PROOF
REVIEW PAPER

Grayanotoxins in Mad Honey: Sources, Chemistry, and Toxicological Effects

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Abstract

Grayanotoxins (GTXs) are found in honey produced by honey bees from the nectar and pollen of *Rhododendron* species, which are prevalent in the Black Sea region of Türkiye. This type of honey has been reported not only in Türkiye but also in Nepal, North America, and some regions of Europe. Poisoning caused by these honeys, commonly referred to as "mad honey," has been documented since 401 BC. Although multiple isomers of GTXs have been identified in honey, GTX I, GTX III and, to a lesser extent, GTX II are primarily responsible for human poisoning. GTXs bind to voltage-gated sodium channels, preventing inactivation and causing prolonged depolarization in cells. This effect is especially pronounced on the cardiovascular system, leading to hypotension, bradycardia, and various arrhythmias. The severity of poisoning depends more on the concentration of GTX in the honey and individual susceptibility than on the amount consumed. Additionally, GTXs can exhibit dose-dependent hepatotoxic, nephrotoxic, and reproductive toxic effects. In conclusion, mad honey poses serious toxic risks to vital organs, particularly the cardiovascular system, due to its GTX content. Therefore, a better understanding of toxic mechanisms, development of regulatory systems, and public awareness are essential.

Introduction

Mad honey is a natural product with toxic properties, derived from the nectar and pollen of plant species belonging to the genus *Rhododendron*, a member of the *Ericaceae* family (Jansen et al., 2012). It is colloquially known as "mad honey" or "bitter honey." Due to the natural distribution of *Rhododendron* species in the Black Sea region of Türkiye, mad honey is extensively produced in this area (Babayiğit et al., 2013; Fatrcová-Šramková & Kačániová, 2020).

Throughout history, mad honey has been consumed both as a foodstuff and for alternative therapeutic purposes. It is traditionally used by the local population as an alternative treatment for conditions such as hypertension, sexual dysfunction, and gastrointestinal disorders (Gündüz et al., 2011). However, the consumption of mad honey can lead to severe poisoning due to the presence of grayanotoxins (GTXs). These toxins are incorporated into the honey when honey bees gather nectar and pollen specifically from *Rhododendron* plants (Haksoy et al., 2020). The historical roots of mad honey poisoning in the region date back to ancient times, with the first case documented in 401 BC. Nevertheless, poisoning cases continue to occur today (Jansen et al., 2012; Lampe, 1988).

The pharmacological effects of these toxins arise from the ability of GTXs to increase the permeability of sodium channels in cell membranes. This interaction prevents the repolarization of nerve cells, leading to prolonged depolarization, which consequently results in cardiovascular symptoms such as hypotension and bradycardia (Turner, 2023; Yang et al., 2022).

The structural similarities among GTXs and the variations in their concentrations across different plant species broaden the clinical spectrum of poisoning cases, creating challenges in diagnosis and treatment (DiSalvo et al., 2022). Therefore, a detailed understanding of the pharmacological and toxicological

properties of honey containing GTX is of paramount importance for public health (Alemdar, 2013). The aim of this review is to comprehensively evaluate the toxicological profile of GTXs based on the available literature, encompassing their botanical sources, historical background, and chemical characteristics. In addition, this review synthesizes recent regulatory developments, including the EFSA risk assessment, together with experimental evidence published up to 2026. The literature included in this review was identified through searches of PubMed, Scopus, Web of Science, and Google Scholar using appropriate keywords relevant to the scope of the review.

Natural Sources of Grayanotoxins

GTXs are toxic diterpenoid compounds that are mainly present in plants belonging to the *Ericaceae* family. These compounds are commonly synthesized in the nectar, pollen, flowers, and leaves of the *Rhododendron* genus, which contains over 1000 species worldwide (Dağ & Özkan, 2025; Gündüz et al., 2011). Honey produced by bees collecting substances from these plants results in the final product known as "mad honey," which can cause poisoning in humans (Silici, 2019).

Botanical Sources and Geographical Distribution

Rhododendron species have a broad distribution, covering much of the Northern Hemisphere. These plants grow naturally not only in Türkiye but also in regions such as Nepal, Japan, Brazil, Europe, and North America (Yan et al., 2021). In Türkiye, five main species of this genus (*R. ponticum, R. luteum, R. smirnovii, R. ungernii, and R. caucasicum*) are distributed, particularly concentrated in coastal forests from the Western to the Eastern Black Sea (Figure 1). Chemical analyses have identified 208 different compounds in the *Rhododendron* genus, most of which are diterpenoids (Mayda et al., 2018; Silici, 2019).

