International Journal of Cosmetic Science, 2002, **24**, 341–348

Tamanu (*Calophyllum inophyllum*) – the African, Asian, Polynesian and Pacific Panacea

A. C. Dweck* **and T. Meadows†**

*Dweck Data, 8 Merrifield Road, Ford, Salisbury, Wiltshire, SP4 6DF, UK and †Concentrated Aloe Corporation, 123 North Orchard Street, #4 A Ormond Beach, FL 32174, USA

Keywords: calophyllolide, *Calophyllum inophyllum*, cicatrising, complex polyphenols, inophyllum, Tamanu, traditional medicine, vulnerary

Synopsis

Tamanu or *Calophyllum inophyllum* has been used traditionally as a local medicine for many different purposes. The oil has been proven to be vulnerary and cicatrising in its effects. The chemicals responsible for this action are calophyllolide and inophyllum in addition to other complex polyphenols.

Résumé

Le Tamanu, ou *Calophyllum inophyllum,* a été utilisé en médecine traditionnelle locale pour de nombreuses et différentes raisons. L'huile a été démontrée comme vulnéraire et cicatrisante. Les substances chimiques responsables de telles actions sont les calophyllide et l'inophyllum, parmi d'autres polyphénols complexes.

Introduction

The beauty of some plants is that they occur in the ethnopharmacy and folklore of more than one country and so we are able to make comparisons between the ways in which that plant has been used medicinally and culturally. This species of *Calophyllum* has proved that its virtues not only withstand the scrutiny of independent traditional use, but also can be proven in modern *in vivo* studies to be as effective as its legend suggested.

The chemistry is complex and unusual, perhaps helping to explain some of the impressive physiological actions possessed by this plant.

Correspondence: A. C. Dweck, Dweck Data, 8 Merrifield Road, Ford, Salisbury, Wiltshire, SP4 6DF, UK. E-mail: dweckdata @aol.com

Botanical names

Calophyllum inophyllum Linn (Syn. *Calophyllum bintagor* Roxb.) (Guttiferae). It is a member of the mangosteen family. *Mesua ferrea* Linn has also been seen as an alternative Latin name.

Common names

Known in English as Alexandrian Laurel, Tamanu, Pannay Tree, Sweet Scented Calophyllum. The wood used to be sold in London as 'Borneo Mahagany'. Bag: Dankaan. Bengali: Punnang. Bombay: Undi. Burmese: Pongnyet. Can: Surahonnae, Namaeru. Cutch: Udi. Duk: Oondi. Hindi: Undi, Surpan, Surpunka, Sultan Champa. Ilk: Bitaog, Pamitaogen. Kon: Undee-phal. Mag: Langkagan. Mah: Undag, Pumag, Surangi, Nagchampa. Mal: Cherupuna, Ponnakum, Bettan. Ponna. Neg: Batarau, Palo Maria. Pamp: Bitaog. Pang: Bitaoi. Sanskrit: Punnaga, Namaeruak, Panchakaeshera, Nagachampa, Nameru, Punnaga, Purasakeshara, Surangai, Tungakeshara. Sbl: Bitaog. Sinhalese: Domba, Dombagaha, Teldomba, Sultan-champa. Sul: Tambotambok. Tag: Bangkalan, Bitaog, Bitok, Butalau, Bitong, Dagkalan, Dangkalan, Palo Maria de Playa. Tamil: Nagam, Nameru, Pinmai, Punnagam, Punnai, Punnagum, Punnaivirai. Pinnay. Tel. Pumagamu, Ponnvittulu, Ponnachettu. Hawaiian: Kamani.

Habitat

Bitaog (as it is most usually called) is found throughout the Philippines along the seashores. It is native to Tropical Asia and its geographical distribution area also includes Melanesia and Polynesia. It grows near the sea coast throughout India. In French

Polynesia, the Tamanu tree is widespread on most of the islands. It grows primarily in the coral sands and on the sea shore, although specimens may be found in valleys. Its seeds sprout easily in muddy and saline soils. The Motu (coral reefs), which surround the volcanic islands, are covered with Tamanu trees; they are very much appreciated for their fragrant flowers and elegant foliage and are thus planted along avenues [1]. Kamani, as it is also known, was brought north to Hawai'i from the South Pacific islands in early migrations of Polynesian settlers. Also called Alexandrian laurel, true kamani was probably introduced by seed, which is how it is propagated. This native of the Pacific and of tropical Africa, grows slowly along sandy shores and in lowland forests. It was cultivated in villages, near houses and also in groves away from villages. When found growing in windy areas, it is sometimes in a picturesque, crooked or misshapen form.

