# PHYTOTHERAPHY

## Chapter 3

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# Gastrointestinal system

## «*Diarrhea*»

- Diarrhea may have a **number causes**.
- The most common factors are **pathogenic bacteria or viruses**, **toxins of non-microbial origin** (including some medicines) or **improper diet**.
- A direct cause of diarrhea may be **increased secretion** and the **decreased absorption of water** in the gastrointestinal system, **increased motility** and **increased osmotic pressure** or a combination of the above factors.

# Gastrointestinal system

## «*Diarrhea*»

- **Uncomplicated acute diarrhea** usually lasts only **for some days** and is typically self-limiting.
- **Chronic diarrhea** persists much longer (**even for weeks**) and may have more severe underlying causes (bowel diseases or endocrinological causes).
- Independently from the cause, **herbal antidiarrheal preparations** may be effective through their **antibacterial or antiviral effects**, by **inhibiting the absorption of toxins and water** and by **decreasing secretion to the gut**.

# Gastrointestinal system

## «*Diarrhea*»

- The majority of antidiarrheal plants act by virtue of their tannin content.
- **Most tannins are catechin derivatives that are resistant to acid hydrolysis.**
- Gallotannins are hydrolyzed in the intestine and therefore have no astringent effects in the colon.
- **By coagulating proteins, tannins have an antibacterial effect and form a protective layer on the mucosal membrane of the gut, thereby inhibiting secretion.**
- Tannins are water-soluble, and their optimal application is therefore in the form of teas. **In high doses or when applied for a long time, tannins may cause gastrointestinal disturbances by inhibiting digestive enzymes and decreasing the bioavailability of several medicines and ions**.

# Gastrointestinal system

## «*Diarrhea*»

- Pectin-containing plants also have a beneficial effect in diarrhea.
- **Pectins are polysaccharides rich in galacturonic acid; they are resistant to digestive enzymes and are fermented by the bacterial flora of the colon to form short-chain fatty acids.**
- These compounds decrease motility and increase water absorption in the colon.
- **Generally used pectin-containing plants are banana, carrot and apple.**
- Since pectins are hydrolyzed into soluble sugars during ripening, **unripe pectin-containing fruits are more effective**.

# Tea

«*Camellia sinensis* (Syn. *Thea sinensis*)»

**Used part:** leaves

**Used type:** water extract,

infusion

**Drog properties: -**

# Tea

## «*Camellia sinensis* (Syn. *Thea sinensis*)»

**Chemical composition and mechanism of action:**

**Methylxanthines.. «caffeine, theophylline, theobromine»**

**Flavanols.. «(-)-epicatechin, (-)-epigallocatechin, (-)-epicatechin-3-O-gallate, and (-)-epigallocatechin-3-O-gallate»**

**Flavonols.. «quercetin, kaempferol and their glycosides»**

**Flavones.. «apigenin, and luteolin as C-glucuronides»**

**amino acids.. «L-Theanine»**

**saponins, phenolic acids and tannins**

# Tea

«*Camellia sinensis* (Syn. *Thea sinensis*)»

## Chemical composition and mechanism of action:

**A cup of tea contains approximately 60 mg of caffeine**

**A cup of coffee contains about 100 mg of caffeine**

# Tea

## «*Camellia sinensis* (Syn. *Thea sinensis*)»

**Chemical composition and mechanism of action:**

- There is **no experimental data** are available for the antidiarrheal effect of tea is directly
- When applied in diarrhea, therefore **green tea** should be preferred.
- The **mild stimulant effect** of green tea can be interpreted on the basis of its **caffeine content**.
- The oral administration of green tea **increased locomotor activity** in rats.

# Tea

## «*Camellia sinensis* (Syn. *Thea sinensis*)»

**Chemical composition and mechanism of action:**

- Tea extracts have a beneficial influence on the **glucose metabolism**.
- A tea extract enriched and standardized to catechins **improved the glucose tolerance** and **insulin sensitivity** in rats.
- After 12 weeks of green tea supplementation, plasma levels of glucose, insulin and triglyceride levels are decreased.

