PHARMACY VISION 2020

CSHP SEMINAR 20 • OCTOBER 21-25

Disneyland RESORT

Essential Oil Essentials

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DISCLOSURE

The speaker has no relevant financial conflicts of interest to disclose

Pharmacist Learning Objectives

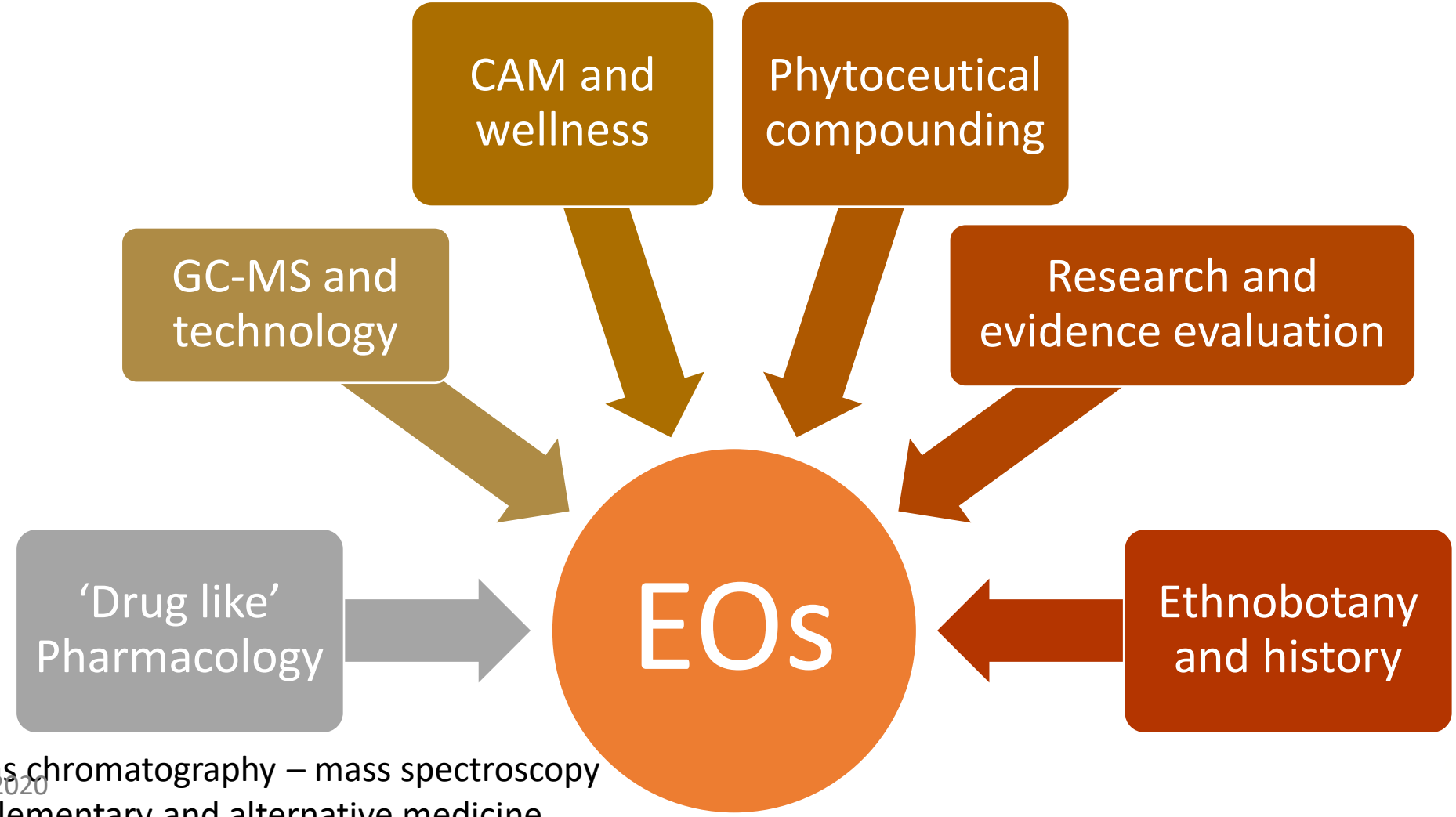
1. Describe the constituents and related pharmacology of Essential Oils (EOs)
2. Explain how EOs are regulated by the Food and Drug Administration (FDA)
3. Identify potential pharmaceutical applications of EOs
4. Summarize evidence from clinical trials for selected therapeutic applications of lavender, eucalyptus, and peppermint oils

Pharmacy Technician Learning Objectives

1. Define essential oils (EOs) and related aromatic extracts
2. Recall how EOs are regulated by the Food and Drug Administration (FDA)
3. List markers of high and low quality EOs

ESSENTIAL OVERVIEW

Why are Essential Oils Interesting to Pharmacy?



GC – MS = gas chromatography – mass spectroscopy
CAM = complementary and alternative medicine

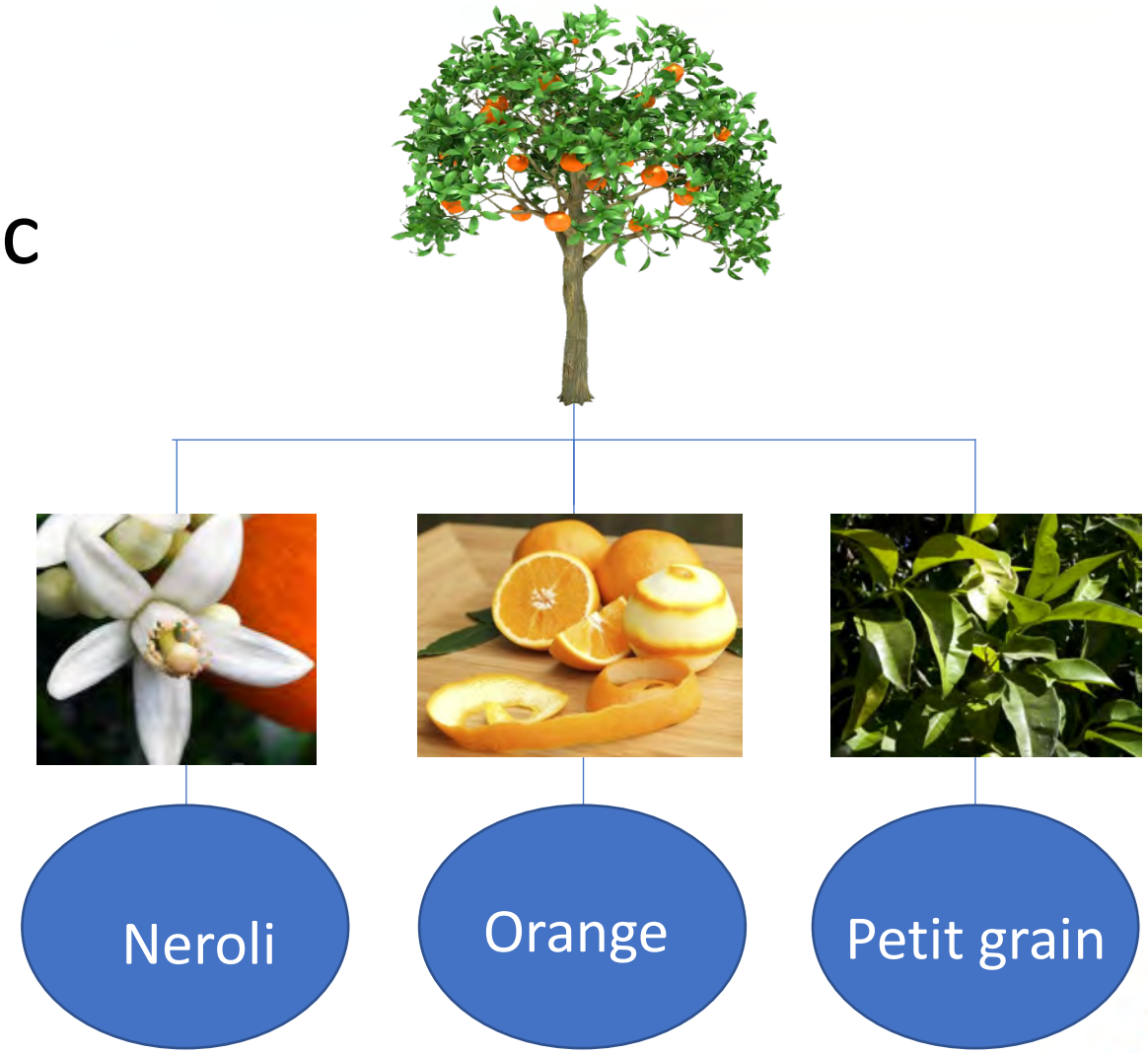
WHAT IS AN ESSENTIAL OIL?

