



INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ

PHYTOPHARMACEUTICALS

academic year 2018/19

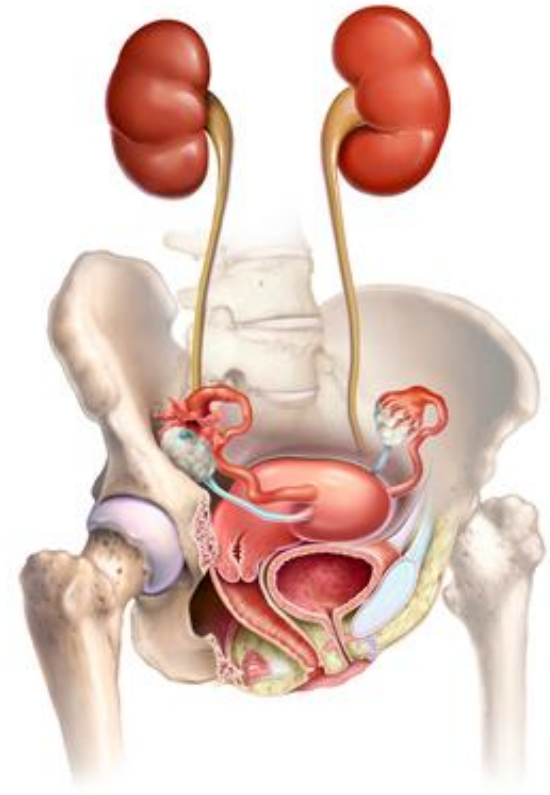
LECTURE 11 – Preparations used to treat some gynaecological disorders

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PHYTOPHARMACEUTICALS vs. Genitourinary system

Genitourinary or urogenital system:

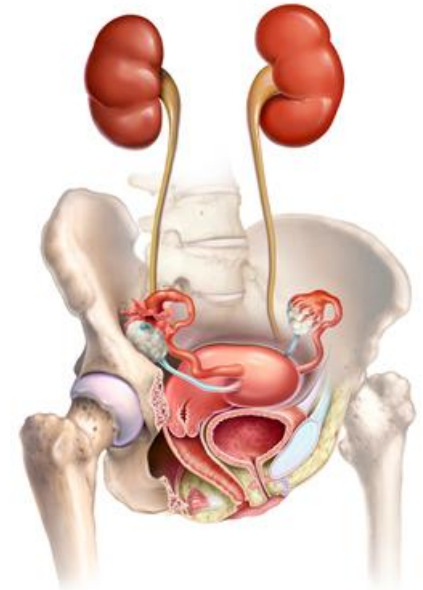
- ▶ the organ systems concerned with reproduction and urinary excretion.
- ▶ These systems are usually grouped together because of their proximity to each other. Although their functions are unrelated, the structures involved in excretion and reproduction are morphologically associated and often use common ducts.



PHYTOPHARMACEUTICALS

used to treat GYNAECOLOGICAL DISORDERS

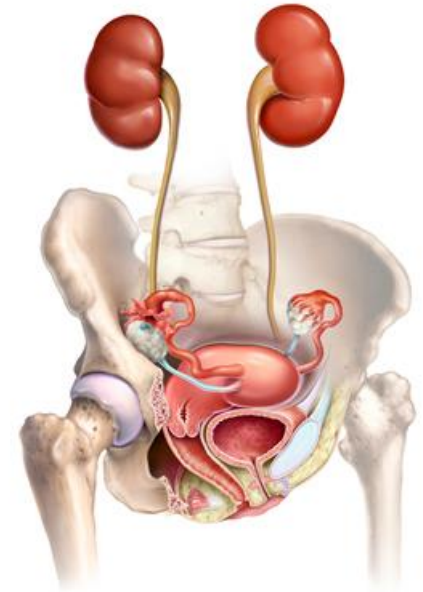
- ▶ **Gynaecological disorders** = any disorder that affects the female reproductive organs
- ▶ The most common disorders are:
 - ▶ **vulvodynia** – is the term used to describe chronic discomfort or pain of the vulva (external genital organs), especially burning, stinging, irritation, or rawness of the area
 - ▶ **vaginitis** – any disorder that causes swelling or infection of both the vulva and the vagina
 - ▶ **pelvic pain** – is a general term that describes the pain in the lower abdomen area. It signals a problem with one of the organs in the pelvic area: uterus, ovaries, fallopian tubes, cervix, vagina. Or, it might be a symptom of an infection.



