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PJMLS

Print ISSN: 2707-4471. Online ISSN: 2707-448X

Review Article	Pak-Euro Journal of Medical and Life Sciences
DOI: 10.31580/pjmls.v5i3.2595	Copyright © All rights are reserved by Corresponding Author
Vol. 5 No. 3, 2022: pp. 521-528	
www.readersinsight.net/pjmls	
Submission: July 06, 2022	**Revised:** September 21, 2022 **Accepted:** September 30, 2022

NUTRITIONAL VALUE OF *PISTACIA KHINJUK* HULL AND KERNEL OIL

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Abstract

Pistacia khinjuk is a deciduous tree of cashew family Anacardiaceae. It is an important medicinal plant that has various pharmacological properties in folk and modern medicine including antidiabetic, antihyperlipidemic, anticholinesterase, antiinflammatory and antiasthmatic. Pistacia khinjuk fruit has potent bioactive phytocompounds significantly present in essential oil having antioxidant, antifungal, antibacterial, antileishmanial and functional potential. Pistacia khinjuk fruit essential oil possesses good therapeutic capability as it has a crucial role in numerous diseases. The main purpose of this review study was to report Pistacia khinjuk characteristics, their composition, bioactive potential and key role in food, cosmetic and pharmaceutical applications.

Keywords: *Anarcardiaceae, Antioxidant activity, Bioactive components, Pharmacological properties, Pistacia khinjuk, Preservation*

INTRODUCTION

Pistacia khinjuk is a potential medicinal plant that plays a vital role in the development of different pharmaceutical products. It has various pharmacological properties in folk and modern medicine including antidiabetic, antihyperlipidemic, anticholinesterase, antiinflammatory and antiasthmatic potential. Its fruits are used as edible wild nuts, for making a coffee-like drink and as a source of oil and colouring agent (1). This plant fruit has been used since ancient times for cooking and making snacks. *Pistacia khinjuk* is used in traditional Persian medicine as a natural remedy that is involved to prevent and treat with several types of diseases including vomiting, nausea, stomach discomfort and motion sickness (2). The respiratory disorder, digestive and cardiovascular problems are cured with different parts of this fruit (3). The major phytochemical elements in the plants as antioxidants are ascorbic acid, flavonoids, flavonols, carotenes, tocopherols, anthocyanins and polyphenols which are present in hull and kernel. The kernel nutritional value is higher as compared to hull in content of unsaturated fatty acid, protein, sugar and elements such as copper, phosphorus, magnesium, zinc and iron in kernel are greater than hull (4).

Pistacia khinjuk fruit extracts have several usages in treatment of numerous infections due to its antibacterial, antifungal and antileishmanial characteristics (5). It promotes stomach diseases, treats hackers, colds, breathes the offspring of the air and gingival secretions. It could be used as a natural preservative in the pharmaceutical and food industry. The essential oil of *Pistacia khinjuk* has antibacterial, antifungal and wound healing properties. The phenolic compounds of fruit like gallic acid, caffeic acid, ascorbic acid, rutin, synaptic acid and ferulic acid possess great effects of antioxidants. Furthermore, this plant fruit (different parts) extract of hull have higher antioxidant activities of antioxidant and 30% - 40% of raw kernel containing protein from where amino acid as hydrophilic for instance, aspartic acid and glutamic are preponderate (1). They contain Phenolic compounds and high essential unsaturated fatty acid content as well as rich in fatty acids like oleic acid and linoleic acid (6). Moreover, its plant nuts reduce the mortality rate of cancer and protect the human body from endothelial cancer, prostate cancer, colon cancer, pancreatic cancer and breast cancer (7).

Pistacia species demonstrate the nutritious characteristics in seed oils for this reason; it is a highly oxidative product of food components including phenolics, tocopherols, tannins, flavonoids and oleic acid

(8). *Pistacia khinjuk* essential oil is famous in the cosmetic industry and beneficial for skin moisturizing. Additionally, skin and hair are both ideally treated with multiple essential oils and *Pistacia khinjuk essential* oil (9).