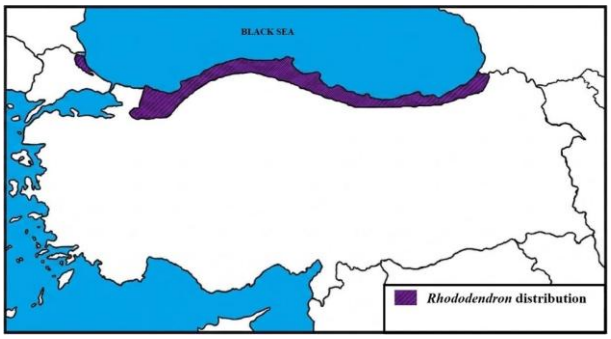

Figure 1. The distribution of *Rhododendron* species in Türkiye

The species most associated with poisoning cases are *R. ponticum* and *R. luteum*. These species contain high concentrations of GTX and are the main botanical sources of the honey involved in poisoning cases. *R. ponticum*, known locally as "ağu" or "komar," is a purple-flowered species (Figure 2). In literature, it is also referred to as "black poison" (Gündüz et al., 2007). Meanwhile, the yellow-flowered *R. luteum* species is known as "sarı ağu" and similarly contains GTX compounds (Bilir et al., 2018). The type and amount of GTX found in the pollen and nectar of these species vary significantly according to plant species and geographical region. During the blooming period of *Rhododendron*, fresh honey contains a higher concentration of GTXs (Gündüz et al., 2011). This variation directly affects the toxicity level of the honey and plays a decisive role in the severity of poisoning incidents (Dursun et al., 2025).

Figure 2. Native *Rhododendron ponticum* in the Black Sea region

Outside of Türkiye, honeys produced from *Rhododendron* nectar in the high-altitude areas of Nepal are also consumed, particularly for recreational or traditional medicinal purposes (Dağ & Özkan, 2025; Gündüz et al., 2007). Furthermore, honeys produced from the *Kalmia latifolia* plant in North America have been reported to contain GTX I and GTX III. Additionally, honey produced from the *Agarista salicifolia* plant on France's Réunion Island also contains GTX (Jansen et al., 2012). This geographical and botanical diversity complicates the distribution of GTXs in honeys and thus the epidemiology of mad honey intoxications (Aryal, 2025; Dursun et al., 2025).

Properties and Historical Background of Mad Honey

Records of the effects of mad honey exist from ancient times to the present. Mad honey has a long history, particularly in the Anatolian and Black Sea regions. In these areas, it has been used in traditional medicine for treating certain ailments, but its uncontrolled consumption has also led to severe intoxications (Sarsmaz et al., 2024).

The earliest records of the toxic effects of mad honey date back to 401 BC. The Athenian historian Xenophon reported that ten thousand soldiers encamped near Trabzon exhibited loss of consciousness, vomiting, and various symptoms of poisoning after consuming local honeys (Gündüz et al., 2011; Eroğlu et al., 2013; Yan et al., 2021). According to Xenophon's Anabasis, during a military campaign against the Persian Empire, soldiers experienced severe gastrointestinal symptoms, loss of balance, excessive intoxication, and neurological disorders after consuming honeycombs along the Black Sea coast. Some soldiers displayed delirium-like conditions and even fell into seemingly fatal collapse; those who consumed a small amount showed signs of intoxication, while those who consumed more collapsed, developing severe clinical pictures (Gündüz et al., 2008; Jansen et al., 2012; Turner, 2023). However, symptoms were temporary, with reports indicating that the soldiers began to recover the next day, fully recovering by the third or fourth day (Daugherty, 2005; Gündüz et al., 2008). This historical record demonstrates that the toxic effects of honey containing GTXs have been known for millennia and that the Black Sea region is an endemic focus for such intoxications (Gündüz et al., 2011). Similarly, the poisoning of Roman troops under Pompey by poisonous honeys strategically placed by the Heptakometes tribe in the Black Sea region in 69 BC suggests that honey containing GTX was used as a kind of chemical weapon in early times (Hanson, 2016).

