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Review Article

Neurologic Effects of Liquorice: A Comprehensive Review

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ABSTRACT

Liquorice (*Glycyrrhiza glabra*) has been widely utilized in traditional medicine for various therapeutic benefits, including its roles in gastrointestinal and respiratory health. Recent research indicates that liquorice and its bioactive components may significantly influence neurological function. This review explores the neurologic effects of liquorice, focusing on its potential in neuroprotection, cognitive enhancement, and management of neurological disorders. Key mechanisms such as neurotransmitter modulation, anti-inflammatory properties, oxidative stress reduction, and regulation of the hypothalamic-pituitary-adrenal (HPA) axis are examined. While liquorice demonstrates potential for neurological applications, concerns regarding neurotoxicity and systemic side effects due to excessive consumption are highlighted. Future research directions and clinical recommendations are discussed to establish safe and effective therapeutic use.

INTRODUCTION

Liquorice (*Glycyrrhiza glabra*) is an herbaceous plant widely recognized for its medicinal properties across various traditional healing systems, including Ayurveda, Traditional Chinese Medicine (TCM), and Unani medicine. Its primary bioactive constituent, glycyrrhizin, exhibits a broad spectrum of pharmacological activities, including anti-inflammatory, antioxidative, and neuroactive effects. The potential neurological applications of liquorice have recently garnered scientific attention, prompting an in-depth investigation of its impact on cognition, neurodegenerative diseases, and mental health disorders. Numerous studies have demonstrated that liquorice extracts can influence brain function through multiple mechanisms, such as neurotransmitter modulation, reduction of oxidative stress, and inhibition of neuroinflammation. Furthermore, research highlights its ability to enhance neuroplasticity, improve learning and memory, and modulate mood disorders. Given its widespread use and potential therapeutic benefits, an extensive review of liquorice's neurological effects is warranted.

This review comprehensively analyzes the neurological effects of liquorice, outlining the physiological mechanisms by which it influences brain health and function. Special emphasis is placed on its therapeutic potential in cognitive disorders, neurodegenerative diseases such as Alzheimer's and Parkinson's disease, and mood-

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related conditions like anxiety and depression. Additionally, the risks associated with excessive liquorice consumption, particularly its neurotoxic and systemic side effects, are discussed.

MECHANISMS OF ACTION

The neuroactive properties of liquorice are mediated through various biochemical pathways:

2.1 Neurotransmitter Modulation

Glycyrrhizin and other flavonoids present in liquorice influence multiple neurotransmitter systems:

- **Gamma-aminobutyric acid (GABA):** Liquorice has been reported to enhance GABAergic transmission, contributing to anxiolytic and anticonvulsant effects. Studies indicate that GABAergic modulation by liquorice leads to reduced neuronal excitability, promoting relaxation and counteracting conditions such as epilepsy and anxiety disorders.
- **Dopaminergic System:** Components of liquorice may modulate dopamine levels, which could be beneficial in neurodegenerative and psychiatric disorders. Increased dopamine activity supports motor control and motivation, making liquorice a potential complementary treatment for Parkinson's disease and depression.
- **Serotonergic Pathway:** The serotonergic system, essential for mood regulation, is influenced by liquorice flavonoids, potentially explaining its antidepressant effects. Enhanced serotonin transmission has been linked to improved emotional stability and cognitive performance.

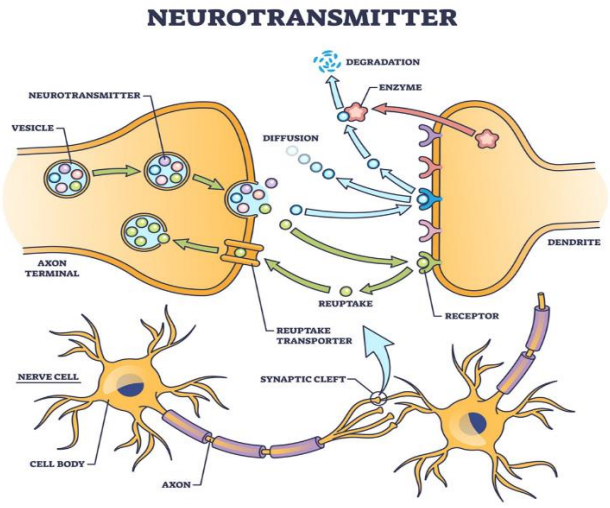
2.2 Anti-inflammatory and Antioxidant Effects

Chronic neuroinflammation is a key driver of neurodegenerative diseases. Liquorice exerts neuroprotective effects by:

- Reducing oxidative stress through scavenging free radicals, thereby preventing neuronal damage and apoptosis.
- Suppressing pro-inflammatory cytokines such as IL-1β, IL-6, and TNF-α, which are implicated in neuroinflammatory disorders like multiple sclerosis and Alzheimer's disease.
- Enhancing endogenous antioxidant defenses (e.g., superoxide dismutase and glutathione peroxidase), which protect against environmental and metabolic stressors that contribute to neuronal aging.

2.3 Hypothalamic-Pituitary-Adrenal (HPA) Axis Regulation

Liquorice influences cortisol metabolism by inhibiting 11β-hydroxysteroid dehydrogenase, thereby modulating stress responses and reducing stress-induced neurological damage. By regulating the HPA axis, liquorice may help mitigate symptoms of chronic stress, anxiety, and adrenal fatigue, supporting overall mental well-being.



3. Neurologic Applications

3.1 Cognitive Function and Memory Enhancement

Liquorice extracts have demonstrated cognitive-enhancing properties in both animal and human studies. These effects are attributed to its antioxidant activity, acetylcholinesterase inhibition, and neurotransmitter regulation. Preclinical studies indicate that liquorice-derived flavonoids can improve spatial learning, memory retention, and synaptic plasticity. Research also suggests that liquorice may counteract cognitive decline in aging populations by preserving neuronal integrity and function.

