

## Could Low-Dose Quinine Prevent or Treat Coronavirus Infection?

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**Received:** March 27, 2020; **Published:** March 31, 2020

**DOI:** 10.31080/ecpt.2020.08.00455

**Keywords:** 2019-nCoV; Cinchona; Chloroquine; Coronavirus; COVID-19; Hydroxychloroquine; Malaria; Pandemic; Quinine

### Abbreviations

2019-nCoV: 2019 Novel Coronavirus; CDC: Centers for Disease Control and Prevention; CoV: Coronavirus; FDA: Food and Drug Administration; PUI: Person Under Investigation; RA: Rheumatoid Arthritis; SLE: Systemic Lupus Erythematosus

### Discussion

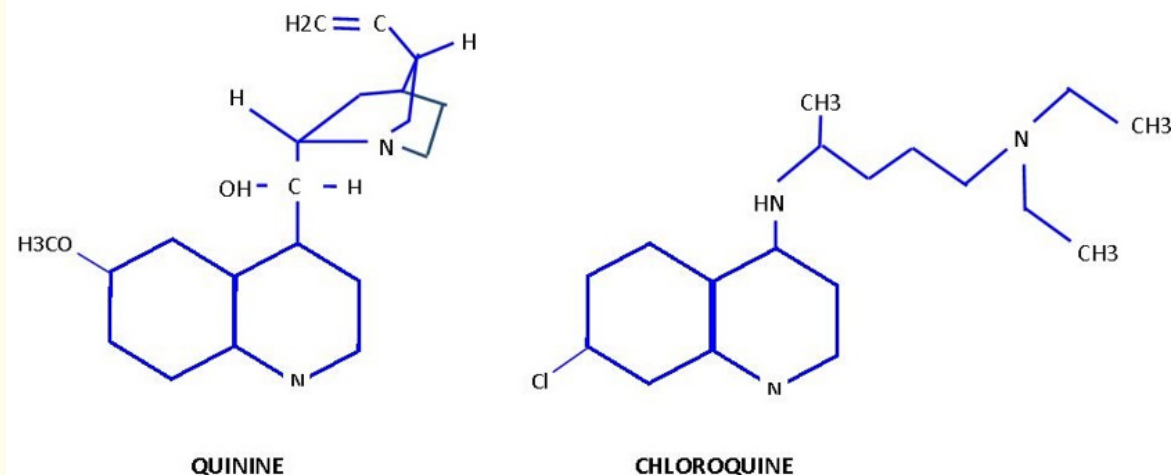
The 2019 novel coronavirus (2019-nCoV) is a single-stranded RNA virus that has affected everyone on the planet in one way or another: as a person infected with 2019-nCoV, a person under investigation (PUI) for coronavirus disease 2019 (COVID-19), and non-infected people around the world that could become infected. A search for a cure, preventive vaccine, or a way to limit the spread of this pandemic-causing contagion is foremost on the minds of governments, medical communities, and people as a whole. Currently, there seems to be some hope for those infected with 2019-nCoV. Two older, commonly prescribed malaria drugs—hydroxychloroquine and chloroquine—have not only been used for malaria but also autoimmune diseases, such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). According to the United State’s Centers for Disease Control and Prevention (CDC):

Both drugs have *in vitro* activity against SARS-CoV, SARS-CoV-2, and other coronaviruses, with hydroxychloroquine having relatively higher potency against SARS-CoV-2. A study in China reported that chloroquine treatment of COVID-19 patients had clinical and virologic benefit versus a comparison group and chloroquine was added as a recommended antiviral for treatment of COVID-19 in China. Based upon limited *in vitro* and anecdotal data, chloroquine or hydroxychloroquine are currently recommended for treatment of hospitalized COVID-19 patients in several countries. Both chloroquine and hydroxychloroquine have known safety profiles with the main concerns being cardiotoxicity (prolonged QT syndrome) with prolonged use in patients with hepatic or renal dysfunction and immunosuppression but have been reportedly well-tolerated in COVID-19 patients. [1]

Hydroxychloroquine and chloroquine are currently being used off-label for hospitalized COVID-19 patients with some anecdotal success outside of the U.S. and, more recently, within the U.S. Many U.S.-based hospitals are putting these FDA-approved, older malaria drugs through fast-track clinical trials to determine COVID-19 efficacy [1].

