

# **Plants and the renal system**

# **Plants and the reproductive system**

Ágnes Alberti  
Semmelweis University  
Department of Pharmacognosy

4. December 2019

# Phytotherapy and the diseases of the urinary tract

- **Urinary tract infections:** urethritis, cystitis, pyelonephritis, uretheritis
- **Bladder stones** (causes: urinary retention, long-standing infections)

*Prophylaxis:* adequate water intake

- **Kidney stones / renal lithiasis, nephrolithiasis** (causes: minerals in concentrated urine crystallize and form stones, inadequate water intake, bladder doesn't empty completely)

*Conservative treatment:* adequate water intake, spasmolytic therapy, medicinal plants to flush out your urinary system

*Prophylaxis:* adequate water intake, avoid carbonated and mineral-rich (e.g. bicarbonate-rich) soft drinks and mineral water, treatment of urinary tract infections, reduction of pungent spices

***Recurrent bladder stones/nephrolithiasis:*** role of diet, high content of oxalate in food: sorrel, spinach, beetroot, rhubarb, green bean, cocoa, chocolate, strong coffee, tea, cola, currants, raspberries

## Examples for the treatment of diseases of the urogenital system

- **Urinary tract infections:**

Uvae ursi folium – bearberry leaf,  
*Herniaria glabra* – smooth rupturewort,  
*Armoracia rusticana* – horseradish,

*Tropaeolum majus* – Indian cress,  
Solidaginis virgaureae herba – European  
goldenrod,  
Orthosiphonis folium – Java tea

- **Diuretic therapy (infections + urolithiasis):**

Juniperi pseudo-fructus – juniper berry,  
Solidaginis virgaureae herba – European  
goldenrod,  
Ononidis radix – restharrow root,  
Graminis rhizoma/Agropyri repentis rhizoma –  
couch grass rhizome,

Equiseti herba – horsetail herb,  
Betulae folium – birch leaf,  
Urticae folium – nettle leaf,  
Violae tricoloris herba cum flore – wild  
pansy,  
*Petroselinum crispum* – parsley

- **Benign prostatic hyperplasia (BPH):**

Cucurbitae semen – pumpkin seed,  
Sabalidis serrulatae fructus – saw palmetto  
fruit,

Pruni africanae cortex – Pygeum africanum  
bark,  
Epilobii herba – willow herb,  
Urticae root – nettle root

# Phytotherapy in the treatment of urinary tract infections I.

## UVAE URSI FOLIUM - bearberry leaf

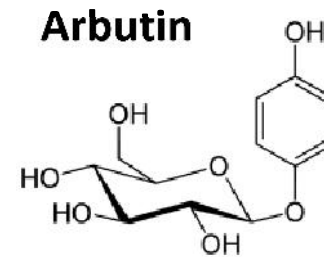
### *Active substances, constituents:*

**arbutin** (Ph.Eur.: min. 7 %)

tannins (10-15%)

### *Application:*

- inflammatory diseases of the urinary tract, in case of mild complaints
- antimicrobial actions: *E. coli*, Gram positive and Gram negative bacteria
- 4 x 3 g / day (400-800 mg hydroquinone)
- tea: pour 150 ml cold water on 3 g chopped herbal drug, steep the tea for several hours (maceration), consume lightly heated (decrease tannin content of the tea)
- potential nephro- / hepatotoxic effect → duration of use < 1 week, max. 5-6 courses/year