# Tea

## «*Camellia sinensis* (Syn. *Thea sinensis*)»

**Chemical composition and mechanism of action:**

- The potential effect of green tea on **body weight** was linked to its **caffeine content**.
- (-)-epigallocatechin-3-O-gallate;
  - significantly reduced food intake in rats.
  - reduced the body weight gain and body fat percentage.
  - treatment attenuated the insulin resistance
  - decreased the plasma cholesterol level
  - showed the antimicrobial activity
  - antioxidant and antitumor activity

# Tea

## «*Camellia sinensis* (Syn. *Thea sinensis*)»

**Efficacy and indications:**

- Theanine increased the cognitive performance at 120 mg doses.
- In a randomized, double-blind, placebo-controlled study, **healthy adult participants** received either **250 mg of caffeine, 200 mg of theanine**, both or neither. **Caffeine increased the self-rated alertness and blood pressure**. **Theanine antagonized the action of caffeine on blood pressure** but **did not significantly affect alertness and mood**.

# Tea

## «*Camellia sinensis* (Syn. *Thea sinensis*)»

**Efficacy and indications:**

- In a 12-week double-blind study, **690 mg of catechins/day decreased the body weight**.
- A green tea beverage (**625 mg of total catechins and 39 mg of caffeine/day**) **reduced abdominal fat**, but had only a marginal effect on body weight.
- The **cardiovascular protective effect** of green tea is supported by epidemiological data from the Far East.
- No human studies are available to confirm the **antidiarrheal activity** of green tea. The basis of the effect is the noteworthy polyphenol content of the herbal drug. For this purpose, **unfermented green leaves are the most appropriate**.

# Tea

## «*Camellia sinensis* (Syn. *Thea sinensis*)»

**Efficacy and indications:**

- On the basis of the traditional application, green tea may be used as a traditional herbal medicinal product
  - **for the relief of fatigue and the sensation of weakness.**
- For this purpose, herbal tea prepared as an infusion from 1.8–2.2 g of whole or comminuted herbal substance, 3–5 times daily, or powdered herbal substance in a single dose of 390 mg, 3-5 times daily, may be applied.

# Tea

## «*Camellia sinensis* (Syn. *Thea sinensis*)»

**Side-effects, interactions & contraindications:**

- The **absorption of alkaline drugs** may be **delayed** because of their chemical binding with the poly phenols of tea.
- **Pregnant women** should limit their caffeine intake to **less than 200 mg of caffeine** per day (this is equivalent to approximately 10 g of tea leaves; at this level, no risk of miscarriage or preterm birth was detected).
- It is not recommended before bedtime since **it may cause sleep disturbances**.
- The consumption of tea products containing >300 mg can lead to restlessness, elevated reflex excitability and tremor.

# Tormentil

«*Potentilla erecta* (syn. *Potentilla tormen-tilla, Tormentilla erecta*)»

**Used part:** rhizoma

**Used type:** dried rhizoma

**Drog properties:**European Pharma-copoeia, Tormentillae rhizoma contains not less than 7% of tannins, expressed as pyrogallol.

# Tormentil

«*Potentilla erecta* (syn. *Potentilla tormen-tilla, Tormentilla erecta*)»

## Chemical composition and mechanism of action:

**catechin-type condensed (high amount)**

**hydrolizable ellagitannins (smaller amounts)**

**flavonoids**

**triterpene saponins**

**phenol carboxylic acids**

# Tormentil

«*Potentilla erecta* (syn. *Potentilla tormen-tilla, Tormentilla erecta*)»

**Chemical composition and mechanism of action:**

- The therapeutic efficacy of tormentil depends on its tannin content.
- These polyphenols coagulate proteins, thereby forming a protective layer on the skin and mucosa, inhibiting the absorption of toxins and exerting an antimicrobial effect.
- Aqueous tormentil extracts exert antimicrobial and antiviral effects on various bacteria (*Shigella* sp., *Pseudomonas aeruginosa*, *Staphylococcus aureus, Escherichia coli* and *Streptococcus faecalis*) and herpes virus.

