Cardiovascular medication

Cursuri Romeo T. Cristina ®

C.10

Image source: http://veterinary.thorne.com/media/images/veterinary/heart.jpg

• Required recollections

Circulatory system is divided into three components :

- heart,
- blood vessels and
- blood.

They are closely related

Disturbance of one component will soon attract other parameters disorder

Blood pressure will be kept constant by heart that will adjust the volume rate pumped into a distribution-return system of the fixed volume of blood

The pressure can be decreased by four mechanisms:

1. decrease of blood volume pumped in heart/minute (minute volume of the heart)

2. decrease in blood volume (hemorrhage)

3. increasing the viscosity of the blood(hemoconcentration),

4. Increasing of circulation space(vasodilatation).

Under normal homeostasis pressure must remain optimal, heart attack =dependent on the pressure that will force the ventricles (in turn dependent on the degree of atrial compensation).

Venous return will depend on that blood pressure that will lead blood to venules.

cardiac pressure = controlled reflex by: the aortic arch and carotid sensors via medullary vital centers and by SNV.

Sanguin volume and hemoconcentration level are kept constant by the following mechanisms: the renin / angiotensin / aldosterone by the action: aldosterone and antidiuretic hormone associated with the activity of natriuretic factor (peptide of atrial muscle).

In this way the heart has endocrine regulatory activities

The physiological basis of cardiac therapy

Cardiac muscle cells contract spontaneously due to a specific contractile protein ,actomyosin and to energy generating system (mitchondrial)

Contraction will be carried out by calcium ions, their release being cyclical after membrane depolarization (which will precede each contraction).

This electrical activity is reversible.

It will allow:

- membrane permeability
- sodium ion penetration
- the release of potassium ions, and then

calcium entering via ion channels voltage / dependent on the concentration gradient.

flow determines:

- Reversal of cardiac membrane electrical polarity that

will be adjusted to balance level of -80 to -90 mV (with Na + ions out the exchange of the K +).

Heart rhythm = determined by sinoatrial node due to the cells that polarize / depolarizes spontaneously and much more frequently than anywhere in the heart.

The heart has:

ά-and especially

β-adrenoreceptors,

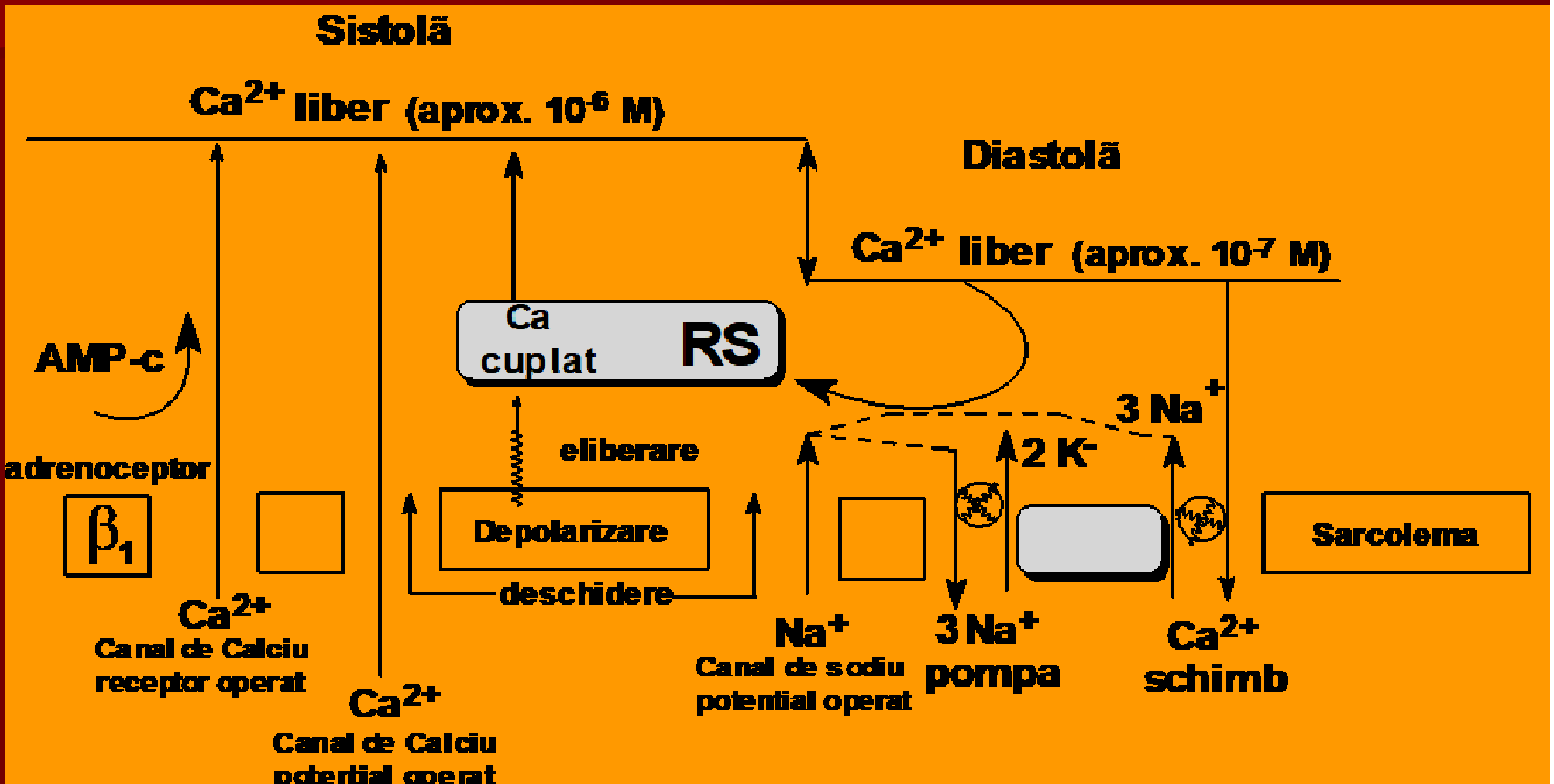
activation: followed by the intrusion of Ca + ions in the cardiac cell, consecutive to the increased contraction and relaxation of cardiac muscle.

When β-adrenoceptors are enabled = increases heart rate and force of contraction, followed by increased intracellular concentrations of c-AMP (cyclic adenosine monophosphate).

β-adrenoreceptors are closely associated with adenylate cyclases , specific enzymes of heart membrane .

β-agonists favors the activation of adenyl cyclase receptors, which convert ATP to AMP-c.

Mechanisms of calcium mobilization in myocardial cytosol
(increased rate in systole, low in diastole)
(Brander, 1991)



Cardiac collapse

when the heart is not able to remove the blood that pervades ventricular, enters in collapse and it will expand.

collapse followed by edema and / ascites as a result of myocardial valve damage .

Treatment, one of two directions:

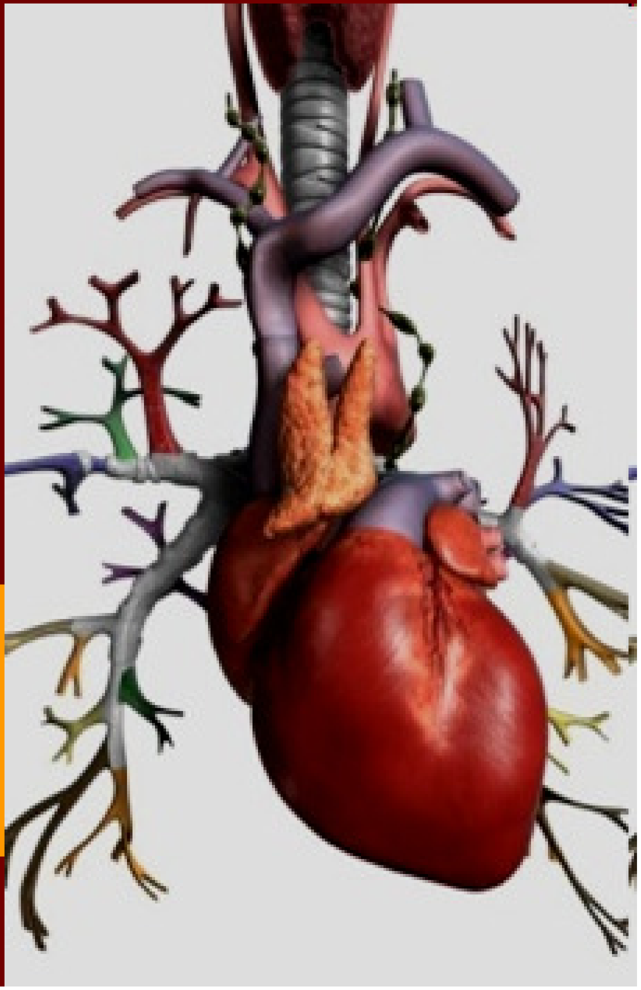
1. improving the pumping capacity of the heart (eg, use of stimulants or glycosides).Valuable stimulants when the pressure is low from heart slowing.

2.In opposition to the first, when the heart activity will be reduced to a level that can cope. This will achieve reducing the volume of blood pumped or by reducing the pressure at which blood is pumped (by vasodilators that reduce peripheral resistance).

