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A REVIEW ARTICLE ON NEUROPROTECTIVE EFFECT OF SHUNTHI

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ABSTRACT Worldwide ginger (the rhizome of *Zingiber officinale* Roscoe) has been in use for centuries in gastronomic and for medicinal purpose. The main pharmacological properties of ginger include anti-inflammatory, antihyperglycemic, antiarthritic, antiemetic and neuroprotective actions. From long time ginger has been used in traditional medicine to treat catarrah, stomachache, rheumatism, dementia, joint and muscle pain, toothache, asthma and diabetes. Ginger rhizome (Zingiber officinale) has been used for centuries to treat dementia in South Asia. The studies proved that ginger significantly improves cognitive function in healthy brain as well as various cognitive disorders. In Ayurvedic references we can see diversity in the references of actions of Ginger on brain. However, the biochemical mechanisms are still unknown and are a point of research.

KEYWORDS : Learning, Memory, Dementia, Shunthi,

INTRODUCTION

"Nootropic" is the name given to any chemical substance that can improve brain function without negatively affecting the brain. Drugs that fall into this group are acknowledged to enhance cognitive abilities such as memory configuration and recall, learning, logical reasoning, creative thinking, concentration and provocation of mood and mental energy.

Ginger is widely used around the world as a culinary spice to add flavor and color to the food. Ginger is generally considered a safe herbal medicine and is on the FDA's Generally Recognized As Safe (GRAS) list1-2. Ginger has been demonstrated to impart significant effects on numerous physiological responses like lipid and glucose levels, blood clotting, blood pressure, GIT, body thermodynamics and intracellular calcium concentration. Numerous evidence demonstrated the pharmacological properties of ginger such as immunomodulatory, anti-oxidative, anti-carcinogenic, anti-hyperglycemic, neuroprotective and antiemetic. Interestingly ginger also has therapeutic effects against nervous system diseases, including insomnia, neurosis, psychiatric disorders, stroke, depression, brain tumors, and dementia.

These multiple physiological and pharmacological properties of ginger make it a particularly promising protective agent against aging and degenerative diseases.

The aging population is particularly vulnerable to memory deficits caused by AD (Alzheimer's Disease), stroke or age-related cognitive decline and many individuals worldwide presently suffer from one or other type of cognitive disorder. Evidence has shown that ginger potently enhances cognitive function in a number of animal models of as well as in healthy individuals. In most parts of South Asia, ginger has long been in use as a folk medicine for the treatment of dementia

Properties of Shunthi according to Ayurveda

सस्नेहं दीपनं वृष्यमुष्णं वातकफापहम्।
विपाके मधुरं हृद्यं रोचनं विश्वभेषजम्॥२९६॥ (च.सू. २७)
कफानिलहरं स्वर्यं विबन्धानाहशूलनुत्।
कटूष्णं रोचनं हृद्यं वृष्यं चैवार्द्रकं स्मृतम् ॥२२७॥ (सु.सू. ४६)

Synonyms- *Vishwa, Vishwam, Nagar, Vishwabheshaj, Ushan, Katubhadra, Shringavera, Mahaushadham*
Rasa- Katu

Guna- *Laghu, Snigdha, Kapha Vata hara , Aamvataghni, Aruchihara, Pachan*

Veerya*- Ushna*
Vipak*- Madhura*

Doshakarma- *Vrishya, Swarya, Vaman, Shwas, Shoola, Kasa, Hridrog, Shleepad, Shotha, Arsha, Anaha, Udar gat Vata, Agniguna Bhuyishtha , Toyanshi Parishoshi, Mala k jal ka sangrahan, Vibandha bhedani* (breakdown obstruction) *but mala ka patan nahi karti* .

Effects of ginger on memory impairment

Researches demonstrated that Z. officinale could protect ischemic brain damage in a rat model of focal cerebral ischemia3. Moreover, it also reduced cognitive deficits induced by focal cerebral ischemia4. Z. officinale is able to increase the neurons' density in the hippocampus of the brain and improve the spatial memory. Z. officinale has previously been reported to induce vasodilation. Therefore, it might be possible that Z. officinale could enhance cerebral blood flow resulting in the improvement of spatial memory. A dose that provided the most beneficial effect was 200 mg/kg body weight. The lower dose failed to show the neuroprotective effect in dentate gyrus while the Z. officinale at a dose of 200 mg/kg body weight could increase the neuronal density in this area. One possible explanation for this phenomenon might be related to the insufficient level of Z. officinale to reach the therapeutic level.