## VACCINIUM VITIS-IDAEAE FOLIUM – LINGONBERRY LEAF

*Constituents:* **arbutin**, hydroquinone

### *Application:*

to treat and prevent acute and chronic urinary tract infections





# Phytotherapy in the treatment of urinary tract infections II.

## Vaccinii macrocarponis fructus – American cranberries

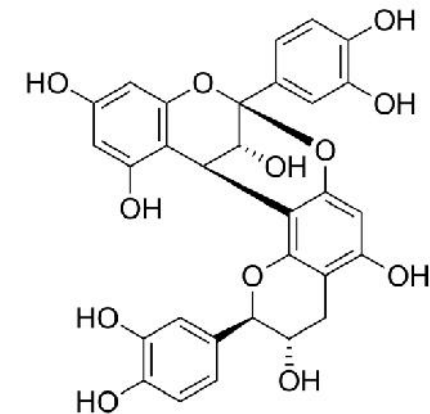
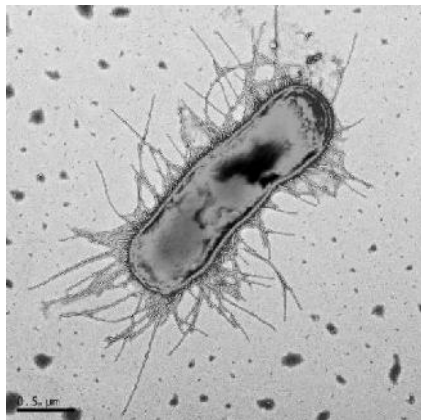
Constituents: **A-type proanthocyanidins, fructose**

**Application:** to prevent frequent/recurrent urinary tract infections (UTIs), for patients more susceptible to infections

Inhibition of bacterial adhesion to the urothelium

type 1 fimbriae: *fructose*

P-fimbriae: *proanthocyanidins*



**Procyanidin A1**

**Cochrane review:** 24 studies, 4473 patients

- cranberry not significantly different to antibiotics for preventing UTIs
- **dropouts/withdrawals** (acceptability of **consuming cranberry juice over long periods**)
- **preparations** need to be **quantified** using **standardised** methods to ensure the appropriate content of the active substances

## Phytotherapy in the treatment of urinary tract infections III.

- **Radish root:** glucosinolates are absorbed from the small intestine, metabolised to mercapturic acid derivatives and excreted with the urine; infections caused by Gram+ and Gram– bacteria, blastomycosis (*Blastomyces*)  
**fresh pressed juice:** 2-3 tablespoons/day
- **Indian cress:** glucosinolates → antibacterial;  
**decoction:** to treat common cold or urinary tract infections
- **Java tea:** causes increased diuresis, elimination of N-containing substances and Na<sup>+</sup>
  - to treat impaired bile production, impaired diuresis, in case of bile or kidney stones
  - to treat urinary tract infections with mild symptoms**tea:** pour 150 ml hot water on 2-3 g chopped herbal drug, steep the tea for 10 minutes, 3-4 times daily

## Phytotherapy in the treatment of urinary tract infections IV.

- **Parsley leaf and root:** essential oil components

**tea:** pour 150 ml boiling water on 1-2 g chopped herbal drug, steep the tea for 10-15 minutes

**apiol** in the essential oil (abortive, neurotoxic)

case study of an overdose: polyneuritis; symmetrical paresis of hands and feet

- **European goldenrod:** **diuretic, smooth muscle relaxant,** analgesic, mild anti-inflammatory action

in inflammatory diseases of the urinary tract

**tea:** pour 150 ml hot water on 3-5 g chopped herbal drug, steep the tea for 10 minutes, 3-4 times daily

- **Smooth rupturewort:** flavonoids, saponins; smooth muscle relaxant; there are not enough data to draw conclusions on the therapeutic efficacy

# Diuretic medicinal plants

- **Juniper berries:** diuretic action; **essential oil** (terpinen-4-ol)

Indications: diuretic treatment of inflammatory diseases of the urinary tract

**tea:** pour 150 ml hot water on 2 g crushed herbal drug, steep the tea for 5 minutes, 3 times a day

**essential oil** renotoxic (in animal studies): excessive doses + inadequate purity of essential oil;

not toxic in human clinical studies, administration of therapeutic doses

**Contraindications:** essential oil in chronic kidney failure, potentially abortive

- **Couch grass rhizome**
- **Restharrow root**
- **Horsetail herb**

## **Betulae folium – Birch leaf (Ph.Eur.)**

**Active substances:** flavonoids, phenolcarboxylic acids

**Effects:** diuretic action

### **Indication:**

- to treat bacterial infections and inflammation of the urinary tract
- to treat kidney stones



