

# Licorice ingestion and blood pressure regulating hormones

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*Nearly half a century ago Revers<sup>1</sup> reported that administration of a paste prepared from succus liquiritiae, a dried watery extract of the roots of Glycyrrhiza glabra, resulted in a reduction in abdominal symptoms as well as radiographic evidence of healing in patients suffering from gastric ulcer. Subsequent studies demonstrated that this preparation could prevent the formation of gastric ulcers in experimental animals and confirmed the salutary effects in patients, but found that approximately 20% of patients so treated developed facial and dependent edema, often accompanied by headache, shortness of breath, stiffness, and pain in the upper abdomen.<sup>2</sup> Although these symptoms suggested an allergic reaction, they were not accompanied by eosinophilia or relieved by antihistamines. These untoward effects usually subsided with a reduction of dose, although in some patients treatment had to be discontinued entirely. Given this profile of side effects, enthusiasm for licorice as a remedy for peptic ulcer disease soon faded. However, the popularity of licorice flavoring in candy and in other products such as chewing tobacco persists to this day, as do the problems in electrolyte and blood pressure homeostasis that can occasionally occur in individuals ingesting large quantities of licorice-containing products.<sup>3,4</sup> Although the pattern of the renal response suggested that the active ingredients in licorice were acting directly on the mineralocorticoid receptors in the kidney, an even more fascinating explanation for the toxic effects of licorice has emerged in the past decade. This article will review the sequence of observations that led to our current understanding of the mechanism by which licorice affects electrolyte metabolism and will pay particular attention to the interaction with hormonal systems involved in blood pressure homeostasis. (Steroids 59:127-130, 1994)*

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## Effect of licorice on electrolyte metabolism

To investigate the mechanism accounting for the licorice-induced edema noted by Revers,<sup>2</sup> Molhuysen et al<sup>5</sup> studied the effects of administration of succus liquiritiae, 20-45 g daily, in normal subjects who were maintained on a constant diet. Urine chloride, sodium, and water excretion decreased, urine potassium excretion increased, and body weight increased by several kilograms over 5-6 days, followed by a return of output to baseline values and the maintenance of a new steady state. None of these subjects developed clinical edema, although dependent edema was noted in several outpatients who were receiving chronic treatment with licorice for gastric ulcer. The authors concluded that "... the main effect of the drug was stimulation of the renal tubules to an excessive reabsorption of water and chlorides (sic), and probably also of sodium." Moreover, they noted that the effects seen with ingestion of licorice were similar to those seen

following injection of large doses of deoxycorticosterone or adrenocorticotropin (ACTH).

## The role of the adrenal in the renal tubular response to licorice

In view of the striking similarity of the renal tubular response to licorice and deoxycorticosterone, several investigators evaluated the effect of licorice extracts on body fluid homeostasis in patients with Addison's disease. This experiment had practical as well as heuristic value, inasmuch as deoxycorticosterone required parenteral administration and was the only remedy then available for treatment of patients with adrenocortical insufficiency. The results were contradictory. Molhuysen et al<sup>5</sup> found no effect whereas Groen et al<sup>6</sup> and Card et al<sup>7</sup> noted weight gain and sodium retention when either a crude licorice extract or a more refined preparation of the active ingredients, glycyrrhizinic or glycyrrhetic acid,<sup>7,8</sup> was administered to patients with Addison's disease following discontinuation of deoxycortone. However, neither glycyrrhetic acid nor crude licorice extract prolonged survival of adrenalectomized rats.<sup>7</sup>

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