# Essential Oils and Human Physiology

An Introduction to Clinical Aromatherapy

Presented by Amanda Lattin
MA, MH, RA



## Defining an Essential Oil

The International Standards Organization (ISO) gives this definition:

> An essential oil is a product obtained from natural raw material, either by distillation with water or steam, or from the epicarp of citrus fruits by mechanical processing, or by dry distillation. The essential oil is subsequently separated from the aqueous phase by physical means.

This describes how the essential oil is obtained, but provides no information on its nature.



## Defining an Essential Oil

Drs. Franchomme and Pénëol use the terms of photosynthesis to describe an essential oil:

Plant essences, in the physiological meaning of the term are most certainly true life essences, elaborated by the secretory cells of the plants that have tapped the photo-electric-magnetic energy of the sun and have converted it, with the intervention of enzymes, into biochemical energy in the form of highly diversified aromatic molecules.



## What Are Essential Oils?

- An essential oil is the distilled, or expressed, product of the volatile components synthesized by various plant tissues of a single plant species.
- The alchemist Paracelsus (1493-1541) coined the term *essence*, which equated to spirit. In alchemy, the term spirit refers to the personality or extract of something that retains the qualities of the original substance.
- The term *essential* was applied to these oils because they held the essence or fragrant part of the plant.



## Concentration and Potency

- Essential oils are highly concentrated forms of the plant or herb part from which they are derived.
- For perspective, 1 drop of essential oil can equal around 30 cups of herbal tea in terms of concentration.
- Essential oils can be up to 75 or 100 times more concentrated than the fresh herb.
- It takes 30 hand-picked blossoms or 2,000 petals to produced 1 drop of rose (*Rosa damenscena*) essential oil.



## Secondary Metabolites

- Are not necessary for the growth and propagation of the plant; however, plants would not survive without them
- Attract pollinators
- Attract beneficial insects to prey on the plant's predators
- Provide protection by repelling harmful insects and herbivores
- Serve as antibiotics and antimicrobial compounds for plants
- Allelopathy: prevent the growth of competing vegetation
- Antitranspirant: reduce the rate of the loss of water

## Where are essential oils found?

- Flowers: jasmine, rose, ylang ylang, neroli
- Leaves: citronella, lemongrass, petitgrain, peppermint
- Bark: cinnamon
- Inner bark or wood: sandalwood, cedarwood, rosewood
- Resin: myrrh
- Seed: fennel
- Fruit peel: bergamot, lemon, lime, orange, mandarin
- Root: ginger, vetiver, valerian
- Berries: juniper



## Our Definition of Essential Oil

- Extracted by various means, including steam and dry distillation or expressing from the plant material of a single species
- Secondary plant metabolites – serving various roles
- Volatile components of aromatic plants:
  - Can be flammable
  - Generally less dense than water
  - Generally non-polar and insoluble in water
  - Can be found in many plant parts depending on the species
  - Highly concentrated forms of the plant or herb



## History of Distillation



## Main Methods of EO Extraction

- Water distillation
- Steam distillation
- Extraction with volatile solvents
- Hydro-diffusion
- Expression
- Enfleurage



## Key Apparatus Changes

- Sources of heat
- Use of steam
- Cooling condensers
- Modern-day use of computer calibration
- Specifics for each individual plant species
- This led to different types of distillation



## When It All Started

Increased availability of essential oils was a result of the advent of the techniques of chemistry in the 19th century. At the time essential oils became the object of intense scientific curiosity. In turn, efforts to elucidate complex structures, like that of pinene, fueled the development of chemistry as a whole.

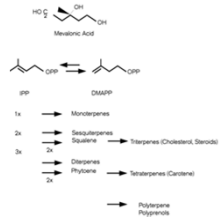
## Main Categories of Essential Oils (EO) Constituents

- Terpenoids
- Phenols and phenyl propanoids
- Non-terpenoid aliphatic molecules
- Heterocyclic compounds



## Mevalonic Acid Pathway

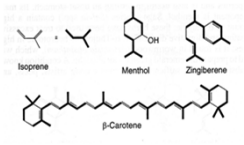
The biosynthesis of terpenes, sesquiterpenes, and ultimately cholesterol and carotenoids is often referred to as Mevalonic Acid Pathway.