CHARACTERISTICS OF *PISTACIA KHINJUK*

OCCURANCE AND BOTANICAL CHARACTERISATION

Pistacia khinjuk is a deciduous tree of cashew family *Anacardiaceae*. This species has been growing for the last 3000 years which is naturally occurring in Middle Eastern and Mediterranean countries (3). It is mostly found in Iran, Syria, Turkey, Egypt, Iraq, India, Afghanistan and Pakistan. In Egypt, two species of *Pistacia khinjuk* are found namely, *var. microphylla* boiss and *var. glabra* schweinf. The three species of *Pistacia khinjuk* including *Pistacia khinjuk var. heterophylla* bornm, *Pistacia khinjuk var. populiphlia* boiss (one to five leaflets-leaves) and *Pistacia khinjuk var. oblonga* bornm (five to seven leaflets-leaves) are generally grow in Iran (1).

Pistacia khinjuk is widely spread in dry, rocky areas of Balochistan, Gilgit, Chitral and Khyber areas of Pakistan. This species grows in warmer areas with lower altitudes and also at high altitude in foothills of mountains. It is found in faraway areas in circumstances of heavy trees destruction of (Northern) areas, especially on rocky cliffs that are out of the way for humans and goats. The species of *Pistacia khinjuk* are best for cultivation in different regions and highly resistant for unfavourable environment, climate change of soil like drought and osmatic stress (10). The word Khinjuk comes from the plant in Afghanistan. *Pistacia khinjuk* are also known in Persian as "Baneh" and "Kolkhoung", respectively. It is called Shinay in Pashto and Jangli Pista in Urdu. It is known for many other names like Gazwan, Buzgai, Kakarsinghee, Bittim, Kasour, Guan, Gulgnoor, Mastix, Ushgai and Mastic show great variety of this species in many areas (11).

Pistacia khinjuk is an evergreen shrub or tree which generally grows 5-15 m tall. Clusters of food are larger and approximately 14-22 cm long. The seeds are yellowish and ready in September and August. Sometimes, it may extend into October. The nuts of this plant are very small and frequently used as rootstock and good eatable variability in the form of roasted and salted nuts (5). It may exist as solitary stands and grow in forests. The species of this plant show modest resistance for (root knot) nematodes as well as species of phythophtora. *Pistacia khinjuk* seed blossoming period is late that chromosome number is (2n= 24) and shows (physical & internal) dormancy. Its plant fruits have a round shape (12.3mm long & 4.8-9.6 mm wide), generally skin (hull) colour is green and seed (kernel) colour is dark green. It is found in different colours, some of the fruits are blackish or blue whereas others are yellowish. Its fruit produces compressed seeds which consist of one-seeded drupe (10).

Fruit of this plant contains fat (57.6%), protein (20.3%), ash (2.8%), water (4.6%) and crude fiber (4.7%). *Pistacia khinjuk* fruit (the green hull of the seeds, kernel and whole seeds) extracts essential oil to 4.0% (v/w). The identified total components of ninety-five compounds from the fruits were found in essential oil. Mainly found constituents are nonaldehyde plus linalool (2.76%), β-caryophyllene (1.95%), p-cymene (2.50%), B-pinene (2.51%), α-pinene (61.13%) and myrcene (8.28%) among them. Main components of fatty acids found in essential oil were linolenic acid (0.95-1.5%), palmitic (8.5-17.82%), margaroleic (0.43%), stearic (1.48-2.61%), gadoleic 0.76%, margaric (0.4%), linoleic (17.44-38.85%), erucic (0.88%) and palmitoleic (1.23-5.73%) were recognized with composition of fatty acid of *Pistacia khinjuk* (12).

BIOACTIVE COMPONENTS

Pistacia khinjuk fruit contain include: phellandrene (52.33%) (w/w), wax (15.45%), triglycerides (62.3%), steroles (2.63%), tocopherols (981.14 mg per kg oil), protein (20.3%), fiber (4.7%) and main components of fatty acids in the oil which were categorized as follows: palmitic acid (8.5-17.82%), oleic acid (51.46-52.12%), linoleic acid (17.44- 38.85%) and many other such as flavonoids, terpenoids, phenolics, and minerals (12).

