Effect of *Pistacia khinjuk* Hydroalcoholic Fruit Extract on Some Biological Parameters in Male Rats

Reza Azadbakht (MD)[1], Mohsen Jafarian Dehkordi (PhD)[2], Reza Fathi Hafshejani (MD)[1], Soudeh Khanamani Falahati-pour (PhD)[3], Sakineh Khanamani Falahati-pour (PhD)[4*]

[1] *Faculty of Veterinary Medicine, University of Islamic Azad of Shahrekord, Shahrekord, Iran*
[2] *Department of Clinical pathology, Faculty of Veterinary Medicine, Shahrekord Branch, Islamic Azad University, Shahrekord, Iran*
[3] *Pistachio Safety Research Center, Rafsanjan University of Medical Sciences, Rafsanjan, Iran*
[4] *Department of Pharmacology, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran*

Information

Article Type:
Original Article

Article History:

Received: 01.01.2021
Accepted: 24.02.2021

Doi: 10.22123/PHJ.2021.284207.1097

Keywords:
Pistacia khinjuk
Hydroalcoholic extract
Biochemical parameters
hypocholesterolaemic properties
glucose-lowering effect

Corresponding Author:

Sakineh Khanamani Falahatipour

Email: Falahatipour@yahoo.com

Tel: +98-34-33221211

Abstract

Introduction: *Pistacia khinjuk* is traditionally used in folk medicine for the treatment of various disorders. This study was aimed to investigate the effect of *Pistacia khinjuk* fruit extract on some selected biochemical parameters using rat model to validate its application in traditional medicine.
Materials and Methods: The fruits of the plant were air-dried and the hydroalcoholic extract was obtained. Twenty-four rats were divided equally into three groups: one group served as the control group and the rest as test groups. The test animals were treated with two concentrations of *Pistacia khinjuk*(200 and 400 mg/kg) orally for twenty-eight days. The biochemical data were analyzed using SPSS software, expressed as means ± SD and were subjected to one-way analysis of variance (ANOVA) followed by post-hoc Tukey.
Results: The results obtained for the selected biochemical parameters revealed that glucose, triglyceride, Blood Urea Nitrogen (BUN), creatinine, urea, bilirubin and GGT levels decreased significantly ($p < 0.05$) in test groups against the control group. The HDL level increased in test group 1 (200 mg/kg), and Cholesterol, AST and ALT levels decreased significantly in test group 2 (400 mg/kg) ($p < 0.05$) compared to the other groups.
Conclusion: The present study showed that the fruit extract of *Pistacia khinjuk* possesses hypocholesterolaemic properties, has a glucose-lowering effect, improves the lipid profile, and may be of enormous benefit in the management of diabetes, cardiovascular, renal and hepatic diseases.

►Please cite this article as follows:

Azadbakht R, Jafarian Dehkordi M, Fathi Hafshejani R, Khanamani Falahatipour S, Khanamani Falahati-pour S. Effect of *Pistacia khinjuk* Hydroalcoholic Fruit Extract on Some Biological Parameters in Male Rats. Pistachio and Health Journal. 2021; 4 (1): 7-17.

1. Introduction

Humans have used natural products, such as plants, animals, microorganisms and marine organisms in medicines to alleviate the symptoms of or treat diseases since prehistoric and ancient times [1]. Many drugs of known therapeutic effects have been developed from different plant species. Some plants are used as medicinal plants because they contain pharmacological components of therapeutic value. The medicinal value of plants lies in some chemical substances (usually secondary metabolites) that produce a definite physiological action on the human body [2].

The wild pistachio or *Khinjuk* (*Pistacia khinjuk*) belongs to the family of Anacardiaceae [3]. This plant is called "khenjuk or kelkhong" in Iran [4]. *Pistacia khinjuk* tress can potentially withstand the severest climatic conditions [5]. Their natural habitat is Iran, Turkey, Egypt, Syria, Iraq, Afghanistan and Pakistan. The fruits are blue and black and the seeds are yellowish [6].

