

Semester II.

Pharmacology

Laboratory 9

Medication of digestive tract

1. Pharmacognosy

2. Pharmacodynamics

3. Pharmaceutical technique

4. Pharmacography

5. Classification of substances with action on the digestive tract

1. Pharmacognosy

- ▶ Digestive substances:
 - ruminants and emetics
 - purgative
 - carminative and anti-foaming agent
 - antiemetics, antacids, antidiarrheal
 - standardized preparations with action on the digestive tract

2. Pharmacodynamics

Producing gastric secretion in dog

Technique

- ▶ a Pavlov stomach is made, and the animal should be accustomed before with gastric juice harvesting.
- ▶ Various parasympathomimetic substances (pilocarpine, vasoperif, arecoline) or histamine which is most effective, may be used to induce gastric secretion. The histamine is given in doses of 0.1 mg/kg body weight in a 0.1% solution, injected subcutaneously.
- ▶ Also by the method of gastric fistula can be followed the effect of bitter (digestive bitter) administered orally, as opposed to administering the same substances with the gastric tube directly into the stomach.

- ▶ In the case of bitter substances, it will be found that gastric secretion is stimulated by a reflex pathway when these substances reach the buccal cavity and exert their action in the taste buds.
- ▶ If the substance does not come into contact with these papillae, being administered with the tube directly into the stomach, it will not influence gastric secretion.

- ▶ In the case of injecting a parasympathomimetic substance, gastric secretion is increased by the cholinergic effect of the substance. Histamine acts directly on the secretory glands, and its effect appears after vagotomy.
- ▶ Currently, it is considered by many researchers to be the final physiological component that acts in the glandular cells of the stomach, and all substances that stimulate secretion would ultimately act by releasing histamine into the cells of the gastric mucosa.
- ▶ At this level, it would produce the activation of carbonic anhydrase, an enzyme that plays an important role in the development of hydrochloric acid.

2. Pharmacodynamics

The action of antacid substances

- ▶ From a dog with a small stomach Pavlov, gastric juice is collected, and 3 ml of each is distributed in a test tube. It is measured using the pH meter, or the indicator paper.
- ▶ To the gastric juice, is then added in each test tube a neutrality agent for acidity. Thus, it will be added to the test tubes: calcium carbonate, sodium bicarbonate, magnesium oxide, magnesium carbonate, sub-nitric bismuth, kaolin.
- ▶ Each substance is used in a 5% aqueous solution or suspension, in an amount of 0.6 ml. The gastric juice is kept in contact with the neutralizing substance, and then measure the pH in each tube.

- ▶ The most active are calcium carbonate, magnesium oxide, and sodium bicarbonate, while the bismuth and aluminum salts have poor action.
- ▶ The acidity of the gastric juice, which is around pH 2, is neutralized by these substances.

The stimulatory effect of pilocarpine on the secretions and motility of the digestive tract

Technique

- ▶ 5 ml of hydrochloric pilocarpine 1% solution can be injected subcutaneously, followed by the effect of the substance.
- ▶ After 5-10 minutes following administration, it is possible to observe the abundance of salivation that the animal initially manages to swallow the saliva.
- ▶ For this, the animal makes frequent chewing movements with the tongue, followed by swallowing. In a short time, the amount of saliva that is secreted is so high that it can no longer be swallowed by the animal and flows abundantly from the mouth.
- ▶ If the hand is inserted, and the tongue of the animal is fixed, the swallowing of the saliva is prevented, the massive, and continuous leakage is observed.

- ▶ After listening to the intestinal noises with the help of the stethoscope, it can observe their intensification, by intensifying the peristalsis. The animal often becomes agitated by presenting abdominal colic as a result of strong contractions of the smooth muscles.
- ▶ Examining the frequency of the heart and breathing, it can observe that tachycardia and tachypnea occurs.
- ▶ In the horse, tachycardia following the administration of parasympathomimetics is a constant phenomenon, although these substances usually cause the heart rate to slow down. Also, there is a slight myosis.
- ▶ Pilocarpine as the other cholinergic substances stimulates not only salivary secretion but also other exocrine secretions throughout the digestive tract. Adding to this the stimulating effect of peristalsis we will understand the favorable action of these substances in some chronic indigestion, either through hyposecretion or through the atony of the digestive tract.

