Guideline of prophylactic use of Kampo Medicine for

new coronavirus infection (COVID-19)

Kampo Industralization Consortium

Member

Kenji Watanabe (Representative director, Kampo Industralization Consortium, Eminent Professor, Yokohama University of Pharmacy)

Sung Joon Kim (Yokohama University of Pharmacy)

Chikano Shibayama (Daiichi University of Pharmacy)

Jun Imai (President, The Japan Kampo Medicine Association,)

INDEX

1. Introduction
2. The concept of Kampo medicine for infectious diseases
3. Guidelines of traditional medicine for COVID-19 in other countries 3
4. How to use this Guideline of prophylactic use of Kampo Medicine for COVID-19 4
5. Kampo medicine "Yojo" regimen4
6. Prophylactic use of Kampo Medicine for COVID-19 in people without an underlying disease4
7. Prophylactic use of Kampo Medicine for COVID-19 in people with underlying diseases 5
8. Prophylactic use of Kampo Medicine for other COVID-19 high-risk individuals7
9. How to handle after the onset of the fever8
10. Summary9
11. Acknowledgement

1. INTRODUCTION

Kampo Industralization Consortium has been working on various issues surrounding Kampo, from the utilization of Kampo to the securing of herbal medicines, and one of the major themes is the utilization of Kampo at the undiseased stage.

This is a summary of Prophylactic use of Kampo Medicine for the current epidemic of the new corona infection (COVID-19). In preparing this " Guideline of prophylactic use of Kampo Medicine for new coronavirus infection (COVID-19)" (hereinafter referred to as " guideline"), the opinions of many experts both in Japan and abroad, including the specialist who spearheaded traditional medicine in Wuhan City, have been referred to and summarized with a focus on Kampo medicine available in Japan.

Therefore, this guideline deals only with the period of time until the diagnosis of COVID-19 infection is confirmed by PCR, and once the diagnosis is confirmed, it is absolutely necessary to treat the disease in accordance with the national policy.

2. THE CONCEPT OF KAMPO MEDICINE FOR INFECTIOUS DISEASES

Infectious diseases have been a major threat in human history in both Western and Oriental medicine during the development of medicine. One of the Chinese classics written at the end of the Later Han Dynasty (late 2nd century AD), is "Shang han lun" 『傷寒論』. In the preface, the author Zhang Zhongjing

(張仲景) states that among 200 relatives, two-thirds died in 10 years and 70% of them died of the plague, which led the author to research and write this book. The history of mankind has been with fights against plagues, and Chinese herbal remedies have developed to overcome every time. We now have to use the wisdom we have developed over the years against this emerging infectious disease.

Traditional medicine says that body's defense function (inner qi) is against the plague (outer evil). At Diamond Princess (cruise ship), there was a case that a husband and wife were in the same room but only one of them developed the disease. That shows it is possible to prevent the virus from multiplying if one's "qi" or body's defense function is strong. Traditional medicine is to strengthen this body's defense function and eliminate the virus.

3. GUIDELINES OF TRADITIONAL MEDICINE FOR COVID-19 IN OTHER COUNTRIES

During current COVID-19 pandemic, 4,900 Chinese medical practitioners from all over China gathered in Wuhan to provide front-line treatment while 42,000 medical practitioners from all over the country also rushed to provide medical support. As a result, Chinese medicine intervention reduced the severity rate from 11% to 4%. Based on this experience, the country developed guidelines for traditional medical treatment (Central People's Government of the People's Republic of China Guidelines for the Treatment of New Type Corona Pneumonia (Trial 7th Edition), <u>http://www.gov.cn/zhengce/zhengceku/2020-03/04/content 5486705.htm</u>). Guidelines for traditional medical treatment have also been published in Korea and Taiwan. For more information, please refer to "The Role of Traditional Medicine in New Coronavirus Infections (COVID-19)" at <u>https://www.jmedj.co.jp/journal/paper/detail.php?id=14426</u>.

4. HOW TO USE THIS GUIDELINE OF PROPHYLACTIC USE OF KAMPO MEDICINE FOR COVID-19

This guideline is open to inform the general public about how Kampo medicine can be used for COVID-19. Therefore, the Kampo and herbal medicines listed here are just representatives of each case, and you should consult a doctor or pharmacist who is familiar with Kampo when actually taking medicines.

