

## A Family Rice Faber an Anti-Viral Activity

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### Abstract

#### Background

A corona pandemic has been spread all over the world emerging some mutant's sub-strains. Many trials were reported including anti-viral agent and vaccines in many developing countries. However, none of the system remained to be absolute for concur this evil corona virus.

Therefore, we tried to review the traditional method for impel the way for this microorganism, especially suggesting traditional food additives. Coronavirus 2 (SARS-CoV-2) and has now spread to more than 200 countries and territories, infecting 222,097 persons at December 2021 and 2.059 daily death in US. Therefore, we tried to review the traditional method for impel the way for this microorganism, especially suggesting traditional food additives. Coronavirus 2 (SARS-CoV-2) and has now spread to more than 200 countries and territories, infecting 222,097 persons at December 2021 and 2.059 daily death in US. The mugwort had been traditionally used as food additive as well as famous health care material, such in muxibution can reported as traditional health care in Eastern Asian countries. Our in vitro experiment also by the human cytomegalovirus (HCMV) of the DNA virus and the coronavirus pneumonia virus of RNA virus were suppressed for replication by this material.

**Keywords:** Anti-virus Agent, Corona Virus, Mugwort, Artemisinin

### Introduction

Mugwort (*Artemisia indica* Willd. var. *maximowiczii*) had been traditionally included in daily life of Japan. For mugwort had been succeeded to employ as medicinal plant in East Asian countries as food additive as well as health care substance, including heating therapy such as in moxybuton. In Japan special rice cake that turn to  $\beta$ - to  $\alpha$ -polysaccharide had been prepared artificially in early spring in order to featuring newly grown mugwort for traditional foods. For the people had been confirmed and including their annual life for health maintenance especially for infectious disease by the microorganism.

### Materials and Methods

Human embryonic pulmonary fibroblast (HEL), obtained from human fetal lungs cultivated in 9.6 cm<sup>2</sup> shell until confluence with Dulbecco Modified Eagle Medium (DMEM) medium was carried out, supplemented with 8% amount of fetal bovine serum (FCS). Towne strain of HCMV has been adsorbed and infected in a variety of infections (MOI) = 1 in HEL cells. After incubation at 37 °C for 1 hour, concentrations of 0.1, 1, 10 m of mugwort or novel compounds

were added and cultivated for 6 days, and infectious HCMV numbers in the culture supernadoting were quantified by the plaque method. In the plaque method, HEL cells cultivated to flow into a 24-wells plate were adsorbed on a culture supernadote that was diluted for 1 hour at 37 °C 1 hour and then superimposed with DMEM medium with 2% FCS and 0.4% agar for cultivation. After several days (6 to 12 days), the number of plaques displayed under the microscope was counted and the viral load measured.

### Results

Mugwort (*Artemisia indica* Wild. var. *maximowiczii*) are reported medicinal plant to improve health maintenance especially in East Asian countries at least in Japan. Mugwort had been succeeded in East Asian countries as food additive as well as health care substance, including heating therapy famous for as in moxybuton. In Japan special rice cake that turn to  $\beta$ - to  $\alpha$ -polysaccharide had been prepared artificially in early spring in order to featuring newly grown mugwort for traditional foods. Comparison of the antiviral effect of GCV, mugwort, Anti-HCMV effects were investigated or several novel compounds found by docking simulation.

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Here the results that show the most significant effect are shown. The novel compound had been found to exhibit a stronger anti-HCMV effect compared to GCV and mugwort. Next EC-50 values were determined and compared. .

## Conclusion

The network pharmacological strategy integrated molecular docking to investigate the mechanism of action of AHI against COVID-19. It provides artemisinin as active component associated with COVID-19 that can be further tested as therapeutic targets of evil viruses.

## Introduction

Novel coronavirus pneumonia (COVID-19) was first reported in Wuhan, China, in late December 2019 and has rapidly spread to more than dozens of countries, including the United States, with thousands of infected people and hundreds of deaths within a month. By February 25, 2021, more than 444 million cases had been identified in the United States, and a total of 50 thousand cases had been reported in Japan [1-4]. It is of great importance to look for fast and effective therapeutic drugs for COVID-19. Drug recycling is a common strategy in the search for antiviral treatment.

