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Spinach: An important green leafy vegetable and medicinal herb

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Abstract

Spinach (*Spinacia oleracea*) in an annual herb belongs to the family Chenopodiaceae. It is native to South-West Asia and widely distributed and cultivated through the world including Iran as vegetables for its high nutritious value. Spinach is a good source of minerals (iron, copper, phosphorous, zinc, selenium), vitamin B complex (niacin and folic acid), ascorbic acid, carotenoids (ß-carotene, lutein, zeaxanthin), phenols (flavonoids, p-coumaric acid), apocynin and Omega-3-fatty acids. It is a relatively quick-growing vegetable and easy to maintain and distinguishable by its green color as well as smooth, oblong shaped leaves that can be either crinkled or smooth. Also, the whole plant is medicinally important and are used in traditional medicine for numerous therapeutic effects because of the presence of biological tannins and phenolic active phytochemicals such as alkaloids, flavonoids, steroids, glycosides, terpenoids. It is used to treat diabetes, leprosy, asthma, urinary diseases, lung inflammation, joint pains, thirst, sore throat, scabies, vomiting, ringworm, sore eye, cold, sneezing, fever and the diseases related to brain and heart.

Keywords: antidiabetes, Chenopodicaceae, leafy vegetables, medicinal plant, pharmacological property.

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Introduction

The use of herbal medicines continues to expand rapidly across the world with many people now resorting to these products for treatment of various health challenges in different national healthcare settings. Ease of availability, least side effects and low cost of preparing herbal are the main key player of all available therapies. Although usage of these herbal medicines has increased, their quality, safety and efficiency are serious concerns in industrialized and developing countries thereupon traditional and folklore medicines play an important role in health services around the world (Ekor, 2013; Jadhav et al, 2015; Keshavarzi et al, 2013; Nikdehghan et al, 2013; Roughani and Miri, 2018).

Green leafy vegetables such as spinach are rich sources of many nutrients and form a major category of vegetable groups that have been designated as 'nature anti-aging wonders' and medicinal value (Gupta and Prakash, 2009). Spinach is a valuable crop for food and medicinal purposes with production of over 26 million tons on about 921000 ha in the world. About 25 million tons produced in Asia and China with about 24 million tons was pioneer and Iran was 6th in the 2016 on spinach production world ranking by commodity about 117000 tons (FAO, 2018). Spinach-derived phytochemicals and bioactives are able to scavenge reactive oxygen species and prevent macromolecular oxidative damage, modulate expression and activity of genes involved in metabolism, proliferation, inflammation, and antioxidant defence, and also curb food intake by inducing secretion of satiety hormones (Roberts et al, 2016).

Botany and distribution

Spinach (*Spinacia oleracea*), belongs to Chenopodiaceae family, is one of the most important vegetables. It is a leafy cool-season vegetable with global cultivation usually consumed after boiling either fresh or frozen leaves or raw consumed in salad (Alessa et al, 2017; Eriksen et al, 2016; Yoon et al, 2017). It is native of Southwest Asia that thought to have originated from Iran and has been grown in China, since at least the 7th century and was used in Europe, since at least the13th century (Cai et al, 2017; Sabaghnia et al, 2016).

Spinach is an annual plant species and the closely related species, *S. tetranda*, is considered to be its ancestor, and other related species comprise *S. spinosa*, *S. inermis* and *S. turkestanica*. The classification of numerous spinach cultivars is based on seed form (round or prickly); leaf texture (smooth or crinkled); leaf colour, shape and pose, and petiole length (Al-Khayri, 2012). The edible leaves are arranged in a rosette, from which a seed stalk emerges. The simple leaves are somewhat triangular or ovate and may be flat or puckered. The flowers are inconspicuous and produce small dry fruits (Hassandokht, 2012). Sex of spinach determined by the XY system. Male and female floral organs differ morphologically, but plants do not differ in the vegetative stage before flowering (Fujita et al, 2017).