Essential oils are blends of ***small molecule, concentrated, aromatic, and lipophilic extracts*** of botanical materials → 'drug-like' pharmacology

May be from flower, leaf, bark, root or other portion of plant

1. Handbook of Essential Oils: Science, Technology, and Applications. (2010). CRC Press, Taylor & Francis Group.

Different parts of plants produce different aromatic compounds and EOs



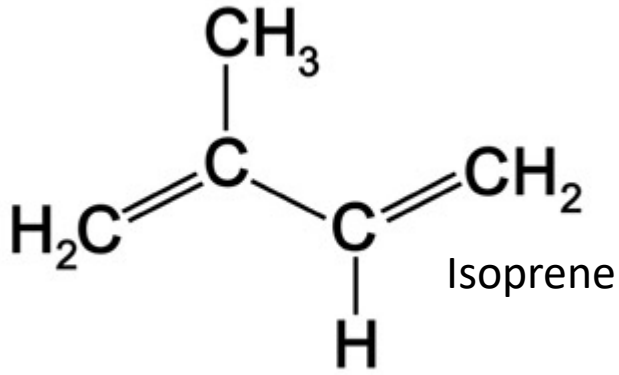
2. Tisserand H. Bitter orange: same plant, three different oils.

WHAT ARE ESSENTIAL OILS COMPOSED OF?

Isoprene → Terpenes → Functional modification ⟶ **Terpenoids**

Terpenes are composed of greater than two 5 carbon isoprene building blocks

Synthesized by terpene synthases



Isoprene

1. Handbook of Essential Oils: Science, Technology, and Applications. (2010). CRC Press, Taylor & Francis Group.

TERPENES ARE FUNCTIONALLY MODIFIED TO TERPENOIDS

Functional modifications

- Alcohol
- Ketone
- Ester
- Aldehyde
- Acid

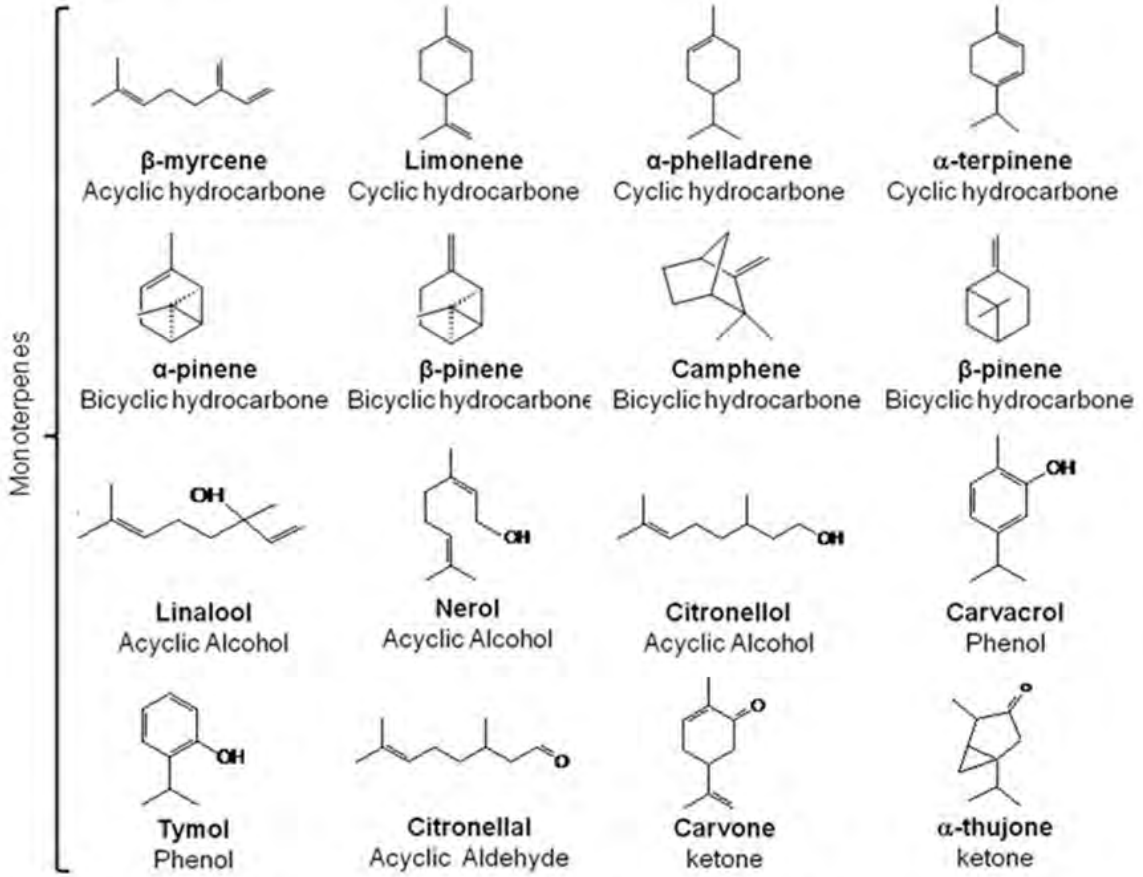


Figure 1. Examples of some monoterpenes compounds found in essential oils of plants.

3. Bayala, B., et al. (2014). *American Journal of Cancer Research, 4*, 591-607.

TERPENE TERMINOLOGY

C = Carbon

Monoterpenes (10C): most common in EO
Sesquiterpenes (15C): less common in EO

} Terpenoids found in EOs

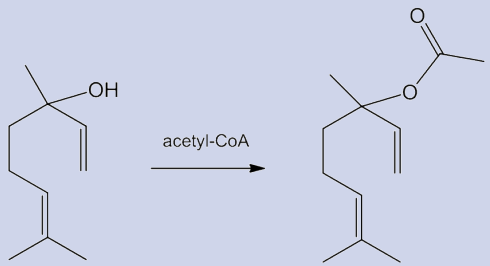
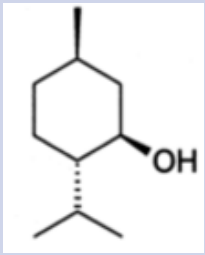
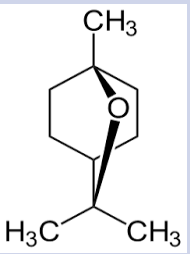
Diterpenes (20C): tetrahydrocannabinol (THC), cannabidiol (CBD)

Triterpenes (30C): cholesterol, bile acids, lovastatin, cholecalciferol, estrogen

Polyterpenes: rubber, latex, polypropylene

1. Handbook of Essential Oils: Science, Technology, and Applications. (2010). CRC Press, Taylor & Francis Group.

CYCLIZATION CREATES ENORMOUS DIVERSITY IN TERPENOIDS

	Acyclic	Monocyclic	Bicyclic
EO	Lavender	Peppermint	Eucalyptus
Primary Terpenoid	Linalool & linalyl acetate	Menthol	Eucalyptol (1,8-cineole)
Terpenoid Structure			

1. Handbook of Essential Oils: Science, Technology, and Applications. (2010). CRC Press, Taylor & Francis Group.

What are The Properties of EO Terpenoids?

