



MINISTERSTVO ŠKOLSTVÍ,
MLÁDEŽE A TĚLOVÝCHOVY



OP Vzdělávání
pro konkurenceschopnost

INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ

PHYTOPHARMACEUTICALS

academic year 2018/19

LECTURE 8 – Preparations used to treat some disorders of digestive system - II

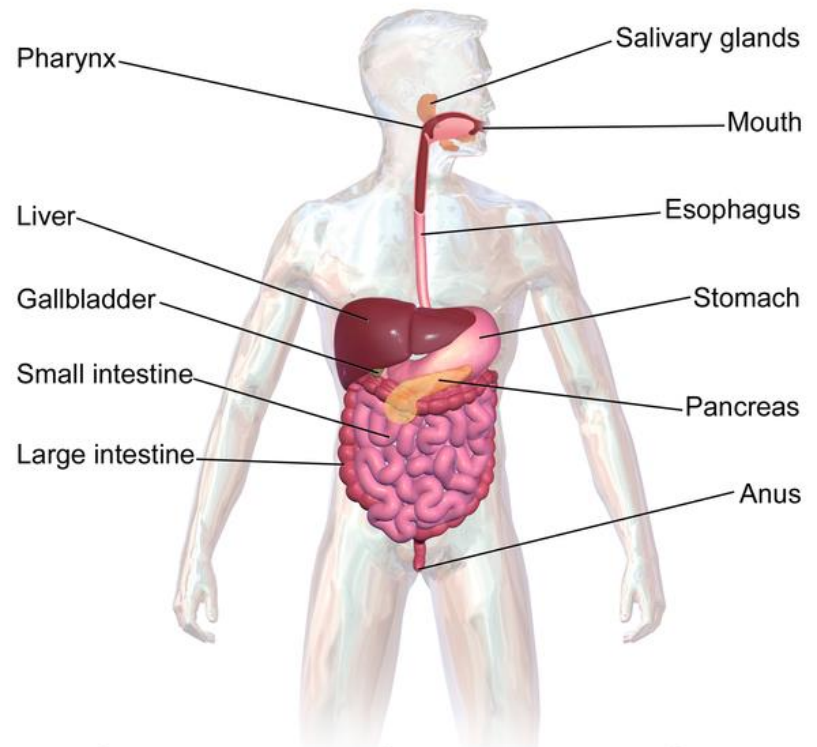
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PHYTOPHARMACEUTICALS

vs. Digestive system (GIT = Gastrointestinal tract)

Major disorders of GIT that can be treated by phytomedicines:

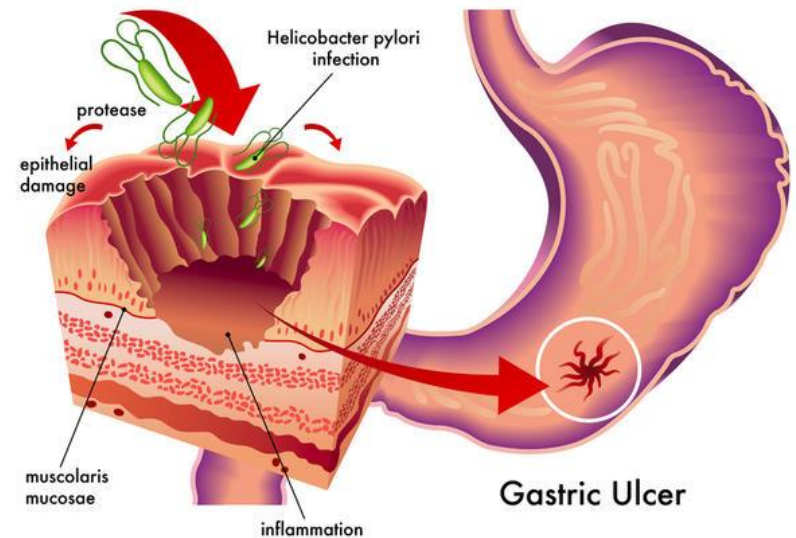
- ▶ digestive disorders
- ▶ damaged mucosa of GIT
 - ▶ ulceration
 - ▶ inflammation (pharyngitis, gastroenteritis)
- ▶ diarrhea/constipation
- ▶ vomiting
- ▶ infection, intoxication