Breeding

The major aims of spinach breeding programs are to develop varieties with traits including increased disease resistance and abiotic stress tolerance such as heat stress (Zhao et al, 2018), drought stress (Xu and Leskovar, 2015), interactive salinity and water stress (Ors and Suarez, 2017) and also improved yield and quality such as decreased levels of nitrate and oxalate, and increased levels of folate in spinach leaves by different physiological and genetical techniques (Hassandokht, 2012; Roughani et al, 2017).

Nutritional value

Spinach is a rich source of fiber, vitamins A, C, E, K, B6, B2 and also magnesium, manganese, iron, calcium, potassium, copper, phosphorous, zinc, selenium, folate, betaine, folic acid, protein, niacin, omega-3 fatty acids, carotenoids beta-carotene and lutein, and bioflavonoid quercetin with many other flavonoids. Spinach with poor source of fat is a suitable food for obese and diabetic people. It is also a good source of chlorophyll, which is known to aid in digestion (Roughani et al, 2011; Gaikwad et al, 2010; Verma, 2018).

Medicinal uses

The leaves of spinach are traditionally used in various folklore medicine as cooling, emollient, wholesome, antipyretic, diuretic, maturant, laxative, digestiblle, anthelmentic, urinary calculi, inflammation of the lungs and the bowels, sore throat, pain in joints, thirst, lumbago, cold and sneezing, sore eye, ring worm scabies, leucoderma, soalding urine, arrest vomiting, biliousness, flatulence and febrile (Metha and Belemkar, 2014; Verma, 2018).

Ameliorative effects of spinach seeds on carbon tetrachloride induced hepatotoxicity. The *in vitro* and *in vivo* hepatoprotective effects of spinach seeds were examined and suggests that these seeds acts as

therapeutic agent in liver diseases. The seeds are useful in fevers, leucorrhoea, urinary discharges, lumbago, brain and heart diseases. Seeds are laxative and cooling (Rao et al, 2015; Verma, 2018).

Pharmacological effects

Antidiabetic effects

The spinach antidiabetic activity may be due to the presence of flavonoids such as kaempferol, qyricetin, quercetin, apigenin and luteolin. It is reported that flavanoids constitute the active biological principles of most medicinal plants with hypoglycemic and antidiabetic properties. The ethanolic and aqueous extract of spinach leaves were orally tested at the dose of 200 and 400 mg/kg for hypoglycaemic effect in normal and alloxan-induced diabetic rats. In addition, changes in body weight, serum cholesterol, triglyceride assessed in the aqueous and ethanolic extract treated diabetic rats, were compared with diabetic control and normal animals histopathological observations during 12 days treatment were else evaluated. Spinach ethanolic and aqueous extract produced a significant reduction in fasting blood glucose levels in the normal alloxan-induced diabetic rats. Also, significant differences were observed in serum lipid profiles including cholesterol and triglyceride and changes in body weight by both ethanolic and aqueous treated diabetic animals. Histopathological studies of the pancreas of these animals showed comparable regeneration by extract which were earlier necrosed by alloxan (Gomathi et al, 2010; Nuutila et al, 2002). Chronic ulcer is still a serious issue for diabetic patients. Diabetes is a prevalent cause of ulcer regeneration delay and disruption. Since spinach extract contains compounds with anti-oxidative and anti-inflammatory effects, this may be effective in accelerating the healing process of ulcers, especially diabetic ulcers. In macroscopic examination of the wounds of the control group and spinach aqueous extract group between 7 and 21 days compared with diabetic group, significant changes were observed. On microscopic examination, epithelial tissue formation, formation of granulation tissue and new blood vessels in the spinach aqueous extract group and non-diabetic group compared to the diabetic group showed significant improvements. Also, significant differences in vascular endothelial growth factor were observed between groups on days 3 and 7. The spinach aqueous extract can be effective in regenerating diabetic ulcers that improvement the speed and structure of the ulcer (Rahati et al, 2015). The protective potentials of the spinach leaf extract (SLE) (50 mg/kg BW) studied against the systemic LPS (5mg/kg BW) induced toxicity by evaluating several toxicological parameters such as increased oxidative burden in organs as depicted from compromised antioxidant defense system (including Glutathione system, MDA levels, Catalase activity), cytokine levels and blood glucose levels. Glucose levels were found to decrease significantly in LPS treated animals as compared to control but SLE normalise the level of glucose. The cytokines IL-1 and TNFα produced in liver regulate glucose metabolism and may lead to hypoglycaemic effect in response to LPS. Whereas, spinach co-administration normalized the blood glucose level in LPS treated animals as it regulates/inhibiting the expression of these pro-inflammatory cytokines i.e., IL-1β and TNF-α. The nutritional value and *in vitro* antioxidant as well as antidiabetic potential of spinach were determined. The methanolic extract of spinach was prepared using Soxhlet extraction technique which was subjected for physicochemical, nutritional value determination along with the OH-scavenging, 2,2-diphenyl-1-picrylhydrazyl and α-amylase inhibition activity. The results demonstrated the good nutritional values such as total crude fiber, proteins, oils and fats, carbohydrate, and vitamins A and C. Moreover, methanolic extract of spinach showed the antioxidant activity and antidiabetic effect with an inhibitory concentration of 3.03 µg/ml, 6.03 µg/ml and 3.046 µg/ml for OH-scavenging, 2,2-diphenyl-1-picrylhydrazyl inhibition and α-amylase inhibition, respectively (Kapoor et al, 2017; Sah et al, 2017).

