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REVIEW

Toxicology

A review: poisoning by anticoagulant rodenticides in non-target animals globally

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ABSTRACT. Worldwide use of anticoagulant rodenticides (ARs) for rodents control has frequently led to secondary poisoning of non-target animals, especially raptors. In spite of the occurrence of many incidents of primary or secondary AR-exposure and poisoning of non-target animals, these incidents have been reported only for individual countries, and there has been no comprehensive worldwide study or review. Furthermore, the AR exposure pathway in raptors has not yet been clearly identified. The aim of this review is therefore to comprehensively analyze the global incidence of primary and secondary AR-exposure in non-target animals, and to explore the exposure pathways. We reviewed the published literature, which reported AR residues in the non-target animals between 1998 and 2015, indicated that various raptor species had over 60% AR- detection rate and have a risk of AR poisoning. According to several papers studied on diets of raptor species, although rodents are the most common diets of raptors, some raptor species prey mainly on non-rodents. Therefore, preying on targeted rodents does not necessarily explain all causes of secondary AR-exposure of raptors. Since AR residue-detection was also reported in non-target mammals, birds, reptiles and invertebrates, which are the dominant prey of some raptors, AR residues in these animals, as well as in target rodents, could be the exposure source of ARs to raptors.

KEY WORDS: anticoagulant rodenticide, comprehensive review, non-target animal, raptor, residue

Worldwide use of anticoagulant rodenticides (ARs) for vertebrate pest control has frequently led to the unintentional exposures of non-target animals, especially raptors, to these poisons. Recently, more than 420 birds, including 46 bald eagles (*Haliaeetus leucocephalus*), died because of a rat-eradication program on an Alaskan island [2]. Reporting that more than 130 dead raptors found in and around Vancouver, Canada, and virtually 100% of the owls and the hawks in this group, had AR residues in their livers, the Nature News article "killing rats is killing birds" had a strong impact on the world [29]. The occurrence of AR poisoning in raptors is related to many factors, such as the exposure pathway, the degree of ARs inhibiting the target molecule (vitamin K 2,3-epoxide reductase, VKOR), and AR metabolism by cytochrome P450 (CYP).

Although it is thought that raptors are sensitive to ARs, the mechanism for this sensitivity has not yet been revealed. Several toxicokinetic of avian species have been studied. Compared to mammals, eastern screech-owls (*Megascops asio*) have a long elimination half-life of diphacinone in the liver [39]. Furthermore, owls have very low CYP-dependent warfarin metabolic activity compared to rats and other avian species [62]. These facts imply that owls have a limited ability to detoxify ARs. However, toxicokinetics of the other raptor species has been rarely studied.

In spite of frequent incidents of primary or secondary AR-exposure and poisoning in non-target animals, including predatory mammals and birds (especially raptors), these incidents have been reported only in individual countries and there has been no comprehensive worldwide study or review. Therefore, we comprehensively reviewed and analyzed the published literature on AR-exposure occurrence based on the kind of ARs, the country type, and the animal groups. In addition, this review discussed diets of raptors. Some possible exposure pathways in addition to the target rodents were also discussed.

The chemical structures of nine typical anticoagulant rodenticides (ARs) are shown in Fig. 1. ARs are classified into two classes:

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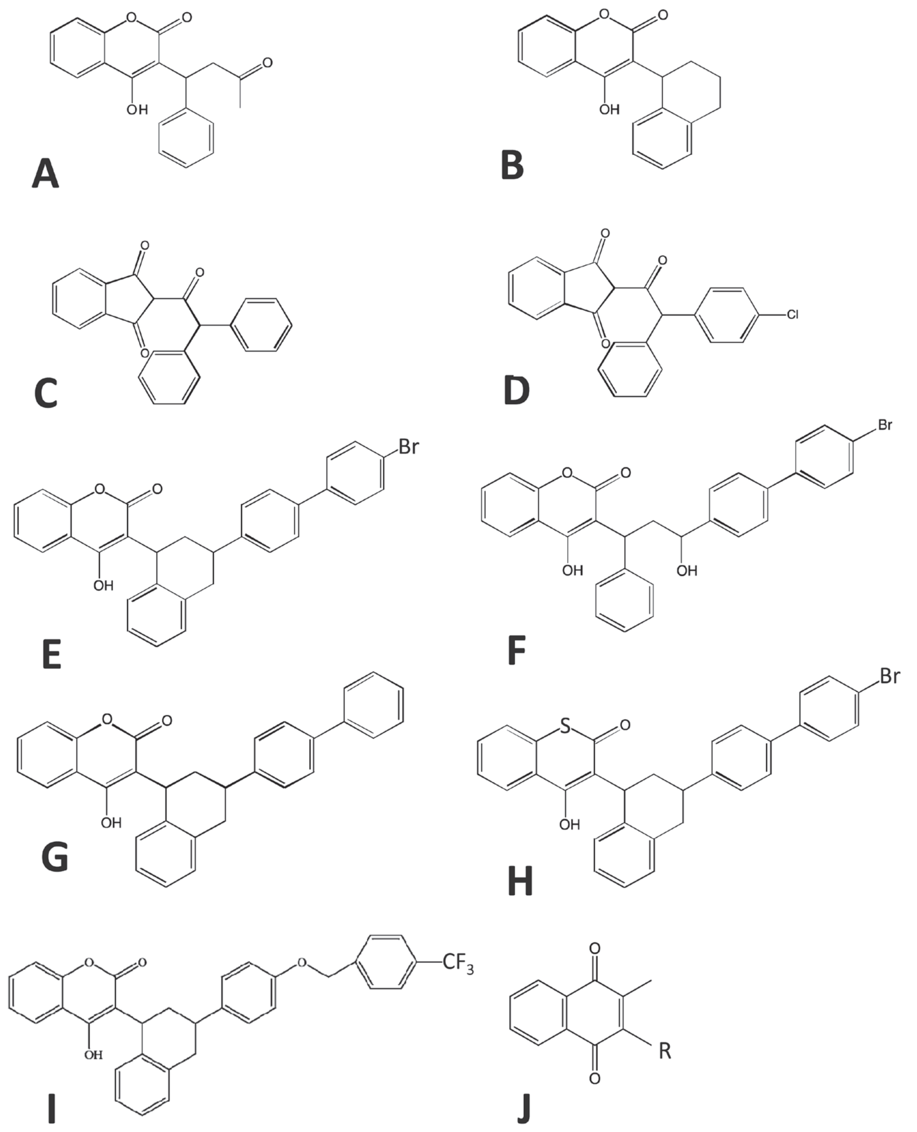

Fig. 1. Chemical structure of nine typical ARs (A to I) and vitamin K (J). First-generation anticoagulant rodenticides (FGARs) are represented by the coumarin (warfarin, A, and coumatetralyl, B) and indanedione (diphacinone, C, and chlorophacinone, D) rodenticides. Examples of second-generation anticoagulant rodenticides (SGARs) are brodifacoum (E), bromadiolone (F), difenacoum (G), difethialone (H) and flocoumafen (I). The main chain structures of ARs are similar to that of vitamin K (J).

4-hydroxycoumarin derivatives (coumarin: warfarin, coumatetralyl, brodifacoum, bromadiolone, difenacoum, difethialone, and flocoumafen), and 1,3-indanedione derivatives (indanedione: chlorophacinone and diphacinone are the most commonly used examples).

