



INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ

PHYTOPHARMACEUTICALS

academic year 2018/19

LECTURE 9 – Preparations used to treat diabetes. Hepatoprotective agents.

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PHYTOPHARMACEUTICALS used to treat DIABETES MELLITUS

Type 1 diabetes

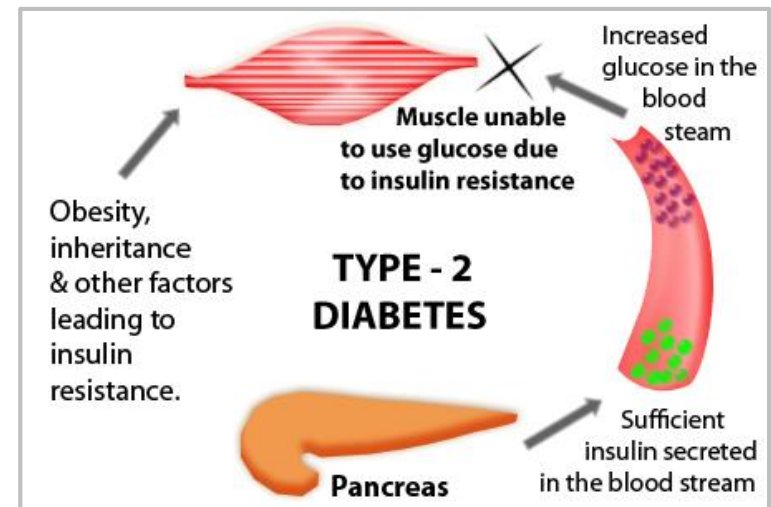
- ▶ = insulin-dependent diabetes → necessity of insulin replacement
 - ▶ insulin administration (insulin pen, insulin pump)
- ▶ prevention of life-threatening hyperglycaemic (diabetic) coma
- ▶ prevention of diabetic complications
 - ▶ angiopathy with blindness, myocardial infarction, renal failure
- ▶ prevention of insulin over dosage leading to life-threatening hypoglycaemic shock (CNS disturbance due to lack of glucose)



PHYTOPHARMACEUTICALS used to treat DIABETES MELLITUS

Type 2 diabetes

- ▶ usually in overweight adults – diabetic metabolic condition
- ▶ there is a relative insulin deficiency – enhanced demand cannot be met by a diminishing insulin secretion
- ▶ therapy of first choice is **weight reduction!**
- ▶ **oral antidiabetics**
 - ▶ the sulfonylurea type antidiabetics
 - ▶ biguanide derivatives
 - ▶ alpha-glucosidase inhibitors
 - ▶ incretin based therapies
 - ▶ etc.



PHYTOPHARMACEUTICALS

used to treat DIABETES MELLITUS

Treatment of diabetes type 2:

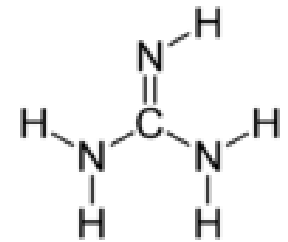
- ▶ **weight reduction** – caloric restriction to restore body weight to normal is associated with an increase in insulin receptor number or cellular responsiveness. The releasable amount of insulin is again adequate to maintain a normal metabolic rate.
 - ▶ dietary management, physical activity
- ▶ **blood glucose (glycaemic) control**
 - ▶ non-glucose sweeteners
 - ▶ glucokinins and other natural compounds that are able to decrease blood sugar
- ▶ prevention and treatment of **microvascular complications** (retinopathy, nephropathy, neuropathy,...)
- ▶ prevention of **macrovascular complications** – treatment of dyslipidaemia and hypertension

