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From the Editor

Hello Prospective Subscriber,

We are pleased to provide with this special compilation issue of the *International Journal of Professional Holistic Aromatherapy* (IJPHA) to give you a taste of what we offer our subscribers.

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The IJPHA provides the reader with informative articles highlighting the practical application of essential oils, research, sustainability and ethics, integrative health, business skills, professionalism and to provide a showcase for practitioner case studies. Each quarterly issue is available in print and contains a variety of articles including profiles of essential oils that are commercially available (but lesser known), chemistry, and how to build and maintain a thriving successful business. Articles often feature therapeutic blends, industry news, book and product reviews, and current information on issues relevant to the field of Aromatherapy and integrative healthcare.

The professional holistic Aromatherapist assesses the client's needs physically, mentally, emotionally and spiritually. Addressing the client's needs goes beyond the use of essential oils alone and may include herbs, homeopathic remedies, flower essences, supplements and advice on nutrition, exercise, and techniques for stress relief. When necessary, a practitioner may make recommendations to a client to seek advice from an integrative practitioner or doctor. The IJPHA provides information and resources about integrative and complementary healthcare methods, as well as additional "tools" for the professional holistic aromatherapist.

We hope you enjoy this sample issue and look forward to receiving your subscription. We encourage you to submit your articles!

Lora Cantele

On the cover: *Mint*
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In this issue

An Exploration of Dalmatian Sage and Thujone

Jennifer Rhind, PhD, CBiol

Salvia officinalis © Eileen Cristina

If we were to examine the essential oil of common Sage in Aromatherapy literature, we might come away with the overriding impression that the risks it presents outweigh any beneficial properties. Indeed, its associated hazards, courtesy of a toxic ketone named 'thujone', led Tisserand and Balacs (1995) to comment that '*the usual thujone content is sufficiently high to warrant its exclusion from aromatherapy*.'

In earlier times, before the essential oil became available, the herb was known as 'Sage the Saviour'. It is even said that Louis XIV of France trusted this herb more than his physician and drank a cup of Sage infusion every morning. Here we will explore the 'common' or 'Dalmatian' Sage (*Salvia officinalis*) and its component, the notorious thujone, with the intent of revealing whether these impressions are justified and how the essential oil might be used in Aromatherapy and in the clinical domain.

Sage in folk belief, traditional medicine and ritual

The botanical name for the Sage genus is *Salvia*[1] – derived from the Latin verb *salvere*, which means 'to be well, or in good health' – a term that is especially relevant to traditional healing and shamanic practices. Interestingly, our word 'sage' also means 'wise'. In Ancient Rome, it was believed that Sage conferred immortality, as can be seen in the proverb recorded in the *Tabula Salerni* which says '*Cur moritur cui Salvia crescit in horto*?' or 'Why should he die who has Sage in his garden?' This refers to a species of Sage known as *Salvia fruticosa* (Gali-Muhtasib *et al*., 2000). In the Salerno school of medicine,[2] it was also said that '*Salvia salvatrix, natura concilatrix*' – 'Salvia is a cure with a calming effect' (Valnet, 1980).

There are many *Salvia* species that have both medicinal and culinary traditions of use. In folk medicine, they have been used to treat many ills, but are especially regarded for helping maintain and restore health, and protect against disease (very much in line with the view of the *Schola Medica Salernitana*), and also to relieve pain, aid digestion (like so many culinary herbs), and treat menstrual problems and infertility (Gali-Muhtasib *et al*., 2000).

To explore what lies behind its reputation for healing mind, body and spirit, we also need to look at what the early herbalists and physicians wrote. Dioscorides maintained that Sage was good for the liver and 'to make blood'; it was a diuretic, and it was of use in consumption, as well as for headaches due to cold rheumatic humors, joint pains, coughs, serpent bites and the plague. He also mentioned its ability to 'help the memory, warming and quickening the senses', while Gerard noted that it was 'singularly good for the head and the brain', that it stimulated the senses and the memory. On the physical level, Sage strengthened the sinews, cured palsy and trembling, and was effective against serpent bites (Grieve, 1992).

Salvia officinalis: Wikimedia Commons

[1] *Salvia* is a genus in the Family Lamiaceae or Labiatae.

[2] The *Schola Medica Salernitana* of Salerno in Campanula, Italy, was a late medieval school of medicine and was the first and most influential of its kind. It grew from a dispensary in a 9th-century monastery. Its teachers and practitioners – both male and female – were considered to be the best in the medieval world. Its ethos was prevention rather than cure.

In Italian folk medicine, Sage was (and is) eaten to maintain good health – and it has a very long tradition of culinary use. Early recipes included traditional stuffings for duck, geese and pork; also, sage and onion sauce, and sage cheese.[3] Is this an example of 'food as medicine' – an old practice enjoying a renaissance?

Dalmatian Sage is well regarded in Palestinian traditional medicine for its antimicrobial actions; it is used as an antiseptic and to treat scabies and syphilis. It is also anti-inflammatory and used for the treatment of skin and eye diseases and pleurisy (Amr and Đorđević, 2000; Al-Qura'n, 2008). In Jordan and the Middle East, it is used for fever, stomach discomfort and digestive problems (Lima *et al*., 2005).

In England, a decoction of Sage leaves with wine was gargled to relieve toothache, while in Germany, Sage was used orally for gastrointestinal problems and excessive perspiration, and topically for inflammation of the mucous membranes of the mouth and throat. Similarly, the Cherokee Native Americans used a Sage leaf infusion to treat colds and coughs, and to prevent diarrhoea (Craft *et al*., 2017).

In many cultures, physical, mental, emotional and spiritual afflictions have been associated with maleficent entities, or harmful influences from the unseen worlds. The use of aromatic species has long been associated with driving out, or repelling, bad spirits and indeed inviting in good ones. Aromatic smokes were important in Native American Indian sweat lodges, shamanic practices and the smudging ceremony.[4] Sage[5] is burned, and its smoke is thought to drive away bad influences, and keep them away, during ceremony – purification and protection – and is believed to induce an altered state of consciousness to enable communication with the Creator and the spirit world. The floors of sweat lodges are often strewn with Sage leaves, so that its volatile oil will scent the air, and its leaves are used to wrap ceremonial pipes.

[3] 'Sage Derby' cheese emerged in 17th-century England and is probably the best-known example of the kind.

[4] Smudging is the burning of specific herbs; the smoke is taken in the hands and directed, or 'brushed', over the body, or a place, and accompanied by prayer; sometimes a feather may be used.

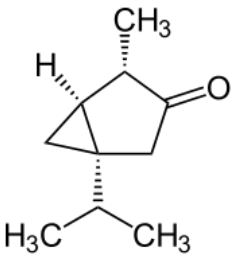
[5] The common Sage, *S. vulgaris*, is often used, as is Sagebrush (*Artemisia californica*) and Mugwort (*A. vulgaris*).

Botanical origins and the essential oil

The genus *Salvia* contains around 900 species and yields several distinct essential oils – many of which are referred to as 'Sage' but with a defining prefix. Cabo *et al.* (1987) suggested that there were three broad types of Sage essential oil based on their dominant constituents: Group I consists of species characterised by α- and β-thujone (Dalmatian Sage *S. officinalis*), Group II by linalool and linalyl acetate (Clary Sage *S. sclarea* and Sardinian Sage *S. desoleana*) and Group III by 1,8-cineole and camphor (Greek or Cretan Sage *S. triloba*, Lebanese Sage *S. libanotica*, and Spanish Sage *S. lavandulaefolia*) (Gali-Muhtasib *et al*., 2000). However, there are others that do not fall into these categories, such as Somalian Sage (*S. somalensis*) which is characterised by bornyl acetate and an absence of α- and β-thujone (Villa *et al*., 2009). *Salvia officinalis* is native to the northern Mediterranean; it grows wild from Spain along the coast up to the eastern Adriatic, and on the mountains of Croatia. It is a perennial, evergreen subshrub, with woody stems, green-grey hued leaves, and blue to purplish flowers. Sage is hardy and has been cultivated in many countries for hundreds of years, and there are many variants within the species. *S. officinalis* essential oil is sometimes referred to as 'Dalmatian Sage' because of its original geographical origins. It is steam distilled from the dried leaves and has a strong, sweet, herbal, camphoraceous odour with warm herbal-minty notes contributed by its ketone α-thujone (Edris *et al*., 2007).

The volatile oil is secreted and stored in the subcuticular cavity in glandular trichomes. Scanning electron microscopy confirmed the presence of two basic types: a capitate stalked form containing a multicellular stalk and surmounted by a unicellular secretory head, and a capitate sessile form containing a unicellular stalk and unicellular or multicellular secretory head. Both types produce volatile oil of similar composition (Venkatachalam *et al*.,1984). The volatile oil also has a biological role, which has yet to be fully elucidated. It displays allelopathy, preventing the germination of treated lettuce seeds and root growth (Bouajaj *et al*., 2013), and the component α-thujone in the ornamental Artemisia arborescens 'Powis Castle' plays a role in the prevention of codling moth infestation in apple fruits (Creed *et al*., 2015).

Genetics and environmental conditions such as temperature, day length, and light influence the balance of the composition of *S. officinalis* essential oil (Figueiredo *et al*., 2008). Lakušić *et al*. (2013) analysed *S. officinalis* essential oils in various stages of development from plants of different geographical origin but grown in the same garden under identical conditions. Young leaves were characterised by high concentrations of α-humulene, viridiflorol, and manool, but had low concentrations of camphor and α-thujone. As the leaves aged, the concentrations of α-humulene, viridiflorol, and manool decreased significantly as camphor and α-thujone increased. We can observe an annual pattern of seasonal variations, where the 1,8-cineole, camphor and thujone vary in a predictable cycle, regardless of geography (Pitarević *et al*., 1984; Putievsky *et al*., 1986) – where 1,8-cineole decreases and α- and β- thujone increase during the vegetative phase between May and October, and camphor peaks in mid-vegetative phase (Grausgruber-Gröger *et al.,* 2012).



α-thujone
NEUROtiker

It has also been established that the distillation time will affect the relative proportions of the principle components in the essential oil. It has been suggested that the minimum time for the hydrodistillation of Sage essential oil to yield the desired characteristic proportions of the components should be one hour (Baj *et al*., 2013).

Tucker *et al*. (1990) cited by Abu-Darwish *et al.* (2013) suggested that within *S. officinalis* oils there are five distinct variants, which are as follows:

i) camphor > α-thujone > 1,8-cineole > β-thujone
ii) camphor > α-thujone > β-thujone > 1,8-cineole
iii) β-thujone > camphor > 1,8-cineole > α-thujone
iv) 1,8-cineole > camphor > α-thujone > β-thujone
v) α-thujone > camphor > β-thujone > 1,8-cineole

More recently, studies on the chemical diversity of *S. officinalis* have led researchers to propose between three and five chemotypes. Lamien-Meda *et al.* (2010) identified a new viridiflorol chemotype from Romania – which has in the region of 20% viridiflorol and low levels of thujones. Stešević *et al.* (2014) proposed three chemotypes: chemotype A, rich in total thujones; chemotype B, with intermediate contents of thujones, α-pinene, camphene, and camphor and a high borneol content; and chemotype C, rich in camphor, camphene, and α-pinene; and intercorrelations between main components were identified. Cvetkovikj *et al*. (2015) proposed four chemotypes; this study also revealed that some of the main components were highly intercorrelated.[6] Craft *et al.* (2017) suggested five major chemotypes of Sage oil, with the most common being an α-thujone > camphor > 1,8-cineole chemotype, an α-humulene-rich chemotype, a β-thujone-rich chemotype, a 1,8-cineole/camphor chemotype, and a sclareol/α-thujone chemotype. Here, in the light of the above, we could suggest that there are in fact six chemotypes including the viridiflorol variant. However, there is no consensus as yet, and it is not known if they are all commercially available.

A 'typical' *S. officinalis* oil from Spain or France[7] contains α-thujone (18-43%), camphor (4.5-24.5%), borneol (trace to 25%), 1,8-cineole (5.5-13%), β-thujone (3-8.5%); with camphene (1.5-7%), α-humulene (0-12%), β-caryophyllene (0-4%), bornyl acetate (0-2.5%), α- (1.0-6.5%) and β-pinene (3-6%), limonene (0.5-3%), linalool (0-1%), and many others, in trace amounts.

There are currently no studies correlating *S. officinalis* oil composition with either fragrance descriptions or with biological activities (Craft *et al*., 2017). Moreover, it is always important to look for evidence of actions of the whole, complete essential oil, rather than attributing properties to individual components in isolation – because of the remarkable phenomenon of synergy, where it is equally possible that minor or even trace components augment or potentiate the actions of principal components, and indeed antagonism and 'quenching', where the actions of some are modified or lessened by the presence of others.

[6] Strong positive correlations were observed between trans-caryophyllene and α-humulene, α-humulene and viridiflorol, and viridiflorol and manool (Cvetkovikj *et al*., 2015); and between α-pinene and camphene, camphene and camphor, as well as between *cis*-thujone and *trans*-thujone. Strong negative correlations were evidenced between cis-thujone and α-pinene, *cis*-thujone and camphene, *cis*-thujone and camphor, as well as between *trans*-thujone and camphene (Stešević *et al*., 2014). The α- and β- positional isomers also exist as stereoisomers, hence the cis- and trans- forms, or (+)- and (-)- forms (Williams *et al*., 2016).
[7] Based on GC-MS data supplied by Jonathan Hinde and Malte Hozzel of Oshadhi Ltd.

However, if one or more components are known to be hazardous, we must acknowledge this. With Dalmatian Sage essential oil, we find not just one, but two ketones that present clear risks and necessitate caution – the α- and β- isomers of thujone, and camphor.

Characterised by ketones – camphor and thujone

Now, camphor is present in many essential oils, often in very small amounts that do not present a problem, but occasionally in significant amounts. It is a bicyclic monoterpenoid ketone that exists in (+)- and (-)- forms. (-)-Camphor is found at > 20% in Ho Leaf (*Cinnamomum camphora*) ct. camphor, Spanish or French Lavender (*Lavandula stoechas*), White Wormwood (*Artemisia herba-alba*), Dalmatian Sage, Feverfew (*Tanacetum parthenium*), Spanish Sage, Madagascan Basil (*Ocimum gratissimum*), Rosemary (*Rosmarinus officinalis*) ct. camphor, and Spike Lavender (*Lavandula latifolia*). Tisserand and Young (2014) summarise the available data and comment that although it is not toxic to the reproductive system or embryos, it is neurotoxic, hepatotoxic and nephrotoxic. Camphor is a powerful stimulant of the central nervous system (CNS) capable of causing grand-mal convulsions; and the mean human lethal dose is 200 mg/kg. It is 6.5 times more toxic to humans than mice.

The two positional isomers of thujone are less common essential oil constituents. Like camphor, thujone is a bicyclic monoterpenoid ketone. The two isomers always occur together, although one often dominates. So, we find warm-herbal-minty α-thujone present at over 20% in Western Red Cedar (*Thuja plicata*), Sea Wormwood (*Artemisia maritima*) and Thuja (*Thuja occidentalis*), and occasionally at over 20% in Dalmatian Sage and White Wormwood. β-Thujone has a camphoraceous-herbal odour and is found at over 20% in White Wormwood, Tansy (*Tanacetum vulgare*) and Great Mugwort (*Artemisia arborescens*). Tisserand and Young (2014) note that thujone is not a reproductive toxin, but it is nephrotoxic, potentially hepatotoxic and certainly neurotoxic; oral doses can cause seizures, especially with large doses (acute toxicity) or prolonged ingestion (chronic toxicity). It would seem that the α-isomer is more toxic than the β-form, and that humans are ten times more susceptible than rats. Thujone, like camphor, can cross the blood–brain barrier. Oral doses can also influence cognitive performance and mood – reducing reactions to visual stimuli and increasing anxiety (Dettling *et al.*, 2004 cited by Tisserand and Young, 2014).

Many compounds that regulate $GABA_A$[8] receptor function interact with membrane lipids, causing changes in the membrane dynamic characteristics that modulate receptor macromolecules (Mariani *et al.*, 2016). High doses of α-thujone cause convulsions by blocking γ-aminobutyric acid (GABA)-gated chloride channels, while chronic exposure can lead to neurotoxicity and carcinogenicity[9] (Craft *et al.*, 2017). Rivera *et al.* (2014) investigated the effects of α- and β-thujone on the fear/anxiety behaviour of 3-day-old chicks and their modulation on the $GABA_A$ receptor. Higher doses were convulsant and had an anxiogenic-like effect. It was also suggested that the modes of action of the two isomers are distinct, although the effects were similar.

In 2011, the National Toxicology Programme published the results of a study with rats and mice, which highlights the hazards of oral doses of thujone, and the effects of gender and species. All male and female rats receiving 50 mg/kg α- and β-thujone died before the end of the study. All those animals, and most receiving the lower dose of 25 mg/kg, had seizures. Species-specific and gender-specific differences were noted – in the males there was an increased incidence of cancers of the preputial gland[10] and a slight, albeit not statistically significant, increase in adrenal gland tumours. No increases in cancers were observed in female rats, or in male or female mice. Waidyanatha *et al.* (2013) found that female rats and mice were more sensitive to α-thujone-induced neurotoxicity than the males. It would seem that in rodents, the bioavailability of thujone is higher in females, which is possibly related to their greater brain:plasma ratio.

[8] Gamma-aminobutyric acid is the principle inhibitory neurotransmitter in the mammalian CNS.

[9] The National Toxicology Programme (2011) study for carcinogenicity only found non-dose-dependent (and therefore of questionable relevance) cancer in the preputial gland – so this claim here (and in the NTP study conclusions) could be viewed as exaggerated and over-cautious. In addition, the preparation used by the NTP only consisted of 81% thujones, so cannot be described as 'thujone'.

[10] The preputial glands of rodents are specialized sebaceous glands located in the adipose tissue near the penis. These glands do not appear to exist in humans.

So, before we look at the potential therapeutic benefits of Dalmatian Sage essential oil, we need to put these hazards into perspective. Pelkonen *et al.* (2013) state that there are important gaps in the knowledge required to properly assess thujone toxicity, notably human dose-concentration-effect relationships, bioavailability and the toxicological consequences of potential pharmacogenetic[11] variations, and modes of administration.

However, it is apparent that the main risk is to the CNS, followed by the kidneys with oral doses. Dalmatian Sage essential oil should not be taken orally; it is contraindicated in pregnancy and breastfeeding, and the maximum dermal use is 0.4% – based on 60% total thujone content (Tisserand and Young, 2014). Abuse can lead to hypoglycaemia, epileptic reactions, loss of balance, tachycardia, muscle cramps, and breathing difficulties – all toxic reactions attributed to the thujones and camphor (Tisserand and Balacs, 1995).

However, the fresh herb itself is quite safe; it has been estimated that between 2 and 20 cups of Sage tea would be required to reach the acceptable daily intake of thujone (Craft *et al*., 2017).

Absinthe, 'la Fée Verte' – a thujone case study (adapted from Rhind, 2013)

The absinthe of the late 19th century was a pale green aperitif, with a very high alcohol content. It was made with several botanicals including Aniseed, Fennel seeds and Wormwood. It had a strong and bitter flavour, and its consumption acquired paraphernalia such as special pierced spoons designed to hold lumps of sugar over the absinthe glass, over which the water was poured (the sweetness would counteract the bitterness to an extent). Absinthe reached its height of popularity with the artists, writers and actors, including Henri Toulouse Lautrec and Vincent van Gogh, who frequented the Parisian cafés in the late 19th century. Some believed that it heightened artistic awareness and aided sexual prowess, despite its adverse psychotropic effects when consumed in excess. Chronic abuse resulted in a syndrome named 'absinthism', which encompassed depression, psychosis and madness.

[11] The individual's responses, which are determined by genetics.

The most dramatic example is that of the painter Vincent van Gogh (1853-1890), who cut off his ear during a psychotic episode. However, based on his own descriptions of his illness, he possibly suffered from temporal lobe epilepsy and manic depression, and so his severe mood swings would have been aggravated by absinthe, brandy, nicotine and turpentine (Morrant, 1993 cited by Tonutti and Liddle, 2010). In the early part of the 20th century, absinthe was banned because of its deleterious effects on individuals and society. Originally the neurotoxic effects of absinthe were blamed on the presence of α- and β-thujones, which in reality were present in relatively low concentrations of up to 4.3 mg/litre, despite earlier claims of 260 mg/kg (Lachenmeier *et al*., 2005). However, a recent investigation of three samples of absinthe – authentic pre-1915, post-ban 1915-1988, and modern commercial absinthe – suggested that 'absinthism' was due to the excessive use of alcohol, not its thujone content, which was in this case reported as β-thujone (Lachenmeier, 2008 cited by Dobetsberger and Buchbauer, 2011). Tonutti and Liddle (2010) comment that the current version of absinthe, advertised 'as being of premium quality', and consequently highly priced, is made by distillation and has an alcoholic strength of at least 45% volume. The thujone content is limited by European and other regulations, as is the case with all vermouths.