The amount of mono- and polyunsaturated fats in nuts is high (70-80%). Fats are essential for a healthful diet and alter the phospholipids in cell membranes, minerals, vitamins, fiber, magnesium and selenium all of which can upgrade insulin sensitivity and glucose homeostasis. The ratio of unsaturated fatty acid in Iranian *Pistacia khinjuk* has been reported to be 76.31% [7,8]. They are noted as a rich source of phenolic compounds which have recently been categorized among the first 50 food resources with antioxidant activity [9]. Seven phenolic compounds, mainly flavonoids and galloylated compounds, were isolated from the aqueous methanol extract of *Pistacia khinjuk* [10]. Bozorgi *et al*. 2013 have described the presence of terpenoids, flavonoids and tannins in *Pistacia khinjuk* extract with respect to phytochemical screening [11].

Previous studies have shown that pistachios can improve blood lipid profiles in individuals with moderate hypercholesterolemia, and in fact, reduce the risk of cardiovascular diseases (CVDs) [9,12]. The results of several interventional studies examining the effects of nut-enriched diets on glycemic control and insulin sensitivity are similar to the present study.[13].

In traditional medicine, the various parts of *Pistacia khinjuk*, for example resin, leaf, bark, fruit and aerial parts have been mainly applied in the treatment and prevention of many diseases including eczema, throat infection, renal stone, asthma, toothaches, stomach discomfort, nausea, vomiting and motion sickness [14-16]. Moreover, in modern medicine, studies have demonstrated antiinflammatory, antioxidant, antitumor, antiasthmatic, antimicrobial, antileishmanial [4], as well as wound healing [8] and scolicidal effects [16] for pistachio Chinju.

Medicinal plants may affect biochemical parameters in many ways. Therefore, it is necessary to investigate the effect of extract of *Pistacia khinjuk* on biochemical parameters such as glucose and lipid. Therefore, this study was carried out to investigate some biochemical effects of hydroethanolic of *Pistacia khinjuk* in normal Wistar male rats.

2. Materials and Methods

2.1. Plant material and extract preparation

Pistacia khinjuk hulls were picked and collected in the central district of Lordegan, Chaharmahal and Bakhtiari province, Iran in July. Then the plant was identified and confirmed (voucher number:1517) at the

Herbarium of Chaharmahal and Bakhtiari, Agricultural and Natural Resources Research and Training Center, Chaharmahal and Bakhtiari, Shahrekord, Iran. Hulls were separated from the fruits. The fruits were dried by natural shadow drying on laboratory benches at room temperature (23-24℃), and powdered in an electric grinder (Philips Mixer Grinder HL1605). The powder was suspended in 1000 ml of ethanol 70% and distilled water solution (7:3, v/v) for 72 h in oven temperature (37℃). The mixture was filtered using a soft cotton cloth followed by filter paper (Whatman No 1). The filtrate was centrifuged for 8 min at 4500 rpm. The supernatant fraction was saved. The obtained clear residue was placed in rotary evaporator for solvent evaporation. Then, the resulting extract was placed at oven temperature (37℃) in order to evaporate the rest of the solvent for 48 h. Afterward, the required amounts of dried extracts were dissolved in distilled water based on the weight of the rats, and the intended doses were prepared and homogenized by shaker. The obtained clear residue was used for the study. The extracts were kept at -20℃ until they were used in the experiment [17].

2.2. Animals

Experiments were conducted using mature Wistar strain male albino rats (180-240 g). The animals were kept in standard controlled laboratory conditions [12 h light/dark cycle, at 22 ± 3℃], and a humidity of 45% with ad libitum access to food and water. The study was conducted in compliance with the principles of the ethical recommendations about using laboratory animal guidelines and the experimental protocol was approved by the Faculty of Veterinary Medicine, Shahrekord Branch, Islamic Azad University, Shahrekord, Iran [18].

