Original Article

Juglans Regia L: A Review of its Traditional Uses Phytochemistry and Therapeutic Applications

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Abstract

Medicinal plants have been used since ancient times for the treatment of different diseases. Natural sources are one of the important fields of research for preventing immunological complications. Herbal extracts have been used in traditional medicine for several thousand years due to a number of reasons including affordability accessibility and low cost and have little side effects.

According to World Health Organization, the use of herbal remedies throughout world exceeds that of the conventional drugs by two to three times because of general belief that herbal drugs are without side effects besides cheap and locally available. Juglans regia L also known as walnut plant is a medicinal plant which possesses various therapeutic properties and used in traditional medicine however it is considered less, Juglans regia l is one such medicinal plant whose all parts namely bark, kernel, leaves, etc. are extensively useful.

Phytochemical analysis of various parts of Juglans regia reveals that it contains reducing sugars, carbohydrates, alkaloid, tannins, phenols and saponins, cardiac glycosides, flavanoids, steroids. Juglans regia possesses wide range of pharmacological properties such as analgesic/anti-inflammatory, antipyretic, antimicrobial, anticancer, antihypertensive properties. Preparations made from Juglans regia are widely used in cardiovascular diseases, type II diabetes mellitus, anti-infective, anti-microbial, anti-fungal, anti-hypertensive, hepatoprotective, anticoagulation, anticancer and lipid lowering agents.

This review aimed to study pharmacological properties possessed by Juglans regia. Review articles pertaining to Juglans regia and its therapeutic effects was searched" in two databases of PubMed, and Google Scholar among published studies. All review articles, original articles, were evaluated.

In present study it was found that Juglans regia was widely used in the treatment of diseases in traditional medicine, and do not have any side effects. Despite the development of many chemical drugs, usage of Juglans regia is highly demanded.

Keywords: Juglans regia L, Herbal medicine, Phytomedicine, Traditional medicine.

INTRODUCTION

Traditional medicine is that the accumulation of data, skills, and practices supported the theories, beliefs, and experiences specific to completely different cultures that are accustomed maintain health, similarly on stop, diagnose, improve, or treat physical and mental sicknesses1.

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The World Health Organization (WHO) reported that eightieth of the rising world's population depends on ancient drugs for medical aid. Throughout the past decades, the developed world has additionally witnessed an ascending trend within the utilization of CAM, especially herbal medicines. 2

The practice of usage of plants for curing many human diseases exist for past many centuries. Plants, even though fullfil need for food, and their rich phytoconstitiuents are extensively studied. Each plant contains many secondary metabolites, such as essential oils, terpenoids, glycosides phenolic compounds, alkaloids, saponins, flavanoids and tannins, which might be responsible for medicinal effects. The remedial significance of medicinal herbs enhances with the increased value of certain compounds of the plants.3 Various parts of plants are being used to prevent, allay symptoms or revert abnormalities back to normal as they exhibit less side effects and are low cost.4 Herbal medicines include herbs, herbal materials, herbal preparations, and finished herbal products that contain parts of plants or other plant materials as active ingredients Numerous studies have been performed so as to establish pharmacological action of medicinal plants and they appear to be a potential source for the development of new drugs, may helps to increase effects of chemical drugs which may result in reduction in cost of treatment and increase in quality of life of patient. Since natural antioxidants for example phenolic compounds reduce the risk of degenerative disease by inhibit the oxidation of macromolecules and reducing oxidative stress they have important and great value for the human health. 5,6

Plant profile:

1. Common names

Arabic: Joz Chinese: Hu ta English: Walnut/Carpathian walnut, English walnut, French: Noyer commun; German: Echte Walnut India: Akhort

2. Taxonomic classification:

Kingdom: Plantae, Subkingdom: Viridiplantae, Infrakingdom: Streptophyta, Superdivision: Embryophyta, Division: Tracheophyta, Subdivision: Spermatophytina, Class: Magnoliopsida, Superorder: Rosanae, Order: Fagales, Family: Juglandaceae, Genus: Juglans, Species: Juglans regia 7

3. Distribution:

Juglans regia was native in Asia i.e Afghanistan, Iran, Iraq, Turkey, Pakistan as well as in Europe esp. in Bosnia , Bulgaria, Croatia, Greece, Macedonia, Montenegro, Serbia, Slovenia8.

