# 「漢方 COVID-19 薬探索 熱研・和漢研プロジェクト」

## The discovery of herbal drugs and natural compounds as inhibitors of SARS-CoV-2 infection in vitro

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## ■背景・目的

The emergence of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic in 2019 has led to a global health crisis. Mutations of the SARS-CoV-2 genome have impeded the development of effective therapeutics and vaccines against SARS-CoV-2. Natural products are important for discovering therapeutics to treat the 2019 coronavirus disease (COVID-19). To identify anti-SARS-CoV-2 drugs we screened 120 herbal extracts, 96 Kampo-related active compounds from a Kampo library which provided by the Institute of Natural Medicine (WAKANKEN) at the university of Toyama. After selected through the first in vitro assay, we detected three positive herbal extracts and two natural compounds for possible antiviral effect on SARS-CoV-2 infection. This study evaluated the inhibitory effects of those herbal drug extracts and natural compounds against SARS-CoV-2 infection in vitro.

## ■結果・考察

The antiviral activity of herbal drug extracts from Polygala Root, Areca, and Quercus Bark and natural compounds derived from herbal drug such as baicalin and glabridin, with $IC_{50}$ values of 9.5 μg/ml, 1.2 μg/ml, 5.4 μg/ml, 8.8 μM and 2.5 μM, respectively, against SARS CoV-2 infection in vitro.

The $CC_{50}$ values of Polygala Root ext., Areca ext., Quercus Bark ext., baicalin and glabridin were 186.3 μg/ml, 89.6 μg/ml, 381.1 μg/ml, > 1000 μM and 21.5 μM, respectively.

Consequently, the selectivity indexes (SI = $CC_{50}/IC_{50}$) of Polygala Root ext., Areca ext., Quercus Bark ext., baicalin and glabridin were 19.7, 73.6, 71.0, > 114.2 and 8.7, respectively.

Certain herbal drug extracts and natural compounds were found to inhibit viral RNA levels by quantitative real time RT-PCR and infectious titers of SARS-CoV-2 by infectivity assay in a dose-dependent manner.

Furthermore, NP expression in infected cells using western blot analysis and quantitative real time PCR for time-of-addition experiments showed that herbal drug extracts and natural compounds effectively inhibited SARS-CoV-2 in entry and post-entry treatments.

Our study revealed that three herbal drugs are good candidates for further in vivo and clinical studies.

## ■結論


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2. Ngwe Tun MM, Luvai E, Nwe K, Toume K, Mizukami S, Hirayama K, Komatsu K, Morita K. Anti-SARS-CoV-2 activity of various PET-bottled Japanese green teas and tea compounds in vitro. 2022. **Arch Virol**. doi: 10.1007/s00705-022-05483-x.