2.3. Experimental design

Twenty-four male Wistar rats weighing 180-240 grams were divided into three groups of eight animals. The hydroalcoholic extract of *Pistacia khinjuk* at a single dose of 200 and 400 mg/kg/day for 28 days was administered orally to the animals of two test groups: Test group 1 (200 mg/kg) and Test group 2 (400 mg/kg). The third group was orally dosed with distilled water and was considered as the control group (Table 1).

Table 1: The groups of the experimental design

Groups	Administered doses
Test 1	**200 mg/kg** hydroalcoholic extract of *Pistacia khinjuk*
Test 2	**400 mg/kg** hydroalcoholic extract of *Pistacia khinjuk*
Control	**300 mg/kg** distilled water

The extract doses were administered using a special stomach tube with a smooth tip to protect the oral mucosa and esophagus from injury. Blood samples were then taken from the heart of the rats and biochemical parameters were measured. All the rats were sacrificed by administrating sodium pentobarbital (120 mg/kg, IP) on day 28, and then the blood samples were used for the respective tests. The samples were collected in plain tubes to obtain serum. The blood was left for one hour to clot and the tube was centrifuged at 3000 rpm for 15 min and the harvested serum was used for biochemical analysis.

2.4. Biochemical Parameters

Most serum biochemical parameters including Blood Urea Nitrogen (BUN), urea, creatinine, glucose, aspartate aminotransferase (AST), alanine aminotransferase (ALT), Gamma Glutamyl Transferase (GGT), serum total cholesterol, triglyceride, High-Density Lipoprotein (HDL) and total bilirubin levels were measured in the samples collected using commercial kits (Parsazmoon, Iran) and an autoanalyzer (BT 3000 Pluse, Italy).

2.5. Statistical analysis

The collected data were analyzed using SPSS software version 20 and expressed as means ± SD and were subjected to one-way analysis of variance (ANOVA) followed by post-hoc Tukey. The results are summarized in Table 2. Values were considered statistically significant at $p < 0.05$.

The results are illustrated in Table 2. The fruit extract of the plant significantly decreased the serum concentrations of Glucose (162.75±31.76, 184.375±24.69), triglycerides (95.5±14.93, 60.375±22.15), BUN (18.25±3.28, 15.75±1.67), creatinine (0.4875±0.099, 0.437±0.074), urea (19.0875±7.035, 13.737±3.57), GGT (3.125±1.46, 2.375±0.744) and total bilirubin (0.2375±0.05, 0.275±0.046) at the two dose levels (in 200 and 400 mg/kg, respectively), ($p<0.05$). The 200mg/kg dose increased the HDL level significantly (49.625±2.72) ($p<0.05$). *Pistacia khinjuk* extract with 400 mg/kg dose increased the HDL level, but it was not significant (44.75±1.49) ($p>0.05$). The 400 mg/kg dose decreased the concentrations of AST, ALT and cholesterol significantly (148.75±22.6, 15.75±1.67, 42±4.44, respectively) ($p<0.05$). Although 200 mg/kg dose of the extract also decreased cholesterol level, it was not significant (48.125±8.36) ($p>0.05$).

Table 2. The effect of hydroethanolic extract of *Pistacia khinjuk* on biochemical parameters in Wistar

Parameters	Control	Kh200	Kh400
Glu (mg/dl)	259.62±35.66	162.75±31.76*	184.375±24.69*
Cho (mg/dl)	55.37±6.67	48.125±8.36	42±4.44*
Tg (mg/dl)	126.12±35.69	95.5±14.93*	60.375±22.15*
HDL (mg/dl)	39.75±6.75	49.625±2.72*	44.75±1.49
AST (u/l)	191.75±41.4	157.125±17.95	148.75±22.6*
ALT (u/l)	47.87±6.83	59.125±21.07	15.75±1.67*
Tbili (mg/dl)	0.375±0.09	0.2375±0.05*	0.275±0.046*
BUN (mg/dl)	22.5±3.34	18.25±3.28*	15.75±1.67*
Crea (mg/dl)	1.45±0.81	0.4875±0.099*	0.437±0.074*
Urea (mg/dl)	28.19±7.14	19.0875±7.035*	13.737±3.57*
GGT (u/l)	4.75±1.49	3.125±1.46*	2.375±0.744*

