



Editorial

Drinks to alleviate liver fibrosis?



In recent years, encouraging beneficial effects of different phytochemicals have been demonstrated. Furthermore, the application of phytochemicals as therapeutic agents has become possible, and the roles that nutraceuticals and pharmaceuticals play are becoming increasingly similar. Such a development, however, is not novel. For instance, phytochemicals such as silymarin have been used for decades to alleviate chronic hepatitis, and its antioxidant and anti-inflammatory effects have generally been proved.

Among known nutraceuticals, noni juice is obtained from the Pacific Basin *Morinda citrifolia* tree's fruits, and currently has aroused considerable attention because of its multiple beneficial functions and its lack of significant side effects and toxicity. It has been suggested that noni juice could be efficacious for a variety of clinical conditions, including bone resorption disorders¹ and cancer.² For a physical condition with excessive bone resorption, noni leaf extract promoted bone regeneration and suppressed bone resorption. The implicated mechanisms in these processes include the enhancement of osteoblast generation and survival, inhibition of osteoclast growth and activities, suppression of inflammation, improvement of bone collagen synthesis, and upregulation of estrogen receptor 1. *Morinda* leaves at a dose of 300 mg/kg body weight mitigated the estrogen deficiency bone loss, indicating benefits for aged and menopausal women.¹ The anticancer effect of noni is worth noting as well: damnacanthal, a noni anthraquinone, induced cell cycle arrest and apoptosis of H400 oral cancer cells.³ Angiogenesis, the crucial stage of carcinogenesis and many diseases, can also be inhibited by the noni anthraquinone damnacanthal via inhibition of multiple kinases, including vascular endothelial growth factor receptor-2, c-Met, and focal adhesion kinase.⁴ Damnacanthal inhibited tubulogenesis, endothelial cell proliferation, and survival, migration, and production of extracellular matrix remodeling enzyme in *ex vivo* and *in vivo* experiments, indicating the potential use of noni in cancer therapy.⁴ Moreover, Lim et al⁵ had demonstrated that noni leaves inhibited lung cancer metastasis via anti-inflammation, antioxidant effect, and activation of apoptotic gene.

Antioxidant and anti-inflammatory activities of noni juice have also been identified in an experimental model with carrageenan-induced paw edema.⁶ Noni juice appeared to

inhibit pulmonary inflammation as well.⁷ In their study entitled “Hepatoprotective effects of naturally fermented noni juice against thioacetamide-induced liver fibrosis in rats”, published in this journal, Lin et al⁸ found that naturally fermented noni juice ameliorated liver fibrosis via enhancing antioxidant capacities and downregulating matrix metalloproteinase-2/matrix metalloproteinase-9 activities. This study is of note because the impacts of noni juice on thioacetamide-induced liver injuries and fibrosis have not been reported previously.

Although the data are promising, one concern that bears further consideration is the possible chronic use of noni fruits in high doses. In female mice with 6-month chronic treatment, noni fruit extract was accompanied by chronic liver toxicity at a high dose of 2 mg/mL drinking water, which was supported by histological evidence of hepatocyte necrosis, an elevated liver enzyme level, a lower circulating albumin level, and 40% mortality rate within 3 months. By contrast, there was no significant toxicity with either a low or a high dose of noni leaf extracts. The authors hypothesized that the toxicity of the *M. citrifolia* fruit extract might be due to the anthraquinones in the seeds and skin, which had potent quinone reductase inducer activity and could damage the liver.⁹ Indeed, the toxicity study applied different methods to extract noni juice from various parts of the plant, and used different doses and animal species from those of the current study performed by Lin et al.⁸ Furthermore, Lin et al⁸ did not find evidence of liver inflammation in Wistar rats with 8-week treatment; by contrast, noni juice even ameliorated thioacetamide-induced liver injuries. Nevertheless, the various results remind us of the necessity of a careful and thorough search of the beneficial and harmful components from the *M. citrifolia* tree, and the need to find a safe dosing schedule for humans.

Our study has further confirmed how nutraceuticals are promising in the control of diseases because the large majority of them do not induce noticeable side effects or adverse response. The accessibility and even good flavor of nutraceuticals compared with the pharmacological agents also make nutraceuticals popular and welcomed by the general population. Indeed, it is never imprudent to be sensibly cautious in the interpretation of different findings and the application of basic studies to clinical practice.

Conflicts of interest

The author declares that she has no conflicts of interest related to the subject matter or materials discussed in this article.

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