SHORT COMMUNICATION

Xanthine Oxidase Inhibiting Effects of Noni (Morinda citrifolia) Fruit Juice

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INTRODUCTION

Morinda citrifolia L. (noni), family Rubiaceae, has been used in Polynesia for over 2000 years for its reputed health benefits, one of which is its therapeutic effects on gout (langa e hokotanga hui). However, its healing mechanism has not been elucidated. This study showed that in an in vitro bioassay that Tahitian Noni® Juice (TNJ) inhibited xanthine oxidase (XO) concentration dependently. Concentrations of 1, 5 and 10 mg/mL of TNJ inhibited XO by 11%, 113% and 148%, respectively, with an IC50 of 3.8 mg compared with an IC50 of 2.4 μM for allopurinol. Noni fruit juice concentrate (NFJC) also inhibited XO concentration dependently. Concentrations of 1 and 5 mg/mL NFJC inhibited XO in vitro by 184% and 159%, respectively. A 0.1 mg/mL methanol extract (NFJME) from the fractionation of noni fruit puree inhibited XO by 64%. It was elucidated that the noni fruit juice inhibitory effect on XO enzymes is the mechanism by which noni ameliorates gout and gout-like diseases. Further, the results also support the traditional usage of noni in the treatment of gout.

MATERIALS AND METHODS

Noni samples. Both noni fruit juice concentrates (NFJC, 50% total solids) and the commercial brand Tahitian Noni® Juice (TNJ) were obtained from the manufacturer. Noni fruit juice methanol extract (NFJME) was obtained from our internal fractionation project. It was extracted as follows: 2 kg of freeze-dried powder of M. citrifolia puree (lot # 52410) was percolated with 20 L of methanol to afford the MeOH extract solution.

Xanthine oxidase inhibition assay. This in vitro assay was done according to an established protocol (Hatano et al., 1990). Briefly, different concentrations (1, 5 and 10 mg/mL) of both TNJ and NFJC samples, and 0.1 mg/mL NFJME were evaluated for their inhibitory effects in duplicates on XO enzymes obtained from bovine buttermilk. A reaction mixture comprising 165 μM of xanthine substrate and noni samples (TNJ, NFJC and NFJME) previously dissolved in 1% DMSO was preincubated for 15 min at 25 °C in 33.3 mM phosphate buffer pH 7.5. A solution of xanthine (100 μL) in phosphate buffer (0.2 units/mL) was added to the reaction mixture and incubated for 30 min at 25 °C. The reaction was stopped by adding 100 μL (0.5 M) HCl. The uric acid productions from each reaction were quantitated using spectrophotometric analysis. Allopurinol was used as a reference alongside the noni samples.

RESULTS AND DISCUSSION

Xanthine oxidase enzymes were inhibited by the noni samples concentration-dependently (Table 1). The inhibition of XO enzyme was more pronounced with NFJC than with TNJ. However, the inhibition of XO by NFJC was higher with 1 mg/mL than with the 5 mg/mL concentration. It is possible that the concentration of the compounds in NFJC, which is five times more concentrated than the normal noni fruit juice, is responsible.
XANTHINE OXIDASE INHIBITING EFFECTS OF NONI (MORINDA CITRIFOLIA)

for the XO inhibitory effects competing with each other, thus reducing the predicted concentration-dependent inhibitory effects. Interestingly, the inhibition of XO by NFJME was about six times more than that of 1 mg/mL TNJ.

Xanthine oxidase is an enzyme involved in the production of free radicals, and is known to be involved in the development of gout disease, due in part to its bio-conversion of hypoxanthine and xanthine to uric acid. Concomitantly, the overproduction and/or under-secretion of uric acid results in hyperuricemic conditions such as gout (Kong et al., 2000; Rasaratnam and Christo-phidis, 1995; Mashino et al., 2000). As such, one of the therapeutic approaches used in treating gout is the use of pharmaceutical drugs such as allopurinol, or medicinal plants that have XO-inhibiting properties to block the conversion of hypoxanthine and xanthine to uric acid. Hence, reducing the amount of uric acid leads to amelioration of gout conditions. Allopurinol has been used clinically in past decades for the treatment of gout (Gilman et al., 1985; Fields et al., 1996). However, its side effects have led others to look for new alternatives which have XO-inhibiting activity.

Traditional healers in various parts of the world treat gout with various medicinal plants. In India and Pakistan, healers use Coccinia grandis, Datura metel, Stychnos nux-vomica, Pistacia integerrima and Vitex negundo. Recently, their XO-inhibitory effects have been elucidated as the mechanism for their antigout effects (Umamaheswari et al., 2007; Ahmed et al., 2008). The Chinese have also used various medicinal plants for centuries to treat gout: Cinnamomum cassia, Chrysan-theum indicum, Lycopus europaeus and Polygonum cuspidatum, to name just a few. Kong et al. (2000) found that these medicinal plants have XO-inhibiting activities, which account for their antigout effects.

Similarly, noni has been used in Polynesia for over 2000 years for treatment of gout and other diseases (Palu et al., 2008; Palu, 2004), but the actual mechanisms of its effect have never been elucidated. The results from this study demonstrate that XO enzymes are inhibited in a concentration-dependent manner by TNJ, NFJC and NFJME (Table 1).

The experiments suggest that the inhibitory effects of noni fruit juice on XO enzymes may be responsible for its inhibitory effects on gout in the traditional usage in Polynesia folk medicine. It is also a novel platform for isolating the active compounds responsible for this effect, which may be useful for therapeutic treatment of gout and/or gout-like conditions. Clinical trials to support our hypothesis on the XO-inhibition are warranted.

Acknowledgements

We thank the Founders of Morinda, Inc. for allocation of funds to carry out this study. Also, we thank Silvia Latai Tulaki Palu, a Tongan traditional healer for sharing her knowledge with us about the traditional usage of noni for gout and gout-like diseases in Tonga.

Potential conflict of interest

All authors are employees of Tahitian Noni International Inc., a subsidiary of Morinda Inc.

REFERENCES


Palu SLT. 2004. Personal conversation with a Tongan traditional healer. Orem Utah 84058, USA.


Table 1. Average percent inhibition of xanthine oxidase enzymes by various noni fruit juice preparations

<table>
<thead>
<tr>
<th>Noni sample</th>
<th>Concentration (mg/mL)</th>
<th>Average % XO inhibition</th>
<th>IC50 (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNJ</td>
<td>1</td>
<td>11</td>
<td>3.8</td>
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<tr>
<td></td>
<td>5</td>
<td>113</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10</td>
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<td></td>
</tr>
<tr>
<td>NFJC</td>
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<td></td>
</tr>
<tr>
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<td>NFJME</td>
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