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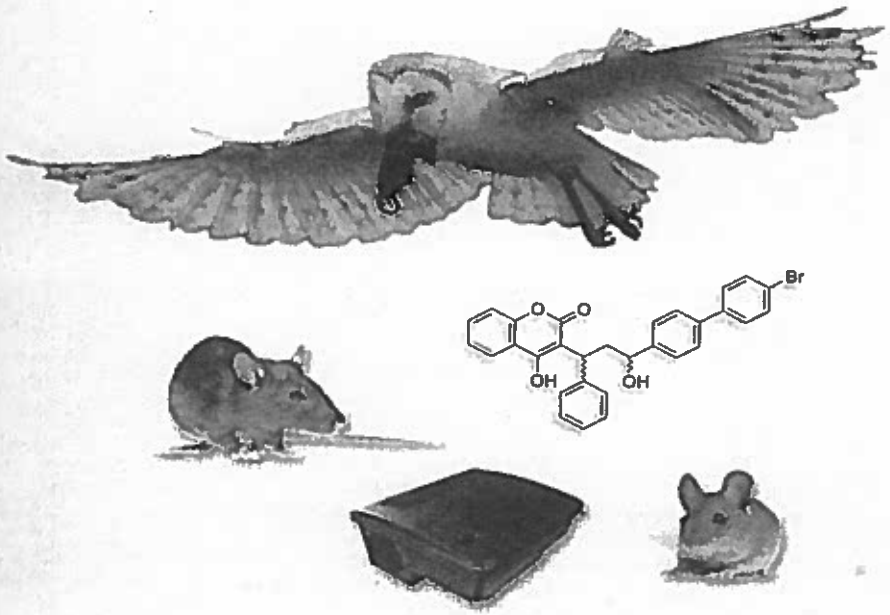
Editors

Anticoagulant Rodenticides and Wildlife



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Chapter 7
Secondary Exposure to Anticoagulant Rodenticides and Effects on Predators

Jhon J. López-Perea and Rafael Mateo

1 The Origin: Rodent-Human Conflict

Rodents are the most important group of mammals in terms of number of taxa with around 2000 species which are widely distributed across the world (Table 7.1; Wilson and Reeder 2005; Singleton et al. 2010). As usually occurs with species considered problematic, competition for food resources is the basis of the conflict between humans and rodents. Additionally, rodents are reservoirs of organisms that cause diseases in humans (i.e. zoonosis) and livestock, so the negative perception of rodents is very well entrenched in our society (Zamorano et al. 1988; Singleton et al. 2003; Stenseth et al. 2003).

Humankind's ongoing struggle with competitors, in this case rodent species, is a long story of adaptation and development of techniques to prevail in the conflict. The most recent tool to solve this conflict was the development of chemical poisons that act with a sufficient time delay to reduce the likelihood that rodents would associate eating the poison with sickness. This delayed mode of action thereby eliminated the potential development for learned aversion and resultant avoidance of bait. However, this group of poisons, the anticoagulant rodenticides (ARs), also have potential to cause collateral damage. Their capacity to bioaccumulate in animal tissues and high acute toxicity can result in the death of the natural predators of rodents, and so poisoning campaigns can also impact, and even potentially extirpate, our natural allies in this battle against rodents (Elliott et al. 2016).

Recent studies around the world have demonstrated the widespread exposure of predators and other non-target species to ARs (Berny et al. 1997; Shore et al. 2003; Albert et al. 2010; Murray 2011; Sánchez-Barbudo et al. 2012). The risk of exposure to ARs in predatory species is closely associated with the consumption of prey

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Table 7.1 Number of rodent species and species producing damage in crops in the world

Continents	N°/rodents species	Rodent species damaging crops	References
Africa	381	77	Singleton et al. (2010)
Asia	418	65	Singleton et al. (2010)
Australia	67	7	Singleton et al. (2010)
Europe	61	16	Singleton et al. (2010)
North America	206	>30	Hafner et al. (1998); Wilson and Reeder (2005); Singleton et al. (2010)
Middle and South America	593	33	Buckle and Smith (2015)

Table 7.2 Summary of the key characteristics of outbreaks and population cycles of vole, house mouse (*Mus musculus*), and black rat (*Rattus rattus*)

Characteristic	Voles[a]	House mouse[b]	Black rat[c]
Periodicity (years)	3–5	4–8	Annual
Density during outbreaks (individuals/ha)	50–500	100–2000+	Up to 1000
Temporal synchrony with other species	Yes	None reported	None reported
Changes in length of reproductive season	Yes	Yes	Yes
Changes in proportion pregnant females	Yes	Yes	Yes
Changes in litter size	Yes	Yes	Yes
Changes in body condition	Yes	Yes	Yes
Most important mortality factor	Predation	Not known	Not known

[a]Information on voles from Hanski et al. (1991, 1993);
[b]Information on house mouse from Singleton et al. (2001);
[c]Information on black rat from Figala (1964); Marsh (1994); Stenseth et al. (2003)

(typically rodents) that are the primary target of control operations (Merson et al. 1984; Alterio et al. 1997; Birks 1998; Alterio and Moller 2000; Chap. 6). Exposure is, in fact, highly probable in predators for which target rodents are key prey species. Consequently, poisoning campaigns with ARs will often lead to the contamination of predators. Moreover, rodent populations, and populations of other prey species, are frequently subject to strong temporal fluctuations related to inter-annual cycles and/or to the reproductive season (Table 7.2). These fluctuations have been typically associated with several factors: food, weather, synchrony and also predation (Krebs and Myers 1974; Singleton et al. 2001; Cavia et al. 2009). Some predators, diurnal and nocturnal birds of prey (such as the pallid harrier *Circus macrourus* and short-eared owl *Asio flammeus*) in particular, are adapted to profit from demographic cycles of prey (Hanski and Korpimäki 1995; Korpimaki and Norrdahi 1998; Terraube et al. 2011) and gravitate towards geographic areas where rodent outbreaks occur. As a result, they may be at particular risk of exposure if ARs are used to control peaks in rodent populations.

2 Scenarios of Exposure

We can identify two different scenarios to explain how predators can become exposed to rodenticides: (1) predators living and feeding around urban or agricultural areas where the use of ARs against commensal rodents is continuous and (2) predators from farmland areas where the type of crop (e.g. intensive production of vegetables or fruits) or the presence of rodent population cycles (e.g. voles of genus *Microtus* or *Arvicola*) lead to the periodic intensive use of ARs. There are other specific scenarios (e.g. rodenticide treatments in islands to protect seabirds colonies from rats – Alterio et al. 1997; Alterio and Moller 2000; Mayol et al. 2012), but these are less common.

Although many rodent species can live in natural or farmland ecosystems, some of them prefer urban areas, and this generates some differences in their demographic fluctuations in comparison with populations in natural environments (Singleton et al. 2003; Korpimäki et al. 2004). In particular, three species with worldwide distributions are responsible for the majority of conflicts with humans because of their adaptation to anthropogenic environments; these are the Norway or brown rat (*Rattus norvegicus*), the roof or black rat (*Rattus rattus*) and the house mouse (*Mus musculus*) (Castillo et al. 2003; Pocock et al. 2004). Rat and mouse outbreaks occur at intervals of 4–8 years, with no correlation in time series between the two species. The density of mice during outbreaks varies widely from 200 to 1000 or more per ha (Channon et al. 2000; Singleton et al. 2001; Korpimäki et al. 2004). In this scenario of anthropic environments, the use of rodenticides can be constant (Morzillo and Mertig 2011; Tosh et al. 2011a), is independent of population cycles, and the risk of chronic exposure to ARs can be elevated in resident predators.

In contrast, species of genus *Arvicola*, *Microtus* and *Apodemus* mostly prefer farmland ecosystems. These have population cycles typically with an amplitude of several years (e.g. voles of *Arvicola* and *Microtus* genus undergo population cycles with 3–5 year periods) and show densities up to 2000 individuals per ha (Korpimäki et al. 2004; Witmer 2007; Jacob and Tradlec 2010; Luque-Larena et al. 2013). In such farmland environments, the use of ARs can be more limited to the periods when rodent populations peak, but treatments are performed at a large spatial scale. That means the risk of exposure to ARs in predators can be more concentrated in time, but the probability of exposure to contaminated prey is elevated and widespread at that time.

In summary, the continuous use of ARs against commensal rodents in environments can lead to long-term chronic accumulation of SGARs in predators. On the other hand, intensive use of ARs in farmland or grassland during vole plagues can produce lethal poisonings in many different species of non-target fauna in addition to secondary poisoning in predators (Olea et al. 2009). The differences between urban and rural environments can affect the probability of exposure to, and accumulation of, ARs in non-target species, especially predators (Morzillo and Mertig 2011; Tosh et al. 2011b), including those that exploit rodent population outbreaks as a food resource.

3 Residues of Rodenticides in Predator's Diet

Secondary exposure and poisoning of predators is caused by the consumption of contaminated prey; i.e. other animals that suffered a primary exposure (and in some cases intoxication) due to bait ingestion (Chap. 6; Bowie and Ross 2006; Giraudoux et al. 2006). These prey animals can either die or survive their AR exposure, but in any case their tissues (especially the liver) will contain a significant amount of ARs that can contribute to the bioaccumulation and biomagnification of ARs in predators (Chap. 6; Dowding et al. 2010; Tosh et al. 2012). Small vertebrates, such as rodents and birds (mainly passerines) constitute part of the diet of most small predators. Such prey may be the targets of AR control or non-target species that, for example, encounter and consume grain bait spread on the ground or in other accessible places (Rammell et al. 1984; Sage et al. 2008; Olea et al. 2009). There is also some evidence that small birds will enter and feed on AR blocks placed in bait stations (Elliott et al. 2014).

Small vertebrates are not the only source of secondary exposure of ARs to predators. Invertebrates feeding on baits can also accumulate rodenticides in their digestive tract and this can be an additional source of exposure to a wide range of insectivorous animals (Craddock 2003; Bowie and Ross 2006). Predators can also be highly opportunistic in their feeding behavior and such behavior increases the risk of direct ingestion of AR baits (Dowding et al. 2010; Jacquot et al. 2013; Coeurdassier et al. 2014).

We compiled different studies that described ARs levels in the potential prey of predators (Rammell et al. 1984; Craddock 2003; Spurr et al. 2005; Sánchez-Barbudo et al. 2012; López-Perea et al. 2015) and the highest residue levels were in small mammals, followed by birds and reptiles (Fig. 7.1). This suggests that predators feeding mostly on small mammals are those with a higher risk of AR poisoning due to the potential that consumptions of relatively few contaminated prey will elevate exposure.

Six different types of ARs have been found in animal species that can be the potential prey of predators. The most commonly reported is bromadiolone, followed by brodifacoum and flocoumafen. In contrast, diphacinone, difethialone and coumatetralyl are more rarely reported in prey species (Table 7.3). As would be expected by their different capacity to bioaccumulate in animal tissues, the three ARs most frequently reported were second-generation ARs (SGARs) and the compounds less frequently detected were mostly first-generation ARs (FGARs). This reflects the fact that SGARs are more persistent, having a longer half-life in liver than FGARs, and so present a greater risk of causing secondary poisoning where they are widely used.