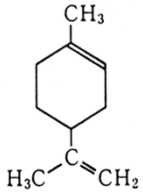



## Isoprene Unit

**Isoprene Example**




**Limonene Example**





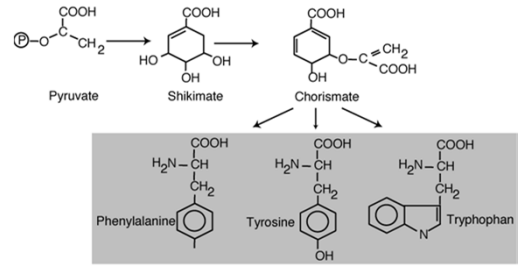

## Functional Group Families Derived From Mevalonic Acid Pathway

- Monoterpenes
- Sequiterpenes
- Monoterpenols
- Sequiterpenols
- Oxides
- Esters
- Aldehydes
- Ketones
- Lactones

- Chemopreventative
- Anti-inflammatory
- Anti-infectious
- Chemopreventative
- Antinociceptive
- Sedative
- Anti-infectious
- Wound healing
- Anti-inflammatory

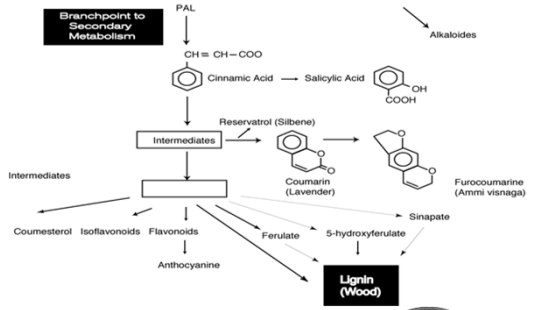


## Phenyl Propanoids: Primary Metabolites



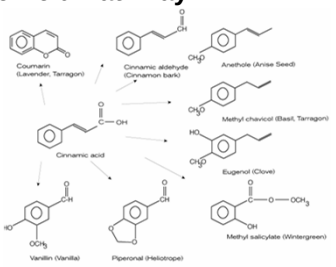



## Phenyl Propanoids: Secondary Metabolites



## Functional Groups Derived From Shikimic Acid Pathway

- Phenols-rubefacient, anti-infectious
- Phenyl methyl ethers-antispasmodic, anti-nociceptive
- Coumarins-antilymphoedemic

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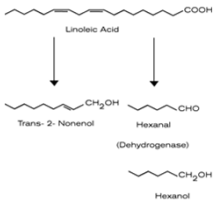
## Fatty Acid Metabolism




Molecules found in essential oils also arise from other biosynthetic pathways, e.g. certain high-impact trace components originate from the fatty acid metabolism.

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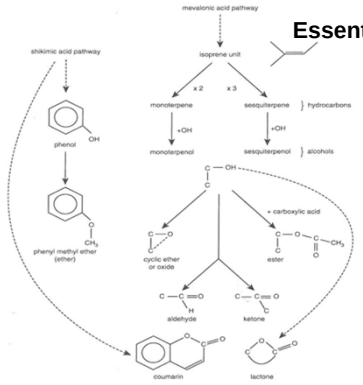
## Essential Oil Road Map

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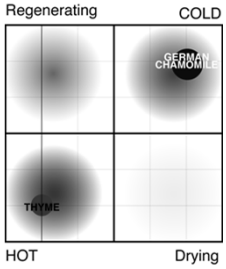
## The Four Qualities

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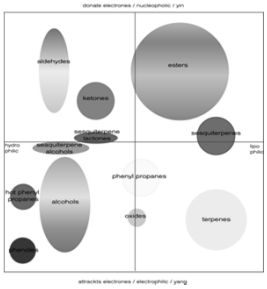
## The 12 Main Classes of Compounds

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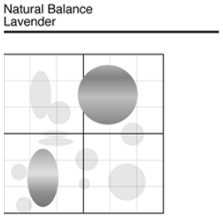
## Natural Balance Lavender




35% Terpen alcohol (tonifying, antiseptic, gentle on the skin)
35% Ester (spasmolytic, relaxing)

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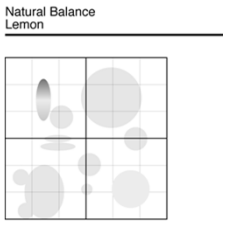
## Natural Balance Lemon

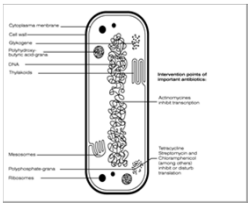



90% Hydrocarbon (dry, irritating)
3% Citral (sedative, antiinflammative)



## The Prokaryotic Cell

- Tri-terpenes are an integral stability piece of the cell wall in prokaryotes.
- The presence of tri-terpenoids in prokaryotes demonstrates the biochemical machinery to produce essential oils and ultimately cholesterol and carotene.
- This has been a feature of living organisms since the beginning of life.





