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Essential oils and single fragrance compounds  
in health care

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**Abstract:**

The positive effects of essential oils and aromatherapy on well-being have been known for centuries. As a consequence the use of this complementary therapy is becoming increasingly popular with nurses and more and more common in hospitals. Because of their diverse effects, essential oils can be used in different areas of care. This paper covers the following areas in detail: insomnia, anxiety, cancer, dementia, pain management, infections, wound healing, and oral care. Numerous studies have shown that aromatherapy goes very well with massage and that massage can amplify the effect of aromatherapy. Since the use of essential oils for inhalation and massage has an effect on the development of a disease, it is difficult to make a precise judgment of when treatment with essential oils is no longer considered as nursing, but as therapy. Sleep quality can be improved by the inhalation of essential oils (e.g. lavender) alone, which causes an increase in the strength of the human body. This can be explained by the fact that many regenerative processes take place during sleep. Essential oils are a mixture of many substances. Several substances contained therein can act either synergistically or antagonistically, but can also have completely different effects on the body. The quality and composition of essential oils play a substantial role and there is a need for accurate quality-control and standardization. It is important to consider several aspects regarding essential oils to ensure their safe use.

## **Zusammenfassung:**

Komplementäre Therapiemethoden werden in der Pflege immer beliebter. Die positiven Wirkungen von ätherischen Ölen und Aromatherapie sind seit Jahrhunderten bekannt. Aufgrund ihrer unterschiedlichen Effekte können ätherische Öle in verschiedenen Bereiche der Pflege eingesetzt werden. In dieser Diplomarbeit wird auf die folgenden Bereiche näher eingegangen: Schlafstörungen, Angst, Krebs, Demenz, Schmerzbehandlung, Infektionen, Wundheilung und Mundpflege. Zahlreiche Studien zeigten, dass durch eine Kombination von Aromatherapie und Massage, die jeweilige Wirkung verstärkt werden kann. Da ätherische Öle auch einen Einfluss auf das jeweilige Krankheitsbild haben, ist es schwierig eine genaue Grenze zwischen Pflege und Therapie zu ziehen. Zum Beispiel kann die Schlafqualität durch die Inhalation von ätherischen Ölen (z.B. Lavendel) verbessert werden. Da während des Schlafes regenerative Prozesse stattfinden, kann dadurch auch der Allgemeinzustand verbessert werden.

Ätherische Öle sind Vielstoffgemische. Die verschiedenen Substanzen in einem ätherischen Öl können nun auf den Körper synergistisch oder antagonistisch wirken oder auch verschiedene Wirkungen haben. Die Qualität und die Zusammensetzung der ätherischen Öle spielen hier eine wichtige Rolle, weswegen eine strenge Qualitätskontrolle und Standardisierung wichtig ist. Bei der Verwendung von ätherischen Ölen ist es wichtig einige Aspekte zu beachten um eine sichere Anwendung zu gewährleisten.

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## **I. Introduction**

**A. Essential oils:** "An essential oil is a concentrated hydrophobic liquid containing volatile aroma compounds from plants. Essential oils are also known as volatile oils, ethereal oils or aetherolea, or simply as the "oil of" the plant from which they were extracted, such as oil of clove. An oil is "essential" in the sense that it carries a distinctive scent, or essence, of the plant." [1] Essential oils consist of mixtures of different terpenes, sesquiterpenes and aromatic compounds. [2]

**B. Aromatherapy:** "Aromatherapy is an independent area of phytotherapy and is defined as the controlled use of essential oils to promote health, to relieve symptoms and to treat disease." [3]

**C. Nursing:** The International Council of Nurses (ICN) defines nursing as the following: "Nursing encompasses autonomous and collaborative care of individuals of all ages, families, groups and communities, sick or well and in all settings. Nursing includes the promotion of health, prevention of illness, and the care of ill, disabled and dying people. Advocacy, promotion of a safe environment, research, participation in shaping health policy and in patient and health systems management, and education are also key nursing roles." [4]

Care can be divided into: [5]

- Health and Nursing
- Child Nursing
- Elderly Care
- Health Education Nursing

In all areas of care, aromatherapy is a very popular alternative method. In Austria, certified nurses can make the additional trainings programm "Complementary Care - Aroma Care" GuKG to § 64 [6]. This course takes 180 hours and includes theoretical and practical knowledge on the use of aromatherapy. [7]

#### **D. Administering of essential oils:**

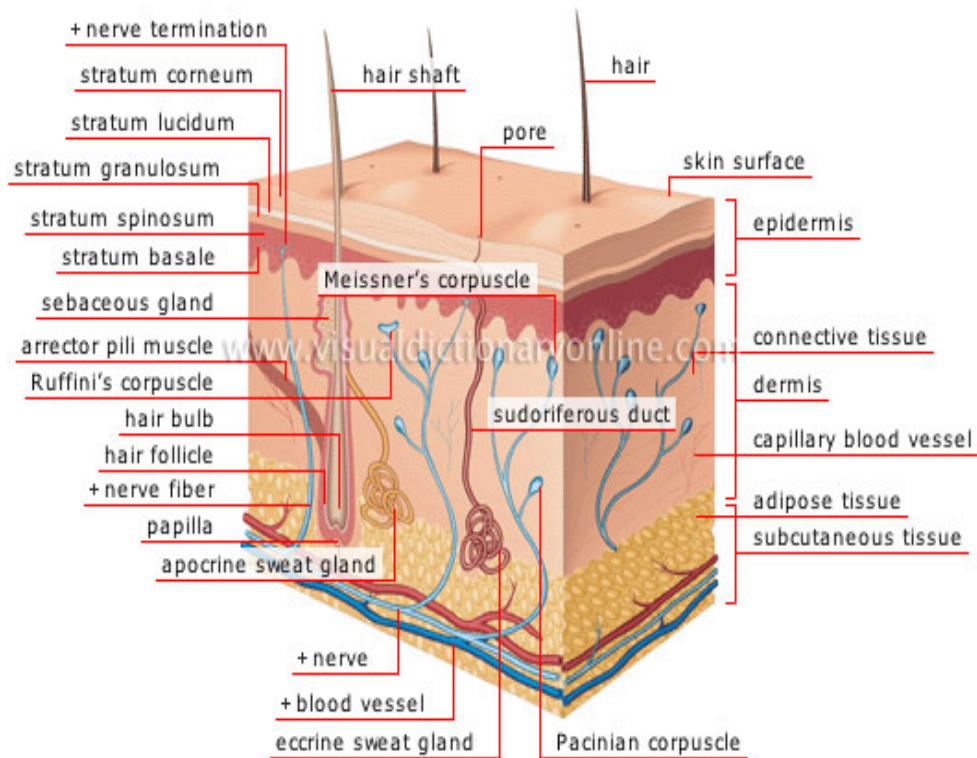
Essential oils can be absorbed through 4 ways: [8]

- Inhalation: with or without steam, with an AromaStreamer, aromatic pillow or sachets..
- Topical: Applied to the skin or combined with massage and baths
- Internal: “mouthwashes, showers, pessaries or suppositories”
- Oral: “via gelatine capsules or diluted in honey, alcohol, etc.” (commercial products) [8]

Ad inhalation: In an animal experiment using mice, Jirovetz et al. showed that linalool and linalyl acetate were detectable in blood after inhalation. The authors were able to demonstrate that the inhaled molecules can be absorbed through the nasal or bronchial mucosa and entered the bloodstream to the organs. A demonstrable physiological effect was detected on the organs. Thus, it could be shown that inhaled essential oils can not only activate the olfactory system, (see below) but can also have a directly effect on different receptors. [9]

Ad topical use: Essential oils can also be absorbed very well through the skin because of their lipophilicity. This allows them to reach the bloodstream. The intake level depends on the concentration of the essential oil, the exposure time, the surface of the skin to which it is applied and whether or not the skin is hyperemic. Essential oils, such as terpenes, can act as a penetration enhancer, which means they can break through the barrier properties of the stratum corneum and allow other substances to be absorbed easily. [10]

Structure of the skin: (Fig. 1) [11]

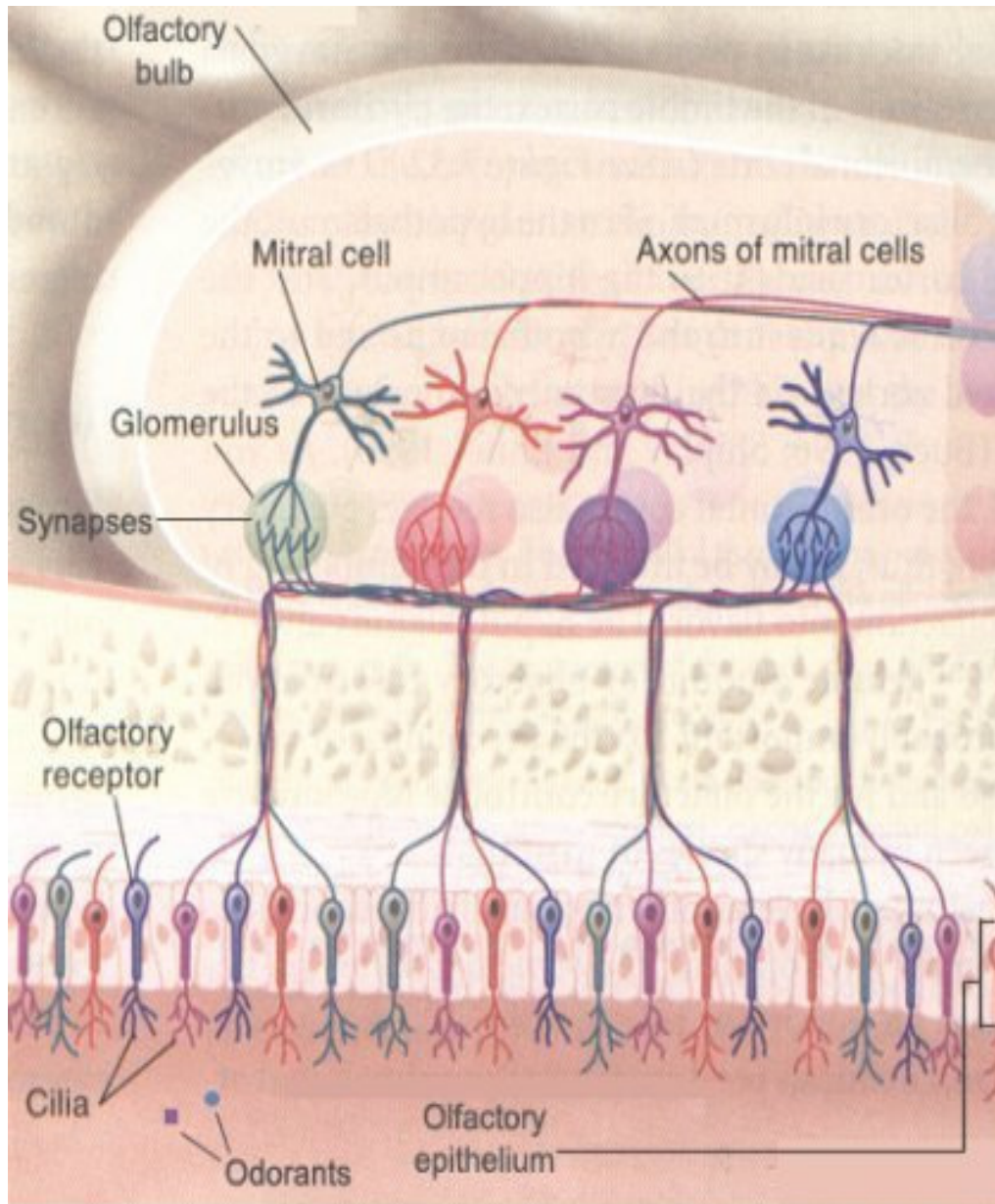


## II. Olfactory system

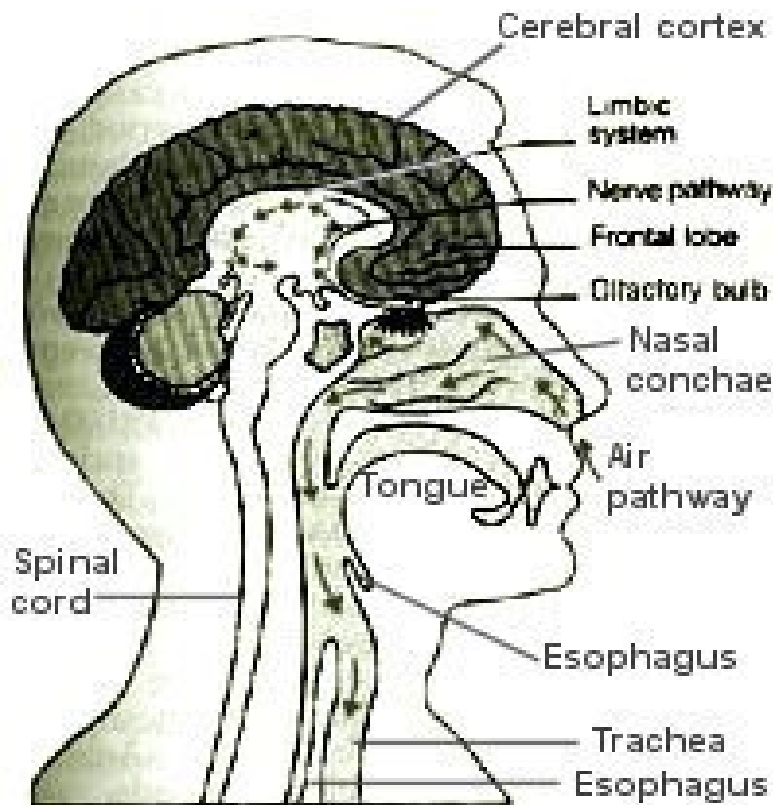
The olfactory mucosa is the odor perceptive part of the nasal mucosa. It covers the upper nasal turbinate and the opposing nasal septum. The olfactory receptors are chemoreceptors, that means they are activated by chemical substances.[12, S.325] The sensory cells of the olfactory mucosa are the primary sensory cells, as they perceive sensory stimuli which they immediately and directly pass into the CNS, without switching to the thalamus. They represent the first neurons in the olfactory tract. With their axons, they form the first Cranial nerve (*F. olfactoria, Nervus olfactorius*) and send signals to the olfactory bulb. There the pulses of the olfactory mucosa are interconnected and draw on the olfactory tract to the cortical projection targets of the olfactory tract. [12, S.201] One of these targets is the *corpus amygdaloideum*, which is part of the limbic system. In addition to the modulating effect on the



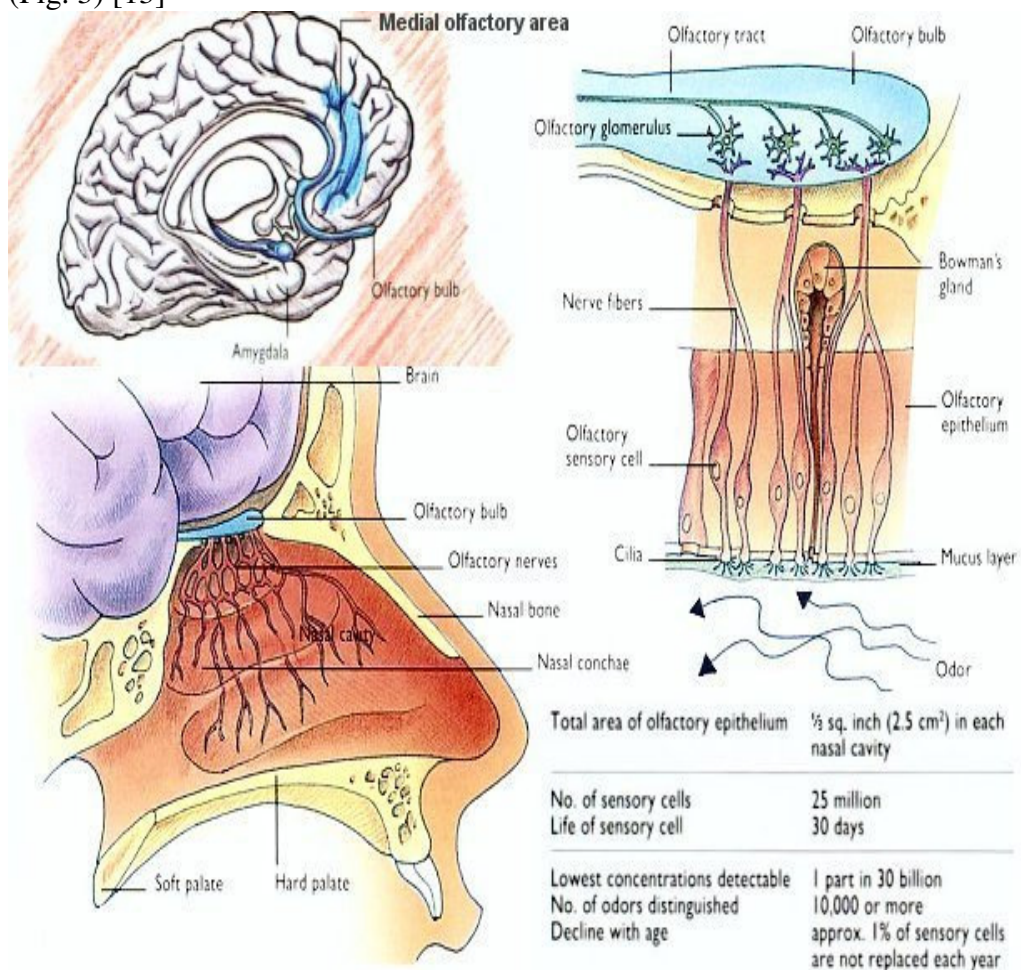
autonomic centers of the hypothalamus (food intake, hormone production, circulatory regulation, etc.), the mediation of behaviors, such as “fight or flight“, and other emotionally induced reactions (laughter, crying), is attributed to the *corpus amygdaloideum* which plays a special role in storing accentuated memories. [12, S. 203] Aromatherapy with suitable essential oils can generate an anxiolytic effect. (see studies below)



(Fig. 2) [13]



(Fig. 3) [13]



(Fig. 4) [13]

The limbic system consists of several structures of the brain, which are closely related. Among them:

- **Hippocampus:** memory, behavior, emotional and autonomic functions
- **Corpus amygdaloideum:** see above
- **Gyrus cingulate:** autonomic modulation, psychological and locomotoric drive
- **Gyrus parahippocampal with area entorhinalis:** Memory, supply of sensory information to other parts of the limbic system
- **Corpus mamillare:** memory, emotional behavior, sexual functions.

