

Jazmin Duarte

Professor Hanson

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## The development of Quinine

Various medicines and treatments have been discovered and developed throughout the centuries, significantly improving our world. One medical finding that significantly impacted society is Quinine, a drug discovered in the 17th century that treats infectious diseases. Quinine has a rich history and a major impact on the medical world; Quinine marked a turning point in the fight against malaria, which caused countless deaths and suffering. Quinine is one of the greatest herbal medicines discovered and has changed our world and the medical field for the better. Throughout this paper, I will discuss the discovery of Quinine in Latin America, malaria and mosquitoes, side effects and reactions to Quinine, how/ what Quinine is being used today, and Quinine in soft drinks.

### **The discovery of Quinine in Latin America:**

The discovery of Quinine has several legends and stories behind its origin and "remains a mystery because of the lack of primary data—in particular, those produced by the Jesuits working in Peru" (Miller et al., 2023). Quinine is also "considered the most serendipitous medical discovery of the 17th century" (Achan, 2011), so to understand the origin of Quinine, let us go back to the 16th century when it all began; legend has it that in the jungles of Andean, an Indigenous person was suffering from a high fever and became lost and dehydrated. The Indian drank from a pool of water, but it tasted bitter. After drinking the bitter-tasting water, the Indian noticed quinquina trees contaminated it. Initially, the Indigenous person believed the

water to be a poisonous substance; however, the opposite occurred; since the water contained extracts from the quinquina trees, it alleviated his fever. The Indians then took their accidental discovery and brought it to neighboring villagers, who, from that point forward, would use the quinquina extract to treat fevers (Erhart, 2011). This was a pivotal moment in medical history. One common fever that spread throughout South America was the yellow fever. This fever was spread by the bite of the *Aedes Aegypti* mosquito, also known as the yellow fever mosquito, and originated in Africa. In the 16th century, fevers were a leading cause of death, making the discovery of Quinine immensely impactful; it healed many individuals' fevers and reduced mortality rates.

Quina-quina is also known as cinchona. The tree got this name after a Spanish Countess of Chinchon who caught a fever in Peru and used the bark of the tree to cure her fever; in 1742, the tree was named in her honor by Carl Linnaeus the Spanish Countess of Chinchon brought back to Spain in 1638 and introduced Quinine to Europe (Yeka, 2011). It was also "referred to as the "Jesuits' bark," "cardinal's bark," or "sacred bark." These names stem from its use in 1630 by Jesuit missionaries in South America" (Talisuna, 2011).

In 1779, the raw bark harvested two to three thousand arrobas. Arrobas is a Spanish unit of weight where one arroba equals twenty-five pounds. In 1780, members of the botanical expedition collected plants in Peru and gathered bark from the valuable trees to take Lima; it was at this point that the "Spanish Botanists [had] an immediate effect on the development of the trade in cinchona as they helped differentiate the species and obtain the quinine extracts" (Science in Latin America pg 137). In 1788, approximately forty thousand arrobas were sent to Lima, which is a significant amount of bark exports that would help develop the extraction of Quinine by "Ruiz and Pavon [researching] the chemistry of producing the quinine extracts to

improve the therapeutic virtues of the bark" (Science in Latin America pg 146) With the



development of Quinine it would provide treatments for individuals suffering from malaria. The image to the left is "a cinchona tree growing in the landscape of Pajal, Huancabamba, Piura, Peru" (Miller, 2023). Further development for Quinine continued in

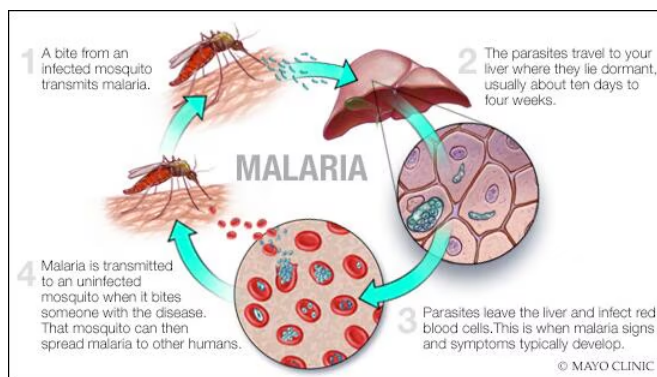
1820 when they isolated the Quinine after extracting it from the quinquina tree bark. Pierre Joseph Pelletier and Joseph Caventou named the drug, which became a primary resource for treating malaria.

