

## Consume drinks, sweets and other foods containing liquorice in moderation

Chronic consumption of large amounts of foods containing liquorice can lead to serious poisoning, in particular a drop in blood potassium levels and hypertension, even in people who have never suffered from high blood pressure. French Poison control centres and ANSES studied the 64 cases of poisoning recorded in the Poison control centres' database from 2012 to 2021. Just under one in two cases were severe, and one death was reported. Here is a reminder of the regulations on maximum intake of liquorice. Prevention measures are based on moderate and occasional consumption.



### Liquorice: a plant used in many food products

Liquorice extract is obtained from the roots of the liquorice plant which, when dried, can be chewed as a treat. Glycyrrhizin is the most abundant compound in the root. It has considerable sweetening power, as well as salt-softening and flavour-enhancing properties. It is used in many sweet products (confectionery, chewing gum, snacks, bakery products, ice creams and sorbets) to reinforce their sweetness, as well as in savoury products (as a softener), cocoa-based products (as a flavour enhancer), soft drinks and syrups, alcoholic drinks based on liquorice extracts (pastis, ouzo, raki, sambuca, etc.), non-alcoholic pastis, beers and food supplements.

### Toxicity of glycyrrhizin

Adverse effects due to liquorice are far from uncommon. A literature review compiling 402 scientific papers, published in 2015, showed that liquorice was responsible for more than 12% of adverse effects associated with the consumption of herbal food supplements or traditional herbal products [1]. In a retrospective study of data from European and Brazilian poison control centres, liquorice was among the ten plants consumed in the diet and most frequently reported as causing adverse effects [2].

Glycyrrhizin induces pseudohyperaldosteronism<sup>1</sup>. It causes the loss of potassium in urine leading to hypokalaemia, water and sodium retention, and elevated blood pressure.

This is mainly due to inhibition in the kidney of an enzyme (11 $\beta$ -hydroxysteroid dehydrogenase type 2 isozyme) that plays an important role in regulating the receptors for aldosterone, a hormone that helps maintain normal blood pressure. After consumption of liquorice ceases, this enzyme's activity continues to be inhibited for about two weeks, and the body's return to a normal physiological state requires two to six months. All adults are at risk of pseudohyperaldosteronism, not just those who already have high blood pressure.

This risk increases with age because this enzyme's activity decreases with age. No cases of pseudohyperaldosteronism from liquorice poisoning have been described in children.

Liquorice poisoning mainly occurs in the event of prolonged consumption (several weeks) of high doses. A regular intake of 100 mg glycyrrhizin/day has been established as the threshold for the lowest observed adverse effect level (LOAEL). For example, depending on the concentration in the product, 100 mg of glycyrrhizin corresponds to about five 15-drop doses of Antésite™ liquorice concentrate, 4 to 50 2 cl doses of non-alcoholic pastis, 25 to 70 2 cl doses of pastis with alcohol, or 60 to 100% of a 6 g tin of confectionery made from pure liquorice extracts.

Some authors have suggested that dividing this dose by ten – daily ingestion of 10 mg of glycyrrhizin – would not have any health consequences for most healthy adults [3].

### What the regulations say

In the European Union, glycyrrhizin is listed as a flavouring substance. Regulation (EU) No 1169/2011 on the provision of food information to consumers imposes specific labelling requirements. The statement "contains liquorice" must be added for confectionery or beverages containing glycyrrhizin at a concentration of 100 mg/kg or 10 mg/l or above, unless the term "liquorice" is already included in the list of ingredients or in the name of the food. The statement "contains liquorice – people suffering from hypertension should avoid excessive consumption" must be added for confectionery with concentrations at 4 mg/g or above and for beverages at concentrations of 50 mg/l or above (or 300 mg/l or above in the case of beverages containing more than 1.2% by volume of alcohol). This statement implies that healthy people are not at risk from excessive consumption, whereas in fact they are.