The Components of the Digestive System

Treatment of PEPTIC ULCERS

- ▶ in the area of a gastric and duodenal peptic ulcer, the mucosa has been attacked by digestive juices = „self-digestion“
- ▶ usually the acid concentration is too high, or the protective effect of mucus on the mucosal surface is decreased
- ▶ other cause is *Helicobacter pylori* infection
- ▶ Therapeutic aims:
 - ▶ relief of pain and acceleration of healing to lessen the risk of dangerous complications
- ▶ Two therapeutic approaches:
 - ▶ reduction of H⁺ concentration
 - ▶ mucosal protection



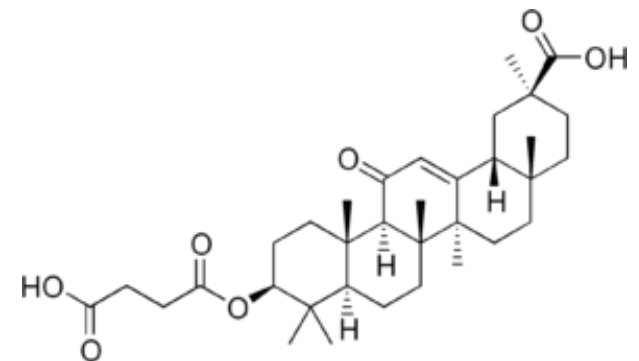
Treatment of PEPTIC ULCERS

- ▶ I. Drugs for lowering acid concentration
 - ▶ Ia – **Acid neutralization** = antacid drugs – containing H⁺ binding groups
 - ▶ sodium bicarbonate, calcium carbonate, magnesium hydroxide, aluminium hydroxide
 - ▶ nonabsorbable antacids are preferred
 - ▶ Ib – **Inhibition of acid production** – acting on their respective receptors
- ▶ II. Protective drugs
 - ▶ promotes the mucus production → coating of mucosal defects
 - ▶ sucralfate, misoprostol, colloidal bismuth compounds
 - ▶ carbenoxolone
 - ▶ **mucilaginous plant drugs**

Treatment of PEPTIC ULCERS

▶ CARBENOXOLONE

- ▶ is a derivative of glycyrrhethinic acid (Liquiritiae radix, *Glycyrrhiza glabra*, Fabaceae – liquorice)
- ▶ stimulates mucus production
- ▶ it is practically obsolete in this indication
- ▶ it has also aldosterone-like effect that promotes renal reabsorption of NaCl and water, therefore, exacerbate hypertension, congestive heart failure, or swellings (oedemas)



Treatment of PEPTIC ULCERS

- ▶ Plant drugs containing **mucilage**, e.g.:
 - ▶ Althaeae radix/ folium – *Althaea officinalis*, Malvaceae, marshmallow
 - ▶ Malvae folium/ flos – *Malva sylvestris*, Malvaceae, common mallow
 - ▶ Farfarae folium flos– *Tussilago farfara*, Asteraceae, coltsfoot
 - ▶ Plantaginis folium – *Plantago lanceolata*, Plantaginaceae, plantain
 - ▶ etc.

