Antifibrinolytics
Plasma substitutes
Blood derrivatives
Haematopoietic growth factors
Veasoprotective drugs

Fibrinolysis

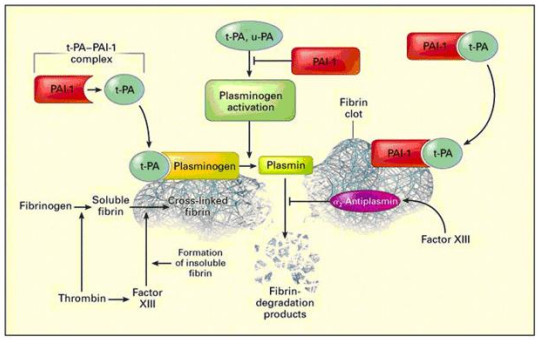
Starts simultaneously with coagulation (coagulum removal)

Plasmin plays major role, is present in inactive form in plasma, is incorporated into coagulum bound on fibrin

So as to prevent decomposition of coagulum is α2-antiplazmin (an bound on plasmin.

Plasmin is then (based on actual circumstances) activated by means of activators: t-PA produced in endothelium and u-PA (source: fibroblasts, epitelium, pneumocytes, placentalcells etc.)

Fibrinolysis

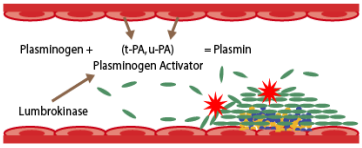


Fibrinolysis

The role of t-PA is regulation of intravascular coagulation, u-PA takes a part on proteolytic processes like tissue remodelation, tumor invasion, oocyte nidation, embryogenesis…

u-PA is metabolized to form urokinase – enzyme present in urine with the conserved ability to cleavage proteins

Activation of fibrinolysis is under the control of inhibitors of plasmin activators PAI 1-3 and nexin.



Fibrinolysis

on the surface of fibrin is bound complex t-PA + plasminogen + fibrin; activated fibrin is immediately inhibited by α2-antiplasmine

coagulum is cleavaged after tPA is released due to hemostasis

- this leads to release of small amount of plasmin, which disrupts fibrin structure and increase its surface and another plasminogen may be bound

- this prevails the activatory processes and coagulolysis is accelerated

Fibrinolysis

Fibrinolysis is balanced on the basis of ratio PA/PAI, which may be influenced by numerous exogenous factors:
physical activity, stress, fear, anger, smoking

↑↑ levels if PAI is in the morning with simultaneous ↓↓ t-PA

=> Most myocardial infarction occurs in the morning

Antifibrinolytics

Are preventing plasmin to bind on fibrin

Are used as adjuvants in coagulation factors supplementation in bleeding after surgery (e.g. tonsilectomy); or in stomatology surgery in haemophilic patients

AE: nausea
CI: DIC
ε-aminocapronic acid (EACA) ↓ plasminogen activation, p.o., i.v.
tranexamic acid, RMP Exacyl
p-aminometylbenzoic acid; RMP Pamba)
aprotinin – protease inhibitor – in bleeding due to defective fibrinolysis (antidote in fibrinolytics overdose) CVS surgery, pancreatitis

Plasma substitutes

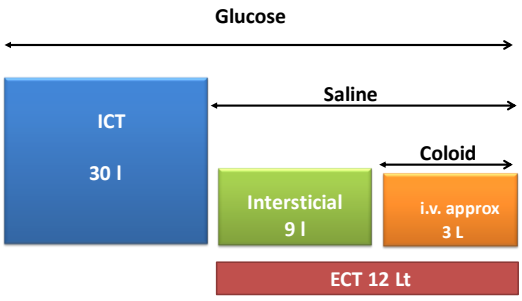
= „**plasma expanders**"

Used for temporaray fluid substitution (to incr. volume) (after bleeding, shock, hypovolaemia)

NOT in hypoxia, lack of ERYS (concentrate of ERYS, transfusion)

