PHARMACOLOGY

Pharmacology is an experimental science dealing with properties of drugs and their effects on living systems. If the substances have medical properties, they are considered pharmaceuticals. Drugs may be used to improve health and quality of life, to treat and prevent diseases, or as a research tool to further explore body functions. Pharmacology also includes the study of sources of drugs (pharmacognosy) or the use of drugs in treatment of disease (toxicology). The word drug is derived from the Old French drogue, which meant herb.

Pharmacology is both an experimental (testing the drug action on animals), and clinical (testing the drug action on human volunteers or target animals for veterinary drugs) science that deals with all types of drugs: medicinal and recreational, legal and illegal, synthetic and naturally occurring, therapeutically beneficial medicines and potentially toxic substances. Clinical pharmacology represents a foundation for the application of pharmacologic principles in the development of drug therapy for animal patients. Controlled evaluation of the drug therapy safety and efficacy in animal patients is a major concern of veterinary clinical pharmacology. Veterinary pharmacology is not an easy subject to master due to the species multiplicity and abundance of drugs on the market. Veterinarians are asked to care for the health of the entire animal kingdom with the only exception— the humans. Different animal species respond to drugs differently, and the veterinarians must bear in mind that a large number of the animals they treat enter the human food supply chain and thus must evaluate the use of drugs accordingly.

Development of a drug is a vital concern to medicine, but also has strong economic and political implications. To protect the consumer and prevent abuse, many governments regulate the manufacture, sale, and administration of medication.

The study of medicinal chemicals requires intimate knowledge of the biological system affected, because chemicals have, from the pharmacological point of view, various properties.

Pharmacodynamics (pharmakon= drug, dynamis= power) is the study of the biochemical and physiological effects of drugs and the mechanisms of their actions, including the correlation of their actions and effects with their chemical structure (desired effects or toxic side-effects, etc.);

Pharmacogenetics (pharmacon+genesis= origin) is the study of the effect of the genetic factors belonging to a group or to an individual on the response of the group or the individual to certain drugs.

Pharmacokinetics (pharmakon+kinesis= motion) is the study of the action of drugs within the body, which can, in many respects, be envisioned more accurately as the actions of the body on an administered drug. It includes studies of the mechanisms of drug absorption, distribution, metabolism, and excretion; onset of action; duration of effect; biotransformation; and effects and routes of excretion of the metabolites of the drug (ADME).

- **Absorption** How is the medication absorbed (through the skin, the intestines, or the oral mucosa)?
- **Distribution** How does it spread through the organism?
- **Metabolism** Is the medication converted chemically inside the body, and into which substances?
• **Excretion**

How is the medication eliminated (through the bile, urine, breath, or skin)?

The term **bioavailability** is used to describe the fraction of an administered dose of medication that reaches the systemic circulation, one of the principal pharmacokinetic properties of drugs. When a medication is administered intravenously, its bioavailability is 100%. However, when a medication is administered via other routes (such as by mouth), its bioavailability decreases (due to incomplete absorption and first-pass\(^1\) metabolism). Bioavailability is one of the essential tools in pharmacokinetics, as bioavailability must be considered when calculating dosages for non-intravenous routes of administration. It is expressed as the letter *F*.

**ROUTES OF DRUG ADMINISTRATION IN ANIMALS**

- **I.M. (intramuscularly)** - administering a drug deep in the muscle for proper absorption. The diameter or gauge (g) should be as small as possible to prevent the drug from running up the needle track and down the side of the animal. This route of administration allows the second fastest rate of absorption. The site of injection is important, particularly in food producing animals, when it is possible to use the muscles on the neck. Injection site abscesses can develop.

- **I.V. (intravenous)** – provides the fastest route of absorption of drugs. In large animals, the jugular vein in the neck is the most frequently used. Drugs should be administered at body temperature and at a slow pace. This route of administration is used a) if a rapid drug effect is required; b) for continuous administration (infusion); c) for large drug dosage volumes; and d) for drugs that cause local tissue damage if given by other routes.

- **I.D. (intradermal)** – drugs are injected into the skin, the absorption rate is very slow, used e.g. for Tuberculosis skin tests

- **I.P. (intraperitoneal)** – drugs are injected directly into the peritoneal cavity, often used in combination with I.V. injections to prolong the availability of the medication to the animal. The drug absorption rate is slow.

- **I.R. (intrarumenal)** – administration similar to that of I.P., but into the rumen (the first part of the compound stomach in ruminants). Can only be accomplished on the left side of the animal. When needle inserted properly, stomach gas will flow out.

- **I.M.F. (intramammary infusion)** – drugs are administered (injected) into the teat canal using a plastic teat infusion cannula; used in the treatment of mastitis.

- **I.N. (intranasal)** – drugs are administered by squirting up the nostril; a suitable way for administration of some vaccines (e.g. Nasogen for IBR vaccination). Currently, many pharmaceutical companies are developing vaccines and other drugs that can be administered via this route to avoid injection site problems and to satisfy animal rights activists.

