

# **PHYTOTHERAPY**

## **Chapter 7**

**Prof. Dr. Müberra Koşar**

**EMU-Faculty of Pharmacy**

# Inflammation, pain

- Pain relief is one of the **most ancient goals of phytotherapy**.
- Plant kingdom is the source of **modern anti-inflammatory drugs**, since the first **non-steroidal anti-inflammatory drug** (NSAID) was developed from a natural product (salicylates of willow bark)

# Inflammation, pain

*«Posttraumatic, muscle and articular pain»*

- **Mild injuries caused** by different traumas (**strains, sprains, bruises and contusions**) can result in injuries of muscles, **edema, hematoma and pain** that limit the motion of the affected limb.
- In modern medicine, **non-steroidal anti-inflammatory drugs** (administered orally or topically) are the first-choice treatment.
- **Edema and hematoma may be relieved by the local application of heparin.**

# Inflammation, pain

*«Posttraumatic, muscle and articular pain»*

- The phytotherapy of posttraumatic states is based on the application of herbal preparations with **anti-inflammatory activities**.
- These are typically **applied topically**.
- The available possibilities also include herbal products with **anti-edematous effects**.

# Arnica

«*Arnica montana* »

**Used part:** flowers

**Used type:** flowers and extracts

**Drog properties:** According to the definition of the Pharmacopoeia, *Arnicae flos* consists of the dried flower heads of *Arnica montana* with a sesquiterpene lactone content of at least 0.4%.



# Arnica

«*Arnica montana*»

**Chemical composition and mechanism of action:**

**sesquiterpene lactones.. «helenalin and 11,13-dihydrohelenanin »**

**Essential oil**

**flavonoids.**

# Arnica

«*Arnica montana*»

## Chemical composition and mechanism of action:

- In an in vitro experiment, **Arnica extracts inhibited activation of the transcription factors NF-κB and NF-AT**
- This effect correlated with their **sesquiterpene lactone** content.
- **Helenalin and 11,13-dihydrohelenalin** (the latter with less pronounced activity) **inhibited the activation of NF-κB**.
- A **methanolic extract reduced the protein level** of inducible NO synthase (iNOS) and COX-2 in vitro.

# Arnica

«*Arnica montana*»

## Chemical composition and mechanism of action:

- Certain **sesquiterpene lactones** may cause **contact hypersensitivity**.
- In an animal experiment, **sesquiterpene lactones** and **tinctures** from Arnica were only **weak inducers of skin inflammation**, and the extracts **decreased experimentally induced eczema**.
- In a subsequent experiment, **contact hypersensitivity could not be induced**, even if the tincture or sesquiterpene lactones were **applied undiluted to the inflamed skin**.

# Arnica

«*Arnica montana*»

## Efficacy and indications:

- In a randomized, placebo-controlled study, patients **with chronic venous insufficiency** were treated for **3 weeks** with an Arnica gel or placebo, and in addition all patients received hydrotherapy.
- The **improvement in venous capacity was significant** in both groups, but with a significantly better effect in the verum group.

# Arnica

«*Arnica montana*»

## Efficacy and indications:

- In a randomized, double-blind study, patients suffering from **hand osteoarthritis** were treated either with ibuprofen gel or with **Arnica gel**.
- The treatment resulted in a **significant reduction** of the total score of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC).
- The **levels of pain, stiffness and function also demonstrated a significant improvement.**

# Arnica

«*Arnica montana*»

## Efficacy and indications:

- Although the clinical data are not sufficient for a well-established **EMA monograph**, the traditional use and the empirical knowledge, justify its use as a traditional herbal medicinal product
  - for the **relief of bruises, sprains and localized muscular pain.**
- In practice, liquid extracts and semi-solid dosage forms containing **20-50% liquid extract may be used topically.**

# Arnica

«*Arnica montana*»

## Side-effects, interactions & contraindications:

- The most frequent adverse events related to the application of Arnica are **allergic skin reactions** such as **itching, redness of the skin and eczema**, and in some cases **contact dermatitis** may also occur.
- **Arnica tincture has much greater allergenicity than semisolid preparations.**
- Hypersensitivity to the active substance and to other plants of the Asteraceae family is a contraindication of the application.
- **The preparation should not be used on broken skin.**

# Capsicum

«*Capsicum annuum*»

**Used part:** fruit

**Used type:** ripe fruits, oleoresin and extracts

**Drog properties:** According to European Pharmacopoeia, *Capsici fructus* should contain a minimum 0.4% of total capsaicinoids.