Requirements:
physiologically iniferent
AB ballance – neutral
sufficiently long lasting effect
physiologically eliminated /excreted
colloid-osmotic pressure
prevent trans -infection
price

Volume efficacy of plasma substitutes



„Fluid management“

- volume substitution→ intravascular liquid substitution for haemodynamics normalization (mostly **sol. of colloids**)
- liquid substitution → extracelular liquid defficiency based on the negative water balance (**crystalloids**)
- electrolytes substitutions → so as to compense changes in ECF and ICF composition (**balanced crystalloids solution**)

Plasma substitutes

crystalloids

hypertonic crystalloids

colloids a) non-human gelatine
dextran
starch

b) human albumin
plasma
blood derrivatives

Plasma substitutes

crystalloids

hypertonic crystalloids

colloids gelatine
dextran
albumin
starch

Plasma substitutes

Colloids

- influence coagulation
- risk of allergy and renal insufficiency
- More effective than crystalloids
- Shelf stable, affordable, cheap
- ↓ risk of transmission of infection
- Improve (or at least do not change) the rheological properties of blood
- Improves microcirculation and thus tissue perfusion
- Reduces swelling

Plasma substitutes

GELATINE

- first used 1915

- derrived from hydrolyzed beef collagen
- GLY-PRO-hydroxyPRO
  - 12 to 15 kDa fragments, cross links (polymers to 35 kDa)

- Circulation half-life about 4 hours

↑ Ca content (patients on digoxin!)

FDA banned 1978 (due allergic reaction)

Ethical issues: vegetarianism, muslims, hindu

risk of BSE not confirmed

Plasma substitutes

DEXTRAN

- Polysaccharide (Leuconostoc mesenteroides)

- Approximately 200,000 glucose units (1 → 6) = 1 molecule dextran
- Formed by the hydrolysis of about 60 kDa fragments

- The efficiency of approx 6 -8 h, excreted in urine

low molecular weight fragments improve rheological properties (reduced platelet aggregation ERYS +trombocytes)

Antigenic properties - can be resolved by use of low molecular weight dextran (1kDa)

Increases coagulation, ↑sedimentation

Plasma substitutes

Albumin (Human)

- 5%, 20%
- Less antigenic than plasma
- M.v. 66500 Da
- Binds water: 18 ml / g
- Areas of application: ascites puncture, neonatology, plasmapheresis

Plasma substitutes

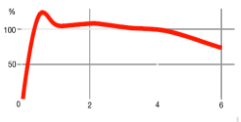
HES - hydroxyethyl starch

- 1 → 4 glycosidic bond
- M.W. 70/200/450 kDa
- origin: amylopectin component in corn starch
- affinity to endogenous glycogen, good biocompatibility
- hydroxyetylation: exchange of H for hydroxyethylic group (CH_3CH_2OH) → prolonged halflife of volume effect + increased solubility

Plasma substitutes

HES

- fragments excreted in the urine after splitting of amylase
- together with albumin lowest risk of anaphylaxis
- profile of effect



improve blood flow

side effects: pruritus (accumulation RES), bleeding complications

Blood derivatives

= ready made medicinal products derived from plasma

collected from donors at transfusion dept.
plasma is processed to the final form of blood products by fractionation in specialized centers.

a) albumin
b) immunoglobulins
c) concentrates of coagulation factor
d) concentrates of inhibitors

Blood derivatives

- Fractionation - a special method of plasma cutting into individual components

Raw material - fresh frozen plasma

Product - individual products

Testing of plasma - HBsAg, anti HCV, HIV

Testing of final product - PCR for HCV

Antiviral treatment - solvent detergent and heat treatment

Albumin

- Sterile solution containing 5% (250 ml, 100 ml, 50 ml) or 20% (100 ml, 50 ml) protein
- Name: Human Albumin 20%
- Human Albumin 5%
- Indications
  - treatment of circulating blood volume loss or insufficient production of albumin

dosage:
100 ml 20% albumin increases the circulating blood volume of 400 ml

Imunoglobulins

- monomeric and dimeric immunoglobulin G
- packing: 2.5 g, 5.0 g, 10.0 g
- Tradename: Flebogamma IV liquid, Kiovig
- Indications: primary and secondary antibody deficiency, prevention and supportive treatment of infections, treatment response in autoimmune diseases (ITP ...)