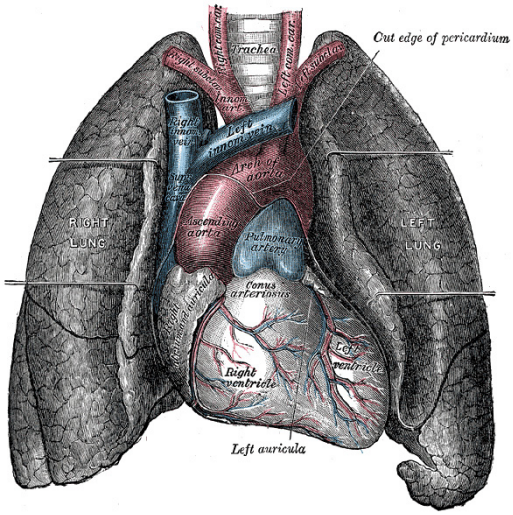
Therapeutic and clinical potential of Sage and thujone

Gali-Muhtasib *et al.* (2000) cite numerous modern studies that have elucidated *Salvia* species' therapeutic and medicinal potentials as antimicrobial agents, as spasmolytics and hypotensives, antioxidants and anti-inflammatories, and for prolonging sleep and treating Alzheimer's disease. More specifically, the essential oil and other preparations of *S. officinalis* are used externally for inflammation and infections of the mucous membranes of throat and mouth (including stomatitis, gingivitis and pharyngitis). Oral doses have been used for dyspeptic symptoms and excessive perspiration (Raal *et al*., 2007).

It has been suggested that the predominant therapeutically valuable components in *S. officinalis* essential oil are α- and β-thujone, 1,8-cineole, and camphor. In the herb there are also active diterpenes such as carnosic acid, triterpenes such as oleanoic

and ursolic acids, and phenolic compounds – notably rosmarinic acid (Abu-Darwish *et al.*, 2013). When evaluating the research findings, we must remain cognisant of the differences between the composition of the essential oil and other types of extracts, such as aqueous infusions and decoctions, and alcoholic tinctures.

When we look for evidence for the actions of *S. officinalis* essential oil it becomes clear that there are a few well-defined areas where therapeutic potential is apparent – it is an antioxidant (Miguel *et al.*, 2011), an antimicrobial (Pereira *et al.*, 2004; Pinto *et al.*, 2007; Hayouni *et al.*, 2008; Sookto *et al.*, 2013; Abu-Darwish *et al.*, 2013; Fournomiti *et al.*, 2015; Stojanović-Radić *et al.*, 2016), an anti-inflammatory/analgesic (Abu-Darwish *et al.*, 2013), an anti-tumoural (Sertel *et al.*, 2011), and an enhancer of cognitive processing (Moss *et al.*, 2010; Moss *et al.*, 2014). Extracts other than the essential oil have antioxidant activity related to the phenolic compounds (Ben Farhat *et al.*, 2009), anti-inflammatory action (Baricevic *et al.*, 2001; Oniga *et al.*, 2007), hepatoprotective properties (Lima *et al.*, 2005), and hypoglycaemic properties which suggest a clinical role in the management of diabetes (Eidi *et al.*, 2005).



Heart and lungs from Gray's Anatomy
WikimediaCommons

There have been some studies on α-thujone itself. Siveen and Kuttan (2011a) demonstrated that it can inhibit the lung metastasis of B16F-10 cells through inhibition of tumour cell proliferation, adhesion, and invasion, as well as by regulating the expression of proinflammatory cytokines and IL-2 in metastatic animals. Siveen and Kuttan (2011b) demonstrated that administration of thujone can enhance the immune response[12] of mice, resulting in a significant reduction in tumour development. It also inhibits proliferation in human colon cancer cells (Zhou *et al.*, 2016). Both isomers have pro-apoptopic and anti-angiogenic actions of glioblastoma tumours (Torres *et al.*, 2016). Thujone has antidiabetic action in rats, but the dose required was considerably higher than the acceptable human daily intake of 0.1 mg/kg bw/day (Lachenmeier and Walch, 2011).

However, since thujone is more toxic in humans than rodents, and because there are still so many gaps in our knowledge about its safety, in the meantime it would seem that any therapeutic benefits of thujone are outweighed by the risks involved.

S. officinalis essential oil

There are a few studies that elucidate the potential therapeutic actions of Dalmatian Sage essential oil, and these are summarised below.

Antibacterial

- Longaray Delamare *et al.* (2007) suggested that 1,8-cineole, thujone, and camphor play an important role in the antibacterial actions of Sage essential oil.

- An *in vitro* study demonstrated that although *S. officinalis* essential oil (characterised by 1,8-cineole, α-thujone, and camphor) showed activity against some clinical isolates of multidrug resistant *Escherichia coli*, *Klebsiella oxytoca*, and *Klebsiella pneumoniae* strains, it was less effective in this respect than Oregano (*Origanum vulgare*) and Thyme (*Thymus vulgaris*) (Fournomiti *et al.*, 2015).

- Hayouni *et al.* (2008) showed that a *S. officinalis* essential oil containing 1,8-cineole (33.27%), β-thujone (18.40%), α-thujone (13.45%), and borneol (7.39%) was active against several Gram +ve and Gram -ve bacteria; it was suggested that it could be used as a natural preservative ingredient in the food and/or pharmaceutical industry, although the strong distinctive flavour could be an issue. In this study, it was also active against *Candida albicans* – see below.

[12] The essential oil of *S. officinalis* did not display immunomodulatory activity, contrary to expectations (Carrasco *et al.*, 2009).

• *Pseudomonas aeruginosa* causes numerous diseases and is known for its ability to produce biofilm.[13] Stojanović-Radić *et al*. (2016) demonstrated that *S. officinalis* essential oil was effective against *P. aeruginosa* clinical strains and suggested that it could be used to treat persistent infections.

• Pereira *et al*. (2004) investigated the activity of several essential oils against clinical isolates of bacteria from the urine of individuals with urinary tract infections. *S. officinalis* oil displayed enhanced inhibitory activity compared to the other two oils (from *Ocimum gratissimum* and *Cymbopogon citratus*), with 100% efficiency against *Klebsiella* and *Enterobacter* species, 96% against *Escherichia coli*, 83% against *Proteus mirabilis*, and 75% against *Morganella morganii*.

Antifungal

• Sookto *et al*. (2013) demonstrated that the essential oil is active against clinical *Candida* strains and had inhibitory effects on the adhesion of the cells to a resin surface. It was suggested that after further testing and development, the essential oil may be used as an antifungal denture cleanser to prevent candidal adhesion and reduce the risk of candida-associated denture stomatitis.

• Pinto *et al*. (2007) evaluated the antifungal activity of Sage essential oils against *Candida* (four clinical isolates and four ATCC type strains), dermatophytes (five clinical strains) and other filamentous fungi (*Penicillium*, *Aspergillus*, *Cladosporium* and *Fusarium*). The oils displayed a broad spectrum of activity, with higher activity against dermatophyte strains. The oil with 10.4% *cis*-thujone and 20.5% camphor was the most active. It was concluded that Sage oils that have a low content of thujones have potential as antifungal agents. It was suggested that thujones do not play an important role against yeasts and filamentous fungi, and that 1,8-cineole and camphor were largely responsible for the antifungal activity in the tested strains.

• Abu-Darwish *et al.* (2013) evaluated the antifungal activity of a *S. officinalis* essential oil from Jordan. This oil belonged to Group IV – 1.8-cineole (40-50%) > camphor (8.0-25%) > α-thujone (1.2-3.7%) > β-thujone (0.1-3.1). It had a low toxicity on macrophages and keratinocytes, which indicated that it would be safe for use in topical preparations. This *in vitro* study demonstrated that the essential oil was active against dermatophytes (*Trichophyton rubrum* and *Epidermophyton floccosum*) and the yeast *Cryptococcus neoformans*. It was less active against *Candida* and *Aspergillus* species. It was concluded that these findings demonstrated that bioactive concentrations of *S. officinalis* oils do not affect the viability of macrophages and keratinocytes, and so they would be suitable for incorporation into skin care formulations for both cosmetic and pharmaceutical purposes.

Analgesic

• *S. officinalis* essential oil can contain over 50% camphor, a TRP (Transient Receptor Potential) modulator[14] (Martinez *et al*., 2009). Other dominant constituents also share this property including α-thujone, borneol and 1,8-cineole, and so this might explain anecdotal reports of the essential oil's ability to relieve pain.

Anti-inflammatory

• Abu-Darwish *et al*. (2013) demonstrated that a *S. officinalis* essential oil from Jordan (1.8-cineole > camphor > α-thujone > β-thujone) had anti-inflammatory activity; it inhibited NO production. Nitric oxide (NO) contributes to oedema, nociception and pain by stimulating the release of cytokines and free radicals, which are pro-inflammatory mediators (Rivot *et al*., 2002 cited by Guimarães *et al*., 2013).

Antioxidant and hepatoprotective

• An *in vivo* rodent study conducted by El-Hosseiny *et al*. (2016) indicated that the concomitant administration of *S. officinalis* essential oil (1,8-cineole > β-pinene > camphor > β-caryophyllene > α-pinene > α-caryophyllene) with the antibiotic Co-amoxiclav exerted a hepatoprotective effect via inducing an antioxidant defence response that eventually partially regressed the liver damage in

[13] Biofilms are complex communities of microorganisms responsible for more than 60% of chronic human infections, and they represent one of the leading concerns in medicine.

[14] Camphor activates TRPV3 receptors and inhibits several other TRP channels, including ankyrin-repeat TRP 1 (TRPA1). The camphor-induced desensitization of TRPV1 and block of TRPA1 may underlie the analgesic effects of camphor (Xu *et al*., 2005).

duced by Co-amoxiclav. It was suggested that Sage essential oil might counteract hepatic injury associated with Co-amoxiclav.

Antitumoural

• Sertel *et al*. (2011) demonstrated the ability of *S. officinalis* essential oil to inhibit human HNSCC (Head and Neck Squamous Cell Carcinoma) cell growth *in vitro*.

Cognition enhancer

• Moss *et al*. (2010) investigated the differential effects of the essential oil vapors of Dalmatian Sage and Spanish Sage on mood, cognitive function and memory. It was demonstrated that the aroma of Dalmatian Sage produced a 'significant enhancement effect' for quality of memory and also for secondary memory (cognitive functions), compared with the 'no odour' control and Spanish Sage. Both aromas significantly increased alertness (a mood effect) in comparison with the control. As both aromas were rated as equally pleasant, the hedonic valence mechanism was probably not a factor. It was suggested that the mechanisms involved in the aromatic modulation of mood are distinct from those involved in cognitive effects, and that cognitive effects are probably pharmacological, via acetylcholinesterase inhibition.

• Miroddi *et al*. (2014) conducted a review of published clinical trials to establish the safety and efficacy of *S. officinalis* and *S. lavandulaefolia* for the management of memory, cognitive impairment and Alzheimer's disease. The review established that *S. officinalis* and *S. lavandulaefolia* essential oils and extracts exert beneficial effects by enhancing cognitive performance both in healthy subjects and patients with dementia or cognitive impairment and are safe for this purpose. However, the review also highlighted several problems: research design and methodological issues, the use of different herbal preparations (extracts, essential oil, use of raw material), compounded by lack of details on the herbal products used in the studies.

• Radulović *et al*. (2017) investigated the behaviour-modulating and toxic effects of the essential oils of *S. officinalis*, *Artemisia absinthium*, *Thuja occidentalis* and *Tanacetum vulgare*. The results strongly implied that the toxic and behaviour-modulating activity of the oils should not be associated exclusively with thujones.

Sage and Aromatherapy

It can be concluded that although Dalmatian Sage essential oil has some useful properties, it must be used with care and respect, and never on the young, the elderly, the vulnerable, or those who suffer from epilepsy or are pregnant or breastfeeding. There will always be alternative oils that are equally useful and without hazard.

It certainly would appear that Sage oil, with its antimicrobial and anti-inflammatory actions and low risk of skin irritation, could be useful in topical antiseptic blends for the prevention of infections. It is also a good candidate for dermatophyte infections. It is important to observe the dilution guidelines in all blends (it should not exceed 0.4%). As an alternative, you might consider Sardinian Sage (*S. desoleana*), which presents no hazards and has considerable potential as an antidermatophytic agent.

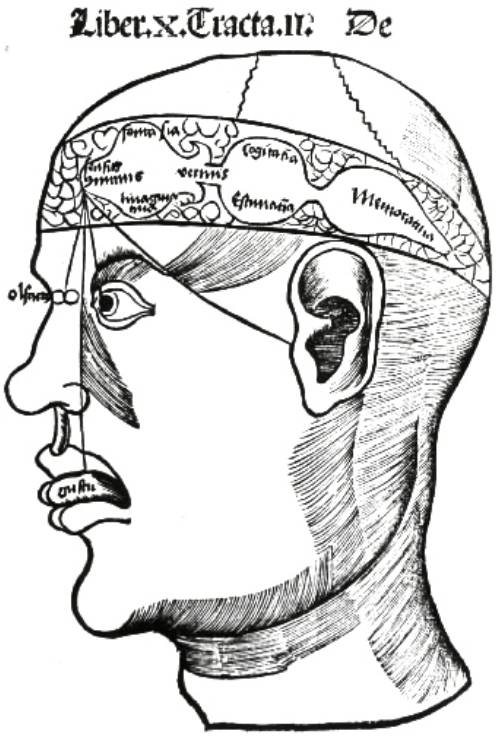


Image: Gregor Reisch, 1512. *Margarita philosophica nova cui insunt sequentia*

New developments in 'carrier' technology might offer another solution. Kodadová *et al.* (2015) demonstrated that if Sage essential oil was formulated into a chitosan and caffeine hydrogel, the release of its components could be controlled. In this *in vitro* study,

it was demonstrated that a hydrogel composed of 3.5% (w/w) Sage essential oil, 2.0% (w/w) caffeine, 2.5% (w/w) chitosan, and 0.1% (w/w) Tween-80 (a surfactant) facilitated an enhanced permeation of the bicyclic monoterpenols with anti-inflammatory and antiseptic properties (namely 1,8-cineole, camphor and borneol) and suppressed the permeation of thujone so that it did not exceed its permitted applicable concentration.

The aroma of Sage can be used, safely, to enhance memory and cognitive functions, but again, exposure must carefully monitored. The essential oil could be blended with other cognition and mood-enhancing oils such as Lemon (*Citrus limon*) and Rosemary (*Rosmarinus officinalis*), and blending will also reduce the aerial 'dose' of the ketones in the Sage oil.

When selecting a Sage essential oil for therapeutic use, you could look for a low α- ,β-thujone content, or you could consider blending with oils that contain 15% (or more) α- and β-pinenes, which might mitigate the neurotoxic effects of thujone. Perhaps of all the essential oils at our disposal, Sage presents us with the biggest challenge, and we should only use it after conducting a risk assessment in each instance. ☙

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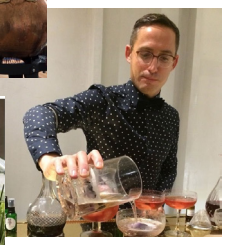
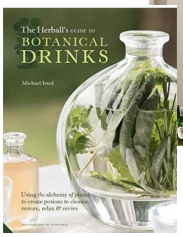
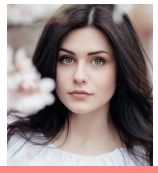




Plants have endless therapeutic qualities on so many levels, physically, spiritually, emotionally, and I think it's important that you are ingesting some good quality organic plants every day. I don't want to say as part of a routine as that sounds boring, but use them prophylactically as a preventative. Have fun with plants, get to know them, enjoy their nature, enjoy their brilliance, it's so rewarding for health and happiness. –Michael Isted

Michael Isted, BSc (Hons)
Author of *The Herball's Guide to Botanical* Drinks



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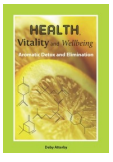

Aromaflexology is the amalgamation of aromatherapy and reflexology created by Shirley Price. The practice of Aromaflexology provides an assessment tool for the practitioner, a lawful hands-on modality for the client, and encourages the client to be proactive in their own healthcare. –Lora Cantele

Lora Cantele, RA APAIA Cert. Aromaflexologist
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Modulating Essential Oil Composition with Distillation Parameters: An Approach to Balance the Oil Composition for Therapeutic: Use An Example with *Picea mariana* (Mill.) Essential Oil

Black Spruce (*Picea mariana*)
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Benoit Roger, PhD and Alexis St-Gelais, MSc

Introduction

Distillers planning to produce a given essential oil may have a lot of questions: What is the best season to harvest the plant? Which plant part is best to use? Is it beneficial to crush, dry or wilt the plant before distillation? Which distillation technique can/should be used: steam distillation, hydro-distillation, both? And so on. The list could be long, and the answers are not always easy to find.

In the absence of any standard or customer specifications, the most logical approach generally is to look for the distillation parameters that allow for the highest practical achievable yield of essential oil with a good scent in a reasonable amount of time. Incidentally, we sometimes hear/read in discussion groups that a given plant must be distilled at least "X" hours to reach an optimal quality. What optimal quality means exactly for a given essential oil is beyond the scope of this discussion, but it is true that distillation parameters (distillation time or others) may have a great impact on essential oil composition (Baydar *et al.*, 2008; Marotti and Piccaglia, 2011; Zheljazkov *et al.*, 2012a and 2013). However, changing distillation parameters does not always produce the outcome we expect. As such, a better understanding of the consequences of specific choices during the course of distillation may be advantageously used to tweak the composition of essential oils we want for therapeutic use.

To illustrate the distillation optimization process, here is an example of how Black Spruce (*Picea mariana* Mill.) essential oil composition can be influenced by distillation time and chipping (making the wood into wood chips prior to distillation).

Material and method

All the distillations were performed using a 40-L full stainless steel still (AlChemia Solutions, "Explorer" model). About 25 kg of branches featuring abundant needles were collected from about 15 black spruce trees of the same forest in the Saguenay region (Québec, Canada) in late April, before the yearly bud burst. All branches were cut in 15-20 cm pieces, and the plant material was separated in two as homogeneous as possible batches. For the batch of branches that was coarsely and roughly chipped prior to distillation, an electric garden chipper was used.

One batch (10 kg of unchipped branches) was distilled right after the harvest. The chipped batch (also 10 kg) was stored at 4°C/40°F and distilled the next day, right after chipping. Uncrushed and crushed branches were steam distilled with cohobation (continuous reinjection of hydrosol in the still) for 4 hours at a condensate rate of approximatively 2.5 L/h, distillate temperature at 15°C/60°F.

The essential oils were collected after each hour and combined with those of the previous hour(s). The combined essential oils were weighted and analysed by GC-FID right after distillation. This procedure gives the composition one would have obtained if one had stopped the distillation after 1, 2, 3 or 4 hours.

GC-FID analyses were carried out at Laboratoire PhytoChemia on an Agilent 7890A GC equipped with a split/splitless injector as well as two FID detectors. Columns: DB-5, 10 m × 0.10 mm × 0.10 µm film thickness (Agilent Technologies, Santa Clara, CA, USA); DB-Wax, 10 m × 0.10 mm × 0.10 µm film thickness (Agilent Technologies). Temperature pro

gram: 35°C/95°F for 1 minute and 9°C/49°F minute up to 250°C/482°F. Injection port temperature: 250°C/482°F. Injection volume: 0.02 µL. Initial inlet pressure: 216.5 kPa, constant flow mode. Carrier gas: H_2, flow rate: 0.7 mL/min. Injection mode: split (300:1). FID (250°C/482°F): H_2 flow: 40 mL/min; air flow: 450 mL/min; make up flow (N_2): 45 mL/min. Sampling rate: 0.01 min.

Results and discussion

Regarding the impact of chipping the branches (Table 1), we noticed quite a significant difference in the distillation yields, but this difference decreased over time. With crushed branches compared to uncrushed ones, we got 117% more essential oil after 1 hour, 52% more after 2 hours, 27% more after 3 hours and 18% more after 4 hours.

Crushing the branches also has a noticeable impact on essential oil composition. The most striking one relates to the relative concentration of bornyl acetate, which is 20% higher after 4 hours of distillation when branches are not chipped. Since this constituent is often cited as being most influential for the beneficial impacts of Black Spruce oil, this difference could be therapeutically significant. On the other hand, we observed 35% more α- and β-pinene, 90% more δ-3-carene, and approximatively twice as many sesquiterpenes in the essential oil obtained from chipped branches compared to whole unchipped plant material, along with some minor differences for other compounds.

These differences in yield and composition can be explained by the fact that needles and wood contain different volatile compounds. The pure wood oil mainly contains monoterpenes (especially δ-3-carene, which reportedly makes for half of needleless twigs' oil) and has a very low concentration of bornyl acetate (<2%) (Rudloff, 1975). When the wood is not crushed, these volatile compounds are mainly retained in the wood. Since these cannot easily diffuse out of the plant material, they are mostly not distilled. When the wood is crushed, it becomes much better exposed to the steam, and the volatile compounds it contains can be distilled, which increases the yield but also modifies the composition. Presumably, the magnitude of these changes could further be controlled by modifying the proportion of wood to needles and modifying the coarseness of the chip ping method, with finer particles being associated with increased contribution of wood volatiles to the resulting oil.

When we compare the chromatogram of essential oils obtained from uncrushed and crushed branches, every single compound is present in both analyses (although with some differences in concentrations), with one exception: (3Z)-hexenol is only found in crushed branches (detection limit of the method we used: 0.0005%). This is known to be a degradation product derived from fatty acids (Hatanaka and Harada, 1973) and may be enzymatically produced upon chipping living plant tissues. This molecule is associated with an intense green odor (i.e. freshly cut grass) and can influence the final aroma of the oil.

Regarding the impact of distillation time, it is generally assumed that one gets the most volatile compounds of the essential oil at the beginning of the distillation and that the heaviest ones only distill later, or at least much more slowly. As we can see in Table 1, this is partly true but not completely. We can see (Table 1 and Figure 1) that sesquiterpenols, featuring a comparatively high boiling point, are much more concentrated in the essential oil if the plant is distilled longer, and this is also the case for diterpenes only present at trace levels in this essential oil. Interestingly, we also see a heavier compound (Unknown PIMA XVIII – the internal designation at Laboratoire PhytoChemia) for which the concentration is quite stable from the first to the fourth hour of distillation (Figure 1). According to GC-MS (data not shown), this unknown compound is a sesquiterpene with two hydroxyl and/or carbonyl functions that make it slightly more polar.