Antioxidant activity

Rao et al (2015) compared the effect of drying in fresh and dried leaves with reference to the phyto-constituents. There was no change in the phytochemical constituents present in fresh and dried leaves of spinach. The anti-inflammatory, laxative and antioxidant property may be due to the presence of glycosides such as coumarins, anthroquinones, steroids and flavonoids, respectively. Loss of water content on drying has no effect on the extractive values of leaves and phyto-constituents. So the dried leaves can be used for its medicinal values and can be stored till its use. The antioxidant properties and stability of spinach polyphenols evaluated by Sun et al (2018) via two common methods including 1,1-diphenyl-2-picrylhydrazyl radical scavenging activity and ferric reducing antioxidant power. Results demonstrated that spinach polyphenol had a certain antioxidant activity, and its antioxidant ability increased with the increase of sample concentration. External factors, such as pH value, temperature, light and preservative, have different effects on their antioxidant stability.

Anti-osteoarthritis effects

Spinach leaves were used as traditional Persian medicine for joint pains which osteoarthritis and rheumatoid arthritis are the most popular ones. The

antiosteoarthritic and chondro-protective effects of spinach extract evaluated on chemically induced osteoarthritis. Results indicated that spinach extract acts as a strong anti-oxidant and an anti-inflammatory agent. Histological analysis of knee joints established its protective effect. Radiological data corroborated the findings with improvement in the joint space and irregularity of the articular and atrophied femoral condyles and tibial plateau. Spinach extract had also the ability to mitigate osteoarthritis effects by increasing bone volume to tissue volume which resulted in decrease of trabecular pattern factor by more than 200%. Serum and urine analysis indicated that it had the potential to down-regulate glutathione S-transferase activity, clinical markers of osteoarthritis. Thereby, this led to a significant improvement in locomotion and balancing activity and it has the ability to alleviate the monosodium iodoacetate induced deleterious effects. (Abolhassanzadeh et al, 2016; Choudhary et al, 2018).

Anti-schizophrenia activity

The protective effects of spinach seed extract were carried out in an experimental model of ketamine-induced schizophrenia (SZ) in mice. Ketamine (50 mg/kg) was used to induce stereotyped psychotic behavioural symptoms in mice. Spinach seed extract reduced dopamine levels, AChE activity and inflammatory surge and increased the levels of gamma-aminobutyric acid (GABA) and reduced glutathione (GSH), thereupon was effective against stereotypic behaviours, positive, negative and cognitive symptoms of SZ induced by ketamine in mice. The extract did not show extra-pyramidal side effects (Yadav et al, 2018).