THERAPEUTIC FUNCTIONS

The best way of treatment of disease is phyto-medicine that has great medicinal and therapeutic effects. It has various pharmacological properties in folk and modern medicine that can be used for antidiabetics, antitumor and antiinflammatory medications (1). Different parts of *Pistacia khinjuk* fruit are

treated for respiratory disorders, digestive and cardiovascular disease. The natural ingredients of essential oil have the best therapeutic effects; its many applications in the pharmaceutical industry (3).

Table I. Bioactive components chemical composition and applications of *Pistacia khinjuk* fruit essential oil

Bioactive components	Types	Function	Applications	References
Phellandrene	Alpha phellandrene, Beta phellandrene	Increase energy levels, reduce pain, as an anticancer	Its pleasing aromas applied for fragrances	(13)
Wax, triglycerides, sterols	Phyto-sterols	Responsible for refining oil color turbidity. Provide insulation. Decreases blood cholesterol level	Probably applied in the pharmaceutical, cosmetics, plasticizer, polymer, leather and food industries	(12)
Tocopherols	α, β, γ, δ-tcopherols	Biological activity in vivo assay and antioxidant	Used as vitamin E for human health	(14)
Protein	—	Physiological activities in human	Serve as vasodilator	(15)
Fiber	Dietry fiber	Control obesity, diabetic, several cancer types, cardiovascular disease	Used as additive. Involved in food processing. Applied for flour product, meat products, dairy products	(16)
Flavonoids, terpenoids phenolics	Flavanol, anthocyanin, monoterpenes, diterpenes, triterpenes	Scavenging ROS ability. Prevent cardiovascular disease and cancer	Food additive, food preservation, food packaging	(17)
Fatty acids	Saturated fatty acid (palmitic acid) unsaturated fatty acid (oleic acid, linoleic acid)	Prevent cardiovascular disease in human body	Used as Food additive in industry. As excipient in pharmaceuticals. Used in cosmetics and personal care products	(18)
Minerals	Micronutrient (B, Cu, Mn ,Mo, Zn, Ni Cl, Fe), Macronutrient (S,P, N, Mg, Ca, K)	Ca role in cell signalling, nervous message transmission. P has function in cell growth and development	K serve as cofactor, Ca functioning as major essential element in human body	(4)

PHYTOCHEMICAL SCREENING

Phytochemical analysis in crude methanolic extract and its fractions demonstrate the presence of tannins, flavonoids, sterols, triterpenoids, saponins, cardiac glycosides, proteins, carbohydrates, and alkaloids in the crude extract of *Pistacia khinjuk* (5). *Pistacia lentiscus* plant different parts such as fruits, twigs and leaves in phytochemical screening revealed flavonoids, tannins, sterols, saponins, holosides, triterpenes, oses, mucilages and reducing sugars presence whereas anthraquinones combined and anthraquinones free showed none presence. However, Fruits showed an abundance of alkaloids presence but in twigs and leaves showed none presence (19). Various parts of *Pistacia chinensis var*. integerrima (galls, roots, bark and leaves) were selected for phytochemical screening. The tannins, flavonoids, alkaloids and terpenoids were present in galls extract where flavonoids and terpenoids were present but tannins and

terpenoids present in roots and leaves extract (20). Berries extract of *Pistacia lentiscus* showed that flavonoids, phenolic compounds, leucoanthocyanins, anthocyanins, tannins, phlobatannins, terpenoids, saponins , mucilage and proteins presence were confirmed in phytochemical activity whereas, carotenoids, quinones and alkaloids showed absence (21).