By the early 1950s, warfarin was being used as a pesticide to control rats and mice [41]. Warfarin and other early ARs, such as coumatetralyl, chlorophacinone, and diphacinone, are called first-generation ARs (FGARs). Multiple ingestions of these compounds are required to cause death in rodents. Since then, FGAR-resistant rats and mice have appeared, so the more potent second-generation ARs (SGARs), such as brodifacoum, bromadiolone, difenacoum, difethialone, and flocoumafen, were developed [41]. SGARs require only a single ingestion to cause death in the targeted rodents. For mice, SGARs have a longer $T_{1/2}$ than FGARs (Table 1): in the plasma, $T_{1/2}$ for SGARs is 20.4–91.7 days, while that for FGARs is 0.52–14.9 days; and in the liver, $T_{1/2}$ for SGARs is 28.1–307.4 days, whereas that for FGARs is 15.8–66.8 days. In addition to longer $T_{1/2}$, SGARs have a lower LD_{50} than FGARs (Table 2): LD_{50} for SGARs and FGARs are 0.4–1.75 and 20.5–1,000 mg/kg in mice; 0.35–0.84 and 11–323 mg/kg in rats; 0.25–8.1 and 0.88–50 mg/kg in dogs; 3.15 and 942 mg/kg in chickens; 0.26–138 and 258–2,150 mg/kg in northern bobwhites; 10 and >100 mg/kg in ring-necked pheasants; and 4.6 and 620–3,158 mg/kg in mallards. In Australian harriers, LD_{50} for brodifacoum (SGARs) is 10 mg/kg; and in American kestrels, LD_{50} for diphacinone (FGARs) is 97 mg/kg. These longer $T_{1/2}$ and lower LD_{50} for SGARs imply that SGARs are more toxic than FGARs.

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Table 1. Eliminated half-life, $T_{1/2}$ (days) for FGARs (warfarin, coumatetralyl, chlorophacinone and diphacinone) and SGARs (brodifacoum, bromadiolone, difenacoum, difethialone and flocoumafen) in animals. Modified from [12, 18, 20, 39, 40, 57]

	FGARs				SGARs				
	Warfarin	Couma-tetralyl	Dipha-cinone	Chloro-phacinone	Brodi-facoum	Broma-diolone	Difen-acoum	Difeti-alone	Flocou-mafen
$T_{1/2}$ in the plasma									
Mouse[a)]	14.9	0.52	-	11.7	91.7	33.3	20.4	38.9	26.6
$T_{1/2}$ in the liver									
Mouse[a)]	66.8	15.8	-	35.4	307.4	28.1	61.8	28.5	93.8
Rat	-	-	3	-	-	-	-	-	-
Pig	-	-	5.43	-	-	-	-	-	-
Screech owl	-	-	11.7	-	-	-	-	-	-

a) dose=half of LD_{50}.

Table 2. Median lethal dose, LD_{50} (mg/kg) for FGARs (warfarin, coumatetralyl, chlorophacinone and diphacinone) and SGARs (brodifacoum, bromadiolone, difenacoum, difethialone and flocoumafen) in animals. Modified from [12, 18, 20, 39, 40, 57]

	FGARs				SGARs				
	Warfarin	Couma-tetralyl	Dipha-cinone	Chloro-phacinone	Brodi-facoum	Broma-diolone	Difen-acoum	Difeti-alone	Flocou-mafen
Mouse	374	<1,000	141–340	20.5	0.4	1.75	0.8	1.29	0.8
Rat	14–323	-	30	11	0.35–0.5	0.56–0.84	-	0.55	-
Dog	20–50	-	0.88–15	-	0.25–1.0	8.1	-	-	-
Cat	2.5–20	-	5–15	-	<25	>25	-	-	-
Chicken	942	-	-	-	3.15	-	-	-	-
Northern bobwhite	>2,150	-	2,014	258	-	138	-	0.26	-
Ring-necked pheasant	-	-	-	>100	10	-	-	-	-
Mallard	620	-	3,158	-	4.6	-	-	-	-
American kestrel	-	-	97	-	-	-	-	-	-
Australasian harrier	-	-	-	-	10	-	-	-	-

AR EXPOSURE GLOBALLY

From 1998 to 2015, altogether 30 papers were published reporting primary or secondary exposure and poisoning by ARs in non-target animals. Of these, 19 papers report poisoning of raptors. There are six publications from the U.S.A. [9, 42, 45, 48–50], three from Canada [1, 18, 55], nine from the U.K. [7, 19, 31, 46, 47, 58–61], two from France [13, 25], three from Spain [28, 43, 44], two from Denmark [5, 11], one from Norway [26], and four from New Zealand (NZ) [6, 8, 14, 35]. These reports and the proposed exposure pathways are summarized below.

Presence of ARs in non-target animals

According to the literatures published between 1998 and 2015, totally 2,694 out of 4,891 (55%) individual non-target animals have been found to have a residual accumulation of ARs in their livers (Table 3A). Because the kinds of analyzed rodenticides were different depending on the papers, the number of analysis was different for each compound. Brodifacoum was detected in 31% (n=1,465 out of 4,790) of non-target animals, bromadiolone in 30% (n=1,346 out of 4,513), and difenacoum in 26% (n=1,048 out of 4,001). The other compounds were detected in less than 10% of the animals: flocoumafen in 5.7% (n=175 out of 3,077), difethialone in 5.0% (n=101 out of 2,035), chlorofacinone in 5.6% (n=113 out of 2,013), diphacinone in 5.0% (n=99 out of 1,972), coumatetralyl in 4.5%, (n=108 out of 2,391), and warfarin in 1.0% (n=27 out of 2,639). Some animals had more than two types of ARs in their liver.

High detection-rates of brodifacoum, bromadiolone and difenacoum reflect the relative frequency of use of these SGARs and differences in tissue $T_{1/2}$ values between compounds. Because brodifacoum has longer $T_{1/2}$ compared with the other ARs (Table 1), it would be expected that brodifacoum is detected for a long time and is over-reported relative to the amount of use compared with the other compounds. Because of the high toxicity of SGARs, as indicated by their longer $T_{1/2}$ values in the liver and lower LD_{50} values relative to FGARs (Tables 1 and 2), the potential adverse effects of SGARs on non-target animals are a particular cause for concern.

AR exposure of non-target animals in each country

In terms of occurrence in each country (Table 3B), residues of rodenticides were detected in 523 out of 560 animals (93%) in Denmark, 241 out of 362 animals (67%) in Canada, 171 out of 288 animals (59%) in NZ, 474 of 812 animals (58%) in the U.S.A.,

Table 3. Detection rates and the numbers of non-target animals in which ARs have been detected in their liver, classified based on (A) type of AR, (B) country and (C) animal groups. Altogether, there were 2,694 out of 4,891 individuals (55%) of non-target animals have been reported to have AR residues in their livers between 1981 and 2013 [1, 5–9, 11, 13, 14, 18, 19, 25, 26, 28, 31, 35, 42–50, 55, 58–61]

(A)	FGARs				SGARs				
	Warfarin	Couma-tetralyl	Dipha-cinone	Chloro-phacinone	Brodi-facoum	Broma-diolone	Difen-acoum	Difeti-alone	Flocou-mafen
Detection rate (%)	1.0	4.5	5.0	5.6	31.0	30.0	26.0	5.0	5.7
The number of detection	27	108	99	113	1,465	1,346	1,048	101	175
The number of analysis	2,639	2,391	1,972	2,013	4,790	4,513	4,001	2,035	3,077

(B)	Denmark	Canada	NZ	U.S.A.	Norway	Spain	U.K.	France
Detection rate (%)	93	67	59	58	53	51	44	23
The number of detection	523	241	171	474	16	437	790	42
The number of analysis	560	362	288	812	30	849	1,809	181

(C)	*Carnivora*	Raptors	Mammals excluding *Carnivora*	Birds excluding raptors	Reptiles
Detection rate (%)	56.8	56.6	52.1	52.1	50.0
The number of detection	382	1,892	212	207	1
The number of analysis	672	3,345	407	397	2

Table 4. The number of non-target animal species in which ARs have been detected in the liver. References are given in Table 5

	U.S.A.	Canada	U.K.	France	Spain	Denmark	Norway	NZ	Total[a)]
Raptors	13	4	7	4	18	11	2	2	34
Other birds	9	1	-	2	9	-	-	16	34
Carnivora	5	-	3	4	8	2	-	-	15
Cetartiodactyla	1	-	-	-	-	-	-	2	3
Erinaceomorpha	-	-	1	-	2	-	-	-	2
Rodentia	2	-	-	-	-	-	-	-	2
Lagomorpha	-	-	-	-	1	-	-	-	1
Chiroptera	-	-	-	-	-	-	-	1	1
Marsupialia	1	-	-	-	-	-	-	-	1
Reptiles	-	-	-	-	1	-	-	-	1
Total	31	5	11	10	39	13	2	21	94

a) This is not necessarily the sum of the values for each country, because some species were reported in several countries.