Network pharmacology is considered a promising approach to cost-effective drug development and has often been used to support the active ingredients of some Traditional Japanese medicine and its mechanisms of action [5-7]. It has transformed the research approach “one goal, one drug” into a strategy “network goal, multi-components”. Using the derivatives of mugwort, the targeting method for natural products was used based on the PubChem database, the targeting method is fast and could provide a relatively accurate result without the support of high-performance computing. Based on the principle of structural biology, molecular docking can be used to perform virtual drug screenings via a computer-aided drug molecular biology design. Therefore, molecular docking is an effective way to find and identify drug targets by filtering the docking energy and space between molecules and targets [8, 9]. The integration of molecular docking and network pharmacology is helpful to accelerate the progress of target determination and experimental verification. In this study, a technology-based strategy integrated with molecular docking was used to investigate the mechanism by which AHI COULD potentially improve COVID-19 to provide scientific evidence for clinical drugs [10].

## Material and Method

Target materials are plant materials derived from Mugwort CAM Derivatives (KCI). The first prejudices for selection are based on the virus infectious diseases, such as small pox, coronavirus pneumonia, hepatitis type B, C and D, cancer, etc.

## Background and invention

### Objective

To date, we have found that Mugwort (main component is Artemisinin), one of the components contained in (Mugwort in Japan), the expression of the human cytomegalovirus (HCMV), a strong antiviral effect against many DNA viruses and RNA viruses (varicella zoster virus, hepatitis B virus, coronavirus pneumonia virus, Zika virus, etc.), and its mechanism of action has been confirmed by a host factor that has not been explained so far (especially chemokine) Furthermore, since Mugwort is present in nature, no significant toxicity has been observed in ex vivo cell toxicity tests and toxicity tests in mouse in vivo.

