



EVROPSKÁ UNIE



MINISTERSTVO ŠKOLSTVÍ,  
MLÁDEŽE A TĚLOVÝCHOVY



OP Vzdělávání  
pro konkurenceschopnost

INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ

# PHYTOPHARMACEUTICALS

academic year 2018/19

## LECTURE 6 – Preparations used to treat some circulatory disorders, venous diseases,...

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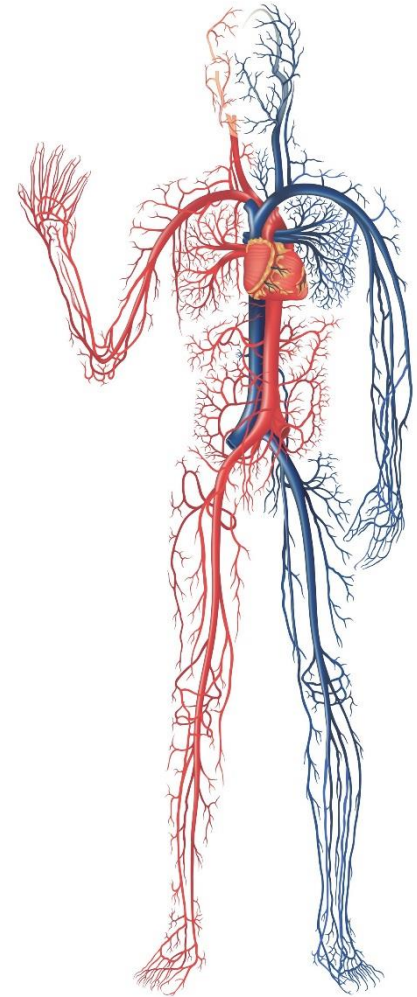
# PHYTOPHARMACEUTICALS

## in the treatment of some CIRCULATORY DISORDERS

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### Circulatory disorders

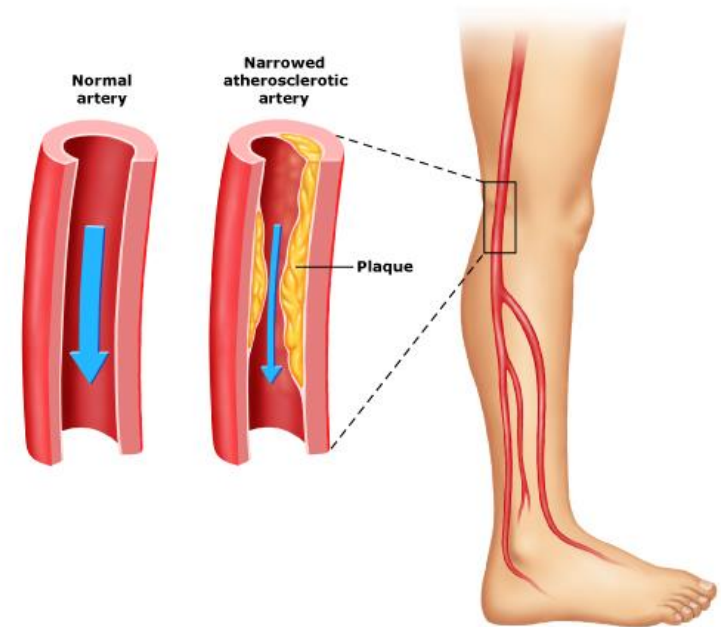
- ▶ is any disorder or condition that affects circulatory system
- ▶ Circulatory disorders can arise from problems with the heart, blood vessels or the blood itself. Disorders of the circulatory system generally result in **diminished flow of blood** and **oxygen supply** to the tissues.
- ▶ They can be classified into 5 groups: traumatic, compressive, occlusive, tumors/malformations and vasospastic (spasm of the artery, which reduces its diameter and thus its blood flow)



# PHYTOPHARMACEUTICALS

## in the treatment of some CIRCULATORY DISORDERS

- ▶ **Peripheral vascular diseases (PVDs)** are circulation disorders that affect blood vessels outside of the heart and brain. PVD typically strikes the veins and arteries that supply „lower body“, the arms, legs = peripheral vessels.
  - ▶ In PVD, blood vessels are narrowed. Narrowing is usually caused by arteriosclerosis = a condition where plaque builds up inside a vessel. It is also called “hardening of the arteries.” Plaque decreases the amount of blood and oxygen supplied to the arms and legs.
  - ▶ As plaque growth progresses, clots may develop. This further restricts the affected vessel. Eventually, arteries can become obstructed.

