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Aromatherapy: The Healing Uses of Essential Oils

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INTRODUCTION

What Is Aromatherapy?

Aromatherapy is the health promoting use of essential oils extracted from various botanical sources. The extraction may be performed by steam or water distillation, cold pressing (for citrus oils), or solvent extraction (primarily with carbon dioxide), the method appropriate to the plant material. The methods of use include diffusion in air, direct inhalation, topical application or ingestion. Health promoting uses include all those beneficial to the physical body, mental states, emotional states and spiritual well-being as these cannot be truly separated from one another. However, the research presented here focuses primarily on the first aspect, as there is much less hard-core research available for the other aspects.

For Whom Is It Suited?

Aromatherapy, using the above broad definition, is suited, in some form or another, for people of all ages, cultures, religions, countries of origin, and shades of skin. It can be used to treat a wide range of symptoms and / or conditions. While this short paper cannot include every use of every essential oil, I will highlight research focused in three main areas of essential oil (EO) use. The first set of research centers on the antimicrobial activity of EOs. The second set focuses on several aspects of the inflammatory and pain responses and ways that EOs influence those processes. The third set includes studies on the metabolic actions of EOs.

What Cautions Should Be Noted?

There are, indeed, a few cautions in using EOs. Essential oils are the most concentrated active botanical substrates that can be obtained from plants. EOs need to be diluted in some fashion before they are used; in fact, as the research here demonstrates, very small concentrations of EOs can have a significant effect and **more is clearly NOT better.**

It is possible for people to develop sensitivities or allergies to EOs, as to anything else. The risk is heightened by use of insufficiently diluted essential oils. If this occurs, that EO should be avoided and cross sensitivities may develop as many EOs share similar constituents (Schaller, 1995). Some EOs, particularly the cold pressed citrus oils, must be used in low concentrations (usually less than 1 %) to avoid sun sensitivity. Some citrus oils contain a constituent that changes with exposure to sunlight; this new substance has a higher risk of sensitization.

As EOs are powerful and concentrated botanical extracts, there is a risk of accidental poisoning if too much is ingested, applied topically or inhaled. As with any other possibly toxic substance, **EOs need to be kept away from children's hands.** Accidental poisonings have occurred in children (Jacobs, 1994; Lee, 1997); few have been fatal. When working with EOs for hours indoors, good ventilation is needed; this will concern the manufacturer of products containing them, the rebottler, and even the massage therapist.

Another major caution is the possible presence of dangerous pesticides remaining in EOs. There is an increasing focus on organic growing of the plant material used for making EOs, but this may not be enough, as evidence of old pesticides is present in EOs grown on land that has not been sprayed for many years. Fractional distillation can remove pesticides, but for crops grown, distilled, and their EO used locally, this is not an option. In addition, it increases the cost of EOs to all.

The last major concern is about adulteration of EOs. As the chemistry of

these oils is increasingly understood, there is the opportunity to adulterate EOs in ways that can be challenging to detect. Sometimes a particular substance, e.g. linalool, may be added to an EO such as lavender to "standardize" it, to diminish variations from year to year or crop to crop. In some instances this is sprayed on the plant material before distillation, so that it can be said that nothing was added to the EO from the time it came from the still. Sometimes adulteration can be detected because some plants make a particular unequal ratio of chiral molecules, mirror images of each other. When adulterants are added, if they have been fabricated in the laboratory, they are usually an even mixture of (+) and (-) molecules. This will alter the expected ratio of these chiral components in the EO. Of course modern laboratory techniques can separate these chiral variations, but this is not economically feasible, except for the most expensive EOs.

Other, more obvious, adulterations have gone on for decades, e.g. unacceptably high levels of hexane solvents in absolutes or diluting the pure EO with a natural carrier oil such as jojoba, almond or fractionated coconut oil or a synthetic carrier such as isopropyl myristate, yet selling the diluted product as a "pure" EO. These adulterations are much easier to detect: by a "nose" (an expert in knowing, identifying, blending EOs, usually for perfumes), by applying a tiny amount topically and noting the carrier residue on the skin, or testing a tiny sample on fabric and washing the sample (EOs will wash out, not all carriers will).

What Benefits Should Be Noted?

There are advantages to using EOs. The EOs are extracted from their botanical sources at their peak. The ratio of EO to plant material is small, making EOs an efficient way to store or transport biologically active components of plants. The EOs do not tolerate bacterial, viral or fungal growth when kept in their concentrated state (Maudsley, 1999). Thus they are not open to this type spoilage. If the EOs are

kept in glass bottles, they are not available for vermin infestation, as are their fresh or dried plant source materials (Brandao, 1998). The glass bottles also minimize oxidation, particularly if dark colored or stored away from light.

Many EOs are distilled in the geographical area where the plants grow. This usually keeps the costs very modest for local use. It is in the transportation around the world and through several custom offices that the costs are increased. In spite of this, the cost of many EOs is still quite modest compared to other treatment methods.

In all forms and methods of holistic healing there is a recognition that the body has within it many methods and mechanisms for healing. When a form of healing is working well, minimal intervention is done, just enough to stimulate the body's own healing mechanisms. When more than that is done, the intervention risks putting the body out of balance, perhaps in a way different than the illness or malady needing care in the first place. An example of this is clearly illustrated by an elderly patient of mine who has osteoarthritis, especially in her knees. One doctor placed her on a non-steroidal anti-inflammatory drug (NSAID) to help with the pain and inflammation. This created a stomach upset. The stomach upset was dealt with by a histamine blocking, anti-ulcer drug. This drug made her light-headed and dizzy; she became frightened that she would fall and break her hip.

After consultation about aromatherapy, we agreed to use a blend of anti-inflammatory EOs in a cream base (3 % total concentration) applied topically to her knees two or three times a day. This afforded enough pain relief that she decreased the NSAIDs by more than half. This allowed her to stop the anti-ulcer drug. Her lightheadedness disappeared. With continued use of the cream, she was able to maintain low pain levels, enjoy increased activity, mobility, sense of well-being and use very little amounts of NSAIDs. The EOs selected for her had not only anti-

inflammatory action, but they were mentally stimulating and pleasantly scented. She enjoyed these added side benefits, particularly compared to the side effects she had just endured. This now happier patient was spending less money for her treatment and felt more involved in her own care, further contributing to her sense of well-being.

