

# Artemisinin From Sweet Wormwood Inhibits SARS-CoV-2

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## STORY AT-A-GLANCE

- › An antimalarial treatment made from the plant *Artemisia annua* (Sweet Wormwood) shows promise as a COVID-19 treatment
- › The drug artesunate – which contains two compounds found in *Artemisia annua*: artemisinin and dihydroartemisinin – is a first-line treatment for malaria
- › In a recent in vitro study, both pretreatment and treatment with artemisinin extracts, synthetic artemisinin and the drug artesunate were able to inhibit SARS-CoV-2 infection. However, artesunate was the most potent in terms of treatment, and from a clinical perspective may be the only one worth pursuing
- › Artesunate’s mechanism of action against SARS-CoV-2 is as yet unknown, but artemisinin does have confirmed antiviral activity
- › The World Health Organization has come out in opposition to artemisinin-based products, warning their use can bolster drug-resistant strains of malaria parasites. For this reason, people living in malaria-prone areas should be cautious about using this plant remedy

**This article was previously published January 4, 2021, and has been updated with new information.**

A second antimalarial treatment is now being seriously considered and evaluated for its efficacy against COVID-19. The treatment is made from the plant *Artemisia annua*,

which most people know as Sweet Wormwood. Other names for this plant include Annual Sagewort and Sweet Annie.

Research over the past few decades has revealed multiple health benefits from this medicinal herb, which has a centuries-long history of use in folk medicine. In 2015, Chinese scientist Tu Youyou received a partial Nobel Prize in Physiology or Medicine for his discovery of artemisinin and dihydroartemisinin,<sup>1</sup> both of which have potent malaria-fighting properties.

As reported by the University of Kentucky,<sup>2</sup> "The popular malaria drug artesunate was developed from those compounds and is still used as a first-line treatment for the disease today."

## **Artemisinin – A Viable COVID-19 Remedy?**

Interestingly, in addition to having a long-standing history of being used as a highly effective antiparasitic, it also has anticancer properties. Additionally, artemisia annua has antiviral activity that might be helpful against SARS-CoV-2.

In an April 8, 2020, SEC filing, Mateon Therapeutics reported<sup>3</sup> that "Artemisinin is highly potent at inhibiting the ability of the COVID-19 causing virus (SARS-CoV-2) to multiply while also having an excellent safety index."

After testing the plant's antiviral effects in a laboratory setting for a couple of years, University of Kentucky researchers are also exploring its use for the treatment of COVID-19,<sup>4</sup> as are researchers in Denmark and Germany.<sup>5</sup> According to the University of Kentucky:<sup>6</sup>

*"Surprisingly, results showed that the plant's leaves, when extracted with absolute ethanol or distilled water, provided more antiviral activity than the actual drug itself – meaning that an Artemisia annua-blended coffee or tea could possibly be more effective than taking the drug."*

Based on these findings, researchers have decided to test artemisinin in patients diagnosed with COVID-19. Some of the first human studies, set to investigate both the extract blended into coffee and tea, as well as the drug artesunate, were implemented by UK HealthCare.

University of Kentucky researchers have founded a company called ArtemiFlow to develop and manufacture the drug, in collaboration with the Kentucky Tobacco Research & Development Center.<sup>7</sup> A sister company, ArtemiLife, is marketing Artemisia tea and coffee to raise research funds.

## **Mechanism of Action Remains Unknown**

As for its mechanism of action, such details still remain to be discovered. C&EN explains:<sup>8</sup>

*"When countering malaria, artemisinin exploits the parasite's taste for hemoglobin in its host's blood. As the parasite digests hemoglobin, it frees the iron-porphyrin heme complex from the protein.*

*Because this heme is toxic to the parasite, the organism normally converts the complex to a more benign crystalline form. 'But artemisinin corrupts this heme-detoxification pathway,' says Paul O'Neill, a medicinal chemist at the University of Liverpool.*

*If artemisinin does have any effect against SARS-CoV-2, though, it likely relies on a completely different mechanism than the one it uses against the malaria parasite, Harvard's [malaria researcher Dyann F.] Wirth says."*

## **In Vitro Study Reports Positive Results**

An in vitro study<sup>9,10</sup> looking at the efficacy of artemisinin-based treatments against SARS-CoV-2, posted on the prepublication server bioRxiv, October 5, 2020, report promising results.

