

# Correspondence

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## Noni juice protects the liver

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We respectfully submit this response to the article by Millonig *et al.*, titled 'Herbal hepatotoxicity: acute hepatitis caused by a noni preparation (*Morinda citrifolia*)' which was published recently in *European Journal of Gastroenterology & Hepatology* [1]. The authors report a case study of a patient with highly elevated liver enzymes which they link to the consumption of a noni (*Morinda citrifolia*) fruit juice.

Spontaneous liver failure is a common phenomenon and the reason for such a reaction remains unknown in a variety of cases [2]. More than 600 medications, occupational, environmental and domestic agents have been reported to cause 'drug induced liver disease' [3]. Among the possible causes are: rare viral infections for which no antiserum is yet available; exposure to fungal toxins or bacterial endotoxins in food; exposure to organic solvents or other hepatotoxic chemicals, and consumption of drugs, such as paracetamol, tetracycline, acetaminophen, for example.

It is impossible for the authors to come to the undisputable conclusion that noni juice caused the elevated liver enzymes. In fact, at least one of the authors (Dr Gunda Millonig) now seems to question her own conclusions as indicated by this recent e-mail statement: 'We have to stress that the association of the consumption of Noni juice and acute hepatitis, as published in our case report is observational and circumstantial. There is no proof of causality.' (E-mail correspondence of 28 July 2005.) The title of the paper: 'Herbal hepatotoxicity: acute hepatitis caused by a noni preparation' is, therefore, not justified and is misleading, because it anticipates a proven relationship between noni juice consumption and elevated liver enzymes.

A clear connection between noni juice and elevated liver enzymes can only be drawn if the same symptoms occur after re-exposure. The authors state that this is not possible due to ethical reasons. Their sense of ethics is

commendable and right, but ethics also demand that the authors should have avoided the propagation of an unproven relationship between the consumption of noni juice and the elevated liver enzymes.

The authors came to the conclusion that the histology of the liver biopsy taken from the patient indicates 'herbal toxicity'. There is no known histology that is specific for elevated liver enzymes caused by herbal products. The same histology could be produced by a variety of 'non-herbal' compounds. The manner in which the dominant findings are reported is inconsistent. Glutamate oxalacetate transferase is outside the normal range, while glutamate pyruvate transaminase is within the normal range.

In the discussion, the authors draw the conclusion that anthraquinones occurring in the noni fruit juice might be responsible for the elevated liver enzymes. The review article [4] cited for this statement does not support this hypothesis. On the contrary, the publication contains research that shows pre-exposure to noni fruit juice protects the liver of rats after exposure to carbon tetrachloride, a well-known hepatotoxic chemical.

Dr Mian-Ying Wang of the University of Illinois at Chicago states:

'Based on the scientific data generated from experiments conducted in my laboratory, Tahitian Noni<sup>®</sup> Juice demonstrated a strong liver protective effect in all female SD [Sprague-Dawley] rats and male C57 mice. Pre-treating animals with 10% Tahitian Noni<sup>®</sup> Juice in drinking water for 7 days was able to reduce DMBA (7,12-dimethylbenz(a)anthracene) induced DNA adduct formation in the liver by 70% compared to that of the positive controls. It indicated that Tahitian Noni<sup>®</sup> Juice is able to block DMBA induced DNA damage in hepatocytes, thus possibly preventing hepatocellular carcinogenesis at the initiation stage' [5].

'Furthermore, pre-treating animals with 10% Tahitian Noni<sup>®</sup> Juice in drinking water was able to significantly protect the liver from carbon tetrachloride (CCl<sub>4</sub>) exposure. The degree of liver damage was significantly decreased, and the appearance of necrotic and apoptotic hepatocytes induced by CCl<sub>4</sub> was dramatically lower compared to that of the positive controls under light and electron microscopic observation' [6].

'The liver function was also protected by Tahitian Noni<sup>®</sup> Juice in acute and chronic carbon tetrachloride induced liver injury models. In test animals receiving CCl<sub>4</sub> plus Tahitian Noni<sup>®</sup> Juice there was a significant reduction in alkaline phosphatase, total bilirubin, direct bilirubin, aspartate aminotransferase (AST) and alanine aminotransferase (ALT), compared to animals receiving CCl<sub>4</sub> plus a placebo' [8].

'The lipoprotein profile in the chronic liver injury model was improved by Tahitian Noni<sup>®</sup> Juice consumption following multiple exposures to CCl<sub>4</sub> for three months' [9]. Therefore, I strongly believe that Tahitian Noni<sup>®</sup> Juice is a liver protective nutritional beverage, rather than a hepatotoxic product. Claiming that Tahitian Noni<sup>®</sup> Juice is a hepatotoxic herb without clear scientific evidence is absolutely misleading. The evidence accumulated about Tahitian Noni<sup>®</sup> Juice over the last six years demonstrates that it has liver protective benefits and behaviors.'