Quinine is one of the most well-known alkaloids. "The molecular formula was determined by Adolph Strecker in 1854. The class of chemical compounds to which it belongs is thus called the cinchona alkaloids." Cinchona alkaloids "are natural products isolated from the bark of the Cinchona tree, and the most known are quinine (Q), quinidine (QD), cinchonine (CN), and cinchonidine (CD)" (Ramić et al., 2021). Quinine "belongs to the aryl amino alcohol group of drugs. It is an extremely basic compound and is, therefore, always presented as a salt" (Anchan et al., 2011). The use of Quinine to treat an infectious disease such as malaria makes Quinine the first chemical compound to be successfully used to treat such a disease (Talisuna, 2011). Quinidine, cinchonine, and cinchonidine were also used to treat malaria; however, in 1890, "quinine took the lead and became the main alkaloid to treat malaria and continued to be the main treatment for malaria throughout the 1920s" (Rosenthal, 2011). Quinine quickly became a necessary resource in society; this herbal medicine helped develop medical treatments and

pivoted our way to finding cures and remedies for malaria, allowing our world to evolve its resources and pharmacology. Despite new discoveries and improved treatments, Quinine is still used. It had such a significant impact on our world, becoming the predominantly used drug to treat malaria and remains to be used to treat malaria for pregnant women, which proves that even in this evolved world, it still plays a critical role and lays the groundwork for modern medicine; quinine "is one of the greatest discoveries of all time in herbal medicine" (Miller, 2023).

### Malaria and Mosquitoes:

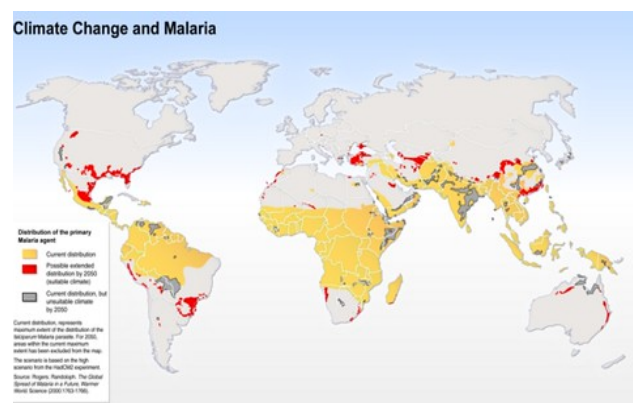
Throughout this paper, we have gone over the discovery of Quinine and now understand that the primary purpose of Quinine is to treat malaria. What is malaria, you may be asking?



Malaria is "a disease caused by a parasite.

The parasite is spread to humans through the bites of infected mosquitoes" (Mayo Clinic 2023). Malaria originated in Africa and is common in tropical countries. This disease originated in a tropical country

because "anopheles mosquitoes thrive in regions with warm temperatures, humid conditions, and high rainfall" (UCAR, 2024). To the right, you will see a map representing the distribution of malaria by 2050 and how the distribution of malaria depends on seasonal patterns and, most importantly, climate change; it shows where malaria is likely to spread by 2050; the "areas shown in yellow indicate the current distribution of malaria. Areas shown in red indicate areas where the climate will be suitable for

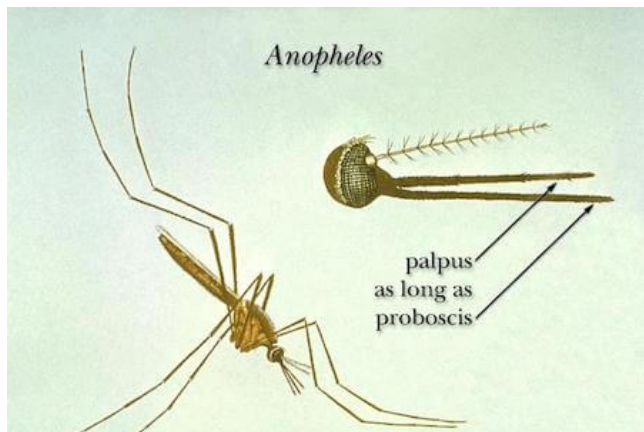


malaria by 2050. Other areas may become [malaria-free] as climate changes" (UCAR, 2024).