PHYTOPHARMACEUTICALS

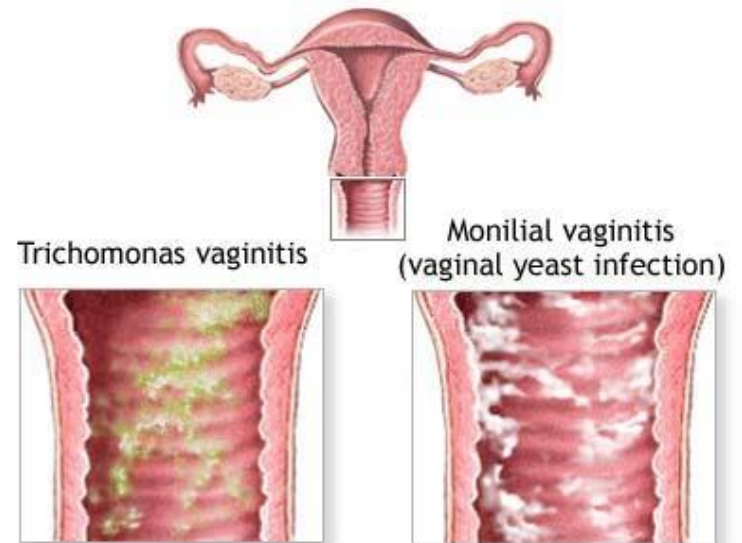
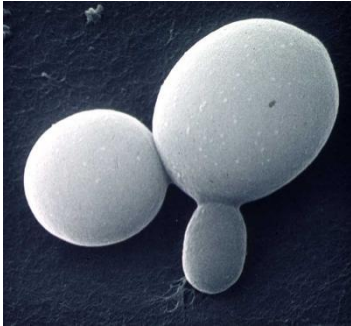
used to treat GYNAECOLOGICAL DISORDERS

- ▶ The most common types of vaginitis:
 - ▶ „yeast“ infections – caused by the fungus *Candida*
 - ▶ **bacterial vaginitis** – caused by an overgrowth of bacteria that are normally present in the vagina (e.g. *Gardnerella vaginalis*) or by other pathogenic bacteria (e.g. enterococci, streptococci, *E. coli*...)
 - ▶ **other infectious vaginitis** – caused by *Chlamydia* sp., *Trichomonas* sp., HSV (Herpes simplex virus), HPV (Human papilloma virus)
 - ▶ **non-infectious vaginitis** – is typically the result of an allergic reaction or an irritation to soaps, detergents, vaginal preparations,...
Once you stop using the product, the symptoms should go away



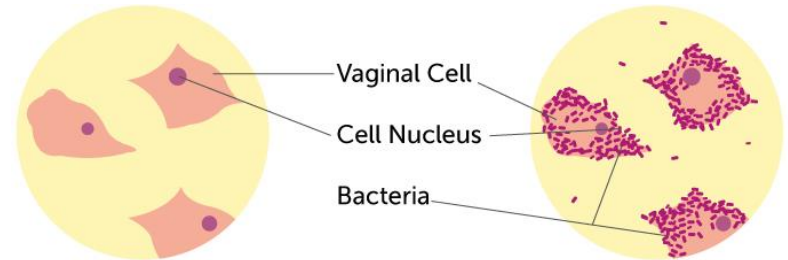
PHYTOPHARMACEUTICALS used to treat GYNAECOLOGICAL DISORDERS

▶ „yeast“ vaginitis



▶ bacterial or other infectious vaginitis

Gardnerella vaginalis



Normal vaginal cells seen under a microscope.

“Clue Cells”, vaginal cells with bacteria stuck to them.

