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Yupingfeng Prescription, a Complementary Strategy against Corona Virus Disease 2019 (COVID-19)?

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Abstract

The Corona virus Disease 2019 (COVID-19) has led to unprecedented health emergency over the world. Till May 2, 2020, over 240,000 people were died due to this serious viral prevalence. Unfortunately, few specific drugs have been developed so far. *Yupingfeng* prescription is a commonly used Chinese preparation to treat lung disease in China. It was showed that *Yupingfeng* prescription had immune regulation, anti-inflammatory and organ protection actions. Recent advances also showed that *Yupingfeng* prescription may protect against COVID-19 patients based on the network analysis. Nevertheless, the clinical data for its use in COVID-19 was lacked. This review will summarize the effects of *Yupingfeng* prescription in the laboratory and clinical researches, in order to provide a complementary strategy in COVID-19 treatment and put forward promising insights for its further studies.

Keywords: Corona virus; SARS-CoV-2; *Yupingfeng* prescription

Abbreviations

ACE2: Angiotensin-Converting Enzyme 2; COPD: Chronic Obstructive Pulmonary Disease; COVID-19: Corona Virus Disease 2019; HIF-1: Hypoxia-Inducible Factor 1; HMGB1: High-Mobility Group Box 1; IL: Interleukin; KEGG: Kyoto Encyclopedia of Genes and Genomes; SARS-CoV-2: SARS Corona Virus 2; TGF-β1: Transformed Growth Factor-β1

Introduction

The Corona Virus Disease 2019 (COVID-19) outbreak which is caused by SARS Corona Virus 2 (SARS-CoV-2) has caused a major challenge to public health. Till May 2, 2020, over 3,400,000 people have been confirmed infected and more than 240,000 people were died due to this serious attack. However, no specific anti-SARS-CoV-2 candidates or vaccines were found yet. Recently, traditional Chinese medicine has been getting more and more attention by the public, governments, as well as World Health Organization.

Yupingfeng prescription (*Yupingfeng* san, *Yupingfeng* powder or *Yupingfeng* granule) is a classical traditional Chinese medicine composing of three herbs including Radix Astragali (Huangqi in Chinese), Rhizoma Atractylodis Macrocephalae (Baizhu in Chinese), and Radix Saposhnikoviae (Fangfeng in Chinese) at a ratio of 3: 1: 1 [1]. Emerging studies showed that *Yupingfeng* prescription had immune regulation, anti-inflammatory and organ protection actions. Recent researches also showed that *Yupingfeng* prescription may protect against COVID-19 patients based on the network analysis. Here the role of *Yupingfeng* prescription in the laboratory studies and clinical trials were summarized to release its current advances. Surprisingly, recent evidence also revealed that *Yupingfeng* prescription may protect against COVID-19 based on its extensive and definite pharmacology actions which would fuel further related researches.

Laboratory Studies of *Yupingfeng* Prescription and Its Extracts

It has been reported that the extracts from *Yupingfeng* could ameliorate bleomycin-induced lung injury by alleviating High-Mobility Group Box 1 (HMGB1) activity and Transformed Growth Factor-β1 (TGF-β1) activation [2]. Further studies also showed that the total glycosides and polysaccharides of *Yupingfeng* could also reverse lung abnormality by inhibiting the excessive deposition of extracellular matrix and continuous lung consolidation [3,4]. In ovalbumin-induced allergic asthma in rats, *Yupingfeng* could reduce the serum Interleukin (IL)-4, IL-5 and IgE levels, increase the level of IFN-γ, reduce the total number of cells in alveolar lavage fluid, and improve the abnormal lung histomorphologic changes [5]. After treatment with *Yupingfeng*, the tumor volume of subcutaneous transplantation of prostate cancer in mice was decreased, the lymphocyte

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proliferation ability and NK cell killing activity were enhanced, while the serum contents of IL-2, IFN-γ and TNF-α were increased, which is related to the enhancement of immune function in mice [6]. This evidence revealed that *Yupingfeng* exerted diverse actions including the anti-inflammatory and immune regulation activities, as well as the lung protection potential.