4. Traditional uses:

According to historical and archeological evidence, humans have been collecting and eating wall nuts since 7300 B.P. near the Mediterranean9. Traditional medicine used various parts of the Juglans regia plant, such as seeds, bark, leaf, and seeds green husks, as remedies for various diseases. Seed or kernel i.e edible part of the walnut fruit was consumed, alone (either toasted or fresh), alone or with other eatables. Wallnut as valued for its nutritional and disease treating as well health promoting properties 10.

Traditionally, walnut plant is used for skin inflammation as well as for excessive perspiration treatment of scrofula and eczema. scalp dandruff itching, superficial and sunburn11In order to relieve fever or to relieve rheumatic pain fresh leaves of wallnut plant are applied to the body12. Kernels of J. regia are used to treat inflammatory bowel disease. It is also used for the treatment of diabetes, asthma, vascular, and prostate disturbances in Palestine 24. In India bark and roots of walnut are used for cleaning teeth as well as to treat toothache. Juglans regia fruit peel is used to treat ringworm infestation 13,14

Wallnut tree leaves were very useful and many times used for treating constipation, chronic dysentery itching frostbite brain tonic as well as mosquito repellant and lice killer. Wallnut fruit was also used as, aphrodisiac, while walnut oil was used as memory enhancer as well as to improve eye sight. 16

5. Chemical constituents

Walnuts had always been known to be high in phytochemistry, what makes them nutritionally more beneficial. In various countries, a plant's chemical composition differs depending on various factors such as location, climate, time, and some other factors. Today, all parts of the walnut tree, such as the bark fruits & leaves, are used in various parts of the world. Phytochemical screening of Juglans regia bark, leaves, and kernels confirmed the presence of reducing sugars, alkaloids, tannins, phenols, and saponins, while phytochemical screening of Juglans regia leaf extract disclosed the presence of alkaloids, carbohydrate, and saponins. cardiac glycosides, flavonoids, saponins, steroids and tannins. Various amino acid presents in walnuts include aspartic acid, threonine, serine, glutamic acid, proline, glycine, alanine, valine, methionine, isoleucine, leucine, tyrosine, phenylalanine, histidine, lysine and arginine. Various Phenolic compounds present in walnut seeds are phenolic acids, namely gallic, ellagic, syringic, 5-Ocaffeoylquinic, caffeic, p-coumaric, ferulic and sinapic acids, and tannins, such as glansrins A, B and C, casuarinin and stenophyllarin.

6. Pharmacological effects

I. Cardiovascular effects

In 2009, Banel DK et al. examined CVD risk factors that were investigated in relation to walnut consumption and concluded that high walnut consumption resulted in substantial differences in lipid profiles when applied to various control diets. Walnuts could also assist to decrease oxidative stress and inflammation markers. Walnuts, despite their high fat content, do not appear to be a high-fat food. 17

Marta Guasch-Ferré et al.in 2018 with an aim to examine impact of walnut consumption on cardiovarcular risk factors

and blood lipids performed a systematic review and meta-analysis of randomized clinical trials. The authors conclude that a meta-analysis of controlled trials presented strong evidence for benefits of walnut intake on blood lipids, with no negative effects on body weight or blood pressure18

Domènech M, et al. 2019 in a randomized control study involving 236 patients, reported that frequent walnut ingestion may aid control high blood pressure in addition to diet and pharmacological approaches19

Joukar S, et al in 2017 studied effects of methanol extract of Juglans regia L on dexamethasone-induced hypertension and It was observed, walnut extract normalized dexamethasone-induced hypertension, like captopril20

II. Neuroprotective and anti-depressant effect

In a study published in 2020, Chauhan et al. examined the impact of walnuts on memory and brain health and observed that having walnuts (1–2 oz per day) may increase cognitive function while still decreasing the risk of other diseases namely cardiovascular disease, depression, and type 2 diabetes, all of which are risk factors for dementia. 21

Ganji A, et al. in 2018 examined at the therapeutic effects of walnut oil on an animal model of multiple sclerosis and found that it lowered disease severity, altered cytokine production, and inhibited plaque formation. 22

Arab L et al. in 2019 carried out a review to see how much of reduced risk of depression is attributable to walnut ingestion. They found a consistent link between nut consumption, particularly walnut consumption, and fewer and less frequent bouts of depression in both males and females. Wall nut eaters tends to show lower depression scores which appear to be linked to increased concentration23

