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## A Silent Threat to Vultures from Veterinary Medicine

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### Introduction

Numerous chemicals have been introduced into our environment since the post-World War II era due to tremendous industrial growth. These consist of industrial wastes, medicines and insecticides. These drugs are intended to enhance human life, animal health and agriculture, but their unforeseen impacts on the environment have frequently gone unnoticed. Scientists have found over time that these substances are not limited to their intended targets. Rather, they damage non-target species by spreading through soil, water and food systems. One of the more startling instances is the decline in vulture populations in India as a result of the veterinary medication diclofenac.

### The Vulture Crisis in India

One of the most significant and concerning reductions in wildlife populations in contemporary ecological history occurred in India in the early 2000s. Millions of birds were lost throughout the Indian subcontinent as a result of the populations of three local vulture species—*Gyps bengalensis*, *Gyps indicus* and *Gyps tenuirostris*—collapsing by more than 99% in a very short amount of time. By scavenging animal carcasses, these vultures, which were previously common and crucial for preserving environmental hygiene, nearly vanished from the ecosystem, raising major ecological and public health issues.

Subsequent thorough scientific studies determined that Diclofenac, a frequently used non-steroidal anti-inflammatory medicine (NSAID) given to animals, especially cattle, for pain and inflammation treatment, was the main reason of this disastrous drop. Diclofenac residues were found in the tissues of animals who died soon after treatment. As natural scavengers, vultures consumed these tainted carcasses and unintentionally came into contact with the medication. Diclofenac showed to be exceedingly toxic to vultures at even very tiny doses,

resulting in acute kidney failure, raised uric acid levels and eventually death in a short period of time. One of the worst cases of drug-induced wildlife mortality ever recorded resulted from this unanticipated and species-specific sensitivity, which transformed a commonly used veterinary medication into a silent but deadly threat.

### **How Diclofenac Kills Vultures**

Diclofenac exposure causes a quick and deadly series of physiological disruptions, according to scientific studies on the mass mortality of vultures. When vultures eat corpses that contain even minute doses of this medication, it disrupts regular kidney function and causes serious renal damage (nephrosis). The kidneys are no longer able to adequately filter metabolic waste, especially uric acid, which is the main nitrogenous waste product in birds. Consequently, dangerously high quantities of uric acid build up in the bloodstream (hyperuricemia).

Visceral gout is the result of this excess uric acid precipitating and forming urate crystals that accumulate all over the body. The function of several internal organs is seriously compromised by these chalky white, pointed deposits. In addition to these distinctive white deposits covering important organs like the liver, heart (particularly the pericardium) and spleen, post-mortem studies of injured vultures regularly show significant kidney impairment.

Toxicity develops quite quickly. Vultures usually exhibit sadness, weakness and lethargy after consuming tainted tissue, which is followed by organ failure. The majority of recorded instances result in mortality between 48 and 92 hours after exposure. Diclofenac's rapid and deadly effect, even at extremely low dosages, explains why vulture populations were so severely impacted by the medication and emphasises how sensitive these birds are to it.

### **Scientific Study: Can Other Birds Predict Toxicity?**

Researchers investigated whether other, more common bird species could be used as experimental models to predict the hazardous effects of Diclofenac because direct toxicity testing on endangered vultures is both practically challenging and unethical. The Japanese quail, Muscovy duck and domestic pigeon were among the species used in controlled experiments for this aim. Due to their ease of upkeep and recommendation in international testing guidelines, these birds are frequently employed in toxicological research. These studies' findings showed that each species' reactions to diclofenac exposure varied significantly. Similar to the clinical symptoms previously noted in vultures, both Japanese quails and Muscovy ducks showed obvious symptoms of toxicity, such as depression, weakness and final death.

These birds' post-mortem results likewise revealed urate accumulation and renal injury, suggesting a similar pathogenic process. Domestic pigeons, on the other hand, shown an

impressive level of drug resistance. Pigeons showed no appreciable harmful effects or mortality even when subjected to same amounts. Their systems were better able to break down and get rid of the medication, which stopped harmful metabolites from building up. These divergent reactions make it abundantly evident that different bird species respond to the same medication in different ways, mostly as a result of differences in physiology, metabolism and biochemical tolerance. Because it emphasises the limitations of employing surrogate species in toxicity testing, this finding is extremely significant. A drug that appears safe in one species may still be highly toxic in another, as seen in the case of vultures and diclofenac.

### **Why Are Vultures So Sensitive?**

The extreme sensitivity of vultures to Diclofenac is not accidental but is linked to fundamental physiological and biochemical differences between species. Scientific studies have identified two major mechanisms that explain why vultures are affected so severely compared to other birds.

The first key factor is metabolic differences. In many bird species, the liver is able to efficiently break down and eliminate diclofenac through metabolic processes. However, vultures appear to lack this capacity or possess it at a much lower level. As a result, when vultures ingest diclofenac-contaminated carcasses, the drug is not properly metabolized and begins to accumulate in the body. This accumulation leads to toxic concentrations in the bloodstream, ultimately damaging vital organs, especially the kidneys. In contrast, species such as the Muscovy duck can metabolize the drug more rapidly, reducing its harmful effects.

The second critical factor is the ability to handle uric acid, which is the primary waste product in birds. Vultures have a very limited tolerance for elevated uric acid levels in their blood. When diclofenac disrupts kidney function, uric acid rapidly builds up, leading to a condition known as hyperuricemia. In vultures, even a small increase in uric acid can trigger the formation of urate crystals throughout the body, causing visceral gout and rapid death. On the other hand, some species like ducks can tolerate much higher levels of uric acid without experiencing fatal consequences. This higher tolerance allows them to survive even when exposed to doses that would be lethal to vultures. Together, these two mechanisms explain the stark differences in survival between species. While ducks may sometimes recover despite exposure, vultures succumb to toxicity at extremely low doses. This highlights the unique vulnerability of vulture species and underscores the difficulty in predicting drug safety across different animals.

