

Semester II.

Pharmacology

Laboratory 8

**Substances acting on ANS and
Antihistamines**

- ▶ **1. Pharmacognosy**
- ▶ **2. Pharmacodynamics**
- ▶ **3. Pharmacography**
- ▶ **4. Classification of ANS substances**

2. Pharmacodynamics

- ▶ Substances with action on SNV are an important chapter in veterinary therapy.
- ▶ Functional changes that occur in various animal disorders are subjected to drug remedies based largely on these substances.
- ▶ On the other hand, a series of drugs that have well-defined therapeutic actions, have some side effects that are reflected in the vegetative nervous system, respectively the territories under its influence.

The distribution of medicinal substances is divided into two groups:

- ▶ substances with action on cholinergic territories
- ▶ substances with action on the adrenergic territories

The parasympathomimetic drug has effects similar to those of acetylcholine, the cholinergic chemical mediator. They may act directly by the substance, or indirectly by the acetylcholine remaining free from blocking acetylcholinesterase (an enzyme that hydrolyzes it).

The sympathomimetic drug, act in the same way as adrenaline and noradrenaline, the chemical mediators of the sympathetic system.

In each group, we distinguish substances that exert a stimulatory effect and others with an inhibitory effect, which antagonize the action of the former. So:

Parasympathomimetic drug - direct
- indirect

Parasympatholytic drug

Sympathomimetic drug - direct
- indirect

Sympatholytic drug

- ▶ **The parasympathomimetic drug** has effects similar to those of acetylcholine, the cholinergic chemical mediator. They may act directly by the substance, or indirectly by the acetylcholine remaining free from blocking acetylcholinesterase (an enzyme that hydrolyzes it).
- ▶ **The sympathomimetic drug**, act in the same way as **adrenaline** and **noradrenaline**, the chemical mediators of the sympathetic system.

The effect of cholinergic and adrenergic substances

The place of action	Cholinergic substance	The adrenergic substance
Eyes		
Pupil	Myosis	active mydriasis
Ciliary muscle	Relaxed	Contracted
Intraocular pressure	decreases	Increases
Tear glands	hypersecretion	normal

The effect of cholinergic and adrenergic

The place of action	Cholinergic substance	The adrenergic substance
Heart		
Frequency	Slowed	Accelerated
Rhythm	bradycardia AV block	Extrasystolic tachycardia
Cardiac output	Low	Grown
Blood vessels		
Brain, Lung, Abdominal	-	Constriction
Coronary	Constriction	Expansion
Skin, Mucous, Skeletal muscle	Dilatation (skeletal muscle)	Constriction

The effect of cholinergic and adrenergic substances

The place of action	Cholinergic substance	The adrenergic substance
Lung		
naso-pharyngeal glands	hypersecretion	normal
bronchial musculature	contraction	relaxation
bronchial glands	hypersecretion	normal or hyposecretion.
Salivary glands		
vascular	vasodilatation	vasoconstriction
secretion	hypersecretion	Hyposecretion

The effect of cholinergic and adrenergic substances

The place of action	Cholinergic substance	The adrenergic substance
Stomach.		
tone	grown	low
motility	grown	low
sphincter	relaxation	contraction
secretion	stimulated	inhibited or normal
Intestine		
tone	grown	low
motility	grown	low
sphincter	relaxation	contraction
secretion	stimulated	inhibited or normal

The effect of cholinergic and adrenergic substances

The place of action	Cholinergic substance	The adrenergic substance
Pancreas		
exocrine secretion	increased	normal
endocrine secretion	increased (insulin)	normal
Gallbladder	contraction	relaxation
Spleen		
tone	unchanged	contraction
Adipose tissue	-	fatty acids into the blood
Skin		
Sweat glands	grows (general).	grows (locally).

The effect of cholinergic and adrenergic substances

The place of action	Cholinergic substance	The adrenergic substance
Medullary adrenal gland		
activity	adrenaline secretion	catecholamine discharge
Ureter		
tone and motricity	unchanged	diminished
Bladder		
bladder detrusor	contraction	relaxation or normal
sphincter	relaxation	contraction
Uterus		
tone	grown	low or normal
motility	grown	low or normal

The action of parasympathomimetic and parasympatholytic substances on the eye

- ▶ Instillation of a **parasympathomimetic substance in the eye** leads to the appearance of myosis, due to the contraction of the ciliary musculature of the iris.
- ▶ The photomotor reflex is diminished or inhibited.
- ▶ The intraocular tension decreases by dilating the Schlemm canal, and the Fontana spaces that appear following the myosis.
- ▶ Tear secretion is increased.