Cardiovascular medication can be classified into::

- Cardiac stimulants
- Sympathicomimetics;
- vasoconstrictors;
- asystolics;
- vasodilators;
- hemostatics.

http://lifesciencefacts.com/wp-content/uploads/2011/01/Cardiovascular_system-SPL.jpg



Cardiovascular

substances

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1. Contractility modifiers (cardiotonics)

Digitalis glycosides

-are cardiotonics (inotropic)

-extracted from plants, role in the therapy of cardiac insufficiencies.

-prevent hypodynamic heart failure by:

activity amplification (without increased energy consumption)

increased heart rate (as Sympathicomimetic).

A glycoside molecule contains:

-a glucidic nucleus, glucone and

a sequence: Genin (or aglycone) = sterol structure.

-activity: very influenced by the glucidic structure attached.

-digitalis glycosides hydrolysis decompose into several gluconate and Genin.

Glucones are mainly represented by:

Strophantines
Genin,
digitalin,
scilarein,
rhamnose.

Sterolic genins are distinguished by their lateral groups . The cardiovascular effect is due to these Genin.

Glucones serve to solubilize and attach in myocardium.

Genines alone are several times less effective than the corresponding glicosides.

On pig cardiovascular glicosides produce: positive inotropism, cronotropism, batmotropism and dromotropism, all negative.

Install:

High blood pressure: cardiac output increases.

systole and diastole become complete,

heart works slowly, but with force,

occurs much better irrigation of the body,

edema and congestion are reduced.

will alleviate disorders of heart failure up to abolition,

in the case of cardiac degeneration, almost zero effect.

at high doses: extrasystoles (positive batmotropism) and heart block with heart stopping in systole.

Therapeutical doses of glicosides may be diuretics.

Genins and Gluons produced by hydrolysis of digitalis glycosides

Glicozida	Genina	Glucona
Digitoxina	Digitoxigenina	Digitoxoză 3 molecule
Gitoxina	Gitoxigenina	Digitoxoză 3 molecule
Gitalina	Gitaligenina	Digitoxoză 3 molecule
Digoxina	Digoxigenina	Digitoxoză 3 molecule
Digitalina	Gitoxigenina	Digitaloză 1moleculă + Glucoză 1 moleculă
Digitonina	Digitogenina	Galactoză 4 molecule + Xyloză 1 moleculă
Gitonina	Gitogenina	Galactoză 3 molecule + Pentoză 1 moleculă
Tigonina	Tigogenina	Glucoză 2 molecule + Galactoză 2 molecule + Ramnoză

Digitalics

Oficina:

woolly foxglove leaves and leaf powder.

Active Principles: Digital digitalina, gitaloxina, gitalina, saponins, potassium salts.

Digoxin

foxglove glycoside officinal and saponins

irritant to the digestive mucosa = vomit and enteritis.

Action: installs gradually after a latent period of 24 hours. Reaches an optimal intensity and then decreases slowly as cardiovascular cumulative glicosids .

Digitalis

one of the best remedies of heart failure.

on: myocardium , vascular wall, the vasomotor center, vagus.

improves circulation,

stagnant blood (stasis, edema) :aspired and pushed toward arteries = decrease local disturbances

Major indication:

chronic and subacute heart failure

valvular insufficiency in decompensation stage,

in functional arterial fibrillations

not in : fibrillations with irreversible organic lesions, hydropsy

Contraindicated in:

-vascular insufficiency,
-Infectious diseases,
-acute gastroenteritis, especially in dogs and cats,
-degeneration of the liver and myocardium,
-acute endocarditis.

Venena storage.

Commercial:

Digitalina solutions for internal use 1 ‰, 0.1 g tablets
Deslanozid, 2ml ampoules 0.2 ‰, compr. 0.2 mg

Dosage: - 1-2 g in large animals and
- 0,02-0,05 g in dogs and cats.

Strophantines

from seeds of tropical vines of the genus Strophantus.

Known strophantines: H, K, G are officinal.

white crystalline powder, colorless crystals, odorless, bitter taste (toxic) water soluble.

Venena storage

work faster and more intense than glicosides of digitalin!

It is recommended in:

severe cases, when a quick intervention is required : acute heart failure, collapse, when digitalin is no longer effective,

Acute infectious diseases.

G Strophantines

-1ml and 2ml ampoules,

-gamma amounts used

K Strophantines (Kombertin, Castrozid)

-In 1 ml ampoules.

Adonis vernalis

-dry aerial parts contain: cardiovascular glycosides, adonidine soluble in water,adonivernozid insoluble in water.

intermediate: between digitalin and strophantines.

contains: convalamarine and convallatoxine.

Side effects: in general weaker than of digital.

associated with valerian in: cardiac neuralgia, with cumulative effect.

Oabain
(Astrobain, Gratibain, Purostrophan, Strodival)

S. Gratus seed (G)

rapid effects and short half-life,

ideal for emergency digitization by parenteral routes.

intestinal absorption: low

does not couple to protein, excreted unchanged.

Dog 10 mcg i.v., repeated every hour until the effect.

In severe heart failure digitization supported on:
vigorous diuresis (furosemide iv: 5 to 20 mg / kg.),
paracentesis, low-dose morphine to quell coughing
and dispeneea and oxygen to combat cyanosis .

Sea onion (Scilla marittima)

contains: scilarein A (white onion variety).

toxicity greater than digitalin and strophantine.

glycoside does not accumulate in the body,

but the drug can cause vomiting.

Tevetine

Alkaloid from the genus Tevetia, is resembling with digitaline but soluble in water, more rapid action, not cumulative.

Disadvantage: it is irritating.

Bipyridine compounds

-increase myocardial contractility and rate,

-decreasing peripheral vascular resistance.

Amrinone and milrinone

Action: it seems to depend on the inhibition of phosphodiesterases.

-on the heart: inotropy, increased output = congestive failure, refractory to diuretics, vasodilators and conventional inotropic.

-very rapidly effect by i.v

-very good disritmogene effect

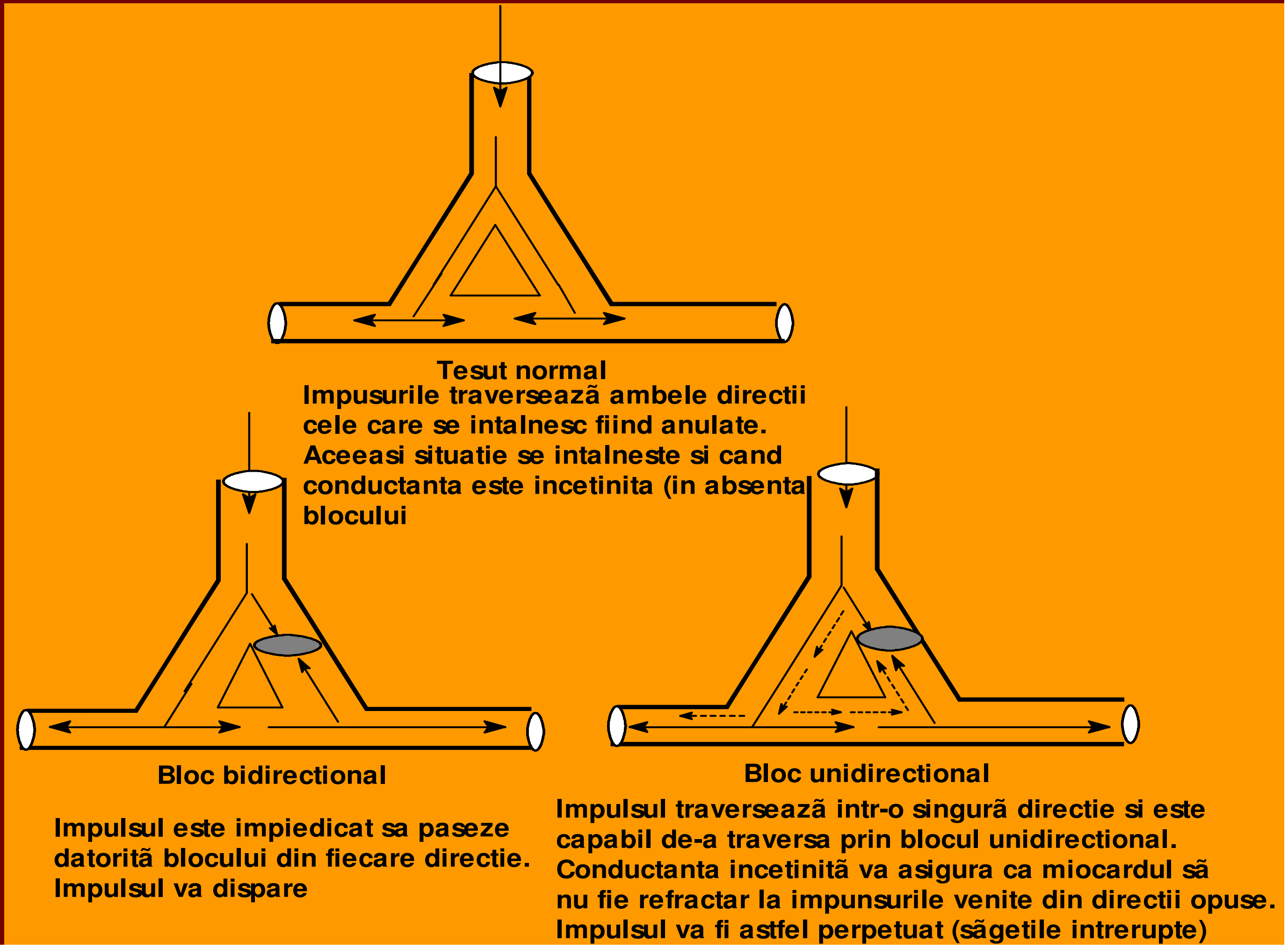
- reversible hepatotoxicity and thrombocytopenia!