- **I.U. (intrauterine infusion)** – drug is infused into the uterus by passing a pipette through the cervix; often used to treat metritis (uterine infection).

- **Topical** – drugs are applied to the skin or surface of the body (e.g. Salves, ointments, pour-on wormers, dusts, etc.).
Oral (drench) – drugs are administered through the mouth in the form of a bolus (pill) or a liquid. Liquids or pastes can be placed in the mouth and animals are allowed to swallow them. Also a stomach tube can be used to administer the drug directly in the digestive tract.

Drug metabolism is the process by which the body breaks down and converts medication into active chemical substances; it is the transformation of a drug by the body tissues, primarily those of the liver, into a more water-soluble metabolite that can be eliminated. This process inactivates many drugs, but some drugs have metabolites that are also biologically active and others are administered as pro-drugs that must undergo drug metabolism to become biologically active.

Drug effect is the ability of a drug or treatment to produce a specific result, regardless of dosage. Knowing the general actions of drugs, both beneficial and harmful, is essential for their proper use in therapy. It is necessary to pay attention to common and potentially serious side-effects, toxic effects (toxicity), adverse effects, and contraindications. Various warnings, adverse and side effects are listed in the package inserts accompanying drugs.

- **Side-effects** are secondary to the main therapeutic effects. They are not necessarily harmful and might be prevented by decreasing the dosage of a drug. They have a tendency to disappear when a patient gets used to the medication. They include a loss of appetite, weight loss or weight gain, nausea, rash, vomiting, etc.
- **Toxic effects (toxicity)** are poisonous and potentially harmful effects caused by certain drugs. They are much more severe than the side or adverse effects. They very often develop if the patient’s dosage greatly exceeds the usual doses of a drug.
- **Adverse effects** are a harmful and undesired effect caused by an incorrect dosage (side-effect), wrong procedure or other medical intervention (surgery). Using a treatment which is contraindicated may increase the risk of adverse effects as well as not knowing other drugs simultaneously taken by a patient (interactions). Allergic reactions are considered to be the most serious (e.g. anaphylaxis, an immediate severe allergic response evoked by an exposure to an antibiotic, a bee sting or various foods). Adverse effects of medical procedures include: haemorrhage, inflammation, gangrene, etc. They can be reversible or irreversible.
- **Contraindications** refer to the factors in a patient’s condition that make use of particular drugs or medical procedures (surgery) life-threatening.

**DRUG ACTIONS AND INTERACTIONS**

Every physiologically active drug has the potential to cause undesirable reactions. In certain cases they may be responsible for illness. A condition which is caused by drug treatment is called iatrogenic. Besides the effects mentioned earlier, patients may experience:

- **Cumulative effects** – if excessive doses of drugs are taken they can accumulate in the body and cause problems with drug elimination. Thus, drug concentrations may reach toxic levels.
- **Tolerance (resistance) and dependence**: Habitual use of some drugs may create a tolerance (reduction in effectiveness of body response after repeated exposure).
Moreover, a physical dependence (development of signs and symptoms of illness when the drug is withdrawn) can also appear.

Various drugs can also interact with one another. When used in combination they may produce effects that are greater than either drug would bring about individually. In such a case we talk about potentiation. Lower or eliminated effects are called antagonism.

MAXIMUM RESIDUE LIMITS (MRLs) AND THE SAFETY OF FOOD FROM ANIMALS

In food-producing animals, veterinary surgeons and farmers must be aware of residues of licensed veterinary medicinal products. They are defined by the EU as pharmacologically active substances (whether active principles, excipients or degradation products) and their metabolites which remain in foodstuffs obtained from animals to which the veterinary medicinal product in question has been administered. An MRL is the maximum concentration of residue following administration of a veterinary medicine which is legally permitted or acceptable in food under the laws of the EU. Use of animal medicines is strictly controlled by European law, and requires observance of the withdrawal period. This is the time which passes between the last dose given to the animal and the time when the level of residues in the tissues (muscle, liver, kidney, skin/fat) or products (milk, eggs, honey) is lower or equal to the MRL. Until the withdrawal period has elapsed, the animal or its products must not be used for human consumption.

1 The first-pass effect (or first-pass metabolism) is a phenomenon of drug metabolism. After a drug is swallowed, it is absorbed by the digestive system and enters circulation. The absorbed drug is carried through the Portal vein into the liver. Some drugs are so extensively metabolized by the liver that only a small amount of unchanged drug may enter the systemic circulation, so the bioavailability of the drug is reduced.