Aromatic – Essential Oils are aromatic and trigger scent-based chemoreceptors

Lipophilic – all essential oils are…oils; may readily traverse cell membranes

Small molecules – typically only mono- and sesquiterpenoids are extracted (10-15 carbon unit backbone)

Bioactive – terpenoids are produced for functional purposes

Concentrated – most oils are 50-100x concentrated relative to plant

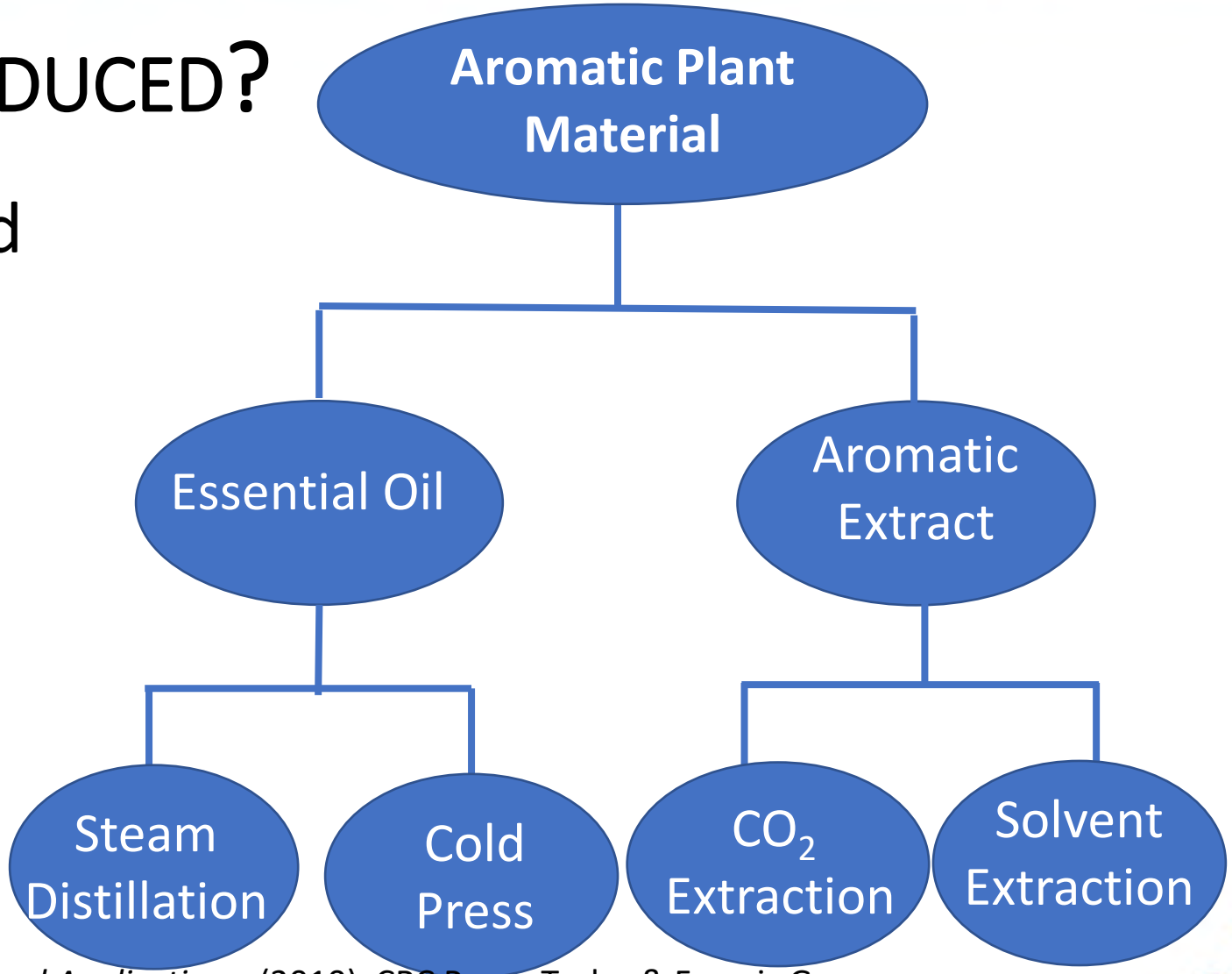
Botanical variability – terpenoid composition has considerable heterogeneity

1. Handbook of Essential Oils: Science, Technology, and Applications. (2010). CRC Press, Taylor & Francis Group.

ESSENTIAL OIL PRODUCTION

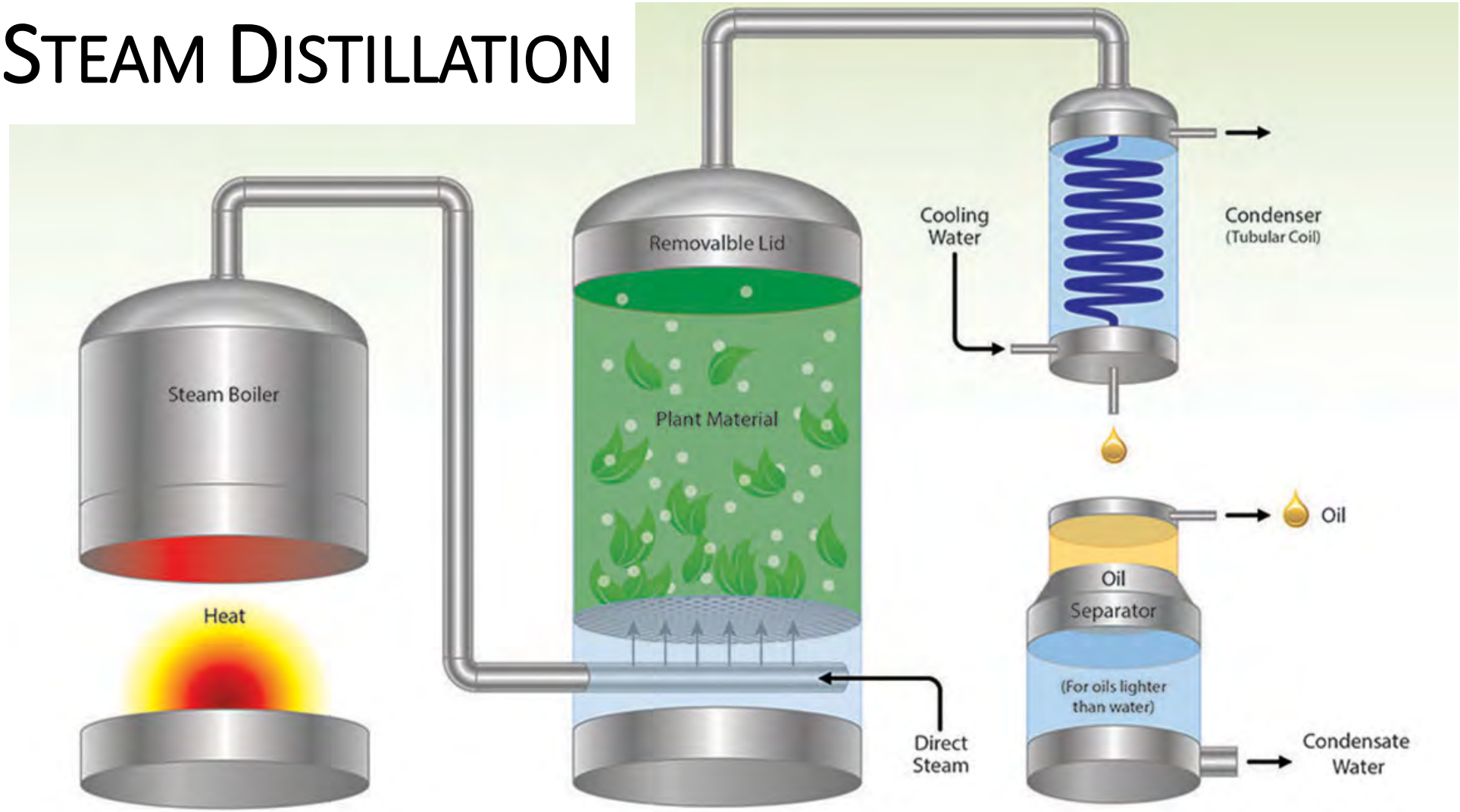
How are EOs Produced?

Most EOs are produced via steam distillation



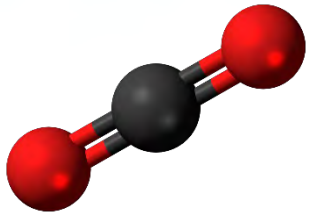
1. Handbook of Essential Oils: Science, Technology, and Applications. (2010). CRC Press, Taylor & Francis Group.