*: Significantly different from control group at $P < 0.05$. Kh200: Test group1, Kh400: Test group2, Kh: Chinju, Glu: Glucose, Cho: Cholesterol, Tg: triglyceride, HDL: High-density lipoproteins, AST: aspartate aminotransferase, ALT: alanine aminotransferase, Tbili: Total bilirubin BUN: Blood Urea Nitrogen, Crea: Creatinine, GGT: Gamma Glutamyl Transferase.

4. Discussion

According to WHO, more than 80% of the world's population rely on traditional medicine for their primary healthcare needs [19]. Because of possessing low toxicity, low cost, high effectiveness, and high accessibility, plant extracts and their pure components promise the discovery of new drugs due to the presence of a variety of chemicals [17].

Our findings revealed the glucose-lowering effect of *Pistacia khinjuk* extract in Wistar rats. Pistachio nuts have antioxidant properties that may contribute to antiglycemic effects. These properties may be due to their richness in natural phenolic compounds, aldohexose inhibition and the presence of magnesium (120 mg in 100 g pistachios) [7]. In agreement with our study, Misra *et al*., 2011 found that daily consumption of pistachios in healthy young men for 4 weeks decreased blood glucose significantly [20]. Ghaseminasab *et al*., 2015 showed that pistachios have a glucose-lowering and insulin-lowering effect, promote a healthy metabolic profile and may reverse some metabolic adverse consequences of prediabetes [12].

The results of this study showed that *Pistacia khinjuk* extract could decrease cholesterol and triglyceride levels and increase HDL levels. These effects were often attributed to the desirable fatty acid profile and the dietary fiber content of nuts [21]. Nuts are cholesterol-free, but their fatty fraction contains great amounts of chemically related noncholesterol sterols known as plant sterols or phytosterols. When phytosterols are present in sufficient amounts in the intestinal lumen, they interfere with cholesterol absorption and thus help lower blood cholesterol. The mechanism of action of phytosterols has been related to their hydrophobicity which is higher than cholesterol because of a large hydrocarbon molecule, entailing a higher affinity for micelles compared to cholesterol. Therefore, cholesterol is dislocated from micelles and the amount available for absorption is limited. Probably the phytosterol content of nuts is responsible for their cholesterol-lowering effect [22]. The low contents of saturated fatty acids may also play an important role in the putative blood-lipid-lowering effect of pistachio nuts since it is now clearly established that partially replacing saturated fat with polyunsaturated or monounsaturated fat may lower LDL cholesterol concentrations and decrease the risk of cardiovascular disease, especially in men [23]. In agreement with our findings, Li *et al*., 2010 showed that pistachio consumption decreased plasma triacylglycerols and reduced body weight when compared with a carbohydrate snack in obese individuals [24]. In addition, Askari *et al*., 2013 showed a significant link between high nut consumption and lower total cholesterol, triglyceride (TG) and low-density lipoprotein cholesterol (LDL-C) levels in female subjects and lower triglyceride and LDL-C in male subjects ($P<0.05$). They concluded that frequent consumption of nuts, particularly ≥ 4 times a week, may result in lower dyslipidemia incidence and may display cardioprotective effects [25]. The *Pistachio Khinjuk* fruit extract may produce beneficial effects to prevent cardiovascular disease. However, further studies in these areas are necessary.