## Co-Evolutionary Language of Plant Secondary Metabolites

- Plants have evolved their secondary metabolite language to match not only their environment, but also the other plants, insects, and mammals they encounter.
- They have two sets of secondary metabolites:
  - One is polar, water soluble, and stays in the plant.
  - The other is non-polar and volatile enough to evaporate and interact with the outside world.



## Essential Oil Communication

- The first way essential oils (EOs) interact with human physiology is via inhalation or smell.
- In Western medicine, it used to be thought that smell did not have much impact beyond an emotional or hunger response.
- However, with breakthroughs in mapping the extensive impact of the olfactory system, we can now see the efficacy of this plant language.



## Smell Olfaction System

- The study of the science of smell is called osmology from the Greek word *osme* – smell, or odor.
- An estimated 1% of our genes are devoted to sensing aromas.
- Humans can distinguish between 2,000-4,000 different aromas.
- Our sense of smell is actually 10,000 times more sensitive than our sense of taste.



## Mechanism of Smell: Detection

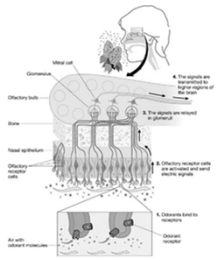
- The molecule travels to the olfactory epithelium.
- The olfactory epithelium is a patch of tissue about the size of a small postage stamp in each nostril and is the primary reception area.
- It is packed with around 40 million sensory neurons.
- It is capable of detecting .0000000013 of an ounce of certain fragrances in a single breath of air.
- Each neuron has tiny finger-like projections called cilia.
- These are bathed in mucus.

## Mechanism of Smell: Detection

- Each cilia has many extremely small odor-binding proteins embedded in its outer membrane.
- These proteins actually 'reach' for the aroma molecules.
- They are also called odor-binding proteins and are the actual binding site where the odor molecule 'docks'.
- When a receptor reacts to an odor molecule, the entire neuron may respond by sending an impulse towards the brain.



## The Mechanism of Smell





## Mechanism of Smell: Transmission

- Once the odor molecule and the receptor protein bind, a sequence of events is initiated and the transmission phase begins.
- The latest theory about receptors is that each type of receptor could recognize a different aspect of an odor molecule. The transmission impulse sent from all of the activated receptors would create an aroma image or fingerprint for the brain.



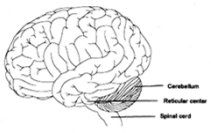
## Mechanism of Smell: Perceive

- The sensory or receptor neuron is activated and sends a transmission of the 'aroma print' in the form of electro-chemical messages and transmits it along the olfactory neurons to the twin olfactory bulbs.
- Then the transmission moves on to other regions for perception. It travels via the olfactory tract to:
  - The olfactory cortex in the temporal lobe for conscious perception of smell.
  - The limbic system in the frontal lobe for interpretation, the hippocampus for memory, and amygdala for emotional response.



## The Mechanism of Smell: Perceive

- It also can travel to the hypothalamus, which triggers glandular responses.
- The reticular formation for visceral responses to smell.






## The Mechanism of Smell: Analyze

- The sense of smell accesses the reticular system, which integrates mind and body and connects them with emotions and memories.
- The reticular formation is composed of interlacing fibers and nerve cells, which form the central core of the brain stem.
- The link between emotion, memory, and fragrance is what is so effective in the process of emotional and spiritual healing.

## Mechanism of Smell: Analyze

- Depending on the aroma perceived, the limbic system may activate the hypothalamus, the human brain's center for basic drives and emotions.
- Signals from the hypothalamus stimulate the pituitary gland to produce various hormones that in turn affect all the glands in the body.
- This then triggers physiological and emotional reactions. These signals have strong influences on feelings and behaviors.