Clinical Trials of *Yupingfeng* Prescription

Recent clinical trials had proven that *Yupingfeng* could restore the immune suppressor function of regulatory B cells *via* inhibiting the expression of Bcl2L12 in allergic rhinitis patients [7]. *Yupingfeng* treatment also had a significantly lower exacerbation rate and a significantly reduced risk of second exacerbation in patients with Chronic Obstructive Pulmonary Disease (COPD) by a randomized, placebo-controlled study [8]. In the treatment of bronchial asthma in children, *Yupingfeng* combined with routine treatment had significant higher total effective rate and obviously improved lung function accompanied with decreased number of asthma recurrence when compared to routine treatment [9]. Meanwhile, the duration of asthma attack was significantly shorter [9]. Further study observed the curative efficacy of adjuvant therapy of *Yupingfeng* in bronchial asthma children with recurrent respiratory tract infection and its influence on humoral immunity function [10]. Adjuvant therapy of *Yupingfeng* therapy had less times of respiratory tract infection, shorter asthma wheeling time, higher levels of serum IgA, IgG (humoral immunity indices), and shorter time of using antibiotics [10].

A systematic review and meta-analysis of randomized controlled trials were performed to evaluate the benefits of *Yupingfeng* in treating primary nephrotic syndrome in children [11]. The analysis showed that *Yupingfeng* could improve total remission rate and decrease the frequency of relapse and infection rate of primary nephrotic syndrome in children, and the beneficial influence of *Yupingfeng* was associated with its immunomodulatory effects [11]. Another meta-analysis suggested that the adjuvant treatment with *Yupingfeng* could improve total clinical effective rate and decrease the frequency of respiratory tract infections in children with recurrent respiratory tract infections [12]. Chen and colleagues demonstrated that *Yupingfeng* could strengthen specific and non-specific immunity of the organism, and improve clinical symptoms and the level of myocardial enzyme spectrum in treating chronic persistent bronchial asthma children [13].

Recent Evidence of *Yupingfeng* Prescription in COVID-19

In addition to the above benefits of *Yupingfeng* in treating different diseases, *Yupingfeng* has also been proved that the core active ingredients in *Yupingfeng* could target SARS-CoV-2 receptor, the Angiotensin-Converting Enzyme 2 (ACE2) [14-17]. Wu et al., have recently reported that *Yupingfeng* may have great application value in the prevention of COVID-19 due to its effects on both strengthening the immune function of the body and improving the ability of disease resistance [14]. Through the network pharmacology and molecular docking analysis, the active compounds such as kaempferol, cleomiscosin A and hederagenin in *Yupingfeng* had certain affinity with SARS-CoV-2 3CL hydrolase and ACE2, by regulating multiple signal pathways [15]. It was also revealed that the quercetin, kaempferol, 5-O-methyramitol and other active compounds in *Yupingfeng* powder could target PTGS2, DPP4, HTR, PTGS1 and HSP90AA1 to regulate multiple signal pathways, through which may play a preventive and therapeutic role in COVID-19 [16]. Zhan et al., recently proved that a total of fifty pathways were obtained from *Yupingfeng* by Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis, such as PIK3R1 target regulation PI3K-Akt signaling pathway, Ras signaling pathway, Hypoxia-Inducible Factor 1 (HIF-1) signaling pathway, MAPK signaling pathways and T cell receptor signaling pathways, which plays a role in the prevention of COVID-19 [17].

Discussion

In the clinical treatments for COVID-19, anti-infection, anti-inflammation, as well as antiviral therapies and organ protection were the basic strategies [18]. Recently, growing oral natural products-derived drugs were confirmed effective against COVID-19. Here we briefly summarized the role of *Yupingfeng* in laboratory and clinical researches, as well as its network analysis focusing on COVID-19. The review showed that *Yupingfeng* has anti-inflammatory and immunomodulatory activity, and protects lung injury as well as the abnormal lesions of other organs. Moreover, recent data also showed the ingredients in *Yupingfeng* has anti-SARS-CoV-2 potential by the Chinese medicine theory or network pharmacology researches.

However, the recent advances lack the direct clinical studies of *Yupingfeng* in treating COVID-19. Whether *Yupingfeng* actually benefits COVID-19 patients is still a question mark. Thus, in order to conquer this viral attack, further efforts are urgent needed to discover the clinical effects of *Yupingfeng* in COVID-19 patients, especially *via* the well-designed randomized controlled trials.

Conclusion

The collected evidence revealed that *Yupingfeng* may be a complementary strategy in COVID-19 treatment by exerting immune regulation, anti-inflammatory and organ protection actions. But more high-quality clinical studies with larger sample sizes are needed to further identify the efficacy of *Yupingfeng* prescription.

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