It is against the purpose of this guideline to be used by some mail order sites that engage in commercial opportunistic sales. Along with the disclosure of these guidelines, reliable medical institutions and pharmacies will be public as well, so please be sure to consult with them and use appropriate Kampo medicine and herbal medicine guided by experts.

5. KAMPO MEDICINE "YOJO" REGIMEN

How to spend everyday life is called "Yojo" (養生), self-curing in Kampo, and it has priority over all drug treatments. Basically, you need to take a well-balanced diet, moderate exercise, enough sleep, avoid stress and relax mentally. To avoid coldness, is always emphasized in Kampo, you need to be careful to your proper clothes according to different seasons. Especially, it is important to warm the lower part of the body below the waist. Try to warm your body from inside by eating and drinking. For instance, avoiding cold drinks or take cooked vegetables rather than raw. Also, smokers should quit immediately.

Before starting Kampo medicine, it is important to review your daily life and take good self-control.

6. PROPHYLACTIC USE OF KAMPO MEDICINE FOR COVID-19 IN PEOPLE WITHOUT AN UNDERLYING DISEASE

- 1) 玉屏風散 (Gyokuheifusan)
 - To whom catch cold and get tired easily, look pale, feel chill when the wind blows.
- 2) 生脈散(Shomyakusan)
- To whom have less physical strength, weak stomach and intestines, sweats frequently.
- 3) 補中益気湯(Hochuekkito) To whom have less physical strength or been exhausted.

The Following are crude drugs used for prevention. They may be added to Kampo medicines mentioned above, or may be used alone.

Herbal medicine with immune-enhancing effects: 薬用人参(Panax Ginseng)・西洋人参(Panax quinquefolius)・冬虫夏草(Cordyceps)・霊芝(Ganoderma lucidum)・紅景天 (Rhodiola rosea)

Herbal medicine with stress-relieving properties: 紅景天(Rhodiola rosea)

Herbal medicine with antiviral effects:板藍根 (Isatis indigotica Radix)・大青葉(Isatis indigotica Folium)・金銀花(Lonicera japonica)

Herbal medicine to enhance lung function: 十薬 (Houttuynia cordata)

7. PROPHYLACTIC USE OF KAMPO MEDICINE FOR COVID-19 IN PEOPLE WITH UNDERLYING DISEASES

The mortality rate of COVID-19 infection is known to be highly dependent on the presence or absence of the underlying disease. If a person has an underlying disease such as heart disease, lung disease, diabetes, or hypertension, it is necessary to treat those well. Yojo (養生) is similar to general prevention, but it requires more strict management of daily life in order to control each disease well.

The following are typical Kampo herbal medicines, which should be taken under the supervision of a doctor/pharmacist who is familiar with Kampo medicine. Side effects may occur when taking long-term medications, so get proper guidance from your doctor/pharmacist about what signs to call in if you see them.

7-1. Lung Disease

1)	人参養栄湯(Ninjinyoeito)
	Whose lung function weakens progressively, accompanied by general weakness.
2)	補中益気湯(Hochuekkito)
	To whom have strong tiredness and fatigue, don't have much appetite.
3)	玉屏風散(Gyokuheihusan)
	To whom have less physical strength, have cold hands and feet, sweat frequently.
4)	蘇子降気湯(Soshikokito)

4) 蘇子降気湯 (Soshikokito) To whom have cold feet, can't stop coughing and flushed face during a coughin.

7-2 Heart Disease

1)	木防已湯(Mokuboito)
	When cardiac hypofunction, accompanied with difficulty of breathing, stridor or edema
	recognized.
2)	生脈散(Shomyakusan)

To whom have a heart disease, weak stomach and intestines, get tired easily.

3) 血府逐瘀湯(Keppuchikuoto)

To whom have high blood pressure and have headache, head heaviness, stiff shoulder, hot flash or palpitation.

4) 炙甘草湯 (Shakanzoto)

5)

To whom have an irregular pulse and get tired easily. 冠元顆粒(Kangenkaryu)

To whom have a headache, head heaviness, stiff shoulders, dizziness, etc.