Prothrombin complex

- The concentrate of coagulation factors II, VII, IX, X, admixture AT III, PC, PS
- Packaging: 200 I.U.; 600 I.U.; 1200 I.U.
- tradename: Prothromplex
- Indications: prophylaxis and treatment of diseases accompanied by deficiency of coagulation factors (hepatopathy, DIC, need of antagonizing anticoagulant therapy ...)

Fibrinogen

- The concentrate of coagulation factor I
- Packaging: 1000 mg, 2000 mg
- tradename: Fibrinogen Immuno, Haemocompletan
- Indications: prophylaxis and treatment of congenital and acquired deficiencies of coagulation factor I,
  below 1.0 g / l - substituting for sepsis, invasive procedures ...
  below 0.6 g / l - substituting in the absence of hemorrhage

Antithrombin III

- The main inhibitor of thrombin and other activated coagulation factors
- Packaging: 500 I.U., 1000 I.U.
- name: Antithrombin III
- indications: congenital deficiency of AT III (prevention and treatment of TEN during high-risk situations - surgery, trauma, immobilization ...)
- acquired AT III deficiency (hepatopathy, sepsis, DIC, drug deficit ...)
- substituting the AT III decrease below 70 %

Factor VIII

- Highly purified factor VIII concentrate
- Packaging: 250 I.U., 500 I.U., 1000 I.U.
- tradename: Fanhdi, Immunate Stim Plus
- Indications: prophylaxis and treatment of bleeding in hemophilia A
- Dosage: 1 I.U. / kg increased levels of 1.5-2 % f.VIII

Factor IX

- Highly purified coagulation factor IX concentrate
- Packaging: 200 I.U.; 600 I.U.; 1200 I.U.
- tradename: Immunine
- Indications: prophylaxis and treatment of bleeding in hemophilia B
- Dosage: 1 IU / kg f IX levels increase by 0.8 %
- Dose calculation: the desired value x weight

Factor VII

- Concentrate of Coagulation Factor VII
- Packaging: 500 I.U.
- tradename: Factor VII Baxter
- Indications: prophylaxis and treatment of bleeding, deficiency of f. VII
- Cave ! due to the short half-life required more frequent application

von Willebrand factor

- Von Willebrand factor concentrate
- Packaging: 500 I.U., 1000 I.U.
- tradename: Haemate P
- Indications: von Willebrand's disease, hemophilia A

Factor VIIa

- Recombinant activated factor VII
- Packaging: 60 kI.U. (1.2 mg)
  120 kI.U. (2.4 mg)
  240 kI.U. (4.8 mg)
- tradename: NovoSeven
- Indications: bleeding in hemophilia with inhibitors, impaired thrombin generation from different causes of bleeding

DRUGS USED IN HAEMATOPOIESIS DISORDERS

Anaemia - *different classification approaches*

- Due to iron deficiency
- Due to lack of vitamin B12
- Due to lack of folic acid or. both
- Due to lack of pyridoxine

Anaema concerning changes of MCV (mean corpuscular volume)

Microcytic MCV ≤ 80 fL

Normocytic MCV = 80-100 fL

Macrocytic (megaloblastic) MCV ≥ 100 fL

Physiological values

	Men		Women
Hemoglobin (g/l)	135 - 175		120 – 160
Hematokrit (l/l)	0,40 – 0,50		0,36 – 0,46
Ery x 10^{12}/l	4,5 – 5,9		3,9 – 5,1
MCV (fl)		80 - 100	
MCH (pg)		27 - 32	
MCHC (g/l)		320 - 370	
RDW (%)		12 - 14	