# Capsicum

«*Capsicum annuum*»

## Chemical composition and mechanism of action:

**Capsaicinoids..** «capsaicin, dihydrocapsaicin,  
nordihydrocapsaicin»

**ascorbic acid**

**carotenoids.**

# Capsicum

«*Capsicum annuum*»

## Chemical composition and mechanism of action:

- The **analgesic activity** of Capsicum extracts is related to their **capsaicinoid** content.
- **Capsaicinoids act as agonists on the vanilloid receptors** (these are transient receptor potential vanilloid (TRPV) channels) located primarily on the ends of substance P-containing axons.
- These **neurons are also responsible for the perception of pain.**

# Capsicum

«*Capsicum annuum*»

## Chemical composition and mechanism of action:

- The analgesic effects of Capsicum and capsaicin have been confirmed preclinically.
- In one study, the **local application of a capsaicin-containing cream decreased the pain** in a peripheral neuropathy.
- It was recently discovered that **TNFalpha-induced NF-κB activation may also play a role** in the chronic effect of capsaicin.

# Capsicum

«*Capsicum annum*»

## Chemical composition and mechanism of action:

- The effect of hot pepper on **gastric acid secretion** is empirical knowledge. This has also been confirmed in animal experiments.
- The application of chilli to rats resulted in a **significant rise of hydrochloric acid production in the stomach, without increasing the peptic activity.**
- In a further experiment, **capsaicin increased the gastrointestinal transit time** in rats; this was limited only to the stomach, the total gut transit time was unaffected.

# Capsicum

«*Capsicum annuum*»

## Chemical composition and mechanism of action:

- The **gastroprotective effect of capsaicin** was reflected in a study where the administration of capsaicin to rats **significantly enhanced the activities of the antioxidant enzymes** (catalase, superoxide dismutase, glutathione reductase and glutathione-5-transferase) in the gastric and intestinal mucosa and had a positive effect on mucosal glycoproteins.

# Capsicum

«*Capsicum annum*»

## Efficacy and indications:

- Clinical trials with Capsicum extract or capsaicin and with **semi-solid dosage forms indicated efficacy in indications relating to muscular or articular pain.**
- In a randomized double-blind study, patients with chronic soft tissue pain were treated with a **cream containing either capsaicin or placebo**. After 3 weeks of treatment, the **median pain sum score had decreased by 49%** (capsicum group) or 23% (placebo group).

# Capsicum

«*Capsicum annum*»

## Efficacy and indications:

- In a double-blind, randomized study, a **Capsicum plaster** was compared with a placebo for 3 weeks in patients with **non-specific back pain**. The rate of responders in the **Capsicum group was 60%**, against 42% in the placebo group.
- In a similar study, **the compound pain subscore was reduced by 42%** (Capsicum) or 31% (placebo) from the values on entry.

# Capsicum

«*Capsicum annum*»

## Efficacy and indications:

- In a double-blind randomized study, patients with osteoarthritis or rheumatoid arthritis received **capsaicin** or placebo for four weeks.
- A **significantly greater relief of pain** was reported by the capsaicin-treated patients.
- Rheumatoid arthritis and osteoarthritis patients demonstrated mean **reductions in pain of 57% and 33%**, respectively.

# Capsicum

«*Capsicum annum*»

## Efficacy and indications:

- In another study, the effect of capsaicin (applied as 2.5 g chili pepper powder/day) on dyspeptic symptoms was analyzed.
- The 5-week study was performed on patients with functional dyspepsia and without gastro-esophageal reflux disease or irritable bowel syndrome.
- The **overall symptom score and the epigastric pain, fullness and nausea scores of the treated group were significantly lower** than those of the placebo group.

