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PLANT REVIEW

Review of Neuro-nutrition Used as Anti-Alzheimer Plant, Spinach, *Spinacia oleracea*

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ABSTRACT

Neuro-nutrition is the nutrition needed to achieve health brain and neurocognitive function. Diets rich in antioxidants, vitamins, flavonoids, and polyphenolic compounds will help suppress the onset of Alzheimer's disease. *Spinacia oleracea* (Family: *Amaranthaceae*) commonly known as spinach or Buai Leng (in Thai), one of the traditional medicinal plants with high in those mention nutrients. The micronutrients in spinach include a range of vitamins and minerals, which can prevent deficiency diseases and are essential for normal physiological function. Its phytochemicals are carotenoids, flavonoids, and phenolic compounds, which can prevent chronic health problems, as well as other diseases associated with aging. The objective of this article was to conduct a review on various ethnomedicinal uses of the spinach and its influences on the pathophysiology of Alzheimer's disease based on a literature review.

Key words: Alzheimer, herb, neuro-nutrition, plant, spinach, *Spinacia oleracea*

INTRODUCTION

Popeye, the popular cartoon sailor man, who famously attributed his strength after his consumption of spinach. This dark green leafy vegetable, *Spinacia oleracea* (SO), referred as "power food" is packed with essential nutrients such as proteins, minerals, and vitamins.[1,2] There is clear evidence that consumption of medicinal plants is beneficial to health. Moreover, recent studies with antioxidant substances indicate that can slow the progression of Alzheimer's disease.[3,4] This review is an attempt to compile information on various ethnomedicinal uses of spinach for anti-Alzheimer's disease. This disease is a multifactorial neurodegenerative disorder which its causes and progression are still not well understood.[5] Chan *et al.*[6] assessed the epidemiology of Alzheimer's disease and other forms of dementia in China, they reported that the prevalence was 1.8% and 2.6% at 65–69 years; 42.1% and 60.5% at 95–99 years in 1990 and 2010, respectively. The number of people with Alzheimer's disease in China was 1.93 million in 1990, 3.71 million in 2000, and progress to 5.69 million in 2010. They also suggested that the burden of dementia seemed to be increasing faster and need to tackle in low- and middle-income countries. Rao *et al.*[7] reported Alzheimer's disease affecting more than 5 million Americans, a number estimated to increase to 7.7 million by 2030. The pathophysiology of Alzheimer's disease is largely represented by the neurotoxic events triggered by the β-amyloid cascade[8] and by cytoskeletal abnormalities subsequent to the hyperphosphorylation of microtubule-associated Tau protein in neurons.[9] These processes lead, respectively, to the formation of neuritic plaques or senile plaques and neurofibrillary tangles, oxidative and inflammatory processes, neurotransmitter disturbances, and cholinergic deficit, which are the pathological hallmarks of this disease.[10] Thus, attempts to restore these features have been a rational target for drugs used to treat the symptoms of Alzheimer's disease. Approaches to enhance cholinergic function have included stimulation of cholinergic receptors or prolonging the availability of acetylcholine released into the neuronal synaptic cleft by inhibiting the acetylcholine hydrolysis by acetylcholinesterase.[11] Currently available treatment, i.e. acetylcholinesterase inhibitors, i.e., rivastigmine,[12] galantamine,[13] and donepezil;[14] and N-methyl-d-aspartate receptor antagonist (memantine) contributes minimal impact on the disease and target late aspects of the disease.[15] These drugs decelerate the progression of the disease, provide symptomatic relief, but fail to achieve a definite cure.[16]

Natural products from medicinal plants have gained huge interests from researchers around the world for new drugs because of their positive bioactivity effects.[17,18] The medicinal plants have been used to enhance cognitive function and to alleviate other symptoms associated with Alzheimer's disease[7,19] such as Ashwagandha (*Withania somnifera)*,[20] Brahmi (*Bacopa monnieri)*,[21] Maca (*Lepidium meyenii)*,[22] and Turmeric (*Curcuma longa)*.[23] Spinach is one of the most important antioxidant plants, usually consumed either fresh or frozen leaves. The 100 g of fresh spinach contain of ascorbic acid (13–53 mg), β-carotene (5626 μg), carotenoids (17.8 mg), flavonoids (1–4 mg), folate (194 μg), folic acid (194 μg), nitrate (31–117 mg), oxalate (400 mg), vitamin A (9377 IU), and minerals such as calcium (99 mg), magnesium