ANTIBACTERIAL ACTIVITY

Pistacia khinjuk essential oil extract inhibited the growth of three pathogenic bacteria *Staphylococcus aureus, Escherichia Coli* and *Pseudomonas aeruginosa*. The small and big both seeds extract of oil pH were equivalent to each other. The wavelength of essential oil of *Pistacia khinjuk* and pure pigment absorption of anthocyanin extract was observed at 479 nm that showed dye highest concentration, respectively. It showed the other some pigments presence as well as pureness of colour quality (22). The oil mastic gum showed an effect against *Bacillus, Staphylococcus aureus* and *Listeria monocytogenes* (Gram positive bacteria). On the other hand, *Listeria monocytogenes* was more effective as comprising values 0.9375µg/ml than *Klebsiella pneumonia, Eschericia coli, Salmonella enterica and Enterococcus faecalis* (gram negative bacteria) that obtain value is 1.875µg/ml. The Gram positive bacteria showed subsequently high MIC values (23).The ethyl acetate, chloroform, diethyl ether and ethyl alcohol were studied in that antibacterial activity were found against bacteria such as *Staphylococcus aureus, Staphylococcus epidermidis, Enterococcus and Bacillus subtilis* that MIC value was recorded 0.02-0.5 mg/mL (24). The results revealed that wild *pistacia* ethanol extract showed antibacterial effects against Gram negative and Gram positive bacteria. In both bacteria the hull extract MIC and MBC was lower than core extract. *Staphylococcus aureus* growth inhibition was greater as compared to *Escherichia coli*. Hull extract inhibition zone of bacterial growth diameter was greater for both bacteria than core extract. The wild *pistacia* fruit ethanolic extract has antibacterial effect against gram positive bacteria but more effect in gram negative bacteria which is due to gram positive cell wall (peptidoglycan layer) resistance (25).

ANTIFUNGAL ACTIVITY

Antifungal Activity of *Pistacia khinjuk* in essential oil showed great activity against *Candida albicans*. The microorganisms which were used show great activity against anti-fungal activity in essential oil that exhibited strong levels of antifungal ability revealed best results. *Candida albicans* in comparison with essential oil was highly sensitive according to MIC and MFC values (26). *Pistacia khinjuk* leaves extracts significantly inhibited growth of fungi. As compared to other extracts, the extracts of chloroform possess great inhibition of fungal growth. The MIC values of *Candida albicans* was 0.10 and *Saccharomyces cerevisiae* was 0.06, respectively (27). The *Pistacia atlantica* leaf and fruit extracts values of MIC were ranging between (6.25-25mg ml^{-1}) and (6.125-12.5 mg ml^{-1}) against *Aspergillus* and *Candida* species. The extracts of olive leaf exhibited not any effect against *Aspergillus flavus* and *Candida* species whereas, it demonstrated the potency of fungi against *Aspergillus fumigatus* and *Aspergillus niger* that MIC was 12.5-25mg/ml (28). The leaf oils of *Pistacia lentiscus*, *Pistacia vera* and *Pistacia terebinthus* some doses and resin of *Pistacia lentiscus* (neutral and total acidic fractions) inhibited the *Rhizoctonia solani* growth. Although antifungal activity was not shown in all samples against *Fusarium sambucinum* and *Phythium ultimum* nevertheless, *Fusarium sambucinum* growth was increased successfully (29).

ANTILEISHMANIAL ACTIVITY

In this MTT assay *Leishmania major* (promastigote form) were tested to evaluate anti-leishmanial activity in essential oil of *Pistacia khinjuk*. It revealed that with the passage of time and concentration antileishmanial activity showed great effect in essential oil of *Pistacia khinjuk* compared with the control group (30). The two species *L.major* and *L.tropica* were used in antileishmanial activity (in vitro & in vivo) against *Pistacia khinjuk* alcoholic extract. Its IC_{50} values and optical density (OD) revealed that alcoholic extract of *Pistacia khinjuk* inhibits the *L.tropica* (promastigote forms) growth. It proves that forms of amastigote were most liable for extract of *Pistacia khinjuk* as compared to forms of promastigote. The promastigote forms of *L. major* that affect male (BALB/c) observed 87.5% recovery in mice also by extract of

Pistacia khinjuk that strong effects of suppression in CL and 30% of concentration was seen in the *in vivo* assay while intermediary exposed suppression effects with 20% of concentration in extract of *Pistacia khinjuk*. In addition, alcoholic extract of *Pistacia khinjuk* (SI value ≥ 10) in macrophage cells showed their safety against it and also to the parasite specificity.