1. Hyperaldosteronism is a condition caused by the excess production of aldosterone. This hormone produced by the adrenal glands helps maintain normal blood pressure by allowing sodium to be reabsorbed by the kidneys

In France, according to the Ministerial Order of 24 June 2014 establishing the list of plants other than fungi authorised in food supplements, as well as the conditions of their use, the recommended daily serving of liquorice-based products must not lead to glycyrrhizin ingestion exceeding 100 mg and the labelling must include the statement "not to be used for more than six weeks without medical advice" along with a warning advising against use in children.

### A first French retrospective study

Considering all the calls and reports of serious poisonings received by poison control centres and the nutriviigilance scheme [4], ANSES conducted a retrospective study of poisoning cases occurring after liquorice consumption that were recorded by poison control centres between 2012 and 2021. During this ten-year period, 64 people presented with clinical or biological signs related to the consumption of liquorice-based beverages or foods. The median age was 55 years (range 10–77 years), and 53% of the poisonings concerned men.

The annual number of cases ranged from three to nine, with no significant variation over the period.

The products consumed were soft drinks such as non-alcoholic pastis, Antésite™ with liquorice, and liquorice syrup (50%), alcoholic beverages such as pastis (11%), confectionery containing liquorice (13%), confectionery made from pure liquorice extract (9%), herbal infusions (13%) and food supplements (5%).

Only two poisonings were reported in children, aged 10 and 12 years, and only after consumption of Antésite™ with liquorice. The first child had an allergic-type reaction within two hours of consumption, which resolved quickly after emergency treatment. The second child developed muscle pain, possibly reflecting hypokalaemia, within two weeks of beginning repeated consumption of the drink, but there was no follow-up information to document the outcome.

Most consumption among adults was chronic (for more than three months in 67% of cases). Most people (70%) reported use exceeding the maximum recommended intake, i.e. estimated consumption of more than 100 mg per day of glycyrrhizin. For chronic consumption, the presentation was typical, with symptoms of pseudohyperaldosteronism whose severity appeared to be correlated with the amount of glycyrrhizin ingested. With acute poisoning, rare cases of allergic-type reactions were observed.

### References

- [1] Di Lorenzo C, Ceschi A, Kupferschmidt H, Lüde S, De Souza Nascimento E, Dos Santos A, Colombo F, Frigerio G, Nørby K, Plumb J, Finglas P, Restani P. Adverse effects of plant food supplements and botanical preparations: a systematic review with critical evaluation of causality. *Br J Clin Pharmacol*. 2015 Apr;79(4):578-92.
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In 42.2% of poisoning cases, severity was high with life-threatening prognosis and one death was reported in a person with severe liver damage. Serious cases were observed with all types of products, except for liquorice syrup and food supplements, and were more common with beverages (pastis with or without alcohol, Antésite™ and large quantities of herbal infusions).

When the outcome was specified (57.8%), it was favourable in almost all cases (91.9%), often after hospital care and sometimes in an intensive care unit. Only one patient had sequelae, following a stroke complicating a hypertensive crisis.

How can liquorice poisoning be prevented?

Liquorice is found in many everyday products (food, cosmetics, medicines, tobacco products) in many forms: plant, liquorice extract, purified glycyrrhizin, solid or liquid.

The risk of toxicity depends on the product consumed (type and quantity) and the person exposed. Indeed, the body's reaction to glycyrrhizin varies greatly from person to person: absorption in the intestine, circulating glycyrrhizin levels, enzymatic activity.

Moreover, some medicines increase the risk of toxicity. This is the case with some diuretics causing a loss of potassium in urine, which is compounded by the glycyrrhizin.

Consumers cannot necessarily tell whether or not their consumption is excessive. The presence of liquorice is specified in the ingredients and/or in a statement, but the maximum recommended daily amount is not always given.

On the basis of current knowledge, it seems reasonable to propose daily consumption of no more than 10 mg/d of glycyrrhizin in the event of chronic consumption, taking care not to multiply the sources of intake through food, medication and tobacco products. Lastly, continuous consumption of products containing liquorice should be avoided.

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