

Semester II.

Pharmacology

Laboratory 10

**Medication of cardio-
vascular and respiratory tract**

1. Pharmacognosy

2. Pharmacodynamics

- ▶ The action of cardiotonics on the isolated heart
- ▶ The action of enhancement of calcium ions on cardiotonic substances
- ▶ Toxic action of large doses of digitalis on the "in situ" heart
- ▶ Peripheral vasodilator action of sodium nitrite and hydrochloric papaverine
- ▶ The action of sodium nitrite on the vascularization of the tongue, mesenterum and interdigital membrane
- ▶ Toxic action of sodium nitrite
- ▶ Use of sodium nitrite as an antidote for cyanide poisoning
- ▶ The action of some medicinal substances on the isolated tracheo-bronchial musculature

3. Pharmaceutical technique

- ▶ Preparation of a Digitalis leaf infusion

4. Pharmacography

5. Classification of substances with action on the circulatory system

6. Classification of substances with action on the respiratory system

1. Pharmacognosy

- **cardiotonic substances**
- **cardiac analeptic substances**
- **vasoconstrictor and vasodilator substances**
- **hemostatic substances and anticoagulants**
- **medications causing cough**
- **bronchodilating substances**
- **respiratory analeptic substances**
- **standardized preparations of these substances**

2. Pharmacodynamics

▶ The action of cardiotonics on the isolated heart

Technique

An isolated heart is prepared using the **Straub technique** and infused with Ringer serum. Normal cardiac contractions are recorded for several minutes.

3-4 drops of chloroformed water are introduced through the infusion cannula, so a decrease in contraction power and heart rate will be observed, due to the toxic effect exerted by chloroform on the myocardium.

Wash the heart by infusion with Ringer's serum, then insert it into the cannula strophanthin 0.1 ‰ solution, so it can be observed the return of the rhythm to normal, force of contraction of the heart and the exceed of the initial amplitudes.

The frequency is usually slightly lower than before, due to the bradycardizing effect of strophanthin.

- ▶ After the heart is washed again with Ringer serum, a few drops of 0.1 digitaline are infused. A greater amplitude of cardiac contractions will appear on the electrocardiogram, more than in the case of strophanthin and a more obvious decrease of the rhythm.
- ▶ Strophanthin and digitalis have effects on all cardiac functions.
- ▶ Thus, they act as a stimulator on the contractile myocardium (adult fiber) and inhibitor on the specific myocardium (embryonic fibers). As such, it has the following effects:
 - ▶ Positive: - inotropic (contractility)
 - bathmotropic (excitability)
 - tonotropic (tonicity)
 - ▶ Negative: - dromotropic (conductivity)
 - chronotropic (rhythmicity)
- ▶ Strophanthine has a faster and shorter duration action, while the digitalis act after a latency period and have a longer effect.

The action of enhancement of calcium ions on cardiotonic substances

Technique

- ▶ A cord isolated by the Straub method is infused with Ringer serum, recording contractions using a chemograph.
- ▶ It is administered by infusion cannula 4-5 drops of calcium chloride in a 1% solution. It is noted that there are no obvious changes to graphic recording.
- ▶ Wash the heart with Ringer's serum and administer digitalin following the cardiotonic effect that appears.
- ▶ Wash the cord again and infuse digitalin and calcium ions. A strong stimulating effect of cardiac activity can be observed.
- ▶ Then by administering a solution of potassium chloride, a depressing action of the heart is recorded.
- ▶ It can be deduced here that while calcium ions potentiate the effect of cardiotonic substances, potassium ions act by antagonizing this effect.

- ▶ It seems that cardiotonic are involved in ion exchange through the cell membrane of the myocardium.
- ▶ Thus, they increase the concentration of calcium in the myocardium, lowering that of potassium.
- ▶ It seems that the transport of electrolytes through membranes is accomplished by binding of ions in the form of chelates.

Toxic action of large doses of digitaline on the "in situ" heart

Technique

- ▶ The heart is discovered and recording the contractions with an electrochemograph.
- ▶ A freshly prepared digitaline infusion (0,2 ml) is then administered into the abdominal vein.
- ▶ There is an increase in the contraction force of the heart, expressed by increasing the amplitude of the movements recorded graphically.
- ▶ Another 0.5 ml of digitaline infusion was administered, observing the appearance of the extrasystoles, after which the partial cardiac block was installed.

Peripheral vasodilator action of sodium nitrite and hydrochloric papaverine

- ▶ The Laewen-Trendelenburg method
- ▶ The animal is eviscerated and a fine glass cannula is inserted into the aorta connected to an infusion vessel containing Ringer's serum.
- ▶ The cannula is fixed in the aorta. Also, in the median abdominal vein a fine glass cannula is attached.
- ▶ Ringer serum infused through the aorta reaches the posterior limbs, returning to the venous tract, and is collected at the level of the abdominal vein. Raise the infusion vessel to adjust the collection flow from the abdominal vein, at 10 drops per minute.
- ▶ 0.25 ml sodium nitrite 1% solution is introduced through the infusion tube.
- ▶ It can be seen that sodium nitrite causes vasodilation and as a result, the number of drops per minute that is collected is increased.
- ▶ By infusing 1 ml hydrochloric papaverine 0.02% solution after washing, we will also find the appearance of vasodilation, but with a shorter duration.

