



EVROPSKÁ UNIE



MINISTERSTVO ŠKOLSTVÍ,  
MLÁDEŽE A TĚLOVÝCHOVY



OP Vzdělávání  
pro konkurenceschopnost

INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ

# PHYTOPHARMACEUTICALS

academic year 2018/19

## LECTURE 5 – Preparations used to treat some disorders of cardiovascular system

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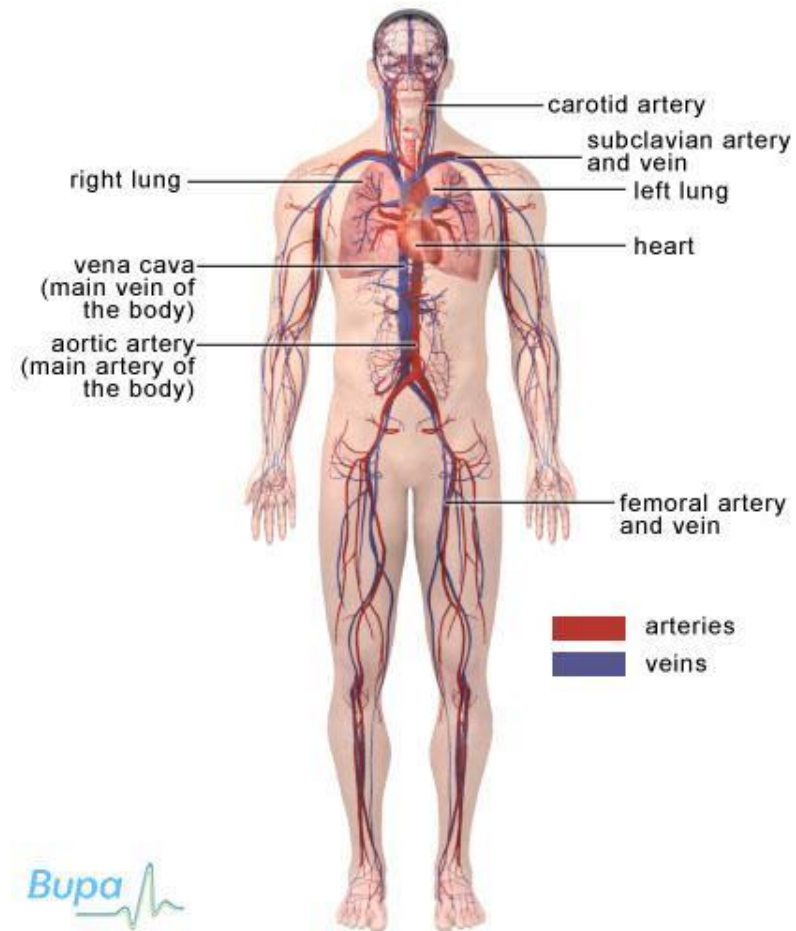
# PHYTOPHARMACEUTICALS

## vs. Cardiovascular system (CVS)

### Major CVS disorders

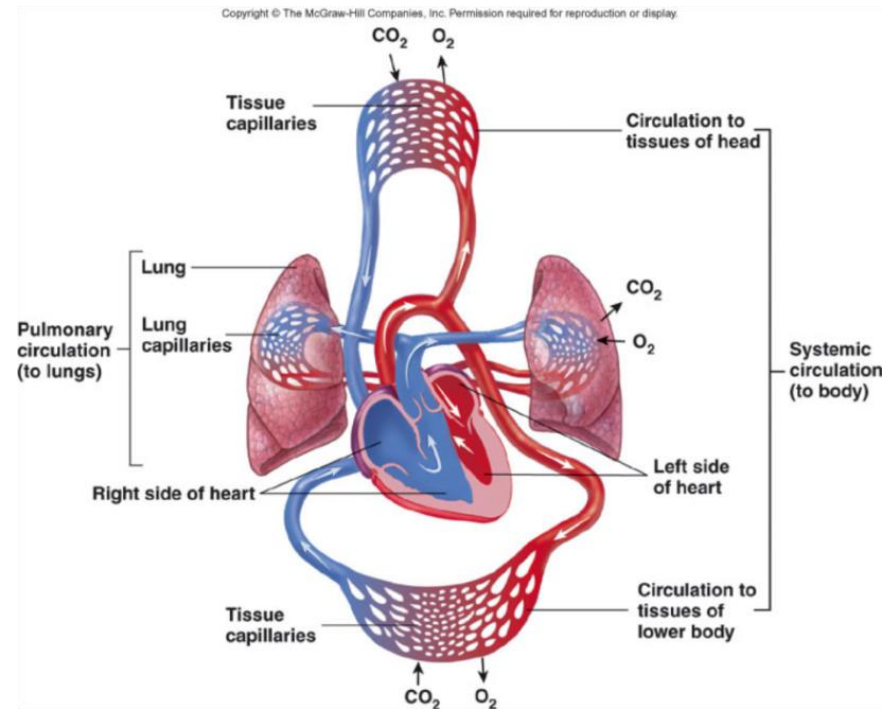
- ▶ Heart failure
- ▶ Angina pectoris, heart attack
- ▶ Abnormal heart rhythms
- ▶ Hypertension/Hypotension
- ▶ Peripheral vascular diseases (arterial/venous)