# Capsicum

«*Capsicum annum*»

## Efficacy and indications:

- According to the (draft) monograph of the European Medicines Agency, the use of Capsicum is well-established
  - for the **relief of muscle pain such as lower back pain**.
- **1 medicated plaster should contain 171-552 mg of soft extract** of Capsici fructus, corresponding to 4.8-11 mg of capsaicinoids. A maximum of **1 plaster per day should be applied to the affected area for at least 4 and up to 12 hours**. Different preparations of semi-solid dosage forms containing **50 mg of capsaicinoids/100 g should be applied 2-4 times daily**.
- The treatment should be continued until the relief of pain is achieved, but after 3 weeks of use a break of at least 2 weeks is required.

# Capsicum

«*Capsicum annum*»

## Side-effects, interactions & contraindications:

- Capsicum preparations **should not be applied on broken skin or wounds**.
- Their use **is not recommended in children below 12 years of age** due to the lack of data on safety and efficacy.
- The preparations **should not be applied near the eyes or to mucous membranes**.
- **Skin hypersensitivity and allergic reactions** (e.g. urticaria, blisters or vesiculation at the application site) may occur.
- Animal studies revealed shown **reproductive toxicity after high subcutaneous doses of capsaicin**.
- **Capsaicin crosses the placenta and may pass into the breast milk**. Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use of capsaicin during pregnancy and lactation is not recommended.

# Willow

«*Salix alba*, *S. nigra* and *S. purpurea*»

**Used part:** cortex

**Used type:** ripe cortex and extracts

**Drog properties:** A willow bark dry extract, also official in the European Pharmacopoeia, contains a minimum of 5% of total salicylic derivatives, expressed as salicin.



# Willow

«*Salix alba, S. nigra and S. purpurea*»

**Chemical composition and mechanism of action:**

**salicylates as glycosides.. «salicortin and tremulacin»**

**salicin**

# Willow

«*Salix alba, S. nigra and S. purpurea*»

## Chemical composition and mechanism of action:

- **Salicin** is the most active **anti-inflammatory** compound in willow.
- In willow bark it can be found in the form of “**prodrugs**” (glycosides); these are **hydrolyzed to salicin**, which is **further metabolized to saligenin** (salicyl alcohol) enzymatically and by the flora of the lower intestines, and **finally to salicylic acid after absorption**.

# Willow

«*Salix alba, S. nigra and S. purpurea*»

## Chemical composition and mechanism of action:

- **Salicin and tremulacin** exerted **antiphlogistic activity** in different in vitro test systems, with a delayed onset of action in comparison with salicyl alcohol or etylsalicylic acid.
- A **Salix extract inhibited prostaglandin synthesis** in vitro and **COX-1 and COX-2 enzymes**.
- It was confirmed experimentally that polyphenols also contribute to the overall enzyme-inhibitory effect of willow bark.

# Willow

«*Salix alba, S. nigra and S. purpurea*»

## Chemical composition and mechanism of action:

- **Salicin** (and willow bark extract) **does not induce gastric lesions** in rats
- In contrast with acetylsalicylic acid, **thrombocyte aggregation is less effectively inhibited by willow bark** (an extract containing 240 mg of salicin as compared with 100 mg of acetylsalicylic acid).
- Pharmacokinetic studies indicate that, based on serum salicylate concentrations, **240 mg of salicin as an extract is bioequivalent to 50-85 mg of acetylsalicylic acid.**

# Willow

«*Salix alba, S. nigra and S. purpurea*»

## Efficacy and indications:

- In a randomized, placebo-controlled double-blind clinical trial **patients with osteoarthritis** of the hip or knee were treated daily for 2 weeks with a willow bark extract containing 240 mg of salicin or placebo. A (borderline) significant superiority of willow bark over placebo with regard to **pain relief** was observed.
- An analysis of the data on patients with osteoarthritis of the hip or knee indicated that the **pain scores decreased** for willow bark (though not significantly), but significantly for diclofenac.