[12, S. 207]

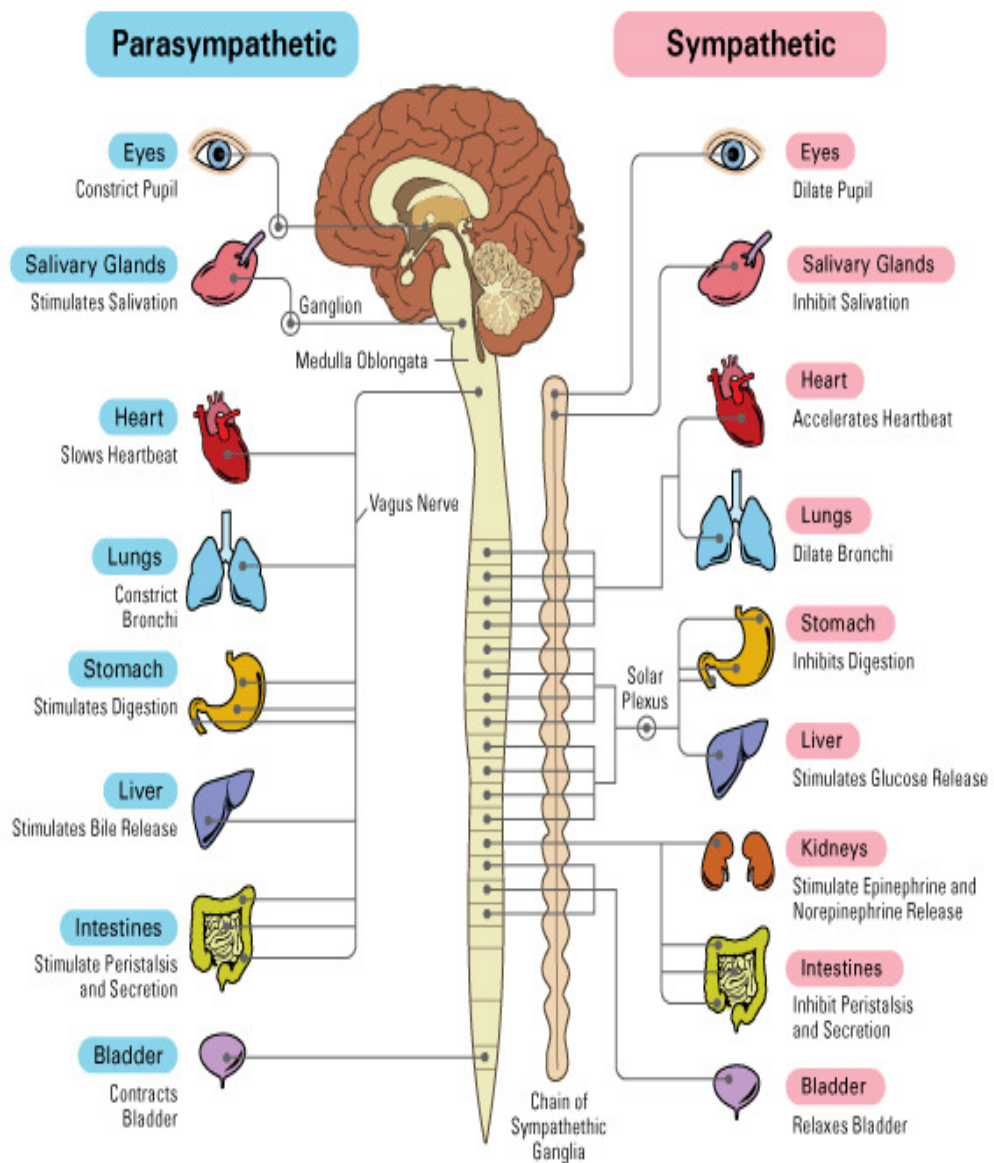
Via the hypothalamus, the most important part of the brain and master control center of the autonomic nervous system, the limbic system affects the autonomic nervous system. The sympathetic or parasympathetic nervous system can be activated depending on the signal, or odor perception of the essential oils. [12, S. 277]

While the sympathetic nervous system activity has a mobilizing and energy-enhancing effect on the body, the parasympathetic nervous system is designed for the preservation and rehabilitation of the body's energy. For example, the sympathetic system causes an increase in heart rate which leads to an increased excitation rate and increased force of contraction: all of this is related to increased cardiac activity. The parasympathetic nervous system on the other hand, causes a lowering of the heart rate and a slowing of the excitation transfer, which corresponds to a reduced heart function. Conversely, in the gastrointestinal tract, the parasympathicus causes an increase in activity in terms of rebuilding the body's energy systems (e.g. increased peristalsis, increased secretion of exocrine glands such as gallbladder and pancreas). In contrast, the sympathetic nervous system has the opposite effect: reduction of peristalsis and gland activity. [12, S. 278]

A "stress function" is often ascribed to the sympathetic nervous system. This suggests that only this part of the autonomic nervous system is activated in

stress and anxiety responses (so called “fight-or-flight” responses). In most cases, however, in stressful situations both parts of the autonomic nervous systems are activated. The stomach ulcer of a manager (due to increased gastric acid production) or the nervousness of a student taking an exam illustrates a partial parasympathetic activation in a stressful situation. [12, S. 279]

## Schema Explaining How Parasympathetic and Sympathetic Nervous Systems Regulate Functioning Organs



(Fig. 5) [14]

### III. Essential oils and Safety

Improper use of essential oils is very dangerous. Some essential oils can cause neuronal damage, liver, and kidney damage as well as skin allergies. [15] The concentration or dose, the route of exposure and the duration of exposure have a significant influence to the toxicity. When using essential oils, it is important to pay attention to quality. [16]

The quality and composition of the essential oils are dependent on: [16]

- Location, level of maturity of the plant, harvest time (time of day, month,..)
- Fresh or dried plants and storage temperature
- Way of distillation and duration
- The composition of the essential oils can be analyzed by gas chromatography and other conventional methods of investigation [16]

The quality factors and characteristics are usually on a label, supplement or the price list. This information should be given: Botanical plant name, stating the plant part, the country of origin, batch quantity in ml, batch number, indication of the vintage, extraction method (steam distillation or expression), quality of the original plant respectively cultivation (certified organic, wild harvest, ..), manufacturer (product liability), safety instructions, .. [16]

- Essential oils should be bottled in tinted bottles for light protection!
- Essential oils should be kept out of reach of children!
- Aromatherapy should be performed only by properly trained personnel!
- Take special care around pregnant women, infants and young children - special knowledge required. [16]

**The following essential oils should not be used for aromatherapy because of their toxicity: [17]**

- Almond (bitter, unrectified) [*Prunus amygdalus var. Amara*, Rosaceae] - neurotoxic!!
- Sage (Dalmatian) [*Salvia officinalis*, Lamiaceae]
- Pennyroyal (European) [*Mentha pulegium*, Lamiaceae] - toxic
- Tarragon [*Artemisia dracuncululus*, Asteraceae]

- Wormwood [*Artemisia absinthium*, Asteraceae]
- Thuja [*Thuja occidentalis*, Cupressaceae]
- Calamus [*Acorus calamus*, Acoraceae]
- Camphor (brown and yellow) [*Cinnamomum camphora*, Lauraceae]
- Cassia [*Cinnamomum cassia*, Lauraceae]
- Cinnamomum bark [*Cinnamomum zeylanicum*, Lauraceae]

**These essential oils should be used fresh: [17]**

- Neroli [*Citrus aurantium*, Rutaceae]
- Orange (bitter, expressed) [*Citrus aurantium*, Rutaceae]
- Orange (sweet, expressed) [*Citrus sinensis*, Rutaceae]
- Bergamot [*Citrus bergamia*, Rutaceae]
- Grapefruit [*Citrus paradisi*, Rutaceae]
- Lemon (expressed or distilled) [*Citrus limonum*, Rutaceae]
- Lime (expressed) [*Citrus aurantifolia*, Rutaceae]
- Pine (Scotch) [*Pinus sylvestris*, Pinaceae]
- Terebinth (=yamor) [*Pinus palustris* etc., Pinaceae] - irritant when oxidised
- Taget [*Tagetes patula*, *T. minuta*, *T. erecta*, Asteraceae]
- Juniper (=juniperberry) [*Juniperus communis*, Cupressaceae]

**A. Oral toxicity**

“Rodent LD 50 values are categorised as follows“: ([17] S. 202)

<b>A</b>	< 1,0 g/kg Toxic (best avoided altogether)
<b>B</b>	1-2 g/kg Mildly toxic (some are safe to use)
<b>C</b>	2-5 g/kg Non toxic (safe to use unless there are other reasons not to)
<b>D</b>	>5 g/kg Non-toxic (safe to use unless there are other reasons not to)

- |                   |                     |                       |
|-------------------|---------------------|-----------------------|
| [An] Annonaceae   | [Aco] Acoraceae     | [A] Apiaceae          |
| [Ast] Asteraceae  | [Bu] Burseraceae    | [Cup] Cupressaceae    |
| [L] Lamiaceae     | [Lau] Lauraceae     | [Myris] Myristicaceae |
| [Myrt] Myrtaceae  | [OI] Oleaceae       | [Pi] Pinaceae         |
| [Pip] Piperaceae  | [Po] Poaceae        | [Ro] Rosaceae         |
| [Ru] Rutaceae     | [San] Santalales    | [Schi] Schisandraceae |
| [Sty] Styracaceae | [Zin] Zingiberaceae |                       |

A	<ul style="list-style-type: none"> <li>- Calamus [<i>Acorus calamus</i>] [Aco]</li> <li>- Wormwood [<i>Artemisia absinthium</i>] [Ast]</li> <li>- Thuja [<i>Thuja occidentalis</i>] [Cup]</li> <li>- Pennyroyal (European) [<i>Mentha pulegium</i>] [L]</li> <li>- Almond (bitter, unrectified) [<i>Prunus amygdalus</i> var. <i>Amara</i>] [Ro]</li> </ul>
B	<ul style="list-style-type: none"> <li>- Tarragon [<i>Artemisia drunculus</i>] [Ast]</li> <li>- Myrrh [<i>Commiphora molmol</i>] [Bu]</li> <li>- Basil [<i>Ocimum basilicum</i>] [L]</li> <li>- Cornmint [<i>Mentha arvensis</i>] [L]</li> <li>- Oregano (Spanish) [<i>Thymus capitatus</i>, <i>Origanum vulgare</i>] [L]</li> <li>- Tea tree [<i>Melaleuca alternifolia</i>] [Myrt]</li> <li>- Clove leaf [<i>Syzygium aromaticum</i>] [Myrt]</li> </ul>
C	<ul style="list-style-type: none"> <li>- Angelica root [<i>Angelica archangelica</i>] [A]</li> <li>- Anise [<i>Pimpinella anisum</i>] [A]</li> <li>- Lovage root [<i>Levisticum officinale</i>] [A]</li> <li>- Caraway [<i>Carum carvi</i>] [A]</li> <li>- Fennel (bitter &amp; sweet) [<i>Foeniculum vulgare</i>] [A]</li> <li>- Cumin [<i>Cuminum cyminum</i>] [A]</li> <li>- Taget [<i>Tagetes patula</i>, <i>T. minuta</i> <i>T. erecta</i>] [Ast]</li> <li>- Marjoram (sweet) [<i>Origanum marjorana</i>] [L]</li> <li>- Thyme [<i>Thymus vulgaris</i>, <i>Thymus zygis</i>] [L]</li> <li>- Sage (Dalmatian) [<i>Salvia officinalis</i>] [L]</li> <li>- Spike lavender [<i>Lavendula latifolia</i>] [L]</li> <li>- Ho leaf (P) [<i>Cinnamomum camphora</i>] [Lau]</li> <li>- Cassia(P) [<i>Cinnamomum cassia</i>] [Lau]</li> <li>- Camphor (yellow &amp; brown) [<i>Cinnamomum camphora</i>] [Lau]</li> <li>- Cinnamomum bark and leaf [<i>Cinnamomum zeylanicum</i>] [Lau]</li> <li>- Laurel [<i>Laurus nobilis</i>] [Lau]</li> <li>- Rosewood [<i>Aniba rosaeodora</i>] [Lau]</li> <li>- Nutmeg (East indian) [<i>Myristica fragrans</i>] [Myris]</li> <li>- Mace [<i>Myristica fragrans</i>] [Myris]</li> <li>- Cajeput [<i>Melaleuca leucadendron</i>] [Myrt]</li> <li>- Eucalyptus [<i>Eucalyptus globulus</i>] [Myrt]</li> <li>- Clove bud, stem [<i>Syzygium aromaticum</i>] [Myrt]</li> <li>- Terebinth (=yamor) [<i>Pinus palustris</i> etc.] [Pi]</li> <li>- Rue [<i>Ruta graveolens</i>] [Ru]</li> <li>- Neroli [<i>Citrus aurantium</i>] [Ru]</li> <li>- Star anise [<i>Illicium verum</i>] [Schi]</li> </ul>
D	<ul style="list-style-type: none"> <li>- Angelica seed [<i>Angelica archangelica</i>] [A]</li> <li>- Ylang-ylang [<i>Cananga odorata</i>] [An]</li> <li>- Chamomile (german) [<i>Chamomilla recutita</i>] [Ast]</li> <li>- Juniper (=juniperberry) [<i>Juniperus communis</i>] [Cup]</li> <li>- Phoenician juniper [<i>Juniperus phoenicea</i>] [Cup]</li> <li>- Cade (rectified) (P) [<i>Juniperus oxycedrus</i>] [Cup]</li> <li>- Marjoram (Spanish) [<i>Thymus masticina</i>] [L]</li> <li>- Clary sage (French) [<i>Salvia sclarea</i>] [L]</li> <li>- Sage (Spanish) [<i>Salvia lavendulaefolia</i>] [L]</li> <li>- Bergamot mint [<i>Mentha citrata</i>] [L]</li> <li>- Spearmint [<i>Mentha spicata</i>] [L]</li> <li>- Lavender [<i>Lavendula angustifolia</i>] [L]</li> <li>- Rosemary [<i>Rosmarinus officinalis</i>] [L]</li> </ul>

D	<ul style="list-style-type: none"> <li>- Camphor (white) [Cinnamomum camphora] [Lau]</li> <li>- Eucalyptus citriodora [Eucalyptus citriodora] [Myrt]</li> <li>- Jasmine [Jasminum officinale] [Ol]</li> <li>- Abies alba (cones and needles) [Pi]</li> <li>- Fir needle (Siberia) [Abies sibirica] [Pi]</li> <li>- Pine (Scotch) [Pinus sylvestris] [Pi]</li> <li>- Pepper (black) [Piper nigrum] [Pip]</li> <li>- Citronella (P) [Cymbopogon nardus] [Po]</li> <li>- Lemongras [Cymbopogon citratus] [Po]</li> <li>- Rose [Rosa damascena] [Ro]</li> <li>- Orange flower [Citrus aurantium] [Ru]</li> <li>- Orange (bitter, expressed) [Citrus aurantium] [Ru]</li> <li>- Orange (sweet, expressed) [Citrus sinensis] [Ru]</li> <li>- Grapefruit [Citrus paradisi] [Ru]</li> <li>- Lemon (expressed) [Citrus limonum] [Ru]</li> <li>- Lemon (distilled) [Citrus limonum] [Ru]</li> <li>- Lemon leaf (Lemon petitgrain) [Citrus limonum] [Ru]</li> <li>- Lime (distilled) [Citrus aurantifolia] [Ru]</li> <li>- Sandalwood [Santalum album] [San]</li> <li>- Benzoin (resinoid) [Styrax benzoin] [Sty]</li> <li>- Ginger [Zingiber officinale] [Zin]</li> <li>- Cardamon Elettaria cardamomum [Zin]</li> <li>- Tumeric Curcuma longa [Zin]</li> </ul>
---	---

(Tab. 1) [17]

## B. Skin irritation

Dermal irritancy: Essential oils can cause skin irritation. They cause inflammation and local hyperemia, without tissue defects. Occasionally, essential oils with skin irritancy effects (e.g. camphor) are used intentionally to provoke a chronic process on the skin or mucous membranes and to transform this process into an acute one, thus accelerating healing. [18] In his book "Essential oil safety," Tisserand examined the potential for skin irritation from essential oils in concentrations between 1% and 30%. He categorized the potential for skin irritation properties of the substances into 5 groups [17]:

A	Severely irritant
B	Strongly irritant
C	moderately irritant
D	very mildly irritant
E	non irritant



[An] Annonaceae	[Aco] Acoraceae	[A] Apiaceae
[Ast] Asteraceae	[Bu] Burseraceae	[Cup] Cupressaceae
[L] Lamiaceae	[Lau] Lauraceae	[Myrs] Myristicaceae
[Myrt] Myrtaceae	[Ol] Oleaceae	[Pi] Pinaceae
[Pip] Piperaceae	[Po] Poaceae	[Ro] Rosaceae
[Ru] Rutaceae	[San] Santalales	[Schi] Schisandraceae
[Sty] Styracaceae	[Zin] Zingiberaceae	