Phytotherapy is suitable only as **supplementary** and **supporting therapy!!**



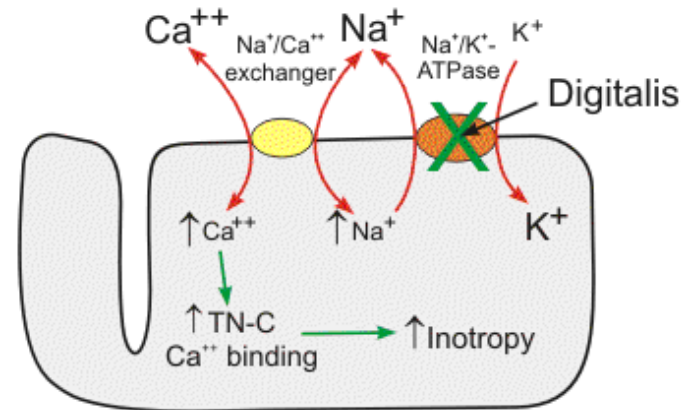
# Therapy of cardiovascular diseases

- ▶ drugs influencing heart
  - ▶ cardiotonics (cardiostimulants)
  - ▶ antirrhythmics
- ▶ drugs influencing vessels
  - ▶ vasodilators
  - ▶ vasoconstrictors
- ▶ antihypertensive drugs
- ▶ vasoprotective drugs
- ▶ antihyperlipidaemic drugs



# CARDIAC GLYCOSIDES

- ▶ = cardiotonic glycosides (CG), „digitalis“ glycosides
- ▶ positive inotropic effect – enlargement of the contractile force of heart muscle (due to the inhibition of  $\text{Na}^+/\text{K}^+$  ATPase → increase of intracellular  $\text{Na}^+$  → increase of intracellular  $\text{Ca}^{2+}$  → ↑ inotropy)
- ▶ Indication: chronic congestive heart failure, atrial fibrillation or flutter
- ▶ Overdose of CG, intoxication can cause life-threatening arrhythmias, contracture
- ▶ **!!!** plant drugs containing cardiac glycosides **are not allowed** to be components of phytopharmaceuticals due to their toxicity and narrow therapeutic margin.



# CARDIAC GLYCOSIDES

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▶ Plant drugs containing CG:

- ▶ *Digitalis lanatae* folium
- ▶ *Digitalis purpureae* folium
- ▶ *Convallariae* herba
- ▶ *Adonidis* herba
- ▶ *Strophanthi* semen
  - ▶ *Strophanthus* sp.

▶ other plants containing CG:

- ▶ *Helleborus niger*, *Nerium oleander*, *Urginea maritima*, *Acokanthera ouabaio*, *Erysimum* sp., *Thevetia* sp.