Climate change plays a role in the distribution of malaria; as I mentioned earlier, mosquitos thrive in tropical weather, so the mosquitoes are likely to migrate to warm, humid weather and transmit diseases in that region. Water also plays a significant factor in where mosquitoes are likely to migrate because they lay their eggs in water (Britannica, 2024). Zoonotic diseases are infections that spread from animals to humans. The increase of climate change can increase the risks of zoonotic disease epidemics from mosquitoes and humans in tropical areas, which could become pandemics across the globe and in other countries. To prevent the risk of this occurring, we must consider our activities to prevent it. Global warming is very apparent and a significant issue that we are dealing with today. There are multiple factors related to global warming, the most obvious being human activity. Due to the amount of human activity, such as burning fossil fuels like coal and oil, we release too much carbon emissions into our atmosphere, which means we are exceeding the amount of resources in our earth's biosphere. In addition to the burning of fossil fuels, the amount of deforestation is another reason for the increase in climate change; this is because our trees absorb the carbon dioxide, which is then released back into our atmosphere, increasing the amount of greenhouse gasses which results in warmer weather for the mosquitoes to thrive. Global warming could also increase malaria because the mosquitoes can survive throughout the winter, and the winters are not getting cold enough to kill the mosquitoes. In order to lessen the chances of malaria, we must mitigate the issues of our current climate conditions.

Mosquitos transmit several infectious diseases, such as "yellow fever, Zika fever, malaria, filariasis, and dengue" (Britannica, 2024). Mosquitoes can transmit their disease by inserting their "proboscis and probes for blood vessels beneath the skin. When it finds one, it injects saliva

into the wound" (Mosquitoes and Disease, n.d). This reveals that the disease is carried in the



mosquito's saliva, and it contains "pathogens such as malaria parasites or encephalitis virus" (Mosquitoes and Disease, n.d.). This also exhibited how easily this disease could be transmitted and cause great suffering and death among millions of people just off one single bite from an infected mosquito. The

small but deadly animal caused the tragedy, but with the miracle of herbal medicine from the quinquina trees, people were cured and relieved of suffering.

Quinine is used to treat malaria, more specifically, uncomplicated malaria. The difference between uncomplicated and severe malaria is "uncomplicated malaria: Symptoms may include fever, chills, sweats, headaches, muscle pains, nausea, and vomiting. Severe malaria: Symptoms may include confusion, coma, focal neurologic signs, severe anemia, respiratory difficulties, and organ dysfunction" (CDC, 2024). Quinine works against malaria by killing the parasites. The World Health Organisation recommends using Quinine "plus doxycycline, tetracycline or clindamycin as second-line treatment for uncomplicated malaria" (Anchan et al., 2011). It was also found that "the addition of either tetracycline or clindamycin to quinine in the Thai study improved cure rates" (Anchan et al., 2011). Quinine could be used alone, or it could be used with other medicines, such as the one just mentioned, to treat malaria as well. Quinine is taken orally and "[reaches its] peak concentration within 1-3 hours. It is distributed throughout the body fluids and is highly protein-bound, mainly to alpha-1 acid glycoprotein. (Anchan et al. 2011). Quinine is vital for malaria because of how easily it is transmitted and how common it is since it



can be transmitted in several tropical regions. Without the discovery and development of Quinine, malaria would still be taking millions of lives and causing great suffering, especially with the current global warming state we are in. Quinine changed our world and the medical field.

### **The side effects and reaction to Quinine:**

Before using Quinine, it would be wise to consult your doctor about the drug, and that goes for any other medication you take. Quinine kills the parasites that enter the red blood cells, which causes malaria, but there could be side effects and reactions associated with its use. People should also take precautions when taking this drug with other medications. When taking Quinine, you should follow the directions provided by your healthcare provider regarding how much you should take and how often. When taking Quinine, one might get better while taking the medication. However, persistence is vital, and one must finish their treatment even after seeing results to ensure that Quinine provides its full effects. It would be best if you also took Quinine with food because consuming the medication on an empty stomach could cause an upset stomach. "Quinine can cause serious side effects on your heart, kidneys, or blood cells" (Drugs.com, 2011). Quinine may also cause allergic reactions that could be serious and life-threatening, such as anaphylaxis, and if this does occur, you should require immediate medical attention. If you experience "rash[es], itching, hoarseness, lightheadedness, dizziness, or fainting, trouble breathing, trouble swallowing, or any swelling of your hands, face, or mouth after you use this medicine," you should call your doctor. Other side effects and reactions could