For sesquiterpenes (Table 1 and Figure 2), we can see varying patterns. Some constituents are more concentrated upon distilling longer, but surprisingly, this is not the case for β-caryophyllene, α-humulene and (E)-α-bisabolene (Figure 2) for which concentration decreases over distillation time. For the moment, we do not have any solid hypothesis to explain the different distillation kinetics observed for these two compounds.

For both crushed and uncrushed branches, monoterpenic esters concentration is quite stable after the second hour of distillation. Interestingly, alco

	Retention index		Uncrushed branches				Crushed branches			
Main compounds	**DB-5**	**DB-Wax**	**0-1 H**	**0-2 H**	**0-3 H**	**0-4 H**	**0-1 H**	**0-2 H**	**0-3 H**	**0-4 H**
(3Z)-hexenol	850	1348	nd	nd	nd	nd	0.06	0.06	0.06	0.05
santene	878	949	1.92	2.39	2.73	2.92	1.39	1.88	2.24	2.46
tricyclene	914	973	0.94	1.16	1.36	1.49	1.31	1.34	1.42	1.47
α-pinene	928	995	10.98	8.77	8.68	8.91	15.17	13.05	12.39	11.99
camphene	941	1031	13.04	15.27	16.84	17.55	13.98	14.72	15.46	15.84
β-pinene*	968	1068	3.54	2.58	2.52	2.26	4.22	3.53	3.29	3.08
myrcene	989	1136	3.10	3.22	3.41	3.51	5.57	3.44	3.44	3.40
δ-3-carene	1005	1114	8.34	5.11	4.20	3.93	12.17	9.53	8.30	7.50
limonene*	1024	1160	3.14	3.25	3.36	3.39	3.11	3.11	3.17	3.14
β-phellandrene*	1024	1167	0.98	0.78	0.74	0.74	1.05	0.92	0.89	0.85
1,8-cineole*	1024	1168	2.33	1.69	1.26	1.03	1.60	1.33	1.14	0.98
terpinolene*	1082	1240	1.02	0.86	0.83	0.82	1.31	1.14	1.08	1.01
linalool	1097	1519	0.51	0.37	0.27	0.24	0.36	0.32	0.28	0.26
camphene hydrate	1139	1548	3.45	2.49	1.86	1.57	1.92	1.69	1.46	1.31
borneol	1158	1652	2.00	1.69	1.40	1.25	1.46	1.50	1.41	1.32
terpinen-4-ol	1170	1556	0.33	0.34	0.32	0.32	0.31	0.31	0.31	0.30
α-terpineol	1184	1652	0.89	0.80	0.71	0.66	0.66	0.70	0.68	0.66
bornyl acetate	1285	1536	29.77	35.57	36.54	35.98	25.03	27.98	29.62	30.02
geranyl acetate	1382	1715	0.32	0.42	0.46	0.47	0.26	0.33	0.37	0.38
β-caryophyllene	1409	1544	0.19	0.11	0.08	0.08	0.25	0.20	0.18	0.16
α-humulene	1443	1610	0.04	0.03	0.02	0.02	0.05	0.05	0.04	0.04
α-muurolene	1493	1671	0.12	0.15	0.18	0.19	0.36	0.37	0.36	0.36
γ-cadinene	1505	1702	0.13	0.15	0.16	0.18	0.39	0.39	0.39	0.39
δ-cadinene	1516	1702	0.43	0.58	0.68	0.79	1.22	1.28	1.32	1.45
E-α-bisabolene	1538	1727	0.13	0.09	0.07	0.07	0.25	0.22	0.21	0.19
T-cadinol*	1631	2108	0.04	0.11	0.19	0.26	0.09	0.15	0.22	0.28
T-muurolol*	1631	2124	0.04	0.11	0.20	0.27	0.08	0.17	0.21	0.29
α-cadinol	1644	2167	0.09	0.23	0.42	0.59	0.16	0.31	0.45	0.61
Cumulative yields	**-**	**-**	**0.12%**	**0.25%**	**0.37%**	**0.45%**	**0.26%**	**0.38%**	**0.47%**	**0.53%**

*Indicates the compounds for which we use the separation on DB-Wax to determine the relative concentration because of a coelution on DB-5. All the other relative concentrations are calculated using the separation on DB-5 column. nd: non-detected (≤ 0.0005%)

Table 1. Composition (% of the main compounds) and yield of Black Spruce essential oils after 1, 2, 3 and 4 hours of distillation for uncrushed and crushed branches.

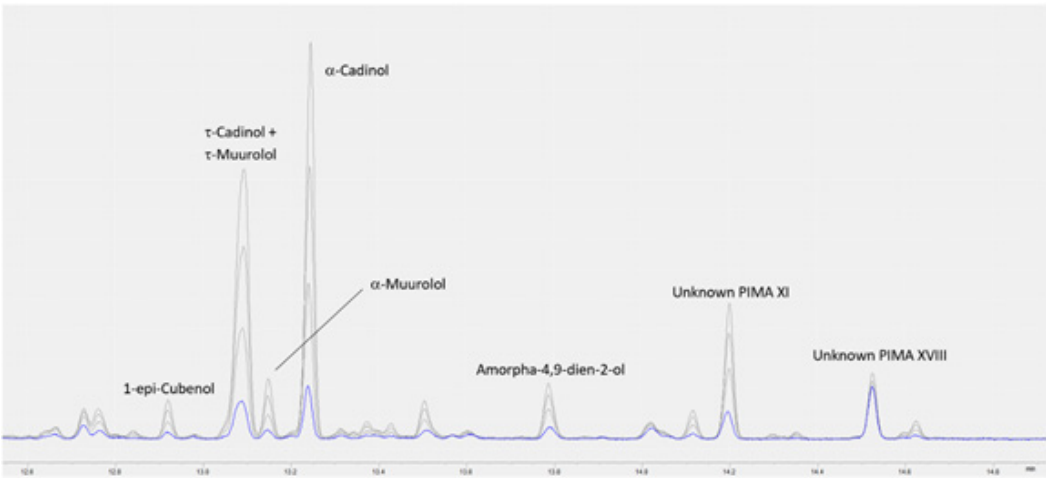

Figure 1. GC-FID chromatograms of essential oil obtained from uncrushed branches focused on the sesquiterpenols retention times. The blue line corresponds to the first hour of distillation, the grey ones correspond to 2, 3 and 4 hours of distillation.

hols, aldehydes and ethers (1,8-cineole), the most polar compounds of the essential oil, are not the most volatile compounds in this essential oil but they distill quickly (Table 1 and Figure 3). Some of them are even two times more concentrated after 1 hour than 4 hours of distillation. This is the case for camphene hydrate, the major monoterpenol in this essential oil.

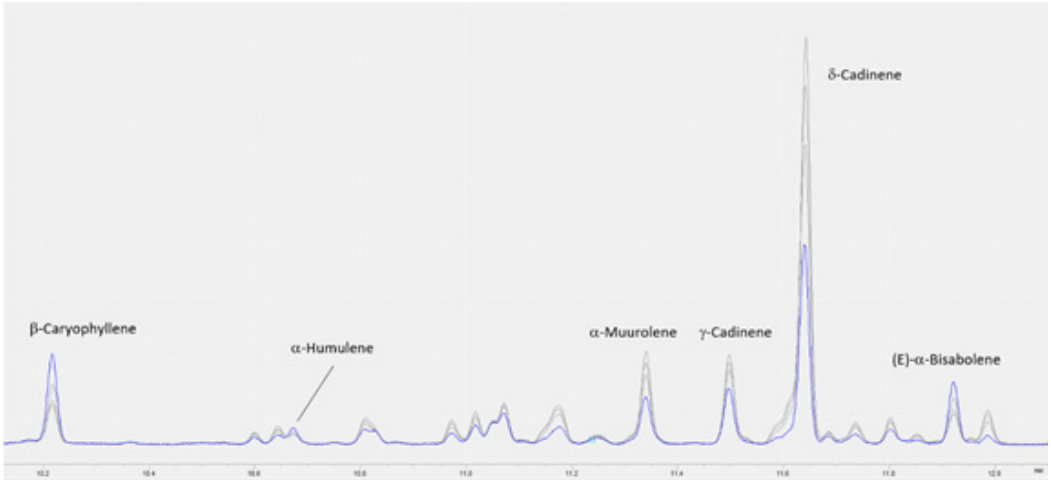

Figure 2. GC-FID chromatograms of essential oil obtained from uncrushed branches focused on the sesquiterpenes retention times. The blue line corresponds to the first hour of distillation, the grey ones correspond to 2, 3 and 4 hours of distillation.

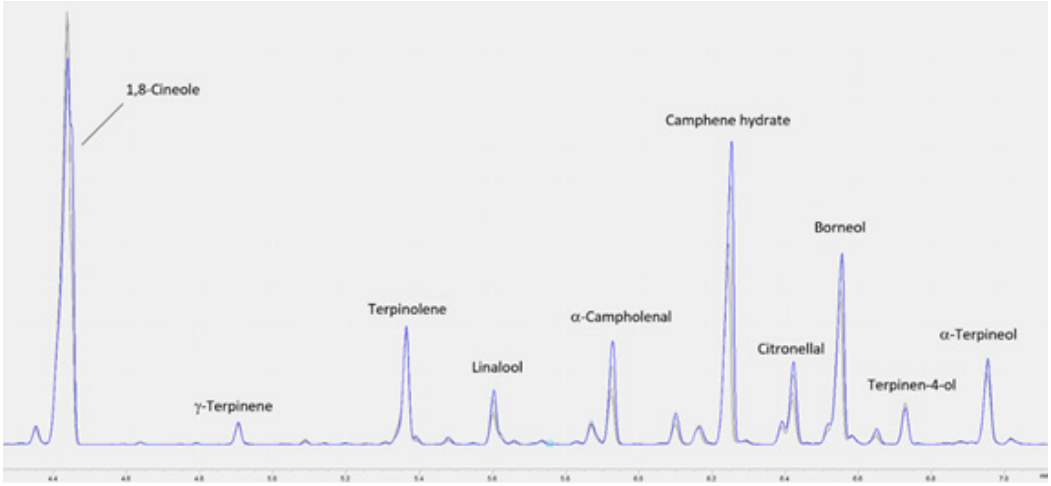

Figure 3. GC-FID chromatograms of essential oil obtained from uncrushed branches focused on the monoterpenols retention times. The blue line corresponds to the first hour of distillation, the grey ones correspond to 2, 3 and 4 hours of distillation.

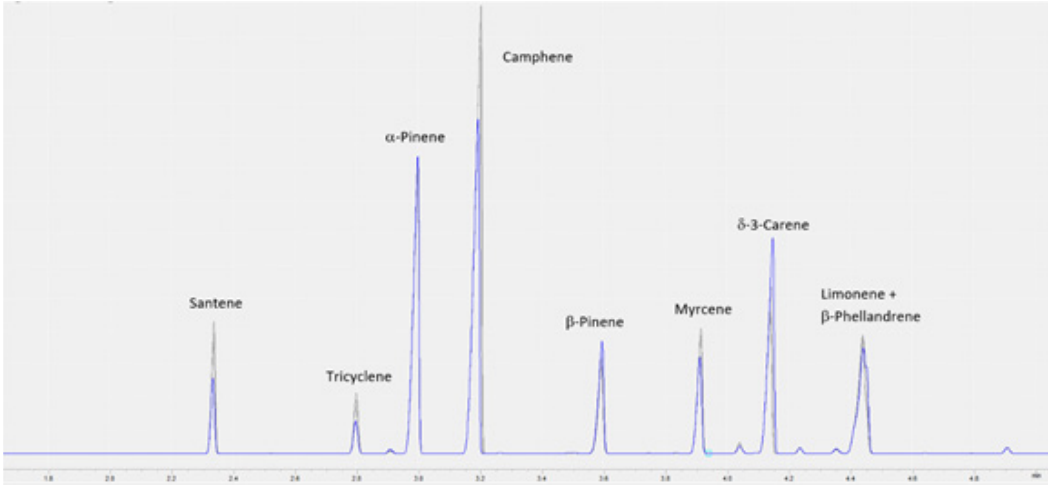

Figure 4. Chromatograms of essential oil obtained from uncrushed branches focused on the monoterpenes retention times. The blue line corresponds to the first hour of distillation, the grey ones correspond to 2, 3 and 4 hours of distillation.

Finally, we may expect non-oxygenated monoterpenes to be distilled very quickly, as they are the most volatile compounds of the plant. This is true for some of them but not in all cases. For example, the proportion of camphene in the oil keeps increasing over time. Also, the most volatile compounds, tricyclene and santene (a nor-monoterpene, which is a monoterpene-based compound with a missing carbon) are much less relatively concentrated if we stop the distillation after one hour (Table 1 and Figure 4). We could think they mainly are found in the wood and that they need time to get out of it, but these compounds are in fact almost absent in needleless wood oil. As with the conflicting patterns for sesquiterpenes, the explanation remains to be found. We just observed noticeable differences in a given compound class.

Conclusion

In Black Spruce (and supposedly other conifers featuring resiniferous, and thus odorant, wood) the chipping of branches prior to distillation seems to have a noticeable impact on yield and composition. In the case we studied, it increased the yield in essential oil (especially for short distillations) but at the same, it decreased the concentration of bornyl acetate, which is generally monitored as a parameter

of quality in the industry. Crushing the branches increased the concentration of various volatile compounds such as pinenes and δ-3-carene. A distiller/practitioner looking for the highest concentration of bornyl acetate in Black Spruce essential oil would thus be advised not to crush the branches prior to distillation and distill long enough to compensate for the ensuing slower yield buildup.

These results regarding the effect of distillation time are in accordance with general literature on the subject (Cannon *et al*., 2013) as well as a study performed on *Pinus ponderosa* (Zheljazkov, 2012b). We globally observed that heavier compounds of the essential oil distill slower than the lightest ones, but the distillation kinetics for all individual compounds do not only follow a simple rule based on volatility. Some sesquiterpenes (β-caryophyllene, α-humulene and (E)-α-bisabolene) are less concentrated in the essential oil after four hours than after one hour of distillation, and we observe the opposite for some mono- and even nor-monoterpenes (santene and tricyclene). For the moment, we cannot explain this phenomenon. For monoterpenes, it seems that the polarity has a positive impact on the distillation kinetics: camphene hydrate distills faster than camphene even if it is less volatile. This has already been described and an interpretation would be that during distillation, water penetrates the plant tissues and dissolves a part of the extractable compounds. This would help the most water-soluble compounds to diffuse out of the plant tissues and would explain why the oxygenated monoterpenes globally distill faster than the non-oxygenated ones, even if they are less volatile (Koedam *et al*., 1979). For sesquiterpenes, the effect of oxygen is less clear, but the particular kinetic we observe for PIMA XVIII, presumably bearing two atoms of oxygen instead of one based on mass spectrometric data and thus being more polar, goes in the same direction as oxygenated monoterpenes. Finally, we observe compounds in the same class that have very different distillation kinetics and we were not able to clearly link these differences to any structural features. However, it should be mentioned that the distillation of a plant is not the distillation of a mixture of more or less volatile compounds. Unless the plant is crushed in very fine dust or paste so that all oil-bearing structures are completely broken, volatile compounds have to diffuse out of these structures and plant tissues before being distilled. This diffusion speed may be affected by several parameters of the volatile compounds themselves (molecular weight, volatility, polarity, water solubility, etc.), the plant part they come from (diffusion out of a needle cuticle is probably not easy compared to the diffusion out of external secretory glands, but much easier than the diffusion through an uncrushed piece of wood) and the process (chipping, soaking, temperature, humidity, etc.). It seems that the distillation kinetic of each compound depends on a complex combination of intrinsic properties and extrinsic conditions. And to add a little more complexity, some volatile compounds may be formed during the distillation (Vuorela, *et al*., 1989) and some others may partially disappear (Kiran and Singh, 2010). But even if we do not know all the reasons why some specific compounds distill faster than others, the distiller can use these observations to slightly modulate the composition of an essential oil distilled for a specific therapeutic use. Also, many other distillation parameters could be explored by comparative tests and some tests such as very fine crushing of the plant to release as many volatile compounds as possible from the bearing structures would presumably help to get a better understanding of the phenomena we observed and described in the present study.

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Santalum album Oil Rejuvenated Part Two: Skin Healing

Robert Tisserand, Essential Oil Consultant

A *Santalum album* seedling

Introduction

Of the several species of Sandalwood oil commercially produced, this article focuses on just one, *Santalum album*. Although *Santalum album* oil (SAO) has been produced in India for centuries, large-scale production there has now entirely ceased and has been replaced by oil from cultivated plantations of *Santalum album* in Australia. The reasons for this are discussed in detail in the first article of this two-part series. Part one covered four subject areas: history, sustainability challenges, quality control and psychodermatology. This second part focuses on the skin-healing properties of SAO and highlights emerging clinical data, linking it with mechanisms of action.

Skin safety

Patch testing is widely used by dermatologists in order to ascertain what might be causing a patient's skin condition, and multiple potential allergens are tested at the same time on the upper back. Generally, there is a standard dilution for each test substance, and for SAO this is 2%, but 10% dilutions have also been used. When a substance used in patch testing is linked to the cause of a patient's skin condition, this is known as clinical relevance. Sometimes patients react to substances that are not clinically relevant.

In terms of patch testing for contact dermatitis (either irritation or allergy), SAO has a good safety profile. Both 10% and undiluted SAO are non-irritant (Burdock and Carabin, 2008). With regard to allergic reactions, in five dermatology reports, 12 of 3,542 patients (0.34%) were sensitive to a 2% dilution of SAO, and in three reports, 69 of 5,595 patients (1.2%) were sensitive to a 10% dilution (Tisserand and Young, 2014). In a subsequent multi-center European study, 656 of 48,956 dermatitis patients (1.38%) showed positive reactions to 10% SAO (Warshaw *et al*., 2017). In a repeat insult patch test for both skin irritation and sensitization conducted by AMA Laboratories, NY, undiluted SAO produced no adverse reactions in 100 test subjects (Santalis Pharm., n.d.).

A total of four reports of photoallergy testing show that nine of 621 patients (1.45%) tested positive to SAO at 2% (Fotiades *et al*., 1995; Greenspoon *et al*., 2013; Scalf *et al*., 2009; Victor *et al*., 2009). It should be noted that clinical relevance was generally not established, and photoallergy to essential oils is very rare.

While this is the best information available, the purity of the SAO used in most of these tests is unclear, as there is no transparent traceability of source. Also, it should be noted that dermatitis patients are more prone to allergic skin reactions than healthy subjects, and that statistics from patch testing do not represent real-world risk (Tisserand and Young, 2014). Finally, the reliability of patch testing is questionable, since results can vary significantly depending on which brand of patch is used (Lazarov *et al*., 2007; Mortz and Andersen, 2010; Sherertz *et al*., 2001).

Skin-healing properties

The therapeutic value of SAO in dermatology can often be ascribed to a combination of antioxidant, anti-inflammatory and antimicrobial properties. In addition, SAO inhibits keratinocyte hyper-proliferation, which is problematic in eczema and psoriasis. Antioxidant action is measured in various ways. SAO scavenged DPPH radicals *in vitro* only very weakly (Inouye *et al*., 2010) but significantly enhanced both hepatic glutathione enzymes and superoxide dismutase, when fed to mice (Banerjee *et al*., 1993; Chhabra and Rao, 1993; Misra and Dey, 2013).

SAO demonstrates significant anti-inflammatory properties. It suppressed the production of 20 of 26 (77%) of tested pro-inflammatory cytokines and chemokines in human dermal fibroblasts (Sharma et al., 2014). Unpublished research by Santalis Pharmaceuticals has confirmed that SAO significantly reduces the production of multiple cytokines and chemokines in reconstituted human skin, in response to inflammation by *P. acnes*. In reconstituted psoriasis tissue, SAO at 0.002% decreased levels of Interleukin (IL) IL-β, IL-6 and IL-8 by 56%, 75% and 83% respectively (Sharma, 2017). Interestingly, SAO reduced inflammation in keratinocytes by inhibiting a pro-inflammatory enzyme, 11β-HSD1 (Itoi-Ochi *et al.*, 2016).

Both α-santalol and β-santalol dose-dependently suppressed prostaglandin E2 production in skin cells, suggesting that the anti-inflammatory action of SAO takes place partly through inhibition of cyclo-oxygenase enzymes (Sharma *et al.*, 2014). In an *in vitro* study for inhibition of 5-lypoxygenase, SAO was more effective than the essential oils of Blue Cypress (*Callitropsis intratropica*) and Blue Chamomile (*Matricaria recutita*) (Baylac and Racine, 2003). Figure 1 illustrates several anti-inflammatory pathways for SAO, and the image at top right shows an important antimicrobial mechanism.

A common side effect of radiation therapy for cancer is skin inflammation and irritation. This is known as radiodermatitis and is related to oxidative stress and an increase in cytokines, including ILβ, IL-6 and IL-8 (De Sanctis *et al.*, 2014). In a nine-week open-label clinical study of 46 head and neck cancer patients undergoing radiotherapy, a proprietary cream (Vicco® Turmeric Skin Cream) containing 16% turmeric extract and 0.5% SAO significantly inhibited the degree of radiodermatitis (24 patients) compared to baby oil (22 patients) (Palatty *et al.*, 2014). In a similar study with the same product in 40 breast cancer patients (20 in each group) radiodermatitis was significantly delayed and mitigated in the sandalwood/turmeric group compared to the baby oil group. Patients had unilateral cancer and had undergone radical mastectomy followed by chemotherapy (Rao *et al.*, 2017). Although this treatment included two active ingredients, it shows a link between antioxidant and anti-inflammatory action, and skin healing/wound healing effects. No adverse events were reported in either study.

