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Introduction to Veterinary Pharmacology

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Pharmacology

(pharmakon = drug; logos = knowledge)

The science concerned with the study of drugs, including their origin, physic and chemical properties, composition, uses, modes of action and their effects on living organisms.



Pharmacology

Can also be defined as the study of the interaction between pharmacons and biological systems.

Pharmacons (drugs)

Are chemical agents that affect the function of biological systems.

The **Veterinarian** is interested in the rational and optimal use of the drugs for the prevention, diagnosis and treatment of disease. This branch of pharmacology is called pharmaco-therapeutics.



In the middle ages the discipline was called

De materia medica and it included elements of:

- pharmacology,
- therapeutics and
- pharmacy



It displayed advanced principles of therapeutics, and was divided into two categories:

- **rational** (if the nature of the disease and the mode of action of the substance was known).
- **empirical** (If the above knowledge was nonexistent or incomplete) which became an experimental field for clinicians.



Two systems of medical practice have established themselves over the centuries, which are also generally accepted to this day:

These are:

- **Allopathy**, and
- **Homeopathy**



Principle of Allopathy

It was introduced in 400 BC, by the famous Greek physician Hippocrates of Kos, called the “Father of Medicine”

Allopathy (*allos = other; pathos =disease*),

Represents a treatment system based on the principle “*Contraria contrariis curantur*” (opposites are cured by opposites), which advocates the use of drugs that produce effects, opposite to the symptoms.



Principles of Homeopathy (*homoios* = similar; *pathos* = disease)

were enunciated at the end of XVIII century by the Saxon doctor **Samuel Hahnemann** (1755-1843) (who was a librarian at the Bruckenthal Palace in Sibiu).

Homeopathy is based on the principle

“Similia similibus curantur” (likes are cured by likes), which advocates the use of drugs that produce effects similar to the symptoms.



It is the exact opposite of allopathy and is based on three fundamental principles:

- ✓ **similarity**
- ✓ **infinitesimal dose (high dilutions);**
- ✓ **treatment individualization**



Pharmacology, evolution and its subdivisions



Pharmacognosy

(pharmakon = drug; gnosis = knowledge)

The branch of knowledge concerned with medicinal substances obtained from plants or other natural sources and their main characteristics and properties.

Pharmacognosy

the medicinal substances, can be:

- **vegetal,**
- **animal,**
- **mineral**



Pharmaceutical chemistry

Deals with the composition and preparation of medicinal active substances (drugs) and studies their physico-chemical properties.

Pharmacodynamics (*dynamis* = power)

the branch of pharmacology concerned with the effects of drugs and the mechanism of their action.



Experimental pharmacodynamics

- Study the effect of drugs on laboratory animals, or on organs and isolated systems, serving informational and research purposes.

Clinical pharmacodynamics

- Follow the effect of drugs during the treatment period in animals or humans.



Pharmacokinetics

(*kinetikos* = motion, movement)

The branch of pharmacology concerned with the circulation of drugs within the body, and the determination of the fate of all substances administered externally to a living organism, in order to describe how the body affects a specific drug after administration.



Pharmacometrics

Analyze interactions between drugs and patients and study methods of measuring the intensity of drug effects.

Pharmacotherapy (*therapoeia* = care)

or clinical pharmacology studies the clinical application of drugs in different diseases, insisting on the mechanism of action, therapeutic efficacy, adverse reactions and toxic potential.



Therapy

Wider notion that includes other non-pharmacological methods of treatment intended to relieve or heal a disorder. (physical agents, diet... etc).

Prescribing

Advise and authorize the use of a medicine or treatment, especially in writing.



It has two subdivisions:

Pharmacography (*graphein = to write*)

studies the prescription of medicines in the form of a recipe.

Pharmaceutical technique (*Galenic technique*)

Studies the drug formulation and preparation methods.



Pharmacotoxicology

Deals with the study of acute or chronic intoxications and the adverse reactions produced by drugs.

Molecular pharmacology

Is a branch of pharmacology which is concerned with the study of pharmacology on a molecular basis.

Pharmacogenetics

It is a newer branch of pharmacology, concerned with the effect of genetic factors on reactions to drugs.



Extensive research in this area has led to the emergence of new sub-branches of the pharmacology domain:

- immunopharmacology,
- chronopharmacology,
- neuropharmacology,
- citopharmacology,
- biochemo-morphology etc.



