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## Artemisinin: A Malaria Drug. What Else Could it be Used For?

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#### **ABSTRACT**

Artemisinin is the chemical compound obtained from the Artemisia annua plant, a component of Chinese traditional medicine and herbolary. Its use has been described for over 2000 years, mainly for its antipyretic activity. In the 1970s the compound was discovered in China and has since been used to treat Malaria. Recently, studies both in vivo and in vitro have shown that artemisinin is not only capable of treating Malaria, but other diseases. Most of these studies have centered on its antineoplastic activity, while others have study it in other fields of medicine, such as dermatology. Because of its low adverse effect rate, artemisinin and its synthetic derivatives could change the current paradigm of chemotherapy against cancer. Interestingly, there is only one report of an artemisinin derivative to treat patients infected with the SARS-CoV-2 virus, responsible for the COVID-19 pandemic.

**Keywords:** Artemisinin, Artesunate, COVID-19, Malaria, Herbolary

#### **REVIEW**

Artemisia annua is plant commonly used in Chinese traditional medicine and herbolary. It has been described for over two thousand years, mainly for its antipyretic effects. However, it was not until the 1970s that the active compound, artemisinin, was found by Dr. Youyou Tu while performing research to find alternative treatments for Malaria, because at the time there was an outbreak that proved to be resistant to chloroquine and quinolones, the standard treatment for the disease in the past [1]. She would eventually be awarded the Nobel prize in Medicine or Physiology for those findings in 2015.

Later on, synthetic derivatives such as artesunate, artemether, arteether, dihydroartemisinin among others, were developed and have proved to be more effective against the Plasmodium parasite than the original compound [2]. The artemisinin compound is a sesquiterpene with an endoperoxide group, which is the main source of its cell toxicity capacities.

Artemisinin is only approved for the treatment of Malaria; however, it has also been used to treat other diseases and is now a prospect drug for cancer treatment. The main breakthrough with these findings is not the anticancer capabilities of the compounds, but rather its minimal adverse effect rates [3,4].

Currently approved chemotherapy schemes include specific medications that partake in stopping the cell cycle or inhibiting proteins and enzymes necessary for cell

replication. Although effective and powerful, those medications tend to cause severe adverse effects to the patient, many times causing to stop treatment.

The way that artemisinin acts to stop the growth of neoplastic cells is vast and still not clearly defined, however, many mechanisms of action have been shown to be a part of this spectrum and include endoperoxide bridges interacting with heme groups in cancer cells, therefore producing cytotoxic radicals, induction of apoptosis via cyclin dependent kinases (CDK) and procaspases, inhibition of cellular replication pathways, assembling of lysosomes, and have also been proved to inhibit metastasis [5-9].

Studies have reported artemisinin and its compounds as synergistic drugs for currently approved cancer medications, as well as sensitizing agents for multidrug resistant cancer cells [4].

Artemisinin or other derivatives have been widely studied as a possible alternative cancer therapy, but recent evidence has shown that it could also be possibly used for other diseases.

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In the field of dermatology, it has been noted as a drug prospect for common pathologies. For example, it has been studied for its ability to modulate scar formation and its beneficial effect on seborrheic keratoses [10,11].

Artesunate was shown to be effective against other parasitic infections such as schistosomiasis and could also be effective against viral pathogens such as Cytomegalovirus, and other members of the Herpesviridae family [12,13]. With this antiviral effect studied, it is noteworthy to mention the possibility of artemisinin and its derivative as a treatment prospect for SARS-CoV-2 virus, which causes the COVID-19 disease, currently a pandemic that has reached all continents and infected over 8 million people as of mid-June 2020 (https://coronavirus.jhu.edu/map.html).

Because of its interaction and inhibition of cell signalling pathways involving NF-kB (Nuclear Factor kappa B) and other interleukins, it is believed that these drugs could be effective and should be considered and studied to treat COVID-19 patients in the setting of a clinical trial [14].

As of mid-June 2020, there is only one article in which artesunate was used to treat COVID-19 patients.

In a study published in April 2020 in the Nanning region of China, artesunate was studied for its possible antiviral effect. The control group of the study consisted of 25 patients and were treated with lopinavir-ritonavir and aerosolized interferon, which they designate as their "standard" treatment, while 18 patients in the experimental group were treated with 60 mg of artesunate twice daily plus the "standard" treatment. At the cut off of 10 days, the experimental group showed a reduced time of symptom improvement, negative SARS-CoV-2 PCR, lung lesion absorption and length of hospital stay, compared with the control group. All data was statistically significant (p < 0.05) [15].

With this brief report in mind, it is quintessential to think of artemisinin and its derivatives as prospects for many diseases. Because of the minimal adverse effect rates, scientists should expand clinical trials both in-vitro and invivo to study its benefits and interactions in other morbidities besides Malaria.

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