# Tormentil

«*Potentilla erecta* (syn. *Potentilla tormen-tilla, Tormentilla erecta*)»

## Efficacy and indications:

- In an open-label study, the safety and clinical efficacy of an ethanolic dry extract (2.4 g/day) were studied in patients with active ulcerous colitis.
- The **colitis activity index was reduced** statistically significantly, and additionally the **stool frequency, bloody stools and C-reactive protein levels decreased**.

# Tormentil

«*Potentilla erecta* (syn. *Potentilla tormen-tilla, Tormentilla erecta*)»

## Efficacy and indications:

- In a study, involving children with **rotavirus diarrhea**, treatment with a **tormentil tincture** was applied until discontinuation of the diarrhea or at most for 5 days.
- In the treated group, the duration of the diarrhea was 3 days, while in the placebo group it was 5 days.

# Tormentil

«*Potentilla erecta* (syn. *Potentilla tormen-tilla, Tormentilla erecta*)»

**Efficacy and indications:**

- Tormentil rhizome may be used as a traditional herbal medicinal product
  - **for the symptomatic treatment of mild diarrhea or**
  - **for the symptomatic treatment of minor inflammations of the oral mucosa.**

- Doses;
  - as an infusion, the maximal daily dose is 12 g;
  - as a decoction it is 6 g.
  - Internally, tinctures or liquid extracts may be used in a daily dose of 3-12 ml,
  - the dry extract is 1.2 g daily.

# Tormentil

«*Potentilla erecta* (syn. *Potentilla tormen-tilla, Tormentilla erecta*)»

**Side effects, interactions & contraindications:**

- On its internal application, the absorption of concomitantly administered medicines may be delayed.
- For this reason, tormentil preparations **should be taken 1 hour or more before or after the intake of other medicinal products**.
- **Safety during pregnancy and lactation has not been established.**
- In cases of oral use, **mild gastrointestinal complaints such as nausea and vomiting may occur.**

# Raspberry

## «*Rubus idaeus* »

**Used part:** leaves

**Used type:** dried chopped

leaves

**Drog properties:-**

# Raspberry

## «*Rubus idaeus*»

**Chemical composition and mechanism of action:**

**hydrolyzable gallo- and ellagitannins**

**flavonoids.. «kaempferol, quercetin and their glycosides»**

**phenolic acids**

# Raspberry
## «*Rubus idaeus*»

**Chemical composition and mechanism of action:**

- In an animal experiment, **raspberry leaf water extracts** were tested on **uterine strips** from both non-pregnant and pregnant rats.
- **Little or no effect was seen in the uteri** from the non-pregnant rats, whereas a **more regular rhythm and less frequent contractions** were observed in the pregnant uteri.
- Ethanol extract had no effect on contractility.

# Raspberry
## «*Rubus idaeus*»

**Efficacy and indications:**

- The clinical data on raspberry leaf focus on its contemporary use during pregnancy.
- A double-blind, randomized, placebo-controlled study was continued from **32 weeks of gestation until the beginning of labor**.
- Tablets containing **2.4 g raspberry leaf daily** had **no significant effect on the length of pregnancy**, the **medical augmentation of labor**, the **need for pain relief during labor**, or the **times of the three stages of labor**.

# Raspberry
# «*Rubus idaeus*»

**Efficacy and indications:**

- Raspberry leaf may be used as a traditional herbal medicinal product for the
  - symptomatic relief of the **minor spasms associated with menstrual periods**,
  - symptomatic treatment of **mild inflammation in the mouth or throat**
  - symptomatic treatment of **mild diarrhea**.

- Doses;
  - maximal dose of a water extract (DER 4:1) is 904 mg.
  - herbal infusions may be used, prepared as 1.5-8 g of the comminuted herbal substance in 150 ml of boiling water, 3 times daily.
  - In cases of mild inflammation in the mouth or throat, it should be used as a gargle.

