

PHYTOTHERAPY

Chapter 4

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Nausea Ginger

«*Zingiber officinale*»

Used part: rhizoma

Used type: rhizoma and extract

Drog properties: According to the European Pharmacopoeia, drug contain at least 1.5% of essential oil



Ginger

«*Zingiber officinale*»

Chemical composition and mechanism of action:

Essential oil- sesquiterpenes.. «alpha-zingiberene, zingiberol, beta-bisabolene and alpha-farnesene»

Gingerols.. «6-gingerol»

During processing, the **gingerols** are partially converted to **shogaols** which may further metabolized to paradols.

Ginger

«*Zingiber officinale*»

Chemical composition and mechanism of action:

- ❖ In nausea induced by chemotherapeutics, a ginger extract and 6-gingerol had antiemetic effects.
- ❖ Both a ginger extract and also 6-, 8- and 10-gingerol inhibited serotonin-induced contractions (in vitro).
- ❖ In human studies, powdered ginger modified the gastric muscular contractions and increased gastric emptying.

Ginger

«*Zingiber officinale*»

Chemical composition and mechanism of action:

- Ginger has anti-inflammatory and analgesic activities, partly through the **inhibition of NF-kappa-B expression and COX-2 and 5-LOX**.
- In vitro, ginger **inhibited the formation of thromboxane B2 and platelet aggregation**.
- The extracts of the plant demonstrated in vitro **antibacterial properties** against both Gram-positive and Gram-negative human pathogenic bacteria (e.g. Escherichia coli, Pseudomonas, Staphylococcus and Proteus sp.).

Ginger

«*Zingiber officinale*»

Efficacy and indications:

- Some studies involved healthy volunteers with experimentally induced motion sickness (e.g. rotating chair), while other studies examined the efficacy during traveling. In 5 of the available 8 studies, **ginger was more effective than placebo** in preventing motion sickness.

Ginger

«*Zingiber officinale*»

Efficacy and indications:

- The most recent systematic review and a meta-analysis of the efficacy of ginger in postoperative nausea and vomiting included 5 randomized and placebo-controlled trials.
- The patients underwent gynecological surgery, laparoscopy or laparotomy. The administered dose corresponded to at least **1 g of crude ginger**, which was **administered 1 hour before anesthesia induction**.
- The meta-analysis found that **ginger was significantly better than placebo** for the prevention of postoperative nausea and vomiting and vomiting alone.

Ginger

«*Zingiber officinale*»

Efficacy and indications:

- The use in the prevention of pregnancy-related nausea is another major focus of clinical research.
- In a systematic review, 6 double-blind randomized studies were analyzed in which ginger was used for the treatment of **675 women with pregnancy-induced nausea and vomiting** (morning sickness and hyperemesis gravidarum).
- In 4 of the 6 randomized trials, ginger was superior to placebo; the remaining 2 trials demonstrated that **ginger was as effective as the reference treatment** (vitamin B6) in relieving nausea and vomiting.
- The **dose of ginger was 1-1.5 g**, and the duration of studies varied from **3 days to 3 weeks**.

Ginger

«*Zingiber officinale*»

Efficacy and indications:

- The efficacy of ginger in chemotherapy-induced nausea is **insufficient**. The only study with a positive outcome demonstrated the non-inferiority to metoclopramide; further studies did not confirm efficacy.
- Some studies assessed the **efficacy of ginger in osteoarthritis**. Although the results were positive, the design (a short treatment period, and high drop-out rates) do not allow the confirmation of efficacy in this indication.

Ginger

«*Zingiber officinale*»

Efficacy and indications:

- The European Medicines Agency has published two monograph for ginger. Well-established use was declared with the indication of
 - **the prevention of nausea and vomiting in motion sickness.**
- The dose of powdered ginger rhizome is 1-2 g 1 hour before the start of travel. Use in children and adolescents under 18 years of age is not recommended

Ginger

«*Zingiber officinale*»

Efficacy and indications:

- The **traditional application** of ginger was the basis of 2 other indications for traditional herbal medicinal products:
 - the symptomatic **relief of motion sickness**, and
 - the symptomatic **treatment of mild, spasmodic gastrointestinal complaints, including bloating and flatulence.**
- For the former indication, **750 mg of powdered rhizome** should be taken **30 min before traveling** (for children between 6 and 12 years: 250-500 mg). Use in children under 6 years of age is not recommended.
- For the latter indication, the dose of the **dried rhizomes is 3x180 mg**. Use in children and adolescents under 18 years of age is not recommended.

