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Is *Artemisia herba-alba* Bioactive Components Useful for Coronavirus (COVID-19 and its Emerging Strains) Prevention?

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Introduction

The new acute respiratory syndrome coronavirus 2 (COVID-19) -and its new emerging variants- is a serious health disease spread quickly all over the world. Currently, multiple candidates of COVID-19 vaccines such as Sputnik V, Pfizer-BioNTech, and Moderna are available in the market but public vaccine hesitancy (loss of public trust) due to potential safety problems might outweigh the perceived pandemic threats in many countries throughout the world. In this context, the continuous use of safety measures and therapeutic approaches are still of great importance to treat COVID-19 and its emerging strains till the disease ceases to pose a risk to public health. Artemisia herba-alba is an aromatic and medicinal shrub well-known for its antioxidant, antiviral, anti-inflammatory and hypoglycemic properties. The aim of this paper is to offer an opinion on the therapeutic benefits of *A. herba-alba* bioactive components against COVID-19.

According to the WHO (2002), about 80 % of the world's population practice herbal medicine to cure their illnesses, due the reasons to be natural, inexpensive and free from adverse effects.

Artemisia herba-alba (white wormwood) that belongs to the Asteraceae family is an important evergreen medicinal and aromatic species in the Mediterranean basin, with antioxidant, antiviral, anti-inflammatory and hypoglycemic effects [1-3]. "Artemisinin" is the main phytochemical bioactive compound isolated from Artemisia sp. and has been shown to treats malaria (Plasmodium falciparum) [4]. Since 2006, the WHO adopted this component as first-line treatment against malaria [5].

SARS-CoV belongs to the Coronaviridae family, included 04 subfamilies namely $\alpha,\beta,\gamma,$ and δ coronaviruses. Three β -coronaviruses reported earlier were: severe acute respiratory syndrome (SARS-CoV) and Middle East respiratory syndrome (MERS-CoV) and severe acute

respiratory syndrome-2 (SARS-CoV-2 or Covid-19) that have caused pneumonic infections and mortality/morbidity risk [6].

SARS-CoV-2 affects the innate immune system by multiple ways, such as dysfunction of the macrophage, induction of oxidative stress, and increased the expression of the inflammatory cytokine, interleukins (IL-2 and IL-6), and tumor necrosis factor- α (TNF- α) [7].

The corona virus disease (COVID-19) or severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is the new respiratory viral infection that has started in Wuhan, province of Hubei (China) in December 2019. The most predominant symptoms of this disease are pneumonic inflammation, high temperature, dry cough, tiredness, and olfaction/gustation failures [8]. On the clinical level, this virus causes a dysfunction of immune system including the decrease of blood immune cells such as natural killer (Nk) cells, T helper (Th) cells and cytokines [9]. Elderly patients with chronic diseases such a hypertension, diabetes, obesity and pulmonary illnesses have a severe vulnerability to this virus [10]. Although the existence of many vaccines, about 9/10 persons from lower-income countries will not have access to SARS-CoV-2 vaccines till 2023 or later [11]. In this critical emergency, there are needs to continuous use of safety processes and all available alternative therapeutic practices to treat COVID-19 infection and lesser its propagation.

Coronavirus is continuously transformed through mutation, and new variants of this virus are emerged in many countries of the world, for example B.1.1.7 stain in United Kingdom, B.1.351 strain in South Africa, P.1 strain in Brazil, and B.1.617.2 strain in india. These variants seem to be more rapidly contagious than other strains, and actually no safe and effective vaccine has been approved to treat these variants.

Many reports were proved the beneficial properties of artemisinin and its derivatives against many respiratory diseases. Based on its

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antiviral and anti-inflammatory properties of *Artemisia herba-alba*, we hypothesis that use of the phytochemical components (artemisinin and artesunate) extracted from this medicinal shrub can enhance immunity against COVID-19 infection.

Artemisinin (sesquiterpene lactone) is the main active component of Artemisia herba-alba and displays antimicrobial and antiinflammatory proprieties (Figure 1). It was demonstrated that this phytochemical agent had an active action against malaria due to its endoperoxidase characteristics and safe toxicity profile [4,12]. Artesunate (an artemisinin derivative) (Figure 2) possess antiinflammatory properties by its inhibition of tumor necrosis factoralpha (TNF-α)-induced production of pro-inflammatory cytokines in human rheumatoid arthritis fibroblast-like synoviocytes [13]. The activation of nuclear factor kappa B (NF-kappa B) has an important role in inflammatory response of many respiratory diseases including coronavirus [14,15]. In this way, it was proved that both artesunate and artemisinin decrease viral protein synthesis and prevent NFkappa B down-regulation under the first phase of viral replication [16,17]. Lu YY, et al. (2010) [18], demonstrated that artemisinin induced apoptosis through reactive oxygen species (ROS). Similar findings were made by Zhou C, et al. (2012) [19], who observed that artesunate stimulated apoptosis via a Bak-mediated caspase in lung adenocarcinoma cells. Artesunate pre-treatment has been shown to prevent lung inflammation through decreasing ROS-promoted NLRP3 inflammasome activation [20] or via down-regulation of inflammatory cytokines [21]. Liu Z, et al. (2018) [20], found that nasally addition of 10-100 mg⁻¹kg⁻¹day⁻¹ of artemisinin significantly inhibits allergic rhinitis [22]. In another study, addition of 10 μM of artesunate improves significantly pulmonary fibrosis, and attenuates asthma (airway inflammation) [23]. Suppression of metastasis was achieved

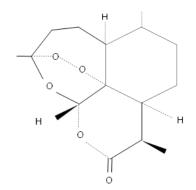


Figure 1: Artemisinin

Figure 2: Artesunate

when 7.5-30 μ M of dihydroartemisinin was applied to non-small-cell lung cancer [24]. It was also determined that application of 5-7 mol L⁻¹ of dihydroartemisinin was effective to alleviate oxidative stress in pulmonary fibrosis [25]. Recently Uzun T, et al. (2020) [26], indicated that Artesunate can substitute chloroquine in coronavirus treatment due its endocytosis inhibition mechanism. Jiang W, et al. (2016) [27], showed that artesunate addition leads to decrease an interleukin 6 receptor (IL-6) level which occurs largely during COVID-19 infection [28.29].

The integration of traditional medicine into conventional preventive cure may be an alternative approach in the absence of approved treatment of COVID-19. *Artemisia herba-alba* could be used as potential therapeutic shrub against COVID-19 and its emerging strains due its antiviral and anti-inflammatory proprieties. However therapeutic efficacy and clinical treatment by *A. herba-alba* ought to be still approved.

Abbreviations

COVID-19: Coronavirus disease-2019;

IL-2: Interleukin-2;

IL-6: Interleukin-6;

MERS-CoV: Middle East respiratory syndrome;

NF-kappa B: Nuclear factor kappa B;

Nk: Natural killer cells;

ROS: Reactive oxygen species;

Th: T helper cells;

TNF-α: Tumor necrosis factor-alpha;

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2;

WHO: World Health Organization.

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Conflicts of Interest

The author declares no conflict of interest.

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