*Digitalis purpurea*



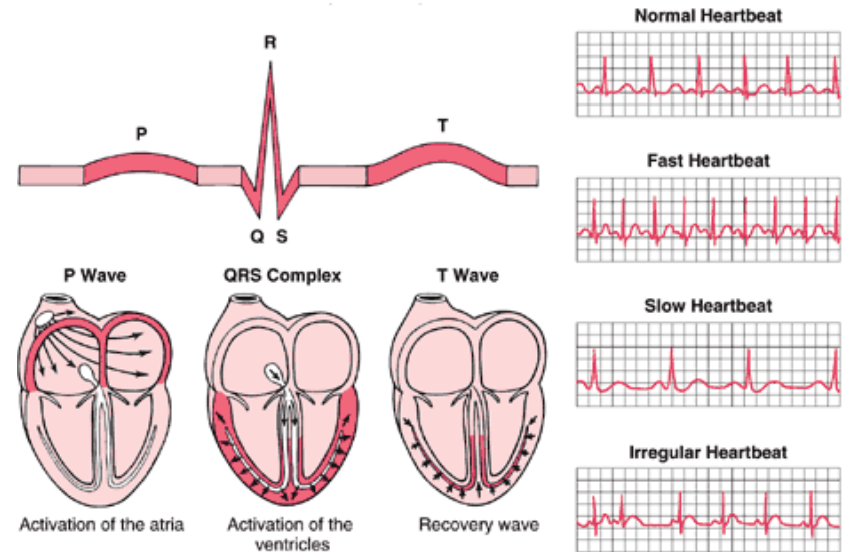
*Convallaria majalis*



*Adonis vernalis*

# Therapy of ARRHYTHMIA

- ▶ abnormal heart rhythms, irregular heartbeat
  - ▶ tachycardia – too fast
  - ▶ bradycardia – too slowly
  - ▶ premature contraction – too early
  - ▶ fibrillation – too irregularly



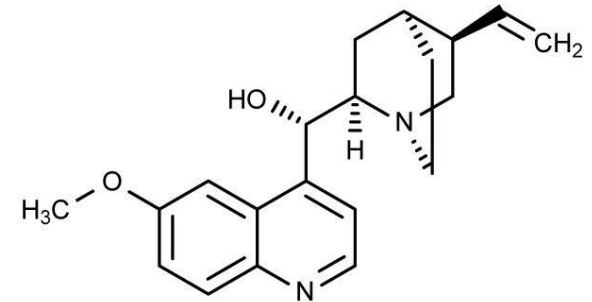
- ▶ partially possible using of phytomedicines

# Therapy of ARRHYTHMIA

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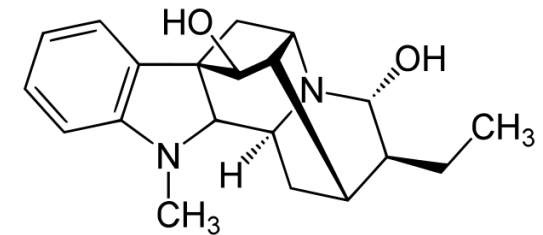
## ▶ quinidine

- ▶ alkaloid from *Cinchona* bark (stereoisomer of *quinine*)
- ▶ acts as a class Ia antiarrhythmic agent
- ▶ prescription-only drugs



## ▶ ajmaline

- ▶ indole alkaloid from *Rauwolfia serpentina* root
- ▶ acts as a class Ia antiarrhythmic agent
- ▶ prescription-only drugs



## ▶ bradycardia

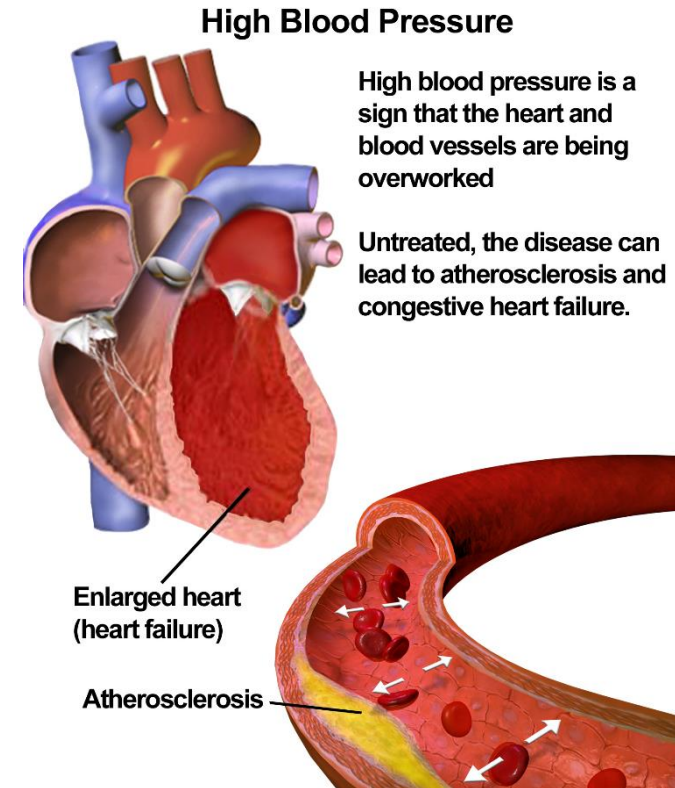
- ▶ plant drugs containing **caffeine**
- ▶ hawthorn leaf/flower – *Crataegus* sp.