# Raspberry
## «*Rubus idaeus*»

**Side effects, interactions & contraindications:**

- Safety during pregnancy and lactation has not been established.
- In the event of hypersensitivity to raspberry leaf, its application is contraindicated.

# Gastrointestinal system

## *«Obstipation»*

- Obstipation is a common complaint in 1-5% of the population and 20–80% of the elderly.
- Obstipation may be a result of **organic causes**, or it can be induced by an **improper diet or by medicines** (chemotherapeutic agents, opioids, sedatives, hypnotics, anxiolytics, antiparkinsonism agents and antidepressants, antacids, diuretics, phenothiazines, and iron and calcium supplementation).
- The most common reasons for obstipation are **dietary habits** (a diet poor in fibre and insufficient water consumption), and **lack of physical activity**.

# Gastrointestinal system

## *«Obstipation»*

- Obstipation is characterized by straining **heavily to produce stools**, in some cases accompanied by a feeling of **incomplete defecation**, and **abdominal cramps**.
- Obstipation may **increase the risk of hemorrhoids** and chronic constipation may be related to an increased risk of **colon cancer**.
- The treatment of obstipation should start with **dietary** (an increase of fibre and water intake) and **lifestyle changes**.
- **Osmotic laxatives** may also be applied. **Stimulant anthranoid-containing laxatives** are agents of second choice, and should be used only occasionally.

# Gastrointestinal system

## *«Obstipation-Bulk-forming laxatives»*

- The safest laxatives belong in the group of bulk-forming agents.
- **These products are especially rich in fibers.**
- Bulk-forming agents stimulate the intestinal activity by causing distension of the bowel.
- **These products provide the bacterial flora with a proper substrate for proliferation, and the bacterial mass and consequently the stool weight are therefore increased.**
- These may have a protective effect on the mucosa, but more importantly act as osmotic laxatives in the colon.

# Gastrointestinal system

## *«Obstipation-Bulk-forming laxatives»*

- Bulk-forming laxatives are not absorbed, and therefore have no systemic effects.
- **They are a safe way of treating the obstipation of pregnant women and also in the case of long-term treatment.**
- The most common side-effect is flatulence and a feeling of fullness.
- **Bulk-forming agents may decrease the absorption of concomitantly taken drugs.**

# Linseed

## «*Linum usitatissimum*»

**Used part:** seed

**Used type:** dried, ripe seeds

**Drog properties:-**

# Linseed

## «*Linum usitatissimum*»

**Chemical composition and mechanism of action:**

**mucilage**

**alimentary fibers of protein**

**polyunsaturated fatty acids.. «linoleic acid»**

**lignans**

**cyanogenic glycoside**

# Linseed

## «*Linum usitatissimum*»

**Chemical composition and mechanism of action:**

- The laxative effect of linseed is attributed to the **swelling of polysaccharides in the intestines**
- An animal experiment confirmed that the oral application of linseed **increased the water content of the feces**.
- Animal experiments have demonstrated that the consumption of linseed **lowers cholesterol levels** because of the unsaturated fatty acid content.
- Linseed extracts exert **estrogenic effect** in different in vitro models.
- The **antioxidant effect** is due to the lignan and unsaturated fatty oil content.

# Linseed

## «*Linum usitatissimum*»

**Efficacy and indications:**

- In a randomized trial, patients with constipation-predominant **irritable bowel syndrome received 6-24 g/day** of either linseed or psyllium for 3 months.
- In the linseed group, the **constipation and abdominal symptoms were decreased significantly**.

# Linseed

## «*Linum usitatissimum*»

**Efficacy and indications:**

- A cholesterol-lowering effect has been observed in several clinical trials.
- The hypothesis that the **alpha-linolenic acid** content of linseed oil may have a **cardioprotective effect** was investigated in a dietary intervention study.
- The **total plasma cholesterol level decreased by 12.3% in the linseed group**.