## **Ononidis radix – Restharrow root (Ph.Eur.)**

**Active substances:** isoflavonoids, stilbenes

**Effects:** diuretic, antiphlogistic actions

**Application:** to treat inflammation of the urinary tract



## **Bursae-pastoris herba – Shepherd's purse**

**Active substances:** flavonoids

**Effects:** antihypertensive, diuretic



## **Violae tricoloris herba cum flore – Wild pansy (Ph.Eur.)**

**Active substances:** flavonoids, salicylic acid derivatives, mucilage

**Application:**

traditionally as a diuretic agent, diaphoretic in upper airway diseases  
externally: to treat seborrhoea



## **Urticae folium – Nettle leaf (Ph.Eur.)**

**Active substances:** silicic acids, flavonoids, biogenic amines (histamine), potassium and calcium salts

**Effects, application:** rheumatism, gout

diuretic and anabolic actions



## **Equiseti herba – Horsetail herb (Ph.Eur.)**

**Active substances:** silicic acids; potassium salts

**Application:** as a diuretic agent



**Can be mistaken!**

***Equisetum palustre* – marsh horsetail**

## **Galeopsidis herba – Hemp-nettle**

**Active substances:** silicic acids, water soluble silicic acids compounds

**Application:** as a diuretic agent

## **Polygoni avicularis herba – Knotgrass herb (Ph.Eur.)**

**Active substances:** silicic acids

**Application:** diuretic; traditionally to treat bronchitis and asthma

# Bardanae radix – burdock root

**Drug:** fleshy tap-root of greater burdock, lesser burdock and woolly burdock  
Roots collected in the first year provide the drug.



**Constituents:** ca. 45% **inulin**, lignans

## Effects

- Antibacterial action
- Anti-inflammatory action
- Anti-hyperglycaemic action, improves glucose-tolerance
- Inulin has prebiotic action: induces the growth or activity of beneficial microorganisms in the large intestine (*Lactobacillus*, *Bifidobacterium*)

## Traditional application

- in combination or as a monocomponent tea: nephrolyticum, diureticum, 'system-purifier', diaphoreticum
- externally to treat eczema, herpes-zoster, as hair care

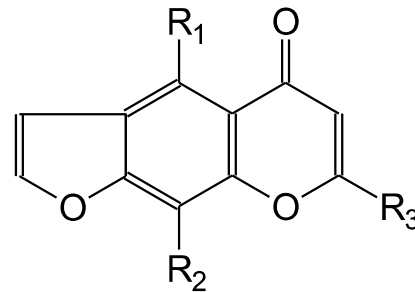


# AMMI VISNAGAE FRUCTUS

## toothpick-plant (khella/Bishop's weed) fruits

### Constituents:

- Essential oil (terpinen-4-ol)
- **Khellin** (furanochromone)



Furano- $\gamma$ -chromones



### Effects:

- diuretic;
- **spasmolytic**; teners spasmolysim of the bronchi, gastrointestinal and *urogenital organs*  
blocks Ca<sup>2+</sup> channels (low doses); in higher doses additional mechanisms

**Undesired effects:** photosensibilisation

# Diuretic tea blendings

## Ph. Helv. VII.

25 g *Betulae folium* (birch leaf)

45 g *Uvae ursi folium* (bearberry leaf)

30 g *Liquiritiae radix* (licorice)

## Kidney and bladder tea

20 g *Betulae folium* (birch leaf)

20 g *Graminis rhizoma* (couch grass rhizome)

20 g *Solidaginis herba* (European goldenrod)

20 g *Ononidis radix* (restharrow root)

20 g *Liquiritiae radix* (licorice)

pour 150 ml boiling water on 2-3 g herbal drug, steep the tea for 15 minutes, 3-4 times a day between meals

to increase the amount of urine in case of the inflammation of the kidney or the bladder, to prevent the formation of kidney stones

# Diuretic herbal tea combinations / Species diureticae EMA-monograph

**Tea combinations**, containing several herbal substances out of the following list (The number of active substances in a herbal tea combination should be limited to a maximum of 4.):

bearberry leaf,

couch grass rhizome,

birch leaf,

horsetail herb,

mate leaf,

juniper berries,

lovage root,

restharrow root,

Java tea,

green bean pods,

common knotgrass,

European goldenrod,

nettle leaf,

**Posology:** pour 150 ml of boiling water on 1.5-2 g of the herbal tea combination, steep the tea for 10 minutes, 3-4 times daily