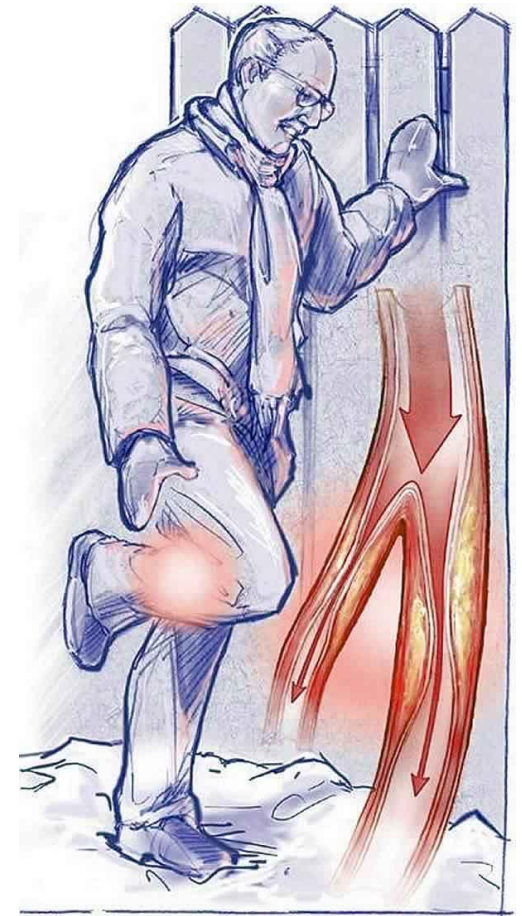


# PHYTOPHARMACEUTICALS

## in the treatment of some CIRCULATORY DISORDERS

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- ▶ PVD that develops only in the arteries is called **peripheral arterial disease (PAD)**. This is the most common form of PVD.
- ▶ PVD may also be referred to as:
  - ▶ arteriosclerosis obliterans
  - ▶ arterial insufficiency of the lower limbs (legs)
  - ▶ claudication
  - ▶ intermittent claudication

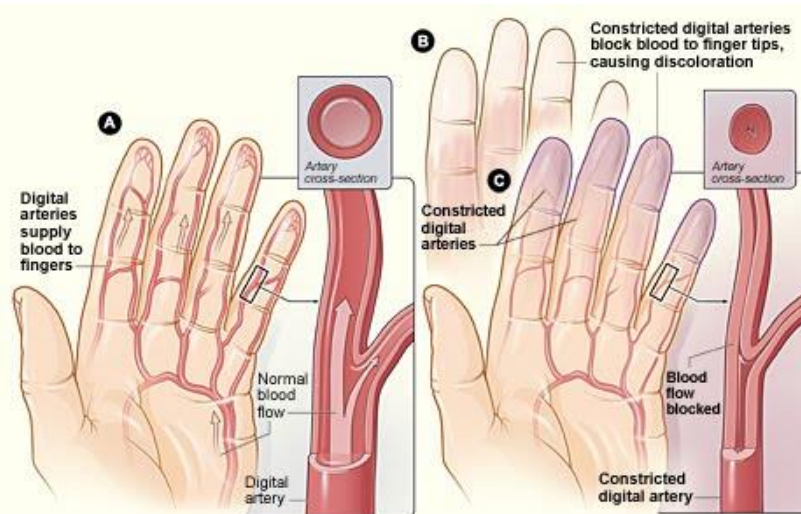


# PHYTOPHARMACEUTICALS

## in the treatment of some CIRCULATORY DISORDERS

### ▶ Raynaud's phenomenon

- ▶ is believed to be the result of vasospasms that decrease blood supply to the respective regions
- ▶ in response to cold or emotional stress (vasoneurosis), causing discoloration of the fingers, toes, and occasionally other areas.



# PHYTOPHARMACEUTICALS

## in the treatment of some CIRCULATORY DISORDERS

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- ▶ Preparations containing Ginkgo bilobae extract
  - ▶ Ginkgo dry extract (22.0-27.0 % flavonoids, 2.6-3.2 % bilobalide, 2.8-3.4 % ginkgolides) = **EGb 761**
- ▶ It has especially following effects:
  - ▶ vasodilating of small arteries (it widens them)
  - ▶ rheological (it improves rheological properties of blood)
  - ▶ it decreases agglomeration of blood platelets and red blood cells
  - ▶ promotes venous tone (tension)
  - ▶ decreases increased permeability of capillaries and so acts against oedemas
  - ▶ improves intracellular utilization of glucose and also acts against the presence of so-called free radicals.



# PHYTOPHARMACEUTICALS

## in the treatment of some CIRCULATORY DISORDERS

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### ▶ **EGb 761**

#### ▶ Indications: vascular disorders

- ▶ peripheral arterial occlusive disease of legs (claudication), vasospasms, Raynaud's phenomenon
- ▶ sensory disorders of vascular and involution origin (tinnitus, vertigo, hearing and sight disorders)
- ▶ treatment of cerebral vascular insufficiency – dementia, mental losses due to organic brain syndrome