The results also demonstrated that Z. officinale at dose of 200 mg/kg body weight could mitigate the brain infarct volume and could decrease oxidative stress by increasing the activity of SOD in cerebral cortex, hippocampus, and striatum and increased the activities of CAT and GSH-Px in cerebral cortex and hippocampus resulting in the decrease of lipid peroxidation level in all areas mentioned earlier. Therefore, the neuroprotective effect of Z. officinale extract might be related to its antioxidant effect.

Ginger improves cognitive function in middle-aged healthy women

Studies validated that *Zingiber officinale* may enhance both the attention and cognitive processing in middle-aged women. Research data showed that the improvement of cognitive function was observed in all attention and cognitive processing domains. *Zingiber officinale* could improve both attention and the competence of cognitive processing. Furthermore, ginger extract and 6-gingerol (an active component) inhibited the cholinesterase activity resulting in increased acetylcholine (ACh) that plays an important role in learning and memory[5].

Effects of ginger on cognitive function under normal conditions

Ginger administration can enhance the cognitive function in normal experimental animals. Data suggest that ginger extract, which has been shown to reduce the memory deficits in the animal models of neurodegenerative diseases, might also enhance learning and memory in normal brain.

Effects of ginger on NGF expression in vivo and in vitro

Nerve growth factor (NGF), which consists of polypeptide growth factors is the best- considered member of the neurotrophic family. NGF influences the proliferation, differentiation, survival and death of cholinergic neurons in the central nervous system. It is believed that cholinergic neurons projecting to the hippocampus are important for memory processes hence NGF is considered as a therapeutic target for dementia, including Alzheimer's disease. NGF plays critical roles in

accelerating neurite outgrowth, facilitating hippocampal long-term potentiation (LTP) and enhancing memory formation. Ginger extracts found to induce the up-regulation of NGF and increase the levels of pERK and pCREB in the hippocampus. Through NGF-induced activation of ERK/CREB signaling, GE may enhance synaptogenesis and memory[6].

The Role of ginger on Inhibiting Amyloid β Protein-Induced Apoptosis in PC12 Cells

AD is characterized pathologically by deposition of extracellular senile plaques and intracellular neurofibrillary tangles.[7] Amyloid-β (Aβ), the major component of senile plaques, is derived from sequential proteolysis of the amyloid precursor protein (APP) by sequential cleavages of β-secretase and γ-secretase and plays a critical role in the pathophysiology of AD[7-8]. Accumulating evidence suggests that oxidative stress and inflammatory responses are the major mechanisms of Aβ-induced neurotoxicity[9-10]. 6-Gingerol, a phenolic compound, is the major gingerol in ginger rhizomes with diverse pharmacological activities, including anti-tumor, anti-inflammatory, and anti-oxidant effects. In a recent study, 6-gingerol exhibited neuroprotective effects against cell apoptosis induced by Aβ through its anti-oxidative role.

Protective effects of ginger root extract on Alzheimer disease-induced behavioral dysfunction in rats.

The aim of this study was to assess the ability of a traditional Chinese medicinal ginger root extract (GRE) to prevent behavioral dysfunction in the Alzheimer disease (AD) rat model. Rat AD models were established by an operation (OP) in which rats were treated with a one-time intra-cerebroventricular injection of amyloid β-protein (Aβ) and continuous gavage of aluminum chloride every day for 4 weeks. GRE was administered intra-gastrically to rats. After 35 days, learning and memory were assessed in all of the rats. Brain sections were processed for immunohistochemistry and Hematoxylin & Eosin (H&E) and Nissl staining. This experiment demonstrated that the administration of GRE reversed behavioral dysfunction and prevented AD-like symptoms in rat models[11].