STEAM DISTILLATION



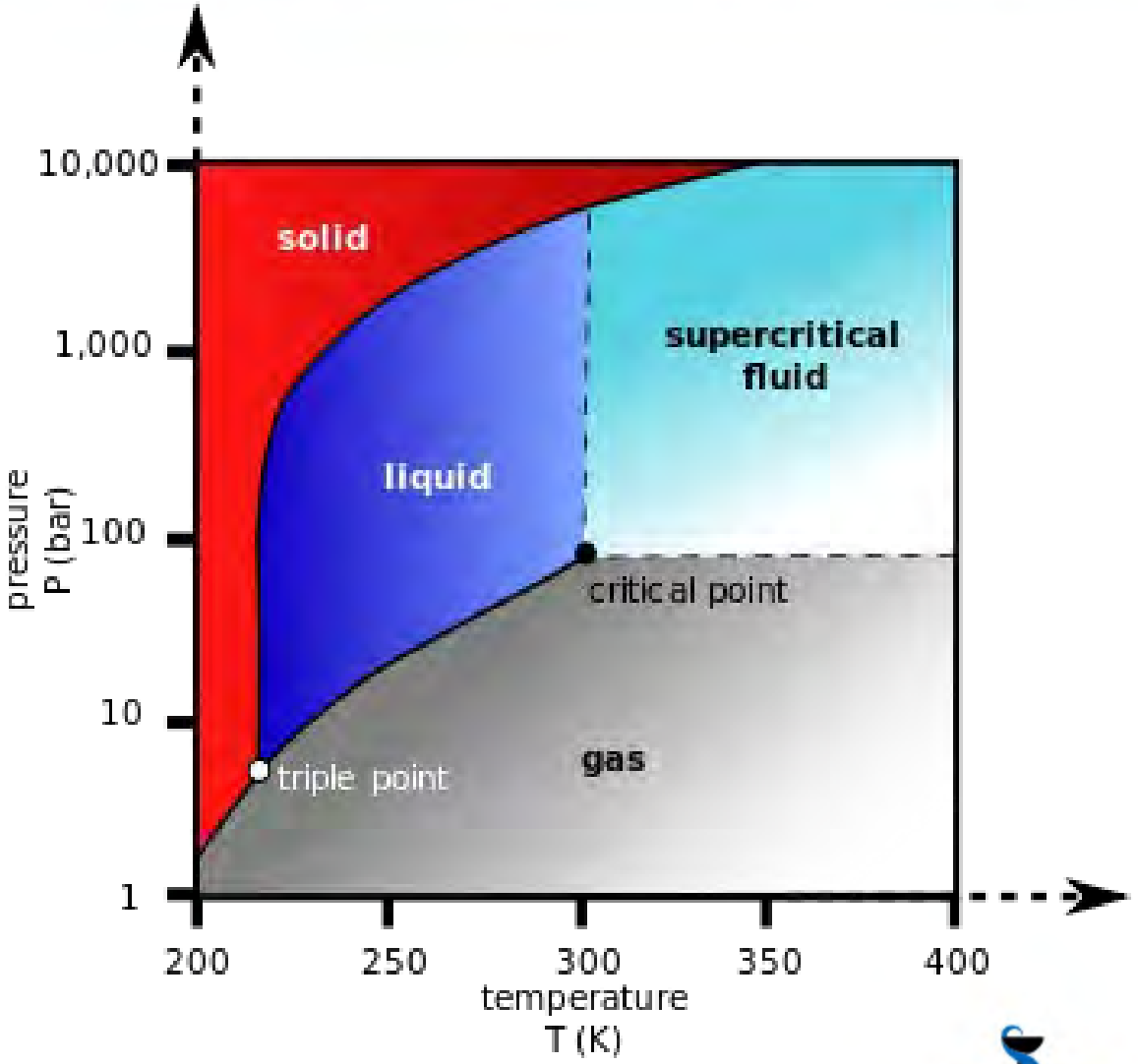
DoTerra Science. https://www.doterra.com/US/en/blog/science-research-news-steam-distillation. Accessed 9/14/20

CO_2 Extraction



Also termed supercritical fluid extraction (SCF)

Under heat and pressure CO_2 becomes a SCF which behaves as a solvent



1. Handbook of Essential Oils: Science, Technology, and Applications. (2010). CRC Press, Taylor & Francis Group.

Regulation of Essential Oils

Application Methods of Essential Oils

Topical or transdermal

Inhaled as aromatherapy

Inhaled as vapor

Internally as sublingual, capsules, beverage or food

Internally as suppository

4. Tisserand R. *Essential Oil Safety: A Guide for Healthcare Professionals* (2013). 2nd Edition: Elsevier.

Regulation Depends on Use Case

Preservative or fumigant

Household cleaning

Flavoring agents

Dietary supplementation

Cosmetics

Therapeutic applications

Intended Use

May be established via several mechanisms:

- Claims
- Consumer perception
- Ingredients that are known to have therapeutic use

Some products may meet the definition of multiple categories

- E.g. if an EO is marketed as a skin lubricant it's a cosmetic, yet if it is being used as a topical pain relief agent, it's also a drug

5. FDA. (2018). Is it a cosmetic, a drug, or both? (or is it a soap?). Retrieved from https://www.fda.gov/cosmetics/cosmetics-laws-regulations/it-cosmetic-drug-or-both-or-it-soap. Accessed 9/14/20

EOs and Key Regulatory Laws

Regulatory Category	Regulatory Authority	Category Description
Cosmetic	Food Drug and Cosmetic Act of 1938	Products intended for cleaning or beautification
Dietary Supplement	Dietary Supplement Health and Education Act 1994	Limited to structure/function claims. Requires substantiation for claim if requested by FDA
Food Additive	Food additives amendment of 1958	Generally Recognized as Safe (GRAS) status defined in CFR §182.20
Drug	Food Drug and Cosmetic Act of 1938	Makes therapeutic claim and requires approval via clinical trials. Intends to diagnose, treat, prevent or cure an illness.

5. FDA. (2018). Is it a cosmetic, a drug, or both? (or is it a soap?). Retrieved from https://www.fda.gov/cosmetics/cosmetics-laws-regulations/it-cosmetic-drug-or-both-or-it-soap. Accessed 9/14/20

Shelf Life and Oil Quality

Storage and Purchasing

ESSENTIAL OILS OXIDIZE OVER TIME, CHANGING THEIR COMPOSITION, SCENT, AND POTENCY.

- Exposure factors that increase oxidation
  - Heat
  - Light
  - Air
  - Time

- Store in a cool, dry, place away from light

1. Handbook of Essential Oils: Science, Technology, and Applications. (2010). CRC Press, Taylor & Francis Group.

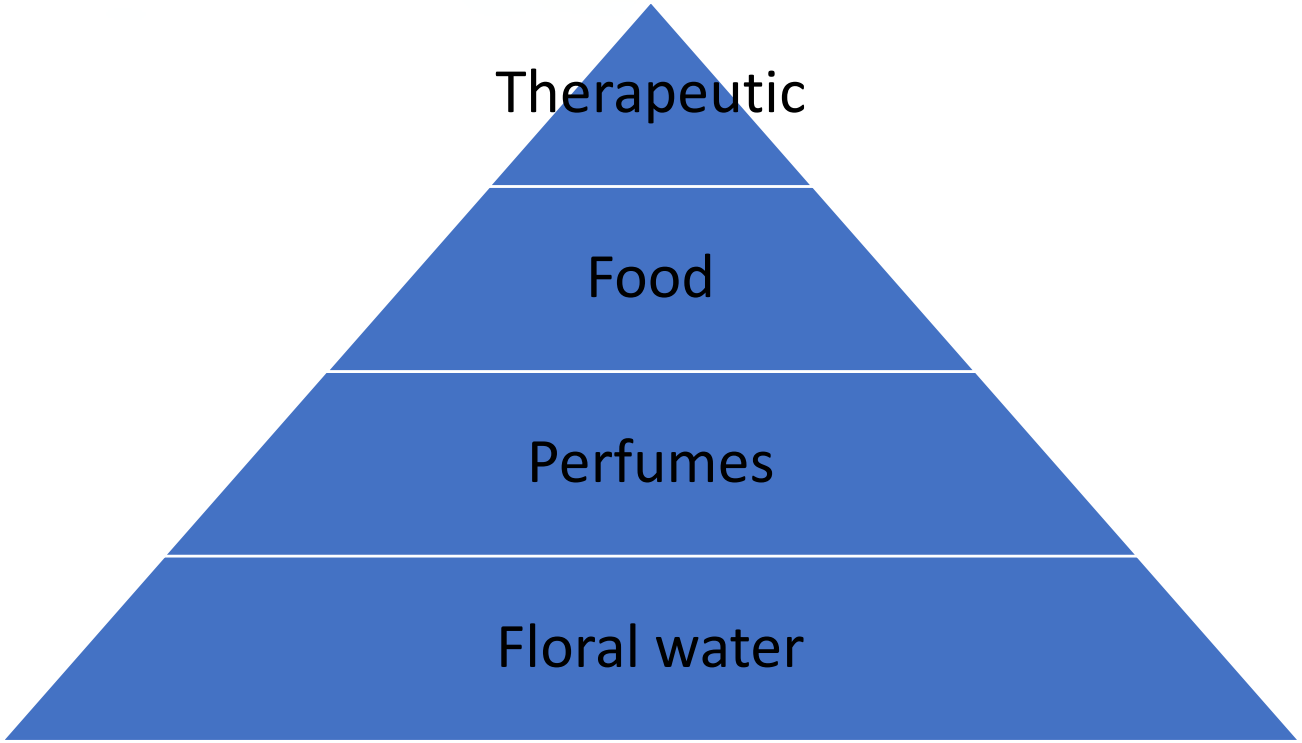
Shelf-Life of Essential Oils

- Oxidation rates vary although most oils can be used for at least 1-2 years
- Cold-pressed oils may have shorter shelf-lives, around 6 months
- Will not smell ‘rancid’ if oxidized, although the scent may change
- Desirable to have production date on label