Topical infection

SAO has shown activity against a range of bacteria, yeasts and fungi associated with skin disease (Table 1). Perhaps surprisingly, in an *in vitro* comparison of 24 essential oils, including Lemongrass (*Cymbopogon citratus*), Clove (*Syzygium aromaticum*) and Oregano (*Origanum vulgare*), SAO was the most effective against *Candida albicans* (Hammer, 1998). SAO dose-dependently inhibited Herpes simplex virus 2 (HSV-2) and was remarkably active against Herpes simplex virus 1 (HSV-1), suggesting a potential use in the treatment of cold sores (Benencia and Courrèges, 1999).

Gram positive bacteria	
Micrococcus flavus	*Staphylococcus aureus*
Micrococcus glutamicus	*Staphylococcus aureus (MRSA)*
Propionibacterium acnes	*Staphylococcus epidermidis*
Sarcina lutea	*Streptococcus equisimilis*
Staphylococcus albus	*Streptococcus pyogenes*
Gram negative bacteria	
Acinetobacter baumannii	*Pseudomonas aeruginosa*
Acinetobacter calcoaceticus	*Pseudomonas florescens*
Klebsiella aerogenes	*Pseudomonas putida*
Klebsiella pneumoniae	
Yeasts & fungi	
Candida albicans	*Microsporum gypseum*
Candida krusei	*Trichophyton asteroides*
Epidermophyton fluccosum	*Trichophyton interdigitale*
Epidermophyton inguinale	*Trichophyton mentagrophytes*
Microsporum canis	*Trichophyton purpureum*

Table 1. Microbes associated with skin disease and against which *Santalum album* oil has shown activity. After Moy and Levenson, 2017.

Several clinical trials have highlighted the potential clinical use of SAO in infective skin conditions, two of them also including salicylic acid, which is already an FDA-approved active ingredient for these disorders. Acne is a skin condition that occurs when hair follicles become plugged with oil and dead skin cells. Two bacteria in particular tend to proliferate in acne lesions: *Staphylococcus epidermidis* and *Propionibacterium acnes*, and both are inhibited *in vitro* by SAO. Acne is most common among teenagers; it causes whiteheads, blackheads or pimples, and usually appears on the face, forehead, chest, upper back and/or shoulders.

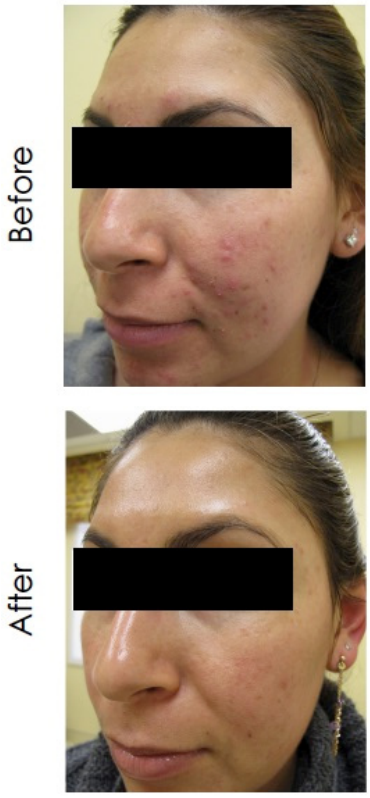

Figure 2. Acne lesions before and after eight weeks of treatment.
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An open-label pilot study of an over-the-counter topical regimen containing 0.5% salicylic acid and up to 2% SAO was conducted in adolescent and adult subjects with mild to moderate facial acne (Figure 2). The regimen consisted of foaming cleanser, serum, spot treatment and mask. Over the course of the eight-week treatment period, 42 of 47 participants (89.4%) experienced an improvement when compared with baseline, using the Global Aesthetic Improvement Scale (GAIS). No adverse events were seen that would limit use of the regimen (Moy *et al*., 2012).

Common warts (*Verruca vulgaris*) are small, grainy skin growths that occur most often on fingers or hands. Rough to the touch, common warts often feature a pattern of tiny black dots which are small, clotted blood vessels. Common warts are caused by the human papilloma virus (HPV) and are transmitted by touch. Children and young adults are more likely to develop common warts, as are people with weakened immune systems (Mayo Clinic, 2015).

A proprietary topical collodion[1] product containing 17% salicylic acid and approximately 2% α-santalol was used in two open-label pilot studies in children and adolescents with common warts. A total of four of 25 (16%) and seven of 33 (21%) of patients experienced complete resolution of treated warts (Figure 3). The treatment was well tolerated with 10-30% of patients experiencing mild to moderate itching, burning, dryness or stinging, symptoms that are common in wart treatment (Browning *et al*., 2017a). In a third open-label pilot study, ten subjects, ranging in age from six to adult, applied undiluted SAO to common warts twice daily for 12 weeks. At the end of the study period, 10 of the 12 (80%) had complete resolution of all treated warts, with the other two subjects experiencing moderate improvement. None of the subjects reported skin irritation, redness, pain or other adverse symptoms (Haque and Coury, 2018).

A randomized, double-blind, placebo-controlled dose range finding trial of SAO ointment (10%, 20%, and 30% strengths) was studied in subjects with common warts (*Verruca vulgaris*) caused by HPV (US National Library of Medicine, 2017a). The primary endpoints of the trial were efficacy, safety, and tolerability. All three treatment arms were deemed to be safe and well tolerated. There were no serious adverse events considered to be related to the study medication, and only four adverse events (three in the 30% arm and one in the 10% arm) were deemed to be related to the study medication; notably, all were mild, reversible irritation at the site of application. All three treatment arms showed greater rates of wart clearance and reduction in wart area than did those in the placebo arm (unpublished results, 2016, Santalis Pharmaceuticals).

A clinical trial using SAO for genital warts with 30 participants is currently in progress (US National Library of Medicine, 2017b).

Molluscum contagiosum is a skin condition caused by a poxvirus of the Molluscipox genus, which is transmitted by close physical contact. Preschool and elementary school-aged children are more commonly affected than are other ages. The condition pres

[1] Collodion is a yellowish, viscous, highly flammable solution of pyroxylin in ether and alcohol. It is used in medicine chiefly for cementing dressings and sealing wounds.

ents as asymptomatic, discrete, smooth, flesh-colored, dome-shaped papules. It typically resolves within months in people without immune deficiency, but treatment may be preferred for social and cosmetic reasons or to avoid spreading the infection (Leung *et al*., 2017; Van der Wouden *et al*., 2017).

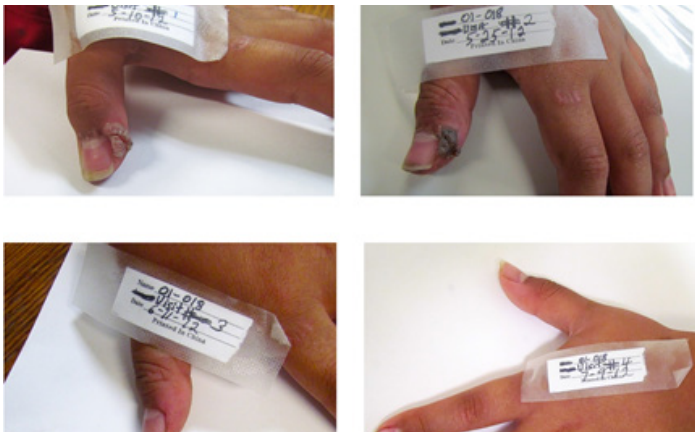

Figure 3. Complete resolution of hand wart over eight weeks. Browning *et al*., 2017a.

In a pilot study, nine subjects used a proprietary sandalwood soap (composition unknown) as a treatment for molluscum contagiosum. All subjects experienced complete resolution of the condition within the 12 weeks of the study. No adverse effects were reported (Haque and Coury, 2018). The subjects had contracted the condition an average of 5.3 months before entering the study. This condition may resolve without treatment in as little as six months, but some cases take several years.

Barrier disruption (eczema and psoriasis)

Eczema (atopic dermatitis) is a condition that causes patches of red and itchy skin. It is common in children but can occur at any age. Eczema is long lasting (chronic) and tends to flare periodically. It may be accompanied by asthma or hay fever (Mayo Clinic, 2018a). Psoriasis is a skin condition that causes cells to build up rapidly on the surface of the skin. The extra skin cells form scales and red patches that are itchy and sometimes painful. There is no known cure for psoriasis, but symptoms can be managed (Mayo Clinic, 2018b).

Both eczema and psoriasis are T-cell mediated chronic inflammatory skin diseases characterized by disruption in the integrity of the skin's barrier function. This is in part associated with depletion of key lipids in the stratum corneum and is associated with keratinocyte hyper-proliferation and faulty keratinocyte differentiation (Sahle *et al*., 2015). Barrier disruption, in turn, permits a low level of chronic infection, as bacteria that normally populate the skin surface become problematic.

Interim results from an on-going Phase 2 clinical trial, in which 10% SAO was topically applied, show that it is well tolerated and alleviates mild to moderate psoriasis symptoms. An anhydrous excipient was used, primarily consisting of caprylic/capric triglyceride (Sharma *et al*., 2017). The researchers hypothesized that SAO might provide therapeutic benefit to psoriasis patients due to its anti-inflammatory and anti-proliferative properties, seen in skin cells (Dickinson *et al*., 2014; Itoi-Ochi *et al*., 2016; Sharma *et al*., 2014). Also, a clinical anti-inflammatory benefit had previously been shown in the Phase 2 study of acne patients already cited (Moy *et al*., 2012).

In nine of the 11 subjects in the psoriasis trial who could be evaluated, the severity of psoriatic plaques was reduced by the end of the study. One patient withdrew from the study with a mild adverse event after three weeks, and their skin reaction resolved. The average immunoglobulin A (IGA) score was significantly reduced by one week and continued to improve at two and four weeks. Overall, 64% of the subjects (7/11) demonstrated a 1.0 or greater reduction in their IGA score during the 28-day treatment period. Two examples are shown of lesions before and after either one or three weeks of treatment (Figure 4). These were both scored as markedly improved. Two additional patients demonstrated moderate improvement. These clinical observations demonstrate that SAO can provide symptom relief for psoriasis patients.

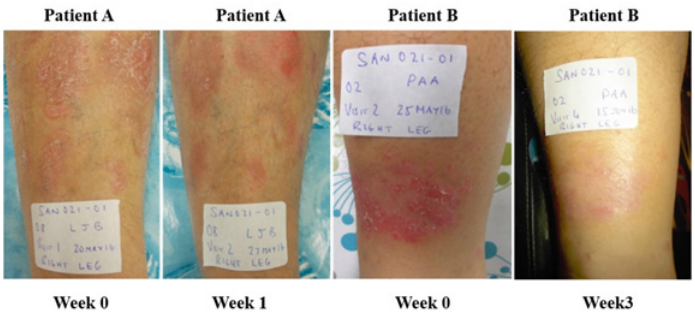

Figure 4. Psoriasis lesions in two patients – before treatment, and after 1 week (patient A) and 3 weeks (patient B). Creative Commons Attribution License, Sharma *et al*., 2017.

Further research evaluated the ability of SAO to affect the psoriatic phenotype using psoriatic and normal human skin models. SAO had no impact on the phenotype of the normal skin tissue model; however, SAO treatment of the psoriasis tissue model reversed psoriatic pathology. This supports the hypothesis that the clinically observed symptom alleviation is due to suppression of intrinsic tissue inflammation in afflicted lesions (Sharma *et al*., 2017).

It has been suggested that *Helicobacter pylori* infection in the stomach might be a triggering factor in psoriasis, probably via inflammatory pathways. *H. pylori* infections are considerably more common in psoriasis patients than in healthy controls, and there are several reports of cases in which psoriatic lesions cleared up following the eradication of *H. pylori* infections (Magen and Delgado, 2014). This is noteworthy, since SAO constituents, including α-santalol and β-santalol, are strongly active against a clarithromycin-resistant strain (TS281) as well as other strains of *H. pylori* (Ochi *et al*., 2005).

Psoriasis patients suffer from impaired quality of life, psychosocial problems and emotional distress, and stress and infection are two of the triggers that can initiate the inflammatory process resulting in keratinocyte hyper-proliferation (Sharma *et al*., 2017). Since stress, barrier disruption, infection and inflammation all cross-promote each other, remedies that address all four factors are arguably most likely to succeed. The anti-stress effects of SAO, and the related study of psychodermatology, are discussed in the first article of this two-part series.

Eczema also appears to be amenable to treatment with SAO. In an open-label study over 60 days, 22 children with eczema (aged three months to 11 years) were treated with three products (daily cleanser, soothing cream and bubble bath gel) all containing 0.1% colloidal oatmeal and SAO. After one week, 91% showed improvement in Eczema Area and Severity Index (EASI) scores. At the end of the trial, 18 children had a 25% or greater reduction in EASI score, and nine were completely clear of eczema or had a greater than 90% EASI score improvement (Figure 5). Adverse events were mild to moderate, and none were considered to be related to the treatment regimen (Browning *et al*., 2017b). Two further clinical trials are currently in progress, each in 72

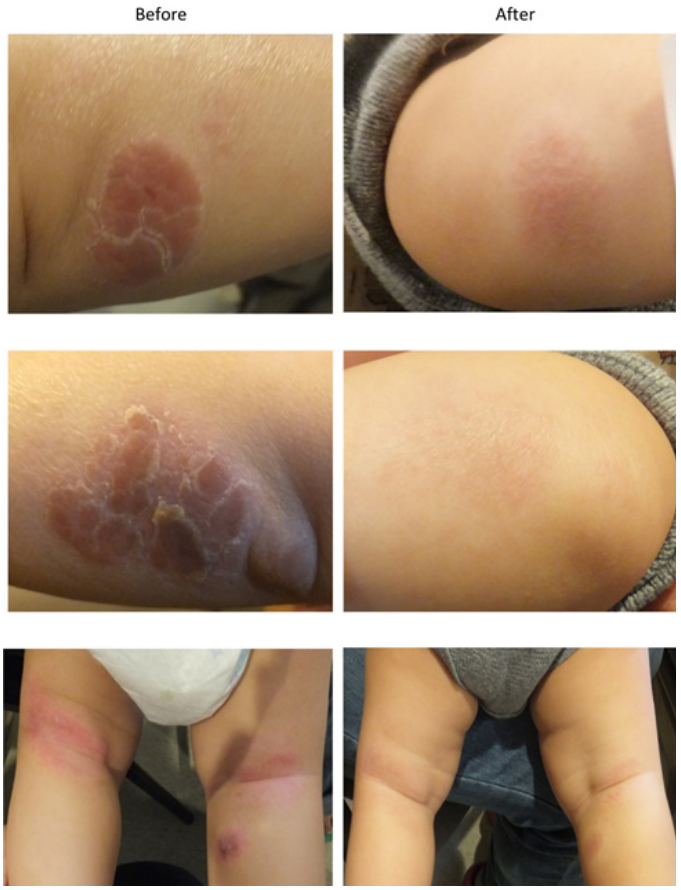

Figure 5. Pediatric eczema in one patient, before treatment and after 60 days. Browning *et al*., 2017b.

eczema patients, using a 5% preparation of SAO, and encompassing a wide age range (US National Library of Medicine, 2017c; US National Library of Medicine, 2017d). Recent interest in inflammation-specific targets for the treatment of skin conditions such as psoriasis and eczema has focused on substances that reduce levels of IL-17 and the activity of PDE412 (Moy and Levenson, 2017). SAO has been shown to specifically inhibit both targets in various *in vitro* models (Sharma *et al*., 2017; Sharma *et al*., unpublished material). This suggests likely mechanisms for the therapeutic activity seen in the clinical studies of SAO in the treatment of these skin conditions.

Skin cancer

Skin cancers are due to the development of abnormal cells that may spread to other parts of the body (National Cancer Institute, 2015). There are three main types: basal-cell skin cancer (BCC), squamous-cell skin cancer (SCC) and melanoma (National Cancer Institute, 2018a). The first two, along with some less common skin cancers, are known as non-melanoma skin cancer (NMSC). Basal-cell cancer grows slowly and can damage the tissue around it

but is unlikely to spread to distant areas or result in death. Squamous-cell skin cancer is more likely to spread (Cakir *et al*., 2012). It usually presents as a hard lump with a scaly top but may also form an ulcer (Dunphy, 2011). Melanomas are the most aggressive. Signs include a mole that has changed in size, shape, or color, has irregular edges, has more than one color, is itchy or bleeds (National Cancer Institute, 2018b). More than 90% of skin cancer cases are caused by exposure to ultraviolet radiation from the sun. This exposure increases the risk of all three main types of skin cancer (Gallagher *et al*., 2010).

In terms of the number of papers published, the most widely researched use of SAO oil in dermatology is for skin cancer, though to date there are no human studies. α-Santalol was significantly effective when tested against human epidermoid carcinoma or melanoma cells *in vitro* (Kaur *et al*., 2005; Zhang *et al*., 2010) and topical application showed good efficacy inhibiting UVB-induced skin cancer in mice when used at 10% (Santha and Dwivedi, 2013) or 5% (Arasada and Bommareddy, 2008; Bommareddy *et al*., 2007; Chilampalli *et al*., 2013; Dwivedi *et al*., 2006). The 5% protocol was also effective for both α-santalol and β-santalol for chemical-induced skin cancer in mice (Dwivedi *et al*., 2003; Kim *et al*., 2006).

The antitumoral mechanisms of action for α-santalol are summarized by Zhang and Dwivedi (2011) and include apoptosis and inhibition of cell growth at the G_2/M phase. Dickinson *et al*. (2014) observed that low concentrations of SAO inhibited rapid proliferation of keratinocytes and suggest that the oil may reduce the risk of actinic keratosis[2] and skin cancer.

An Australian practitioner found that a mix of essential oils including 13% *Santalum spicatum* was an effective treatment in several cases of actinic keratosis (Tisserand Institute, 2011).

Applied at 5% topically, SAO inhibited chemical-induced skin cancer in mice (Dwivedi and Abu-Ghazaleh, 1997) and the 5% dilution was more effective than 1.25%, 2.5% or 3.75% (Dwivedi and Zhang, 1999). Although there has been no clinical research,

[2] An actinic keratosis (also known as a solar keratosis) is a rough, scaly patch on your skin that develops from years of exposure to the sun. It's most commonly found on your face, lips, ears, back of your hands, forearms, scalp or neck (Mayo Clinic, 2018c).

Santalum album, showing lighter colored sapwood and darker colored heartwood © Quintis Limited.

SAO shows promise in terms of both prevention and treatment for skin cancers. For treatment, 5-10% concentration of SAO might be appropriate. For prevention, lower concentrations would make sense as the conditions of mouse testing were quite severe.

For other cancers, SAO has shown promise in *in vitro* testing with human cells for bladder, colon, and breast cancers, α-santalol for liver cancer, breast cancer (both ER-positive and ER-negative) and prostate cancer, β-santalol for leukemia, and both α-santalol and β-santalol for oral cancer (Bommareddy *et al*., 2012, 2015; Dozmorov *et al*., 2014; Lee *et al*., 2015; Matsuo *et al*., 2014; Mitoshi *et al*., 2012; Ortiz *et al*., 2016; Santha *et al*., 2013; Saraswati *et al*., 2013a, 2013b). Topically applied at 10% to female rats, α-santalol demonstrated good transdermal absorption, and in breast cancer it significantly reduced tumor incidence (Dave *et al*., 2017).

Whether SAO would be an effective anticancer treatment is not known, but the above findings suggest its use in prevention.

Summary

Santalum album oil (SAO) is proving to be an effective treatment for a wide range of skin conditions. Data from patch testing suggest a low level of risk, and this is borne out by clinical results, which show encouraging risk-benefit ratios. *In vitro*, and some *in vivo* studies, demonstrate properties that include antibacterial, antifungal, antiviral, anti-inflammatory and antitumoral effects, and some mechanisms of action have been elucidated. The efficacy of SAO in terms of anti-

inflammatory and antimicrobial action compared with certain other essential oils may be surprising. Clinical studies are ongoing, and show promise in the treatment of facial acne, common warts, psoriasis, radiodermatitis, molluscum contagiosum and eczema. Concentrations varying from 2% to 10% (up to 100% for common warts) have been used in a variety of excipients. Other skin conditions that may be amenable to SAO therapy include cold sores, sensitive skin, rosacea, genital warts, skin cancers, and fungal infections such as onychomycosis, diaper rash and athlete's foot.

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Notes

The suppliers given for SAO in the reports cited include Cauvery (Bangalore), Dragoco (Austria), Karnataka Emporium (New Delhi), Mountain Rose Herbs (OR), NOW Foods (IL), Organic Infusions (CA), Phytoaroma Labs (Yokohama), Santalis Pharmaceuticals (TX), Shiseido (Japan), Synthite Industrial Chemicals (Cochin), and Young Living (UT). Haque and Coury (2018) gave no source. Only two papers (Misra and Dey, 2013 and Sharma *et al*., 2017) included a detailed analysis of the essential oil used.

The article was also published on the Tisserand Institute blog http://tisserandinstitute.org/blog/.

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Robert Tisserand is an international speaker, educator and consultant. Since 2010 he has inspired live audiences internationally. He tracks all the published essential oil research and often collaborates with doctors, herbalists and academics, integrating scientific data with holistic principles. He is familiar with the foundations of oriental medicine, and Western herbal and naturopathic traditions. Robert has 40 years of experience in essential oil blending and Aromatherapy product development. He is a co-author of the 780-page book *Essential Oil Safety*, 2nd edition.