Megaloblastic anaemia

Anemia pernicious
(approx 80 % of megaloblastic anaemias)

- It may also be induced by drug admin.! (e.g. azathioprin, trimethoprim, PPI)
- The most important treatment goal: adjustment of missing inventory vitamin
- Two forms of vitamin B12
  - cyanocobalamin
  - hydroxocobalamin
    - easily utilized for the cells
    - initial vitamin retention is better

Vitamins of megaloblastic anaemia treatment

	folic acid	B_{12}
Daily requirements	**200 ug**	**5 ug**
Reserves in the body	**5-10.000 ug**	**3.000 ug**
Total Reserve (days)	**25-50**	**600**

Vitamin B_{12} in pernicious anaemia

- Dose of 1 ug/day parenterally induce haematological remission
- Parenteral regime (2000 ug/6 weeks)

Oral treatment of pernicious anaemia with vitaminm B_{12}

⇒ patients refusing injections
⇒ patients with hypersensitivity
⇒ impairment of haemostasis

- 1% B12 absorbed independently of the intrinsic factor
- single dose of 300-1000 ug
- need for more rigorous monitoring of patients

Treatment with folic acid

- Folic acid tablets 10 mg
- 1 mg tablets would be sufficient
- minimal toxicity
- Contraindications: untreated vitamin B_{12} deficiency
- B_{12} deficiency may develop during treatment with folate
- neurological symptoms

Anemie sideropenic = a consequence of negative Fe balance

Oral treatment with ferrous or ferric preparations

- simpler, safer than parenteral treatment
- is safer than parenteral
- lower risk of overdose
- no risk of anaphylactic reactions
- potential for poisoning if abused
- long-term need substitution

Oral preparations with Fe

- **divalent Fe $^{++}$**
  - Fe-sulphate
  - Fe-fumarate
  - Fe-gluconate
  - Fe-chloride
- **trivalent Fe $^{+++}$**
  - ferric hydroxide
  - complex of Fe $^{+++}$ hydroxide
  - polymaltose

Bioavailability of Fe in oral treatment

- In the deficit, there is absorbed up to 15% of the administered Fe
- Proportion absorbed is reduced after adjustment deficit
- overdose risk only in hemochromatosis, (even in asymptomatic heterozygotes)

Oral preparations with Fe

- capsules, syrups, suspensions, drops, chewable tablets
- Vit. C increases the bioavailability of orally administered Fe
- Fiber, milk, coffee, tannins reduce the availability!

Influencing Fe oral bioavailability

- Increased resorption
  - fasting
  - together with ascorbic acid (commonly Org. acids)
  - with orange (citrus, fruits) juice
- Reduction of resorption
  - Food reduces absorption by up to 50%
  - especially with tea, milk or cereal
  - together with antacids -hydroxides of Al, Mg and Ca salts
  - with cholestyramine
  - with tetracyclines

Adverse effects of oral Fe preparations

- GIT: heartburn (pyrosis), nausea, abdominal pain, cramps up, diarrhea
  (in the elderly rather constipation)

  problems have approximately ¼ of patients

Dosing of Fe preparations

- Optimal initial dose of 200 mg Fe / day
  leads to the maximum recovery of Hb
  resorption up to 15% in a patient with sideropaenia
- resorption decreases after treatment of Fe deficiency
- resorption is increased in formulations with modified release
- The maintenance dose is lower (individual)
- In case of intolerance to try to form tablets, suspensions or other salt of Fe

Toxicity of Fe

- Accidentally ingested Fe
- lethal dose in children 3-10 g
- mucosal ulceration, bleeding in the gastrointestinal tract
- The course of intoxication Fe
  First stage: vomiting, diarrhea, melena, shock
  2nd: transient improvement for 6-24 h
  3rd: metabolic acidosis
  4th: bowel obstruction