PHYTOPHARMACEUTICALS

used to treat GYNAECOLOGICAL DISORDERS

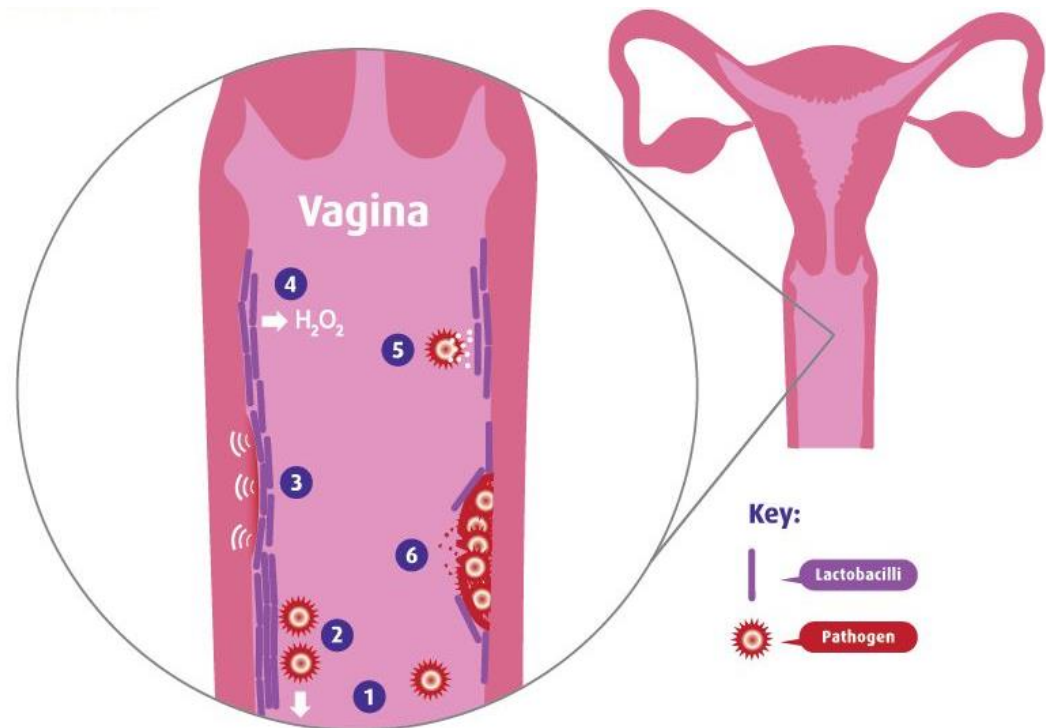
- ▶ Treatment of vaginitis and vulvodynia
 - ▶ preventive administration of probiotics, prebiotics, eubiotics - vaginally or orally, especially in the treatment of other infectious diseases with antibiotics
 - ▶ two-stage procedure:
 - ▶ provision of the normal physiological condition of the vaginal medium and mucosa
 - ▶ provision of the normal microbiocenosis – the use of vaginal eubiotics was shown to be highly efficient
 - ▶ local and general treatment – total antibiotics, antimycotics, antiinflammatory drugs;
 - ▶ topical medicines with disinfectant, antibacterial, anti-inflammatory effect,...

PHYTOPHARMACEUTICALS used to treat GYNAECOLOGICAL DISORDERS

▶ Vaginal eubiotics

- ▶ lactobacterin (*Lactobacillus* sp.)
- ▶ bifidumbacterin (*Bifidobacterium* sp.)
 - fermenting sugars into lactic acid

- 1 Restores a healthy pH < 4.5
- 2 Competitive inhibition
- 3 Modulates cytokines to decrease inflammation
- 4 Produces H_2O_2 (kills pathogens and lowers pH)
- 5 Bacteriocin production (kills pathogens)
- 6 Produces biosurfactants, which breakdown pathogen biofilms



PHYTOPHARMACEUTICALS

used to treat GYNAECOLOGICAL DISORDERS

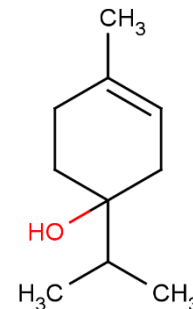
▶ TEA TREE OIL

Melaleuca alternifolia, Myrtaceae

- ▶ most *Melaleuca* species are native to Australia
- ▶ essential oil (isolated from the leaves) is an efficacious natural antiseptic (antibacterial, fungicide) agent
- ▶ composition: mainly monoterpenes
terpinen-4-ol (30-48 %), γ -terpinene (10-28 %),
 α -terpinene (5-13 %) and others (1,8-cineole,
 α -pinene, *p*-cymen,...)



terpinen-4-ol



PHYTOPHARMACEUTICALS

used to treat GYNAECOLOGICAL DISORDERS

▶ FEMIGEL

(Australian Body Care)

- ▶ hormone free vaginal moisturiser with 3 % of *Melaleuca alternifolia* oil
- ▶ The **tea tree oil** acts as a natural **antibacterial** and **antifungal** agent and so helps to prevent recurrent thrush and candidal infection.

Femigel coats the mucous membranes, to provide long lasting moisturisation and maintains healthy vaginal flora.



▶ TEA TREE OIL Vaginal gel

(Dr. Müller Pharma)



PHYTOPHARMACEUTICALS

used to treat GYNAECOLOGICAL DISORDERS

▶ FEMIBION® Intima (Merck)

- ▶ a food supplement, with probiotic strains *Lactobacillus rhamnosus* GR1, *Lactobacillus reuteri* RC-14 which helps to maintain the natural balance of the vaginal flora by:
 - protecting against bacteria and fungal growth that can cause vaginal yeast infections.
 - sustaining the protective bacteria in the vagina that can be destroyed by factors (such as antibiotics, etc.)
- ▶ available in topical and oral formats



PHYTOPHARMACEUTICALS

used to treat GYNAECOLOGICAL DISORDERS

▶ CANDIVAC® cps

(Bioveta, Czech Rep.)