### **Shocking Toxicity Differences Across Species**

The wide range in toxicity between bird species is one of the most startling discoveries

from Diclofenac study. Vultures have a very low fatal dosage (LD<sub>20</sub>) of about 0.1 mg/kg, although other species, including ducks and quail, have much higher LD<sub>50</sub>'s of about 190 mg/kg and 405 mg/kg, respectively. This means that vultures can be quickly killed by a dose that is innocuous or very slightly poisonous to species like the Japanese quail or Muscovy duck. A crucial principle in veterinary pharmacology and toxicology is demonstrated by this striking contrast: a medication that is safe in one species may be extremely hazardous in another, rendering cross-species safety assumptions untrustworthy.

### **Impact on the Environment Outside of Vultures**

There were significant ecological and social repercussions from the reduction in vulture numbers. As natural scavengers, vultures are essential because they quickly devour carcasses and stop the spread of illness. As a result of their disappearance, carcasses stayed in the environment for extended periods of time, which sharply increased the number of other scavengers like rats and stray canines. This change directly affected human health and upset the natural equilibrium. Growing rodent numbers increased the risk of diseases like the plague, while feral dog populations increased the number of rabies cases. The impact on the economy was particularly significant, with estimates indicating losses of over \$2.43 billion per year in India as a result of disrupted ecosystems and higher healthcare bills.

### **Why Existing Drug Testing Failed**

The diclofenac incident revealed serious flaws in the safety assessment and drug licensing procedures. Traditionally, target animals like dogs and cattle, as well as lab animals like rats and mice, are used to evaluate veterinary medications. Nevertheless, the possible effects on wildlife, particularly birds, are mostly ignored by these testing procedures. The environmental implications of soil and water contamination are the primary focus of regulatory frameworks like those created by VICH, with scavenging and other indirect exposure pathways receiving less attention. Consequently, an extremely dangerous medicine entered widespread use without sufficient ecological controls since the risk to vultures and other scavenging birds was not anticipated.

### **Can We Use Other Birds to Predict Toxicity?**

Organisations like the Organization for Economic Co-operation and Development advise utilising surrogate bird species like quail, ducks and chickens to solve the problem of proving drug safety without exploiting endangered species. The larger avian group is thought to be represented by these species. However, studies have made it abundantly evident that this strategy has significant drawbacks. The fact that each species has distinct metabolic pathways and genetic traits is highlighted by these models' incapacity to forecast diclofenac toxicity in

vultures. These variations affect drug absorption, metabolism and excretion, resulting in wildly disparate reactions. Therefore, while evaluating drug safety, depending only on a small number of model species may lead to risky mistakes.

### **Are All NSAIDs Dangerous?**

Importantly, not all non-steroidal anti-inflammatory drugs pose the same level of risk to wildlife. While diclofenac has proven to be toxic, safer alternatives do exist. For example, Meloxicam has been extensively studied and found to be safe for vultures, making it a recommended substitute in veterinary practice. On the other hand, several other NSAIDs—including Ketoprofen, Flunixin and Phenylbutazone—have also been identified as toxic to certain bird species. This variation underscores the importance of careful drug selection and awareness among veterinarians, particularly in regions where livestock carcasses are accessible to scavengers.

### **Practical and Ethical Difficulties**

Drug testing on endangered animals, such as vultures, is one of the main obstacles to preventing such ecological catastrophes. Direct experimentation is severely constrained by ethical constraints and the procedure is further complicated by pragmatic concerns like cost and time. Because of this, researchers are actively looking for different strategies, such as enhanced prediction models, in vitro testing systems and sophisticated computational tools. Developing techniques that can precisely evaluate environmental risks without endangering sensitive species is the aim.

### **Veterinary Science Lessons**

Several significant lessons for contemporary veterinary science and environmental management can be learned from the diclofenac disaster. First, it strengthens the idea of "One Health," which acknowledges the close connections between human, animal and environmental health. Second, it emphasises the necessity of responsible drug use, stressing that veterinary medications should be chosen for both their safety in the larger environment and their efficacy in the intended animals. Third, it increases knowledge of how pharmaceutical residues affect the environment, which might have unforeseen and significant repercussions. Lastly, it emphasises how critical it is to include wildlife issues in drug safety assessments.

### **Prospective Routes**

A multifaceted strategy is needed to stop similar tragedies in the future. Scientists are attempting to create species-specific toxicity models that take genetic and metabolic variations into consideration. Molecular biology developments, such as PCR and toxicogenomics, provide promising methods for comprehending the biological responses of many species to

medicines. At the same time, raising awareness among farmers and veterinarians and encouraging the use of safe substitutes like meloxicam are vital actions. Protecting biodiversity will also need tightening environmental laws and incorporating ecological risk assessment into medicine clearance procedures.

### Conclusion

The diclofenac tragedy serves as a strong reminder of how a useful veterinary medication can unintentionally cause a significant ecological catastrophe. The near-extinction of vulture populations in India showed serious flaws in the current safety evaluation processes and demonstrated the unexpected nature of medication toxicity across species. Since every species reacts differently due to its distinct biology, it is evident from current research that toxicity cannot always be predicted using traditional models. Environmental safety must be given top priority going ahead and veterinary medicine must take a more comprehensive approach.

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Sharma, P., Patel, R., & Singh, K. (2023). Pharmacokinetics and toxicity of NSAIDs in avian species: Implications for environmental safety. *Veterinary Pharmacology and Therapeutics*, 46(2), 210–220. <https://doi.org/10.xxxx/vpt.2023.xxxx>

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