Good to Know...

Prophetic Medicine–*Nigella Sativa* (Black Cumin Seeds) – Potential Herb for COVID-19?

Abstract:
Coronavirus disease-19 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Currently, the management of patients with COVID-19 depends mainly on repurposed drugs, which include chloroquine, hydroxychloroquine, lopinavir/ritonavir, ribavirin, remdesivir, favipiravir, umifenovir, interferon-α, interferon-β and others. In this review, the potential of *Nigella sativa* (Black Cumin seeds) to treat patients with COVID-19 is analyzed, as it has shown to possess antiviral, antioxidant, anti-inflammatory, anticoagulant, immunomodulatory, bronchodilatory, antihistaminic, antitussive, antipyretic and analgesic activities. Medline/PubMed Central/PubMed, Google Scholar, Science Direct, Directory of Open Access Journals (DOAJ) and reference lists were searched to identify articles associated with antiviral and other properties of *N. sativa* related to the signs and symptoms of COVID-19. Various randomized controlled trials, pilot studies, case reports, and *in vitro* and *in vivo* studies confirmed that *N. sativa* has antiviral, antioxidant, anti-inflammatory, immunomodulatory, bronchodilatory, antihistaminic, antitussive activities related to causative organism and signs and symptoms of COVID-19. *N. sativa* could be used as an adjuvant therapy along with repurposed conventional drugs to manage patients with COVID-19.

Maideen N M P. (2020). Prophetic Medicine-*Nigella Sativa* (Black cumin seeds) - Potential herb for COVID-19? *J of Pharmacopunct.* 23 (2), p62-70.

Aromatherapy Featured in (Un)Well

Netflix launched a six-part docuseries called "(Un) Well" that aims to balance stories about how non-medical treatments are making a difference in various clinical settings with stories about people selling these treatments as unproven cures, and the big business that some of those people generate. Episode one features Aromatherapy and looks at its up- and downside. Participants include authentic practitioners, those selling online and for multi-level marketing companies, as well as those harmed.

Geranium and Lemon Essential Oils and Their Active Compounds Downregulate Angiotensin-Converting Enzyme 2 (ACE2), a SARS-CoV-2 Spike Receptor-Binding Domain, in Epithelial Cells

Abstract:
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), also known as coronavirus disease-2019 (COVID-19), is a pandemic disease that has been declared modern history's gravest health emergency worldwide. Until now, no precise treatment modality has been developed. The angiotensin-converting enzyme 2 (ACE2) receptor, a host cell receptor, has been found to play a crucial role in virus cell entry; therefore, ACE2 blockers can be a potential target for anti-viral intervention. In this study, we evaluated the ACE2 inhibitory effects of 10 essential oils. Among them, Geranium and Lemon oils displayed significant ACE2 inhibitory effects in epithelial cells. In addition, immunoblotting and qPCR analysis also confirmed that Geranium (*Pelargonium graveolens*) and Lemon (*Citrus limon*) oils possess potent ACE2 inhibitory effects. Furthermore, the gas chromatography-mass spectrometry (GC-MS) analysis displayed 22 compounds in Geranium oil and 9 compounds in Lemon oil. Citronellol, geraniol, and neryl acetate were the major compounds of Geranium oil, and limonene represented the major compound of lemon oil. Next, we found that treatment with citronellol and limonene significantly downregulated ACE2 expression in epithelial cells. The results suggest that Geranium and Lemon essential oils and their derivative compounds are valuable natural anti-viral agents that may contribute to the prevention of the invasion of SARS-CoV-2/COVID-19 into the human body.

Kumar *et al*.. (2020). Geranium and Lemon Essential Oils and Their Active Compounds Downregulate Angiotensin-Converting Enzyme 2 (ACE2), a SARS-CoV-2 Spike Receptor-Binding Domain, in Epithelial Cells *Plants* (Basel). 9 (6), p770.

2021 AIA Conference Early Registration

With the theme "Aromatherapy Hot Topics: From Self-Care to Clinical Trials" the Alliance of International Aromatherapists will be holding its international conference September 16-19, 2021, in Chicago. They are offering an *early* Early Bird rate starting 12/1/2021. For more info: **www.aromatherapyconference.com**

Every oil is hand-poured with love and intention just for you. I look forward to continuing our aromatherapy, wellness and healing journey together!

Tutte Cose Buone,

Virginia Joy

Case Study: Treating Eczema And *Staphylococcus aureus* With Herbs And Essential Oils In An Infant

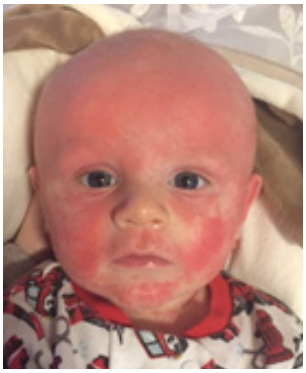

Image: "Mikey" at four months with Eczema and infection.

Inga Wieser, ND, MS, APAIA, MH
Board Certified Traditional Naturopath

Introduction

This case study discusses an infant (four months old) with severe eczema and a potentially controversial treatment involving the use of essential oils. Using essential oils on an infant requires additional knowledge in the risks associated with using essential oils on such young clients. The first two visits were generally concerned with treating the infant via the nursing mother to clear the eczema enough for an allergist to be able to provide testing on his condition, which later revealed the existence of a *Staphyloccocus aureas* infection alongside the infant's eczema. The latter visits were focused on a more aggressive treatment using essential oils with the infant to clear the infection. I realize that this goes against the general teaching and beliefs held in the field, but the mother was faced with the use of a dangerous antibiotic with side effects that had the potential to be extremely risky to the infant. I consulted with another doctor who agreed the risk of the higher percentage of essential oils was much less than the antibiotics the prescribed by the infant's pediatrician and recommended the use of essential oils over the use of antibiotics. A great deal of thought, research, consulting, and counseling was taken into consideration prior to employing this treatment.

Description of the case

"Mikey" is a four-month-old infant with a happy disposition despite struggling with severe eczema. He was constantly itching and wore mittens, to avoid scratching himself. His care team consisted of a pediatrician, dermatologist, and an allergist. Mikey's mom had heard essential oils could cure her son but did not want to experiment with what she found on the internet or advice shared from well-meaning friends who sold essential oils.

Eczema is considered by some to be as an autoimmune disease with an allergic component while others consider it to be an allergic reaction. The allergy most often is caused by dietary issues, but it can stem from environmental issues. While all eczema patients have positive allergy test results, only about 80% have serum IgE levels (Murray and Pizzorno, 2012). These results indicate an allergy compotent. In looking at 260 orginal studies, Garcia-Larsen *et al*., found that there is also an immune component influenced by the diet of the mother during pregnancy which can trigger an allergy and/or autoimmune response in the child (Garcia-Larsen *et al*., 2018). They conclude that the supplementation of fish oil and probiotics during pregnancy and breasting feeding reduces the risk of eczema and allergic sensitization to food for the child.

As Mikey was being nursed by his mother, I chose to work with him through his mother.

Mikey's mother never had eczema, although his sister had some minimal issues that did not require intervention. His father had skin issues, including eczema, in the past. An intelligent woman, Mikey's mother had done a lot of research about eczema before seeking my expertise. She was healthy and had a great, although limited, diet as she was nursing her son. She had already eliminated gluten and most non-gluten grains, dairy, eggs, tomatoes, and nightshade vegetables. We began with an elimination diet to see if we could find the problematic allergen(s) that were affecting Mikey's eczema. Working with the mother; is safer for the infant and changes in the mother's diet would be reflected in the infant's health if the cause of the eczema was related to her diet.

Treatment protocol for Mikey's mother
We began with an elimination diet to detect the problematic allergen(s) for that were affecing Mikey. She was concerned about producing the necessary quality and quantity of milk needed to feed her son. Mikey's mother kept a food diary and noted her son's eczema each day on a scale from 1 to 10 with 10 being the worst. Each time Mikey had a flare up she was instructed to look back over the past 72 hours to see if any foods consistently showed up on only those days. I was hoping to identify a pattern that would indicated possible food or several foods that were causing her son's eczema to flare up. Due to her already restricted diet, her milk supply was dwindling. If the elimination diet caused a further reduction in her milk supply, I instructed her to add back in any foods she felt she needed to provide for her son.

Other supports
Omega 3 — 2 gm daily to support both her and Mikey during this restricted diet and to reduce inflammation caused by the eczema.

Probiotics — double the recommend dose to support gut health for both mother and son.

Mikey's mother drank a tea three times daily between meals to build up and enrich her milk.

Tea for Mom
33% - 0.4 oz/12 gm Blessed Thistle (*Cnicus benedictus*)
17% - 0.2 oz/ 6 gm Dandelion (*Taraxacum officinale*)
17% - 0.2 oz/ 6 gm Fennel (*Foeniculum vulgare*)
17% - 0.2 oz/ 6 gm Red Raspberry (*Rubus idaeus*)
16% - 0.2 oz/ 6 gm Cinnamon (*Cinnamomum* spp.)

Preparation: Add one teaspoon (5 ml) in one cup (237 ml) of hot water, steep for ten minutes and strain.

Rationale
Blessed Thistle was selected to increase mother's milk. Dandelion is a bitter herb to help increase the assimilation of nutrients. Fennel was selected to increase mother's milk supply and to enhance the flavor. Red Raspberry is an herb that is high in the vitamins needed for milk supply and for enhanced flavor. Cinnamon was to reduce inflammation and to improve the flavor of the tea (Kunnumakkara *et al*., 2018).

Treatment for Mikey
A skin nourishing butter made from carrier oils was prepared for Mikey to relieve the dry itchy red spots. I planned to make a cream with hydrosols and herbal infused base oil for eczema support before they came back for their next visit.

Skin Nourishing Butter
3 oz (90 g) Coconut (*Cocos nucifera*) oil
2 oz (60 g) Jojoba (*Simmondsia chinensis*) wax
1 oz (30 g) Cocoa (*Theobroma cacao*) butter
1 oz (30 g) Beeswax (*Cera alba*)

The skin butter was to be lightly rubbed on the spots to soothe the hot, red, and itchy skin when "Mikey" was scratching the spots. I explained to his mother that his scratching and rubbing the spots would be her cue for reapplying the cream. I instructed his mother to use the skin butter up to four times daily.

Rationale
According to Sade (2017), Coconut oil is an excellent moisturizer and antibacterial.

Jojoba has been shown to be useful in cases of psoriasis and eczema and is an emollient (Battaglia, 1995). Cocoa butter is recommended to help to soothe the skin (Sade, 2017). The beeswax is an emollient and included to harden the butter (Sade, 2017).

Clients' response to treatment
At their second visit two weeks later, there was no improvement to Mikey's eczema, although his skin was softer with the use of the skin nourishing butter. His mother was able to isolate oats as a trigger; however, Mikey continued to have flare ups after she stopped eating oats.

During the two weeks, Mikey had several flare ups. One was severe enough in which his mother took him to the hospital emergency room (Figure 1). The emergency room doctors referred him to an allergist. Mikey was seen the following day however the allergist wouldn't do any testing because his skin was in such poor condition. Mikey's mother was instructed to give her son water baths with bleach until the severe eczema rash was cleared. Mikey's mother gave him two baths but was not willing to continue even though she saw some slight improvement.

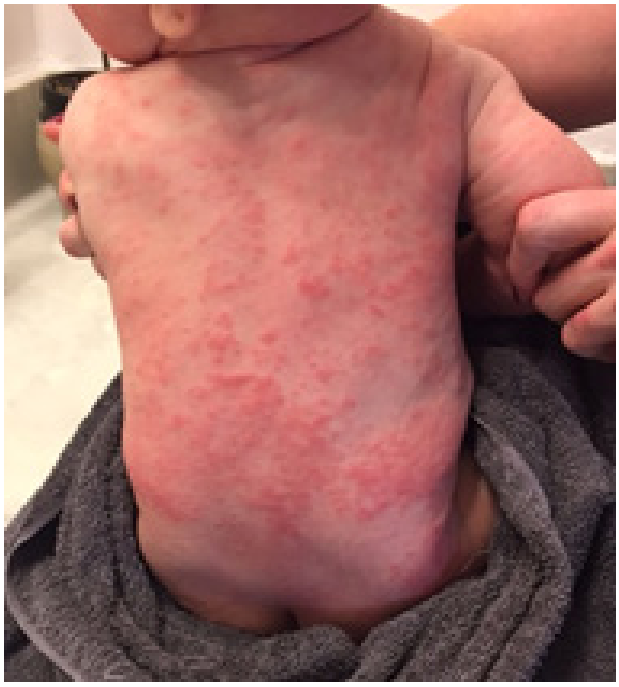

Figure 1. "Mikey's" severe rash during his emergency room visit

Treatment protocol for Mikey's mother
Due to the very restrictive diet, her milk almost dried up. She returned the diet she was on when she came in two weeks ago but continued to eliminate oats. The restricted diet did not was not having a positive impact and adding back some of the other foods did not change anything either. She continued the supplements and food diary from the first visit

Treatment protocol for Mikey
Chickweed (*Stellaria media*) bath
Add 0.5 oz (14 gm) of Chickweed and steep in 8 cups (1.9 L) of water for 20 to 30 minutes. Strain out the herbs and add the remaining liquid to the bath water to help to reduce itching and inflammation.

Eczema cream
3 oz/90 ml Olive (*Olea europaea*) oil that has been infused with Burdock (*Arctium lappa*), Chickweed, Echinacea (*Echinacea angustifolia*), and Cleavers (*Galium aparine*)[1].

1.5 oz/45 ml Coconut (*Cocos nucifera*) oil
0.5 oz/15 gm Beeswax (*Cera alba*)
1 oz/ 30 ml Helichrysum (*H. italicum*) hydrolat
2 oz/ 60 ml Aloe vera (*Aloe barbadenis*) gel

[1] One half ounce of each herb was extracted in 8 oz of olive oil over 7 days in a dehydrator at 105˚F/41˚C.

Rationale
According to Sade, Coconut oil is an excellent moisturizer and antibacterial. Helichrysum and Aloe Vera (*Aloe barbadenis*) gel, is good for wound healing (Sade, 2017). Olive oil infused with Burdock, Chickweed, Echinacea, and Cleavers. Burdock is known for skin conditions and a mast cell stabilizer (Easley and Horne, 2016). Chickweed is anti-inflammatory, emollient and reduces itching (Duke, 2002). I chose Echinacea for its antiseptic, anti-inflammatory, antibacterial, and immunostimulant properties (Duke, 2002). Cleavers is anti-inflammatory, antibacterial, and a hemostat to soothe irritated skin (Duke, 2002).

Clients' response to treatment
At their third visit five weeks later, Mikey did improve with the eczema cream and Chickweed baths but continued to have flare ups from time to time. Some spots were very resistant to improvement. Mikey had improved enough for the allergist to run tests. His tests showed he had a Staphylococcus aureus infection within the eczema spots. The allergist wanted to put Mikey on antibiotics but could not prescribe for them children under one year old, so he sent Mikey"back to his pediatrician with the biopsy results.

The pediatrician prescribed an antibiotic for Mikey however the allergist was horrified and suggested the mother not give the antibiotic to Mikey, now 5 1/2 months old. Mikey's mother wanted me to make a cream to treat the staph infection. Despite discussing the pros and cons of using essential oils on a child under a year old, his mother was still very interested - especially after the allergist's response to the antibiotic prescribed by the pediatrician. She said she would be very careful to apply the cream only on the spots, which at this point covered a great deal of Mikey's body.

Treatment Protocol
Mikey's mother really wanted an essential oil preparation to treat the staph infection, since she was not going to use the prescribed antibiotics. The allergist agreed that a different approach needed to be employed. I consulted with another alternative medicine doctor who agreed that, considering the risks versus the benefits, the cream with the addition of the essential oils was a better option to the antibiotics. Mikey's mom expressed her concern for the Co

conut oil in the eczema cream as she believed that Mikey might be having a reaction to it. I replaced the Coconut oil with Mango (*Mangifera indica*) butter.

Staph infection cream - 8 oz (227 gm)
1.5 oz/45 ml Jojoba (*Simmondsia chinensis*) wax
1.5 oz/45 ml Avocado (*Persea Americana*) oil
1 oz/30 g Mango (*Mangifera indica*) butter
0.5 oz/15 g Shea (*Vitellaria paradoxa*) butter
0.5 oz/15 g Beeswax (*Cera alba*)
1 oz/30 ml Helichrysum (*H. italicum*) hydrolat
2 oz/60 ml Aloe vera (*Aloe barbadenis*) gel

Essential oil blend (1.4% essential oil blend)
25% (24 drops) Roman Chamomile (*C. nobile*)
25% (24 drops) Geranium (*Pelargonium graveolens*)
20% (20 drops) Cardamom (*Elettaria cardamomum*)
15% (14 drops) Oregano (*Origanum vulgare*)
15% (14 drops) Thyme (*Thymus vulgaris* ct. thymol)

The total amount of the strong phenolic essential oils is 0.6% of the cream. (2 x 0.30 = 0.6%).

Rationale
According to Battaglia (1995), Jojoba can help in cases of psoriasis, eczema, and as an emollient. In addition, Avocado oil is moisturizing for the skin and has been found useful in cases of eczema (Battaglia, 1995). Mango butter is good for skin repair due to its wound healing properties (Manadawgade and Patravale, 2008). Shea butter is good emollient as it traps moisture and keeps it from evaporating, which is helpful with irritated skin. It has been found to repair damaged skin and improves wound healing (Sade, 2017; Lin *et al*., 2018). Helichrysum hydrosol is anti-inflammatory, relieves itching, is a mild analgesic, and is wound and tissue healing (Brownley and Musacchio, 2018; Purchon and Cantele, 2014). Aloe vera gel is anti-inflammatory, antibacterial, antihistaminic, emollient, immunomodulatory stimulant, and moisturizer (Duke, 2002).

In selecting essential oils, I investigated which are kind to the skin and effective against staph infections. Roman Chamomile, according to Battaglia, is one of the gentlest essential oils and an excellent choice for children given its effectiveness against red, dry skin. It is also a vulnerary and used to treat fresh cuts and wounds. (Battaglia, 1995). Geranium has been found effective against staphylococcal skin infections (Kwiatkowski, 2017). Cardamom was selected as it anti-inflammatory and antiseptic (Battaglia, 1995). I also chose it because it had been very successful in a previous blend I used for *Staphylococcus aureus* infection. According to Lu *et al.* (2018), Oregano essential oil is effective against *Staphylococcus aureus*. I selected Thyme essential oil as it has been shown to be effective against *Staphylococcus aureus* and has a lower lower risk of skin irritation (Kot *et al*., 2018; Tisserand and Young, 2014). Oregano essential oil is shown to damage the bacterial cell membrane of *Staphylococcus aureus* (Tavares *et al*., 2013). Thyme essential oil can strongly inhibit the activity of *Staphylococcus aureus* according to Zarringhalam *et al.* (2013).

Clients' response to treatment
At their fourth visit two months later, Mikey's mother was very impressed with his improvement. The eczema was almost completely cleared, except for some spots on Mikey's face (Figure 2). She was interested in trying a little stronger percentage of essential oil in the cream. Mikey was now 7 1/2 months old. We talked at length about the possible consequences of using essential oils on an infant. According to the guidelines established by Tisserand and Young (2014), the maximum essential oil concentration for an infant three to 24 months old should be 0.5%. As Mikey's condition was so severe, I did not think that concentration would be effective in dealing with the staph infection. In my experience, I believed the situation called for a stronger preparation and in previous cases I found a 4% dilution was very effective. Three of the essential oils: Roman chamomile, Geranium and Cardamom did not pose direct dermal concerns of skin sensitization. Cardamom is high in 1,8-cineole, which can cause breathing problems and depress the central nervous system in young children (Tisserand and Young, 2014). Oregano and Thyme (and their components carvacrol and thymol) are not recommended for children under two years of age. In discussing the approach to care with Mikey's mother, we agreed


Figure 2. "Mikey" two months after using the Staph infection cream

to start with a 1.4% dilution, which was effective on 95% of the body. I agreed to mix her the additional 2% blend of essential oils for her to add to a new 1.4% essential oil cream, making it a 2.8% essential oil cream. I informed "Mikey's" mother that I was not comfortable with making the 2.8% preparation for use on her son. As a compromise, I made her a new one-ounce jar containing essential oils diluted at 1.4% and I bottled the same amount of the essential oil formula in a separate amber bottle. Mikey's mother took the responsibility of adding the additional essential oils into the one-ounce jar with the 2% blend of essential oils herself therefore adjusting the ratio of essential oils to a 2.8% blend in the cream. I instructed her to use the cream only with one spot to start and to check for any negative reactions. If there were no adverse skin reactions, then it was ok for her to proceed with using the cream on the few remaining spots.

Two weeks later the mom called to say Mikey had no problems with the higher percentage of essential oils in the cream and all the spots had totally cleared up. She was very pleased with how well it worked. She said she used it on all spots twice, except for one remaining spot in which she needed to use it four times (Figure 3).

Evaluation

The goal was to clear the skin of eczema. Using only a blend of carrier oils did not provide any resolution. When herbs were added to a carrier oil, there was marked improvement but not total resolution. Shortly afterwards, it was discovered we were dealing with more than just eczema, as testing completed by Mikey's allergist found *Staphylococcus aureus* alongside the eczema. The antibiotic prescribed by Mikey's pediatrician was deemed a risky choice by his allergist. The allergist insisted that another approach should be considered. After consulting another clinician, I began with a more conservative dilution of a blend that I had previous success with against a *Staphylococcus aureus* infection. I was aware that my choice was considered beyond the safety standards of essential oil use with infants; however, under the circumstances Mikey's mother approved use of the Staph infection cream at a 1.4% dilution given the circumstances. While it was my desire to mitigate the infection with a lower dose of essential oils, it was not entirely successful until the dilution was increased to 2.8% of the

essential oils in the cream. Mikey's parents were very happy with the progress and the results. They were appreciative of the attempt to accomplish eradication of the infection with minimal invasive intervention, even though it took several attempts.