A	-
B	<ul style="list-style-type: none"> <li>- Cade (rectified) [Juniperus oxycedrus] [Cup]</li> <li>- Terebinth (=yamor) [Pinus palustris etc.] [Pi]</li> <li>- Fir needle (Siberia) [Abies sibirica] [Pi]</li> </ul>
C	<ul style="list-style-type: none"> <li>- Fennel sweet [Foeniculum vulgare] [A]</li> <li>- Tarragon [Artemisia dracunculus] [Ast]</li> <li>- Taget [Tagetes patula, T. minuta T. erecta] [Ast]</li> <li>- Phoenician juniper [Juniperus phoenicea] [Cup]</li> <li>- Oregano (Spanish) [Thymus capitatus, Origanum vulgare] [L]</li> <li>- Thyme [Thymus vulgaris, Thymus zygis] [L]</li> <li>- Sage (Dalmatian) [Salvia officinalis] [L]</li> <li>- Laurel [Laurus nobilis] [Lau]</li> <li>- Cassia [Cinnamomum cassia] [Lau]</li> <li>- Cinnamomum bark and leaf [Cinnamomum zeylanicum] [Lau]</li> <li>- Clove bud, leaf and stem [Syzygium aromaticum] [Myrt]</li> <li>- Abies alba (cones) [Pi]</li> <li>- Rue Ruta graveolens [Ru]</li> </ul>
D	<ul style="list-style-type: none"> <li>- Lovage root [Levisticum officinale] [A]</li> <li>- Anise [Pimpinella anisum] [A]</li> <li>- Angelica root and seed [Angelica archangelica] [A]</li> <li>- Caraway [Carum carvi] [A]</li> <li>- Fennel (bitter) [Foeniculum vulgare] [A]</li> <li>- Cumin [Cuminum cyminum] [A]</li> <li>- Chamomile (german) [Chamomilla recutita] [Ast]</li> <li>- Wormwood [Artemisia absinthium] [Ast]</li> <li>- Juniper (=juniperberry) [Juniperus communis] [Cup]</li> <li>- Thuja [Thuja occidentalis] [Cup]</li> <li>- Clary sage (French) [Salvia sclarea] [L]</li> <li>- Basil [Ocimum basilicum] [L]</li> <li>- Marjoram (Spanish) [Thymus masticina] [L]</li> <li>- Bergamot mint [Mentha citrata] [L]</li> <li>- Rosemary [Rosmarinus officinalis] [L]</li> <li>- Spearmint [Mentha spicata] [L]</li> <li>- Pennyroyal (European) Mentha pulegium [L]</li> <li>- Spike lavender Lavendula latifolia [L]</li> <li>- Lavender [Lavendula angustifolia] [L]</li> </ul>

D	<ul style="list-style-type: none"> <li>- Ho leaf [Cinnamomum camphora] [Lau]</li> <li>- Camphor (white &amp; yellow) [Cinnamomum camphora] [Lau]</li> <li>- Tea tree [Melaleuca alternifolia] [Myrt]</li> <li>- Eucalyptus Eucalyptus globulus [Myrt]</li> <li>- Eucalyptus citriodora [Eucalyptus citriodora] [Myrt]</li> <li>- Nutmeg Myristica fragrans [Myris]</li> <li>- Abies alba (needles) [Pi]</li> <li>- Pepper (black) [Piper nigrum] [Pip]</li> <li>- Lemongras [Cymbopogon citratus] [Po]</li> <li>- Citronella [Cymbopogon nardus] [Po]</li> <li>- Rose [Rosa damascena] [Ro]</li> <li>- Almond (bitter, unrect.) [Prunus amygdalus var. Amara] [Ro]</li> <li>- Orange (bitter, expressed) [Citrus aurantium] [Ru]</li> <li>- Orange flower [Citrus aurantium] [Ru]</li> <li>- Orange (sweet, expressed) [Citrus sinensis] [Ru]</li> <li>- Grapefruit [Citrus paradisi] [Ru]</li> <li>- Lemon (expressed) [Citrus limonum] [Ru]</li> <li>- Lemon (dist.) [Citrus limonum] [Ru]</li> <li>- Lemon leaf (Lemon petitgrain) [Citrus limonum] [Ru]</li> <li>- Lime (distilled) [Citrus aurantifolia] [Ru]</li> <li>- Sandalwood [Santalum album] [San]</li> <li>- Star anise [Illicium verum] [Schi]</li> <li>- Tumeric [Curcuma longa] [Zin]</li> <li>- Ginger [Zingiber officinale] [Zin]</li> <li>- Ylang-ylang [Cananga odorata] [Zin]</li> </ul>
E	<ul style="list-style-type: none"> <li>- Calamus [Acorus calamus] [Aco]</li> <li>- Myrrh [Commiphora molmol] [Bu]</li> <li>- Marjoram (sweet) [Origanum marjorana] [L]</li> <li>- Clary sage (Russian) [Salvia sclarea] [L]</li> <li>- Sage (Spanish) [Salvia lavendulaefolia] [L]</li> <li>- Cornmint [Mentha arvensis] [L]</li> <li>- Rosewood [Aniba rosaeodora] [Lau]</li> <li>- Camphor (brown) [Cinnamomum] [Lau]</li> <li>- Cajeput [Melaleuca leucadendron] [Myrt]</li> <li>- Jasmine [Jasminum officinale] [OI]</li> <li>- Pine (Scotch) [Pinus sylvestris] [Pi]</li> <li>- Neroli [Citrus aurantium] [Ru]</li> <li>- Cardamon [Elettaria cardamomum] [Zin]</li> </ul>

(Tab. 2) [17]

## C. Phototoxicity

**Phototoxie (also phototoxicity):** "Describes the strength with which a chemical substance causes under effects of sunlight poisoning (toxic) effects on the skin surface." A change occurs in phototoxic substances in their structure which is caused by UVA and UVB radiation from sunlight. This change increases their toxicity. The toxic effect on skin can be observed as redness, itching, rash, dryness, and flaking. [19]

- The more concentrated a photo-toxic substance is used, the greater the risk! [17]
- When using several phototoxic essential oils, the phototoxicity is increased proportionally. [17]

### **Phototoxic essential oils: [17]**

- Angelica root (*Angelica archangelica*) [Apiaceae]
- Cumin (*Cuminum cyminum*) [Apiaceae]
- Taget (*Tagetes patula*, *T. minuta*, *T. erecta*) [Asteraceae]
- Cassia (*Cinnamomum cassia*) [Lauraceae]
- Grapefruit (*Citrus paradisi*) [Rutaceae]
- Orange (bitter, expressed) (*Citrus aurantium*) [Rutaceae]
- Lemon (expressed) (*Citrus limonum*) [Rutaceae]
- Lime (expressed) (*Citrus aurantifolia*) [Rutaceae]
- Bergamot (*Citrus bergamia*) [Rutaceae]
- Rue (*Ruta graveolens*) [Rutaceae] [17]

## **IV. Massage**

Massage: “The therapeutic practice of manipulating the muscles and limbs to ease tension and reduce pain. Massage can be a part of physical therapy or practiced on its own. It can be effective for reducing the symptoms of disorders of or pain in the muscles and nervous system, and it is often used to reduce stress.” [20]

### **“General effects of massage: [21]**

- Local increased blood flow
- Lowering of blood pressure and pulse rate
- Relaxing muscles
- Loosed adhesions and scars & improved wound healing
- Pain relief
- Effects on internal organs via reflex arcs
- Reduced stress & mental relaxation
- Improved cell metabolism in tissues
- Relaxation of skin and connective tissue
- Effects on the autonomic nervous system” [21]

### **Safety & contraindication:**

- A powerful massage should not be performed on patients with low platelet count, bleeding disorders, or on patients who take blood thinners (e.g. warfarin) [22]
- No massage should be applied to skin areas with open or healing wounds, weakened or broken bones (e.g. osteoporosis or cancer), skin infections, areas with blood clots, or areas where a surgery recent has been performed [22]
- In patients with cancer, first consult an oncologist to make sure that a massage will not be harmful [22]
- Pregnant women should be careful and consult a doctor first. [22]
- Massage must not be given to patients with cases of acute inflammation (febrile diseases, diseases of the blood vessels, etc.)! The body is already highly stressed and would be additionally burdened by massage. [23]

- It should be noted, that during massage, essential oils are absorbed very well (because of hyperemia and the long exposure time ..). Therefore, only dilutions of 0.2% should be used. [24]

It has been shown in numerous studies that essential oils and massage are highly complementary, and have a paired effect. There are many massage techniques. The following techniques should be discussed in more detail:

- Swedish Massage
- Acupressure
- Lymph-Massage
- Reflexology

## **B. Swedish Massage**

The classic, or Swedish massage, is one of the best known forms of massage and is practiced worldwide by massage therapists, physical therapists, and doctors. [23]

In classical massage, five basic strokes are used:

- **Effleurage** (sliding or gliding) is used for distributing or spreading the oil or cream and to warm up the muscle. Sliding can be used to relax the patient and to speed recovery of stressed muscles. [23]
- **Petrissage** (kneading): „Massage movements with applied pressure which are deep and compress the underlying muscles. Petrissage techniques include kneading, wringing, skin rolling, and picking up and squeezing. They are all performed with the padded palmar surface of the hand, the surface of the fingers, and the thumbs. During kneading, the hands should be moulded to the area and the movements should be slow and rhythmical. Knuckling is another form of kneading, but one must use the knuckles to knead and lift in circular, upward motions. Scissoring is another petrissage movement that is performed only over a flat area with very little pressure. The index and middle fingers of both hands are used for this movement. They are placed opposite each other and then are slowly worked towards each other lifting and releasing as they go.“ [25]

- **Frikktion** (cross fiber) : "The fingers or the palm of your hand make small, circular movements on the muscles." [23] It is a very effective grip to use to harden muscles. As it is very powerful, it must be used with caution. [23]
- **Tapotement** (rhythmic tapping): "With the edge of the hand, the palm of the hand, or the fingers short, percussive movements are performed." This function may promote the peripheral circulation and change muscle tone. In lungs with mucus "rapping with the palm at the level of the lung" can help. [23]
- **Vibration** (vibration/shaking): "The fingers or the palm of the hand are placed and the masseur produces tremors. The effect can extend to deeper tissues and organs. This grip is loosening effect and thus has among other anticonvulsant effect." [23]

**Indication:**

- Tension, hardening, musculoskeletal disorders such as spinal syndromes or post-traumatic changes
- Nervous system disorders, such as paralysis, spasticity, neuralgia and sensory disturbances
- attributable to stress, psychosomatic symptoms, which are mainly related to the heart and the circulatory system [23]

**Effect:**

- improved blood circulation in the circuit, especially in the lower extremities.
- The performance of myocardial sufficient heart is increased by depletion of blood banks (propagation of cardiac output)
- endocrine effect by acting on the pituitary gland and other endocrine glands (acts vagoton and improves blood pressure, pulse, breathing, sleeping and has a relaxing effect and mood improving effect) [23]

**Contraindication:** see introduction massage "Safety & contraindication"

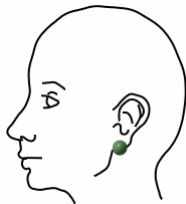
## C. Acupressure

Acupressure, like acupuncture is based on the meridian theory. Using acupressure one stimulates the acupuncture meridian points without needles. One massages or presses. Traditional Chinese Medicine (TCM) suggests that there are a number of meridians in the human body. Meridians are invisible lines in which the energy of life circulates. TCM assumes that a disease occurs when the energy in the meridians can not flow freely. By stimulating the meridian points, one can affect the body's organs and thereby provide relief from ailments. [26]

Here is a small overview of how different sets of symptoms can be treated with acupressure [26] :

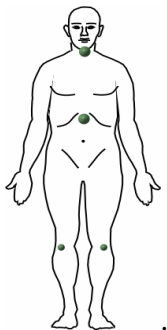
### Acupressure points for fatigue:

- Main points: earlobe (massage both earlobes with the thumb and forefinger and then pull repeatedly on the earlobe)



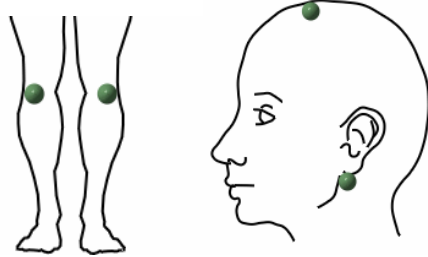
### Acupressure points for anxiety

- Main points: the end of the sternum (at the lower end of the sternum)  
chin (directly under the tip of the chin to the bottom of the mandible)
- Auxiliary points: kneecaps (on the outer bottom of the patella: the points of the "divine indifference")



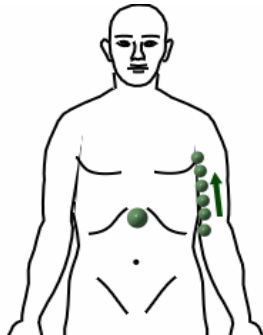
### Acupressure points for nervousness:

- Main points: knee (press outside below the kneecaps on the points of the "divine indifference")  
head (the middle of the skull pressing for 5 seconds)
- Auxiliary points: pine (press behind the jaw below the ears)



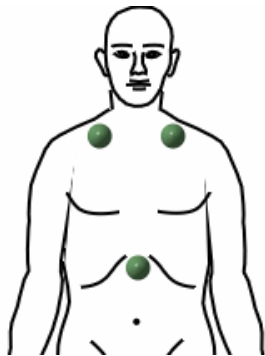
### Acupressure points against nervous heart complaints:

- Main points: arm (the left arm from the elbow inside press upwards point by point)  
breastbone (press the sternum gently to the gut)



### Acupressure points against Nervous stomach discomfort:

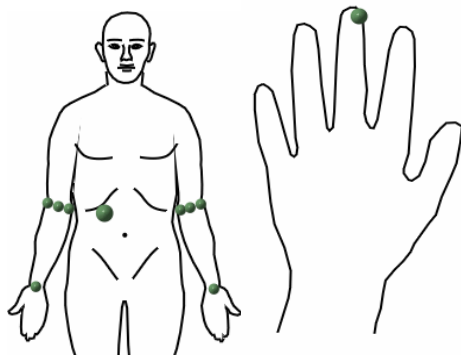
- Main points: sternal (press in the stomach under the breastbone)  
collarbone (press in the middle of the clavicle bone)



### Acupressure points for depression:

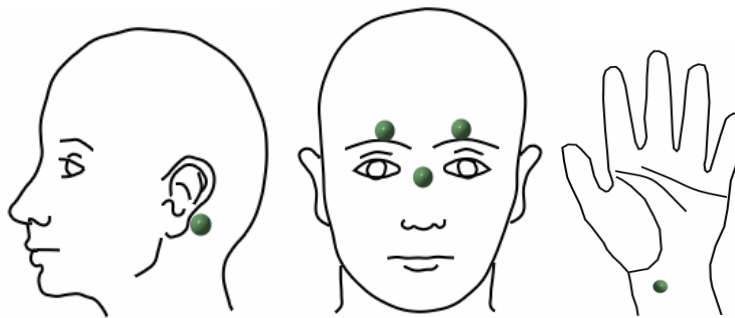
- Main points: elbow crease (press the elbow from the inside out inch by inch)  
right upper abdomen (press under the right costal margin in the upper abdomen on the most sensitive area)
- Auxiliary points: wrist (press the wrist on the pulse point)  
middle finger (press the middle finger at the nail on the side of the index finger)





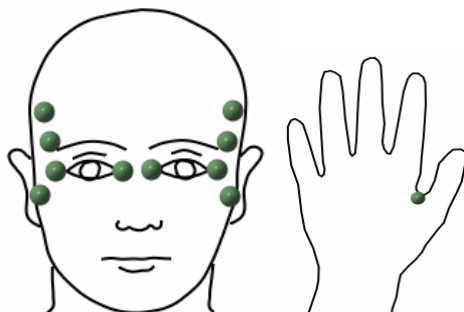
### Acupressure points for headache:

- Main points:
  - eyebrow (press the middle of the nose with thumb and forefinger)
  - nose (press in the recesses behind the ears)
  - ear (massage over the eyebrows to the point of pain)
- Auxiliary points:
  - wrist (press the wrist on the pulse point)



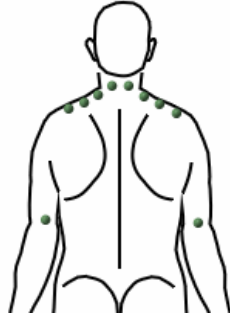
### Acupressure points for migraine:

- Main points:
  - eyebrows (press outside above the eyebrows)
  - inner corner of the eye (press at the inner corners of eyes gently)
  - temporomandibular joint (press above the TMJ)
  - temples (press into the depressions on the temples)
  - outer corner of the eye (press at the outer corners of the eyes)
- Auxiliary points:
  - hand (massage between thumb and forefinger of the left hand)



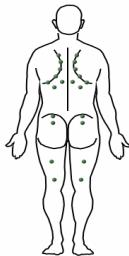
### Acupressure Points for Neck Pain:

- Main points: neck (press on the neck or at the widest point of pain)  
shoulder (push on the shoulder in the hollows between the bones from the inside out)
- Auxiliary points: elbow (massaging the elbow)



