PHYTOTHERAPHY

Chapter 3

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Gastrointestinal system

«Liver and biliary diseases»

- The **liver**, as an exocrine gland secretes bile, which is essential for normal **lipid digestion**.
- In case of **insufficient bile secretion** or **gallbladder emptying**, **dyspeptic symptoms** develop.
- The most common liver diseases are **cirrhosis** and **hepatitis**.
- **Hepatitis**, which is characterized by the **inflammation of the liver** and consequent **functional lesion**, is usually caused by toxins (e.g. alcohol, medicine abuse) or viruses (hepatitis A, B and C).
- **Cirrhosis** is a chronic state characterized by the **fibrosis and necrosis of the liver**.

Gastrointestinal system

«*Liver and biliary diseases*»

- The therapy of liver diseases aims at the **protection** of liver cells.
- There are **no herbal remedies to eliminate the virus** and it is not possible to achieve complete remission in case of **chronic liver diseases**.
- The **improvement of liver functions** and **life expectancies** and the **support of life quality** may be viable goals of the treatment.

Gastrointestinal system

«Liver and biliary diseases»

- **Cholagog** plants improve the flow of the bile into the intestinal system.
- The two large groups of these plants are the **cholekinetics** (which **promote the emptying of the gallbladder**) and the **choleretics** (which **improve the production of bile in the liver**).
- A lack of bile may result in the imperfect digestion of fats and oils, and this may cause subjective symptoms.

Turmeric

«*Curcuma xantho-rrhiza* Roxb. (*C. xanthorrhiza* D. Dietrich)»

Used part: rhizoma

Used type: dried rhizoma

Drog properties: should contain a minimum of 1% of dicinnamoyl methane derivatives, expressed as curcumin.

Turmeric

«Curcuma xantho-rrhiza Roxb. (*C. xanthorrhiza* D. Dietrich)*»*

Chemical composition and mechanism of action:

Curcuminoids.. **«curcumin»**

Essential oil

Turmeric

«*Curcuma xantho-rrhiza* Roxb. (*C. xanthorrhiza* D. Dietrich)»

Chemical composition and mechanism of action:

- Turmeric essential oils **increase bile secretion** in rat.
- The essential oil of *C. xanthorrhiza* proving **slightly more active** than that of *C. longa*.
- The effect of curcumin (in the same dose) **was weaker** than that of the essential oils.
- A **single oral dose of 20 mg of curcumin** stimulated contraction of the human gall-bladder.
- Orally administered turmeric **extracts** **inhibited gastric juice secretion and ulcer formation** comparable to the effects of ranitidine. This effect may be mediated through H2 receptors.

Turmeric

«Curcuma xantho-rrhiza Roxb. (*C. xanthorrhiza* D. Dietrich)*»*

Chemical composition and mechanism of action:

- Various turmeric **extracts** (and also pure curcumin and xantorrhizol) have been shown to have marked **antioxidant, antiphlogistic, hepatoprotective and chemopreventive effects**.
- Curcuminoids inhibit the enzymes.
- **Wound healing activity for locally** applied turmeric has been documented.
- This may be linked to its antiphlogistic and its elastase, **hyaluronidase and collagenase-inhibiting properties**.

Turmeric

«*Curcuma xantho-rrhiza* Roxb. (*C. xanthorrhiza* D. Dietrich)»

Efficacy and indications:

- For *C. xanthorrhiza*, no clinical studies are available.
- *C. longa* has been investigated more thoroughly, the majority of the studies focusing on **its gastrointestinal effect**.
- Curcuma products (typically food supplements) are most widely used in the **treatment of articular pains and cancer**.
- It should be noted that the confirmed **chemopreventive effect of Curcuma extracts** **does not imply efficacy in the treatment of malignant tumors**.

Turmeric

«*Curcuma xantho-rrhiza* Roxb. (*C. xanthorrhiza* D. Dietrich)»

Efficacy and indications:

- In a study with patients with **irritable bowel syndrome**, half of the patients received **72 mg of turmeric (*C. longa*) extract**, and the others the double dose. Relative to the baseline, the intake of turmeric resulted in a **significant reduction in the prevalence of this syndrome**, though the efficacy was similar within the two groups.
- In a randomized, double-blind, placebo-controlled multicenter study patients with **dyspeptic complaints** were treated daily for **7 days with 2 g of turmeric (*C. longa*)**, a herbal combination or placebo. At the end of the study, 87% of the patients in the turmeric group, 83% in the herbal extract mixture group and 53% in the placebo group reported a notable improvement. The **difference between turmeric and placebo was significant and clinically relevant**.