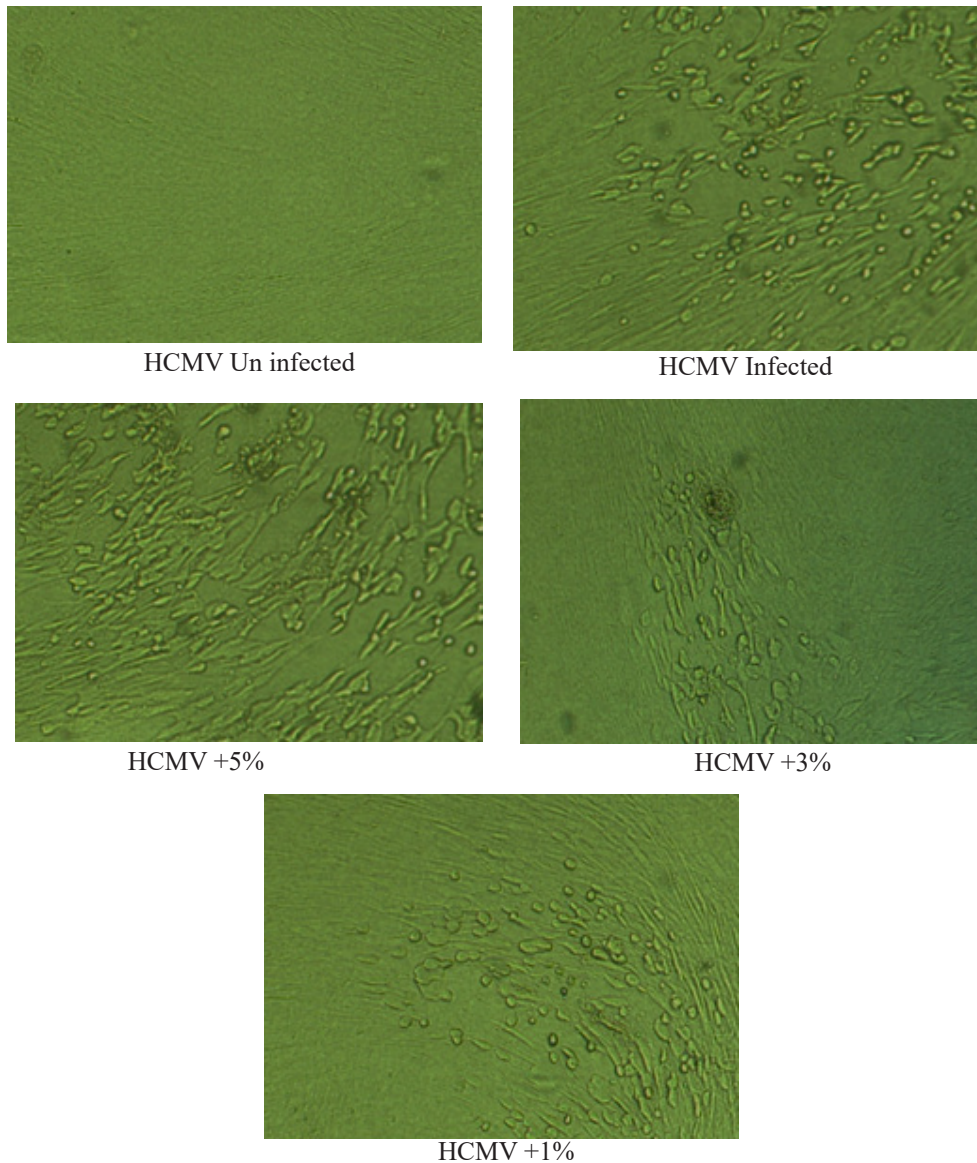
Ganciclovir (GCV) currently used worldwide as an anti-HCMV drug has a strong specificity for HCMV infected cells and acts as a viral DNA synthesis inhibitor and exhibits strong anti-HCMV effects. However, as it is used over a long period of time, the pressure on medical expenditure and the appearance of viruses resistant to GCV is becoming a major social problem, and it is desirable to introduce new novel drugs with different mechanisms of action. Therefore, we looked for ingredients in herbal medicine and discovered Mugwort, which is more contained in Gramineae plants (we extract from Mugwort), and as a result of the study it showed antiviral effects on host factor, chemokine, dependence, which I made clear. However, since the anti-HCMV effect of Mugwort is slightly weaker than GCV, it aimed to look for new compounds that show strong activity via GCV and Mugwort.

## Strategy

With Mugwort as a key drug, we wanted to discover new compounds via Mugwort and GCV by adding compounds. Several candidate compounds with fluorine were found and synthesized from the docking simulation for cyclin - dependent kinase 9 (CDK - 9) by imaging with the in silico, and the antiviral effect was compared and investigated.

## Experimental method for anti-HCMV action

Human embryonic pulmonary fibroblast (HEL), obtained from human fetal lungs cultivated in 9.6 cm<sup>2</sup> shell until confluence with Dulbeccos Modified Eagle Medium (DMEM) medium was carried out, supplemented with 8% amount of fetal bovine serum (FCS). Towne strain of HCMV has been adsorbed and infected in a variety of infections (MOI) = 1 in HEL cells. After incubation at 37 °C for 1 hour, concentrations of 0.1, 1, 10 mg of Mugwort or novel compounds were added and cultivated for 6 days, and infectious HCMV numbers in the culture supernatant were quantified by the plaque method. In the plaque method, HEL cells cultivated to flow into a 24-wells plate were adsorbed on a culture supernatant that was diluted for 1 hour at 37 °C 1 hour and then superimposed with DMEM medium with 2% FCS and 0.4% agar for cultivation. After several days (6 to 12 days), the number of plaques displayed under the microscope was counted and the viral load measured.



**Figure 1:** Comparison of the antiviral effect of GCV, mugwort extracts, day 9th culture in vitro.

The antiviral activity against HCMV of GCV, mugwort, a novel compound was compared and investigated for EC50.

As a result, the EC50 values of GCV, H and novel compounds were 27.5, 54.3 and 0.13 nM, respectively. It has been revealed that the novel compound shows anti-HCMV effect of about 200 times GCV and about 400 times of mugwort.

In addition, neither nor novel compounds as a result of the study of cytotoxicity showed cytotoxicity and a direct injury effect on the virus to at least 10 M.