#### ▶ TANAKAN (Ipsen Ltd.)

- ▶ SUKL code : 0062914; ATC: N06DX02

#### ▶ TEBOKAN (Dr. Willmar Schwabe GmbH & Co)

- ▶ SUKL code: 0075124; ATC: N06DX02



# *Ginkgo bilobae folium*

## ▶ food supplements

- ▶ solid forms – tablets, capsules, content usually 40, 80 mg to 120 mg
- ▶ producers: Walmark, Dr. Müller Pharma, MedPharma, NefDesanté, Swiss, GS, Favea...
- ▶ composite preaparations, e.g.:
  - ▶ GINKOPRIM (Walmark) – contains 40 mg Egb 761 and 150 mg Mg<sup>2+</sup>
- ▶ liquid preparations – herbal drops, tinctures
- ▶ herbal teas





# PHYTOPHARMACEUTICALS

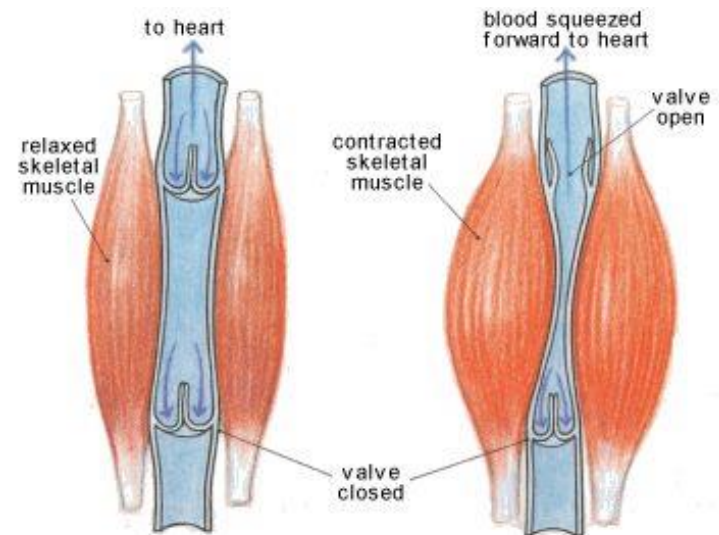
## in the treatment of VENOUS DISEASES

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### VENOUS DISEASES

- ▶ refers to all conditions related to or caused by veins that become diseased or abnormal
- ▶ about **15 percent** of adult population is affected
- ▶ In the normal circulation, arteries carry oxygen rich blood from your heart to the body, and veins return the blood to your heart.

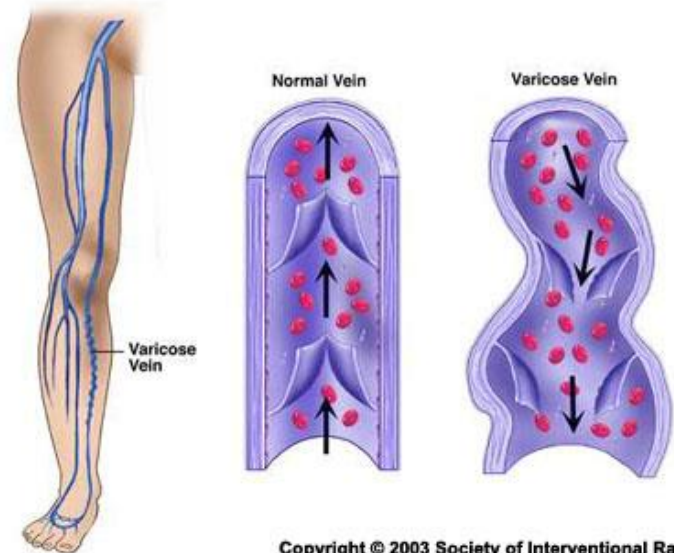
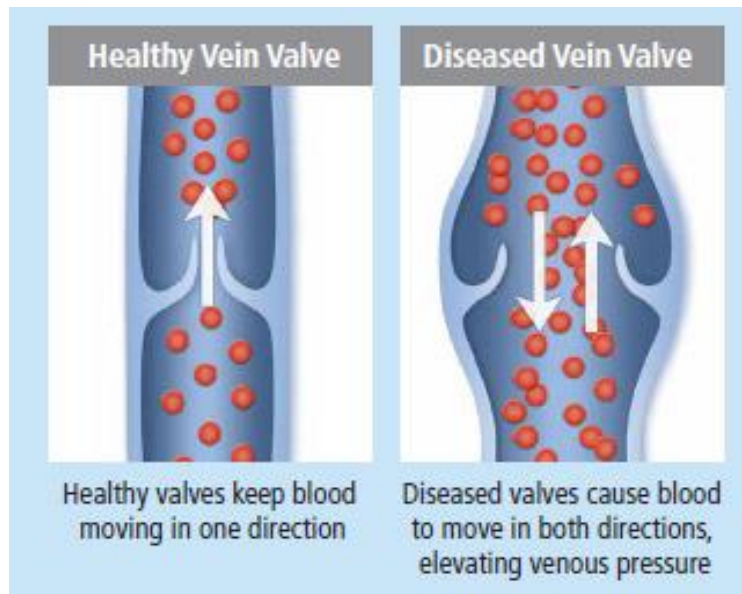
Veins have one-way valves along their length to keep the blood flowing to the heart. As **muscles contract**, the blood is squeezed forward in the veins. When muscles relax, the **valves shut to prevent blood from flowing backward**.