16 out of 30 animals (53%) in Norway, 437 out of 849 animals (52%) in Spain, 790 out of 1809 animals (44%) in the U.K., and 42 out of 181 animals (23%) in France. Although these rates seem to imply the degree of AR exposure in each country, it is difficult to compare the percentage with each country, because these percentages probably reflect residue detection limits as well as the relative frequency of use. The minimum detectable amounts of individual ARs described in the study of Denmark and Canada were lower than those of France (e.g. 2–5 to 70–80 μg/kg for brodifacoum respectively) [1, 5, 11, 13, 18, 25, 55]. On the other hand, the detection limits for brodifacoum were 10–50, 2–20, 5, 1–6, and 1.4–50 μg/kg of NZ [8, 14, 35], the U.S.A. [9, 42, 45, 48–50], Norway [26], Spain [28, 43, 44], and the U.K. [7, 19, 31, 46, 47, 58–60], respectively. Therefore, high (or low) sensitivity of detection seemingly not always cause over (or under)- estimation, but in some cases might affect accounting of AR exposure. We would like to note that, although AR detection rates were various in eight countries (from 23 to 93%), AR exposure of non-target animals might certainly occur in all eight countries.

The largest number of species in which AR residues have been found in one country (Table 4) was 39 (Spain), followed by 31 (the U.S.A.), 21 (NZ), 13 (Denmark), 11 (the U.K.), ten (France), five (Canada), and two (Norway). In all of these countries except NZ, raptors constituted the majority of exposed species: 18 in Spain, 13 in the U.S.A., 11 in Denmark, seven in the U.K., four in France and Canada, and two in Norway. In NZ, the majority of exposed species were in the group “birds excluding raptors” (16 species). Various species (totally 94 species), especially raptors (34 species), were exposed to ARs.

AR residues in non-target animals have only been reported in these eight countries. This is probably because this research is implemented only in North America, Europe and NZ. However, ARs have been frequently used worldwide [21]. Global AR market data is difficult to obtain because of confidential business information, but estimates are described as hundreds of millions dollars annually in the U.S.A. and European countries [41]. Primary and secondary AR exposure of non-target animals may indeed occur all over the world, so increased surveys are needed worldwide to determine the extent of the problem.

Classification of animal species exposed to ARs

Table 3C shows that the accumulation of AR residues was detected in 382 out of 672 individuals of *Carnivora* (56.8%), 1,892 out of 3,345 raptors (56.6%), 212 out of 407 mammals excluding *Carnivora* (52.1%), 207 out of 397 birds excluding raptors (52.1%), and 1 out of 2 reptiles (50%). Percentages of *Carnivora*, raptors and reptiles are presumed to be secondary exposure degree, and those of mammals excluding *Carnivora* and birds excluding raptors seem to be primary exposure degree.

Although secondary exposure seems to occur in *Carnivora* and raptors at a comparable frequency, secondary poisoning should be considered to occur in raptors frequently relative to *Carnivora*. Critical liver SGAR concentrations associated with hemorrhaging and mortality have not been defined for most raptor species. However, the potentially lethal range for SGARs in raptors has been described as >100–200 μg/kg [5, 55, 60]. On the other hand, the lethal concentration of SGARs in *Carnivora* livers have been reported that brodifacoum of 700 μg/kg was detected in stoat and weasel, bromadiolone of 230 μg/kg accumulated in stoat, and difenacoum of 1,400 μg/kg was measured in polecats [31, 46]. Because most of the cited references in the current review did not mention AR concentrations of individual animals, we could not calculate AR-poisoning rate of individual species. However, raptors are presumed to be poisoned by ARs frequently rather than *Carnivora*, because of the low lethal range for SGAR residues in raptors. Moreover, screech owls have longer $T_{1/2}$ for diphacinone compared with rats and pigs (Table 1), and owls have very low warfarin metabolic activity relative to rats and other avian species [62]. The adverse effect of AR exposure on raptors is of interest.

The high AR-exposed rate was reported in various raptor species rather than *Carnivora* species. The number of species ARs detected in more than 60% of individuals was 11 in raptors, and it comprised 48% of 23 raptor species that the number of analysis was more than nine individuals (Note: We did not include the species whose analyzed individual sample size was less than 8. This was to avoid the over-estimation e.g. 100% of detection rate such a case that the one individual detected from the one individual analyzed.). In contrast, 3 species, which had over 60% AR-detection rate, composed 27% of 11 *Carnivora* species that AR residue was examined in more than nine individuals. AR exposure to extensive raptor species implies that various kinds of raptors have a risk of AR poisoning.

SECONDARY EXPOSURE TO AR IN RAPTORS

Frequently reported raptor species

Of the 39 raptor species analyzed, 34 species were reported to have AR accumulation in their liver, and 17 species had more than 60% detection rate of ARs (Table 5): two out of two turkey vultures (*Cathartes aura*; 100%), one out of one short toed snake-eagle (*Circaetus gallicus*; 100%), three out of three marsh harriers (*Circus aeruginosus*; 100%), five out of five moreporks (*Ninox novaeseelandiae*; 100%), 15 out of 17 little owls (*Athene noctua*; 88%), 33 out of 39 Eurasian eagle owls (*Bubo bubo*; 85%), 20 out of 24 bald eagles (*Haliaeetus leucocephalus*; 83%), five out of six short-eared owls (*Asio flammeus*; 83%), 26 out of 32 rough-legged buzzards (*Buteo lagopus*; 81%), 116 out of 145 sparrowhawks (*Accipiter nisus*; 80%), 108 out of 138 red kites (*Milvus milvus*; 78%), 62 out of 80 long-eared owls (*Asio otus*; 78%), 154 out of 206 kestrels (*Falco tinnunculus*; 75%), 26 out of 38 barred owls (*Strix varia*; 68%), 14 out of 22 golden eagles (*Aquila chrysaetos*; 64%), and 192 out of 308 great horned owls (*Bubo virginianus*; 62%).

Of these 17 species, ten species included some individuals, which had liver SGAR concentrations more than 100 μg/kg (Table 5). The potentially lethal level for brodifacoum residues were reported in some individuals of all ten species: at least five moreporks (610–3,440 μg/kg), one little owl (574 μg/kg), four Eurasian eagle owls (133–2,008 μg/kg), 18 bald eagles (429–2,599 μg/kg), one sparrowhawk (112 μg/kg), three red kites (129–222 μg/kg), two kestrels (240 and 298 μg/kg), one barred owl (927 μg/kg), one golden eagle (110 μg/kg), and 15 great horned owls (100–970 μg/kg). High bromadiolone concentrations were reported in six species: at least one Eurasian eagle owl (208 μg/kg), one red kite (490 μg/kg), one kestrel (679 μg/kg), one barred owl (1,012 μg/kg), one golden eagle (154 μg/kg), and four great horned owls (226–1,080 μg/kg). High difenacoum accumulations were reported in two Eurasian eagle owls (181 and 281 μg/kg) and one kestrel (450 μg/kg), at least. High flocoumafen accumulations were reported in one red kite (400 μg/kg) and one golden eagle (117 μg/kg). High difethialone accumulations were reported in one Eurasian eagle owl (200 μg/kg). Four sparrowhawks were reported to have sum SGAR concentrations of 100–157 μg/kg. Because of the high AR exposure rates and including some individuals that have high liver SGAR concentrations, these ten species are seemingly affected by ARs more severely than other raptor species.

