ASSESSMENT OF THE POTENTIAL EFFECTS OF DICLOFENAC ON SPANISH AVIAN SCAVENGERS GUILD

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The most important European vulture populations (>90%) are in Spain (Margalida *et al*., 2010) (Table 1). However, on 2013 the veterinary use of diclofenac, a non-steroidal anti-inflammatory (NSAID) drug, was authorized. The generalized use of this product between 1990 and 2006 resulted in the death of >95% of three *Gyps* species in the Indian Subcontinent (Oaks *et al*., 2004; Green *et al*., 2006). Diclofenac is fatal to vultures when they ingest residues of recently treated animals and die from kidney failure within days of exposure to contaminated tissues (Oaks *et al*., 2004). In India, lethal contamination of just 0,13% to 0,75% of ungulate carcasses may explain the observed vulture declines (Green *et al*., 2004). In Spain, between 0,11% and 0,22% of all carcasses available to vultures could include diclofenac in 5 years (VCF, Public consult).

The law (RD 1632/2001) allows some dead animals to remain within the field or in certain areas (feeding stations); there are 235 stations for scavenging birds registered and many unauthorized. Annually, 70.000 animal carcasses are available to scavenger birds (40.000 in stations, the remainder on field). It would be complex, expensive and not fully reliable to create a system to ensure that these carcasses do not contain toxic concentrations of diclofenac. The identification of meloxicam as non-toxic alternative drug (Cuthbert *et al*., 2007) and the wide variety of published literature about the toxicity of diclofenac, reflect an enormous contradiction between science and application of knowledge. The objective of this work is to make a literature review on the impact caused by the veterinary use of diclofenac on the avian scavengers guild in Spain, which plays a key role on the conservation of these species at an European level. Possible exposure scenarios that currently exist in Spain are defined and, finally, applicable preventive and control measures are also mentioned.

1. DICLOFENAC

NSAID with multiple therapeutic uses (treatment of pain, fever and inflammation); its efficacy is fully demonstrated in both human medicine and veterinary. Its mechanism of action is to block prostaglandin synthesis by inhibition of cyclooxygenase.

2. TOXICITY TO BIRDS

Vultures that consume a lethal dose die within 1 - 2 days of exposure from renal failure. They show clinical signs of extensive visceral gout, and diclofenac residues are detected in kidney and liver tissues (Oaks *et al*., 2004). Toxicity mechanism is related to the accumulation of uric acid in plasma (Naidoo and Swan, 2009).

Diclofenac is toxic to other species such as Steppe eagle (*Aquila nipalensis*) (Sharma *et al*., 2014). This discovery suggests the possibility that diclofenac is also toxic to other *accipitri* raptors, increasing the risk to a much wider range of birds. By contrast, other species such as turkey vulture (*Cathartes aura*), pied crow (*Corvus albus*), domestic chickens (*Gallus gallus domesticus*) and all of the New World Vultures are much less sensitive to diclofenac.

3. RISC ASSESMENT (EMA/CVMP 2014)

The European Commission (EC) asked the European Medicines Agency (EMA, Committee for Medicinal Products for Veterinary Use –CVMP-) to assess the risk in the EU. Non-toxic concentration for vultures and other raptors has been estimated on 3µg/kg. The highest concentrations of residues are found at the injection site for cattle and pigs (Figure 1).

Many raptors may be susceptible to a wide range of NSAIDs; a review with numerous treatments with NSAIDs to 79 bird species suggests that diclofenac, carprofen and flunixin are highly toxic and that more studies for ketoprofen and dexamethasone are required (Cuthbert *et al*., 2007). Recently, the first poisoning of a griffon vulture by ingestion of residues of flunixin in Andalucia has been demonstrated (Zorrilla *et al*., 2014).