# PHYTOPHARMACEUTICALS

## in the treatment of VENOUS DISEASES

- ▶ If the vein walls become weak or damaged, or if the valves are stretched or injured, the system stops working normally and the blood begins to flow backward when the muscles relax. This creates unusually high pressure in the veins, resulting in even more stretching, twisting, and swelling of veins.

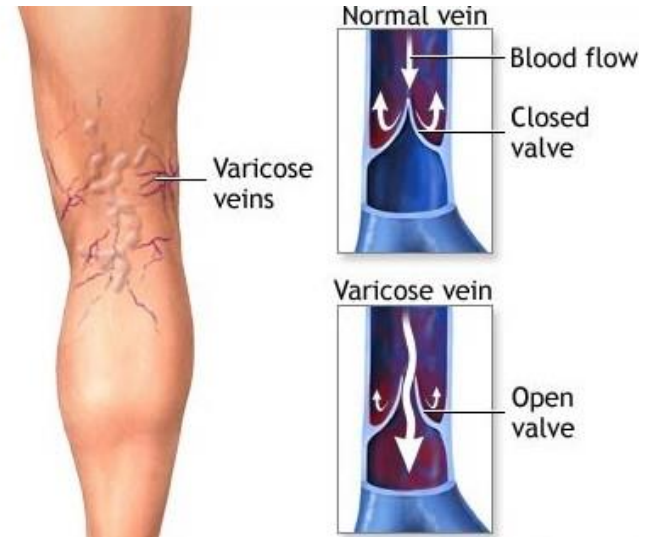


# PHYTOPHARMACEUTICALS

## in the treatment of VENOUS DISEASES

Venous diseases of lower limbs (legs) include:

- ▶ spider veins, varicose veins
- ▶ leg swelling, leg pain
- ▶ chronic venous insufficiency (CVI)
- ▶ leg skin changes, leg ulcers
- ▶ phlebitis = inflammation of the vein, usually accompanied with thrombosis – **thrombophlebitis**
- ▶ **phlebotrombosis** – deep vein thrombosis

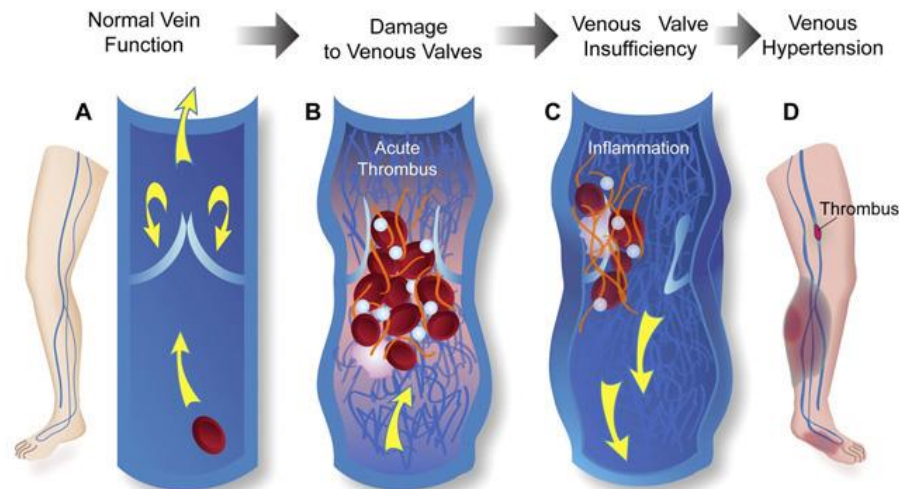


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# PHYTOPHARMACEUTICALS

## in the treatment of VENOUS DISEASES

- ▶ Venous diseases are caused by a damage of the vein wall – lower elasticity and tensile strength of the vein wall → increased **permeability** and **fragility** of the capillaries
- ▶ → local bleeding, swelling, inflammation, thrombosis
- ▶ The poorly functioning valves allow blood to flow backward, which causes pooling (congestion) in the veins, worse venous return → increasing pressure inside the veins → veins become „leaky“



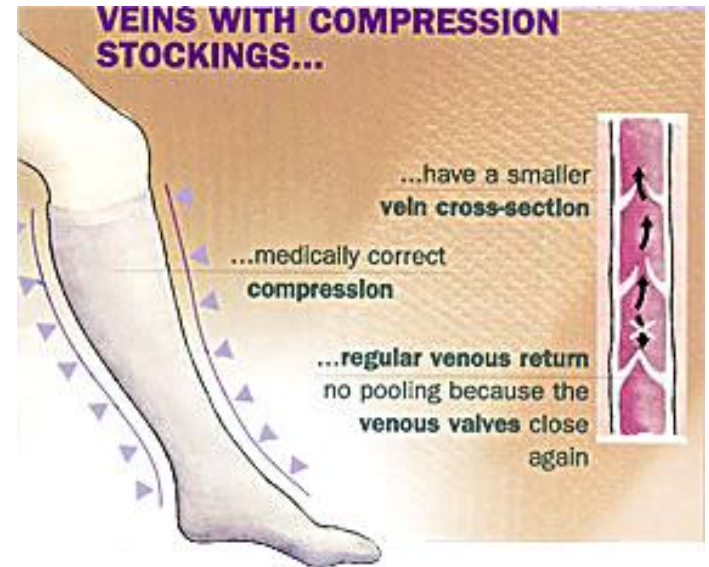
# PHYTOPHARMACEUTICALS

## in the treatment of VENOUS DISEASES

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### Therapy of venous diseases:

- ▶ supporting of venous return
  - ▶ physical training
  - ▶ massage
  - ▶ compression stockings
- ▶ sclerotherapy, endovenous laser ablation, phlebectomy,...
- ▶ phytomedicines – preparations with especially **FLAVONOIDS** and **SAPONINS** content



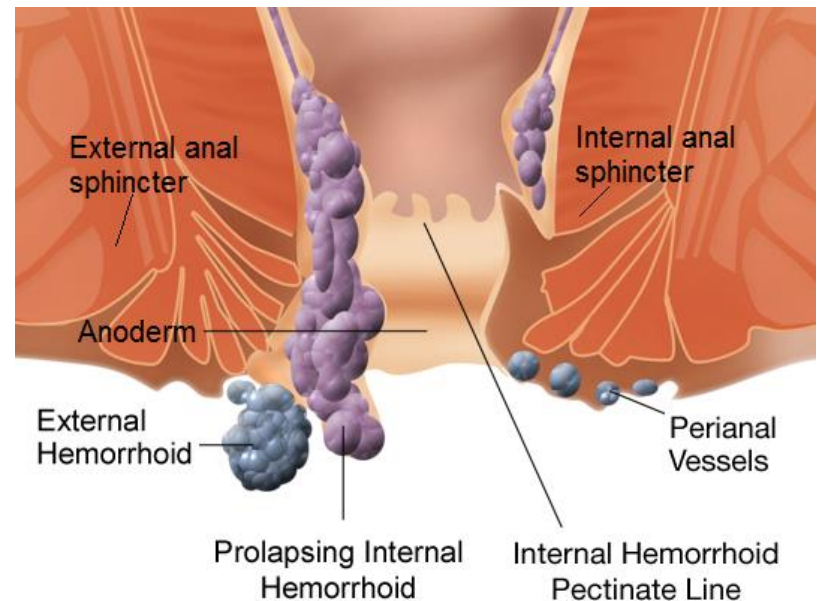
# PHYTOPHARMACEUTICALS

## in the treatment of VENOUS DISEASES

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### HAEMORRHOIDS

- ▶ smaller varicose veins in the rectum
- ▶ symptoms: itching, skin flare, pain discharge,...
- ▶ natural compounds/plant extracts containing mainly **flavonoids** and **saponines** that provides beneficial influence on venous tonus and venous wall elasticity
- ▶ **tannins** have astringent effect in case of bleeding (only external application forms)



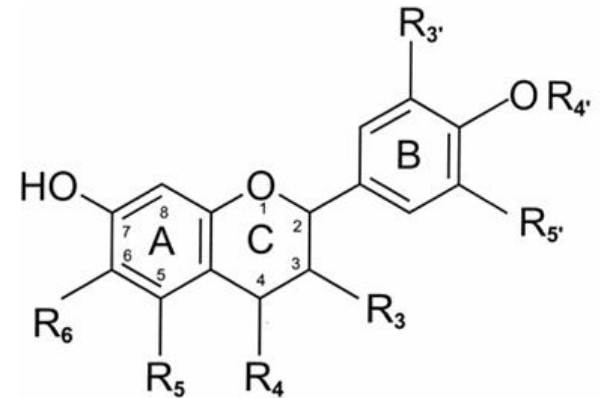
# PHYTOPHARMACEUTICALS

## in the treatment of VASCULAR DISEASES

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### **FLAVONOIDS** in the treatment of venous diseases:

- ▶ prolong the vasoconstrictor effect of norepinephrine on the vein wall, increases venous tone
- ▶ improve lymphatic drainage
- ▶ reduce capillary hyperpermeability and increase capillary resistance by protection the microcirculation from damaging processes
- ▶ reduce the expression of endothelial adhesion molecules, and inhibit the adhesion, migration, and activation of leukocytes at the capillary level



