Effect of *Peganum harmala* seeds alcoholic extract on kidney efficiency, thyroid stimulating hormone and thyroid gland hormones in local female rabbits

Shaymaa Kadhim Noor Alzamili
Coll. of Vet. Med. / Univ. of Al-Qadisiyah
email: Shaymaa.Alzamili@qu.edu.iq
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Abstract

Peganum harmala belong to the Jigo phalluses family has many compounds as alkaloids, Saponines steroids and lignin which are used as a medicinal components which serve as a regulator to endocrine activity, in this study, twenty adult female local rabbits with weighing 1500±100gms, and aged 240 ±10 days were divided into 2 groups: the control group which fed on diet and water *ad libitum* and the treatment group which administrated orally (by stomach tube) 10cc with 13.5% of *peganum harmala* alcoholic extract daily for 14 consecutive days, and at the 15th day, blood samples were collected. Serum level of Triiodothyronin (T3), Thyroxin (T4) and Thyroid-stimulating hormone (TSH), uric acid and creatinine were measured by using radioimmunoassay method. Results were revealed that the 90mg/kg dosage of *peganum harmala* alcoholic extract increased significantly ($p<0.05$) the levels of the urea and uric acid when compared with control, while the creatinine has not recorded significant variances when compared with the control group, on the other hand, the effect of *Peganum harmala* seed alcoholic extract on the TSH, T3, T4 levels revealed that these hormones decreased significantly ($p<0.05$) when compared with the control group. In conclusion the results of this study indicate that the 90mg/kg of alcoholic extract of *Peganum harmala* seeds has increased blood urea and uric acid, decreased blood TSH as well as hormones of thyroid gland

Key words: *Peganum harmala* seeds, alcoholic extract, urea, creatinine, thyroid gland, TSH, rabbits.

تأثير المستخلص الكحولي لبذور نبات الحرمل *Peganum harmala* على كفاءة الكلية والهرمون المحفز للغدة الدرقية وهرمونات الغدة الدرقية في إناث الأرانب المحلية

شيماء كاظم نور الزاملي
كلية الطب البيطري/ جامعة القادسية

الخلاصة

ينتمي نبات الحرمل الى عائلة Jigo phalluses والذي يحوي عدة مركبات مثل القلويدات والصابونيات والستيرويدات واللكنين والذي يستعمل كمركب طبي يعمل على تنظيم الفعالية الصماوية ، لقد استخدم في هذه الدراسة عشرون انثى بالغة من الأرانب المحلية بوزن 1500 غم ±100 وبعمر 240 ± 10 يوم. قسمت الحيوانات الى مجموعتين: مجموعة السيطرة والتي تم تغذيتها وإروائها ومجموعة المعاملة والتي جرعت بالمستخلص الكحولي للحرمل10 مل وبتركيز 13.5 % يوميا لمدة اربعة عشر يوم متتالي ، وفي اليوم الخامس عشر تم جمع عينات الدم من جميع حيوانات التجربة ، وتم قياس مستوى هرمون Triiodothyronin (T3) وهرمون Thyroxin (T4) والهرمون المحفز للدرقية Thyroid-stimulating hormone (TSH) بالإضافة الى اليوريا وحامض اليوريك والكرياتنين وتم القياس باستخدام طريقة التحليل المناعي الشعاعي radioimmunoassay ، اظهرت النتائج ان جرعة 90 ملغم/كغم من المستخلص الكحولي قد سببت زيادة معنوية في كل من اليوريا وحامض اليوريك عند مقارنتها مع مجموعة السيطرة ، بينما لم يسجل مستوى الكرياتنين أي فرق معنوي عن مجموعة السيطرة ومن ناحية اخرى فان المستخلص الكحولي لنبات الحرمل على T3هرمونات و T4 و TSH قد سبب زيادة معنوية في مستوياتها عند مقارنتها مع مجموعة السيطرة.

نستنتج من نتائج الدراسة ان جرعة 90 ملغم /كغم من المستخلص الكحولي لبذور نبات الحرمل قد سببت زيادة في كل من مستوى يوريا الدم وحامض اليوريك وسببت انخفاضا في الهرمون المحفز للدرقية بالإضافة الى هرمونات الغدة الدرقية.