3.2 Neurodegenerative Diseases

3.2.1 Alzheimer's Disease

Liquorice bioactives reduce beta-amyloid aggregation, a hallmark of Alzheimer's disease. Additionally, anti-inflammatory actions help mitigate neuronal loss. Certain flavonoids in liquorice enhance cholinergic function, which is crucial for learning and memory processes.

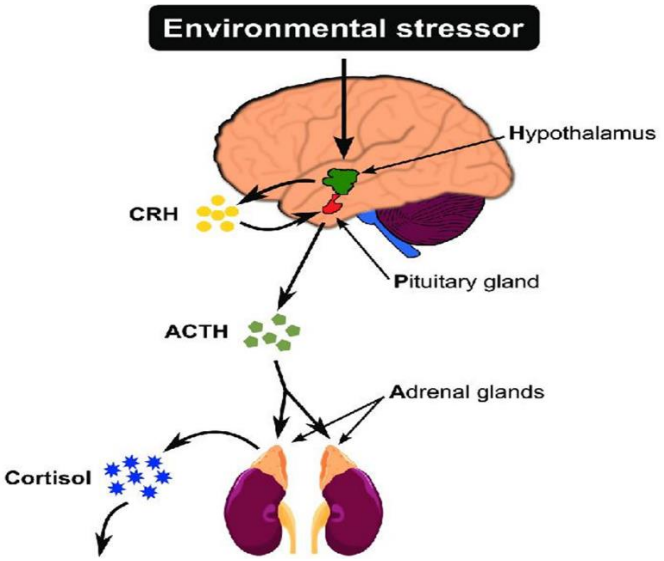
3.2.2 Parkinson's Disease

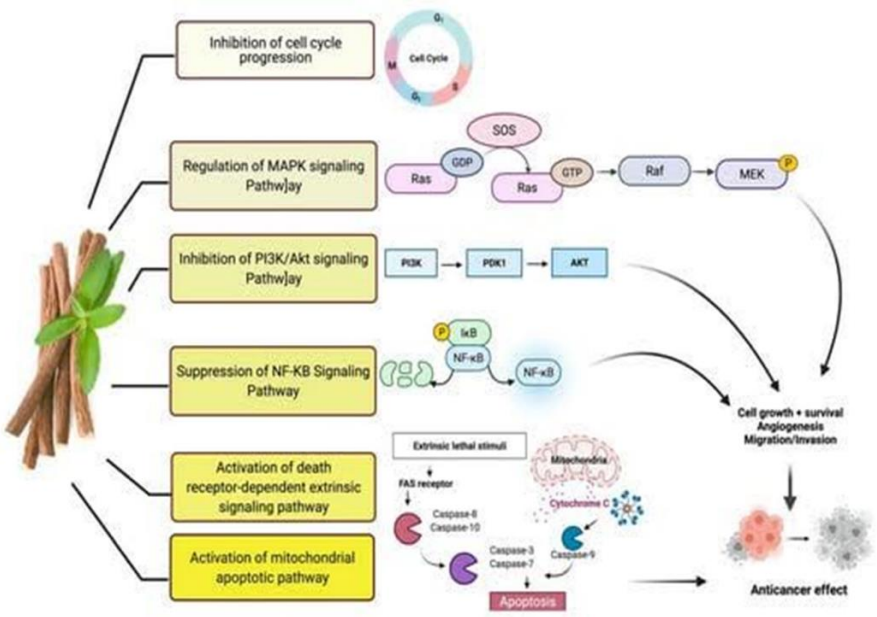
Preliminary research suggests that liquorice compounds may exert neuroprotective effects in dopaminergic neurons, reducing oxidative damage and inflammation in Parkinson's disease models. Additionally, its potential to inhibit neurodegeneration and support mitochondrial function is currently under investigation.

3.3 Mood Disorders and Stress Regulation

Liquorice has been studied for its potential role in treating depression and anxiety. By modulating the serotonergic and GABAergic systems, liquorice exerts anxiolytic and antidepressant effects. The adaptogenic properties of liquorice also contribute to emotional resilience, making it a candidate for stress management.

4. Safety, Toxicity, and Clinical Considerations





4.1 Adverse Effects of Excessive Liquorice Consumption

- **Hypertension and Hypokalemia:** Chronic intake of glycyrrhizin can lead to pseudoaldosteronism, resulting in electrolyte imbalances and cardiovascular complications.
- **Neurotoxicity:** High doses of liquorice may impair cognitive function due to excessive HPA axis stimulation, potentially leading to symptoms such as headaches, dizziness, and confusion.
- **Drug Interactions:** Liquorice may interact with corticosteroids, antihypertensive medications, and psychotropic drugs, necessitating caution in individuals undergoing pharmacological treatment.

4.2 Recommended Dosage and Safe Use

Current research suggests moderate intake (less than 100 mg/day of glycyrrhizin) to avoid adverse effects. More extensive clinical trials are needed to establish standardized doses for neurological applications. Personalized recommendations based on genetic and metabolic factors should be considered in future studies.

5. Future Directions and Conclusion

Liquorice and its bioactive components present a promising avenue for neurological research and therapeutic applications. While preclinical evidence supports its neuroprotective and cognitive-enhancing properties, well-controlled clinical trials are needed to confirm efficacy and safety.

Future research should focus on:

- Elucidating precise molecular pathways of liquorice in neurological health.
- Conducting large-scale human trials to validate findings.
- Exploring novel formulations to maximize therapeutic benefits while minimizing toxicity.

In conclusion, liquorice holds significant potential as a natural neuroprotective agent. However, safe consumption guidelines must be established to balance its benefits against potential risks.

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