- ▶ Care should be taken, however, that parasympathomimetic substances should not be administered in gestation because produce uterine contractions, and can cause abortion.
- ▶ They will also not be used in animals with heart or respiratory conditions (it causes bronchial hypersecretion and contraction of the smooth muscles in the bronchi).
- ▶ After administering 5 ml of sulfuric atropine 1 ‰ solution all effects of pilocarpine disappear immediately.
- ▶ Salivary secretion stops, as do other digestive secretions. Moreover, the buccal mucosa becomes dry. Intestinal noises are quiet and the phenomena of colic disappear. Breathing returns to normal. At the pupil level, mydriasis appears.
- ▶ Thus, it can be observed that atropine and its successors have an opposite effect on parasympathomimetic substances and can be successfully used in spasmolytic and hyposecretory medication.
- ▶ It is also the specific antidote for poisoning with parasympathomimetic substances.

- ▶ These substances are not used in tympanism and indigestion through overload, as there is a danger of breaking the wall in the overloaded digestive organ (stomach, cecum in horse, rumen in cow, etc.).
- ▶ Also, these substances can be used as a reflex purgative by the stimulatory effect they exert on peristalsis.

The action of spastic and antispastic substances on the isolated intestine

Technique

- ▶ Collect a portion of the terminal ileum, record the normal tone of the intestinal musculature, and then add 1-2 drops of a 1 / 10,000 pilocarpine solution.
- ▶ The contraction of the intestinal fragment, marked by its shortening, is observed. By successive washes, pilocarpine can be partially removed, also it can be repeated using vasoperif, with similar effects.
- ▶ To counteract the cholinergic effect of the substances used, add 1-2 drops of sulfuric atropine 1 / 10,000, and there will be a strong relaxation of the smooth muscle of the intestine.
- ▶ It results from this experience how the parasympathomimetic substances act on the intestine, and generally on the smooth muscles, as well as the spasmolytic effect of atropine.

Demonstration of the vomiting action of apomorphine in dogs

- ▶ hydrochloric apomorphine 1% solution is injected at a dose of 5 mg/kg subcutaneous.
- ▶ After a few moments, it is noticed the appearance of nausea, translated by restlessness, tremors, polypnea, sialorrhea, ingestion of grass (when the animal is on a lawn with grass), vomiting movements.
- ▶ In a short time, vomiting occurs, which lasts until the stomach contents are evacuated.
- ▶ The vomiting produced by apomorphine is central, the substance acting at the level of the bulb, where the vomiting center is located.

Demonstration of the vomiting action of sulfathiazole in dogs

- ▶ Sulfathiazole is one of the most commonly sulfonamides used in veterinary medicine.
- ▶ Its administration is strictly intravenous due to the strong alkaline pH of the solution.
- ▶ In dogs, the use of the substance intravenously is not possible due to the vomiting effect it has on this species.
- ▶ This effect has not been observed in other animal species.
- ▶ It does not appear if the substance is administered orally.
- ▶ In a dog, 5 ml of sulfathiazole 20% solution is injected into the external saphenous vein. After a few minutes, sometimes even faster, the signs of nausea appear that have already been mentioned in the case of apomorphine, followed immediately by vomiting. After the evacuation of the stomach contents, the animal usually calms down.
- ▶ Vomiting triggered by sulfathiazole also has a central mechanism. As with apomorphine, it is about the stimulation of the bulb chemoreceptor area.

Production of peripheral vomiting by copper sulfate solution in dogs

- ▶ Administration of copper sulfate, 50 mg/kg in 1% warm aqueous solution orally, through its irritating action on the gastric mucosa, it will trigger vomiting as a reflex act of defense of the body.
- ▶ The vomiting effect of copper sulfate is therefore peripheral.