Turmeric

«*Curcuma xantho-rrhiza* Roxb. (*C. xanthorrhiza* D. Dietrich)»

Efficacy and indications:

- The effect of turmeric on **peptic ulcers** was examined in an uncontrolled trial in which, after taking **600 mg of turmeric/day for 12 weeks, 19 of the 25 patients had no ulcers**.
- **Curcumae xanthorrhizae rhizoma** is considered plausible with the indication
  - **symptomatic treatment of digestive disturbances, such as a feeling of fullness, slow digestion and flatulence.**
- As a herbal tea, the single dose is 1 g of comminuted herbal substance in 100 ml of boiling water (3 times daily). The following dry extracts are also in use: DER 20-50:1, extraction solvent ethanol (daily dose 24-39 mg), and DER 9-12:1, extraction solvent acetone (daily dose 100-200 mg).

Turmeric

«*Curcuma xantho-rrhiza* Roxb. (*C. xanthorrhiza* D. Dietrich)»

Efficacy and indications:

- **Curcumae longae rhizoma**, a traditional use monograph has been prepared with the indication of
  - **increasing the bile flow for the relief of symptoms of indigestion (such as a sensation of fullness, flatulence, and slow digestion).**
- For this purpose, the daily dose of the herbal substance (either as powdered rhizome or as tea) is 1.5-3 g. Tinctures may be used in a dose of 1.5-3 ml (1:10) or 10 ml (1:5) daily. The daily doses of the different dry extracts range from 80 to 400 mg.

Turmeric

«*Curcuma xantho-rrhiza* Roxb. (*C. xanthorrhiza* D. Dietrich)»

Side-effects, interactions & contraindications

- **Curcumin and turmerone inhibit arachidonic acid-induced platelet aggregation** with IC50 values similar to that of acetylsalicylic acid.
- Curcumin is a **potent inhibitor of certain cytochrome P450 enzymes**, and in therapeutic doses the development of interactions is not probable.
- *C. xanthorrhiza* is **not recommended in cases of obstruction of the bile duct, cholangitis, liver disease, gallstones and any other biliary diseases**.
- Mild gastrointestinal symptoms such as dry mouth, flatulence and gastric irritation may occur.
- The safety of its therapeutic application during pregnancy and lactation has not been established.

Artichoke

«*Cynara scolymus*»

Used part: leaves and buds

Used type: dried leaves and extracts

Drog properties: dried basal leaves of *Cynara scolymus* containing a minimum of 0.8% chlorogenic acid.

Artichoke

«*Cynara scolymus*»

Chemical composition and mechanism of action:

Phenolic acids.. «cynarin, chlorogenic acid and caffeic acid»

Sesquiterpene lactones.. «cynaropicrin»

Artichoke

«*Cynara scolymus*»

Chemical composition and mechanism of action:

- Artichoke **leaf extracts** **inhibited the biosynthesis of cholesterol** in rat hepatocytes (Luteolin and **cynaroside**).
- In vitro, artichoke **increased the secretion of biliary substances** in cultured hepatocytes and in the isolated liver, different extracts dose-dependently enhanced the bile flow.
- The choleretic activity is linked to **mono- and dicaffeoylquinic acids**.
- A dose-dependent **increase in bile flow** was registered following a **single intravenous administration of cynarin.**

Artichoke

«*Cynara scolymus*»

Chemical composition and mechanism of action:

- **Chlorogenic acid** administered orally to rats had a significant **choleretic effect and also stimulated peristalsis**.
- An extract of the plant exerted **spasmolytic activity on isolated smooth muscles**.
- Artichoke has **strong antioxidant, cytoprotective and hepatoprotective activities**.

Artichoke

«*Cynara scolymus*»

Efficacy and indications:

- In one clinical trial on 20 male volunteers with acute or chronic metabolic disorders, the **choleretic effect of a single dose of an artichoke product was investigated**. The bile secretion was 127% higher at 30 minutes after administration, 150% after 60 minutes (the maximum effect) and 94% after 90 minutes (compared to the placebo group).
- 960-1920 mg of artichoke extract daily resulted in a significant **decrease of the digestive complaints within 6 weeks of treatment**.
- In a double-blind, randomized placebo-controlled trial with patients with **functional dyspepsia**, the overall symptom improvement **over the 6 weeks of treatment was significantly greater with artichoke leaf extract** than with the placebo.