The results revealed that alcoholic extract of *Pistacia khinjuk* possesses super antileishmanial activities and in mice regulate cutaneous leishmaniasis which is also affected by (*L. major*) promastigotes forms (3). It suggested that essential oil of *Pistacia vera* inhibited ($P < 0.05$) forms of amastigotes growth rate in the *in vitro assay*. The IC_{50} observed in a dose-dependent response was 21.3 ± 2.1 μg/ml comparable with glucantime. This clinical stage, Meglumine antimoniate showed antileishmanial activity that IC_{50} was (44.6 ± 2.5 μg/ml), respectively. The essential oil represented great suppression effect on cutaneous leishmaniasis showed recovery 87.5% in BALB/c mice in the *in vivo assay* (31). Obtained gum of *Pistacia atlantica var. kurdica* and Glucantime decreased BALB/c mice skin lesion size affected by *Leishmania major* comparison with this $P < 0.01$ of control. BALB/c mice treated with gum and Glucantime also decreased the number of parasitological positive mice $P < 0.05$ (32).

ANTIOXIDANT ACTIVITY

Pistacia khinjuk antioxidant activities have been reported according to the fruit of *Pistacia khinjuk* phenolic compound (ascorbic acid, rutin, caffeic acid, gallic acid and synaptic acid) has potent antioxidant effects. Among different parts of the fruit, hull extract exhibited great antioxidant activity. Moreover, kernels in raw form consist of (30% - 40%) protein in which glutamic acid and aspartic acid hydrophilic amino acid predominate (33). The gas chromatography analysis of the composition of hull and kernel oil fatty acids of *Pistacia khinjuk* and high performance of liquid chromatography analysis of tocopherols were done to evaluate antioxidant activity. Anisidine and peroxide values under the process of heating of 100°C, 110°C, 120°C were shown oxidative stability of oil. The Essential oil (hull and kernel) were major fatty acids based on oleic acid determined by gas chromatography that showed (high content monounsaturated and low content saturated) fatty acids. During the process of heating it shows high oxidative stability in (hull and kernel) oil which is based on tocotrienols that are attributed to high content. The results revealed that hull oil as compared to kernel oil of *Pistacia khinjuk* acted slightly better (34). The obtained results showed TPC value (46.0 mg/g) of *Pistacia khinjuk* extract. It revealed that DPPH radicals 73.5% scavenging while (8.3 μmol TE/g DW) was recorded in FRAP assay that proved *Pistacia khinjuk* extract exhibited great antioxidant activity (2).

The fruit essential oil of *Pistacia lentiscus L.* contained maximum amount of total phenol content was 810 mg GAE/kg while BHA (butylated hydroxyanisole) was 0.012 ± 0.0001mg/mL by comparing capacity of DPPH radical scavenging was permissible IC_{50} = 20.619 ± 0.312 mg/ml (35). *Pistacia vera var. sarakhs* (hull and kernel) ethanolic extract revealed highest phenolic content of dried plant was 169.53 and 113.21 mg GAE/g whereas, flavonoid content of dried plant (139.47 and 87.03 mg QE/g). The antioxidant activity was assessed in hull and kernel ethanolic extract that DPPH radical scavenging of IC_{50} least value (6.08 and 3.04 μg/ml) while greatest IC_{50} of FRAP (5.59 and 5.59 mmol/g), respectively (36). Hydro-alcoholic extract of *Pistacia atlantica* subsp of kurdica exhibited modest antioxidant effects that IC_{50} was 75μg ml-1. Hydro-alcoholic extract of total phenol was 15.9 mg GAE/g (dry weight) while hydro-alcoholic extract of total flavonoids was 28 mg QE/g (dry weight) (37).