RESEARCH

Antimicrobial Action of EOs: Anti-bacterial Section

There is ample evidence of the anti-bacterial properties of EOs. Ross, in 1980, and many who followed presented laboratory studies about the efficacy of EOs and / or their constituents inhibiting the growth of numerous types of bacteria. This substantiated common folk knowledge about EOs as they have been used around the world for hundreds of years. Currently, laboratory studies from Australia, Brazil, Canada, China, England, France, Greece, India, Italy, Japan, Kenya, Korea, Scotland, South Africa, Spain, Turkey, USA, Zaire and more are available to confirm this folk knowledge.

Several aspects of EOs make these studies challenging. First, EOs have a complexity of constituents and concentration of constituents which vary not only from year to year, but also with place of origin and exact methods of distillation. Second, EOs are volatile at room temperature, and third, EOs are water insoluble. This last characteristic makes them difficult to test in the laboratory, yet this attribute contributes to their mode of action, particularly on lipophilic cell membranes, as we will see in a moment.

Studies have been done with a wide range of EOs and a wide range of both Gram positive and Gram negative bacteria [Bacteria stained by the Gram method

either pick up the stain (+) or they do not (-); this is a common method used in bacterial identification.]. In general, the bacteria have been selected because they contribute to food spoilage and/or poisoning, are common human pathogens and some have developed antibiotic resistance or are common plant pathogens. In general, the EOs are more effective in inhibiting growth of Gram positive bacteria than Gram negative bacteria.

There are two primary laboratory methods utilized by these studies to measure efficacy of EOs against bacteria. The first method measures a zone of inhibited growth around an EO impregnated disc (varying EO and/or concentration) on a known bacterium plated agar dish. The second uses a broth as the culture medium. A known bacterium and a known EO at a specific concentration are added. Turbidity is measured after a specific amount of time and compared to controls; the more turbid the broth, the higher the concentration of bacteria.

Some of the many EOs that have proven successful in inhibiting bacterial growth include: Artemisia afra, other Artemisia varieties, Cistus creticus, Cymbopogon densiflorus, other Cymbopogon varieties, Helichrysum amorginum, Helichrysum italicum, Lavendula officinalis, Melaleuca alternifolia, Melissa officinalis, Ocimum basilicum linalool, Ocimum basilicum methyl chavicol, Rosemarinus officinalis and Thymus capitus and Thymus vulgaris. There are others identified by their common names: citronella, eucalyptus, geranium, orange, palmarosa, patchouli, peppermint and more. (This difference in style of reporting studies and results, botanical name vs. common name, makes it more difficult to compare studies with each other or to compile good review data. The botanical name is more precise; a common name may refer to more than one plant. They are not always equivalent. The studies most useful for comparisons use both names; hopefully, using both names will be the method for future studies.)

Not all the studies use the same bacteria, but certain trends emerge. Mangena

(1999) found his South African Artemisea and Rosemary effective against salmonella, shigella, and staphylococci, as well as many more. Pattniak (1996) found his Indian eucalyptus, lemongrass, orange, and peppermint effective against 22 of 22 different bacteria, aegle and palmarosa effective against 21 of 22 and ageratum and patchouli effective against 20 of 22. Wan (1998) worked with two varieties of Basil-linalool (BL) and -methyl chavicol (BMC). He found them effective against all bacteria except Clostridium sporogenes, Flavimonas oryzihabitans and three species of Pseudomonas. He was not alone in finding **Pseudomonas resistant to EOs in the concentrations that inhibited most other tested bacteria.** This was a more prevalent finding than antibiotic-resistant Staphylococcus aureus failing to be inhibited. Pattniak (1995) found Pseudomonas aeruginosa VR-6 resistant to all his tested EOs at 20 microliters/ml. concentration. After altering the bacteria, it was then susceptible to eucalyptus and palmarosa, but at higher concentrations than other bacteria required.

Many researchers, impressed with the effective action of EOs inhibiting bacterial growth, sought to find the active constituents in the EOs. Pattniak (1997) found cineol inhibited 16 of 18 bacteria; citral, 14 of 18; geranial, 16 of 18; linalool, 17 of 18; and menthol, 15 of 18. Chinou (1996) reported his Helichrysums were composed mainly of geraniol, geranyl acetate, neryl acetate and nerolidol, but did not test these constituents individually. Mangena (1999) suggested camphene and alpha-pinene were particularly effective. Tirillini (1996), in his study of Piper augustifolium, suggested camphor and camphene could be the active constituents. Carson and Riley (1995), studying the major components of Tea Tree Oil found 1-terpinene-4-ol most effective, with linalool and alpha-terpineol very close seconds. (Again, the resisters were Pseudomonas.) Demetzos (1999), working with Cistus creticus subsp. creticus against Staphylococcus aureus, S. epidermidis and S. hominis found diterpene sclareol was the effective component of his EO.

In our modern world of high antibiotic use we are interested in antibiotic resistant Staphylococcus aureus. Carson, Cookson, et al (1995) studied 66 isolates of S. aureus with Melaleuca alternifolia, also known as Tea Tree Oil (TTO). **He found 64 of 66 isolated S. aureus were methicillin resistant and 33/66 were mupirocin resistant, yet 66 /66 were susceptible to TTO.** Here the mean inhibitory concentration (MIC) was 0.25% and the mean bactericidal concentration (MBC) was 0.5%. His British collaborators found comparable results in their S. aureus strains.

Antimicrobial Action of EOs: Mode of Anti-bacterial Action

Takaisu-Kikuni (1996), studying the effects of Cymbopogon densiflorus on Staphylococcus aureus found that high doses impaired growth in a bacteriostatic manner (like chloramphenicol), while low doses caused an energy/heat loss that caused the bacterial cell metabolism to become ineffective. Ultrastructure studies showed cell morphology changes that were characteristic of bactericidal antibiotics (like penicillin), causing bacteriolysis. This showed that EOs can have both bacteriostatic and bactericidal action. This study also suggested EOs may have anti-bacterial activity specifically on cytoplasmic and cell wall metabolism.