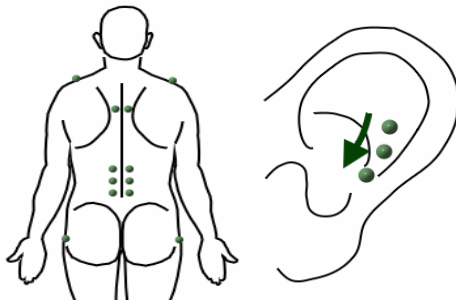
### Acupressure points and back pain:

- Main points: hips (press above and below the hip bone in the middle of the buttocks)  
ribs (press at the ribs parallel to the lower edge of the shoulder blade)  
scapula (press on the edge of the shoulder blade, point by point along)
- Auxiliary points: popliteal fossa (press a few inches above the popliteal fossa)  
thigh (press in the middle, a few inches below the buttocks to the thighs)



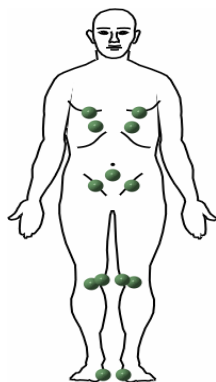
### Acupressure points for low back pain:

- Main points: sacrum (massage the spinal above the sacrum)  
upper leg (press the thigh at the approach)  
shoulder blades (press between the shoulder blades)  
shoulders (presses on the shoulders)
- Auxiliary points: ear (press at the edge of the ear from top to bottom)



### Acupressure points for menstrual cramps:

- Main points: groin (press in the middle of the groin)  
navel (press a few inches below the navel)  
pubic bone (presse two finger widths above the pubic bone)
- Auxiliary points: great toe joint (metatarsophalangeal joint of the big toe massage at the ball)  
knee (press inside the knee joint)  
kneecap (press on the inner side of the patella)  
big toe joint (massage the metatarsophalangeal joint of the big toe at the ball) [26]



### D. Lymph-Massage

The lymphatic system plays a central role in the immune system and is also responsible for the transport of substances with high molar mass, which can not be transported in the blood (proteins, lipids (chylomicrons), cellular debris, toxins, disarmed bacteria and viruses). [27] If the lymphatic system is impaired in its function, water backs up into the body tissue, edema occurs, and the immune system may be impaired. Here, lymphatic drainage intervenes and tries to restore the efficiency of the lymphatic system, thereby restoring tissue and water balance. The subcutaneous tissue is massaged with gentle pressure (by circular movements, pump handles using thumbs and fingers, cupping handles, twist grips, where the skin is pushed against a subcutaneous). The order of the massage is first on the face and neck, then the arms, abdomen, legs (front and back), and finally the back. [28]

Effects: [28]

- Improved lymph
- Decongested localization

- Freedom from pain
- Improved muscle movement of the lymphatic vessels
- Immune system is stimulated
- Soothing and tonic effect on the autonomic nervous system
- Relaxation of muscles
- Calming and relaxing effect on the CNS
- New lymphatic vessels at break points
- Normalization of the muscle tension in the vessel wall.

Applications: [28]

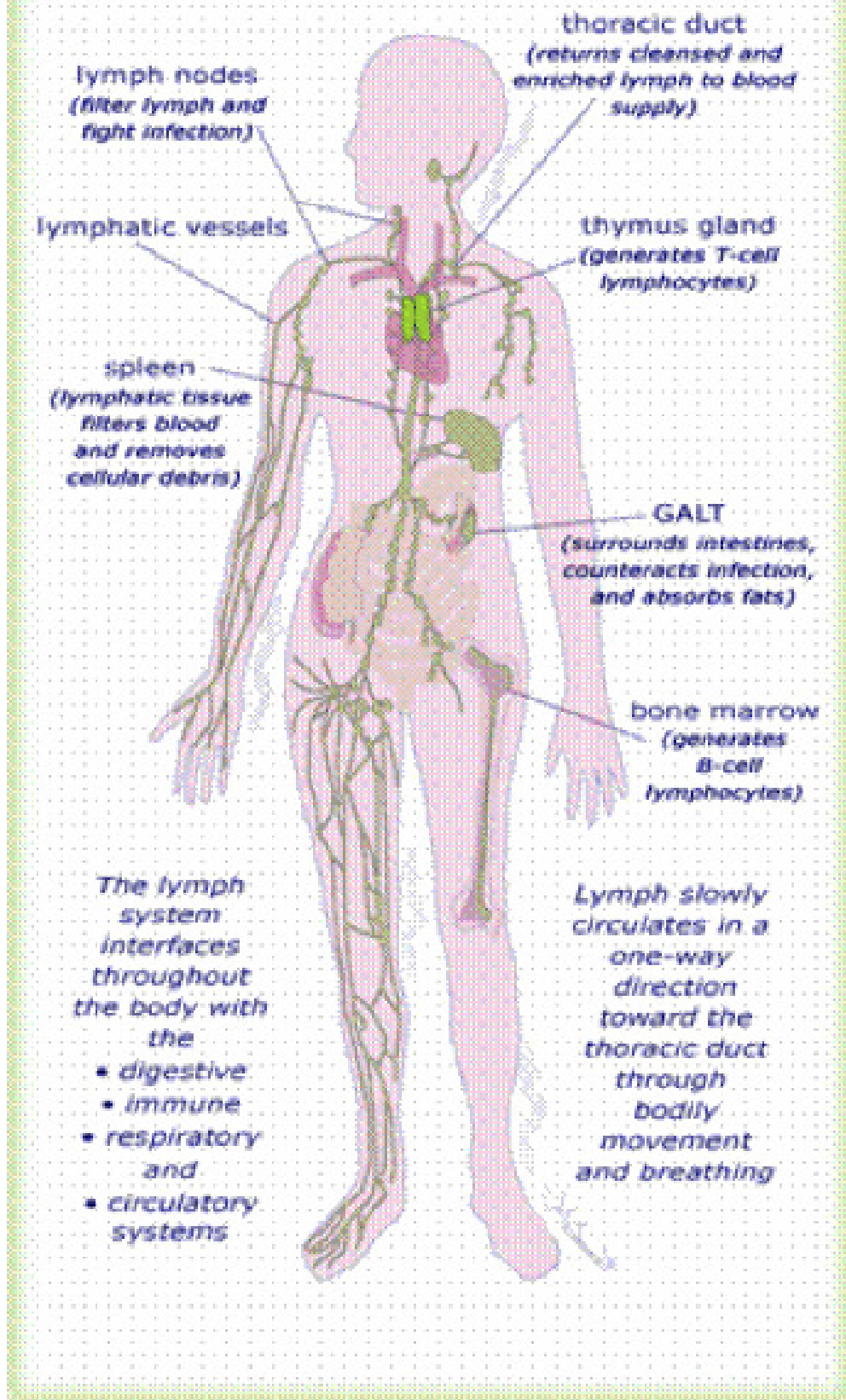
- Secondary lymphedema after surgical removal of the tumor and / or radiation to the regional lymph nodes, such as tumors of the breast (arm lymphedema), the pelvis (leg lymphoedema), in the ear, nose and throat area (facial lymphoedema)
- Edema in rheumatic diseases
- Swelling after injury or swelling of various causes
- Cosmetic problems (acne, bruises, facial edema, eye bags, scars and cellulite).
- Respiratory disease with severe congestion
- Neuralgia
- Neurovegetative syndromes: migraine, trigeminal neuralgia

**Safety & contraindication:** [28]

Additional to “general safety and contraindication” - no lymphatic drainage should be performed:

- For acute allergic reactions
- Heart failure (congestive heart failure)
- Water retention in the legs due to heart disease (insufficiency)
- Bronchial asthma

# Lymphatic System



(Fig. 6) [29]

## E. Reflexology (Zone therapy)

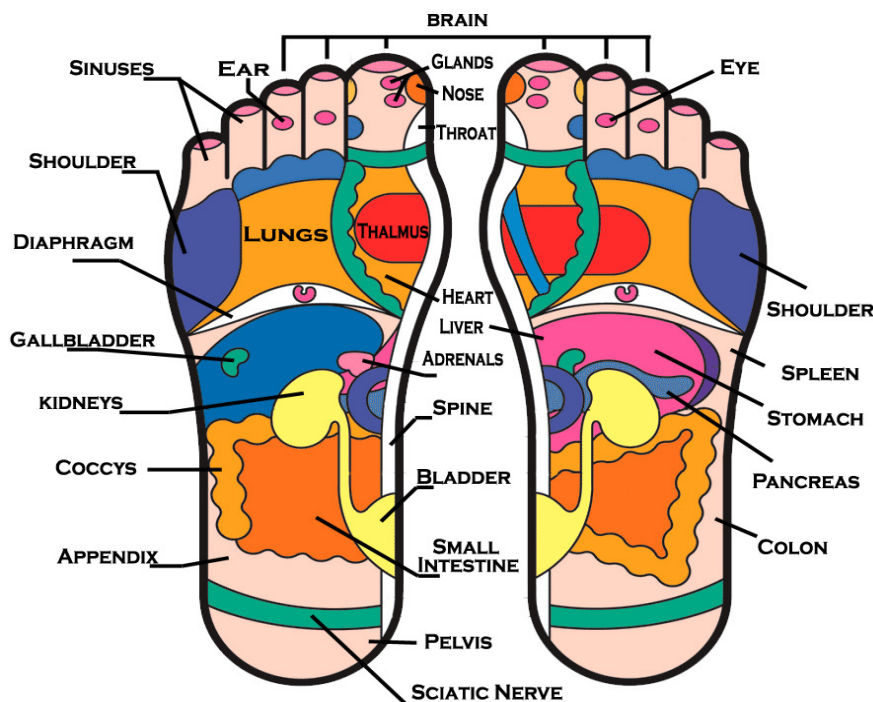
Also reflexology should be described briefly, even though the therapeutic effects of this massage technique are more controversial. "The in reflex massage intentioned reflex zones in the body should reflect all the organs and muscle groups on the skin surface and the skin-subcutaneous area." These reflex zones are located at the foot, the hand, the ear, nose and skull, and are not identical to the head zones of medicine. [30]

"There are several theories that explain the mechanisms behind reflexology, but none of these are scientifically proven.

- Reflexologists propose that when invisible forces or energy fields in the body are blocked, illnesses can result.
- Reflexology may also promote healing by releasing endorphins, which are natural pain killers in the body. Reflexology could also stimulate nerve circuits, promote lymphatic flow, or help dissolve uric acid crystals." [31]

"There is no standard "map" of the reflex zones, such as on feet and hands, instead, there are many different ways by different conflicting figures." [30]

For example: (Fig 7) [32]



## **V. Essential oils and Sleep**

Common causes of insomnia are poor sleeping conditions, stress, mental and physical disorders and diseases, such as cardiovascular or brain disease, a respiratory disease known as apnea, or other physical disorders. When insomnia occurs only for a short period, it is not harmful. When, however, insomnia becomes chronic and appears regularly, it can cause negative effects on the function of organs and body parts. [33] Insomnia occurs very commonly in patients in hospitals and institutions, this is, why it is very important to put a special focus on it. [34]

In a study of Vgontaz et al. with fifteen young adults (<40 years) a correlation between chronic insomnia and release of stress hormones was found. During 24 hours, urinary free cortisol (UFC), catecholamines and growth hormone (GH) were measured and it was demonstrated that the blood level of these hormones increased with increasing insomnia. It could also be shown that chronic, severe insomnia is a substantial stress. [35] Especially in sick people, it has an effect on the course of their disease and plays an important role in nursing science. During the sleep phase, regeneration processes are set in motion. [33]

Too little sleep and rest can also adversely affect the cardiovascular system. Lack of sleep and the consequent activation of the sympathetic nervous system increase the release of stress hormones in blood pressure and can lead to an increased heart beat. Lack of sleep can also increase the activation of nociceptors and thus cause pain. “So there is a direct correlation between the quality of sleep and pain.” [36] The causes of sleep disorders are multifactorial. Nurses have an important role to see the patient’s reasons and factors for insomnia individually and if possible try to reduce them. [37]

### **VALERIANA OFFICINALIS**

Chen et al. investigated the sleep-promoting effect of valerian acupuncture in patients in the Intensive Care Unit (ICU). The effects of valerian acupuncture

were measured by observations with actigraphy measurements between 10 p.m. and 6 p.m., and with the Stanford Sleepiness Scale (SSS) on the consecutive morning. 41 patients in the experimental group received a massage on the Shenmen, Pe and Yongquan acupoints with valerian between 7.00 pm to 10.00 pm, while the control group consisting of 44 people received regular treatment. Five minutes before and after the valerian acupressure the heart frequency was measured. Furthermore it could be detected that acupressure with valerian increases sleep hours, while the excitation frequency and the SSS scores decreased. Thus, it was shown that valerian acupressure is a very effective method to improve the quality of sleep. [38]

Dietz et al. could show “that both dichloromethane-extracts (DCM) and polyethylene-extracts (PE) of Valerian excited a strong binding affinity to the 5-HT (5a) receptor, but only a weak binding affinity to the 5-HT (2b) and other serotonin receptors.” So, Dietz et al. realized that “valerian and valerenic acid are partial agonists on the 5-HT (5a) receptor.” The 5-HT (5a) receptors are present in the suprachiasmatic nucleus in high numbers, which is a part of the brain and responsible for the sleep-wake cycle. [39] The suprachiasmatic nucleus controls, among other things, the production and release of the hormone melatonin from the pineal gland. Melatonin is involved in the timing of the sleep. [40]

#### VALERIAN & LEMON

In a study by Komori et al. the effects of inhalation of various essential oils on the sleep-wake times of rats were examined and particularly the role of olfactory receptors. Volatile substances can affect the body in 3 different ways, due to the absorption by the mucous membranes of the nose and respiratory tract, stimulating the bronchial and pulmonary chemical receptors, and the olfactory sensory neurons as odors. Komori et al. tested on anosmic rats, whether activation of the odor cells plays an important role in the effects of essential oils. In the experiment “cloves, jasmine, lavender, lemon, peppermint, pine, rose, sandalwood, valerian, and ylang-ylang” were used. By the inhalation of valerian the pentobarbital-induced sleep time increased



significantly and the gamma-aminobutyric acid (GABA) transaminase assay showed that by inhalation of valerian the activity of the degradation enzyme is reduced and consequently the activity of GABA is increased. It can also lead to a significant prolongation of total sleep time by inhalation using valerian. From this, the valerian may improve sleep very effectively. In contrast, during the inhalation of lemon the pentobarbital-induced sleep time shortened considerably and observed a significant increase in sleep latency. It follows that inhalation with lemon causes a worsening of insomnia symptoms. In anosmic rats, however no significant effect of the above odors on the pentobarbital sleep time could be found. This suggests that the sense of smell possesses an important significance on the effect on pentobarbital sleep time by the inhalation of valerian and lemon. [41]

#### CITRUS

Park et al. demonstrated by using an *in vitro* radioligand binding assay that limonene, an aromatic compound from citrus peel, directly binds to the adenosine A (2A) receptor. Limonene has a selective affinity to the A (2A) receptors and thus can cause sedative effects. [42] “The A(2A) receptor is present mainly in the brain, where it plays an important role in the regulation of glutamate and dopamine release. This receptor is a potential therapeutic target for the treatment of conditions such as insomnia, pain, depression, drug addiction, and Parkinson's disease.” [43]

In a study by Guzman-Gutierrez the sedative and calming effects of methanol and DCM extracts from the flowers of *Citrus sinensis* (L.) Osbeck (Rutaceae) were examined and “the pharmacological mechanisms of action” of the extracts of these sedative drugs were recorded. “In an exploratory cylinder model in mice“, a dose-dependent sedation was noted and assumed that the reason for the sedation is the activity of hesperidin on adenosine receptors. [44]

#### LAVENDER

Lee et al. examined the effect of aromatherapy with lavender oil on insomnia in 42 female college students in a 4-week protocol. The study was conducted

as a single blind repeated measured experiment. The first week was the check-week, in the second week students received 60 % lavender scent, the third week was a wash-out period and in week 4 all students received the treatment with 100 % lavender scent. Parameters were measured on patterns of sleep disorders, e.g. insomnia severity scale, self-satisfaction with sleep, and recorded the severity of depression weekly. Lee et al. realized that this therapy significantly reduced insomnia. The “sleep time, the severity of insomnia and satisfaction with sleep” were significantly improved in both the 100% and 60% lavender week. “The severity of depression was significantly improved only in the 100% lavender week. Thus, it was shown that lavender fragrance had a beneficial effect on insomnia and depression.” [45]

In a randomized, single-blind pilot study with cross-over design by Lewith the effect of aromatherapy with lavender was tested for 4 weeks on ten volunteers (five male and five female) with defined insomnia. These four weeks were divided as follows: in the first week the acclimatization of the baseline was aspired, then two weeks were treated and the last week was the washout period. The results showed that lavender oil aromatherapy compared with the control group (sweet almond oil was administered as a placebo) effected an improvement in the Pittsburgh Sleep Quality Index (PSQI) of 2.5 points. Treatment with lavender oil also reduced the insomnia and improved the quality of life significantly. Especially “women and younger subjects with a mild insomnia” responded well to the aromatherapy with lavender. [46]

Also in a clinical study of Moeni et al. on 64 patients with ischemic heart disease in an intensive care unit, the effects of aromatherapy on the quality of sleep were examined. The study was designed placebo-controlled. Patients in the experimental group received nine hours of aromatherapy with lavender oil, and the control-group got no-intervention. Patients in both groups were measured by the SMHSQ (St Mary’s Hospital Sleep Questionnaire) before and after the intervention, and they were asked about the quality of their sleep. The results of the intervention group showed positive changes in sleep quality compared to the control group. It was shown in this study that the quality of

sleep was significantly improved in ischemic heart disease patients after an aromatherapy with lavender oil and that these results can have a further positive impact on the well being and health. [36]