Serum aminotransferases such as aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are the markers for hepatocellular injury [26]. A high concentration of AST and ALT indicates tissue damage and changed membrane permeability [27]. The results of the present study indicated that oral administration of hydroalcoholic extract of *Pistacia khinjuk* in test group 2 (400 mg/kg dose) decreased liver functional factors, including serum ALT and AST levels remarkably. By reducing oxidative stress and inhibiting liver lipid peroxidation, *Pistacia khinjuk* extract can protect liver tissue from reactive oxygen species (ROS) damaging role, thereby reducing the ALT and AST activities in serum [28]. In fact, consumption of fruit of this plant can help the body to fight against continuously produced harmful free radicals and further potentiate scavenging capacity of the liver [29]. The antioxidant activity of methanolic extract of *Pistacia khinjuk* has been reported by Ahmed *et al*., 2017 [6]. In agreement with our results, Iranmanesh *et al*., 2016 evaluated the effects of *pistachio vera* hydro-alcoholic extract on carbon tetrachloride-induced hepatotoxicity in male rats. They reported that gavage of hydro-alcoholic extract of *Pistachio vera* (10, 50, 100 mg/kg) significantly decreased ALT and AST indices ($p<0.05$) [29].

Creatinine and blood urea nitrogen (BUN) are metabolic waste products eliminated from the blood by the kidneys [30]. Urea is the main

nitrogen-containing compound in the urine of mammals. When urea is high in the blood, it can cause tissue damage, e.g. haemorrhage [31]. The results of the present research showed a statistically significant decrease in urea, BUN and creatinine concentrations of treated rats compared to the control group ($P<0.05$). Because urea synthesis in the liver is the major pathway of nitrogen excretion released into the blood and excreted by kidneys, the reduction in animals receiving *Pistacia khinjuk* extract may be either due to a lower rate of urea synthesis in the liver or a higher rate of urea excretion in kidneys. Since large amounts of urea are passively reabsorbed from the medullary collecting duct, the reduction of BUN in animals receiving *Pistacia khinjuk* extract is interpreted as a mechanism of reabsorption inhibition of urea in nephrons [32]. Because serum creatinine is easily measured as a by-product of muscle metabolism, is excreted unchanged by the kidneys, and can overestimate renal function, it is an important indicator of renal health. When the kidney is deficient in its filtration ability, creatinine blood level increases. Since the result of this research showed a decrease in creatinine level, the extract is assumed to be nephroprotective. However, this decrease in creatinine level may be attributed to the chemical components of the extract such as flavonoids, which shows that the plant extract may have beneficial effects for the management of cardiovascular diseases and oxidative stress [31].

Bilirubin (BR) is the breakdown product of the haem moiety of haemoglobin and other haemoproteins in mammals [33]. It transported to the liver by albumin for further metabolism. *Pistacia khinjuk* in both doses could reduce total bilirubin, suggesting that the compounds in this extract may have health benefits for the liver, improve its bilirubin conjugating property and help clear bilirubin from circulation. In fact, the following mechanisms could be suggested for the bilirubin-lowering potential of *Pistacia khinjuk*. *Pistacia khinjuk* extract might activate the Constitutive Andostane Receptor, a key regulator in the bilirubin clearance pathway, and increase the activity of glucuronyl transferases, the synthesis of ligandin, a transporter of bilirubin, and the conjugation of bilirubin in the liver. Also, *Pistacia khinjuk* extract may inhibit the activity of haem oxygenase, the rate-limiting enzyme of the bilirubin pathway [34]. In addition, the presence of glucosides in the extract might be converted to glucorunic acid for conjugating with bilirubin for excretion [11].

Gamma-glutamyltransferase (GGT) is a cell-membrane bound enzyme with high secretory activity that is found in the liver, kidneys, and pancreas. Any damage to the plasma membrane causes the release of GGT into the serum. Serum GGT is an indicator of liver dysfunction and excessive alcohol consumption. *Pistacia khinjuk* extract significantly lowered the GGT level in both test groups, which indicates that the extract tends to prevent liver damage by maintaining the integrity of the plasma membrane [35,36].