Today, mad honey continues to be used as a traditional remedy in the treatment of conditions such as hypertension, stomach pain, digestive disorders, and sexual dysfunction (Mayda et al., 2018; Yan et al., 2021). Consequently, serious poisonings originating from GTX occur, with reports of emergency department visits in the Black Sea region (Akça & Kahveci, 2012; Gündüz et al., 2006; Ullah et al., 2018). Some studies have reported the average amount of mad honey causing poisoning to be between 5 and 30 grams (Gündüz et al., 2008). However, analyses have shown no direct correlation between the amount of honey consumed and the severity of clinical symptoms; the severity of poisoning depends more on the GTX concentration in the honey and individual susceptibility than on the quantity of honey consumed (Fatrcová-Šramková & Kačániová, 2020; Tekinsoy et al., 2017).

Mad honey, due to the toxins it contains, possesses a sharp and bitter taste. Its color can range from light yellow to brown, and its viscosity can vary widely depending on its botanical source (Mayda et al., 2018; Silici, 2019). This physicochemical diversity presents additional challenges in quality control and toxicity assessments while the variation of GTX content concerning seasonal, geographical, and botanical factors makes risk analysis critical. The primary factor complicating the management of this risk is the structural stability of the toxins. There is no scientific evidence in the literature indicating that heating reduces toxin levels in mad honey. Moreover, it has been reported that toxin concentrations remain unchanged even after storage at room temperature for 12 months (EFSA Panel on Contaminants in the Food Chain [CONTAM] et al., 2023).

In addition to its toxic GTX content, mad honey is rich in phenolic compounds, which possess certain levels of antioxidant activity (Kurtdede & Baran, 2021; Şahin et al., 2017; Silici et al., 2014). A study on mad honey reported that coumaric acid derivatives were the major components, with gallic acid and ferulic acid identified as common phenolic components in all samples (Silici et al., 2014). In another study, qualitative and quantitative analyses of 17 different phenolic compounds from mad honey samples were performed. According to the results of this study, p-OH benzoic acid was identified as the major component in all honey samples. Furthermore, some samples were found to contain other phenolic compounds such as p-coumaric and caffeic acid at high concentrations. The presence of phenolic compounds indicates that mad honey is rich not only in toxic GTX content but also in secondary metabolites that might have antioxidant and other biological activities (Şahin et al., 2017). This can play an important role in determining the overall pharmacological profile and potential health effects of the honey. In this regard, it is crucial to thoroughly investigate the effects of phenolic components in mad honey on health, along with carefully evaluating toxicological risks (Ciulu et al., 2016; Ruško et al., 2021).

Chemical Structure of Grayanotoxins

GTXs, also known as andromedotoxins, are classified as nitrogen-free, polyhydroxylated cyclic hydrocarbons with a tetracyclic diterpene structure (Gündüz et al., 2008, 2011). The basic skeleton of these compounds is composed of carbon, hydrogen, and oxygen atoms and is characterized by specific formulas like their chemical structures (Jansen et al., 2012; Silici, 2019). Structurally, these toxins are observed to consist of various hydroxyl and acetate groups located on a "grayan" skeleton with a 5/7/6/5 ring system (Gündüz et al., 2011; Yan et al., 2021). These structural variations lead to the formation of different subtypes of GTXs. The chemical structures of GTX I, II, and III are shown in Figure 3 (Gündüz et al., 2011).

To date, dozens of GTX isomers have been identified, but there are three main forms primarily responsible for "mad honey" poisonings observed in humans (Gündüz et al., 2007; Jansen et al., 2012). These are known as GTX I, GTX III, and to a lesser extent, GTX II (Gündüz et al., 2008). The fundamental structural differences between these isomers are based on the hydroxylation positions on the molecular skeleton and the presence of acetate groups, and these variations affect the pharmacokinetic and pharmacodynamic properties of the toxins. Especially GTX I is the most frequently encountered and primarily responsible for cardiac effects in human poisonings (Aryal, 2025; DiSalvo et al., 2022). Sensitive analytical methods like LC-MS/MS and UHPLC-Orbitrap-HRMS are used to

