

LETTER TO THE EDITOR**Artemisia annua: Trials are needed for COVID-19**

Beginning in December 2019, an increasing number of cases of novel coronavirus, designated SARS-CoV-2, has caused worldwide outbreak of respiratory infection now termed coronavirus disease 2019 (COVID-19) (Cao et al., 2020). As of March 26, 2020, coronavirus disease 2019 (COVID-19) has been confirmed in 462,684 people and the death had reached over 20,834 globally (WHO, 2020). Until yet, there are no vaccine and no specific antiviral agents for coronavirus infections, so it is a great challenge for scientists to find antiviral agent to treat this disease. Researcher endeavoring for antiviral agents, some of them are natural products, ritonavir, chloroquine phosphate, arbidol, ribavirin, and traditional Chinese medicines that demonstrated preliminary efficacy against SARS-CoV, the virus that causes SARS in humans (Dong, Hu, & Gao, 2020). Scientific attention is needed toward efficacious therapies against COVID-19.

There are relevant information regarding therapies from the 2002–2003 outbreak of SARS-CoV in China. The researcher tested in vitro antiviral activities of *Artemisia annua* whole plants preparation in ethanolic extract against SARS-CoV, with 50% effective concentration (EC50) value of 34.5 ± 2.6 $\mu\text{g}/\text{mL}$ and 50% cytotoxic concentration (CC50) of $1,053 \pm 92.8$ $\mu\text{g}/\text{mL}$. The result affords strong support for the usage of *A. annua* to treat SARS-CoV infectious diseases (Li et al., 2005). In China, natural compounds has been frequently used in combination with conventional medicine to treat SARS. Some evidence demonstrated that the traditional herbal medicine is effective against SARS-CoV infectious diseases (Lin, Han, & Yang, 2003).

Artemisinin is derivatives of *A. annua* that have been commercialized as antimalarial drugs (Efferth et al., 2008). As well as the value of artemisinin is not limited to the treatment of malaria, it is most promising natural products that is important candidates accounting for the antiviral effects (Karamodini, Emami, Ghannad, Sani, & Sahebkar, 2011). In addition *A. annua* contain sterols that show virus inhibitory potential (Khan, Jain, Bhakuni, Zaim, & Thakur, 1991).

Currently, there are supportive and nonspecific treatment to relieve patient symptom. For prophylaxis and treatment of virus the antiviral agent must be safe, adequate, and cost should be preferably low. In China, most of the infected patient receiving traditional Chinese medicine for treatment of COVID-19 (Yang, Islam, Wang, Li, & Chen, 2020). The subset methanolic extracts obtained from aerial parts of *A. annua* had the highest antiviral activity than acyclovir against Herpes Simplex virus type 1. Aerial subsets extracts of *A. annua* contain bioactive compound that may be an appropriate candidate for antiviral therapies (Karamodini et al., 2011). It has a history of being safe and easily available for therapies.

Pulmonary fibrosis are observed in SARS coronavirus-2 (SARS-CoV-2) infection with increased severity, mediated by Interleukin-1

(Conti et al., 2020). Several studies suggesting that oxidative stress is associated with pulmonary diseases and it is likely that the consumption of natural antioxidant are effective in lung fibrosis (Day, 2008). *A. annua* extract exhibit significant antioxidant activity that is most likely due to its high phenolic content (Ferreira, Luthria, Sasaki, & Heyerick, 2010). *A. annua* derivatives, artesunate, is a promising novel drug to treat pulmonary fibrosis by inhibiting pro-fibrotic molecules associated with pulmonary fibrosis (Wang, Xuan, Yao, Huang, & Jin, 2015). The rationale for testing antioxidants and antifibrotic effect in *A. annua* is appealing that might play a key role in lung fibrosis.

The recent emergence of COVID-19 warrants the urgent development of potential antiviral therapies to protect population from high risk of infection (Mitjà & Clotet, 2020). There is immediate need for approved therapies to reduce the ongoing mortality, so it is important to emphasis the proven safety profiles of *A. annua* for the treatment of COVID-19. Natural products found in *A. annua* as chemical weapons to protect against infections by viruses, specifically herpes simplex virus type 1, hepatitis B virus, hepatitis C virus, bovine viral diarrhea virus, and Epstein–Barr virus (Efferth et al., 2008). Meanwhile this plant *A. annua* is cheap and widely available, although the final analysis is therefore technically demanding. It will be of the great value to know the efficacy of these compound associated specifically SARS-CoV-2. If a distinct antiviral compound is identified in *A. annua*, it may be lead to active pharmaceutical compound production. These compound may contribute to reducing the use of high cost agent. The option of using *A. annua* in the treatment of COVID-19 from SARS-Cov-19 should be studied with attention in light of the previous studies. The experimental study on *A. annua* may contribute to the identification of anti-coronavirus compounds that may successful and safe antiviral in in the treatment of COVID-19. We urge international scientific community to get focused on the efficacy of proposed agent against current ongoing pandemic. Further careful analysis of *A. annua* for anti-coronavirus will be crucial before the discovery of new antiviral agent.

There is the possibility that studies on *A. annua* preparations have been not carried according to more recent scientific qualitative standards for plant-derived products (Heinrich et al., 2020). As the pandemic spreads, scientists around the globe are actively exploring drugs for combating an ongoing challenge. It is important to develop safe drugs for treatment of COVID-19. The efficacy and safety of *A. annua* in the therapy of COVID-19 is needed to be assessed in clinical trials.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

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