Herbal remedies for DIABETES

▶ „glucokinins“

= compounds that are able to reduce blood-sugar level

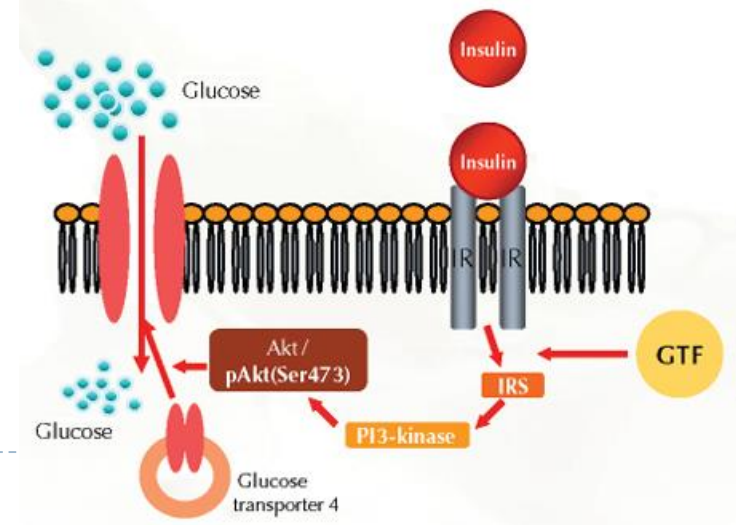
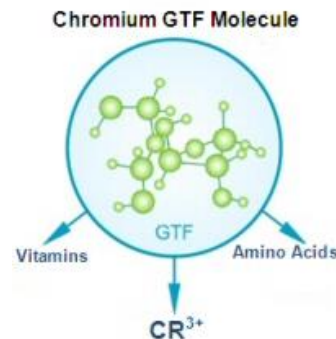
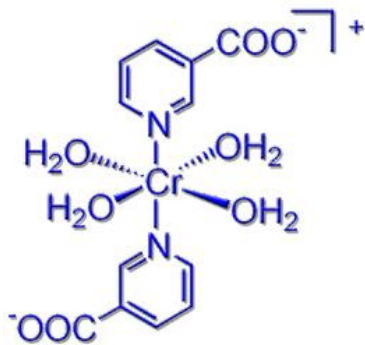
- ▶ e.g. natural **guanidine** derivatives – are able to low glycaemia by inhibiting absorption and promoting metabolism of glucose



GUANIDINE

▶ chromium

- ▶ a component of the so-called **glucose tolerance factor** – a low molecular weight chromium(III) complex



Herbal remedies for DIABETES

Plant drugs containing „**glucokinins**“, **chromium** e.g.:

- ▶ Galegae herba – *Galega officinalis*, Fabaceae, goat's-rue
 - ▶ **galegine**, the guanidine derivative, present in all parts; chromium salts
- ▶ Myrtilli folium/herba – *Vaccinium myrtillus*, Vacciniaceae, bilberry
 - ▶ **neomyrtillin** – a methoxylated glucoside of gallic acid; chromium salts (chromium content about 9.0 ppm)
- ▶ Phaseoli fructus sine semine (Phaseoli pericarpium) – *Phaseolus vulgaris*, Fabaceae, kidney-bean pods (without seeds)
- ▶ Foenugraeci semen – *Trigonella foenum-graecum*, Fabaceae, fenugreek seeds

- ▶ Cinnamomi cortex – *Cinnamomum zeylanicum*, *C. verum*, Lauraceae
- ▶ (Salviae folium, Zingiberis rhizoma)

Herbal remedies for DIABETES



Galega officinalis
herb



Vaccinium myrtillus
leaf/herb



Phaseolus vulgaris
pericarp (pods without seeds)



Cinnamomum zeylanicum
bark



Trigonella foenum-graecum
seeds



Herbal remedies for DIABETES

Natural alternative sweeteners for diabetics

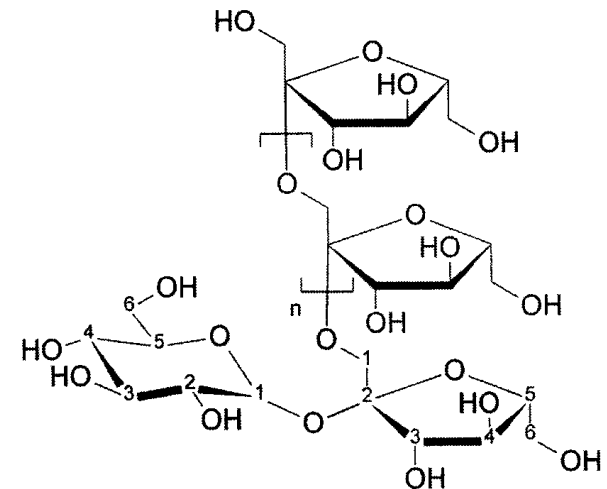
- ▶ they do not raise blood sugar levels
 - ▶ sugar alcohols – **xylitol** and **erythritol**. They are absorbed into the blood stream more slowly than sugar and are low in carbohydrate. Rather than being stored in the body they are eliminated efficiently in the urine.
 - ▶ **inulin**
 - ▶ **Stevia leaf** – *Stevia rebaudiana*, Asteraceae
 - ▶ contains sweet-tasting substances – **stevioside, rebaudiosides** (many times sweeter than sugar)
 - ▶ helps bring down high blood sugar