Cox (1998) studied some of the active constituents of Melaleuca alternifolia (TTO) against Escheria coli. He studied 1-terpinene-4-ol, alpha-pinene, linalool, and alpha-terpineol. He found that terpenes accumulate in liposome membranes causing loss of membrane integrity and dissipation of the proton motive force. At 0.5% TTO (2 x MBC in his laboratory), he found respiration in the exponential phase cell suspensions was completely inhibited and in the stationery phase cell suspensions partially inhibited. The death rate of cells was higher in the exponential phase cells.

Cox (1998) also studied whole TTO with E. coli to further investigate its action on membrane functions and cell respiration. He measured oxygen consumption as

a reflection of glucose-dependent respiration and K^+ ion concentration as a measure of K^+ leakage from cells in both exponential and stationery phases. He found 0.5% TTO (2 x MBC) completely inhibited respiration in the exponential phase and decreased it to 43% of control in the stationery phase. When 0.25% and 0.5% TTO was added to to exponential and stationery phase cells, K^+ leakage began within one minute, but was slower in stationery phase cells. He concluded that TTO kills bacteria in a manner similar to membrane active disinfectants.

Gustafson (1998) also studied TTO (whole oil) with E. coli. He found that TTO stimulates autolysis in exponential and stationary phase cells. Electron micrographs of cells grown in the presence of TTO showed loss of electron dense material, coagulation of cell cytoplasm and formation of extra-cellular blebs. This was more pronounced in the exponential phase cells. In the stationary phase cells he found less autolysis and a sub-population of stationary phase cells demonstrated increased tolerance to TTO's bactericidal effects. **This is an important finding as it indicates that bacteria can possibly develop resistance to EOs as well as antibiotics.**

Hamner (1999) did a study of TTO inhibiting growth of various organisms under conditions that might be encountered outside the laboratory. He found that 1% TTO and organic matter compromised the concentration of TTO it took to inhibit growth of S. aureus and Candida albicans. 10% TTO plus organic matter compromised activity against Pseudomonas aeruginosa. Organic matter affected 1% and 2% TTO, but not 4% and 8%, against E. coli. He also measured surfactants and found they, too, disrupt the anti-microbial action of TTO. He found the degree of disruption varies with organisms.

Soderberg (1996) concerned aromatherapists when he reported on the **toxicity of conifer resin acids (known cytotoxins), a tapped resin from Pinus merkusii and TTO on epithelial cells and fibroblasts.** A careful reading of his paper reaffirms the

toxicity of the conifer resin acids, the pine resin, but TTO **only in concentrations above 30%. As noted earlier, the MBC was 0.25% to 0.5%, depending upon researcher and laboratory.** Whole conifer resins are little used in aromatherapy because they are known sensitizers. In aromatherapy, a conifer EO is generally distilled from a part of the tree (e.g. needles) or sometimes distilled from the resin. This practice eliminates most of the risks of sensitization in using conifer EOs. Soderberg mentions that one significant risk is that "... abietic acid, one of the main components from conifer oleoresin, has been shown to cause lysis of alveolar epithelial cells and is suggested responsible for asthmatic reactions occurring in some wood workers."

Antimicrobial Action of EOs: Anti-fungal Section

With the proven anti-bacterial action of EOs, along with the time-honored use of culinary herbs and spices, it should be no surprise that research proves EO activity against food spoilage organisms. Outtara (1997), Lachowicz (1998), Smith-Palmer (1998) and many others present convincing evidence that EOs will likely have an increasing role as food preservatives.

The studies with EOs and food spoilers usually include fungi. In addition to those studies, there are some that have focused upon several specific fungi. Caccioni (1998) studied citrus fruit EOs and constituents on the growth of Penicillum digitatum and P. italicum. He found monoterpenes, except limonene, and susquiterpene constituents had positive correlation with pathogenic fungi growth inhibition. Of his group, citrange and lemon EOs performed the best.

Pattniak (1996) used the same EOs that he tested against bacteria against 12 fungi: 3 yeast-like and 9 filamentous. He found aegle, citronella, geranium, lemongrass, orange, palmarosa and patchouli effective in inhibiting growth of 12 of 12 fungi; peppermint and eucalyptus worked with 11 of 12, but ageratum inhibited

only 4 of 12. He then studied constituents of these EOs against the 12 fungi (1997). He found citral and geraniol best (12/12), linalool next (11/12) and cineol and menthol following (7/12). It seems that **although an EO may be bactericidal and fungicidal, it is not necessarily the same constituents working in both instances.**

Viollon (1994) studied EOs and their constituents against the fungus Cryptococcus neoformans, originally obtained from an HIV patient. She found EOs of palmarosa, clove, origanum, savory, tea tree, thyme, geranium and cinnamon had the lowest minimum fungicidal concentrations (MFC), all 400 microliters per liter or less. Of the constituents she tested thymol (MFC = 50 microliters per liter), carvacrol (100), citral, citronellol (150), geraniol, beta-ionone (200), carvone, eugenol, farnesol, cis-jasmone and nerol (400) were the most effective against this fungus.

Lima (1993) tested 13 EOs against dermatophytes isolated from symptomatic patients. Of his Brazilian EOs tested, Cinnamomum zeylanicum, Ocimum gratissimum, Eugenia uniflora, Alpinia speciosa, Cymbopogon citratus, Acanthospermum hispidum and Pneumus boldus inhibited a great majority of test organisms. Other EOs were unsuccessful inhibiting the test organisms, although these oils had major constituents in common with the EOs that did inhibit growth.