Artichoke

«*Cynara scolymus*»

Efficacy and indications:

- In a randomized double-blind, placebo-controlled study, over 12 weeks, the **triglyceride level significant reduced**.
- European Medicines Agency granted a traditional use monograph for artichoke with the indication of the
  - **symptomatic relief of digestive disorders such as dyspepsia with a sensation of fullness, bloating and flatulence.**
- The posology is 6 g of the comminuted herbal substance as a herbal infusion daily or 600-2400 mg of dry or soft extract daily.

Artichoke

«*Cynara scolymus*»

Side-effects, interactions & contraindications:

- The use of the plant is contraindicated in cases of **hypersensitivity** to artichoke or to plants of the Asteraceae family, obstruction of the **bile ducts, cholangitis, gallstones and any other biliary diseases or hepatitis**.
- As **adverse effects**, **slight diarrhea with abdominal spasms, epigastric complaints such as nausea, and heartburn** have been reported.

Dandelion

«*Taraxacum officinale*»

Used part: leaves, herba, radix

Used type: dried leaves, herba and radix

Drog properties: -

Dandelion

«*Taraxacum officinale*»

Chemical composition and mechanism of action:

Roots

«inulin»

Sesquiterpenes.. «eudesmanolides and guaianolides»

Sterols.. «taraxasterol and its derivatives»

Leaves

phenolic acids and flavonoids

Dandelion

«*Taraxacum officinale*»

Chemical composition and mechanism of action:

- The efficacy of **aqueous extracts** obtained from dandelion **leaves** was **more pronounced** than that of those from **the root extracts**.
  - **Its saluretic effect may be due to the high potassium salt content of the plant.**
- The **choleretic effect** of the **leaves** has been confirmed in different animal species.
- The extracts **of leaves and roots** proved to possess **anti-inflammatory activity**.
- The **extract** of the plant **inhibited ADP-induced human platelet aggregation** in vitro.
- The **extracts** of the plant exerted a **glucose level-lowering effect**. This may be a result of the **inulin content and the moderate alpha-amylase and alpha-glucosidase-inhibitory activities**.

Dandelion

«*Taraxacum officinale*»

Efficacy and indications:

- European Medicines Agency published a monograph for traditional herbal medicinal products
  - for the **relief of symptoms related to mild digestive disorders (such as a feeling of abdominal fullness, flatulence, and slow digestion) and a temporary loss of appetite**, and
  - to **increase the amount of urine so as to achieve flushing of the urinary tract as an adjuvant in minor urinary complaints.**

Dandelion

«*Taraxacum officinale*»

Efficacy and indications:

- With this indication, the comminuted **dried root with herb** should be used, **3-4 g as a decoction or 4-10 g as an infusion**, up to 3 times daily.
- For the **leaves**, the European Medicines Agency considered only the use as a **diuretic acceptable**. The daily dose of the leaves is **4-10 g as an infusion**, 3 times daily.
- The **expressed juice from the fresh leaves** can be used in a dose of **10-20 ml daily**.

Dandelion

«*Taraxacum officinale*»

Side effects, interactions & contraindications:

- In cases of **bile duct obstructions, cholangitis, liver diseases, gallstones, active peptic ulcer and any other biliary disease, or hypersensitivity** to the plant or other species of the Asteraceae family, its use is **contraindicated**.
- Its use in patients with **renal failure or heart failure** should be avoided because of the possible risks due to **hyperkalemia**.
- Its use in children under 12 years of age and during pregnancy and lactation has not been established due to lack of adequate data.
- **Epigastric pain and hyperacidity may occur as adverse effects**.