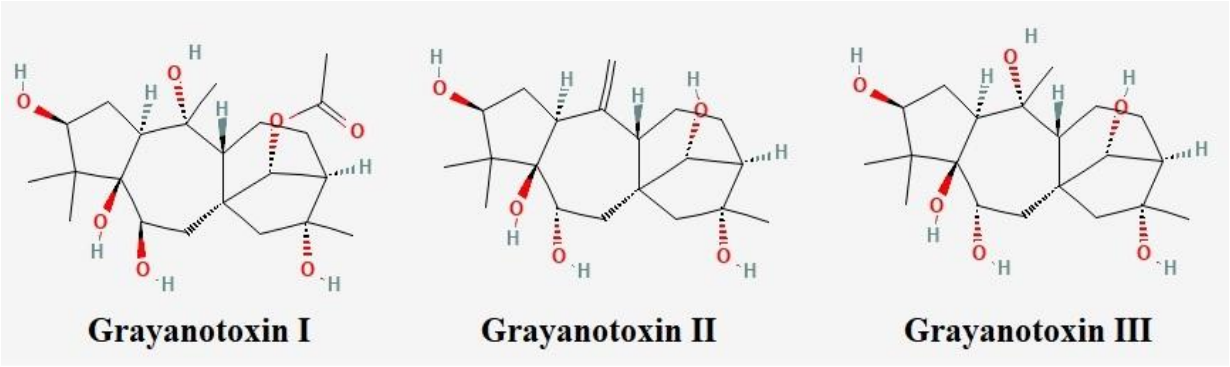

Figure 3. Chemical structure of GTX I, II, and III (Source: NCBI PubChem, 2026).

determine the GTX levels in mad honey samples (Dursun et al., 2025). These methods play a critical role in determining the potential toxicity level of honey, particularly allowing for the quantitative analysis of known forms such as GTX I, II, and III (Abashidze et al., 2024; Dönmez & Kaya, 2020).

Toxicological Effects of Grayanotoxins

GTXs bind to voltage-gated sodium channels, preventing their inactivation and leading to prolonged depolarization by allowing continuous sodium influx into the cell membrane (Haksoy et al., 2020; Ullah et al., 2018). As a result of this ionic imbalance, the spontaneous firing rate of pacemaker cells decreases, and myocardial contractility is suppressed (Adhikari & Bhandari, 2021). Various cardiovascular and electrophysiological disorders, such as bradycardia, hypotension, and atrioventricular block, may develop due to the impact on the cardiac conduction system (Çağlı et al., 2009; Thapa et al., 2024). The sequential molecular, cellular, and clinical events underlying GTX toxicity are summarized in Table 1.

Differences in toxicity have been reported among GTX isomers. Although GTX II is generally considered less toxic than GTX I and III, the precise structural and molecular mechanisms responsible for these differences in toxicity have not yet been fully elucidated. Some studies suggest that the toxicity ranking of grayanotoxins follows the order GTX III > GTX I > GTX II (Ullah et al., 2018; Silici, 2019).

At low doses, GTXs can cause mild symptoms such as dizziness, vomiting, sweating, nausea, paresthesia, blurred vision, hypotension, and bradycardia, whereas at high doses, life-threatening conditions such as loss of consciousness and severe cardiac arrhythmias may occur (Dursun et al., 2025). In a systematic review involving 1199 cases, no deaths were reported related to mad honey poisonings (Ullah et al., 2018; Silici, 2019). However, mad honey poisoning can have serious consequences in elderly patients or individuals with cardiac conditions. This emphasizes the critical significance of the dose in GTX-induced toxicity and the influence of individual sensitivity factors in shaping the clinical picture (Yaylacı et al., 2015).

Toxicology studies investigating the toxic effects of GTXs on the kidneys, liver, and reproductive organs, in addition to their neurological effects, have revealed dose-dependent hepatotoxicity, nephrotoxicity, and reproductive damage. For example, congestion,

Table 1. Sequential molecular, cellular, and clinical events underlying GTX toxicity

Molecular event	Cellular consequence	Clinical consequence
GTXs bind to voltage-gated sodium channels	The channel is stabilized in the open conformation	Initiation of toxic effects
Channel inactivation is inhibited	Persistent Na^+ influx into the cell occurs	Sustained membrane depolarization develops
Membrane repolarization is impaired	Normal action potential generation and impulse conduction are disrupted	Dysfunction of excitable tissues, particularly neuronal and muscular cells, occurs
Stimulation of vagal afferent pathways	Vagal tone is increased and cardiac impulse conduction is slowed	Bradycardia, atrioventricular block, hypotension, syncope, and dizziness develop

steatosis, and inflammatory cell infiltration were observed in the liver after intraperitoneal injection of GTX III in rats (Haksoy et al., 2020; Kükner et al., 2016), while increases in blood urea nitrogen and creatinine levels and minimal tubular changes were reported in the kidneys (CONTAM et al., 2023; Silici et al., 2015), and decreased seminiferous tubule diameter, increased apoptosis, and hormonal imbalances were identified in the testes (Doğanyiğit et al., 2019). These findings demonstrate that GTXs exhibit broad-spectrum toxic effects not only on the cardiovascular and neurological systems but also on vital organs and that these effects vary according to the dose and duration of exposure (Fatrcová-Šramková & Kačániová, 2020).

