



A Closer Look at Some Medical Use of Green Persian Walnut Shell

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ABSTRACT: Persian walnut (*Juglans regia* L) is a tree species that has been of interest to humans since its medicinal and nutritional effects. The wild population of this species has been recorded in the temperate and semi-arid mountainous regions of Central Asia, East and South Asia, the Middle East and the Caucasus region. The origin of Iran's walnut communities is in the Hyrcanian forest in the north of Iran. Walnut is a source of various medicinal compounds such as various biologically active substances such as polyphenols, flavonoids, steroids, phospholipids, triterpenes, kinins, fatty acids, tannins, gallic acid and ellagic acid, and plays an important role in medicine, especially in traditional Iranian medicine. All these compounds have turned walnut into an important commercial product that is of high value in the pharmaceutical and food industry. In this study, various medicinal effects of this valuable species such as anti-cancer, anti-oxidant and anti-diabetic effects have been investigated according to recent researches and it shows that depending on the different climatic conditions, the medicinal compounds of walnut can change and this phenomenon is necessary. It creates more research in this field.

Keywords: Hyrcanian, Anti-cancer, medicinal effects, traditional medicine, Walnut

INTRODUCTION

Juglans regia L. (Persian Walnut) is a tree species that has been of interest to humans since the past. The fruit of *J.regia* is 5 cm long with a leathery, wrinkled exocarp and a hard 4-lobed endocarp. Fruits are born in clusters. The seeds are edible. The nuts are round and measure 1.5-2 inches. Wild populations of *J. regia* have been recorded in temperate and semi-arid mountainous regions of Central Asia, East and South Asia, the Middle East, and the Caucasus region. These forests are characterized by an extraordinary morphological and physiological diversity and are home of numerous wild relatives of cultivates species, highlighting the importance as a global biodiversity hot-spot (Verma et al., 2020).

J. regia has been introduced to a much wider area in the past due to its special nutritional importance and significant economic value. Walnuts were cultivated on a commercial scale in 48 countries of the world on a total area of 647,497 hectares in 2016. Global annual walnut production was estimated at 3,763.725 metric tons (in shell) in 2016, equaling a total production value of more than USD 14 billion. China and the United States accounted for 47 and 31 percent of the total global walnut production, respectively. Further major producer countries include Chile, Iran and Ukraine (Ahandani et al., 2014; Shigavea and Darr, 2020).

The origin of Iranian walnut communities in the Hyrcanian forest in northern Iran is very complex, and more efforts are needed to protect the diverse populations of this valuable genetic resource. In modern times, it is very difficult to find remaining natural populations of Persian walnut (*J. regia*) in its native range, but natural populations of this species can still be found in Hyrcanian forests. Recent studies have listed the presence of this species in North Iran in Talesh, Astara, Dino Chal, Goli Daghi (1500 m) and Bandargaz. The distribution of this species is mostly in Golestan province, including the cities of Bandar Gaz, Zarin Gol (900 m), Rabat Gezlaq (2400 m), Mazandaran province, including Farsang Dar, Haraz Valley. (100 meters) and the mountain slopes of this province and in Gilan province near Hashtpar (60 meters) the existence of this valuable species has also been reported (6-9). Some very valuable wild cultivars were identified and named for the first time by Alinia-Ahandani et al, in Lahijan region in Guilan province in Iran, which have potential capacities in the field of moisture-resistant cultivars and also very old generations of Hyrcanian walnut in this region (Ahandani et al., 2014; Alinia-Ahandani et al., 2019).

The origin of the walnut tree is from the eastern Balkans to the Himalayas and southwestern China. Persian or common walnut (*J. regia*) is the most well-known member, found mainly in temperate regions and commercially cultivated in many parts of the world. Now the walnut trees are growing. In parts of the world, including Asia (the foothills of the Himalayas, Iran, China and Japan), southern and eastern Europe, as well as North and South America. The walnut tree grows in some other provinces of Iran, such as Fars, Hamadan, Kohgiluyeh, Boyer Ahmad and Lorestan. A species of walnut tree with the scientific name *J.*

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regia grows in Iran. The walnut tree is sensitive to very hot and very cold weather in summer and winter. Walnut trees are single-stemmed plants with a height of about 10 to 25 meters. They have claw-shaped compound leaves. It appeared with male and female flowers separately on them. During the hibernation period, walnut trees can tolerate cold weather up to -11 degrees Celsius. The maturity of the walnut tree is directly related to various factors such as the species, race, climate and place of its growth (Aryapak and Ziarati, 2014; Habibi et al., 2022).

