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Giloy and the Liver: Correlation Is Not Causation. Comment on Philips and Theruvath (Medicine, 2024)

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Dear Editor,

We read with concern the recent review by Philips and Theruvath, which lists *Tinospora cordifolia* (giloy, guduchi) among Ayush herbs with liver toxicity potential [1]. Giloy has been used safely in Ayurveda for over two thousand years, and in our view the evidence cited does not support the conclusion that it causes liver injury. We wish to highlight four problems.

First, most of the reported patients had pre-existing liver disease or autoimmune features. In the original case series, all six patients had features of autoimmune hepatitis [2], and in the multicentre study the commonest presentation was acute worsening of chronic liver disease [3]. These patients were already ill; their liver disease would have progressed with or without giloy. A herb cannot be blamed for a disease that was already present.

Second, none of these studies confirmed that the product consumed was actually *T. cordifolia*. As Singh and Bajwa have shown, the reported toxicity is better explained by *Tinospora crispa*, a look-alike species that is commonly substituted in the market [4]. Without botanical authentication, the case reports implicate a name rather than a plant.

Third, causality assessment in these reports relied on scales such as RUCAM, which at best classify a case as 'probable' [5]. A probable association is not proof. By the same standard, almost any widely used substance could be implicated in liver injury.

Fourth, the number of cases is tiny relative to use. During the pandemic, giloy was consumed by tens of millions of Indians as part of government-recommended immunity measures. Forty-nine cases in a nationwide study [3] therefore represent a negligible risk, far lower than that of paracetamol or anti-tuberculosis drugs. If giloy were genuinely hepatotoxic, India's hospitals would have been overwhelmed.

Fifth, the review relies heavily on earlier work from the same group. In their 2018 single-centre study of patients with severe liver injury after Ayurvedic and herbal medicines, Philips and colleagues reported that 11 patients had obtained their medicines from unregistered traditional healers, and that intake from such healers was associated with higher mortality [6]. This finding, which the review does not emphasise, shows that the problem lies with unqualified practitioners and unregulated preparations, not with registered Ayurvedic medicines prepared according to the classical texts. Products from licensed manufacturers, made under Good Manufacturing Practice, were not the cause of the deaths reported.

The relationship between the reports is summarised in Table 1. When the cited evidence is traced back to its sources, it becomes clear that the case against giloy rests on a small number of patients, most of whom were seriously ill before they took the herb, and on products whose identity was never verified. Each subsequent publication has cited the earlier ones, creating an impression of a large body of evidence where in fact there is very little.

Sixth, the scientific community has already responded. In July 2021, after the first reports appeared, the Ministry of Ayush issued a detailed statement explaining that linking giloy to liver damage was misleading, that the authors had not analysed the contents of the herb consumed, and that giloy is among the most commonly prescribed medicines in Ayurveda [7]. This official assessment, made by the national authority responsible for Ayurveda, should settle the question. It is surprising that a 2024 review should revive concerns that were addressed three years earlier without engaging with the Ministry's analysis.

Seventh, the pharmacological literature points in the opposite direction. Reviews of *T. cordifolia* describe immunomodulatory, antioxidant, anti-inflammatory and hepatoprotective activity in experimental models, and note that the plant is valued precisely because, unlike synthetic drugs, it is free of side effects [8]. A herb that protects the liver in the laboratory cannot reasonably be expected to damage it in patients. Where liver injury occurs after giloy use, a contaminant, an adulterant or a coincidental illness is a far more plausible explanation than the herb itself.

We do not dispute that clinicians should ask about herbal use when they see a patient with unexplained liver injury. But we are concerned about the wider consequences of reviews such as this. Ayurvedic physicians already report that patients are stopping giloy, and other well-tolerated Rasayana herbs, out of fear generated by media coverage of these papers. Patients who abandon traditional care may turn instead to unregulated supplements bought online, which carry genuinely higher risks. Scientific caution must be balanced against the harm of discouraging a safe and culturally important practice.

Table 1. The principal Indian reports cited as evidence of giloy hepatotoxicity, and our assessment.

Report	Design	What was found	Our assessment
Nagral et al. 2021 [2]	Case series, Mumbai	Six patients with jaundice after giloy-containing immune boosters	All had autoimmune features; pre-existing disease unmasked, not caused
Kulkarni et al. 2022 [3]	Multicentre, 13 centres	Liver injury attributed to giloy across India	Mostly chronic liver disease; product not authenticated
Philips et al. 2018 [6]	Single centre, Kochi	Severe injury linked to Ayurvedic and herbal medicines	Injury confined to unregistered healers' products
Philips and Theruvath 2024 [1]	Narrative review	Giloy listed among hepatotoxic Ayush herbs	Built on the three reports above; adds no new cases

Assessment by the authors of this letter.

We therefore make three requests. First, that the authors clarify how many of the patients in the cited studies had liver disease before taking giloy, and exclude them from any estimate of risk. Second, that future reports of herb-associated liver injury be accepted for publication only when the product has been botanically authenticated and chemically analysed. Third, that the authors acknowledge the Ministry of Ayush's assessment and the substantial experimental evidence for the hepatoprotective action of giloy. Without these steps, the review risks presenting a weak and biased body of evidence as settled fact.

We would add that the review's broad concern about 'Ayush herbs' risks frightening patients away from a safe and effective system of care. Giloy is classically described as a hepatoprotective Rasayana, and it remains one of the most valuable herbs in the Ayurvedic pharmacopoeia. We urge the authors and readers to interpret these isolated case reports with appropriate caution, and to recognise that the weight of traditional and modern evidence supports the safety of giloy.

Competing interests. None declared.

References

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