Amrinone will not mix with: detroza or Lasix (excipient) only with normal saline solutions

2. Modifiers of cardiac rythm

Antiarrhythmic:

- membrane stabilizers,
- β-adrenoceptor blockers and
- calcium channel blockers



Quinidine sulfate
(Cin-Quin, Quinidex, Quinicardine, Quinora)

Cinchona alkaloid, dextro-isomer of quinine,
decreases excitability of heart muscle
refractory period extends to:
blocks sodium channels potentially operated (voltage sensitive)
nodal rhythm dominates thus cardiac activity.
blocks: the vagus nerve and acetylcholine = extension of refractory period and increased heart rate.
At: horse and dogs = restoration of sinus rhythm, by p.o
Side reactions:
fall of blood pressure, gastrointestinal disorders and
Hypersensitivity reactions:
hives, respiratory edema ,dyspnea, laminitis.

Procainamide

(Procan, Promine, Pronestyl, Procanbid)

sodium channel blocker,

effects similar to those of quinidine,

especially in controlling intravascular atrial arrhythmias.

Directions: **by all means, doses: 25 mg / kg.**

Lidocaine (lignocaine)

The only anesthetic with activity also as myocardial depressant

with sodium channel blocking increases potassium conductance

similar effects of quinidine, except that it does not affect the atrial action potential.

decreases blood pressure

Depresses myocardium: indirect action on the heart is not significant.

effective dose levels: very close to toxic.

- local anesthetics containing also epinephrine will not be used for the correction of ventricular arrhythmias!

dog: 1-2 mg / kg, repeating as needed.

Will not be administered p.o: liver decomposes lidocaine.

Phenytoin (diphenylhydantoin)

- control of digitalis-induced arrhythmias and of the ventricularnes.

-counteracts the arrhythmogenic activity of digitalis, preserves its response inotropo-positive unaltered.

When the membrane and action potentials are low (hypokalaemia and hypoxia), phenytoin amplifies both counteracting undesirable effect of digitalis.

-improve ventricular or intraventricular conduction-.

p.o in dogs: 20 mg / kg daily up to amend of signs.

i.v.: 5-10 mg / kg slowly minutes.

propranolol

β-adrenoceptor blocker prototype,
in: sinusal tachycardia, artrial flutter, atrial fibrillation, ventricular arrhythmias.
remarkable local anesthetic activity.
when: heart is aggressed by catecholamines, halogenated anesthetics, digitalis overdose or myocardial infarction,
Action: extension of the AV node refractory period,
Side effects: vasoconstriction, bronchoconstriction,
iv slow: 0.1-1 mg / kg, which may be increased in digitalis intoxication.

3. That affect heart and vascularization

Adrenoceptor agonists and antagonists

therapeutic agents used as:

-direct circulatory stimulants of heart and blood vessels.

The sympathetic system = major role in coordinating the circulatory function to the needs of the organism, mainly by:

-adjustment of cardiac output,

-modulation rate and force of cardiac muscle

Adrenaline

classic circulatory stimulant, pressor agent, when blood pressure is low

acts by the: α and β-adrenoceptors in vascular zone

increases the rate and force of myocardial muscle,

installs:

Vasoconstriction in: skin, intestines and veins,

Vasodilation in: muscle,

in other forms of shock ► ► ► correction of hypovolemia.

Noradrenaline

-relatively selective for β-adrenoceptors,

-favoring vasoconstriction rather than cardiostimulation,

-baroreceptors via the vagus nerve slow heart rate.

Isoprenaline

highly selective for β-adrenoceptors,

effect: positive inotropic and chronotropic response from β1-myocardial receptors .

β2-adrenoceptors mediate vasodilation, particularly in the voluntary muscles, blood pressure effects being mild.

β-agonists importance: adjustment of bradycardia, heart block or attack (Adams-Stokes type).

The short-term effect of adrenaline, noradrenaline and isoprenaline makes them unsuitable for long-term effects, but for short term and in emergencies are highly recommended. (intracardiac: 5ml / 1:10.000 dogs).

Isoxuprin
(Dilavase, Duvadilan, Vasodilan, Vasoplex, Vasotran)

-a β-agonist used in human medicine,
-good vasodilator in the treatment of equine navicular conditions

Methoxamine
- effective α-agonist with long lasting activity.
- significant cardiopresor effect, often accompanied by bradycardia

direct action = useful in severe progressive hypotension by anesthesia.

Metaraminol

α-agonist with direct and indirect effects on the heart.

strong long-acting action for one hour after i.v administration

in: **dramatic drop in blood pressure (eg acute** pancreatitis in dogs or anaphylactic shock).

Dopamine and Dobutamine

vasodilators: splachnic coronary and renal territories.

action: on the **myocardial-D1 receptor** population that mediates the increase of contraction force (not rate) by mediating adenylyl cyclase.

amplifies: venous return and cardiac output without increasing contraction rate = disarrhy or decreases the risk of ventricular fibrillation.

Major disadvantage: inhibits release of norepinephrine.

Xanthine derivatives

-Alkaloids: caffeine, theophylline and theobromine,

-activity: peripheral and coronary vasodilator.

disadvantage:

irritants and are of low solubility, which triggers more soluble compounds:

- **aminophylline** (theophylline + ethylenediamine injectable sol.)
- **Diprophiline** and **etamphilina** also derivatives a.u.v. of theophylline

Activity: myocardial stimulant, diuretic, mild respiratory and vasomotor.

in: stages of acute decompensated heart, as adjuvant in the therapy with digitalis glycoside

Vasodilator substances

a. Atrial vasodilators

Hydralazine (Hydrapress)

- inhibiting the flow of Ca + + into the cell, followed by relaxation.
- Another mechanism: conversion to NO and increased GMP-c = iontrope positive effects: stimulation of adenylyl cyclase via β-receptor

At: old dogs in hypertensive crisis = blood pressure is rapidly decreased, as well as systemic resistance = increased cardiac performance.

-good absorption both in humans and in dogs.

-elimination: renally via acetylation, at dog (deficient in acetylation) the renal passage is not important.

-use: related to intolerance to angiotensin converting enzyme (ACE) a much newer remedy that has replaced the use of hydralazine in animals.

Diazoxide

another arterial dilator but non-diuretic from the benzotiadiazinic family.

determines:

hyperglycemia,

hyperuricemia and

sodium retention.

For the present its effects on the dog are still being studied.

b. Calcium channel blockers

- mistaken for Ca + + antagonists though it does not directly antagonize
- on: V-dependent channels in the smooth heart muscles, inhibiting them even at low concentrations (below those required to release the intracellular calcium).
- in cardiovascular system there are at least three voltage-dependent channels different by: conductance and electrical sensitivity.
- These are: T, N and L.
- Clinically : Ca + + channel blockers = block only type L.

They are classified into three groups:

- fenilalkil-amine (Verapamil)
- benzothiazepine (Dilthiazem)
- dihydropyridine (Nifedipine, Amlodipine)
- Vasodilators order: Nifedipine> Verapamil> Dilthiazem
- new representative: the first T channel blocker = mibefradil

Verapamil

- derivative of papaverine,
- first used in humans as a dilator of the coronary vessels and to prevent arrhythmias of atrial origin.
- Action: Ca++ channel blockade and decreasing conductivity rate and heart frequency via the AV node.
- decreases heart rate, as a result of arteriolar vasodilation.

c. Inhibitors of angiotensin converter enzymes (ACE)

- role: vasodilator and neuro-hormonal and compensatory responsive for heart failure.

-acting on the heart: directly.

-reduced renal perfusion accompanies the decrease cardiac output = renin release from the kidney into the circulation.

-determines: synthesis of angiotensin I ► ► angiotensin II in lungs = role: to maintain cardiac volume and the CV insufficiency

-blood volume = increases due to the release of aldosterone and consecutive the water and salt retention.

-angiotensin II = strong vasoconstrictor, increases vascular resistance = maintaining blood flow to the organs involved

The most important representatives belong to the groups:

- sulfhydryl (Captopril),
- dicarboxyl (Enalapril, Benazepril, Quinapril)
- phosphorus (Fosinopril)

d Classic arterial and venous vasodilators

Nitrates

vasodilators of: cephalic extremity and neck area
install: coronary vasodilation
reflex: heart acceleration.
high dose = methemoglobin activity (in hydrocyanic acid poisoning= will form cianmethemoglobin).
organic nitrates =activate GMP- c = the interaction actin - myosin decreases.
Therefore: all vascular smooth muscles will: relax and will dilate venous or arterial vessel.

