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A Review on Medicinal Importance of *Juglans regia* (Walnut)

			
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ABSTRACT

As we know, dire need for novel drugs are needed for various diseases and the demand for herbal medicines is increasing day by day. The reason may be due to fewer side effects and good therapeutic value. One such medicinal plant is Walnut or scientifically named *Juglans regia*. It is a potential traditional medicine with numerous therapeutic values ranging from diabetes, rheumatic pains, fever, diabetes, skin diseases, malaria, and rheumatic pain. Also, they show good activity as an analgesic, antidiarrheal, antiparasitic, and antimicrobial. This review focuses on discussing the details of walnut or *Juglans regia* and its pharmacological uses.



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INTRODUCTION:

Walnut (*Juglans regia* L.)

Walnut, scientifically known as *Juglans regia* and a member of the Juglandaceae family, is a medicinal plant that, like most herbal remedies used in traditional medicine, is underappreciated despite its therapeutic potential¹. Walnut roots are used to treat diabetes, walnut leaves are used to treat rheumatic pains, fever, diabetes, and skin problems, and walnut flowers are used to treat malaria and rheumatic pain in traditional medicine²⁻⁵. This plant is commonly utilized in Persian cuisine to treat several ailments, according to Iranian traditional medicine. Walnut leaves have been used for centuries in traditional medicine to lower blood sugar and improve diabetes. According to research, walnut leaves contain health-promoting components, and they are commonly used in traditional medicine to treat venous insufficiency and hemorrhoids symptoms. They are sometimes used as an anti-diarrheal and anti-parasitic medication, as well as a blood purifier⁶⁻⁷. The findings indicate that substantial study on the pharmacological effects of walnut has been undertaken during the last two decades. In diabetic animals, different components of this plant, such as the leaves, bark, and fruits, show hypoglycemic characteristics⁸. In streptozotocin-induced diabetic rats, studies on the impact of walnut leaves on lipid variables revealed lower levels of lipids. Furthermore, recent investigations have revealed that this herb has analgesic and antibacterial properties⁹⁻¹⁰. Walnut extract is high in total phenol, which has anti-cancer and anti-inflammatory characteristics, according to studies¹¹. The goal of this study was to review the distribution of walnuts, their chemical content, and therapeutic qualities, according to studies completed on walnuts and their attributes [Figure 1].



Figure 1: *Juglans regia*

Ecology and geographical distribution

The vegetative origin of the walnut tree is the Eastern Balkans to the Himalayas and Southwestern China. The Persian or common walnut (*J. regia*) is its best-known member, found primarily in the temperate areas and commercially cultivated in many parts of the world [Figure 2]. Now, walnut trees are growing many in parts of the world, including Asia (foothills of the Himalayas, Iran, China, and Japan), Southern and Eastern Europe, as well as North and South America. Walnut trees grow in some provinces of Iran such as Fars, Hamedan, Kohgiluyeh and Boyerahmad, and Lorestan. A species of walnut tree with the scientific name of *J. regia* grows in Iran. Walnut tree is sensitive to too hot and too cold weather in summer and winter¹². Walnut trees are monoecious plants with a height of about 10–25 m. They have pinnately compound leaves; with male and female flowers appeared on them separately. During winter dormancy, walnut trees can stand the cold weather up to -11°C . The puberty of walnut trees has a direct relationship with the species, breed, weather, and the location of its growth.