- ▶ Czech patented preparation – purified lysate from 4 most common vaginal inflammation agents
- ▶ 1 capsule contains 5 mg of active substance prepared by lyophilisation of inactivated microorganisms (lysatum cryodessicatum):

<i>Candida albicans</i>	0,83 mg
<i>Candida krusei</i>	0,83 mg
<i>Candida glabrata</i>	0,83 mg
<i>Propionibacterium acnes</i>	2,50 mg

- ▶ dosage: 1 capsule once a day, for 10 days, then pause for 20 days. Next 2 months to repeat the same procedure.



PHYTOPHARMACEUTICALS

used to treat GYNAECOLOGICAL DISORDERS

- ▶ **PM-CHLAMYDIL[®]** (Purus-Meda, Czech Rep.)
 - ▶ cleansing cure (especially when chlamydia occurs)
 - ▶ contains:
 - extr. from *Filipendula ulmaria* - 5: 1,104.3 mg
 - extr. from *Salix alba* - 10: 1, 11.6 mg
 - extr. from *Alnus glutinosa* - 4: 1, 11.6 mg
 - Propolis Moravia PM[®] - 12.5 mg



- ▶ Dosage: 2-4 tablets a day for 3-7 months. The treatment should last at least 4 months, ideally 7-9 months.
During the first 4 months of dechlamydosis, the organism is purified from active forms of *Chlamydia trachomatis*, between 4-7 months of chlamydia are unable to reproduce and disappear from the organism, between 7-9 months there is probably residual detoxification of the organism from chlamydial endotoxins.

PHYTOPHARMACEUTICALS

used to treat GYNAECOLOGICAL DISORDERS

▶ MENSTRUAL DISORDERS

- ▶ painful cramps during menstruation (dysmenorrhea) – caused by menstruation itself (contraction of the smooth muscle), or by other condition – e.g. endometriosis, or uterine fibroids
 - ▶ heavy bleeding (menorrhagia) includes prolonged menstrual periods or excessive bleeding
 - ▶ absence of menstruation (amenorrhea)
 - ▶ light or infrequent menstruation (oligomenorrhea)
 - ▶ premenstrual syndrome (PMS)
- ▶ **Treatment:**
- ▶ hormone preparations, ergot alkaloids, NSAIDs, spasmolytics
 - ▶ **herbal preparations** – can be used as support therapy

PHYTOPHARMACEUTICALS

used to treat GYNAECOLOGICAL DISORDERS

- ▶ Active principles of drugs:
 - ▶ mostly **flavonoids** (spasmolytic effect), **tannins** (astringent), **essential oils** (spasmolytic), **coumarins** (spasmolytic)
- ▶ Plant drugs used to treat menstrual disorders
 - ▶ Alchemillae herba – *Alchemilla vulgaris*, Rosaceae, lady's mantle
 - ▶ contains mainly tannins, flavonoids
 - ▶ Anserinae herba – *Potentilla anserina*, Rosaceae, silverweed
 - ▶ contains mainly tannins
 - ▶ Lamii albi flos/herba – *Lamium album*, Lamiaceae, white deadnettle
 - ▶ contains mainly tannins, flavonoids
 - ▶ Agni casti fructus – *Vitex agnus-castus*, Lamiaceae, chaste tree
 - ▶ contains flavonoids, diterpenes, essential oils

PHYTOPHARMACEUTICALS used to treat GYNAECOLOGICAL DISORDERS



Alchemilla vulgaris
herb



Lamium album
flower/herb



Vitex agnus-castus
fruits



Potentilla anserina
herb



PHYTOPHARMACEUTICALS

used to treat GYNAECOLOGICAL DISORDERS

- ▶ Plant drugs used to treat menstrual disorders
 - ▶ Matricariae flos – *Matricaria recutita*, Asteraceae, German chamomile
 - ▶ Chamomillae romanae flos – *Anthemis nobilis* (*Chamaemelum nobile*), Asteraceae, Roman chamomille
 - ▶ Millefolii herba – *Achillea millefolium*, Asteraceae, yarrow
 - ▶ Petasitidis folium – *Petasites hybridus*, Asteraceae, butterbur
 - ▶ contains sesquiterpene derivatives (petasin, isopetasin,...), flavonoids,...
 - ▶ spasmolytic activity
 - ▶ Bursae pastoris herba – *Capsella bursa-pastoris*, Brassicaceae, shepherd's-purse
 - ▶ contains biogenetic amines, saponins, flavonoids, glucosinolates
 - ▶ haemostyptic action (due to a peptide with oxytocin-like activity)

PHYTOPHARMACEUTICALS

used to treat GYNAECOLOGICAL DISORDERS



Matricaria recutita
flower



Anthemis nobilis
flower



Achillea millefolium
herb



Petasites hybridus
leaf



Capsela bursa-pastoris
herb



PHYTOPHARMACEUTICALS used to treat GYNAECOLOGICAL DISORDERS

▶ LADY'S MANTLE

- ▶ Alchemillae herba
Alchemilla vulgaris, Rosaceae
- ▶ loose tea or tea bags
- ▶ Leros, Megafyt Pharma,
Apotheke, Fytopharma,...