J. regia is a rich source of various types of chemical compounds. It plays a big role in Ayurveda and homeopathy system of medicine. It contains various biologically active substances such as polyphenols, flavonoids, steroids, phospholipids, triterpenes, kinins, fatty acids, tannins such as gallic acid and ellagic acid. Ellagic acid is responsible for anti-cancer and immunity properties. The active ingredient of *J. regia* is juglone (quinone). The bark of *J. regia* contains higher polyphenolic compounds which are responsible for antioxidant and antibacterial activities. The leaves of *J. regia* are rich in alkaloids, saponins, flavonoids, which show anti-diabetic effect. Walnut oil contains omega-3 and omega-6 unsaturated fatty acids, mono, di, triacylglycerol, free fatty acids, oleic and linoleic acids, which are beneficial for heart diseases, lowering cholesterol and blood sugar. The green husk contains juglone and polyphenols, which are used in textile dyeing industries. *J. regia* plant contains monoterpenes, sesquiterpenes, juglone, sterols, tocopherols, proteins, dietary fibers, melatonin, and folate. This study showed that *J. regia* contains a variety of chemical compounds with different biological activities (Alinia-Ahandani, 2018; Liu et al., 2021; Verma and Sharma, 2022).

Walnuts are a good source of essential fatty acids and tocopherols. Some sources reported that 17 compounds were identified in walnut leaves. 9 of them are epicatechin, syringtin-o-hexoside, myristicin-3-o-glucoside, myristicin-3-o-pantoside, scoltin, taxifolin-pantoside, quercetin glucuronide, kaempferol pantoside, and kaempferol rhamnoside. Depending on various factors such as geographical location, temperature, time, a plant has a different chemical composition in different countries. Recently, different parts of the walnut tree such as leaves, bark and fruit are used in the world. Researchers have reported that the chemical composition of walnuts varies in different climates. The fruits of walnut trees are valuable and edible. And their oil is rich in polyunsaturated fatty acids, tocopherols and phytosterols (Zhao et al., 2014; Hassani et al., 2020; Sheydaei and Alinia-Ahandani, 2021).

Juglone with a molecular weight of 174.16 and a formula of $C_{10}H_5O_2$ (OH) is the most prominent substance in different organs of the walnut tree which is then converted to juglone through hydrolysis. Juglone is an alkaloid substance that is slightly soluble in hot water and moderately soluble in alcohol. As a result, it can be one of the effective ingredients in walnut leaves because other substances in walnut leaves are often water-soluble or fat-soluble. The green shell of the walnut tree fruit contains emulsion, glucose and organic substances such as citric acid, malic acid, phosphate and calcium oxalate. Juglone and phenolic compounds are the most important compounds found in the leaf and green shell of walnut (Jaimand et al., 2004).

As a toxic compound, juglone is found only in fresh and green walnuts, but it does not have such properties. The green shell of the walnut is a by-product with little use. Due to its phytochemical source, walnut shell has been shown to increase the value of walnut products. Compared to using a by-product produced in large quantities (Delaviz et al., 2017; Sheydaei et al., 2021).

We mentioned on the title of this paper as a practical look at the medical use of Iranian green walnut skin in the world, and we focused on expressing the medicinal uses of walnut. Although in various climatic conditions, we can see varieties in medicinal compounds depending on temperature, humidity and even acidity. Remarkably, some secondary metabolites like phenolic and flavonoid compounds are synthesized in different conditions. Finding these differences needs regarding relevant tests on species from various climates (Zhao et al., 2014; Jahanbani et al., 2016; Sheydaei and Alinia-Ahandani, 2020).

The purpose of this research is to investigate the medicinal effects of walnuts in different climates and the effect of the environment on the medicinal effects of species. We reviewed various researches in this field and presented their results in this report.

MATERIALS AND METHOD

In order to collect the needed materials, it was tried to use 40 related papers which were between 2000 till 2022 and sites in related journals and indexed in sources such as SID, Springer, ScienceDirect, Wiley, Taylor & Francis and etc. For this purpose, the search was done through key words such as “Walnut and Medical applications”, “*J. regia* and medical applications”, “Medical use of walnut shell” and etc. At the end, it was tried to summarize and compare the contents in a concise and useful way.

