



Centrum für Therapiesicherheit in der Chinesischen Arzneitherapie

Center for Safety of Chinese Herbal Medicine

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C T C A l e t t e r F e b r . 2 0 2 0

Coronavirus – risk from Chinese medicinal substances?

Individual inquiries on this topic have been raised by patients and healthcare professionals. The coronavirus SARS-CoV-2 is widely considered to have originated from animal sources and subsequently adapted to humans. Certain animal-derived materials used in Traditional Chinese Medicine (TCM) have occasionally been suggested as possible sources, including the snake *Bungarus multicinctus* (*jin qian bai hua she*) and the scales of the pangolin (*Manitis Squama*, *chuan shan jia*). However, there is no confirmed evidence supporting these claims.

Irrespective of these considerations, transmission of disease in Europe via Chinese medicinal substances is extremely unlikely. Each year, goods with a value exceeding 100 billion euros are imported from China to Germany, including fresh food products. The Bundesinstitut für Risikobewertung (German Federal Institute for Risk Assessment, BfR) currently states:

“Can imported goods from regions where the disease is prevalent serve as a source of infection in humans? Based on the transmission pathways identified to date and the relatively low environmental stability of coronaviruses, it is unlikely, according to current knowledge, that imported goods—such as food products or consumer items including toys, tools, computers, clothing, or footwear—could constitute a source of infection with the novel coronavirus.”

Any unlikely considerations relevant to fresh food products are further diminished for dried medicinal substances due to extended storage prior to their import into Germany, and are even less applicable to granulated preparations obtained through prolonged boiling. Accordingly to the best currently available evidence, these concerns are therefore unfounded.

Recommendation for patient information

In response to numerous inquiries, the CTCA has decided to issue a recommendation for patient counselling. This is intended to serve as a practical guideline in a clinical setting. We consider it particularly important to inform patients about possible symptoms of a – albeit very rare – hepatic reaction, as patient awareness is essential for detecting such reactions at an early stage and preventing more serious outcomes.

It is explicitly stated that this constitutes a non-binding recommendation that has not been subject to legal review and does not absolve the treating practitioners from their personal

responsibility regarding the content of patient information and counselling. In certain situations, for example when using medicinal substances with a higher risk potential, in the presence of possible drug interactions, or in specific patient risk constellations (e.g., certain pre-existing conditions or pregnancy), the counselling should be appropriately expanded.

Patient information:

Chinese herbal medicine, in comparison with treatments using chemically defined pharmaceuticals, is a relatively safe therapeutic approach. A prerequisite is that the Chinese medicinal substances are sourced from reputable suppliers (certified pharmacy-grade products) that ensure quality control, including verification of identity, testing for heavy metals and pesticides, as well as other analyses required under pharmacopoeial standards. Nevertheless, adverse effects may occur.

Often enough, gastrointestinal symptoms or nonspecific feelings of unwellness may occur, which are generally harmless, including mild diarrhea, nausea, constipation or sensations of heat or cold. Occasionally headaches, fatigue or more pronounced diarrhea may occur, and in women, menstrual irregularities.

As with other natural substances and foods, allergic reactions to Chinese herbal medicines are possible. These may present as pruritus and/or skin rashes. Very rarely, systemic reactions such as dyspnea and/or circulatory disturbances may occur.

In extremely rare cases, serious hepatic reactions may arise. Therefore, it is important that you contact me/us immediately if symptoms such as unusual fatigue, persistent nausea, dark urine, pale stools or yellowing of skin occur. If timely contact is not possible, treatment with the Chinese herbal medicines should be discontinued and not resumed until a causal relationship with the Chinese medicine has been excluded. In certain cases, monitoring of liver function parameters prior to and during therapy may be appropriate.

Interactions with other medications cannot be ruled out. Please inform me/us about any medications you are taking, as well as any changes in your medication regimen.

Please also inform me/us if pregnancy is planned, has occurred, or if you are breastfeeding, as in such cases certain Chinese herbal medicines must not be used or should only be used with restrictions.

Chinese medicine and doping

At the Olympic Games in Beijing, a number of Chinese TCM patent medicines resulted in positive doping test results. This may be attributable, on the one hand, to adulteration with undeclared pharmacologically active substances or to contamination. On the other hand, certain Chinese medicinal substances themselves may, in specific cases, lead to positive test results.

This is known, for example, for Ephedrae Herba (*ma huang*) due to its content of ephedra alkaloids (including ephedrine, pseudoephedrine, and others). Another substance listed by the World Anti-Doping Agency (WADA) that may occur in Chinese medicinal substances is **higenamine**:

https://www.wada-ama.org/sites/default/files/wada_2020_english_prohibited_list_0.pdf

Higenamine is a constituent of aconite drugs, *Asarum (xi xin)*, and various lotus-derived materials, including *Nelumbinis Plumula (lian zi xin)*, *Nelumbinis Semen (lian zi)*, and *Nelumbinis Folium (he ye)*. Its presence in other lotus-related materials cannot be excluded. Higenamine is a β 1- and β 2-adrenergic receptor agonist and has been investigated in several pharmacological and clinical studies. It appears to have been included on the WADA prohibited list only recently.

The aforementioned substances should not be prescribed to competitive athletes, as their intake is likely to result in a positive doping test.

Interstitial pneumonia associated with Kampo formulations

Since 1989, reports from Japan have repeatedly described cases of interstitial pneumonia attributed to Kampo formulations. The most recent report dates from 2019. A substantial proportion of cases have been associated with the formula *sho-saiko-to*, which corresponds to the Chinese formulation *xiao chai hu tang*. However, Kampo medicine sometimes employs different plant species than Chinese Medicine. Other Kampo formulations have also been linked to this clinical condition. It is characterized by cough, dyspnea, and fever. Inflammatory markers are not markedly elevated, and indications of an allergic aetiology is found in only a minority of cases. Radiological findings include ground-glass opacities, ring-shaped opacities, infiltrates, or combinations thereof. A notable higher proportion of patients affected had a prior history of hepatitis C.

In a review analysing 73 cases, the most frequently reported constituents in the formulations were *Scutellariae Radix* (86%), *Glycyrrhizae Radix* (85%), ginseng (62%), *Bupleuri Radix* (59%), and *Pinelliae Tuber* (58%). Accordingly, no single medicinal substance can be identified as solely responsible for the observed reactions. The formulation *gosha-jinki-gan*, implicated in 4% of cases, does not contain any of the aforementioned individual components. In a smaller subset of cases, symptom onset was temporally associated with interferon therapy. Since 1994, interferon treatment has been considered a contraindication for *sho-saiko-to*, and in 1996 the Japanese Ministry of Health issued an official warning. Interestingly, the formulations involved are also associated with hepatic adverse reactions in Japan, where *sho-saiko-to*, often prescribed in patients with pre-existing liver disease, is prominently represented in reported cases.

In Europe, interstitial pneumonia has so far not played a role in this context. Nevertheless, this adverse effect should be considered if relevant symptoms occur. Hepatic reactions to similar formulations have, however, been reported in Europe as well, including a case notified to the CTCA involving an extended form of *xiao chai hu tang*. Further details on “Interstitial Pneumonia and Kampo Medicine” are available on our website (<https://www.ctca.center/de/aktuelles/interstitielle-pneumonie-und-kampomedizin.html>).

With kind regards,
Axel Wiebrecht

Have you experienced adverse effects under Chinese herbal therapy?

Please report them using our reporting form:

<http://www.ctca.de/images/files/CTCAMeldebogen.pdf>

➤ **Do you have questions regarding risks, interactions, or quality issues?**

Please do not hesitate to contact us at: info@ctca.center