 苓桂朮甘湯(Ryokeijutsukanto)
 To whom being aware of palpitation, short breath or dizziness, and whose lower limb swells.

7-3 High blood pressure

1)	釣藤散(Chotosan)
	To whom have high blood pressure since their late middle age, progressive arteriosclerosis, and
	have a headache sometimes when they wake up.
2)	八味地黄丸:(Hachimijiogan)
	To whom have cold hands and feet accompanied with frequent urination in nighttime.
3)	杞菊地黄丸:(Kogikujiogan)
	To whom have hot flashes, dry mouth, dizziness, and poor vision.
4)	血府逐瘀湯(Keppuchikuoto)
	To whom have headache, head dullness, stiff shoulder, hot flash or palpitation
5)	冠元顆粒(Kangenkaryu)
	To whom have a headache, heavy head, stiff shoulders, dizziness, etc.
6)	半夏白朮天麻湯(Hangebyakujutsutenmato)
	To whom have dizziness or headache, and feel a pressure on the chest or solar pleus.
7)	真武湯(Shinbuto)
	To whom have weak constitution, sensitive to cold, and have dizziness, swelling or palpitation,
	etc.

7-4 Diabetes

1)	八味地黄丸 or 牛車腎気丸:(Hachimijiogan or Goshajinkigan)	
	To whom have cold hands and feet, back pain, polyuria, frequent urination in nighttime, ear	
	noise, etc.	
2)	六味丸(Rokumigan)	
	To whom have symptoms similar to 八味地黄丸(Hachimijiogan), but the chillness is not as	
	strong.	
3)	清心連子飲(Seishinrenshiin)	
	To whom have weak stomach and intestines, and frequent urination.	
4)	生脈散(Shomyakusan)	
	To whom have weak constitution, week stomach and intestines, get tired easily, don't have	
	much appetite.	
5)	血府逐瘀湯 or 冠元顆粒(Keppuchikuoto or Kangen Karyu)	
	To whom have high blood pressure and whose arteriosclerosis is progressing.	
The Following are crude drugs used for patients with underlying diseases. They may be added to Kampo		

The Following are crude drugs used for patients with underlying diseases. They may be added to Kampo medicines mentioned above, or may be used alone.

Herbal medicine with immune-enhancing effects: 薬用人参(Panax Ginseng)・西洋人参(Panax quinquefolius)・冬虫夏草 (Cordyceps) ・霊芝 (Ganoderma lucidum) ・紅景天 (Rhodiola rosea)

Herbal medicine with antiviral effects:板藍根(Isatis indigotica Radix)・大青葉(Isatis indigotica Folium)・金銀花(Lonicera japonica)

Herbal medicine that improves blood flow and is effective for patients with heart disease and hypertension: 鶏血藤(Millettia reticulata Benth) ・紅花 (Carthami Flos)

8. PROPHYLACTIC USE OF KAMPO MEDICINE FOR OTHER COVID-19 HIGH-RISK INDIVIDUALS

8-1 A close contact

2 weeks observation period is required. During this time, each individual will take immune-boosting herbal medicines (e.g., Hochuekkito and Juzentaihoto), combined with herbal medicines with antiviral effects. Alternatively, take a Kampo medicine that is similar to an infection (e.g., Gingyosan and Kakkoshokisan), combined with a combination of immune-boosting herbal medicines.

- 1) 補中益気湯(Hochuekkito) Immune-boosting Kampo medicine with antiviral effects
- 2) 十全大補湯 (Juzentaihoto) To whom get tired easily and looks pale.
- 3) 銀翹散 (Gingyosan)
 It is a remedy for cold with less chillness, but may be used preventatively.
 4) 藿香正気散 (Kakkoshokisan)

To whom have swelling, weak stomach and intestines, coating of tongue.

8-2 Frail and elderly person

The elderly has been reported to be at a higher risk of becoming seriously ill, as have those with underlying diseases. It is also said that refraining from going out can lead to inactivity in life and increase the likelihood of developing frail syndrome for the elderly. In addition to taking Kampo medicine, it is also important to take exercise that can be done at home, eat three proper meals, and take good oral care.