Combinations containing the following drugs **only for adults or elderly**: juniper berries (Juniperi galbulus), lovage root (Levistici radix), mate leaf (Mate folium), Java tea (Orthosiphonis folium), green bean pods (green bean pods), bearberry leaf (Uvae ursi folium)

# Species diureticae – EMA-monograph

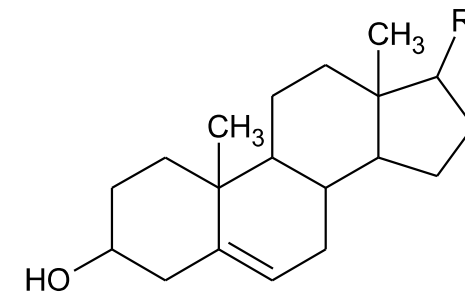
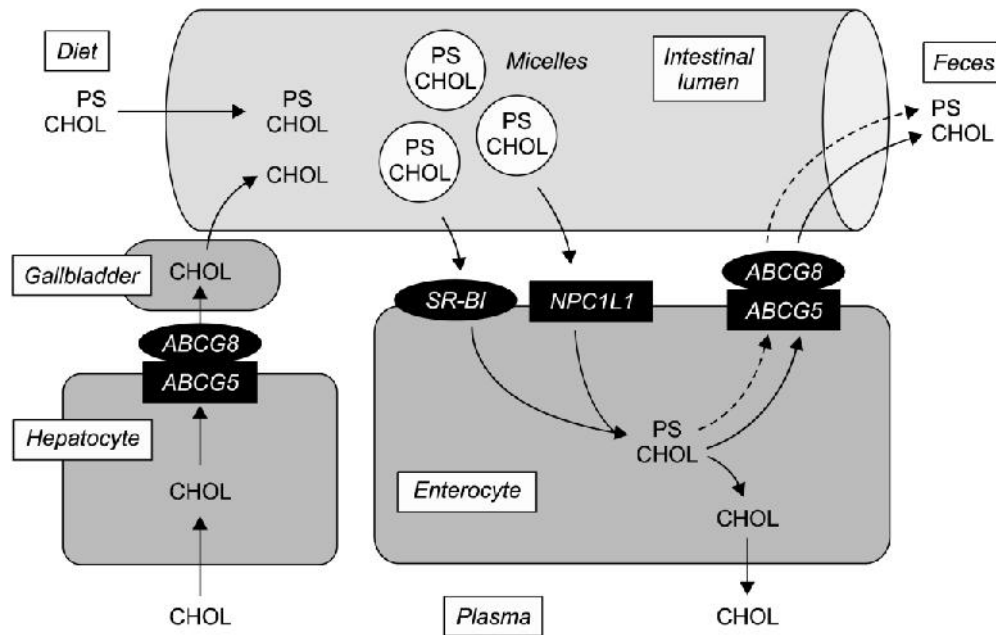
Well-established use								Traditional use							Range in a combination (excl. excipients)
Betulae folium	Equiseti herba	Graminis rhizoma	Juniperi galbulus	Levistici radix	Mate folium	Ononidis radix	Orthosiphonis folium	Phaseoli fructus	Polygoni avicul. herba	Solidaginis virg. herba	Urticae herba / folium	Uvae ursi folium			
Betulae folium	+	+	+	+	+	+	+	+	+	+	+	+	+	10–57%	
Equiseti herba	+		+	+	+	+	+	+		+	+	+	+	10–61%	
Graminis rhizoma	+	+		+			+	+					+	10–25%	
Juniperi galbulus	+	+	+		+		+	+			+			10–50%	
Levistici radix	+	+		+			+							20–33%	
Mate folium	+	+						+	+				+	10%	
Ononidis radix	+	+	+	+	+			+		+		+	+	10–50%	
Orthosiphonis folium	+	+	+	+		+	+		+		+		+	10–50%	
Phaseoli fructus	+	+				+		+					+	10–20%	
Polygoni avicul. herba	+						+					+	+	12%	
Solidaginis virg. herba	+	+		+				+					+	18–29%	
Urticae herba/folium	+	+					+			+			+	11–22%	
Uvae ursi folium	+	+	+			+	+	+	+	+	+	+		20–50%	

A + indicates the evidence of traditional medicinal use of a certain combination.

