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SHORT COMMUNICATION

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

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***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 IC_{50} of 3.8 mg compared with an IC_{50} 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.**

Keywords: xanthine oxidase; noni; gout; *Morinda citrifolia*.

INTRODUCTION

Morinda citrifolia L. commonly known as noni, from the family Rubiaceae, has been used in Polynesia for over 2000 years for food, medicine and dyeing of traditional clothes. Its medicinal usage has been purported to include the amelioration of diabetes (*suka*), gout (*kauti*), high blood pressure (*toto ma'olunga*), cancer (*kanisā* or *kahi*), boils (*hangatāmaki*), and other skin and internal ailments (Wang *et al.*, 2002; Palu, 2004; Palu *et al.*, 2008).

Traditionally, noni fruit juice was also consumed after a long voyage to help strengthen and restore vigor to the body (Thaman, 1990, 1992). It has also been used to treat gout. However, the mechanism responsible for this effect has not been elucidated. The inhibitory effects of noni fruit juice on the enzyme xanthine oxidase are reported.

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. The solution was concentrated to a syrup using a rotary evaporator. A small portion of the syrup was taken and dried to result in 2 g of the MeOH extract of the noni fruit powder. The remaining syrup was added with 3 L of H_2O, and then partitioned sequentially against petroleum ether (3 L × 4) and EtOAc (3 L × 3), to afford petroleum ether (41.7 g) and EtOAc (47.7 g) partitions.

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 spectrophotometic 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

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

Noni sample	Concentration (mg/mL)	Average % XO inhibition	IC_{50} (mg)
TNJ	1	11	3.8
	5	113	
	10	148	
NFJC	1	184	
	5	159	
NFJME	0.1	64	

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 undersecretion of uric acid results in hyperuricemic conditions such as gout (Kong *et al.*, 2000; Rasaratnam and Christophidis, 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*, *Chrysanthemum 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.

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Potential conflict of interest

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

REFERENCES

Ahmed NS, Farman M, Najmi MH, Mian KB, Hasan A. 2008. Pharmacological basis for use of *Pistacia integerrima* leaves in hyperuricemia and gout. *J Ethnopharmacol* **117**: 478–482.

Fields M, Lewis CG, Lure MD. 1996. Allopurinol, an inhibitor of xanthine oxidase, reduces uric acid levels and modifies the signs associated with copper deficiency in rats fed fructose. *Free Radic Biol Med* **20**: 595–600.

Gilman AG, Goodman LS, Rall TW, Murad F. 1985. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*, 7th edn. Macmillan: New York.

Hatano T, Yasuhara T, Yoshihara R, Agata I, Noro T, Okuda T. 1990. Effects of interaction of tannins with co-existing substances. VII. Inhibitory effects of tannins and related polyphenols on xanthine oxidase. *Chem Pharm Bull* **38**: 1224–1229.

Kong LD, Cai Y, Huang WW, Cheng CHK, Tan RX. 2000. Inhibition of xanthine oxidase by some Chinese medicinal plants used to treat gout. *J Ethnopharmacol* **72**: 199–207.

Mashino T, Takigawa Y, Saito N, Wong LQ, Mochizuki M. 2000. Antioxidant activity and xanthine oxidase inhibition activity of reductic acid: ascorbic acid analogue. *Bioorg Med Chem Lett* **10**: 2783–2785.

Palu AK, Kim AH, West BJ, Deng S, Jensen J, White L. 2008. The effects of *Morinda citrifolia* L. (noni) on the immune system: its molecular mechanisms of action. *J Ethnopharmacol* **115**: 502–506.

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

Rasaratnam I, Christophidis N. 1995. Gout: a disease of plenty. *Aust Fam Physician* **24**: 849–851, 855–856, 859–860.

Thaman RR. 1990. Kiribati agroforestry: trees, people and the atoll environment. *Atoll Res Bull* **333**: 1–29.

Thaman RR. 1992. Batiri kei baravi: the ethnobotany of Pacific island coastal plants. *Atoll Res Bull* **361**: 1–62.

Umamaheswari M, AsokKumar K, Somasundaram A, Sivashanmugam T, Subhadradevi V, Ravi TK. 2007. Xanthine oxidase inhibitory activity of some Indian medicinal plants. *J Ethnopharmacol* **109**: 547–551.

Wang MY, West BJ, Jensen CJ *et al.* 2002. *Morinda citrifolia* (Noni): A literature review and recent advances in Noni research. *Acta Pharmacol Sin* **12**: 1127–1141.