DOI 10.1002/lite.200900071

Feature

Western Australian sandalwood seed oil: new opportunities

Dhanushka Hettiarachchi, Yandi Liu, John Fox and Bruce Sunderland

Dhanushka Hettiarachchi is a Doctoral Candidate, School of Pharmacy, Curtin University of Technology and a scientist at Wescorp Sandalwood Ltd, Bibra Lake, WA 6157 Australia. Tel: +61-8-9418 2888; e-mail: danny@wescorp.com.au

Yandi Liu is an adjunct Professor; John Fox Professor, Dept of Environmental & Aquatic Science, Curtin University of Technology, Bentley, WA 6152 Australia. e-mail: Y.Liu@curtin.edu.au; J.E.Fox@curtin.edu.au

Bruce Sunderland is a Professor, School of Pharmacy, Curtin University of Technology, Bentley, WA 6152 Australia. Tel: +61-8-9266 7377; e-mail: B.Sunderland@curtin.edu.au

Summary

Western Australian Sandalwood (Santalum spicatum R.Br.) is an economically important timber crop. Sandalwood seeds have been identified as a potential secondary source of income prior to harvesting the tree. Chemical and toxicological studies of the seed have found that the kernels contain nearly 50% of a drying oil. This oil is comprised mainly of unsaturated fatty acids. The presence of an unusual acetylenic fatty acid has been confirmed. The oil was found to cause no pathological abnormalities in mice but reduced fat deposition. Acetylenic fatty acids are known to inhibit eicosanoids and stimulate certain enzymes, even though dietary consumption is yet to be trialled. The oil has potential uses in cosmetic and external pharmaceutical applications. Vegetable oils used in pharmaceutical and cosmetic formulations require high oxidation stability and antioxidant activity and benefit from the presence of other compounds such as sterols and tocopherols. This article summarises the research conducted over a half a century on sandalwood seeds and considers suitable uses and the future research needed to commercialise this oil.

Introduction

The species of sandalwood found in Western Australia (WA) is known as WA sandalwood (*Santalum spicatum* R.Br.) and produces scented wood valued in cosmetics and traditional Asian religious practices. Sandalwood oil, the steam distilled essential oil from the heartwood, has been used as a perfumery agent for over 150 years. Many perfume manufacturers depend upon sandalwood oil as a fixative agent despite its high price. Sandalwood was traditionally supplied from India and Pacific nations but due to decreasing availability of these sources *S. spicatum* has gained wide popularity. WA sandalwood has developed from natural growth harvesting to a commercial forestry industry. Seeds of this tree are a potential source of income during the long growth period before the trees are harvested. The high oil content of these seeds is a valuable resource in the ever-increasing global demand for vegetable oils. Although some research has been done on the seed oil, finding new market opportunities is seen as an important requirement to support WA's sustainable sandalwood industry.

Western Australia Sandalwood

WA sandalwood is mostly found in the arid rangelands of Western Australia and South Australia. It is one of five endemic *Santalum* species (family Santalaceae) found in Australia. In contrast to its Indian and Pacific cousins, it is a small tree or shrub with moderate foliage, dull grey/green leaves, a trunk diameter of 10–30 cm and growing on average to 5 m in height. This tree is a root hemi-parasite dependent upon a host plant throughout its life. After 3-4 years the tree bears annually significant numbers of a large fruit in the form of a drupe containing a hard-shelled seed. These become ripe from September to November (spring). The seed has a weight varying from 1–5 g. A hard endocarp shell covers the kernel which on average is 28% of the total seed weight.