WOUNDHEALING ACTIVITY

The wound healing activity was determined by in vivo experiment commenced with methanolic extract of *Pistacia khinjuk* which were tested in wistar rats by using excision wound model. It showed that extract of *Pistacia khinjuk* plant is the best therapeutic drug with wound healing properties (24). The total flavonoid, phenol and antioxidant capacity, DDPH (2,2-diphenyl-1-1-picrylhydrazyl) assay was used to evaluate wound healing activity. It revealed that IC_{50} of butylated hydroxytoluene around (3.9 μg/ml) whereas IC_{50} of (3,650 μg/ml) inhibit (50%) concentration decrease free radical stability that were measured in methanolic extract of unripe fruits of *Pistacia khinjuk*. As compared to control wounds the percentage of

wound healing showed increasing value at $P < 0.05$ (38). The results showed that wound contraction level was greater and in the PLVO group the healing time was faster as compared to CRL group, VAS group and MAD group. The different epithelization periods obtained in days were PLVFO group (30 ± 3.994), MAD group (33.5 ± 3.78), VAS group (34.66 ± 3.88), CRL (37.16 ± 3.54), respectively. It revealed that fatty oil of *Pistacia lentiscus* stimulates $P < 0.05$ wound contraction and period of epithelization reduces in rabbit model (39). It was reported by different studies that both oleoresins as a wound healing agent have great effects and seems in wound healing to rationalize their traditional usage in many countries and provide scientific provision for traditional healers' treatment (40).

ANTIINFLAMMATORY ACTIVITY

The anti-inflammatory activity was evidenced by decreased PGE2 elevation and carrageenan-induced rat paw edema. In the croton oil–induced ear edema model, MPO activity was significantly inhibited and inflammatory histopathological changes were ameliorated. In the rat air pouch model, NO generation and TNF-a release were significantly inhibited. For the first time, isolation and nuclear magnetic resonance spectral data of compound 6 from the genus *Pistacia* are measured. In several experimental models *Pistacia khinjuk L. aqueous* methanol extract shows anti-inflammatory activity (41).

Oleoresin exhibited anti-inflammatory activity among the screening of different extracts against carrageenan-induced hind paw edema models in mice that did not harm gastric system at doses of 500 and 250 mg/kg while the remaining extracts were not found to be active. Whereas, antinonociceptive effect was seen significantly at dose of 500 mg/kg in oleoresin. *Pistacia vera ethanolic* and aqueous extracts of peduncle, branch, leaf and fruit did not manifest antinociceptive inhibition in (p-benzoquinone-induced) abdominal contraction in mice (42). The anti-inflammatory activity was assessed by using leaves of *Pistacia lentiscus L.* in carrageenan-induced paw edema assay in rats. The leaves methanolic (MeOH) and aqueous (AQ) extract showed anti-inflammatory activity in a dose-dependent manner. For this both extract effects were matched with control drugs (43). The leaves extracts of *Pistacia integerrima* exposed reaction significantly against chemically induced pain $P < 0.001$ while extracts of galls with dose dependent response showed higher substantial protection ($P < 0.0001$).The galls extracts of *Pistacia integerrima* with (200 mg/kg) p.o, exhibited ($P < 0.05$) response in thermally induced algesia nevertheless, a lesser amount of positive references diclofenac and pentazocine, respectively. *Pistacia integerrima* extracts between (50-200 mg/kg) p.o, showed moderate activity against chronic inflammation induced by formalin ($P < 0.01$) and hind paw acute (44). Anti-inflammatory activity was found in *Pistacia lentiscus* hydrosol due to suppressed TNF- α proinflammatory, IL- β *and* IL-6 cytokines secretion in LPS (lipopolysaccharide) activate primary human monocytes.The NF-κB inhibited in LPS triggered U937 cells, the main aspect of transcription because of cascade of inflammatory that regulate the expression of ATP citrate lyase genes and mitochondrial citrate carrier. *Pistacia lentiscus* hydrosol modulated the citrate pathway of these two main components. Consequently, PGE_2, NO and ROS levels (inflammatory mediators) downward the citrate pathway were lessened. Results showed the *Pistacia lentiscus* anti-inflammatory properties suggest its potential as a therapeutic agent (45).

