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CORRESPONDENCE

Reply

> Some people create their own storms and then get upset when it rains.
>
> —Anonymous

We welcome the opinions of Balkrishna et al. on our multicenter study, which demonstrated a strong association of Tinospora cordifolia (Giloy) and autoimmune-like hepatitis.[1] The authors' arguments supporting the "safety" of Giloy come from multiple preclinical sources; these unpublished, non-peer-reviewed work have misinterpreted published data on Giloy, or the lack of it, to suit their narrative. They claim that 40 ml/day of Giloy was akin to an "overdose" and provide a misleading citation. In fact, their own product page and that of the Ministry of Ayush Guidelines on coronavirus disease 2019 mention a maximum daily dose of 60–80 ml/day.[2,3] Nonetheless, the authors' claims are fictitious, as the efficacy and safety Giloy for the prevention or mitigation of any disease condition in humans is not yet identified through robust clinical trials.

Contrary to what Balkrishna et al. argue, our patients consumed properly identified Giloy and authentically marketed Giloy-based products, which were advertised and recommended via public and private Ayush promotions. The presence of a pre-existing liver condition does not exclude Giloy liver injury, but enforces the importance of diagnosing herb-induced acute worsening of chronic liver disease, which is known to be associated with high mortality.[4]

The type, concentration, effective dose, safety limits, and toxicity of bio-active phytocompounds in Giloy products should ideally be disclosed by the manufacturer. The authors lay out irrational arguments leveraged on their confirmation biases, in support of the safety of Giloy, using various preclinical rat models. However, it is well known that animal models have sizeable limitations for predicting toxicity in human clinical trials.[5]

Balkrishna et al. appeal to ignorance regarding liver-toxic furano-diterpenoids, based on inaccurate citations that do not support their claims that these hepatotoxic compounds are lost during purification. The preparatory process for various Giloy-based formulations is not standardized. Nonetheless, they have missed the fact that Ayush Ministry guidelines explicitly state the use of aqueous-base extracted Giloy and not alcohol or chloroform processed decoctions.[3]

The authors have misinterpreted our study, taken to strawman arguments and red-herring fallacies on cherry-picked aspects of chemical analysis, all the while trying to find closure for their labyrinthine, but flawed narrative on the safety of Giloy.[6] Giloy liver injury is a clinical diagnosis of exclusion, based on causality assessment and temporal association which we have succinctly proven. Finally, Balkrishna et al. willfully ignore the editorial on Giloy liver injury by experts from the US Drug-Induced Liver Injury Network, which re-assessed that Giloy can lead to liver injury with autoimmune features as well as worsen silent autoimmune hepatitis, which was also confirmed in our study.[7]

Therefore, the evidence presented in our study strongly associates Giloy with observed hepatotoxicity and restates that non-evidence-based, poorly regulated traditional herbal products must be curbed. A "supervised" prescription is not the solution here, but awareness of the potential toxicity of Giloy, which has no proven clinical benefits. Our study demonstrates that preventing a modifiable disease is far more important than treating inadvertent complications.

CONFLICT OF INTEREST

Nothing to report.

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