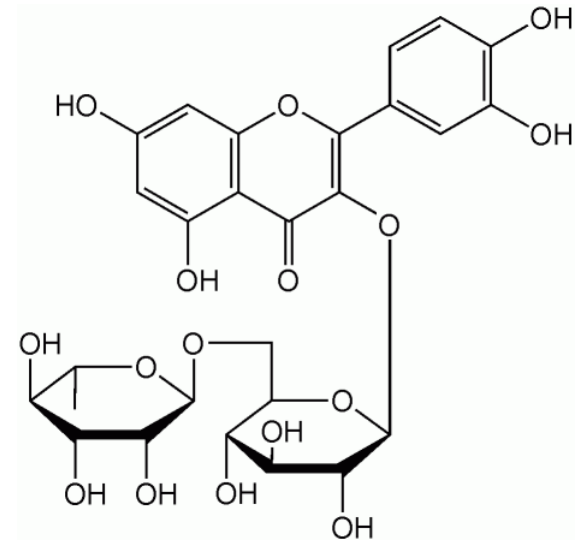
# PHYTOPHARMACEUTICALS

## in the treatment of VASCULAR DISEASES

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The most frequently used flavonoids in the treatment of venous diseases:

- ▶ **RUTIN, RUTOSIDE** (quercetin-3-rutinoside)  
rutinose = disaccharide of rhamnose and glucose
- ▶ **TROXERUTIN** = rutin derivative  
(hydroxyethylrutoside)
- ▶ **DIOSMIN** (diosmetin-7-rutinoside)
- ▶ **HESPERIDIN** (hesperetin-7-rutinoside)
- ▶ **QUERCITRIN**  
(quercetin-3-rhamnoside)
- ▶ Preparations: mostly oral solid forms containing isolated compounds/flavonoid fractions or plant extracts



**RUTIN**



# PHYTOPHARMACEUTICALS

## in the treatment of VASCULAR DISEASES

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Plants with high content of RUTIN

- ▶ Japanese pagoda *Sophora japonica*  
Sophorae flos
- ▶ tree  
contains about 20 % of rutoside
- ▶ Buckwheat  
*Fagopyrum esculentum*, *F. sagittatum*,  
Fabaceae – Fagopyri herba
  - ▶ contains about 1-2 % of rutoside
  - ▶ difficult isolation
- ▶ citrus fruits – source of **rutin**,  
**diosmin**, **hesperidin**



# PHYTOPHARMACEUTICALS

## in the treatment of VASCULAR DISEASES

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### ▶ ASCORUTIN

POR TBL FLM 50 (Zentiva)

- ▶ Acidum ascorbicum 100 mg  
Rutosidum trihydricum 20 mg
- ▶ SUKL code: 0096303  
OTC medicinal product
- ▶ ATC: C05CA51 (Rutoside, combinations)
- ▶ use 1-2 tablets 3 times daily



### ▶ RUTIN 50 mg tbl. (Walmart)

- ▶ food supplement
- ▶ use 1 tbl daily



### ▶ RUTIN 50 mg tbl. (Nature's Bounty)



# PHYTOPHARMACEUTICALS

## in the treatment of VASCULAR DISEASES

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- ▶ **VENAVIT tbl. (FAVEA)**
- ▶ **1 tablet (500 mg) contains:**
  - ▶ Rutoside 50 mg
  - ▶ Ascorbic acid/ Ca<sup>2+</sup> salt 20 mg
  - ▶ Ginkgo biloba extr. siccum 10 mg
  - ▶ Lecithin 5 mg
  - ▶ Beta-carotene 0.1 mg
  - ▶ citrus pectin 20 mg
- ▶ use 1 tablet 2 times daily
- ▶ not available at present



# PHYTOPHARMACEUTICALS

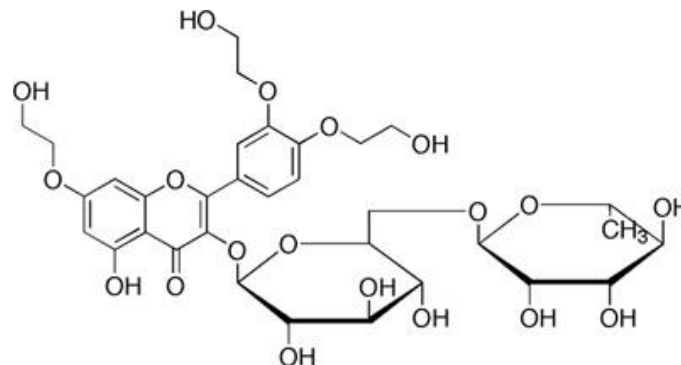
## in the treatment of VASCULAR DISEASES

### ▶ CILKANOL POR CPS DUR 30X300MG (ZENTIVA)

- ▶ Troxerutinum 300 mg
- ▶ SUKL code: 0004336  
OTC medicinal product
- ▶ ATC: C05CA04
- ▶ dosage: 1 capsule 3 times  
per day

### ▶ VENORUTON 300 POR CPS DUR 50X300MG (NOVARTIS)

- ▶ Oxerutinum 300 mg
- ▶ SUKL code: 0015297  
OTC medicinal product
- ▶ ATC: C05CA04
- ▶ dosage: starting dose 900-1200 mg  
per day (= 3-4 capsules)