RESULTS

Recently, the use of medicinal plants has increased significantly. So that today it is necessary to use traditional medicine as well as medicinal plants with the aim of producing more effective drugs with less side effects and determining effective doses. *J. regia* is a medicinal plant with different properties, which is less considered in traditional medicine despite its great therapeutic potential. The green skin of the immature fruit of *J. regia* (Persian walnut) has a wide range of medicinal effects, which has a

long history in the treatment of malignant tumors in traditional Chinese medicine. Flavonoids are the primary constituents of *J. regia* green peel as well as the main active components. In recent years, compounds extracted from traditional Chinese medicine have attracted more attention with their antitumor activity against gastric cancer. In traditional Chinese medicine, the green skin of the unripe fruit is called Qinglongi and it is used to expel heat and toxins, expel wind and ringworm, and relieve pain and dysentery. Modern pharmacological studies have shown that the green bark of *J. regia* has a wide range of medicinal effects, including anti-inflammatory, analgesic, antibacterial, antioxidant and antitumor. Effects There are complex chemical compounds in the bark of *J. regia*, including naphthoquinones, glycosides, polysaccharides, flavonoids, diarylheptanoids, terpenoids, organic acids and tannins (Croitoru et al., 2019; Wei et al., 2022). To extract the phenolic compounds of the green peel, double solvent systems (ethanol/water) are used, which are preferable to single solvent systems, and the extracts are taken using a shaker incubator (Taheri et al., 2020). In the world market, there are so many herbs which have some medical activities and reactions and are a good source for curing minor to major issues such as colds, coughs, skin rashes, bacterial and fungal infections, diabetes, cancer, arthritis, tuberculosis, etc. Various parts of herbs such as roots, bark, fruit, flowers, seeds, leaves, stems, etc. and their secondary products such as gum, resin demonstrate biological activity which could be applied as important parts in traditional medicine (Verma and Sharma, 2020).

In traditional medicine, walnut root is used to treat diabetes, its leaves are used to treat rheumatic pains, fever, diabetes, and skin diseases. And its flowers are used to treat malaria and rheumatic pains. As far as Iranian traditional medicine is concerned, this plant is widely used in Iranian cooking to treat various diseases. Walnut leaves are used in traditional medicine to reduce blood glucose and improve diabetes. According to studies, walnut leaves contain compounds that are effective for health. And they are widely used in traditional medicine to treat venous insufficiency and hemorrhoid symptoms. In some cases, they are used as anti-diarrheal and anti-parasitic drugs, as well as blood purifiers. The results show that extensive research has been done on the medicinal effects of walnuts in the last two decades. Different parts of this plant, such as its leaves, skin and fruit, have the property of reducing blood sugar in diabetic animals (Delaviz et al., 2018).

Anti-Cancer Activity

The green skin of the immature fruit of *J. regia* (walnut) has a wide range of medicinal effects, which has a long history in the treatment of malignant tumors in traditional Chinese medicine. Flavonoids are the primary constituents of *J. regia* green peel as well as the main active components. Recent studies show the anti-cancer effects of green walnut shell. Gastric cancer is a malignant tumor of the gastrointestinal tract. This cancer has a high incidence and low survival rate and is the fifth most common cancer and the third leading cause of cancer death worldwide. The 5-year survival rate of gastric cancer patients is only 25-30%. Cyclophosphamide has been the drug of choice for the treatment of gastric cancer, but it has serious side effects. In contrast, traditional Chinese medicines with immunomodulatory function are characterized by mild side effects, good antitumor activity, and are not harmful to immune function. In this study, tumor inhibition rate in mice was 39.86, 32.87 and 22.03% respectively. Lymphocyte proliferation and macrophage phagocytosis of model mice were increased, indicating that JRF (whole green walnut skin flavonoids) can inhibit the growth of gastric cancer in mice, and this effect can be attributed to its immune regulation. The immune system is the main defense system of the body against tumor (Alinia-Ahandani et al., 2019; Wei et al., 2022).