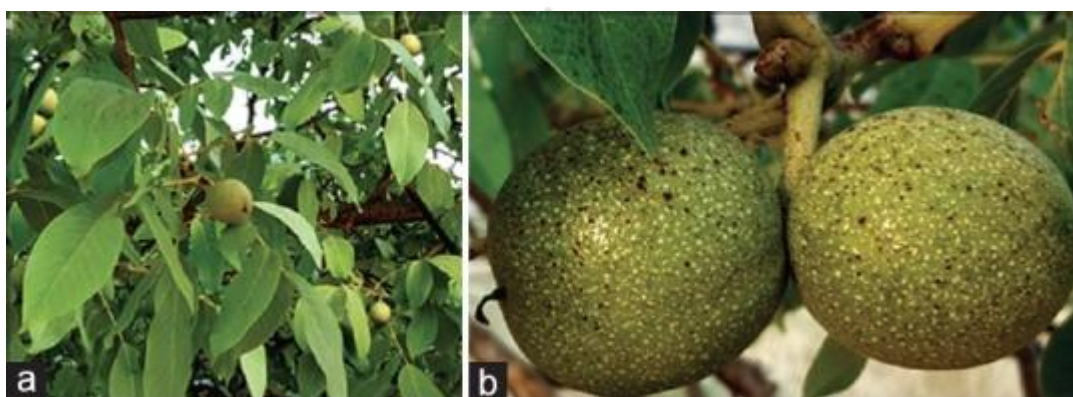


Figure 2: (a) Leaves of *Juglans regia* (b) Fruits of *Juglans regia*

Chemical compositions

Depending on the different factors such as geographic location, temperature, time, and other factors, a plant has a different chemical composition in different countries. Today, different parts of the walnut tree such as leaves, bark, and fruits are used in the world. Researchers have reported that chemical compounds found in walnuts are different in different climates. Fruits of walnut trees are valuable and edible; and their oil is rich in polyunsaturated fatty acids, tocopherols, and phytosterols. Walnuts are a good source of essential fatty acids and tocopherols. Zahoo reported that 17 compounds have been identified in walnut leaves; nine of them are epicatechin, syringetin-o-hexoside, myricetin-3-o-glucoside,

myricetin-3-o-pantocid, aesculetin, taxifolin-pantocid, quercetin glucuronide, kaempferol pantocid, and kaempferol rhamnoside. The leaves of this plant contain phenolic acids, tannins, essential fatty acids (linoleic acid is its major fatty acid), ascorbic acid, flavonoids, caffeic acid, and paracomaric acid. The most important flavonoids in the walnut leaves include quercetin galactoside and quercetin pantocid derivatives, quercetin arabinoside, quercetin xyloside, and quercetin rhamnoside. Furthermore, Shah et al. also reported phytochemical screening of the crude leaf extracts of *J. regia* revealed the presence of carbohydrates, cardiac glycosides, phenolics, flavonoids, alkaloids, proteins, steroids, and tannin¹³. Amaral et al. reported that there are phenolic compounds including 3- and 5-caffeoylquinic acid, 3- and 5-p-coumaroylquinic acid, quercetin 3-galactoside, quercetin 3-pantocid derivatives, quercetin 3 arabinoside, quercetin and quercetin 3-o-xyloside, and quercetin 3-rhamonocid in the walnut leaves¹⁴. Quercetin 3-galactoside is the main ingredient among the mentioned compounds^{14,15}. Furthermore, it has been reported that the leaves of this plant contain naphthalene derivatives, particularly 5-hydroxy-1-4-naphthoquinone. Juglone (5-hydroxy-1, 4-naphthoquinone) is a naphthoquinone compound found in the fresh leaves and green husk of the walnut tree fruits. Juglone is the most obvious ingredient in different organs of the walnut tree, with a molecular weight of 174.16, and formula C₁₀H₅O₂ (OH), the precursor of which is a glycoside that is found as a compound in aerial parts of the plant, especially leaves, which is then converted to juglone through hydrolysis^{16,17}. Juglone is an alkaloid substance that is slightly dissolved in the hot water and moderately in alcohol; therefore, it can be one of the effective compounds in the walnut leaves because other substances in the leaves of the walnut are often water-soluble or fat-soluble. The green husk of walnut tree fruits has emulsion, glucose, and organic materials such as citric acid, malic acid, phosphate, and calcium oxalate. Juglone and phenolic compounds are the most important compounds found in the leaves and green husk of walnuts¹⁷. Juglone, as a toxic compound, is only found in fresh and green walnuts, but there is no such property in its dried leaves^{18,19}. Walnut green husk has a by-product with little use. It has been demonstrated that due to its phytochemical source, walnut husk increases the value of the walnut products; compared to the use of a by-product produced in a large quantity^{19,20}.

Therapeutic treatment:

Antioxidant activity

Possible mechanisms of the effectiveness of pharmacological properties of different parts of walnuts. Several studies have demonstrated the antioxidant potential of walnut products, particularly their fruits, leaves, and alcoholic substances produced from green fruits. In biological systems, oxidative stress resulting from an imbalance between the production of reactive oxygen species (ROS) and antioxidant defense systems are some of the effects of major cellular components, including lipids, proteins, and DNA. Overproduction of ROS or reduced antioxidant defense may be involved in creating several dangerous diseases²¹. Green walnut husk extract shows a strong effect of lowering oxidative stress. The reduction capability of a compound is based on its potential antioxidant activity²². In their study, Ahmad et al. reported that walnuts are associated with antioxidant properties that are useful in the treatment of chronic diabetic patients²³. Some studies have shown that the fruits of walnut trees contain Vitamin C and polyphenols, with antioxidant effects^{24,25}. Based on recent empirical research, the leaves of walnut trees have secondary metabolites that provide a powerful antioxidant effect²⁵. The existence of antioxidant compounds in walnuts may lead to the collection of free radicals and inactivation of them; and consequently, the protection of cell membranes and various compounds of alive organisms against harmful effects. In addition, the selections with relatively antioxidant activity may offer significant marketing advantages, due to consumer preference for antioxidant-rich products²⁶.

Antidiabetic activity

Due to its fatal complications, diabetes mellitus is the seventh leading cause of death in human society and the third in the world. Although the most common way to treat diabetes is the use of insulin, a nutritional approach to the treatment of diabetes is very effective in developing countries. Several studies have confirmed the therapeutic potential of some medicinal plants in the treatment of diabetics. So far, the positive effect of more than 1200 medicinal plants in reducing blood glucose levels or reducing complications of diabetes has been identified. The use of different types of medicinal plants in Morocco indicates how fourteen plant samples such as walnut leaves are used to treat diabetes²⁷.

Lipid-lowering activity

Researchers have reported that dose-dependent consumption of the Persian walnut oil extract decreases the level of triglyceride, cholesterol, and LDL-C cholesterol in nondiabetic rats with high cholesterol. The results of the administration of alcoholic extract of walnut leaves on the level of triglyceride and serum cholesterol indicate that the active ingredient in walnut leaves somehow has managed to reduce the level of triglyceride and total serum cholesterol and increase the level of HDL. The results of previous studies shown that walnut administration would change the distribution of lipids in different lipoprotein groups; and the use of walnuts is likely associated with anti-atherogenic effects. It was also reported that a diet containing walnuts will lead to a better distribution of fats among fat subgroups, even when the amount of total fat has not changed. This effect of walnuts may be an additional process involved in the prevention of vascular plaque formation. As far as the effects of hydroalcoholic extract of walnut leaves in lowering blood glucose levels are concerned, it is likely that juglone, as an effective factor in the walnut leaf extract, causes a higher reduction of blood glucose level by stimulating the insulin-producing system or enhancing the response of cells to insulin. At the beginning of the experiment, more urea is produced due to the development of diabetes in the rats. But with the increase in blood glucose consumption and decreased level of protein, urea production is also reduced. Therefore, the existence of multiple chemical compounds in walnuts and their mechanism of action is a factor to reduce the level of fats²⁸⁻³¹.

Antihypertensive activity

In a study in Morocco, 320 diabetic patients and 380 patients with high blood pressure and cardiovascular disorders were interviewed. Eighty percent of patients were taking herbal medicine to treat their illness. They reported that herbal therapy is cheaper and better than the treatment with synthetic drugs. It has been reported that in young people prone to heart disease, eating walnuts play an important role in changing blood lipid concentrations. In another study, it has been reported that the administration of walnut leaf aqueous extract reduced systolic, diastolic, and mean arterial pressure compared to the control group. In a study, Perusquia et al. examined the effect of walnut leaf aqueous extract on aortic segments of rats and reported that their blood pressure and noradrenaline-induced contraction in the isolated aorta were reduced. This reduction in blood pressure is attributed to the relaxant effects of the extract on the muscles of arterial walls³². Perez-Vizcaino et al. demonstrated

that a diet rich in flavonoids, especially quercetin reduces blood pressure. Furthermore, in another study, it was reported that the ethanol extract of the thin husk around the walnut fruit can inhibit the effect of angiotensin-converting enzyme CE by 40%. In a study, Javadi et al. reported that the extract of walnut blades decreased systolic and diastolic blood pressure. In another study, it has been reported that coadministration of walnut leaf aqueous extract and acetylcholine reduced systolic, diastolic, and mean arterial pressure compared with the control group; and pretreatment with walnut leaf aqueous extract reduced blood pressure caused by the injection of adrenaline³³⁻³⁹.

