Veterinary Pharmacology

Veterinary pharmacology is defined as the study of the properties of drugs and all aspects of their interaction with living organisms. Drugs include any chemical agent (other than food) used in the treatment, cure, prevention or diagnosis of disease, or the control of physiological processes. The science of pharmacology draws on the knowledge and methods of many allied clinical and non-clinical disciplines, including chemistry, biochemistry, biology, physiology, pathology, toxicology, and medicine.

Veterinary pharmacology is an experimental science dealing with the properties of drugs and their effects on living systems. It has included study of sources of drugs (pharmacognosy), magnitude, and time course of the observed pharmacological effect on the body pharmacodynamics (PD), relationship between administered doses, the observed biological fluid/tissue concentrations of the drug, and time in the body pharmacokinetics (PK), use in the treatment of diseases (therapeutics), and poisoning effects (toxicology).

The residue definition for veterinary drugs in edible commodities of animal origin is obtained from metabolism studies conducted in target species and livestock animals. The metabolites, degradation products, and other transformation products are typically identified and quantified with methods based on the use of substances labeled with radioactive isotopes. Metabolites obtained in these studies are qualitatively compared with metabolites identified in laboratory animals, usually rats, to ensure that substances occurring in significant amounts in edible commodities have been included in the toxicological testing or to determine whether additional testing of individual metabolites is necessary. Metabolism studies in laboratory animals also serve to identify mammalian metabolism.

Drug–drug and drug–feed additive interactions deserve especial attention: a particular reference should be made to side effects and residue formation, and the likelihood of these interactions has to become part of the evaluation procedure. However, the most effective approach to prevent the occurrence of residues is certainly the rationally based selective use of veterinary drugs for which well-educated veterinarians are needed.

The form and the distribution of the residues that result from each authorized mode of application in each species should be determined, and the depletion of the residues from edible tissues or animal-derived foods should be studied. Total residue and metabolism study provides information to establish the appropriate marker residue (is the parent drug or any of its metabolites or a combination of any of these with a known relationship to the concentration of the total residue in each of the various edible tissues at the expected withdrawal time) and to determine the target tissue. A “marker residue” should be identified, which is usually the form of the drug (parent compound or metabolite) that is found at the highest concentration for the longest period in the target food. The tissue in which the highest residues are found is usually designated as a “target tissue” (represents the edible carcass from which residue depletes most slowly and is the edible tissue selected to monitor for the marker residue in the target animal) .

The extent to which such differences can be extrapolated to humans should be evaluated; for example, many sex differences in metabolism observed in rats do not occur in humans. The enzymes involved in the metabolism of foreign compounds represent the most important source of interspecies differences and human variability in the biodisposition of the compound and, for many cases, in the generation of toxic effects.

A further important role of such *in vitro* experiments is to investigate similarities and differences between humans and test species in the metabolism and effects of xenobiotics that may provide information critical to the extrapolations normally used in risk assessment.

Veterinary clinical pharmacology is a subset matter of the broad study of pharmacology and is devoted to the study of the clinical effects of drugs on animal patients with a goal of optimizing therapeutic dosage regimens. Knowledge of the PK and PD properties of drugs and their toxic effects is inherent in this veterinary discipline. Clinical pharmacology in the veterinary setting is the clinical discipline devoted to the optimal use of drugs in veterinary patients, maximizing their prophylactic or therapeutic benefits while ensuring that the adverse consequences of drug use are minimized.

Veterinary clinical pharmacology is a clinical science that integrates disease pathophysiology with fundamental concepts of pharmacology to provide a rational basis for drug therapy in animal patients . Brown states that the goal of veterinary clinical pharmacology is to apply the principles of pharmacology to more successfully treat animal patients and to more rationally use medications in veterinary medical practice. A fundamental understanding of veterinary clinical pharmacology is essential for good clinicians. The demonstration of efficacy includes the following test phases: (1) description of the mode of action, (2) determination of dose and dosing interval(s), (3) dose confirmation trials, including persistent efficacy trials, and (4) where applicable, clinical field trials. Similarly, knowledge of the pharmacological action of drugs is meaningless unless one also has a basic understanding of the relevant physiology and pathophysiology of the system or tissue adversely affecting the health or welfare of the patient.