Anticancer activity was performed on *J. regia*, which affects the survival of human breast and colon cancer cells. The 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) method was used to detect the viability of cancer cells. Hydrolyzed walnut protein was used against breast and colon cancer cell lines. Chymotrypsin shows good anticancer activity. Chymotrypsin hydrolyzate inhibits breast MDA-MB 231 and HT-29, a colon cancer cell line. Peptide fraction showed inhibition of cell growth by 63%±1.73% for breast cancer and 51%±1.45% for colon cancer cells (Jahanbani et al., 2016).

Anti-diabetic activity

The medical uses of walnut have been mentioned many times in the sources of Iranian traditional medicine. Walnut leaves are one of the natural medicines that are recommended to diabetic patients in traditional medicine. One of the major compounds in different parts of the walnut plant is juglone, which has been limited in research. It has been reported in a research that walnut skin extract reduces the complications of diabetes. Leaves and fleshy green fruits of walnut trees are used as blood sugar lowering agents in traditional Iranian medicine. The results of some previous studies have shown that the infusion of walnut and olive leaves has the effect of reducing blood sugar in diabetic patients. In another study, it has been proven that walnut leaf infusion was effective in reducing blood glucose levels in diabetic patients. Some researchers have also reported that the consumption of hydroalcoholic extract of walnut leaf dose-dependently reduces the blood glucose level in diabetic rats. They also believed that the effect of the hydroalcoholic extract of walnut leaves in reducing blood glucose levels was comparable to drugs such as metformin (Alinia-Ahandani et al., 2020; Wang et al., 2020).

Antioxidant activity

Antioxidant activity on different extracts of bark and green peel of *J. regia* showed that they investigated the inhibitory effect of DPPH (2,2-diphenyl-1-picrylhydrazyl) and cyclophosphamide-induced urinary toxicity in rats. With the increase in the concentration of the extract, the radical scavenging activity also increased. It was researched that all parts of walnut such as shell, leaf, seed, fruit show antioxidant activity. All the methanol extracts show higher antioxidant activity than the petroleum ether extract (Rusu et al., 2020; Werma et al., 2020). Antioxidant activity mostly is assessed by measuring thiobarbituric acid reactive substances (TBARS) and by oxidative hemolysis inhibition methods (OxHLIA). It must be said that, extract is diluted at a concentration of 10 mg/mL (distilled water and PBS solution for TBARS and OxHLIA assay, respectively), next, the subsequent dilutions (25-500 µg/mL) are carried out. The TBARS assay is done by measuring of the color intensity of malondialdehyde-thiobarbituric acid (MDA-TBA) at a wavelength of 532 nm, following the methodology (Vieira et al., 2020).

Several studies have shown the antioxidant potential of walnut products, especially fruits, leaves, and alcoholic substances produced from green fruits. In biological systems, oxidative stress is caused by an imbalance between the production of reactive oxygen species (ROS) and the antioxidant defense systems of some of the main cellular components, including lipids, proteins, and DNA (Akgül et al., 2016; Kına et al., 2021; Pehlivan et al., 2021). Excessive production of ROS or reduced antioxidant defenses may contribute to the development of several dangerous diseases. Walnuts are associated with antioxidant properties that are useful in the treatment of chronic diabetic patients. Some studies have shown that the fruits of walnut trees contain vitamin C and polyphenols with antioxidant effects (Sevindik et al., 2016; Uysal et al., 2021). According to recent research, the leaves of walnut trees have secondary metabolites that provide a strong antioxidant effect. The presence of antioxidant compounds in walnuts may lead to the collection of free radicals and their inactivation. As a result, protecting the cell membrane and various compounds of living organisms against harmful effects. Additionally, choices with moderate antioxidant activity may provide a significant marketing advantage due to consumer preference for antioxidant-rich products (Vinson and Cai, 2012; Wang et al., 2015; Sevindik et al., 2018; Alinia-Ahandani et al., 2019).