Herbal remedies for DIABETES

INULIN

- ▶ = fructan, a nondigestible polysaccharide of fructose units (about 2 to 5 % of glucose)
- ▶ a storage carbohydrate found in many plants, especially in roots and rhizomes of Asteraceae family plants (usually obtained from cichory root), or in some fruits, seeds,... (e.g. banana, onion)
- ▶ as a food ingredient can decrease the blood sugar level



Herbal remedies for DIABETES

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

- ▶ Cichorii radix – *Cichorium intybus*, Asteraceae
- ▶ Inulae radix – *Inula helenium*, Asteraceae
- ▶ Taraxaci radix – *Taraxacum officinale*, Asteraceae
- ▶ Bardanae radix – *Arctium lappa*, *A. minor*, *A. tomentosum*, Asteraceae, burdock root – 27-45 % of inulin
- ▶ Yacon – *Polymnia sonchifolia* (*Smallanthus sonchifolius*), Asteraceae – tubers (tuberous roots)
- ▶ Graminis rhizoma – *Elymus* (*Agropyron*) *repens*, Poaceae – common couch
 - contains „triticin“, a polysaccharide related to inulin which on hydrolysis yields fructose



Plant drugs containing INULIN



Cichorium intybus
root

Inula helenium
root



Arctium lappa
root



Polymnia sonchifolia
„yacón“ – tuberous roots

ANTIDIABETIC PREPARATIONS

Herbal teas

▶ **DIABETAN** (Leros)

▶ POR SPC 20X1GM, 1X100GM

▶ composition, in 100 g:

Phaseoli fructus sine semine 17 g

Myrtilli herba 15 g

Salviae officinalis herba 15 g

Galegae herba 12 g

Polygoni avicularis herba 10 g

Taraxaci radix cum herba 8 g

Rubi fruticosi folium 8 g

Foeniculi amari fructus 8 g

Bardanae radix 5 g

Liquiritiae radix 2 g

▶ SUKL code: 0056234, 0001918

▶ ATC: V11

▶ It positively influences increased blood sugar levels. It has diuretic, antiseptic and slightly spasmolytic effects.

▶ For diabetics, the tea is suitable as a part of diet

▶ CI: Patients with gall bladder and gall-duct ailments (especially with bile stones), fresh peptic ulcers

▶ be careful in case of hypertension (Liquiritiae radix)



ANTIDIABETIC PREPARATIONS

Herbal teas

▶ Herbal tea for DIABETICS (Megafyt Pharma)

- ▶ 20 x 1.5 g
- ▶ Galegae herba
Phaseoli fructus sine semine
Myrtilli folium
Urticae folium
Salviae folium
Taraxaci radix



▶ Pavel VÁŇA DIABETIC TEA

- ▶ 40 X 1.6 g
- ▶ Myrtilli herba
Galegae herba
Inulae radix



ANTIDIABETIC PREPARATIONS

Herbal teas

▶ DIAHERB Herbal Tea (Grešík)

- ▶ loose tea 50 g or tea bags
- ▶ Myrtilli folium
- Phaseoli fructus sine semine
- Urticae folium
- Galegae herba
- Cichorii radix
- Graminis rhizoma
- Bardanae radix
- Salviae folium
- Equiseti herba
- ▶ too many plant drugs!