ANTICANCER ACTIVITY

Anti-cancer activity was tested to examine cytotoxic effects in aqueous and methanolic *Pistacia khinjuk* seed extract on murine mammary adenocarcinoma (AMN-3), its mitogenic effects on blood lymphocytes, normal cell lines murine fibroblast (L20B) and different tumors rhabdomyosarcoma (RD). The *Pistacia khinjuk* seed extract of cytotoxic effects were assessed on one normal cell line murine fibroblast, RD, murine mammary adenocarcinoma and two tumor cell lines. Furthermore, the blood lymphocytes in humans were premeditated to extract of plant mitogenic effects. The aqueous and methanolic both *Pistacia khinjuk* seed extracts with higher concentrations generate normal cell line and tumor cell line proliferation. It revealed that proliferation of blood lymphocytes in humans at (72h) increased by extracts which induced this activity. The activity that was determined in the extracts of the plant suggests it as a good mitogenic agent for experimental studies. The results showed that all cell line that were tested in which *Pistacia khinjuk* generate

proliferation moreover, the *Pistacia khinjuk* methanolic and aqueous both seed extracts with highest concentration displayed mitogenic effects (46).

All samples were tested to determine anticancer activity which showed apoptotic effects against (colon cancer) HT-29 cell lines and (breast cancer) MCF-7. In vivo extracts for root parts of females revealed great cytotoxic effects as compared to other extracts of testing in HT-29 cell series (IC_{50} = 59.60_0.69g/ml) and MCF-7 (IC_{50} = 31.86_ 1.40g/ml). The best activity of butyrylcholinesterase enzyme inhibition (BChE) activity was seen in samples of all extracts. In vivo female and male genotypes of *Pistacia khinjuk* were shown by toxic effects in extracts and in healthy cell lines (PDF). These plant samples were tested in vitro. In terms of cytotoxic activity the *in vivo* sample extracts showed high performance comparison with *in vitro*. The extracts of (female) root parts revealed high effects of cytotoxicity on cytotoxic effects on (breast cancer) MCF-7 cell lines. Accordingly, the extracts of root including male genotypes and female genotypes exhibited great cytotoxic activity in (breast cancer) MCF-7 (male IC_{50}= 36.11_0.44g/mL, female IC_{50} = 31.86_1.40g/mL) and HT-29 (male IC_{50} = 68.47_2.41g/mL, female IC_{50} = 59.60_0.69g/mL) cell lines by comparing extracts of leaf and stem (7).

Pistacia atlantica extract revealed antiproliferative inhibition of HDFS, HeLA and AGS (IC_{50} = 896.3 mu g/m, 382.3 mu g/m, 332.3 mu g/m). The results showed that *Pistacia atlantica* suppressed cervical cancer cells and gastric carcinoma proliferation. It suggests *Pistacia atlantica* containing higher amounts of phytocomponents might have a great source of anticancer drugs (47). *Pistacia lentiscus* methanolic extract (8:2) exhibited super cytotoxic activity in MTT assay. The extract of leaf showed significant proliferation with IC_{50} value of 250.45 ± 1.96 g/ml and 135.67 ± 2.5 g/ml in AGS cells and $CaCO_2$ while leaves, stems and fruits infusion extracts were not found to be active (48).

The mastic gum resin of *Pistacia atlantica* persuades cancer cells to die with time and is dose-dependent at concentration ranging from (0.01 to 100 μM). The mastic gum resin inhibited human cancer cells proliferation within 2 days (IC_{50} = 5.2 ± 0.8 μg/ml, 8.11 ± 0.23 μg/ml, 11.52 ± 0.18 μg/ml and 15.34 ± 0.21 μg/ml) of colonic adenocarcinoma (COLO205) cells, gastric adenocarcinoma (CRL-1739), pancreatic carcinoma (PANC-1) and bile duct cancer (cholangiocarcinoma)(KMBC). Flow cytometry demonstrated cell cycle G2/M Phase in that mastic gum significantly ($P < 0.05$) halted proliferation of COLO205 cells. Due to this COLO205 cells morphologically changed, initiated by resin. (49). *Pistacia terebinthus* induced dose dependent and time at 24 h for anticancer activity in which A549 cell lines (human lung cancer) proliferation of cell inhibited. After 24 hrs treatment with *Pistacia terebinthus* the A549 cell lines (cell viability) was recorded (16.13 ± 2.42 to 99.81 ± 4.01%) with concentration ranging between (0.5-500 μg/ml) and (IC_{50} = 123.8±39.41μg/ml) (50).