- 1) 玉屏風散(Gyokuheifusan)
 - To whom have weak constitution, sweat easily.
- 2) 補中益気湯(Hochuekkito)
- To whom get tired easily, have no appetite.
- 3) 十全大補湯(Juzentaihoto)
 - To whom tending to anemia, get tired easily.
- 4) 人参養栄湯(Ninjinyoueito) To whom is rather frail have w
- To whom is rather frail, have weak legs.
- 5) 六君子湯(Rikkunshito)
 - To whom having a small appetite, could not get enough nutrition.
- 6) 生脈散 (Shomyakusan)
 - To whom is rather dehydrate, have less appetite, short breath, and dry cough.

The Following are crude drugs used for high-risked patients. They may be added to Kampo medicines mentioned above or may be used alone.

Herbal medicine with immune-enhancing effects: 薬用人参(Panax Ginseng)・冬虫夏草 (Cordyceps)・霊芝(Ganoderma lucidum)

Herbal medicine with antiviral effects: 板藍根 (Isatis indigotica Radix) ・大青葉(Isatis indigotica Folium)・金銀花(Lonicera japonica)

9. HOW TO HANDLE AFTER THE ONSET OF THE FEVER

The speed of viral propagation is determined by the initial viral load that enters and the ability of the organism to defend itself. If Kampo medicine is taken as a preventive measure, various biological defense functions are activated, and the virus growth can be suppressed at an early stage. After the onset of the disease, the main treatment is herbal medicine to eliminate the virus, but it is more effective if it is combined with continued immune-enhancing medicine.

The initial symptoms of COVID-19 infection are the usual symptoms of the common cold, which may begin with fever, headache, and sore throat. Those symptoms may go away, but it also may bring various symptoms such as cough and sputum, diarrhea (sometimes constipation), olfactory disorder, loss of appetite and decreased urine output. Coronaviruses bind to the ACE2 receptor and invade cells, and because the receptor is spread over multiple organs, a variety of symptoms are thought to appear.

It is important to recover at this stage. However, patients may have cytokine storm suddenly and blood clot may form and cause a myocardial or cerebral infarction. Thus, it is important to see a health care provider as soon as possible.

Based on the above, here are some Kampo herbal medicines that you can take until you see the doctor or have a PCR test.

9-1 When patient have a fever

If there are no other symptoms within 1-2 days after the onset of fever, take 葛根湯(Kakkonto)or 麻 黄湯(Maoto)combine with 薬用人参(Panax ginseng), 冬虫夏草(Cordyceps)and 霊芝

(Ganoderma lucidum) in order to enhance immunity. If more than 3 days have passed since the onset of symptoms, or if the fever does not decline even the patient take 葛根湯 or 麻黄湯 constantly for 3 days, take 柴葛解肌湯(Saikatsugekito). Or combine of 葛根湯 (Kakkonto) and 小柴胡湯 (Shosaikoto) until the fever declines.

When taking a combination of extracts, the amount of 甘草(Licorice), one of the herbal medicines contained in Kampo medicine, is increased, and side effects such as dullness in the hands and feet, numbness, and weakness may appear. Contact your doctor or pharmacist as soon as you develop symptoms of side effects.

- 1) 葛根湯(Kakkonto)
 - Take it immediately after the onset of the disease, when there is a chill, the back of the neck is stiff and the fever rises.
- 2) 麻黄湯(Maoto)
- To whom feels chill strongly, have joint pain, back pain, etc.
- 3) 麻黄附子細辛湯(Maobushisaishinto)
- To the elderly.
- 4) 銀翹散(Gingyosan)
 - To whom have sudden fever without a strong chill
- 5) 藿香正気散(Kakkoshokisan)

To whom have chilling and fever, headache, chest tightness, vomiting, diarrhea and coating of tongue.

9-2 When patient have a cough and phlegm

If the fever is persistent, it is better to use: 柴葛解肌湯(Saikatsugekito), 麻杏甘石湯

(Makyokansekito),麻杏甘石湯 + 銀翹散(Makyokansekito + Gingyosan). If the fever is calm: 小柴胡湯加桔梗石膏(Shosaikoto ka Kikyosekko), if the patient complains chest pain: 柴陥湯(Saikanto). In every case, continue to take them until the fever declines.