▶ Diabetic tea with cinnamon (Fytopharma, Slovakia)

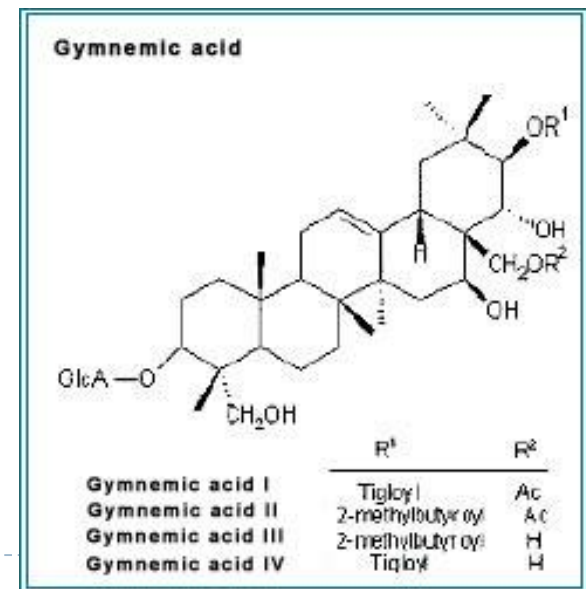
- ▶ 20 X 1.5 g
- ▶ Myrtilli herba
- Cichorii radix
- Cinnamomi cortex



Herbal remedies for DIABETES

Gymnemaefolium

- ▶ *Gymnema sylvestre*, Asclepiadaceae, „gurmar“
- ▶ a woody climbing plant native to the tropical forests of southern and central India
- ▶ chewing the leaves suppresses the sensation of sweet – „sugar-killer“
- ▶ has been used in Indian herbal medicine as a treatment for diabetes for nearly 2.000 y.
- ▶ active principles: **gymnemic acids** (oleanane-type triterpenoid saponins)
- ▶ inhibition of glucose absorption, stimulation of insulin secretion (due to regeneration of the pancreatic B cells), increase of glucose utilization



ANTIDIABETIC PREPARATIONS

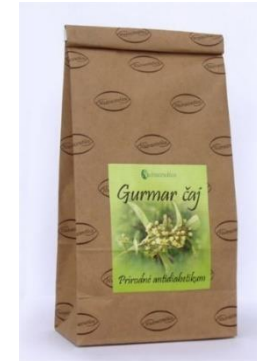
Herbal teas

- ▶ Diabetic tea with gymnema (Leros)
 - ▶ 10 (20) tea bags x 1g
 - ▶ Myrtilli herba 30 %
 - ▶ Galegae herba 15 %
 - ▶ Rooibos (*Aspalathus linearis*) 10 %
 - ▶ Phaseoli fructus sine semine 10 %
 - ▶ Myrtilli fructus 10 %
 - ▶ Polygoni avicularis herba 10 %
 - ▶ Salviae officinalis herba 5 %
 - ▶ Liquiritiae radix 5 %
 - ▶ **Gymnema folium 5 %**



Herbal remedies for DIABETES

- ▶ **GURMAR tea (Nutraceutica)**
 - ▶ loose tea – 150 g
 - ▶ drink warm; 2-3 cups per day
- ▶ **Edenpharma GYMNEMA SYLVESTRE (Medinterra)**
 - ▶ oral capsules
 - ▶ 350 mg of herbal extract (25%)
- ▶ **GURMAR 50 cps. (Brainway Inc.)**
 - ▶ gelatine capsules
 - ▶ 200 mg of herbal extract in 1 capsule
 - ▶ 1-3 capsules per day

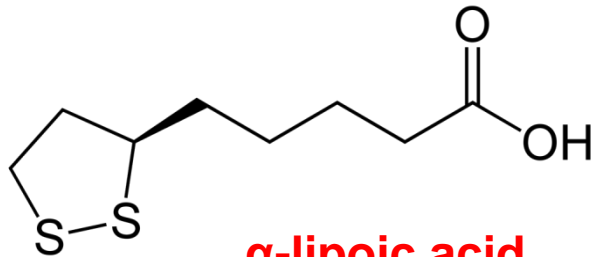


Herbal remedies for DIABETES

▶ DIABEN

(Advance Nutraceuticals)

- ▶ oral capsules
- ▶ *Gymnema sylvestre*, „gurmar“
- ▶ cinnamon – contains chromium salts and polyphenolics that helps to decrease blood sugar
- ▶ α -lipoic acid – antioxidant properties (e.g. treatment of diabetic neuropathy)