3.1 ARs in Small Mammals

ARs residues have been described at least in four families of small mammals (Muridae, Cricetidae, Erinaceidae, Leporidae). Two of these families (Muridae and Cricetidae) belong to the group of rodents, which are the main target for these compounds. Mean

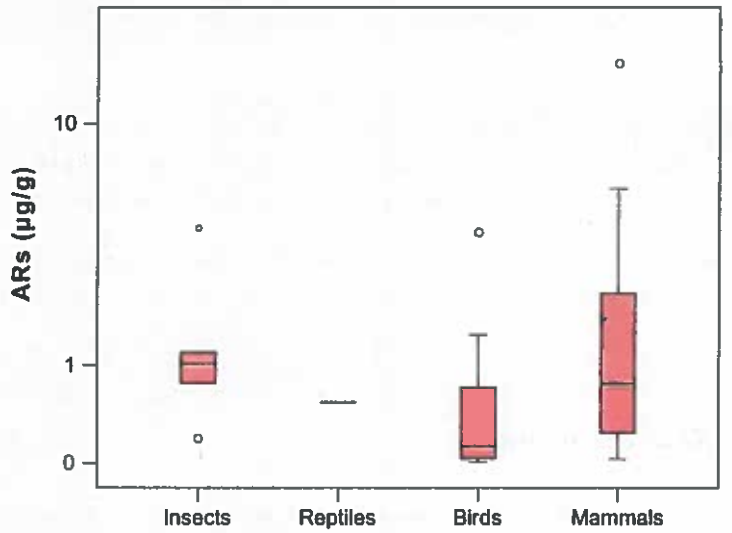

Fig. 7.1 Box-plots (median, 25–75%, range) of the concentrations of anticoagulant rodenticides (ARs) detected in tissues of potential prey of predators (Data was obtained from studies with mean values for mammals (n = 20), birds (n = 7), reptiles (n = 1) and insects (n = 6). References: Alterio et al. (1997), Berny et al. (1997), Bowie and Ross (2006), Craddock (2003), Dowding et al. (2010), Giraudoux et al. (2006), López-Perea et al. (2015), Murphy et al. (1998), Ogilvie et al. (1997), Rammell et al. (1984), Sage et al. (2008), Sánchez-Barbudo et al. (2012), Spurr et al. (2005), Tosh et al. (2012), Winters et al. (2010))

Table 7.3 Average (maximum) values of the mean concentrations (µg/g) of anticoagulant rodenticides described in several studies of the potential prey of predators

Compound	Insects	Reptiles	Birds	Mammals
Brodifacoum	1.418 (4.3)		0.181	1.745 (15.97)
Bromadiolone			0.127	1.034 (5.95)
Chlorophacinone			1.875 (4.15)	2.205 (2.3)
Diphacinone	0.39			
Difenacoum			0.056	0.041 (0.1)
Difethialone				0.096 (0.169)
Flocoumafen		0.540	0.006	0.058 (0.092)
Warfarin				0.207 (0.611)
∑ARs	1.418 (4.3)	0.540	0.857 (4.15)	2.188 (15.97)

Data are from references cited for Fig. 7.1

levels of total ARs in liver vary from 0.026 µg/g in European hedgehog (*Erinaceus europaeus*) to 15.97 µg/g in black rat (Alterio et al. 1997; Sánchez-Barbudo et al. 2012), but levels above 10 µg/g have been detected for brodifacoum in rabbit (*Oryctolagus cuniculus*) from New Zealand (Rammell et al. 1984) and for bromadiolone in water voles (*Arvicola amphibious*) from France and voles (*Microtus spp.*) from Canada (Giraudoux et al. 2006; Sage et al. 2008; Elliott et al. 2014) (Fig. 7.1). Further information on residues in small mammals is also presented in Chap. 6.

3.2 ARs in Small Birds

Birds are the second group of prey in which ARs have been most frequently detected. The geometric mean level of the sum of ARs reported in the livers of non-predatory birds ranged from 0.006 µg/g in red-legged partridge (*Alectoris rufa*) to 4.15 µg/g in rock dove (*Columba livia*) (Sánchez-Barbudo et al. 2012). The maximum concentration of ARs has been reported in Spain by Sánchez-Barbudo et al. (2012) in an individual rock dove that had 55.1 µg/g of chlorophacinone in the liver. Elliott et al. (2014) found one song sparrow (*Melospiza melodia*) with 0.073 µg/g of brodifacoum in the liver.

3.3 ARs in Invertebrates

Although this group of prey does not suffer AR-induced adverse effects on blood clotting like vertebrates, invertebrates feeding on poisoned baits can act as carriers of ARs to predators. As baits are prepared with cereal grain in different formulations (whole grain, milled grain in paraffin, etc.), these baits can be attractive for many species, including invertebrates. The mean values of the sum of ARs detected in invertebrates range from 0.21 µg/g in ground beetles (*Coleoptera*) to 4.3 µg/g in cave weta (*Gymnoplectron spp.*) (Ogilvie et al. 1997; Craddock 2003). In New Zealand, where most of research on ARs in invertebrates has been done, levels as high as 2.3–5.9 µg/g of brodifacoum have been found in weta (Craddock 2003; Bowie and Ross 2006). Elliott et al. (2014) found 0.39 µg/g of diphacinone in a pooled sample of carrion beetles (*Dermestes spp.*) from Canada that fed on the carcasses of poisoned animals.

3.4 ARs in Reptiles

There are few studies on AR residue levels in this group of vertebrates. Sánchez-Barbudo et al. (2012) described the presence of 0.54 µg/g of flocoumafen in the liver of a horseshoe whip snake (*Hemorrhois hippocrepis*) that was found dead on a Mediterranean island where this AR had been used against rats for the protection of seabird colonies. Many species of reptiles predate on rodents that may contain AR residues, so this group can be at risk of secondary poisoning in the same way as predatory birds and mammals. Bishop et al. (2016) recently described the exposure and poisoning risk of the gopher snake (*Pituophis catenifer deserticola*) to another rodent control compound, strychnine. In addition, reptiles are also potential prey for mammalian and avian predators, including mongooses (*Herpestidae*) and other species such as snake eagles (*Circaetus spp.*) which specialize on feeding on them. Reptiles may therefore form part of a tertiary exposure pathway for such predators.

4 Bioaccumulation from Prey to Predator

The presence of ARs in prey presents a risk to predators that may bioaccumulate ARs in tissues, especially the liver. Several factors contribute to the calculation of the risk of AR accumulation in predators. The first is the frequency of occurrence of ARs in prey. Intensive baiting with ARs in sites with elevated densities of rodents (such as population peaks of vole species) will result in an elevated availability of contaminated prey for scavenging predators over extended periods (Sage et al. 2007, 2008; Vidal et al. 2009; Montaz et al. 2014). The second factor is the concentration of ARs in the tissues of those prey that are exposed. In many cases, it can be expected that the dose ingested is high enough to cause the death of the rodent (or other non-target vertebrate), but there is usually a period of some days between lethal exposure and death during which some residues in prey may be eliminated. Furthermore, rodents sometimes ingest sub-lethal rather than lethal amounts of AR; for instance, Giraudoux et al. (2006) found 0.75 µg/g of bromadiolone per body mass in voles that were trapped alive after being exposed to field treatments. A third factor is the gut bioavailability and absorption of ARs in predators. Not all the AR dose ingested by prey is absorbed. In raptors, it is estimated that around 25% of the ingested dose is lost through elimination in regurgitated pellets (Newton et al. 1990; Gray et al. 1994; Elliott et al. 2014; Salim et al. 2014). A fraction of ingested dose may also either not be absorbed or undergo biliary excretion, although Sage et al. (2010) estimated that the maximum amount of bromadiolone eliminated via faeces by foxes (*Vulpes vulpes*) exposed daily to 1000 µg was only 69.9–73.3 µg. The fourth factor to take into account is the excretion rate of accumulated ARs. This is another parameter that can vary markedly between compounds and species. The half live ($t_{1/2}$) for ARs in animal tissues can range from 15.8–55 days for FGARs to 108–307 days for SGARs (Eason et al. 2002; Vandenbroucke et al. 2008); daily first-order excretion rates ($0.693/t_{1/2}$) can therefore be estimated to range between 0.002 to 0.044 d^{-1}, assuming a single-compartment model.

If we consider all the above parameters, a simple bioaccumulation model can be developed and the outputs compared with reported AR concentrations in predators from biomonitoring studies. If the barn owl (*Tyto alba*) is used as a sentinel predator in the model, the daily food intake in this species is about 10% of body mass (Marti 1973). The tissue concentration of ARs in prey that are associated with toxicity are usually based on the liver but these compounds are also found at lower levels in muscle and other tissues (Giraudoux et al. 2006). In fact, the proportion of AR body burden in the liver has been estimated to be about 25% of total body burden, which implies a ratio between liver and body concentrations of 7.9, according to data given by Giraudoux et al. (2006), although Shore and Coeurdassier (Chap. 6) estimate this ratio may be lower (5.2).

Information on food intake rates and AR concentrations in prey can be incorporated in a bioaccumulation model assuming a single-compartment distribution and a first-order elimination rate (Lazarus et al. 2014) as follows:

$$LC_n = BC_n \times LR \quad (7.1)$$

n is the life of the predator in days.
LC the liver concentration of ARs.
BC the total body concentration of ARs.
LR the concentration in liver relative to the total body concentration (×7.9).where

$$BC_n = \left(BC_{n-1} \times e^{-ER}\right) + DI_n \quad (7.2)$$

ER is the excretion rate (proportion of body burden excreted daily – 0.002 to 0.044 d^{-1}).
DI the daily intake of ARs (μg/kg bw).and

$$DI_n = FI \times CF \times BA \quad (7.3)$$

FI the daily food intake (100 g/kg bw);
CF the concentration of ARs in food (0.75 μg/g food-voles from Giraudoux et al. 2006);
BA the bioavailability of ingested ARs (0.75).

Figure 7.2 shows the modelled bioaccumulation of ARs in barn owls and how this varies with frequency of ingestion of contaminated prey (daily or every four days) and with two different tissue elimination rates based on $t_{1/2}$ having a value of either 15.8 days or 307 days. The modelled output indicates

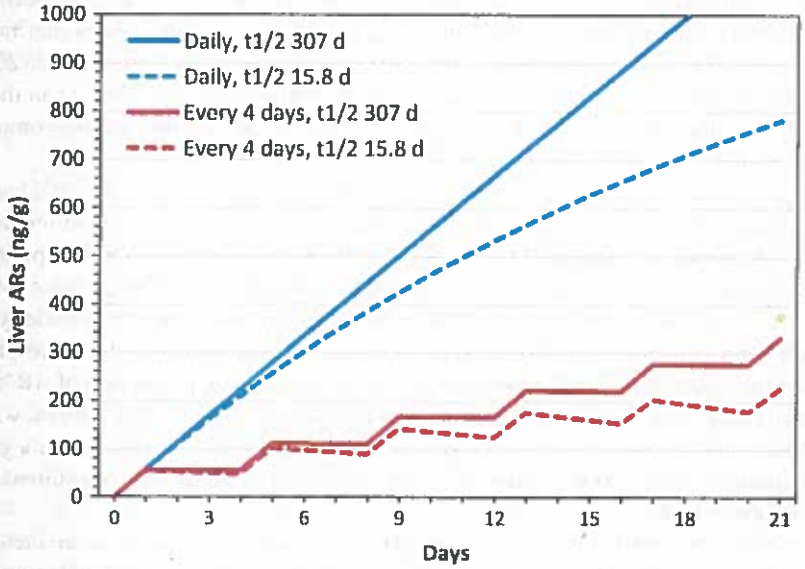

Fig. 7.2 Estimated levels of ARs in liver of barn owls exposed to contaminated prey daily or every 4 days (See details in the text for model parameters)

how bioaccumulation of ARs may lead to liver concentrations of concern in predators (see Sect. 8, this chapter) after 3–4 days of continuous ingestion of contaminated prey with variation in elimination rate making a minimal difference. Ingestion of contaminated prey every 4 days is estimated to result in liver concentrations of concern after 12–13 days when the excretion rate is just 0.002 d^{-1}, and after 20–21 d when the excretion rate is 0.049 d^{-1}. These results highlight the importance of the availability of contaminated prey, and the importance of the excretion rate when the consumption of contaminated prey is sporadic. Moreover, the assumption of a single-compartment model is probably not realistic, because $t_{1/2}$ of ARs is not equal in different tissues (Rattner et al. 2014a). Although additional information is needed to refine this model, the estimated bioaccumulation process with a constant exposure to ARs in contaminated prey (blue lines in Fig. 7.2) is similar to the experimental results obtained with owls, in which the exposure to contaminated prey for a period comprising up to 15 days produced ARs levels (i.e. brodifacoum) in liver of 0.63–3.7 μg/g accompanied by signs of coagulopathy or even death (Mendenhall and Pank 1980; Newton et al. 1990; Gray et al. 1994). The results of the discontinuous exposure to ARs in contaminated prey (red lines in Fig. 7.2) also gives similar results to the range of concentrations shown in many field monitoring studies (see Table 7.4).

5 Predators at Risk

The risk of secondary poisoning of the different species of predator may depend on their feeding habits. The factors associated with the elevated exposure to ARs in predators can be summarized as: (1) specialization in rodent predation, (2) scavenging behavior, either opportunistic or facultative and (3), in conjunction with the previous two, the use of anthropic environments where ARs are used.

