

Quinine

Quinine belongs to the group of quinoline alkaloids and has a complex chemical structure. It consists of a quinoline framework, a quinuclidine ring, and functional groups like hydroxyl (-OH) and methoxy (-OCH₃), which influence its physical and pharmacological properties. Its weakly basic character derives from the nitrogen atoms in the quinoline and quinuclidine rings, which act as proton acceptors. In acidic solutions, quinine forms highly soluble salts such as quinine sulfate, which is used in medications.

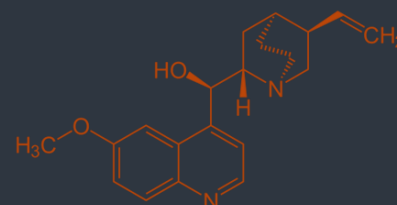
Quinine alkaloids are synthesized in plants via two distinct biosynthetic pathways: the shikimate pathway and terpenoid biosynthesis. The alkaloids are secondary metabolites, likely serving as a defense mechanism against herbivores.

Quinine is extracted from the bark of cinchona trees, particularly species such as *Cinchona officinalis* and *Cinchona ledgeriana*. The quinine content in the bark ranges from 5–10%. The complete chemical synthesis of quinine was first described in 1944 by Woodward and Doering. However, due to its complexity, quinine continues to be primarily sourced from natural extracts.

Malaria Treatment

Malaria is one of the most prominent infectious diseases globally. Quinine's effectiveness as an antimalarial agent is based on its ability to inhibit the development of Plasmodium parasites, the causative agents of the disease. The parasites are transmitted through the bite of an infected female Anopheles mosquito.

Quinine disrupts the heme polymerization process within the food vacuole of the parasites, leading to their death. While modern, less toxic antimalarial drugs have largely replaced quinine, it remains a reserve treatment for cases involving drug-resistant parasites.



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Quinine: A Bitter Threat?

The taste of quinine, a naturally occurring alkaloid extracted from the bark of the cinchona tree (*Cinchona spp.*), is familiar to many people. It is the compound that gives beverages like tonic water their bitter flavour.

The development of tonic water, however, was not the result of a creative food manufacturer's idea. The Inca are said to have already used the bark of the cinchona tree to reduce fevers. One theory is that this knowledge reached Europe in 1633 through the Spanish Jesuit priest José de Acosta. From the 1850s onward, British colonial officers and soldiers used quinine as a prophylactic against malaria. To make the pure medication more palatable due to its extremely bitter taste, they began mixing quinine with water, sugar, and later lemon; and the drink tonic water was born.

To minimize health risks, the concentration of quinine in modern beverages is clearly regulated and far below the concentration of the liquids consumed for malaria prophylaxis.

The therapeutic dose for treating malaria ranges from 200–600 mg per day. In comparable doses (200–400 mg per day), quinine is prescribed in Germany under the brand name Limptar® to treat nocturnal leg cramps, a painful muscle disorder. Although primarily prescribed in Germany similar or other quinine-based treatments are also available in other EU countries. It is believed that quinine reduces muscle hyperexcitability by influencing calcium channels. However, it can take up to four weeks for the number of cramps to decrease.

Quinine's pharmacological activity also reveals toxic potential when taken in higher doses. Acute poisoning usually occurs from intentional or accidental overdoses. A dose of just 2–4 g can cause severe poisoning symptoms in adults, while the lethal dose is approximately 8–10 g.

Permissible Concentration of Quinine in Beverages

In the European Union, the allowed concentration of quinine is limited to a maximum of 85 mg/L in non-alcoholic beverages and 300 mg/kg in spirits. These concentrations are considered generally safe for public consumption. However, sensitive individuals and pregnant women are exceptions. The German Federal Institute for Risk Assessment (BfR) advises these groups to avoid quinine-containing beverages as a precaution.

Interactions with Other Medications

Quinine is metabolized in the liver via the cytochrome P450 enzyme system, which can lead to interactions with other substances that use the same metabolic pathway.

Simultaneous use with antidepressants, antiarrhythmics, or other potentially cardiotoxic substances may increase side effects. Additionally, quinine can enhance the effect of blood thinners like warfarin or alter the efficacy of certain antibiotics. These interactions can result in unexpected and potentially dangerous health conditions, making medical supervision essential. Particularly at risk are sensitive individuals, the elderly, pregnant women, and those with liver or kidney impairments.

The term quinine syndrome (cinchonism) encompasses symptoms such as tinnitus, visual disturbances, dizziness, nausea, and headaches, which can occur with prolonged use or overdose. These symptoms are generally reversible.

In cases of high-dose poisoning, quinine has cardiotoxic effects, potentially causing arrhythmias that, in severe cases, can be fatal. Additionally, quinine is neurotoxic, which may lead to seizures, confusion, and, in extreme cases, permanent neurological damage. Hematological reactions, such as allergic or idiosyncratic responses, may also occur, potentially causing severe hemolytic anemia or thrombocytopenia. Rarely, irreversible damage to the eyes and ears has been reported.

Treatment for quinine poisoning is symptomatic, often involving gastric lavage and the administration of activated charcoal to minimize absorption.

While the consumption of quinine up to the acceptable daily intake (ADI) level in beverages is considered safe, sensitive individuals may still experience side effects such as nausea, tinnitus, or allergic reactions, even at these low levels. Caution should be taken when using prescription quinine for treating nocturnal leg cramps. Its efficacy is limited, while the risk of side effects such as cardiac arrhythmias, allergic reactions, and hemolytic anemia remains significant. Consequently, in 2015, Germany's Federal Institute for Drugs and Medical Devices (BfArM) classified the previously over-the-counter medication as prescription-only. In some countries, prescribing quinine for leg cramps has even been banned.

By Ute Haßmann

Literature and links:

- [QUININE | Poisoning & Drug Overdose, 7e | AccessMedicine | McGraw Hill Medical](#)
- [Chininhaltige Getränke können gesundheitlich problematisch sein - Aktualisierte Gesundheitliche Bewertung Nr. 020/2008 des BfR vom 9. Mai 2008](#)
- [Chininhaltige Getränke sind nichts für Schwangere! - BfR](#)
- [BfArM - Risikoinformationen - Chinin gegen nächtliche Wadenkrämpfe \(Limptar® N\): Bescheid des BfArM zu Änderungen der Produktinformation, einschließlich Einschränkung der Indikation, u.a. wegen des Risikos für schwere Blutbildveränderungen \(Thrombozytopenien\) im Rahmen eines nationalen Stufenplanverfahrens](#)
- [File:Chinin.svg - Wikimedia Commons](#)
- <https://unsplash.com/de/fotos/ein-krug-wasser-der-in-ein-mit-eis-und-limetten-gefulltes-glas-fliesst-zGRSfzI7HLA>