Biopharmacy (biopharmaceutics)

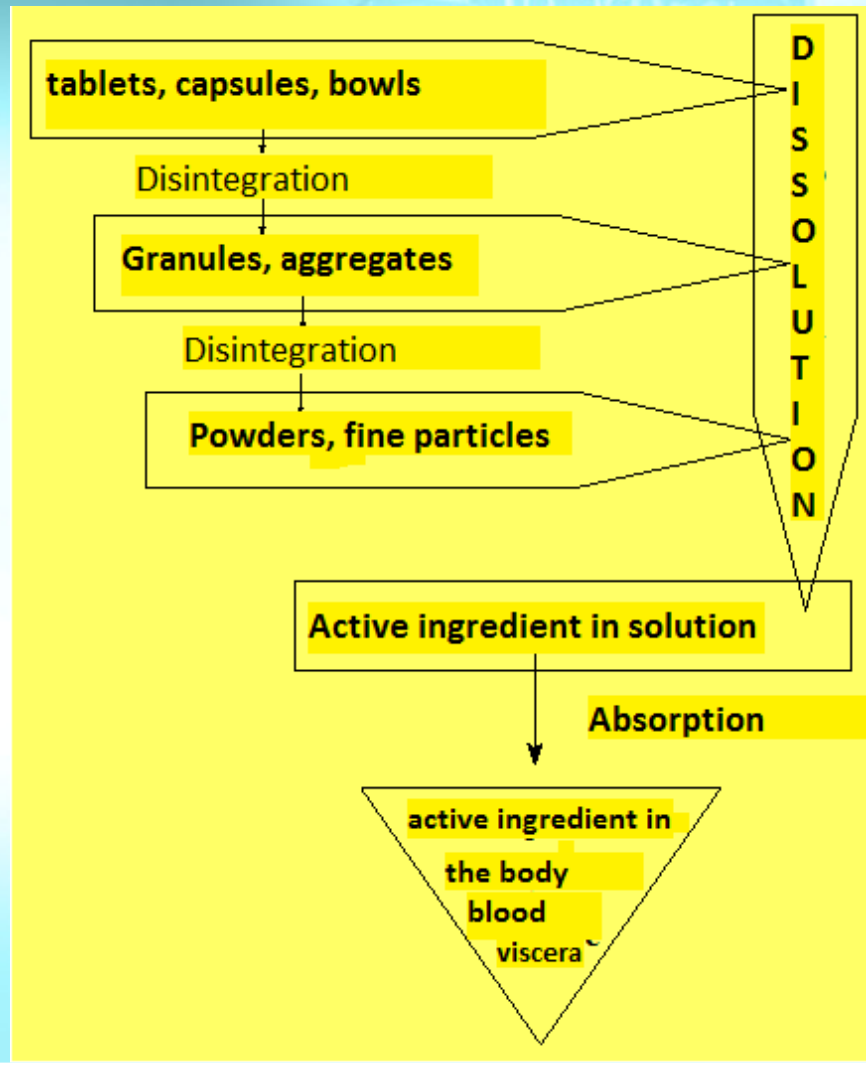
Deals with the study of:

- physico-chemical properties of substances,
- conditioning form and administration,
- pharmacokinetic parameters
- obtained bio-pharmacologic effects.



Bioavailability

basic notion of biopharmacy, which refers to the proportion of a drug or other substance which enters the circulation when introduced into the body and so is able to have an active effect.





The concept of medicinal product



The food - drug - toxic relationship

By **food** we understand:

“any nutritious substance of vegetal, animal or mineral origins, which enters the body’s metabolism, in order to maintain life and growth”.



The **Drug** as defined by WHO (World Health Organization), means:

“any product used in diagnostics, treatment, attenuation or prevention of diseases and abnormal physical states, or their symptoms, in humans or animals”.



Drug

A medicine or other substance which has a physiological effect when ingested or otherwise introduced into the body in order to :

- a)** diagnose, cure, mitigate, treat or prevent disease.
- b)** recognize and affect the structure or function of organic structures.



The pharmacon:

Any biologically active substance or product used or proposed for use, in order to influence or investigate physiological systems or pathological states, in the patient's benefit.



An ***“ideal”*** drug, will present:

- an accurate activity,
- a known mechanism of action,
- a constant effectiveness,
- the absence of adverse effects
- economic accessibility.



Drugs (medicines) can be obtained from the following sources:

- vegetal
- animal
- mineral
- synthetics

By **toxic** we understand:

“any substance which introduced into the body, produces general disorders known as intoxication”.