The use of natural antimicrobial compounds to produce food additives in factories is increasing due to the desire of consumers to avoid chemical preservatives and increasing resistance to antibiotics. In a way, access to plant resources is unlimited and affordable, and the ability of plants to treat all kinds of diseases has been proven from the past to the present (Sevindik et al., 2017; Zhao et al., 2018; Alinia-Ahandani et al., 2020). Some experienced methods for analyzing of antimicrobial effects are being worked. As mentioned, The hydroethanolic extract of walnut green shell would be dissolved in a mixture of dimethyl sulfoxide (DMSO) + Mueller-Hinton broth (MHB) / tryptic soy broth (TSB) (95 + 5%, v/v) to obtain a final concentration of 100. mg/ml for the stock solution. In some researches, antimicrobial potential is assessed applying five Gram-negative bacteria (*Escherichia coli*, *Proteus mirabilis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Morganella morganii*) and three Gram-positive bacteria (*Enterococcus faecalis*, *Listeria monocytogenes*-Rs A-Morganius) (Vieira et al., 2020). In some other herbal assessment, leaves and fruits have been used in medicine. Studies have shown that walnut products, especially the shell, bark, leaves, fruit, and special compounds of juglone are associated with antimicrobial activities. Considering the economic value of the walnut fruit and the properties of its various parts, especially the oil and antioxidant compounds of the shell, we need more extensive studies in this field, especially since the properties and compounds of walnut can be different depending on different climates, as a result of the effects It can also have a different medicine that this changing feature of properties dependent on geography prompts us to advance our studies according to a more specialized climate (Ahandani et al., 2013; Fukuda and Yoshida, 2004).

DISCUSSION

Research results show. Walnut green shell (WGH) has a special place as an effective medicine in the treatment of diseases in traditional Iranian medicine. Different parts of Iranian walnut have been used to treat a wide range of diseases, including skin disorders, cancer, infectious diseases, diarrhea, blood sugar, anorexia, worm arthritis, sinusitis, eczema, asthma. Although various medicinal forms of walnut green husk (WGH), extract and burnt residue have been mentioned as wound healing agents in TIM/PM sources, previous reports indicate that this plant is a good source of phenolic compounds with high antioxidant potential. which can be used in the pharmaceutical industry. The obtained results are a step for the development of future applications using green walnut shell as well as other parts of the fruit as a source of value-added compounds with bioactive potential.

CONCLUSION

We must conclude that Persian walnut, due to its high medical and nutritional capacities, can be recognized as a main supplement in preventing cancer and also preventing cancer cells, and it should also be noted that despite the presence of many species, It requires more extensive research in the world every year.

