

PHARMACOLOGICAL RISKS OF LICORICE ROOT: HORMONE-MIMICKING COMPOUNDS AND NEPHROTOXIC EFFECTS

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Abstract: For centuries, *Glycyrrhiza glabra*, commonly known as licorice root, has been applied in both Eastern and Western medical traditions due to its wide spectrum of pharmacological benefits. Nevertheless, its active constituents, primarily glycyrrhizin and glycyrrhetic acid, may elicit hormone-like effects that disturb the endocrine axis and renal physiology. This paper provides an in-depth exploration of the biochemical processes underlying these effects, the pharmacokinetic behavior of licorice metabolites, and the potential systemic consequences of chronic or excessive consumption.

Keywords: *Glycyrrhiza glabra*, glycyrrhizin, endocrine disruption, nephrotoxicity, pseudoaldosteronism, renal physiology, pharmacokinetics.

Introduction

Licorice root, a botanical derivative of the *Glycyrrhiza glabra* plant, occupies an important position in herbal pharmacology and nutraceutical production. It is commonly incorporated into respiratory and digestive formulations for its anti-inflammatory and protective effects on mucosal tissues. However, the misconception of licorice as a harmless natural sweetener has resulted in unregulated usage, contributing to adverse physiological outcomes. Among its major constituents, glycyrrhizin—a triterpenoid saponin—exerts pharmacodynamic activity comparable to corticosteroids, accounting for both therapeutic and toxic properties.

Chemical Composition of Licorice Root

The phytochemical composition of licorice root encompasses saponins, flavonoids, coumarins, and polysaccharides. Glycyrrhizin, constituting up to one quarter of the dry root mass, undergoes microbial hydrolysis within the intestinal tract to form glycyrrhetic acid—the bioactive metabolite responsible for its systemic activity. In addition, compounds such as liquiritin, isoliquiritin, and glabridin enhance its antioxidant capacity while contributing to its endocrine-modulating potential.

Hormone-Mimicking Mechanisms

The bioactive molecules of licorice interfere with the physiological regulation of cortisol by suppressing the enzyme 11β -hydroxysteroid dehydrogenase type 2 (11β -HSD2). This inhibition allows cortisol to remain in its active form, thereby overstimulating mineralocorticoid receptors. The resulting physiological cascade promotes sodium and water retention, potassium depletion, and increased arterial pressure, a constellation of symptoms referred to as pseudoaldosteronism. This endocrine interference demonstrates how plant-derived compounds can imitate and disrupt steroid signaling pathways.

Pharmacokinetics of Glycyrrhizin

Glycyrrhizin displays limited gastrointestinal absorption and is predominantly metabolized by intestinal microbiota. Following conversion to glycyrrhetic acid, the compound undergoes hepatic conjugation to glucuronide and sulfate derivatives, which are excreted via the biliary system. Enterohepatic recycling significantly extends its biological half-life, explaining the delayed manifestation of toxic effects after prolonged intake. Variability in microbial activity and liver function among individuals contributes to diverse toxicological responses.

Nephrotoxic and Systemic Adverse Effects

The renal system is among the most vulnerable targets of licorice toxicity. Sustained exposure to glycyrrhizin-containing products frequently results in potassium depletion, metabolic alkalosis, fluid retention, and arterial hypertension. Prolonged sodium retention may cause edema, cardiac stress, and reduced glomerular filtration rate. Extreme cases have been associated with acute renal insufficiency and muscle breakdown (rhabdomyolysis). Beyond renal implications, patients may experience fatigue, dizziness, and endocrine imbalance, including suppressed testosterone levels and menstrual irregularities.

Therapeutic Considerations and Safe Dosage

According to the European Food Safety Authority (EFSA, 2015), the acceptable daily intake for glycyrrhizin should not exceed 100 mg in adults. Lower dosages are advised for individuals with compromised renal or cardiovascular function. Therapeutically, licorice-based preparations can be beneficial for short-term management of respiratory or gastric inflammation under professional supervision. However, long-term self-medication may provoke pseudoaldosteronism, particularly when combined with diuretics or corticosteroids.

Public Health Implications

The increasing inclusion of licorice in dietary supplements and confections necessitates enhanced public awareness regarding its pharmacological potency. Clearer labeling of glycyrrhizin content, coupled with public health education on dosage thresholds, could prevent many adverse incidents. Healthcare systems should incorporate adverse event reporting for herbal products to strengthen pharmacovigilance frameworks and prevent licorice-related

toxicity.

Discussion

Licorice exemplifies the paradox of natural therapeutics—its bioactivity provides therapeutic efficacy but also toxic potential. While its antiviral and hepatoprotective properties have been documented, the compound's interference with steroid metabolism and cytochrome P450 enzymes introduces risk when consumed excessively. Future investigations should focus on pharmacogenetic variability and the establishment of standardized safety protocols to identify populations at heightened risk.

Conclusion

Licorice root serves as both a medicinal ally and a pharmacological challenge. Its main constituent, glycyrrhizin, possesses hormone-like characteristics that can disrupt endocrine and renal balance if consumed without caution. Maintaining moderate intake, guided by evidence-based dosage recommendations, ensures therapeutic benefits while minimizing toxic manifestations. Greater awareness and regulatory oversight are essential to prevent complications associated with licorice overconsumption.

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