The specificity of predation on rodents is a characteristic that can fluctuate in some species according to prey abundance. Some predators prey mostly on rodents and their migratory and breeding strategies are highly dependent on the spatial distribution of demographic peaks of rodents on a continental scale. On the other hand, these rodent cycles may also determine the predatory behavior of less specific predators, just because prey availability offers an important food resource that can be exploited temporarily (Hanski et al. 1991; Terraube et al. 2011). Such generalist predators exploit a wide range of food items and feed on small rodents when they are easily available. For instance in Europe, fox, common buzzard and some mustelids such as European pine marten (*Martes martes*), European polecat (*Mustela putorius*) and European badger (*Meles meles*) feed on small rodents when they are easily available (Redpath and Thirgood 1999; Dell'Arte et al. 2007). In contrast, specialist predators use a narrow range of food resources. This is true of the least weasel (*Mustela nivalis*) and many owl species, which are adapted specifically for hunting on rodents. This relationship between prey and predators can be so close as

Table 7.4 Frequency of occurrence, and mean concentrations, of anticoagulant rodenticide (AR) residues in the livers of birds of prey and carnivorous mammals. N is the number of animals tested for liver residues and N+ is the number that contained detectable AR concentrations

Class/family/ species		Country	N	N+	%	Mean ΣARs[a] (µg/g)	Ref[b]
BIRDS							
Accipitridae							
Cooper's hawk	*Accipiter cooperii*	USA	50	18	36	0.175	38
Northern goshawk	*Accipiter gentilis*	Spain	2	1	50	0.038	29
		USA	1	0	0		38
European sparrowhawk	*Accipiter nisus*	Spain	14	12	86	0.035	27
Sharp-shinned hawk	*Accipiter striatus*	USA	11	1	9		38
Spanish imperial eagle	*Aquila adalberti*	Spain	8	1	13	0.008	29
Golden eagle	*Aquila chrysaetos*	France	1	1	100	6.200	6
		Spain	4	1	25	0.006	29
		USA	1	1	100	0.030	37, 38
Common buzzard	*Buteo buteo*	Denmark	141	132	94	0.074	8
		France	43	41	95	0.318	6, 9, 15
		Spain	83	44	53	0.082	17, 23, 27, 29
		UK	519	227	44	0.047	14, 34
Red-tailed hawk	*Buteo jamaicensis*	Canada		58		0.005	39
		USA	263	201	76	0.437	20, 36–38
Rough-legged buzzard	*Buteo lagopus*	Denmark	31	26	84	0.040	8
		USA	1	0	0		38
Broad-winged hawk	*Buteo platypterus*	USA	11	0	0		38
Short toed snake-eagle	*Circaetus gallicus*	Spain	1	1	100	0.111	29
Marsh harrier	*Circus aeruginosus*	Denmark	3	3	100	0.012	8
Harrier hawk	*Circus approximans*	NZ	2	2	100	0.230	24
Montagu's harrier	*Circus pygargus*	France	1	1	100	6.100	6
		Spain	1	0	0		23

(continued)

Table 7.4 (continued)

Class/family/ species		Country	N	N+	%	Mean ΣARs[a] (µg/g)	Ref[b]
Bald eagle	*Haliaeetus leucocephalus*	USA	5	1	20	1.400	37, 38
Black kite	*Milvus migrans*	France	5	5	100	0.400	6
		Spain	5	3	60	0.054	29
Red kite	*Milvus milvus*	Denmark	3	3	100	0.413	8
		France	90	55	61	5.525	5, 9
		Spain	8	7	88	0.107	29
		UK	115	80	70	0.185	14, 33, 41
Falconidae							
Merlin	*Falco columbarius*	USA	1	0	0		38
Barbary falcon	*Falco pelegrinoides*	Spain	16	5	31	0.020	27
Peregrine falcon	*Falco peregrinus*	USA	2	1	50	1.480	37, 38
Common kestrel	*Falco tinnunculus*	Denmark	66	59	89	0.099	8
		France	4	3	75	0.080	15
		Spain	21	14	67	0.118	27
		UK	45	23	51	0.190	14, 33
Strigidae							
Saw-wet owl	*Aegolius acadicus*	USA	3	1	33		38
Short-eared owl	*Asio flammeus*	Denmark	5	5	100	0.015	8
		USA	1	0	0		38
Long-eared owl	*Asio otus*	Denmark	38	36	95	0.019	8
		Spain	35	24	69	0.036	17, 27
		USA	7	2	29		38
Little owl	*Athene noctua*	Denmark	9	9	100	0.118	8
		Spain	8	6	75	0.127	17, 29
Eagle owl	*Bubo bubo*	Denmark	10	10	100	0.193	8
		Spain	21	18	86	0.192	17, 29
Great horned owl	*Bubo virginianus*	Canada	250	166	66	0.043	1,39
		USA	93	79	85	0.141	20, 36–38
Screech owl	*Megascops asio*	USA	83	39	47	0.251	13, 20, 37, 38
Morepork	*Ninox novaeseelandiae*	NZ	2	2	100	2.005	19, 22
Snowy owl	*Nyctea scandiaca*	USA	2	0	0	0.260	37, 38
Scops owl	*Otus scops*	Spain	33	16	48	0.016	17

(continued)

Table 7.4 (continued)

Class/family/ species		Country	N	N+	%	Mean ΣARs[a] (μg/g)	Ref[b]
Tawny owl	*Strix aluco*	Denmark	44	41	93	0.078	8
		France	5	2	40		15
		Spain	27	21	78	0.095	17
		UK	206	46	22	0.047	14, 42
Barred owl	*Strix varia*	Canada	25	23	92	0.126	1
		USA	53	33	62	0.004	20, 38
Tytonidae							
Barn owl	*Tyto alba*	Canada	78	48	62	0.037	1
		Denmark	80	75	94	0.114	8
		France	17	8	47	0.206	6, 15
		Spain	66	47	71	0.088	17, 27, 29
		UK	313	81	26	0.083	14, 21, 33, 34
MAMMALS							
Canidae							
Red fox	*Vulpes vulpes*	France	82	72	88	1.132	6, 28
		Spain	31	12	39	0.122	29
		UK	155	97	63	0.117	40
Felidae							
Feral cat	*Felis catus*	NZ	47	36	77	1.297	2, 19, 35
Eurasian lynx	*Lynx lynx*	France	1	1	100	1.300	6
Bobcat	*Lynx rufus*	USA	39	35	90	1.352	25
Mountain lion	*Puma concolor*	USA	4	4	100	1.650	25
Mustelidae							
European otter	*Lutra lutra*	France	35	5	14	3.323	11, 16
		Spain	3	1	33	0.353	29
Stone marten	*Martes foina*	France	1	1	100	1.600	6
		Spain	19	11	58	0.353	29
Fisher	*Martes pennanti*	USA	58	46	79	1.610	12
Eurasian badger	*Meles meles*	France	1	1	100	0.900	6
Stoat	*Mustela erminea*	Denmark	61	59	97	0.150	10
		NZ	209	118	56	0.730	2–4, 7, 19, 35
		UK	40	9	23	0.022	18
Feral ferret	*Mustela furo*	NZ	24	16	67	1.030	2, 19, 35
European mink	*Mustela lutreola*	France	31	1	3	5.000	11
Least weasel	*Mustela nivalis*	Denmark	69	66	96	0.141	10

(continued)

Table 7.4 (continued)

Class/family/ species		Country	N	N+	%	Mean ΣARs[a] (μg/g)	Ref[b]
		NZ	61	42	69	0.747	2, 19, 35
		Spain	1	1	100	2.930	29
		UK	10	3	30	0.039	18
Polecat	*Mustela putorius*	France	33	5	15	3.400	11
		Spain	1	0	0		23
		UK	105	33	31	0.092	30–32
American mink	*Mustela vison*	France	47	7	15	4.300	11
American badger	*Taxidea taxus*	USA	1	1	100	4.400	26
Procyonidae							
Northern raccoon	*Procyon lotor*	Spain	10	2	20	2.720	29
		USA	1	1	100	2.070	26, 37
Viverridae							
Common genet	*Genetta genetta*	Spain	7	2	29	0.284	29
ALL			4187	2414	58	0.744	

[a]Concentration of ARs in individuals with detected levels. Sample size was 2551, higher than in column N+, because in some studies only positive cases were recorded and these individuals were not considered for the calculation of occurrence (%) because the number of monitored animals was not clearly stated

[b]References: 1. Albert et al. (2010); 2. Alterio (1996); 3. Alterio and Moller (2000); 4. Alterio et al. (1997); 5. Berny and Gaillet (2008); 6. Berny et al. (1997); 7. Brown et al. (1998); 8. Christensen et al. (2012); 9. Coeurdassier et al. (2014); 10. Elmeros et al. (2011); 11. Fournier-Chambrillon et al. (2004); 12. Gabriel et al. (2012); 13. Hegdal and Colvin (1988); 14. Hughes et al. (2013); 15. Lambert et al. (2007); 16. Lemarchand et al. (2010); 17. López-Perea et al. (2015); 18. McDonald et al. (1998); 19. Murphy et al. (1998); 20. Murray (2011); 21. Newton et al. (1990); 22. Ogilvie et al. (1997); 23. Olea et al. (2009); 24. Rammell et al. (1984); 25. Riley et al. (2007); 26. Ruder et al. (2011); 27. Ruiz-Suárez et al. (2014); 28. Sage (2008); 29. Sánchez-Barbudo et al. (2012); 30. Shore et al. (1996); 31. Shore et al. (1999); 32. Shore et al. (2003); 33. Shore et al. (2005); 34. Shore et al. (2006); 35. Spurr et al. (2005); 36. Stansley et al. (2014); 37. Stone et al. (1999); 38. Stone et al. (2003); 39. Thomas et al. (2011); 40. Tosh et al. (2011b); 41. Walker et al. (2008a); 42. Walker et al. (2008b)

to determine the density of rodents and the presence of these specialist predators (Andersson and Erlinge 1977; Brandt and Lambin 2007). In summary, how rodents contribute to the ingested biomass of a predator will determine the likelihood of exposure to ARs and the consequent risk of secondary poisoning.

The second risk factor is the facultative or scavenging behavior of predators. Rodents killed by ARs can contain elevated residue levels in their tissues, so the species feeding on small carrion items (e.g. rodents) may be at high risk of exposure to ARs [although it has been questioned as to the extent AR concentrations actually do differ between dead and living AR contaminated prey (Chap. 6)]. This is the case, for instance, for the red kite (*Milvus milvus*) in Europe, where it has been found to be lethally exposed to ARs used against voles in France (Coeurdassier et al. 2012). The list of opportunistic scavengers is extensive, including many species of carnivores,

diurnal birds of prey and corvids. Some facultative scavengers (i.e. vultures) also feed on small carcasses. In Europe, this includes the Egyptian vulture (*Neophron percnopterus*) and the bearded vulture (*Gypaetus barbatus*).

Finally, the third risk factor of use of anthropic environments is linked to the feeding behavior of predators and may explain spatial variation in the risk of AR exposure (also see Chap. 8). Several studies have pointed to higher exposure to ARs in predators from urban areas (Riley et al. 2007; López-Perea et al. 2015), especially areas of low-density development formed by single-family housing units (Nogeire et al. 2015), or around farms of intensive livestock production (Shore et al. 2006; Geduhn et al. 2015), because in both cases the use of ARs is often sustained over time to prevent the spread of rodent pests.

6 Monitoring Studies

Monitoring of AR levels in predators and other species of wildlife has been undertaken during the last three decades in some jurisdictions, particularly since the development of more sensitive analytical techniques whereby the detection of these compounds is now common in many studies carried out in different parts of the world. Initially, methods of detection were based on thin-layer chromatography (TLC) (Welling et al. 1970), but that technique was rapidly replaced by those based on high-performance liquid chromatographic (HPLC) methods (Hunter 1985; Newton et al. 1990). HPLC can be coupled with fluorescence (FLD) and high-resolution mass spectrometry (MSD) detection. The limits of detection for most of the ARs by FLD range between 0.001 and 0.1 μg/g (Shore et al. 1996; Berny et al. 1997; Fournier-Chambrillon et al. 2004; Christensen et al. 2012; Elmeros et al. 2011). Mass spectrometry, in addition to a very low limit of detection (0.002–0.25 μg/g) also gives a high specificity in the identification of the ARs in biological samples (Albert et al. 2010; Dowding et al. 2010; Gabriel et al. 2012; Hughes et al. 2013; López-Perea et al. 2015).