- at low concentrations = venules dilation predominant without affecting systemic vascular resistance,
-pharmacological effects= occur very fast,
-metabolism: very rapid and complete,
-sublingual use unused a.u.v.,
-used: i.v or topical (gel)
-Nitrates = vasodilators only after being reduced to nitrite.

-recommendations:
-- coronarian, cerebral and of bronchial muscle spasm.

Nitroglycerin (Trinitrin)

in M. V. are used. alcohol sol.1%, topical gel 2%, sol i.v

on: small vessels = general vasodilatation

scope: coronary and cerebral

may be associated with caffeine (older dogs).

applications: with gloves (for preventing percutaneous absorption)

on: hairless skin areas, abdomen or ear.

Modern variants with increased temporal effects (hours) are:

pentaeritrinol-tetranitratul and

Isosorbide dinitrate-.

Sodium nitrite

crystal-white, bitter, easily soluble, even hygroscopic.

effect: after 10-15 minutes.

At: large animals and dogs in cyanide poisoning, just i.v

Amyl nitrite

volatile liquid, yellowish, fruit characteristic odor, flammable.

in: Angina crisis,

result = prompt ,does not last more than 10-15 minutes.

Sodium nitroprusside (Nitroprusside)

Action: inside smooth cardiac muscle

-nitroprusside metabolised to NO = triggers on GMP-c activation and then vasodilation of arteries and veins.

-disadvantage: iv administration, slow infusion requires close monitoring (due to hypotension), but being a very efficient structure in emergencies makes disadvantages to be incurred.

Prazosin

-α-adrenergic receptor blocker, but important as venous dilator (probably due to inhibition of c-AMP).

-p.o administrations advantage,but the disadvantage of tolerance after several treatments.

- to avoid this shortcoming prazosin may be associated with other representatives of the group.

e. Indirect vasodilators

Inhibitors of angiotensin

system: renin - angiotensin - aldosterone = regulator of renal blood perfusion.

Action: increase of blood volume by: retaining Na + ions (aldosterone) and vasoconstriction (angiotensin II).

Captopril

Heart failure = local effects (low blood pressure in glomerular arterioles) + central ef. (amplification activity Sy) on glomerular apparatus = renin.

Renin = will cleave angiotensin I on the precursor plasma: angiotensinogen, angiotensin I = from a inactive decapeptide ► ► octopeptidă: angiotensin II, which is activated by the endothelial enzyme: angiotensin-convertase.

- the enzyme can also inactivate vasodilatory bradykinin,
- it may be inhibited in this way also by Captopril
- both vasoconstriction and aldosterone secretion caused by angiotensin will be removed and the medicinal effect disposed .
- the volume and cardiac workload will be reduced.
- venous return volume will be much lower and
- Myocardium less expanded = removing blood efficiently in peripheral areas where capillaries are less permeable.

Captopril will further reduce heart overuse and thus indirectly will reach the desired therapeutic desiderates:

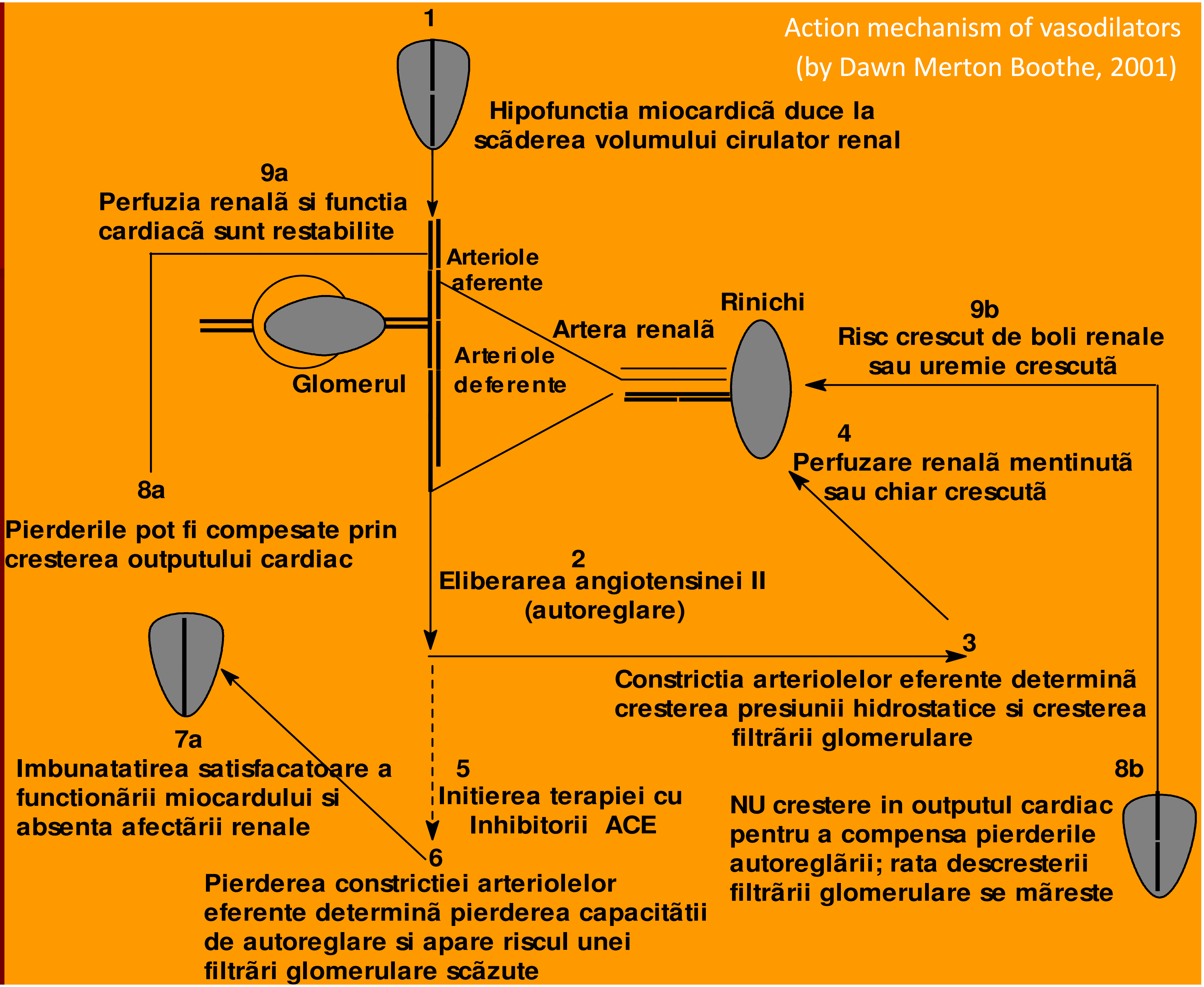
diuretic,

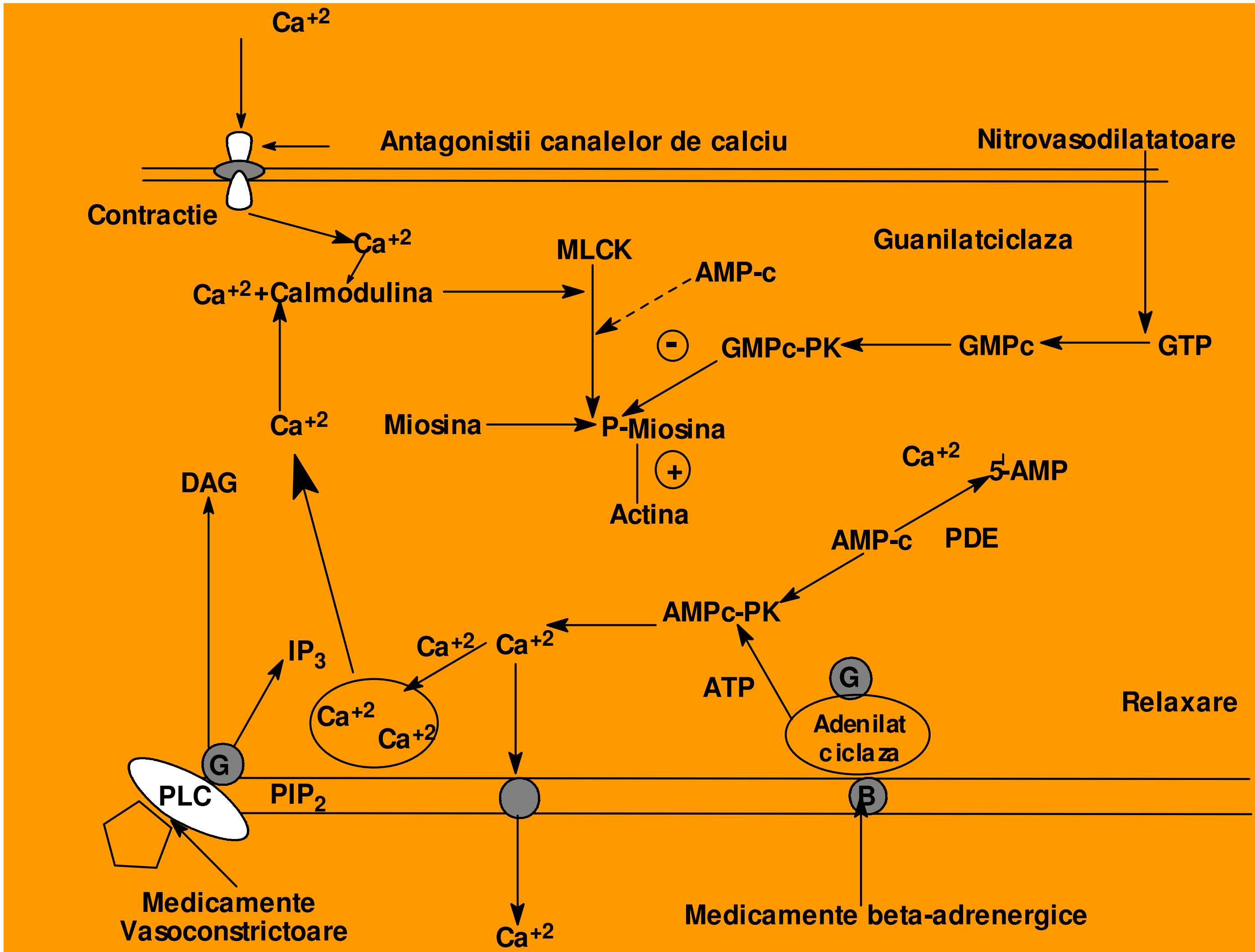
sympathicolytic and vasodilator, all in a single remedy without affecting autonomous mechanisms and interfering other systems.