Threatened raptors

A wide variety of raptor species was found to have been exposed to ARs. Furthermore, these reported raptors include species with special conservation status, such as red kites (Near Threatened, IUCN Red List [54]) and the Spanish imperial eagle (*Aquila adalberti*, Vulnerable, IUCN Red List [51]).

Although there are no reports of AR residues in the livers of raptors from Russia or Mongolia, it has been reported that the numbers of breeding pairs of Eastern imperial eagles (*Aquila heliaca*, Vulnerable, IUCN Red List [52]) and Saker falcons (*Falco cherrug milvipes*, Endangered, IUCN Red List [53]) decreased following bromadiolone application [15, 36]. In Japan, diphacinone was used on Ogasawara Island and it was reported that at least three Eastern buzzards (*Buteo japonicus toyoshimai*), classified as locally Endangered (Ministry of the Environment, Government of Japan [33]), might have been poisoned as a result [4, 16]. These

Table 5. Presence of ARs in animal species reported in various countries. AR concentrations (µg/kg) given are in the form minimum–maximum, or mean ± S.D. (values marled with an asterisk are medians, with a sharp are standard error, S. E. and † means prevalence of any ARs); N gives the number of analysis; n+ gives the number of individuals with detectable residues; % means detection rate; and n is the total number of individuals in which each AR has been detected

Species	Year	Country	N	n+	%	Warfarin	Coumatetralyl	Diphacinone	Chlorophacinone	Brodifacoum	Bromadiolone	Difenacoum	Difetialone	Flocoumafen	References
Raptors (39 species analyzed)															
Turkey vulture *Cathartes aura*	1998–2001	U.S.A.	2	2	100	n=0	n=0	n=1	n=0	n=1	n=1	n=0	n=0	-	[50]
Short toed snake-eagle *Circaetus gallicus*	2005–2010	Spain	1	1	100	n=0	n=0	n=0	n=0	n=1 9	n=1 10	n=0	n=0	n=1 2	[44]
Marsh harrier *Circus aeruginosus*	2000–2009	Denmark	3	3	100	-	n=†	-	-	n=†	n=†	n=†	-	n=†	[5]
Morepork *Ninox novaeseelandiae*	1994–1999	NZ	5	5	100	-	-	-	-	n=5 610–3,440	-	-	-	-	[8, 35]
Little owl *Athene noctua*			17	15	88					n=5	n=1	n=2		n=1	
	2005–2013	Spain	8	6	75	n=0	-	-	-	62–574	79.5	2, 56	n=0	33	[28, 44]
	2000–2009	Denmark	9	9	100	-	n=†	-	-	n=†	n=†	n=†	-	n=†	[5]
Eagle owl *Bubo bubo*			39	33	85					n=20	n=13	n=11	n=3	n=7	
	2005–2013	Spain	21	18	86	n=0	n=0	n=0	n=0	10–2,008	2–208	1–281	35–200	3–90	[28, 44]
	2000–2009	Denmark	10	10	100	-	n=†	-	-	n=†	n=†	n=†	-	n=†	[5]
	2009–2011	Norway	8	5	63	-	-	-	-	74–158	n=0	39, 181	-	13	[26]
Bald eagle *Haliaeetus leucocephalus*	1995–2009	U.S.A.	24	20	83	n=1 1,400	n=0	n=0	n=0	n=18 429–2,599	n=0	n=1	n=0	-	[9, 49, 50]
Short-eared owl *Asio flammeus*			6	5	83										
	1998–2001	U.S.A.	1	0	0	n=0	n=0	n=0	n=0	n=0	n=0	n=0	n=0	-	[50]
	2000–2009	Denmark	5	5	100	-	n=†	-	-	n=†	n=†	n=†	-	n=†	[5]
Rough-legged buzzard *Buteo lagopus*			32	26	81		n=3			n=19	n=5	n=23			
	1998–2001	U.S.A.	1	0	0	n=0	n=0	n=0	n=0	n=0	n=0	n=0	n=0	-	[50]
	2000–2009	Denmark	31	26	84	-	1–3	-	-	3*–34	0–130	14*–105	-	n=0	[5]
Sparrowhawk *Accipiter nisus*			145	116	80				n=3	n=53	n=62	n=90	n=1		
	2000–2013	U.K.	131	104	79	n=0	n=0	n=0	n=0	n=48	n=57	n=85	3.3	n=0	[19, 59]
	2009–2012	Spain	14	12	86	n=0	n=0	-	0.34 ± 0.57	13.2 ± 8.1	31.9 ± 22.6	3.6 ± 2.0	n=0	-	[43]
Red kite *Milvus milvus*			138	108	78					n=40	n=74	n=78	n=1	n=5	
	1994–2011	U.K.	127	98	77	n=0	n=0	n=0	n=0	71–222	56–94	40–67	n=1	15	[19, 58, 60]
	2005–2010	Spain	8	7	88	n=0	n=0	n=0	n=0	129, 210	5–490	1	n=0	53, 400	[44]
	2000–2009	Denmark	3	3	100	-	n=†	-	-	n=†	n=†	n=†	-	n=†	[5]
Long-eared owl *Asio otus*			80	62	78		n=4	n=1	n=1	n=39	n=22	n=36		n=3	
	1998–2001	U.S.A.	7	2	29	n=0	n=0	n=1	n=0	n=1	n=1	n=0	n=0	-	[50]
	2009–2013	Spain	35	24	69	n=0	n=0	-	0.5 ± 0.4	12–42	77.2 ± 29.6	1–53	n=0	n=0	[28, 43]
	2000–2009	Denmark	38	36	95	-	0*–29	-	-	3*–40	0*–33	7*–52	-	0*–2	[5]
Kestrel *Falco tinnunculus*			206	154	75		n=12		n=3	n=71	n=94	n=106	n=1	n=18	
	2000–2011	U.K.	115	78	68	-	-	-	-	n=21	n=52	n=58	n=1	n=0	[19, 58, 60]
	2003	France	4	3	75	n=0	n=0	-	-	80–250	80–250	n=0	-	-	[25]
	2009–2012	Spain	21	14	67	n=0	n=0	-	0.6 ± 1.8	57.4 ± 34.6	79.8 ± 34.4	8.2 ± 6.9	n=0	-	[43]
	2000–2009	Denmark	66	59	89	-	0*–64	-	-	2*–298	0*–679	6.5*–450	-	0*–20	[5]

Table 5 (continued)