# Willow

«*Salix alba, S. nigra and S. purpurea*»

## Efficacy and indications:

- From the clinical evidence, one dry extract (8-14:1, ethanol 70%, 15% total salicin) was considered by the European Medicines Agency to possess well-established use
  - for the **short-term treatment of low back pain**. The daily dose is 1572 mg of dry extract.
- For further extracts and the comminuted herbal substance, the clinical evidence is insufficient, but their documented long-standing use and the plausibility of the effect due to their salicin content, led to a **traditional use** monograph being granted with the indication of
  - **minor articular pain,**
  - **fever associated with common cold,** or
  - **headache.**
- The doses of the **dry extracts are about 1.2 g**, while those of the **liquid extract and tincture are 9-24 ml**.
- 1-3 g of comminuted herbal substance should be used for tea preparation, 3 or 4 times daily. The posology of the powdered herbal substance is 260-500 mg three times daily.

# Willow

«*Salix alba, S. nigra and S. purpurea*»

## Side effects, interactions & contraindications:

- In the event of chronic use, the **duration should be restricted to a maximum of 4 weeks.**
- The use of willow bark is **contraindicated in cases of hypersensitivity to salicylates or to other NSAIDs** (e.g. a history of angioedema, bronchial spasm or chronic urticaria in response to salicylates or to other NSAIDs), **asthma, active peptic ulcer disease and in the third trimester of pregnancy.**
- It is **contraindicated in children and adolescents under 18 years of age** because of the risk of Reye's syndrome.

# Willow

«*Salix alba, S. nigra and S. purpurea*»

## Side effects, interactions & contraindications:

- Willow bark **may increase the effects of anticoagulants such as coumarin derivatives.**
- **Allergic reactions such as rash, pruritis, urticaria, asthma or exanthema, and gastrointestinal symptoms such as nausea, vomiting, abdominal pain, dyspepsia, heartburn or diarrhea, may occur.**
- Its use during the first and second trimesters of pregnancy and during lactation is not recommended.

# Inflammation, pain

## «Migraine, headache»

- **Tension type headache is the most common** type of headache, accounting up to 90% of the cases and as many as 80% of the population experience tension headache at least once during their lifetime.
- The exact underlying mechanisms is not known, but **peripheral pain mechanisms are most likely involved.**
- **If tension headache is chronic, peripheral and central pain mechanism** are also involved.

# Inflammation, pain

*«Migraine, headache»*

- The therapy of **tension headache** relies on the application of **non-steroid anti-inflammatory drugs**.
- From plants, **salicylate-containing drugs, e.g willow bark** may be applied.
- **Peppermint oil** is a unique tool which allows **topical, clinically confirmed therapy for headache**.

# Inflammation, pain

## «Migraine, headache»

- **Migraine is a neurological disease** accompanied by severe headache.
- The **therapy of migraine is complex, for pain management usually NSAIDs are applied.**
- **Preventive treatment** includes the application of different medicines; from phytotherapeutics, **feverfew** may be applied.

# Feverfew

«*Tanacetum parthenium*»

**Used part:** herbs

**Used type:** herbs and extracts

**Drog properties:** According to the European Pharmacopoeia, *Tanacetum parthenii* herba consists of the dried, whole or fragmented aerial parts of *Tanacetum parthenium*, and it contains no less than 0.2% of parthenolide.



# Feverfew

«*Tanacetum parthenium*»

## Chemical composition and mechanism of action:

Sesquiterpene                      alpha-methylenebutyrolactones..

«parthenolide»

flavonoids

monoterpenes

# Feverfew

«*Tanacetum parthenium*»

## Chemical composition and mechanism of action:

- The parthenolide has an important role in its bioactivity.
- This moiety reacts with the sulfhydryl groups of proteins.
- **Parthenolide has anti-inflammatory activity.**
- It **inhibits the expression of COX-2 and proinflammatory cytokines and nitric oxide production** by inducible nitric oxide synthase (iNOS) in vitro.
- The anti-inflammatory effects of different extracts have been demonstrated in animal experiments.

# Feverfew

«*Tanacetum parthenium*»

## Chemical composition and mechanism of action:

- The extract **inhibits blood platelet aggregation**.
- The **release of serotonin from platelets induced** by various aggregating agents was inhibited.
- Feverfew **extracts and parthenolide inhibit smooth muscle contractility** in vitro, and also **inhibit the neuronal release of 5-HT**, but in contrast with some anti-migraine medicines without interfering with the 5-HT receptors.
- A feverfew **extract inhibited stimulated histamine release** in vitro.