Sources:
HAVLIČKOVÁ, DOSTALOVÁ, KATEROVÁ: English for Pharmacy and Medical Bioanalytics. The Karolinum Press, 2008. s. 175-181
Maximum Residue Limits (MRLs) and the Safety of Food from Animals accessed at <http://www.yoah.co.uk/issues/briefing/doc99-mrls.htm>
affinity (n)  /aˈfɛnətɪs/  vtzah k, chápání čeho  uprostřed, mezi
amid (prep)  /ˈaɪmd/  nepřátelství, opačné působení
antagonism (n)  /ænˈtæɡənɪzəm/  antipatogenník
antipathogenic (adj)  /ænˌtɪpəˈθætɪk/  antipatogenník
bile (n)  /baɪl/  žluř
bioavailability (n)  /ˌbaɪəˈvɒlərətɪs/  biologická dostupnost, využitelnost
bolus (n)  /ˈbɒləs/  pilulka
camulla (n)  /ˈkæmələ/  kanya
correlation (n)  /kərəˈleɪʃən/  korelace, vzájemný vztah
digitals (n)  /ˌdɪgɪtəlz/  digitální, nápříslušník
disintegration (n)  /ˌdɪsˈɪntɪgrətʃən/  rozpad, rozklad
dispersal (n)  /dɪˈspɜːsəl/  rozptylení, disperze
dissolution (n)  /ˌdɪzəˈluːʃən/  rozpuštění, rozložení
drench (v)  /drent/  nasáknout, namoč
efficacy in (n)  /ˈɛfɪkəsɪ/  účinnost, působivost
eclipse (v)  /ˈɛkləs/  uplynout, projít, vypršet
encompass (v)  /ɪnˈkʌmpəs/  obklopit, zahrnout
envisage (v)  /ɪnˈvɪzɪdʒ/  představovat si, předvídať
excipient (n)  /ɪkˈsɪpiənt/  mastový základ
excretion (n)  /ɪkˈskriʃən/  výměšek, vylučování
exert (v)  /ɪkˈzɜːrt/  vynaložit silu, činit se, projevovat se
exogenous (adj)  /ɪkˈzɔʊnɪəs/  vnější, působící zvědějku
foundation for (n)  /ˈfɑːnəˈdeɪʃən/  důvod pro
gangrene (n)  /ˈgænɡriːn/  snět
gauche (n)  /gɔːʃ/  míra, šablonu, mlíčlo
genomic (adj)  /ˈdʒɛməstɪk/  genomový
give rise to (phr)  /gɪv rɪz tə/  dát vzniknut čemu
hemorrhage (n)  /həˈmɔːrɪdʒ/  hemoragie, krvácení
iatrogenic (adj)  /ɪəˈtrɒgənɪk/  iatrogenní
implication (n)  /ɪmplɪˈkeɪʃən/  důsledek, souvislost, následek
in recognition of (phr)  /ɪn rɪˈkɒrəns əv/  jako projev uznání za co
in vivo (adv)  /ɪn ˈvɪvəʊ/  v živém organismu, zaživa
intramammary (adj)  /ˌɪntrəˈmeɪmərəri/  intramamární
intravenously (adv)  /ˌɪntrəˈveɪnəsli/  nitrožilně
liberation (n)  /ˈlɪbərəʃən/  zvonnopravění, osvození
margin (n)  /ˈmɑːrɪndʒ/  kraj, okraj, hranice
mastitis (n)  /ˈmɑːstɪtɪs/  mastitida
mediate (v)  /ˈmedɪteɪt/  zprostředkovat, sjednat, zakročit
medicinal (adj)  /ˈmedɪsɪnəl/  léčivý, působící jako lék
metabolite (n)  /meɪtəˈbɒlit/  metabolit
metritis (n)  /meɪtrɪtɪs/  metritida
morpheine (n)  /mɔːrˈfɪn/  morfin, morfin
mucosa (n)  /ˈmjuːkəsə/  mukóza, sliznice
nausea (n)  /ˈnɔːziə/  náuza
novel (adj)  /ˈnɔvəl/  nový, neobvyklý
onset of (n)  /ˈɔnˌset/  začátek, příchod; záchvat (choroby)
outcome (n)  /ˈaʊtkwɔːm/  výsledek, závěr, konec
pathway (n)  /ˈpæθweɪ/  stezka, cestovka (vyšlapánek)
peritoneal (adj)  /pɜːrɪˈtɒnɪəl/  peritoneální
pharmacognosy (n)  /ˌfɑːrməˌɡɒnɪs/  farmakognosie
posology (n)  /pəˈsɒlədʒi/  ven a portálu
quinine (n)  /kwɪˈnɪn/  chinin
residue (n)  /rɪˈziːd/  reziduum
resurgence of (n)  /rɪˈsɜːrʤən/  obnovení, obnova
rume (n)  /ˈrʌm/  bachor
salve (n)  /ˈsælv/  mast
teat (n)  /tɛt/  struk
therapeutic (adj)  /θəˈræpɪtɪk/  léčebný, terapeutický
uterus (n)  /ˈjuːtərəs/  děloha, uterus
vaguely (adv)  /ˌveɡəli/  nejasně, vyhýbavé