# Phytosterols

## Biological actions of phytosterols and phytostanols:

**Decrease of plasma cholesterol level**, anti-inflammatory, antibacterial, antifungal actions

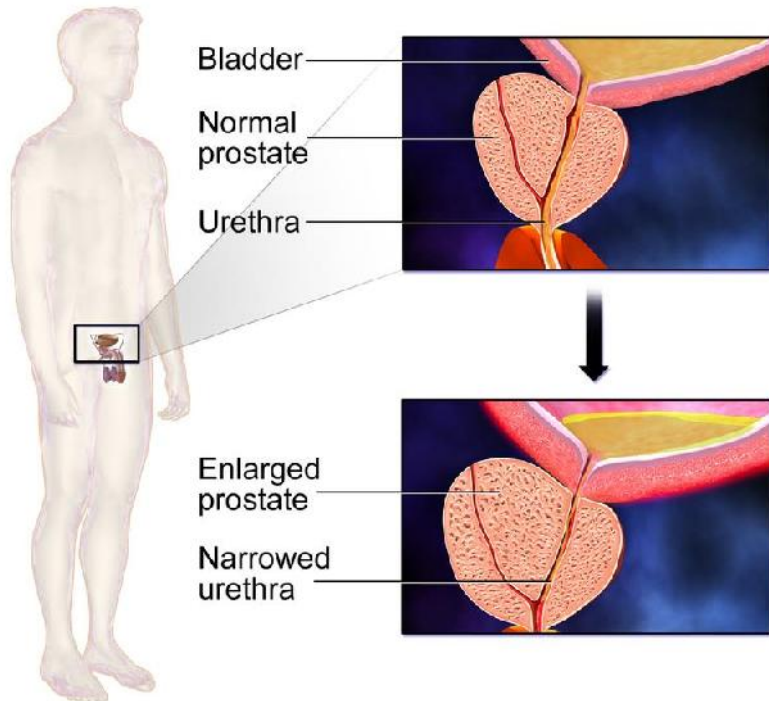


Potential actions on the lipid and lipoprotein metabolism:

**reduction of absorption of cholesterol;**

limited uptake of cholesterol into the liver → increase of endogenic cholesterol synthesis and expression of LDL receptors in the liver

# Herbal medicinal products for the relief of lower urinary tract symptoms related to benign prostatic hyperplasia



## Benign Prostatic Hyperplasia (BPH)

- prostate enlargement, noncancerous increase in size of the prostate gland
- **to alleviate mild symptoms** (need to urinate frequently, waking at night to urinate, urgency, involuntary urination, urinary hesitancy and intermittency, involuntary interruption of voiding, weak urinary stream, a sensation of incomplete emptying, and uncontrollable leaking)

- relief of symptoms, but **no reduction of enlargement**
- no treatment of erectile dysfunction!
- **long-term use** is needed: relief of symptoms in ca. 6 weeks, maximum effect after ca. 3 months

## Pruni africanae cortex / Pygeum africanum bark

- **5 $\alpha$  reductase inhibitor**, regenerates prostatic epithelium
- to relief lower urinary tract symptoms related to BPH; outcome of the clinical trials supports the plausibility in the proposed indication (Cochrane/EMA: 18 studies, 1562 patients)

## Sabalıs serrulatae fructus / Saw palmetto fruit

- anti-inflammatory (COX and 5-LOX inhibitory effect), immuno-modulatory effect (*in vivo*): polysaccharides
- **antigonadotrope action**: lipophilic extracts have **5 $\alpha$  reductase inhibitory action**, **inhibit receptor binding** of testosterone and dihydrotestosterone
- these effects occurred **without influencing the secretion of prostate specific antigen/PSA** (Cochrane/EMA: 32 studies, 5666 patients)