Treatment of PEPTIC ULCERS



Althaea officinalis
leaf/root



Malva sylvestris
leaf/flower



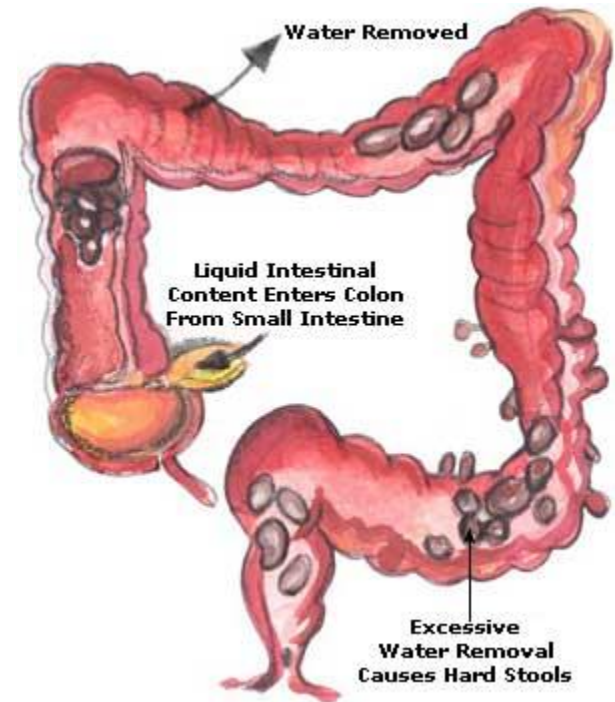
Plantago lanceolata
leaf/seed coat



Tussilago farfara
leaf/flower

LAXATIVES

- ▶ = drugs that relieve **constipation**, a symptom that refers to irregularly passing stools due to decreased bowel function or diet that doesn't include enough fluids and fiber
- ▶ Laxatives can increase bowel movements, promote bowel evacuation by acting locally to
 - ▶ stimulate intestinal peristalsis
 - ▶ to soften bowel content
 - ▶ or both



LAXATIVES

- ▶ **Classification of laxatives:**
 - ▶ **Bulk laxatives** – distention of the intestinal wall by bowel contents (increased filling of the bowel) stimulates propulsive movements of the gut musculature (peristalsis)
 - ▶ **Irritant laxatives** – purgatives, cathartics – exert an irritant action on the enteric mucosa. Consequently, less fluid is absorbed than is secreted – increased filling of the bowel promotes peristalsis. Excitation of sensory nerve endings elicits enteral hyper motility.
 - ▶ **Lubricant laxatives** – no absorbable liquids (e.g. glycerol) make faeces softer and more easily passed

LAXATIVES

BULK LAXATIVES

- ▶ **vegetable fibers** – rich in cellulose (component of plant cell walls) = indigestible polysaccharide that is resistant to digestive enzymes
 - ▶ e.g. bran = cereals pericarp
- ▶ **hydrophilic colloids, bulk gels** – insoluble and nonabsorbable carbohydrate substances (polysaccharides) that expand on taking up water in the bowel
 - ▶ **mucilage drugs**
- ▶ **osmotically active laxatives** – soluble but nonabsorbable particles that retain water in the bowel due to their osmotic activity
 - ▶ salts (e.g. Glauber's salt – *sodium sulphate*), polyhydric alcohols (*mannitol, sorbitol*), disaccharide *lactulose*

LAXATIVES

IRRITANT LAXATIVES (PURGATIVES, CATHARTICS)

- ▶ these laxatives are distinguished according to the site of irritation
- ▶ the small bowel irritant
 - ▶ ricinoleic acid – in Castor oil
- ▶ the large bowel irritant
 - ▶ anthraquinone derivatives
 - ▶ synthetic drugs
 - diphenolmethane derivatives

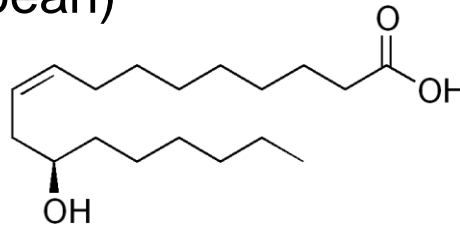


LAXATIVES

▶ RICINI OLEUM = Castor oil

– the oil obtained from the first cold-pressing of the seed of *Ricinus communis*, Euphorbiaceae (castor bean)

- ▶ **ricinoleic acid**
– major component



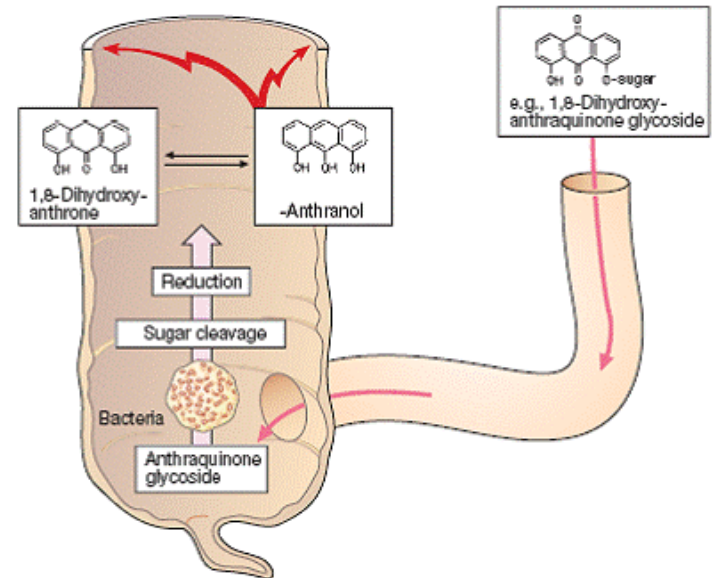
- ▶ oral administration of 10-30 mL of castor oil is followed within 0.5 to 3 hours by discharge of water stool
- ▶ **very strong, massive effect !** – castor oil is hardly suitable to treat ordinary constipation
- ▶ it can be employed after oral ingestion of a toxin in order to hasten elimination and to reduce absorption of the toxin from the gut