A study by Chien with climacteric women suffering from insomnia showed that the inhalation of lavender has “a persistent short-term effect on heart rate variability (HRV)” and may lead to an enhancement of the parasympathetic modulation. Also this study in climacteric women showed a significant improvement in the quality of sleep after aromatherapy with lavender. In a long-term follow up there were no changes in HRV. [47]

In another study the effect of lavender oil “on the quality of sleep in healthy Japanese students” was tested (M age = 19.0). The study was single-blind and randomized, designed for 11 days with seven students in the intervention group (two men, five women) with nocturnal exposure with lavender aroma and eight in the control group (three men, five women) with no flavor. There was a three day evaluation phase, the actual five-day intervention and three more days of the intervention assessment. Also here the results clearly suggest that lavender aromatherapy reduces the drowsiness on next morning and it was easier for the participants to get up. There were no gender differences and “daily variations in the quality of sleep during this period” observed. It was constant effective. [48]

In 31 young healthy volunteers, (15 women and 16 men, aged between 18 and 30 years) the influence of lavender oil on the quality of sleep was measured in the sleep laboratory for three days. The first night both groups (experimental group and a control group) had to stay in the sleep laboratory without olfactory stimuli for acclimatization. The two following nights both groups got olfactory stimuli (with lavender oil in the experimental group and the control group got distilled water for inhalation) between 11:10 p.m. and 11:40 p.m. in ten minutes intervals for two minutes. The self-reported sleepiness and mood were evaluated. Under the influence of lavender the proportion of deep or slow-wave sleep (SWS) increased in male and female subjects. The subjects felt

more vital next day. So, there was a significant improvement in the quality of sleep after aromatherapy compared to the control group. [49]

#### JASMINE TEA & LAVENDER

Kuroda et al. studied the effect of the smell of jasmine tea and lavender and their main ingredients (R)-(-)-linalool and (S)-(+)-linalool on the mood and the autonomic nervous activity (ANS) in 24 healthy volunteers. They worked with jasmine tea and lavender in the lowest concentration still perceptible. The blood pressure (RR), heart rate, and the Profile of Mood States test (POMS) were measured before and after 5 minutes of inhalation. Both lavender and jasmine tea odors perceived at similar intensity induced a significant decrease in heart rate compared to the control group. In the POMS test, these two flavors had a positive effect on mood, the subjects felt calm and vital. Also the effects of pure (R)-(-)-linalool, one of the largest odor components both in jasmine tea and in lavender, were tested “at the same concentration as in the jasmine tea.” (R)-(-)-linalool caused a significant decrease in heart rate compared to the control and set off a quiet and good atmosphere in the subjects. The enantiomer (S)-(+)-linalool showed no physiologic effect. Kuroda was able to show in his study, that jasmine scent in less concentration and (R)-(-)-linalool, one of its components, had sedative effects on both autonomic nervous activity as well as on the mood. [50]

#### MELISSA OFFICINALIS

The anxiolytic, anti-stress and relaxing effect of *Melissa officinalis* L. [Lamiaceae] have been known for a long time. Cyracos®, a standardized extract of *M. officinalis* L., inhibits gamma-aminobutyric acid degradation, which has already been tested in mice. Cases et al. examined in a prospective, open-label, 15-day trial, the efficacy of Cyracos® on mild-to-moderate anxiety disorders and insomnia in 20 stressed subjects. 14 of them reported a complete remission of both anxiety and insomnia, in 17 of the 20 subjects, the insomnia decreased significantly. [51]

## VI. Essential oils and Anxiety

Anxiety is a psychological and physiological state characterized by cognitive, physical, emotional and behavioral problems. [52] The physiological responses to fear are controlled by the limbic system, particularly the *amygdala nuclei* are responsible for the assignment of emotions and fear. [53] There is an activation of the sympathetic nervous system and central noradrenergic systems and this, in consequence, releases the stress hormones, e.g. adrenaline, noradrenaline, dopamine and cortisol. [52] The physical symptoms of anxiety are consequences of the release of stress hormones and due to a real or imagined danger to their survival. All these reactions have to function to prepare for a fight or flight situation (“fight or flight“). Among these physical symptoms are the following: [54]

- Increased attention, pupils dilate, visual and auditory nerves are more sensitive
- Increased muscle tension, increased reaction rate
- Increased heart rate, increased blood pressure
- Flatter and faster breathing
- Energy supply in muscles
- Physical reactions such as sweating, trembling and dizziness
- Bladder, bowel and stomach function can be inhibited during the state of fear.
- Nausea and shortness of breath occur in some cases as well

The physical symptoms are the same, regardless of whether it is a real threat or a panic attack. Every fourth patient with anxiety disorders complains about chronic pain. [54]

In a study by Satou et al. “the effectiveness of aromatherapy massage on elderly patients” was examined in a long-term stay in a nursing home. Unfortunately, the authors did not give precise information about the used essential oils. Patients received aromatherapy massage twice a week over 4

weeks. “The questionnaire survey (face-scale, General Health Questionnaire-12 [GHQ-12]) and a salivary amylase activity measurement” were made before and after the first, fifth and eighth aromatherapy massage. “A decrease in stress after aromatherapy massage was observed.” The face scale and the salivary amylase activity could be observed decreasing trends, but no significant reduction. In the GHQ-12 a significant reduction was observed in the long term. In this study it could be shown, that aroma massage is a very effective way in reducing psychological stress in elderly patients in long-term hospitalization. [55]

#### CANANGA ODORATA (YLANG-YLANG)

Hongratanaworakit et al. investigated in a controlled study of 40 healthy volunteers the effect of transdermal absorbed ylang-ylang oil (*Cananga odorata*, (LAM.) HOOK F. et T. THOMSON, Annonaceae) on physiological parameters in the human body (pulse, skin temperature, blood pressure and respiratory rate), and a self-evaluation using a visual analog scale (VAS). Volunteers in the ylang-ylang group showed a significant increase of skin temperature and a significant decrease of blood pressure. Participants in this group also felt much calmer and were more relaxed compared to the control group. [56]

#### JASMINUM SAMBAC

Hongratanaworakit proved in another study based on 40 healthy volunteers that topically applied jasmine oil (*Jasminum sambac* L., Oleaceae) onto the skin of the abdomen had a significant increase in respiratory rate, oxygen saturation of the blood, and both systolic and diastolic blood pressure. So in comparison to placebo a significant increase in autonomic arousal was observed. After the massage with jasmine oil, the participants felt more attentive, more energetic and less heavily sedated than those in the control group. All this points, like the stimulating and activating effect of topically administered jasmine oil, indicate that it could be useful in treatment of depressions. [57]

## ROSA DAMASCENA

Hongratanaworakit also examined the effect of transdermal absorbed rose oil (*Rosa damascena* Mill, Rosaceae) on vegetative parameters such as blood pressure, heart rate, respiratory rate, skin temperature and blood oxygen saturation, as well as emotional reactions as measured by rating scales, in 40 healthy subjects. To exclude any olfactory stimulation, the subjects were required to wear respirators. Rose oil caused, compared to placebo, a significant decrease in respiratory rate, systolic blood pressure and oxygen saturation, all of these were signs of a relaxing effect of rose oil. Even with the self-evaluation rating scales the subjects of the rose oil group reported to be relaxed, quiet and felt sedated. The author came to the conclusion that rose oil could be used in the alleviation of depression and stress in humans due to its relaxing effects. [58]

## MATRICARIA RECUTITA, CHAMOMILE

Amsterdam et al. investigated the effect of *Matricaria recutita* L. (chamomile) [Asteraceae] extract therapy in 57 “patients with mild to generalized anxiety disorder (GAD)” for eight weeks in a double-blind, placebo-controlled study. 28 of them were assigned to the experimental group and 29 to the placebo group. The Hamilton Anxiety Rating (HAM-A), changes in the Beck Anxiety Inventory, the Clinical Global Impression Severity and psychological well-being were measured. The results showed a large reduction in mean Ham-A Rating, which means a significant reduction of fear in the chamomile group compared to the placebo group. Even in the secondary endpoints Beck Anxiety Inventory, the Clinical Global Impression Severity and psychological well-being chamomile caused positive results. It was shown that chamomile excited an anxiolytic activity on patients with mild GAD. [59]

## CITRUS SINENSIS

Goes et al. examined the effect of sweet orange (*Citrus sinensis* L. (L. OSBECK) [Rutaceae]) flavor to healthy volunteers in anxiogenic situations. For this purpose 40 health male subjects were divided into five groups, three of them were administered the essential oil of sweet orange for inhalation (1st

group: 2.5 drops, 2nd: 5 drops, and the 3rd: 10 drops of the aroma test). Furthermore, there was a group that inhaled the essential oil of tea tree (2.5 drops) and a placebo group that got water (2.5 drops) for inhalation. After the inhalation volunteers underwent the Stroop Color Word Test (SCWT) with video monitors. The physiological parameters (gastrocnemius electromyogram and heart rate) and psychological parameters (anxiety, subjective stress, calming, and sedation) were measured prior to inhalation as well as during and after the SCWT. The results showed no significant changes in the verum group in state-anxiety, subjective stress and rest levels, but in the anxiogenic situation a significant anxiolytic activity of sweet orange essential oil was noticed. [60]

#### LAVENDER

In a double-blind study conducted by Bradley et al., the anxiolytic effect of Lavender essential oil, taken orally, was assessed without olfactory stimuli. To 97 subjects were administered lavender capsules (placebo, 100  $\mu$ l, 200  $\mu$ l). At the beginning of the study baseline measurements, namely “heart rate (HR), galvanic skin response (GSR), heart rate variability (HRV), State-Trait Anxiety Inventory (STAI), mood and the positive and negative affect scale (PANAS)” were performed. After the baseline was adjusted the capsules were given. To generate a sense of fear, movie clips, only a neutral, then a fear-inducing, and finally a film clip for carefree relaxation have been shown to the participants. The results showed that students, that had been administered the 200  $\mu$ l lavender dose felt very relaxed after ingestion. During the neutral film clip they were in a reduced anxiety state, with a reduced galvanic skin response and heart rate, and an increased heart rate variation. During anxiety-provoking film clips the relaxing effect of lavender was a little higher in females, but only based on heart rate variation. In men the sympathetic arousal was increased during the anxiety-provoking film. Women who had taken the 200  $\mu$ l lavender capsules, showed an increased HRV in all three film clips, suggesting a decreased anxiety. Bradley et al. supposed on these results that lavender excited anxiolytic effects in humans in situations where the fear is not so great. However, in situations of very great anxiety it probably would not show the



desired effect. [61]

Also in a study of Kritsidima et al. the anxiolytic effect of lavender oil was assessed. The authors tested 340 people waiting for a dentist appointment. The study was conducted randomized-controlled and the subjects therefore were divided into two groups and were allocated either to the lavender group or to the placebo group. The current fear, using instantaneous State-Trait Anxiety Indicator (STAI) and the basic fear of the dentist with the help of changes in the Modified Dental anxiety Scale (MDAS) were determined. Although in the general dental anxiety the MDAS of both groups showed similar results, the current STAI was better in the lavender-group than in the control one. The results suggest that the subjects in the lavender group would not be less afraid on subsequent visits to the doctor, but their state anxiety during visits with lavender scent was reduced. [62]

Muzzarelli et al. examined the anxiolytic effects of lavender oil. In their controlled, prospective study of 118 patients, the reduction of anxiety was assessed using aromatherapy with lavender oil before elective colonoscopy or esophago-gastro-duodenoscopy. According to the STAI, the anxiety scores of patients were evaluated before and after aromatherapy. The experimental group inhaled the essential oil of lavender, while the control group an inert oil (placebo) was given. The control group and the intervention group showed similar results before the start of the study in terms of fear. The STAI state-anxiety of women was well 3 percentiles higher (at 99) than in men (96). As expected, in the control group, there was no difference in the state-anxiety level before and after the inhalation of inert oil. But also in the lavender group, no difference after intervention was observed. [63]

A similar study was conducted in 2008 by Hoya et al. with better results. The authors examined the effect of optimal soothing environment (OSE) for the reduction of anxiety in patients undergoing gastroscopy. The study was conducted over 6 months in a 150-bed acute care hospital in Japan. Fifty outpatients were divided randomly into 2 groups (OSE group n = 26 patients;

and the control group n = 24 patients). The reduction of anxiety was measured using the Face Scale score and systolic blood pressure pre- and postprocedural and was compared with the blood pressure at the time of the arrival at the hospital. For the intervention of the OSE a safe essential oil burner (produced by NHK software, Japan Broadcasting Corporation) with lavender flavor and a digital video disk program called "Flow" as used in the waiting room before gastroscopy. The self-assessment of anxiety in the control group was significantly higher before gastroscopy than at the time of arrival at the hospital and returned after the gastroscopy back to the initial value. Also, the systolic blood pressure measurements in the control group were significantly higher before and during gastroscopy than at the arrival at the hospital. Patients in the OSE group showed no increase in anxiety and the systolic blood pressure was not raised before the gastroscopy. Thus the production of an optimal soothing environment with lavender scent is an inexpensive, simple and safe way to minimize fear and anxiety of patients prior to and during gastroscopy. [64]

Saeki investigated in a randomized controlled crossover study "the effect of foot-bath with or without the essential oil of lavender on the autonomic nervous system". The study was conducted at a nursing college in Japan with young women. They got a foot bath for 10 minutes with warm water and with or without lavender oil. Respiratory rate and finger tip blood-flow were measured and an electrocardiogram was recorded, even the autonomic function was assessed by heart rate variability. The footbath alone showed no changes in heart or respiratory rates, but there was a significant increase in blood flow. By a spectral analysis it could be established that "the parasympathetic nerve activity increased significantly" in both cases during the foot bath with and without essential oil. The foot bath with lavender resulted in delayed changes in autonomic activity and seemed relaxed. A hot foot bath with lavender leads to positive changes in autonomic activity and relaxation. [65]

Woelk and Schläfke conducted a controlled clinical trial to compare the efficacy of silexan, a new oral formulation of lavender oil in capsules, with

benzodiazepine. In patients with a GAD oral administration of silexan was compared with the benzodiazepine lorazepam over 6 weeks. To determine the severity of anxiety, the HAM-A total score was used both at the beginning of the study and after 6 weeks of therapy. Woelk and Schläfke came to the conclusion that lorazepam and silexan both sat down the HAM-A score very well and were almost equally well in relief of generalized anxiety. Also the “SAS (Self-Rating Anxiety Scale), PSWQ-PW (Penn State Worry Questionnaire), SF-36 Health Survey Questionnaire and the Clinical Global Impressions (CGI)“ of severity of the disease were measured. A sleep diary was performed and the same positive results for silexan and lorazepam were found. Woelk and Schläfke showed in their study that silexan is equally good in the treatment of GAD as the benzodiazepine lorazepam. [66]

#### LAVENDER & BERGAMOT

Hongratanaworakit tested in a placebo-controlled study whether the mixture of essential oils of lavender and bergamot excited a synergistic effect in the treatment of depression or anxiety. The author examined the effects of blended essential oil (lavender and bergamot) topically applied onto the skin of the abdomen on vegetative parameters (blood pressure, breathing rate, pulse and skin temperature) and emotional reactions (relaxation, vitality, calmness, alertness, mood and attention). Forty subjects took part in the study. Blended essential oil showed, compared to placebo, a significant decrease in systolic and diastolic blood pressure and heart rate. On an emotional level it showed the same results, the subjects in the experimental group rated themselves more "quiet" and "relaxed" compared to those in the control group. Interesting at this point would be a direct comparison with bergamot and lavender oil alone. [67]

#### EUCALYPTUS GLOBULUS & UNCARIA TOMENTOSA

The aim of the study of Quilez et al. was to determine the interactions between diazepam (2 mg/kg) and one of the two sedating phytopharmaceuticals *Eucalyptus globulus* Labill. (Myrtaceae) and *Uncaria tomentosa* (Willd. ex Roem. & Schult, Rubiaceae) each two different concentrations. *E. globulus* (6 mg / kg and 3.25 mg / kg) excited an inhibitory and sedative effect at both

doses and it could produce an anxiolysis without muscle relaxation at the higher dose. *U. tomentosa* (Willd. ex Roem. & Schult). DC. increased at both doses (7.14 mg / kg and 3.54 mg / kg) the effect of diazepam on the spontaneous motor activity, and at the lowest dose an exploratory ability was found. According to Quilez et al. these two herbal medicines may be useful in musculoskeletal disorders when treated with benzodiazepines because of their anti-inflammatory activity. [68]

#### NEROLI

Hu et al. also examined the effect of aromatherapy on patients undergoing coloscopy. The randomized and controlled study was carried out between 2009-2010 in order to investigate the effect of aromatherapy on anxiety, stress and physiological parameters in patients prior to a coloscopy. The 27 subjects had a mean age of 52.26 + / - 17.79 years and were divided into two groups: 14 were allocated to the experimental group and received neroli oil for inhalation, while ordinary sunflower oil for inhalation was given to 13 subjects in the placebo group. „The fear index was measured by the STAI-S before and after the procedure and the pain index post-procedural by visual analog scale (VAS).“ Also physiological parameters such as heart rate, blood pressure and respiratory rate were measured before and after aromatherapy. Procedural anxiety by STAI-S score and procedural pain by VAS showed no significance. On the other hand a significant lower pre- and post-procedural systolic blood pressure was detected in the neroli group compared to the control group. Although there were no significant results on the reduction of anxiety with neroli oil aromatherapy, it could be seen that the systolic blood pressure was reduced. So, aromatherapy with neroli is certainly a cost effective, but still safe and effective intervention before a coloscopy. [69]