The anti-vomiting action of major tranquilizers

- ▶ In a dog with central or peripheral vomiting, chlorpromazine 10 mg/kg body is injected intravenously or intraperitoneally.
- ▶ It will be observed that immediately after the administration of the substance, the vomiting and nausea disappear, and the animal recovering in total.
- ▶ The same effect can be obtained by using delazine, prochlorpromazine, and romergan.
- ▶ This effect is better observed if the substances are given before vomiting. It will thus be found that vomiting no longer occurs, regardless of the vomiting substance we use.
- ▶ Neuroleptics can act as an inhibitor in the bulb chemoreceptor area, thereby exerting their antiemetic effect.

The purgative action of sodium sulfate

- ▶ 10 ml of methylene blue 1/1000 can be administered by gavage to one animal, and to another animal the same amount of methylene blue together with 4 g of sodium sulfate.
- ▶ After 30 minutes both are sacrificed, and the bowel examined.
- ▶ It will be seen that while in the one who received only methylene blue no obvious changes occur, in the one who received also sodium sulfate, the intestine is expanded and strongly hyperemic, having rich liquid content.
- ▶ This is due to the osmotic effect of drawing water into the intestine by saline purgative.
- ▶ By opening the bowels, it will be found that methylene blue traveled a long way on the digestive tract of the animal that received sodium sulfate.

Demonstration of the action of magnesium sulfate on the intestine

Technique

- ▶ After a 24-hour diet, pentobarbital sodium 3% is injected intravenous in doses of 30 mg/kg is injected into a laboratory animal.
- ▶ After the animal has fallen asleep, carefully open the abdomen, and attach to about 5 cm under the pylori, three separate portions of the intestine with 5-8 cm each, taking care not to damage the mesenteric vessels.
- ▶ Then, with a very thin needle are injected 1 ml magnesium sulfate 25% solution in the first portion, 1 ml magnesium sulfate 0.2% solution in the second portion, and 1 ml saline solution in the third portion
- ▶ Throughout the operation, and administration, the bowels will be moistened with saline solution at body temperature. After administration, the abdomen is closed immediately.

- ▶ After 30 minutes the abdomen is opened again, and the three ligated portions are examined.
- ▶ It can be seen that in the case of the hypertonic solution of magnesium sulfate the intestine is strongly expanded, containing a significant amount of fluid.
- ▶ The other two portions did not undergo any obvious changes.
- ▶ It can deduce from here the osmotic effect of magnesium sulfate, which thus exerts its purgative action.
- ▶ Magnesium ions are also known to stimulate intestinal chemoreceptors, leading to increased peristalsis.

3. Pharmaceutical technique

► Preparation of the *Riviere' s potion*

A *Riviere potion* or *solution-effervescens* is an official preparation used as an antivomitive, especially in small animals.

It is composed of 2 solutions that are administered separately, and which by their contact in the stomach releases carbon dioxide with a calming effect on the gastric mucosa.

The two solutions have the following composition:

1. Natrium bicarbonicum 4.0

Sirupus simplex 15.0

Aqua q.s. at 100.0II.

2. Acidum citricum 3.5

Sirupus citri 15.0

Aqua q.s. at 100.0

- ▶ The preparation of the solutions is made simple, first dissolving the crystalline substance in water, after which the syrup is added and homogenized.
- ▶ The release is made in two bottles, the name of the preparation being noted and numbered I and II separately.
- ▶ One teaspoon from each bottle, 1-3 times daily, is given to the dog or cat, in peripheral vomiting.

▶ Calcium hydroxide (traditionally called slaked lime) preparation

- ▶ The slaked lime or solutio calcii hydroxydati is an official preparation, commonly found in the pharmacy, but which is usually prepared on the ground by veterinarians in larger quantities being used as an ***anti fermenting***, especially in ruminant meteorism.
- ▶ The preparation is made of 2 tablespoons dried lime to 1 l of water. Mix well then allow to settle. The clear liquid after sedimentation is slaked lime, which contains 0.16% calcium hydroxide. It is preferable to use slaked lime prepared for several days.
- ▶ In the pharmacy the preparation is made of calcium oxide (lime unstained) as follows:
Calcium oxydatum 2.0
Aqua q.s.

