

SUMMARY

Nowadays, anthelmintic therapy is the main method in the fight with parasitic worms. Anthelmintics, as well as other xenobiotics, undergo structural changes by effect of biotransformation enzymes, when lipophilic substances are transformed to polar substances more easily eliminable from the organism. Generally, biological effects of metabolites and parent compound are different. Activity of biotransformation enzymes is thus the fundamental factor influencing velocity of detoxification and elimination of the compound from the body and duration of drug effect as well. Modulation of biotransformation enzymes' activities can lead to changes in pharmacokinetic parameters of drug itself as well as other xenobiotics and thus to the risk of decrease in desired effect and/or increase in adverse effects with corresponding impact on the quality of drug therapy. In addition, possible risk of drug residues' presence in animal products has to be considered in farm animals.

Biotransformation of xenobiotics is affected by many physiological as well as pathological factors. These factors can be divided into inter-individual (species, gender, genetic polymorphism) and intra-individual (age, diet, medication, disease, etc.). All these factors cause wide variability in occurrence and activity of biotransformation enzymes and are main cause of big differences in biotransformation of xenobiotics in different individuals. Variability in drug metabolism is often the cause of therapy failure or of many unexpected or undesired reactions to drugs.

In presented work, the effect of disease of animals (microcoeliosis, haemonchosis) on the activity of biotransformation enzymes and metabolism of ABZ and FLU *in vitro* in mouflons, further modulation of the CYP1A activity and metabolism of ABZ *in vitro* in mouflons by single administration of ABZ, and at last effect of age and gender on pharmacokinetics of orally administered FLU to domestic sheep were studied. Age of animals and medication had the most significant influence from all studied factors (pathological status, medication, age, and gender). We found out that pharmacokinetics of FLU in sheep essentially differs in adult and young individuals, and treatment of mouflons by ABZ leads to pronounced induction of CYP1A and accelerated deactivation of ABZ. These findings should be taken into account during the pharmacotherapy of sheep by these anthelmintics.

Thus, given substance must be studied on target species of appropriate age with respect to gender, health condition, pregnancy, route of administration and formulation of

drug, and with respect to other factors as composition of diet or state of the environment in the place of breeding.