# Feverfew

«*Tanacetum parthenium*»

## Efficacy and indications:

- Feverfew is applied in modern phytotherapy with the very specific indication of **preventing migraine attacks**.
- Some of its pharmacological effects overlap with those of certain anti-migraine medicines, e.g. the **inhibition of blood platelet aggregation and 5-HT secretion** similar to the effects of triptans.

# Feverfew

«*Tanacetum parthenium*»

## Efficacy and indications:

- A double-blind placebo controlled-trial involving patients who already ate **fresh leaves of feverfew daily** as prophylaxis against migraine was carried out.
- The patients were allocated randomly to receive either freeze-dried feverfew leaves or identical placebo capsules.
- The treatment with feverfew was associated with a **reduction in the number and severity of the attacks and the frequency of vomiting in a two-month period**, while the duration of the individual attacks was unaltered.

# Feverfew

«*Tanacetum parthenium*»

## Efficacy and indications:

- The efficacy of a supercritical extract of feverfew in migraine prevention was investigated in a randomized, double-blind, placebo-controlled study with migraine patients.
- After **16 weeks of treatment, the migraine frequency was significantly decreased** in the feverfew group as compared with the placebo group.

# Feverfew

«*Tanacetum parthenium*»

## Efficacy and indications:

- On the basis of its long-standing use, the use of feverfew is accepted as a traditional herbal medicinal product
  - for the **prophylaxis of migraine headaches** after serious conditions have been excluded by a physician.
- The average daily dose of powdered **feverfew leaf is 100 mg.**

# Feverfew

«*Tanacetum parthenium*»

## Side effects, interactions & contraindications:

- Its use in children and adolescents under 18 years of age and during pregnancy and lactation is not recommended due to the lack of adequate data.
- **Gastrointestinal disturbances may occur** as adverse effects.
- In cases of hypersensitivity to feverfew and other plants of the Asteraceae family, its use is not recommended.

# Skin disorders

- The skin is composed of two layers, the **epidermis and the dermis**.
- The epidermis consists of 5 layers, and only the deepest one, the **germinative layer**, is able to reproduce itself and form new cells.
- The connective tissue, containing **sudoriferous and sebaceous glands**, is **part of the dermis**.
- The integrity and physiological functioning of this very complex system may be affected on different levels.
- However, treatment is usually carried out cutaneously (though there are some instances of oral treatment too).

# Skin disorders

- In the treatment of inflammations, infections, traumas and different lesions, a series of medicinal plants containing different active components may be applied.
- In order to achieve a targeted therapy, **the active constituents of the products must reach different layers of the dermis and/or epidermis**; nevertheless, a systemic effect is usually undesirable.
- In the dermal application of medicinal plants, therefore much depends on the pharmaceutical form (cream, ointment, lotion, etc.) and the vehicles used.

# Skin disorders

## «*Inflammatory skin disorders*»

- Various skin disorders are caused by a superficial injury of the skin, followed by infection and inflammation. Inflammation may be a result of different causes, e.g. burns.
- **Eczema and atopic dermatitis** involve chronic inflammation of the skin, accompanied by pruritus, erythema, exudation and crusting.
- In simple forms of inflammatory skin disorders, herbal products may ensure **causal therapy**, whereas in cases of **eczema the goal of the treatment** is the temporary relief of the symptoms.

# Skin disorders

## «*Inflammatory skin disorders*»

- In the treatment of inflammatory skin disorders, plants with different mechanisms of action may be applied.
- One cornerstone of the therapy is the application of plants with confirmed **anti-inflammatory activity**.
- This is usually achieved similarly to synthetic antiphlogistics (e.g. inhibition of the enzyme COX), but the the manner in which herbal extracts act is more complex.
- For example, **camomile acts primarily by inhibiting COX** through its azulenes, but the overall effect is a result of the activities of polysaccharides, flavonoids and bisabolol derivatives.

# Skin disorders

## «*Inflammatory skin disorders*»

- Herbal preparations with strong **antimicrobial activities** are indispensable constituents of preparations intended to be used for infectious diseases.
- These are usually **essential oils** with a broad antibacterial and antifungal spectrum.
- A very special group of phytotherapeutics applied **in inflammatory skin diseases are the astringents**.
- These contain **water-soluble polyphenolic substances** which **coagulate proteins**, and thereby exert antimicrobial and anti-inflammatory action.