Note: Images of "Mikey" used with his mother's permission.

Editor's note: Though the formula used in this case study saw success in treatment, the IJPHA recommends that any multiple-phase product containing aqueous substances must be appropriately emulsified and preserved to both stabilize the product and reduce the risk of microbial exposure to the client if it is not to be kept in cold storage and used up in under one week.

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Essential Oil Research Interpretation Part Four: Negative Findings

Jessie Hawkins, PhD

When reading research and striving for an evidence-based approach to interpretation, one of the most frustrating things to encounter is a study with negative findings. Many professionals have been there. After exploring scientific journals for hours on end, you find what seems to be 'the perfect study.' It is relevant to the essential oil in question, it seems to be a good study, the outcome of interest is relevant, everything looks great – until you reach the results section.

The essential oil did not work. Or perhaps worse yet, it made things worse.

How can this be? You know from years of experience that this essential oil is capable of this task. Perhaps this action is described in respected textbooks. Perhaps it is even taught in popular Aromatherapy training programs.

When this happens, it can be extremely tempting to toss the study. The arguments are numerous. "It must be junk research." "Perhaps the researchers have conflicts of interest." "Maybe they were not even using legitimate essential oils." "Clearly, something is flawed." Social media and popular blogs are laden with justifications and even smear campaigns that attempt to disqualify legitimate research and highly skilled scientists who have published essential oil research with negative findings.

This is a serious mistake.

Ignoring, rejecting, or disparaging studies with negative findings is one of the greatest threats to the legitimacy of any scientific field. There is a name for this approach: 'confirmation bias.' Confirmation bias occurs when personal beliefs and preferences influence the interpretation of facts, findings, and outcomes. Confirmation bias results in errors, inaccuracies, and in the case of health-related professions, harm to clients and patients as a result. Because the body of scientific evidence grows extensively on a regular basis, professionals in any scientific related field have an obligation to monitor new findings and update practices and protocols accordingly.

Unlike personal preference, scientific evidence is neither for nor against a particular outcome; it just exists. Regardless of outcome, all scientific research provides a professional with evidence of some kind. It is up to the reader to determine the meaning of that evidence and how it may impact practice. Learning how to value and appreciate studies with negative findings is not merely a habit that will make you a better Aromatherapist; it separates the science-based professional from the pseudoscience-based professional.

An evidence-based approach literally means to base a practice on all of the available scientific evidence. As such, any approach that dismisses negative findings or cherry-picks evidence only from studies with desirable outcomes, fails to meet that minimum standard. Negative findings ensure that we critically evaluate commonly held practices and beliefs.

What are negative findings?

Outcomes in clinical research are commonly referred to as negative findings any time they do not find that the intervention was beneficial. In everyday conversation, however, negative findings can refer both to null results – the absence of results from the intervention – and studies which find that the intervention actual

ly worsened the outcome of interest. This distinction is important when interpreting a research study.

During the analysis phase of a clinical trial, researchers use statistical hypothesis testing to evaluate whether any difference between the groups in a study can be attributed to the intervention rather than to mere chance. This requires advanced statistical methods which are able to take into account variables such as age, sex, or baseline measurements. This method of testing uncovers whether or not there is a true difference between the two groups aside from variations which can be expected due to chance.

The bar for demonstrating that a legitimate difference has actually occurred as a result of the intervention is set pretty high to avoid producing false positives – known as type 1 errors. This is accomplished by calculating the probability that any difference between the two groups naturally occurred due to chance. If that probability is less than 5% (notated as $P < 0.05$), then the idea that the two groups had the same outcome is rejected and it is accepted that the intervention caused some sort of difference. This is referred to scientifically as rejecting the null hypothesis.

Because of this high bar for accepting results, many studies are unable to produce evidence of a statistically significant difference between the two groups using the methodology selected during the design phase. These outcomes are easily spotted in the study by looking at the *p*-value related to the outcome in question. In a clinical trial, it does not matter if the *p*-value is 0.99 or 0.06, anything above 0.05 results in a study with null findings. This should not be interpreted as finding that the intervention will never work, nor should it be interpreted as finding that the intervention worsened the situation.

If the *p*-value is less than 0.05, the study produced outcomes with statistical significance. This is still not a guarantee that the study found that the intervention was beneficial. The next step is to look to see what kind of difference occurred between the two groups. Did the intervention group experience outcomes which were better than the control group? Or did the intervention group experience outcomes which were worse than the control group?

Differentiating between these two potential clinical trial findings is the first step to interpretation of these difficult studies. Once the outcome has been identified, the next step is to interpret the findings within that context.

Studies without statistically significant effects

Studies which do not find statistically significant effects, or studies with null results, are often understood to provide evidence that the intervention does not work. These studies are often used by opponents of natural health as evidence against the use of herbalism or Aromatherapy. Such arguments, however, reflect a fundamental misunderstanding of the interpretation of clinical research. Studies with null results are not to be automatically interpreted as evidence against a practice as a whole.

For example, a 2006 study published in the journal *Gastroenterology Nursing* evaluates the effect of Lavender (not specified other than where purchased and the year) essential oil inhalation on pre-procedural anxiety among patients being prepped for a gastrointestinal endoscopy (Muzzarelli *et al.*, 2006). In this study, 118 patients were randomized to either a control group or a lavender Aromatherapy group. Researchers diluted lavender essential oil to 10%, then placed three drops of the oil on a cotton ball for exposure via inhalation. Anxiety was measured using a validated instrument before the exposure and again after the 5-minute exposure. After simple analysis, the study's authors did not find any difference between the control group and the lavender inhalation group.

Given the widespread acceptance of lavender essential oil as a tool to reduce anxiety, what does this mean for the Aromatherapy field?

Let's start by looking at what it does not mean. It does not mean that…

- All lavender essential oil does not work.
- Lavender essential oil cannot reduce anxiety.
- Essential oils do not reduce anxiety.
- Aromatherapy doesn't work.
- Lavender essential cannot reduce anxiety in a hospital.

So what does it mean? Here is an accurate interpretation of these findings:

> For adult patients preparing to undergo gastrointestinal endoscopy, five minutes of heavily diluted lavender essential oil inhalation did not produce an immediate reduction in anxiety scores that could be detected in this analysis.

The most important takeaway from this specific type of clinical trial is that the absence of evidence of an effect is not to be interpreted as evidence of the absence of an effect. This type of methodological design does not provide evidence that the essential oil and placebo have the same effect; it merely does not provide evidence that the essential oil was more effective. This distinction may seem subtle but dramatically changes the interpretation of these findings. If a researcher wanted to demonstrate that two effects were the same or that an essential oil does not work, a researcher would use a different methodological design to conduct equivalence or noninferiority studies.

In the above example, perhaps the researchers would have been able to detect a difference had they measured the effects after 10 minutes or 15 minutes. Perhaps they would have detected effects had they used an undiluted essential oil for inhalation or a different lavender oil product. Perhaps they would have detected effects if they used a larger quantity of essential oils. Perhaps they would have detected effects on a different population preparing for a different type of procedure. Perhaps the effect size is so small that it could not be detected with this specific study design. Or in this case, perhaps the researchers did not use analytical methods that were sensitive enough to detect differences of this size. The potential changes to the study design which could impact the outcome are practically limitless. As a result, the findings cannot be applied to these hypothetical scenarios which do not reflect the specific design of the study.

Bottom line: this study does not indicate that lavender essential oil does not reduce anxiety. Its interpretation must include the parameters that were used in the research.

Scientific studies answer research questions which are precise and specific. Broad, abstract questions cannot be answered using scientific tools because the foundation of scientific evidence requires that a hypothesis be testable and falsifiable. As a result, findings of scientific studies must be interpreted in this context. A study finding that this specific dose of this specific essential oil administered to this specific population in this specific setting in this specific manner for this specific condition means nothing more than what is outlined above. It cannot be generalized to make broad, sweeping generalizations such as those in the list of inaccurate interpretations.

Aside from interpreting the findings accurately, it is also important to recognize the value in the research methodology which does exist to identify situations in which an essential oil might not be effective or where the oils might not be the best choice for a situation. These findings are important because they tell us what does not work, which is information that is just as important as knowing what does work. Some studies may identify a simple detail, such as finding that an essential oil's actions do not apply to a specific population. Other studies could identify a more groundbreaking finding, such as an alternate explanation for positive outcomes that have long been attributed to an essential oil.

Again, this does not mean that Aromatherapy does not work or that a certain essential oil does not work; it simply means that the combination of oil selection, application, dose, population, and condition which were tested is not an ideal match. It is useful to recognize when a protocol is not optimal so that professional attention and scientific research can be focused on protocols which are effective.

Studies with harmful outcomes

Studies with a lack of identified effects, or null results, differ from studies in which researchers find that the patients who were exposed to the intervention actually had worse outcomes than patients who were in a placebo, control, or other group. In this scenario, the essential oil exposure worsened the situation for the participants. This is frustrating because the oil has shown to not only be ineffective in this particular setting, but potentially harmful.

It is important to remember that statistical analysis relies on probability, not guarantees. So, despite being extremely small, there is the possibility that these findings are a fluke and that future studies will not find the results to be reproducible. However, because this chance is so small, the safest approach is to use caution until more information is available and the potential for risk is clarified through additional scientific research. This is known as the 'precautionary principle.'

The in-between time which occurs after findings indicate that a practice may be harmful and before these findings can be replicated or investigated further in additional studies can be frustrating for the Aromatherapist who is trying to practice safely and effectively without fear mongering. Determining protocols in the absence of certainty can be difficult. In these situations, the details of the study provide important clarification and parameters within which to interpret the potential for harm. It is important to avoid the temptation to extrapolate the findings beyond the setting in which they were discovered unless additional studies provide evidence to justify such an approach.

The evidence-based approach to such findings is to continue to explore the situation further with new studies. When additional studies are available, the new findings may provide parameters that define when this harm occurs, how it occurs, or other details that help to clarify the risk. This information is useful for updating protocols, educational materials, and resources which make recommendations regarding the use of the affected essential oils.

Application

In most cases, studies with negative effects, whether null effects or harmful effects, clarify rather than completely negate existing ideas and practices, provided they are interpreted correctly. These studies provide context that reveals when a commonly held practice may need to be updated, revised, or limited. This is crucial to the growth of a field because ideas and practices that are incorrect should be addressed. If a long-held approach to Aromatherapy turns out to be harmful, professionals should be the first to update materials and help to disseminate this information to the public.

False right.
Image in publicdomainpictures.net

Conclusion

The value of negative findings is found in their ability to help us to stop making mistakes in the field. These important research studies identify weaknesses in practice, and ultimately move us forward towards a better, more accurate profession. Learning how to appreciate these studies and integrate their findings will improve individual Aromatherapy practice success rates, as well as the success of the field as a whole.

Studies which find positive results are equally important tools for moving the field forward. These studies are also frequently misinterpreted and inaccurately applied. In the next installment, we will take a closer look at studies which do produce statistically significant, positive effects, and how to apply them accurately and effectively.

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Mithridatium and Theriac: Early Pharmacological Remedies

Cinnamon bark and Rose petals © Michael Isted

Michael Isted, Herbalist, BSc (Hons.)

As an herbalist, I am obsessed with delicious prophylactic medicines and creating preventative rituals that my clients, friends and guests can integrate into their lives. I have a passion for creating engaging and contemporary plant portals that my clients can step through to interact with nature on a whole new level. My work in food and beverage allows me to create novel ways to connect people with nature. I really want my patients and clients to enjoy the plants and medicines that they are taking. I want to move away from and try not to work with the non-descript brown liquids in brown bottles that are so often prescribed by herbalists. It is our duty as herbalists, Aromatherapists, nutritionists, naturopaths and plant workers to engage people with nature as it is such a vital part of the therapeutic exchange.

I'm often researching ancient recipes and texts for inspiration. Whilst researching the roots of alchemy and plant medicines through the texts of ancient Egypt, India, Persia, China, Greece and Alexandria, I came across a semi-mythical plant preparation called the Mithridatium. Trying to trace its roots, I found myself treading in very similar alchemical footprints of others, following a path from ancient Egypt to Alexandria, Arabia and into Europe, while also being inspired by the ancient healing arts of Asia and India. I'm not sure if there is a more influential therapeutic plant preparation than the Mithridatium. It is arguably the first polypharmic drug of sorts – the precursor to numerous other drugs and even confectionery.

The semi-mythical Mithridatium, which has been called a "pharmacological ghost" (Totelin, 2004) was used as an antidote or anti-venom, and as a cure for all. Numerous stories and recipes chart its influence across millennia, people, places and cultures. Here I will shed as much light on the Mithridatium as I am able to and discuss its continued influence.

Mithridates VI, King of Pontus (135 BC), is an extremely influential figure in the roots of therapeutic plant preparations, one of the first experimental toxicologists and ethnobotanists of our time (Griffin, 1995). Mithridates was obsessed with poisons and antidotes; his father was poisoned by his mother, so he lived in fear that he himself would also be poisoned.

Inspired by the bountiful nature of the Black Sea region and the previous work of King Attalus III of Pergamon (170 BC), himself an expert in cultivating and preparing concoctions and antidotes with local toxic flora, Mithridates found his fascination with toxicology growing. He looked further afield, amassing a huge library of ethnobotanical texts and treatises from around the world. He drew inspiration from the ancient Ayurvedic texts, the long-life Hindu practitioners, the antidote recipe of Sushruta (ca. 550 BC), which boasted 85 different ingredients, and the Mahagandhahasti theriac of Charaka (300 BC), which contained 50. It is believed that Mithridates was also inspired by the alchemical writings of Democritus of Egypt who was influenced by King Menes's (3000 BC) previous work on poisons and cultivating medicinal plants (Mayor, 2010).

Mithridates teamed up with a brilliant botanist, physician and skilled pharmacologist called Krataeus. They forged a strong bond and became an early dream team of phytotherapy, crafting and studying mixtures of plants, resins and extracts to create exceptionally powerful potions as antidotes to all poisons. They observed the bees working on the nectar of poisonous

plants such as Rhododendrons (*Rhododendron* spp.) and watched ducks thriving on Hellebore (*Helleborus* spp.) and wondered how these creatures were so immune to these poisons.

Mithridates and Krataeus started to experiment with micro-doses of poisons, ingesting (or getting royal tasters to ingest) plants such as Belladonna (*Atropa belladonna*), Hemlock (*Conium maculatum*), Black Henbane (*Hyoscyamus niger*) and Aconite (*Aconitum napellus*). They even ingested vipers's flesh and beaver secretions from the testicles of the beaver, called "castoreum," as it was a prized remedy for treating fevers, boosting immunity and as an aphrodisiac (Mayor, 2010).

Mithridates and Krataeus discovered that by ingesting small amounts of poisons they would be immune to larger, more fatal doses of the same chemicals. They would then go on to compound some of the most effective herbs, resins and extracts to try to produce a prophylactic universal cure for all. The key being to combine beneficial plant secondary metabolites with anti-toxins and small amounts of poisons. Mithridates and Krataeus's cure for all was named the "Mithridatium," a combination of over 70 ingredients, including herbs and resins sourced locally and from around the world.

Although it is impossible to find the original Mithridatium recipe, research suggests that it included some of the plants from the traditional Egyptian kyphi incense mixtures including Cassia (*Cinnamomum cassia*), Cinnamon (*Cinnamomum zeylanicum*), Myrrh (*Commiphora myrrha*) and oil of balanos (from the Balanites aegyptiaca tree, native to North Africa) combined with ingredients such as honey, Castor (*Ricinus communis*), musk, Frankincense (*Boswellia* spp.), Rue (*Ruta graveolens*), tannin, Garlic (*Allium sativum*), red earth of Lemnos (*Lemnia sphragis*), fermented Grape (*Vitis vinefera*), charcoal, curdled milk, Centaury (*Centaurium erythraea*), Birthwort (*Aristolochia clematitis*), Ginger (*Zingiber officinale*), Iris (*Iris* x *germanica*), Orris (*Iris* x *germanica*; *Iris* x *pallida*) root, Eupatorium (*Eupatorium cannabinum*), Rhubarb (*Rheum rhabarbarum*), Hypericum (*Hypericum perforatum*), Saffron (*Crocus sativus*), Walnuts (*Juglans regia* or *Juglans* spp.), Figs (*Ficus carica*), Parsley (*Petroselinum crispum*), Acacia (*Acacia* spp.), Carrot (*Daucus carota*), Cardamom (*Elettaria cardamomum*), Anise (*Pimpinel la anisum*), Opium (*Papaver somniferum*), and other ingredients from North and East Africa, India, Arabia Asia, Mediterranean and Black Sea (Mayor, 2010; Totelin, 2004; Watson, 1966).

The Mithridatium was developed further over the years by Andromachos (50 AD), physician to Emperor Nero. He created a version named the "Galene" or "*Galeni Theriaca*," *galene* meaning "tranquillity" as it appears that Andromachos significantly increased the amount of opium in the preparation. The Galene was used for a wider variety of ailments including respiratory problems such as asthma, for circulatory disorders such as dropsy and as a general anti-inflammatory and health tonic (Karaberopoulus *et al.*, 2012).

Research suggests that the Galene contained around 55 herbs and up to 70 other ingredients, using a base of honey, wine, vipers' flesh, lots of Opium, Cinnamon, Opobalsam (*Balsamodendron opobalsamum*) or Balm of Gilead, Hedychium (*Hedychium* spp.), Long Pepper (*Piper longum*), Black Pepper (*Piper nigrum*), Myrrh, Turpentine (*Pistacia terebinthus*) resin, Lemnian earth (*Lemnia sphragis*), roasted copper (*Cuprum*), bitumen (asphalt) and excretions of beaver (Griffin, 2004; Mayor, 2010; Watson, 1966). It took 40 hours to prepare and was matured for the optimum potency for 12 years before administering orally directly, taken with water or wine, or applied topically (Griffin, 2004).

As with the Mithridatium the influences of Egypt and India can be seen in the ingredients used to formulate the Galene. A multi-drug prescription with bioavailability-enhancing phytochemicals, it shares similarities to Ayurvedic preparations such as *Trikatu* – a mixture of Long Pepper, Black Pepper and Ginger.

Contrary to popular belief, the term "Galene" was not associated with famous Greek physician Galen of Pergamum (131–200 AD); however, Galen did further develop the Mithridatium, creating Theriac 64, a drug containing 64 different herb preparations, based on the Mithridatium. The term "theriac" is said to have come from the Greek word *theria* / *theriakos* meaning "wild beasts," as it referred to an ointment or compound used as an antidote for venomous bites (Griffin, 2004). Galen would advance the Theriac, based on his humoural theory (developed from Hippocrates and sharing similarities with the ancient systems of

Chinese and Ayurvedic medicine). He classified traits and personalities into four simple categories: the phlegmatic type, the melancholic type, the choleric type and the sanguine type. Galen believed that any imbalances in these humours would lead to disease and the way to address the imbalances was through the administration of herbal extracts in the form of a theriac (Karaberopoulus *et al.*, 2012).

Galen also improved the taste of the Mithridatium by including more honey and wine, forming the precursor to the "*electuarium*" or "*electuary*." An electuary was a Greek medicine traditionally made with honey in combination with herbs and extracts to create a delivery method of dispensing therapeutic quantities of plant secondary metabolites for consumption – some of the first herbal confectionary. The term "electuary" comes from the Greek word *ekleikton*, meaning "to be licked." Electuariums or electuarys used to form the largest group of therapeutic pharmaceutical antidotes (Wexler, 2014).

Versions of Galen's Theriac 64 appeared in Islamic toxicology manuscripts. The Arabic theriac (*tiryaq-i-faruq, mithruditus*) and Persian (*daryaq*) recipes were inspired by Mithridates's concept of combining poisons with antidotes (Mayor, 2010; Wexler, 2014). The great Arabian physicians such as Avicenna (980 AD) started to introduce sugar cane and plant distillates into similar preparations. With the introduction of sugar, we begin to see the origins of preparations such as syrups, conserves, sherbets and confectionery (Mann, 1988).

It is worth noting it would have been very expensive to create these preparations with herbs, spices and resins coming from India, Arabia and East Africa. Only the wealthy people of the time would have had access to these medicines. Spices and exotic plant resins were attractive to wealthy clientele and as the attraction to such expensive and exclusive "drugs" grew, more exotic ingredients were added to impress clients. Mithridatium became fashionable and the drug of choice. This created problems with ingredients becoming more difficult to source. Adulteration became an issue and many cheaper variations of the drug became commonplace. The popularity of the Mithridatium and its contemporaries grew and waned under different emperors (Mayor, 2010; Wexler, 2014).

Uses of the theriac were recorded in the *Leechbook of Bald*, in which King Alfred the Great was sent a variant of the Theriac 64 by Abel the Patriarch of Jerusalem. Its use was also recorded via Arabian influences in the Greek and Roman medical writings at the University at Salerno (Griffin, 2004; Watson, 1966). Later, in the 12th century, a commercialised 55-component version of the theriac was manufactured in Venice and exported around the world. In the UK this became known as "Venetian Treacle" (Griffin, 2004; Watson, 1966).