Seo examined in a two-group cross-over study, the effect of aromatherapy on stress responses in adolescents. Essential oils were applied on a necklace for inhalation in the aroma group and an inert carrier oil was applied for the placebo group. With 36 female high school students the “Fisher’s exact test, t-test and t-test using SPSS / WIN program“ were conducted to investigate the

effects of aromatherapy on stress. It was shown that the stress level of the aroma-group was significantly lower than in the placebo group. The stress responses were significantly reduced whereas the salivary IgA levels were not. Seo could demonstrate that the inhalation of essential oils is an effective method in stress management. [70]

#### MELISSA & VALERIANA

Kennedy et al. investigated the effect of a combination of *Melissa officinalis* L. [Lamiaceae] (lemon balm) and *Valeriana officinalis* L. [Valerianaceae] (valerian) on laboratory-induced stress in 24 healthy volunteers. The study was double-blind, placebo-controlled and randomized, conducted as a balanced cross-over experiment. The 24 subjects were divided into four groups and received “three doses (600 mg, 1200 mg, 1800 mg) of a standardized product, *M. officinalis* and *V. officinalis* extracts, plus a placebo“, on different days, separated by a 7 day wash period. “Modulation of mood and anxiety were assessed“ before the dose administration and 1 h, 3 h and 6 h after ingestion using the Defined Intensity Stressor Simulation (DISS) battery. Also cognitive function was assessed at the four concurrent tasks of the battery. It was found that 600 mg dose of the combination of lemon balm and valerian, improved the negative effects of the DISS on ratings of anxiety. At a dose increase to 1800 mg, however, a slight increase of anxiety during a testing session was recorded. With all 3 doses, a reduction in the performance was found on the Stroop task module within the battery. Thus, it was shown that a combination of *M. officinalis* and *V. officinalis* possesses anxiolytic properties. [71]

## VII. Essential oils and Cancer

43 patients with terminal cancer (including 22 in the experimental group and 21 in the comparison group) were tested in order to improve the oral health care using essential oils. The experimental group received a special oral care with essential oils (lavender, geranium, tea tree and peppermint), while the control group received a special oral care with 0.9% saline. Both groups received their oral care twice a day for a week. The authors recorded the patient's subjective feeling of the tooth-purity and the colony forming units of *Candida albicans* were measured before and after the treatment. The patients in the experimental group had a good feeling about their oral care and the elimination of *C. albicans* strains was effective. The oral care with essential oils could therefore have a positive effect in patients with terminal cancer. [72]

Chang investigated 58 hospice patients with terminal cancer and the effect of aroma hand massage on pain, anxiety and depression. 28 of them belonged to the experimental group and received an aroma hand massage, and 30 were assigned to the control group and received a hand massage with an ordinary almond oil. Patients in both groups were given a 5-minute hand massage every day for 7 days. In the experimental group, the oil was a mixture of lavender, bergamot and frankincense in the ratio of 1:1:1, which were mixed with 50ml almond oil. The results showed a significant reduction in pain scores as well as in depression both compared with the control group. [73]

In a randomized, controlled pilot study of the effects of aromatherapy massage on mood, quality of life and physical symptoms cancer patients were investigated. 46 participants were assigned to either conventional day care alone or day care plus a weekly aromatherapy massage for four weeks. The aromatherapy massage was performed using a standardized mixture of essential oils. At the beginning and at the end of every week the patients evaluated their mood, quality of life and those two symptoms that distressed them most on a questionnaire. „Only 11 of the 23 (48%) patients in the aromatherapy group and 18 of 23 (78%) in the control group“ completed the four-week study, due

to a large number of withdrawals. Quality of life, mood and physical symptoms were improved in both groups, however, no significant difference between aromatherapy and placebo was observed. [74]

The effect of aromatherapy massage on psychological and immunological parameters of 12 breast cancer patients was observed in an open semi-comparative study by Imanishi et al. The results of one month prior to treatment were compared with those during and one month after the aromatherapy massage. In a four-week period patients were given an aromatherapy massage for 30 minutes twice a week. The comparison showed a reduction in anxiety within these four weeks determined by the STAI test and also a reduction in the basis of the Hospital Anxiety and Depression Scale (HADS) test. The authors also assumed that the immune status had been improved. [75]

In a small study, Hadfield tested eight patients with primary brain cancer, whether aromatherapy massage (AM) could reduce the anxiety of patients at their first follow-up appointment after radiotherapy. Assessed were the HADS and physical parameters. No positive effects of aromatherapy massage were observed in the HADS, however, a significant reduction of all four physical parameters, thus showing a relaxing effect of AM on the autonomic nervous system could be observed. In the interview patients also confirmed that they felt relaxed. Aromatherapy massage can be supportive and improve the quality of life. [76]

Soden et al. tested in a four-week randomized study with 42 patients with advanced cancer the effects of a weekly aromatherapy massage with lavender oil. The authors compared the effects of a weekly aromatherapy massage with lavender oil and inert carrier oil and massage with only inert carrier oil with no treatment. Changes in physical and psychological symptoms were assessed using the “VAS of pain intensity, the Verran and Snyder-Halpern (VSH) Sleep Scale, the HADS and the Rotterdam Symptom Checklist (RSCL).” While pain, anxiety and quality of life showed no significant improvement, the

quality of sleep was significantly improved in both the massage and the aromatherapy plus massage group. There was also a statistically significant reduction in depressive symptoms in the two massage groups. The addition of lavender oil led to an improvement compared to a massage alone. [77]

In a study by Stringer et al. aroma sticks were used, similar to those of Vicks® Vapor Inhaler®, against anxiety, nausea and insomnia of 160 cancer patients in a hospital. The study was conducted as a retrospective evaluation service. Scent-sticks with lavender were offered to the patients on a voluntary basis. In the score sheet, which had been used by those patients who accepted these sticks, they also documented how often the scent sticks were used and which benefits they perceived. 123 of 160 patients (77%) reported at least one positive benefit of aroma sticks. 65% of patients reported that they felt more relaxed and 51% felt less stressed. 47% of patients reported an improvement suffering of nausea by aroma sticks and 55% of those affected, reported that aroma sticks helped them to sleep better. In this study, it was also shown that the effects of the fragrance stick was directly proportional to the frequency of administration. [78]



## VIII. Essential oils and Dementia

**Dementia:** “Dementia is characterised by memory loss (initially of recent events), loss of executive function (such as the ability to make decisions or sequence complex tasks), other cognitive deficits, and changes in personality. This decline must be serious enough to affect social or occupational functioning, and reasonable attempts must be made to exclude other common conditions, such as depression and delirium.” [79]

**Alzheimer's disease :** “Alzheimer's disease is a type of dementia characterised by an insidious onset and slow deterioration, and involves impairments in memory, speech, personality, and executive function. It should be diagnosed after other systemic, psychiatric, and neurological causes of dementia have been excluded clinically and by laboratory investigation. The median life expectation for people with Alzheimer's is about 6 years after diagnosis, although many people may live far longer.” [79]

**Behavioral and psychological symptoms of dementia (BPSD)** is very common in patients with dementia and it is often a major challenge for nursing staff . It manifests in the patient often in psychological and physical aggression and anxiety. [88] Snow (2004) et al. showed that in patients with dementia, the olfactory system is affected. [83] According to Burns (2011), the olfactory dysfunction could be a marker of Alzheimer's disease in order to determine an early stage. [89]

### LAVENDER

In 2001, Smallwood compared the effect of aromatherapy massage (PM) with only aromatherapy (CA) and only a massage (M) on the disordered behavior in patients with dementia. The 21 patients with dementia were randomized into one of 3 groups. At various times of the day, video recordings of the participants were made at specified times. The observers did not know at what time and which intervention took place, so they were able to assess the video objectively. The best results were found in aromatherapy and massage (AM). Agitation was subdued in this category the most. Patients in the aromatherapy

massage group also showed the least disturbance between 3 and 4 PM. Smallwood and his colleagues showed that aromatherapy could be very good when supplemented with massage. [80]

Holmes et al. conducted a placebo-controlled study to see whether lavender oil (Lamiaceae) had a calming effect on patients with severe dementia and agitation. Holmes et al. used the Pittsburgh Agitation Scale (PAS) to measure anxiety. 15 subjects participated in the study. In a common room, an AromaStreamer was provided to give the room a scent. Aromatherapy with 2% lavender oil was given to the patients for 10 days, every second day. On the other days, the AromaStreamer was filled with water as a placebo. During the observation of the participants, the appraisers wore nose clips to ensure blinding. In nine patients, there was an improvement in their condition from experiencing the aromatherapy compared to the placebo. In 5 of the 15 patients there was no improvement observed and in one patient a negative change occurred. On the Pittsburgh Agitation Scale, a significant improvement was observed from lavender oil aromatherapy, compared to placebo. [81]

The same year, Gray et al. conducted a study of 13 nursing home residents with dementia (7 men and 6 women) who resisted their medication physically or through vocalizations. They tested whether the behavior of the subjects would change in regards to their medication administration from a pleasant aroma. They successively used lavender vera (*Lavendula officinalis*, Lamiaceae), sweet orange (*Citrus aurantium*, Rutaceae), tea tree (*Melaleuca alternifolia*, Myrtaceae) or a neutral flavor (control). The drug administration was filmed so that the duration and frequency of negative behavior of the subjects in all four flavors could be later evaluated. In this study, no positive results for aromatherapy were noted on the aggressive behavior of the patients. [82]

A similar study was carried out by Snow et al. in 2004. In a 16-week program. They tested the effect of aromatherapy on agitation of 7 patients with advanced dementia in nursing homes. In the first 4 weeks, no intervention took place and

at that time the patients' states and agitation without aromatherapy were measured by the Cohen-Mansfield Agitation Inventory. In the following 10 weeks, they got aromatherapy with a different scent every 2 weeks in the following sequence: ABCBA ("A = lavender oil, B = thyme oil, C = unscented grapeseed oil"). At the end, 2 weeks of post-intervention measurements followed. Patients wore a large cotton pad on their T-shirt for 3 hours per day, which had 2 drops of the essential oils on it. This study also measured the olfactory function of patients and Snow et al. came to the conclusion that in people with dementia, the sense of smell is impaired. Every second day the agitation was evaluated by the Cohen-Mansfield Agitation Inventory. In this study, no differences between the various aromatherapy oils were identified. It was surprising, that there were no differences between patients with good and impaired olfactory function. This study had a small number of participants and there was no placebo group for comparison, so I think this study may not be a good representation. [83]

In a study by Lee done one year later, the effect of aromatherapy with lavender oil was compared to a massage with jojoba oil. The patients with Alzheimer's were divided into 3 groups. Depending on the group, they got a massage with lavender oil, a massage with jojoba oil, or no treatment (control group) for 2 weeks. The lavender oil massage was observed to have no effect on cognitive function compared to the jojoba oil massage or the no intervention group. However, lavender oil was shown to significantly influence emotions and the aggressive behavior in patients was positively affected compared to the other two groups. [84]

In 2007, a similar study was performed by Lin et al. Lin and his colleagues evaluated the effectiveness of *Lavandula angustifolia* (Lamiaceae) on agitation in 70 Chinese patients with dementia. The study was designed in a randomized cross-over trial and lasted 6 weeks. The patients were divided into 2 groups. The first group had lavender aromatherapy (inhalation of lavender oil) for 3 weeks and for the next 3 weeks they inhaled sunflower oil as a placebo. The other group had the same interventions, but started with the sunflower oil.

Agitation was measured by the Cohen-Mansfield Agitation Inventory (CMAI). Aromatherapy with lavender was shown to reduce the agitation by a quarter. [85]

Jimbo et al. dealt with the effect of aromatherapy on 28 elderly patients who suffer from dementia (17 of them from Alzheimer's). The study was divided into 3 parts (control phase, aromatherapy, and washout phase) and lasted 28 days per phase. Aromatherapy expired so that the lounge was clouded in the morning and evening by two diffusers with different oils. From 9:00 AM to 11:00 AM lemon and rosemary oil were used. From 7:30 PM to 9 PM they used lavender and orange. The study was based on the hypothesis that lemon and rosemary are able to activate the sympathetic nervous system and may lead to better memory and concentration. Lavender and orange, in contrast, can activate the parasympathetic nervous system and act as dampeners, able to calm and promote sleep. Based on various scales, the course of the disease and the effects of aromatherapy were measured 4 times (before and after the control period, after the aromatherapy, and after the washout period). Jimbo et al. reported a significant improvement in personal orientation, and cognitive functions in all patients. In patients suffering from Alzheimer's disease, the improvement was significant. [86]

#### MELISSA

Akhondzadeh et al. 2003 conducted a multicenter study to test the effectiveness and safety of 60 drops of *Melissa officinalis* (Lamiaceae) extract in patients suffering from mild to moderate Alzheimer's. This placebo-controlled study lasted 4 months and took place at 3 centers in Tehran, Iran. 42 patients (18 women and 24 men) between 65 and 80 years old took part in the study. They had a "score of  $\geq 12$  on the cognitive subscale of the Alzheimer Disease Assessment Scale (ADAS-cog) and  $\leq 2$  on the clinical dementia rating (CDR)." Patients were either in the Melissa group or the placebo group. After 4 months, the changes in ADAS-cog and CDR-SB were measured. Treatment with *M. officinalis* showed significant improvement in cognitive function compared to the placebo group or to baseline. [87]

Ballard et al. 2002 examined the effect of *Melissa officinalis* (lemon balm, Lamiaceae) on agitation in 72 patients with severe dementia. The study was conducted using a double-blind placebo-control. Half of the patients were assigned randomly to the Melissa group and half of the patients received the placebo (sunflower oil). Both the lemon balm oil and sunflower oil were mixed with a base lotion to create a 10% solution. Patients' faces and arms were creamed twice a day by nurses. The nurses tried to apply the lotion quickly to the skin in order to exclude massage effects. After four weeks, changes to the quality of life and social behavior were measured by the Cohen Mansfield Agitation Inventory (CMAI) scale. The study was completed by 71 patients. Patients in the Melissa group showed a significant reduction in agitation on the CMAI scale. There was an improvement in agitation by 35% in the active treatment group and 11% in the placebo group. Patients in the active treatment group spent more time on constructive activities during the four weeks and were also less socially withdrawn compared to the placebo group. [88]

In a double-blind, placebo-controlled randomized trial in 2011, Burns et al. compared the effectiveness of a hand massage with lemon balm oil (*M. officinalis*, Lamiaceae) in the treatment of agitation in Alzheimer's patients to cholinesterase inhibitors donepezil. A hand massage with sunflower oil was used as a placebo. The patients with Alzheimer's disease were divided into three groups and received one of the three treatments. 94 patients participated in the four-week study, and the change or reduction of their agitation was measured by the Pittsburgh Agitation Scale (PAS) and the Neuropsychiatric Inventory (NPI). After 12 weeks agitation was measured again in 81 participants. To ensure blinding, caregivers used nose clips. Among the 3 groups there were no significant differences. In all 3 groups, an 18% improvement on the Pittsburgh Agitation Scale and a 37% improvement in the Neuropsychiatric Inventory were found after 12 weeks. It was shown that after a few weeks, even hand massage alone could significantly improve agitation and was as effective as donepezil. [89]

## IX. Essential oils and pain management

In 1999, Buckle examined the effect of aromatherapy on chronic pain. She was convinced that by stimulating the sense of touch and smell, a parasympathetic response was being promoted, and thus would lead to relaxation on a deeper level. In previous studies, it had already been shown that during relaxation perception of pain is changed. [90] Steflitsch et al. examined this same question: "Aromatherapy works on the sensory system and appears to enhance the parasympathetic response, which is closely linked with endorphins, through the effects of touch and smell, encouraging relaxation at a deep level." [91] Steflitsch et al. assumed that the analgesic effect of aromatherapy is attributable to several factors:

- The mixture of volatile substances reach certain parts of the brain
- Certain components of the essential oils act as agonists to receptors of the neurotransmitters dopamine, serotonin and norepinephrine in the brain
- contact of essential oils with sensory fibers of the skin can influence the transmission of referred pain.
- Rubefacient effect (counter-irritant effect) [91]

Essential oils for pain management include: "black pepper (*Piper nigrum*, Piperaceae), clove bud (*Syzygium aromaticum*, Myrtaceae), frankincense (*Boswellia carterii*, Burseraceae), ginger (*Zingiber officinale*, Zingiberaceae), Juniper (*Juniperus communis*, Cupressaceae), spike lavender (*Lavandula latifolia*, Lamiales), true lavender (*Lavandula angustifolia*, Lamiaceae), Lemongrass (*Cymbopogon citratus*, Poaceae), marjoram (*Origanum majorana*, Lamiaceae), myrrh (*Commiphora molmol*, Burseraceae), peppermint (*Mentha piperita*, Lamiaceae), rose (*Rosa damascena*, Rosaceae), rosemary (*Rosmarinus officinalis*, Lamiaceae), verbena (*Aloysia triphylla*, Verbenaceae) and ylang ylang (*Cananga odorata*, Annonaceae)." [91]

In a randomized, crossover study, Gedney et al. tested the effect of olfactory admission of 2 essential oils on the affective and sensory responses on experimentally induced pain. In the study, 26 patients (13 women and 13 men)

took part and were divided into 3 groups. The first group received the essential oil of lavender for inhalation, the second group received the essential oil of rosemary for inhalation. The third group was the control group and inhaled distilled water. Changes in the pain intensity and pain assessment were measured and recorded using a visual analog scale. At first, no quantitative changes in pain perception through aromatherapy appeared. Retroactively, the subjects stated that there had been a reduction in pain intensity and the sensation of pain with lavender aromatherapy compared to the control group. In the treatment with rosemary, this effect was also seen, but only slightly. Gedney et al. concluded that aromatherapy has no direct analgesic effect but can have a positive influence on the affective pain-assessment. [92]

