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Letter to the Editor

Is the traditional Chinese herb "*Artemisia annua*" possible to fight against COVID-19?

Artemisinin is a natural product derived from traditional herbal medicine, *Artemisia annua* (*qinghao*). It's also known as "Qinghaosu" and "Sweet wormwood" in China and African countries respectively. "Qinghao" was earlier mentioned in "The recipes for 52 kinds of diseases" at West Han Dynasty (168BC) because it's noted as an anti-inflammatory traditional herbal medicine in *Shennong Bencaojing*. Meanwhile, Ge Hong at 341 AD recorded the anti-febrile properties of "Qinghao" in zhou hou bei ji fang. Thereafter, it is used for the anti-malarial from the ben cao gan mu who written by Li Shizen in wen bing tiao bian.[1]

Artemisinin is the most important bioactive component in *Artemisia annua*. The chemical structure of artemisinin is a sesquiterpene lactone containing an unusual endoperoxide bridge with chemical formulas $C_{15}H_{22}O_5$ and a molecular weight of 282.332 g/mol. This unusual endoperoxide bridge is the key active site for its drug mechanism of action. However, artemisinin has certain limitations such as poor water insolubility and bioavailability, so various semi-synthetic derivatives developed including dihydroartemisinin, β-artemether and artesunate which exhibit greater potency, improve the water solubility, favorable metabolic as well as the hydrolytic stabilities.[2]

Over the past, artemisinin and its semi-synthetic derivatives have been reported for the treatment of fever and Plasmodium falciparum malaria. These acts as an excellent anti-infect agent and anti-malarial agent. Artemisinin-based combination therapies (ACTs) fight against infections and malarial fever which has been recognized by the World Health Organization (WHO) in 2001. Nowadays, many researchers still investigate the effect of artemisinin and its analogues on Plasmodium parasites by modification of the structure of peroxides, ethers and ozonides in artemisinin. This improves the killing rate of plasmodium parasites for both *in vitro* and *in vivo* models as well as a faster clinical response for humans.[3]

In 2003, Li et al. have been indicated that artemisinin is one of the candidates to treat severe acute respiratory syndrome coronavirus (SARS-CoV) in Vero cell-based CPE/MTS screening. It's inhibited the coronavirus replication and showed antiviral activity against SARS-CoV with 34.5 ± 2.6 μg/mL in 50% effect concentration (EC50), CC_{50} value of 1053.0 ± 92.8 μg/mL in cytotoxicity assay and a selective index (SI) is greater than 31 which shown that artemisinin could be further developed as a drug for coronavirus.[4]

Recently, coronavirus disease-2019 (COVID-19) has been spread all around the world. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the virus strain which as a causative agent. It is a positive-sense single-stranded RNA virus, also called betacoronavirus often causing cold and other mild upper respiratory tract infections in the human body. This is the most lethal because it is the incorporation of a polybasic cleavage site to increase the pathogenicity and its transmission rate is much higher than the other coronavirus.

At present, there are no effective treatments against COVID-19 such as vaccines. Traditional Chinese herb "*Artemisia annua*" may be a good choice as the acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is extremely similar to the severe acute respiratory syndrome coronavirus (SARS-CoV) in 2003. The pharmacological mechanism of *Artemisia annua* has mainly inhibited the enzymatic activity of CLPro (chymotrypsin-like protease) which is an enzyme produced by SARS-CoV-2 during COVID-19 infection. It is expected to be improved exhausting adaptive immunity and modulating the inflammatory response through regulating the production of pro-inflammatory cytokines such as prostaglandin E2 (PGE2), IL-6, IL-10 and TNF alpha. The genesis of CD4, CD8 and interferon-gamma would be increased when a combination of the minerals and biomolecules. The principle is the same as artemisinin-based combination therapies (ACTs) and well developed previously in 2003.[5]

To conclude the above information, the traditional Chinese herb "*Artemisia annua*" is possible to combat COVID-19. However, much more work needs to be done for supporting the evidence including its safety and efficacy to fight against COVID-19.

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Not applicable.

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Siukan Law [a,b,*]

[a] *Department of Science, School of Science and Technology, The Open University of Hong Kong, Ho Man Tin, Kowloon, Hong Kong*

[b] *School of Chinese Medicine, Faculty of Medicine, The Chinese University of Hong Kong, Shatin, Hong Kong*

Albert Wingnang Leung

Asia-Pacific Institute of Aging Studies, Lingnan University, Tuen Mun, Hong Kong

Chuanshan Xu

Key Laboratory of Molecular Target and Clinical Pharmacology, State Key Laboratory of Respiratory Disease, School of Pharmaceutical Sciences & Fifth Affiliated Hospital, Guangzhou Medical University, Guangzhou 511436, China

* Corresponding author at: Department of Science, School of Science and Technology, The Open University of Hong Kong, Ho Man Tin, Kowloon, Hong Kong.

E-mail address: siukanlaw@hotmail.com (S. Law)

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