1. Handbook of Essential Oils: Science, Technology, and Applications. (2010). CRC Press, Taylor & Francis Group.

There is little or No government regulation of EO quality and high variability of EO quality available.

Buyer beware!



Contamination with organic solvents or misrepresentation with synthetic substitutes is common

JUDGING ESSENTIAL OIL QUALITY

Low Quality Oils

- Labeled as natural oil or perfume oil
- Packaged in plastic or non light-resistant container
- Little information about oil disclosed on label
- Large quantity for price

High Quality Oils

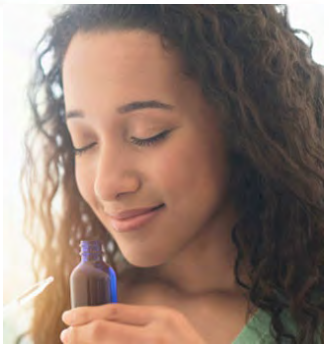
- From ‘organic, non-sprayed, or wild crafted’ plant materials
- Packaged in light-resistant glass
- Method of production, species of plant, date produced, and country of origin on label
- GC-MS or other pedigree data for oil available from seller
- Smaller quantities sold – price variability among product offerings

- *1. Handbook of Essential Oils: Science, Technology, and Applications*. (2010). CRC Press, Taylor & Francis Group.

Use of Essential Oils

Aromatherapy & Topical Application

WHAT IS AROMATHERAPY?



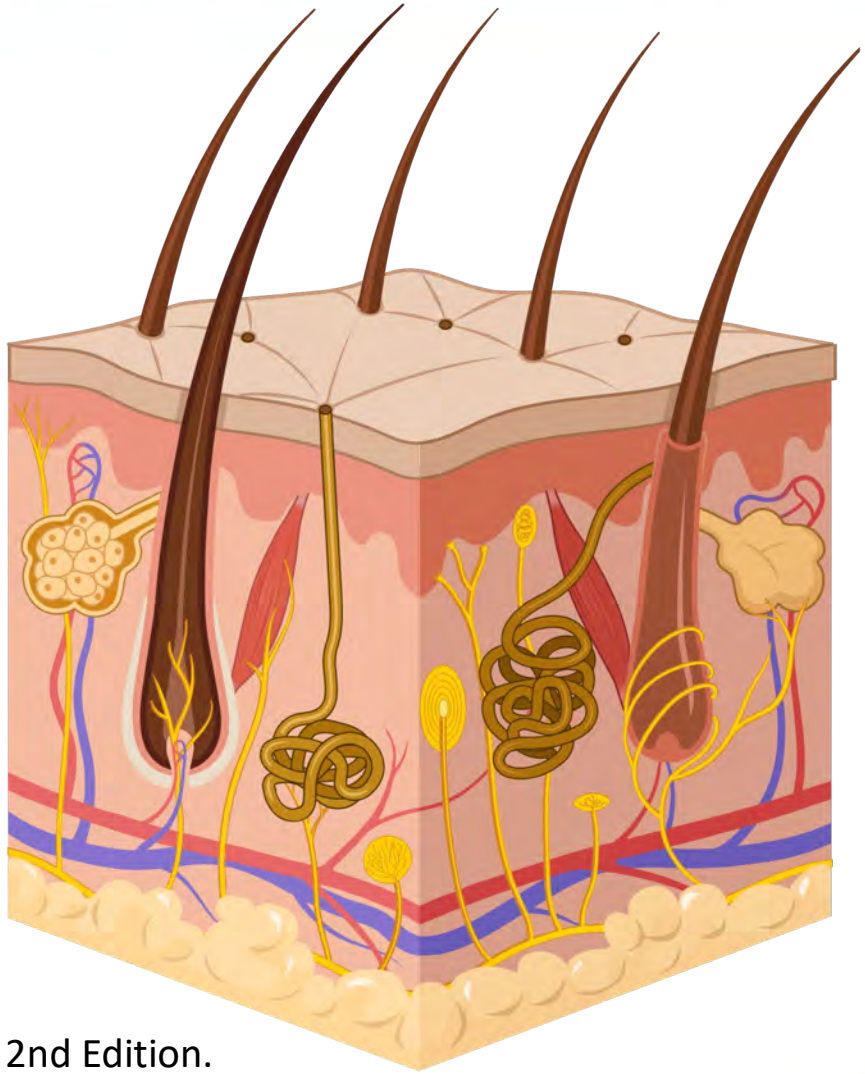
"The art and science of utilizing naturally extracted aromatic essences from plants to balance, harmonize and promote the health of body, mind and spirit"

"Seeks to unify physiological, psychological and spiritual processes to enhance an individual's innate healing process"

6. NAHA. What is Aromatherapy? Retrieved from https://naha.org/explore-aromatherapy/about-aromatherapy/what-is-aromatherapy/. Accessed 9/14/20

INTEGUMENT'ARY

- EO may be absorbed via the epidermis or hair follicles
- EOs may enhance the penetration of other drugs through the stratum corneum
- Caution with widespread application of high potency oil blends
- Hypersensitivity reactions possible



4. Tisserand R, Essential Oil Safety: A Guide for Healthcare Professionals (2013). 2nd Edition.
7. Jiang, Q., et al (2017). Pharm Biol, 55(1), 1592-1600.

Topical Use and Oil Dilution

Most essential oils require dilution prior to topical application

Amount of dilution required depends upon:

- The intended use
- The oil(s) being used
- Individual sensitivity → skin patch allergen testing (rule out hypersensitivity)

Dilution performed with carrier oil ('inert' oil that carries EO)

- Gel or lotion can be used along with emulsifier and preservative

4. Tisserand R, Essential Oil Safety: A Guide for Healthcare Professionals (2013). 2nd Edition.

SOME* CONSIDERATIONS FOR TOPICAL EO DILUTION

AGE

Age range	Dilution range
Up to 3 months	0.1-0.2%
3-24 months	0.25-0.5%
2-6 years	1-2%
6-15 years	1.5-3%
15 or older	2.5-5%

USE

End use	Dilution range
Facial cosmetics	0.2-1.5%
Body massage	1.5-3%
Bath & body products	1-4%
Specific problems	4-10%
Pain, wounds	5-20%

*Individual EOs can have wide ranges of appropriate dilutions including some that can be applied undiluted (neat)!