The tissue of choice for monitoring the presence of ARs is the liver because of long-term accumulation in that tissue but residues are also detectable in other tissues. While most studies have analysed liver samples for ARs (Berny et al. 1997; Elmeros et al. 2011; Gabriel et al. 2012; Ruiz-Suárez et al. 2014), a few have also used muscle (Sánchez-Barbudo et al. 2012). The two other commonly used sample types are blood and regurgitated pellets, especially in studies involving live animals, toxicokinetics, coagulopathy or other adverse effects, and to determine exposure levels to inform risk assessment (Newton et al. 1994; Rattner et al. 2010, 2011, 2014a; Brooke et al. 2013).

We reviewed scientific papers and reports describing the presence of ARs in predatory birds and mammals with different feeding habits and from different geographical areas. This information is from 40 published studies with a total number of 4187 animals from 53 species of predators, of which 17 were mammals and 36 were birds (Table 7.4). The number of positive animals was 2414, so the occurrence

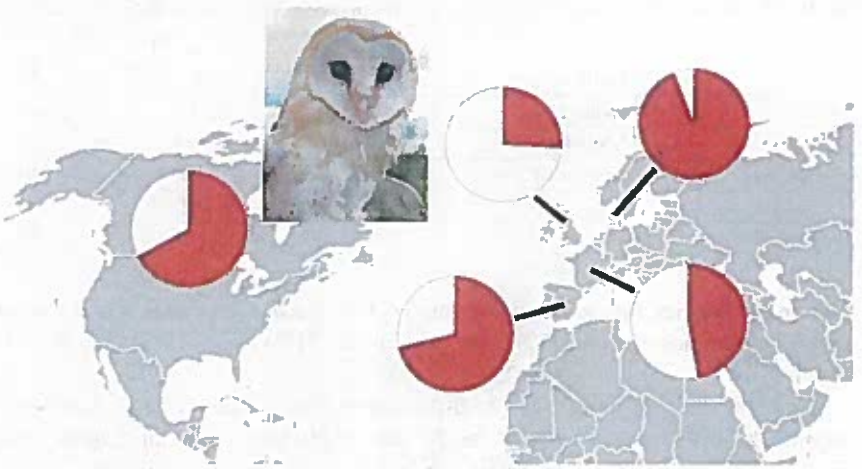

Fig. 7.3 Prevalence (*red portion*) of ARs in liver of barn owl (*Tyto alba*) in the northern hemisphere (From left to right: Canada, Spain, United Kingdom, France and Denmark-data from Table 7.4). This cosmopolitan species could be a good bioindicator of the risk of secondary poisoning by ARs in predators)

of ARs averaged 58% amongst studied predators. This is a value that should be considered of concern for the conservation of biodiversity in top-down regulated food-chains because it may reduce the numbers of top predators leading in the mid or long-term to rodent overabundance.

Seven countries contributed most of the available information: Canada, USA, UK, Denmark, France, Spain and New Zealand. Some cosmopolitan species, like the barn owl, can be good bioindicators of the risk of secondary poisoning in generalist predators and the calculated prevalence of AR residues can be compared among studies or geographic areas (Fig. 7.3). However, care must be taken when interpreting any such comparisons as limits of detection and the time frames over which data have been collected may not be similar; detection limits have decreased as analytical technology has advanced (Dowding et al. 2010), and the prevalence of rodenticides in barn owls may have changed over time (Newton et al. 1990, Walker et al. 2014). In terms of the types of anticoagulant, coumarin derivatives such as brodifacoum, bromadiolone, coumatetralyl, difenacoum, flocoumafen, warfarin, and indandione derivatives such as diphacinone and chlorophacinone have been documented. The most widely detected compounds have been brodifacoum, bromadiolone and difenacoum, all of them SGARs and therefore potentially bioaccumulative and toxic (Eason et al. 2002).

We also used the data from the studies we compiled to compare AR levels between birds and mammals and between generalist and specialist predators. We considered weasels and owls as specialist species, whereas diurnal raptors and carnivorous mammals (excluding weasel) were considered generalists (Hanski et al. 1991; Andersson and Erlinge 1977). Interestingly, specialist and generalist predatory birds had the same frequency of occurrence of AR residues in liver (58%). For

Table 7.5 Occurrence of ARs in avian and mammalian predators in relation to their feeding habits

Class	Predator type	N	With ARs	
			N+	%
Birds	Generalist	1296	755	58
	Specialist	1752	1012	58
Mammals	Generalist	688	349	51
	Specialist	451	298	66
All		4187	2414	58

mammals, species that are more specialized in feeding on rodents had a slightly higher occurrence of ARs (66%) than generalists (51%) (Yates' $\chi^2 = 25.5$, $p < 0.001$) (Table 7.5).

Detected concentrations tend to differ more than frequency of occurrence with significant differences between birds and mammals (General Linear Model, $F_{1,120} = 7.65$, $p = 0.007$) and between types of feeding behavior ($F_{1,120} = 7.96$, $p = 0.006$). Figure 7.4 shows that liver AR concentrations are generally higher in mammals than in birds, and in generalists than specialist. This finding may indicate that some specialist species mostly feed on non-target rodents.

Nine families of predators have been monitored for liver AR residues and the percentage of positive animals in each of them is shown in Fig. 7.5. The number of species included in each family were 17 Accipitridae, 4 Falconidae, 12 Strigidae, 1 Tytonidae, 1 Canidae, 4 Felidae, 11 Mustelidae, 1 Procyionidae and 1 Viverridae (Table 7.4). Although the calculated occurrence of ARs is derived from studies on several species and from multiple locations, the data provides an indication of the worldwide scenario for exposure and accumulation of ARs in predatory birds and mammals. It is notable that the detection of ARs has been above 50% in most of the studied families (Fig. 7.5).

Although the frequency of occurrence of liver ARs was similar in birds of prey and carnivorous mammals, liver concentrations in animals with residues were generally higher in mammals (especially Felidae, Mustelidae and Procyonidae) than in birds and at levels that could be indicative of the implication of ARs in the death of many of the studied individuals (Fig. 7.6).

The genus *Buteo* is among the diurnal raptor taxa with higher exposure to ARs in Europe and North America. Three species of this genus have shown prevalence of ARs between 44% and 94% in studies involving sample size >27. Mean ΣAR concentrations in this genus ranged between 0.04 and 0.318 μg/g (Table 7.4). Another raptor of the Accipitridae family widely studied has been the kites of *Milvus* genus. Black (*M. migrans*) and red kites (*M. milvus*) in Europe have shown prevalence of AR residues between 44% and 100% and concentrations from 0.054 to 5.525 μg/g (Table 7.4). In the case of Falconidae, common kestrel (*Falco tinnunculus*) has been the species with higher number of individuals monitored, and the occurrence of ARs has been between 51% and 89% in different European countries. Mean ΣARs levels in common kestrel ranged from 0.099 to 0.190 μg/g (Table 7.4).

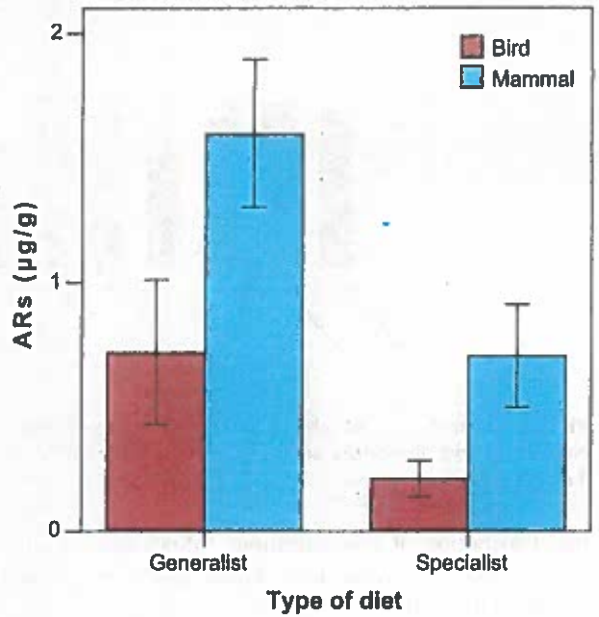

Fig. 7.4 Mean (±SE) of ARs concentrations described in generalist and specialist predatory species of birds and mammals. Mean values were calculated from the means of studies on different species in different countries (see Table 7.4)

Among the nocturnal raptors of the family Strigidae, *Strix* genus has been studied in Europe and North America and the occurrence of ARs has been between 22% and 93% with mean ΣARs levels of 0.004–0.126 μg/g (Table 7.4). Even higher occurrence of ARs has been found in the larger *Bubo* species from Europe and North America, with detectable levels in 66–100% of the individuals and mean levels of 0.043–0.192 μg/g (Table 7.4). In the family of Tytonidae, barn owl has been also widely used to monitor the prevalence of ARs exposure in Europe and North America. This cosmopolitan species have shown occurrence of ARs ranging from 26% to 94% and with mean ΣAR levels of 0.037–0.206 μg/g (Table 7.4).

In the case of carnivorous mammals, the highest occurrence of ARs was reported for Felidae species with values of prevalence between 77% and 100% and mean ΣARs levels of 1.297 and 1.650 μg/g (Table 7.4). Those concentrations are well above the levels detected in raptorial birds. Red fox has been the only Canidae species studied and the prevalence of AR exposure has been between 39% and 91% in Europe. The mean detected concentrations in red fox have been between 0.117 and 1.132 μg/g (Table 7.4). The family of carnivores with the highest number of species analysed for ARs has been the Mustelidae. The species of that group monitored with a sample > 30 show prevalence values between 3% and 97%, so there can be important differences related to the habitat use and feeding habits within this group of species. Similarly, the mean concentrations ranged from 0.022 to 5 μg/g (Table 7.4).

The major differences in the concentrations detected in the different studies of the same species (Table 7.4) deserve some consideration. Some of these differences may be explained by differences in the analytical methods used, because the most sensitive would increase the incidence of positive individuals in the lower range of

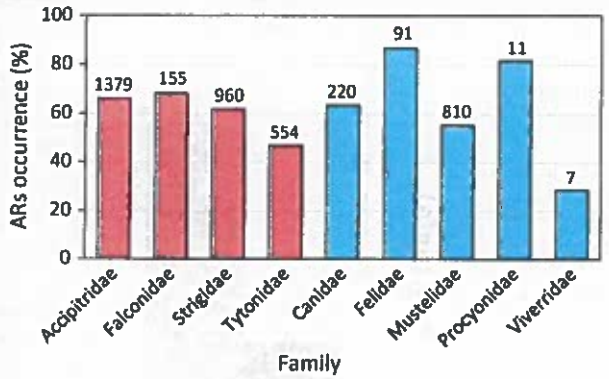

Fig. 7.5 Occurrence of ARs by families of birds of prey (*red*) and carnivorous mammals (*blue*). Numbers shown above bars are the sample size in each family (Data are from studies cited in Table 7.4)

the distribution of concentrations. Mean concentrations are calculated with individuals containing detectable levels, so the inclusion of individuals with very low levels could significantly reduce the arithmetic mean. On the other hand, some of the compiled studies have been performed during large-scale treatments with ARs against rodents at their demographic peaks or in areas specially affected by rodents, so the high availability of contaminated prey could lead to excessive accumulation in predators (Berny et al. 1997; Giraudoux et al. 2006) and affect their populations (Jacquot et al. 2013). For instance, stoats (*Mustela erminea*) and least weasel monitored in New Zealand have been exposed after broader scale poisoning operations against mice and black rats, so the high observed levels (brodifacoum in liver: up to 1.72 μg/g) may be explained by these treatments (Alterio 1996; Alterio et al. 1997; Alterio and Moller 2000). Similarly, pellet samples from screech-owls (*Megascops asio*), exposed to brodifacoum after broadcast application in an orchard in the USA to control voles (*Microtus spp.*), contained 0.06–0.09 μg/g (Merson et al. 1984). It is also noteworthy that monitoring surveys are usually conducted using animals found dead and, if there is a large number of poisoned animals in such samples, this may introduce a bias in the overall observed mean AR value for a species.

