Sunyer L.; Lara-Pezzi E.; Maldonado-Rodriguez A.; Lopez-Cabrera M. and Moreno O.R. (2004):

N-Acetyl-cysteine modulates inducible nitric oxide synthase gene expression in human hepatocytes. J Hepatol , 40: 632–637.

Mehrzadi S.; Tavakolifar B.; Huseini H.F.; Mosavat S.H.and Heydari M. (2016):

The Efficacy of Boswellia Serrata Gum Resin for Control of Lipid Profile and Blood Glucose in Diabetic Patients, Iran J Med Sci, 41(3):S66.

Pandey R.S.; Singh B.K. and Tripathi Y.B. (2005):

Extract of gum resins of Boswelliaserrata L. inhibits lipopolysaccharide induced nitric oxide production in rat macrophages along with hypolipidemic property. Indian J ExpBiol , 43: 509–516.

Rahman M.; Smith A. and Michael C. (1998):

Chronic renal insufficiency: A diagnostic and therapeutic approach.*158:1743- 52*.

Reeves P.; Nielsen F. and Fahmy G. (1993):

AIN-93.Purified diets for laboratory rodents: Final reports of the American Institute of Nutrition adhocwriling committee of reformulation of the AIN-76 A Rodent Diet. J. Nutr. 123, Pp. 1939-51.

Safayhi H.; Rall B.; Sailer E.R. and Ammon H.P. (1997):

Inhibition by boswellic acids of human leukocyte elastase. J. Pharmacol Exp. Ther.281:460–3.

Sakata C.; Tanaka, H Takemura, S.; Hirohashi K.; Minamiyama Y.; Nakamura A.; Inoue M. and Kinoshita H. (2000):

Post-ischemic intraportal adenosine administration protects against reperfusion injury of canine liver. J. Hepatobiliary. Pancreat. Surg.; 7(1):78-85.

Snedecor G.W. and Cochran W.G. (1986):

Statistical Methods. Iowa State University Press, Ames, Iowa, USA, 4th ed., 1986, page 91-9.

Trevisan R.; Dodesini A.R. and Lepore G. (2006):

Lipids and Renal Disease. J. Am. Soc. Nephrol.; 17: S145– S147.

Yokozawa T.; Zheng P.D.; Oura H. and Koizumi F. (1986):

Animal model of adenine-induced chronic renal failure in rats. Nephron. 44: 230-234.

Young D. (2001):

Effect of disease on clinical lab Tests, 4th ed, vol(1).AACC press.

Yousef J.M. (2011):

Identifying frankincense impact by biochemical analysis and histological examination on rats, Saudi J BiolSci, 18(2): 189–194.

Zhao W.; Entschladen F.; Liu H.; Niggemann B.; Fang Q. and Zaenker K. (2003):

Boswellic acid acetate induces differentiation and apoptosis in highly metastatic melanoma and fibrosarcoma. Cancer Detect Prev. 27:67–75.

Zoellner N. and Kirsch K. Z. (1962):

fur die Gesampte.,Exp Med., 135:545.

تأثير اللبان المر على الجرذان المصابة بمرض الفشل الكلوي المزمن

أحمد على أمين ، هانى جابر المصرى ، فردوس محمود محمد

قسم التغذية وعلوم الاطعمة , كلية الإقتصاد المنزلي , جامعة حلوان

الملخص العربي

اللبان المر مستخلص من عائلة البرسيريسيا، تنمو في الصومال واليمن والهند. استخدمه الأطباء في علاج العديد من الأمراض منذ القدم. وكان الهدف من الدراسة هو التحقق من تأثير مستويات مختلفة من اللبان المر على الجرذان المصابه بالفشل الكلوي المزمن .أجريت التجربة على خمس وثلاثين جرذا، ثم قسمت الجرذان عشوائيا إلى مجموعتين رئيسيتين، وكانت المجموعة الرئيسية الأولى (ضابطة سالبة) سبعة جرذان تغذت على الغذاء الأساسي. والمجموعة الرئيسية الثانية عددها ثماني وعشرين جرذا تغذت على غذاء محتوي على 0.7% أدينين لمدة أربع أسابيع لاحداث مرض الفشل الكلوي المزمن . بعد هذه المدة يتم تقسيم الجرذان في المجموعة الثانية الرئيسية إلى أربع مجموعات فرعية، تغذت المجموعة الأولى الفرعية (ضابطة موجبة) على الغذاء الأساسي ، أما باقي المجموعات الفرعية تغذت على الغذاء الأساسي بجانب اللبان المر بنسب (1% ,2% ,3%) على التوالي . بعد أربع وعشرين ساعة من انتهاء التجربة (أربع أسابيع) تم أخذ عينات الدم للتحاليل الكيميائية. وأشارت النتائج أن استخدام اللبان المر بالمستويات الثلاثة قد حسن من وظائف الكبد والكلى. وخلصت الدراسة أن اللبان المر قد يساعد في تحسن وظائف الكلي. وقد أوصت هذه الدراسة بتجربة تناول المشروبات الغنية باللبان المر على مرضى الفشل الكلوي المزمن.

كلمات البحث:اللبان المر- الفشل الكلوي المزمن- الأدينين- الجرذان-الغذاء الأساسي.