LAXATIVES

▶ ANTHRAQUINONE DERIVATIVES

- ▶ compounds derived from anthracene and have a variable degree of oxidation, in plants usually present as glycosides
- ▶ in the colon, they are hydrolyzed by the β -glucosidases of the intestinal flora, and the free anthraquinones are reduced into active form = **anthrones**
- ▶ anthrones increase the secretion of electrolytes and water and affect intestinal motility
- ▶ the latency between drug intake and laxative effect is 6 to 12 hours.
- ▶ daily dose is max. 30 mg of hydroxyanthracene derivatives



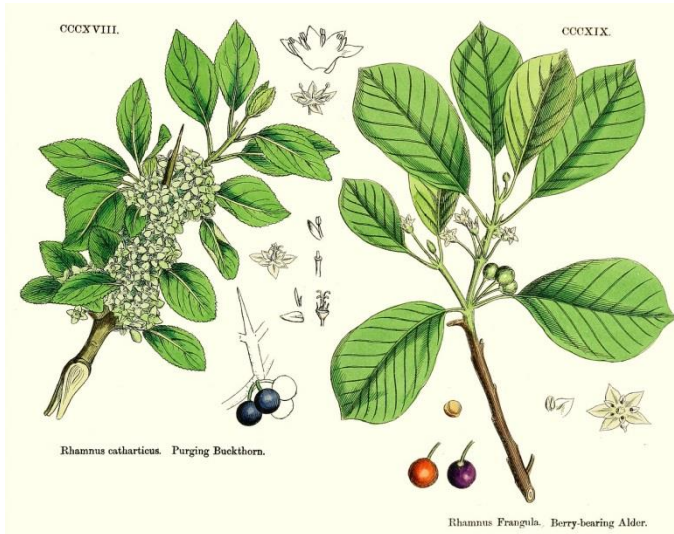
Large-bowel irritant laxatives: anthraquinone derivatives

LAXATIVE HERBAL DRUGS

Plant drugs containing **anthraquinone derivatives**, e.g.:

- ▶ **Frangulae cortex** – *Rhamnus frangula* (*Frangula alnus*), Rhamnaceae, frangula
- ▶ **Rhamni purshianae cortex** – *Rhamnus purshianus* (*Frangula purshiana*), Rhamnaceae, Cascara sagrada
- ▶ **Rhamni cathartici fructus** – *Rhamnus catharticus*, Rhamnaceae, purging buckthorn
- ▶ **Rhei radix** – *Rheum officinale* and/or *R. palmatum* Polygonaceae, rhubarb
- ▶ **Sennae folium/fructus** – *Cassia senna* (*C. acutifolia*) and/or *C. angustifolia*, Fabaceae, Alexandrian or Tinnevely senna
- ▶ **Aloe** – *Aloe barbadensis*, *A. capensis*, Xanthorrhoeaceae, aloe

LAXATIVE HERBAL DRUGS



Rhamnus catharticus
fruit



Rhamnus frangula, R. purshiana
bark



Cassia senna, C. angustifolia
leaves/fruits



Rheum officinale Bail.
Image processed by Thomas Schoepke
www.plant-pictures.de



Rheum officinale
Rheum palmatum
root/rhizome



Aloe barbadensis
Aloe capensis
leaves – juice

LAXATIVES

- ▶ **Contraindication of purgatives, irritant laxatives:**
 - ▶ intestinal congestion, sudden abdominal episodes, inflammatory diseases of the colon, abdominal complaints of unclear origin
 - ▶ children up to 10 years of age
 - ▶ pregnant and nursing women



Warning:

- ▶ persons with heart and kidney illnesses, accompanied by swellings, should be careful
- ▶ chronic usage can lead to dependence (habit-forming syndrome) which can cause fluid and electrolyte imbalance



LAXATIVE HERBAL DRUGS

Plant drugs containing **mucilage** and **gums**, e.g.:

- ▶ **Lini semen** – *Linum usitatissimum*, Linaceae, flax
- ▶ **Psyllii semen** – *Plantago afra* (*Plantago psyllium*), *Plantago indica* (*P. arenaria*), Plantaginaceae
- ▶ **Plantaginis ovatae semen** – *Plantago ovata* (*P. ispaghula*), Plantaginaceae, blond plantain, Indian plantago
- ▶ **Agar** – obtained from red algae – *Gelidium*, Rhodophyta
- ▶ a vegetable **gums** produced mostly as an exudate of various plants:
 - Gummi arabicum, Acaciae gummi – *Acacia senegal*, Fabaceae
 - Tragacantha, gum tragacanth – *Astragalus gummifer*, Fabaceae
 - Guma guar – from the seeds of *Cyamopsis tetragonoloba*, Fabaceae
 - Karaya gummi – trees of the genus *Sterculia*, Malvaceae

LAXATIVE HERBAL DRUGS



Linum usitatissimum
seed



Gelidium
„agar“



Psyllium afra (*Plantago psyllium*)
seed (seed coat)



Psyllium indica (*P. arenaria*)
seed (seed coat)



Plantago ovata (*P. ispaghula*)
seed (seed coat)

LAXATIVE PREPARATIONS

Herbal teas

▶ LAXATIVE Herbal Tea (Megafyt Pharma)

- ▶ POR SPC 20X1.5GM
- ▶ Sennae folium 750 mg
Menthae pip. herba 300 mg
Foeniculi fructus 150 mg
Liquiritiae radix 150 mg
Millefolii herba 150 mg
in 1 tea bag (1.5 g)
- ▶ SUKL code 0084374
- ▶ ATC: V11

- ▶ laxative preparation, mild antiphlogistic and carminative effects
- ▶ one tea bag (1.5 g) contains 12.5 mg of hydroxyanthracene derivatives, sennosides (maximal daily dose = 30 mg)
- ▶ suitable for adults and children over 12y.



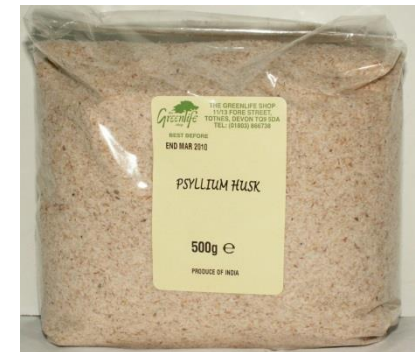
LAXATIVE PREPARATIONS

- ▶ **Bio PSYLLIUM – ISPAGHULA**
(Megafyt Pharma)

- ▶ 150 g
- ▶ *Plantago psyllium*
Plantago ovata
– seed coat (testa)



- ▶ **PSYLLIUM**
– many producers, various packages



LAXATIVE PREPARATIONS

- ▶ **PSYLLIUM cps.**
(Medicol, Dr. Popov, PharmaLine...)



- ▶ **LEPICOL (ASP Czech s.r.o.)**

- ▶ various products – as loose powder or in capsules
- ▶ a multi-fibre source product containing gentle psyllium husk
- ▶ + inulin (fructooligosaccharides from *Cichorium intybus* root)
- ▶ + probiotics (*Lactobacillus* sp., *Bifidobacterium bifidum*)
- ▶ + digestive enzymes
- ▶ suitable also for children



LAXATIVE PREPARATIONS

▶ FRUCTOLAX (ORTIS Laboratoires)

▶ chewing cubes, tablets, syrup

▶ *Ficus carica*

Rheum palmatum/R. officinale

Guma guar (*Cyamopsis tetragonoloba*)

Tamarindus indica pulp

Phoenix dactylifera concentrate

wheat syrup



LAXATIVE PREPARATIONS

▶ LAXAFRUIT (Vaminter S.L.)