Treatment of Fe intoxication

- always lavage 1% bicarbonate
- deferoxamine 3-5 g / 50 ml of water into the stomach via gastric probe
- Systemically deferoxamine 1 g i.v. / i.m. repeated after 4-6 hours
- or sc. / iv. infusion into max. dose 6 g / day

Treatment with parenteral Fe^{+++}

Indications: failure of oral therapy
patient does not tolerate iron orally
inflammation / ulceration of the stomach

rapid loss of Fe (unidentified cause)
disorder of resorption in the GIT

AE of parenteral Fe administration

- **Local**
  pain at i.m. injection
  sensitivity of the regional lymph nodes after i.m. administration
  painful veins after i.v. application, metallic taste in mouth
- **Systemic:** early
  anaphylactic reactions, hypotension, weakness, headache, nausea
- **Systemic**: late
  lymphadenopatia, myalgia, arthralgia, fever

Hematopoietic growth factors - erythropoietin

is produced by kidney cells in the juxtatubular apparatus
recombinant human erythropoietin - epoetin α
- epoetin β
difference is not clinically relevant

stimulates the formation of erythrocytes

Pharmacokinetics: given i.v., s.c. i.p.
effect even fastest after the i.v., greatest after s.c.

Side effects: flu-like syndrome
hypertension - encephalopathy, headache, disorientation, convulsions
Fe deficiency
Increased viscosity, hematocrit (↑ thrombosis)

Hematopoietic growth factors - erythropoietin

Main indications:

Anemia associated with chronic disease (e.g., renal insufficiency)

anemia associated with cancer chemotherapy

prevention of anemia of premature delivered newborns
chronic inflammatory conditions

Anemia in AIDS patients

Increasing the amount ERYS before autologous donation

Hematopoietic growth factors - CSF

CSF = Colony-stimulating factors

factor stimulating granulocyte-macrophage colony (GM-CSF)

granulocyte colony stimulating factor (G-CSF)

platelet-stimulating factor (in development)

recombinant derrivates:

- Filgrastim (G-CSF)
- Lenograstim (G-CSF)
- Molgrasmostim (GM-CSF) (+ monocytes neutrophilic granulocytes)

Hematopoietic growth factors - CSF

CSF used in cancer centers during chemotherapy or after as imunostimulans

- to stimulate stem cell release into circulation
- conventional anticancer therapy
- Intensive chemotherapy chemotherapy damaging haematopoiesis
- therapy after bone marrow transplant

Neutropenia in HIV infection

Induction of progenitor cells ex vivo

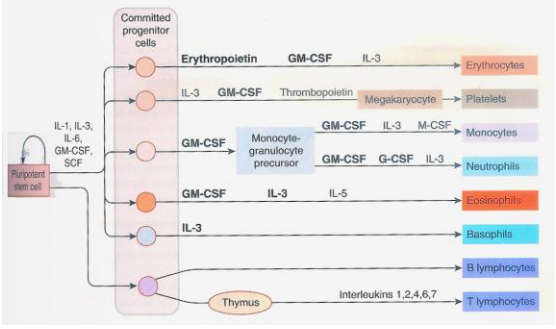
aplastic anemia

Hematopoietic growth factors - CSF

Administration: s.c., i.v.

Generally well tolerated, though:

Side effects: fever, bone pain, muscle lethargy, pain at the injection site hypotension, tachycardia, nausea, vomiting, lack of O_2 saturation, thromboembolism



Vasoprotectives and drugs influencing rheology of blood

Vasoprotectives (ATC C05) =

Drugs for the treatment of venous diseases, especially chronic venous insufficiency.