Therefore captopril: is used with results in old dogs.

A congener of captopril is enalapril.

Action mechanism of vasodilators
(by Dawn Merton Boothe, 2001)





NOTA:

AMP = Adenozinmonofosfat

ATP = Adenozintrifosfat

c = ciclaza

MLCK = Myosin Light Chain Kinase

DAG = Diacilglicerol

PIP_2 = Phosphaditilinozitol

PI_3 = Inozitol- trifosfat

PK = Proteinkinaza

PDE = Phosphodiesteraza

PLC = Phospholipaza C

→ = stimulează

- - - → = inhibã

Schema situsurilor de acţiune a principalelor cardio-modificatoare

(după Dawn Merton Boothe, 2001)

Blood medication

- **Animal Blood Groups**

Antigens

Blood cells are grouped for each species according to antigens located on the surface of red blood cells.

The number of antigens detected is variable from species to species.

example:

-the dog has reached over 11 blood groups, of which 8 are recognized and classified as canine erythrocyte antigens (AEC) and categorized as: 1.1, 1.2, 3, 4, 5, 6, 7 and 8. of which the most frequently identified in the current casuistic were AEC-1 and AEC-7.

The cat knowns three blood groups: A, B and AB (below 0.1% of cats).

-no specimen of the Siamese breed had gr. Blood B.

-up to now have not been identified individuals who possess antigens –for both group A and group B.

To note that blood types in cats are unrelated to human ones.

Blood group A is dominant (75-99% of cats) on others, the groups being allelic .

Blood group B was identified only in 1-10% of cases mostly in pure breeds of cats (eg Abyssinian, Persian, Himalayan, Rex).

Interestingly, no specimen of the Siamese breed had blood group B .So far have not been identified individuals who possess antigens for both group A and B.

Izoantibodies

Plasma contains izoantibodies (aloantibodies) genetically determined, whose activity is related to antigens of red blood cell from the same animal species that occurr after the first transfusion in an animal.

-the clinical incidence of izoantibodies is low, antigen-antibody reactions in animals being practically nonexistent at the first transfusion.

-most frequent izoantibodies in dogs: izoantibodies AEC-7, present at over 50% of dogs tested

- in cats with blood groups A and B was identified the emergence of izoantibodies, anti-A antibodies (cats with blood type A) being responsible for the most severe reactions.
- in cats possessing the blood group B have been identified high titres of haemagglutinines and hemolysins of anti-A-izoantibodies.
- in contrast cats with blood type A, contain over 35% anti-B izoantibodies.
- in cats with blood type AB, has not been identified so far izoantibodies anti-A or anti-B, intravascular destruction being complete and immune mediated (IgM).
- formation of new antibody in receiving bodies occurs in 10-14 days.
- In 25% of the cases in dogs there will be noticed after the first transfusion the presence of antibodies anti-AEC-1.1. In the case of administration of total blood from the group A - 1.1 = severe immunological reactions.

- Blood substitutes

- an alternative in emergencies but cannot replace total blood.
-low viscosity recommends them in microcirculatory disorders

Free hemoglobins

-have short half-life (20 min.) and specific weight ,smaller than blood with large storage capacity and oxygen donation.

-Oxiglobina (Oxyglobin-Biopure)

-hemoglobin-carrier, a derivative polymerized bovine hemoglobin.

-Increased plasma concentrations and total hemoglobin = arterial blood oxygen increases.

-colloidal properties (MW 180kD) close to Dextran 70.

-being a polymerized hemoglobin , its molecular size will be bigger than that of hemoglobin = avoid renal filtration and side effects (eg, hemoglobinuria).

- absence of plasmatic izoantibodies reduces the risk of sensitization,
- antigenicity of the bovine hemoglobin = antibodies and anaphylaxis, especially when administered over a week.
- the product can be heated to body temperature,
- can not be frozen but is stable two years.
- properties = four days after opening the packs.
- oxiglobina will be removed, like hemoglobin by RE cells in 30-40 hours at dogs.

- Fluorocarbones
- miscible structure with the blood, which are capable of carrying 5.25 ml of oxigen/100 ml blood
- activities similar to oxiglobine.

- **Anemia therapy**

Erythropoietics

In anemia ,therapeutical conduct will:

- provide the components necessary for the production of red blood cells: protein, vitamin B12, folic acid,

-stimulate the formation of hemoglobin: iron and minerals

-stimulate the bone marrow.

Hematopoiesis begins in embryonic life through stem cell differentiation.

Erythropoietin (EPO)

The most important regulator of the proliferation of erythrocytes,

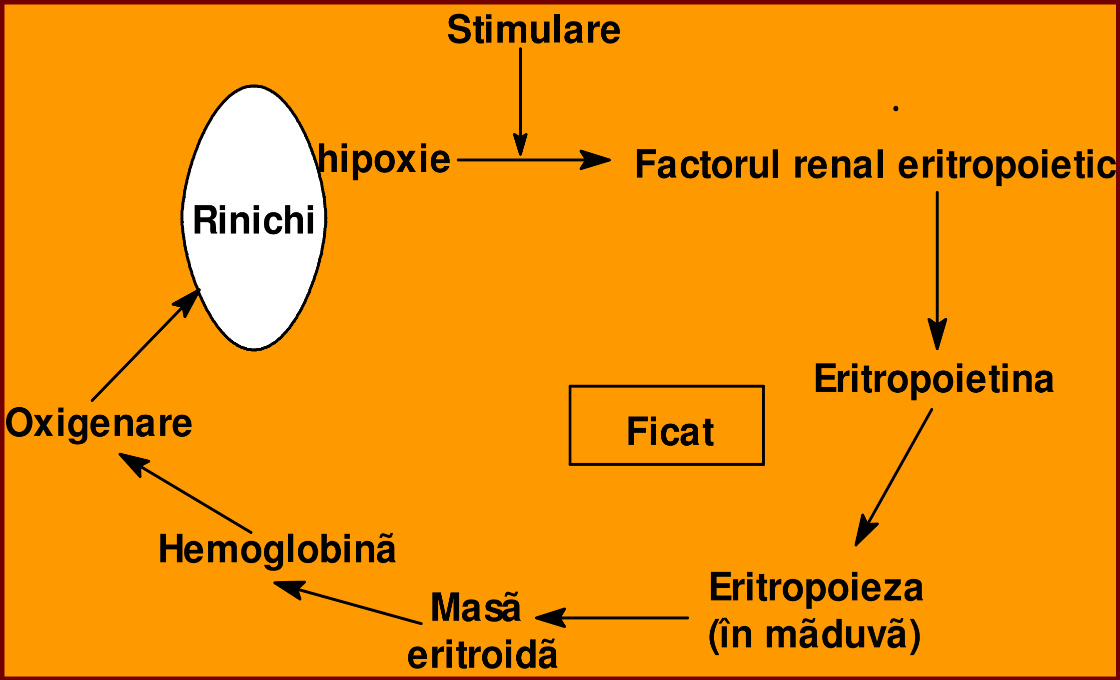
Initial EPO couples to the receptors of erythrocyte precursors,

then it will initiate intracellular phosphorylation,

After it will stimulate the proliferation and differentiation of erythrocyte precursors: eritroizii, erythroblasts and reticulocytes

- EPO stimulates the release of reticulocytes from the bone marrow into the blood.

Phases of the hematoformator process



Granulopoetics

Granulopoesis is stimulated by at least six factors named granulopoetines.

Supplementation with exogenous factors factors will favor the proliferation of several cell types: macrophages, granulocytes, platelets etc., according to the stimulant involved.

Other products that stimulate granulopoesis are extracts of Serratia marcescens that were identified as activators of α and γ interferons and interleukins IL-1 ,IL-6.

This induces mieloproliferation , either directly or through other cytokines.

Anabolic and androgenic steroids

-synthetic products related to testosterone.