Research conducted on laboratory animals reveals the effects of GTX I and GTX III isomers on physiological systems within certain dose ranges. In a study with GTX III, it was found that an intravenous dose of 5 µg/kg administered to rats did not cause toxic effects; however, doses of 50 µg/kg and above were fatal due to cardiac arrest within the first 10 minutes after administration (Yılmaz et al., 2017). In research concerning the GTX I isomer, proteinuria and hematuria were observed in the urine starting from a dose of 0.25 mg/kg. At a dose of 1 mg/kg, in addition to kidney effects, significant liver damage was also observed (Aşçıoğlu et al., 2000). Furthermore, GTX I and GTX III isomers were detectable in human blood and urine following mad honey poisoning. In a study reviewing the data of twenty-five patients, levels of 4.82 ng/mL GTX I and 6.56 ng/mL GTX III were reported in the blood, while levels of 0.036 µg/mL GTX I and 0.391 µg/mL GTX III were reported in the urine (Aygün et al., 2018).

Given the toxic effects of GTXs, advanced research is needed to elucidate the long-term outcomes of chronic exposure. The 0.05 mg/kg upper limit value set by the European Food Safety Authority (EFSA) for the sum of GTX I and GTX III found in *Rhododendron*-derived mad honey aims to provide at least 75% protection across all age groups based on the acute reference dose. However, it is noted that this value may be insufficient for individuals with heart disease or those undergoing anti-ischemic/antihypertensive treatment (CONTAM et al., 2023).

Conclusion

For centuries, mad honey has been consumed as a traditional food and therapeutic substance in specific regions, especially in the Black Sea area. However, the GTXs present in this product pose significant toxicological risks to human health, as they can induce severe and potentially life-threatening clinical manifestations, particularly affecting the cardiovascular system (Babayiğit et al., 2013; Hossain & Kharel, 2025). This underscores how critical it is for public health to regularly monitor mad honey consumption and the levels of GTXs in honeys. Studies have shown that these toxins can lead to significant histological damage in vital tissues like the liver over time (Haksoy et al., 2020).

The molecular mechanisms of action, bioavailability, and elimination pathways of GTXs from the body should be investigated more deeply. The recent report prepared by EFSA emphasizes that the genotoxic effects of these toxins and the lack of data on chronic exposure obscure the risks of long-term low-dose consumption. Filling these data gaps will allow for the development of more reliable risk assessment methodologies. Additionally, it is crucial to thoroughly examine the GTX concentrations in *Rhododendron* species in the Black Sea region and the effects of environmental factors on GTX production.

In conclusion, to prevent mad honey intoxications, comprehensive control mechanisms should be established at the national level, and the GTX levels in marketed products should be meticulously monitored. In this regard, it is of great importance to develop and standardize rapid and reliable analysis methods for distinguishing honeys containing GTX. Furthermore, limits for GTXs should be established in the Turkish Food Codex Honey Communiqué. Moreover, it is vital to inform consumers about the use of this product based on scientific data.

Ethical Statement

There are no ethical issues with the publication of this article.

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Conflict of Interest

The author declares that there is no conflict of interest.

Author Contributions

The author was responsible for the conceptualization, methodology, data curation, formal analysis, investigation, and writing.

References

Abashidze, N., Djafaridze, I., Vanidze, M., Khakhutaishvili, M., Kharadze, M., Kartsivadze, I., Davitadze, R., & Kalandia, A. (2024). Physicochemical characterization and antioxidant activity of Jara honey produced in Western Georgia. *Applied Sciences,* 14(16), 6874. https://doi.org/10.3390/app14166874

Adhikari, S., & Bhandari, A. (2021). Wild honey poisoning: A case report from remote mountains. *Global Journal of Medical Research,* 21(5), 33-35. https://doi.org/10.34257/gjmrkvol21is5pg33