The *London Pharmacopoeia* in December 1618 detailed formulations for a Theriac and a Mithridatium. During the Great Plague of London, it was recommended that people ingest variations of the Mithridatium and Galene. It was not until the efficacy of these preparations was really brought into question in 1746 that the Mithridatium and its variants disappeared from the public domain, although versions of the Galene still appeared across Europe late in the 1800s (Griffin, 2004).

So, what about the efficacy of these preparations? How could they have been a cure for so many ailments? How were these drugs popular for so long? If you look at the recorded recipes, they contain many health-giving, anti-inflammatory, anti-bacterial, peripheral circulatory stimulating, bioavailability-enhancing plants, resins and extracts, many of which are still used regularly today. What cannot be ignored is the high content of opium. Anything with such a high content of opioids would feel not only effective, but also very addictive.

One cannot underestimate the powerful nature of consuming complex prophylactic mixtures of herbs through diet or by creating and ingesting herbal remedies or potions. The commercialisation of the Mithridatium and Theriac 64, in the form of the Venetian Treacle, I'm certain was the beginning of the end for these preparations. As the popularity and influence of the Mithridatum and Theriac grew, they would have become adulterated with simplified ingredients and lost their potency and their identity.

The golden question often asked about herbs is, what do they do? However, it is not what the plants do as such, but how our bodies or the complex biological processes of the body interact with the raft of plant

secondary metabolites in the plants or plant preparations. This exchange is a complex dynamic interaction that will change from person to person, plant to plant, and preparation to preparation. Through experience, scientific research and historical data, there is a reasonable amount of information on what interactions and biological effects may take place. This is by no means conclusive. Almost all research papers on the efficacy of herbs conclude with "this study suggests that such and such plant / extract may be of help for such and such disorders, but more clinical studies required." As much as I admire and work with scientific research, nature just does not always conform to the very limited, narrow spectrum and linear logic of science; it's much more complex than this.

These ancient preparations and their complex natures are deeply inspiring, although it is impossible to reconstruct the original recipe of the Mithridatium. (I would not be as agreeable to the idea of incorporating beaver secretions either.) From existing documentation, we cannot doubt their influence as they have certainly directly and indirectly influenced a variety of preparations and drugs. I like to work with complex mixtures of plant constituents to craft delicious (where possible) prophylactic medicines. I believe it is key to wellness and so a great way to interact and connect with the nature that surrounds you. Like Mithridates and Krataeus, I look to the nature that surrounds me for inspiration. I also use combinations of herbs and spices from all around the world: Southern Indian spices, North and East African resins, American herbs, Chinese mushrooms and herbs closer to home to create these medicines and potions.

Below is a version of the Galene, designed to use prophylactically as a delicious drinking medicine, but particularly useful for those with stagnant or sluggish digestion.

Galene 'Tranquillity' 1.0

Long Pepper	*Piper longum*
Californian Poppy	*Eschscholzia californica*
Cinnamon	*Cinnamomum zeylanicum*
Peru Balsam	*Myroxylon balsamum*
Myrrh	*Commiphora myrrha*
Black pepper	*Piper nigrum*
White pepper	*Piper nigrum*
Ginger	*Zingiber officinale*
Rose	*Rosa* spp.
Lemon	*Citrus limon*
Copper	*Cuprum*
Medicinal red clay	
Sugar	
Honey	
Distilled water	

Lemnian earth and copper compound (all dried herbs)

0.2oz	Long Pepper
0.2oz	Red Clay
0.4oz	Californian Poppy
0.4oz	Cinnamon (*C. zeylanicum*) bark
0.2oz	Myrrh
0.3oz	Black peppercorns
0.2oz	White peppercorns
0.4oz	Ginger powder
10oz	Raw honey
4oz	Distilled water (hot)

Method

Add all to a blender, blend for 30 seconds, decant into copper flask and shake. Leave flask to infuse for several weeks; if you are impatient, you can use after two weeks but try to leave for longer – at least one month, preferably six months. Warm copper flask and strain off the liquid through muslin or super bag, making sure to squeeze out as much of the liquid as possible (you may wish to use a tincture press), bottle and seal.

Rose sherbet

2	Un-waxed lemons
0.5oz.	Rose water
Handful	Fresh or dried Rose (*Rosa* spp.) petals
3oz.	Cane sugar

Peel the lemons, then put the zests in a container with the Rose petals, rose water and sugar. Muddle/press the zest, petals, flowers and sugar together for a minute or so, then juice the leftover lemons and stir the juice into the mixture. Seal and leave to infuse overnight, or for at least six hours. Stir, strain and bottle. This will keep refrigerated for at least one month.

Copper-infused water
© Michael Isted

Copper-infused water*

Simply fill a copper flask with spring water and leave for at least eight hours. If you do not have access to a copper flask you can infuse a jug of water with a copper coil.

*Note that drinking from copper regularly can have adverse effects on health and can be toxic. If any doubts please use a glass mason jar for the compound and spring water for the serve.

Recipe for Serve

1.75oz	Rose sherbet
0.2oz	Lemnian earth & copper compound
2.5oz	Copper-infused water*

Method

In the bottom of a copper cup add all the ingredients, ¾ fill the cup with crushed ice and churn the ingredients through the ice. Top with more crushed ice, stir and serve with a copper straw, freshly picked flowers and a dust of fine red clay.

Rose sherbet © Michael Isted

Conclusion

Although we now live in a world where danger from venoms and poisons has declined (in most places), we still face toxicity and the risk of disease from elsewhere – our food, environmental toxins, media-based mind pollution and increased electromagnetic radiation are just a few examples. These original pharmacological remedies such as the Mithridatium and Theriac 64 were packed with potent prophylactic, anti-inflammatory, antiseptic and anti-bacterial compounds, combined with tonic and stimulating herbs and tempered with high doses of morphine from Opium (*Papaver somniferum*). Classic diuretic substances such as Squill (*Drimia maritima*) were then added to help facilitate elimination. Although extremely old, these preparations were still created with reason, thought and great skill. The Mithridatium and Theriac are arguably two of the greatest medicines devised in the ancient world; although not used today, they should still be admired, revered and looked to for inspiration. The ingestion of complex phytochemicals and plant secondary metabolites and our relationship with nature is key to enhancing our ability to deal with toxicity and disease – that much has not changed. ☙

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Putting Consciousness Back Into Conservation of Aromatic Medicinal Plants

Illegal *Aniba roseodora* stockpile at the port of Rantabe, adjacent to the Makira Forest Protected Area © Eric Patel

Kelly Ablard, PhD, MSc, EOT, RA

Earth provides enough to satisfy every man's needs but not every man's greed. -Mahatma Gandhi

When Gandhi said this over five decades ago, he was highlighting an imbalance between need and greed, and as a visionary, reminding those accountable for future generations to be mindful of it. Although this imbalance is nothing new, it has taken a more serious and impending turn regardless of his wise words. This is evident in our modern-day world where concepts and words like "conservation," "sustainability," "recycle," and "biodiversity" are so common and pervasive that they may not be consciously understood.

A conscious understanding encompasses all these important concepts under the umbrella of conservation. And part of cultivating "conservation consciousness" is extending our healing of others to the healing of those plants in imminent danger of extinction because of the imbalance between man's need and greed. Unfortunately, this imbalance has become a global problem for nearly 13,000 threatened land-plant species (IUCN, 2020), including aromatic medicinal plants. The scope of this article will focus on roughly 8% of 400 threatened and near-threatened essential plant species commonly traded on the world market today. Also, we will explore how to help create a more harmonized and healthy relationship with these plants now as well as for future generations.

The sixth extinction and biodiversity

Scientists revealed in 2010 that Earth is undergoing the sixth extinction defined as species are being lost at a rapid rate that far outruns the origin of new species. Unlike the five preceding mass extinctions of geological history, this extinction is one in which the human race is nearly entirely responsible. It is currently estimated that there are at the very least two million unique species on Earth and experts calculate that1,000,000 are facing extinction (IPES, 2019). We are in a biodiversity crisis.

The year the sixth extinction was revealed, the United Nations named 2010 to be the International Year of Biodiversity (Mace, 2010). Biodiversity is the diversity of ecosystems, species, and genetics of species (Krishnamurthy, 2003). An ecosystem is a biological community of interacting organisms and their physical environment, a species is the largest group of organisms in which two individuals can reproduce fertile offspring, and genetic diversity refers to both the vast numbers of unique species as well as the diversity within a species (Frankham *et al*., 2002; Krebs, 2008). The greater the genetic diversity within a species, the greater that species' chance of long-term survival. So, why is it important that we conserve biodiversity?

One reason is that we do not have the right to drive other species to extinction. Without biodiversity, oxygen, natural pest control, and pollination of crops will be lost. Resources such as food, clothing, housing, and medicine would be depleted (Frankham *et al*., 2002). When we lose biodiversity, we lose more than just precious species — we lose preservation of culture.

This was the case for the now extinct aromatic medicinal plant Silphium (*Ferula* sp.). Considered a gift from Apollo, it strengthened the Egyptian economy, symbolized the connection of heart, was depicted on Cyrene currency (Figure 1), and medicinally contained numerous therapeutic properties (Hippo-

crates, 400 B.C.E; Pliny, 1669; Favorito and Baty,1995; Tataman, 2000). Unfortunately, overexploitation drove it to extinction — a human-driven factor which today impacts many plant species. Other factors which plants are impacted by include urban sprawl, agricultural invasion, road construction, mining, illegal trade and logging, pollution, invasive species and unsustainable management.

Figure 1. Silphium depicted on an ancient Cyrenian silver coin.

Sustainability and conservation

The concept of sustainability is associated with the Seven Generation Stewardship, which is a Great Law of the Iroquois Nation. This Great Law urges the current generation to live and work for the benefit of the seventh generation; in other words, make decisions and live a life that will benefit children seven generations into the future. This way of thinking and living helps to protect and preserve species because it demonstrates "conservation consciousness."

One organization that can facilitate our protection of species is the International Union for Conservation of Nature (IUCN). The IUCN implements the most accepted approach for evaluating and categorizing species on a global and regional level that are facing a higher risk of extinction. One reason they are respected worldwide is that their evaluations encompass ecosystems, species, and genetic diversity. In other words, they focus on biodiversity (IUCN, 2020). Many countries implement IUCN protocol to assess the conservation status of native plant species as represented for example in the Global Forest Resource Assessment (GFRA) (2005).

Threatened species are categorized by the IUCN as Critically Endangered, Endangered, or Vulnerable. Although species are categorized within individual countries, if population numbers have declined drastically in one country, then the status is applied globally. For example, more than 80% of the wild population of Spikenard (*Nardostachys jatamansi*; *N. grandiflora*) has declined in the Himalayan region of India. Because factors impacting its survival are going on in other countries, the status in India represents the status of Spikenard globally, which is Critically Endangered (Ved *et al*., 2015).

When a species is categorized as threatened, one criterion or several criteria are used to assign it to the correct category. For example, Critically Endangered criterion include, but are not limited to: the actual or projected reduction in population size has decreased by ≥80% over the last 10 years or three generations, and/or, there are less than 250 mature adults, and the numbers are declining, and/or there is a ≥50% probability of extinction within 10 years or three generations. There are at least five essential oil-bearing plant species listed as Critically Endangered globally: Spikenard, Guggul (*Commophora wightii*), Costus (*Saussurea costus*), and Agarwood (*Aquilaria rostrata*; *A. malaccensis*) (Table 1).

Endangered criterion include, but are not limited to: the actual or projected reduction in population size has decreased by ≥50% over the last 10 years or three generations, and/or there are less than 2500 mature adults and the numbers are declining, and/or there is a ≥20% probability of extinction within 20 years or five generations. There are at least eight essential oil-bearing plant species listed as Endangered globally: Angelica (*Angelica glauca*), Rosewood (*Aniba rosaeodora*) (Figure 2), Atlas Cedarwood (*Cedrus atlantica*), Guaiacwood (*Gonopterodendrdon sarmientoi*) Araucaria (*Nelocallitropsis pancheri*), Sandalwood (*Santalum freycinetianum*), Taiwan Cypress (*Chamaecyparis formosensis*), and Vanilla (*Vanilla planifolia*) (Table 1).

Figure 2. Rosewood (*A. rosaeodora*) wood pieces: Peru © Kelly Ablard

The essential oil of Dorado Azul (*Hyptis suaveolens*), native to Ecuador, has become high in demand. Although Dorado Azul has not yet received a status by the IUCN, *H. argutifolia*, *H. diversifolia*, *H. florida*, and *H. pseudoglauc*a (all native to Ecuador) have recently

been classified as either Critically Endangered or Endangered (IUCN, 2020). Until H. suaveolens has been assessed or there is evidence in place that its essential oil is sourced from sustainably managed plants, it is recommended to avoid purchasing it or to ensure ethical sourcing.

Vulnerable criterion include, but are not limited to: the actual or projected reduction in population size has decreased by ≥30% over the last 10 years or three generations, and/or there are less than 10,000 mature adults with those numbers are declining, and/or there is a ≥10% probability of extinction within 100 years. There are at least ten threatened essential oil-bearing plant species listed as Vulnerable globally: Sandalwood (*S. album*, *S. haleakalae* var. *haleakalae*, *S. paniculatum*), Camphor (Borneo) (*Dryobalanops sumatrensis*), Spanish Cedar (*Cedrela odorata*), Brazilian Sassafras (*Ocotea pretiosa*), Opopanax (*Commiphora guidotti*), and Siam Wood (*Chamaecyparis hodginsii*), Taiwan bian mai (*Chamaecyparis* var. *formosana*), and Phoebe (*Oreodaphne porosa*) (Table 1).

Common name	Latin name	Location	Conservation status; CITES*	Year Assessed
Agarwood	*Aquilaria rostrata*; *A. malaccensis*	Global	*Critically Endangered	2018
Costus	*Saussurea costus*	Global	*Critically Endangered	2014
Guggul (Common myrrh)	*Commiphora wightii*	Global	Critically Endangered	2014
Spikenard	*Nardostachys jatamansi* (syn: *N. grandiflora*; *N. chinensis*)	Global	*Critically Endangered	2014
Angelica (Himalayan)	*Angelica glauca*	Global	Endangered	2014
Araucaria	*Neocallitropsis pancheri*	Global	Endangered	2009
Atlas cedarwood	*Cedrus atlantica*	Global	Endangered	2013
Guaiacwood	*Gonopterodendron sarmientoi*	Global	*Endangered	2017
Rosewood	*Aniba rosaeodora*	Global	*Endangered	1998
Sandalwood	*Santalum freycinetianum*	Global	Endangered	2016
Taiwan cypress	*Chamaecyparis formosensis*	Global	Endangered	2010
Vanilla	*Vanilla planifolia*	Global	*Endangered	2017
Brazilian Sassafras	*Ocotea pretiosa*	Global	Vulnerable	1998
Camphor (Borneo)	*Dryobalanops sumatrensis*	Global	Vulnerable	2017
Cedrela (Spanish cedar)	*Cedrela odorata*	Global	Vulnerable	2017
Opopanax	*Commiphora guidotti*	Global	Vulnerable	2018
Phoebe	*Oreodaphne porosa*	Global	Vulnerable	1998
Sandalwood (East Indian)	*Santalum album*	Global	Vulnerable	2018
Sandalwood (Haleakala)	*Santalum haleakalae* var. *haleakalae*	Global	Vulnerable	1998
Sandalwood (Mountain)	*Santalum paniculatum*	Global	Vulnerable	2017
Siam Wood	*Chamaecyparis hodginsii*	Global	Vulnerable	2010
Taiwan bian mai	*Chamaecyparis* var. *formosana*	Global	Vulnerable	2010
Elemi (Piling-liitan)	*Canarium luzonicum*	Global	Near Threatened	2019
Frankincense	*Boswellia sacra*	Global	Near Threatened	1998
Hemlock spruce	*Tsuga canadensis*	Global	Near Threatened	2011
Himalayan fir needle	*Abies spectabilis*	Global	Near Threatened	2010
Hinoki cypress	*Chamaecyparis obtusa*; *C. obtusa var. obtusa*	Global	Near Threatened	2011; 2010
Muhuhu	*Brachylaena huillensis*	Global	Near Threatened	1998
Port Orford cedarwood	*Chamaecyparis lawsoniana*	Global	Near Threatened	2011
Sandalwood (New Caledonian)	*Santalum austrocaledonicum*	Global	Near Threatened	2020
Tonka bean (Cumaru)	*Dipteryx odorata*	Global	Data Deficient - population decreasing	2017

Table 1. The Airmid Institute Biannual List of Threatened and Near-Threatened Essential Oil-Bearing Plant Species (July 1 – Dec 31, 2020). Common name, Latin name, Global or Regional location, Assessment year, and *CITES protected. Data were gathered from IUCN and CITES unless otherwise noted.

Common name	Latin name	Location	Conservation status; CITES*	Year Assessed
Frankincense	*Boswellia serrata*	Sri Lanka	Critically Endangered	2012
Frankincense	*Boswellia serrata*	India	Critically Endangered	2015
Rose root	*Rhodiola rosea*	Bulgaria	Critically Endangered	2011
Rose root	*Rhodiola rosea*	Czech Republic	Critically Endangered	2012
Spruce (Norway)	*Picea abies*	Albania	Crtically Endangered	2013
Calamus	*Acorus calamus*	India (Kerala)	Endangered	2000
Calamus	*Acorus calmus*	Norway	Near Threatened	2006
Calamus	*Acorus calmus*	Hungary	Near Threatened	2007
Cistus	*Cistus ladanifer*	France (continental)	Near Threatened	2012
Elecampane	*Inula helenium*	United Kingdom	Near Threatened	2014
Juniper berry	*Juniperus communis*	United Kingdom	Near Threatened	2014
Valerian	*Valeriana officinalis*	Norway	Near Threatened	2013
Valerian	*Valeriana officinalis*	United Kingdom	Near Threatened	2014
Calamus	*Acorus calamus*	India (Tamil Nadu)	Vulnerable	2000
Calamus	*Acorus calmus*	Switzerland	Vulnerable	2002
Juniper berry	*Juniperus communis*	Albania	Vulnerable	2013
Rose root	*Rhodiola rosea*	Mongolia	Vulnerable	2011
Spanish broom	*Spartium junceum*	Switzerland	Vulnerable	2002
Valerian	*Valeriana officinalis*	Albania	Vulnerable	2013
Benzoin	*Styrax benzoin*	Singapore	Vulnerable	1994
White Sage	*Salvia apiana*	USA	At-risk (UpS)	2019

Table 1 (continued). Common name, Latin name, country where classified by IUCN and/or GFRA, and conservation status of threatened and near-threatened essential and carrier oil-bearing plants. *indicates CITES protected.

Many threatened species are also protected by the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES). Their aim is to ensure that international trade in specimens of wild animals and plants does not threaten their survival. CITES plant specimens listed under Appendix II (www.CITES.org, n.d.) include essential oils/extracts and require a CITES permit for exportation. Exportation of CITES-protected plants, their parts, and extracted material should be traceable and backed by a CITES certificate available to the importer, which offers some assurance that growers and distillers are practicing sustainable management. There are approximately 30,000 CITES-protected plants which are under the protection of the US Lacey Act. Young Living, in 2017, was in violation of the Lacey Act and fined $760,000 USD for the illegal trafficking of Rosewood (Endangered) oil and Spikenard (Critically Endangered) oil. Essential oils and extracts which require a CITES permit for exportation include Rosewood (Figure 3), Agarwood, Costus, Guaiacwood, Vanilla, and Spikenard.

Figure 3. Evidence of equipment used for illegal logging of Rosewood: Peru © Kelly Ablard

Thirty-two percent of the 22 threatened plants are facing extinction primarily because of overexploitation for their essential oil. They are Spikenard, Sandalwood, Guggul, Agarwood, Rosewood, Atlas cedarwood, and Brazilian Sassafras. Essential oils found to be in great demand globally are Atlas Cedarwood, Angelica, Taiwan Cypress, Rosewood, Spikenard, and Sandalwood.

Were it not for ongoing conservation initiatives, species categorized as Near Threatened would be at a much higher risk of extinction. There are at least eight essential oil-bearing species listed as Near Threatened: Spruce Hemlock (*Tsuga canadensis*), Fir needle (Himalayan) (*Abies spectabilis*), Port Orford Cedarwood (Rose of Cedar) (*Chamaecyparis lawsoniana*), Hinoki cypress (*C. obtusa*), Frankincense (*Boswellia sacra*), Muhuhu (*Brachylaena huillensis*), Elemi (*Canarium luzonicum*), and New Caledonian Sandalwood (*Santalum austrocaledonicum*) (Table 1).

How to become a threatened-plant protector

Join forces

The first step to protecting plants is keeping up to date on which ones are threatened and/or trade-protected. This information is made available by the IUCN: www.iucnredlist.org; CITES: www.cites.org; TRAFFIC: http://www.traffic.org/medicinal-plants/; and the Airmid Institute: https://www.kellyablard.com/subscribe-to-the-biannual_list/ This information provides the required foundation for your work as a plant-protector.

Not using oils from unsustainably managed threatened and near-threatened plants

Do not use oils or extracts sourced from unsustainably managed threatened or near-threatened plants. Instead work with oils from sustainably-managed cultivated plants categorized by the IUCN as Least Concern (i.e. low risk of extinction). They include Roman Chamomile (*Chamaemelum nobile*), Cypress (*Cupressus sempervirens*), Grapeseed (*Vitis vinifera*), Virginian Cedarwood (*Juniperus virginiana*), Texas Cedarwood (*J. ashei*), Yarrow (*Achillea millefolium*), Hazelnut (*Corylus avellana*), Lavender (*Lavandula angustifolia*), Rosemary (*Salvia rosmarinus*), Calamus (*Acorus calamus*), Himalayan Cedarwood (*Cedrus deodara*), and Copaiba (*Copaifera langsdorfii*).