All drugs which are absorbed in the body can become toxic, when significantly exceeding the therapeutic dosages.

Long before the appearance of modern pharmacology, **Paracelsus** (1493-1541) showed that all substances are “poisons” and everything depends on the dose affirming that: *“Dosis sola facit venenum”* (The dose alone makes the poison).



Denomination and classification of drugs

Questions that pharmacologists are preoccupied with:

- What pharmaceutical preparation **should be used**?
- What is the **optimal dose**?
- Which is the **optimal frequency** of drug administration?

The answers to these questions depend on the pharmacist and the manufacturer's ability to prepare compounds from raw materials and to calculate the correct dosages, so that further recommendations can be made.

This ideal has been achieved by **standardizing drugs and remedies.**



The essential elements of such a system are:

- ▶ Definition of tests in order to establish identity, purity and strength of a medicinal source, of a substance or a preparation.
- ▶ Recommendations on dosage, administration frequency and indications for each drug.

However there it is still a high degree of confusion over drug nomenclature, because each chemical may be known under a variety of different names worldwide.



The “blame” lies on the drug manufacturers who, in order to protect and standardize their products, consider convenient to use brand names or *trademarks* to name their products.

Brand names are, most of the time, registered as a trademark.



Thus, chemical compounds with different formulations, can be produced in a number of unrelated names by several manufacturers.

An even greater confusion is created by the fact that the same drug can be used as a component in a number of compounds that contain multiple active ingredients.



- In an attempt to clarify this situation, the drafting committees of pharmacopoeia give each compound an **accepted name** (known as **official** or **generic name**).



Most of the time the **approved name**, is an abbreviation that derives from the chemical name of the substance, because most of the time, chemical names are long and difficult to memorize.

There are several "**versions**" of the names used by the chemists. Therefore a compound can have multiple chemical names (different, but correct).

So, the best solution is the one **accepted and internationally approved** name.



Due to these considerations we see a multitude of drug names (received after various criteria).

Medications extracted from **vegetal drugs** have names **close to the plants or yeasts** from which they are extracted:

- atropine (*Atropa belladonna*),
- strychnine (*Strychnos nux vomica*),
- caffeine (*Coffea arabica*),
- digitalin (*Digitalis purpurea*),
- penicillin (*Penicillium notatum*),
- streptomycin (*Streptomyces griseus*).... etc.



Chemical name

A term referring to the chemical makeup of a drug rather than to the advertised brand name under which the drug is sold. (ex: phenyl-ethyl barbituric acid is the chemical name of barbiturate derivative, known in over 120 commercial names).

Officinal name

is the name provided by the Pharmacopoeia and it is expressed in Latin (ex: *Coffeinum et natrii benzoas* for caffeine sodium benzoate).



The officinal name

It is used mostly by *researchers* and by those working in the preclinical stage.

To put order into the medicines nomenclature, the W.H.O. through its specialized committees, has agreed on an easier to remember, **Common International Name (or DCI)** for each substance, based on the chemical structure or on other criteria (ex: *aminophenazonum* for piramidone, *methenaminum* for urotropine, *pethidinum* for mialgin, etc.)



Pharmacopoeia



Pharmacopoeia

Is the basic book for the preparation of medicinal formulations, whose name derives from the Greek words: *pharmacon = remedy and poise = to make.*

Pharmacopoeia

Is a government publication containing a list of drugs, their formulas, methods for making medicines, and other related information.



The first reference dates to **2100** BC in Sumer (Pharmacopoeia from Nippur, written on burned clay).

In **Japan** the first pharmacopoeia appeared around 900 AD, describing 1025 products, from Chinese sources.

The first **Arab** pharmacopoeia includes over 200 medicinal plants, many still in use today.

The first **European** Pharmacopoeia appeared in the late XVII-th and early XIX-th century.

The first **International Congress of Pharmacology** took place in **1865** in Paris, where, for the first time, the need of an unitary Pharmacopoeia was determined.



The first Romanian Pharmacopoeia appeared in **1862**, during the ruler **Alexandru I. Cuza**, under the care of **Constantinos C. Hepites** (a Greek origin pharmacist), being one of the first works of its kind in Eastern Europe.

The first edition of the Veterinary Pharmacopoeia appeared in **1977**, and was published in Great Britain.



In the USA the equivalent of the European pharmacopoeia is the **United States Pharmacopoeia - National Formulary (USP).**

The ancient pharmacopoeias were abundant in preparations of natural origin, mainly vegetal.