REFERENCES

- Ahandani, E.A., Gawwad, M. R. A., Yavari, A. (2013). Extraction and preparation of psoralen from different plant part of *Psoralea corylifolia* and psoralen increasing with some elicitors. J Plant Biol, 2, 25-37.
- Ahandani, E.A., Ramandi, H.D., Sarmad, J., Samani, M.A., Yavari, A., Ahandani, R.A. (2014). Evaluation of morphological diversity among somepersian walnut accessions (*Juglans regia* L.) in Guilan, Northern Iran. Int J Plant Biol Res, 2(3), 1015.
- Akgül, H., Nur, A. D., Sevindik, M., Doğan, M. (2016). *Tricholoma terreum* ve *Coprinus micaceus*’ un bazı biyolojik aktivitelerinin belirlenmesi. Artvin Çoruh Üniversitesi Orman Fakültesi Dergisi, 17(2), 158-162.
- Alinia-Ahandani, E. (2018a). Medicinal plants with disinfectant effects. J Pharm Sci Res, 10, 1-1.
- Alinia-Ahandani, E., Alizadeh-Terepoei, Z., Boghוזian, A. (2019). Positive role of green tea as an anti-cancer biomedical source in Iran northern. health-promotion, 6(13), 15-18.
- Alinia-Ahandani, E., Alizadeh-Terepoei, Z., Sheydaei, M., Peysepar-Balalami, F. (2020). Assessment of soil on some heavy metals and its pollution in Roodsar-Iran. Biomed J Sci & Tech Res, 28(5), 21977-21979.
- Alinia-Ahandani, E., Fazilati, M., Boghוזian, A., Alinia-Ahandani, M. (2019). Effect of ultraviolet (UV) radiation bonds on growth and chlorophyll content of *Dracocephalum moldavica* L herb. J Biomol Res Ther, 8(1), 1-4.
- Alinia-Ahandani, E., Nazem, H., Boghוזian, A., Alizadeh, Z. (2019). Hepatitis and some effective herbs: A review. EAS J Parasitol Infect Dis, 1(1), 20-27.
- Alinia-Ahandani, E., Sheydaei, M., Shirani-Bidabadi, B., Alizadeh-Terepoei, Z. (2020). Some effective medicinal plants on cardiovascular diseaaes in Iran-a review. J Glob Trends Pharm Sci, 11(3), 8021-8033.
- Aryapak, S., Ziarati, P. (2014). Nutritive value of Persian walnut (*Juglans regia* L.) Orchards. Am. Eurasian J. Agric. Environ. Sci, 14, 1228-1235.
- Bahmani, M., Shirzad, H., Majlesi, M., Shahinfard, N., Rafieian-Kopaei, M. (2014). A review study on analgesic applications of Iranian medicinal plants. Asian Pac J Trop Med, 7, S43-S53.
- Bedia, B., Çelik, İ., Turan, A. (2019). Determination of Antioxidant Effect of Walnut (*Juglans regia* L.) on Lung and Muscle Tissue. Doğu Fen Bil Der, 2(1), 29-39.
- Chauhan, A., Chauhan, V. (2020). Beneficial effects of walnuts on cognition and brain health. Nutrients, 12(2), 550.
- Croitoru, A., Fica, D., Craciun, L., Fica, A., Andronescu, E. (2019). Evaluation and exploitation of bioactive compounds of walnut, *Juglans regia*. Curr Pharm Des, 25(2), 119-131.
- Delaviz, H., Mohammadi, J., Ghalamfarsa, G., Mohammadi, B., Farhadi, N. (2017). A review study on phytochemistry and pharmacology applications of *Juglans regia* plant. Pharmacogn Rev, 11(22), 145.
- Fukuda, T., Ito, H., Yoshida, T. (2004). Effect of the walnut polyphenol fraction on oxidative stress in type 2 diabetes mice. Biofactors, 21(1-4), 251-253.
- Habibi, A., Hamedpour-Darabi, M., Vahdati, K. (2022). Local cultural values of Persian walnut in Iran. The Cultural Value of Trees, 162-173.
- Hassani, D., Sarikhani, S., Dastjerdi, R., Mahmoudi, R., Soleimani, A., Vahdati, K. (2020). Situation and recent trends on cultivation and breeding of Persian walnut in Iran. Scientia Horticulturae, 270, 109369.
- Jafri Sayadi, M. H., Vahdati, K., Mozafari, J., Mohajer, M. R. M., Leslie, C. A. (2011). Natural Hyrcanian populations of Persian walnut (*Juglans regia* L.) in Iran. In I International Symposium on Wild Relatives of Subtropical and Temperate Fruit and Nut Crops, 948, 97-101.
- Jahanbani, R., Ghaffari, S. M., Salami, M., Vahdati, K., Sepehri, H., Sarvestani, N. N., Moosavi-Movahedi, A. A. (2016). Antioxidant and anticancer activities of walnut (*Juglans regia* L.) protein hydrolysates using different proteases. Plant Foods Hum Nutr, 71(4), 402-409.