include "serious skin reactions [such as] blistering, peeling, or loosening of the skin, red skin lesions, severe acne or a skin rash, sores or ulcers on the skin, or fever or chills with this medicine. Quinine may cause hypoglycemia (low blood sugar). If your blood sugar gets too low, you may feel weak, drowsy, confused, anxious, or very hungry. You may also sweat, shake, or have blurred vision, a fast heartbeat, or a headache that will not go away" (Quinine (Oral Route) Description and Brand Names - Mayo Clinic, n.d.). If an individual experiences any of these reactions after taking Quinine, it would be in their best interest to call their doctor and let them know about any side effects they are experiencing. Other side effects that could be caused by taking Quinine that are less common include "anxiety behavior change, similar to drunkenness, bloody urine, blurred vision or change in vision, chills, cold sweats, confusion, cool pale skin, cough, difficulty concentrating, drowsiness, excessive hunger, fast heartbeat, fever, headache, hoarseness, loss of consciousness, lower back or side pain, nervousness, nightmares, painful or difficult urination, pinpoint red spots on the skin, restless sleep, seizures, shakiness, slurred speech, sore throat, unusual bleeding or bruising, unusual tiredness or weakness" (Quinine (Oral Route) Description and Brand Names - Mayo Clinic, n.d.). Some of the rare side effects are "difficulty breathing or swallowing disturbed color perception, double vision, hives, increased sweating, muscle aches, night blindness, reddening of the skin, especially around ears, ringing or buzzing in the ears, swelling of the eyes, face, inside of the nose, fingers, feet, or lower legs" (Quinine (Oral Route) Description and Brand Names - Mayo Clinic, n.d.). Taking Quinine comes with several risks of reactions, side effects, etc., which makes it essential to keep strong communication with your doctor and let them know any of the reactions you may be experiencing after taking Quinine, as it is crucial to make sure you are following the directions your doctor gave you when being prescribed this drug.



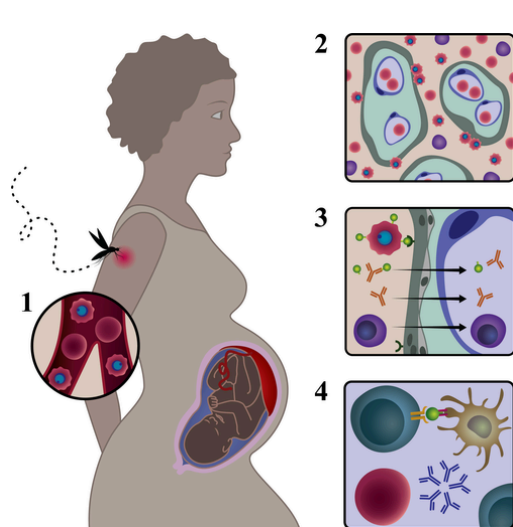
Some of these side effects will not last, and as your body gets used to the medication, the side effects will alleviate on their own, but it is always a good idea to let your doctor know to ensure that the side effects or reaction to Quinine are not life-threatening. If an individual overdoses on Quinine, it could have a severe negative effect on the eyes. The toxic effect quinine has "on the retina that can result in blindness. At one time, vasoconstriction of retinal arterioles resulting in retinal ischemia was thought to be the cause of blindness" (Darracq, 2024). Some of the other symptoms of an overdose of Quinine may include: "chest pain, dizziness, double vision, fainting, lightheadedness, rapid or irregular heartbeat, sleepiness" (Quinine (Oral Route) Description and Brand Names - Mayo Clinic, n.d.). From this, we could conclude that Quinine comes with a lot of risks. Quinine was a life-changing discovery that saved so many lives. It relieves so many people from suffering, but with the medication comes side effects and reactions, so it is vital to be aware of what medications you are taking and how they might affect your body. Quinine and other medication should be taken with precaution and awareness to ensure your safety and health.

While taking Quinine, you should be aware of changes you may be experiencing and ensure that you are doing whatever you can to ensure that your body is not in any type of life-threatening reaction to the drug. Communication is critical when taking Quinine or any other medication. Talk to your doctor about side effects or reactions to medication that could negatively affect your body. It would also be wise to consult your doctor about past reactions to Quinine and any health conditions you may have. Individuals with "a heart rhythm disorder called Long QT syndrome; an enzyme deficiency called glucose-6-phosphate dehydrogenase deficiency (G-6-PD); myasthenia gravis; optic neuritis (inflammation of the optic nerve); or if you have taken quinine in the past and it caused a blood cell disorder, severe bleeding, or kidney

problems" (Drugs.com, 2011) should not take Quinine. Safety and health always come first, so one must keep that in mind when taking medications.

### **How/ what Quinine is being used for in the present day:**

Today, Quinine is still used to treat malaria, and interestingly, Quinine plays a critical role in the first trimester for pregnant women when treating malaria. "Pregnant women are 3 times more likely to suffer from severe disease as a result of malarial infection..." (Schantz-Dunn & Nour, 2024). Malaria in pregnant women could be severe and life-threatening for the baby.