Suresh (1997) studied the EO of Santolina chamaecyparissus against Candida albicans. After he found it effective to inhibit growth of the fungus (MIC = 62.5 - 125 micrograms/ml), he tested it in vivo in mice and guinea pigs. He tested a 4% EO vs. 2% clotrimazole p.v. in treating an induced Candida vaginal infection in mice. The two treatments were equally effective, although the EO took a little longer to work. He also tested EO vs. ketoconazole, both 60 mg/Kg, p.o., against induced systemic candidosis. The survival rate was better for the ketoconazole (and both much better than controls), but the growth of fungi from harvested organs showed better results for the EO treatment. He inoculated guinea pigs dermally to infect their hair roots. They were then treated with 4% EO or 2% clotrimazole. Clinically they showed the

same improvement, but there was more fungal growth from hair roots taken from the EO treated guinea pigs. **These are interesting studies, not only because he shows efficacy in treatment against the standard, but with a treatment that may have less toxicity and fewer side effects than the standard.**

Buck (1994) did a clinical trial of TTO (100% concentration) vs. clotrimazole (1% solution) in 117 patients with onychomycosis confirmed by culture. At the end of six months, after twice daily treatment and debridement at 0, 1, 3, and 6 months, clinical assessment was cure for 61 % using clotrimazole and for 60 % using TTO; cultures were negative for 11% using clotrimazole and 18% using TTO. Three months later, at follow up, those showing continued improvement or resolution was 55% for those using clotrimazole and 56 % using TTO.

Syed (1999) used a different protocol for onychomycosis. He used a cream containing 2% butenafine HCl and 5% TTO vs placebo in 60 patients. He found an 80% cure rate in his treatment group after 16 weeks. At follow up, there was no relapse in the cured group and no improvement in the treatment resistant or placebo groups.

Nenoff (1996) tested for MIC for 26 strains of dermatophyte species, 54 yeasts (including 32 strains of C albicans) and 22 Malassezia furfur strains. After determining the geometric mean MIC for these 3 groups, he suggests that a TTO ointment might be useful *invivo* for fungal infections of the skin and mucous membranes and dandruff.

Mishra (1994) screened EOs for antifungal activity against Aspergillus flavus. He found Cymbopogon citratus to have a MIC of 1000 ppm in stored feed. He supports its wide fungitoxic spectrum, non-phytotoxic nature and superiority over synthetic fungicides. He states the fungitoxic potency remained unaltered over 7 months, even upon introduction of high doses of inoculum of test fungi, and remained thermostable from 5°C to 100°C.

Mahmoud (1994) also worked with A flavus, but he also measured aflatoxin production. He was working with EO constituents in an aerosol form. He found that thymol (200 ppm), cinnamaldehyde (250 ppm), geraniol, nerol, and citronellol (500 ppm) all suppressed A flavus growth and aflatoxin production. He also stated that citral, citronellol and eugenol prevented fungal growth and toxin formation for up to 8 days, but after 15 days the toxin production was more than the controls.

With extensive evidence for the antibacterial and antifungal efficacy of EOs, it might seem natural that a dilute solution of EOs would make a good mouthwash. Gingivitis and dental caries are very common disorders. Aroma Medica$_{TM}$, aware of these two facts, used these beneficial properties of EOs to develop a mouthwash that does decrease plaque and tarter accumulation and helps heal the chronic infection and inflammation in gingivitis. The mouthwash, containing TTO, peppermint, thyme, and more EOs, was effective in healing mouth ulcers in an AIDS patient, permitting him to resume eating.

Anti-inflammatory Action of EOs

In order to understand the anti-inflammatory and analgesic actions of EOs, it is helpful to understand some of the variety of inflammatory responses the body has. One immediate type inflammatory reaction is mediated by histamine release, primarily from mast cells. This often instigates the formation of prostaglandins (PG) and leukotrienes (LT). The body's numerous PGs have many functions in the body, with the number and position of double bonds and hydroxyl groups determining the physiologic properties of the various PGs. The inflammatory PGs, especially PGE $_{1+2}$, PGD_2 and PGG_2, cause increased permeability of capillaries, loss of plasma and plasma proteins from vascular space with evident edema and tissue swelling, and increased immune cellular response, even in very low concentrations.

When the polymorphoneuclear white cells arrive at the site of inflammation, they add further LTs, with potent pro-inflammatory (even more than PGs) and bronchoconstrictor properties. LTs have 200 -20,000 times the bronchoconstrictor action of histamine.

PGs and LTs are formed from dietary essential fatty acids, primarily from arachidonic acid, in a cascade of chemical reactions facilitated by certain cyclooxygenase enzymes. In one pathway, aspirin, indomethacin and other non-steroidal anti-inflammatory drugs (NSAIDs), inhibit cyclooxygenase. In another pathway, 5-lipoxygenase results in the formation of LTs A_4, B_4, C_4, D_4, E_4, and F_4.

Numerous studies have been done that demonstrate EOs diminish the inflammatory response to various noxious stimuli. Miller (1996) affirmed that "The lipophilic character of the constituents of EOs must be regarded as the basis of their pharmacological activity. This property enables their small molecules to interact with the components of biological membranes. In this way they may influence the membrane permeability and the activity of the carriers, ionic channels, receptors, or membrane integrated enzymes, e.g. cyclooxygenase and lipoxygenase." In this 1996 study Miller presents the results of his study with three constituents of Chamomilla recutita (German camomile) on histamine release from rat peritoneal mast cells. Protamine sulfate was used to trigger release of histamine. Chamazulene, in concentrations from 10^{-9} to 10^{-5} M, mildly inhibits and, in concentrations above 10^{-5} M, stimulates release of histamine. En-yne-dicycloether had a moderate stimulation effect at concentrations lower than 10^{-4} M and a strong inhibiting effect at concentrations above that.

Safayhi (1994) studied matricine and its transformation product, chamazulene. He noted that Chamomilla recutita is used in commercial preparations for treating inflammatory skin and bowel disease. He studied LT production in neutrophilic granulocytes (PMNs). He found that chamazulene, but

not matricine, inhibited formation of LT B_4 in intact cells (IC_{50} = 15 microM) and in the supernatant of lysed cells (IC_{50} = 2 microM). He found chamazulene, but not matricine, blocked the chemical peroxidation of arachidonic acid by cyclooxygenase and 12-lipoxygenase activity in human platelets. **This indicates that the water distilled EO of Camomilla recutita would be a more effective anti-inflammatory agent than the carbon dioxide extracted EO because the chamazulene is a transformation product formed in the heat of distillation.**

Kim (1999) found that lavender EO inhibits immediate-type allergic reaction in mice and rats. In concentrations ranging from 1:500 to pure EO, he found lavender EO in mice inhibited, in a concentration-dependent manner, the mast cell-dependent ear swelling response stimulated by compound 48/80 by both topical and intradermal application. He found the same concentrations of lavender EO in rats inhibited, in a concentration-dependent manner, the passive cutaneous anaphylaxis induced by topical and intradermal application of anti-dinitrophenyl (DNP) IgE. He also found the same concentrations of lavender EO in rat peritoneal mast cells inhibited, in a concentration-dependent manner, the release of histamine by compound 48/80 or anti-DNP IgE. Additionally, Kim noted that lavender EO, in concentrations of 1:1000, 1:100, 1:10 and pure, had a significant inhibitory effect on anti-DNP IgE - induced tumor necrosis factor secretion from peritoneal mast cells.