- ▶ chewing cubes

- ▶ in 100 g:

paste from *Ficus carica* 62.9 g

syrup from *Agave* 12.6 g

Psyllium Husk (from *Plantago ovata*) 10.5 g

Rheum rhabarbarum (leaf stalks) 4.2 g

Tamarindus indica – legume pulp 3.4 g

plums (*Prunus domestica*) 2.1 g

oat fibre (*Avena sativa*) 2.5 g

Anisi fructus 0.8 g

yoghurt powder 0.5 g

inulin 0.5 g

- ▶ dosage usually 1 cube a day,
wash down with 2 dL of water.

LAXAFRUIT
12 žvýkacích kostek



Čistě přírodní produkt
s obsahem vlákniny
a ovoce, podporující
přirozené vyprazdňování.



DIARRHEA, DIARRHOEA

Causes	Examples
Viral infections	Rotavirus, Norwalk virus
Bacterial infections	<i>E. coli</i> , <i>Vibrio cholerae</i> , <i>Campylobacter</i> , <i>Shigella</i> , <i>Salmonella</i>
Parasites	<i>Giardia</i> , <i>Entamoeba</i>
Helminths (intestinal worms)	Strongyloides
Allergic	Lactose intolerance, celiac sprue, medication side effects
Autoimmune	Ulcerative colitis, Crohn's disease
Malabsorptive	Pancreatic deficiency, biliary disease
Nutritional	Zinc deficiency, vitamin A deficiency, enteral feedings consisting of liquid nutritional formulas delivered straight to the bowels
Functional	Irritable bowel syndrome, short bowel syndrome, cancer



ANTIDIARRHEAL AGENTS

- ▶ Causes of diarrhea – gastroenteritis:
 - ▶ bacteria/viruses – invade the gut wall cause inflammation characterized by increased fluid secretion into the lumen. The enteric musculature reacts with increased peristalsis. Some bacterial toxins (e.g. *Vibrio cholerae*) inhibit ability of mucosal enterocytes to absorb sodium (Na^+) and water, and, at the same time, stimulate mucosal secretory activity
- ▶ The aims of antidiarrheal therapy are:
 - ▶ to prevent dehydration and electrolyte depletion
 - ▶ to prevent excessively high stool frequency



ANTIDIARRHEAL AGENTS

▶ Classification:

- ▶ **adsorbent powders** – nonabsorbable material with a large surface area. These binds different substances including toxins, permitting them to be inactivated and eliminated.
Medicinal charcoal – the recommended effective dose is in the range of 4-8 g. Other absorbents: *kaolin* (hydrated aluminium silicate), *chalk*.
- ▶ **oral rehydration solution** – solution containing salts and glucose
- ▶ **opioids** – inhibition of propulsive peristalsis.
Opium tincture (CNS effects !) → synthetic derivatives with peripheral action
- ▶ **antibacterial drugs**
- ▶ **astringents – tannins** – cause precipitation of mucosa surface proteins, „sealing“ of mucosa



ANTIDIARRHEAL AGENTS

Plant drugs containing **tannins**, e.g.:

- ▶ **Tormentillae rhizoma** – *Potentilla erecta* (*P. tormentilla*), Rosaceae, tormentil
- ▶ **Bistortae rhizoma** – *Polygonum bistorta* (*Bistorta major*), Polygonaceae, common bistort
- ▶ **Quercus cortex** – *Quercus robur*, *Q. petraea*, Fagaceae, oak
- ▶ **Sanguisorbae radix** – *Sanguisorba officinalis*, Rosaceae, great burnet
- ▶ **Agrimoniae herba** – *Agrimonia eupatoria*, Rosaceae, agrimony
- ▶ **Myrtilli fructus/foolium** – *Vaccinium myrtillus*, Ericaceae, bilberry
- ▶ **Fragariae folium** – *Fragaria vesca*, Rosaceae, wild strawberry
- ▶ **Alchemillae herba** – *Alchemilla vulgaris*, Rosaceae, lady's mantle