Folklore

Before the conversion of the Polynesians to Christianity, the Tamanu trees were considered as sacred. They were planted inside the royal marae (sacred areas). There, according to ancient beliefs, the Gods would hide in the Tamanu trees and watch human sacrifices without being seen. Idols were also carved out of Tamanu wood. It is still considered a sacred relic of the past.

Plant description

The Tamanu tree is 2–3 m high, and has a thick trunk covered with a rough, black and cracked bark. It has elliptical, shiny and tough leaves. Its flowers, arranged in axilliary cymes, have a sweet, lime-like fragrance. The tree, which flowers twice a year, is said to attain a great age.

The numerous fruits, arranged in clusters, are spherical drupes. Once ripe, their smooth, yellow epidermis discloses a thin layer of pulp, which tastes somewhat of apple. The grey, ligneous and rather soft nut contains a pale yellow kernel, which is odourless when fresh. Once chewed, it coats the mouth and emulsifies saliva, and its insipid taste becomes bitter.

Tamanu kernels have a very high oil content (75%). It is obtained by cold expression and yields a refined, greenish yellow oil, similar to olive oil, with an aromatic odour and an insipid taste. Once grown, a Tamanu tree produces up to 100 kg fruits and about 18 kg oil.

Oil processing

Unlike most vegetable oils, Tamanu oil is not contained in fresh ripe fruits. It forms in the course of the nuts' desiccation.

The oil production process is as follows: ripe and non-germinating fruits are slightly crushed in order to crack the shells without damaging the kernels. The latter are quickly removed, arranged in thin layers and exposed to the sun. They must not be exposed to humidity in any case. In spite of these precautions, some kernels mould and must be eliminated.

During the desiccation process, kernels lose weight (from a mean 7 g for fresh kernels to about 4.5 g for dry and oil-rich ones). They become brownish, develop an aromatic odour and increase their oil content. In the meantime they lose their germinative power. The transformation is completed within 2 months provided the weather has been dry enough. Kernels can then be stored for a long time.

Use of the plant and its parts

The bark, seeds and leaves are used with a bitter oil coming from the seeds together with a resin and a gum. When mature, it has a thin leathery dark grey-brownish skin which covers a bony shell that holds a partly poisonous kernel or seed surrounded by a cork-like substance. A lamp oil for light was produced from the kernel and was used at times instead of kukui nut oil. The kernel is called a 'punnai nut' in some areas of the Pacific, and the oil is dark, green, thick and called 'dilo' oil or Pinnay oil [2]. Sometimes this oil is useful for lomi lomi, massage, especially when enhanced with coconut oil or flower fragrances. The oil may have been useful in waterproofing tapa cloth and is used as a varnish. In the old days an extract from the fruit was used to make a brown dye to colour tapa cloth. The oil can also be used to make soap.

In Java, the tree is believed to have diuretic properties, whereas in Samoa every part of the plant is considered a virulent poison, with the milky juice causing blindness, the sap once introduced into the circulation causing death and so used as an arrow poison. The piscicidal activity reported in some species of *Calophyllum* may be due to the coumarin derivatives, whereas some of the irritating components reported for some species are likely to be cyanogenic compounds, tannins, saponins or pigments present [3].

The flowers

The fragrant flowers are used to make bouquets and wreaths and are also worn in the hair by Philippino women.

The shell

The round, thin shells are used as a receptacle for 'buri sugar', which is a popular confection.

External application of the plant

The application of the gum

The gum extracted from the plant (from the wounded bark) is emetic and purgative but also has use for the treatment of wounds and ulcers. It can also be mixed with strips of bark, and leaves are infused in water, and the oil that rises to the surface is another application for sore eyes [4, 2]. The resin is said to be responsible for the colour and the odour of the oil and may be poisonous; it is also said to contain benzoic acids [5]. The gum resin is said to be good for old sores and wounds [5]. The resin may be useful for chronic catarrh.