Ginger

«*Zingiber officinale*»

Side-effects, interactions & contraindications:

- The use of ginger is contraindicated in cases of hypersensitivity to the plant.
- A moderate number of data on pregnant women indicate no malformative or feto/neonatal toxicity of ginger root.
- In the absence of sufficient data, use during lactation is not recommended.
- Minor gastrointestinal complaints, and particularly stomach upset, eructation, dyspepsia and nausea, have been reported as adverse reactions.

Cardiovascular System

«Chronic venous insufficiency»

- Chronic venous insufficiency is a very common problem, afflicting about 20% of the population.
- The frequency of the disease increases with age, resulting in a deterioration of the quality of life, due to the symptoms relating to varicose veins and more serious consequences such as leg ulcer.
- **Varicose veins develop as a result of the destruction of proteoglycans in the elastic tissue of the vein wall.**
- **This leads to dilation of the vessels and edema formation.**

Cardiovascular System

«Chronic venous insufficiency»

- Apart from surgical treatment, chronic venous insufficiency cannot be cured, but the **symptoms may be relieved** and the **process of vessel wall destruction may be slowed down**.
- The pharmacotherapy of chronic venous insufficiency is usually based on the **local or systemic application of natural or semisynthetic flavonoids**.

Cardiovascular System

«Chronic venous insufficiency»

- The aim of the treatment is **to increase the capillary resistance** and **venous tone and relieve the symptoms**.
- This can be achieved by the application of flavonoids (in many cases **“bioflavonoids”** are applied, i.e. a flavonoid-rich fraction gained from different plants).
- Some **triterpene saponins** also have a beneficial effect on vessel walls. Their mechanism of action is partly different, involving the **inhibition of certain enzymes that are responsible for the breakdown of the vein wall structure**.

Cardiovascular System

«Chronic venous insufficiency»

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Horse chestnut

«*Aesculus hippocastanum*»

Used part: seed

Used type: seed extract

Drog properties: bitter taste



Horse chestnut

«*Aesculus hippocastanum*»

Chemical composition and mechanism of action:

Saponin mixture.. «aescin, especially beta-aescin»

Flavonoids

Sterols

Essential oils

Horse chestnut

«*Aesculus hippocastanum*»

Chemical composition and mechanism of action:

- Different experimentally induced edemas have been **inhibited by the application of beta-aescin** in animals.
- Different **extracts and beta-aescin contracted isolated veins and exhibited antiedematous activity after oral administration.**
- **Aescin inhibited the enzyme hyaluronidase** in vitro.

Horse chestnut

«*Aesculus hippocastanum*»

Efficacy and indications:

- The effect of a special extract (DER 5:1, 50% ethanol), standardized to 50 mg aescin/capsule (240-290 mg extract/capsule) on transcapillary filtration has been assessed by **measuring capillary filtration coefficients** in clinical studies.
- The **capillary filtration coefficient proved to be decreased significantly** as compared with placebo.
- The **inhibitory effect on edema formation may improve** the edema-related symptoms in venous diseases.

Horse chestnut

«*Aesculus hippocastanum*»

Efficacy and indications:

- In a study on patients with varicose veins, oral administration of the **extract** **decreased the activity of three hydrolases** (beta-N-acetylglucosaminidase, beta-glucuronidase and arylsulfatase) that catalyze the breakdown of the proteoglycans of the capillary walls.

Horse chestnut

«*Aesculus hippocastanum*»

Efficacy and indications:

- The above-mentioned special extract was applied (the daily dose of **beta-aescin was 100-150 mg**), and the studies lasted for **2-16 weeks** and were usually placebo-controlled and double-blind.
- The endpoints were symptoms related to the chronic venous insufficiency (**leg pain, edema and pruritus**) and objective measures such as **leg volume and circumference**.
- The effects on the subjective symptoms and edema were found to be **reduced significantly** by the active treatment relative to placebo.

