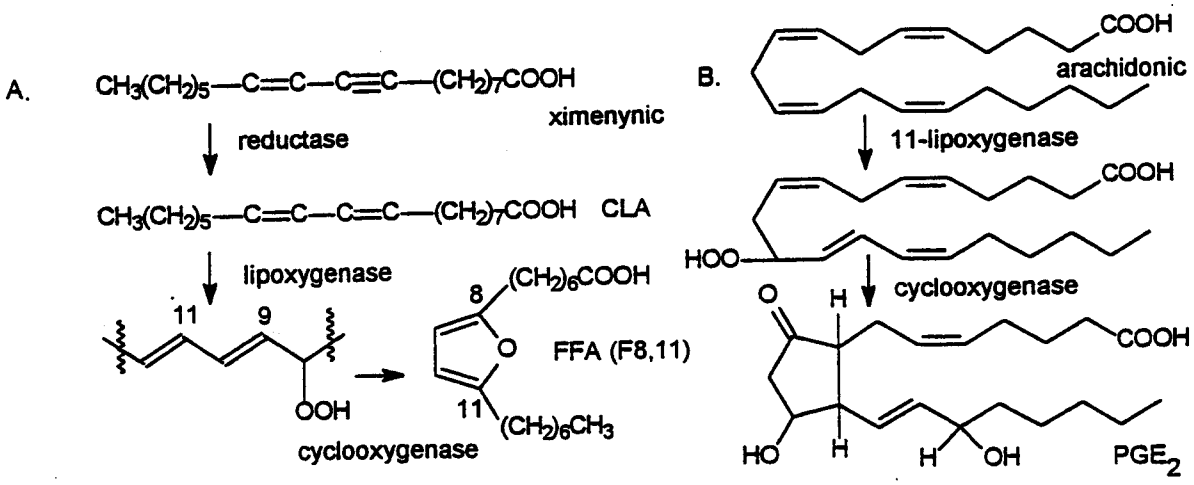
A biotransformation product of ximenynic acid and its significance.

YD Liu, RB Longmore

School of Pharmacy, Curtin University of Technology, Perth, WA 6102

The seed kernels of sandalwood, *Santalum spicatum*, have formed a valuable part of the traditional Aboriginal Australian diet and were also used for a therapeutic effect to treat arthritis by oral ingestion and when macerated as a topical application for skin lesions. Ximenynic acid (XMY), a significant fatty acid in the seed oil triglycerides, may interact in aspects of eicosanoid pharmacology (1). This study investigated the metabolism of XMY to explain its potential for anti-inflammatory activity.

Six week old female mice were fed a 15% sandalwood seed oil diet and killed by cervical dislocation eight weeks later. The mouse liver total lipids were extracted from homogenised organ tissue and were converted to the 4,4-dimethyloxazoline (DMOX) fatty acid derivatives which were then characterised and quantified using gas chromatography (GC) with mass spectral (MS) detection. GC/MS analysis showed the presence of a minor exotic fatty acid derivative in addition to the other expected fatty acid components such as palmitic, stearic, oleic and XMY acids. The derivative has been determined to be a furanoid fatty acid (FFA), 8,11-epoxy-8,11-octadecadienoic ($F_{8,11}$) acid, previously reported as an oxidation product of conjugated linoleic acid (CLA). A possible metabolic pathway for XMY (A) and its relationship to the biosynthesis of prostaglandin PGE_2 from arachidonic acid (B) are shown in the Figure:



Inhibition of the first oxygenation step in prostaglandin biosynthesis is significant in anti-inflammatory drug treatments for rheumatoid arthritis (2). XMY has a structure analogous to the normal substrate, arachidonic acid, and may thus act as a competitive inhibitor and alternative substrate for the essential cyclooxygenase and lipoxygenase enzymes which produce inflammatory prostaglandins. Thus sandalwood (*S. spicatum*) seed kernels may be both a food and a medicine.

1. Croft KD, Beilin LJ, Ford GL. Differential inhibition of thromboxane B_2 and leukotriene B_4 biosynthesis by two naturally occurring acetylenic fatty acids. Biochim Biophys Acta 1987;921:621-4.
2. Gilman AG, Rall TW, Nies AS, Taylor P. The pharmacological basis of therapeutics. New York: Pergamon Press, 1991:602-3