Spatial memory

The effects of ethanolic extracts of spinach on spatial memory in wistar rat induced by diazepam were studied. There is an effect of 200 mg/kg BW spinach ethanolic extracts in preventing impairment on spatial memory by accelerating escape latency time (Leonita et al, 2015).

Anti-bacterial acticity

Spinach extract can be used as a natural antibiotic and preservative in food industries and pharmaceuticals (Issazadeh et al, 2017). It is very rich in the flavonoids including querecetin, myricetin, kampeferol, apigenin, luteolin, patuletin and spinacetin. The polyphenols para-coumaric acid, ferulic acid and orthocoumaric acid also reported from this plant which may be responsible for antibacterial activity. The methanolic extracts of spinach were tested against twelve Gram-positive and eighteen Gram-negative bacteria at 1000 µg/disc concentration by disc diffusion method and it exhibited activity against three Gram-positive and one Gram- negative bacteria (Ali et al, 2017). Sun et al (2017) demonstrated that the antibacterial activity of spinach polyphenol against Gram-negative bacteria was stronger than that of Gram-positive bacteria. In addition, the effects of pH value, temperature and NaCl concentration on the antibacterial stability of spinach polyphenol were also discussed. Issazadeh et al (2017) studied alcoholic extract of spinach that showed more potent antibacterial activity than aqueous extract on *Escherichia coli* (*E. coli*). Also, the effect of its alcoholic extract on *E. coli* was comparable with Erythromycin on *Listeria innocua* at disc diffusion test. Finally, it can be concluded that high amounts of flavonoids and terpenes, unsaturated fatty acids and inorganic materials are probably the most important inhibitory agents of spinach on Gram-negative bacteria such as *E. coli*.

Anti-inflammatory activity

The polyphenols have anti-inflammatory, anti-oxidant and anti-DNA damaging effects. Based on the epidemiological evidence and laboratory studies conducted using *in vitro* and *in vivo* systems, it is suggested that routine consumption of these polyphenols may provide efficient protection. The investigation of phytochemically evaluated ethanolic and aqueous extracts of spinach leaves for its anti-inflammatory activity in rats demonstrated that ethanolic as well as aqueous extract at a dose level of 1100 mg/kg have shown significant activity which is comparable to the standard drug (Indomethacin, 20 mg/kg). The findings with spinach are significant, because it used as a dietary vegetable and is available all over the world. Therefore, it is worthwhile to conduct detailed studies in order to explore the full potential of this plant in reducing inflammation in humans from the point of view of cost and availability for people at all socioeconomic levels (Garg et al, 2010; Gupta et al, 2018).

Anti-cancer effects

Spinach is considered as a beneficial source for various carotenoids and lipophilic active compounds including neoxanthin, lutein, zeaxanthin, and chlorophylls. Dietary intake of spinach extract has beneficial effects on various types of cancer, such as ovarian, lung, prostatic, breast, and colon. Natural antioxidant mixture is composed of the main active compounds contained in spinach, mainly flavonoids, and cumaric acid derivatives. Natural antioxidant mixture can easily be used for chemoprevention or dietary intervention in humans because it is stable at high temperature and lacks toxicity (Lomnitski et al, 2003). The spinach glycoglycerolipids fraction can also inhibit mammalian pol activity, human cultured cancer cell growth, and *in vivo* solid tumor proliferation with oral administration that could help

to prevent cancer (Verma, 2018). Glycoglycerolipids from spinach including monogalactosyl diacylglycerol were extracted from dried spinach and using four human pancreatic cancer cell lines and normal human dermal fibroblasts. The effects of radiation and monogalactosyl diacylglycerol were assessed inhibitory effects on tumor growth in a mouse xenograft tumor model though monogalactosyl diacylglycerol enhances the cytotoxicity of radiation to induce apoptosis of cancer cells *in vitro* and *in vivo* (Akasaka et al, 2016).

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