Milk thistle

«*Silybum marianum*»

Used part: fruit

Used type: dried fruit ad extract

Drog properties: minimal silymarin content of 1.5%, expressed as silibinin

Milk thistle

«*Silybum marianum*»

Chemical composition and mechanism of action:

flavonolignans .. «silibinin and isosilibinin, silicristin and silidianin»

flavonols .. «taxifolin, quercetin and kaempferol»

flavones.. «apigenin and chrysoeriol»

phytosterols

fatty oil.. «linoleic and oleic acid»

Milk thistle

«*Silybum marianum*»

Chemical composition and mechanism of action:

- The **pharmacological effects** of milk thistle are linked to its **flavonolignans**.
- The **hepatoprotective effect** depends in part on the **protein synthesis-increasing action of flavonolignans** in the hepatocytes.
- **Silybin** activates **DNA-dependent RNA polymerase 1**, this enzyme increasing the rate of synthesis of ribosomal RNAs and consequently protein biosynthesis.

Milk thistle

«*Silybum marianum*»

Chemical composition and mechanism of action:

- The **antifibrotic effect of silymarin** may be explained by the **inhibition of the activation of hepatic starry cells** (which transform to myofibroblasts).
- This activity is **related to the inhibition of the NF-κB activation**.
- Silybin prevented the transformation of **fat-storing liver cells** into myofibroblasts.
- Milk thistle extract **prevented the development of hepatic fibrosis, and it decreased collagen accumulation** in different experimental models.

Milk thistle

«*Silybum marianum*»

Chemical composition and mechanism of action:

- **Flavonolignans** possess strong **antioxidant activity** and exert **scavenging activity** against different radicals.
- **Silymarin** administration led to a higher total glutathione content and **improved the redox state of the liver**.
- The **effects of several hepatotoxins are neutralized** by the marked antioxidant action of **flavonolignans**.
- Milk thistle **extract attenuated the liver injury caused by alcohol** in animal experiments (as reflected in the liver enzyme activities).

Milk thistle

«*Silybum marianum*»

Chemical composition and mechanism of action:

- The efficacy in **viral hepatitis** may be due to the inhibition of the RNA-polymerase-dependent hepatitis C viruses.
- **Silymarin inhibits the entrance of the virus into the host cell**, probably as a result of its effects on the cell membrane.
- **The antitoxic effects of flavonolignans** are due to their influence on (hepatocyte) cell membranes.
- **Silybinin changes membrane permeability**, which prevents the uptake of mushroom (*Amanita phalloides*) toxins into liver cells.

Milk thistle

«*Silybum marianum*»

Efficacy and indications:

- The **efficacy of silymarin** has been studied in a number of trials.
- Many of these involved several hundreds of patients with alcoholic liver disease. **Most of them showed improvements in clinical symptoms**, but with **no changes in the laboratory parameters**.
- Several studies have been conducted on patients with **viral hepatitis** (acute or chronic, hepatitis A, B or C). In earlier studies, **a positive tendency was found in the biochemical parameters**, but an antiviral effect was not observed.

Milk thistle

«*Silybum marianum*»

Efficacy and indications:

- The majority of the well-designed trials were carried out with a **dry extract** (DER 36-44:1, extraction solvent: ethyl acetate, standardized to contain 40-65% of silymarin). For this extract, a well-established indication was accepted as follows:
  - **supportive treatment of alcoholic liver disease.**

- The dose is 173-186.7 mg of extract standardized to a content of 108.2 mg of silymarin, calculated as silibinin, 3 times daily. The average duration of use is 2 months.

Milk thistle

«*Silybum marianum*»

Efficacy and indications:

- For **other extracts and preparations**, clinical efficacy has not been confirmed conclusively, and they can therefore be applied as traditional herbal medicinal products
  - **for the symptomatic relief of digestive disorders with a sensation of fullness, bloating and flatulence.**

- For this purpose, the tea prepared from the fruits (6-15 g daily), the dry plant material (up to 1800 mg daily) or its different dry or liquid extracts prepared with ethyl acetate, ethanol or acetone may be used.

Milk thistle

«*Silybum marianum*»

Side effects, interactions & contraindications:

- **The only contraindication is hypersensitivity to this or other plants of the Asteraceae family.**
- Its **use is not recommended in children and adolescents below 18 years of age, or for pregnant or lactating women**, due to the lack of data on safety and efficacy.
- **Mild gastrointestinal symptoms such as dry mouth, nausea, gastric irritation and diarrhea, headache and allergic reactions (urticaria, skin rash, pruritus, anaphylaxis, asthma) may occur**.