The application of the bark

The bark is astringent (contains 11–19% tannin) and its juice is purgative [5]. It is considered medicinal in Asia, being used in India (according to some this is Indo-China) for orchitis [5]. In Indonesia, it is used after childbirth for vaginal discharge, the passing of blood and also for use in gonorrhoea [6]. It is used in decoction for internal haemorrhages and as a wash for indolent ulcers [4].

The bark acts as an antiseptic and disinfectant. Rubbed with water lime juice, it makes a useful application on armpits, groins and feet in bromidrosis. The bark taken internally acts as an expectorant and is useful in chronic bronchitis and phthisis. The resin is mixed with strips of bark and leaves, steeped in water and the oil which rises to the surface is a household application for sore eyes. The astringent juice of the bark is a purgative and given in the form of a decoction for internal haemorrhages.

The application of the roots

A decoction of the root is employed for dressing ulcers and also for application in heatstroke. It is taken internally for a stitch [5].

The application of the leaves

The leaves soaked in water yield a bluish colour and natural scent is applied to inflamed eyes [4], also used for this purpose in Linga and Fiji. The leaf infusion is also taken internally for heatstroke and used in combination with an external application of the root decoction. A reverse treatment is used for a stitch where the hot poultice of leaves is applied externally and the root decoction taken internally [5].

In Cambodia, the leaves are prescribed as an inhalation for migraine and vertigo and the oil for scabies. In Madagascar, the leaves are applied to sore eyes, the pounded bark for orchitis; the gum resin is a vulnerary, resolvent and anodyne; oil from seeds is used against psoriasis and is antirheumatic. In Java, the tree is supposed to possess diuretic properties, while in Samoa the plant is considered a virulent poison and the sap from the bark is used for the preparation of an arrow poison [7].

The leaves impart a pleasant odour when soaked in water, which is used in the Philippines as an astringent for haemorrhoids (piles) [5, 6] and is used in Indonesia as an eye lotion [5, 6].

The plant has a rich history of use. Primitive tribes of native blacks throughout Papua New Guinea utilize the leaves frequently for different kinds of skin problems. On Manus, the leaves are heated over a fire until soft and then applied to skin ulcers, boils, cuts, sores, and pimples, while on Dobu Island, leaves are boiled and a skin rash is washed periodically with the solution. The natives in New Caledonia and in Samoa also utilize these leaves for treating skin inflammations, leg ulcers and wounds.

Water in which the macerated leaves have been soaked for some time has been used by them and other tribes for haemorrhoids [5].

The application of the fruits

The fruits according to some authors are more or less poisonous and only the endosperm of the still immature fruit is safe to eat. In fact, the mature fruit is sufficiently poisonous to be ground and used as a rat bait [6]. An infusion of the fruit is said to be pectoral and stimulates the mucous membrane of the lungs [5].

The application of the plant sap

The balsam (oleoresin) from the bark is used for its cicatrising properties. The Negritos of the Philippines

mix the plant sap with sulphur as an ointment to apply on boils, open sores and wounds [5].

Native blacks of Jamaica used another species *Calophyllum calaba* for healing wounds and sores in the 18th century. The resin was melted and poured into gangrenous and incised wounds requiring only a couple of changes in dressing and producing recovery [8].

A material (calophyllolide) isolated from the seeds reduced histamine inflammation and carrageenan-induced tissue swelling in rats [9].

Properties of Tamanu oil

The oil expressed from the seeds (about 60%) is sometimes called Domba oil in Europe and has proved useful in the treatment of rheumatism as well as in the treatment of itch or scabies. The figure quoted can be as high as 70–75% [2]. The oil was once thought by the old pharmacologists to be Tacamahaca oil (balsam poplar or *Populus balsamifera*). It is similar to myrhh (*Commiphora molmol*) and is also useful for indolent ulcers [2].The oil is also used in cases of gonorrhoea and gleet [4]. The oil from the seeds is used externally on rheumatism and gout and is specific for scabies [7] and may also be used for ringworm [5].