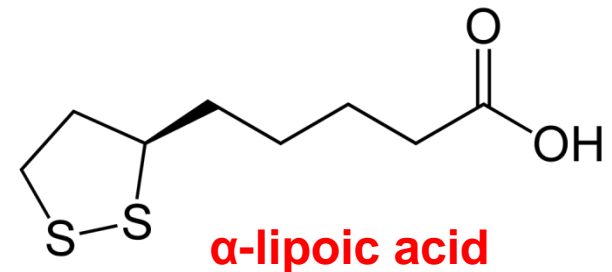
Active constituents	Content in 1 capsule
Gurmar (75% extract of <i>Gymnema sylvestre</i>)	200 mg
α -lipoic acid	100 mg
Cinnamomi cortex extract	100 mg
Gelatine capsules	

Herbal remedies for DIABETES

▶ DIALEVEL

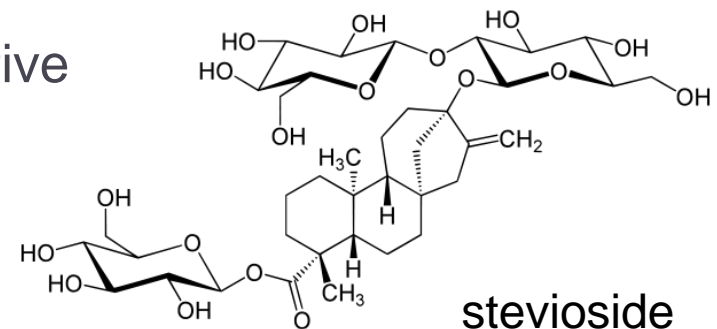
(Walmart)

- ▶ food supplement suitable for diabetics, prediabetics with general preventive measures (diets and exercising), for people with impaired glucose tolerance and for overweight people
- ▶ **α -lipoic acid** 200 mg
- ▶ ***Cinnamomum cassia* extract** 55.6 mg
- ▶ **Chromium(III)** 60 μ g
- ▶ use 1-2 tablets per day



Herbal remedies for DIABETES

- ▶ *Stevia rebaudiana*, Asteraceae
 - ▶ commonly known as „sweet leaf“, „sugar leaf“, „honey herb“, „yerba dulce“
 - ▶ leaves contain sweet-tasting substances that are 300 times sweeter than sugar (sucrose)
 - ▶ diterpene glycosides – mainly **stevioside**, **rebaudioside A**
 - ▶ used as a component of herbal teas and other remedies for diabetes treatment; as a dietary supplement and food additive (but some countries restrict its use as a sweetener)



Herbal remedies for DIABETES

▶ STEVIA

- ▶ natural sweetener – good solubility, nice taste
- ▶ suitable for diabetics, in diets
- ▶ available as tablets, in powder or liquid form
- ▶ one tablet contains usually about 7,5 mg of stevioside
- ▶ use maximally 2,5 mg of stevioside on each kg of body weight per day
- ▶ as a sweetener in some phytomedicinal products, e.g. Aromatica Herbal syrup with plantain leaf and stevia

▶ producers and brand names, e.g.:

- ▶ Advance Nutraceuticals - Steviadiet
- ▶ Dr. Popov – Fytostevin,
- ▶ Naturprodukt – Additiva, Teekanne – Kandisin,...