Akça, A. S. D., & Kahveci, F. O. (2012). An indispensable toxin known for 2500 years: Victims of mad honey. *Turkish Journal of Medical Sciences,* 42(4), 718-723. https://doi.org/10.3906/sag-1109-41

Alemdar, R. (2013). ST elevasyonu ile acile başvuran sıradışı bir deli bal zehirlenme olgusu. *Konuralp Tıp Dergisi, 5*(2), 51-54. https://izlik.org/JA36KG99SG

Aryal, M. (2025). Grayanotoxins in mad honey: Mechanisms of toxicity, clinical management, and therapeutic implications. *Journal of Applied Toxicology,* 45(11), 2240-2255. https://doi.org/10.1002/jat.4855

Aşçıoğlu, M., Özesmi, Ç., Doğan, P., & Öztürk, F. (2000). Effects of acute grayanotoxin-I administration on hepatic and renal functions in rats. *Turkish Journal of Medical Sciences*, 30(1), 23-28.

Aygün, A., Sahin, A., Karaca, Y., Turkmen, S., Turedi, S., Ahn, S. Y., Lermer, R., & Gunduz, A. (2018). Grayanotoxin levels in blood, urine and honey and their association with clinical status in patients with mad honey intoxication. *Turkish Journal of Emergency Medicine*, 18(1), 29-33. https://doi.org/10.1016/j.tjem.2017.05.001

Babayiğit, M., Tutal, Z. B., Güleç, H., Kütük, S., Şahap, M., & Horasanlı, E. (2013). Wild honey intoxication: Case report. *Gaziosmanpaşa Üniversitesi Tıp Fakültesi Dergisi,* 5(3), 183-190.

Bilir, E. K., Tutun, H., Sevin, S., Kısmalı, G., & Yarsan, E. (2018). *Rhododendron ponticum* L. extract'ın prostat karsinomu ve adenokarsinoma hücre hatları (DU145, PC3) üzerindeki sitotoksik etkileri. *Kafkas Üniversitesi Veteriner Fakültesi Dergisi,* 24(2), 241-247. https://doi.org/10.9775/kvfd.2017.19219

Çağlı, K., Tüfekçioğlu, O., Şen, N., Aras, D., Topaloğlu, S., Basar, N., & Pehlivan, S. (2009). Atrioventricular block induced by mad-honey intoxication: Confirmation of diagnosis by pollen analysis. *Texas Heart Institute Journal,* 36(4), 342-344.

Ciulu, M., Spano, N., Pilo, M. I., & Sanna, G. (2016). Recent advances in the analysis of phenolic compounds in unifloral honeys. *Molecules,* 21(4), 451. https://doi.org/10.3390/molecules21040451

Dağ, Ş. R. O., & Özkan, A. M. G. (2025). *Rhododendron* spp. (Ericaceae). In *Poison or remedy? Case reports on selected plants* (pp. 141-160). Bentham Science Publishers. https://doi.org/10.2174/9789815274318125010014

Daugherty, C. (2005). Toxic honey and the march up-country. *Journal of Medical Biography,* 13(2), 104-106. https://doi.org/10.1177/096777200501300210

DiSalvo, P., Khorolsky, C., Filigenzi, M. S., Poppenga, R. H., & Hoffman, R. S. (2022). Confirmed grayanotoxin poisoning with bradycardia from a gift of imported honey. *The Journal of Emergency Medicine,* 63(2), 260-263. https://doi.org/10.1016/j.jemermed.2022.05.009

Doğanyiğit, Z., Silici, S., Demirtaş, A., Kaya, E., & Kaymak, E. (2019). Determination of histological, immunohistochemical and biochemical effects of acute and chronic grayanotoxin III administration in different doses in rats. *Environmental Science and Pollution Research,* 26(2), 1323-1331. https://doi.org/10.1007/s11356-018-3700-9

Dönmez, M., & Kaya, E. (2020). Separating mad honey from other honeys with grayanotoxin analysis in LC-MS/MS. *International Journal of Traditional and Complementary Medicine Research,* 1(2), 86-94.