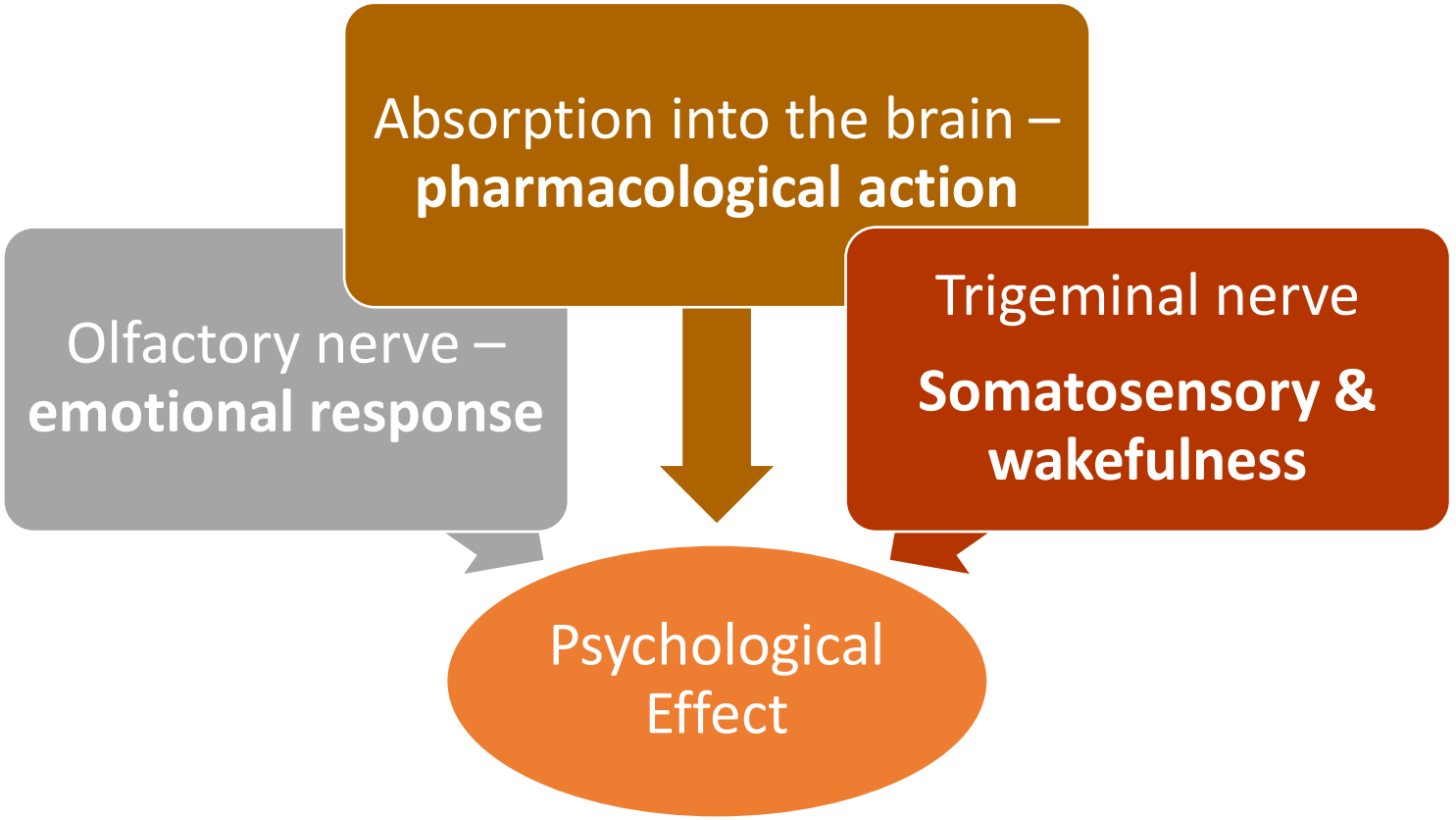
8. Tisserand R. How to Use Essential Oils Safety. https://tisserandinstitute.org/safety/safety-guidelines/. Accessed 9/24/20

OL'FACT'ORY

- Evolutionarily critical sense for survival and well-being
- Humans can recognize and remember ~10,000 different odors
- Smell mediated by superfamily of G-protein coupled receptors comprised of ~1000 unique receptors
- Smell receptors compose ~3-4% of the human genome