HEPATOPROTECTIVE DRUGS

LIVER = HEPAR

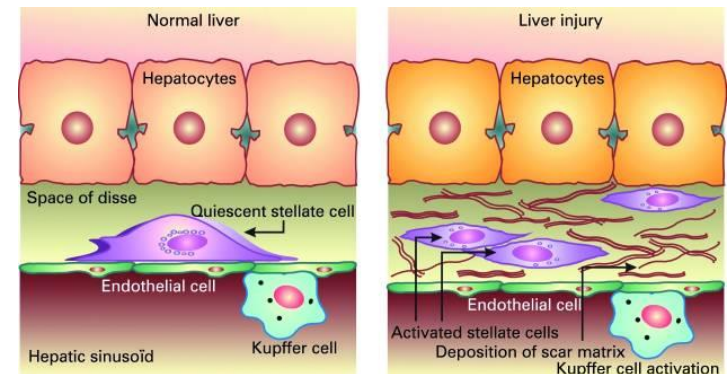
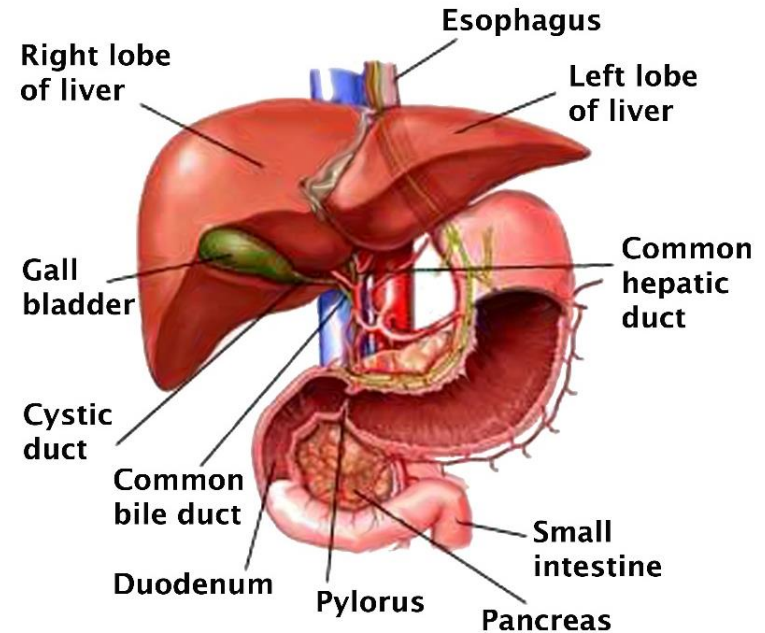
- ▶ a vital organ (gland) that performs essential functions related to digestion, metabolism, immunity and the storage of nutrients, e.g.:
 - ▶ synthesis of proteins, hormones, enzymes,...
 - ▶ production of biochemicals necessary for digestion (e.g. bile)
 - ▶ storage of glycogen, fatty acids, vitamins, minerals,...
 - ▶ decomposition of blood cells
 - ▶ detoxification
 - ▶ drug biotransformation and elimination



HEPATOPROTECTIVE DRUGS

LIVER = HEPAR

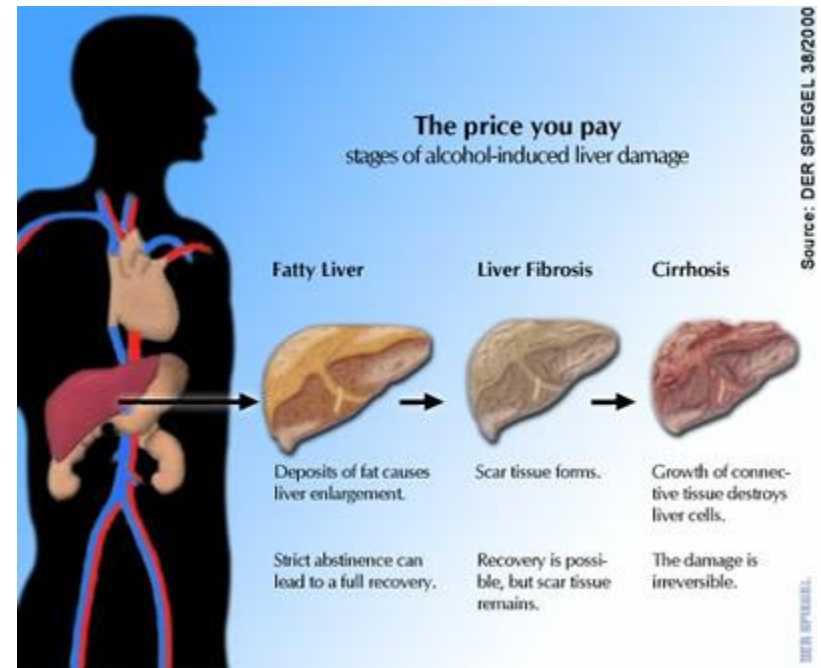
- ▶ is necessary for survival; without liver the tissues of the body would quickly die from lack of energy and nutrients
- ▶ the liver is the only human internal organ capable of natural **regeneration**; it has an incredible capacity for regeneration of dead or damaged tissues; it is capable of growing to restore its normal size and function
- ▶ in case of irreversible liver failure there is the only option of liver transplantation



HEPATOPROTECTIVE DRUGS

LIVER FAILURE

- ▶ **acute liver diseases** is less common but more deadly (mortality 80 %)
 - ▶ multi-organ failure, adult respiratory distress syndrome (ARDS), acute renal failure, cirrhosis
- ▶ **chronic hepatic disease** is the most common cause:
 - ▶ chronic active hepatitis
 - ▶ widespread necrosis from severe damage of hepatocytes (due to alcohol, poisonous mushrooms, microorganisms, hepatotoxic plants, medications,...)