7 Effects on Predators in Field and Experimental Studies

ARs have an anticoagulant mode of action, inhibiting the vitamin k epoxide reductase enzyme necessary for recycling of vitamin K, a cofactor of primary importance for activation of blood clotting factors II, VII, IX and X (Watt et al. 2005; Krieger 2010). Because of AR exposure, rodents or other vertebrates accidentally exposed to baits can die and predators feeding on poisoned prey may suffer secondary poisoning with effects ranging from subclinical signs to mortality. More detailed

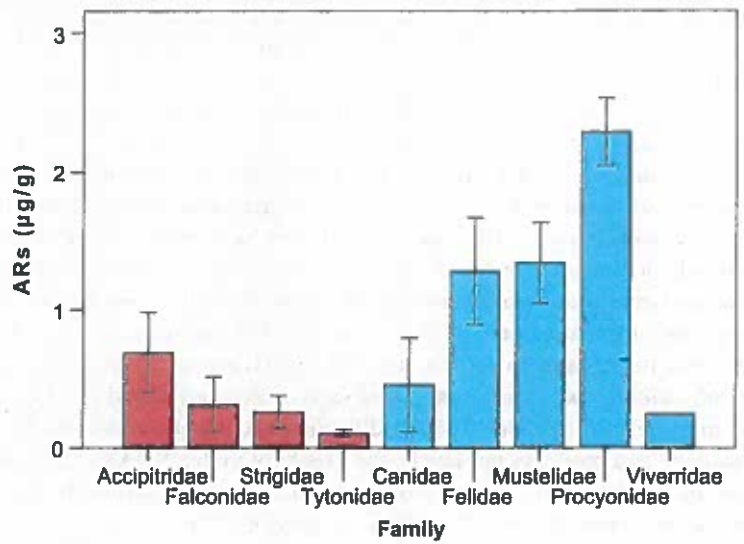

Fig. 7.6 Concentration (arithmetic mean ± SE) of ARs by families of birds of prey (*red*) and carnivore mammals (*blue*)

information on the toxicity and pharmacokinetics of ARs and on clinical signs of intoxication and effects are given in Chaps. 3, 4 and 5 of this book.

7.1 Mortality

Secondary poisoning of predators by ARs has been documented in several European countries. In France, which conducts toxico-vigilance monitoring of wildlife, AR poisoning of predators has been confirmed in several wildlife species over recent decades. For instance, Berny et al. (1997), analyzed 31 red foxes and 16 common buzzards (*Buteo buteo*) suspected of bromadiolone poisoning; poisoning was confirmed in all foxes and 15 buzzards. Later, Berny and Gaillet (2008) published another survey conducted between 1992 and 2002 that involved 62 cases of suspected poisonings of red kites. In total, 27 birds were confirmed to have died by AR exposure, 24 with liver bromadiolone residues between 0.2–5.6 μg/g and three with chlorophacinone residues between 0.9–5.2 μg/g. Also in France, Fournier-Chambrillon et al. (2004) analyzed 122 carcasses of four species of free ranging mustelids collected between 1990 and 2002 and found two European polecats with 0.6 μg/g and 2.6 μg/g and one American mink (*Mustela vison*) with 2.0 μg/g of ARs in liver together with generalized and massive hemorrhages, severe anemia and dehydration; ARs were therefore considered to be directly responsible for their death. In the United Kingdom, Newton et al. (1990) diagnosed AR poisoning as the cause of death in one out of 145 barn owls; that single bird had 0.43 μg/g

brodifacoum in its liver and had hemorrhages. Hughes et al. (2013) assessed the presence of ARs in the liver tissues of raptors from the United Kingdom and the highest frequency of exposure was in red kite, with 70% of positive individuals (n = 114) and mean liver ΣAR concentrations of 0.155 μg/g; it was concluded that 10% died because of rodenticide exposure.

In North America, several studies have described cases of lethal poisoning of predators by ARs. Stone et al. (1999) found hemorrhages associated with AR exposure in 33 predators between 1971 and 1997 in New York State (USA). AR residues in those predators ranged from 0.01 to 5.3 μg/g in liver and their necropsy revealed subcutaneous hemorrhages, pallor of muscle and/or internal organs, hemorrhages in lungs and inter- and intramuscular hemorrhages, most likely caused by vitamin K deficiency due to exposure to ARs. Stone et al. (2003) also analyzed the presence of ARs in 265 individuals from 12 species of raptors and they found residues in 49% of them, in some cases with levels of brodifacoum >0.36 μg/g. Based on the finding of hemorrhage and brodifacoum levels, the exposure to that SGAR was considered the cause of death in nine cases (14.6% of positives). Similarly, Murray (2011) detected the presence of liver ARs in 86% of individuals of four species of birds of prey admitted to wildlife rehabilitation centers; mortality from AR toxicosis was diagnosed in 6% of birds, which had AR levels from 0.012 to 0.29 μg/g. More detailed information about AR poisoning in predatory birds in the USA is given by Murray in Chap. 5 of this book.

AR poisoning has also been observed in carnivorous mammals in the USA: two mountain lions (*Puma concolor*) with 0.51–1.27 μg/g of bromadiolone and 0.31–0.57 μg/g of brodifacoum in the liver, a raccoon (*Procyon lotor*) and an American badger (*Taxidea taxus*) with 1.4–4.4 μg/g of chlorophacinone in liver and four fishers (*Martes pennant*) with 0.12 μg/g bromadiolone and 0.22 μg/g brodifacoum in the liver; coagulopathy and bleeding into tissues or cavities were common findings in these cases (Riley et al. 2007; Ruder et al. 2011; Gabriel et al. 2012). Albert et al. (2010) monitored the exposure to ARs in three owl species in Canada between 1988 and 2003. The analysis of 164 liver samples revealed that 70% of the studied birds had detectable residues of at least one AR and six of the owls were diagnosed as having died by AR poisoning with ARs levels ranging from 0.060 to 1.065 μg/g.

The intensive use of ARs in the Oceania region to control invasive rodents also represents a risk for predators, including some non-native species. For instance, Brown et al. (1998) described AR poisoning in ten stoats that had between 0.54 μg/g and 0.81 μg/g of brodifacoum in liver after a treatment against mice in New Zealand.

All of the above cases are evidence of the risk secondary poisoning by ARs can pose to predators in the wild. Many non-target wildlife around the world have suffered lethal effects from AR exposure, with two SGARs, bromadiolone and brodifacoum, most commonly involved. Lethal effects were documented in animals with liver levels of those SGARs ranging from 0.01 to 5.3 μg/g ARs in liver. In summary, those findings confirm that secondary exposure to ARs in predators can be a cause of mortality, and should be taken into account in the conservation and population management of many species of predators.

Recent studies have experimentally assessed AR effects on diurnal and nocturnal birds of prey. The toxicity and the potential risk of diphacinone (FGAR) have been assessed by Rattner et al. (2010, 2011, 2014a) in two species (i.e. American kestrel (*Falco sparverius*) and eastern screech-owls), which are representative of Falconidae and Strigidae families. Rattner et al. (2010, 2011) orally administered diphacinone to American kestrels with daily dosages ranging from 35.1 to 675 mg/kg body weight. They documented mortality and sub-lethal effects during seven days of monitoring. American kestrels survived with dosages ranging from 35.1 to 79.0 mg/kg, but died when given doses of 118.6 mg/kg to 675 mg/kg. All birds that survived exhibited varying degrees of hemorrhage in liver and prolonged clotting times. In a study carried out with eastern screech-owls, individuals were fed diets containing 10 μg/g of diphacinone (by wet weight) for 7 days to evaluate sub-lethal effects (Rattner et al. 2014a). Russell's viper venom time was prolonged by day 3, when birds had diphacinone levels of 1.63 μg/g in liver and 5.83 μg/g in kidney; prothrombin time was prolonged by day 7 when several owls already exhibited external signs of bruising and internal evidence of hemorrhage. After termination of exposure, coagulopathy and anemia were resolved within 4 days, and residues decreased to <0.3 μg/g after 7 days. Liver and kidney elimination occurred with overall half-lives of 11.7 days and 2.1 days, respectively.

7.2 *Sub-lethal Effects*

In many cases, exposure to ARs in predators is not sufficient to kill the animals, but sub-lethal effects may impair the fitness of individuals. The best known effect of ARs is related to blood clotting, which is clinically diagnosed by the increase of the coagulation time measured through different laboratory tests (i.e. thrombin time, prothrombin time, activated partial thromboplastin time) (Brakes and Smith 2005; Sage et al. 2010; Rattner et al. 2010, 2011, 2012, 2014a). All of those measures are indicative of impairment of blood coagulation and can represent an early signal of AR poisoning, but are all in fact indicators of the mechanism causing lethality.

Some other adverse effects have been associated with AR exposure, but sometimes there is not a clear mode of action to establish such associations. Exacerbated blood loss during molt in AR-exposed birds can be explained by vitamin K antagonism but this mechanism is not obviously directly related to other effects attributed to sub-lethal AR exposure, such as impaired body condition, susceptibility to disease, reduced resilience or tolerance to extreme weather, and even sensitivity to other toxicants (Rattner et al. 2014b). In this respect, observed infestations with notoedric mange in bobcats (*Lynx rufus*) and mountain lions (*Puma concolor*) have been linked to exposure to SGARs in the wild (Riley et al. 2007); felines of these two species found dead with mange lesions had detectable liver AR residues with concentrations >0.05 μg/g. The mechanism by which exposure to ARs may be linked to occurrence of mange is uncertain although Riley et al. (2007) suggested that SGARs could act as stressors and have increased the susceptibility of bobcats to mange.

Knopper et al. (2007) assessed SGAR effects in bones of raptors because of the role that vitamin K also plays in bone metabolism, where it is required for the formation of γ-carboxyglutamyl, a component of bone proteins such as osteocalcin (Weber 2001). The density and breaking strength of humerus and femur of barn owls and kestrels was measured and its relationship with liver SGARs residues was evaluated, but no significant relationship was found.

Sub-lethal adverse effects mediated by ARs may occur not only at the individual level but may also disturb population dynamics and other factors essential to maintenance of wildlife populations. One such adverse effect is on reproduction. Several studies have shown evidence of adverse effects of AR treatments on the breeding success of predators. Naim et al. (2011) studied the clutch size, hatching and fledging success of the Eastern barn owl (*Tyto alba javanica*) in an area where rodent control was practiced using three treatments (warfarin, brodifacoum and a biological control with the parasite *Sarcocystis singaporensis*). They found that breeding success in treatment plots was lower than in control plots (areas where there was no rodent control). In particular, brodifacoum treatment plots had the lowest rates of hatching and fledging, and brodifacoum was also the most effective for rodent control. SGAR residues were not assessed in the raptors, but the observed reproductive effects seemed to have been caused by a reduction in prey availability (Naim et al. 2011), and so may represent an indirect effect of rodenticides.

Effects on population dynamics from the use of ARs can also occur in carnivorous mammals. An example has been reported for American badger and red fox populations in two study areas with different levels of AR use. In the study area with relatively lower use of ARs, American badger had a relative abundance index of 0.11 individuals/km and red fox of 0.16 individuals/km, while in the area with higher use of ARs the relative abundance of both species was only 0.05 individuals/km (Proulx and MacKenzie 2012). Another example of effects on populations of predators was reported by Jacquot et al. (2013) who monitored the fox population in relation with a bromadiolone treatment in France. These authors found a negative relationship between fox populations and bromadiolone treatments, and these effects were detectable more than one year after treatments.

With regards birds of prey, Coeurdassier et al. (2014) found 28 red kites and 16 common buzzards (*Buteo buteo*) dead during surveys after an intensive treatment with bromadiolone for water vole control in France. Bromadiolone poisoning was either confirmed or highly suspected as the main cause of death and there was a possible impact of bromadiolone on the breeding population of red kites in the area during that year. ARs poisoning has been also identified as a main conservation issue for the red kite in Spain due treatments against common vole (Viñuela et al. 1999; Mougeot et al. 2011).

Another aspect of potential sub-lethal effects to consider is the maternal transfer of ARs to progeny. Gabriel et al. (2012) described the neonatal transfer of AR in one fisher kit (*Martes pennant*), who was still suckling when the mother died. The kit showed trace levels of brodifacoum in liver tissue, but it was not associated with hemorrhaging in any tissues or body cavities; therefore, the cause of death was determined to be acute starvation and dehydration because of mother's death. In

birds, Fisher (2009) confirmed the maternal transfer of ARs in hens administered with a single dose of brodifacoum at 0.5 mg/kg of body weight; hens laid eggs that had brodifacoum concentrations of up to 0.035 µg/g.