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(79 mg), and potassium (558 mg).[24] The scientific classification of SO is following (Kingdom) *Plantae*; (Subkingdom) *Tracheobionta*; (Superdivision) *Spermatophyta*; (Division) Magnoliophyta; (Class) Magnoliopsida; (Subclass) *Caryophyllidae*; (Order) *Caryophyllales*; (Family) *Amaranthaceae*, formerly *Chenopodiaceae*; (Subfamily) *Amaranthoideae*; (Genus) *Spinacia*; (Species) SO L.[25]

Nomenclature

SO was originated from the Central and Southwestern Asia and later was distributed widely in Europe, America, Africa, and Australia. The vernacular name of SO also known as spinach (English), palang (Bengali), bo cai (Chinese), spinat (Deutsch), épinard (French), spinat (German), palak (Hindi), pinni (India), horenso (Indonesian), spinacio (Italian), horenso (Japanese), sigeumchi (Korean), bayam (Malaysian), espinafre (Portuguese), chhurika (Sanskrit), espinaca (Spanish), spenat (Swedish), pasalai (Tamil), mathubucchali (Telugu), Buai leng (Thai), ispanak (Turkish), and rau chan vit (Vietnamese).[25,26]

Morphological Characters

SO has two varieties, one is the wavy or curly leaf [Figure 1], whereas the other is the flat leaf.[26] The leaves are alternate, simple, ovate to triangular-based, and varying in size from about 2–30 cm long and 1–15 cm broad. The larger leaves are at the base of the plant and small leaves higher on the flowering stem.[27] The flowers are inconspicuous, yellow-green, 3–4 mm in diameter, maturing into a small, hard, dry, lumpy fruit cluster about 5–10 mm across containing several seeds.[28-30]

Figure 1: *Spinacia oleracea* showing wavy leave

PHYTOCHEMICAL SUBSTANCES

The extracts of SO consist of the important constituents of pharmacological activities.[28] Phenolic compounds: The polyphenols isolated from this plant are ortho-coumaric acid, para-coumaric acid, and ferulic acid.[31,32] Flavonoids: Various flavonoids isolated from this plant are apigenin, glucuronide, flavone, jaceidin, kaempferol, myricetin, methoxyflavone, patuletin, quercetin, and spinacetin.[33,34] Carotenoids: The carotenoids isolated from this plant are lutein, β-carotene, violaxanthin, and neoxanthin.[35,36] Vitamins: Spinach contains a high concentration of vitamin A, E, K, and C, and also folate, folic acid, and oxalic acid.[37] Minerals: The minerals isolated from this plant are calcium, copper, iron, magnesium, manganese, phosphorus, potassium, and zinc.[28]

Traditional Uses

SO is traditionally used for antianemia,[38] antibacterial,[39-41] anticonvulsant,[42] antidiabetic,[43] anthelmintic,[44] antihyperlipidemic,[45,46] anti-inflammatory,[36,47] antioxidant,[2,48] antiulcer,[49] and antiviral activities.[50,51] It is also used in the prevention of nervous,[42] hepatic,[52,53] and respiratory diseases.[54]

Neuropharmacological Effects

There are still not many data available about the neuroprotective potential of this medicinal plant, SO. During the review searches were done on the scientific databases, i.e. Science Direct, Springer Link, PubMed, Google Scholar, and so on. Moreover, internet searches were undertaken on the search engine. Different combinations of keywords as well as synonyms for keywords were used during the searches.

Wang *et al.*[55] have demonstrated that rats which received spinach-enriched diet have a significant reduction in the volume of infarction in the cerebral cortex, lower caspase-3 activity in the ischemic hemisphere, and an increase in poststroke locomotor activity. Those authors also postulated that besides antioxidant activity, anti-inflammatory mechanisms might be involved reducing brain damage.