-hematin action of heme steroids happens at cellular level,they increase the rate of glycolysis and form 17-keto-metabolites.

-they are released into tissues, including bone marrow where interact with cytosolic receptors and are transferred to the cell nucleus.

in the nucleus will initiate: formation of RNA and protein synthesis effect.

Vitamin B12 (cyanocobalamin)

-porphyrin compound ,contains a ring with a central Co atom.

-also referred to as factor of maturation, is essential for DNA synthesis,

- Its deficiency leads to many effects of which the most important are inhibition of maturation and nuclear division.

-first affect will register in marrow.

-erythroblasts will not divide and grow continuously in a megaloblast= installation of megaloblastic anemia.

Folic acid (glutamic –pteroil acid)

-cofactor required for DNA synthesis,

-promotes the formation of nucleotides necessary for the formation of DNA .

-needed for RNA synthesis where serves as a donor of methyl groups in the synthesis of vitamin B12.

-in humans daily requirement is 50 mcg / day ,it may be increased to 100-200 mg / day (hemolytic anemia).

-in animals may be administered human conditioning

Iron and its derivatives

Hemoglobin is composed by:

a heme portion and a globulin one .

Heme portion is formed from a pyrrole ring, proto-porphyrin formation. This structure will combine with iron to heme structure, which in turn will associate (four) and then will associate with globulins to form hemoglobin.

Iron is a component part of:

hemoglobin (65%)

mioglobulin(4%)

cytochrome

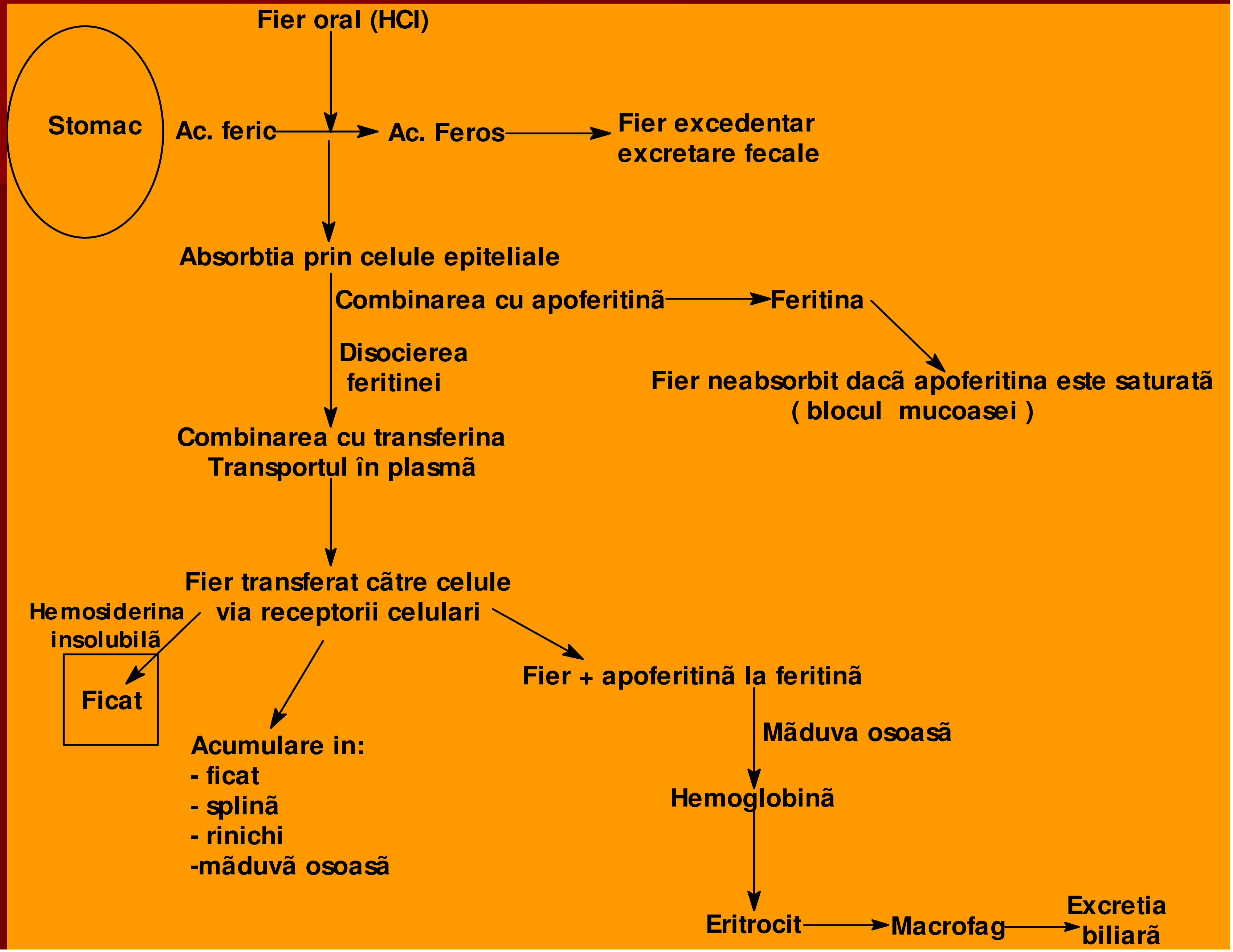
electron transport systems (1%.)

The remaining iron (30%) is stored:

or in the form of ferritin (soluble)

or as hemosiderin (insoluble).

Mobilization of iron in the body



Representatives:

Reduced iron.
ferrous sulphate
Iron lactate
ferrous chloride
Iron and iron carbonate
Dextriferonul (Astrafer).
Iron Hausmann
ferrous fumarate
Farmafer
Ferronat
glubifer
Myofer
Bioferan
Ferrodex
Ursoferan 75

Cobalt

deficiencies in Co in ruminants associated with:

-severe anemia,

-loss of appetite,

-loss of weight and productions,

-decrease of blood volume and

oxygen transport capacity by 30% (sheep).

Copper

-necessary for the recovery of iron and hemogobin in hemoglobin formation processes in mammals and birds.

-experimental studies discovered that iron absorption is much reduced in copper deficiency.

-will be reduced also the mobilization of iron from RE and will reduce the rate of synthesis of heme.

-copper and iron are associated in many enzymes;

-copper is essential for the metabolism of ascorbic acid (as oxidases, polyphenol oxidase, lactase and other compounds with unknown function).

Are known:

-a conditioning i.m. retarded copper glycinate

-dose: 120 mg (in cattle), and 40 mg (in sheep).

-other injectable formulations contain:

-copper calcium edetate or

-metionate copper.

Copper oxide

-conditioned as ruminal capsules and

-administered simultaneously with selenium and cobalt.

-grasslands sprayed with sol. $CuSO_4$ = improved grassland

-dose: 6kg/ha.

- **Hemostatic substances**

Clotting obtained by physiological clotting factors :
- thromboplastin (trombokinaze)
- thrombin,
- fibrinogen
- fibrin

Hemostasis occurs also by medicinal means.

Trombokinaze from blood platelets and plasma Ca++ ions determines prothrombin passage (pro-trombinogen in the presence of vitamin K in liver) to thrombin.

It provides conversion of fibrinogen into fibrin which is the basis of thrombus.

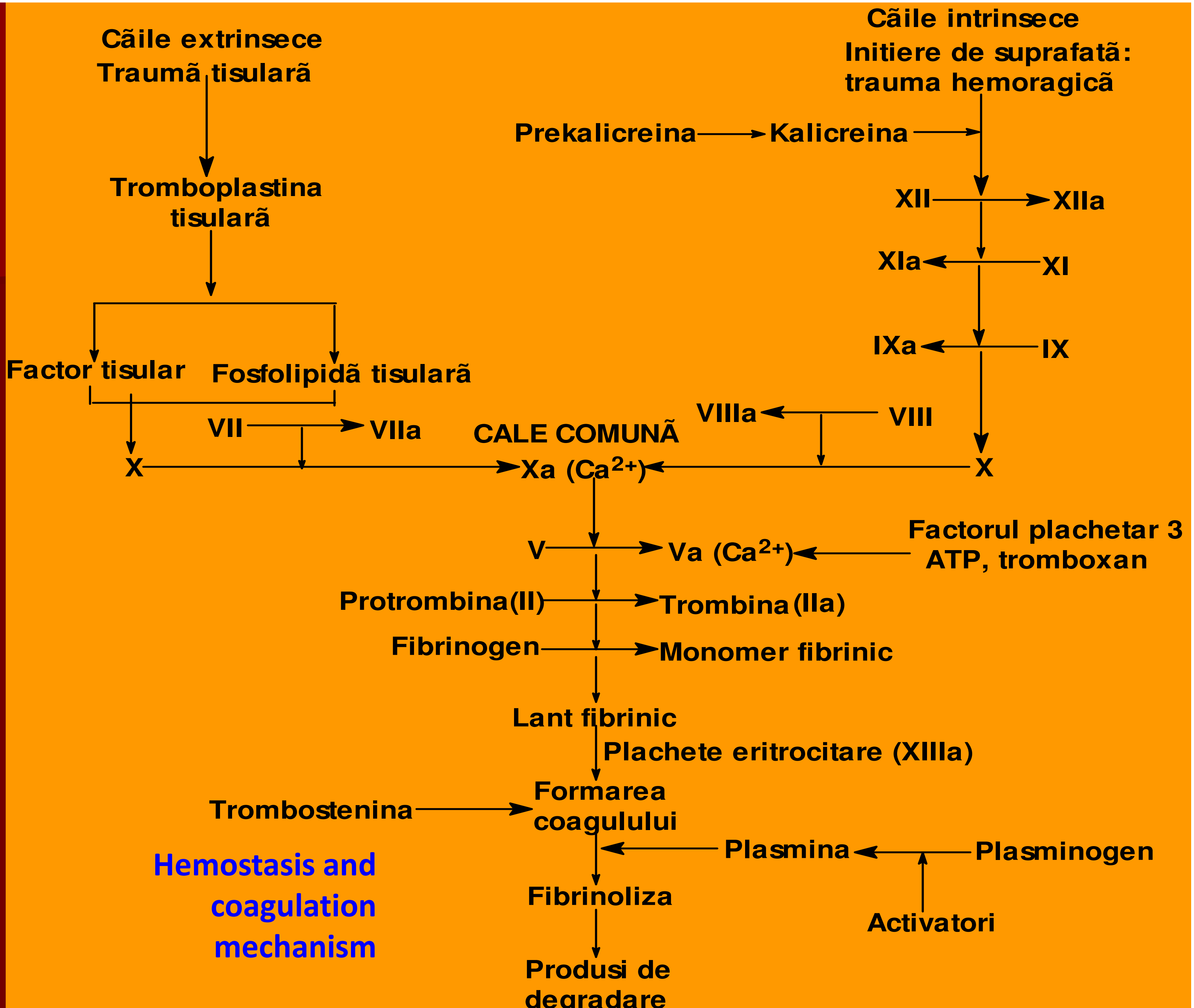
Hemostatic medication is recommended in:

internal and external hemorrhages,

the hemorrhagenic diathesis,

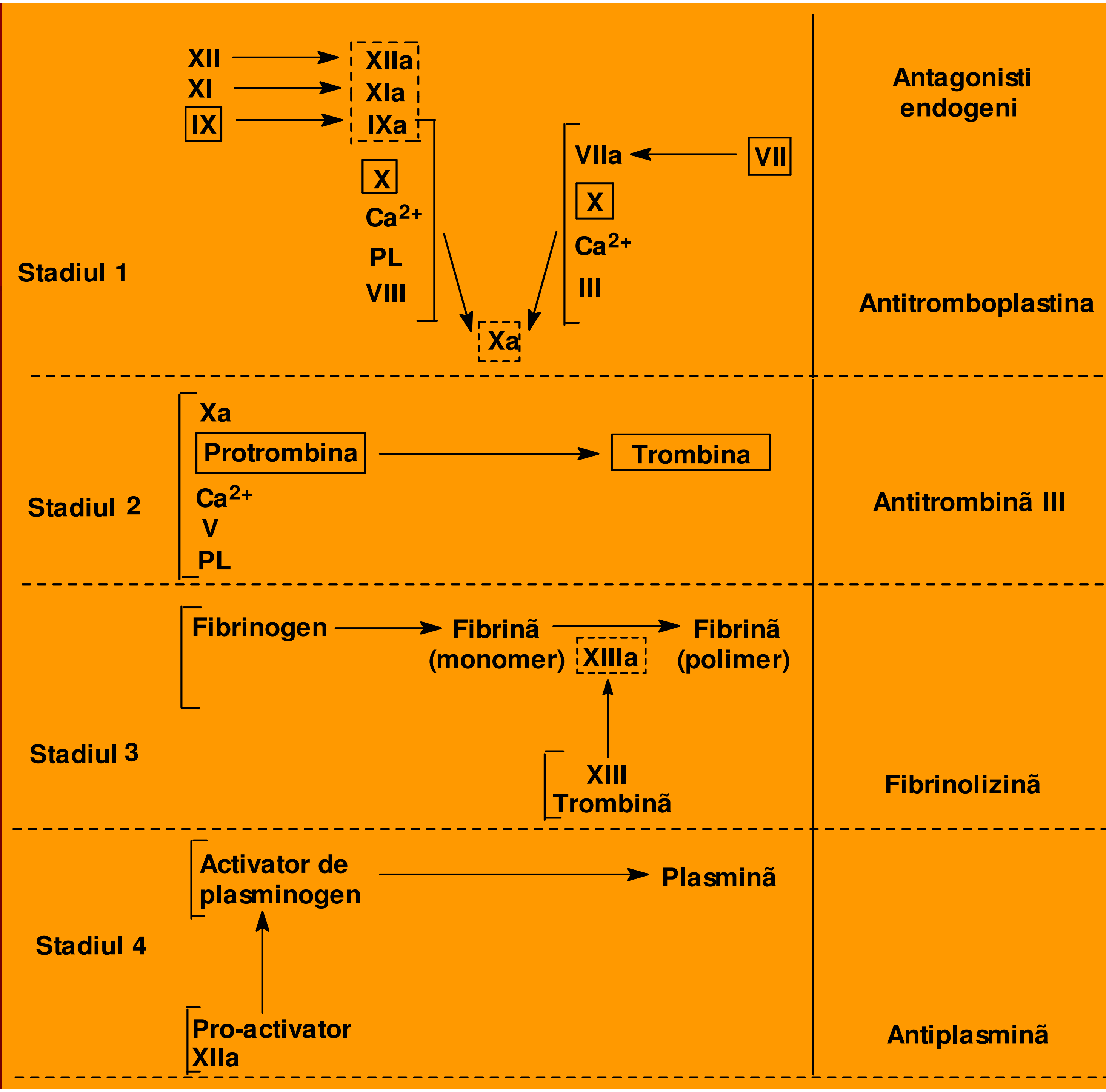
in hemorrhagic poisoning

preventive before surgery



Hemostasis and coagulation mechanism

stages of formation and elimination of fibrin



Calcium chloride

colorless crystals, bitter, very hygroscopic.

at over 30 ° C is dissolved in water of crystallization, is officinal.

Hemostatic by the presence of Ca ions, in hypertonic sol. disturbs isotonicity ,destroys platelets that release trombochinaza.

Effect: 30 min.

Is injected strictly i.v., in 10% solution .

There is a risk of necrosis.

If the solution has reached perivenously are recommended perifocale and focal injections with physiological serum.

20-40% Glucose solutions and 5-10% sodium chloride, i.v, will increase the power of clotting three times for 30 minutes.

Gelatins (Surgicel)

administered: s.c., i.m. or i.v. , 5-10% solution

effect: 8 hours.

haemostasis = by increasing the viscosity of the Ca content and the specific protein that will lead to an increase in the amount of fibrinogen in blood.

destruction of leukocytes = trombochinasis titer increase.

commercial: Gelaspon

- Gelatin sponge in plagues induces local hemostatic effect by absorbing blood and formation of adherent clots

K vitamin

liposoluble in nature - spinach, cabbage, tomatoes, nettles, liver, eggs, milk.

phytomenadione in animals (vitamin K1) is synthesized by the intestinal flora of mammals, at these animals is not found, hypo or avitaminosis.

Deficiency is common in birds (hemorrhagic diathesis).

in: hemorrhage diathesis, hypoprothrombinaemia.

Can increase capillary resistance.

vitamin K1

produces: rapid hemostatic effect and vitamin K3 acts longer.

vitamin K3

birds: drinking solution, adjuvant in coccidiosis, drinking water.

Vitamin C

works by increasing blood platelets and decrease of vascular permeability.

epsiloaminocaproic acid

inhibiting fibrinolysis, is antiallergic and antiphlogistic.

administered i.v. and p.o

Dicynone

- Systemic hemostatic on small vessels.

Fibrin and human fibrinogen,

Normal dog serum,

Blood and serum immunotherapy.

works by the contained proteins,

improve fibrinogen titer,

results increased clotting power 2 times for three days.

- **Anticoagulant substances**

Decrease coagulation and formation of thrombus within the body.

Dicumarin

inactivated form of coumarin.