## Cucurbitae semen / Pumpkin seed

- $\Delta_{7-8}$  sterols: **5 $\alpha$  reductase inhibitors**;
- to relief symptoms related to BPH



# Effects and active substances of Saw palmetto fruit and *Pygeum africanum* bark

## Biological actions:

inhibition of activity of BPH specific enzymes, reduction of cell proliferation, anti-inflammatory action

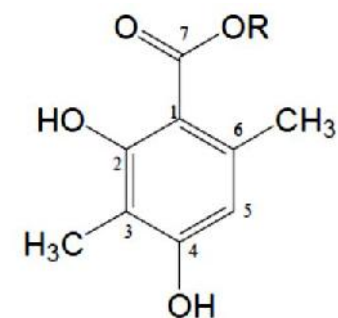
complex mechanisms → multicomponent mixture of active substances

active substances (*Pygeum africanum* bark and *Saw palmetto* fruit)

- sterols
- free and esterified fatty acids

active substances (*Pygeum africanum* bark)

- long-chain aliphatic alcohols
- triterpenes
- atraric acid (antiandrogenic)
- *N*-butyl benzenesulfonamide (antiandrogenic)



**Atraric acid, R = H**

**pumpkin seed** (5-alpha reductase inhibitor, anti-inflammatory)

**nettle root** (5-alpha reductase inhibitor, inhibits SHBG binding, inhibits cell proliferation)

**rye pollen** (anti-inflammatory)



## Nettle root / *Urticae radix* (Ph.Eur.)

**Constituents, active substances:** **phytosterols**; silicic acids, organic aliphatic acids

**Leaf:** potassium salts, silicic acids, flavonoids; in the non-glandular trichomes: acetylcholine, histamine

### **Application:**

root: in the early phase of BPH

leaf: diureticum, as an adjuvant in rheumatic and urinary tract diseases

## Willow herb / *Epilobii herba*

**Constituents, active substances:** **phytosterols**, tannins, flavonoids

**Application:** in BPH



# Herbal medicinal products with Saw palmetto fruit for the relief of BPH symptoms

## Germany

- **Sabalvit® / Sabalvit® uno** soft capsule: 160 mg / 320 mg **Sabalıs serrulatae fructus** extract, extraction solvent: **ethanol 96%** (V/V)
- **Prostagutt® uno** capsule: 320 mg **Sabalıs serrulatae fructus** extract, extraction solvent: **ethanol 90%** (m/m)
- **Eviprostat®-S UNO** soft capsule: 320 mg **Sabalıs serrulatae fructus** extract, extraction solvent: **ethanol 90%** (V/V)

## France

- **Prodinan** gelatine capsule: 160 mg **Sabalıs serrulatae fructus** dry extract, extraction solvent: **CO<sub>2</sub>**
- **Permixon** gelatine capsule: 160 mg **Sabalıs serrulatae fructus** dry extract, extraction solvent: **hexane**

## Italy

- **Serpens** soft capsule: 320 mg **Sabalıs serrulatae fructus**, dry extract, extraction solvent: **hexane**
- **Saba** soft capsule: 320 mg **Sabalıs serrulatae fructus**, dry extract, extraction solvent: **hexane**
- **Rilaprost** soft capsule: 160 mg **Sabalıs serrulatae fructus** purified extract

## Additional herbal medicinal products for the relief of BPH symptoms

### Germany

- **Nomon<sup>®</sup> mono** capsule: 105 mg **Cucurbitae semen** dry extract
- **Prostamed<sup>®</sup> Tab** chewable tablet: 200 mg **Cucurbitae semen powder**, 100 mg **Cucurbitae semen** dry extract, extraction solvent: **water/NaCl/NaHCO<sub>3</sub>** (90.9:6.1:3.0), 6.3 mg **Populi tremulae folium** dry extract, extraction solvent: ethanol 60% (V/V), 2.6 mg **Solidaginis virgaureae herba** dry extract, extraction solvent: ethanol 60% (V/V)

### France

- **PRUNIER D'AFRIQUE ARROW** soft capsule: 50 mg **Pruni africanae cortex** extract
- **Tadenan** soft capsule: 50 mg **Pruni africanae cortex** extract

# Cimicifugae rhizoma – black cohosh rhizome

(Ph.Eur.)