The dark-skinned natives of Fiji value the oil of the fruit as a liniment for joint pains, arthritis and bruises. The oil is applied to suppurating wounds including coral sores and is commonly used for rubbing on the limbs of children who are slow in learning to walk. Some Fijan mothers rub the fruit oil of *Calophyllum inophyllum* onto their babies to prevent nappy/diaper rash. The oil also is occasionally used in the place of a chap stick for chapped, parched lips [10]. The oil (once used in Indian oil lamps) is useful for dermal problems and is an ancient treatment for leprosy [6].

Externally, the bruised seeds and oil are applied to chronic rheumatism, inflammation of bones and joints and ankylosis. The oleoresin taken internally is supposed to be beneficial for lung ailments and externally applied on chronic ulcers and wounds with beneficial results.

In most of the South Sea islands,Tamanu oil is used as an analgesic medicine (natives use it in frictions for sciatica and rheumatism) and to cure ulcers and bad wounds. At the beginning of the century, missionaries had noticed that leprous people often came to the leper house with a bottle of oil they used to rub over their wounds. The idea occurred to them to prepare a solution of this oil in an alcoholic ether. Injections of this preparation proved effective against neuritis due to leprosy or other origins, sciatica, zona, as well as pains caused by serious diseases. This medicine is still successfully used in hospitals in Tahiti and neighbouring islands.

Tamanu oil can be applied on skins as well as mucous membrane lesions. It heals small wounds such as cracks and chaps, but is also efficient on more serious cutaneous problems: atonic wounds, physical and chemical burns, radiodermatitis, anal fissures or postsurgical wounds. Tamanu oil activity was studied in numerous clinical cases. Those healing, anti-inflammatory and antibiotic properties make Tamanu oil an excellent raw material for cosmetics, in regenerating and protective formulations [1].

This oil is especially recommended for all kinds of burns (sunburns or chemical burns), most dermatoses, postsurgical cicatrization, certain skin allergies, acne, psoriasis, herpes, chilblains, skin cracks, diabetic sores, haemorrhoids, dry skin, insomnia, hair loss, etc. In cosmetology, it is used in the preparation of regenerative creams. This soothing oil has long been a beauty secret of the Tahitian Vahine.

The oil from the seeds is used for soap making and is a rubefacient and irritant, but on the mucous membranes of the genitourinary organs it is specific. It is only employed externally and can be used as a stimulating application in cases of rheumatism [4].

In Southern India, the oil of the seeds of the plant is used specifically for treating skin diseases. It is also applied topically in cases of rheumatism [9].

Plant activity

The root bark contains and antibacterial principle [11]. The plant is also reported to have novel inhibitors of HIV-1 reverse transcriptase [12].

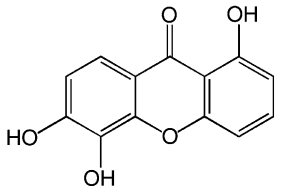
Constituents

The two main actives in this oil were discovered by a Frenchman named Professor Lederer; he succeeded in isolating two essential components of the oil of *Calophyllum*. He found a totally new fatty acid, Calophyllic acid and a lactone endowed with antibiotic properties to be at the origin of the oil's amazing cicatrizing power. The dark yellow oil extracted from the seeds contains a poisonous resin, which has a parsley-like odour. The resin is similar to myrrh and is alcohol soluble.

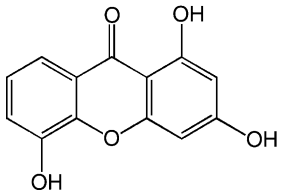
The bark contains tannin [6] and exudes an oleoresin which contains benzoic acids [7]. The oleoresin is officinal in the Mexican and Spanish Pharmacopoeias [5].

The leaves of *Calophyllum inophyllum* contain friedelin and triterpenes of the friedelin group, namely canophyllal, canophyllol and canophyllic acid [13], and from the heartwood xanthones such as mesuaxanthone B and calophyllin B are obtained [14].