5. Conclusion

In conclusion, the results suggest that balanced consumption of *Pistacia khinjuk* nuts may be beneficial for reducing risk factors for diabetes and cardiovascular diseases, especially those related to hypercholesterolemia. Our results also provided scientific evidence on the use of *Pistacia khinjuk* as a nephro-protective, hepato-protective and cardio-protective agent.

List of abbreviations

ALT: Alanine Aminotransferase; **ANOVA**: One Way Analysis of Variance; **AST**: Aspartate Aminotransferase; **BR**: Bilirubin; **BUN**: Blood Urea Nitrogen; **CVD**: Cardiovascular Disease; **GGT**: Gamma Glutamyl Transferase; **HDL**: High Density Lipoprotein; **LDL**: Low Density Lipoprotein; **LDL**-C: Low-Density Lipoprotein Cholesterol; **TG**: Triglyceride; **WHO**: World Health Organization

Declarations

Ethics approval and consent to participate

The study was conducted in compliance with the principles of the ethical recommendations about using laboratory animal guidelines, and the experimental protocol was approved by the Faculty of Veterinary Medicine, Shahrekord Branch, Islamic Azad University, Shahrekord, Iran.

Consent for publication

Not applicable

Availability of data and material

Not applicable

Competing interests

All authors declare that they have no conflict of interest.

Funding

This study was financially supported by Islamic Azad University, Shahrekord Branch, Shahrekord, Iran.

Acknowledgements

The authors are thankful to the Faculty of Veterinary Medicine, Islamic Azad University, Shahrekord Branch (IAUSHK), for the financial support. The results described in this paper are part of Dr. Reza Fathi Hafshejani's thesis.

References

1- Yuan H, Ma Q, Ye L, Piao G. The traditional medicine and modern medicine from natural products. Molecules. **2016**;*21(5):559.*

2- Daradka HM. Evaluation of Hematological and Biochemical Activity of Ethanolic Extract of Zygophyllum simplex Linn. in Wistar Rats. Pak J Biol Sci. **2016**;*19(4):179.*

3- Aminifard Z, Chaji M, Mohammadabadi T. The replacement value of corn silage with wild pistachio (Pistacia khinjuk) leaf in the diet of sheep and its effect on digestibility of fiber and protein. JLST. **2015**;*3(1):17-23*.

4- Ezatpour B, Saedi Dezaki E, Mahmoudvand H, Azadpour M, Ezzatkhah F. In vitro and in vivo antileishmanial effects of Pistacia khinjuk against Leishmania tropica and Leishmania major. Evid Based Complement Alternat Med. **2015**;*2015:149707*.

5- Asif S, Ahmad M, Bokhari A, Chuah LF, Klemeš JJ, Akbar MM, et al. Methyl ester synthesis of Pistacia khinjuk seed oil by ultrasonic-assisted cavitation system. Ind Crops Prod. **2017**;*108:336-47.*

6- Ahmed S, Saeed-Ul-Hassan S, Islam M, Qureshi F, Waheed I, Munawar I, et al. Anti-oxidant activity of Pistachia khinjuk supported by phytochemical investigation. Acta Pol Pharm. **2017**;*74:173-78.*

7- Parham M, Heidari S, Khorramirad A, Hozoori M, Hosseinzadeh F, Bakhtyari L, et al. Effects of pistachio nut supplementation on blood glucose in patients with type 2 diabetes: a randomized crossover trial. The review of diabetic studies: Rev Diabet Stud. **2014**;*11(2):190-6.*

8- Tohidi M, Khayami M, Nejati V, Meftahizade H. Evaluation of antibacterial activity and wound healing of Pistacia atlantica and Pistacia khinjuk. J Med Plants Res. **2011**;*5(17):4310-4.*