8 Interpreting Liver Residue Levels and Exposure Doses

As considered above, there is a high occurrence of ARs in the liver tissues in many predatory species and in many geographical areas. Most studies have used animals found dead in the wild and so it is only possible to estimate how many individuals died because of their exposure and accumulation of ARs. There is still a lack of consensus among researchers about how and if it is possible to determine AR levels in liver tissue that are indicative of lethal poisoning. In general, the diagnosis of AR poisoning has been performed by researchers on the basis of evidence of hemorrhage and the presence of liver AR residues over a specific threshold level (0.1–1 µg/g) (Berny et al. 1997; Murray 2011). That approach seems to be appropriate but is problematic both in terms of considering hemorrhagic lesions and residue magnitude. Firstly, animals poisoned by ARs do not always show macroscopic hemorrhage (Sarabia et al. 2008; Rattner et al. 2011). Moreover, many predators die because of trauma (e.g. road kills, collision with power lines or shooting) that may involve bleeding which can confound the interpretation of an effect of ARs (Chap. 5; Murray 2011; Sánchez-Barbudo et al. 2012; López-Perea et al. 2015). On the other hand, there seems to be a high degree of variability among species and individuals in vulnerability to ARs, and so a probabilistic approach has been proposed as an alternative to the establishment of a unique threshold level (Thomas et al. 2011). For instance, based on this probabilistic approach, barn owls with a liver summed SGAR concentrations of 50 ng/g, 90 ng/g, 130 ng/g and 180 ng/g may have a 5%, 10%, 15% and 20% probability, respectively, of having been poisoned by SGARs.

The development of such models or the establishment of threshold levels could also require information from experimental studies in predators fed with contaminated prey. Some laboratories have tested the secondary poisoning risk from SGARs by giving poisoned prey to predators. For example, the risk posed by brodifacoum has been tested in owls fed with poisoned mice or rats for up to 15 days. The owls under those treatments consumed amounts of brodifacoum ranging from 0.046 to 0.184 mg and had liver brodifacoum levels of 0.63–1.67 µg/g. In all tests, the owls showed signs of poisoning such as internal hemorrhage and liver pallor and/or died. Clinical signs began to occur after 1–21 days of exposure, and the earliest death occurred six days after the onset of the treatment (Mendenhall and Pank 1980; Newton et al. 1990; Gray et al. 1994).

The sub-lethal and lethal toxicity of bromadiolone has been studied in several species of predators. Barn owls fed bromadiolone-contaminated rats for seven days had an accumulated total dose of 1.12 mg and a mean bromadiolone blood concentration of 13.25 µg/L at day 1 and 0.02 µg/L at day 7 post-treatment. Although none

died, some exhibited hemorrhages (Salim et al. 2014). In another experimental exposure of barn owls, Mendenhall and Pank (1980) found that all the birds fed bromadiolone poisoned rats died after 11 days, but tissue concentrations of bromadiolone were not analyzed in that study. In carnivorous mammals, bromadiolone was also found to cause sub-lethal and lethal effects; one red fox receiving bromadiolone in pheasants for 5 days containing around 0.52 μg/g of bromadione in the liver showed longer prothrombin time and partial activity of prothrombin time at day 20, and died 36 days after the onset of exposure. That fox had 0.198 μg/g of bromadiolone in liver (Beklova et al. 2007). In another survey, four foxes were fed for 2 or 5 days with water voles spiked with 200 μg bromadiolone/vole, which is a concentration close to that measured in voles in the field. The foxes did not die but two presented very severe external hemorrhages that required administration of the antidote vitamin K1. At the end of the experiment, the foxes were euthanized and bromadiolone concentrations in liver ranged from 2 to 2.54 μg/g (Sage et al. 2010).

In the case of flocoumafen, barn owls fed for one day on poisoned mice (containing 0.23 μg/g of flocoumafen in the liver) eliminated the compound in eight days without any mortality or signs of altered blood clotting (Eadsforth et al. 1991). However, other studies with barn owls fed flocoumafen-poisoned mice for 1–15 days described the presence of hemorrhage at day 1 and mortality at day 5. Dead birds had liver flocoumafen concentrations of 0.25–1.15 μg/g (Newton et al. 1994; Gray et al. 1994).

Difenacoum has been also tested in several studies. Barn owls fed with poisoned mice and receiving a total dose of up to 0.1 mg of difenacoum showed sub-lethal hemorrhages and elongation of the coagulation time between 6 and 23 days after treatment (Mendenhall and Pank 1980; Newton et al. 1990). Gray et al. (1994) studied the exposure of difenacoum in barn owls and observed that one dead bird had 0.25 μg/g of this AR in liver and showed internal hemorrhages.

Finally for the SGARs, the risk of secondary poisoning from difethialone was tested in barn owls. Three of barn owls ate poisoned rats during 54 days in three phases; in phase 1 (1–20 days), owls received a dose of 0.05 mg/kg body weight (BW), in phase 2 (21–50 days) a dose of 0.16 mg/kg BW and in phase 3 (51–54 days) a dose of 0.13 mg/kg BW of difethialone. All barn owls survived phases 1 and 2, with signs of poisoning (i.e. bleeding on the foot and dullness) manifest only in phase 2. The three owls died in phase 3 showing internal hemorrhage after accumulative doses of 0.27, 0.36 and 0.39 mg/kg (Saravanan and Kanakasabai 2004).

The risk to predators from FGARs is lower than for SGARs according to the results of experimental studies. For instance, American kestrels exposed to an undetermined amount of chlorophacinone during 21 days showed only hematomas on the pectoral muscle, lung, liver and heart (Radvanyi et al. 1988). In a more recent study, clotting times increased in American kestrels given 0.079 mg/kg body weight chlorophacinone over a 7-day exposure period; a liver reference residue level associated with coagulopathy was estimated at 0.076 mg/kg (Rattner et al. 2015). Barn owls with up to 10.14 μg/L of chlorophacinone in blood displayed hemorrhages, but no mortality occurred (Mendenhall and Pank 1980; Salim et al. 2014). Diphacinone

is the other FGAR tested in diurnal and nocturnal raptors. Golden eagles (*Aquila chrysaetos*) feeding on diphacinone-poisoned sheep for 5–10 days showed longer prothrombin time, but no mortality occurred after the consumption of up to 1.6 mg/kg of diphacinone (Savarie et al. 1979). In another study, great-horned owls (*Bubo virginianus*) and saw-whet owls (*Aegolius acadicus*) exposed to an undetermined amount of diphacinone showed changes in the coagulation time after 8 days of exposure, displayed hemorrhages and died at 7–14 days (Howard et al. 1970). More recently, Rattner et al. (2011) estimated the 7-day acute oral LD50 of diphacinone for American kestrels to be 96.8 mg/kg (95% confidence interval 37.9–219 mg/kg). This value was 20 times lower than the LD50 estimated in Northern bobwhite quail (2014 mg/kg), which reveals a great variability in the toxicity of diphacinone among bird species (Rattner et al. 2010). Diphacinone concentration in liver of lethally or severely poisoned American kestrels was in the range of 0.591–56.3 μg/g wet weight, while in those that survived to sub-lethal exposures this was ≤0.280 μg/g (Rattner et al. 2011). Eastern screech-owls exposed to diphacinone showed overt signs of intoxication at a single dose of 130 mg/kg of body weight, but in 7-day feeding trials toxic effects occured with diets containing as low as 2.15 ppm (dose of 0.24 mg/kg body weight/day). In this study, two owls that died at 22.6 ppm of diphacinone in diet had 1.26 and 1.29 mg/g of dipahcinone in liver. In a subsequent study, Rattner et al. (2014a) concluded that coagulopathy can occur in owls with more than 0.1 mg/kg of dipahcinone in liver.

Based on results of the toxicity assays carried out with barn owls and other species, the scale of toxicity from the most to least toxic compound generally follows this order: brodifacoum > bromadiolone > flocoumafen > difenacoum > difethialone > diphacinone > chlorophacinone. The greater toxicity of SGARs compared to FGARs is evident from their low LD_{50} and high persistence in the hepatic tissue of rodents and their predators (Watt et al. 2005; Ishizuka et al. 2008). Brodifacoum, in particular, is the compound with lowest LD_{50} for most species (Godfrey 1985; Erickson and Urban 2004; Valchev et al. 2008).

9 Risk of Secondary Poisoning in Humans

The effects of some anticoagulants in humans are well known due to their use as pharmaceuticals. Warfarin has been extensively used for antithrombotic therapy and clinical human studies have also been conducted to establish a therapeutic dose of diphacinone for its use on patients requiring anti-clotting medication (Eisemann and Swift 2006; Cavallari and Limdi 2009). In the case of warfarin, the reported LD in humans is 6.667 mg/kg (ChemIDplus 2017). Human LD values have not been calculated for other anticoagulants but clinical assays have established the therapeutic dose of diphacinone in humans at 5–63 mg per day (Willis et al. 1953; Duff et al. 1953; Katz et al. 1954).

Consideration of pharmaceutical use is not the purpose of this chapter, although the available information can be of interest for the evaluation of the risk posed to humans from the consumption of game containing ARs residues. This may result in exposure in humans that is analogous to that in other predators and the consequences have been assessed in some countries where game is commonly consumed.

In New Zealand, brodifacoum concentrations in wild boar (*Sus scrofa*) ranged from 0.01 to 0.07 mg/kg in muscle and from 0.007 to 1.7 mg/kg in liver; in red deer (*Cervus elaphus*) it was 0.02 mg/kg in muscle and between 0.01 and 0.03 mg/kg in liver and the liver concentration in goat (*Capra hircus*) was 0.01 mg/kg (Eason et al. 1999, 2001). Those studies highlighted that if humans had a similar LD_{50} for brodifacoum as dogs (0.25 mg/kg; ChemIDplus 2015), a 60-kg man would need to eat approximately 15 kg of liver containing 1 mg/kg to achieve a lethal exposure level.

Diphacinone levels have been measured in the liver and muscle of several domestic and wildlife species that can be consumed by humans. Pigs used for diphacinone toxicity assays had diphacinone concentrations between 0.004 and 0.37 mg/kg in muscle and between 0.04 mg/kg and 3.22 mg/kg in the liver (Keith et al. 2009; Fletcher 2002; Fisher 2006). In the field, wild boar exposed to diphacinone had concentrations of 0–3.07 mg/kg in liver and 0–0.25 mg/kg in muscle (Pitt et al. 2005). Several species of game birds have also been found to contain diphacinone residues in their liver: residues were 0.09–0.18 mg/kg in Kalij pheasants (*Lophura leucomelana*) (Spurr et al. 2003a, b), 0.23 mg/kg in ring-necked pheasant (*Phasianus colchicus*), and up to 0.56 mg/kg in California quail (*Callipepla californica*) (Hegdal 1985). It is important to highlight the assays done by Pitt et al. (2011) who assessed the effect of cooking on diphacinone residues in meat and the potential hazard for human consumers. In that study, pigs were exposed to diphacinone baits designed to deliver doses of 3.5 and 7.4 mg/kg/day over two days. The resultant diphacinone wet weight concentrations in the uncooked tissues of the pigs were 0.223–0.562 mg/kg in fat, 0.660–1.733 mg/kg in liver and 0.048–0.209 mg/kg in muscle. After boiling, diphacinone was undetected in fat and was present at concentrations of 0.910–1.940 mg/kg in liver and 0.107–0.296 mg/kg in muscle. Roasted tissue had mean concentrations of 0.648 mg/kg in fat, 1.116–2.335 mg/kg in liver and 0.132–0.348 mg/kg in muscle. The highest concentration of diphacinone was detected in a roasted liver sample (3.650 mg/kg), which may indicate that water loss during heating tends to concentrate diphacinone in samples.