▶ TEA FOR WOMEN (Leros)

- ▶ 10(20) x 1.5 g
- ▶ Alchemillae herba (30 %)
Origanum herba (15 %)
Menthae pip. herba (15 %)
Callunae herba (15 %)
Lamii albi herba (10 %)
Melissae herba (10 %)
Millefolii herba (5 %)



PHYTOPHARMACEUTICALS

used to treat GYNAECOLOGICAL DISORDERS

▶ GYNASTAN

Feminine Herbal tea
(Fytopharma)

- ▶ 20 x 1.0 g
- ▶ Lamii albi herba
- Alchemillae herba
- Menthae pip. herba
- Millefolii herba



▶ GYNOTON

(Dr. Müller Pharma)

- ▶ 20 x 1.5 g
- ▶ content in one tea bag (1.5 g):
 - Lamii albi herba 450 mg
 - Alchemillae herba 450 mg
 - Millefolii herba 450 mg
 - Menthae pip. herba 150 mg



PHYTOPHARMACEUTICALS

used to treat GYNAECOLOGICAL DISORDERS

- ▶ **AGNUCASTON** POR TBL FLM 30
(Bionorica)

- ▶ content in 1 tbl:
4 mg of Agni casti fructus extractum siccum
(7-11:1), extracted with ethanol 70%

- ▶ SUKL code: 0010045

Prescription-only medicinal products

- ▶ ATC: V11, G02CX03

- ▶ used for the harmonization of menstrual disorders and complaints occurring ahead of the onset of menstruation (premenstrual syndrome), as well as in case of tension and swelling of the breasts (mastodynia)



PHYTOPHARMACEUTICALS

used to treat GYNAECOLOGICAL DISORDERS

▶ SARAPIS Mensis (Sanamed, Austria)

- ▶ content in 1 cps:
 - 90 mg flower pollen
 - 50 mg fermented flower pollen
 - 22.5 mg Magnesium
 - 21.25 mg cranberries (*Vaccinium macrocarpon*) extr.
 - 18.75 mg soy beans (*Glycine soya* seeds) extract
 - 12.5 mg red clover (*Trifolium pratense*) extract
 - + vitamins B, vit. E, folic acid, zinc, phosphatidylserin
- ▶ used for the harmonization of menstrual disorders (dysmenorrhea, irregular menstruation), premenstrual syndrome (tension and sensitivity of the breasts, loss of appetite, nervousness,...)
- ▶ dosage: 1 capsule 2 times a day



PHYTOPHARMACEUTICALS

used to treat GYNAECOLOGICAL DISORDERS

▶ MASTODYNON

POR GTT SOL 1X50ML (Bionorica)

- ▶ **!!** homeopathic remedy (in decimal dilution)

- ▶ content in 100 mL:

Agnus castus D1 20 g

Caulophyllum thalictroides D4 10 g

Cyclamen europaeum D4 10 g

Strychnos ignatii D6 10 g

Iris versicolor D2 20 g

Lilium tigrinum D3 10 g

53 % of ethanol by volume

- ▶ SUKL code: 0045546
OTC medicinal products

- ▶ ATC: V11

- ▶ available also as tablets

- ▶ preparation is included into Phytopharmaceuticals (ATC group V11), but in fact it is homeopathic preparation

- ▶ used in case of complaints prior to menstruation such as, e.g. feeling of tension and swelling of the breasts (mastodynia), complaints during menstruation and menstrual cycle



PHYTOPHARMACEUTICALS used to treat MENOPAUSAL DISORDERS

▶ MENOPAUSE, CLIMACTERIUM

- ▶ is defined as the state of an absence of menstrual periods for 12 months when the function of the ovaries and secretion of estrogen/progesterone is coming to stop
- ▶ symptoms of menopause can include **abnormal vaginal bleeding, hot flashes, sweating, vaginal and urinary symptoms, and mood changes**
- ▶ complications that women may develop after menopause include **osteoporosis, metabolic syndrome and cardiovascular diseases**
- ▶ **Treatment** is directed toward relieving uncomfortable or distressing symptoms
 - ▶ hormone replacement therapy (HRT)
 - ▶ herbal remedies with content of **phytoestrogens**