In 2016, Pribis P. et al. investigated the impact of walnut consumption on mood in young adults and confirmed that supplementation of walnuts enhanced mood in healthy, non-depressed males in a randomized, double-blind, placebo-controlled feeding trial. 24

III. Antioxidant effect

Rusu ME et.al, in 2020 assessed the antioxidant effects of walnut kernel and walnut septum extract in a D-galactose (D-gal)-induced aging model and in a naturally aged rat model for a period 56 days.At the end of 56 days samples from, blood, liver, brain were collected and analysed for blood examination biochemical examination as well as biomarkers for oxidative stress . histological, as well as immunohistochemical analyses was also performed.Results showed considerable improvement in cellular antioxidant activity alongwith /or decrease of reactive oxygen species 25

Fizesan et.al in 2021 examined the antitussive, antioxidant, and anti-inflammatory effects of a walnut (Juglans regia L.) septum extract. The antitussive and anti-inflammatory effects in walnut septum were demonstrated and also potent antitussive effects. Walnut septum's antitussive effect could be due to a cellular defensive effect as well as an anti-inflammatory effect, which could be due to activation of t cells. The antitussive effect of walnut septum could be due to a cellular defensive effect and an anti-inflammatory effect, which may be due to antioxidant enzyme system stimulation. 26

Soussi A, et al. in 2018 carried out a study. to examine the potential protective effect of Juglans regia vegetable oil on the lead nephrotoxicity in rats together with its relationship with oxidative stress. It was found that Juglans regia oil supplementation shows a protective antioxidant effect against lead intoxication and hence provides scientific proof in support of usefulness of Juglans regia vegetable oil against lead-induced toxic oxidative stress on the kidney tissue. 27

In 2018, Cheraghali F, et al. investigated its encapsulation efficiency total phenol content antioxidant and antimicrobial activities structural , and release properties of WGH extract-loaded microcapsules and uncovered its possibility of using WGH extract-loaded microcapsules as herbal treatments in food and pharmaceutical products, microcapsules serve as natural antioxidant and antibacterial agents 28

Hatamjafari F et.al 2013 conducted a study with a view to study antioxidant properties of Juglans regia leaves. in their study it was found that methanol extract of Juglans regia displayed strong concentration dependent antioxidant activity was shown in DPHH and reductive power test. 29

IV. Anti diabetic effect

Saeed Hosseini et.al. Investigated the hypoglycemic effect of J. regia leaves aqueous extract in type 2 diabetes patients and found that Juglans. regia improves glycemia in the type 2 diabetic patients without any adverse effects on the kidney and hepatic function and J. regia extract treatment significantly lowered fasting blood glucose and HbA1c, and increased the insulin level in diabetic patients at the end 30

Abdoli, et.al in 2017 wanted to evaluate the effect of aqueous extract of Juglans regia leaf on blood glucose in type 2 diabetic patient.It was found that his study suggests that aqueous extract of J.regia leaf had a lowering effect of FPG, PPG and HbA1c in type 2 Diabetic patients. 31

Teimori M et.al 2009 investigated mechanism of hypoglycemic action of Juglans regia Leaves methanolic extract and found that plant extract had a significant hypoglycemic action in both short and long term models. Decrease in PBG level was the most at 8 hour after treatment and permanent post prandial blood glucose was evident in treated groups 32

V. Anti Cancer Effect

Jahanbani R, et.al in 2016 studied anti cancer as well as antioxidant activities of Walnut protein hydrolysates and found that the peptide fractions showed cell growth inhibition for breast cancer as well as for colon cancer cells thereby confirming existence of direct correlation between antioxidant and anticancer activities of walnut peptide fractions . 33

Catanzaro E,et.al in 2018 in his review Natural product to

fight cancer concluded that walnut tree, also called common walnut, possess incontestible fascinating anticancer potential on totally different cell lines and animal models. Single molecules keep in varied elements of plants, and fully-fledged extracts, displayed effective antitumor effects. 34

Salimi M et.al in 2012 evaluated antiproliferative activity of total extract similarly as many fractions from the leaves of J. regia. Antiproliferative activity was evaluated against human carcinoma, breast glandular cancer and colon glandular cancer cell lines. Total phenolics, flavonoids, and condensed tannins were calculable. The methyl alcohol fraction have had highest quantity of total phenolics, flavonoids, and condensed tannins, suggesting that walnut fraction might contain effective compounds that may be used as a therapy agent, per quantitative analysis strategies.35