Use analogs not sourced from threatened, near-threated and/or trade-protected plants

Although an oil can never replace the unique chemistry of another oil, explore safe analogs that share major key chemical constituents, fragrance profiles, therapeutic benefits, and which are not sourced from threatened, near-threatened and/or trade-protected plants. Here are some suggested analogs to use for Atlas Cedarwood and Rosewood essential oil.

Atlas cedarwood

Atlas cedarwood's primary constituents are β-himachalene, and α-himachalene, (E)- α-atlantone, and γ-himachalene (Aberchane and Fechtal, 2004) (Table 2), it has a dry and woody fragrance profile, and numerous therapeutic properties. Although the essential oil of Himalayan Cedarwood is chemically more like Atlas Cedarwood than to Virginian or to Texas Cedarwood, Virginian cedarwood essential oil is reported to have numerous therapeutic properties that mirror those of Atlas cedarwood essential oil (Table 3). Texas Cedarwood oil shares many of these properties as well but to a lesser amount. Further, Virginian and Atlas Cedarwood essential oils are uniquely similar (Mojay, 1997; Bowles, 2003; von Marksfeld-Fuhrherr, 2004; Gray, 2006; Lis-Balchin, 2006; Farrer-Halls, 2009; Wanner *et al*., 2010; Guba, 2012; Price *et al*., 2012; Martins *et al*., 2015; Worwood, 2016; Orchard and van Vuuren, 2017).

Virginian Cedarwood has a similar fragrance profile (dry and woody) and would likely support healing in a similar way to Atlas Cedarwood essential oils. It would also positively impact the preservation and protection of Atlas Cedar and help to control the Virginian Cedar population numbers. Virginian and Texas Cedar are so abundant, they are considered pest species, which is one reason the IUCN has categorized them as 'Least Concern' (Tumen et al., 2013). An additional benefit is that also like Atlas Cedarwood essential oil, Virginian and Texan Cedarwood essential oils have insecticide properties and no known contraindications or hazards (Gawde, 2009; Tisserand and Young, 2014).

From a chemistry rather than a therapeutic standpoint, Himalayan Cedarwood essential oil could be a promising alternative to Atlas Cedarwood essential oil (Table 2). These essential oils are significantly and similarly unique in their chemical composition com-

Chemical constituent	Atlas (Wood)	Himalayan (Wood)	Port Orford (Wood)	Chinese (Wood)	Texas (Wood)	Virginian (Wood)	Western Red (Needles)	Eastern White (Needles/ Branches)
β-himachalene	30.8-40.4	8.0-13.0 [1](43.9)			1.1-1.4	2.1		
α-himachalene	10.3-16.4	20.0-30.0 [1](16.9)						
(E)-α-atlantone	5.2-13.4	5.0-7.0						
γ-himachalene	6.7-9.7	[1](11.3)						
deodarone	1.2-6.7	4.0-6.0						
Iso-α-cedrene				32				
thujopsene				21.6	25.0-46.8	21.3-23.4		
cedrenol				6.1				
cuparene				4.9				
longifolene				4.2				
α-cedrene		12.0-16.0		2.1	22.6-30.7	21.1-38.0		
α-terpineol			14.3					
δ-cadinene	0.5-2.6		8.2					
α-pinene			6.5				0.5-2.9	
camphor			5.9					2.2-2.5
α-fenchol			5.5					
cedrol					12.2-19.1	12.3-22.2		
β-cedrene					5.5	8.2-9.2		
α-cadinol			5.3					
(E)-γ-atlantone	1.2-3.9							
himachalol	1.7-3.7							
isocedranol	1.2-3.1							
(Z)-α-atlantone	1.0-2.8	2.0-3.0						
1-epi-cubenol	1.1-2.5							
(Z)-trans-α-bergamotol	0-2.0							
fenchone			4.7					12.2-12.8
α-muurolene			4.2					
T-cadinol			3.4					
β-terpineol			3.3					
(+)-limonene			2.7					
T-muurolol			2.7					
citronellol			2.3					
α-selinene					0-1.5	3		
widdrol					1.1-1.6	1.9-2.3		
α-thujone							63.5-84.0	48.7-51.5
β-thujone							4.9-15.2	7.9-9.9
sabinene							1.1-8.8	1.8-4.4
bornyl acetate								2.3-3.2
terpinen-4-ol							1.4-4.6	1.5-2.5
β-myrcene							0.5-3.3	1.8-2.1
geranyl acetate							0.1-3.9	
rimuene							0.1-2.6	
γ-terpinene							0.3-2.0	

Table 2. Percentages of key chemical constituents of each cedarwood/leaf essential oil. Although all chemical constituents play an important role in the activity of the oil, only those ≥2% were included with exceptions made to highlight further similarities between chemical profiles. The essential oil source or plant part is denoted within ( ) under the common name of each cedar. Constituents highlighted in green are cedars in family Pinaceae, and those in orange are in family Cupressaceae (Gupta *et al.*, 2011).

	Cedarwood		
Therapeutic properties	**Atlas**	**Texas**	**Virginian**
Antiacne	X		X
Antibacterial	X	X	X
Anticatarrhal	X		X
Antifungal	X	X	X
Antihyperalgesic	X		
Anti-inflammatory	X		
Antiseborrheic	X		X
Antiseptic	X		X
Astringent	X	X	X
Depurative	X		X
Diuretic	X		X
Emmenagogue		X	X
Expectorant	X	X	X
Lipolytic	X		X
Decongestant	X		X
Pectoral	X		X
Restorative	X		
Sedative	X		X
Tonic	X		X
Additional properties			
Insecticide	X	X	X

Table 3. Most common therapeutic properties for Atlas Cedarwood, Virginian Cedarwood and Texas Cedarwood essential oils. 'X' indicates properties are present.

pared to cedars in the family Cupressaceae. This is predominantly because of the himachalenes and atlantones which likely are linked to insecticide properties. (Chaudhar *et al*., 2011). However, more research is needed on the therapeutic and non-therapeutic properties of Himalayan cedarwood. Contraindications and hazards are none (Atlas Cedarwood) and mildly toxic (Himalayan Cedarwood) (Tisserand and Young, 2014). And finally, Himalayan Cedar is classified as 'Least Concern.'

Rosewood

Analog essential oils to Rosewood oil should be high in the linalool enantiomer (3R)-(-)-linalool (licareol), which is the prevalent form of linalool in rosewood ranging between 78.0 – 90.3% (Lupe *et al*., 2008; Chantraine *et al*., 2009; Maia *et al*., 2016). An ideal alternative would also have a floral, woody, and spicy fragrance profile and the following therapeutic properties: sedative, analgesic, antibacterial, antispasmodic, anticonvulsant, antidepressant, antimicrobial, antiseptic, aphrodisiac, and tonic (Elisabetsky *et al*., 1995; Peana *et al*., 2002; Souza *et al*., 2011; Sampaio *et al*., 2012; Raintree, 2018).

An ideal candidate is Ho leaf (ct. linalool) (*Cinnamomum camphora* NEED) essential oil. It contains 66.7 – 90.6% (3R)-(-)-linalool, has a similar fragrance profile, and the following therapeutic properties: antispasmodic, anticonvulsant, anti-inflammatory, sedative, and antibacterial. It has not yet been assessed by the IUCN as there is no apparent threat of extinction (Letizia *et al*., 2003; Aprotosoaie *et al*., 2014; Zhu *et al.* as cited in Tisserand and Young, 2014; ITHMA, 2017). According to Tisserand and Young (2014), this may contain methyleugenol, and no contraindications are known. Although this oil can contain up to 1% of potentially carcinogenic constituents, it also contains as much as 90% linalool which is anticarcinogenic.

If you use oils sourced from threatened and/or trade-protected plants

Investigate growers of these plants. Growers who practice sustainable management should have an economically viable farm, maximize reliance on renewable sources, recycle organic material, understand the biology of the plant species, implement crop diversification, consider environmental health, practice sustainable harvesting, manage soil, replant, incorporate multiple fields of science, and engage in community outreach and education. When obtaining plant material directly from a cultivated source, request a certificate or other assurance that it has been sustainably managed and/or exported legally.

Question distillers of threatened and near-threatened plants. Extracting oils from these plants require extra costs (e.g. money for permits; efficient distillation equipment) and consequently may be done with illegally obtained material and/or makeshift equipment. This is a problematic in countries where resources are often not affordable or easily accessible. Consequently, these oils are routinely adulterated and/or contaminated. Ethical distillers and suppliers should be transparent and willing to provide you with a GC-MS profile and any other relevant paperwork requested. If local distillers are unable to afford GC-MS profiles, you have the option to have the analysis done on your own, or you can work with the distiller or supplier, or other interested parties, on ways to share the cost. It is important to support distillers and suppliers who are taking extra measures to ensure sustainably-managed plants, and pure and high-quality essential oils.

Suppliers of essential oils sourced from plants which are CITES-protected should be able to verify that the exportation was done legally by obtaining or viewing a CITES certificate from the exporter.

Get involved

There are ways you can help to obtain needed data. Tools have been specifically designed for the public to use for collecting data points on the reduction in species' populations size, area of occupancy, and population number. These collective data are pooled, compiled, and used to help determine the conservation status of a species. Tools one can explore include the United Plant Savers Species At-Risk Assessment tool and the IUCN Assessment tool.

Collective projects also take the form of community outreach and engagement. You can support local aromatic medicinal plant gardens, get involved in replanting and reforestation projects, help with seed saving and sharing, and support relevant conservation efforts abroad. It is amazing what can be accomplished in small numbers.

Conclusion

We are now in the sixth extinction. It is time to protect and preserve biodiversity. Even by protecting just one plant, a multitude of another species benefit. Unlike the past, we live in a technology-rich world that gives us the power and resources to make a positive difference and help others gain "conservation consciousness." If we can make decisions today that will benefit children seven generations (~140 years) into the future, imagine the sweet scent our trail would leave behind. Walk in the visionary path of Gandhi and be protectors, healers and messengers on behalf of the aromatic plants we both rely on and deeply value. ☙

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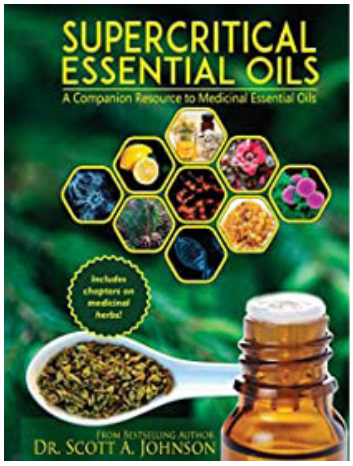
Supercritical CO_2 Extracts – Are They Merely Essential Oils? A Book Review



Kenneth Miller, Functional Aromatic/Herbal Medicine Practitioner

If you have been following the Aromatherapy community, you have probably seen the debate over the subject of "supercritical extracts." A book by author Scott Johnson entitled *Supercritical Essential Oils* fostered the debate. The contents of the book itself were not included in the debate, but rather the debate circled around whether supercritical CO_2 extracts could (or should) be termed "essential oils" – specifically "select" supercritical CO_2 extracts.

The book author asserted the following:

1. That because of the similarities in the major components of select supercritical CO_2 extracts with the steam-distilled product, select supercritical CO_2 extracts could (and should) be defined as "essential oils."

2. Many research papers refer to select supercritical CO_2 extracts as "essential oils" in their titles and/or in the content of their published works, and therefore Aromatherapy should be following the lead of the research scientists whom the author claims are the authority on these matters.

Are these assertions correct? Are select supercritical CO_2 extracts so close to the steam- to hydro-distilled product that the Aromatic community should, in fact, be generalizing them as "essential oils"?

What is an essential oil?

To begin our discussion, we must define "essential oil." According to the International Organization for Standardization (ISO), an essential oil is defined as:

> *An essential oil is a product made by distillation with either water or steam or by mechanical processing of citrus rinds or by dry distillation of natural materials. Following the distillation, the essential oil is physically separated from the water phase.*

This is the definition upon which the entire Aromatherapy community has based its teachings and literature for decades. An essential oil is a steam-distilled product or hydro-distilled product; furthermore, included in this definition is the oil obtained from the mechanical processing of citrus rinds.

The argument by the book author is that this definition is 20 plus years old and was created at a time when supercritical CO_2 products in general did not exist. Therefore, he argues, the definition should be revised to include select supercritical CO_2 products.

But would it be profitable to include select supercritical CO_2 products in that ISO definition? What would be the consequences of altering that definition?

Are select supercritical CO_2 products different than essential oils?

The claim by the author of this book is that select supercritical CO_2 products are similar enough in nature that they should be considered "essential oils." He asserts that the major components are essentially the same, so the end justifies the means. In other words, because the properties of select supercritical CO_2 products are so like major components of the steam- or hydro-distilled product, grouping them into the definition of "essential oil" is justified.

The problem with this assertion is two-fold:

1. The minor components will vary, and those minor components do matter. In the case of Rose (*Rosa damascena*) essential oil, for example, some

of the minor components have been identified as the most medicinal.

2. Furthermore, there are often components in the select supercritical CO_2 extract that are not at all present in the essential oil.

Yes, there are some select supercritical CO_2 extracts that are so close to the essential oil in even minor components that one might justify the assertion that it is basically an essential oil, but there are myriad cases in which this justification is unwarranted. There are many examples of this, and here are just a few.

German Chamomile (*Matricaria recutita*) select supercritical CO_2 is quite different from the steam- or hydro-distilled product (essential oil). One of the most marked differences is its lack of the compound chamazulene. Chamazulene is an artifact of the steam-distilled or hydro-distilled product, created (and almost completely consumed) by the conversion of matricin via the application of heat. In the select supercritical CO_2 product (and the total product as well), the matricin fully remains. While chamazulene in the steam-distilled product is itself considered a powerful anti-inflammatory, matricin has been estimated to be ten times more powerful in anti-inflammatory property. In addition, the component α-bisabolol in the steam- or hydro-distilled product is often less than 1%, while in the select supercritical CO_2 extract it is around 43%. On these two factors alone, it is quite a reach to attempt to classify this product as an essential oil.

Frankincense (*Boswellia carterii*) select supercritical CO_2 is also quite different from the steam- or hydro-distilled product. Although it shares many of the major components of its steam- or hydro-distilled counterpart, the select supercritical CO_2 contains diterpenes that are not found in the steam- or hydro-distilled product – namely incensol, isosembrene, cembrene A, and incense acetate. These compounds alone differentiate, and they also change the therapeutics of the product, most especially from a mental and emotional treatment standpoint.

Beyond the examples above, it is also worth noting that almost all supercritical CO_2 extracts (select and total) will contain some non-volatiles. In select supercritical CO_2 extracts, the non-volatiles will be minute, but they will be there; in the total supercritical CO_2 extracts they will be quite prominent. Whether the major components of the volatiles from both the supercritical extracts and steam- or hydro-distilled extracts are similar, there are no non-volatiles in steam- or hydro-distilled products. Furthermore, gas chromatography-mass spectrometry (GC-MS) testing will only reveal the volatiles, and that is all the testing that is really needed to determine composition for steam- or hydro-distilled products, while all supercritical CO_2 products will need high performance liquid chromatography (HPLC) testing.

Should Aromatherapy and ISO follow the research scientist?

The second argument presented by the author of the book (and the book title) in question is that because many research scientists use the term "essential oil" in their published works when the extraction is later revealed as a select supercritical CO_2 extract, the research scientist has thus equated a steam- or hydro-distilled product (essential oil) to the select supercritical CO_2 extract, and therefore ISO and Aromatherapy at large are not "keeping up with the times" nor are they "keeping up with science."

The problem with this argument is that researchers are not the authorities on the definition of the two products. And the further problem with this is that often researchers fail to make distinctions because of, well, either pure laziness or because they really don't understand or care to understand the distinction. How many of us practitioners, vendors, and students have read the title of an article during our research, observed that "essential oil" is mentioned, and then began to read the article only to find that the extraction method is not steam- or hydro-distilled, but rather supercritical, or even an alcoholic extraction (methanol or ethanol in particular)? I know that I have seen this more times than I can count. So, do we now say that an alcoholic extraction should be considered an essential oil because the authors of the research paper (scientists) have decided to make that claim in their title? Should we now also include absolutes in the definition of essential oils because a research scientist says so in a publication?

The fact remains that ISO and the Aromatherapy community are in a much better position to make the delineations because those bodies are most knowledgeable about the subject matter. Here's why.

It's all about the therapeutics…and the client notes

One of the most important reasons why absolutes, supercritical extracts, and even florasols are not included in the definition of "essential oils" is because of the therapeutics. As mentioned above, the select (and total) supercritical CO_2 extracts may differ greatly in properties, and most importantly in dose compared to the steam- or hydro-distilled product.

A good example of this among the select extracts is surprisingly Peppermint (*Mentha* x *piperita*). The menthol content of the select supercritical CO_2 is about 24%, while the steam-distilled product is about 50%. According to Aromatherapy practitioner Madeleine Kerkhof who specializes in end-of-life care and pain management, and who also is an authority on subcritical and supercritical CO_2 extracts, this difference (even as a major component) will give us reason for pause when deciding on the use of one product above the other. She indicates in her courses that it would be better to use the steam-distilled product in cases of itching because of the high menthol content. However, in cases of pain management, because of the higher levels of β-caryophyllene, the select supercritical CO_2 product would be preferred. Furthermore, because of the more refreshing odor profile of the select supercritical CO_2 extract, its use in mental and emotional Aromatherapy work would be much more desirable.

If we take a moment to examine the profiles of Ginger (*Zingiber officinale*) total supercritical CO_2 extract or Black Pepper (*Piper nigrum*) select or total supercritical CO_2 extract, we find components that will need extra caution – components such as higher piperine content in the case of Black Pepper; and the gingerols and shogaols in the case of Ginger. Therapeutically, these two products alone would be used very differently than would their steam- or hydro-distilled counterparts.

In addition to the change in therapeutic use itself is the need for precision when taking client notes. Many doctors use SOAP (subjective, objective, assessment, and plan) notes when taking client notes. Many practitioners in Aromatherapy and in herbalism tend to use this note structure or some other note-taking structure. The reason for the use of SOAP notes is so that if the Aromatherapy or herbal practitioner needs to work in coordination with the medical doctor, there is a common language that is being spoken.

In the SOAP notes (or other note systems) it is imperative that precision be recorded. This is firstly for the practitioners to understand what product was used in treatment. It is important to note if the product was an absolute, an essential oil (steam- or hydro-distilled), a subcritical CO_2 extract, a select supercritical CO_2 extract, a total supercritical CO_2 extract, or even a florasol extract. The differences in the products can be integral in pinpointing any issues that might arise in the therapeutic use of these products – i.e., adverse reactions. Secondly, sharing this information with medical doctors can also be helpful. Being as precise as possible can make all the difference in the world in some cases, and even can lead us to choosing a more appropriate product. If we do not make the delineation between the products in our notes (simply calling them essential oils), then we cannot make better decisions in client care when referring to our notes.

Generalization is rarely helpful…and is anti-science

The author of the book asserts that it would be easier and less confusing to simply classify supercritical CO_2 extractions (particularly select supercritical CO_2 extractions) as "essential oils." Because of their similarities to the steam- or hydro-distilled products – particularly with respect to the major volatiles – he contends that the two products are essentially the same, and delineation is simply "semantics." But, for the very reasons previously stated, semantics in this case are important.

It is rarely helpful to generalize, especially when it comes to therapeutics. In some cases, select supercritical CO_2 products are so similar that they and their steam- or hydro-distilled counterparts are used exactly the same way. But in other cases, as stated above, they are very different. So, to classify all select supercritical CO_2 products into the same category generalizes to the point of indistinction, causing confusion with the plethora of products that are not quite as similar. Furthermore, the author titles the book *Supercritical Essential Oils*, generalizing total supercritical CO_2 extracts, which are more often than not far different than select supercritical CO_2 extracts, and even far more different than total su

percritical extracts, into the "essential oil" category. This can be dangerous, especially where therapeutics are concerned.

The book author also argues that "science" should be followed rather than established definitions – that definitions must change with science. This is very true. However, science almost never pushes the specific into the general. To do so is actually "anti-science." Scientific method does not follow specific to general, but rather general to specific. Science is known for "digging into things" not "digging out of them."

For those who are familiar with herbalism, what the book author is trying to do with the erasure of delineation by generally classifying all plant extracts used in Aromatherapy as "essential oils" is equivalent to classifying all plant extracts used in herbalism as "tinctures." By the author's rationale, a "tincture" would not only include pure alcohol extracts or aqueous-alcohol extracts, water extracts (infusions and decoctions), acetic extracts, and glycerin extracts, but would also generalize extraction methods within those very categories. For instance, pure alcohol or aqueous-alcohol extraction methods such as maceration, percolation, fluid extracts, and Soxhlet extracts would be generalized into the simple "tincture" category. The problems with this are dosing. Each of these extracts may – and often do – require different dosing because some are more concentrated than others.

So, the idea of putting all plant extracts used in Aromatherapy into the general box of "essential oils" is unfounded.

In conclusion

Although the author of the book might mean well by attempting to generalize plant extracts utilized in Aromatherapy as "essential oils," it is a misguided effort; all the reasons stated above show the folly and even the dangers of doing so. These are the reasons why the ISO definition of "essential oil" has not been updated to include any supercritical (or even subcritical or florasol) CO_2 products. The delineation among the products is necessary and useful; if it was not, the definition would have been updated long ago. Aromatherapy has its own language. This language has been established for years. When changes need to be made, they are often made, but changes are never made without considerable thought; and those changes must be agreed upon by the Aromatherapy community, not as a result of the preference of one person.

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Image of sunflower and sunflower oil.

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