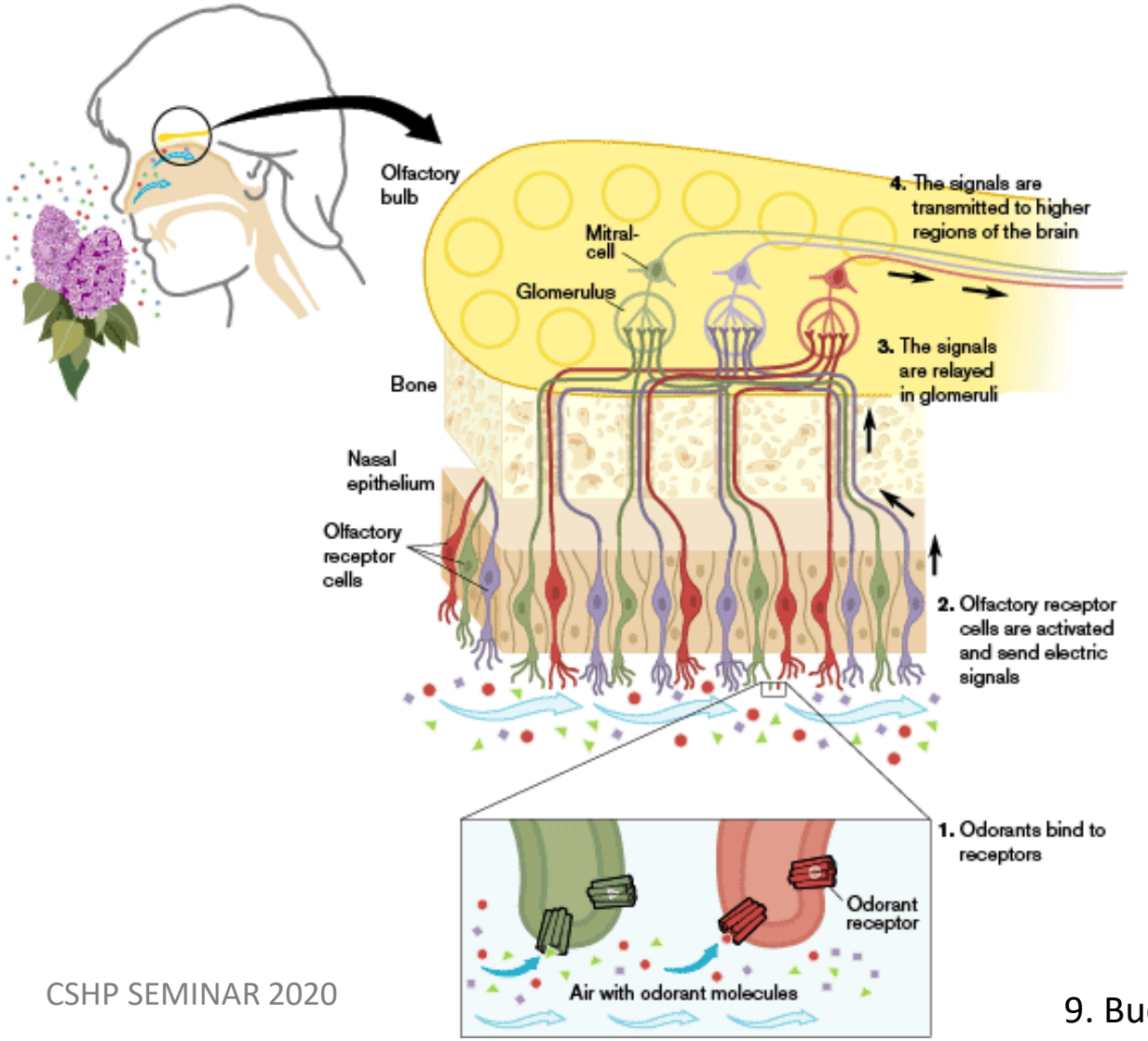
9. Buck L & Axel R. Cell 1991;65:175-87

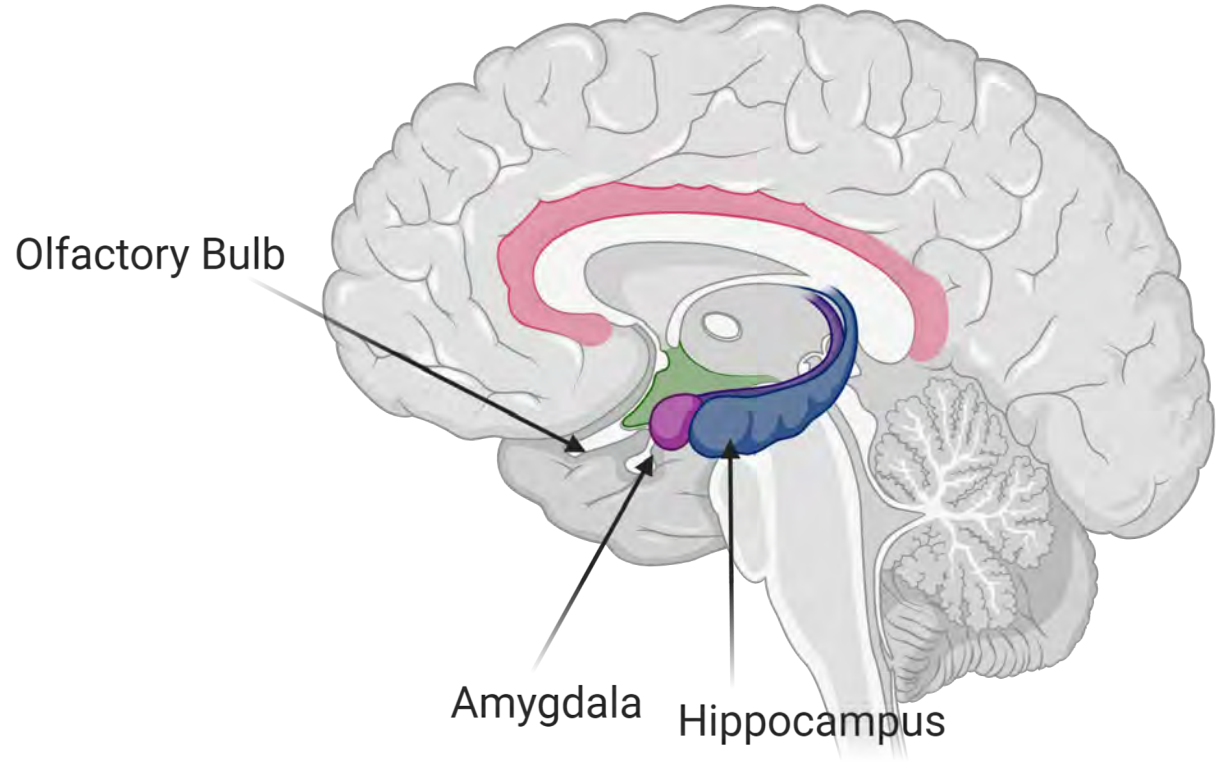
MECHANISMS OF AROMATHERAPY



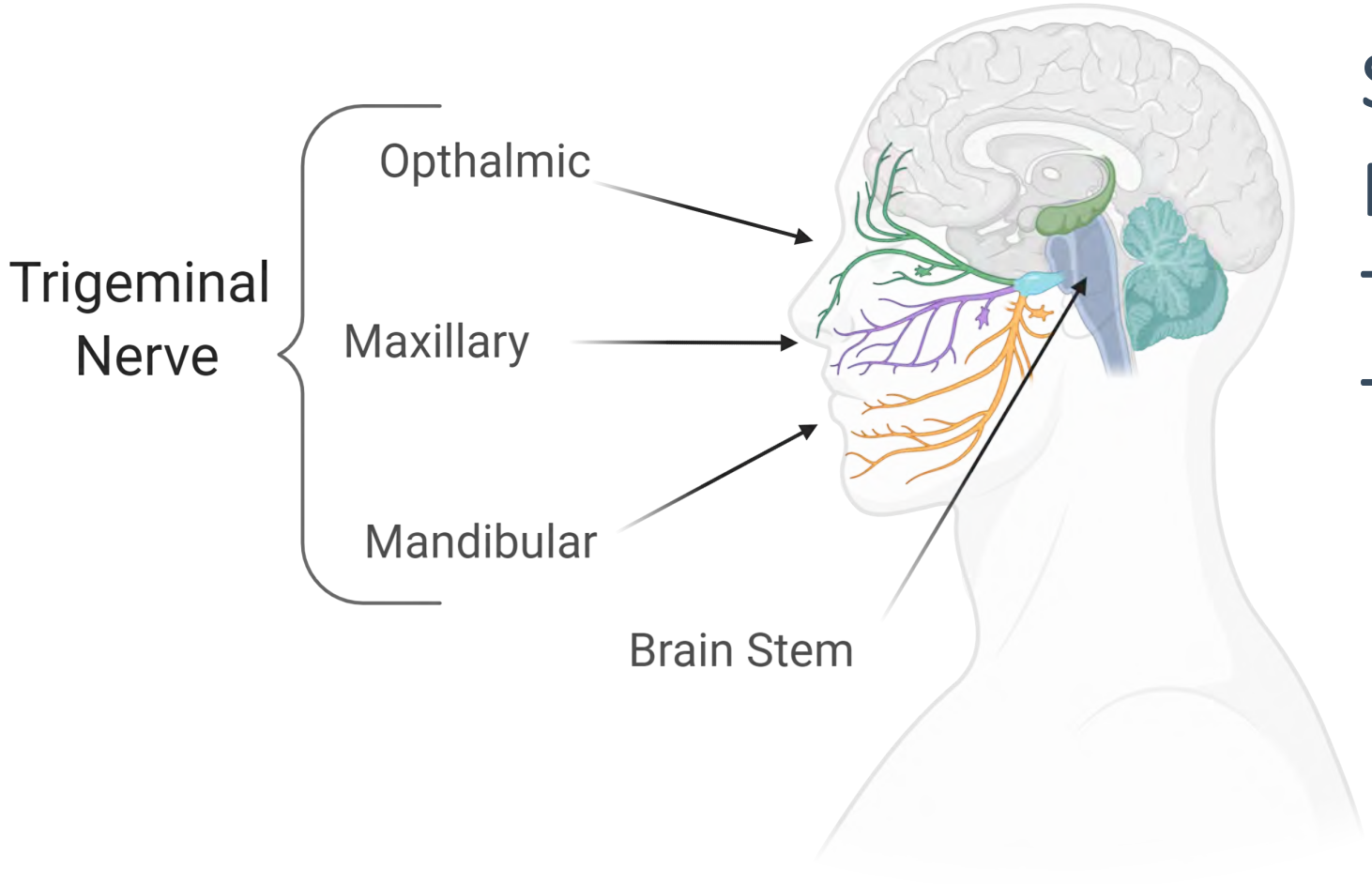
1. Handbook of Essential Oils: Science, Technology, and Applications (2010). CRC Press, Taylor & Francis Group.

Smell Detection and Processing





9. Buck L & Axel R. Cell 1991;65:175-87



THE TRIGEMINAL NERVE SERVES A SOMATOSENSORY FUNCTION AND PROJECTS TO AROUSAL CENTERS IN THE BRAINSTEM.

1. Handbook of Essential Oils: Science, Technology, and Applications (2010). CRC Press, Taylor & Francis Group.

Is Aromatherapy Evidence-Based?

Studies of aromatherapy are difficult to conduct with methodologic rigor

- Inability to blind participants to scents
- Variability in participant response due to psychological effect
- Confounding variables (massage or human touch - placebo)
- Small sample sizes and low funding
- Variability in oil quality and constituents

10. Howard, S., & Hughes, B. M. (2008). Br J Health Psychol, 13(Pt 4), 603-617.

AROMATHERAPY HAS MANY POTENTIAL APPLICATIONS AND IS TYPICALLY A LOW-RISK INTERVENTION.

- Applications: anxiety/stress, post-operative nausea & vomiting, productivity in the workplace, calming for nap-time at day care
- Risk is low if oil directly inhaled or diffused, risk is increased when aromatherapy is combined with topical application
- May combine with other therapeutic concepts such as ritual or the placebo effect to achieve outcomes

11. Malcolm, B.J. and K. Tallian. Mental Health Clinician, 2017. 7(4): p. 147-155.

Therapeutic Use of Essential Oils

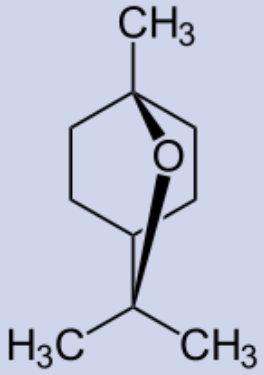
Lavender, Eucalyptus, Peppermint

Use of Essential Oils by Mouth

- Contact with mucous membranes
- Higher systemic exposure
- Small amounts of GRAS oils likely safe
- Use of studied constituent may be safer than use of full spectrum oil
- Requires professional oversight with therapeutic intention
- Allows double-blinded and placebo-controlled experimentation

4. Tisserand R, Essential Oil Safety: A Guide for Healthcare Professionals (2013). 2nd Edition.

EUCALYPTUS OIL – EUCALYPTUS SPP.