Species	Year	Country	N	n+	%	Warfa-rin	Couma-tetralyl	Dipha-cinone	Chloro-phacinone	Brodi-facoum	Broma-diolone	Difen-acoum	Difeti-alone	Flocou-mafen	References
Barred owl			38	26	68	n=1		n=2	n=4	n=18	n=20		n=1		
Strix varia	1998–2001	U.S.A.	13	3	23	n=0	n=0	n=1	n=0	n=1	n=1	n=0	n=0	-	[50]
	1988–2003	Canada	25	23	92	2.6	-	10	2.5–15	1–927	2–1,012	-	3	-	[1]
Golden eagle			22	14	64			n=1		n=9	n=7			n=3	
Aquila chrysaetos	1996–2001	U.S.A.	2	2	100	n=0	n=0	n=1	n=0	30	n=0	n=0	n=0	-	[49, 50]
	2005–2010	Spain	4	1	25	n=0	n=0	n=0	n=0	n=0	n=0	n=0	n=0	6	[44]
	2009–2011	Norway	16	11	69	-	-	-	-	11–110	13–154	n=0	-	15, 117	[26]
Great horned owl			308	192	62	n=4		n=4	n=3	n=157	n=111	n=1	n=7		
Bubo virginianus	1994–2012	U.S.A.	136	74	54	730	n=0	n=0	n=0	7–970	28–1,080	22	n=0	-	[48–50]
	1988–2003	Canada	172	118	69	2.5–720	-	8–12	2.5–14	1–610	1–570	-	3–30	-	[1, 55]
Black kite *Milvus migrans*	2005–2010	Spain	5	3	60	n=0	n=0	n=0	n=0	n=1 25	n=0	n=0	n=0	n=2 55, 84	[44]
Common buzzard			639	380	60	n=4	n=31		n=2	n=130	n=238	n=236	n=3	n=35	
Buteo buteo	2000–2010	U.K.	407	195	48	n=0	n=0	n=0	n=0	n=24	n=122	n=110	-	-	[19]
	2003	France	11	10	91	350–2,000	n=0	-	-	80–250	80–290	80–250	-	-	[25]
	2005–2013	Spain	80	43	54	n=0	n=0	n=0	0.3, 120	4.9–1,356	1–586	2.9–1,921	85–539	1–175	[28, 43, 44]
	2000–2009	Denmark	141	132	94	-	0*–435	-	-	2*–613	7.5*–282	10*–170	-	0*–115	[5]
Australasian harrier *Circus approximans*	1994–1999	NZ	4	2	50	-	-	-	-	n=2 610, 660	-	-	-	-	[8, 35]
Screech owl *Otus asio*	1997–2001	U.S.A.	24	12	50	n=0	n=0	n=0	n=0	n=10 7–800	n=3 50–500	n=0	n=0	-	[49, 50]
Red-tailed hawk			362	176	49			n=1	n=1	n=155	n=59				
Buteo jamaicensis	1994–2010	U.S.A.	297	137	46	n=0	n=0	340	180	6–1,600	31–543	n=0	n=0	-	[48–50]
	2011	Canada	65	39	60	-	-	-	-	1–170	1–64	-	n=0	-	[55]
Scops owl *Otus scops*	2011–2013	Spain	33	16	49	n=0	n=0	n=0	n=0	n=9 3–158.4	n=5 2–44	n=8 1–10	n=0	n=2 3, 10	[28]
Barn owl			769	370	48	n=1	n=13	n=3	n=3	n=149	n=235	n=203	n=22	n=25	
Tyto alba	1988–2003	Canada	78	48	62	2.5	-	10–20	n=0	10–470	5–720	-	2.5–720	-	[1]
	2000–2011	U.K.	535	193	36	-	-	-	-	n=33	n=111	n=115	n=4	n=9	[19, 58, 60]
	2003	France	10	7	70	n=0	640	-	-	n=0	80–260	80–260	-	-	[25]
	2005–2013	Spain	66	47	71	n=0	n=0	-	1.2 ± 1.0	2–839	7.1–180	1–198	45–4,463	14–299	[28, 43, 44]
	2000–2009	Denmark	80	75	94	-	0*–18	-	-	4*–957	16*–252	11*–223	-	0*–34	[5]
Tawny owl			276	109	40		n=6			n=53	n=65	n=51	n=4	n=12	
Strix aluco	1990–2010	U.K.	200	45	28	-	-	-	-	n=12	n=26	n=13	-	n=0	[19, 60]
	2003	France	5	2	40	n=0	n=0	-	-	n=0	80, 250	n=0	-	-	[25]
	2011–2013	Spain	27	21	78	n=0	-	-	-	2–1582	2–77	1–84	93–430	0–118	[28]
	2000–2009	Denmark	44	41	93		0*–39	-	-	3*–220	8*–496	7*–90	-	0*–42	[5]
Cooper's hawk *Accipiter cooperii*	1998–2001	U.S.A.	50	18	36	n=1 100	n=0	n=1 100	n=0	n=12 8–220	n=5 40–600	n=0	n=0	-	[50]

Table 5 (continued)

Species	Year	Country	N	n+	%	Warfa-rin	Couma-tetralyl	Dipha-cinone	Chloro-phacinone	Brodi-facoum	Broma-diolone	Difen-acoum	Difeti-alone	Flocou-mafen	References
Peregrine falcon *Falco peregrinus*			30	10	33	n=1		n=1		n=3	n=8				
	1986–2009	U.S.A.	4	3	75	1,480	n=0	n=1	n=0	n=2	n=1	n=0	n=0	-	[9, 49, 50]
	2000–2010	U.K.	24	7	29	n=0	n=0	n=0	n=0	n=1	n=7	n=0	-	n=0	[19]
	2009–2011	Norway	2	0	0	-	-	-	-	n=0	n=0	n=0	-	n=0	[43]
Northern goshawk *Accipiter gentilis*			3	1	33					n=1					
	1998–2001	U.S.A.	1	0	0	n=0	n=0	n=0	n=0	n=0	n=0	n=0	n=0	-	[50]
	2005–2010	Spain	2	1	50	n=0	n=0	n=0	n=0	38	n=0	n=0	n=0	n=0	[44]
Saw-whet owl *Aegolius acadicus*	1998–2001	U.S.A.	3	1	33	n=0	n=0	n=1	n=0	n=1	n=1	n=0	n=0	-	[50]
Bearded vulture *Gypaetus barbatus*	2005–2010	Spain	3	1	33	n=0	n=0	n=0	n=0	n=0	n=1 1	n=0	n=0	n=0	[44]
Snowy owl *Nyctea scandiaca*	1993, 1998–2001	U.S.A.	3	1	33	n=0	n=0	n=1 260	n=0	n=0	n=0	n=0	n=0	-	[49, 50]
Barbary falcon *Falco peregrinoides*	2009–2012	Spain	16	5	31	n=0	n=0	-	n=1 0.1	n=1 0.8	n=3 26.2 ± 18.6	n=1 1.4	n=0	-	[43]
Eurasian griffon *Gyps fulvus*	2005–2010	Spain	23	3	13	n=0	n=0	n=0	n=1 4	n=0	n=1 208	n=1 1	n=0	n=0	[44]
Spanish imperial eagle *Aquila adalberti*	2005–2010	Spain	8	1	13	n=0	n=0	n=0	n=0	n=0	n=0	n=1 8	n=0	n=0	[44]
Sharp-shinned hawk *Accipiter striatus*	1998–2001	U.S.A.	11	1	9	n=0	n=0	n=1	n=0	n=1	n=1	n=0	n=0	-	[50]
Broad-winged hawk *Buteo platypterus*	1998–2001	U.S.A.	11	0	0	n=0	n=0	n=0	n=0	n=0	n=0	n=0	n=0	-	[50]
Black vulture *Coragyps atratus*	1998–2001	U.S.A.	1	0	0	n=0	n=0	n=0	n=0	n=0	n=0	n=0	n=0	-	[50]
Merlin *Falco columbarius*	1998–2001	U.S.A.	1	0	0	n=0	n=0	n=0	n=0	n=0	n=0	n=0	n=0	-	[50]
Gyrfalcon *Falco rusticolus*	2009–2011	Norway	1	0	0	-	-	-	-	n=0	n=0	n=0	-	n=0	[43]
Osprey *Pandion haliaetus*	2009–2011	Norway	3	0	0	-	-	-	-	n=0	n=0	n=0	-	n=0	[43]
Birds excluding raptors (40 species analyzed)															
Common myna *Acridotheres tristis*	1994–1999	NZ	3	3	100	-	-	-	-	n=3 540–1,270	-	-	-	-	[8]
Gray duck *Anas superciliosa*	1994–1999	NZ	1	1	100	-	-	-	-	n=1 910	-	-	-	-	[8]
Gray heron *Ardea cinerea*	2005–2010	Spain	1	1	100	n=0	n=0	n=0	n=0	n=0	n=1 10	n=0	n=0	n=0	[44]
Lapland longspur *Calcarius lapponicus*	2009	U.S.A.	2	2	100	n=0	n=0	n=0	n=0	n=2 560, 2,989	n=0	n=0	n=0	-	[9]
Rock sandpiper *Calidris ptilocnemis*	2009	U.S.A.	1	1	100	n=0	n=0	n=0	n=0	n=1 43	n=0	n=0	n=0	-	[9]