HEPATOPROTECTIVE DRUGS

LIVER PROTECTION

- ▶ high-quality diet – eat organic foods (be careful about pesticides), use natural household products, limit harmful foods
- ▶ drink alcohol only in moderation (if at all)
- ▶ avoid smoking
- ▶ be careful with consumption of mushrooms and some plants (e.g. from the family Asteraceae, Boraginaceae...)
- ▶ prevention of viral infections (hepatitis B, C – vaccination)
- ▶ be careful with medications – e.g. paracetamol (acetaminophen)
- ▶ do physical exercises
- ▶ detoxify your body regularly
- ▶ **consider liver health supportive supplements**

HEPATOPROTECTIVE DRUGS

- ▶ **Silybi mariani fructus**
(*Cardui mariae fructus*)

Silybum marianum (*Carduus marianus*),
Asteraceae, milk-thistle herb

- ▶ 1.5-3% **silymarin**, a mixture of various flavanone derivatives (flavolignans) present only in the fruit – the principal components are silybin, silichrystin, silydianin, dehydrosilybin, silybinomer
- ▶ as hepatoprotective agent – provides relief for chronic liver problems; protects and promotes the growth of liver cells, helps to reduce the level of fat in the liver; antioxidative properties.



HEPATOPROTECTIVE PREPARATIONS

Herbal teas

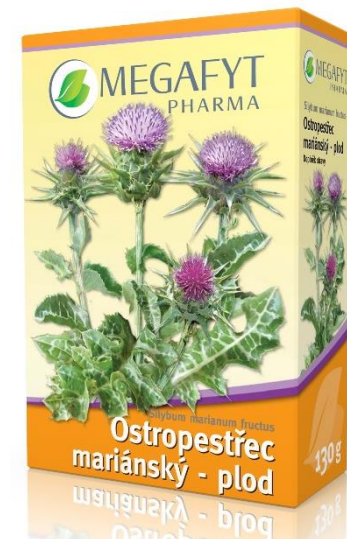
▶ Milk thistle fruit (Leros)

- ▶ loose tea, 150 g
- ▶ **Boil** 1 teaspoon of the drug for 5 minutes in $\frac{1}{4}$ L of water; allow to steep for 10 minutes in a covered container.
- ▶ Always prepare a fresh serving.
- ▶ As a dietary supplement, consume 1 cup per day.



▶ Milk thistle fruit (Megafyt Pharma)

- ▶ loose tea, 130 g
- ▶ pour boiling water over the **crushed** fruit; after 10-15 min passed through a strainer



HEPATOPROTECTIVE PREPARATIONS

Herbal teas

▶ LIVER Herbal tea (Megafyt Pharma)

- ▶ 20 x 1.5 g
- ▶ **Silybi mariani fructus**
Coriandri fructus
Schisandrae fructus
Rooibos (Aspalathi herba)
Taraxaci radix cum herba
Menthae piperitae herba
Cynarae flos
Curcumae rhizoma
soluble silymarin (4 %)



▶ LIVER Herbal tea with helichrysum (Apotheke)

- ▶ 20 x 1.5 g
- ▶ Helichrysi flos (Stoechados flos)
Cardui benedicti herba
Agrimoniae herba
Taraxaci radix
Foeniculi fructus
Menthae piperitae herba
Cichorii radix



HEPATOPROTECTIVE PREPARATIONS

▶ FLAVOBION

POR TBL FLM 50X70MG
(Takeda GmbH, Germany)

- ▶ **Silymarinum** 70 mg in one coated tablet
- ▶ SUKL code: 0163138
OTC medicinal product
- ▶ ATC: A05BA03 (Silymarin)

- ▶ Indications: auxiliary treatment of chronic persistent and active hepatitis, liver cirrhosis, toxic-metabolic liver injuries (liver steatosis, poisoning,...)
- ▶ no evidence of toxicity – suitable for long-term usage
- ▶ dosage: 1-2 tablets 3 times daily
- ▶ CI: hypersensitivity to any component, not suitable for children up to 5y.