The Australian sandalwood industry is evolving from naturally grown wood harvesting starting in 1845 to cultivation and sustainable harvesting in this new millennium. Initially wood was exported to Asia mainly for the joss stick industry. Timber was largely exploited from near coastal locations but remain abundant in the rangelands of WA. Land clearing during the mid 19^{th} and 20^{th} centuries provided an enormous sandalwood resource that initially provided the highest source of foreign income to the new colony. Once it was identified as an important natural resource which needed protection, the WA State Government implemented strict measures to control harvesting which still apply. Currently, wild harvested wood is the total industry resource under the control of the Forest Products Commission of WA and WA supplies about 50% of the global demand for sandalwood. It was identified a few decades ago that wild harvesting should be balanced with cultivation to maintain a sustainable industry. The Department of Environmental Biology, Curtin University of Technology has conducted research since 1980 on different aspects of sandalwood cultivation (1). The Forest Products Commission has taken the initiative to develop *S. spicatum* plantations and sustainable harvesting has been welcomed by many indigenous communities, farmers and private organisations. Plantations require a 15 years growth period before income is generated from harvesting the plantation. The seeds have been identified as a suitable source to provide some regular income during the growth period and encourage more investment.

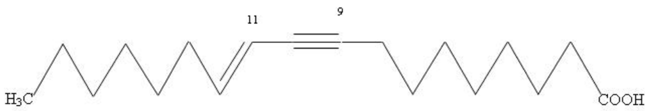

Figure 1. *trans*-11-octadecene-9-ynoic acid.

Sandalwood seed oil

In addition to the valuable wood and in contrast to other Santalum species, the WA species produces a large fruit with edible kernels. There is some evidence of nutritional, cosmetic and medicinal uses by the aboriginal population of WA though its suggested use for arthritis is only anecdotal. The seed is rich in a drying fixed oil (50-60%), useful in soaps and other preparations, and the oil is characterised by containing a high percentage of unusual acetylenic fatty acids such as ximenynic acid (*trans*-11-octadecen-9-ynoic acid, santalbic acid) (Figure 1).

The oil also contains a high percentage of oleic acid. Oil extracted from sandalwood seeds contains important fatty acids which are listed with their average composition in Table 1 (2).

Several studies have been conducted on seeds of the Santalaceae family. Gunstone and Russell (3) reported the structural similarity between ximenynic acid identified previously form Ximenia species with the santalbic acid, which was then considered a trienoic acid. This unusual acetylenic acid is found only in the seeds of the Oleaceae and Santalaceae families. Work carried out by Hatt *et al.* in the late 1950's identified ximenynic acid from the Australian *Santalum* species (4).

Several lipid metabolic studies have used ximenynic acid isolated from *S. accuminatum* (Australian Sweet Quondong). The acid was reported to inhibit the biosynthesis of thromboxane B_2, leukotriene B_4 and 6-ketoprostaglandin F_{1a} in rat peritoneal leukocytes. Ximenynic acid was found to be a potent inhibitor of leukotriene B_4 with IC_{50} values of 60 μM. Cyclooxygenase inhibition activity was evident in ximenynic acid by affecting the bioconversion of arachidonic acid to prostaglandins. Animal studies conducted by feeding rats with *S. accuminatum* seed oil, showed no histopathological changes but the hepatic and renal P-450 levels increased. Increased P-450 levels is an indication of a xenobiotic effect from ximenynic acid, with the authors questioning the safety of consuming quandong seeds, where the ximenynic acid concentration was 15–25% of the total kernel weight. Ximenynic acid and its sodium salt have significantly inhibited Gram positive bacterial strains and pathogenic fungi but not the growth of Gram negative bacteria. Certain chloramphenicol and co-trimoxazole resistant *Staphylococcus aureus* strains were inhibited, with the free acid ten times as potent as its sodium salt (5). The ethyl ester of ximenynic acid has been found to exert significant pharmacological properties which may be important for cosmetic and therapeutic uses. Considerable microvasculokinetic properties were observed, which were anecdotally beneficial in treating cellulitis and hair loss. Further ximenynic acid ethyl ester was found to produce vasoconstrictor effects in subjects suffering from venous insufficiency cellulitis (6).