VI. Antimicrobial Effect

Floriana D'Angeli et.al in 2021 in their study found that HSV replication, bacterial and fungal growth, and colorectal cancer cell viability was efficiently and significantly reduced by J. regia pellicle extract. Further they found that Juglans extract pellicle possessed significant antioxidant properties 36

Arjji Parham et.al in 2021 studied anticandidal activities of extracts of walnut fruit, peel, and leaves on different Candida species. They concluded that there exist considerable therapeutic antifungal potential in methanol extracts of walnut leaves and peels against candida species with minimum side effects37

In 2014, Emira Noumi, Mejdi, and colleagues conducted a comparative study on the antifungal and antioxidant properties of natural and colored Juglans regia L. barks. They found that Methanolic extract of natural walnut has massive anti vaginal Candida strains and suggested that J. regia can be used to treat vaginal candidiasis because it is a cheap and easily accessible source of effective natural antifungal and antioxidant agent38

Eswayah A, et.al in 2019 studied Antibacterial and anti-inflammatory activities of methanolic extract of Juglans regia L. leaves (Walnut) and found that methonalic extract possess antimicrobial and antinflammatory activities as it was active against Gram positive bacteria, and fungus39

VII. Hepatoprotective Effect

Akram Eidi, et.al in 2013 conducted a study to assess hepatoprotective effects of Juglans regia extract. Results of this study suggested that walnut leaf extract has potent hepatoprotective activity.Walnut leaves may have antioxidant properties that guard against the damage caused by free radicals. Flavonoids, polyphenolic and other constituents of walnut leaf extract might be responsible for the protective effects 40

Choi Yet.al in 2016 evaluated the underlying mechanism as well as protective effects of dietary walnuts on high fat diet induced fatty liver. It was found that dietary walnuts significantly decreased the amounts of hepatic triglyceride observed in high fat diet fed mice. Walnuts drastically altered the levels of proteins involved in hepatic lipid homeostasis, such as AMP-activated protein kinase, fatty acid synthase, and peroxisome proliferator-activated receptor. thereby demonstrating protective effects of walnuts against HFD-induced hepatic TG accumulation 41

VIII. Effects in Oral Cavity

Ausama Abbas Faisal et.al in 2019 conducted a study on 40 volunteers with stained teeth so as to assess the use of walnut tree bark powder as tooth whitener and found that walnut tree bark powder is a useful material for teeth whitening and has antibacterial effects because the presence of polyphenolic compounds42

Saimbi C S et.al in 2009 studied clinical effects of Juglans regia on dental plaque and found that antiplaque activity of Juglans regia may be because of juglone, caffeic acid and crumicidin. Presence of enzymes peroxidase, lipase and amylase in Juglans regia may also be responsible for plaque inhibition, which too may play a role in inhibition of plaque accumulations. Results of study suggested that Juglans regia can be used as an anti-plaque agent and could be considered a potent adjunct to oral hygiene regime43

Faramarz Zakavi et.al in 2013 conducted as study evaluate the antimicrobial activities of ethanolic and aqueous extracts of Juglans regia bark against four species of oral bacteria namely Streptococcus mutans, Streptococcus salivarius, Streptococcus sanguis, and Staphylococcus aureus. Results of this study showed that S. sanguis and S. mutans were the most sensitive and the most resistant bacteria against ethanolic and aqueous extracts, respectively44

Conclusion

In present review an attempt was made to mention most of the information available in literature including description chemical constituents, therapeutic properties of Juglans regia as medicinal plant which possess wide number of pharmacological properties which can be used to treat variety of medical conditions Various studies have revealed that Juglans regia contain alkaloids, flavonoids, and terpenoids monoterpenes, coumarin, flavonoids, tannins, saponins, alkaloids, and other components. Juglans regia l commonly known as Walnut possess many medicinal properties because of which it has been widely used in traditional medicine for treatment of many diseases. Juglans regia is known to possess antihypertensive, cardioprotective, antioxidant, anticancer, neuroprotective, hepatoprotective antimicrobial and antiplaque properties. Since Juglans regia contains multiple compounds as well as unknown pharmacological properties, other unknown useful properties of Juglans regia should be examined further before it could be used as a drug to treat human diseases.

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