Structure of Mesuazanthone-B

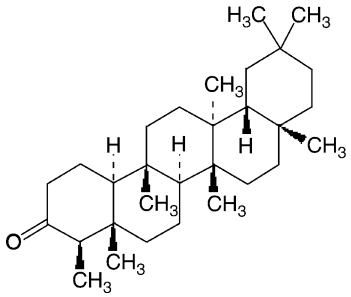


Structure of Mesuazanthone-A



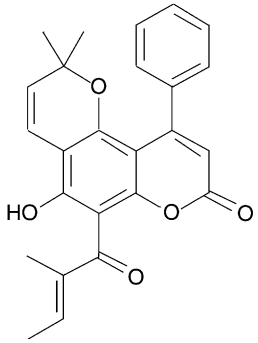
Interestingly, many of these substances, i.e. canophyllal and friedelin, are also found is *Syzigium* species [15].

Structure of Friedelin [Merck, 1996]



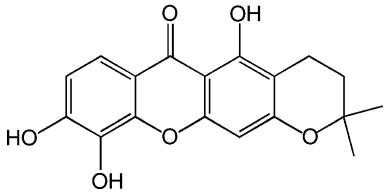
Calophyllolide was isolated from the nuts ([16–18]. ED_{50} was 140 mg kg^{-1} orally. It showed anti-inflammatopry and antiarthritic activity in formaldehyde-induced arthritis and adjuvant arthritis in rats. LD_{50} was 2.5 g kg^{-1} orally. It was devoid of ulcerogenic activity up to twice the ED_{50} dose.

Structure of Calophyllolide



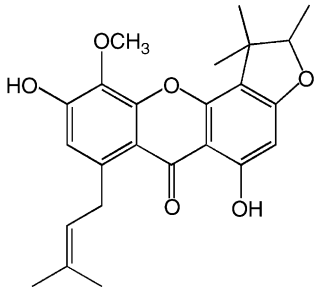
Dehydrocycloguanindin, calophyllin-B, jacareubin and 6-deoxyjacareubin produced varying degrees of CNS depression, characterized by ptosis, sedation, decreased spontaneous motor activity, loss of muscle tone, potentiation of phenobarbitone sleeping time and ether anaesthesia in mice and rats. All the xanthones exhibited anti-inflammatory activity by both intraperitoneal and oral routes in rats. Jacareubin and 6-deoxyjacareubin also showed antiulcer activity in rats [19].

Structure of Jacareubin

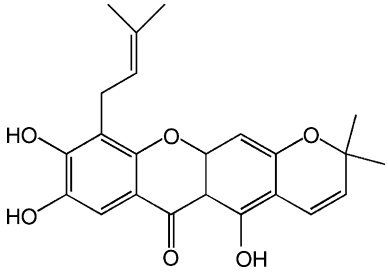


Calophyllolide, isolated from the seeds [9], reduced histamine inflammation and carrageenan-induced tissue swelling in rats. Together with inophyllide, it reduced oedema by 60.7 and 29.8%, respectively (compared to hydrocortisone, which reduced inflammation by about 44%). The safety margin of calophyllolide is very similar to that of oxyphenbutazone (21.4 and 25 mg kg^{-1}, respectively) [16].

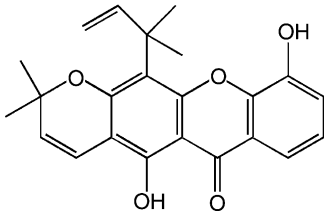
Caloxantone A



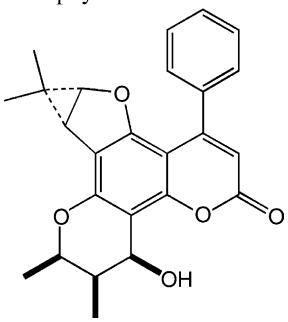
Caloxanthone B



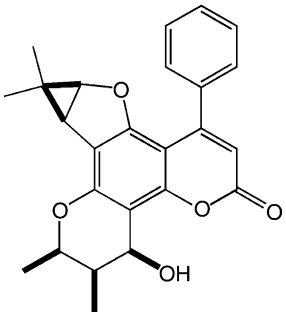
Caloxanthone C



Inophyllum G-1

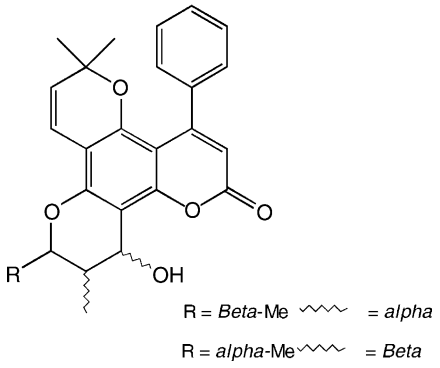


Inophyllum G-2



Inophyllums B and P inhibited HIV reverse transcriptase (IC_{50} 38 and 130 nm, respectively).