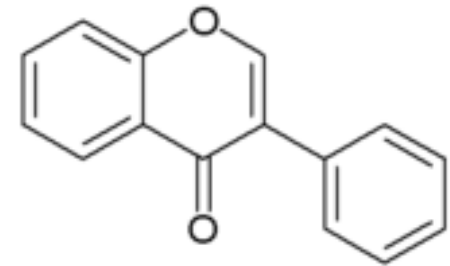


PHYTOPHARMACEUTICALS

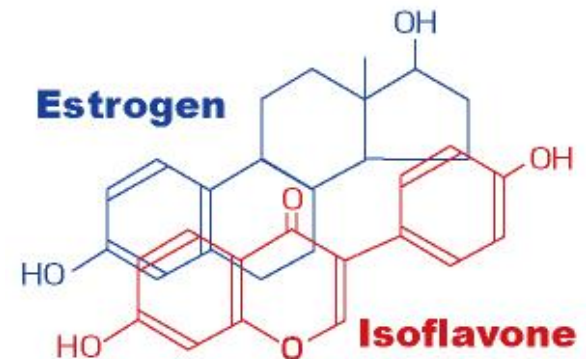
used to treat MENOPAUSAL DISORDERS

▶ PHYTOESTROGENS

- ▶ **Isoflavones** are non-steroidal, polyphenolic compounds related to flavonoids that are capable of exerting estrogen-like effects
- ▶ the chemical structure of isoflavones is quite similar to that of our own estrogens that is why they can interfere with the estrogen receptors (ER) on the cells – reduce or activate the estrogen activity
- ▶ the consumption of isoflavones may have a positive effect in prevention of
 - ▶ adverse menopausal manifestations
 - ▶ hormone-dependent cancer
 - ▶ cardiovascular disease
 - ▶ osteoporosis – improve bone health
 - ▶ cognitive decline



Similarity of Isoflavone to Estrogen

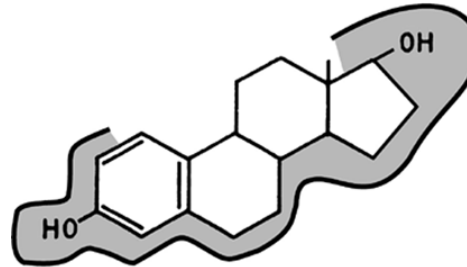


PHYTOPHARMACEUTICALS

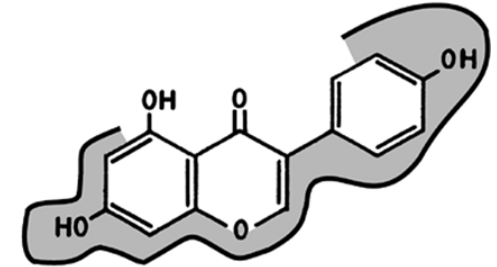
used to treat MENOPAUSAL DISORDERS

▶ ISOFLAVONES, e.g.:

- ▶ genistein, (genistin)
- ▶ daidzein, (daidzin)
- ▶ biochanin A
- ▶ formononetin



Estradiol



Genistein

▶ Plant drugs containing **isoflavones**, especially from the family Fabaceae:

- ▶ *Glycine max*, soy beans
- ▶ *Trifolium pratense*, red clover
- ▶ *Medicago sativa*, alfalfa
- ▶ *Ononis spinosa*, spiny restharrow