# Skin disorders

## «*Inflammatory skin disorders*»

- Astringents decrease exudation by coagulating the superficial injured tissue and creating a protective layer, thereby promoting wound healing.
- These compounds possess mild local painkiller activity.

# Marigold

«*Calendula officinalis*»

**Used part:** petals

**Used type:** petals and extracts

**Drog properties:** According to the European Pharmacopoeia, *Calendulae flos* is the whole or cut, dried, fully-opened flowers, which have been detached from the receptacle, of the cultivated, double-flowered varieties of *Calendula officinalis* L. The drug should contain not less than 0.4% of flavonoids, calculated as hyperoside.



# Marigold

«*Calendula officinalis*»

**Chemical composition and mechanism of action:**

**triterpene mono-, di- and triols.. «faradiol derivatives»**

**triterpene saponins**

**Polysaccharides**

**Carotenoids.. «lutein and zeaxanthine»**

**flavonoids and coumarins**

**essential oil**

# Marigold

«*Calendula officinalis*»

## Chemical composition and mechanism of action:

- The **anti-inflammatory effect** of marigold has been reported in animal experiments.
- One of the most active substances is the triterpene diol **faradiol**, with a molar activity comparable to that of indomethacin.
- **Faradiol esters and monools are less active.**
- The **essential oil, the flavonoids and different extracts** of the plant **inhibit the growth of several bacteria and fungi.**

# Marigold

«*Calendula officinalis*»

## Chemical composition and mechanism of action:

- A water extract of the drug **exerted an angiogenic effect** in vitro, referring to the **wound-healing activity** of the plant.
- Dry 70% ethanolic and aqueous extracts of Calendula flower **accelerated the healing of surgically inflicted skin wounds** in rats.

# Marigold

«*Calendula officinalis*»

## Efficacy and indications:

- In an observational study, patients with venous leg ulcers were treated with a **Calendula extract-containing cream** or placebo for 3 weeks. In the treated group, a **significant acceleration of wound healing** was observed.
- In a randomized, controlled, open study patients with 2nd or 3rd degree burns were treated with either a **Calendula ointment**, a proteolytic ointment or a control (vaseline). A slightly **significant difference in favor of the Calendula** over the vaseline was observed.

# Marigold

«*Calendula officinalis*»

## Efficacy and indications:

- In a phase III randomized single-blind trial, Calendula was compared with trolamine for the prevention of **acute dermatitis during irradiation for breast cancer**.
- Patients who had been operated on for breast cancer and who were to receive postoperative radiation therapy were treated on the irradiated fields. The occurrence of **acute dermatitis of grade 2 or higher was significantly lower following the use of Calendula in comparison with trolamine**.

# Marigold

«*Calendula officinalis*»

## Efficacy and indications:

- Based on the folk medicinal application of the plant, marigold may be used as traditional herbal medicinal products
  - for the **symptomatic treatment of minor inflammations of the skin** (such as sunburn) and as an aid in the healing of minor wounds, and
  - for the **symptomatic treatment of minor inflammations in the mouth or the throat.**
- An infusion for cutaneous and or mucosal application should be prepared from **1-2 g of dry flowers**. Externally, different liquid extracts may be applied. As a gargle or mouth wash marigold tincture should be applied in a 2% solution.

# Marigold

«*Calendula officinalis*»

## Side-effects, interactions & contraindications:

- Hypersensitivity to plants of the Asteraceae (Compositae) family is a contraindication of the treatment.
- **Skin sensitization may develop as an adverse effect** in cases of cutaneous application.

# Centella

«*Centella asiatica*»

**Used part:** herbs

**Used type:** herbs and extracts

**Drog properties:** According to the European Pharmacopoeia, the herbal substance consists of the dried, fragmented aerial parts, containing a minimum of 6% of total triterpenoid derivatives, expressed as asiaticoside.