# Linseed

## «*Linum usitatissimum*»

**Efficacy and indications:**

- Euroepan Medicines Agency with the following indication:
  - treatment of habitual constipation or in conditions in which **easy defecation with soft stool is desirable**.
- The daily dose is **20-45 g**.
- Linseed may therefore be used as a traditional herbal medicinal product with the indication of a
  - demulcent preparation for the symptomatic relief of **mild gastrointestinal discomfort**
- The daily dose is **15-30 g**.
- It should be consumed with a **sufficient water intake and at least 1/2-1 hour before or after the intake of other medicines**. The effect starts 12-24 hours later. It should not be taken immediately prior to bedtime.

# Linseed

## «*Linum usitatissimum*»

**Side effects, interactions & contraindications:**

- Although **100 g of linseed** may contain **cyanogenic glycosides** equivalent to 30 mg of hydrogen cyanide (the **lethal dose of which is about 50-100 mg**), linseed consumption **is not dangerous** from this aspect.
- Linseed **should not be used** by patients with a sudden change in bowel habit that has persisted for **more than 2 weeks**, with undiagnosed rectal bleeding or with a failure to defecate following the use of a laxative.

# Linseed

## «*Linum usitatissimum*»

**Side effects, interactions & contraindications:**

- The **long-term use of linseed may have an estrogenic effect**, and its use is therefore not recommended in women with hormonally dependent tumors.
- As an **adverse effect, meteorism** is common.

# Gastrointestinal system

## *«Obstipation-Stimulant laxatives»*

- Stimulant laxatives have a direct effect on the intestinal mucosa and relieve obstipation by increasing the water content of the fecal matter and the intensity of bowel peristalsis.
- Since the **active components** are known, there are products on the market containing pure **anthranoids** rather than dry herbal material or a crude extract.
- These products (especially medicines) are standardized to their active components.

# Gastrointestinal system

## *«Obstipation-Stimulant laxatives»*

- The main components of the **mechanisms of action of anthranoids** are
  - **inhibition of the Na+-K+-ATPase in the bowel epithelium, resulting in decreased water and Na+ absorption**,
  - **the increase of cyclic AMP (cAMP) in the enterocytes, which results in the increased secretion of Na+ and water**
  - **stimulation of the synthesis of certain autacoids and neurotransmitters (NO and 5-HT), resulting in increased intestinal motility, a shortened transit time and decreased water and electrolyte absorption**

# Gastrointestinal system

## *«Obstipation-Stimulant laxatives»*

- The **pharmacokinetics** of anthranoid-containing herbs and pure compounds (except sennosides) is only **poorly understood**.
- **The aglycones are pharmacologically active, the glycosides are pharmacologically inert.**
- Anthranoid glycosides are metabolized by the bacteria of the colon.
- **Only a small proportion of the aglycones is absorbed, the majority is excreted with the feces.**

# Gastrointestinal system

## *«Obstipation-Stimulant laxatives»*

- The most **common side-effect of anthranoids is spastic abdominal pain**.
- **Long-term application may lead to water and electrolyte loss and hypokalemia.**
- **Anthraquinone-containing plants may be applied for the short-term treatment of atonic constipation and before surgery or endoscopy of the gastrointestinal tract.**

# Senna

## «*Cassia acutifolia, Cassia angustifolia*»

**Used part:** leaves, fruits

**Used type:** dried leaves and fruits, standized extract

**Drog properties:** The herbal substance contains not less than 2.5% of hydroxyanthracene glycosides, calculated as sennoside B

# Senna

«*Cassia acutifolia, Cassia angustifolia*»

## Chemical composition and mechanism of action:

**Anthranoids.. «dianthrones, anthrones»**

- **Sennosides.. «sennoside A and B»**

# Senna

## «*Cassia acutifolia, Cassia angustifolia*»

**Chemical composition and mechanism of action:**

- Anthranoid glycosides **are not absorbed from the intestinal tract**.
- Neither the acidic milieu of the stomach nor alpha-glycosidase enzyme in the small intestine is able to hydrolyze the beta-O-glycosidic substituents of sennosides.
- As regards the time of transport to the colon and metabolization into active compounds, **Senna extracts act within 8-12 hours**.
- The laxative effect is based on the **increased colonic motility**, the **inhibition of absorption and stimulation of the secretion of water and electrolytes**.