Dursun, İ., Kanbur, E. D., Kara, Y., & Kolaylı, S. (2025). Determination of grayanotoxin-III amount in the *Rhododendron* honey and flowers samples using UHPLC-Orbitrap®-HRMS. *Toxicon,* 257, 108294. https://doi.org/10.1016/j.toxicon.2025.108294

EFSA Panel on Contaminants in the Food Chain (CONTAM), Schrenk, D., Bignami, M., Bodin, L., Chipman, J. K., del Mazo, J., Grasl-Kraupp, B., Hogstrand, C., Hoogenboom, L., Leblanc, J., Nebbia, C. S., Nielsen, E., Ntzani, E., Petersen, A., Sand, S., Vleminckx, C., & Wallace, H. (2023). Risks for human health related to the presence of grayanotoxins in certain honey. *EFSA Journal,* 21(3), e07866. https://doi.org/10.2903/j.efsa.2023.7866

Eroğlu, S. E., Urgan, O., Onur, Ö., Denizbaşı, A., & Akoğlu, H. (2013). Grayanotoxin (mad honey) - ongoing consumption after poisoning. *Balkan Medical Journal,* 30(3), 293-295. https://doi.org/10.5152/balkanmedj.2013.8100

Fatrcová-Šramková, K., & Kačániová, M. (2020). Selected toxicological aspects of honey. *Archives of Ecotoxicology, 2*(4), 95-99. https://doi.org/10.36547/ae.2020.2.4.95-99

Gündüz, A., Durmuş, İ., Türedi, S., Nuhoğlu, İ., & Öztürk, S. (2007). Mad honey poisoning-related asystole. *Emergency Medicine Journal,* 24(8), 592-593. https://doi.org/10.1136/emj.2006.045625

Gündüz, A., Tatlı, Ö., & Türedi, S. (2008). Geçmişten günümüze deli bal zehirlenmesi. *Türkiye Acil Tıp Dergisi,* 8(1), 46-54.

Gündüz, A., Türedi, S., & Ayaz, F. A. (2011). The poisonous content of "mad honey": Grayanotoxin. *Journal of Academic Emergency Medicine,* 10(2), 95-97. https://doi.org/10.5152/jaem.2011.018

Gündüz, A., Türedi, S., Uzun, H., & Topbaş, M. (2006). Mad honey poisoning. *The American Journal of Emergency Medicine,* 24(5), 595-598. https://doi.org/10.1016/j.ajem.2006.01.022

Haksoy, H., Çakmak-Arslan, G., Rasgele, P. G., & Kekeçoğlu, M. (2020). Deli bal ve grayanotoksin'in karaciğer dokusu üzerindeki etkilerinin zamana bağlı araştırılması. *Konuralp Tıp Dergisi,* 12(1), 97-104. https://doi.org/10.18521/ktd.598739

Hanson, J. R. (2016). From 'mad honey' to hypotensive agents, the grayanoid diterpenes. *Science Progress,* 99(3), 327-336. https://doi.org/10.3184/003685016x14720691270831

Hossain, M. F., & Kharel, M. (2025). Mad honey poisoning in Nepal: A case report. *Clinical Case Reports,* 13(1), e70069. https://doi.org/10.1002/ccr3.70069

Jansen, S. A., Kleerekooper, I., Hofman, Z. L. M., Kappen, I. F. P. M., Stary-Weinzinger, A., & van der Heyden, M. A. G. (2012). Grayanotoxin poisoning: 'Mad honey disease' and beyond. *Cardiovascular Toxicology,* 12(3), 208-215. https://doi.org/10.1007/s12012-012-9162-2

Kükner, A., İlter, G., Söyler, G., Rasgele, P. G., Kekeçoğlu, M., & Acar, M. K. (2016). The effect of *Rhododendron* honey on mice liver tissue. *International Journal of Morphology,* 34(3), 842-847. https://doi.org/10.4067/s0717-95022016000300004

Kurtdede, E., & Baran, B. (2021). Evaluation of the antioxidant potential of the mad honey collected from the Black Sea region in Turkey. *Journal of Advances in VetBio Science and Techniques,* 6(3), 243-250. https://doi.org/10.31797/vetbio.960851

Lampe, K. F. (1988). *Rhododendrons*, mountain laurel, and mad honey. *JAMA,* 259(13), 2009. https://doi.org/10.1001/jama.1988.03720130073034

Mayda, N., Özkök, A., & Sorkun, K. (2018). Some characteristic properties of chestnut and *Rhododendron* honeys in Turkey. *Hacettepe Journal of Biology and Chemistry, 46*(1), 135-144. https://doi.org/10.15671/hjbc.2018.223

National Center for Biotechnology Information. (2026). PubChem: Grayanotoxin I (CID 119041), Grayanotoxin II (CID 114828), Grayanotoxin III (CID 119541). Retrieved April 26, 2026, from https://pubchem.ncbi.nlm.nih.gov/