The action of sodium nitrite on the vascularization of the tongue, mesentery and interdigital membrane

- ▶ Inject 1 ml sodium nitrite 5% solution, or apply 1-2 drops of 1% solution directly to the respective tissues.
- ▶ Following the effects on the vessels, the appearance of vasodilation, and the existence of a more abundant blood flow can be observed.
- ▶ The experience can be performed with other vasodilating substances.

Toxic action of sodium nitrite

- ▶ The skin is examined at the level of the abdomen, and also the reflexes are investigated.
- ▶ A toxic dose of 1 ml sodium nitrite 10% solution is administered.
- ▶ After 15 minutes can see the decrease of reflexes, which disappear gradually, in the final phase appearing paralysis.
- ▶ The skin is colored reddish-brown.
- ▶ If the abdominal and thoracic cavities are opened, organ congestion, and a reddish-brown coloration of the blood can be observed.
- ▶ By diluting a few drops of blood into the physiological serum, it can be seen that it is hemolysed.

Use of sodium nitrite as an antidote for cyanide poisoning

- ▶ After administration of 4 mg/kg potassium cyanide 1% solution, injected subcutaneously, it is observed within minutes that severe respiratory crisis phenomena occur, as a result of blocking the cellular respiration under the action of cyanide.
- ▶ Intervening in the first 2 minutes after stopping the breathing with sodium nitrite 15 mg/kg in 1% solution, injected intravenously, followed shortly after administration of 4.5 ml solution 20% sodium thiosulphate, also injected intravenously, it can be seen that the breathing gradually returns to normal after 5-10 minutes.
- ▶ Cyanides act by blocking tissue respiration, following the reversible inhibition of cytochrome oxidase and other oxidative enzymes.

- ▶ Nitrites by their methemoglobinizing property, remove CN ions from their connections with cellular oxidative enzymes and give rise to cyanmethemoglobin.
- ▶ Sodium thiosulphate takes up the CN ion from cyanmethemoglobin, giving rise to thiocyanate, which is a non-toxic product and subsequently releasing hemoglobin.

The action of some medicinal substances on the isolated tracheobronchial musculature

Technique

- ▶ The thoracic cavity is opened and the entire trachea and primary bronchus are excised.
- ▶ The fragment is mounted in an organ bath and is attached to the writing pen of a chemograph.
- ▶ In the bath, there is a Krebs-Henseleit, Hastings or van Kyke solution at 37°C. Oxygenation is done by air bubbling.
- ▶ Place 1 ml of Acetylcholine solution in the bath, then wash, then 0.5 ml of adrenaline, followed by washing again and 1 ml of acetylcholine, followed by a new wash.
- ▶ The following administration: 0.5 ml ephedrine, washing; 0.5 ml adrenaline, 1 ml acetylcholine; washing, 1 ml acetylcholine, washing; 1 ml atropine, washing; 1 ml histamine, washing; 1 ml promethazine; 1 ml of histamine.

- ▶ Wait for 2-4 minutes after each substance and after each wash.
- ▶ Following the effects, it can be seen that acetylcholine and histamine cause the tracheobronchial muscles to contract.
- ▶ It yields more easily after washing in the case of histamine than in acetylcholine.
- ▶ The spasm of the tracheobronchial musculature produced by acetylcholine disappears under the action of antagonistic substances such as parasympatholytic or sympathomimetic.
- ▶ Their effectiveness in increasing order is atropine, ephedrine, adrenaline.
- ▶ The spasm produced is prevented by romergan (promethazine) which blocks histaminergic receptors.

Comparative picture between the actions of adrenaline and ephedrine:

Actions	Adrenalin	Ephedrine
C.N.S	weak stimulation	stimulation
Hearts	stimulation; pronounced tendency for arrhythmias	stimulation; weak tendency to arrhythmias
Arterioles	<p>Constriction:</p> <ul style="list-style-type: none"> - quick installation - short duration <p>- followed by Dilation:</p> <ul style="list-style-type: none"> - strengthened by cocaine - is maintained by repeated doses - reversed by the sympatholytics 	<p>Constriction:</p> <ul style="list-style-type: none"> - slow installation - lasting 10 times longer than adrenaline - there is no Dilation - cocaine decreases or does not influence it - Decreases by repeated doses (tahifilaxy)
Bronchi	<p>Dilation:</p> <ul style="list-style-type: none"> -intense -sudden -short-term 	<p>Dilation:</p> <ul style="list-style-type: none"> - less intense - slow installation - longer duration
The striated muscles	they are not influenced	active in myasthenia

3. Pharmaceutical technique

▶ Preparation of a Digitalis leaf infusion Technique

Weigh 0.5 g of Digitalis leaves, gently chopped, and prepare 100 ml of infusion, according to the technique learned in extractive solutions.

More concentrated infusions can be prepared, which go up to 4%.

Along with cardiotonic glycosides, saponins are also extracted from the leaves of the digitalis, which favors their absorption and fixation on the myocardium.

