Efficacy of Frankincese on Rats Suffering from Chronic kidney Disease

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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 using the 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 (Eknoyan et 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 (Rahman et al., 1998 and Martinez-Castela et al., 2014).

Frankincense (Boswellia Species) is a French word, meaning “pure incense”. It is popularly known as Indian olibanum, salaiguggal, loban, or kundur (Afsharypour 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-arthritis, anti-proliferative, and analgesic agent for the treatment of related diseases. In Traditional Chinese Medicine, frankincense is
Ahmed A. Ameen, et al

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. They reported significant reduction in serum creatinine as well as a decrease in blood urea nitrogen. So it 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 bitartrate were 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 basal diet for 4 weeks. (Yokozawa et 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 the biological 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 diet and Group (5) received 3% Frankincense/kg diet. At the end of the experiment (4 weeks) rats were sacrificed 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 (Fossati et al., 1980), creatinine (Young,2001), serum cholesterol (Allain et 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 FI was 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 change compared to the negative control group while the FER in group 5 showed higher value than the negative control. Frankincense supplementation has a greater enhancement of 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 decreased with 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 control positive 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 hydroxytoluene (BHT). The renoprotective 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 Aminotransferase(ALT) and Aspartate Aminotransferase(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 frankincense in the diet these parameters improved the best result in the group treated with (3%) Frankincense, where the levels of liver enzyme became significantly lower 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 Aminotransferase (AST), Alanine Aminotransferase (ALT) as compared to negative control 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.
Ahmed A. Ameen, et al

Treatment with Boswelliaserrata at different doses induce a 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 Frankincence 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).

Moreover, 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 Frankincence improved total cholesterol, total lipids, and triglycerides, as compared non – treated group (control positive group). A similar result was reported by Azadmehr et al.,(2014) who reported significant 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 Feed Efficiency Ratio (FER) of rats |
|---------------------------------|-------------|-------------|-------------|
| Groups                         | Feed Intake (g/day) | BWG%        | FER         |
| G1: Control (-ve)              | 10.20        | 11.26±1.92* | 0.070±0.011*|
| G2: Control (+ve)              | 6.20         | -7.06±1.29* | -0.070±0.15*|
| G3: 1% Frankincence           | 8.12         | 4.28±0.82*  | 0.033±0.008*|
| G4: 2% Frankincence           | 8.70         | 10.28±0.51* | 0.073±0.003*|
| G5: 3% Frankincence           | 9.00         | 16.13±2.23* | 0.113±0.013*|

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

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

Mean values are expressed as means ± SE.
Means with different superscript letters in the same column are significantly different at P > 0.05.

Table 3:
Effect of Frankincense on liver functions in rats suffering from chronic kidney disease and on treatment

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

Mean values are expressed as means ± SE.
Means with different superscript letters in the same 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

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

Mean values are expressed as means ± SE.
Means with different superscript letters in the same column are significantly different at P < 0.05.
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تأثر اللبن المر على الجرذان المصابة بمرض الفشل الكلوي المزمن

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اللبان المر مستخلص من عائلة البرسيريسيا، تنمو في الصومال واليمن والهند. استخدم الأطباء في علاج العديد من الأمراض منذ القدم. وكان الهدف من الدراسة هو التحقق من تأثير مستويات مختلفة من اللبان المر على الجرذان المصابة بالفشل الكلوي المزمن. أجريت التجربة على خمس وثلاثين جرذًا، 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 جرذًا تغذت على غذاء محتوي على 0.7% أدينين لمدة أربع أسابيع لاحترم مرض الفشل الكلوي المزمن. بعد هذه المدة، يتم تقييم 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 بسبب اللبان المر بنسبة (1%, 2%, 3%) على التوالي. بعد أربع وعشرين ساعة من الانتهاء التجربة (أربع أسابيع) تم أخذ عينات الدم للتحليل الكيميائي. وأظهرت النتائج أن استخدام اللبان المر بالمستويات الثلاثة قد حسن من وظائف الكبد والكلى. وخلاصة 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: اللبن المر، الفشل الكلوي المزمن، الأدينين، الجرذان-الغذاء الأساسي.