- ▶ The calcium oxide is moistened with 5 g of water, and then 100g of water is added gradually.
- ▶ Shake and leave to stand for 12 hours, after which the clear liquid is decanted and removed. Repeat the operation twice. Then add 100 g of water and leave this.
- ▶ At the time of use, the aqueous solution is decanted and filtered.

▶ Preparation of Rumisan solution

- ▶ **Rumisan** is a veterinary preparation that is presented as an aqueous solution, having the following contents:

Tincture of junipers

Tinctura absinthi

Extractum veratri aa 170.0

Acidum Hydrochloricum 140.0

Distilled aqua. qs at 1000.0

- ▶ The preparation is presented in 1-liter bottles, for administration, take 1-2 tablespoons of Rumisan, which is mixed in 0.5-1 liters of water and given to the cow in the form of a drink.
- ▶ 1 teaspoon in 300-400 ml of water is given to the calves.
- ▶ In weaned piglets 2 teaspoons, and at baby piglets 1 teaspoon, each in 100-300 ml liquid.
- ▶ Rumisan is used with good results as ruminant and appetite stimulant, in ruminant atones and acute and chronic indigestion, dyspepsia in calves and piglets.

5. Classification of substances with action on the digestive tract

Digestive substances

pure bitter

- *radix gentianae*
- *herba centaurii*
- *radix taraxaci*

pure aromatic

- *menianthes juniperi*
- *fructus anisi*
- *fructus carvi*
- *folia menthae*
- *semen sinapis*
- *bulbus alii sativi*
- *radix armoraciae*

aromatic bitter

- *menianthae trifoliata*
- *herba absinti*
- *herba achilei*
- *flores camomillae*

saline

- *natrium chloratum*
- *natrium bicarbonicum*
- *natrium sulfuricum*

others

- *alcohol acetilicus*
- *acetum*
- *fructus capsici et pipermeni*

Cholecystokinetic and Choleric

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- *cynara scolymus* extracts and infusions
- fats, acids, natrium benzoicum,
- magnesium sulfuricum
- natrium salicylicum
- peptone
- egg yolk

Substituents of digestive secretions

- ruminal juice
- horse stomach juice
- pepsinax and hydrochloric acid
- Triferment

Digestive excito-motors

ruminants drug

- kalium stibiltartaricum
- rhizoma veratri
- farina sinapis
- veratrinum,
- rumisan, ruminol

emetic

- sulfatiazolum, radix ipeca
- apomorphinum, veratrinum

Purgative

on all segments

- *natrium sulfuricum*
- *magnezium sulfuricum*

on the small intestine

- *oleum ricinus*
- *oleum vaselinae, helianthi*
- *oleum crotonis*

on the large intestine

- *aloe, istizinum*
- *cortex frangulae*
- *sulfur sublimatum depuratum*
- *phenolphthaleinum*

Antizymotic

- *liquor amonii dilutum*
- *fomaldehydum dilutum*
- *suspensio creolini*
- *acetum*

Carminative

- *foliae menthae piperithae*
- *fructus anisi, carvi*
- *coriandri, foeniculi*

Carminative and antifoaming agents

Antifoaming

- *Blo-trol*
- *silicones*

Antacids

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- *natrium bicarbonicum*
- *magnezium oxidatum*
- *calcium carbonicum*

Mucilaginous protectors

- *radix althea*
- *amilum*
- *guma arabica*
- *semen lini*

Adsorbent

- *bolus alba*
- *carbo medicinalis*

Antidiarrheal

Astringent

- *aqua calcis*
- *bismuth carb. basic*
- *bismuth subnitricum*

Intestinal antiseptics

- *chemotherapeutic agents*
- *sulfonamides*
- *antibiotics*
- *benzoflitol*