Licorice (or liquorice) is a plant of ancient origin and steeped in history. Natural licorice is an extract from the root of *Glycyrrhiza glabra*, a 4- to 5-foot woody shrub that contains glycyrrhizic acid (GZA) and grows in subtropical climates in Europe, the Middle East, and Western Asia.

Licorice extracts and its principle component, glycyrrhizin, have extensive use in foods, tobacco products, and snuff, and in traditional and herbal medicine. As a result, there is a high level of use of licorice and glycyrrhizin in the US with an estimated consumption of 0.027-3.6 mg glycyrrhizin per kilograms per day. Licorice extract (block, powder, or liquid) may be applied to cigarette tobacco at levels of about 1-4% to enhance and harmonize the flavor characteristics of smoke, improve moisture-holding characteristics of tobacco, and act as a surface active agent for ingredient application.

Licorice flavor is found in a wide variety of licorice candies. Licorice is also found in some soft drinks (eg, root beer) and in some herbal teas where it provides a sweet aftertaste. Licorice has also been used as a medicinal agent in a number of cultures dating back to ancient Egypt and China. Medicinal uses have included cough suppression, gastric ulcer treatment, treatment of early Addison disease, treatment of liver disease, and as a laxative.

**Pathophysiology**

Natural licorice possesses both mineralocorticoid properties and glucocorticoid properties. Most licorice-flavored foods available in the United States do not contain GZA, and they do not produce the hypermineralocorticoid syndromes observed with the long-term consumption of moderate-to-significant amounts of natural licorice.

Large doses of GZA in licorice extract can lead to hypokalemia and serious hypertension, a syndrome known as hypermineralocorticoidism. Biochemical studies indicate that glycyrrhizinates inhibit 11-beta-hydroxysteroid dehydrogenase (type 2), the enzyme responsible for inactivating cortisol. As a result, a continuous, high-level exposure to glycyrrhizin compounds can produce hypermineralocorticoid-like effects in both animals and humans. These effects are reversible upon withdrawal of licorice or glycyrrhizin.

In the kidney, cortisol activation of mineralocorticoid receptors alters renal tubular exchange of sodium (retained), potassium (excreted), and hydrogen ions (excreted); producing an increased extracellular volume (hypertension, edema), hypokalemia (weakness, muscle spasm), and metabolic alkalosis. Pseudoparimary aldosteronism of chronic licorice ingestion is characterized by low serum and urinary aldosterone levels and decreased serum renin activity. This differs from true primary hyperaldosteronism caused by aldosterone producing adenomas or primary adrenal hyperplasia; it is characterized by elevated urine and serum aldosterone levels.

Licorice can reduce serum testosterone level, probably by blocking 17-hydroxysteroid dehydrogenase, and 17,20 lyase. Licorice has therefore been considered an adjuvant therapy of hirsutism and polycystic ovary syndrome.

The exact amount of ingested GZA that produces mineralocorticoid toxicity is unclear. Avoiding ingestion of natural licorice in the setting of hypertension, diuretic use, sexual dysfunction, or pregnancy is probably wise.

**Epidemiology**

**Frequency**

**United States**

Licorice poisoning is rare in the United States.

**International**

The frequency is unknown.

**History**
Most patients report chronic toxicity from daily excessive ingestion of natural licorice products (not artificial licorice flavoring); acute toxicity is not reported. Symptoms of licorice toxicity may include the following:

- Fatigue and muscle cramping
- Dark urine (myoglobinuria)
- Weakness (hypokalemia, myopathies)
- Polyuria/nocturia (increased extracellular volume)
- Edema (increased extracellular volume)
- Dyspnea (pulmonary edema)
- Headache (hypertension)
- Paresthesias/dysesthesias (eg, burning sensations of extremities)
- Impotence and diminished libido
- Amenorrhea

**Physical**

- Edema (peripheral, pulmonary), secondary to increased extracellular fluid from water retention, rales
- Licorice has been reported to cause high blood pressure, including dangerously high blood pressure with symptoms such as headache, nausea, vomiting, and hypertensive encephalopathy with stroke-like effects (eg, one-sided weakness).
- Spasms/tetany
- Hyporeflexia, muscle wasting, weakness, flaccid paralysis
- Myoglobinuria/rhabdomyolysis
- Trousseau and Chvostek signs (from hypokalemia with alkalosis)

- Cardiac arrest, dysrhythmias (rare) from hypokalemia

**Differentials**

- Acute Respiratory Distress Syndrome
- Congestive Heart Failure and Pulmonary Edema
- Encephalitis
- Hypernatremia
Hypertensive Emergencies

Hypokalemia

Myopathies

Pediatrics, Respiratory Distress Syndrome

Plant Poisoning, Herbs

Respiratory Distress Syndrome, Adult

Rhabdomyolysis

**Laboratory Studies**

Diagnosis is generally confirmed by combination of hypokalemia, increased urinary free cortisol, elevated cortisol-cortisone metabolite ratio, and low or absent urinary aldosterone.

Low serum potassium level is the most helpful screening result for establishing mineralocorticoid excess in patients with hypertension.

Elevated urinary potassium level may be present.

Dilutional anemia may be present, and hematocrit may be depressed.

Licorice poisoning can cause hypokalemic rhabdomyolysis with resultant myoglobinuria and elevated serum creatine kinase level. Elevated creatine phosphokinase level can cause acute tubular necrosis.

In so-called pseudo-primary hyperaldosteronism, plasma and urinary aldosterone levels are not elevated.

References


