Commentary Article

Evaluation of Traditional Chinese Medicine Xuanfei Baidu Decoction in Immune Modulation that may Contribute to COVID-19 Treatment

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DESCRIPTION

Coronavirus disease 2019 (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) continues its damages and has become a serious health risk all over the world. Despite several vaccines have been marketed, the symptomatic treatment is still the main therapeutic way for COVID-19 patients. Identification of effective medication consequently is vital and highly-considered all over the world. Traditional Chinese Medicine (TCM) has been actively participated in prevention and suppression of COVID-19 in China. With the understanding and experience in treating viral infectious pneumonia, doctors of TCM have proposed a series of prescriptions against COVID-19. Early of 2020, the National Health Commission of the People's Republic of China and the National Administration of Traditional Chinese Medicine recommended a notable medication regimen of TCM known as "three medicines and three formulas", which Xuanfei Baidu Decoction (XFBD) was included. It is consequently highly concerned and great expected that treatment with TCM may help win the battle with SARS-CoV-2. Based on the clinical data, XFBD combined with conventional medicine may improve clinical symptoms, shorten the time for temperatures to return to normal, and increase the number of white blood cells and lymphocytes to improve immunity. However, the mechanism for regulating immunity needs to be further confirmed.

In this paper, we focused on the regulatory effect of XFBD on the immunosuppressive state, one of the early typical symptoms for COVID-19, and results showed that XFBD enhanced the immune function in immunosuppressive mice [1]. XFBD significantly suppressed body weight loss and increased the indices of spleen and thymus in cyclophosphamide-treated mice. The pathological alteration in liver, spleen and thymus were all much improved after XFBD administration. The reductions of TNF-α, IFN-γ, IgG and IgM levels in serum and IL-2, IL-4, and IL-6 expressions in spleen were all significantly alleviated by XFBD. Splenic lymphocyte proliferation in response to LPS was further enhanced after treatment with XFBD. The reduction of $CD4^+$ and $CD8^+$ T lymphocytes in cyclophosphamide-treated mice were also highly increased in XFBD groups. These findings supported one of the possible ways of XFBD that suppressed the worsen process of COVID-19 by early prevention of virus infection because of a strong immune defense ability of the host.

As far as we have known, an intricate regulatory mechanism including combatting viral infections, immune modulation, anti-inflammation, and the suppression of lung injury and fibrosis is involved in TCM against COVID-19. Therefore, the holistic mechanisms of XFBD against COVID-19 have also been elucidated in our group. For instance, the anti-inflammatory activity of XFBD has been found in LPS-induced acute inflammatory mice model and XFBD significantly alleviated pulmonary inflammation and decreased the levels of serum pro-inflammatory cytokines. Transcriptomic profiling suggested that genes related to macrophage function were differently expressed after XFBD treatment. For cellular assay, the anti-inflammatory effect of XFBD has been investigated in LPS-induced THP-1 monocytes and RAW 264.7 macrophages. As we expected, XFBD significantly inhibited LPS-induced IL-6, IP-10 and TNFα expressions in THP-1 cells and TNF-α, IL-6 and IL-1β secretions in RAW 264.7 cells, indicating an immune-modulatory effect of XFBD in a bidirectional manner. Compounds from XFBD also inhibited spike protein of SARS-CoV-2 binding to Angiotension-Coverting Enzyme 2 (ACE2) receptor and virus replication. The effect of XFBD on the immune regulation is also being well-investigated particularly in natural killer cells and neutrophils. Of course, the effects on virus-infection are being detected in BSL-3 laboratory. Pre-experiments data indicated the roles of XFBD in different areas, which may together help anti-SARS-COV-2 for COVID 19 patients.

As a mixture, identification of active compounds in decoction is a crucial issue that requested and concerned for its therapeutic effect. By employing high-resolution mass spectra combined molecular networking to apply for the profiling major substances of XFBD, a total of 154 compounds have been identified or tentatively characterized, including flavonoids, terpenes, carboxylic acids. UPLC data showed that the top ten contents in the freeze-dried powder of XFBD are: ephedrine, amygdalin, sinapine, hastatoside, verbenalin, polydatin, liquiritin, acteoside, naringin and glycyrrhizic acid. Previously, the roles of herbs in XFBD have also been defined according to the classical composition theory of TCM known as "Monarch, Minister, Assistant and Guide". Consistently, the network pharmacology-based analysis identified the biological pathways including viral infection and anti-inflammation is also highly related with the main active herbs *Polygoni Cuspidati Rhizoma Et Radix*. and *Verbenae Herba*. Currently, we are trying to uncover the active components XFBD in immunomodulation, especially immune-enhancement.

It is still a long way to give comprehensive explanation of XFBD for COVID-19 treatments. Many attempts and joint researches from sino and international groups are making concerted efforts, and at least, the founding of XFBD in enhance host immune function may be considered as a first step and it strongly encouraged us to continue the research and uncover the mechanism of XFBD and also provide ways that contribute to the final victory when beat COVID-19 in the future.

REFERENCES

1. Yan H, Lu J, Wang J, et al. Prevention of Cyclophosphamide-Induced Immunosuppression in Mice with Traditional Chinese Medicine Xuanfei Baidu Decoction. Front Pharmacol.2021.

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