Horse chestnut

«*Aesculus hippocastanum*»

Efficacy and indications:

- On the basis of the clinical evidence, extracts standardized to **100 mg aescin** may be applied orally as well-established medicines
 - for the **treatment of chronic venous insufficiency** (characterized by swollen legs, varicose veins, a feeling of heaviness, pain, tiredness, itching, tension and cramps in the calves).
- At least 4 weeks of treatment may be needed to achieve a beneficial effect.

Horse chestnut

«*Aesculus hippocastanum*»

Efficacy and indications:

- In view of the traditional application of horse chestnut seeds, some extracts may be applied topically as traditional herbal medicinal products
 - to **relieve symptoms of discomfort and heaviness of the legs related to minor venous circulatory disturbances**, or
 - for **the relief of signs of bruises, such as local edema and hematoma**.
- For this purpose, a dry extract (ethanol 25-50% v/v) in a strength corresponding to ca 1% aescin in an ointment/gel base, or a tincture (1:5; extraction solvent: 50% ethanol v/v), 20% in an ointment/gel base, may be applied 1-3 times daily.

Horse chestnut

«*Aesculus hippocastanum*»

Side-effects, interactions & contraindications:

- In clinical trials, **no treatment-related adverse events have been recorded.**
- The frequency of a specific, **mild side-effects** (nausea, headache, gastrointestinal disorders and pruritus) was the same as in the placebo group.
- Absolute contraindication of the treatment is limited to hypersensitivity to the active substance.
- **Saponins may have an irritative effect in the stomach, resulting in nausea.**
- **However, high tolerance has been demonstrated for controlled-release dosage forms.**

Horse chestnut

«*Aesculus hippocastanum*»

Side-effects, interactions & contraindications:

- Although the hemolytic activity of saponins led to the suggestion that **aescin might increase the effect of anti-coagulants**, this was not confirmed by the clinical data.
- **Oral application is not intended for those under 18; for topical application, the age limit is 12 years.**
- If there is inflammation of the skin, thrombophlebitis or subcutaneous induration, severe pain, ulcers, sudden swelling of one or both legs, or a cardiac or renal insufficiency, the products may be applied only after a medical doctor has been consulted.
- **Topical application should be avoided on broken skin, around the eyes or on the mucous membranes.**

Cardiovascular System

«Cardiac insufficiency»

- Chronic cardiac insufficiency, or congestive heart failure (CHF) is one of the most common causes of death in the elderly population.
- The **reduction of the pump function** results in an insufficient oxygen supply to the organs, including the heart, leading to a wide range of symptoms (**edema, cyanosis, tachycardia, hypertension and arrhythmia**).

Cardiovascular System

«Cardiac insufficiency»

- According to the classification of the New York Heart Association (NYHA), heart failure may be grouped as follows:

Class	Patient symptoms
I	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation or dyspnea (shortness of breath).
II	Slight limitation of physical activity. Comfortable at rest. Ordinary physical activity results in fatigue, palpitation, or dyspnea.
III	Marked limitation of physical activity. Comfortable at rest. Less than ordinary activity causes fatigue, palpitation or dyspnea.
IV	Unable to carry on any physical activity without discomfort. Symptoms of heart failure at rest. If any physical activity is undertaken, discomfort increases.

Cardiovascular System

«Cardiac insufficiency»

- In the history of phytotherapy, a myocardial insufficiency was usually treated with cardiac glycoside-containing plants.
- In Europe, the most widely applied species applied for the treatment of chronic cardiac failure belonged in the genus *Digitalis*.
- In acute cases, the **quick-acting glycosides of *Strophanthus* seeds** were used.
- More recently, **pure digitaloids have been used instead of the extracts** of the plants since the **narrow therapeutic range** of the compounds may result in intoxications.