الكلمات المفتاحية: بذور نبات الحرمل ، المستخلص الكحولي ، اليوريا ، الكرياتنين ، الغدة الدرقية ، الهرمون المحفز للغدة الدرقية ، الارانب.

Introduction

The Zygophyllaceae plant (*Peganum harmala*) is known as (Espand) in Iran, (Harmel) in North Africa and (African Rue), (Mexican Rue) or (Turkish Rue) in the United states, habitant to arid and Semiarid area distributed mainly in the Mediterranean region, North Africa and Middle east (1,2,3,4). The flowering period is March to April. The fruits are globose capsule have three chambers containing many angular blackish seeds (5), due to its bitter taste, the plant is not usually grazed and repels animals, all species of animals are susceptible to poisoning by this plant, but camels are the most often affected (6). The seeds of *P. harmala* plant contain tens of chemical compounds including amino acids, flavonoids, volatile compounds, polysacch-arides and several kinds of alkaloids compounds (7).The extracts of its seeds contain B-carbolin alkaloids, small quantity of flavonoid glycosides and anthroquinons (8,9). Several studies have clarified various biological activities and pharmacological characteristics of the seeds such as hypothermia (10), factor hallucinogen (11), antidepressant (12), monoamine oxidase (MAO) inhibitor (13) antibacterial, anti-fungal and antiviral effects (14,15). It has effect for the treatment of dermatosis disease (16), its leaves used as antinociceptive activity (17).The seeds of this plant are widely used in treatment of several diseases in livestock or domestic anthelmintic and protozoacidal agent besides treatment of asthma, eczema and malaria (18), experiments have showed the insecticidal effects (19,20), The antibacterial effect and antioxidant effects (15). A study was done in adult male rats; they found that the TSH level also T3 and T4 hormones were reduced by using of *peganum harmala* extract in adult male rats (21). The present study aimed to investigate the physiological changes following repeated administration of alcoholic extract of *peganum harmala* seeds for 14 days on the levels of urea, uric acid and creatinine as well as T3, T4 and TSH hormones of rabbits.

Materials and methods

The seeds of *Peganum harmala* L. (Zygophylaceae) were collected from local market in AL-Diwaniyah Province; powdered seeds were placed in percolator with ethanol 70% in 1:10 w/v, and allowed to stand at room temperature overnight. The percolate was collected and the process of extraction was repeated, the combined extract was dried in 45ºc and stored in 4ºc (22).Twenty adult females of local rabbits with approximate weight of 1500±100 gm. were divided into 2 groups. The control group did not take any medicine, the experimental group administered orally with 90mg/kg of *Peganum harmala* alcoholic extract daily for 14 consecutive days. At the 15^{th} day, blood samples were collected from all animals and then serum obtained to detect level of Triiodothyronin (T3), Thyroxin (T4) and Thyroid-stimulating hormone (TSH) by using radioimmunoassay method (23).The data were analyzed by using SPSS software, the statistical significance of differences between means was calculating using one way analysis (ANOVA), at ($P \leq 0.05$) level of significance (24).

Results

The effect of alcoholic extract of *Peganum harmala* seeds on urea, uric acid and creatinine were shown in table (1). Results represented that there were significant differences ($P<0.05$) in urea and uric acid levels of the treated group when compared with the control group, whereas the creatinine of the treated group recorded no significance in comparison with control group. Alcoholic extract of *Peganum*

harmala seeds causes a significant increment in urea when compared with the control group (34.411±0.137, 32.634± 1.774) mg/dL respectively as well as the same action in the uric acid when compared with control group (4.391±0.11 and 3.45±0.056)mg/dL respectively while in post-treatment the creatinine did not recorded any changes in its level when compared with control group (0.553±0.012 and 0.553±0.021) mg/dL respectively. Table (2) showed the levels of T3, T4 and TSH hormones of the treatment group and the control group. Alcoholic extract of *Peganum harmala* seeds on thyroid gland had registered a significant decrement in T3 and T4 hormones. The T3 hormone level after treatment was (1.134±0.0157) and T4 hormone level become (6.532±0.03) while they were in the control groups (1.583±0.025), (7.692±0.05) respectively. The decrement effect of alcoholic extract of *Peganum harmala* seeds involved TSH hormone which was in the control group 0.504±0.294 and became 0.302±0.198 mg/L.