Noni juice does not contain anthraquinones. Dr Johannes Westendorf of the University of Hamburg in Germany has confirmed this in his laboratory several times. Recently, the sample of Tahitian Noni<sup>®</sup> Juice which was suspected of being consumed by the Austrian patient was tested by Dr Westendorf and no anthraquinones were detected in it (J. Westendorf, University of Hamburg 2005, unpublished). The absence of anthraquinones in the suspected batch of noni juice was also confirmed and reported by the Austrian Agency for Health and Nutrition Safety (AGES). After being made aware of the article in *European Journal of Gastroenterology & Hepatology* the Agency initiated an independent analysis of Tahitian Noni<sup>®</sup> Juice in a laboratory that specializes in the analysis of anthraquinones. No anthraquinones or other hepatotoxic compounds were detected. Their conclusion was, 'Due to the current findings the above described product has no toxic effects on the liver' [10].

Moreover, the absence of anthraquinones in Tahitian Noni<sup>®</sup> Juice was a prerequisite for its approval as a novel food by the European Union. Tahitian Noni<sup>®</sup> Juice was registered in the EU as a 'novel food' in 2003 [11]. Tahitian Noni<sup>®</sup> Juice has been used since 1996 worldwide by several million people: there are no other reports of it elevating liver enzymes. Extensive toxicological studies, including acute and sub-chronic exposure to laboratory animals and humans, testing for allergenicity, genotoxicity and mutagenicity, have been performed on it. These tests were thoroughly reviewed and approved by the EU Commission's Scientific Committee on Food (SCF) [12].

A randomized, double blind, placebo controlled human trial with 96 healthy volunteers was conducted in the United Kingdom. The highest dose group received

750 ml of Tahitian Noni<sup>®</sup> Juice per day for a total of 6 weeks. Extensive examination of blood chemistry and haematology including liver enzymes did not show any abnormalities. The consumption of Tahitian Noni<sup>®</sup> Juice has been shown to have no effect on liver enzymes (Davies and Mugglestone. A single centre, double-blind, three dose level, parallel group, placebo controlled safety study with Tahitian Noni Juice in healthy subjects. BIBRA International Ltd, UK, 2003, unpublished). We therefore have considerable doubt that the patient's liver damage was related to the consumption of noni juice as reported in the article by Millonig *et al.*

In e-mail correspondence Dr Millonig stated that the causation of the elevated liver enzymes, reported in the *European Journal of Gastroenterology & Hepatology*, by noni juice 'remains an open question'. She suspects 'an idiosyncratic reaction'. This is contradictory to her statement in the article, 'this is the first case report on the hepatotoxicity of noni', which anticipates a toxic reaction (e-mail correspondence of 20 May 2005). We conclude that the paper by Millonig *et al.* contains speculative statements, lacking sufficient experimental evidence or research. The causal relationship between toxic hepatitis as stated in the title and body of the article is conjectural, unproven and damaging.

After the paper had been published an Austrian consumer protection agency, *Konsument*, initiated an aggressive campaign against noni juice, calling it a 'dangerous fruit juice' [13]. Several newspapers in Austria and Germany, as a result, published their own concerns about the consumption of noni juice, causing considerable negative impact on the sale of the product. *Konsument* justified their campaign by citing the now disputed article written by Millonig *et al.*

From the research completed on Tahitian Noni<sup>®</sup> Juice by independent laboratories and by the laboratory at Tahitian Noni International, Inc. the results show noni protects the liver. Case studies involve one person under conditions that are not statistically valid. The experiments on noni were conducted in laboratories under controlled conditions and yielded significant conclusions that noni protects the liver.

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## Reply

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Thank you for giving us the opportunity to reply to Mr Jensen's letter [1]. We would like to stress that our publication was a case report [2]. Case reports are by definition clinical observations that aim to work up an unusual clinical finding with appropriate clinical methods. A case report never substitutes for clinical trials and never claims statistical significance. On the other hand, case reports enable clinicians to share experiences and to create awareness of a particular problem. It is always possible that our patient's abnormal liver function and biopsy were due to an idiosyncratic reaction, but this can only be clarified by further experience with the juice. We have to stress that the association of the consumption of noni juice and acute hepatitis as published in our case report is observational and circumstantial. There is no proof of causality to be expected from a case report.

We would like to point out that an association between the consumption of noni juice and hepatotoxicity has been suggested by other workers. Stadlbauer and colleagues [3] have recently reported two other cases independently of our own observations. This indicates that a high level of suspicion is appropriate.

With our case report we intended to add to the discussion of herbal hepatotoxicity. The fact that this report was

chosen for publication with an accompanying editorial and has raised so much interest in people from the medical/scientific community as well as in the general population merely indicates the need to evaluate and reassess novel food products that are offered in increasing number.

We declare that there is no conflict of interest pertaining to either of the authors.

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