The evidence for lavender EO inhibiting release of histamine from mast cells and for German camomile blocking the formation of inflammatory LTs and PGs gives ample support to the efficacy of Aroma Medica™'s Allergy Cream. The Allergy Cream, containing both of these EOs (and others), acts to prevent allergic reactions and to quell allergic reactions that have already begun.

The monograph (1998) on Boswellia serrata (Indian Frankincense) explains that Boswellia specifically, and in a dose-dependent manner, blocks 5-lipoxygenase, thus blocking the formation of 5-hydroxyeicosate, iaenoic acid and LT B_4. These

cause bronchoconstriction, chemotaxis and increased vascular permeability. It reports that Boswellia has been observed to inhibit human leukocyte elastase (HLE) which stimulates mucus secretion and may be involved in the pathogenesis of emphysema. The monograph states that NSAIDs can cause disruption of glycosaminoglycan synthesis. This can increase cartilege degeneration and articular damage in arthritic conditions. Boswellia reduced the degradation of glycosaminoglycan compared to controls, whereas NSAIDs (here, ketoprophen) caused decreased total tissue glycosaminoglycan content.

SaiRam (1997) worked with NIM-76, the steam distilled volatile fraction of neem oil, a cold pressed seed oil. NIM-76 has high spermicidal activity, but not the abortificient effect of whole neem oil. In this research rats were pretreated for five days with either 120 mg/Kg or 300 mg/Kg i.p.. At the end of five days there was an increase in PMN and a decrease in lymphocytes for the 120 mg/Kg group and a marked increase in PMN and a decrease in lymphocytes for the 300 mg/Kg group over controls. However, the PMN activity was examined. The 120 mg/kg group's PMNs showed enhanced yeast uptake and NBT reduction, but the 300 mg/Kg group showed no significant difference from controls, **indicating that 300 mg/Kg was a supraoptimal dose and that too much of a good thing is not better.** In further support of this, SaiRam showed there was no change in antibody levels in the lower dose and an actual decrease in antibody titers in the higher dose.

Ocete (1989) examined the anti-inflammatory activity of Bupleurum gibraltaricum. He compared the whole EO, its three major constituents (beta-pinene, alpha-pinene and delta-3-carene) and indomethacin against a control in carrageenan induced pedal edema and exudative inflammation in rats. He tested the EO p.o. and i.p.; both were effective, but the oral dose needed to be about thirty times the peritoneal dose to obtain comparable results. The EO showed dose-dependent anti-inflammatory activity, comparable to indomethacin; this suggests a

possible inhibition of prostaglandin synthetase. In testing the three named constituents, all showed activity against carrageenan induced inflammation. Delta-3-carene showed dose dependent results; 8 mg/Kg of beta-pinene was more effective than 42 mg/Kg of alpha-pinene. Moreover, throughout the 24 hour timeframe of the study, the dose dependency seen at shorter intervals, was no longer necessarily evident. This revealed differences in potency of the components and that not all the anti-inflammatory responses are dose dependent over time. Ocete, in this same report, demonstrated that the EO of Bupleurum gibraltaricum diminished the chronic proliferative inflammation in foreign body granuloma formation, compared to controls, after implanting a cotton wool pellet into the dorsal superficial fascia. Ocete also tested the EO and its major constituent, delta-3-carene, in rat uterus smooth muscle. Both antagonized (blocked) oxytocin induced contractions, suggesting a PGF_2 inhibition, but did not antagonize acetylcholine (ACh) contractions.

Lorente (1989) examined the effects of the EO of Bupleurum fruticosum as well as its major constituents, alpha-pinene and beta-pinene, and a combination of the two pinenes. Against carrageenan induced inflammation he found the whole EO effective and more so than either alpha-pinene or beta-pinene or alpha-pinene plus beta-pinene. This suggests that there are additional constituents adding to the anti-inflammatory response. He found the whole EO effective in a dose dependent manner, but that 40 mg/Kg of beta-pinene was more effective that 80 mg/Kg. He also tested the EO on rat uterus smooth muscle. With this EO the ACh contractions were antagonized in a non-competitive way, whereas oxytocin contractions were inhibited in both competitive and non-competitive ways. He noted this latter antagonism was not as strong as what Ocete found with Bupleurum gibraltaricum and he postulated that this was because Bupleurum fruticosum did not contained delta-3-carene.

Martin (1993) studied the anti-inflammatory effects of the EO of Bupleurum fruticescens. The major constituents varied from the two previous studies with Bupleurum, demonstrating that EO constituents can vary widely from variety to variety, from year to year, from location and/or altitude grown to another location and/or altitude. This is important to remember when making generalizations about EOs. He, too, used carrageenan induced paw edema, but he also tested some rats that had been adrenalectomized. He found the whole EO more effective than its major constituent beta-caryophyllene and the EO approximately equal to a combination of beta-caryophyllene and alpha-pinene. He found the alpha-pinene effective only in the normal rats, but not in the adrenalectomized rats. This implies intact adrenal glands are needed for the anti-inflammatory action of alpha-pinene, presumably through stimulation of release of cortisol or other adrenal steroid hormone. When he tested the beta-caryophyllene in normal and adrenalectomized rats, he found it exhibited an anti-inflammatory effect in both, but the adrenalectomized rats needed higher doses to obtain a similar result, implying that beta-caryophyllene has at least two modes of action working synergistically. Martin also tested these two constituents against the inflammation induced by PGE_1. Beta-caryophyllene, at 300 and 600 mg/Kg exerted its maximal activity 45 minutes after the administration of the PGE_1. Alpha-pinene, at the same doses, exhibited it effect at 15 minutes after the PGE_1 administration and exerted it's effect as long as the experiment lasted. Again, this suggests different modes of action for these two constituents.