Table (1): Effects of alcoholic extract of *Peganum harmala* seeds (90mg/kg) on female rabbit serum urea, uric acid and creatinine concentrations

Group	Urea mg/dL M±SE	Uric acid mg/dL M±SE	Creatinine mg/dL M±SE
Control	32.634A ±1.774	3.45A ±0.056	0.541A ±0.022
Treatment	34.411B ±1.037	4.391B ±0.11	0.559A ±0.031

Different letters mean significant differences (p≤0.05)

Table (2): Effects of alcoholic extract of *Peganum harmala* seeds (90mg/kg) on T3, T4,TSH hormones of female rabbit

Group	T3 ng/ml M±SE	T4mg/dl M±SE	TSH mg/L M±SE
Control	1.583A ±0.025	7.692A ±0.05	0.504A ±0.294
Treatment	1.134B ±0.015	6.532B ±0.03	0.302B ±0.198

Different letters mean significant differences (p≤0.05)

Discussion

The present study stated the changes in the kidney function tests and thyroid gland hormones as well as thyroid stimulating hormone following repeated administration of alcoholic extract of *Peganum harmala* seeds. In a study done in chicks fed diets including 10% of *peganum harmala* for a period of 14 days, the histological changes in the kidney noticed the degeneration of epithelial cells of the renal proximal convoluted tubules (23) and this agreed with the recent study which lead to increase the uric acid and urea, whereas this study was agreed with a study done in mice injected subcutaneously with aqueous extract of *peganum harmala* which showed no toxic effect on kidney (25), this may be due to differences in the experimental animals, the status of extract and the route of administration. The present study has similarity with previous studies conducted on large animals (26); furthermore, (21) found that 90mg/kg as well as 270mg/kg dose of the *pagnum harmala* extract reduce the T3, T4 and TSH levels in rats and that accord with the present study. The increase in the levels of urea and uric acid after treatment with alcoholic extract of *Peganum harmala* seeds is considered as an indicator of renal function failure, results showed that alcoholic extract of *Peganum harmala* seeds has the ability to normalize the creatinine level post treatment. This effect may be due to the presence of many active compounds in the alcoholic extracts of *P. harmala* as alkaloids and flavonoids. On the other hand (27) found that alkaloids impaired the kidney function. In contrast (28) stated that alkaloids have been exerted protective effects on the renal function, in the same way (29) reported that flavonoids compounds may prevent nephrotoxicity and improve the function of kidney and promote kidney primary epithelial tubular cell regeneration, besides that identically (30) clarified that flavonoid mixture lowers plasma creatinine and urea concentrations and these results contrast with those in the present study except the uncharged of level of creatinine where the animals in the other study were rats, but the

animals of the present study were rabbits with dose of 90mg/kg. A study was done on patient (31) found that adding herbal medicine as alcoholic extract of *Peganum harmala* seeds did not change the level of Creatnine and this accord with the present study. Furthermore (32) clarified that 200 and 400 mg/kg of *P. harmala* extract significantly reduced the levels of TSH, T3 and T4 in rats and this compatible with this study. Similarly, a study was done on rats revealed that this herbal plant reduces the TSH level and levels of T3 and T4 (21). The obtained data revealed that *P. harmeala* caused a significant decrement in the level of plasma T3, this is consistent with (14) who found that this plant effect decreasingly on that hormone. The conducted results revealed that there is an elevation in the level of uric acid and this is not accord with (33) who found that the *P.harmala* decreased the plasma uric acid level and this may be due to the experimental animals where chickens. A present study conducted on male rats (34) represents that *P. harmala* cause decrement of T3, T4 and this due to decrease of thyroid hormones transporter proteins and this is in agreement with the present study. According to the results of this study the effect of *P. harmala* ethanolic extract on pituitary–thyroid axis is examined, it is obtained that the inhibitory action of compounds in *P. harmala* seed extract effect on the secretion of thyroid hormones. In conclusion, the results of this study showed that administration alcoholic extract of *Peganum harmala* seeds caused a significant decrement in thyroid gland hormones and TSH, while caused a significant increase of urea and uric acid with still unchanged creatinine level in both pre- and post-treatment groups in local female rabbits.

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