Antimicrobial and antifungal activity

The use of natural antimicrobial compounds for the production of food additives in factories is increasing because of the desire of consumers to avoid chemical preservatives and increased resistance to antibiotics. Various components of walnuts such as their green husks, barks, leaves, and fruits have been used in pharmaceuticals. Studies have demonstrated that walnut products, particularly husks, barks, leaves, fruits, and special compounds of juglone are associated with antimicrobial activities. But so far there is no information about the effects of the green husk of walnuts. With its antioxidant activity, the Portuguese walnut extract significantly inhibited the growth of Gram-positive bacteria, in particular, *Bacillus cereus*¹⁵. Some researchers demonstrated, that walnut green husks aqueous extracts presented a strong antioxidant activity and inhibited the growth of different pathogenic bacteria¹⁴. Several studies have demonstrated that apart from the antioxidant activities of phenols and/or phenolic extracts, their antimicrobial activities have led the researchers to consider them as an alternative to antibiotics and chemical protection²⁶. In a study, Sharafati-chaeshtori et al. reported that the walnut leaf extract is effective on *Propionibacterium acnes*. Methanolic components derived from walnut leaves have demonstrated a strong antifungal activity. In a study, Amaral et al. reported that walnut leaves could be useful for employment as an antimicrobial agent against bacteria responsible for human gastrointestinal infections. Thus, according to the results of a lot of studies, it can be said that, due to having compounds such as juglone and phenolics, walnut leaves are associated with antibacterial activities.

Protective of liver and kidney

eidi et al. have reported that the hydroalcoholic extract of walnut leaves can protect the liver against oxidative damages induced by carbon tetrachloride. This liver protective effect is likely effective in meeting the changes in detoxifying and antioxidant enzymes and sweeping

free radicals away. Another study showed that after subcutaneous injection of mercuric chloride to rabbits and induction of experimental acute renal failure, the administration of walnut extract had a significant impact in the treatment of acute renal failure and could be effective in nephron cell regeneration, *in vivo* or *in vitro*. Laboratory studies have shown that the intraperitoneal injection of walnut extract into rats reduced the amount of alanine aminotransferase, aspartate aminotransferase, total protein, and plasma albumin, while there were no significant changes in the levels of bilirubin, BUN, creatinine, and alkaline phosphatase enzyme activity. The results of several studies have shown that walnuts are associated with a lot of effects due to having antioxidants. Some other walnut activity walnut leaves are the major source of flavonoids. Flavonoids have antioxidant properties that are involved in the regulation of immune function and increase the anticancer activities of the body.

Antifungal activity

Pathogenic fungi are the main infectious agents in plants, causing alterations during developmental stages including post-harvest. In fruit and vegetables, there is a wide variety of fungal genera causing quality problems related to aspect, nutritional value, organoleptic characteristics, and limited shelf life. In addition, in some cases, fungi are indirectly responsible for allergic or toxic disorders among consumers because of the production of mycotoxins or allergens. Generally, phytopathogenic fungi are controlled by synthetic fungicides; however, the use of these is increasingly restricted due to the harmful effects of pesticides on human health and the environment. The increasing demand for production and regulations on the use of agrochemicals and the emergence of pathogens resistant to the products employed justifies the search for novel active molecules and new control strategies. Since antiquity, the plant kingdom has provided a variety of compounds of known therapeutic properties, like analgesics, anti-inflammatories, medicines for asthma, and others. In recent years, the antimicrobial properties of plant extracts have been reported with increasing frequency from different parts of the world. For example, a large proportion of the South American population use plant extracts obtained from traditional medicinal plants as medicine for many infectious diseases. Plants from the genus *Pterocaulon*, known as "quitoco", are commonly used in veterinary medicine in southern Brazil to treat animal problems popularly diagnosed as "mycoses". Several works have demonstrated in laboratory trials that different plant tissues, such as roots, leaves, seeds, and flowers possess inhibitory properties against bacteria, fungi, and insects. Currently, there is little evidence on the

antimicrobial properties of the medicinal plants under investigation against phytopathogen fungi¹⁶⁻²⁶.

CONCLUSION:

With the increase in demand for herbal formulations in the market, there comes the need for the search for drugs having good therapeutic activities and very few side effects. Thus, one such drug is Walnut (*Juglans regia*,) which shows various medicinal properties and can be used in various forms in the pharmacological industry with proper research. They show good activity in diabetes, rheumatic pains, fever, diabetes, skin diseases, malaria, and rheumatic pain. Furthermore, they may also act as an analgesic, antidiarrheal, antiparasitic, and antimicrobial. Thus, further research needs to be focused on the development of good and effective medicine from this *Juglans regia* medicinal plant.

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