



Centrum für Therapiesicherheit in der Chinesischen Arzneitherapie

Center for Safety of Chinese Herbal Medicine

www.ctca.center info@ctca.center

CTCA letter – Febr 2018

Potential discontinuation of TCM granules in Germany – open letter to pharmaceutical supervisory authorities and decision-makers

We previously reported in the CTCA letter on increasing restrictions affecting the distribution of Traditional Chinese Medicine (TCM) granules in Germany. Initially emerging in Bavaria, numerous TCM pharmacies across different federal states have since received or been notified of distribution prohibitions. This development raises concerns regarding a potential nationwide discontinuation of availability.

The underlying issue is that, in addition to already existing and valid certificates, a secondary identification procedure for the plant species used must be conducted within the pharmacy setting. Previously applied methods are reportedly no longer being accepted and, according to subject-matter experts, are considered insufficient. However, rather than limiting additional analyses to excluding potential misidentification of medicinal substances already verified by accredited institutions, authorities are requiring more sophisticated procedures such as thin-layer chromatography (TLC). TLC represents a resource-intensive analytical method with substantial requirements regarding personnel expertise and material resources, including reference standards. Pharmacies generally consider its implementation economically impractical. A possible consequence could be an increasing shift toward procurement of granules from less regulated EU markets or third-country suppliers, where quality-control procedures may be less rigorous and products are often not dispensed through pharmacies.

Major societies for Chinese Medicine and the CTCA have therefore drafted an open letter to the pharmaceutical supervisory authorities, official pharmacists, and health care decision-makers in Germany, which can be accessed here:

<https://www.ctca.center/de/stellungnahmen/stellungnahmen-des-ctca.html>.

To our knowledge, discussions are currently taking place between individual pharmacies, the TCM Pharmacy Working Group (TCM-Apo AG), and relevant decision-makers regarding implementation of thin-layer chromatography requirements. Even if some (larger) pharmacies were to adopt such procedures, this would likely lead to a substantial reduction in supply options and a considerable increase in the cost of TCM granules. Consequently, products originating from countries not subject to these requirements could gain a competitive advantage. A foreseeable outcome may be a signifi-

cant increase in purchases from sources against which caution has repeatedly been advised. (It should be noted, however, that high-quality international suppliers do exist.)

The signatories of the open letter support a simplified procedure limited to excluding potential misidentification of granules that have already undergone quality assessment. The optimal implementation of such a procedure should be determined on the basis of pharmaceutical expertise and agreed upon collaboratively between decision-makers and pharmacies. We further emphasize the importance of informed TCM-specific expertise and a balanced, proportionate approach in this context.

New large-scale study on hepatic reactions under Chinese herbal medicine published

A recently published study by Melchart and colleagues (2017) investigated the frequency of hepatotoxic reactions in the TCM Clinic Bad Kötzing, Bavaria, between 1994 and 2015. A total of 21,740 patient cases were evaluated. An elevation of liver enzymes above the normal range occurred in 3.93% of cases. Liver injury, defined as at least a fivefold increase in ALT, was observed in 26 patients (0.12%). An increase in ALT up to five times the upper limit of normal was interpreted as an adaptive hepatic response, whereas higher increases were classified as liver injury. Among the herbal substances used, Bupleuri Radix (*chai hu*) and Scutellariae Radix (*huang qin*) were particularly notable; they were involved in seven “probable” and “possible” cases each, and co-occurred in 12 of these cases.

The study provides a previously unavailable level of data quality for assessing the hepatotoxicity risk of Chinese medicines. However, parts of the evaluation are considered methodologically flawed. A critical analysis with a reassessment of the results is available here:

<https://www.ctca.center/en/statements-comments/comments.html>.

On the basis of the available evidence, a—albeit rare—hepatotoxic potential of Bupleuri Radix or Scutellariae Radix, or both in combination, must be considered likely, although further differentiation is currently not possible. A possible hepatotoxicity is also suggested for Toosendan Fructus (*chuan lian zi*) at standard dosages, previously only associated with overdose. Drug-induced liver reactions typically occur between 5 and 90 days after treatment initiation, and in some cases may also appear after discontinuation of therapy.

These findings are not intended to diminish interest in or appreciation of the fascinating therapeutic approach of Chinese herbal medicine, but rather to contribute to improving its safety profile.

Yours sincerely,

Axel Wiebrecht

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