**“ Both pretreatment and treatment with artemisinin extracts, synthetic artemisinin and the drug artesunate were able to inhibit SARS-CoV-2 infection. However, artesunate was the most potent in terms of treatment, and from a clinical perspective may be the only one worth pursuing.”**

The study was a collaboration between researchers from Germany, Denmark and Hong Kong, led by Kerry Gilmore, Ph.D., from the Max Planck Institute for Colloids and Interfaces in Potsdam, Germany.

Three artemisinin extracts, as well as pure, synthetic artemisinin, artesunate and artemether were evaluated. During the initial screening for antiviral activity, a German SARS-CoV-2 strain obtained from Munich was used.

Later on, during the concentration-response phase of the trial, they used a Danish SARS-CoV-2 strain from Copenhagen. These two strains are said to be "more closely related to the majority of SARS-CoV-2 strains circulating worldwide than the Wuhan strain."<sup>11,12</sup>

In summary, they found that both pretreatment and treatment with artemisinin extracts, synthetic artemisinin and the drug artesunate were able to inhibit SARS-CoV-2 infection of Vero E6 cells and human hepatoma Huh7.5 cells. That said, artesunate was the most potent in terms of treatment, and from a clinical perspective may be the only one worth pursuing.<sup>13,14</sup>

## **World Health Organization Warns Against Its Use**

While the world is eager to add another remedy to its COVID-19 treatment list, the World Health Organization has come out in opposition to artemisinin-based products. In a May 27, 2020, article, C&EN reported:<sup>15</sup>

*"One of the most high-profile advocates for using the herbal remedy against the novel coronavirus is Madagascar president Andry Rajoelina, who has been touting Covid-Organics, a tonic containing A. annua that the Malagasy Institute of Applied Research developed ...*

*But health officials are deeply concerned about the promotion and use of these herbal remedies for three principal reasons. First, no evidence exists that A. annua extracts can prevent or cure COVID-19 ...*

*Second, A. annua preparations such as teas, tonics, or herbal capsules also contain a cocktail of bioactive compounds in addition to artemisinin that can have side effects such as dizziness, hearing problems, and vomiting.*

*Third, and perhaps most worrying of all, widespread use of A. annua herbal extracts could bolster drug-resistant strains of malaria parasites such as Plasmodium falciparum.<sup>16</sup>*

*For people living in regions where malaria is endemic, exposure to subtherapeutic doses of artemisinin in A. annua may be enough to kill off some of the parasites in their bodies, but not all of them. Clearing out weakling parasites leaves more room for drug-resistant siblings to proliferate, rendering vital ACTs [artemisinin-based combination therapies] ineffective."*

According to Pascal Ringwald, who heads up the drug resistance and response unit of the WHO Global Malaria Program, artemisinin resistance is a significant problem in Southeast Asia, where Artemisia readily grows and is commonly used.<sup>17</sup>

That said, this risk is bound to be slight for Americans and people in many other Western countries where malaria is exceedingly rare. According to C&EN,<sup>18</sup> "Scientists interviewed by C&EN agree that although this use is against WHO recommendations, it does not risk accelerating resistance because there are so few cases of malaria in the U.S."

## Sources and References

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- <sup>1</sup> NobelPrize.org Tu Youyou
- <sup>2, 4, 6</sup> University of Kentucky August 11, 2020
- <sup>3</sup> SEC Database April 8, 2020
- <sup>5, 7, 8, 15, 17, 18</sup> C&EN May 27, 2020
- <sup>9, 11, 13</sup> bioRxiv October 5, 2020 DOI: 10.1101/2020.10.05.326637
- <sup>10, 12, 14</sup> News-medical.net October 6, 2020
- <sup>16</sup> WHO.int Use of Non-Pharmaceutical Forms of Artemisia October 10, 2019