Eisemann and Swift (2006) calculated several exposure scenarios for human consumers based on maximum diphacinone residues in pig muscle (0.25 mg/kg), pig liver (3.07 mg/kg), and game bird liver (0.56 mg/kg). Those authors concluded that a person weighing 55 kg would need to eat 28.49 kg of pig muscle, 2.33 kg of pig liver or 12.77 kg of game bird liver to ingest a dose of diphacinone equivalent to that which affects blood clotting in rats. In terms of potential risk to pregnant women, the ingested amounts would be 5.50 kg, 0.45 kg or 2.46 kg, respectively, to receive a dose equivalent to that which caused fetal reabsorption in rats. These exposure scenarios do not seem likely to occur in a single day. However, the risk of such exposure should not be totally discounted because ARs have much lower effective doses at repeated exposures and because some SGARs are highly accumulative. Moreover, the potential interaction with factors such as antithrombotic therapies should be considered as an additional risk for the development of possible adverse drug interactions. Despite the evidence of wide distribution of ARs in the environment (Gómez-Canela et al. 2014a, b) and wildlife (Rattner et al. 2014b), there is a distinct lack of toxico-epidemiological studies about the presence of AR residues in humans that is unrelated to pharmacological use.

10 Summary

Anticoagulant rodenticides (ARs) are currently the most common pesticides and biocides used to control rodents that pose economic and health problems for humans. However, the long-term persistence of ARs in animal tissues, especially the second-generation anticoagulant rodenticides (SGARs), causes this type of compound to bioaccumulate. This, in conjunction with the high toxicity of SGARs, poses consequences for predatory species that are, otherwise, natural allies in this struggle against pest rodents. The available information about rodenticide levels in the potential prey of predators, including insects, reptiles, granivorous birds and rodents, can be used to calculate expected bioaccumulation based on literature data on AR bioavailability, excretion rate and tissue distribution under scenarios of continuous and sporadic exposure to contaminated prey. The modeled results highlight the importance of excretion rate as a key factor in determining whether an animal's liver burden reaches a level of concern in the case of sporadic exposures. The potential of ARs to bioaccumulate explains the finding that 58% (2414 out of 4187) of predators analyzed in field monitoring studies worldwide had detectable AR residues. This data compilation reveals that specialist and generalist predatory birds have equal occurrence of AR residues in liver (58%), but in the case of mammals, those more specialized on rodents showed slightly higher occurrence of ARs (66%) than the generalist species (51%). Diagnosis of lethal poisoning is usually based on the co-occurrence of ARs residues in liver and signs of obvious hemorrhage, but AR levels associated with poisoning vary among species and individuals and the development of macroscopic bleeding is not a constant finding in poisoned animals. Thus, it is difficult to establish a diagnostic threshold level and a probabilistic approach of the dose-residue-effect relationships seems more appropriate for this type of toxicant. With regards secondary exposure risk in humans, the available information indicates a risk of exposure for game meat consumers when hunted animals contain ARs residues, but at levels well below those that are likely to be lethal. In summary, the fate and distribution of ARs need to be monitored in depth using predatory species, including humans. The consequences for the top-down regulation of rodent populations should be evaluated in greater detail and considered as part of the regulation on use of this group of pesticides/biocides.

References

Albert CA, Wilson LK, Mineau P, Trudeau S, Elliott JE (2010) Anticoagulant rodenticides in three owl species from Western Canada, 1988-2003. Arch Environ Contam Toxicol 58:451–459

Alterio N (1996) Secondary poisoning of stoats (*Mustela erminea*), feral ferrets (*Mustela furo*), and feral house cats (*Felis catus*) by the anticoagulant poison, brodifacoum. New Zeal J Zool 23:331–338

Alterio N, Moller H (2000) Secondary poisoning of stoats (*Mustela erminea*) in a South Island podocarp forest, New Zealand: implications for conservation. Wildl Res 27:501–508

Alterio N, Brown K, Moller H (1997) Secondary poisoning of mustelids in a New Zealand Nothofagus forest. J Zool London 243:863–869

Andersson M, Erlinge S (1977) Influence of predation on rodent populations. Oikos 29:591–597

Beklova M, Krizkova S, Supalkova V, Mikelova R, Adam V, Pikula J, Kizek R (2007) Determination of bromadiolone in pheasants and foxes by differential pulse voltammetry. Int J Environ Anal Chem 87:459–469

Berny PJ, Gaillet J-R (2008) Acute poisoning of Red Kites (*Milvus milvus*) in France: data from the Sagir network. J Wildl Dis 44:417–426

Berny PJ, Buronfosse T, Buronfosse F, Lamarque F, Lorgue G (1997) Field evidence of secondary poisoning of foxes (*Vulpes vulpes*) and buzzards (*Buteo buteo*) by bromadiolone, a 4-year survey. Chemosphere 35:1817–1829

Birks JDS (1998) Secondary rodenticide poisoning risk arising from winter farmyard use by the European polecat *Mustela putorius*. Biol Conserv 85:233–240

Bishop CA, Williams KE, Kirk DA, Nantel P, Reed E, Elliott JE (2016) A population model of the impact of a rodenticide containing strychnine on Great Basin Gophersnakes (Pituophis catenifer deserticola). Ecotoxicology 25:1390–1405.

Bowie MH, Ross JG (2006) Identification of weta foraging on brodifacoum bait and the risk of secondary poisoning for birds on Quail Island, Canterbury, New Zealand. N Z J Ecol 30:219–228

Brakes CR, Smith RH (2005) Exposure of non-target small mammals to rodenticides: short-term effects, recovery and implications for secondary poisoning. J Appl Ecol 42:118–128

Brandt MJ, Lambin X (2007) Movement patterns of a specialist predator, the weasel *Mustela nivalis* exploiting asynchronous cyclic field vole *Microtus agrestis* populations. Acta Theriol (Warsz) 52:13–25

Brooke M, Cuthbert RJ, Harrison G, Gordon C, Taggart MA (2013) Persistence of brodifacoum in cockroach and woodlice: implications for secondary poisoning during rodent eradications. Ecotoxicoly Environ Saf 97:183–188

Brown KP, Alterio N, Moller H (1998) Secondary poisoning of stoats (*Mustela erminea*) at low mouse (*Mus musculus*) abundance in a New Zealand Nothofagus forest. Wildl Res 25:419–426

Buckle AP, Smith RH (2015) Rodent Pests and Their Control, 2nd edn. CABI

Castillo E, Priotto J, Ambrosio AM, Provensal MC, Pini N, Morales MA, Steinmann A, Polop JJ (2003) Commensal and wild rodents in an urban area of Argentina. Int Biodeterior Biodegrad 52:135–141

Cavallari LH, Limdi NA (2009) Warfarin pharmacogenomics. Curr Opin Mol Ther 11:243–251

Cavia R, Cueto GR, Suárez OV (2009) Changes in rodent communities according to the landscape structure in an urban ecosystem. Landsc Urban Plan 90:11–19

Channon D, Cole M, Cole L (2000) A long-term study of *Rattus norvegicus* in the London borough of Enfield using baiting returns as an indicator of sewer population levels. Epidemiol Infect 125:441–445

ChemIDplus (2015) ChemIDplus. A Toxnet Database. https://chem.nlm.nih.gov/chemidplus/name/brodifacoum. Accessed 20 June 2015

ChemIDplus (2017) A Toxnet Database. https://chem.nlm.nih.gov/chemidplus/name/warfarin. Accessed 4 August 2017.

Christensen TK, Lassen P, Elmeros M (2012) High exposure rates of anticoagulant rodenticides in predatory bird species in intensively managed landscapes in Denmark. Arch Environ Contam Toxicol 63:437–444

Coeurdassier M, Poirson C, Paul J-P, Rieffel D, Michelat D, Reymond D, Legay P, Giraudoux P, Scheifler R (2012) The diet of migrant red kites *Milvus milvus* during a water vole *Arvicola terrestris* outbreak in eastern France and the associated risk of secondary poisoning by the rodenticide bromadiolone. Ibis 154:136–146

Coeurdassier M, Riols R, Decors A, Mionnet A, David F, Quintaine T, Truchetet D, Scheifler R, Giraudoux P (2014) Unintentional wildlife poisoning and proposals for sustainable management of rodents. Conserv Biol 28:315–321

Craddock P (2003) Aspects of the ecology of forest invertebrates and the use of brodifacoum. Doctoral dissertation University of Auckland, New Zealand

Dell'Arte GL, Laaksonen T, Norrdahl K, Korpimäki E (2007) Variation in the diet composition of a generalist predator, the red fox, in relation to season and density of main prey. Acta Oecol 31:276–281

Dowding CV, Shore RF, Worgan A, Baker PJ, Harris S (2010) Accumulation of anticoagulant rodenticides in a non-target insectivore, the European hedgehog (*Erinaceus europaeus*). Environ Pollut 158:161–166

Duff IF, Dennis EW, Hodgson PE, Coon EW (1953) Clinical experience with a new indandione derivative; a preliminary report. Med Bull (Ann Arbor) 19:43–48

Eadsforth CV, Dutton AJ, Harrison EG, Vaughan JA (1991) A barn owl feeding study with [^{14}C] flocoumafen-dosed mice – validation of a non-invasive method of monitoring exposure of barn owls to anticoagulant rodenticides in their prey. Pestic Sci 32:105–119

Eason CT, Milne L, Potts M, Morriss G, Wright GRG, Sutherland ORW (1999) Secondary and tertiary poisoning risks associated with brodifacoum. N Z J Ecol 23:219–224

Eason CT, Wright GRG, Milne LM, Morriss GA (2001) Laboratory and field studies of brodifacoum residues in relation to risk of exposure to wildlife and people. Sci Conserv 177:11–23

Eason CT, Murphy EC, Wright GRG, Spurr EB (2002) Assessment of risks of brodifacoum to non-target birds and mammals in New Zealand. Ecotoxicology 11:35–48

Eisemann JD, Swift CE (2006) Ecological and human health hazards from broadcast application of 0.005% diphacinone rodenticide baits in native Hawaiian ecosystems. In: Timm RM, O'Brien JM (eds) Proceedings 22nd of the Vertebrate Pest Conference, Berkeley, 6–9 March 2006. University of California, Davis, pp 413–433

Elliott JE, Hindmarch S, Albert CA, Emery J, Mineau P, Maisonneuve F (2014) Exposure pathways of anticoagulant rodenticides to nontarget wildlife. Environ Monit Assess 186:895–906

Elliott JE, Rattner B, Shore RF, van den Brink N (2016) Paying the pipers: mitigating the impact of anticoagulant rodenticides on predators and scavengers. Bioscience 66:401–407

Elmeros M, Christensen TK, Lassen P (2011) Concentrations of anticoagulant rodenticides in stoats *Mustela erminea* and weasels *Mustela nivalis* from Denmark. Sci Total Environ 409:2373–2378

Erickson W, Urban D (2004) Potential risks of nine rodenticides to birds and nontarget mammals: a comparative approach. EPA P.2004.27 A. Office of Prevention, Pesticides and Toxic Substances, U.S. Environmental Protection Agency, Washington, DC

Figala J (1964) The reproduction and population structure of the black rat, *Rattus rattus* (L.) in the Czechoslovak habitats. Acta Soc Zool Bohemoslov 28:48–67

Fisher PM (2006) Persistence of residual diphacinone concentrations in pig tissues following sublethal exposure. DOC Research & Development Series 249. Department of Conservation, Wellington, p 19

Fisher PM (2009) Residual concentrations and persistence of the anticoagulant rodenticides brodifacoum and diphacinone in fauna. Lincoln University. PhD Thesis. 166 pp

Fletcher DW (2002) Seven-day range-finding oral toxicity study of Ramik Green (0.005% diphacinone) in domestic swine (*Sus scrofa*). Unpublished Genesis Midwest Laboratories Report 203–0023-17, Neillsville, WI, p 38

Fournier-Chambrillon C, Berny PJ, Coiffier O, Barbedienne P, Dassé B, Delas G, Galineau H, Mazet A, Pouzenc P, Rosoux R, Fournier P (2004) Evidence of secondary poisoning of free-ranging riparian mustelids by anticoagulant rodenticides in France: implications for conservation of European mink (*Mustela lutreola*). J Wildl Dis 40:688–695

Gabriel MW, Woods LW, Poppenga R, Sweitzer RA, Thompson C, Matthews SM, Higley JM, Keller SM, Purcell K, Barrett RH, Wengert GM, Sacks BN, Clifford DL (2012) Anticoagulant rodenticides on our public and community lands: spatial distribution of exposure and poisoning of a rare forest carnivore. PLoS One 7:e40163

Geduhn A, Jacob J, Schenke D, Keller B, Kleinschmidt S, Esther A (2015) Relation between intensity of biocide practice and residues of anticoagulant rodenticides in red foxes (*Vulpes vulpes*). PLoS One 10:e0139191