9- Tomaino A, Martorana M, Arcoraci T, Monteleone D, Giovinazzo C, Saija A. Antioxidant activity and phenolic profile of pistachio (Pistacia vera L., variety Bronte) seeds and skins. Biochimie. **2010**;*92(9):1115-22.*

10- Esmat A, Al-Abbasi FA, Algandaby MM, Moussa AY, Labib RM, Ayoub NA, et al. Anti-inflammatory activity of Pistacia khinjuk in different experimental models: isolation and characterization of its flavonoids and galloylated sugars. J Med Food. **2012**;*15(3):278-87.*

11- Bozorgi M, Memariani Z, Mobli M, Salehi Surmaghi MH, Shams-Ardekani MR, Rahimi R. Five Pistacia species (P. vera, P. atlantica, P. terebinthus, P. khinjuk, and P. lentiscus): a review of their traditional uses, phytochemistry, and pharmacology. Sci World J. **2013**;*2013: 219815.*

12- Ghaseminasab PM, Ahmadi A, Mazloomi SM. A review on pistachio: Its composition and benefits regarding the prevention or treatment of diseases. JOHE. **2015**; *4 (1):57-69.*

13- Hernández-Alonso P, Salas-Salvadó J, Baldrich-Mora M, Juanola-Falgarona M, Bulló M. Beneficial effect of pistachio consumption on glucose metabolism, insulin resistance, inflammation, and related metabolic risk markers: a randomized clinical trial. Diabetes care. **2014**;*37(11):3098-105.*

14- Mirian M, Behrooeian M, Ghanadian M, Dana N, Sadeghi-Aliabadi H. Cytotoxicity and antiangiogenic effects of Rhus coriaria, Pistacia vera and Pistacia khinjuk oleoresin methanol extracts. Res Pharm Sci. **2015**;*10(3):233-40.*

15- Fattahi A, Sakvand T, Hajialyani M, Shahbazi B, Shakiba M, Tajehmiri A, et al. Preparation and characterization of Pistacia khinjuk gum nanoparticles using response surface method: Evaluation of its anti-bacterial performance and

cytotoxicity. Adv Pharm Bull. **2017**;*7(1):159-164.*

16- Mahmoudvand H, Mirbadie SR, Kia MG, Badparva E, Lori SS, Harandi MF. Efficacy of Pistacia khinjuk fruits on viability of hydatid cyst protoscoleces and its acute toxicity in mice model. Iran J Parasitol. **2016**;*11(3):383-388.*

17- Farahpour MR, Mirzakhani N, Doostmohammadi J, Ebrahimzadeh M. Hydroethanolic Pistacia atlantica hulls extract improved wound healing process; evidence for mast cells infiltration, angiogenesis and RNA stability. Int J Surg. **2015**;*17:88-98.*

18- Memariani Z, Sharifzadeh M, Bozorgi M, Hajimahmoodi M, Farzaei MH, Gholami M, et al. Protective effect of essential oil of Pistacia atlantica Desf. On peptic ulcer: role of α-pinene. J Tradit Chin Med. **2017**;*37(1):57-63.*

19- Karunamoorthi K, Jegajeevanram K, Vijayalakshmi J, Mengistie E. Traditional medicinal plants: a source of phytotherapeutic modality in resource-constrained health care settings. Evid Based Complement Alternat Med. **2013**;*18(1):67-74.*

20- Misra A, Sharma R, Gulati S, Joshi SR, Sharma V, Ibrahim A, et al. Consensus dietary guidelines for healthy living and prevention of obesity, the metabolic syndrome, diabetes, and related disorders in Asian Indians. Diabetes Technol Ther. **2011**;*13(6):683-94.*

21- Fischer S, Glei M. Potential health benefits of nuts. Ernaehrungs Umschau International. **2013**;*60(12):206-215.*

22- Ros E. Health benefits of nut consumption. Nutrients. **2010**;*2(7):652-82.*

