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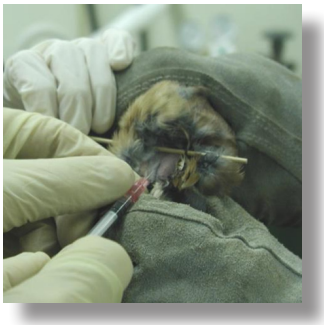
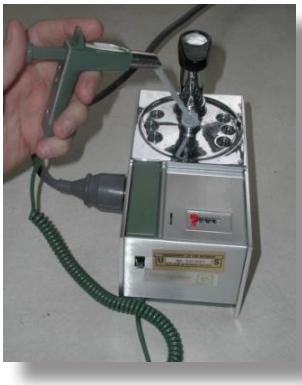
Patuxent Wildlife Research Center

Development of a Physiologically-based Pharmacokinetic Model for the Rodenticide Diphacinone in Kestrels and Owls





- ***The Challenge:*** Anticoagulant rodenticides have been identified as hazards to predatory and scavenging birds on a worldwide scale. Restrictions on the sale, distribution and packaging of brodifacoum, difethialone, bromadiolone and difenacoum by the US EPA in 2008 will likely cause the expanded use of other anticoagulant rodenticides, including diphacinone. The hazard of diphacinone to non-target organisms is inadequately characterized, hence toxicological data are being generated that underlie development of a pharmacodynamic model and a more complete risk assessment of diphacinone for birds.

- ***The Science:*** Data on the acute oral toxicity of diphacinone are being collected in bobwhite quail, American kestrels and Eastern screech owls. The effects of sublethal exposure to diphacinone on blood clotting time, histopathology, and the half-life of diphacinone in various tissues are being determined as well. A pharmacokinetic model for diphacinone in various species of wild birds will be useful in evaluating the hazard of this rodenticide.

- ***The Future:*** The acute oral toxicity of diphacinone was found to be over 20 times greater in American kestrels than in Northern bobwhite and mallards. Residue analysis suggests that the half-life of diphacinone in liver of kestrels is relatively short, with the majority of the dose cleared within days of exposure. However, histopathological examination of various tissues in exposed birds revealed extensive evidence of microscopic bleeding, and both prothrombin and Russell's Viper venom clotting times were lengthened. Prolongation of in vitro clotting time reflects impaired coagulation complex activity, and generally corresponded with the onset of overt signs of toxicity and lethality. In view of the implication of diphacinone in some raptor mortality events, and the paucity of threshold effects data following short-term dietary exposure for birds of prey, additional feeding trials with captive raptors may be warranted to more fully characterize the risk of secondary poisoning.

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