PHYTOPHARMACEUTICALS used to treat MENOPAUSAL DISORDERS



Trifolium pratense
herb



Glycine max, soy
seeds



Medicago sativa
herb/germs



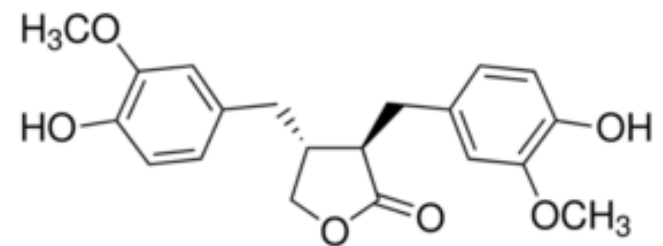
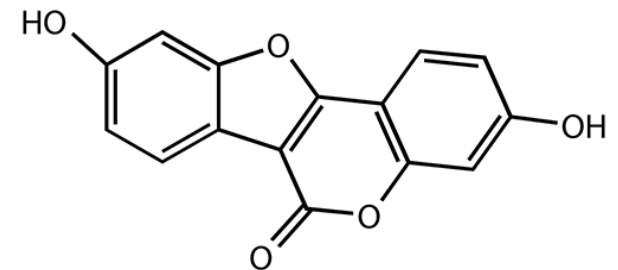
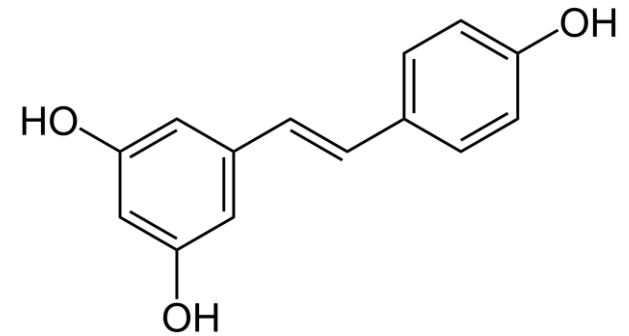
Ononis spinosa
root



PHYTOPHARMACEUTICALS

used to treat MENOPAUSAL DISORDERS

- ▶ Other natural compounds with estrogen-like activity:
 - ▶ stilbenes
 - ▶ **resveratrol** – *Vitis vinifera* var. *rubra*, Vitaceae, red wine
 - ▶ coumestans
 - ▶ **coumestrol** – e.g. in alfalfa, soy beans, red clover
 - ▶ lignans
 - ▶ **matairesinol, secoisolariciresinol** – major food sources: oil seeds and nuts, whole grains, vegetables, fruits, e.g. *Linum usitatissimum* seed, flax seed



PHYTOPHARMACEUTICALS

used to treat MENOPAUSAL DISORDERS

- ▶ Other plant drugs used in herbal teas for reduction of menopausal complaints:
 - ▶ to calm down, eliminate psychological disorders, e.g.:
 - ▶ Hyperici herba, Melissa herba/folium,...
 - ▶ against excessive sweating, hot flashes, e.g.:
 - ▶ Salvia herba/folium
 - ▶ drugs with diuretic activity, e.g.:
 - ▶ Betulae folium, Urticae folium/herba,...
 - ▶ drugs that improve the functioning of the cardiovascular system
 - ▶ Crataegi folium cum flore/fructus
 - ▶ drugs with astringent effect, e.g.:
 - ▶ Alchemillae herba

PHYTOPHARMACEUTICALS

used to treat MENOPAUSAL DISORDERS

▶ FYTOKLIMAN Planta (Leros)

▶ POR SPC 20X1.5 GM

▶ composition, in 100 g:

Hyperici herba	20 g
Alchemillae herba	20 g
Crataegi folium cum flore	20 g
Betulae folium	15 g
Melissae herba	10 g
Origani herba	10 g
Lupuli flos	5 g

▶ SUKL code: 0089824

▶ ATC: V11

▶ be careful about the content of Hyperici herba !

- ▶ An herbal preparation combining different herbs with different properties – to calm and relax (Hyperici herba, Melissae herba, Lupuli flos), as an astringent to control bleeding (Alchemillae herba), to help reduce blood pressure (Crataegi folium cum flore) and as a diuretic (Betulae folium).



PHYTOPHARMACEUTICALS

used to treat MENOPAUSAL DISORDERS

▶ KLIMAKTERIN (Dr. Müller Pharma)

- ▶ 20 x 1.5 g
- ▶ content in one tea bag (1.5 g):
Trifolium rubri flos 1050 mg
Melissae herba 450 mg



▶ GYNASTAN Meno (Fytopharma)

- ▶ 20 x 1.5 g
- ▶ **Trifolium rubri flos**
Melissae herba



PHYTOPHARMACEUTICALS

used to treat MENOPAUSAL DISORDERS

- ▶ **MENOFILAVON Classic cps.**
MENOFILAVON Forte cps.
(Melbrosin International, Austria)



- ▶ content in 1 capsule:
standardized extract of *Trifolium pratense*,
RCE 40, corresponding to 40 (80) mg of isoflavones
(genistein, daidzein, biochanin A, formononetin)
- ▶ according to the research of Vienna University, the activity of 1 g
of *Trifolium pratense* extract corresponds to the activity of 85 µg
17-β-estradiol (20 times more than in soy)
- ▶ dosage: 1 tablet daily
- ▶ no side effects
- ▶ not recommended in pregnancy and lactating



PHYTOPHARMACEUTICALS

used to treat MENOPAUSAL DISORDERS

- ▶ **MENOFILAVON OSTEO cps.**
(Melbrosin International, Austria)
 - ▶ content in 1 capsule:
 - standardized extract of *Trifolium pratense*, corresponding to **50 mg of isoflavones**
 - + OSTEO complex:

calcium	350 mg
magnesium	30 mg
zinc	2,5 mg
vitamin D3	2,5 µg
 - ▶ dosage: 1-2 tablet daily



PHYTOPHARMACEUTICALS

used to treat MENOPAUSAL DISORDERS

▶ FEMIFLAVON Forte tbl.