Substances used for sclerotherapy of varicose veins

Vasoprotectives

Drugs for the treatment of venous diseases

Indications: primary and secondary venous insufficiency

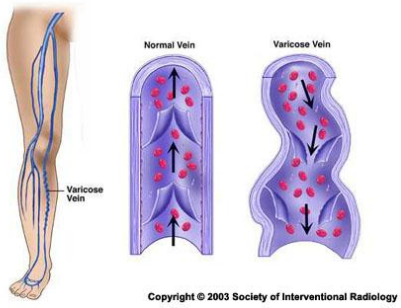
local swelling of the limbs and of lymphatic origin posttraumatic oedema

microangiopathy (e.g. diabetic angiopathy)

states with increased capillary fragility hemorrhoids

Contraindications: pregnancy and lactation?

Side effects: allergic skin reactions, dyspepsia, headache



Vasoprotectives

Drugs for the treatment of venous diseases:

varicose veins, vein inflammation, atherosclerosis, venous ulcers

increase venous tone → lumen reduction in affected veins, accelerating outflow (slow blood flow is one of the main mechanisms of thrombosis).

improve microcirculation, reduce permeability and fragility of capillaries and improve lymphatic drainage.

Prevent swelling and improve trophics in tissue.

Vasoprotectives

Drugs of the treatment of venous diseases

anti-inflammatory effect (tribenoside, calcium dobesilate)

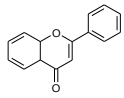
improve metabolism

Occasionaly are combined with dihydrogenated ergot alkaloids (DH-ergocristin) - arteriolodilating, venotonic and capillarotonic effect

Very often: flavonoids / flavonoid fraction

Vasoprotectives

Flavonoids



Currently over 2.000 flavonoids known

2 - fenylbenzopyren ring

normalize metabolism between blood and tissue

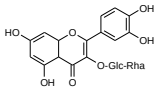
inhibit hyaluronate lyase = slow down degradation of hyaluronidase - cleaves proteoglycans extracellular space = accelerate the absorption of edema, hematoma

most of flavonoids have antioxidant properties (scavenger activity)

Vasoprotectives
- Drugs for the treatment of venous diseases

Rutin (rutoside) – Ruta graveolens *(Herb-of-grace*), Sophora Japonica *(Pagoda Tree)* , Fagopyrum vulg., F. esculentum *(common buckwheat)*

= glukorhamnoside of quercetin



Vasoprotectives
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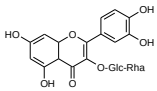

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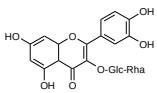
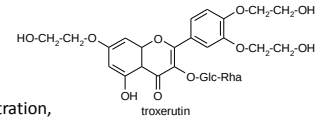


Vasoprotectives
- Drugs for the treatment of venous diseases

Troxerutine



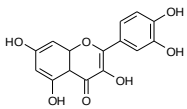
troxerutin

MA:
Reduction of capillary filtration,
decr. microvascular permeability for proteins
reduce the gaps between endothelial cells, interendotelial matrix modification
Increase adhesion of endothelial cells to the microvascular wall
Inhibit erythrocyte aggregation and increase their deformability
Improve microvascular perfusion and oxygen content in the skin.
reduce oedema

I: chronic venous insufficiency, idiopathic edema, liver cirrhosis, diabetic retinopathy.

Vasoprotectives
- Drugs for the treatment of venous diseases

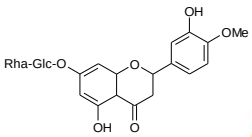
Quercetin – aglycone of Rutoside
Ruta graveolens, Sophora Japonica, Fagopyrum Vulgate., F. esculentum



antioxidant, ROS scavenger
CVS smooth muscle relaxation
stimulation of adenosine release

Vasoprotectives
- Drugs for the treatment of venous diseases

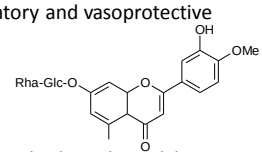
Hesperidin – pericarpium spp. Citrus



Vasoprotectives
- Drugs for the treatment of venous diseases

Diosmine

flavonoid with anti-inflammatory and vasoprotective effect



Hesperidin + diosmine

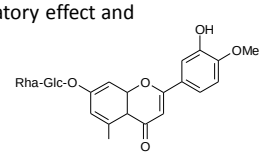
Improve the venous return in CVS

- at veins decreases venous stasis and reduces distenzibility
- normalize capillary permeability and increases capillary resistance,
- increase the level of lymphatic flow
- incr. venous tone