Structure Inophyllum P

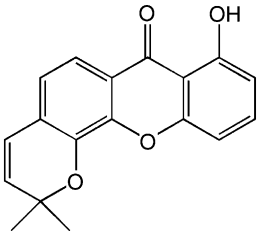


Tamanu oil contains terpenic essences, benzoic and oxi-benzoic acids. Small amounts of vitamin F and phospho-aminolipids come along with glycerides and saturated fatty acids. The plant contains 4-phenylcoumarins that have antitumour activity [20].

The following active principles have been found in the oil:

- calophyllolide ($C_{25}H_{22}O_5$) the molecule of which contains a lactonic and a methoxyl group.
- calophyllic acid ($C_{25}H_{24}O_6$), which results from the saponification of the calophyllolide.

Structure of dehydrocycloguanandin



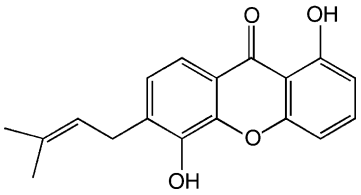
These active principles are coumarine derivatives [1].

Composition of the oil:

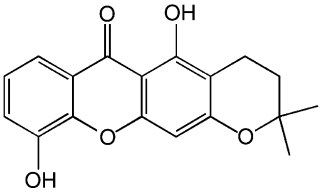
- Free fatty acids, glycerides, sterols.
- Terpenoids and steroids (canophyllal, canophyllol, canophyllic acid).

Coumarinic derivatives: calophyllolids (natural neo-flavonoids with antibacterial, anti-inflammatory and antiblood coagulation properties), inophyllolids (natural neo-flavonoids with antiviral properties), calophyllic acid (natural neo-flavonoid with antimolluscidal and healing activities).

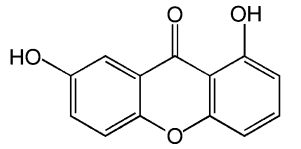
The structure of Calaphyllin-B



The structure of 6-desoxyjacareubin



The structure of Euxanthone



Preparations made from the plant

There is a local remedy made from the pounding together of the seeds of the plant (Undi) with the seeds of cachew nut, gamboge and borax, which is used as a paste and liniment.

The modern evaluation

This study evaluated the ability of one test product to improve the appearance of scars. Six subjects with visually obvious, aged scars (1 year or more) were utilized for the study. The subjects were restricted from using any moisturizing products on the scarred area for a 7-day pretest period and throughout the 9-week test period. The 0.5-ml aliquots of the product were applied to the scarred area twice a day for nine consecutive weeks. Product applications were performed by the subjects and recorded on a product application tracking form provided to them. The subjects were evaluated prior to product application

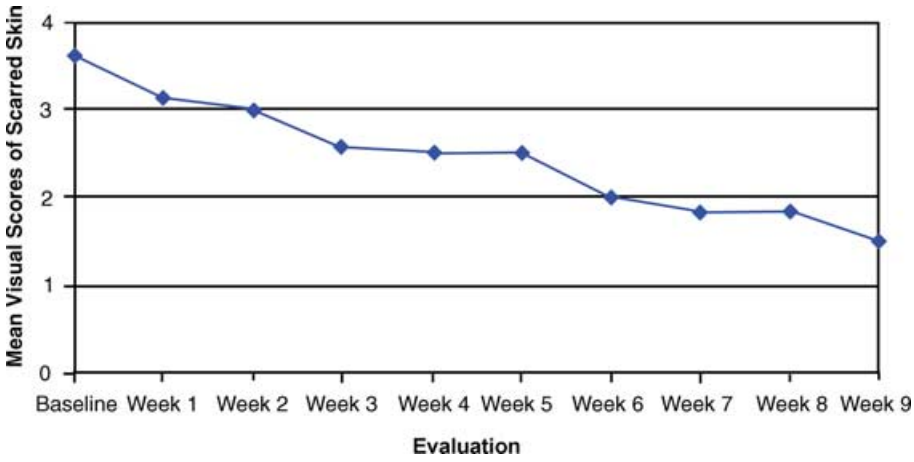


Figure 1 Graphical presentation of the mean visual scores of the scarred skin.