Gastrointestinal system

«*Loss of appetite*»

- may be a result of different diseases (ranging from simple gastrointestinal disorders to infections and tumors) or
- the side-effect of certain medications (e.g. antibiotics or chemotherapeutics).
- very frequently related to stress or a symptom of a psychic disease (anorexia nervosa).
- **Appetite is directly linked to the sensation of the taste of the meal**.
- **Decreased taste reflexes (which is common in the elderly) may lead to a loss of appetite.**

Gastrointestinal system

«*Loss of appetite*»

- A lack of digestive enzymes may also lead to a lack of appetite.
- The appetite may be improved through the stimulation of taste sensors and the improvement of digestion.
- The most traditional herbal remedies for the treatment of a lack of appetite are based on bitter plants.
- The sensation of the bitter taste in the mouth stimulates (within 30 minutes) salivary, gastric and biliary secretion, at least in conditions where the reflex secretion of gastric juice is inhibited in the cephalic phase.

Gastrointestinal system

«*Loss of appetite*»

- Overdosed bitters reduce gastric secretions, presumably through their direct effect on the gastric mucosa.
- Some bitter plants may induce headache in susceptible patients.
- In high doses, bitter herbs cause nausea and vomiting.
- As a consequence of their stimulant effect on gastric acid secretion, bitters are contraindicated for those suffering from gastric or duodenal ulcer.

Fenugreek

«*Trigonella foenum-graecum*»

Used part: seed

Used type: dried seed

Drog properties:

chracteristic odour

Fenugreek

«*Trigonella foenum-graecum*»

Chemical composition and mechanism of action:

galactomannan-type polysaccharides

saponins

protoalkaloids (trigonelline)

sterols

flavonoids

Fenugreek

«*Trigonella foenum-graecum*»

Chemical composition and mechanism of action:

- The majority of the preclinical trials **focused on the blood glucose-lowering effect** of fenugreek seeds.
- Fenugreek seeds and water and ethanol extracts exerted a **hypoglycemic effect** in normal and in diabetic rats and other animal species.
- It is supposed that **fenugreek polysaccharides decrease the intestinal glucose absorption**.

Fenugreek

«*Trigonella foenum-graecum*»

Chemical composition and mechanism of action:

- Some studies indicated the **potential stimulation of pancreatic insulin secretion**.
- **Inhibition of intestinal glycosidases may also play a role**.
- More recent studies concluded that **fenugreek increases the translocation of glucose transporter GLUT4 to the cell surface**.

Fenugreek

«*Trigonella foenum-graecum*»

Chemical composition and mechanism of action:

- The **hypolipidemic effect** of fenugreek has also been thoroughly investigated.
- In animals with normal lipid levels, the contents of **total cholesterol, VLDL and LDL were decreased**.
- The impact on HDL levels is contradictory. This activity may be related to the polysaccharides and saponins of the seeds.

Fenugreek

«*Trigonella foenum-graecum*»

Efficacy and indications:

- In contrast with the huge amount of preclinical data, the body of evidence from **clinical trials is insufficient**.
- In one 6-week trial, the effects of a fenugreek seed extract on the eating behavior of overweight subjects were studied. **The fasting serum insulin and plasma glucose levels decreased** significantly.
- In a clinical trial study, **type 2 diabetic patients** were given 10 g/day fenugreek seeds for 8 weeks. **The triglyceride and VLDL levels decreased** significantly in the treated group.

Fenugreek

«*Trigonella foenum-graecum*»

Efficacy and indications:

- European Medicines Agency has published a monograph classifying it as traditional herbal medicinal product with the indications of a
  - **temporary loss of appetite and for the symptomatic treatment of minor inflammations of the skin.**
- Internally, it can be used as a tea (**1 to 6 g daily in divided doses**) or as dry (water-ethanol) extracts. Externally, the infusion prepared from **50 g/250 ml** of water should be used in a cataplasm.

Fenugreek

«*Trigonella foenum-graecum*»

Side effects, interactions & contraindications:

- **Its use in children and adolescents under 18 years of age and during pregnancy and lactation has not been established due to the lack of adequate data.**
- On oral use, close of glycemic control monitoring should be considered in patients with **diabetes mellitus** due to the possible hypoglycemic effect of fenugreek.
- **Gastrointestinal disorders (flatulence and diarrhea) and dizziness may also occur.**
- In cases of cutaneous use, allergic reactions have been reported (facial angioedema and wheezing).