If these drugs work, to a greater or lesser degree, then, it could be asked, “Is there another more expedient and less expensive way to proactively treat the world’s population? Is there another way to prevent 2019-nCoV from infecting a host, causing COVID-19, and the infected patient’s hospitalization?” If the fast-tracked drug trials mentioned above prove successful, we may look to the bark of the Cinchona tree (native to the Andes of South America) as a cure for COVID-19 or preventive agent against 2019-nCoV.

Hydroxychloroquine and chloroquine are derivatives of their natural predecessor, quinine (derived from the bark of the Cinchona tree), and thus share similar molecular configurations with quinine (Figure 1). Quinine, as well as quinidine, cinchonine, and cinchonidine, found in cinchona bark, are alkaloids and stereoisomers of each other [2].



*Figure 1: Illustration depicting the chemical similarity between quinine and chloroquine. Note. Image by Mitchell G Jomsky (2020).*

### Historical context of quinine

In the 17<sup>th</sup> century, Spanish explorers observed that the indigenous people in what is now Peru used a specific bark to ameliorate various “fevers” [3]. Microbiology professor, I. Edward Alcamo, reported that in 1638, the Countess of Chinchon, wife of the Spanish Ambassador to Peru, had developed malaria, and agreed to be treated with an extract of the bark of the “fever tree”. When the Countess experienced a complete recovery from malaria, news of her miraculous recovery spread throughout Europe. Subsequently, and for the next few centuries, the bark of the Cinchona tree (as it came to be called), remained a staple in fighting malaria [4]. In 1820, Pelletier and Caventou isolated quinine from cinchona [4]. According to Raustiala K (2020):

But it [quinine] was also a powerful new weapon in the European quest to conquer and rule distant lands. Quinine powder quickly became critical to the health of the [British] empire. By the 1840s, British citizens and soldiers in India were using 700 tons of cinchona bark annually for their protective doses of quinine. Quinine powder kept the troops alive, allowed officials to survive in low-lying and wet regions of India, and ultimately permitted a stable British population to prosper in Britain’s tropical colonies. Quinine was so bitter, though, that British officials stationed in India and other tropical posts took to mixing the powder with soda and sugar. “Tonic water,” of a sort, was born. [3]

To meet the growing demand of overseas British nationals who needed quinine to prevent malaria, the Schweppes Company of Geneva launched a commercial version, known as “Indian Quinine Tonic” [5]. Soon thereafter, British soldiers began mixing their daily tonic with lime and gin, which made the herbal concoction more palatable. According to Winston Churchill, “The gin and tonic has saved more Englishmen’s lives, and minds, than all the doctors in the Empire” [6].

### Quinine tonic as a COVID-19 preventive agent

Perhaps drinking quinine tonic (without the gin) can help save even more lives around the world—in this case, from 2019-nCoV? The risk of adverse effects in consuming a controlled amount of quinine or quinine tonic seems low. There might be no, or little, harm in drinking a 3–4 ounce-daily prophylaxis dose of tonic water. However, if taken in excessive amounts, quinine can be toxic. The sequella of quinine toxicity (typically seen in an overdose) can include pulmonary edema, immune thrombocytopenic purpura, irreversible deafness, or arrhythmias [5]. Nevertheless, the level of quinine in tonic water is quite low; therefore, toxicity would be an unlikely outcome. However, some people are sensitive to any quinine and may experience tinnitus. If so, they should discontinue drinking the tonic water immediately [5]. An interesting side note, tinnitus is also known as cinchonism, named after the tree that was named for the Countess of Chinchon [2].

### Conclusion

Finding a cure, preventive vaccine, or a way to limit the spread of 2019-nCoV is paramount to stop this COVID-19 pandemic. According to DiRuzzo and Kerna (2020), “To date, little is known about this [2019-nCoV] coronavirus, although it shares characteristics and presentations of SARS-CoV and MERS-CoV, which predated 2019-nCoV [7]. Hydroxychloroquine and chloroquine are currently being used off-label for hospitalized COVID-19 patients and are being fast-tracked through clinical trials to determine efficacy in the treatment of COVID-19. Hydroxychloroquine and chloroquine are derivatives of quinine and have similar chemical structures. Quinine has been known for hundreds of years as a cure and preventive agent in malaria. If hydroxychloroquine and chloroquine can help in the treatment or prevention of COVID-19, perhaps quinine, consumed as a tonic, can be of benefit, singularly or multimodally, to the world’s population for the same purpose.

### Conflict of Interest Statement

The authors declare that this paper was written in the absence of any commercial or financial relationship that could be construed as a potential conflict of interest.

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**Volume 8 Issue 4 April 2020**

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