Table 5 (continued)

Species	Year	Country	N	n⁺	%	Warfa-rin	Couma-tetralyl	Dipha-cinone	Chloro-phacinone	Brodi-facoum	Broma-diolone	Difen-acoum	Difeti-alone	Flocou-mafen	References
Emperor goose *Chen canagica*	2009	U.S.A.	1	1	100	n=0	n=0	n=0	n=0	n=1 27	n=0	n=0	n=0	-	[9]
Great spotted cuckoo *Clamator glandarius*	2005–2010	Spain	1	1	100	n=0	n=0	n=0	n=1 6	n=0	n=0	n=0	n=0	n=0	[44]
Common crow *Corvus brachyrhynchos*	1997	U.S.A.	1	1	100	n=0	n=0	n=0	n=0	n=1 1,340	n=0	n=0	-	-	[49]
Raven *Corvus corax*			14	14	100					n=14					
	1996	U.S.A.	1	1	100	n=0	n=0	n=0	n=0	1,040	n=0	n=0	-	-	[49]
	1995	Canada	13	13	100	-	-	-	-	980–2,520	-	-	-	-	[18]
Chaffinch *Fringilla coelebs*	1994–1999	NZ	3	3	100	-	-	-	-	n=3 120–2,310	-	-	-	-	[8]
Southern black-backed gull *Larus dominicanus*	1994–1999	NZ	1	1	100	-	-	-	-	n=1 580	-	-	-	-	[8]
Gray-crowned rosy finch *Leucosticte tephrocotis*	2009	U.S.A.	1	1	100	n=0	n=0	n=0	n=0	n=1 1,219	n=0	n=0	n=0	-	[9]
Kaka *Nestor meridionalis*	1994–1999	NZ	3	3	100	-	-	-	-	n=3 1,200–4,100	-	-	-	-	[8]
Pukeko *Porphyrio porphyrio*	1994–1999	NZ	8	8	100	-	-	-	-	n=8 520–1,350	-	-	-	-	[8]
Spotless crake *Porzana tabuensis*	1994–1999	NZ	1	1	100	-	-	-	-	n=1 40	-	-	-	-	[8]
Paradise shelduck *Tadorna variegata*	1994–1999	NZ	4	4	100	-	-	-	-	n=4 240–800	-	-	-	-	[8]
Black bird *Turdus merula*	1994–1999	NZ	13	13	100	-	-	-	-	n=13 10–1,100	-	-	-	-	[8]
Northern fulmar *Fulmarus glacialis*	2009	U.S.A.	1	1	100	n=0	n=0	n=0	n=0	n=1 57	n=0	n=0	n=0	-	[9]
Pelagic cormorant *Phalacrocorax pelagicus*	2009	U.S.A.	1	1	100	n=0	n=0	n=0	n=0	n=1 44	n=0	n=0	n=0	-	[9]
Glaucous-winged gull *Larus glaucescens*	2009	U.S.A.	10	9	90	n=0	n=0	n=0	n=0	n=9 709–4,189	n=1 n =1	n=2 n =2	n=0	-	[9]
Rock dove *Columba livia*	2005–2010	Spain	97	64	66	n=0	n=0	n=0	n=64 550–55,100	n=0	n=0	n=0	n=0	n=0	[44]
Weka *Gallirallus australis*	1994–1999	NZ	55	31	56	-	-	-	-	n=31 10–2,300	-	-	-	-	[8]
Kakariki *Cyanoramphus sp.*	1994–1999	NZ	2	1	50	-	-	-	-	n=1 30	-	-	-	-	[8]
Saddleback *Philesturnus carunculatus*	1994–1999	NZ	4	2	50	-	-	-	-	n=2 50, 600	-	-	-	-	[8]
Brown kiwi *Apteryx australis*	1994–1999	NZ	29	14	48	-	-	-	-	n=14 10–690	-	-	-	-	[8]

Table 5 (continued)

Species	Year	Country	N	n+	%	Warfa-rin	Couma-tetralyl	Dipha-cinone	Chloro-phacinone	Brodi-facoum	Broma-diolone	Difen-acoum	Difeti-alone	Flocou-mafen	References
Lesser black-backed gull *Larus fuscus*	2005–2010	Spain	8	3	38	n=0	n=0	n=0	n=0	n=0	n=3 2–5	n=0	n=0	n=0	[44]
Common starling *Sturnus vulgaris*	2005–2010	Spain	3	1	33	n=0	n=0	n=0	n=0	n=0	n=1 15	n=0	n=0	n=0	[44]
Calandra lark *Melanocorypha calandra*	2005–2010	Spain	7	2	29	n=0	n=0	n=0	n=2 1,040, 2,090	n=0	n=0	n=0	n=0	n=0	[44]
Mallard *Anas platyrhynchos*			23	6	26				n=3	n=2	n=1				
	2003	France	15	1	7	n=0	n=0	-	-	-	80–250	-	-	-	[25]
	2005–2010	Spain	6	3	50	n=0	n=0	n=0	710–2,170	-	n=0	n=0	n=0	n=0	[44]
	1994–1999	NZ	2	2	100	-	-	-		900, 1,230	-	-	-	-	[8]
Black coot *Fulica atra*	2003	France	13	3	23	n=1 23,520	n=0	-	-	n=1 80–250	n=1 80–250	n=0	-	-	[25]
Magpie *Gymnorhina tibicen*	1994–1999	NZ	30	6	20	-	-	-	-	n=6 80–990	-	-	-	-	[8, 35]
Robin *Petroica australis*	1994–1999	NZ	10	2	20	-	-	-	-	n=2 350, 580	-	-	-	-	[8, 35]
Red-legged partridge *Alectoris rufa*	2005–2010	Spain	7	1	14	n=0	n=0	n=0	n=0	n=0	n=0	n=0	n=0	n=1 143	[44]
Eurasian collared-dove *Streptopelia decaocto*	2005–2010	Spain	8	1	13	n=0	n=0	n=0	n=0	n=0	n=1 127	n=0	n=0	n=0	[44]
Bellbird *Anthornis melanura*	1994–1999	NZ	2	0	0	-	-	-	-	n=0	-	-	-	-	[8, 35]
Northwestern crow *Corvus caurinus*	1995	Canada	9	0	0	-	-	-	-	n=0	-	-	-	-	[18]
Common moorhen *Gallinula chloropus*	2003	France	1	0	0	n=0	n=0	-	-	n=0	n=0	n=0	-	-	[25]
Whitehead *Mohoua albicilla*	1994–1999	NZ	12	0	0	-	-	-	-	n=0	-	-	-	-	[8, 35]
Tomtit *Petroica macrocephala*	1994–1999	NZ	5	0	0	-	-	-	-	n=0	-	-	-	-	[35]
Fantail *Rhipidura fuliginosa*	1994–1999	NZ	2	0	0	-	-	-	-	n=0	-	-	-	-	[8, 35]
Carnivola (15 species analyzed)															
Skunk *Mephitis mephitis*	1996	U.S.A.	3	3	100	n=0	n=0	n=0	n=0	n=0	n=3 20–280	n=0	-	-	[49]
Mountain lion *Puma concolor*	1997–2006	U.S.A.	4	4	100	n=0	-	n=1 <250	n=0	n=4 310–570	n=4 370–1,270	-	n=1 <250	-	[42]
Bobcat *Lynx rufus*	1988–2012	U.S.A.	169	148	88	n=11 n=11	-	n=67 30 ± 120	n=10 n=10	n=135 140 ± 200	n=133 380 ± 550	-	n=50 40 ± 310	-	[42, 45]