(Favea)

▶ content in 1 tbl:

50 mg *Silybum marianum* extract (standardized to 20 % content of silybin)

50 mg *Vitis vinifera* leaves and fruit extract

40 mg isoflavones from *Trifolium pratense*

4 mg natural carotenoids from algae *Dunaliella salina*
(halophile green micro-algae)

400 µg folic acid

4 mg vitamin B6

2.5 µg vitamin B12

250 mg non-soluble fibre

▶ dosage: 1 tablet daily



PHYTOPHARMACEUTICALS used to treat MENOPAUSAL DISORDERS

- ▶ **IVE® inkontin stop cps.**
(SWISS Pharmaceutical Investments)
 - ▶ content in 1 capsule:
 - 175 mg of microsomal flavolignane complex (extract from the *Silybum marianum* fruits, lecithin, squalen,...)
 - 90 mg dry extract from *Trifolium pratense* herba
 - 75 mg dry extract from *Glycine max* semen
 - 40 mg dry extract from *Linum usitatissimum* semen
 - inulin
 - ▶ dosage: 1 capsule daily
- ▶ **IVE® 50 InkontinStop cps.**
 - ▶ contains also extract from *Cucurbita pepo* semen



PHYTOPHARMACEUTICALS

used to treat MENOPAUSAL DISORDERS

▶ SARAPIS Soja (Sanamed, Austria)

- ▶ content in 1 cps:
 - 24 mg lyophilized royal jelly (= 72 mg of crude r. j.)
 - 180 mg flower pollen
 - 100 mg fermented flower pollen
 - 37.5 mg soy beans extract
 - 25 mg red clover extract
 - 20 mg vitamin C
 - 3 mg iron (Fe)
- ▶ dosage: 1 capsule 2 times a day
- ▶ CI: hypersensitivity to any component, especially to bee products
- ▶ **royal jelly** (bee secret that is used in the nutrition of larvae) health benefits: reducing the symptoms of PMS and menopausal syndrome, lowering cholesterol levels, serving as a general tonic for rejuvenation, improving immune system function



PHYTOPHARMACEUTICALS

used to treat MENOPAUSAL DISORDERS

- ▶ **Cimicifugae rhizome/radix**
Cimicifuga racemosa (*Actea racemosa*),
Ranunculaceae
black cohosh
 - ▶ active principles are triterpenoid glycosides – **actein, cimicifugosid** and also isoflavones – **formononetin**
 - ▶ the possible mode of action – lowering of LH (luteinizing hormone) due to the influencing of hypothalamic-hypophyseal system
 - ▶ in 2006, European Medicines Agency (EMA, previously EMEA) called attention to possible hepatotoxicity in high doses of *Cimicifuga racemosa* extract



PHYTOPHARMACEUTICALS

used to treat MENOPAUSAL DISORDERS

Preparations with *Cimicifuga racemosa*:

- ▶ **MENOFEM POR TBL FLM 60X20MG**
(Bionorica/Schwabe)
 - ▶ content in 1 coated tablet:
2.80 mg Cimicifugae extractum
siccum 5-10:1, extracted with ethanol 58 %
 - ▶ SUKL code: 0125119; OTC medicinal product
 - ▶ ATC: G02CX04
 - ▶ Indication: symptoms of pre- or postmenopausal neurovegetative disorders – hot flashes, sweating, headaches, sleep disorders, mood changes,...
 - ▶ Dosage: 1 tablet 2 times a day
recommended duration of therapy: 8 weeks
 - ▶ CI: hypersensitivity to any component, pregnancy, lactation
Be careful in case of any liver disease!



PHYTOPHARMACEUTICALS

used to treat MENOPAUSAL DISORDERS

Preparations with *Cimicifuga racemosa*:

▶ **KLIMADYNON/KLIMADYNON Uno**
(Bionorica)

- ▶ dry extract of the black cohosh rhizome
(*Cimicifuga racemosa*)



▶ **GS MERILIN Harmony**
(Green-Swan Pharmaceuticals)

- ▶ content in 1 tbl:
standardized dry extract of *Cimicifuga racemosa*
(equal to 20 mg of dry rhizome)
250 mg Calcium
10 µg vitamin D₃
extr. Hyperici herba (equal to 150 mg of dry
herba)