Vasoprotectives
- Drugs for the treatment of venous diseases

Diosmine

flavonoid with anti-inflammatory effect and venoprotektivním



Hesperidin + diosmine

Improve the venous return in CVS

- At veins decreases venous stasis and reduces distenzibility
- Normalize capillary permeability and increases capillary resistance,
- increase the level of lymphatic flow

- Enhances venous tone

Vasoprotectives
- Drugs for the treatment of venous diseases

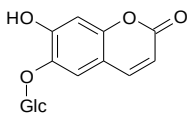
Esculin

Coumarin derivatives contained in the seeds hippocastani (chestnut, horse-chestnut)

decreases the permeability of capillaries

reduces capillary fragility

anti-inflammatory effect



Vasoprotectives
- Drugs for the treatment of venous diseases

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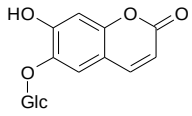


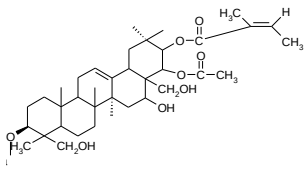
Vasoprotectives
- Drugs for the treatment of venous diseases

Aescin

amorphous, water-soluble mixture of triterpene saponins, sapogenin glycosides
Effects: antiedematous, anti-inflammatory, vasoprotective
seals capillaries, normalizes the permeability, reduces transcapillary transudation.
reduces the inflammatory response
decr. exsudative phase of inflammation
accelerates the absorption of traumatic hematoma
improves venous-lymphatic circulation
facilitates emptying of varicose veins in patients with flebopathy

Vasoprotectives
- Drugs for the treatment of venous diseases

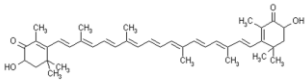
Aescin



Glc- Glc- Glucur. Ac.

Vasoprotectives
- Drugs for the treatment of venous diseases

Astaxanthin



http://en.wikipedia.org/wiki/

carotenoid

orange-red natural pigment

antioxidant, potentially venoprotective action

improves blood rheology

Vasoprotectives
- Drugs for the treatment of venous diseases

Ginkgo bilobae extractum siccum normatum

Active ingredients: flavonoid glycosides, ginkoflavon glucosides, ginkgolides, bilobalid

http://www.growsundews.com

MA: different mechanisms,
are not yet cmpletely understood

Vasoregulatory, improve blood rheology, antioedematous
effects and positive effect on the intracellular metabolism (neurons).

↑ synthesis of ACh and release + ↑ number of cholinergic rcp.

Vasoprotectives
- Drugs for the treatment of venous diseases

Ginkgo bilobae extractum siccum normatum

Vasodilating effect in the arterioles (EDRF, eventually. PgI_2),

experimentally reduces arterial spasm and increases venous tone wall.

Increases capillary resistance and reduces capillary hyperpermeability

Antioedematous effect.

Effect on intracellular metabolism: ↑ ATP and lactate

at the cortical level, utilization of oxygen and glucose,

inh. lipoperoxidation of cell

membranes and the production and the presence of free

oxygen and hydroxyl radicals.

Interactions !!

http://da.wikipedia.org

Vasoprotectives
- Drugs for the treatment of venous diseases

DH ergocrystin - semi-synthetic ergot alkaloid

partial agonist $\alpha 1$, antagonist of 5-HT receptors, no effect on uterus

Improving the distribution of oxygen, weak vasodilatory effect (arterioles)

Extends arterioles and precapillary sphincters,

increases venous tone by acting on the smooth muscle of blood vessels and thus improves the supply of oxygen to the tissues.