Cardiovascular System

«Cardiac insufficiency»

- The cornerstone of the efficacy of **cardiac glycosides is the inhibition of Na⁺-K⁺-ATPase**, which results in an **increased intracellular Ca²⁺ level** and an **improvement of the heart muscle contraction** (a positive inotrope effect).
- For this purpose, **beta-adrenoreceptor agonists and ACE-inhibitors are used most widely in modern therapy**.
- From among the “classical” phytomedicines, only one plant, **hawthorn**, is of noteworthy importance in the treatment of a cardiac insufficiency. However, hawthorn has the major limitation that it is clinically effective only in mild and moderate cases.

Hawthorn

«*Crataegus spp*»

Used part: dried flower-bearing branches

Used type: dry leaves with flowers and standardized extract

Drog properties: The latter contains 0.8-3% of flavonoids, expressed as hyperoside.



Hawthorn

«*Crataegus spp*»

Chemical composition and mechanism of action:

Proanthocyanidins..

- Flavan derivatives «(+)-catechin and (-)-epicatechin»
- Flavones and flavonoles «vitexin, hyperoside»

Triterpenes

Aromatic amines

Hawthorn

«*Crataegus spp*»

Chemical composition and mechanism of action:

- The most important effect of hawthorn as concerns its efficacy is the **positive inotropic activity**.
- Ex vivo studies confirmed **that *Crataegus* extracts significantly increase the force of contraction of the human myocardium**.
- The extract of the plant **inhibits Na⁺-K⁺ adenosine triphosphatase**, which indirectly hampers the Na⁺-Ca²⁺ antiport leading to an increased intracellular Ca²⁺ level.

Hawthorn

«*Crataegus spp*»

Chemical composition and mechanism of action:

- Hawthorn **improves the coronary blood flow**, presumably through the endothelial nitric oxide (NO) synthesis-enhancing properties of the extract.
- In an animal experiment, treatment with a *Crataegus* extract **dose-dependently lowered the pathologically increased blood pressure**, but had no effect in normal control animals.
- *Crataegus* extracts prolonged pacemaker repolarization, indicating **anthyarrhythmic class III-like activity**.

Hawthorn

«*Crataegus spp*»

Chemical composition and mechanism of action:

- In an animal experiment, following the application of **oral doses of 100 mg/kg for 12 weeks** (this is markedly higher than the human therapeutic dose), the **levels of serum cholesterol and triglycerides decreased significantly** as compared with the control values.
- In a further experiment, **i.v. administration of different *Crataegus* extracts resulted in a decrease of the blood pressure.**

Hawthorn

«*Crataegus spp*»

Efficacy and indications:

- In a recent meta-analysis (2011);
- *Crataegus* dry extracts (4-6.6:1, ethanol 45% m/m) were used.
- The results showed that the physiological outcome parameters (the **maximal workload** (MWL), the **left ventricular ejection fraction** (LVEF), and the **exercise tolerability**) improved.
- The typical symptoms such as **reduced exercise tolerance, exertional dyspnea, weakness, fatigue** and **palpitations** improved.

Hawthorn

«*Crataegus spp*»

Efficacy and indications:

- European Medicines Agency has granted a traditional-use monograph to the plant, with the following indications:
 - traditional herbal medicinal product used to relieve symptoms of **temporary nervous cardiac complaints** (e.g. palpitations, perceived extra heart beat due to mild anxiety) after serious conditions have been excluded by a medical doctor, and
 - traditional herbal medicinal product for the **relief of mild symptoms of mental stress and to aid sleep.**

Hawthorn

«*Crataegus spp*»

Efficacy and indications:

- There are several extracts (apart from the dry plant material) that can be used in therapy: **dry extract** (DER 4-7:1, extraction solvent aqueous methanol or ethanol), **liquid extract** (DER 1:1-2, extraction solvent aqueous ethanol), **expressed juice**, etc. Typical **daily doses are 0.25-1 g of the dry extracts, 1.5-5 g for the liquid extracts.**

Hawthorn

«*Crataegus spp*»

Side-effects, interactions & contraindications:

- With regard to **its effect on the Na⁺-K⁺ pump and phosphodiesterase inhibitory activity**, it may be presumed that **hawthorn may potentiate the effect of digitalis glycosides, beta-blockers and other antihypertensives**, but in human studies no such interactions have been recorded.
- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, its use during pregnancy and lactation is not recommended.