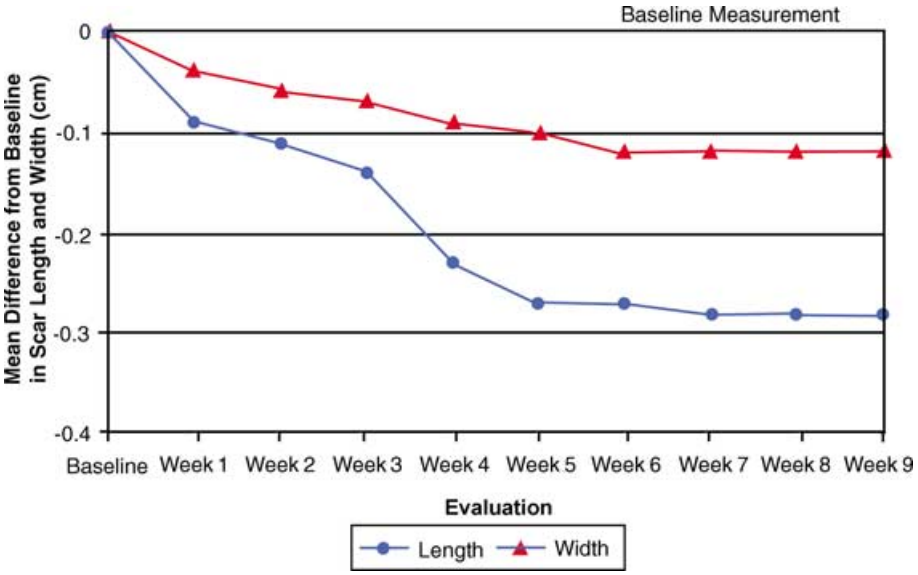


Figure 2 Graphical presentation of the mean difference from baseline in scar length and width.

(baseline) and each week for 9 weeks at the testing facility. Visual ratings of scar appearance (colour, roughness and degree of difference from surrounding normal skin) and scar size measurements (length and width) were performed. Quantitative measurements of skin colour for melanin (darkness) and haemoglobin (redness) were made on the scarred and adjacent normal skin areas using a Mexameter MX 18. Quantitative measurements of skin hydration were also performed on the same sites. Digital photographs of the scar were taken prior to product application (baseline) and again at the end of week 9. The subjects completed a self-evaluation questionnaire regarding their scar's appearance prior to product application (baseline) and again at the end of week 9. The subjects also completed a product questionnaire that assessed their likes and dislikes of the product.

A significant improvement in the appearance of scars after 6 weeks of Tamanu oil use was observed visually (Fig. 1). This improvement continued through to week 9 of the study. The overall size of the scars consistently decreased throughout the study (Fig. 2). The length of scars was reduced by an average of 0.28 cm, and the width by an average of 0.12 cm [21].

Conclusions

This plant always promised to be interesting from a survey of the literature and folklore. The fascinating chemistry, coupled with a modern evaluation of the oil, justified that interest.