Al-Zuhair (1996) studied the effects of cardamom (Elettaria cardamomum) EO. In the toxicology study, doses from 50 - 1600 microl/Kg, produced drowsiness, staggering gait and absence of pain reflex in mice. Pedal edema was induced by carrageenan; it was countered with indomethacin (30 mg/Kg) or 175 or 280 microl/Kg of EO. The indomethacin dose was intermediate in effectiveness

between the two EO doses. In the writhing response test of analgesia, aspirin at increasing dosages was compared to EO at similarly increasing dosages against para-benzoquinone induced writhing. They had similar dose-response curves. The EO was also tested on prepared rabbit intestine; gradually increasing doses of EO inhibited spontaneous movement in a dose-dependent manner. When ACh was added to the rabbit intestine, it inhibited the stimulation in a dose-dependent manner; atropine (3 micrograms) and EO (400 nanoliter) both produced a 50% reduction in the stimulant action of ACh, suggesting a muscarinic receptor antagonistic action.

Analgesic Action of EOs

Moran (1989) reported about the EO of Artemesis caerulescens subsp gallica. The analgesic effects were compared to lysine acetylsalicylate in three doses administered i.p. prior to i.p. injection of acetic acid or para-phenylbenzoquinone. Reduction in writhing response was effective and dose-related against both test irritants, although slightly less against para-phenylbenzoquinone. In the anti-pyretic tests, i.p. lipopolysaccharide was administered 1 or 3 hours prior to the tests levels of the EO or lysine acetylsalicylate. In the 1 hour post-lipopolysaccharide tests, initially the EO created a temperature drop below starting temperatures, but by 3 hours, when the lipopolysaccharide hyperthermic effect was maximal, the temperature returned to normal, but not more. The anti-inflammatory activity was measured against carrageenan induced pedal edema; the activity was dose-related and comparable to the activity of lysine acetylsalicylate. All these effects were seen at 25 -33% of the LD_{50}.

Lorenzetti (1991) studied the analgesic activity of Brazilian lemongrass (Cymbopogon citratus) tea, EO and various chromatographic fractions of the EO. He used GC and thin-layer chromatography to determine that the major fraction with

analgesic activity corresponded to myrcene; this was confirmed by mass spectrometry. He used variations on the carrageenan pedal injection: first, he measured pressure applied before postural freezing, not edema, and second, he measured against carrageenan, PGE_2, dibutyryl cyclic AMP and isoprenalin. The tea, EO, and especially its myrcene fraction, were effective against inflammation induced by carrageenan and PGE_2, but not dibutyryl cyclic AMP. In the writhing tests, the EO and myrcene were tested against the effects of i.p. acetic acid or iloprost. The dose response curves were similar. Myrcene was also tested in mice using the hot plate test, measuring reaction time for withdrawal. The myrcene enabled a non-significant prolongation of reaction time, but not near the prolongation enabled by administration of morphine. The rat paw hyperalgesic testing done in this study permits the differentiation of peripheral from central acting analgesia. The dibutyryl cyclic AMP-induced hyperalgesia is blocked by a central acting substance, such as morphine, by not by a peripheral acting analgesic. This site of action is suggested for lemongrass EO and myrcene and is further supported by the lack of effect for the hot plate test and its inability to cause tolerance after successive administration. For peripherally acting analgesics, there are two major modes of action: one prevents the development of sensitization of the nociceptor (like aspirin and related drugs) and the other down-regulates the sensitized nociceptors (like dipyrone). The former is unable to produce analgesic effect on PGE_2 or isoprenalin-induced hyperalgesia. That lemongrass EO and myrcene have a direct peripheral acting analgesic effect, similar to opiates, was further supported by the absence of antipyretic effects on fever induced by endotoxin in rabbits.

Aydin (1998) reported his studies of EOs from several Nepeta species, particularly Nepeta caesarea. This EO, which showed marked sedation in test animals, was screened with the tail-flick and tail immersion (in 52.5 ^{o}C water) tests

in the rat. It showed activity on mechanical, but not thermal, analgesic response. This activity was blocked by naloxone, which blocks opioid receptors. Together, these suggest that this EO acts on specific opioid subtype receptors, excluding mu-opioid receptors.

Aydin (1999) reported on additional Nepeta species from different locations in Turkey. He found Nepeta italica (but from only one of three locations) was able to inhibit the tail-flick response in mice; this was blocked by naloxone. It showed no effective analgesia in the tail immersion test. In prepared rat ileum, it inhibited ACh-stimulated contractions in a non-competitive manner and showed no significant effect on the isolated rat aorta. These findings, along with the high concentration of 1,8-cineole in this EO, led Aydin to suggest that kappa (OP_2) opioid receptors were affected by 1,8-cineole.

This variety of studies in animals suggests there may be more than one mode of action for EOs and their constituents for the anti-inflammatory and analgesic effects. Note, **it is not the efficacy that is in question, but rather the mode of action.**

We can observe that these studies concern a considerable variety of EOs exerting these actions. Additionally, these EOs are selected because they are local botanical species used in the "folk medicine" of the region. This means that if distillation equipment and skills were available to people they could prepare their own, locally available, inexpensive EOs for their own use.