Primary constituent	Uses	Safety	Regulatory Designation	Application
1,8-cineole 	Vasodilator, asthma, congestion, expectorant, upper respiratory infection, bronchitis, analgesia, cooling, anti-inflammatory	Dilute for topical application in sensitive individuals **<u>Not a GRAS oil</u>**	Supplement	Diffusion Aromatherapy Topical (neat or dilute 1:1) Disinfectant

12. Galan, D.M., et al., Journal of Essential Oil Research, 2020: p. 1-8.

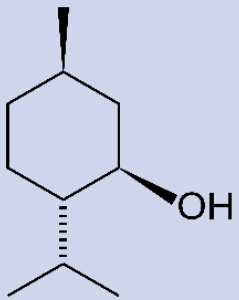
Trials of Eucalyptol (1,8-cineole) in Respiratory Disorders

2 in Asthma, 1 in Chronic Obstructive Pulmonary Disease, 1 in Rhinosinusitis, 1 in Bronchitis

- All give eucalyptol 200mg PO TID a.c.
- Trials with varying lengths and endpoints (weeks – 6 months)
- All produced safe and beneficial outcomes
- Eucalyptol 200mg available as standardized products

12. Galan, D. M., et al. (2020). Journal of Essential Oil Research: 1-8.

PEPPERMINT - *MENTHA PIPERITA*

Primary constituent	Uses	Safety	Regulatory Designation	Application
menthol 	Alertness, cooling, respiratory conditions, irritable bowel syndrome, muscle aches	Dilute at least 1:1 for topical application, avoid application close to eyes. Enteric Coated (EC) Capsules internally	GRAS	Diffusion Aromatherapy Topical (dilute) Internal (therapeutic)

Use enteric coated capsules for internal use – menthol relaxes the lower esophageal sphincter and can cause acid reflux if ingested in regular capsule

13. Stacy L. Haber, Shareen Y. El-Ibiary. American Journal of Health-System Pharmacy Jan 2016, 73 (2) 22-31

MENTHOL

- Used as a flavoring agent in foods
- ↑ addictive risk of cigarettes
- Use in cough drops
- Often combined with camphor and methyl salicylate in muscle rubs

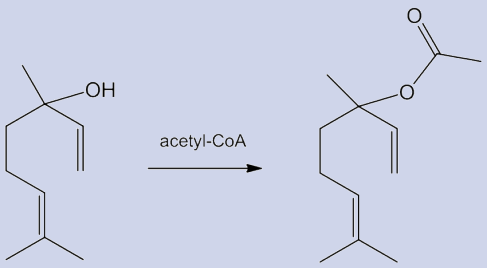
14. Alexander LA et al. Nicotine Tob Res. 2016 Apr;18 Suppl 1:S91-101

Peppermint Oil and Irritable Bowel Syndrome (IBS)

- Carminative, antiemetic, and antispasmodic
- **Efficacy and safety improved in 6 trials that use EC peppermint capsules**
  - GERD, perianal burning, high trial attrition rates
  - Given as 0.2-0.4ml peppermint oil TID (standardized) x 8 weeks
- Drug-Drug Interactions
  - CYP 1A2, 2C19, 2C, and 3A4 inhibition
  - Agents that interfere with gastric pH; space by at least 2 hours
- Contraindication
  - Achlorhydria, pregnancy or nursing, hypersensitivity

13. Haber SL, El-Ibiary SY. *Am J Health Syst Pharm*. 2016;73(2):. doi:10.2146/ajhp140801

LAVENDER - *LAVANDULA ANGUSTIFOLIA*

Primary constituents	Uses	Safety	Regulatory Designation	Application
Linalool and linalyl acetate 	Anxiety, relaxation, analgesic, wound healing, bug bites, poison ivy relief, insomnia, migraine, perfumery	Contact dermatitis possible, although overall **one of the safest EOs**	GRAS	Diffusion Aromatherapy Topical (neat ok) Internal

11. Malcolm, B.J. and K. Tallian. Mental Health Clinician, 2017. 7(4): p. 147-155.

Lavender Oil and Anxiety Disorders

- 5 RCTs with positive results
  - 3 with placebo, 2 with active control (lorazepam 0.5mg or paroxetine 20mg)
  - 4-8 weeks in length
- All trials use a standardized lavender oil extract
  - Linalool and linalyl acetate (36.8% and 34.2%) 80mg gel capsules
- Once or twice daily
- Well tolerated, lacks withdrawal syndrome in week after use
  - Lavender taste upon eructation

11. Malcolm, B.J. and K. Tallian. Mental Health Clinician, 2017. 7(4): p. 147-155.

SUMMARY & CONCLUSIONS

- Relative to other botanical and herbal products, EOs have pharmacology that is considerably more ‘drug-like’
- EO regulation depends on use case, however there is little regulation on product quality overall and discretion in product use is required
- Data with eucalyptus, peppermint, and lavende oil constituents support potential for internal use in various therapeutic indications
- Pharmacy professionals have an important role to play in safeguarding public health and educating persons on how to use EOs effectively

POST-TEST QUESTIONS

WHICH OF THE FOLLOWING ARE COMMON PROPERTIES OF ESSENTIAL OILS?

A. Hydrophilic and dilute
B. Lipophilic and concentrated
C. Aromatic and dilute
D. Hydrophilic and concentrated

Select the Statement Regarding FDA Regulation of Essential Oils that is Accurate:

A. The FDA regulates essential oils like drugs
B. The FDA regulates essential oils like supplements
C. The FDA regulates essential oils like cosmetics
D. All of the above; the FDA regulates essential oils based on intended uses

Choose the Markers which can Indicate High Oil Quality:

A) Clear plastic container, labeled as natural oil
B) Large quantity for price, labeled as perfume oil
C) Light-resistant glass, labeled with origin country and production date
D) Clear glass container, found on clearance rack at large retailer

WHICH IS TRUE OF PEPPERMINT OIL?

A) Internal use is contraindicated in pregnancy
B) Enteric Coated (EC) capsules reduce incidence of acid-reflux
C) Peppermint oil may treat Irritable Bowel Syndrome (IBS)
D) Menthol is found in cough lozenges and muscle rubs
E) All of the above

SELECT THE INDICATION FOR WHICH LAVENDER OIL HAS GOOD QUALITY EVIDENCE FROM RANDOMIZED TRIALS?

A) Generalized Anxiety Disorder
B) Schizophrenia
C) Insomnia
D) Asthma
E) Chronic idiopathic urticaria

REFERENCES

1. Handbook of Essential Oils: Science, Technology, and Applications, ed. K.B.G. Baser. 2010: CRC Press, Taylor & Francis Group.
2. Tisserand H. Bitter orange: same plant, three different oils. Available from: https://tisserandinstitute.org/learn-more/bitter-orange-same-plant-three-different-oils/. Accessed 9/14/20
3. Bayala, B., et al., Anticancer activity of essential oils and their chemical components -a review. American Journal of Cancer Research, 2014. 4: p. 591-607.
4. Tisserand R, Y.R., Essential Oil Safety: A Guide for Healthcare Professionals. Vol. 2nd Edition. 2013: Elsevier.
5. FDA. Is it a cosmetic, a drug, or both? (or is it a soap?). 2018; Available from: https://www.fda.gov/cosmetics/cosmetics-laws-regulations/it-cosmetic-drug-or-both-or-it-soap. Accessed 9/14/20
6. NAHA. What is Aromatherapy? ; Available from: https://naha.org/explore-aromatherapy/about-aromatherapy/what-is-aromatherapy/. Accessed 9/14/20
7. Jiang, Q., et al., Development of essential oils as skin permeation enhancers: penetration enhancement effect and mechanism of action. Pharm Biol, 2017. 55(1): p. 1592-1600.

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8. R., T. *How to Use Essential Oils Safely: General Safety Guidelines*. Available from: https://tisserandinstitute.org/safety/safety-guidelines/. Accessed 9/14/20

9. Buck, L. and R. Axel, *A novel multigene family may encode odorant receptors: a molecular basis for odor recognition.* Cell, 1991. **65**(1): p. 175-87.

10. Howard, S. and B.M. Hughes, *Expectancies, not aroma, explain impact of lavender aromatherapy on psychophysiological indices of relaxation in young healthy women.* Br J Health Psychol, 2008. **13**(Pt 4): p. 603-17.

11. Malcolm, B.J. and K. Tallian, *Essential oil of lavender in anxiety disorders: Ready for prime time?* Mental Health Clinician, 2017. **7**(4): p. 147-155.

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