Liu *et al.* researched the biochemical and pharmacological properties of *S. spicatum* seed oil employing three major approaches (2). First the fatty acid composition in seeds was analysed in different stages of development, then the presence of triacylglycerol molecular species of ximenynic acid in the oil were studied. Potential toxicity and bioactivity of the oil was based on consumption studies in mice. It was observed that palmitic, linoleic and α-linolenic acids tended to decrease during the maturation of the seed whilst ximenynic and oleic acids tended to increase. Although Liu *et al.* hypothesised that oleic acid could be the precursor for ximenynic acid biosynthesis, this has not been established to date. In the seed kernel ximenynic acid is known to exist as triacylglycerols with one, two, or three ximenynic acid chains. Pharmacological studies were carried out on mice fed on sandalwood seed oil enriched diet. A control group was given a standard laboratory diet and a reference group fed on canola oil enriched diet was also employed. Mice fed with sandalwood seed oil were reported to gain the least weight of the three groups, whilst the serum aspartate aminotransferase enzyme levels of sandalwood seed oil fed mice were slightly elevated possibly indicating liver damage. Additionally mice fed with sandalwood seed oil were reported to lose whiskers in the third week. In adipose tissue the ratio of unsaturated to saturated fatty acids increased; In certain tissues there were higher levels of 18:1 (n-9) and docosahexaenoic acid (omega-3 fatty acids) and lower levels of arachidonic acid. The researchers suggested ximenynic acid might stimulate the Δ9-desaturase enzyme, which is responsible for the above biochemical activity. However histopathological examinations of liver, kidney, brain and adipose tissue showed no pathological differences upon feeding with sandalwood seed oil (7).

Table 1. The Average Fatty Acid Profile of Sandalwood Seed Oil

Fatty acid	Notation	Relative percentage
Palmitic	16:0	3.4
Palmitoleic	16:1 (n-7)	0.7
Stearic	18:0	2.7
Oleic	18:1 (n-9)	52.7
Linoleic	18:2 (n-6)	1.2
α-Linolenic	18:3 (n-3)	1.3
Stearolic	18:1 (9a)	1.0
Ximenynic	18:1 (9a,11t)	30.9
Others		6.3

Novel vegetable oils

Global demand for vegetable oils has steadily increased. Traditionally vegetable oils have been used as food, and for medicinal and cosmetic uses. Increased use of edible oils in the food industry is now challenged by the development of biodiesel technology. Increased prices of petrochemicals and environmental considerations have forced the cosmetic industry to seek plant alternatives for oils and oleochemicals derived from fossil fuels. Novel oils are emerging as nutraceuticals. Many of these oils were either used traditionally or recently been identified for their pharmacological properties. For example, omega-3 fatty acids have been a major focus of any oil used as a supplementary food and neutraceutical. Several oils have reached the food industry as speciality foods or widely known as boutique oils. Examples are avocado oil, macadamia nut oil and red palm oil, which are from known food sources. In recent times many different types of oils have been introduced into cosmetics. Their exceptional properties or simply the novelty of the product has driven this demand. Certain vegetable oils have been identified with excellent topical pharmacological characteristics such as antimicrobial, antioxidant and anti-inflammatory. The cosmetic industry requires oils which have a high oxidative stability and no distinctive odour or flavour. The presence of minor components in oil is beneficial for their bioactivity as well as the shelf-life of the formulation.

Potential uses of sandalwood seed oil

In the light of the above information any potential uses of sandalwood seed oil should be carefully considered. If this oil is to be used as a nutraceutical or specialty oil the requirements to qualify as a food would require an assessment of its toxicity in humans and its nutritional value. A comprehensive pharmacological study needs to evaluate any potential cyclooxygenase inhibition activity including the ethno-pharmacological evidence. To be recognised for therapeutic purposes the mechanism of action, toxicity and efficacy needs to be established. Adverse reactions reported in several animal studies could limit such potential. Immediate action is required by the sandalwood industry as the cultivators are eager to find a market for seeds. An obvious target is the cosmetic industry which requires more natural novel oils to manage a growing demand and competition. Certain studies have found beneficial effects of ximenynic acid in certain cosmetic formulations. The free ximenynic acid has been reported to a produce foaming capability with diethanolamine or alkali-hydrolysates of gelatin. The previously discussed vascular kinetic properties and antimicrobial properties of ximenynic acid esters and salts could link to valuable topical effects and formulation advantages in cosmetics. Skin irritation and contact toxicity testing are primary requirements in cosmetics. Nut oils should be free of common allergens, odour and prominent colour. The texture of the oil also plays an important role. Oxidative stability is a major requirement when oils are used in formulations as the stability of the oil determines the shelf-life of the product. The established use of sandalwood essential oil as a perfume would facilitate the acceptance of this fixed oil in cosmetics.