# Centella

«*Centella asiatica*»

**Chemical composition and mechanism of action:**

**triterpenoid glycosides.. «asiaticoside,  
madecassoside»**

**their aglycones.. «asiatic acid, madecassic acid»**

**carotenoids and flavonoids,**

**polysaccharides.**

# Centella

«*Centella asiatica*»

## Chemical composition and mechanism of action:

- In the literature, experimental data can be found on the following special extracts:
- **Madecassol<sup>®</sup> or Centellase<sup>®</sup> or Blastoestimulina<sup>®</sup>, TECA, TTFCA and TTF**, all containing **40% of asiaticoside and 60% of the aglycones** (asiatic acid and madecassic acid).
- These (practically identical) highly purified extracts, fractionated and enriched in triterpenic acid and triterpenic sugar ester fractions, have a long history of use in Europe for the therapy of wounds.

# Centella

«*Centella asiatica*»

## Chemical composition and mechanism of action:

- The medicinal effects are attributed primarily to the **triterpene saponins**.
- Topically applied preparations **accelerate wound healing, stimulating epithelization and increasing the rate of wound contraction**.
- This effect has also been **observed in the case of oral administration**.
- *Centella asiatica* **promoted angiogenesis** in an experimental model.

# Centella

«*Centella asiatica*»

## Chemical composition and mechanism of action:

- In a study carried out on animals, the **extent of radiation injury was reduced after the topical application** of a Centella product.
- Aqueous extracts of *Centella asiatica* **inhibited keratinocyte replication**, which suggests the potential use of the plant extracts **as a topical anti-psoriatic agent**.
- The effects of *Centella asiatica* and asiaticoside in the prevention of experimentally induced **gastric lesions** in animals were confirmed in a series of experiments.

# Centella

## «*Centella asiatica*»

### Efficacy and indications:

- The effect of skin aging was studied with several cosmetic preparations.
- A randomized double-blind study was carried out on the photoaged skin of female volunteers to investigate the effects of **topically applied 5% vitamin C and 0.1% madecassoside**.
- The cream was applied twice daily for 6 months to the face, and to the assigned half of the neck and upper chest and one of the arms of each volunteer.
- After the treatment, **significant improvements of the clinical scores for deep and superficial wrinkles, suppleness, firmness and skin hydration** were observed.

# Centella

«*Centella asiatica*»

## Efficacy and indications:

- Prophylaxis with an antistria cream containing a *Centella asiatica* extract as active constituent was assessed in a double-blind trial in **pregnant women**.
- In the placebo group, 56% of the women presented striae, whereas in the treated group only **34% of the women developed striae** in this pregnancy.
- The **intensity of the striae was also lower** in the treated group.

# Centella

## «*Centella asiatica*»

### Efficacy and indications:

- Several Centella products are available on the market on the basis of their clinically confirmed efficacy. The following are the most important applications:
  - Cream containing 1% extract: for the **treatment of moderate or benign problems in wound formation, such as atonic wounds, hypertrophic scars**, keloids in the active phase, cutaneous ulcerations and cutaneous gangrene.
  - Cutaneous powder containing 2% extract: **for cutaneous ulcerations and wound healing agent** (scars, keloid scars and burns).
  - Ointment containing 1% extract: for the **treatment of leg ulcers, decubitus scabs, gangrene, defective scars, fistulas, traumatic and surgical wounds, burns and cutaneous-mucosal injuries**.

# Centella

## «*Centella asiatica*»

### Efficacy and indications:

- Pharmaceutical forms for oral use containing special extracts (typically 60-120 mg triterpenes daily) are authorized in different European countries
  - for the **treatment of atonic wounds, hypertrophic scars, keloids** in the active phase, for the **improvement of symptoms of venous stasis, and for the treatment of prevaricose syndromes and of complications of varicose veins** (phlebitis, varicose ulcers and cutaneous dystrophy).
- According to the ESCOP monograph, for internal use the adult dose is 0.6 g of dried drug as an infusion, tincture or extract, up to four times daily, and for external use semi-solid preparations containing 1% of extract or tincture.

# Centella

«*Centella asiatica*»

## Side-effects, interactions & contraindications:

- In the event of oral administration of Centella, **gastrointestinal complaints and nausea may occur**, but the frequency is not higher than for placebo.
- If there is allergy to Apiaceae, the use of Centella is contraindicated.
- It **should also be avoided during pregnancy, due to its reputed emmenagogue effect.**