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Editorial

Drug Metabolism in Veterinary Pharmacology

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EDITORIAL NOTE

Pharmacology is the study of the properties of chemicals used as drugs for therapeutic purposes. It is divided into the study of pharmacokinetics and pharmacodynamics. Veterinary pharmacology focuses on drugs that are used in domestic animals.

Drug metabolism/biotransformation is the term used to describe the chemical alteration of drugs (xenobiotics) as well as normally found substances in the body. Following filtration at the renal glomerulus most lipophilic drugs are reabsorbed from the filtrate. Biotransformation of drugs to more water-soluble (polar) chemicals reduces their ability to be reabsorbed once filtered by the kidney. This enhances their excretion and reduces their volume of distribution. The liver is the most important organ for biotransformation but the lung, kidney, and GI epithelium also play a role. Drug biotransformation frequently reduces the biological activity of the drug/chemical/toxicant. Drug metabolism/biotransformation is not synonymous with drug inactivation as the parent chemical may be transformed to a chemical with greater or significant biologic activity

The differences in the rate of elimination for drugs that are metabolized by the liver usually accounts for most of the differences in the values between species. Cattle and horses oxidize drugs more efficiently than dogs and cats. Because pharmacokinetic parameters including t1/2 values are more available for humans, it is important to appreciate that human values are usually longer than those of domestic animals (except cats). It is also important to be careful about comparing duration of action between different species of birds. There is significant variation between t1/2values of chickens, turkeys, and different wild birds which is again related to differences in metabolism. Although there are different types of cholinesterase in the tissues and blood, the overall levels in ruminants are lower than in horses and humans. This means that sheep, goats, calves, and cattle, are more sensitive to organo phosphorous compounds than horses and humans.

IONIZED DRUGS

There is much less variation in the t1/2values between the species for drugs that are more ionized, and have a lower volume of distribution: renal excretion is the main route of elimination. For example, the t1/2of gentamicin for cats is 82 minutes, for dogs it is very similar, 75 minutes. Penicillins and cephalosporins also have short t1/2values of 30-90 minutes in different species. Thus, highly "ionized drugs" are less likely to show species variation.

COLD-BLOODED ANIMALS

Fish and reptiles have longer t1/2values compared to mammalian species due to the much lower metabolic rates. However, the temperature of the ambient environment affects the metabolic rate of the animals and this, in turn, affects the t1/2values of the drug. The t1/2value of trimethoprim given IV to carp is 41 hours at 10°C but 20 hours at 24°C. Fish also have a lower renal function and more enterohepatic recycling than warm-blooded animals.

DISTRIBUTION AND SPECIES VARIATION

Distribution does vary with species. There is a significant difference between non-ruminant and ruminants in the distribution of lipid-soluble organic base drugs. The rumen has a pH of 5.5-6.5 and is a large volume relative to the whole body water; because of the large capacity of the rumen, which is up to 25 liters in sheep and up to 220 liters in cattle, the phenomenon of "ion-trapping" leads to the accumulation of weak bases in the rumen fluids. This means that xylazine, furosemide, and phenylbutazone have larger volumes of distribution in ruminants so that these compounds have a greater clearance in ruminants than non-ruminants.

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