Ruško, J., Vainovska, P., Vilne, B., & Bartkevičs, V. (2021). Phenolic profiles of raw mono- and polyfloral honeys from Latvia. *Journal of Food Composition and Analysis, 98*, 103813. https://doi.org/10.1016/j.jfca.2021.103813

Sarsmaz, H. Y., Gürgen, S. G., Cansu, A., Türkmen, S., & Gündüz, A. (2024). The relationship between oxidative stress and apoptosis of histopathological changes in the ovary made by mad honey containing grayanotoxin. *Food and Chemical Toxicology,* 187, 114634. https://doi.org/10.1016/j.fct.2024.114634

Silici, S. (2019). Orman gülü balı (deli bal) toksikasyonu: Orman gülü balı toksikasyonu. *Türk Bilimsel Derlemeler Dergisi,* 12(2), 35-44.

Silici, S., Doğan, Z., Şahin, H., Atayoğlu, A. T., & Yakan, B. (2015). Acute effects of grayanotoxin in *Rhododendron* honey on kidney functions in rats. *Environmental Science and Pollution Research,* 23(4), 3300-3307. https://doi.org/10.1007/s11356-015-5534-z

Silici, S., Sarıoğlu, K., Doğan, M., & Karaman, K. (2014). HPLC-DAD analysis to identify the phenolic profile of *Rhododendron* honeys collected from different regions in Turkey. *International Journal of Food Properties,* 17(5), 1126-1134. https://doi.org/10.1080/10942912.2012.698441

Şahin, H., Can, Z., & Kolaylı, S. (2017). Bazı ormangülü ballarının fenolik içerik kompozisyonu. *Anadolu Arıcılık Dergisi, 9*(1), 1-9.

Tekinsoy, A., Yaşlı, S. O., Sarıtaş, A., Güneş, H., Kaya, E., & Sönmez, F. T. (2017). Analysis of mad honey (grayanotoxin) cases admitted to Duzce University School of Medicine Emergency Department. *Open Journal of Emergency Medicine,* 5(1), 13-21. https://doi.org/10.4236/ojem.2017.51003

Thapa, A. J., Chapagain, S., Lamichhane, S., Aryal, E., Sapkota, A., Ghimire, A., Bhatt, B., Agarwal, S., Khadka, A., & Parajuli, S. (2024). Mad honey (wild honey) poisoning: Clinical case series from Nepal. *Annals of Medicine and Surgery,* 86(9), 4975-4979. https://doi.org/10.1097/ms9.0000000000002448

Turner, M. D. (2023). Mad honey and the poisoner king: A case of mass grayanotoxin poisoning in the Roman military. *Cureus,* 15(4), e38289. https://doi.org/10.7759/cureus.38289

Ullah, S., Khan, S. U., Saleh, T. A., & Fahad, S. (2018). Mad honey: Uses, intoxicating/poisoning effects, diagnosis, and treatment. *RSC Advances, 8*(33), 18635-18654. https://doi.org/10.1039/c8ra01924j

Yan, S., Wang, K., Naggar, Y. A., Van Heyden, Y., Zhao, L., Wu, L., & Xue, X. (2021). Natural plant toxins in honey: An ignored threat to human health. *Journal of Hazardous Materials,* 424, 127682. https://doi.org/10.1016/j.jhazmat.2021.127682

Yang, J., Zhao, J., & Zhang, J. (2022). The efficacy and toxicity of grayanoids as analgesics: A systematic review. *Journal of Ethnopharmacology,* 298, 115581. https://doi.org/10.1016/j.jep.2022.115581

Yaylacı, S., Ayyıldız, O., Aydın, E., Ösken, A., Karahalil, F., Varım, C., Demir, M., Genç, A., Şahinkuş, S., Can, Y., Kocayiğit, İ., & Bilir, C. (2015). Is there a difference in mad honey poisoning between geriatric and non-geriatric patient groups? *European Review for Medical and Pharmacological Sciences,* 19(23), 4647-4651.

Yılmaz, İ., Kaya, E., Yaykaşlı, K. O., & Türker, Y. (2017). The dose-dependent cardiovascular effects of intravenous grayanotoxin-III in rats. *Journal of Dr. Behçet Uz Children's Hospital,* 7(2), 121-128. https://doi.org/10.5222/buchd.2017.121