When taking a combination of extracts, the amount of 甘草(Licorice), one of the herbal medicines contained in Kampo medicine, is increased, and side effects such as dullness in the hands and feet, numbness, and weakness may appear. Contact your doctor or pharmacist as soon as you develop symptoms of side effects.

1) 柴葛解肌湯 (Saikatsugekito)

If a cough starts to appear, switch to 柴葛解肌湯.

- 麻杏甘石湯 + 小柴胡湯 (Makyokansekito + Shosaikoto)
 To whom have airway stenosis and feel short of breath. When using the extract, be careful of swelling as 甘草 (Licorice) will be 4g.
- 麻杏甘石湯 + 銀翹散(Makyokansekito + Gingyosan)
 The formula used during the 2009 influenza epidemic. It is widely used for fever, cough and phlegm. Be careful of over taking 甘草(Licorice).
- 4) 小柴胡湯加桔梗石膏 (Shosaikoto ka Kikyosekko) To whom have a swollen and sore throat.
- 5) 柴陥湯(Saikanto)
- To whom have a chest pain.
- 6) 蘇子降気湯 (Soshikokito)

To whom are tangled in phlegm and feel short of breath.

This is the end of the guideline of prophylactic use of Kampo Medicine for new coronavirus infection (COVID-19), which is summarized by Kampo Industralization Consortium. In Wuhan City, China, PCR-positive COVID-19 also played a major role in the prevention of severe disease in patients with mild disease. Please refer to "The Role of Chinese Medicine in New Coronavirus Infection (COVID-19)" <u>https://www.jmedj.co.jp/journal/paper/detail.php?id=14426</u> for specific treatment options.

10. SUMMARY

To summarize this guideline, we heard directly from Prof. Zhang Boli (張伯礼) of Tianjin Chinese Medical University and Prof. Zhang Zhongde (張忠徳) of Guangzhou Chinese University, both of whom contributed to the suppression of COVID-19 in Wuhan City. It was stressed that this virus is persistent, seemingly stable, but can rapidly deteriorate, so it was important to have a daily reminder (to raise your inner "Qi"). It should be noted that 4,900 traditional medicine doctors who treated COVID-19 infection in Wuhan City took their own herbal medicines and no one was infected.

I would be happy if this guideline could contribute to saving as many precious lives as possible.

11. ACKNOWLEDGEMENT

In summarizing this guideline, we received a lot of information from the members of Kampo Industralization Consortium. Ms. Aki Ito, who is a member of the academic committee of the Japan Kampo Medicine Association, gave us a lot of advice.

Prof. Jianping Liu of Beijing University of Chinese Medicine, Prof. Liqun Jia of China-Japan Friendship Hospital, Division of Oncology Chief, Prof. Yong-Sueok Kim of Kyung Hee University and Prof. Hung-Rong Yen of College of Chinese Medicine / China Medical University, Vice Dean gave us the information about the guidelines of traditional medicine and the actual treatment. I would also like to express my heartfelt gratitude to Prof. Zhang Boli (張伯礼) of Tianjin Chinese Medical University and Prof. Zhang Zhongde (張 忠徳) of Guangzhou Chinese University, for teaching me the practicalities of traditional medical treatment in Wuhan.

Finally, we would like to express our deepest gratitude to Mr. Koji Fujimoto of Medical Excellence Japan and Yokohama University of Pharmacy for their support of this activity.

References

<Kampo drugs>

葛根湯

- □ Okabayashi S, et.al. Non-superiority of Kakkonto, a Japanese herbal medicine, to a representative multiple cold medicine with respect to anti-aggravation effects on the common cold: a randomized controlled trial. Intern Med. 2014;53:949-56.
- □ Kurokawa M, et.al. Effect of interleukin-12 level augmented by Kakkon-to, a herbal medicine, on the early stage of influenza infection in mice. Antiviral Res. 2002;56:183-8.