The existence of saponins is observed by the presence of foaming that appears when stirring the infusion.

It can also be highlighted by their hemolytic action, demonstrated by mixing with a small amount of blood in the tube.

4. Pharmacography

Rp./ Fol. Digitalis pulv. 12,0
Rad. Altheae pulv. 50,0
Fruct. Juniperi pulv. 100,0
M.D.S int 3 tablespoons per day
to horse (cardiotonic)

Rp./ Fol. Digitalis pulv 1,0
Sacchari pulv 9,0
M.Div. p. aeq X
D.S int 2x1/day to dog in ascites
(cardiotonic and diuretic)

Rp./ Camphorae 15,0
Tinct. Strophanti
Rad. Altheae pulv aa 50,0
Aquaе font Q.S
Ut.f boli II
D.S int 1/day to horse or cow
(analeptic or cardiotonic)

Rp./ Tinct. Digitalis
Tinct. Strophanti aa 100,0
M.D.S int 2X1 spoon per day
to cow in foot and mouth disease
(cardiotonic)

Rp./ Tinct. Strophanti 5,0
Theobromini natrii-salicylici 2,5
Sirupi simplicis
Aquae destill. aa 75,0
M.D.S int. 3x1 teaspoons / day
in the dog in ascites
(cardiotonic and diuretic)

Rp./ Coffeini natrii benzoici sol. 25% vial a 5 ml N X
D.S ext. 2x2 vials/day in inj. s.c. to cow
(cardiac analeptic)

Rp./ Oleum camphorati sol. 20% vials a 10 ml N XII
D.S. ext in inj. i.m 2x3 vials/day to horse
(cardiac analeptic)

Rp./ Stibii sulfurati rubri 100,0
Natrii chlorati 150,0
Fruct. Juniperi pulv. 150,0
M.D.S int 3x1 spoon/day to horse mixed
in grits (expectorant)

Rp./ Inf. Rad. Ipeca 0,3/140,0
Natrii benzoici 3,0
Sirupi codeini 20,0
M.D.S int 3x1 spoon/day to dog
In bronchitis
(expectorant and antitussive)

Rp./ Codeini phosphorici 0,05
Sacchari pulv. 0,3
M-f pulv.
D.t.d. IX
S. int 3x1/day to dog
(antitussive)

5. Classification of substances with action on the circulatory system

Cardiotonic

- *folia digitalis purpureae*
- *folia digitalis lanatae*
- *strophantinum*
- *bulbus scillae*
- *adonis vernalis*
- *convallariae majalis*
- *sparteinum*
- *nerium oleander*

Cardiac medication

Analeptic

- *coff. natr. benzoicum*
- *camphora*
- *pentetrazolum*
- *nicetamidum*

Antiarrhythmics

- *quinidine*
- *procainamide*
- *procaina*
- *ephedrine*

5. Classification of substances with action on the circulatory system

	vasodilators	<i>-natrium nitrosum -papaverinum hydrochloricum -iodum și natrium iodatum</i>
Vascular medication	vasoconstrictor	<i>-coffeinum natr. benzoicum -pentetrazolum -stricninum -adrenalin and noradrenalin -efedrinum -vasopressin</i>

5. Classification of substances with action on the circulatory system

	Stimulants of erythropoiesis	<i>-products with Fe +++ -vitamin B12 -folic acid -microelement -liver extract</i>
Blood medication	Stimulants of leukopoiesis	<i>- biogenic stimulants</i>
	Hemostatics	<i>-vitamin K3 -calcium chloratum -calcium gluconicum -gelatine -thrombin -local hemostatics</i>
	Anticoagulants	<i>-heparin -coumarin derivatives</i>

6. Classification of substances with action on the respiratory system

Antitussive medication	Central	<ul style="list-style-type: none">-codeinum-dioninum-bromoformium-tusomag, calmotusin
	Peripheral	<ul style="list-style-type: none">- radix althaea-species pectoralis-radix liquiritiae-t-ra belladonna, aconiti

6. Classification of substances acting on the respiratory system

Fluidifiers and excretomotors

- stybium sulfuratum*
- ammonium chloratum*
- ammonium aceticum*
- bromhexim*

Expectorant

- natrium benzoicum*
- radix ipecacunahae*

Antisecretori

- ol. terebenthinae*
- ol. eucalipti, menthae piperithae*
- terpin hidratum*
- creozotum*
- gaiacolum*
- *camfoteprin*
- *pneumosept*

6. Classification of substances acting on the respiratory system

Musculotrope

- *coff. natr. benzoicum*
- *papaverinum hydrochloricum*
- *natrium nitrosum*

Neurotrope

- *atropinum, extr. belladonnae*
- *adrenaline, ephedrine*
- *Tranquilizers: largactil*
- *ACTH, cortisone*
- *vasopressin*
- *antihistamine: romergan*
- *feniramin*

Bronchodilatory medication

Respiratory analeptic

- *pentetrazole, nicetamide,*
- *lobelin, ether*
- *reflexotherapy with ammonia, ether, ethereal oils, chlorine*
- *artificial respiration*