## Other Olfactory Receptors

- Olfactory receptors have been found in other locations in the body
- Skin
- Intestines
- Sperm
- Frontal cortex



## Olfactory Receptors In Skin

- The skin contains receptors to interact with many aspects of the environment, especially in keratinocytes.
- Activation (antagonist) of the olfactory receptor OR2AT4 by synthetic sandalwood odorant Sandalore, produce stimulation of proliferation and wound-healing activity.



## Olfactory Receptors in the Intestines

- In experiments with rats, several olfactory receptors found in the duodenum were found to be selectively regulated by a high-fat diet fed to obesity prone rats.
- Researchers felt these receptors may play a part in sensing and managing dietary fat
- Important for future research in genetic predisposition to obesity.



## Olfactory Receptors in the Intestines

- Recent research is pointing to the olfactory bulbs working as an independent circadian rhythm system.
- The mechanism behind this has been unknown.
- Recently through real-time imaging of gene expression, a link was found.
- Vasoactive intestinal peptides had to be present for the olfactory bulbs to maintain circadian rhythm.



## Olfactory Receptors and Neurodegenerative Disease

- Up or down regulation of olfactory and taste receptors has been found in relation to several neurodegenerative diseases
- Parkinson disease, schizophrenia, Alzheimer's disease
- These changes in receptor expression are found in found in several parts of the brain, including the frontal cortex.

## Efficacy of Essential Oil Inhalation

- A 2012 study at the Shanghai School of Pharmacy demonstrated metabolic changes in rats after 10 days of essential oil inhalation at 45 min. per day.
- Brain tissue and urinary metabonomic analysis identified a number of altered metabolites in response to aromas intervention.



## Symmetry

Chirality Enatiomers… and why it matters.



## Chirality in Physiological Molecules

In enzymatic processes a specific molecule (substrate) is altered by attaching to a specific site on an enzyme. But the enzymatic reaction will only proceed if there is a precise fit between substrate and enzyme. In the case of chiral molecules, only one of the enantiomers will fit. The other enantiomer may not have biological activity.



Enantioselective Gas Chromatography, University of Messina, Itlay

Michelangelo Merisi, detto Il Caravaggio (1573-1610), Narciso, Roma, Galleria Nazionale



## Selected Enantiomeric Pairs

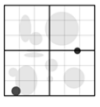
Different enantiomers of the same molecule usually have different odor:

Linalool (R)-(-) fresh, lily of the valley like
(S)-(+) slightly different odor
Limonene (R)-(-) pleasant, orange like
(S)-(-) faint mint, turpentine note
Carvone (R)-(-) herbaceous, reminiscent of dill
(S)-(+) spearmint

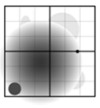


## Manmade Emphasis: Oregano

Manmade Emphasis
Thyme



natural Oregano:
50% Phenols
5% Caryophyllen



'improved Oregano'
60% Phenols
traces of Caryophyllen

irritant qualities
enhanced

## Pharmacodynamics of EOs

- Drug molecules work by binding or interacting with target molecules
- Essential oil molecules are active with several types of target molecules, these include:
  - Cell membranes, neuronal and muscular ion channels, neurotransmitter receptors, G-protein coupled and second messengers, enzymes, even DNA molecules (rarely)



## Selectivity

- Lock and Key Model
- In reality, drugs, including EOs, bind to many sites
- Want some selectivity or drug is not useful
- EOs generally have low selectivity
- Diverse components of EOs show potent selective effects. Also, the large number of constituents found in EOs allow one 'drug' to address many aspects of one disease, e.g. nervous anxiety and eczema
- Lavender can reduce anxiety on CNS level and provide topical anti-inflammatory actions



## Primary Physiological Actions of Essential Oils

- Antibacterial, antimicrobial, antiviral
- Anti-inflammatory, anti-spasmodic
- Antinociceptive (analgesic), anesthetic
- Chemopreventative (cytoprotective/cytotoxic)
- Emmenagogue
- Skin penetration and regeneration



## Antibacterial/Antimicrobial

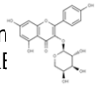
Here are top picks for antibacterial oils that show biological activity against methicillin-resistant *Staphylococcus aureus*:

- Bay *Laurus nobilis*
- Geranium *Pelargonium graveolens*
- Lavender *Lavandula angustifolia*
- Rose *Rosa damascena*
- Tea Tree Australia *Melaleuca alternifolia*



## Antibacterial
### Bay *Laurus nobilis* Essential Oil

A 2008 study isolated two compounds from bay oil. Both showed strong antibacterial activity not only against methicillin resistant *Staphylococcus aureus*, but also again *vancomycin-resistant enterococci* (VR



These two compounds from bay were found to not only have a direct action against MRSA, but also were able to enhance the effect of anti-MRSA drugs (synergism).