There are methods for conducting clinical efficacy studies for infectious diseases and non-infectious diseases. These approaches may include studies in a model of the disease, or alternate methods for evaluating the response to the therapeutic agent in order to get utility in the new animal drug development process. The choice of the clinical endpoint is critical and determines the study design. There are many compounds (e.g., antibacterials, anthelmintics), where efficacy endpoints are reasonably easy to identify (i.e., clinical and bacteriological response as determined by the use of appropriate clinical, postmortem, and bacteriological diagnostic methods, and the determination of mortality rate; decrease in worm count, decreased temperature). However, identification of efficacy endpoints for non-antibacterial or non-growth enhancement compounds is more difficult to determine. Veterinary pharmacology aids in the identification of appropriate endpoints, helping to make them more quantitative, reproducible, and representative of the clinical field situation. Whereas “therapeutics” is a term describing treatment of disease in general and includes use of drugs, surgery, radiation, behavioral modification, and other modalities. Demonstration of efficacy of veterinary drugs is usually dealing with general requirements for the assessment of efficacy of such products. Depending on the aim of the trial, it can be classed in one of the following three categories: (1) confirmatory, (2) exploratory, or (3) composite trial. Confirmatory trials can concern dose-determination trials, dose confirmation trials as well as controlled field trials.

For antimicrobials, the dose, the dosing interval, and the number of administrations of product should always be justified by considering the PK/PD relationship, if established, as well as the severity of the disease. In some cases, where the PK/PD relationship is well established using validated models, it may be possible to omit dose-determination studies and to evaluate in a clinical trial the efficacy of one or a very few regimens. However, to be acceptable, the choice of the PK/PD parameter considered as best predictive of efficacy must be prospectively justified by independent data.

A prerequisite for clinical studies is to perform toxicological testing of new drugs with the objective to know potential undesirable effects of the drug candidates and drugs in the therapeutic range and above

## Veterinary Toxicology

Veterinary toxicology is a very complex subject as it deals with a wide variety of poisons. The field of toxicology is very broad, including the identification and characterization of a number of toxicants (pharmaceuticals, food and feed additives, natural toxins, consumer products, and specific chemicals), their physical and chemical properties, their fate in the body, and their biological effects. Currently, synthetic compounds constitute the largest number of chemicals that are frequently encountered in animal poisonings. Acute poisoning is a common presentation in emergency veterinary medicine. Moreover, veterinary toxicology is concerned with the treatment of disease conditions caused by poisons. Currently, there is a need to integrate veterinary medicine and specifically veterinary toxicology into environmental medicine.

The nature of the toxic responses depends not only on the toxicant but also on the route of exposure, the duration, and intensity of the exposure, and the characteristics of the exposed individual (i.e., species, gender, age, preexisting disease states, nutritional status, and prior exposure to the agent or related compounds). The subject of veterinary toxicology is complicated greatly by the wide variations in responses of domestic, aquatic, wild, and zoo species to toxicants. Of course, there are many other factors that can be involved in the overall toxicity of a chemical. Understanding the complete profile (especially mechanisms of toxicity) of each toxicant is the biggest challenge for today’s veterinary toxicologists ([21](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5020047/#B21)).

Veterinary toxicology is a multifaceted hybrid that draws on and contributes to the veterinary medical profession, the scientific field of toxicology and, broadly, to medical science. Some have characterized toxicology as a distinct scientific discipline. I view toxicology as an applied area of science addressing important societal issues by drawing on multiple scientific disciplines and professions. Veterinary toxicology had a much applied origin, involves the evaluation of toxicosis and deficiencies, identification and characterization of toxins and determination of their fate in the body, and the diagnosis and treatment of toxicoses in domestic animals and companion animals. However, the field has broadened to include concern for contaminants in human food products originating from animals and for contributing to the conduct and interpretation of safety/risk evaluations for pharmaceuticals, food additives, consumer products, and specific chemicals.

The recent worldwide melamine contamination in pet and swine feed indicates the relevancy of veterinary toxicology to current animal health and food safety, particularly on its toxicological aspects. Veterinary toxicology can be challenging because of the low frequency of cases observed in a practice setting. When a toxicosis occurs, it often involves a large number of animals and may also involve litigation .

Veterinary toxicologists who understand both normal and disease processes extending from the molecular level to the integrated mammalian organism and, indeed, populations, have an array of opportunities for making significant contributions to society .

In veterinary medicine, the discipline of clinical toxicology concerns the protection of companion, exotic/wildlife, and food-producing animals. Veterinary clinical toxicology links preventive and experimental toxicology with clinical veterinary medicine. Clinical animals are exposed to natural toxicants in their native environments, as well as to synthetic chemicals and drugs. The practicing veterinarian and the diagnostic or clinical veterinary toxicologist are often the first to respond to these problems, which may appear as a clinical syndrome of unknown cause. In veterinary medicine, understanding of sources of poisons, circumstances of exposure, diagnosis of the type of poisoning, treatment, and application of management or educational strategies to prevent poisoning is of much interest. The clinical diagnosis may be used initially to determine the organ systems affected, and the disturbances that must be controlled to save the animal’s life and etiologic diagnosis is the most important diagnosis because it enables specific therapy and preventive measures to proceed. Clinical toxicology evaluation depends heavily on the determination of exposure and evidence for the contribution of interacting factors than can alter toxicity.