ANTIDIABETIC ACTIVITY

The methanolic extract of *Pistacia khinjuk* was tested to determine the hypoglycemic effect in six groups of swiss albino mice. In alloxan monohydrate all the mice were injected. After alloxan monohydrate induction they received no treatment in Group 1 and 3 in comparison with group 2 that received glibenclamide (5mg/kg) whereas group 4, 5 received 500 and 250 mg/kg of *Pistacia khinjuk* extract and group 6 received 500 mg/kg of *Pistacia khinjuk* wax after alloxan monohydrate induction. The blood glucose level decreased and showed hypoglycemic activity in a group of mice (4, 5, 6) of extract of *Pistacia khinjuk.* It is considered as excellent antidiabetic medicine due to methanolic extract in which phenolic constituents were measured (9). The diabetic mice were allocated to keep in four groups. *Glibenclamide*, *Artemisia scorpia* and *Pistacia atlantica* extract were used for three groups with a dose of 200 mg/kg for 15 days whereas the untreated fourth group was given normal dose. Remaining ten mice (non- diabetic) were treated for normal control group. The results directed the ability of those plants that can diminish blood glucose comparable to diabetic control group ($P < 0.05$). The extract of *Pistacia atlantica* had more effectiveness compared with the extract of *Artemisia scorpia* (51).

Pistacia lentiscus crude gum of 100 mg/kg showed significantly ($P < 0.001$) reduced blood glucose comparable to the control group. Comparison with alloxan-treated group liver function test indicated changes significantly ($P < 0.01$). It revealed that crude gum of *Pistacia lentiscus* has hepatoprotective effect

and great efficiency for diabetic treatment (52). The extracts of PT in streptozotocin induced diabetic rats for antidiabetic activity of *Pistacia terebinthus*. 40 male rats (wistar albino) assigned into five groups including PT.DM, diabetic + PT (DM + PT), diabetic + acarbose (DM+ AC), diabetic (DM) and control (C) were entrenched through intraperitoneal injection of streptozotocin. It was shown in the pancreas of diabetic rat streptozotocin induce. Contrarily, immunoreactivity of insulin in the pancreatic PT (β cells) served for diabetic rats was significantly increased. In the PT supplemented diabetic group decreased levels of blood glucose such as low density lipoprotein (LDL), high density lipoprotein (HDL), total cholesterol (TC), total triglycerides, glucose, lactate dehydrogenase (LDH), alkaline phosphatase (ALP), alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were established. The enzyme levels of antioxidant defense system and malondialdehyde (MDA) were stabilized in DM + PT group. PT showed protective effects in pancreas, kidney and liver harmed through streptozotocin induced DM (53).

ANTIHYPERLIPIDEMIC ACTIVITY

Anti-hyperlipidemic test was performed to evaluate in leaves of *Pistacia khinjuk* proximate analysis which exhibited 6.8% fat, 12.8% crude fiber and 6.8% ash content. Both extract dosages of *Pistacia khinjuk* in albino rats enhanced better quality profile of lipid serum due to total cholesterol, total lipids, triglycerides and low density lipoprotein reduction and also increase levels of lipoprotein, high density of *Pistacia khinjuk* treated groups. The observation for weight of body to (0-60 days) shows great effect of increasing weight of body in all groups. Before sacrifice it was observed decreasing in hyperlipidemic and high dosages of *pistacia khinjuk* whereas *Pistacia khinjuk* low dosages and increasing in control, correspondingly (54).

CONCLUSION

Pistacia khinjuk has comestible fruit that is a great source of essential oil. Its oil is valuable and essential oil has folkloric uses. The chemical composition of essential oil is the key dynamic of discovering diverse bioactive constituents. It has been proved that *Pistacia khinjuk* exhibited remarkable antimicrobial, antioxidant, anti-inflammatory, anticancer, antidiabetic and antihyperlipidemic activities. It is the best wound healer that acts as a therapeutic agent for treating various ailments. Due to a wide range of medicinal and functional values, extensive studies have needed to explore potential bioactive constituents which could be a good candidate in treating disease

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