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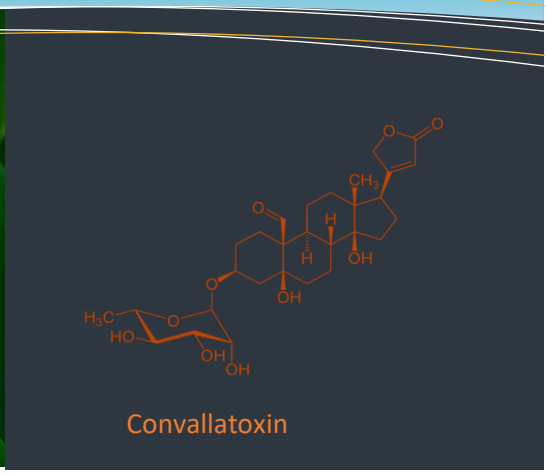
Poison of the month



Lily of the Valley was selected as Poison of the Month for May by the Working Group on Biogenic Toxins

…because *Convallaria majalis* is a clear example of the toxicological relevance of plant-derived natural products. The cardiac glycosides it contains are biogenic toxins with a well-defined molecular mode of action.

Chemistry of cardiac glycosides

Cardiac glycosides consist of a steroidal core structure, an unsaturated lactone ring, and a sugar moiety. The steroidal structure, the aglycone, is essential for binding to the sodium-potassium pump, whereas the sugar residues influence properties such as solubility, absorption, and duration of action.

Chemically, cardiac glycosides are mainly divided into cardenolides, which contain a five-membered lactone ring, and bufadienolides, which contain a six-membered lactone ring. Many well-known plant-derived cardiac glycosides are cardenolides, including digoxin and digitoxin from foxglove species, convallatoxin from lily of the valley, oleandrin from oleander, thevetin from yellow oleander, and ouabain from *Strophanthus* species.

Although they originate from different plant species, they all act by inhibiting the sodium-potassium pump in cardiac muscle cells.

Lily of the Valley: Between a Symbol of Spring and Cardiac Glycoside Toxicity

Lily of the valley is one of the best-known spring plants. Its white, bell-shaped flowers and intense fragrance make *Convallaria majalis* a symbol of the month of May. Many people are aware that lily of the valley is poisonous. Thanks to broad media coverage, many also know about the risk of confusing it with wild garlic. Less well known, however, is what the plant's toxicity is actually based on.

Lily of the valley contains a range of cardioactive steroid glycosides, particularly convallatoxin, as well as other cardenolides such as convalloside and convallamarin. It is therefore not merely a plant with unspecific irritant properties, but one containing pharmacologically highly active compounds with a clearly defined target organ: the heart.

The toxic effects of cardiac glycosides are primarily based on inhibition of the sodium-potassium pump in the cell membrane of cardiac muscle cells. This alters transmembrane ion gradients, indirectly leading to increased intracellular calcium availability. Since calcium is essential for cardiac muscle contraction, this increases the force of contraction. In toxic exposure, however, the electrophysiological stability of the heart is impaired. Possible consequences include bradycardia, conduction disturbances, and cardiac arrhythmias.

After oral ingestion, gastrointestinal symptoms often occur first. Typical symptoms include nausea, vomiting, abdominal pain, and diarrhoea. These symptoms may be partly caused by the saponins contained in the plant and by local irritation of the mucous membranes and, at the same time, they may limit further absorption. However, this should not be interpreted as an all-clear, as relevant amounts of cardiac glycosides can trigger cardiac effects, particularly in susceptible individuals.

It is difficult to define a universally valid toxic dose level for lily of the valley. The risk depends on the amount ingested, the plant part involved, the form of preparation, body weight, pre-existing cardiovascular disease, electrolyte disturbances, and concomitant medication.

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Controlled use of cardiac glycosides

Cardiac glycosides are among the oldest pharmacologically used natural products with effects on the heart. The use of foxglove (*Digitalis purpurea*) was particularly influential.
The English physician William Withering described the use of foxglove for treating “dropsy”, a term historically used for fluid accumulation, which can occur, among other conditions, in heart failure. Withering recognized that the effect was not merely an unspecific diuretic action, but was substantially related to an effect on the heart.
From this historical form of plant-based medicine, defined drugs such as digoxin and digitoxin were later developed. They inhibit the sodium-potassium pump in cardiac muscle cells, indirectly increase intracellular calcium availability, and thereby exert a positive inotropic effect, meaning that they increase the contractile force of the heart. In addition, they influence conduction at the atrioventricular node. For this reason, they have been used medically in certain forms of heart failure and for rate control in atrial fibrillation.

Children are a particularly vulnerable group, as their lower body weight means that markedly smaller amounts may already cause signs of poisoning. Older people, individuals with cardiac arrhythmias, and patients receiving digitalis, diuretics, or antiarrhythmic drugs may also be more sensitive.

Severe courses are rare after low-level accidental exposure. However, persistent vomiting, dizziness, palpitations, or an unusually slow pulse may indicate relevant ingestion of cardioactive glycosides and should prompt medical evaluation.

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By Ute Haßmann

Literature and links:

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