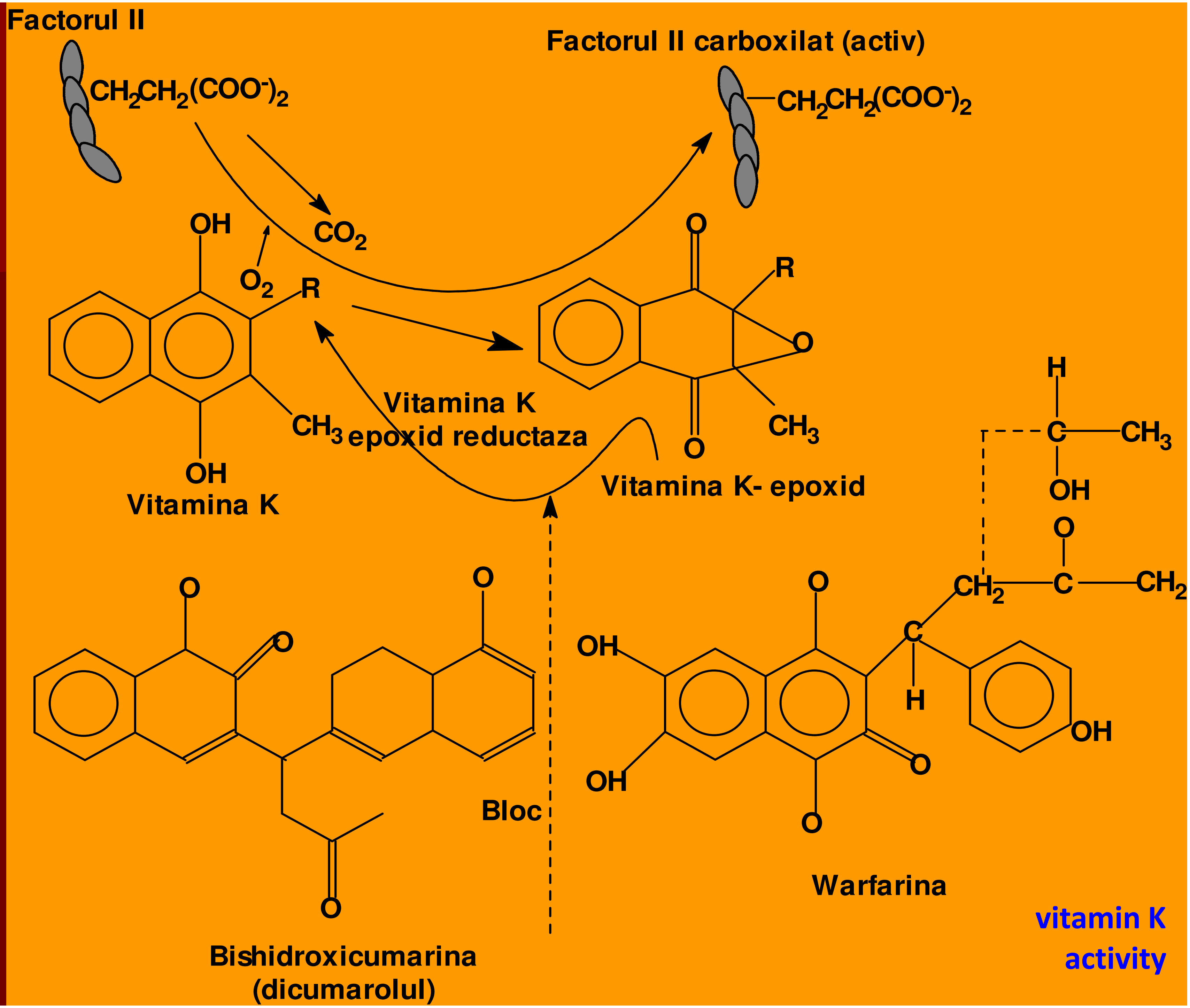
naturally found in melilot and any leguminous plant, which by conservation in humidity and under the influence of bacteria passes into the active form dicoumarol which is antivitamin K.

Trombostop

oxicumarin active derivative,

slow anticoagulant in thromboembolic disease.

Dicumarin and its preparations are contraindicated in: dismicrobism, hypovitaminosis K, hemorrhagic diathesis, digestive ulceration, liver disease.



vitamin K
activity

salicylic acid

structurally resembles cumarol.

by: decrease of prothrombin in blood which will reduce its coagulability , occurring also the reduction and aggregation of platelets.

Dipyridamole (Persantine)

vasodilator, as well as anticoagulant.

in: prevention of arterial embolism, venous thrombosis, thrombocytopenic purpura. It is associated with aspirin.

dextran

minimizes postoperative thromboembolic accidents,

in: i.v. perfusions

- polysaccharides produced by Leuconostoc mesenteroides and L. dextranicum
- these produce dextran being seeded on a sucrose substrate.
- produced by depolymerization or synthesis
- are composed by sequences of α-D-glucopyranosyl.

- Depending on the molecular weight multiple conditionings:
- Dextran 40 (Rheomacrodex, Eudextran, Rheotran), product of L. mesenteroides (MW = 40,000).
- Dextran 70 (Hyskon, Macrodex) (MW = 70,000)
- Dextran 75 (Gentran 75) (MW = 75,000).
- Dextran sulfate Na (Asuro, Colyonal, Dexulate, Dextrarine)

Heparin

- Officinal sodium salt, in fact mixture of sodium salts and mucopolysaccharides.

Prolongs coagulation: preventing transformation of prothrombin to thrombin (inhibition of trombokinasis and maintaining the integrity of platelet).

Is administered s.c., i.v., i.m., 100 I.U.

Not to be used orally.

Commercial vials of 1 ml Calcipirin 25.000 IU / ampoule.

Lasonil (ointment)

heparinoid, 5000 IU + 15,000 UI/100g hyaluronidase.

minimizes blood coagulability,

reduces viscosity,

increases the permeability of connective tissue.

in: resorption of edema, hematoma and exudates.

Hemofilin

in: oral glands of Hirudo medicinalis .

action: over thrombin: prevents turning fibrinogen into fibrin.

increases the amount of antithrombin.

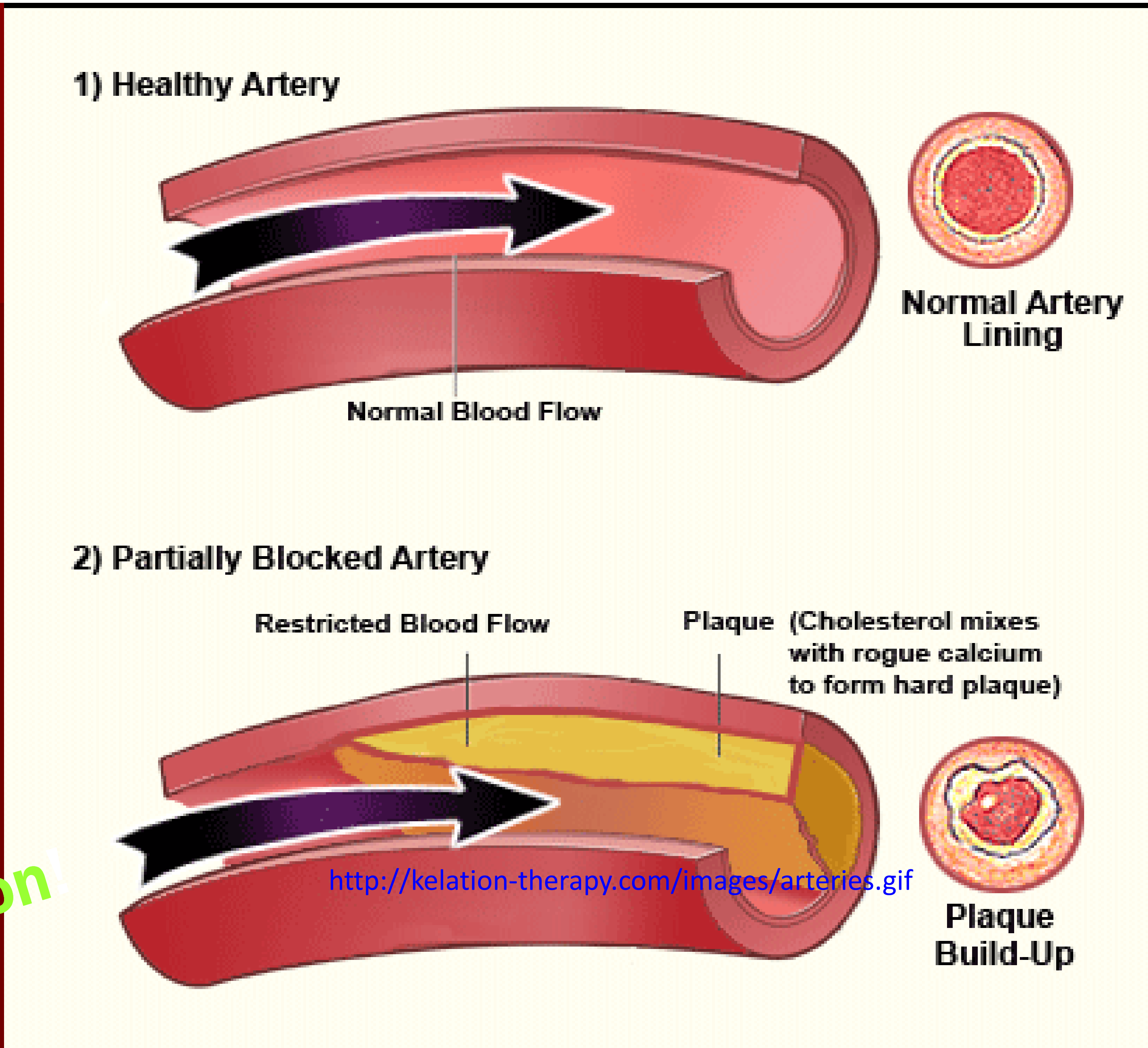
Sodium citrate , trisodium salt.

colorless crystals or white crystalline powder, odorless, salty, soluble in water.

If MA is exceeded by 10g, i.v. occurs hypocalcaemia.

Sodium oxalate

- Good anticoagulant being used in vitro.



http://kelation-therapy.com/images/arteries.gif

Thank you for attention!