In 2006, Kim et al. tested in a placebo-controlled study the analgesic effect of lavender oil in 50 patients after breast biopsy. They were divided into two groups. 25 received a face mask with two drops of 2% lavender oil. The other 25 patients were in the placebo group and received a face mask with no additive. 5, 30 and 60 minutes after the operation the pain was evaluated with the numeric rating scale. The satisfaction of patients with pain management was also recorded. Postoperative aromatherapy did not have a significant effect on the perception of pain, but in the lavender group there was a significantly higher satisfaction with pain management. [93]

In 2007, Kim et al. designed a randomized placebo controlled study to evaluate the reduction of opioid medication after LAGB (laparoscopic adjustable gastric banding) with the help of aromatherapy with Lavender. 54 patients took part in this study. After surgery, patients in the experimental group were given lavender oil and an oxygen mask in the recovery room. Patients in the control group received non scented baby oil. The post-operative pain of patients in both groups was treated with morphine. After 5, 30 and 60 minutes, pain was measured using numerical rating scores (0-10). Sedation was also measured. Patients in the lavender group needed significantly less analgesia respectively morphine compared to the control group (2.38 mg vs. 4.26 mg). [94]

In 2000, Dolara and his colleagues found that the essential oils of myrrh [*C. myrrha* (Burseraceae)] are able to block the inward sodium current in mammalian excitable membranes and thus it is able to numb the skin and act as a local anesthetic. [95]

In 2007, Burns and his colleagues conducted a randomised controlled trial (RCT) to test whether aromatherapy is a good care option during labor and whether the well-being of pregnant women and newborns was improved compared to standard care during labor. The participants were randomly allocated to an aromatherapy group or control group (251 vs. 262). The midwives who carried out the aromatherapy were trained. The perception of pain in aromatherapy was minimally reduced, but not significantly. [96]

In 2005, Kim et al. investigated the effect of aromatherapy on depression and pain in patients with arthritis in a placebo-controlled sample test on 40 patients in a rheumatism center in South Korea. The following essential oils were used: lavender, eucalyptus, marjoram, peppermint and rosemary - in the ratio of 2:2:1:1:1. This mixed essential oils had been diluted to 1.5% with almond oil (45%), apricot oil (45%), and jojoba oil (10%). There was a significant reduction in pain and depression compared to the control group. [97]

In a double-blind, placebo-controlled experimental study, Yip and Tam examined the effect of a massage with essential oils (1% *Zingiber officinale* [Zingiberaceae] & 0.5% *Citrus sinensis* [Rutaceae]) in 59 patients with moderate to severe knee pain. The patients were divided into 3 groups. The treatment group received 6 massages with essential oils within three weeks, the placebo control group received the same massage with olive oil and the control group received no intervention. The condition of the patient was checked at baseline, after one week, and after four weeks of the treatment. Compared to baseline knee pain intensity, stiffness and physical function was significantly improved in the experimental group, but compared to the other groups there was only slight improvement. After a week the experimental group was significantly better in terms of physical function and pain, but their



improvement was not sustained. After four weeks, the values adjusted back to those of the other two groups. Yip and Tan came to the conclusion that an aromatherapy massage has the potential for short-term knee pain relief. [98]

In a randomized, controlled study done by Shin and Lee the effect of acupressure with essential oils and only acupressure on 30 stroke patients with hemiplegic shoulder pain was compared. 15 subjects received acupressure, the other 15 patients received acupressure with aromatherapy (lavender, rosemary, peppermint). The acupressure sessions were conducted for two weeks twice a day. Each session lasted 20 minutes. Shoulder pain and motor performance were measured. Pain was significantly reduced in both groups after the treatments, but in the aroma group the results were better. [99]

In a randomized, placebo-controlled trial, Han et al. tested the effectiveness of aromatherapy (with *L. officinalis* [Lamiaceae], *Salvia sclarea* [Lamiaceae], *Rosa centifolia* [Rosaceae]) as treatment for menstrual cramps and symptoms of dysmenorrhea. In the study, 67 female students took part, who were suffering from menstrual cramps with greater than 6 on a 10-point visual analog scale. The participants were randomly divided into one of three groups: the treatment group (n = 25) / the placebo group (n = 20) / the control group (n = 22). For the treatment group, 2 drops of lavender (*L. officinalis*), one drop of rose (*R. centifolia*) and one drop of clary sage (*S. sclarea*) were mixed with 5 ml of almond oil and used for abdominal massage. The placebo group got an abdominal massage with almond oil but without essential oils. The control group had no intervention. The menstrual cramps were measured on the first and second day of menstruation after treatment. In the aromatherapy group there was a significant pain reduction compared to the other two groups. [100]

In 2012, Hur and his colleagues compared the effect of aromatherapy on menstrual cramps to the painkiller paracetamol. 55 Korean high school girls participated in this study and were divided into 2 groups: The aromatherapy-group (n = 32) and the paracetamol-group (n = 23). For aromatherapy massage, geranium, ginger, marjoram, sage and cinnamon were mixed with almond oil

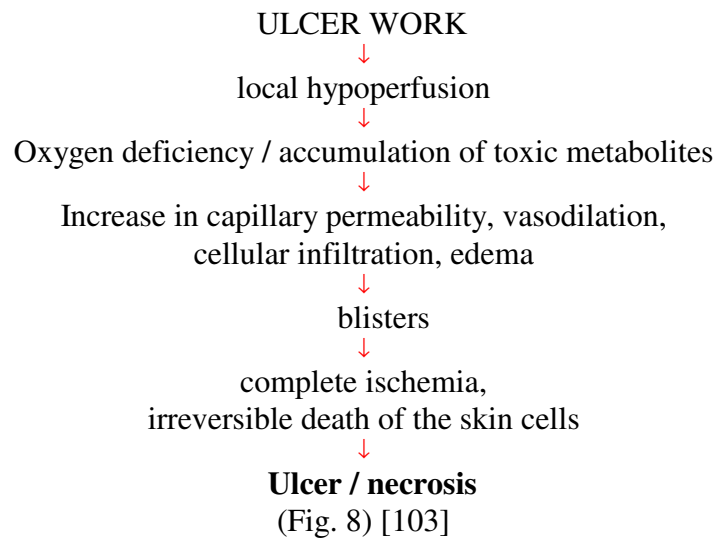
and massaged onto the patient's stomach. The visual analogue scale was used for the measurement of menstrual pain and was measured before the treatment and after 24 hours. In the aromatherapy group, the reduction of menstrual pain was significantly higher than in the paracetamol group. [101]

## **X. Decubitus (pressure ulcers)**

Prevention of pressure ulcers is an important issue for nurses and medical staff. Pressure ischemia is the most common cause for the occurrence of ulcers. There are many risk factors that contribute to the development of an ulcer. [102] A decubitus is caused by a prolonged pressure effect, resulting in ischemia in the areas of the skin and to damage and the death of skin cells, and the underlying tissue. Usually a decubitus arises in areas over bony areas. Generally, "a decubitus arises when the size of the contact pressure exceeds a value of 25mmHg for more than 2 hours." Even in healthy people, it can sometimes lead to large production runs, but these are usually short-lived, because healthy people move consciously or unconsciously regularly and counteract such a decubitus. However, in sick people who suffer for example, from dementia, cerebrovascular events, paresthesia or general weakness these voluntary or involuntary movements are often lacking and thus favors the formation of bedsores. According to Hirsch, it is a fallacy to believe a decubitus would start from the outside and as long as you don't see it, there will be no bedsores. He says, "A pressure ulcer, and thus the subsequent death of tissue usually starts in depth, namely directly on the abutment of the bone." When a decubitus is accrued, it is a major challenge for the nursing staff and a long and painful affair for the patient. The general condition of the patient can also thereby deteriorate drastically; complications can occur and pressure ulcers can lead to infection, sepsis or even death. For a 60-year-old patient, the regeneration of the skin area takes three times longer compared to 20-year-olds. The development of a pressure ulcer is preventable relatively easily through good maintenance. [103]

ULCER RISK FACTORS
PRIMARY RISK FACTORS = FACTORS REDUCE MOTILITY
<ul style="list-style-type: none"> <li>• Neurological diseases with paralysis (all): cerebrovascular stroke, hemiplegia, hemiparesis, paraplegia, quadriplegia, comatose conditions of any origin</li> <li>• Surgical procedures: anesthesia (premedication, anesthesia, recovery period), long operating time</li> <li>• Psychiatric disorders and psychiatric drugs: acute psychosis as catatonia and acute depression, sedatives as neuroleptics, benzodiazepines, and similar medication</li> </ul>
SECONDARY RISK FACTORS
<p><b>Factors that reduce intravascular pressure:</b></p> <ul style="list-style-type: none"> <li>• Arterial hypotension: shock (hypovolemic, septic, cardiogenic), antihypertensive drugs overdose</li> <li>• Dehydration: diuretics, diarrhea, summer heat</li> </ul> <p><b>Factors that reduce oxygen transport to the cell:</b></p> <ul style="list-style-type: none"> <li>• Anemia: hemoglobin &lt;9 g / dl</li> <li>• Peripheral arterial disease</li> <li>• Diabetic microangiopathy</li> <li>• Hypotension, bradycardia</li> <li>• Hypovolemic shock</li> </ul> <p><b>Factors that increase oxygen consumption in the cell:</b></p> <ul style="list-style-type: none"> <li>• Fever &gt; 38 ° C</li> <li>• Hypermetabolism</li> <li>• Infections, cytokine anemia</li> </ul> <p><b>Factors, which lead to a lack of nutrients in the cell:</b></p> <ul style="list-style-type: none"> <li>• Malnutrition: lack of protein, vitamins, minerals, trace elements</li> <li>• Cachexia: immobility by muscle weakness and catabolism</li> <li>• Lymphopenia in malnutrition: immune deficiency, wound healing</li> </ul> <p><b>Factors that weaken the resistance of the skin:</b></p> <ul style="list-style-type: none"> <li>• Aging skin: thin, atrophic, with fewer immune cells</li> <li>• Skin disorders: eczema, thrush</li> <li>• Dry, cracked skin: promotes skin infections with bacteria and fungi</li> <li>• Pressure injured, irritated skin: as a sign of harmful shunt circulation</li> <li>• Heat, inflammatory redness: circumvention of nutritive microcirculation</li> <li>• Steroid-induced skin atrophy: thin, easily damaged skin</li> </ul>

(Tab. 3) [103]



### **PRINCIPLES OF PRESSURE ULCER PREVENTION [103]**

Effective prevention studies have been conducted to find the influence of primary and secondary risk factors regarding pressure ulcers (see Tab.). This means the reduction in the length of stay and size of the contact pressure and the improvement of the general condition of the patient. The principles of pressure ulcer prevention are therefore:

- Reduce the pressure dwell time by regular, two-hour patient transfer into the 30°- degree, lean angles right and left and in the supine position.
- reducing the size of the contact pressure at all five classical decubitus localisations below 25 mmHg by using the 30 ° - inclined storage and the use of soft mattresses.
- improving the general condition of the patient through treatment and influence of other risk factors such as malnutrition, anemia, pneumonia, depression, etc. [103]

The combination of all three methods is very effective and should be used routinely. Furthermore, the circulation of bedridden patients can be improved by passive exercises and mobilization. Even a brief lifting of the affected body parts improves microcirculation in the affected skin area. [103] This type of circulation support does not replace the regular repositioning! [103] It is very dangerous when wounds are infected! (See next Chapter)

## **XI. Essential oils with antimicrobial activity**

Due to the spread of antibiotics, more and more bacteria are developing a resistance and the effectiveness of treatment with antibiotics can be weakened. Essential oils often act very well against these multi-resistant bacteria (nosocomial bacteria). The bactericidal effect of essential oils can also be used in hospitals or nursing homes, for example, the growth of bacteria can be inhibited by using an antibacterial room spray with essential oils. Bacterial infections can delay the healing process, degrade overall health and also be very dangerous. For example, bacterial infections in wounds (see pressure ulcer) can lead to sepsis and even death.

### **LAVENDER**

The essential oil of lavender is used with increasing popularity and antimicrobial activity has been demonstrated in numerous studies, however, one must not lose sight of the dangers. The possibility of contracting dermatitis must be considered when using lavender oil. One study showed, for example, that with increasing exposure, more patients have these complications. There was an increased incidence of contact dermatitis with lavender (from 1.1% to 13.9% over 8 years). For everyday work in nursing science, it is also important to realize the effect of lavender oil as a potential allergen. [104]

Lavender oil is one of the most popular and commonly used essential oils in aromatherapy. In a study done by Huang in 2012, the effect and the mechanism of essential oils from lavender to lipopolysaccharide induced inflammation was investigated. The results showed that treatment with 0.1% lavender oil, increased cell viability significantly, and the authors demonstrated that lavender oil increased the inhibition of the IL-1 $\beta$  and the expression of heat shock protein 70 (HSP70) in LPS-stimulated THP-1 cells. This also suggests that lavender oil inhibites the LPS-induced inflammatory effects by means of the expression of HSP70. [105]

In a study by Vegh et al., different types of lavender (*Lavandula vera* L., *L.*

*pyrenaica* DC., *L. intermedia* and *L. stoechas* subsp. *Stoechas* [Lamiaceae]) were tested for their ingredients and their antibacterial effects on *Pseudomonas* strain. Linalool is the main component of the essential oils from a variety of lavender species. In *L. stoechas* subsp. *stoechas* L., fenchone was identified in the greatest amount. Using the tube dilution method, Vegh et al. found that each of the eight studied essential oils of lavender species had an inhibitory effect on the *Pseudomonas* strain, and the minimum bactericidal concentrations (MBC) were between 12.5 and 50 microL / mL in all seven types of lavender. [106]

In another study, the essential oils from 5 different varieties of lavender (*L. angustifolia* L.) were tested for their chemical compositions and their biological activity against *Pseudomonas aeruginosa* and *Staphylococcus aureus*. The following lavender varieties were tested: 'Munstead', 'Munstead Strain', 'Lavender Lady', 'Ellegance Purple' and 'Blue River'. The main ingredients were found in all varieties in different concentrations: "linalool (23.9 to 15.8%), linalyl anthranilate (12.3 to 1.6%), 1-terpinen-4-ol (9.7 to 5.5%), p-menth-1-en-8-ol (7.9 to 4.0%) and linalool oxide (4.7 to 1.1%)." In testing "Munstead" and "Blue River" varieties showed the greatest antibacterial activity against *P. aeruginosa* and *S. aureus*. [107]

Sienkiewicz et al. tested the microbial growth inhibition of essential oils of the plants *Thymus vulgaris* and *L. angustifolia* on 120 bacterial strains. The antibacterial activity of the two essential oils were tested with an agar diffusion method on all *Enterococcus*, *Escherichia*, *Staphylococcus* and *Pseudomonas* species, using different concentrations of the essential oils. The results indicate very strong antibacterial activity of the essential oil of *T. vulgaris* against all clinically relevant bacterial strains. Even with antibiotic resistant strains, thyme oil showed very good activity. Lavender oil was found to be not as good as thyme oil. [108]

## THYMUS

In an *in-vitro* study, Ichrak et al. tested the antibacterial effect of the essential oils of *T. pallidus* (Tp) and *T. satureioides* (Ts) [Lamiaceae] against Gram-positive and Gram-negative bacteria by the agar diffusion and broth dilution methods. The Gram-positive *Bacillus subtilis* was very sensitive to the essential oils of the two *T.* species. *P. aeruginosa*, a resistant strain, reacted very sensitively. [109]

Sienkiewicz et al. also investigated the antibacterial activity of the essential oils of *T. vulgaris*. They used standard bacterial strains but also multiresistant strains of *Pseudomonas*, *Enterococcus*, *Escherichia* and *Staphylococcus* species. 120 clinical strains from patients with infections of the respiratory and urogenital tract, abdominal cavity, oral cavity, and skin were isolated. They examined the sensitivity of bacteria to antibiotics with a disk diffusion. The antimicrobial and bactericidal potential of thyme oil was carried out at different concentrations with agar diffusion and the inhibition of growth was measured. The results showed that the essential oil of thyme can be very effective to inhibit the growth of the bacterial strains. Sienkiewicz and his colleagues confirmed that the essential oil of thyme can be very effective in inhibiting the growth of bacteria. [110]

## TEA TREE

Tea tree oil (*Melaleuca alternifolia*, Myrtaceae) has been used for 100 years in Australia as an antiseptic and anti-inflammatory agent. [111] In a controlled study at a referral acute teaching hospital in Australia, Caelli et al. tested the antibacterial effect of “4% tea tree oil nasal ointment and 5% tea tree oil“ gel on methicillin-resistant *S. aureus* compared to “a standard 2% mupirocin nasal ointment and triclosan body wash“. The study involved 30 people. 15 patients were in the tea-tree oil group and 15 in the control group. The combination of tea tree oil showed a better effect than the standard combination. [112]

Dryden et al. conducted a similar study in 2004. The authors investigated the clearance of MRSA colonization using 10% tea tree oil cream & tea tree 5%

body wash versus the standard treatment: 2% mupirocin nasal ointment, chlorhexidine gluconate 4% soap, silver sulfadiazine 1% cream. The study was conducted at an acute district hospital in England. 236 patients took part in the study and it lasted five days. Nose ointment was applied three times daily, and the lesions were washed and treated daily. 12 patients were lost in the follow-up (5%). There were 110 patients in the intervention group and 114 in the comparison group. The clearing of the nasal mucosa with mupirocin was significantly more effective than tea tree cream, but tea tree oil treatment was more effective in clearing superficial skin sites and skin lesions than chlorhexidine and silver sulfadiazine. [113]