# Senna

«*Cassia acutifolia, Cassia angustifolia*»

## Efficacy and indications:

- The clinical efficacy of senna has been evaluated in clinical trials in the **treatment of obstipation** and for **bowel cleansing before medical interventions**.
- The **bowel-cleansing efficacy** was tested with a **senna fruit dry extract preparations** with a single dose corresponding to **150 mg of sennoside** in patients referred for colonoscopy.

# Senna

## «*Cassia acutifolia, Cassia angustifolia*»

**Efficacy and indications:**

- EMA granted a well-established use monograph to senna. Preparations containing standardized herbal substances or extracts may be indicated for
  - **short-term use in cases of occasional constipation.**

- Doses;
  - 15–30 mg/day of hydroxyanthracene derivatives, calculated as sennoside B for adolescents, adults and the elderly.
  - The maximum daily dose of hydroxyanthracene glycosides is 30 mg.

# Senna

«*Cassia acutifolia, Cassia angustifolia*»

**Side-effects, interactions & contraindications:**

- In theory, anthranoids may increase hyperemia in the pelvic region, and **stimulation of uterine muscles** is also presumed.
- It is not recommended for use in children under 12 years of age.
- It is **contraindicated** in cases of intestinal obstructions and stenosis, atony, appendicitis, inflammatory colon diseases (e.g. Crohn's disease and ulcerative colitis), abdominal pain of unknown origin, or a severe dehydration state with both water and electrolyte depletion.

# Aloe

## «*Aloe barbadensis, Aloe ferox* »

**Used part:** juice

**Used type:** juice collected after cutting of the leaves

**Drog properties:** light-colored jeleous juice

# Aloe

«*Aloe barbadensis, Aloe ferox* »

**Chemical composition and mechanism of action:**

**anthrone-10-C-glycosides.. «aloin A, B» (barbaloin)**

**other anthranoid derivatives**

**aglycones.. «aloe emodin and chrysophanol»**

# Aloe

## «*Aloe barbadensis, Aloe ferox* »

**Chemical composition and mechanism of action:**

- The anthranoid-glycosides of aloe are not absorbed in the upper gut.
- The intestinal flora is able to break down O-glycosides fully, but C-glycosides (the major constituents of aloe) only to a certain extent.
- Aloe-emodin is quickly oxidized to rhein. The absorbed aglycone is conjugated with glucuronide in the liver and excreted via the urine and the bile.

# Aloe

«*Aloe barbadensis, Aloe ferox* »

## Chemical composition and mechanism of action:

- The mechanism of action of aloe includes a direct effect on the motility, leading to a **reduced transit time**, **inhibition of the absorption of water, Na+ and Cl-**, and an **increase of the secretion of water and electrolytes** into the lumen.

# Aloe

## «*Aloe barbadensis, Aloe ferox* »

**Efficacy and indications:**

- The medicinal use of aloe is regarded as well-established for the **short-term treatment of occasional constipation**.
- For adolescents over 12 years of age and adults, the daily dose should contain 10– 30 mg of anthranoid derivatives, calculated as barbaloin, to be taken once daily at night (if necessary, 2-3 times weekly).
- **Use for more than 1-2 weeks requires medical supervision.**

# Aloe

## «*Aloe barbadensis, Aloe ferox* »

**Side-effects, interactions & contraindications:**

- Porolonged use or an overdosage may lead to **hypokalemia** which may enhance the effects of cardiac glycosides and interfere with the antiarrhythmic agents.
- **It is contraindicated for children under 12.**
- **Aloe is contraindicated in cases of intestinal obstruction and stenosis, inflammatory colon diseases, abdominal pain of unknown origin, and a severe dehydration state with water and electrolyte depletion.**
- **Aloe preparations may lead to colicky abdominal pain, especially in patients with an irritable colon.**