### Discussion

Coronavirus pneumonia is a highly infectious acute respiratory disease caused by coronavirus [11-16]. The World Health Organization estimates that about 1 billion people are infected with

coronavirus pneumonia each year, coronavirus pneumonia resulting in over 120,000,000. Patients in the world. The virus is highly infectious and has a high mortality rate, making it one of the biggest infectious diseases that seriously threaten human health. The appearance of coronavirus pneumonia-resistant strains has been accelerated by the strong use of antiviral drugs such as oseltamivir [17]. Therefore, it is particularly urgent to develop safe and efficient new anti-coronavirus pneumonia drugs [18-21].

In Japan, traditional Japanese medicine has been used for thousands of years to treat pneumonia in coronavirus with good safety and remarkable efficacy [22-26]. KCI comes from the book “Treatise on differentiation and treatment of epidemic febrile disease” and has been used for hundreds of years. At the same time, it is also one of the prescriptions recommended treatment for coronavirus pneumonia in Japan and its anti-coronavirus pneumonia and its

anti-corona virus pneumonia efficacy has been confirmed by clinical and experimental studies. In this study, network pharmacology was used to predict and investigate the targets of KCI against the coronavirus pneumonia virus and to investigate the mechanism of KCI in the treatment of coronavirus pneumonia [27-30], which provided a theoretical basis for subsequent in vivo and in vitro experimental studies of mugwort.

More and more studies have confirmed that TCM has a good effect on viral infectious diseases. A prospective, randomized, controlled study of participants confirmed that mugwort had a decoction of a shorter fever deposition time than oseltamivir in the treatment of coronavirus corona virus. The challenge experiment of the coronavirus virus also confirmed that KCI had a protective effect on mice. Mugwort derivatives could prolong the survival of infected mice and improve survival rates [31-36].

Currently, the Database of the Traditional Japanese Medicine Systems Pharmacology Database and Analysis Platform is the most widely used database for screening active ingredient components and targets in network pharmacology research. The general method of network pharmacology research is to review the components for achieving oral bioavailability (OB) and drug similarity (DL) in the TCMSP database and then to verify their corresponding objectives. The Sym Map platform integrates target information from HIT, TCMSP, HPO, Drug Bank and NCBI databases and is one of the largest target databases to date. However, only OB data from components is provided by this database, while DL data does not, and the corresponding targets of components cannot be retrieved directly. Therefore, we have skipped the step of screening active ingredients, and the goal with FDR (Benjamini-Hochberg Multiple Testing Correction) < 0.05 corresponds to any traditional Chinese medicine has been directly included.

This suggests that KCI may play an anti-coronavirus role corona virus by regulating TLR7/NF-B. As far as the MAPK pathway is concerned, some studies have reported that Raf/MEK/ERK signaling plays an important role in the spread of corona virus viruses. Mutation of Raf and ERK or treatment with MEK inhibitors (U0126) could significantly inhibit virus spread. Berberin is an important component of a variety of traditional Chinese medicines, and it can hinder the replication of coronavirus A by inhibiting the coronavirus nucleola export of viral ribonucleoproteins mediated in vitro by the ERK signaling pathway.

Through the antiviral drug market, 5.7 billion people are a major market in the world. In addition, there will be a large market for drug delivery, even due to the bias for the frequency of the outbreak and the appearance of drug-resistant virus strains [37-41]. The aim of this project is to supply a new antiviral agent KCI for the global market. The detailed amount of the production of antiviral agents includes USD 568 million after domestic production; 351 million U.S. dollars from underwater production. The use and production of antiviral agents will continue to increase, an increase in the market of about five times the previous year. The expanding

KCI market also allows for veterinary use. The development of KCI for the current market is much more necessary to promote the spread of resistant strains to the former clinical antiviral agents.

## Conclusion

From the above, it has been shown that 6F-Mugwort of a novel compound shows an anti-HCMV effect in a concentration of 1/200 to less than that of a known drug GCV widely used around the world, and no cytotoxicity has been observed. This suggested that the novel compound might be a promising new drug candidate. .

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