Metabolic Effects of EOs: Lipid Metabolism

Yasni (1994) built upon his previous work that showed the EO of Curcuma xanthorrhiza (Javanese tumeric) exerted glucose lowering activity in diabetic rats and triglyceride lowering effects in normal and diabetic rats. In this study he used the EO and 10 hexane-soluble subfractions of the EO to find the primary active

constitutents. 65% of the EO is alpha-curcumene. He added EO (0.02%) to rat chow; this resulted in lower hepatic triglyceride concentration and no change in serum triglyceride levels in two weeks time. When he added the hexane-soluble fraction (0.5%) to rat chow, it resulted in lower liver and serum triglyceride levels and higher concentrations of HDL in two weeks time. Examination of the livers after these trials revealed both groups had lower hepatic fatty acid synthase. In cultured rat hepatocytes, the hexane soluble fraction containing alpha-curcumene most suppressed the synthesis of fatty acids from [14C]acetate, demonstrating alpha-curcumene is an active principle exerting influence in the triglyceride lowering effect of Curcuma xanthorrhiza. There was another unidentified constituent in another subfraction that also suppressed the synthesis of fatty acids from [14C]acetate in cultured rat hepatocytes, as well as some measurable, but lesser, effect from other fractions, indicating that there are probably several constituents of Curcuma xanthorrhiza affecting liver and serum lipids. In this study **it took only two weeks, and at a very low concentration of EO, to begin to see a change in liver enzymes that affect liver and, eventually, serum triglycerides and cholesterol.** It would be interesting to see a longer trial done with people and this EO.

Nikolaevskii (1990) studied the EOs of lavender, monarda and basil on the course of experimental atherosclerosis in rabbits. Inhalation of lavender and monarda in concentrations of 0.1 - 0.2 mg/m^3 produced no change in serum cholesterol, but did diminish its content in the aorta and reduce, "...affection of the aorta by the atherosclerotic plaques."

Elson (1989) studied the impact of 140 mg daily of lemongrass EO on the serum cholesterol of 22 hypercholesterolemic patients for 90 days. Previous studies indicated that geraniol and citral, non-sterol plant mevalonate pathway end products, would suppress mevalonate synthesis and thus act in the regulation of 3-hydroxy-3-methylglutaryl coenzyme A reductase. The patients were selected because

they had each undergone coronary bypass surgery within the previous seven years and had a serum cholesterol of over 250 mg/dl in spite of being on a diet with strict limitations on fat, energy and cholesterol intakes. The group as a whole showed a decrease average cholesterol that almost reached significance ($p<0.06$), but the investigators noticed that the results fell into a bimodal distribution. Eight subjects responded well to the trial and fourteen were resistant. The responders tended to have higher starting triglycerides, a higher body mass index and required 20% fewer calories to maintain body weight. **It appears that for a portion of people with elevated serum lipids, something as simple as 140 mg of lemongrass EO a day can make a significant difference in lowering cholesterol levels.** It would be valuable to have additional serum lipid measurements, especially triglycerides, during the clinical trial. After the lemongrass supplement was discontinued, by 90 days, the cholesterol returned to pre-study levels.

Metabolic Effects of EOs: Glucose and Insulin

Al-Hader (1994) studied the effects of the EO of Rosmarinus offinalis on glucose and insulin levels in normal and alloxan diabetic rabbits. Previous work demonstrated rosemary EO has antispasmodic and tracheal smooth muscle relaxing effects; it was suggested this smooth muscle relaxation is attributed to inhibition of the increase in cytosolic free calcium concentrations. Other work demonstrated that elevated cytosolic free calcium concentration is a trigger for exocytotic insulin release from beta-pancreatic cells. The normal rabbits were subjected to an i.p. glucose tolerance test (GTT) with serum glucose and insulin levels measured, one group received EO i.m. before the glucose and the other group did not. The group that received the EO had higher glucose levels, with the differences from controls growing more significant from 60 to 90 to 120 minutes. The insulin level was lower at 30 minutes and not significantly different after that. In the diabetic rabbits, at six

hours of the GTT, the rabbits that received EO had significantly higher glucose levels, but not prior to that. It appears that the hyperglycemic effect requires a normal pancreas to have inhibition of insulin release. While this will not dramatically effect the diabetic pancreas, **rosemary is an EO to keep in mind for helping the hypoglycemic patient whose pancreas and insulin release may be overactive in response to a glucose challenge.**

STANDARDS

The most important standards to maintain concern the purity of the EOs and truth in labeling the EOs. Today there are people and companies that mislabel what a bottle contains. For example, birch and wintergreen oils contain methyl salicylate in high percentages. Often the pure chemical methyl salicylate is sold as one of these oils. There is no warning that methyl salicylate in repeated small dosages or one large dose can be toxic [Lee (1997)]; there is no warning that people sensitive to aspirin should avoid this product. There is often no warning that EOs should be diluted. Some people and companies in the USA tell people to use these EOs neat (undiluted) on the skin. Recently, a woman phoned Aroma Medica™ looking for these two EOs. We told her that we did not sell them because they are rarely what they say they are and that people tend to misuse them. We told her they **always** need to be diluted in a carrier because they can be strong skin irritants. Her response was, "Oh, is that why I have a red, burning mark on my face where I put some just a while ago?"

Truth in labeling is important because if someone dilutes an oil, for example, oregano, and tells people it is pure, the unsuspecting person who buys the diluted oil, first overpays, often dearly, for the product and then s/he comes to think it is

safe to use in high concentrations. If, the next time, s/he buys a pure oregano oil and uses it in the dilutions s/he used with the previous purchase, the EO will irritate the skin. S/he will believe the second oil is defective!

Previously in this paper I mentioned a number of ways that EOs can be adulterated. All of those present a deviation from good, ethical standards especially since someone can be injured physically by the substitution. If not injured physically, the person is injured financially, because they have overpaid for a lesser product.

Another standard that is important has to do with the packaging of pure EOs. For retail purposes, EOs should come in small glass bottles with a orifice reducer. The glass is inert and will protect the oils. Many oils interact chemically with plastic, dissolving molecules of plastic into the EO, even weakening the plastic container. In addition, plastic is porous, so that oxidation of the EO will occur even in a closed plastic container. The orifice reducer serves two purposes; it assists the person using the oil to measure by counting drops when using the oils and it makes accidental poisoning more difficult by preventing a child from inadvertently drinking a whole bottle of EO.

The next issue of safety is respect for the EOs. As I stated previously, EOs are the most powerful concentration of active botanical constituents that we have. People using and/or recommending EOs for one reason or another need to know what they are doing. This leads directly into our next section on education.