# PHYTOPHARMACEUTICALS

## in the treatment of VASCULAR DISEASES

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- ▶ **DETRALEX 30X500MG POR TBL FLM**  
(Les Laboratoires Servier)
  - ▶ Flavonoidorum fractio purificata micronisata: Diosminum 450 mg, Flavonoida 50 mg (determined as Hesperidinum)
  - ▶ SUKL code: 0132633
  - ▶ medical prescription-only product
  - ▶ ATC: C05CA53 (Diosmin, combinations)



# PHYTOPHARMACEUTICALS

## in the treatment of VASCULAR DISEASES

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- ▶ **DIOREX 60X500MG**  
(Glenmark Pharmaceuticals)
  - ▶ micronized purified flavonoid fraction  
(MPFF = Diosmin 450 mg,  
Hesperidin 50 mg)



- ▶ **MOBIVENAL micro Simple tbl.**  
(VULM, Slovakia)
  - ▶ MPFF = Diosmin 450 mg,  
Hesperidin 50 mg



# PHYTOPHARMACEUTICALS

## in the treatment of VASCULAR DISEASES

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- ▶ **ANTISTAX 360 MG**  
POR TBL FLM 30X360MG  
(Boehringer Ingelheim)
  - ▶ Vitis viniferae rubrae folii extractum aquosum siccum (4-6:1) 360 mg
  - ▶ SUKL code: 0023698
  - ▶ OTC medicinal product
  - ▶ ATC: C05CA (Bioflavonoids)
  - ▶ Dosage: 1 tablet daily (in the morning before breakfast).  
For fast effect – increase dosage to 2 tablets daily (for 3 weeks)
  - ▶ available also as cooling gel, spray



# PHYTOPHARMACEUTICALS

## in the treatment of VASCULAR DISEASES

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### **Rusci radix** (syn. *Rusci rhizoma*)

*Ruscus aculeatus*, Ruscaceae

Butcher's broom

- ▶ **ruscogenins** = steroid saponins (min. 1 %)
- ▶ flavonoids, coumarins, sterols, triterpenes
- ▶ vasoprotective effect
- ▶ Indications: CVI (chronic venous insufficiency), varicose veins, haemorrhoids, swellings





# PHYTOPHARMACEUTICALS

## in the treatment of VASCULAR DISEASES

- ▶ **CYCLO 3 FORT POR CPS DUR 30**  
(Pierre Fabre Medicament Production)
  - ▶ Rusci extractum siccum (Butcher's broom extract) 150 mg
  - ▶ Hesperidinum methylchalconum 150 mg
  - ▶ Acidum ascorbicum 100 mg
  - ▶ SUKL code: 0098194
  - ▶ **!** prescription-only product
  - ▶ ATC: C05CA51
  - ▶ Dosage: 2-3 capsules a day



The image shows a screenshot of the Cyclo3Fort website. At the top, there is a navigation bar with the following links: ACCUEIL, L'INSUFFISANCE VEINEUSE, LE VEINOTONIQUE CYCLO 3 FORT, and LA DÉMARCHE DES LABORATOIRES PIERRE FABRE. The main content area features a woman sitting on a bed, a box of Cyclo3Fort capsules, and the product name and description. The box is labeled 'Cyclo3Fort JAMBES LOURDES' and 'Traitement des troubles de la circulation veineuse'. The website also includes a 'DÉCOUVRIR' button and a footer with contact information and legal notices.

**Cyclo3Fort**  
Traitements des troubles de la circulation veineuse

**Cyclo3Fort**  
JAMBES LOURDES  
Traitement des troubles de la circulation veineuse

**Cyclo3Fort**  
Brevet exclusif  
Hesperidines méthyl-chalcones  
Aide osseuse

Traitement des troubles de la circulation veineuse

DÉCOUVRIR

PIERRE FABRE | SITES INTERNET DU GROUPE | VISA GP N° : 0434610X112 | SERVICES | MENTIONS LÉGALES | PLAN DU SITE | CRÉDITS

Cyclo 3 Fort est un médicament de la classe des veinotoniques destiné au traitement des troubles de la circulation veineuse (jambes lourdes, douleurs, impatiences du primodécubitus). Lire attentivement la notice. Demander conseil à votre pharmacien. Si les symptômes persistent, consulter votre médecin. Les traitements veinotoniques sont des traitements symptomatiques complémentaires des mesures d'hygiène de vie limitant l'insuffisance veineuse et des moyens de contention (bas, collants...)