ANTIDIARRHEAL AGENTS



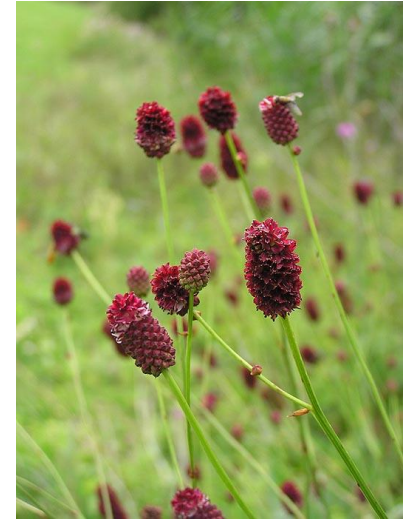
Potentilla tormentilla
rhizome



Bistorta major
rhizome



Quercus robur
Quercus petraea
bark



Sanguisorba officinalis
root

Vaccinium myrtillus
leaf/fruit



Agrimonia eupatoria
herb



Alchemilla vulgaris
herb

ANTIDIARRHEAL AGENTS

Plant drugs containing **tannins**, e.g.:

- ▶ Rubi idaei folium – *Rubus idaeus*, Rosaceae, bramble leaf
- ▶ Rubi fruticosi folium – *Rubus fruticosus*, Rosaceae, raspberry leaf
- ▶ Juglandis folium – *Juglans regia*, Juglandaceae, walnut leaf
- ▶ Hamamelidis folium/cortex – *Hamamelis virginiana*, Hamamelidaceae, witch hazel leaf/bark
- ▶ Salviae officinalis folium – *Salvia officinalis*, Lamiaceae, sage
- ▶ Theae folium – *Thea sinensis*, Theaceae, fermented (black) tea

ANTIDIARRHEAL PREPARATIONS

Herbal teas

▶ **TORMENTAN** (Leros)

▶ POR SPC 20X1.5GM

▶ Myrtilli fructus	480 mg
Tormentillae rhizoma	300 mg
Sanguisorbae radix	300 mg
Matricariae flos	105 mg
Salviae officinalis folium	105 mg
Menthae piperitae herba	105 mg
Liquiritiae radix	105 mg
in 1 tea bag (1.5 g)	

▶ SUKL code: 0043957

▶ ATC: V11

▶ do not allow the tea to boil

▶ drink warm and unsweetened
3 times a day after meals.

- ▶ traditional herbal preparation for diarrhoeal ailments. It has anti-inflammatory properties, soothes flatulence and relieves spasm.
- ▶ suitable for adults and children over 12y.



ANTIDIARRHEAL PREPARATIONS

Preparations containing tannins

▶ TASECTAN

CPS 15x 500 MG or sachets 20x 250 MG
(Pharma Swiss/Ocean Healthcare, Ireland)

- ▶ contains **gelatin tannate**
- ▶ suitable for babies, children and adults as well
- ▶ use every 6 hours until the symptoms disappear. It is usually effective within 12 hours.



ANTIDIARRHEAL PREPARATIONS

Adsorbent powders

- ▶ **CARBO MEDICINALIS**
POR TBL NOB 20X300MG
(Icn Polfa)
 - ▶ SUKL code: 0057338
 - ▶ ATC: A07BA01
 - ▶ dosage:
 - in case of mild disorders:
600-1500 mg (2-5 tbl.) 3-4 times a day
 - in case of serious diarrhoeal ailments – 3000-3600 mg (10-12 tbl.) 3-4 times a day

- ▶ **CARBOSORB**
POR TBL NOB 20X320MG
POR PLV 1X25GM
(Imuna Pharm)
 - ▶ SUKL code: 0031951;
0000982
 - ▶ ATC: A07BA01



ANTIDIARRHEAL PREPARATIONS

Oral solid forms

▶ EUCARBON POR TBL NOB 30 (SEDICO/F. TRENKA, Austria)

- ▶ Sennae folium pulveratum 105 mg
- ▶ Rhei extr. siccum normatum 25 mg
- ▶ Carbo vegetalis 180 mg
(vegetable charcoal)
- ▶ Sulfur depuratum 50 mg
- ▶ Foeniculi etheroleum 0.5 mg
- ▶ Menthae pip. etheroleum 0.5 mg
- ▶ SUKL code: 0049998
- ▶ OTC medicinal product
- ▶ ATC: A06AB56 (Sennosides, combinations)
- ▶ dosage: 1-2 tablets up to 3 times daily

- ▶ Eucarbon® is a mild laxative with prominent regulatory properties to the intestinal functions.
- ▶ charcoal adsorbs metabolic/bacterial toxins
- ▶ the addition of Senna & rhubarb hastens the elimination of the charcoal-toxins complex, reduces intestinal desorption of the drug.
- ▶ The essential oils relieve flatulence