The development of biological simulation systems on which the expressions of potency were based, was a major contribution from the pharmacologists.



Biological simulation

will continue to be a standard methodology in the analysis of qualitative and quantitative pharmacology for years to come.

Quantitative biological simulation expresses :

“the potency of a batch of medicinal products in relation to their ability to produce selective biological responses, related to a **standard preparation** of the same product”



The first synthetic organic drugs introduced in medicine were the volatile anesthetics, followed by the phenolic antiseptics.

Another big step was the **molecular modification of natural products** (*ex: 6-aminopenicillanic acid, product of fermentation, which was the starting point for semisynthetic penicillins*).



From a **toxicity point of view**, drugs are divided into three major groups :

- **Venena** (poisonous)
- **Separanda** (to be kept separately)
- **Anodina** (means “painless” or “harmless”)



Venena group

Includes toxic substances, with a very strict regime of keeping, release, use, and which are usually to be kept locked away in special cabinets.

In these medications the toxic dose is very close to the maximal therapeutic dosage and is usually expressed in milligrams or fractions of mg.

Drugs in this group require special recipes to be released.



The **Separanda** group includes:

highly active substances whose manipulation and use are highly dangerous.

They do not have the same degree of toxicity as the Venena group, but their administration requires strict supervision. They also must be kept locked in separate cabinets.



Anodina group includes:

non-toxic or substances of reduced toxicity, generally without risk in the actual use. By the **way of prescribing and manufacturing**, medicinal forms can be classified as:

- ▶ magisterial
- ▶ officinal
- ▶ standardized.

By **drug form**, we understand :

„the finite form of presentation of a drug for administration“.



Magisterial preparations

In pharmacy, *after a doctor's prescription*, composition can be different in each case.

Officinal preparations

in pharmacy, the prescriptions from the Pharmacopoeia, have a fixed composition. These are prescribed by enouncing the exact name, without explanation of the formula.

Standardized preparations (pharmaceutical specialty, industrial medicines)

They are industrially made, in drug factories, and have a fixed composition and preparation.



From this point of view there are:

Solid drugs: powders, granules, tablets, pills, bolts, capsules, etc.

Soft drugs: ointments, pastes, plasters, electuaries.

Liquid drugs of:

- **extraction** (macerates, infusions, decoctions, tinctures)
- **preparation** (molecular solutions, colloids, mixtures, emulsions).



**By their predominant
pharmacodynamic
actions**

drugs are categorized in:

*antiseptics,
disinfectants,*

*vasodilators,
vasoconstrictors,*

purgatives,

*chemotherapeutics
antimicrobials,
antiparasitics,*

*analgesics,
antipyretic,
hypnotics,
narcotics,
tranquilizers,
neuroleptics,*

diuretics,



The biologic drug

Is the product containing biological substances that are used for :

- **diagnostic,**
- **prophylactic and/or**
- **curative purposes.**

This category includes :

- **serums,**
- **vaccines and**
- **immunostimulating products.**



The veterinarian & the drugs



The clinician

characterizes a drug based on its:

- *effect* or, (ex: bacteriostatic, diuretic, stimulant etc.),
- *symptoms* from the *indications for use* (ex: analgesic, antacid, antispasmodic etc.).

The chemist

Is more “interested” by the drugs’ chemical structure than the pharmacists’ activity.



Activity of the drug

often forms the basis for different criteria of classification.

For example, to describe a drug as being a surfactant, diuretic osmotic, emollient etc. reference is made on their **physical terms**.

Description of a drug as being, for example:

- parasympathomimetics,
 - adrenergic
 - neuromuscular blocking agent,
- requires a **functional physiological** terminology.



Another older classification was based on the source and preparation of the product (for example identification by naming the plant sources and vegetal structure ex.:

- Gentiana root (*Gentiana*),
- Juniper berries(*Juniperis*),
- Chrysanthemum flowers(*Pyrethrum*).



Developing drugs with similar activities, led to obtaining **type-compounds**, against which new compounds are compared. This practice led to *the expression of terms* such as :

- histamines,
- atropines,
- chlorpromazines etc.



The discoveries that, drugs act by binding to the active macromolecular sites and the development of radio-labeled ligands for these sites, had made possible the use of the ligands for revealing un-identified binding sites, or for identification of the endogenous ligands (*ex: enkephalins, opioid receptors, etc.*).