Constituents, active substances: **phytosterols**

Biological actions: ,**oestrogen-like**' effect,

osteoprotective (inhibits osteoclasts)

antiproliferative (*in vitro*, on human breast cancer cell lines)



**Indication:** used for the **relief of menopausal complaints** such as hot flushes and profuse sweating.

continued **use over 2-3 weeks** needed

Cimicifugae rhizoma should not be taken for more than 6 months without medical advice.

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

- **Liver toxicity:** patients with a history of liver disorder should use with caution.
- Patients with **breast cancer** or other **hormone-dependent tumours** should not use without medical advice.
- Preparations with **Hyperici herba: interactions!!!** / photosensitivity

# Agni casti fructus – agnus castus fruit

(Ph.Eur.)

**Constituents, active substances:** **iridoid glycosides, phytosterols,**  
lipophilic flavonoids

**Biological actions:** probable prolactin decreasing effect

**Indication:** used for the treatment of **premenstrual syndrome**

*(not to treat: menstruation disorders: dysmenorrhoea, oligo-menorrhoea, polymenorrhoea, etc.)*

To achieve an optimal treatment effect, continued **use over three months** is recommended.

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

- possible dopaminergic and oestrogenic effects → interactions with dopamine agonists, dopamine antagonists, oestrogens and antioestrogens cannot be excluded
- patients with an **oestrogensensitive cancer** should consult their doctor
- thought to **act on the pituitary-hypothalamic axis** and therefore patients with a history of a pituitary disorder should consult a doctor before use



# Herbal medicinal products with black cohosh rhizome and agnus castus fruit

for the treatment of **premenstrual syndrome**

## Germany

- **Agnolyt® MADAUS** tincture: 90 mg **Agni casti fructus** tincture, extraction solvent: **ethanol 68%** (V/V)
- **Gynocastus®** solution: **Agni casti fructus** extract, extraction solvent: **ethanol 60%** (V/V)
- **Agnucaston®** film-coated tablet: 4 mg **Agni casti fructus** dry extract, extraction solvent: **ethanol 70%** (V/V)

for the **relief of menopausal complaints**

## Germany

- **Remifemin® Plus** film-coated tablet: 58-85 mg **Hyperici herba** dry extract (equivalent to 0.25 mg Hypericin), 2.5-5 mg **Cimicifugae rhizoma** extract (equivalent to 1 mg 27-desoxyactein), extraction solvent: **ethanol 60%** (V/V)

## Italy

- **Mensifem** film-coated tablet: 2.8 mg **Cimicifugae rhizoma** dry extract, extraction solvent: **ethanol 58%** (v/v)

# Medicinal plants frequently used in folk medicine

## EFFICACY SCIENTIFICALLY NOT PROVEN

*to treat menstruation disorders, irregular cycles, menopause:*

agnus castus fruit (*Agni casti fructus*),  
yarrow (*Millefolii herba*),  
common lady's mantle (*Alchemillae herba*),  
shepherd's purse (*Bursae pastoris herba*),  
juniper (*Juniperi pseudo-fructus*),  
raspberry (*Rubi idaei folium*),

basil / *Ocimum basilicum* (estragol!),  
fennel (*Foeniculi fructus*),  
evening-primrose oil (*Oleum oenotherae*),  
mistletoe (*Visci stipes*)  
dong quai / *Angelica sinensis* (furanocoumarins!)

- *to treat low progesterone level:* agnus castus fruit, dong quai, common lady's mantle
- *to reduce prolactin level:* common lady's mantle
- *to regulate irregular cycles, imbalanced hormone metabolism:* yarrow, shepherd's purse, evening-primrose oil
- *to treat menorrhagia (heavy menstrual bleeding):* yarrow
- *to treat menstrual pain and uterine pain:* common lady's mantle
- *to strengthen the uterine wall:* mistletoe
- *to prevent abortion AND facilitate labour:* raspberry