Table 5 (continued)

Species	Year	Country	N	n$^+$	%	Warfa-rin	Couma-tetralyl	Dipha-cinone	Chloro-phacinone	Brodi-facoum	Broma-diolone	Difen-acoum	Difeti-alone	Flocou-mafen	References
Weasel			80	69	86		n=15			n=39	n=17	n=60		n=20	
Mustela nivalis	1996–1997	U.K.	10	3	30	n=0	8.5–60	-	-	n=0	250	n=0	-	n=0	[31]
	2005–2010	Spain	1	1	100	n=0	n=0	n=0	n=0	2,930	n=0	n=0	n=0	n=0	[44]
	1984–2008	Denmark	69	65	94	-	4–45	-	-	4–159	7–1,610	5–292	-	3–49	[11]
Feral cat *Felis catus*	2005–2010	Spain	4	3	75	n=0	n=0	n=0	n=0	n=2 34, 350	n=1 52	n=1 70	-	n=1 72	[44]
Stoat			101	68	67		n=22			n=31	n=34	n=49		n=25	
Mustela erminea	1996–1997	U.K.	40	9	23	n=0	4.6–9.7	-	-	120	40–380	n=0	-	n=0	[31]
	1993–2007	Denmark	61	59	97	-	2–61	-	-	2–317	3–1,290	2–280	-	1–86	[11]
Stone marten *Martes foina*	2005–2010	Spain	19	11	58	n=0	n=0	n=0	n=0	n=5 19–390	n=6 7–17,900	n=3 7–520	n=1 926	n=5 8–230	[44]
Raccoon			16	8	50					n=6	n=2				
Procyon lotor	1992–1997	U.S.A.	6	6	100	n=0	n=0	n=0	n=0	320–5,300	n=0	n=0	-	-	[49]
	2005–2010	Spain	10	2	20	n=0	n=0	n=0	n=0	n=0	1,090, 6,800	n=0	n=0	n=0	[44]
Red fox			33	14	42					n=7	n=8	n=1			
Vulpes vulpes	1996	U.S.A.	2	2	100	n=0	n=0	n=0	n=0	1,320, 4,010	n=0	n=0	-	-	[46]
	2005–2010	Spain	31	12	39	n=0	n=0	n=0	n=0	5–4,500	5–12,300	78	n=0	n=0	[44]
Domestic dog *Canis familiaris*	2005–2010	Spain	11	4	36	n=0	n=0	n=0	n=0	n=0	n=3 6–308	n=1 4	n=0	n=0	[44]
Common genet *Genetta genetta*	2005–2010	Spain	7	2	29	n=0	n=0	n=0	n=0	n=2 16, 2,020	n=2 1, 350	n=1 12	n=0	n=1 60	[44]
European otter			14	4	29				n=1		n=2			n=1	
Lutra lutra	1990–2002	France	11	3	27	n=0	n=0	-	5,000	n=0	6,00, 7,100	n=0	n=0	-	[13]
	2005–2010	Spain	3	1	33	n=0	n=0	n=0	n=0	n=0	n=0	n=0	n=0	353	[44]
Polecat			133	36	27					n=3	n=17	n=22			
Mustela putorius	1992–1999	U.K.	100	31	31	-	-	-	-	8–70	16–217	5–917	-	n=0	[49, 50]
	1990–2002	France	33	5	15	n=0	n=0	-	n=0	n=0	600–9,000	n=0	n=0	-	[13]
American mink *Mustela vison*	1990–2002	France	47	7	15	n=0	n=0	-	n=4 3,400–8,500	n=0	n=3 1,900–4,200	n=0	n=0	-	[13]
European mink *Mustela lutreola*	1990–2002	France	31	1	3	n=0	n=0	-	n=0	n=0	n=1 5,000	n=0	n=0	-	[13]
Cetartiodactyla (3 species analyzed)															
White-tailed deer *Odocoileus virginianus*	1994–1997	U.S.A.	7	7	100	n=0	n=1 500	n=2 200, 930	n=0	n=5 120–410	n=0	n=0	-	-	[49]
Red deer *Cervus elaphus*	1994–1999	NZ	37	33	89	-	-	-	-	n=33 <30	-	-	-	-	[8, 35]
Domestic pig *Sus scrofa*	1994-1999	NZ	40	26	65	-	-	-	-	n=26 7–1,780	-	-	-	-	[8, 35]

Table 5 (continued)

Species	Year	Country	N	n+	%	Warfa-rin	Couma-tetralyl	Dipha-cinone	Chloro-phacinone	Brodi-facoum	Broma-diolone	Difen-acoum	Difeti-alone	Flocou-mafen	References
Erinaceomorpha (2 species analyzed)															
Algerian hedgehog *Atelerix algirus*	2011–2013	Spain	106	61	58	n=1 611.8	-	-	-	n=18 5–1,533	n=35 6–2,548	n=29 1–659	n=4 71–256	n=0	[28]
European hedgehog *Erinaceus europaeus*			170	57	34					n=29	n=28	n=28	n=2	n=6	
	2004–2006	U.K.	120	27	23	-	-	-	-	50 ± 10#	590 ± 240#	100 ± 30#	-	n=0	[7]
	2005–2013	Spain	50	30	60	n=0	-	-	-	3–1,390	2–1,110	0–672	4, 142	1–29	[28, 44]
Rodentia (2 species analyzed)															
Gray squirrel *Sciurus carolinensi*	1981–1997	U.S.A.	7	7	100	n=1 228	n=0	n=1 2,000	n=1 620	n=5 530–4,100	n=0	n=0	-	-	[50]
Eastern chipmunk *Tamias striatus*	1992	U.S.A.	1	1	100	n=0	n=0	n=0	n=0	n=1 3,800	n=0	n=0	-	-	[50]
Lagomorpha (1 species analyzed)															
Iberian hare *Lepus granatensis*	2005–2010	Spain	25	8	32	n=0	n=0	n=0	n=7 580–9,520	n=2 130, 270	n=0	n=1 15	n=0	n=0	[44]
Chiroptera (1 species analyzed)															
NZ lesser short-tailed bats *Mystacina tuberculata*	2009	NZ	12	10	83	-	-	n=10 190–680	-	-	-	-	-	-	[6]
Marsupialia (1 species analyzed)															
Opossum *Didelphis virginiana*	1996, 1997	U.S.A.	2	2	100	n=0	n=0	n=0	n=0	n=1 180	n=1 800	n=0	-	-	[49]
Reptile (1 species analyzed)															
Horseshoe whip snake *Hemorrhois hippocrepis*	2005–2010	Spain	1	1	100	n=0	n=0	n=0	n=0	n=0	n=0	n=0	n=0	n=1 540	[44]

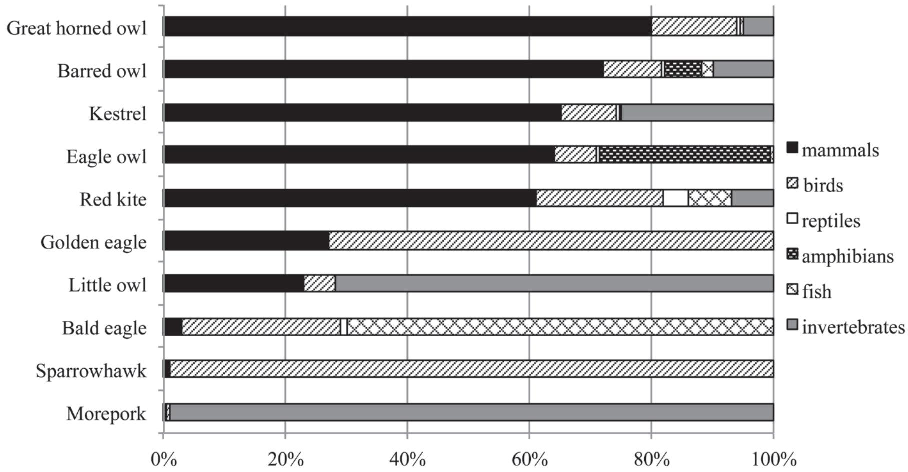

Fig. 2. Diet composition of ten raptor species, which frequently reported AR-exposure. Predominant prey of raptors is mammal in great horned owls (80%), barred owls (72%), kestrels (65%), Eurasian eagle owls (64%), and red kites (61%), whereas it is bird in sparrowhawks (99%) and golden eagles (73%), fish in bald eagles (70%), and invertebrate in moreporks (99%) and little owls (72%) [3, 17, 22, 24, 27, 32, 34, 37, 56, 63].

incidents imply that poisoning by ARs could have occurred worldwide, despite the lack of studies on the existence of AR residues in the livers of raptors from these areas.

