



Contents lists available at ScienceDirect

Journal of Integrative Medicine

journal homepage: www.jcimjournal.com/jim

Traditional Chinese medicine is a resource for drug discovery against 2019 novel coronavirus (SARS-CoV-2)

Novel coronavirus pneumonia, named as COVID-19 by the World Health Organization, has spread widely since December 2019 [1–3], with more than 40,000 confirmed cases in China and exportations to over 20 countries [4]. On January 30, 2020, the World Health Organization declared the epidemic to be a public health emergency of international concern in the second meeting of the Emergency Committee [5]. It was recommended that potential vaccines and antiviral medicines should be developed. However, the development of these therapeutics will take months, even years. For this specific indication, rapid performance of traditional Chinese medicine (TCM) can contribute as an alternative measure.

In 2003, patients with severe acute respiratory syndrome (SARS) who were treated with TCM benefited from shorter hospitalization, decrease in steroid-related side effects, and improvement of symptoms [6]. Notably, genomic and *in silico* structural characterization of novel coronavirus revealed that it is closely related to the SARS coronavirus, further suggesting that TCM may have potential use in the current outbreak [7]. Indeed, the China government is advising doctors to consider combining Western antiviral drugs with TCM remedies in combating novel coronavirus pneumonia. However, there were few studies to help select suitable herbal drugs before costly biological experiments and clinical trials.

Classically, whether a TCM remedy can be clinically used for viral infections depends on two aspects: 1) clinical symptoms and signs of the patient, and 2) the type of TCM remedy and its traditional indications. TCM formulas have been used in China over 2000 years. According to their effectiveness, TCM remedies are divided into various types, each corresponding to a group of diseases. On the other hand, research has shown that many TCM remedies have antiviral ingredients. Selecting specific TCM formula through integrative methods based on both disease symptom and pathogen-directed cause will greatly increase the clinical potential. However, it is still a challenge to experimentally screen many TCM remedies for the treatment of novel coronavirus pneumonia in a short time.

In this issue of the *Journal of Integrative Medicine*, Zhang et al. [8] provided *in silico* methods to narrow down TCM remedies that may directly inhibit the coronaviral reproduction. Two principals for selection were proposed: oral effectiveness to inhibit viral infection and compatibility of patient manifestation. The identified TCM remedies should contain anti-novel coronavirus chemicals that meet the requirement for orally administered medical drugs. Meanwhile, the identified TCM remedies should be of the types

of TCM remedy that have activity against virus-caused pneumonia. To this end, the authors conducted a series of *in silico* analyses. A number of natural compounds were selected, which were experimentally validated for their potential activity against SARS or Middle East respiratory syndrome coronavirus. These chemicals were then evaluated for their suitability for oral administration. Most importantly, the molecular structures of these natural compounds were evaluated for their ability to interact, or dock, with the main proteins of the novel coronavirus. Positive docking suggested their ability to inhibit the novel coronavirus infection. In order to comply with patient manifestation, the authors conducted another three rounds of screening. First, TCM herbs that contained at least two of the above natural compounds were selected from the Traditional Chinese Medicine Systems Pharmacology (TCMSPT) database [9]. These medicinal plants were classified by the types of diseases they are used to treat. Only those belonging to the types that have been classically used to treat viral pneumonia were selected for further studies. Next, comprehensive evaluation of the effectiveness of these TCM herbs was performed. The authors downloaded its documented chemical constituents of each herb and analyzed their cellular protein targets for network pharmacological analysis. All these processes found that at least 26 TCM herbs have potential *in vivo* anti-novel coronavirus effects and can simultaneously regulate host inflammation responses.

This work highlights the prospect of computer-aided, structure-based TCM drug discovery for the novel coronavirus pneumonia. These approaches helped to narrow down the large libraries of compounds into a subset in a relatively short time with limited resources; they also provided guidance for the future clinical use of TCM formulas. Although the potential is great, at the same time, we need to be fully aware of challenges and limitations faced by these tools. Computational prediction is a bridge between theory and experiment, and further research is needed. Inhibitory assays and crystallography should be performed to confirm the interaction of the herbal compounds with viral proteins and structures. It is worth noting that in a recent study to identify potent ebolavirus inhibitors, only two of the eight compounds selected by *in silico* screening showed inhibitory properties, reflecting the limited reliability of the computational scoring functions [10]. The decoction of the selected 26 TCM herbs should be tested for their effectiveness and safety in both cell cultures and animal models. Eventually, TCM remedies should be evaluated in carefully

designed clinical trials, either used alone or integrated with Western medicine, to cover the prevention, treatment and recovery of patients suffering from the novel coronavirus pneumonia. Before the release of successful clinical trial data, we shall keep cautiously optimistic. Lessons from a recent public panic buying spree, in which results from a preliminary study were announced and triggered irrational purchases overnight, should be heeded.

It is a pivotal moment in defeating the current outbreak of the novel coronavirus. With the data published by Zhang's group, TCM practitioners around the world may speed up the experimental research and clinical use of these remedies, especially in those countries, territories or areas with reported and confirmed cases of COVID-19. Although the difficulties and challenges are fully recognized, we are looking forward to increasing the contribution and benefits from TCM professionals that will provide treatment to many patients with pneumonia caused by 2019 novel coronavirus (2019-nCoV), a new virus also named as SARS-CoV-2 by the International Committee on Taxonomy of Viruses.

Funding

This study was supported by National Natural Science Foundation of China (No. 81430101). The funding source had no role in writing or submission of this article for publication.

Conflicts of interest

The author declares that there is no conflict of interest.

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Received 11 February 2020

Accepted 13 February 2020

Available online xxxx