References

1. Muller, A. The Pacific Ocean oils (L'Ami September 1993, no. 5).
2. Drury, C.H. The useful plants of India; with notices of their chief medicinal value in commerce, medicine and the arts. Higginbotham Madras (1873). ISBN no. not available.
3. Schultes, R.E. and Raffauf, R.F. *The Healing Forest – Medicinal and Toxic Plants of the Northwest Amazonia*. Dioscorides Press, Portland, Oregon (1990, reprint 1995). ISBN no. 0-931146-14-3.
4. Nadkarni, K.M. and Nadkarni, A.K. *Indian Materia Medica – with Ayurvedic, Unani–Tibbi, Siddha, Allopathic, Homeopathic, Naturopathic and Home Remedies*, Vol. 2. Popular Prakashan Private Ltd., Bombay, India (1999). ISBN no. 81-7154-143-7.
5. Quisumbing, E. *Medicinal Plants of the Philippines*. Department of Agriculture and natural Resources, Bureau of Printing, Manila (1951).
6. Burkill, H.M. *The Useful Plants of West Tropical Africa*, 2nd edn, Vol. 2. Families E–I. XX, Royal Botanic Gardens Kew (1994). ISBN no. 0-947643-56-7.
7. Jayaweera, D.M.A. *Medicinal Plants Used in Ceylon*, Part 3. National Science Council of Sri Lanka, Colombo. (1981).
8. Grimé, W., ed. *Ethno-Botany of the Black Americans*. Reference Publications Inc., Algonac, Michigan (1979).
9. Oliver-Bever, B. *Medicinal Plants in Tropical West Africa*. Cambridge University Press, Cambridge (1986).
10. Steiner, R.P. *Folk Medicine – the Art and Science*. American Chemical Society, Washington, DC (1986).
11. Potti, G.R. and Kurup, P.A. Antibacterial principle of the root bark of *Calophyllum inophyllum*: isolation and antibacterial activity. *Indian J. Exp. Biol.* **8**(1): 39–40 (1970). ISSN 0019-5189.
12. Patil, A.D., Freyer, A.J., Eggleston, D.S. *et al.* The inophyllums, novel inhibitors of HIV-1 reverse transcriptase isolated from the Malaysian tree, *Calophyllum inophyllum* Linn. *J. Med. Chem.* **36**(26): 4131–4138 (1993). ISSN 0022-2623.
13. Govindachari, T.R., Viswanathan, N, Pai, B.R, Rao, R. and Srinivasan, M. Triterpenes of *Calophyllum inophyllum* Linn. *Tetrahedron* **23**(4): 1901–1910 (1967). ISSN 0040-4020.
14. Govindachari, T.R. *et al.* Chemical components of the heartwood of *Calophyllum inophyllum*. Part I. Isolation of mesuaxanthone B and a new xanthone, calophyllin B. *Indian J. Chem.* **6**: 57 (1968).
15. Merck. *The Merck Index*, 12th edn. Merck Inc., Whitehouse Station, NJ, USA (1996). ISBN no. 0911910-12-3.
16. Rastogi, R.P. and Mehrotra, B.N. *Compendium of Indian Medicinal Plants*, Vol. 5. 1990–94. Central Drug Research Institute, Lucknow and Publications and Information Directorate, New Delhi (1998). ISBN no. 81-85042-14-4.
17. Rastogi, R.P. and Mehrotra, B.N. *Compendium of Indian Medicinal Plants*, Vol. 3. 1980–84. Central Drug Research Institute, Lucknow and Publications and Information Directorate, New Delhi (1993). ISBN no. 81-85042-11-X.
18. Bhalla, T.N., Saxena, R.C., Nigam, S.K. *et al.* Calaphyllolide – a new non-steroidal anti-inflammatory agent. *Indian J. Med. Res.* **72**, 762–5 (1980).
19. Gopalakrishnan, C., Shankaranarayanan, D., Nazimudeen, S.K., Viswanathan, S. and Kameswaran, L. Anti-inflammatory and CNS depressant activities of xanthones from *Calophyllum inophyllum and Mesua ferrea*. *Ind. J. Pharmac.* **12**(3), 181–191 (1980).
20. Itoigawa M., Ito C., Tan H.T., Kuchide M., Tokuda H., Nishino H. and Furukawa H. Cancer chemopreventive agents, 4-phenylcoumarins from *Calophyllum inophyllum*. *Cancer Lett.* **169**(1): 15–9 (2001). Faculty of Pharmacy. Meijo University, Tempaku, Nagoya 468-8503, Japan.
21. Beausoleil, C., Lehman, L. *et al. Evaluation of the Ability of One Test Product to Improve the Appearance of Scars*. Bioscience Laboratories, Inc., Boxeman, MT (2001). Report #010514-111.