EDUCATION DESIRED

To use EOs one needs to respect the concentration and power of plant essences, to appreciate that tiny doses are needed to bring about a shift toward

healing in the body. As I have pointed out in the research section, more is not better when using essential oils. When using a holistic approach to healing, using the least force or influence to stimulate the body's own healing mechanisms, generally only very tiny quantities of EOs are used or needed at any one time. If one is using them by inhalation, it takes only a few molecules to stimulate olfactory sensations. These olfactory sensations go directly from the olfactory nerve to major control centers in the brain, to the limbic system, thalamus, hypothalamus and then to the cortex and the rest of the body. Years ago, John Steele studied EEG changes evoked by smelling EOs. The changes were almost instantaneous. (These are unpublished data learned from a personal communication.) I have recommended inhalation of some EOs, such as frankincense, benzoin or sandalwood, to slow and deepen respiration, useful for meditation or for quelling anxiety. I have also used inhalation of other EOs to stimulate a somnolent audience. Once, confronted with being the second to last speaker late one night, I asked the audience to compare organoleptically two varieties of basil. What I was really doing was using EOs with mental stimulating properties so we could have an interesting discussion together. It worked beautifully!

There are many "first-aid" type uses of EOs that populations in general can learn, just as these populations learn any OTC healing remedies. As more and more remedies and supplements are available ad lib, more and more general education of the public is necessary. Recently, I wrote an article titled *Lavender Essential Oil: First Aid Kit in a Bottle* for an alternative/ complementary/ integrated health newsletter. Many people were quite interested to learn about the many uses of lavender EO and the advantages of having a small bottle handy at home. One story in particular was about a woman who burned her hand extensively removing sticky buns from her oven. First, the caramelized goo overran the pan and burned her; she withdrew her hand, dropped the potholder, then grabbed the pan with her bare

hand. She ran her burned hand under cold water and then placed it in a bowl with water and ice. Her hand was intensely red and very painful. I gently dabbed some lavender EO on the burned areas of her hand. The people present, over the next forty minutes, watched her hand return to its normal color, witnessed her move all her fingers and heard her say that it did not hurt her any longer. Those present who were unfamiliar with lavender EO were incredulous. I saw another burn of similar magnitude, not treated this way, require an emergency room visit, extensive dressings, several visits to a plastic surgeon, topical antibiotics, and an unhappy woman who could not use her hand for six weeks.

Using EOs for first aid or in ways that OTC remedies are used can be learned by many with focused training. In the arena of aromatherapy, many people in the USA, Canada and Great Britain are working to establish educational standards. There will be standards for an introductory program of education: this would enable a person to use a few EOs safely for their own or their family's benefit. This level of education should include some elementary knowledge about the physiological effects of the EOs in the body, as well as introductory EO chemistry. Many of the educational programs then advance to standards for more in-depth education in all the subjects, including a wider range of EOs.

When it comes to the practice of aromatherapy, of diagnosing and prescribing for others, and using EOs as an integral part of a person's health and well-being, it is important to have some training in the healing arts and sciences, including: medicine (allopathic or a traditional system), nursing, chiropractic, massage, herbal studies and so forth. Here, because the dimensions of diagnosis and treatment are required, the practitioner needs a system of understanding good health and function, as well as deviations from that. The practitioner needs to understand the actions of the EOs, including how they influence the deviation from well-being to help a person return to balance. With a solid framework, the practitioner can make

a diagnosis and create a treatment plan incorporating EOs. The practitioner needs to understand blending EOs and describing to patients / clients exactly how to best use the prescriptions given. The practitioner also needs to understand at least the basic organic chemistry behind the oils and the variations that are naturally present. The practitioner must understand the safety issues involved in using EOs and be able and willing to teach this to others. The practitioner also needs to understand how the treatment s/he prescribes may complement or fight any other treatment her/his patient may already be receiving, even if from another healer. For example, a patient may benefit greatly from aromatherapy massage as an integral part of a total care program for arthritis, cancer, depression, anxiety or high blood pressure.

There is no licensure, or even certification, for aromatherapy in USA, Canada or Great Britain. In order to practice aromatherapy currently, it needs to be combined with another modality, e.g. medicine, nursing, massage, chiropractic, naturopathy, etc. that does have a license in the location of the practitioner. The exception would be a traditional healer within the healer's traditional culture. In these situations there is usually a long training or apprenticeship to adequately learn ranges of safety. The extent of the individual's practice would be limited legally by the license (s)he holds, but morally or ethically, by the limits of the individual's knowledge and experience.

I believe in the benefits of aromatherapy and want to make EOs available to more people, in a safe and ready to use form. This is the reason I founded Aroma Medica$_{TM}$ and its line of "healing products." They can be used like other OTC remedies, without any basic knowledge of chemistry or EOs. A person need only have an understanding of when to use it, where to use it and how much, to benefit from an Aroma Medica$_{TM}$ product.

COST-EFFECTIVENESS

Aromatherapy can be a very cost effective modality, either to stand alone for first aid or other small issues, or integrated into a larger program of health care for an individual. Many of the "workhorse" EOs, those used most commonly for healing purposes, are not expensive compared to alternatives. The expensive EOs tend to be the floral, perfumy ones. They are healing, but often a tiny amount is sufficient, or a less expensive alternative will be fine to substitute.

Recently (August 30, 1999) the Wall Street Journal had an article "Americans to Spend More on Prescription Drugs," detailing that the National Association of Chain Drug Stores estimates that consumers will spend $121.6 billion on prescription drugs in 1999. This continues a trend of more prescriptions and at a higher average cost, even in the face of more formerly-prescription drugs available over-the-counter. This cost for medical care does not include: visits to doctors, laboratory studies, diagnostic procedures, imaging studies, treatments, hospitalizations, surgeries or the administrative charges and profits for insurance companies. Aromatherapy, like many of the complementary/integrated modalities, is low-tech. It involves talking with patients, touching patients, asking them to participate in their own care and well-being, and encouraging them to be aware of their sensations. Literally asking people to stop to smell the flowers. In our too busy, increasingly impersonal world, aromatherapy can, indeed, be a fragrant respite and one that benefits the individuals using EOs.

I do believe that aromatherapy and the other complementary / integrated modalities represented at the conference will change the way people take care of themselves in the years to come. And I believe our grandmothers' and greatgrand-mothers' remedies will come full-circle to find a beneficial place in our lives again.

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