Side effects: nasal congestion, headache, metrorrhagia

(Combination with Rutoside, esculine)

Vasoprotectives
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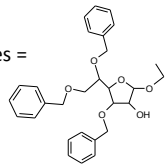
Tribenoside - a semisynthetic derivative of glycide, glucofuranosid

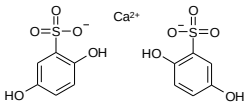
decreases the permeability of capillaries = antioedematous effect



antagonizes the effects of various endogenous substances that play important role as mediators of inflammation and in the pathophysiology of pain.

Vasoprotectives
- Drugs for the treatment of venous diseases

Calcium dobesilate



regulates impaired the capillary walls,

reduces its permeability and increases its resistance.

reduces the degradation of collagen, reduces blood viscosity and increases blood circulation,

improves lymphatic drainage and reduces swelling

Vasoprotectives
- Drugs for the treatment of venous diseases

Pentoxyfylin - semi-synthetic derivative of methylxanthine

Directly relaxes arteriolar smooth muscle, or through inhibition of PDE

reducing blood viscosity mainly in the microcirculation

improve blood flow and tissue oxygen saturation

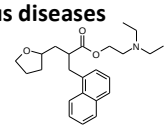
Inhibits platelet aggregation and adhesivity

↑ ATP in erythrocytes, improves elasticity

anti-inflammatory and cytoprotective effect, the inhibition of cytokine production (mainly tumor necrosis factor – TNF)

Vasoprotectives
- Drugs for the treatment of venous diseases

Naftidrofuryl - synthetic substance



musculotropic spasmolytic effect on the smooth

muscles of arteries, arterioles

reduces the tone and peripheral vascular resistance

improvement of blood circulation in the peripheral tissues (especially CNS) reduces ischemic pain.

nicotine and bradykinin antagonist

stimulates energy metabolism and decreases the production of neuron algogenic substances (lactic acid)

activates succinyldehydrogenase, increasing the supply of oxygen to tissues, improves glucose utilization, increases the production of ATP

Vasoprotectives
- Drugs for the treatment of venous diseases

Sulodexide – medium- MW - glycosaminoglycan composed of heparin (80%) and dermatan component (20%).

Antithrombotic effect (inhibition of factor Xa - activation of antithrombin III)

Weak fibrinolytic effect (stimulation of tPA, PAI inhibition)

Lipolytic effects (activation of lipoprotein lipase)

Vasoprotectives
- Drugs for the treatment of venous diseases

Sulodexide – medium- MW - glycosaminoglycan composed of heparin (80%) and dermatan component (20%).

- reduction of plasma viscosity
- protective and reparative effects on the endothelium, prevents adhesion of platelets, lymphocytes, monocytes and neutrophils to the vascular wall
- supports neoangiogenesis and enhances the natural antithrombotic properties of endothelium

Vasoprotectives
- Drugs for the treatment of venous diseases
LIMITATIONS

A number of products registered for more than **30 years ago**

Venoprotective effects are sometimes considered controversial in recent years; there has been a **revision** of medicinal products containing venoprotective drugs **concerning payment** from general health insuarance system

Evaluation of the quality of evidence on the effectiveness

A – Calcium dobesylate, micronised purified flavonoid fraction (hesperidine, diosmine), hydroxyethylruotsides

B – escin, ruscucs extr.

C - troxerutin, extr. Ginkgo bilobae

Drugs for sclerotherapy

- Injected into the varicose distended vein
- subsequent proliferation of fibrous tissue occurs and this cause obliteration of varices.

CI: intraarterial administration; oral contraception, in pregnancy and lactation.

Side effects: allergic skin reactions, pain at the injection site, necrosis after extravasal administration and pain.

Drugs for sclerotherapy

Polidokanol v 0,5-3% conc. (lauromacrogol 400)
- administration-compression-physical activity
- may be repeated after 7 days

Tetradecylsulphate sodium

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