## ▶ tachycardia, palpitations

- ▶ plant drugs with sedative effect

# HYPERTENSION

- ▶ blood pressure („arterial“ BP) over 140/90 mmHg
  - ▶ primary (essential) hypertension = high BP with no obvious underlying medical cause
  - ▶ secondary HT– as a consequence of other disturbances (e.g. in renal diseases, by endocrine conditions, obesity,...)
- ▶ phytomedicines can be used only as a part of **supplement therapy !!**
- ▶ first steps
  - ▶ low sodium intake diet (be careful about using of *Liquiritiae radix*)
  - ▶ reduction of body weight





# Therapy of HYPERTENSION

- ▶ **Crataegi folium cum flore**  
**Crataegi fructus**
  - ▶ *Crataegus oxyacantha*, *C. monogyna*, and other species, Rosaceae = hawthorn
  - ▶ major constituents:
    - ▶ flavonoids – quercetin glycosides (e.g. *hyperoside* – mainly in fruits), and apigenin glycosides (*vitexin* derivatives – mainly in leaves)
    - ▶ oligomeric procyanidines, triterpene acids, phenylpropanoid acids, aminopurines, xanthines, K<sup>+</sup> salts



# Therapy of HYPERTENSION

- ▶ **Crataegi folium cum flore**  
**Crataegi fructus**
  - ▶ improvement of blood circulation, also in coronary arteries; effect on the control of the intracellular  $\text{Ca}^{2+}$  concentrations
  - ▶ Indications:
    - ▶ hypertension (used to treat both high BP and low BP)
    - ▶ It might be effective against initial cardiac insufficiency (congestive heart failure), as well as for the ageing heart, against a feeling of pressure and tightness in the cardiac region (chest pain) and mild bradyarrhythmia



# Therapy of HYPERTENSION

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- ▶ **Hawthorn tea**  
(MEGAFYT Pharma)
  - ▶ POR SPC 20X1.5GM
  - ▶ *Crataegi folium cum flore*
  - ▶ SUKL code: 0076436, OTC medicinal product
  - ▶ ATC: V11 (Phytopharmaceuticals and animal products)
  - ▶ herbal preparation suitable for treatment of mild forms of hypertension, for improvement of heart blood flow, as a cardiostimulant
- ▶ **Hawthorn drops** (Grešík, Herba Vitalis, Topvet, ...)
  - ▶ alcoholic extracts of *Crataegus oxyacantha* and/or *Crataegus monogyna*



# Therapy of HYPERTENSION

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- ▶ **Visci albi herba**
  - ▶ *Viscum album*, Santalaceae  
– mistletoe



major constituents: proteins and polypeptides (*viscotoxins*), *lectins*, polysaccharides

BUT active principles in therapy of hypertension are probably flavonoids, phenylpropanes and lignans, biogenic amines

- ▶ **!!** A clear distinction must be made between *oral* use of the drug in the form of **aqueous extract** (herbal tea – as an adjuvant in the treatment of high BP), and the *parenteral* use of isolated constituents, e.g. in the form of intradermal injections (for treating degenerative inflammation of the joints, or as palliative therapy for malignant tumours).

# Therapy of HYPERTENSION

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- ▶ **Visci albi herba**
  - ▶ *Viscum album*, Santalaceae
    - mistletoe
  - ▶ There are no real grounds for the use of mistletoe tea as a supportive agent in treating of high BP
  - ▶ **!!** It has indeed been shown that the isolated **viscotoxins** have **hypotensive effect** on parenteral administration, but they can not be considered as the active principle since they **are not absorbed orally**; moreover they are highly irritating to the skin, at high dose they even cause necrosis.



# Therapy of HYPERTENSION

## ▶ ALVISAN Neo (LEROS)

- ▶ POR SPC 20 x 1.5 g or 1x 100g
- ▶ SUKL code: 0004364, 0043954
- ▶ OTC product
- ▶ ATC: V11 (Phytopharmaceuticals and animal products)
- ▶ not suitable for children until 18 years, for pregnant and lactating women
- ▶ **!** mind the presence of Hyperici herba
  - ▶ photosensitivity, interactions with certain concurrently administered drugs, loss of concentration,...

- ▶ Matricariae flos
- Crataegi folium cum flore**
- Crataegi fructus**
- Equiseti herba
- Hyperici herba
- Melissae herba
- Menthae piperitae herba
- Visci albi herba**



# Therapy of HYPERTENSION

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## ▶ Hypotonic herbal tea (MEGAFYT)

- ▶ POR SPC 20 x1.5 g
- ▶ SUKL code: 0084373
- ▶ OTC product
- ▶ ATC: V11
- ▶ herbal preparation suitable for treatment of mild forms of hypertension

Composition (in one tea bag = 1.5 g):

- ▶ **Crataegi folium cum flore** 375 mg
- Visci albi herba** 375 mg
- Polygoni avicularis herba 225 mg
- Rubi fruticosi folium 225 mg
- Crataegi fructus** 150 mg
- Melissae herba 150 mg