Muscarinic, Ca (++) antagonist and specific butyrylcholinesterase inhibitory activity of dried ginger extract might explain its use in dementia.

In South Asia region ginger is traditionally used as a treatment of Dementia. Dried ginger was tested positive for the presence of terpenoids, flavonoids, secondary amines, phenols, alkaloids and saponins. Specific inhibition of butyrylcholinesterase (BuChE) rather than acetylcholinesterase enzyme was shown by Zo.Cr and 6-gingerol in an in-vitro study. Ginger also showed spasmolytic activity in stomach fundus in which 6-gingerol was found as the most potent component.This study shows a unique combination of muscarinic, possible Ca(++) antagonist and BuChE inhibitory activities of dried ginger, indicating its benefit in dementia, including Alzheimer's disease[12].

Ayurvedic references

When searched in Ayurvedic references, Shunthi has been mentioned in Shirovirechana, Shoolaghni (analgesic), Raktatisaaraghna (diarrhea with blood), Mutrakrichhra (diuretic), Pipasaghni (anti dyspepsia), Triptighna (anti anorexic), Stanyashodhan (improves lactation), Medohara (anti-obesity) Gana. It is indicated in a lot of diseases including Jwara, Raktapitta, Gulma, Udavarta, Kushtha Rajyakshma, Unmaad, Apasmaar etc.

When looked up for memory enhancing effect it is seen that Shunthi is a component of a lot of Kalpas in Manovaha and Sangyavaha Srotas diseases like Unmaad and Apasmara. Shunthi is a ingredient of Hingwadi Ghrita which is Unmaad, Bhuta and Apasmaranut (As. Hr. Ut. 6/22). It is metioned in Brahmi Ghrita (As. Hr. Ut. 6/23-25) which is indicated in Unmaad, Kushtha, Apasmara, Vandhya, Vak-Swara-Smriti- Medha- Buddhi Vriddhi kara. Unmaad Sudani Varti (As. Hr. Ut. 6/38-40) containing Shunthi is indicated in Unmaad for Nasya, Anjan, Alepa and Dhupan. Mahapanchgavya Ghrita (As. Hr. Ut. 7/19-23) contains Shunthi which is indicated in Jwara, Apasmara, Jathara, Bhagandara, Shofa, Arsha, Kamala, Pandu, Gulma and Kasa. Shunthi as a component of Siddharthaka Ghrita (Su. Sa. Ut. 61/31-33) is indicated in Krimi, Kushtha, Garvisha, Shwas, Balas, Visham Jwara, Unmaad and Apasmara. Panchagavya Ghrita (Su. Sa. Ut. 61/34-35) containing Shunthi is indicated in Apasmara, Chaturthak Jwara, Kshaya, Shwasa and Apasmara.

DISCUSSION

The detailed study of Shunthi according to its Guna, Karma, formulations and indications, we can say that it mainly acts on Kapha Vata Pradhan Srotorodh Janya Samprapti, which also include pathologies like Dementia. It is a drug of combination of properties having Katu Rasa, Snigdha- Laghu, Pachan Guna, Ushna Veerya, Madhura Vipak Agni guna bahulya it increases Agni and possess Kapha Vata Shamak property. Correlating the Ayurvedic pathogenesis of Dementia, it appears that disturbance in the natural course of Dosha specially Vata and accumulation of Kapha due to Dhatwagnimandya (Majja) is responsible for Srotorodha leading to accumulation of Aam (Neurofibrillary Tangles and Tau proteins) that leads to degeneration and death of neurons resulting in Dementia. Shunthi, due to its peculiar properties like Vibandh Bhedan it breaks the accumulated Aam or NFTs and Tau proteins and because of Agni Vardhan, Pachan and absorption of excess water (Toyansh Parishoshi) it decreases the secretion of beta amyloid it may break the pathology of formation of new NFTs and tau proteins. The combined effect may result in normalizing of the Dosha imbalance on one hand and reversing the pathology of Dementia on the other hand.

We can conclude that Shunthi or ginger, which has no side effects and possesses multiple functions, can be a potential drug candidate for memory disorders and neurodegenerative diseases.

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