Therapeutic Effects of Ginseng on Psychotic Disorders

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Abstract: Ginseng, the root of Panax species, a well-known herbal medicine has been used as a traditional medicine for thousands of years and is now a popular and worldwide used natural medicine. Ginseng has been used primarily as a tonic to invigorate weak bodies to help the restoration of homeostasis in a wide range of pathological conditions such as cardiovascular diseases, cancer, immune deficiency and hepatotoxicity. Although conclusive clinical data in humans is still missing, recent research results have suggested that some of the active ingredients ginseng exert beneficial effects on central nervous system (CNS) disorders and neurodegenerative diseases, suggesting it could be used in treatment of psychotic disorders. Data from neural cell cultures and animal studies contribute to the understanding of these mechanisms that involve inhibitory effects on stress-induced corticosterone level increasing and modulating of neurontransmitters, reducing Ca2+ over-influx, scavenging of free radicals and counteracting excitotoxicity. In this review, we focused on recently reported medicinal effects of ginseng and summarized the possibility of its applications on psychotic disorders.

Key words: Panax ginseng; Ginsenoside; Psychotic disorders; Learning and memory; Anxiolytic effect; Sleep; Neurotransmitters.

INTRODUCTION

Psychotic disorders are mental disorders in which the personality is seriously disorganized and contact with reality is impaired. During psychotic disorders a person is confused about reality and often experiences delusions, anxiety or depression. Psychotic disorders include schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder, brief psychotic disorder, shared psychotic disorder, psychotic disorder due to a specific general medical condition, substance-induced psychotic disorder and psychotic disorder unspecified. These disorders share many features and also have important features that set them apart from each other.1)

Experts believe that many factors may play a role and there may be different causes for different illnesses within this group. Some researchers believe that individuals may inherited a tendency for developing a psychotic disorder for psychotic disorders tend to run in families.2,3) The role of neurotransmitters is also under study.4,5) On the other hand, the cause of this disorder is also typically an extremely stressful event or trauma for environmental factors seem to play a role and stress seems to set off schizophrenia in certain susceptible individuals.6)

Severe stressful conditions are responsible for the etiopathogenesis of various psychotic disorders. Mental homeostasis is controlled by various physiological mediators working in concert by interacting with receptors placed at various physiological levels and the functional identity of neurotransmitters is challenged during stressful conditions. Out of various neurotransmitters - noradrenaline (NA), dopamine (DA) and 5-hydroxy tryptamine (5-HT) are the important neurotransmitters which are widely distributed in brain and their functional role is well established during stressful conditions.7) Recent neurobiological studies indicates that psychotic disorders may be induced by neurodevelopmental and progressive disorders with multiple biochemical abnormalities involving DA, 5-HT, glutamate and gamma-aminobutyric acid (GABA)ergic systems. Changes in their activity result in behavioral changes as well as a cascade of hormonal release from the hypothalamus-pituitary-adrenal (HPA) axis. Alternation of HPA axis and dysfunction of these neu-

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rotransmitters due to prolonged stressful conditions have been associated with a wide range of central and peripheral disorders like depression, anxiety, drug abuse, obsessive compulsive disorder, eating and sleeping disorders, hyperglycemia and decreased immune response. Due to increased physical and psychological demands in the present day lifestyle and advent of various stress related disorders, there is an urgent need to develop agents to overcome these abnormalities.

The drugs of plant origin are gaining importance and being investigated for remedies of a number of psychotic disorders and other stress-related diseases. Since the introduction of adaptogen concept, several plants have been investigated, which were used earlier as tonics due to their adaptogenic and rejuvenating properties in traditional medicine. 

Panax ginseng, one of the most popular herbal medicines, has been widely used for the therapy of stress related disorders. In oriental medicine, ginseng is referred to as an agent that stimulates brain activity, invigorates mental capacity, improves vision, audition, power of thought and memory, thereby enhancing concentrations. In the early 1960s, scientists suggested that ginseng improved mental and intellectual performance in people. Ginseng extract and ginseng saponin improved memory acquisition, physical performance and learning disorders and confronted loss of memory in a memory-damaged animal model. Later, animal and clinical experiments carried out with ginseng as well as the active ingredients isolated from the ginseng have further supported the beneficial role of ginseng in brain activity.

**EFFECTS OF GINSENG ON PSYCHOTIC DISORDERS**

**Improving learning and memory (Anti-dementia)**

The specific mechanisms of learning and memory improving effects of ginseng are still unknown. Hyperglycemia has been shown to cause impairments in cognition and worsen the outcome of brain ischemia in several animal models. Some research work indicated that cognitive improvements may be related to the glycemic properties of ginseng because single doses of the ginseng have been shown to lower blood glucose levels and elicit cognitive improvements in healthy, overnight-fasted volunteers. In a double-blind, placebo-controlled, balanced-crossover design, ginseng and glucose were proved to be effective in enhancing performance of a mental arithmetic task and ameliorated the increase in subjective feelings of mental fatigue experienced by participants during the sustained, cognitively demanding task performance. Accuracy of performing the Rapid Visual Information Processing task was also improved following the glucose load. There was no evidence of a synergistic relationship between Panax ginseng and exogenous glucose ingestion on any cognitive outcome measure. Panax ginseng caused a reduction in blood glucose levels 1 hour following consumption when ingested without glucose. These data confirm that ginseng may possess glucoregulatory properties and enhance cognitive performance. It also suggests that there might be other mechanisms in the cognitive improving effects of ginseng.

Ginsenosides or ginseng saponins as the active ingredients have antioxidant, anti-inflammatory, anti-apoptotic and immunostimulant properties. Recent studies have revealed that ginsenosides possess neuroprotective and cognitive improving effects through activation of antioxidant enzymes, which raised speculations that these compounds could positively affect neurodegenerative disorders and delay neuronal aging. Although conclusive clinical data in humans are still missing, results from animal studies and neuronal cell culture experiments indicate that many ginsenosides, such as Rg1, Rg2, Rg3, can counteract and attenuate factors promoting neuronal death as environmental toxins, excitotoxic action of glutamate and increases in intracellular calcium ([Ca$^{2+}$]), excessive release of free radicals and apoptotic events. In cellular model of Alzheimer’s disease established by amyloid-beta treated primary cultured cells, ginsenoside Rg2 significantly attenuated [Ca$^{2+}$], lipid peroxidation and the protein expression levels of calpain II, caspase-3 increasing induced by amyloid-beta and increased cell viability. Besides, ginsenosides Rb1, Rb2, Re and Rg1 were also effective in reducing astrocytic death induced by oxidative stress, while Rb1, Rb2, Rd, Re and Rg1 decreased formation of reactive oxygen species, ginsenoside Re being the most active compound. Thus, researchers believe neuroprotective actions of ginsenosides could be an important reason for learning and memory improving effects of ginseng and come about as a valuable option to slow down neurodegenerative diseases such as Alzheimer’s disease.

**Anxiolytic and anti-depressive effects**

Ginseng has also been widely used for the management of anxiety and emotional instability and studies have already proved that ginseng induces anxiolytic-like effects in the elevated plus-maze test. Administration of red