- Jaimand, K., Baghai, P., Rezaee, M. B., Sajadipoor, S. A., Nasrabadi, M. (2004). Extraction and Identification of Juglone from Leaves and fresh peels of *Juglans regia* L. by High-Performance liquid Chromatography. J Appl Res Med Aromat Plants, 20(3), 323-331.
- Kına, E., Uysal, İ., Mohammed, F. S., Doğan, M., Sevindik, M. (2021). In-vitro antioxidant and oxidant properties of *Centaurea rigida*. Turkish JAF Sci Tech, 9(10), 1905-1907.
- Liu, M., Li, C., Cao, C., Wang, L., Li, X., Che, J., Liu, X. (2021). Walnut fruit processing equipment: academic insights and perspectives. Food Engineering Reviews, 13(4), 822-857.
- Pehlivan, M., Mohammed, F. S., Şabik, A. E., Kına, E., Dogan, M., Yumrutaş, Ö., Sevindik, M. (2021). Some Biological activities of ethanol extract of *Marrubium globosum*. Turkish JAF Sci Tech, 9(6), 1129-1132.
- Rusu, M. E., Georgiu, C., Pop, A., Mocan, A., Kiss, B., Vostinaru, O., Popa, D. S. (2020). Antioxidant effects of walnut (*Juglans regia* L.) kernel and walnut septum extract in a D-galactose-induced aging model and in naturally aged rats. Antioxidants, 9(5), 424.
- Sevindik, M., Akgül, H., Günal, S., Doğan, M. (2016). *Pleurotus ostreatus*' un doğal ve kültür formlarının antimikrobiyal aktiviteleri ve mineral madde içeriklerinin belirlenmesi. J Kast Forf, 16(1), 153-156.
- Sevindik, M., Akgul, H., Pehlivan, M., Selamoglu, Z. (2017). Determination of therapeutic potential of *Mentha longifolia* ssp. *longifolia*. Fresen Environ Bull, 26(7), 4757-4763.
- Sevindik, M., Akgul, H., Korkmaz, A. I., Sen, I. (2018). Antioxidant potantials of *Helvella leucomelaena* and *Sarcosphaera coronaria*. J Bacteriol Mycol, 6(2), 00173.
- Sheydaei, M., Alinia-Ahandani, E. (2020). Cancer and Polymeric-Carriers. Biomed J Sci Tech Res 31(2), 24107- 24110.
- Sheydaei, M., Alinia-Ahandani, E. (2021). Breast cancer and the role of polymer-carriers in treatment. Biomed J Sci Technol Res, 34(5), 27057-27061.
- Sheydaei, M., Edraki, M., Javanbakht, Sh., Alinia-Ahandani, E., Soleimani, M., Zerafatkhah, A. (2021) Poly(butylene disulfide) and poly(butylene tetrasulfide): Synthesis, cure and investigation of polymerization yield and effect of sulfur content on mechanical and thermophysical properties. Phosphorus Sulfur Silicon Relat Elem, 196(6), 578-584.
- Shigaeva, J., Darr, D. (2020). On the socio-economic importance of natural and planted walnut (*Juglans regia* L.) forests in the Silk Road countries: A systematic review. For Policy Econ, 118, 102233.
- Taheri, A., Mirghazanfari, S. M., Dadpay, M. (2020). Wound healing effects of Persian walnut (*Juglans regia* L.) green husk on the incision wound model in rats. Eur J Transl Myol, 30(1), 210-218.
- Uysal, İ., Mohammed, F. S., Şabik, A. E., Kına, E., Sevindik, M. (2021). Antioxidant and Oxidant status of medicinal plant *Echium italicum* collected from different regions. Turkish JAF Sci Tech, 9(10), 1902-1904.
- Verma, G., Sharma, V. (2020). A Scientific Update on *Juglans Regia* Linn. Asian J Pharm Res Dev, 8(3), 166-175.
- Vieira, V., Pereira, C., Abreu, R. M., Calhelha, R. C., Alves, M. J., Coutinho, J. A., Ferreira, O., Barros, L., Ferreira, I. C. (2020). Hydroethanolic extract of *Juglans regia* L. green husks: A source of bioactive phytochemicals. Food Chem Toxicol, 137, 111189.
- Vinson, J. A., Cai, Y. (2012). Nuts, especially walnuts, have both antioxidant quantity and efficacy and exhibit significant potential health benefits. Food Funct, 3(2), 134-140.
- Wang, J., Wu, T., Fang, L., Liu, C., Liu, X., Li, H., Min, W. (2020). Anti-diabetic effect by walnut (*Juglans mandshurica* Maxim.)-derived peptide LPLLR through inhibiting α -glucosidase and α -amylase, and alleviating insulin resistance of hepatic HepG2 cells. J Funct Foods, 69, 103944.
- Wang, X., Zhao, M., Su, G., Cai, M., Zhou, C., Huang, J., Lin, L. (2015). The antioxidant activities and the xanthine oxidase inhibition effects of walnut (*Juglans regia* L.) fruit, stem and leaf. Int J Food Sci, 50(1), 233-239.
- Wei, B., Zhu, H., Wang, K., Liu, S., Dai, Y., Liu, D., Sun, H. (2022). Antitumor and immunomodulation of total flavonoids from the green peep of *Juglans regia* L. in mouse forestomach carcinoma gastric cancer-bearing mice. Phcog Mag, 18(78), 328.

- Zhao, H., Li, J., Zhao, J., Chen, Y., Ren, C., Chen, Y. (2018). Antioxidant effects of compound walnut oil capsule in mice aging model induced by D-galactose. *Food Nutr Res*, 62, doi: 10.29219/fnr.v62.1371
- Zhao, M. H., Jiang, Z. T., Liu, T., Li, R. (2014). Flavonoids in *Juglans regia* L. leaves and evaluation of in vitro antioxidant activity via intracellular and chemical methods. *Sci World J*, doi:10.1155/2014/303878