# PHYTOPHARMACEUTICALS

## in the treatment of VASCULAR DISEASES

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- ▶ **VALOVEN Diosmin: Hesperidin forte** (Valosun)
  - ▶ micronized purified flavonoid fraction (MPFF):  
Diosmin 450 mg, Hesperidin 50 mg  
Butcher's broom extract (*Ruscus aculeatus*) 110 mg  
L-ascorbic acid (vitamin C) 70 mg
  - ▶ 1 tablet once daily during meals





# PHYTOPHARMACEUTICALS

## in the treatment of VASCULAR DISEASES

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### ▶ AESCIN-TEVA

POR TBL ENT 30X20MG  
(TEVA Pharmaceuticals)

- ▶ Escinum alfa 20 mg
- ▶ SUKL code: 0107806
- ▶ OTC medicinal product
- ▶ ATC: C05CX
- ▶ Dosage: 40 mg (2 tablets)  
3 times per day



### ▶ REPARIL-DRAGÉES

POR TBL OBD 40X20MG  
(Madaus)

- ▶ Escinum alfa 20 mg
- ▶ SUKL code: 0057352
- ▶ OTC medicinal product
- ▶ ATC: C05CX
- ▶ Dosage: 40 mg (2 tablets)  
3 times per day



# PHYTOPHARMACEUTICALS

## in the treatment of VASCULAR DISEASES

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- ▶ **AESCIN VULM tbl.**  
(VULM, Slovakia)
  - ▶ Escinum alfa 30 mg (150 mg of standardized extract of horse-chestnut seed – 20 %)
  - ▶ coated tablets
  - ▶ Dosage: 1 tablet 3 times a day
  
- ▶ **ESCIRUTIN tbl.**  
(STYLPHARMA)
  - ▶ Aescins (aescin complex) 30 mg
  - ▶ Rutoside 10 mg



# PHYTOPHARMACEUTICALS

## in the treatment of VASCULAR DISEASES

- ▶ **MOBIVENAL micro tbl.**  
(VULM, Slovakia)
  - ▶ MPFF: Diosmin 450 mg, Hesperidin 50 mg, Escinum alfa 30 mg (150 mg Aesculi hippocastani extract 20%)
- ▶ **DIOSMINOL tbl.**  
(FAVEA)
  - ▶ MPFF: Diosmin 450 mg, Hesperidin 50 mg, 162 mg of standardized Aesculi hippocastani extract
- ▶ **HEMODIN (Valosun)**
  - ▶ MPFF: Diosmin /Hesperidin (90:10) 445 mg, Aesculi hippocastani extract (20%) 60 mg Troxerutin 15 mg Selenized yeast 25 mg, Inulin 175 mg



# PHYTOPHARMACEUTICALS

## in the treatment of VASCULAR DISEASES

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- ▶ **VENITAN** DRM CRM 1X50GM (Sandoz)
  - ▶ Hippocastani extr. siccum normatum – extracted with ethanol 60% (V/V) – 5 g in 100 g of hydrophilic cream
  - ▶ SUKL code: 0066788  
OTC medicinal product
  - ▶ ATC: V11 (Phytopharmaceuticals and animal products)
  - ▶ apply 1-3 times per day
- ▶ **HORSE CHESTNUT Gel** (Valosun)
  - ▶ *Aesculus hippocastanum* extr.  
Lavandulae etheroleum  
Cymbopogoni etheroleum and other natural volatile oils
  - ▶ apply 1-3 times per day



# PHYTOPHARMACEUTICALS

## in the treatment of VASCULAR DISEASES

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### ▶ VARIXINAL tbl. (Walmart)

- ▶ food supplement
- ▶ Horse chestnut - positive effect on venous functions (flow rate, distension, tonus).  
Butcher's broom and gotu kola support venous circulation in legs. Blueberries are known as effective antioxidants, which help to keep veins elastic and also may help to maintain vascular integrity. Composition is enriched by bioflavonoid hesperidin and vitamin C that is essential for normal function of blood vessels.
- ▶ ! enhanced amount of horse-chestnut extract

- ▶ Horse chestnut extract **1000 mg**  
(*Aesculus hippocastanum* seed)
- ▶ Butcher's broom extract 800 mg  
(*Ruscus aculeatus* root)
- ▶ Blueberries extract 200 mg  
(*Vaccinium myrtillus* fructus)
- ▶ Gotu kola extract 100 mg  
(*Centella asiatica* herb)
- ▶ Hesperidin 100 mg
- ▶ Vitamin C 250 mg





# PHYTOPHARMACEUTICALS

## in the treatment of VASCULAR DISEASES

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### ▶ VARIXINAL gel (Walmark)

- ▶ cosmetic product
- ▶ is recommended for people with symptoms of vascular insufficiency (feeling of heavy legs, frequent lumps, varicose veins, etc.)
- ▶ Enriched by extract of horse chestnut for proper blood circulation
- ▶ Massage the gel into your legs, apply when needed throughout the day.

- ▶ *Ruscus aculeatus* extract
- ▶ *Aesculus hippocastanum* extract
- ▶ *Centella asiatica* extract
- ▶ *Vaccinium myrtillus* fruit extract



# PHYTOPHARMACEUTICALS

## in the treatment of VASCULAR DISEASES

### ▶ VENUREGEN herbal tea

(Topvet)

- ▶ Fagopyri herba
- Ribes nigri folium
- Hibisci flos
- Meliloti herba
- Equiseti herba
- Millefolii herba



### ▶ TEA FOR VEINS

(Pavel Váňa)

- ▶ Fagopyri herba
- Sambuci nigri flos
- Violae tricoloris herba
- Agrimoniae herba
- Calendulae flos