かんげんかりゅう 冠元顆粒

- \square Paudel P, et.al. Rosmarinic Acid Derivatives' Inhibition of Glycogen Synthase Kinase-3 β Is the Pharmacological Basis of Kangen-Karyu in Alzheimer's Disease. Molecules. 2018;23:2919.
- □ Yokozawa T, et.al. Scientific evidence for therapeutic effects of Chinese prescription Kangen-karyu from pre-clinical animal experiments. Drug Discov Ther. 2017;11:6-14.
- □ Yokozawa T, et.al. The protective role of Kangen-karyu against fructose-induced metabolic syndrome in a rat model. J Pharm Pharmacol. 2007;59:1271-8.
- □ Pu F, et.al. Ameliorating effects of Kangen-karyu on neuronal damage in rats subjected to repeated cerebral ischemia. J Nat Med. 2010;64:167-74.
- 牛車腎気丸
- □ Watanabe K, et. al. Long-term effects of Goshajinkigan in prevention of diabetic complications: A randomized open-labeled clinical trial. Evid Based Complement Alternat Med. 2014; 2014:128726.

まであっげきとう 柴葛解肌湯

- □ 村井 政史ら。10年間続いた不明熱に柴葛解肌湯が奏効した1例。日東医誌 2020;71:24-29.
- □ 秋葉哲生、渡辺賢治。秋田魁新報記事に見る 1918 年から 1919 年にかけてのスペイン風邪 流行状況。漢方の臨床 2009;56(2):331-342.

しゃかんぞうとう 炙甘草湯

□ Sugiyama A. et.al. Chronotropic and Inotropic Effects of Kampo Extracts in the Canine Isolated, Blood-Perfused Heart Preparations Jpn J Pharmacol. 1989;51:239-46.

じゅうぜんたいほとう

 Munakata K, et.al. Microarray Analysis on Germfree Mice Elucidates the Primary Target of a Traditional Japanese Medicine Juzentaihoto: Acceleration of IFN-α Response via Affecting the ISGF3-IRF7 Signaling Cascade BMC Genomics. 2012; 13: Article number 30.

小柴胡湯

- □ Ara T, et.al. Preventive effects of a Kampo medicine, Shosaikoto, on inflammatory responses in LPStreated human gingival fibroblasts. Biol Pharm Bull. 2008;31:1141-44.
- □ Cheng PW, et.al. Xiao chai hu tang inhibits CVB1 virus infection of CCFS-1 cells through the induction of Type I interferon expression. Int Immunopharmacol. 2006;6:1003-12.
- □ Kawakita T, et.al. Protective effect of a traditional Chinese medicine, xiao-chai-hu-tang (Japanese

name: shosaiko-to), on Pseudomonas aeruginosa infection in mice. Immunopharmacol Immunotoxicol. 1987;9:523-40.

上1 派散

- □ Nishida H, et.al. Shengmai-san Enhances Antioxidant Potential in C2C12 Myoblasts Through the Induction of Intracellular Glutathione Peroxidase. Journal of Pharmacological Sciences 2007; 105:342-352.
- Li Y, et.al. Antioxidant Synergism among Component Herbs of Traditional Chinese Medicine Formula, ShangMai San Studied In Vitro and In Vivo. Journal of Health Science. 2015;53; 692-699.

しんぶとう 真武湯

□ Horiba Y.et.al.Kampo Extract of Shinbuto Improved Refractory Diarrhea in Milroy's Disease. Glob Adv Health Med. 2013;2:14-7.

^{ちょうとうさん} 釣藤散

- □ Shimada Y, et.al. Choto-san prevents occurrence of stroke and prolongs life span in stroke-prone spontaneously hypertensive rats. Am J Chin Med. 2003;31:79-85.
- □ Sugimoto A., et.al. Effect of Choto-san, a Kampo medicine, on the cerebral blood flow autoregulation in spontaneously hypertensive rats. Jpn J Pharmacol. 2000;83:135-42.

はんじんようえいとう

- Ohsawa, et.al. A Possibility of Simultaneous Treatment with the Multicomponent Drug, Ninjin'yoeito, for Anorexia, Apathy, and Cognitive Dysfunction in Frail Alzheimer's Disease Patients : An Open-Label Pilot Study. J Alzheimers Dis Rep. 2017;1:229-235.
- □ Takayama S, et.al. Perspectives on the Use of Ninjin'yoeito in Modern Medicine: A Review of Randomized Controlled Trials. Evid Based Complement Alternat Med. 2019;2019:9590260.