Drugs conditioning

Knowledge of the drugs' molecular structure allowed the observations regarding the :

- the sites conformation at which level they link and act,
- offers a basis in order to suggest the hypothetical structures of the drugs with "*high potency*", *selective activity* and with *specific antagonism*.



In order to facilitate the discovery and to lower the costs of the new remedies, **computerized techniques** are employed in an attempt to specify the best possible parameters, before the synthesis of a molecule.

By doing this, it's possible to recognize the portions of the drug molecule responsible for the therapeutic action, and to synthesize only the substances that are corresponding in this regard, excluding those that prevent the drug association with its molecular target.



When the coupling is engaged in only a small portion of the molecule, specificity will allow the identification of a group of structurally different compounds, with a common biological activity.

This creates the potential for discovering structurally simpler analogs, easier to synthesize(ex: pethidin instead of morphine).



The opposite phenomenon is increasing the molecule's size (volume) and therefore, to convert a product into an antagonist (ex: beta blocker drugs), or make inaccessible the part of a structure that is uncovered for the unwanted enzymatic attack.

For example, the modification of a natural product, ex. Penicillin, in a semisynthetic penicillin which is resistant to the penicillinase attack).



These indicators are used in some methods based on analytical regression, defining correlations between them and the activity of the drug (ex: Hansch analysis and Hammett correlations).

These have established **QSAR**

Quantitative Structure Activity Relations



The presence of a drug in the body and the resulting chemical responses, are of a great importance to clinical utility.

Knowledge gained in this field enables the drugs administration, which are biologically inactive until their *activation in the body* and sometimes at the site of action. Such drugs are referred to as: **pro-drugs**.



Efficient use of the medicines:

It is obvious that rational therapy can only exist when establishing a certain diagnostic procedure.

However, the effective use of drugs involves a little more than selecting the best drug and the use of a potent formulation.



After the diagnosis, before administrating any drug, the clinician has to consider the:

- benefits
- disadvantages
- stopping the treatment with a drug and/or switching to another one, more suited
- correct dosage which will lead to the desired effect



Pharmaceutical Science is evolving rapidly and constantly.

Currently the drug market faces an excess of the “copies” of “renowned” preparations (cases where the patent copyright infringement is involved).

Unfortunately, the sales of a product depend directly on advertising and not on its qualities. This is where “aggressive advertising” interferes (including here veterinary field).



Pharmaco – clinical studies in the veterinary medicine



Biomedical research

In human and/or animal subjects the recognized scientific rules must be followed. The research has to be based on laboratory studies, on a sufficient number of animals and a complete knowledge of the literature.

Planning and conducting the experiment

A research protocol made by a specialized committee must be established (this committee must be neutral to the experiment and is empowered to supervise, make comments and give advice regarding the experiment).



Any project must be preceded, by establishing with certainty the **risks involved**, in relation to the benefits they bring to the subjects.

Veterinarians should be **cautious** when performing experiments whose risks can not be assessed.

Any experiments in which potential risks outweigh the potential positive results, **should be abandoned**.
Veterinarians have the duty to publish the experiment results, unaltered.



The clinical research



Concerning treatments, the practitioner **must feel free** to use new diagnostic and therapeutical methods, when, in his opinion, they could increase the chance of survival or cure, or to reduce the suffering.

Possible advantages, risks or side effects of new methods must be reported to the benefits of the best known methods.



- For every medical experiment, each patient or control group must be provided with the best methods of diagnosis and therapy.
- A veterinarian can perform clinical trials in order to obtain new scientific information, only when these experiments are in accordance with the medical act itself.



Placebo therapy in veterinary medicine



The therapeutic effect of the placebo drug is dependent on how is administered by the physician: ***optimistic or pessimistic.***

Administration of placebo drugs (apparent drugs) to humans, may lead to improvement or healing.



In **veterinary medicine,**

especially for pets where the level of owner - animal affection is raised, the therapeutic effect may be sometimes dependent on the owner's state of mind.

In these situations, one can speak of "placebo therapy" (closely dependent on the owner's affection and personality which can be influenced by the suggestion of the veterinarian).



Placebo substances in veterinary medicine may be used only in two circumstances:

- when a real pharmacotherapy is not necessary;
- the veterinarian is aware that he can perform psychotherapy on the owner with the help of the drugs administered to the pet.

However :

in contrast to placebo therapy in human medicine, which could be monitored in veterinary medicine it was not possible to monitor the occurrence of conditioned reflexes or some side effects in animals.



Thanks for your attention!