Das and Guha[42] reported the treatment with SO extract (400 mg/kg body weight) decreased the locomotor activity, grip strength, increased pentobarbitone-induced sleeping time, and also markedly altered pentylenetetrazole-induced seizure status in rats. They also mentioned SO increased serotonin level and decreased both norepinephrine and dopamine levels in cerebral cortex, cerebellum, caudate nucleus, midbrain, and pons and medulla. The result suggested that SO exerts its central nervous system depressive effect on pentylenetetrazole-induced seizure by modulating the monoamines in different brain areas.

Das and Guha[56] also reported the protective role of fresh, young, and healthy leaves of SO against the development of amygdala-kindled (AMK) experimental epileptogenesis. Thirty-six rats were equally divided into (1) control, (2) 400 mg/kg of SO, (3) AMK, (4) SO + AMK, and (5) diazepam + AMK group, oral treated one daily for 14 consecutive days. The afterdischarge duration (ADD) was used as index of kindled seizures. In AMK group, seizure stages reached up to stage 4–5 within the 2nd week. Electroencephalographic tracings showed that pretreatment with SO in AMK group decreased the ADD and seizure stages of SO pretreated rats were limited within stage 1–2 from 1st to 4th week of kindling. The brain monoamine content of serotonin was decreased in cerebral cortex, cerebellum, caudate nucleus, midbrain, and pons-medulla of AMK group which was increased by SO pretreatment. Alteration of dopamine and norepinephrine in different brain regions of AMK group was also modulated by SO pretreatment. Thus, the authors

summarized SO pretreatment retards the development of AMK epilepsy in experimental animals by modulating behavioral and neurochemical aspects.

Moreover, Sharma *et al.*[57] studied the possible neuroprotective mechanism of SO against lipopolysaccharide, a bacterial endotoxin, induce neurodegenerative disease by injected intraperitoneally (5 mg/kg) in mice. They found that lipopolysaccharide produced symptoms as impaired motor functions, total locomotor activity, catalepsy and rotarod, increased oxidative burden, enhanced mRNA expression of pro-inflammatory cytokines, and decreased dopamine turnover in striatum. However, spinach leaf extract (50 mg/kg) administration intraperitoneally for 21 days significantly attenuated the lipopolysaccharide-induced behavioral, biochemical, neurochemical, and cellular alterations.

SO possesses the anti-Alzheimer effect using multiple mechanisms. From the literature reviews that can be summarized these mechanisms as following:

Improvement of cognition

The Vitamin B plays a particular role in the memory healing diet. It helps synthesize and regulate the neurotransmitter, which can protect cognitive decline.[58] The study of more than 200 women found that a diet high in folate and vitamin B6, such as that found in spinach and other dark leafy greens, helped improve mental ability and short-term memory.[59]

Antioxidant activity

It was found that the intake of antioxidant-rich diet is effective in reducing the deleterious effects of aging and behavior.[60] It suggested that the combination of polyphenolic compounds found in spinach may show efficacy in Alzheimer's disease.[61]

Protection against senile plaques

Flavonoids, i.e., kaempferol, apigenin, luteolin, and quercetin significantly lowered the β-amyloid-induced neuronal death and increase in reactive oxygen species production. Hence, the flavonoids-rich spinach is able to protect Alzheimer's disease against β-amyloid peptides and/or oxidative stress-induced toxicities.[62]

Anticholinesterase activity

One of the currently available drugs is rivastigmine, acetylcholinesterase inhibitor. Hence, the natural plants, which show anticholinesterase activities, will be the candidates for anti-Alzheimer's disease. Boga *et al.*[63] found the high amount of anticholinesterase activities from the dichloromethane, ethanol, and water extracts of spinach.

CONCLUSION

It was suggested that an increase in acetylcholine in the hippocampus may be the neurochemicals basis for improved learning and memory. The other mechanism is a neurogenic growth promoter that will increase in survival, growth, and development of the newborn neurons, critical for the repair, and restoration of the normal neural circuitry in various diseases, especially Alzheimer's disease. The present article reviews that SO may also be the anti-Alzheimer's plant.

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Conflicts of interest

There are no conflicts of interest.

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