はちみじおうがん 八味地黄丸

- □ Yamada N, et.al. Activity of the Chinese prescription Hachimi-jio-gan against renal damage in the Otsuka Long-Evans Tokushima fatty rat: a model of human type 2 diabetes mellitus. J Pharm Pharmacol. 2006;58:535-45.
- □ Kim HY, et.al. Protective effects of the Chinese prescription Hachimi-jio-gan against diabetic oxidative stress. J Pharm Pharmacol. 200;56:1299-305.

ほちゅうえっきとう 補中益気湯

□ Dan K, et.al. A Kampo (traditional Japanese herbal) medicine, Hochuekkito, pretreatment in mice prevented influenza virus replication accompanied with GM-CSF expression and increase in several defensin mRNA levels. Pharmacology. 2013;91:314-21.

- Dan K, Takanashi K, Akiyoshi H, Munakata K, Hasegawa H, Ogawa O, Watanabe K: Action Mechanism of the Anti-Influenza Virus Active Kampo (Traditional Japanese Herbal) Medicine, Hochuekkito. Pharmacology, 2018; 101:148-155.
- □ Takanashi K, Dan K, Kanzaki S, Hasegawa H, Watanabe K, Ogawa K: Hochuekkito, a Japanese Herbal Medicine, Restores Metabolic Homeostasis between Mitochondrial and Glycolytic Pathways Impaired by Influenza A Virus Infection. Pharmacology, 2017; 99:240-249.
- □ Takanashi K, Dan K, Kanzaki S, Hasegawa H, Watanabe K, Ogawa K: The Preventive Effect of the Traditional Japanese Herbal Medicine, Hochuekkito, against Influenza A Virus via Autophagy in vitro. Pharmacology, 2017; 99:99-105.

まおうとう 麻黄湯

- □ Yoshino T, Arita R, Horiba Y, Watanabe K. The use of maoto (Ma-Huang-Tang), a traditional Japanese Kampo medicine, to alleviate flu symptoms: a systematic review and meta-analysis. BMC Complement Altern Med. 2019;19:68.
- □ Arita R, et.al. National cost estimation of maoto, a Kampo medicine, compared with oseltamivir for the treatment of influenza in Japan. Traditional & Kampo Medicine. 2016; 3: 59-62.

ますずしきいしんとう麻黄附子細辛湯

□ Shirayama R, et.al. Inhibition of PA endonuclease activity of influenza virus RNA polymerase by Kampo medicines. Drug Discov Ther. 2016;10:109-13.

まきょうかんせきとう 麻杏甘石湯

- □ Iida Y, et.al. Diffuse Alveolar Hemorrhage Associated with Makyo-kanseki-to Administration. Intern Med. 2016;55:3321-23.
- □ Yuan D, et.al. Pharmacological properties of traditional medicines (XXVII). Interaction between Ephedra Herb and Gypsum under hyperthermal conditions in rats. Biol Pharm Bull. 2002;25:872-874.
- □ Miyagoshi M, et.al. Antitussive effects of L-ephedrine, amygdalin, and makyokansekito (Chinese traditional medicine) using a cough model induced by sulfur dioxide gas in mice. Planta Med. 1986;275-8.

もくぼういとう

- Ezaki H, et.al. Effects of Mokuboito, a Japanese Kampo medicine, on symptoms in patients hospitalized for acute decompensated heart failure - A prospective randomized pilot study. J Cardiol. 201;74:412-417.
- □ Miho E, et.al. Acute and chronic effects of mokuboito in a patient with heart failure due to severe aortic regurgitation. J Med Sci. 2019;65:61-67.

りっくんしとう 六君子湯

- □ Tominaga K, et.al. Rikkunshito simultaneously improves dyspepsia correlated with anxiety in patients with functional dyspepsia: A randomized clinical trial (the DREAM study). Neurogastroenterol Motil. 2018;30:e13319.
- □ Hoshino N, et.al. Rikkunshito for upper gastrointestinal symptoms: A systematic review and meta-

analysis. Complement Ther Med. 2019;42:255-263.