The action of parasympathomimetic and parasympatholytic substances on the eye

- ▶ If a parasympatholytic substance (atropine) is instilled in the eye, exactly the opposite changes occur.
- ▶ Thus, it can be seen the installation of passive mydriasis by paralysis of the circular iris muscle, the lack of accommodation of the pupil through the photomotor reflex, the increase of the intraocular tension and the decrease of the tear secretion.

The action of parasympathomimetic and parasympatholytic substances on the eye

- ▶ Atropine can counteract the effect of the parasympathomimetic substance, and its characteristic changes are observed.
- ▶ On the other hand, if it is desired to add Pilocarpine or Ezerine to the atropinized eye it does not exert any effect, the lithic substance having the predominant action.

The action of pilocarpine and atropine on the heart

- ▶ If from a solution of 1% of hydrochloric pilocarpine, 2-3 drops are deposited directly on the tip of the heart, a marked decrease of the heart rate is observed due to the parasympathomimetic effect of pilocarpine.
- ▶ If, after washing, 2-3 drops of atropine sulfuric solution 1% are added, after a short time we will be able to see the recovery of the heart rate, and then the appearance of a tachycardia.
- ▶ This is due to the blocking of cholinergic receptors by atropine and thus removing the parasympathetic component.

Comparative action of atropine and scopolamine on CNS

- ▶ The administration of scopolamine leads to lazy, heavy and uncoordinated movements, shortness of breath and shallow breathing.
- ▶ The administration of atropine, on the contrary, causes lively movements, increased reflexes, increased breathing as well as frequency.
- ▶ The effects are because the two parasympatholytic substances act differently on the CNS.
- ▶ While atropine is a CNS stimulant, scopolamine exerts a depressing action.

The action of adrenaline on the isolated heart

By adding a few drops of adrenaline 0.1‰, a tachycardia is observed through the effect on the intrinsic nervous system of the heart as well as an increase in the amplitude of the cardiac contractions due to the direct effect of adrenaline on the heart muscle.

The action of adrenaline on the eye

- ▶ Adrenaline acts at the pupil's level, producing the contraction of the radial musculature of the pupil, thus causing the appearance of active mydriasis.
- ▶ The sympathomimetic action occurs in two types of adrenergic receptors called alpha and beta, so alpha receptors have generally stimulatory effects, whereas those of beta receptors are predominantly inhibitory.
- ▶ Mydriatic action is accomplished through alpha receptors.

The effector organ	Effects due to receptor activation	
	alpha	beta
Heart		
Sinoatrial node	-	positive chronotropic
The atrioventricular node	-	increasing the speed, shortening the refractory period
atrium - ventricle	-	Positive inotropic, positive bathmotropic
Blood vessels		
In skeletal muscle	contractions (constriction)	relaxation (dilation)
In mucous, skin and splanchnic territor	contraction	-
Bronchial muscles	-	relaxation
Digestive tube		
Salivary glands	secretion	-
Gastric smooth muscles	-	relaxation
Smooth intestinal muscles	relaxation	relaxation
Intestinal sphincter	contraction	-
Gallbladder	-	relaxation
Bladder		
Detrusor	-	relaxation
Trigon and sphincter	contraction	-
Ureter, deferent	contraction	-
Eyes		
Radiation muscle of the iris	contraction (midriasis)	-
Ciliary muscle	-	relaxation
Spleen	contraction	-
Uterus	contraction	relaxation
Pilomotor muscles	contraction	-
Nictitating membrane	contraction	decrease in tone
Metabolism	-	hyperglycemia, hyperlactacidemia, hyperkalemia
CNS	-	stimulation

The effect of adrenaline, noradrenaline, and ephedrine on blood pressure and respiration

- ▶ In dogs narcotized with chloralosis, which is subsequently injected with hydrochloric adrenaline 30 mcg/kg intravenously in 0.1 % solution, it is observed accentuated hypertension (180-200 mm Hg), followed by tachycardia, positive inotropic alternated with the compensatory decrease of the heart rate, and after a few minutes, the blood pressure decreases for a short time even below the normal limits. Respiratory is initially an apnea, followed by tachypnea and then returns to normal.
- ▶ Hypertension is the consequence of peripheral vasoconstriction and direct stimulatory action on the myocardium. Hypotension at the end is the effect of small amounts of adrenaline, that have vasodilatory action.
- ▶ Tachycardia is due to the action of the substance on Keith and Flack nodules from intrinsic innervation of the heart, and as a compensation for vascular hypertension.
- ▶ Initial apnea is a reflex due to the large amount of adrenaline that reaches the level of the sinocarotid receptors as well as due to ischemia that occurs in the respiratory center.
- ▶ Tachypnea is the consequence of the bronchodilatory effect of adrenaline.