Adaptogenes

- If stress is above the level of tolerance or if it is permanent, it may lead to the exhaustion and damage of the organism.
- Gastric ulcer, irritable bowel syndrome and anxiety are typical consequences of excessive stress.
- Stress tolerance is decreasing with age.
- Resistance to stress may be improved by adaptogens.

Adaptogenes

- The group of adaptogens consists of drugs only of herbal origin.
- Adaptogens have **multiple physiological activities** and their overall **effect is the adaptation to stress**, the **normalization of physiologic functions** affected by stress.
- This effect is **non-specific**, i.e., independent from the nature of the stress and results in the prolongation of adaptation phase and prevention of exhaustion.

Ginseng

«*Panax ginseng*»

Used part: root

Used type: root and dry
extract

Drog properties: The roots of
the plants are widely used in
Traditional Chinese Medicine



Ginseng

«*Panax ginseng*»

Chemical composition and mechanism of action:

Ginsenosides (saponins)..

- dammarane-type.. «**protopanaxadiol** and **protopanaxatriol**»
- oleanolic acid-type

Ginseng

«*Panax ginseng*»

Chemical composition and mechanism of action:

- There are many contradictory results in the literature about the effects of ginseng related with antistress activity.
- Individual ginsenosides, contrary to the fact that they are chemically very similar, may have opposite effects.
- Ginsenosides exhibited both CNS-depressant and CNS-stimulant effects in animal experiments.
- However, this is fully in line with the normalizing effect of adaptogens.

Ginseng

«*Panax ginseng*»

Chemical composition and mechanism of action:

- Ginseng has corticosteroid-like action presumably by increasing adrenal steroidogenesis.
- Increased physical endurance, which may be related to this effect, was described in several animal experiments after the administration of ginseng.

Ginseng

«*Panax ginseng*»

Chemical composition and mechanism of action:

- The **hypotensive, antiarrhythmic and positive inotropic effect** of ginseng extracts and certain individual ginsenosides has been confirmed experimentally.
- *Panax ginseng* **reduced serum cholesterol and triglycerides**, and **increased high-density lipoprotein levels** of animals.
- It also had **antiplatelet effect**, presumably by **inhibiting thromboxane formation**.

Ginseng

«*Panax ginseng*»

Chemical composition and mechanism of action:

- Ginseng has **hypoglycaemic activity** as demonstrated in several preclinical trials.
- Ginsenosides **promoted insulin release in pancreas** in vitro.
- **Hypoglycaemic effect was demonstrated** in healthy animals.
- **Antioxidant, antiproliferative and antiviral** activities of different ginseng extracts have been demonstrated in in vitro studies.

Ginseng

«*Panax ginseng*»

Efficacy and indications:

- Clinical trials support the activity of ginseng on **cognitive performance**.
- In one of study, administration of root extract led to **significant improvements in speed of memory and attention**.
- Efficacy was also confirmed with combination products (ginseng with caffeine-containing plants or *Ginkgo*).

Ginseng

«*Panax ginseng*»

Efficacy and indications:

- The 200-400 mg ginseng extract reduced blood glucose concentrations in healthy subjects.
- The **chronic use of ginseng may have effect on life quality and expectancy.**
- The usual **dose of ginseng roots is 0.5-1 g daily**, however in China larger doses (up to 9 g) are used in processed form. The **standardized extract G115 has been applied at doses of 100–400 mg daily** in clinical studies.

Ginseng

«*Panax ginseng*»

Side-effects, interactions & contraindications:

- Consumption of **large doses of ginseng together with caffeine-containing drugs** was reported to cause “**ginseng abuse syndrome**”, characterized by **diarrhea, hypertension and anxiety**.
- **Overdosage may lead to nausea, vomiting, cardiovascular symptoms** (palpitation).
- **Ginseng may interfere with oral anticoagulants.**
- The safety of ginseng during pregnancy, breastfeeding and in children has not been established.