Future studies

Research in the near future should target the cosmetic uses but pharmacological research leading to potential medicinal or nutritional uses would be highly beneficial for the long term growth of the industry. Effective industrial extraction methods are needed to provide an oil of suitable quality for the cosmetic industry. The current tendency towards greener sourced cosmetic and nutraceutical products requires oil to be extracted by non-chemical means such as by cold pressing. Some seeds need a chemical agent as physical expression is not capable of extracting oil from the kernel. Some methods have emerged in lipid technology to overcome this problem. Among them enzymatic extraction and supercritical fluid extraction are the most commonly used or in experimental development. These are relatively expensive compared with physical expression or solvent extraction, however more acceptable than the latter to potential users. These methods extract and preserve the minor components in the oil better than conventional methods. In a small-scale industry such as sandalwood seeds specificity of the end use of the product(s) and exclusion of refining steps will be beneficial. Most nut oils are rich in tocopherols and phytosterols which are known for their health benefits both internally and topically. Tocopherols and other natural antioxidants not only produce a health benefit but improve the shelf-life of oils. The composition of minor components in any of the Santalaceae family seeds has not been reported. A future study should identify and quantify these compounds, along with the best method to extract them in maximum concentrations. Moreover an oil used for cosmetics or other oleochemical possibilities should have high oxidative stability; this will be one of the main factors required by formulation technologists. There are many accelerated stability measurement methods for lipids, the active oxygen method measuring peroxide value is the most conventional method and methods like Rancimat© and oxy-tester© methods are widely accepted for edible oil evaluation. Auto-oxidation of ximenynic acid or any other acetylenic fatty acids have not been reported to the author's knowledge. Several chemical and enzymatic oxidative studies are needed along with a stability study as previously mentioned. Oxidative by-products of ximenynic acid also need to be identified to confirm the safety and stability of the product.

Conclusion

The sandalwood industry needs to find a use for the annual seed harvest to improve its sustainability. These seeds are rich in oil and contain ximenynic acid as glycerol esters. Acetylenic fatty acids have unique bioactivity including cyclo-oxygenase inhibition. This pharmacological activity could substantiate the claims of aboriginal people of Australia in their use of these seeds to treat arthritic pain and skin lesions. Adverse effects from the oil when taken internally have been reported in several animal studies. Detailed pharmacological and toxicological research is necessary to establish the oil as a medicinal, nutraceutical or cosmetic agent. Considering the chemical and basic pharmacological research undertaken in the past, future studies should focus on more specific potential uses. Extraction methods need to be developed in order to address the specific market needs followed by an evaluation of the requirements concerning the potential cosmetic use of this oil. Considerable further research will be necessary to establish any nutritional and medicinal value.

References

1. Fox, J.E.D. (2000) Sandalwood: the royal tree, *Biologist*, 47, 31.
2. Liu, Y. (1997) A study of the biochemical development and toxicology of the seed of *Santalum Spicatum*, *Doctor of Philosophy,* School of Pharmacy, Curtin University of Technology, Perth.
3. Gunstone, F.D. and W.C. Russell. (1955) Fatty Acids Part III The constitution and properties of santalbic acid, *J. Chem. Soc.*, 3782–3787.
4. Hatt, H.H. (1956) Some seed fats of the Santalaceae family, *Journal of the Science of Food and Agriculture*, 7, 130.
5. Jones, G.P., *et al.* (1999) Santalbic acid from quandong kernels and oil fed to rats affects kidney and liver P450, *Asia Pacific Journal of Clinical Nutrition*, 8, 211–215.
6. Bombardelli, E., *et al.* (1994) Microvasculokinetic activity of ximenynic acid ethyl ester, *Fitoterapia*, 65, 195.
7. Liu, Y. and R.B. Longmore. (1997) Dietary sandalwood seed oil modifies fatty acid composition of mouse adipose tissue, brain and liver, *Lipids*, 32, 965–969.