# PHYTOPHARMACEUTICALS

## in the treatment of VASCULAR DISEASES

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- ▶ Tea for high blood pressure  
(Fytopharma, Slovakia)

- ▶ **Visci albi herba**  
Millefolii herba  
**Leonuri herba**  
Melissae herba



*Leonurus cardiaca*  
Lamiaceae

- ▶ Tea for blood pressure  
(Pavel Váňa)
- ▶ **Crataegi folium cum flore**  
Filipendulae herba  
Melissae herba  
**Leonuri herba**





# Therapy of HYPERTENSION

Formerly used plant drugs:

- ▶ **Veratri albi radix**  
*Veratrum album*, Melanthiaceae
  - ▶ steroid alkaloids
- ▶ **Rauwolfiae radix**  
*Rauwolfia serpentina*, Apocynaceae
  - ▶ alkaloids – *reserpin* – formerly used in composite medicinal preparations (e.g. CRYSTEPIN)
- ▶ **Secale cornutum**  
*Claviceps purpurea*, Clavicipitaceae
  - ▶ alkaloids, especially dihydroderivatives (e.g. dihydrocristine, in CRYSTEPIN)



*Veratrum album* L.  
Image processed by Thomas Schoepke  
www.plant-pictures.de



*Rauwolfia serpentina*



PLATE XXXVII.—*Claviceps purpurea* (Ergot). (From Jackson: *Experimental Pharmacology and Materia Medica*.)



# Therapy of HYPERTENSION

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## Supplementary and support therapy:

- ▶ Diuretics (!) – plant drugs containing:
  - ▶ flavonoids
  - ▶ saponins
  - ▶ essential oils
  
- ▶ Plant drug with significant antioxidative activity, e.g.:
  - ▶ *Oleae folium* (*Olea europea*)

- ▶ *Allii sativi bulbus*



# Therapy of HYPERTENSION

## ▶ OptiTensin® (Walmart)

- ▶ Oleae folium extract 350 mg
- ▶ Olive leaves extract helps to maintain normal blood pressure and helps to protect organism against negative effects of free radicals.
- ▶ Dosage: 1-2 tablets daily. It is recommended to use minimally for the period of 8 weeks



## ▶ Garlic (Walmart)

- ▶ highly concentrated oil extract from *Allium sativum* 2.0 mg in 1 capsule (eqv. 1000,0 mg of fresh garlic)
- ▶ Garlic contributes to normal function of immune system.
- ▶ Garlic helps to maintain normal cholesterol level and the health of heart.



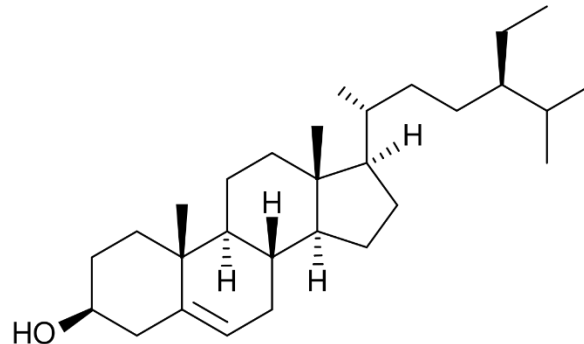
# Therapy of HYPERTENSION

## ▶ $\omega$ -3 fatty acids

- ▶ EPA and DHA cause vasodilation, low blood pressure
- ▶ source: oil seeds and fruits, sea fish, cereals, some vegetables...

## ▶ plant sterols

- ▶ have positive influence on blood cholesterol level
- ▶ *beta-sitosterol, beta-sitostanol*
- ▶ source: oil seeds (e.g. rapeseed), nuts, cereals (e.g. corn),...



### Omega 3 Fatty Acids

Alpha Linolenic Acid (ALA)

EPA (Eicosapentaenoic Acid)

DHA (Docosahexaenoic Acid)

Anti-inflammatory;  
promotes blood thinning,  
artery dilation, lower blood  
pressure, improved arthritis  
pain, elevation of  
depression, mood  
stabilization.

# HYPOTENSION

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- ▶ **chronic hypotension – systolic BP below 105 mmHg**
  - ▶ primary hypotension – generally has no clinical importance. If symptoms such as lassitude and dizziness occur, a program of physical exercise instead of drug is advisable
  - ▶ secondary hypotension – is a sign of an underlying disease that should be treated first
- ▶ **acute hypotension**
  - ▶ failure of orthostatic regulation
- ▶ **Therapy of hypotension**
  - ▶ increase sodium intake in a diet
  - ▶ physical activity
  - ▶ *caffeine* plant drugs