"Malaria in pregnancy causes several adverse outcomes that include maternal anemia, intrauterine growth retardation, low birth weight, preterm deliveries, and abortion. Prevention and treatment of malaria in pregnancy is, therefore, critical to avoid these adverse outcomes" (Achan et al., 2011). Malaria affects the development of the foetal. Contracting malaria during pregnancy exposes the foetus to

parasite antigens as well as altering the foetus, which may lead to the development of "immune responses directed against parasite antigens, including malaria-specific T cells and IgM-producing B cells" (Harrington et al., 2018). If the mother contracts malaria, the placenta and the baby will be exposed to the disease; however, the placenta is more likely to be infected than the baby. What does this mean for the baby? If the placenta is infected, then this "may prevent the baby from getting proper amounts of oxygen and nutrients" (Malaria, 1994). Some of the symptoms of malaria a pregnant woman should watch out for are "fever[s], low oxygen levels, or low blood sugar, [which] may also raise the chance of pregnancy complications"

(Malaria, 1994). This could also affect the child in the future in that "malaria can cause behavior or learning issues for a child who was exposed during a pregnancy, and malaria infections in pregnancy, especially in late pregnancy, could be related to motor delay (rolling over, crawling, walking)" (Malaria, 1994).

While Quinine is used to treat malaria in pregnant women to reduce the risks of maternal anemia, intrauterine growth retardation, low birth weight, and preterm deliveries, as well as future effects on the child, the medication also comes with its risks and side effects as we went over in the previous topic on the side effects and reaction to Quinine. More specific effects Quinine has on pregnant women in the case of an overdose on the medication include: "stillbirth, congenital deafness, hypoplasia of the optic nerve, and anomalies of the CNS, limbs, face and heart" (Use of Quinine in Pregnancy – Uktis, 2023). Another factor to consider when a mother is taking medication such as Quinine is breastfeeding. While malaria can not be passed to the child through breast milk, "some medications used to treat malaria might enter the breast milk" (Malaria, 1994), which is why it is essential to have strong communication with your doctor if you have any issues or questions about the medication you take. No matter what medication the mother takes, she is responsible for taking it as directed by her doctor and following the directions for its use. It is vital to watch out for symptoms and side effects of Quinine and consult her doctor to ensure it is not life-threatening for her baby or herself.

### **Quinine in soft drinks:**

Quinine is used not only to treat malaria but also as an ingredient in soft drinks. Quinine is bitter-tasting, and a carbonated soft drink that contains Quinine is tonic water. Often, tonic water is consumed to relieve leg cramps; however, the FDA did ban using Quinine in leg cramp medications. "Tonic water contains no more than 83 mg of quinine per liter—a much lower

concentration than the 500 to 1,000 mg in the therapeutic dose of quinine tablets" (Will Tonic Water Prevent Nighttime Leg Cramps? 2016). Since the amount of Quinine in tonic water is so little, it may not alleviate the leg cramp. There are few nutritional benefits to drinking tonic



water. For some, tonic water does help with leg cramps and restless legs syndrome, and they may also enjoy the flavor and drink the tonic water to stay hydrated; however, the tonic water contains a diluted amount of Quinine; however, there are some side effects one may experience in rare cases such as: "ringing in the ears, vomiting, stomach cramps, nervousness, nausea, diarrhea, and confusion" (Fletcher, 2018). While tonic

water may have rare side effects after consuming the drink, it will not cure malaria. Tonic water has a minimal amount of Quinine and has minimal impact on the body, so if one has malaria, this will not cure the disease. One must be prescribed quinine tablets to treat malaria.

### **Conclusion:**

Throughout this paper, we took a journey on the development of Quinine; we discussed the discovery of Quinine in Latin America, malaria and mosquitoes, side effects and reactions to Quinine, how/ what Quinine is being used for the present day, and Quinine in soft drinks. After reading, learning, and comprehending the topics of this paper, I would assume that the discovery and development quinine was quite impactful and, some would say, a miracle.

The mysterious discovery of Quinine in the 16th century and its ongoing use of the drug today reveals the profound and significant impact quinine had on our world, the medical field, public health, and the very history of medicine itself. One accidental discovery can remarkably change

our world and transform lives. Quinine was the first effective treatment to cure fevers and colds that claimed millions of lives. It creates an infectious disease, malaria, which too took so many lives and caused much suffering; it is truly a life-saving medicine. Despite the evolution and advancement of medicine and the discovery of new treatments, Quinine continues to be used today. Throughout the centuries, our world has encountered several diseases, illnesses, infections, etc. Just recently Covid-19. Quinine and other remarkable discoveries remind us that research and discovery are vital; we must continue to gain knowledge and research to make discoveries that will improve our world and open opportunities. Quinine served as both a treatment and a token of hope. What a miracle the discovery of Quinine; individuals dying of fevers and colds and the miracle substance discovered alleviated the suffering and death of many.

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