Remarks on "Herbal Immune Booster-Induced Liver Injury in the COVID-19 Pandemic - A Case Series"

Sir,

We read the case series by Nagral et al.[1] in "JCEH" with great interest, wherein the authors have reported six cases with drug-induced autoimmune-like hepatitis and proclaimed it secondary to the consumption of *Tinospora cordifolia* (TC). The case series has highlighted a very limited set of observations without covering several beneficial aspects of TC.

1. There is published evidence in animal models and clinical studies suggesting TC as a safe and natural remedy for hepatoprotection.[2–6]
2. Nagral et al. do not clarify from the patient's history, which variety of Tinospora was consumed by the patient, as the two varieties (*T. cordifolia* and *T. crispa*) look similar in the morphology, and people may mistake *T. crispa* for *T. cordifolia*.[7] *T. cordifolia* is referred to as *Giloy* in Ayurveda; however, *T. crispa* is known to be hepatotoxic.[8,9] The same concern about the nature of the prescribed medicine has also been raised by Ministry of AYUSH in a press release.[10]
3. Case 1 may have self-consumed TC in excess. The reported findings of drug-induced liver injury (DILI) are further weakened as the patient took two additional herbs in an undefined dosage. Cases 2 and 4 were diabetic, Case 3 had beta-thalassemia minor, while Cases 5 and 6 had hypothyroidism, which are also confounders. Therefore, presenting TC as a sole factor for autoimmunity development in these patients has confounding factors. Further, the authors have mentioned that certain non-hepatotropic viruses were not tested in the study, which could alter the findings.
4. Cases 2 to 6 might be taking some concomitant conventional medications (unclear from the publication) e.g. for diabetes and hypothyroidism, which may be associated with DILI as confounders.[11,12] Effect of all drugs and drug-drug interactions on liver health should have been discussed.
5. All cases had a history of unsupervised consumption of TC. Four cases consumed twigs (undefined amount), while Ayurveda clearly advocates using thumb-sized mature stems.[7] Two cases consumed commercial syrup and tablet with TC as one of the ingredients where a chance of adulteration is possible. Excessive, prolonged, and unscrupulous use of any herb could be dangerous. Ayurveda does not recommend the continuous unsupervised use of TC for several months. Also, the methods to prepare a decoction or any dosage form and administration methods are unique in Ayurveda, and such medications should be taken only under the supervision of a qualified physician.[7,12]
6. The authors have not studied whether the patients had subclinical COVID-19 infection. It is also quite possible these 6 patients already were suffering from an autoimmune condition that may have manifested due to drug-drug interactions after consumption of over-the-counter TC-based preparations.

Contrary to widespread belief, natural products with medicinal value are not always safe. One needs to be cautious while administering herbal medications, and administration should always be under the supervision of a trained physician in prescribed doses.[13] We recommend that Ayurvedic guidelines for therapeutic use should be followed, and hazards of misuse of any Ayurvedic herbal medicine should be clearly understood before projecting it as "unsafe" or "toxic." It seems that the author's claim of the TC inducing liver injury is not substantiated, and they have not accounted for many important basic criteria to conclude the hepatotoxicity of the drug.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

Conceptualization, data collection, and writing - original manuscript, **R.S.**; Editing and proofreading, **P.K.P.** All authors approved submission of the final manuscript.

CONFLICTS OF INTEREST

The authors have none to declare.

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Abbreviations: DILI: drug-induced liver injury; TC: *Tinospora cordifolia*

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Rohit Sharma
Department of Rasashastra and Bhaishajya Kalpana, Faculty of Ayurveda, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, 221005, India

Pradeep K. Prajapati
Department of Rasashastra and Bhaishajya Kalpana, All India Institute of Ayurveda, New Delhi, 110076, India

Address for correspondence: Rohit Sharma, Assistant Professor, Department of Rasashastra and Bhaishajya Kalpana, Faculty of Ayurveda, Institute of Medical Sciences, Banaras Hindu University, Varanasi, 221005, India.
E-mail: rohitsharma@bhu.ac.in or dhanvantari86@gmail.com

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