HEPATOPROTECTIVE PREPARATIONS

▶ LAGOSA

POR TBL FLM 50X150MG
(Wörwag Pharma, Germany)

- ▶ Cardui mariae fructus extractum siccum (35-40:1)
204 mg (= **150 mg of silymarin**)
- ▶ SUKL code: 0019570
- ▶ ATC: A05BA03
- ▶ on medical prescription only



- ▶ Indications: see FLAVOBION
- ▶ Dosage: depending on the severity of the disease and the treatment phase use 3 to 6 mg of silymarin/kg of body weight per day – 1 tablet twice (up to 3 times) per day. The interval between doses should be at least 4 hours. Treatment with the initial dose lasts for 1-6 weeks, once the condition is improved, the daily dose may be reduced. The total duration of treatment may last from 3 months to 1 year.
- ▶ The tablets are taken after a meal, swallowed whole, not blown.

HEPATOPROTECTIVE PREPARATIONS

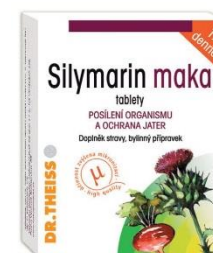
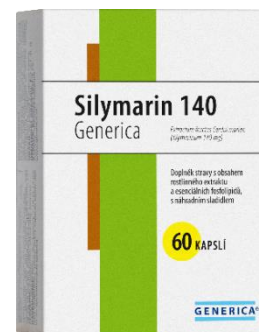
- ▶ **LIPOVITAN S tbl.** (Herbacos-Bofarma)
 - ▶ *Silybum marianum* fructus extract 80% (140 mg of silymarin)
 - ▶ maximal daily dose of silymarin = 420 mg
- ▶ **LIPOVITAN Duo tbl.** (Herbacos-Recordati)
 - ▶ cholin 255 mg
 - ▶ SIM complex (silymarin 65 mg, inositol 50 mg, L-methionin 25 mg)
 - ▶ B vitamins (B1, B2, B3, B5, B6, B12), vit. E
- ▶ **SILYMARIN DUO** (DaVinci Academia)
 - ▶ oral capsules
 - ▶ *Silybum marianum* fructus extract
 - ▶ *Scutellaria baicalensis* root extract



doplňěk stravy

HEPATOPROTECTIVE PREPARATIONS

- ▶ **SILYMARIN 140 (Generica)**
 - ▶ 60 capsules
 - ▶ *Cardui mariae fructus extractum* 175 mg (silymarinum 140 mg)
+ essential phospholipids 40 mg
- ▶ **Dr. Theiss SILYMARIN forte (Generica)**
 - ▶ for liver and veins protection
 - ▶ silymarin, blackcurrant seed oil, mixture of ω -3 and ω -6 fatty acids
- ▶ **Dr. Theiss SILYMARIN**
 - ▶ + yacon (*Polymnia sonchifolia*)
 - ▶ + maca (*Lepidium meyenii*, Brassicaceae)
 - ▶ + Selenium, + vit. D



HEPATOPROTECTIVE PREPARATIONS

▶ LIVERAX

(Advance Nutraceuticals)

- ▶ oral capsules
- ▶ *Astragalus membranaceus*
 - used in Chinese traditional medicine for favourable activities on immune system and liver



Active constituents	Content in 1 capsule
<i>Silybi mariani fructus</i> (content of silymarin 80 %)	200 mg
<i>Astragalus membranaceus</i>	50 mg
Cholin	50 mg
Curcuma	50 mg
α -lipoic acid	20 mg

HEPATOPROTECTIVE PREPARATIONS

▶ ESSENTIALE FORTE N POR CPS DUR (Sanofi-Aventis)

- ▶ 1 capsule contains:
phospholipida sojae praeparata
300 mg
- ▶ SUKL code: 0125752
OTC medicinal product
- ▶ ATC: A05BA



- ▶ essential soya phospholipids
- ▶ Indications: toxic-metabolic liver damage, hepatitis. In the small intestine, phospholipids are absorbed, transformed into phosphatidylcholine, which enters the liver through the lymphatic and blood vessels. Here it participates in regeneration of damaged liver cells, restoration of cell membranes.
- ▶ Dosage: 2 capsules 3 times a day
- ▶ KI: Hypersensitivity to soya, peanut, or any other excipient
- ▶ Treatment with the product can not prevent liver damage due to the use of harmful substances (e.g. alcohol) !!