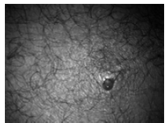
## Antibacterial
### Rose *Rosa damascena* Essential Oil

A March 2010 study showed positive antimicrobial activity of rose *Rosa damascena* against *Candida albicans* and methicillin-resistant *Staphylococcus aureus*.*

## Antibacterial
### Tea Tree *Melaleuca alternifolia* Essential Oil

Antibacterial activity of Australian tea tree oil (TTO) compared to cajuput oil niaouli oil, kanuka oil, manuka oil, and eucalyptus oil.

Tea tree oil was the highest with a Minimum Inhibitory Concentration (MIC) value of 0.25% with different bacteria that cause a wide range of infections.*





## Antibacterial
### Cinnamon *Cinnamomum Zeylanicum*



## Antibacterial Activity of Cinnamon Cinnamomum Zeylanicum Essential Oil

- A study published in March 2014 showed *Cinnamomum zeylanicum* had antibacterial activity towards 7 pathogenic strains:
- H. pylori
- E. coli
- Proteus sp
- Bacillus cereus
- K. pneumoniae
- C. freundii
- S. aureus
- Researchers felt these results showed promise for using Cinnamon EO for gastro-intestinal disorders.



## Antibacterial Activity of Cinnamon Cinnamomum Zeylanicum Essential Oil

- An in vitro study presented at the 2014 ISEO in Istanbul, Turkey.
- Found the essential oils of clove, cinnamon, and thyme to be effective against several strain of multi-drug resistant strains of bacteria.
- The researchers felt using essential oils to produce an additive effect on antibacterial drugs may be the direction of research.



## Immunomodulatory Effects of Cinnamon *Cinnamomum Zeylanicum* Essential Oil

- A study published in 2014 showed the immunomodulatory effects of Cinnamon essential oil in immune compromised mice.
- Results showed administration of Cinnamon essential oil showed a stimulatory effect on several aspects of immunity.
- Even in induced lethal E. coli abdominal sepsis in the immune compromised mice.



## Anticancer Activity of Cinnamon *Cinnamomum Zeylanicum*

- An in vitro study in 2010 compared 10 essential oils for their antibacterial and anticancer activity.
- Thyme, cinnamon, and rose had strongest antibacterial activity again *P. acnes*.
- Cinnamon had the strongest anticancer effect towards the 3 human cancer cells lines:
- A-549 (lung carcinoma), PC-3 (prostate cancer),
- MCF-7 (breast cancer)

## Effects of Blocking $Ca^{+2}$ Channel

- These channels occur in cardiac muscle, smooth muscle, and neurons.
- The nerve endings responsible for detecting pain use calcium ion channels to transmit pain messages.
- They can be deactivated if channel is blocked.
- Peppermint sensitizes cold-sensitive neurons to give cooling effect.
- Local anesthetic activity of both isomers of menthol are from calcium ion channel blocking.
- Eugenol in clove is anesthetic.

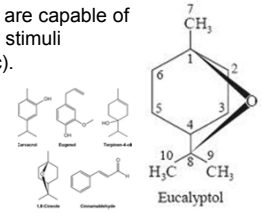


## Anti-Inflammatory/Antinociceptive

Anti-inflammatory essential oils are capable of counteracting or suppressing inflammation.

Antinociceptive essential oils are capable of reducing sensitivity to painful stimuli (also referred to as analgesic).

Cineole, also known as eucalyptol, is the active constituent.



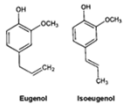



## Basil *Ocimum basilicum* Essential Oil



## Analgesic and Anti-Inflammatory Basil *Ocimum basilicum* Essential Oil

In a Brazilian study, basil *Ocimum gratissimum* was shown to be antinociceptive. In specific, it's thought the eugenol in basil is the active constituent as it can inhibit nerve conduction and prostaglandin biosynthesis.




