

# Grayanotoxin

**NIH/PubMed****1. Name of Toxin:**

Grayanotoxin (formerly known as andromedotoxin, acetylandromedol, and rhodotoxin)

**2. Name of Acute Disease:**

Honey Intoxication

Honey intoxication is caused by the consumption of honey produced from the nectar of rhododendrons. The grayanotoxins cause the intoxication. The specific grayanotoxins vary with the plant species. These compounds are diterpenes, polyhydroxylated cyclic hydrocarbons that do not contain nitrogen. Other names associated with the disease is rhododendron poisoning, mad honey intoxication or grayanotoxin poisoning.

**3. Nature of Disease:**

The intoxication is rarely fatal and generally lasts for no more than 24 hours. Generally the disease induces dizziness, weakness, excessive perspiration, nausea, and vomiting shortly after the toxic honey is ingested. Other symptoms that can occur are low blood pressure or shock, bradyarrhythmia (slowness of the heart beat associated with an irregularity in the heart rhythm), sinus bradycardia (a slow sinus rhythm, with a heart rate less than 60), nodal rhythm (pertaining to a node, particularly the atrioventricular node), Wolff-Parkinson-White syndrome (anomalous atrioventricular excitation) and complete atrioventricular block.

**4. Normal Course of the Disease:**

The grayanotoxins bind to [sodium channels](#) in cell membranes. The binding unit is the group II receptor site, localized on a region of the sodium channel that is involved in the voltage-dependent activation and inactivation. These compounds prevent inactivation; thus, excitable cells (nerve and muscle) are maintained in a state of depolarization, during which entry of calcium into the cells may be facilitated. This action is similar to that exerted by the alkaloids of veratrum and aconite. All of the observed responses of skeletal and heart muscles, nerves,

and the central nervous system are related to the membrane effects.

Because the intoxication is rarely fatal and recovery generally occurs within 24 hours, intervention may not be required. Severe low blood pressure usually responds to the administration of fluids and correction of bradycardia; therapy with vasopressors (agents that stimulate contraction of the muscular tissue of the capillaries and arteries) is only rarely required. Sinus bradycardia and conduction defects usually respond to [atropine](#) therapy; however, in at least one instance the use of a temporary pacemaker was required.

### 5. Diagnosis of Human Illness:

In humans, symptoms of poisoning occur after a dose-dependent latent period of a few minutes to two or more hours and include salivation, vomiting, and both circumoral (around or near the mouth) and extremity paresthesia (abnormal sensations). Pronounced low blood pressure and sinus bradycardia develop. In severe intoxication, loss of coordination and progressive muscular weakness result. Extrasystoles (a premature contraction of the heart that is independent of the normal rhythm and arises in response to an impulse in some part of the heart other than the [sinoatrial node](#); called also premature beat) and ventricular tachycardia (an abnormally rapid ventricular rhythm with aberrant ventricular excitation, usually in excess of 150 per minute) with both atrioventricular and intraventricular conduction disturbances also may occur. [Convulsions](#) are reported occasionally.

### 6. Associated Foods:

Grayanotoxin poisoning most commonly results from the ingestion of grayanotoxin-contaminated honey, although it may result from the ingestion of the leaves, flowers, and nectar of rhododendrons. Not all rhododendrons produce grayanotoxins. *Rhododendron ponticum* grows extensively on the mountains of the eastern Black Sea area of Turkey. This species has been associated with honey poisoning since 401 BC. A number of toxin species are native to the United States. Of particular importance are the western azalea (*Rhododendron occidentale*) found from Oregon to southern California, the California rosebay (*Rhododendron macrophyllum*) found from British Columbia to central California, and *Rhododendron albiflorum* found from British Columbia to Oregon and in Colorado. In the eastern

half of the United States grayanotoxin-contaminated honey may be derived from other members of the botanical family Ericaceae, to which rhododendrons belong. Mountain laurel (*Kalmia latifolia*) and sheep laurel (*Kalmia angustifolia*) are probably the most important sources of the toxin.

**7. Relative Frequency of Disease:**

Grayanotoxin poisoning in humans is rare. However, cases of honey intoxication should be anticipated everywhere. Some may be ascribed to a increase consumption of imported honey. Others may result from the ingestion of unprocessed honey with the increased desire of natural foods in the American diet.

**8. Target Population:**

All people are believed to be susceptible to honey intoxication. The increased desire of the American public for natural (unprocessed) foods, may result in more cases of grayanotoxin poisoning. Individuals who obtain honey from farmers who may have only a few hives are at increased risk. The pooling of massive quantities of honey during commercial processing generally dilutes any toxic substance.

**9. Analysis in Foods:**

The grayanotoxins can be isolated from the suspect commodity by typical extraction procedures for naturally occurring terpenes. The toxins are identified by thin layer chromatography.

**10. Selected Outbreaks:**

Several cases of grayanotoxin poisonings in humans have been documented in the 1980s. These reports come from Turkey and Austria. The Austrian case resulted from the consumption of honey that was brought back from a visit to Turkey. From 1984 to 1986, 16 patients were treated for honey intoxication in Turkey. The symptoms started approximately 1 h after 50 g of honey was consumed. In an average of 24 h, all of the patients recovered. The case in Austria resulted in cardiac arrhythmia, which required a temporal pacemaker to prevent further decrease in heart rate. After a few hours, pacemaker simulation was no longer needed. The Austrian case shows that with increased travel throughout the world, the risk of grayanotoxin poisoning is possible outside the areas of Ericaceae-dominated vegetation, namely, Turkey, Japan, Brazil, United States, Nepal, and British Columbia. In 1983 several British veterinarians reported a incident of grayanotoxin poisoning in goats. One of the four animals

died. Post-mortem examination showed grayanotoxin in the rumen contents.

**For more information on recent outbreaks see the [Morbidity and Mortality Weekly Reports](#) from CDC.**

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