23- Schwab U, Lauritzen L, Tholstrup T, Haldorsson TI, Riserus U, Uusitupa M, et al. Effect of the amount and type of dietary fat on cardiometabolic risk factors and risk of developing type 2 diabetes, cardiovascular diseases, and cancer: a systematic review. Food Nutr Res. **2014**;*58(1):25145.*

24- Li Z, Song R, Nguyen C, Zerlin A, Karp H, Naowamondhol K, et al. Pistachio nuts reduce triglycerides and body weight by comparison to refined carbohydrate snack in obese subjects on a 12-week weight loss program. J Am Coll Nutr. **2010**;*29(3):198-203.*

25- Askari G, Yazdekhasti N, Mohammadifard N, Sarrafzadegan N, Bahonar A, Badiei M, et al. The relationship between nut consumption and lipid profile among the Iranian adult population; Isfahan Healthy Heart Program. Eur J Clin Nutr. **2013**;*67(4):385-9.*

26- Hyder MA, Hasan M, Mohieldein AH. Comparative levels of ALT, AST, ALP and GGT in liver associated diseases. Eur J Exp Biol. **2013**;*3(2):280-4*.

27- Akomolafe SF, Oboh G, Oyeleye SI, Olasehinde TA. Toxicological effects of aqueous extract from African walnut (Tetracarpidium conophorum) leaves in rats. Evid Based Complement Alternat Med. **2017**;*22(4):919-25.*

28- Su J, Wang X, Song W, Bai X, Li C. Reducing oxidative stress and hepatoprotective effect of water extracts from pu-erh tea on rats with high-fat diet. Food Sci and Hum Wel. **2016**;*5(4):199-206.*

29- Iranmanesh F, Mousaei Amin A, Shamsizadeh A, Fatemi I, Malaki Rad A, Rahnama A. Effects of Pistacia vera hydro-alcoholic extract on carbon tetrachloride-induced hepatotoxicity in male rats. Iran J Pharmacol Ther. **2016**;*14(2):35-40.*

30- Fathi M, Asiaban M. Elevated levels of blood urea nitrogen and creatinine in the last trimester of pregnancy of dromedary camels (Camelus dromedarius). Iran J Vet Med. **2016**;*9(4):249-55.*

31- El-Newary SA, Sulieman A, El-Attar S, Sitohy M. Hypolipidemic and antioxidant activity of the

aqueous extract from the uneaten pulp of the fruit from Cordia dichotoma in healthy and hyperlipidemic Wistar albino rats. J Nat Med. **2016**;*70(3):539-53*.

32- Mehrdad M, Messripour M, Ghobadipour M. The effect of ginger extract on blood urea nitrogen and creatinine in mice. Pakistan journal of biological sciences: PJBS. **2007**;*10(17):2968-71*.

33- Ayeni M, Akanmu M, Bolaji O, Osasan S, Olayiwola G, Afolabi M, et al. Bilirubin Lowering Potential of Aqueous Carica Papaya Extract in Induced Jaundice in Rats. J Pharm Pharmacol. **2017**;*7:457-66.*

34- Arthur FK, Woode E, Terlabi EO, Larbie C. Bilirubin lowering potential of Annona muricata (Linn.) in temporary jaundiced rats. Am J Pharmacol Toxicol. **2012**;*7(2):33-40.*

35- Staudigl C, Concin N, Grimm C, Pfeiler G, Nehoda R, Singer CF, et al. Prognostic relevance of pretherapeutic gamma-glutamyltransferase in patients with primary metastatic breast cancer. PLoS One. **2015**;10(4):*e0125317.*

36- Rajesh V, Perumal P. Chemopreventive and antioxidant activity by Smilax zeylanica leaf extract against N-nitrosodiethylamine induced hepatocarcinogenesis in wistar albino rats. Orient Pharm Exp Med. **2014**;*14(2):111-26.*