Antibiotic-resistant bacteria are a very big problem in healthcare. *S. aureus* can cause severe skin infections and the infection can spread to the underlying tissue, particularly if the bacteria are methicillin-resistant the treatment is very difficult. Tea tree oil (*M. alternifolia*) oil has been used in botanical medicine for centuries and in the past two decades more and more studies have been conducted, demonstrating the antimicrobial and antiinflammatory effect. The ability of tea tree oil to activate monocytes has also been demonstrated. Infections can be treated very effectively with tea tree oil. The side effects are well above the minimum value. However, one must be careful not to produce contact dermatitis, which may occur in susceptible individuals with topical use of tea tree oil in very low concentrations. Case studies and small clinical trials have demonstrated the effectiveness of tea tree oil in the treatment of osteomyelitis and infected chronic wounds. [114]

Mondello et al. examined the antifungal and fungicidal effect of the essential oil of *M. alternifolia* Cheel (Tea Tree Oil, TTO) in vaginal candidiasis *in vitro* and *in vivo*. The two main ingredients of the antifungal tea tree oil are terpinen-4-ol and 1,8-cineole. In this study “oophorectomized, pseudoestrus rats under estrogen treatment“ were vaginally infected with azole (fluconazole, itraconazole)-sensitive or -resistant strains of *Candida albicans*. The minimal inhibitory concentration (MIC<sub>90</sub>) values were determined. They were 0.06% (v / v) for terpinen-4-ol and 4% (v / v) for 1,8-cineole *in vitro*, regardless of



whether they were fluconazole- or itraconazole -resistant or -sensitive. Terpinen-4-ol accelerated the clearance of all *Candida* strains from the vagina of the rats. These data indicate that terpinen-4-ol has the main antifungal capacity of tea tree oil. Further investigation would be necessary, particularly *in vivo* in order to demonstrate that TTO especially terpinen-4-ol would be a good option for the treatment of vaginale candidiasis, especially when fluconazole- or itraconazole -resistant *Candida* strains are involved. [115]

In the studies above, it could be shown that tea tree oil (TTO) is very effective in the removal of MRSA of the skin. In 2008, Thompson et al. examined in a “multicenter phase II / III prospective, open-label, randomized controlled trial“, whether treatment with 5% TTO is also effective in preventing MRSA colonization compared with a standard gel (Johnson's Baby Softwash) in the intensive care unit. On admission to the ICU, swabs were taken from the nose and groin and were tested for methicillin-resistant *S. aureus*. Then, patients were randomly assigned to the experimental group or the control group. Smears were taken and the results were compared. This study also showed that TTO is very effective against MRSA. [116]

Tea tree oil is known for its antimicrobial, anti-inflammatory and wound healing properties and it can also lead to decolonization of methicillin-resistant *S. aureus* (MRSA) strains. In an Australian study, which was conducted as an uncontrolled case series, it was examined whether tea tree oil is able to decolonize MRSA strains in acute and chronic wounds of mixed etiology. The secondary objective of this study was to examine whether the tea tree oil solution had an impact on wound healing ability. 19 subjects with wounds and suspicion of colonised MRSA took part in this pilot study. Seven of them, which had been tested negative on colonized MRSA, were withdrawn from the study. One participant left the study before treatment, so a total of 11 patients participated. Their wounds were washed with a water-miscible tea tree oil solution (3.3%) with at each dressing change. Bandages were changed between every day and 3 times a week depending on the assessment of the nurses. After the treatment, none of the participants were tested negative on MRSA. In 8 of

the 11 treated wounds an incipient cure and a reduction in the wound could be observed by computer planimetry. Although the primary objective, the decolonization of MRSA strains, wasn't reached, a positive effect was observed on wound healing. [117]

The fungicidal activity of tea tree oil was demonstrated in an in vitro study by Hammer et al. The authors used dermatophytes (n = 106) and filamentous fungi (n = 78). It was found that MICs of tea tree oil were between 0.004% to 0.25% for all fungi and had a minimum fungicidal concentrations (MFCs) of <0.03% to 8.0%. At a dose of 1-4 x MFC three of the four test organisms could be detected after 8 hours and after 24 hours all four test organisms were removed. It was also shown that germinated conidia of *Aspergillus niger* were not as susceptible to tea tree oil. Tea tree oil had a fungicidal and inhibitory activity. [118]

#### SALVIA

In 2006, El-Saved et al. demonstrated anti-inflammatory effects of *Salvia triloba* [Lamiaceae] on both chronic and acute inflammation by an oral dose of 25 mg / kg. The chloroform extract of *S. triloba* was particularly effective. [119]

In the pathogenesis of inflammatory diseases, granule proteases and reactive oxygen species produced by neutrophils, play a major role. Chan et al. found that the extracts of *Salvia nipponica* var. *formosana* leaves and roots show a strong “inhibitory effect on superoxide anion production in fMLP / CB-activated human neutrophils“. An anti-inflammatory effect of the extracts of *S. nipponica* var. *formosana* was detected. In addition, significant anticholinesterase and antioxidant activities were detected. [120]

In one study, the antimicrobial activity of *Salvia x jamensis* and its main components, “beta-caryophyllene (14.8%), beta-pinene (6.8%), caryophyllene oxide (6.0%), delta-cadinene (5.5%), alpha-pinene (5.2%) and spatulenol (5.2%)” were examined. The essential oils of *S. jamensis* showed antimicrobial

activity against three Gram-positive bacteria (*S. aureus*, *S. epidermidis* and *Bacillus cereus*) and three *Candida* strains: *C. albicans*, *C. tropicalis* and *C. glabrata*. No antibacterial effects could be detected against Gram-negative bacteria, such as *Escherichia coli*, *Enterobacter cloacae* and *P. aeruginosa*. [121]

## EUCALYPTUS

In 2004, Mulyaningsih examined the antimicrobial potency of the essential oils obtained from the leaves of *Eucalyptus radiata* Sieber ex DC (ERL), *E. citriodora* Hook (ECL) and fruits and leaves of *E. globulus* Labill (Myrtaceae) (EGF) & (EGL). The effect of the essential oils against multidrug-resistant (MDR) bacteria was investigated using broth microdilution. The essential oil from the fruit of *E. globulus* Labill was found to have a very significant antibacterial effect against methicillin-resistant *S. aureus*. The other essential oils were also very effective against MDR Gram-negative bacteria. The antibacterial effectiveness of the oils was in the following order: EGF > ECL > ERL ~ EGL. [122] Marzoug et al. confirmed the significant antimicrobial activity of essential oils from stems, flowers, leaves and fruits of *E. oleosa* against Gram-positive and Gram-negative bacteria. [123]

## ROSEMARY

Jiang et al. examined the antimicrobial and antifungal activity of *Rosmarinus officinalis* [Lamiaceae] on three Gram-negative bacteria (*Proteus vulgaris*, *E. coli* and *P. aeruginosa*), three Gram-positive bacteria (*Bacillus subtilis*, *S. epidermidis* and *S. aureus*) and on two fungi (*Aspergillus niger* and *C. albicans*). The oil of Rosemary, with the main ingredients 1,8-cineole and  $\alpha$ -pinene, was very effective against all of the aforementioned bacteria and fungi. [124]

## **XII. Essential oils with wound healing effect**

Many of the following wound healing essential oils have been used for centuries in folk medicine of different countries, and some even go back to antiquity.

In a randomized, double-blind, placebo-controlled study the clinical effectiveness of lavender oil was measured in the treatment of recurrent aphthous ulcers (RAU). The study consisted of 4 parts:

1) The first one was to determine the healing ability of lavender oil in rabbits with induced ulcers compared with placebo. The healing ability was determined by measuring the area of the ulcer and inflammation. It turned out that in animals treated with lavender oil, a significant reduction in ulcer size occurred compared with baseline. Within 3 days after treatment rabbits treated with lavender oil had an “increased rate of mucosal repair and healing” compared to baseline or placebo group.

2) The safety and toxicity and the median lethal dose (LD50) in albino mice was also tested. The skin irritation was tested using the patch-test on the intact skin of albino rabbits. The intraperitoneal LD50 was 6.5 kg /g in mice. The skin irritation test showed no signs of redness or irritation.

3) The antibacterial properties of lavender oil was tested using swab specimens and the disc diffusion method on the skin of human participants with RAU. Lavender oil showed antibacterial activity against all tested strains.

4) The last part of this study was to evaluate the healing properties of lavender oil. 115 patients with RAU (mean age 38 years) took part in this study and were divided into 2 groups. The experimental group received lavender oil, the other group received a placebo.

Duration and size of the ulcer, healing time, inflammation level and intensity of pain were judged. In patients treated with lavender oil, a reduction of the inflammation and ulcer size was found, and, depending on the concentration, there was a shorter healing time between 2-4 days [2 days (40%), 3 days (50%), 4 days (10%)] compared with baseline or placebo. A slight pain reduction was observed. There were no side effects. [125]

Rosenbaum wrote in his study: “The quality of life of patients with chronic wounds may be negatively affected by chronic and procedural pain, sleep disturbance, social, and emotional concerns.” [126]

Nayk et al. examined the wound-healing effect of *Matricaria recutita* (Asteraceae) extract on “excision, incision and dead space wound models in rats“. For each wound-model, there were 6 rats in the verum-group and 6 rats in the placebo-group. Animals in the test group received a treatment with the aqueous extract of *M. recutita* (120mg/kg/day) and for rats of the placebo group, normal tap water was used. On the 15th day the speed of the wound contraction, epithelialization, weight of the granulation tissue, wound breaking strength and the content of hydroxyproline were measured. The group which was treated with *M. recutita* extracts showed a significant reduction in wound area compared to the control group (61% versus 48%). Also a “faster epithelialization and a significantly higher wound breaking strength“ was noted in the experimental group. The granulation tissue weight and hydroxyproline content were also much higher. So, it was shown that the treatment of wounds with *M. recutita* extract is very promising. [127]

The group of Martins et al. compared the healing effect of *Chamomilla recutita* (Asteraceae) with corticosteroids and no treatment in 125 male rats. It was found that the rats that were treated with chamomile had a significantly faster rate of healing than those of the corticosteroid group. [128]

Orafidiya et al. compared *Ocimum gratissimum* L. (Lamiaceae) “with two antibacterial preparations Cicatrin® (Glaxo Wellcome) and Cetavlex® (AstraZeneca)” on wound healing. For this placebo-controlled study albino rabbits were used. On the rabbits’ back excisional and incisional wounds were inflicted under anesthesia. The test substance was added in drops for 15 days on the wound surface. The wounds were measured and observed for the following six days. In the *O. gratissimum* group a significant improvement of the proliferative and inflammatory phase was observed. It was found that *O. gratissimum* can accelerate wound healing and provides significantly better

results than the reference products and the control group. [129]

Süntar et al. compared the wound-healing and antibacterial properties of a new cream formulation of *Hypericum perforatum* L. (Hypericaceae), *Salvia* L. species (Lamiaceae), *Origanum* Tourn ex L. (Lamiaceae) and Olive (Oleaceae) with the reference ointment Madecassol® in rats and mice. Tissue sections were histopathologically valued and the healing progress was documented. This formulation showed an advantage in the wound-healing effect as well as in the candidicidal and bactericidal activities. [130]

Saddige et al. reported an anti-bacterial effect of the *H. perforatum* L. (Hypericaceae) against Gram-positive and Gram-negative bacteria and found that one of the main ingredients, tetraketone hyperforine was probably responsible. [131]

Tumen et al. compared the dividend wound healing and anti-inflammatory effect of the essential oils from the cones of various *Cupressus* species (Cupressaceae) and different essential oils extracted from the berries of different *Juniperus* species (Cupressaceae) with the reference ointment Madecassol®. *In vivo* experimental wound models were used with linear incision and circular excision. To determine the wound-healing effect, histopathological analyzes were performed and the hydroxyproline content was measured. It was found that the essential oils of *J. oxycedrus* subsp. *oxycedrus* and *J. phoenica* had the highest wound healing activity and the highest anti-inflammatory effect. The other species showed no significant wound healing effect. [132]

Tumen et al. examined the healing potential and anti-inflammatory activity of four different types of firs (*Abies nordmanniana* subsp. *Bornmulleriana*, *Abies nordmanniana* subsp. *equiangular* *Trojani*, *Abies cilicica* subsp. *cilicica*, and *Abies nordmanniana* subsp. *Nordmanniana* [Pinaceae]), *Cedrus libani* [Pinaceae] and *Picea orientalis* [Pinaceae] in comparison to reference ointment Madecassol®, which contains 1% of the extract of *Centella asiatica*.

Wounds were inflicted using linear incision and circular excision, and then they were analyzed histopathologically. The essential oils of *A. cilicica* subsp. *cilicica* showed a very significant wound healing effect, and anti-inflammatory activity in comparison to the other types. [133]

In an study by Vakilian et al., the wound healing activity of lavender oil was examined at an episiotomy after birth and was compared to a treatment of povidone-iodine. The study was randomized on 120 primiparae “who had undergone normal spontaneous vaginal delivery and episiotomy“ performed. They were randomly assigned to the experimental group or control group. 10 days after birth, the incision sites were examined. The results showed that 25 of the 60 young mothers in the lavender group and 17 women in the control group had no more pain. In addition, the lavender group showed significantly less redness at the incision sites compared to the povidone-iodine group. There were no differences in regards to complications at the surgical site. This study showed that lavender oil can be an effective alternative to povidone-iodine for episiotomy wound care.[134]

Hur et al. tested in a placebo-controlled clinical trial the use of aromatherapy in healing of episiotomy on vaginal postpartum mothers. For aromatherapy, essential oils of “lavender, neroli, rose, myrrh, grapefruit, orange, mandarin and roman chamomile” were used. There were three different treatment groups, the 1st group was given a seat bath with essential oils, the 2nd group received an aromatic soap and the 3rd group was the control group. The healing progress of the perineal wounds were judged using the REEDA scale and the number of bacteria was determined by a swab. After the 5th and 7th day the results on the REEDA scale in the experimental group were significantly lower compared to the control group. The authors came to the conclusion that the post-partum, pernieale care with essential oils is very effective for healing the perineum. [135]

### **XIII. Essential oils and oral care**

Ouhayoun noted in 2003 that essential oils in mouthwash has the ability to break cell walls of bacteria, inhibit their enzymatic activity, and kill the microorganisms. Furthermore, the essential oils prevent bacterial aggregation and slow their reproduction. [136]

In a 6-month study Charles and his colleagues compared antigingivitis and antiplaque effectiveness of mouthwash with essential oils with a chlorhexidine containing mouthwash. The 108 eligible patients were aged 20-57 and were randomly divided into three groups. The first group was given a mouth rinse with essential oils (Listerine®Antiseptic), the 2nd group received 0.12% chlorhexidine mouthwash (Peridex®), and the third group was the control group with 5% hydroalcohol. A complete examination of the oral soft tissues was performed at baseline and assessed with "Loe Silness gingival index (GI), Quigley-Hein Plaque Index (PI), Volpe-Manhold calculus index (CI) and Lobene tooth stain index (SI)." At the beginning of the study, participants received a complete dental prophylaxis. In addition to tooth brushing, they rinsed twice a day with their assigned mouthwash. After 3- and 6- months, the oral tissues and the teeth were evaluated again. After 3 months, all 108 subjects were still participating and after 6 months 107 patients were evaluated. After 3 months, there were no significant differences, but the control group showed significantly worse results compared to the other two groups according to the PI. Mouthwash with essential oils could keep up very well with the chlorhexidine mouthwash. After 6 months, subjects using mouthwash with essential oils and with chlorhexidine, showed, according to the GI and the PI, an inhibitory effect on plaque as well as on gingivitis. In the study group, that used chlorhexidine mouthwash, more dental stones and tooth stain occurred. [137]

Due to the side effects of chlorhexidine, there is a search for alternative anti-plaque agents. Pizzo et al. compared the plaque inhibitory activity of essential



oils (EO) to 10 and 20 ml of amine fluoride / stannous fluoride (ASF). The authors used a 0.12% chlorhexidine solution as a positive and a saline solution as a negative control. In the masked, randomized, cross-over designed study, 15 volunteers participated in a four-day plaque regrowth model. On the first day, participants received a professional oral hygiene checkup began to flush with the assigned mouthwashes. It was shown that while flushing with essential oils as well as the ASF in both doses plaque formation was significantly inhibited compared to the control group with saline. The strongest anti-plaque effect could be accomplished by using the solution with chlorhexidine. No side effects occurred using any of the mouthwashes. It was shown that ASF and mouth rinses containing essential oils represent an effective alternative to chlorhexidine. [138]

In a study by Rasooli and colleagues, the antibacterial activity of essential oils of *Mentha spicata* and *Eucalyptus camaldulensis* was analyzed by gas chromatography and GC-mass spectrometry against *Streptococcus mutans* and *Streptococcus pyogenes*. *S. mutans* is present in almost everyone's saliva and it is the main cause of dental cavities. Dental care is also an important part of nursing, especially in patients who can no longer care for themselves. It is important for their mental and physical wellbeing. *S. pyogenes* is a common bacterium that can cause scarlet and bilateral purulent tonsillitis in humans. Both *M. spicata* and *E. camaldulensis* oils were very effective against *S. pyogenes* and *S. mutans* biofilm formation and could slow down their multiplying significantly. [139]

Gupta et al. compared the use of cinnamon oil (Lauraceae) with clove oil on oral caries favoring bacteria. They found out that cinnamon oil had a higher antibacterial activity than clove oil against a broad spectrum of all ten test bacteria. [140]

Park et al. reported a strong antimicrobial activity of linalool and  $\alpha$ -terpineol against periodontal diseases and cavity causing bacteria. The authors also mentioned that the concentration of these components has a value of 0.4 mg / ml in toothpastes and gargles should not be exceeded. [141]

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