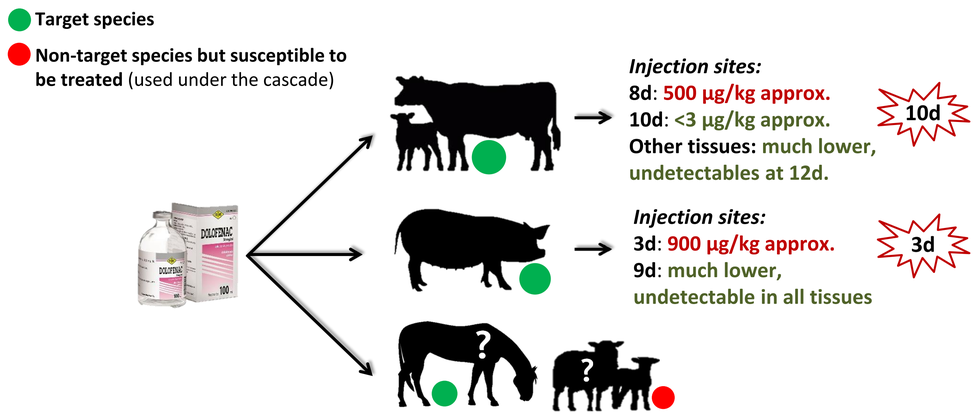
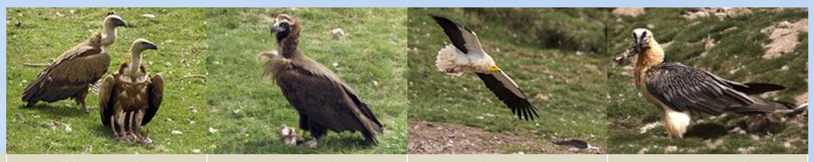


Figure 1. Diclofenac residues on treated animals (EMA/CVMP 2014)

Table 1. European vultures, population census and conservation status.



Name	Griffon vulture	Black vulture	Egyptian vulture	Bearded vulture
EU Population (pairs)	26.967 – 28.063	2.126 – 2.127	1.547 – 1.748	199 – 200
% population Spain/EU	**91**	**97**	**67**	**85**
Global status (IUCN)	Least concern	Near threatened	Endangered	Near Threatened
EU status	Secure	Rare	Endangered	Vulnerable
Spain Status (CEEA)	-	Vulnerable	Vulnerable	Endangered

Other facultative scavenger bird species threatened and potentially susceptible to diclofenac are: **Red kite** (*Milvus milvus*), **Black kite** (*Milvus migrans*), **Spanish imperial eagle** (*Aquila adalberti*) and **Golden eagle** (*Aquila chrysaetos*).

4. EXPOSURE ROUTES: 2 main scenarios (EMA/CVMP 2014)

1. EXPOSURE AT FEEDING STATIONS:

a) **From animal by-products from slaughterhouses: no risk** is identified (diclofenac concentration <3µg / kg).

a) **From treated animals that die on farms and are taken directly to stations: high risk** when the animals die within few days after treatment.

2. EXPOSURE FROM FALLEN STOCK: opinions about whether animals can be treated before they are moved to pastures (or during the stay) differ. **The bodies remaining on field are not subject to any control.**

5. PREVENTIVE AND CONTROL MEASURES

- **To always evaluate the toxicity of NSAIDs and other veterinary compounds widely used against carrion birds.**
- **To include on current pharmacovigilance services systems to routinely determine the presence of certain veterinary drugs in animal tissues.**
- **To establish official control measures on farms to ensure that carcasses from treated animals will not enter the food chain of carrion birds. All dead animals treated should be collected by a specialized company.**
- **At slaughterhouse level, to take on specific analysis to determine the presence of diclofenac in animal carcasses.**
- **In authorized dumps, to analyze through official sampling the animal carcasses, especially those from farms.**

These measures include multiple controls at different levels, which are complex and expensive. Whereas there is an alternative drug (meloxicam), it seems ineffective and impractical. Conservation experts and scientists agree that the same measures as in South East Asia should be applied here: the prohibition of the product and the promotion of the use of meloxicam. At the same time, they suggest a new exchange policy based on jointly promoting research and policy knowledge (Margalida *et al*., 2015).

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