<Herbs>

きの時間

- □ Toyama T, et.al. <u>Reactive oxygen species scavenging activity of Jixueteng evaluated by electron</u> <u>spin resonance (ESR) and photon emission.</u> Nat Prod Commun. 2014;9:1755-9.
- □ Liao H,et.al. <u>Antioxidant activity of 45 Chinese herbs and the relationship with their TCM</u> <u>characteristics.</u> Evid Based Complement Alternat Med. 2008;5:429-34

こうけいてん 紅景天

- □ Lekomtseva Y, et.al. Rhodiola rosea in Subjects with Prolonged or Chronic Fatigue Symptoms: Results of an Open-Label Clinical Trial. Complement Med Res. 2017;24:46-52.
- □ Cropley M, et.al. The Effects of Rhodiola rosea L. Extract on Anxiety, Stress, Cognition and Other Mood Symptoms. Phytother Res. 2015;29:1934-9.
- □ Ishaque S, et.al. Rhodiola rosea for physical and mental fatigue: a systematic review. BMC Complement Altern Med. 2012;12:70.

じゅうやく 十薬

- □ Zhu H, et.al. Houttuynia cordata polysaccharides ameliorate pneumonia severity and intestinal injury in mice with influenza virus infection. J Ethnopharmacol. 2018;218:90-99.
- □ Chen MY, et.al. Houttuynia cordata polysaccharide alleviated intestinal injury and modulated intestinal microbiota in H1N1 virus infected mice. Chin J Nat Med. 2019;17:187-197.
- □ Lu Y, et.al. Beneficial effects of Houttuynia cordata polysaccharides on "two-hit" acute lung injury and endotoxic fever in rats associated with anti-complementary activities. Acta Pharm Sin B. 2018;8:218-227.

とうちゅうかそう 冬虫夏草

- □ Kwon HK,et.al. Immune-enhancing activity of C. militaris fermented with Pediococcus pentosaceus (GRC-ON89A) in CY-induced immunosuppressed model. BMC Complement Altern Med. 2018;18:75.
- □ Lee HH, et.al. Anti-influenza Effect of Cordyceps militaris through Immunomodulation in a DBA/2 Mouse Model. Journal of Microbiology. 2014;52:696–701.

板藍根・大青葉(ホソバタイセイの根が板藍根、葉が大青葉)

- □ Wang T, Antiviral activity of a polysaccharide from Radix Isatidis (Isatis indigotica Fortune) against hepatitis B virus (HBV) in vitro via activation of JAK/STAT signal pathway. J Ethnopharmacol. 2020:112782.
- □ Govindarajan M, et.al. One-pot biogenic fabrication of silver nanocrystals using Quisqualis indica: Effectiveness on malaria and Zika virus mosquito vectors, and impact on non-target aquatic organisms. J Photochem Photobiol B. 2016;162:646-655.
- □ Phatthalung PN, et.al. Thai ethnomedicinal plants as resistant modifying agents for combating Acinetobacter baumannii infections. BMC Complement Altern Med. 2012;12:56.
- □ Roxas M, et.al. Colds and influenza: a review of diagnosis and conventional, botanical, and nutritional

considerations. Altern Med Rev. 2007;12:25-48.

やくようにんじん 薬用人参

- □ Jin ZH, et.al. Enhancement of oral bioavailability and immune response of Ginsenoside Rh2 by coadministration with piperine. Chin J Nat Med. 2018;16:143-149.
- □ Yin S-Y, et.al. Comparative Study of the Effects of Whole Red Ginseng Extract and Polysaccharide and Saponin Fractions on Influenza A (HINI) Virus Infection. Biol Pharm Bul. 2013:36;1002-1007.

^{れいし} 霊芝

- □ Meng J, et.al. Analysis of maturation of murine dendritic cells (DCs) induced by purified Ganoderma lucidum polysaccharides (GLPs). Int J Biol Macromol. 2011; 49: 693-9.
- □ Sun LX, et.al. Promoting effects of Ganoderma lucidum polysaccharides on B16F10 cells to activate lymphocytes. Basic Clin Pharmacol Toxicol. 2011;108:149-54.