Inhibitory effect of albendazole and its metabolites on cytochromes P450 activities in rat and mouflon in vitro

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Abstract:
Cytochromes P450 (CYP) belong to the most important biotransformation enzymes, therefore, their inhibition may lead to serious pharmacological and toxicological consequences. Albendazole (ABZ) is a benzimidazole anthelmintic widely used in human and veterinary medicine. The effects of ABZ on CYP were investigated on the rat (Rattus norvegicus) and mouflon (Ovis musimon) hepatic microsomes. Besides ABZ, its two main metabolites (albendazole sulfoxide, ABZSO, and albendazole sulfone, ABZSOO) were tested to clarify which compound is responsible for the inhibitory effect. After preincubation of microsomes with the benzimidazoles (1, 5 and 25 µM), CYP activities, ethoxyresorufin O-deethylase (EROD) and benzyloxyresorufin O-dearylase activities were measured. The results showed that both ABZ and ABZSO, but not ABZSOO, exhibited significant potency to inhibit CYP activities measured in both tested species. Since ABZ as well as ABZSO are known inducers of EROD activity, our results clearly demonstrate that the drug can act as inducer and also as inhibitor of the same enzyme. In in vitro studies the CYP inhibition may mask the CYP induction. The extent of inhibition observed in mouflon was significantly higher than in rat. This finding emphasizes the importance of performance of inhibition studies in target animal species. Possible consequences of CYP inhibition should be taken into account during the anthelmintic therapy of mouflons with ABZ.

Key words:
albendazole, benzimidazole anthelmintic, enzyme inhibition, rat, mouflon