- ▶ The injection of 10 mcg/kg noradrenaline also produces hypertension, but this time constant and lasting, the fact is due to the pronounced vascular action of this substance. Breathing is less modified.
- ▶ Injection with 1 mg/kg ephedrine leads to a slower but longer-lasting hypertension. Breathing after a short, mild apnea is strongly stimulated by the effect of the substance at the level of the bulbar respiratory center, and sympathetic bronchodilation.

The following table shows the comparative actions of adrenaline and noradrenaline

The organ and function	Adrenaline	Noradrenaline
Heart		
Frequency	increased	low
Cardiac output	increased	minor changes
Excitability	much increased	increased
Blood pressure		
systolic	increased	increased
diastolic	low	increased
Blood vessels		
Muscle	constriction	constriction
Skin and viscera	constriction	constriction
Heart	expansion	expansion
Total peripheral resistance	low	increased
Capillary permeability	low	Weak effect
Metabolism		
Oxygen consumption, glucose release	low	insignificant
CNS	simulation, anxious state, stimulated breathing, tremor	insignificant effects
Smooth muscles		
bronchi	relaxation	weak effect
Intestine	relaxation	relaxation
sphincters	constriction	constriction
Bladder	relaxation	relaxation
Uterus (pregnant)	usually inhibition	stimulation

The action of horned rye extract

- ▶ After injecting a rye fluid extract into the chickens, it is observed the presence of progressive cyanosis that goes until the crest is blackened, effects that last for several hours.
- ▶ The cyanosis of the crest is due to a strong vasoconstriction action produced by the alkaloids of the horned rye. This vasoconstriction results in blood stasis in the extremities. When the duration of this stasis is longer than several hours, gangrene of the extremities may occur.
- ▶ At the level of the uterus, the derivatives of horned rye produce strong contractions of the musculature, being used at eutocic births to expose the fetus. Also, by increasing the tone of the uterine muscles, they have good anti-hemorrhagic effects in this organ.

The antihistamine action of Romergan

- ▶ It can be demonstrated: Inject 0.01g/kg Romergan, s.c., and after 10-15min. inject 1 ml/kg trypan blue 10% solution. An area is depilated of the animal, where 0.1ml of 1% histamine solution is injected intradermally.
- ▶ So, without the administration of Romergan, it is observed the appearance of blue coloration in the skin in the depilated area, however, no changes occur if Romergan is administered. The effect is due to the protection against histamine.
- ▶ The trypan blue does not diffuse out of the vascular bed unless it is slow and allows its extravasation. This effect is taken up by histamine. However, under the antihistamine action of Romergan, vascular changes no longer occur.
- ▶ Romergan also exerts a mildly hypnotic and anti-vomiting effect. Also, due to its structural relation with phenothiazine neuroleptics, it borrows a number of the characteristics of these substances.

The antihistamine action of chlordelazine in anaphylactic shock

- ▶ Administration of chlordelazine 0.01 / kg s.c, followed by 20 minutes of administration of 1% glycerinated histamine, it is observed that the antihistamine substance will induce drowsiness, without any changes due to histamine.
- ▶ In contrast, the single administration of glycerinated histamine 1% results in anaphylactic shock.

3. Pharmacography

Rp./

Vasoperif sol. 1% vials a 10 ml N II
D.S ext in inj. s.c., to horse, 1/day in 2 calves
(intestinal atony)

Rp./

Miostin vials a 1 ml N III
D.S ext in inj. i.m. 1/day, to dog, in 2 calves
(bladder atony)

Rp./

Adrenalin sol. 1% vials a 5 ml N II
D.S ext. s.c. to cow in 2 calves (serum disease)

Rp./

Arecoline sol. 1% vials a 5ml N II
D.S.ext inj. s.c. to cow 1/day, in 2 calves

Rp./

Atropină sol. 1% vials a 5 ml N II
D.S ext în inj. s.c. 1/day in 2 halves to horse
In colic through intestinal spasm

Rp./

Efedrină sol. 5% vials a 1 ml N V
D.S ext în inj. s.c. to horse bronchial spasm

Rp./

Secale cornuti pulv. 3,0
D.S int mixed in the middlings, to sow (placenta
retention)

Rp./

Romergan sol. 2,5% vials a 2 ml N X
D.S ext. i.m., to cow, in 2 halves (urticaria)

Rp./

Procaini hydrochlorici sol.5% vials a 5 ml N III
D.S ext inj. slow i.v. to horse (ganglioplegic in colic)

4. Classification

CNS modifiers

- depressant substances

- central anesthetics (narcotics)
- general sedatives and motor
- tranquilizers and neuroplegics
- analgesics and antipyretics

- exciting substances

Modifiers to the A.N.S.

- parasympathomimetic and parasympatholytic substances
- sympathomimetic and sympatholytic substances
- antihistamines
- ganglioplegic substances