In addition, 1,8 cineole, another major active constituent in basil essential oil, has both anti-inflammatory and antinociceptive properties.*



## Analgesic and Anti-inflammatory Basil *Ocimum Basilicum* Essential Oil

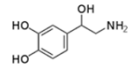
- A study presented at the 2014 International Symposium on Essential Oils.
- Showed estragole (methyl chavicol) and one of its isomers, anethole, both showed significant anti-inflammatory activity.
- Estragole has been shown in other studies to also have anticonvulsant and anesthetic activity.

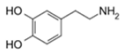


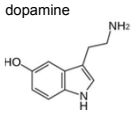
## Anti-Spasmodic Effect

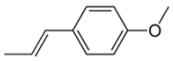
- Also due to Ca+2 Ion Channel blockage
- Can reduce hypertension
- Reduce smooth muscle contractions in heart
- Reduced smooth muscle contractions in intestines
- Prevent skeletal muscle contractions
- Methyl chavicol
- Anethole
- Esters – linalyl actate, isobutyl angelate
- Linalool

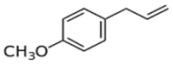
## Plant Secondary Metabolites Mimic Neurotransmitters


noradrenaline


dopamine


serotonin


anethole


methyl chavicol



## Other Areas of Application

- Cytotoxicty: potential treatment of growing cancers or tumors
- Cytoprotective: liver and skin
- Inflammation: mediating the inflammation cascade. Wound healing
- Antioxidant: radical scavengers. Prevent oxidative damage



## Chemopreventive

Chemopreventive is an essential oil helpful in preventing, slowing, stopping, healing, or reversing cancer.




## Chemopreventive Essential Oils

Here are top picks for chemopreventive essential oils:

- Clove *Syzygium aromaticum*
- Lavender *Lavandula angustifolia*
- Sandalwood *Santalum album*
- Frankincense *Boswellia carterii*



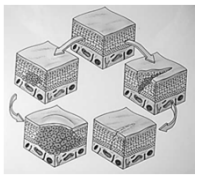
## Clove *Syzygium aromaticum* Essential Oil



## Chemopreventative

**Clove *Syzygium aromaticum* Essential Oil**

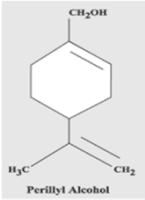
Effective in reducing abnormal cell development leading to malignant cancer.



Caused overall decline in the number of multiplying cancer cells and also boosted the numbers of cancer cell deaths.*

**Chemopreventative**
**Lavender *Lavandula angustifolia* Essential Oil**

Monoterpenes-perillyl alcohol shown to help prevent breast, lung, and liver cancers; tumor developments in leukemia; and may decrease tumor actions in pancreatic cancer.






Sandalwood *Santalum album* Essential Oil



## Chemopreventative
**Sandalwood *Santalum album* Essential Oil**

Sandalwood *Santalum album* significantly reduced the incidence of skin papillomas (or skin tags) by 67% and multiplicity of skin papillomas by 96%.

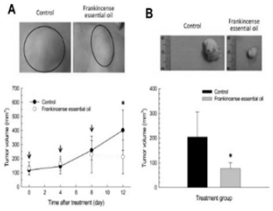


**Chemopreventative**
**Frankincense *Boswellia Carterii***

- Found to induce apoptosis / be anti-proliferative in vitro for breast cancer, prostate cancer, and bladder cancer cell lines.
- Was shown Frankincense EO disrupted cell metabolism and thus causing cell death.
- In the case of bladder cancer, it was demonstrated frankincense had no ill effect on health bladder cells.
- Preliminary research has looked at two Boswellia EOs to suppress the activation of cancer signaling molecules.



**Chemopreventative**
**Frankincense *Boswellia Carterii***




- Shown to suppress pancreatic tumor growth in mice using human pancreatic tumor xenograph.
- "30 µl Frankincense essential oil plus 70 µl PBS (phosphate buffered saline) through subcutaneous injections. Animals were treated every 4 days; and a total of 3 injections were administered."



## Internal Use of Essential Oils

- Oral administration of essential oils is common in Europe.
- A 2009 British study used capsules of lavender to study internal administration efficacy for anxiolytic effects.
  - Showed interesting, positive results.
  - Lavender reached the blood stream in 15 min.
  - Left blood stream in 60 min.

**American College of Healthcare Sciences**
**Amanda Lattin MA, MH, RA**

For questions or comments, please contact me…
amandalattin@achs.edu

www.achs.edu
www.terracinaherbals.com



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