

Toxicity of the Non-Steroidal Anti-Inflammatory Drug Diclofenac



The Challenge: Diclofenac is a non-steroidal anti-inflammatory drug used by veterinarians for the treatment of inflammation, fever and pain in domestic livestock. This drug appears to have been the principal cause of a severe population crash of vultures of the genus *Gyps* in India and Pakistan. Vultures unintentionally ingested diclofenac when scavenging livestock treated shortly before death. This is perhaps the only well-documented instance of a veterinary drug resulting in an adverse population-level effect in non-target free-ranging birds. Diclofenac is registered for veterinary use in many Western hemisphere countries (e.g., Chile, Argentina, Peru, Ecuador, and provisional use in the United States), and there is potential for non-target exposure of birds of prey, including endangered California condors (*Gymnogyps californianus*) in the western U.S.



The Science: Studies were undertaken to determine the potential toxicity of orally administered diclofenac to New World vultures (*Cathartes aura*) and American kestrels (*Falco sparverius*). Birds were examined for overt signs of toxicity, gross and microscopic pathological lesions, biochemical effects, tissue residues, and diclofenac half-life in blood.

The Future: Diclofenac failed to evoke overt toxicity, visceral gout, renal necrosis, or elevate plasma uric acid when administered at concentrations greater than 100 times the estimated median lethal dose for *Gyps* vultures. The plasma half-life of diclofenac was estimated to be 6 hours, and it was apparently cleared after several days as no residues were detectable in liver or kidney. Findings suggest that New World vultures are considerably more tolerant to diclofenac than *Gyps* vultures. However, because differential sensitivity among avian species is a hallmark of cyclooxygenase-2 inhibitors like diclofenac, additional studies in related scavenging species and raptors are being conducted through multinational collaborative investigations.

