

## Network Pharmacology Study of Boosting effect from Aiye Herb on Anti-covid Properties of Cangzhu

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### Abstract

**Introduction:** Cangzhu, an herbal medicine used to treat symptoms of respiratory pneumonia in traditional Chinese medical system, has shown its effectiveness in combating fever, cough, and fatigue of current pandemic while no specialty drugs are available. Latest research in network pharmacology has confirmed the theoretical mechanism behind, the drug itself is commonly prescribed alone side another herb Aiye, which believed to be able to improve the effectiveness of Cangzhu. In this study, network pharmacology will be applied in search of potential mechanism behind.

**Method:** The Traditional Chinese Medicine Systems Pharmacology (TCMSP) is used to filter the active compounds and the target of the prescription compound. The Genecard and OMIM database are applied to identify the target related to our aim symptom fever, cough, and fatigue. The STRING database is used to analyse the intercepted targets. Compound-target interaction and protein-protein interaction networks are constructed using the Cytoscape between target disease Covid and our medicine mixture Cangzhu and Aiye. The Kyoto Encyclopaedia of Genes and Genome (KEGG) pathway and Gene Ontology (GO) enrichment analysis are performed for investigation of the molecular mechanisms. Finally, the interaction probability between the targets and the active compounds can be determined by molecular docking technology.

**Results:** A total of 14 target are identified, in which are 10 most important targets and 2 key compounds. Besides, 216 biological processes items are obtained ( $P < 0.05$ ). Two hundred and seventy-one pathways are obtained ( $P < 0.05$ ). The result of molecular docking shows a stable binding between the active compounds and the target.

**Keywords:** Cangzhu; Aiye; Covid-19; Network pharmacology; molecular docking; symptoms; Efficacy boost

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## 1 Introduction

From the disease firstly reported in Wuhan China on 31<sup>st</sup> December 2019 [1], Covid 19 has been around us for almost two years. As of 7:37 pm CEST 14<sup>th</sup> July 2022, there have been 556 897 312 confirmed cases of infections including 6 356 812 deaths reported to the World Health Organization [2]. Alone in the country of United States of America, despite widespread of availability of Covid 19 vaccines and advanced medicinal technology, a death toll of 675 455 was reported by John Hopkins University on 20<sup>th</sup> September 2021, surpassing the record number from 1918 Influenza Pandemic, marking a shameful and painful milestone in the human history [3].

Major clinical diagnostic feature of Covid 19 is Ground-Glass-Opacity (GGO) in lung CT scans, accompanied by more common symptoms of cough, fever and fatigue, and more rarer symptoms as body pain, diarrhoea, loss of taste and smell, body discoloration as well as more severe symptoms such as chest pain, breathing difficulties and loss of mobility [4]. In China, parallel to the modern medical diagnosis and treatment method, the well preserved and refined traditional medical system has proved its value and efficacy on treating patients and ending pandemics in the nerve wracking 76 days in the battle of the disease in the city of Wuhan. In TCMSP Covid-19 is classified as a Pandemic with a sub-classification of wet toxic pandemic. The basic Pathogenesis is explained as invasion of foreign toxicity, negative influence on lungs and related respiratory system, lack of positive physical inertia, with pathological properties of humid, heat, toxicity, weakness, and inadequate blood flow [5].

Traditional Chinese Medicinal System is a summary and inheritance of diagnosis and treatment measurements from pharmacist, physicians, and therapist, with a documented and traceable history for more than 2000 years. As Miss Youyou Tu being awarded the Nobel Prize in Physiology and Medicine in 2015 for finding a cure of Malaria based on traditional Chinese medical science, which saved life of millions [6], the long ignored and vilified traditional medical system gradually becoming popular research field of modern medical science.

Cangzhu, also known as Black Atractylodes rhizome or Rhizoma Atractylodes, is the dried rhizome of *Atractylodes Lancea* (Thunb.) DC., *Atractylodes Chinensis* (DC.) Koidz, or certain other local species including *Atractylodes Japonica koidz* [7]. Compounds isolated from a hexane extract of *A. Lancea* included atractylochromene, a potent inhibitor of 5-lipoxygenase (IC<sub>50</sub> 3.3 μmol L<sup>-1</sup>) and cyclooxygenase (IC<sub>50</sub> 0.6 μmol L<sup>-1</sup>); 2-[(2E)-3,7-dimethyl-2,6-octadienyl]-6-methyl-2,5-cyclohexadiene-1,4-dione, a selective inhibitor of lipoxygenase (IC<sub>50</sub> 0.2 μmol L<sup>-1</sup>); atractylon and osthol, weak inhibitors of lipoxygenase, and atractylenolides I, II, and III [8]. A prenylated dihydrobenzofuran derivative isolated from *A. Lancea*, trans-2-hydroxyisoxypyl-3-hydroxy-7-isopentene-2,3-dihydrobenzofuran-5-carboxylic acid, was found to be cytotoxic to two cancer cell lines tested [9]. In ancient application in TCMSP, *A. Lancea*, according to *Compendium of Materia Medica*, has the ability to counter respiratory inflammation and to stabilize the blood circulatory system. It is also recorded by the same source, that *A. Lancea* is widely burned in open air during pandemic to decrease the viral transmission [10]. In modern TCMSP, it is proven chemically that *A. Lancea* and the β-eudesmol, hinesol containing volatile oil extract can significantly improve the human blood circulation and bloody oxygen level [11]. In China, despite the herb has been widely used for epidemic prevention and control, the mechanism of function is only being confirmed by the latest Network Pharmacology research [12]. In order to boost the efficacy, portion of Aiyue is also commonly prescribed alongside. In this research, the boosting effect will be researched with Network Pharmacology.