EXPOSURE PATHWAYS

Diets of raptors

Although it is widely thought that preying on the target rodents is the dominant pathway by which raptors are exposed to ARs, there have been a few studies on the relationship between the diets of raptors and the incidence of AR-exposure. This study is the first to discuss the exposure pathways for ARs based on both a comprehensive analysis of primary and secondary AR-exposure worldwide and the diets of raptors.

The most affected raptor species have commonly been thought to prey predominantly on mammals, especially the targeted rodent species. Figure 2 shows the diet composition of raptors whose AR-exposure are frequently reported. Because mammals constitute 60–80% of the diets of great horned owls [3], barred owls [27], kestrels [24], Eurasian eagle owls [37], and red kites [34], targeted rodents can be the source of ARs in some cases. Moreover, ARs were detected in barn owls (*Tyto alba*) pellets that contained rat fur [10]. However, the Eurasian eagle owls occasionally prey on larger mammals (e.g., hares, foxes, and deer) [37], and red kites sometimes feed on hares, rabbits, and as carrion, foxes, stoats, polecats and deer [34]. Therefore, a wide range of mammals can be the source of ARs as well as target rodents. On the other hand, raptors also prey on other animals, such as birds, reptiles, amphibians, fish, and invertebrates. Birds constitute even 99 and 73% of the diets in sparrowhawks [63] and golden eagles [22], respectively; and 26, 21 and 14% in bald eagles [32], red kites [34] and great horned owls [3] following, respectively. In addition, the Eurasian eagle owls occasionally prey on other raptors (e.g., buzzards, falcons, tawny owls, and long-eared owls), and the diets of Eurasian eagle owls also consist of amphibians (28%) [37]. Diets of bald eagles consist of fish (70%) [32]. Invertebrates compose 99, 72 and 25% of prey of moreporks [17], little owls [56] and kestrels [24], respectively. Therefore, preying on targeted rodents does not necessarily explain all causes of secondary AR-exposure in raptors.

AR residues in the prey of raptors

Relatively high concentrations of AR residues have been detected in the livers of mallards (chlorophacinone, 710–2,170 μg/kg, and brodifacoum, 1,230 μg/kg), rock doves (chlorophacinone, 550–55,100 μg/kg), chaffinches (brodifacoum, 120–2,310 μg/kg), Algerian hedgehogs (brodifacoum, 5–1,533 μg/kg and bromadiolone, 6–2,548 μg/kg), European hedgehogs (brodifacoum, 3–1,390 μg/kg and bromadiolone, 2–1,110 μg/kg), Iberian hares (chlorophacinone, 580–9,520 μg/kg), and a horseshoe whip snake (flocoumafen, 540 μg/kg) (Table 5). Because all of these animals are the prey of raptors, non-target animals (i.e., non-target rodents, birds, hedgehogs, hares and snakes) could also be a source of exposure to ARs.

Some studies have also reported AR residues in other reptiles (geckos) and invertebrates such as ants, cockroaches, beetles, slugs, and snails [10, 23, 38]. In addition, recent studies have shown that ARs can be detected not only in shorebirds and seabirds, but also in marine biota, including fish, crabs, sea urchins, and shellfish [30, 38]. These papers suggest exposure pathways for ARs from marine biota to shorebirds and/or seabirds, and from shorebirds and seabirds to raptors. In the case of Rat Island in Alaska, when gulls died after eating bait containing brodifacoum, their carcasses attracted bald eagles [9]. During the study period, 46 bald

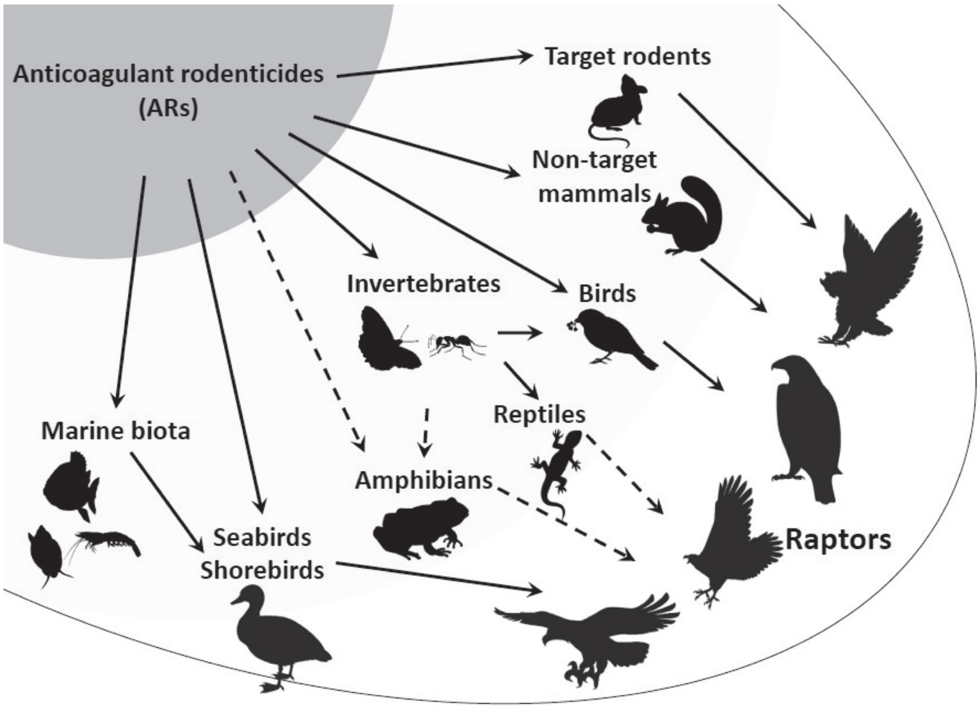

Fig. 3. Proposed pathways by which raptors are exposed to ARs. Primary poisoning occurs in target rodents, non-target mammals, reptiles, invertebrates, marine biota, and birds, including land birds, shorebirds and seabirds. It is possible that AR residues in these animals are transferred to raptors, causing secondary poisoning.

eagle carcasses were collected, and the brodifacoum residues were detected in the livers of all the carcasses tested (18 bald eagles).

In conclusion, primary AR exposure has occurred in non-target mammals, reptiles, invertebrates, marine biota, and birds, including land birds, shorebirds and seabirds. It is possible that AR residues in these animals constitute exposure pathways for raptors, resulting in the secondary exposure (Fig. 3). In some cases, these exposure pathways are presumed to cause secondary poisoning in raptors. More studies focusing on the dose-response relations between hepatic AR concentration and both hemorrhage and mortality of various raptor species are necessary to understand incidents of secondary AR poisoning in raptors accurately. Furthermore, toxicokinetics studies of raptors (e.g. AR metabolism, and degree of ARs inhibiting the target molecule) are also necessary to reveal the risk of raptors poisoned by ARs.

CONFLICTS OF INTEREST. The authors declare no conflict of interest.

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