Giraudoux P, Tremollières C, Barbier B, Defaut R, Rieffel D, Bernard N, Lucot É, Berny P (2006) Persistence of bromadiolone anticoagulant rodenticide in *Arvicola terrestris* populations after field control. Environ Res 102:291–298

Godfrey MER (1985) Non-target and secondary poisoning hazards of "second generation" anticoagulants. Acta Zool Fenn 173:209–212

Gómez-Canela C, Barata C, Lacorte S (2014a) Occurrence, elimination, and risk of anticoagulant rodenticides and drugs during wastewater treatment. Environ Sci Pollut Res 21:7194–7203

Gómez-Canela C, Vázquez-Chica A, Lacorte S (2014b) Comprehensive characterization of rodenticides in wastewater by liquid chromatography-tandem mass spectrometry. Anal Bioanal Chem 406:345–358

Gray A, Eadsforth CV, Dutton AJ, Vaughan JA (1994) The toxicity of three second-generation rodenticides to Barn Owls. Pestic Sci 42:179–184

Hafner DJ, Yensen E, Kirkland Jr GL (Compilers and eds) (1998) North American rodents. Status survey and conservation action plan. IUCN, Gland, Switzerland and Cambridge, UK

Hanski I, Korpimäki E (1995) Microtine rodent dynamics in Northern Europe: parameterized models for the predator-prey interaction. Ecology 76:840–850

Hanski I, Hansson L, Henttonen H (1991) Specialist predators, generalist predators, and the microtine rodent cycle. J Anim Ecol 60:353–367

Hanski I, Turchin P, Korpimäki E, Henttonen H (1993) Population oscillations of boreal rodents: regulation by mustelid predators leads to chaos. Nature 364:232–235

Hegdal PL (1985) Primary hazards to game birds associated with the use of ramik brown (diphacinone bait) for controlling voles in orchards. Unpublished Report U02591, Denver Wildlife Research Center, U.S. Fish and Wildlife Service, Denver, CO, p 60

Hegdal PL, Colvin BA (1988) Potential hazard to eastern screech-owls and other raptors of brodifacoum bait used for vole control in orchards. Environ Toxicol Chem 7:245–260

Howard WE, Marsh RE, Cole RE (1970) A diphacinone bait for deer mouse control. J For 68:220–222

Hughes J, Sharp E, Taylor MJ, Melton L, Hartley G (2013) Monitoring agricultural rodenticide use and secondary exposure of raptors in Scotland. Ecotoxicology 22:974–984

Hunter K (1985) High-performance liquid chromatographic strategies for the determination and confirmation of anticoagulant rodenticide residues in animal tissues. J Chromatogr 321:255–272

Ishizuka M, Tanikawa T, Tanaka KD, Heewon M, Okajima F, Sakamoto KQ, Fujita S (2008) Pesticide resistance in wild mammals mechanisms of anticoagulant resistance in wild rodents. J Toxicol Sci 33:283–291

Jacob J, Tradlec E (2010) Rodent outbreaks in Europe: dynamics and damage. In: Singleton GR, Belmain S, Brown P, Hardy B (eds) Rodent outbreaks: ecology and impacts. International Rice Research Institute, Los Baños – Philippines, pp 207–224

Jacquot M, Coeurdassier M, Couval G, Renaude R, Pleydell D, Truchetet D, Raoul F, Giraudoux P (2013) Using long-term monitoring of red fox populations to assess changes in rodent control practices. J Appl Ecol 50:1406–1414

Katz R, Ducci H, Roeschmann W, Toriello L (1954) Clinical experience with dipaxin and with the combined use of prothrombopenic agents. Circulation 10:685–690

Keith JO, Hirata DN, Espy DL, Greiner S, Griffin D (2009) Field evaluation of 0.00025% diphacinone bait for mongoose control in Hawaii. Unpublished Report QA-16, Denver Wildlife Research Center, Denver CO

Knopper LD, Mineau P, Walker LA, Shore RF (2007) Bone density and breaking strength in UK raptors exposed to second generation anticoagulant rodenticides. Bull Environ Contam Toxicol 78:249–251

Korpimaki E, Norrdahl K (1998) Experimental reduction of predators reverses the crash phase of small-rodent cycles. Ecology 79:2448–2455

Korpimäki E, Brown PR, Jacob J, Pech RP (2004) The puzzles of population cycles and outbreaks of small mammals solved? Bioscience 54:1071–1079

Krebs CJ, Myers H (1974) Population Cycles in Small Mammals. Adv Ecol Res 8:267–273

Krieger R (ed) (2010) Hayes' handbook of pesticide toxicology, vol Vol. 1. Academic, Amsterdam

Lambert O, Pouliquen H, Larhantec M, Thorin C, L'Hostis M (2007) Exposure of raptors and waterbirds to anticoagulant rodenticides (difenacoum, bromadiolone, coumatetralyl, coumafen, brodifacoum): epidemiological survey in Loire Atlantique (France). Bull Environ Contam Toxicol 79:91–94

Lazarus RS, Rattner BA, Brooks BW, Du B, McGowan PC, Blazer VS, Ottinger MA (2014) Exposure and food web transfer of pharmaceuticals in ospreys (*Pandion haliaetus*): predictive model and empirical data. Integr Environ Assess Manag 11:118–129

Lemarchand C, Rosoux R, Berny P (2010) Organochlorine pesticides, PCBs, heavy metals and anticoagulant rodenticides in tissues of Eurasian otters (*Lutra lutra*) from upper Loire River catchment (France). Chemosphere 80:1120–1124

López-Perea JJ, Camarero PR, Molina-López RA, Parpal L, Obón E, Solá J, Mateo R (2015) Interspecific and geographical differences in anticoagulant rodenticide residues of predatory wildlife from the Mediterranean region of Spain. Sci Total Environ 511C:259–267

Luque-Larena JJ, Mougeot F, Viñuela J, Jareño D, Arroyo L, Lambin X, Arroyo B (2013) Recent large-scale range expansion and outbreaks of the common vole (*Microtus arvalis*) in NW Spain. Basic Appl Ecol 14:432–441

Marsh RE (1994) Roof rats. In: Hygnstrom SE, Timm RM, Larson GE (eds) The handbook: prevention and control of wildlife damage. Digital Commons@University of Nebraska, Lincoln, pp 125–132

Marti CD (1973) Ten years of barn owl prey data from a Colorado nest site. Wilson Bull 85:85–86

Mayol J, Mcminn M, Rodriguez A, Domenech O, Oliver J (2012) Sa Dragonera, la mayor isla mediterranea (posiblemente) libre de roedores. Quercus 314:27–33

McDonald RA, Harris S, Turnbull G, Brown P, Fletcher M (1998) Anticoagulant rodenticides in stoats (*Mustela erminea*) and weasels (*Mustela nivalis*) in England. Environ Pollut 103:17–23

Mendenhall VM, Pank LF (1980) Secondary poisoning of owls by anticoagulant rodenticides. Wildl Soc Bull 8:311–315

Merson MH, Byers RE, Kaunkeinen DE (1984) Residues of the rodenticide brodifacoum in voles and raptors after orchad treatment. J Wildl Dis 48:212–216

Montaz J, Jacquot M, Coeurdassier M (2014) Scavenging of rodent carcasses following simulated mortality due to field applications of anticoagulant rodenticide. Ecotoxicology 23:1671–1680

Morzillo AT, Mertig AG (2011) Urban resident attitudes toward rodents, rodent control products, and environmental effects. Urban Ecosyst 14:243–260

Mougeot F, Garcia JT, Viñuela J (2011) Breeding biology, behaviour, diet and conservation of the red kite (*Milvus milvus*), with particular emphasis on Mediterranean populations. In: Zuberogoitia I, Martínez JE (eds) Ecology and conservation of European dwelling forest raptors and owls. Editorial Diputación Foral de Vizcaya, Bilbao, pp 190–204

Murphy EC, Clapperton BK, Bradfield PMF, Speed HJ (1998) Brodifacoum residues in target and non-target animals following large-scale poison operations in New Zealand podocarp-hardwood forests. New Zeal J Zool 25:307–314

Murray M (2011) Anticoagulant rodenticide exposure and toxicosis in four species of birds of prey presented to a wildlife clinic in Massachusetts, 2006-2010. J Zoo Wildl Med 42:88–97

Naim M, Noor HM, Kasim A, Abu J (2011) Comparison of the breeding performance of the barn owl *Tyto alba javanica* under chemical and bio-based rodenticide baiting in immature oil palms in Malaysia. Dyn Biochem Process Biotechnol Mol Biol 5:5–11

Newton I, Wyllie I, Freestone P (1990) Rodenticides in British barn owls. Environ Pollut 68:101–117

Newton I, Wyllie I, Gray A, Eadsforth CV (1994) The toxicity of the rodenticide flocoumafen to barn owls and its elimination via pellets. Pestic Sci 41:187–193

Nogeire TM, Lawler JJ, Schumaker NH, Cypher BL, Phillips SE (2015) Land use as a driver of patterns of rodenticide exposure in modeled Kit Fox populations. PLoS One 10(8):e0133351

Ogilvie SC, Pierce RJ, Wright GRG, Booth LH, Eason CT (1997) Brodifacoum residue analysis in water, soil, invertebrates, and birds after rat eradication on Lady Alice Island. N Z J Ecol 21:195–197

Olea PP, Sánchez-Barbudo IS, Viñuela J, Barja I, Mateo-Tomás P, Piñeiro A, Mateo R, Purroy FJ (2009) Lack of scientific evidence and precautionary principle in massive release of rodenticides threatens biodiversity: old lessons need new reflections. Environ Conserv 36:1–4

Pitt WC, Eisemann JD, Swift CE, Sugihara R, Dengler-Germain B, Driscoll L (2005) Diphacinone residues in free-ranging wild pigs following aerial broadcast of a rodenticide bait in a Hawaiian forest. Unpublished Report QA-1077. National Wildlife Research Center, Fort Collins, p 35

Pitt WC, Higashi M, Primus TM (2011) The effect of cooking on diphacinone residues related to human consumption of feral pig tissues. Food Chem Toxicol 49:2030–2034

Pocock MJO, Searle JB, White PCL (2004) Adaptations of animals to commensal habitats: population dynamics of house mice *Mus musculus domesticus* on farms. J Anim Ecol 73:878–888

Proulx G, Mackenzie N (2012) Relative abundance of american badger (*Taxidea taxus*) and red fox (*Vulpes vulpes*) in landscapes with high and low rodenticide poisoning levels. Integr Zool 7:41–47

Radvanyi A, Weaver P, Massari C, Bird D, Broughtont E (1988) Effects of chlorophacinone on captive kestrels. Bull Environ Contam Toxicol 41:441–448

Rammell CG, Hoogenboom JJL, Cotter M, Williams JM, Bell J (1984) Brodifacoum residues in target and non-target animals following rabbit poisoning trials. New Zeal J Exp Agric 12:107–111

Rattner BA, Horak KE, Warner SE, Day DD, Johnston JJ (2010) Comparative toxicity of Diphacinone to Northern Bobwhite (*Colinus virginianus*) and American Kestrels (*Falco sparverius*). In: Timm RM, Fagerstone KA (eds) Proceedings 24th of the Vertebrate Pest Conference, Sacramento 22–25 February 2010. University of California, Davis, pp 146–152

Rattner BA, Horak KE, Warner SE, Day DD, Meteyer CU, Volker SF, Eisemann JD, Johnston JJ (2011) Acute toxicity, histopathology, and coagulopathy in American kestrels (*Falco sparverius*) following administration of the rodenticide diphacinone. Environ Toxicol Chem 30:1213–1222

Rattner BA, Horak KE, Lazarus RS, Eisenreich KM, Meteyer CU, Volker SF, Campton CM, Eisemann JD, Johnston JJ (2012) Assessment of toxicity and potential risk of the anticoagulant rodenticide diphacinone using Eastern screech-owls (*Megascops asio*). Ecotoxicology 21:832–846

Rattner BA, Horak KE, Lazarus RS, Goldade DA, Johnston JJ (2014a) Toxicokinetics and coagulopathy threshold of the rodenticide diphacinone in eastern screech-owls (*Megascops asio*). Environ Toxicol Chem 33:74–81

Rattner BA, Lazarus RS, Elliott JE, Shore RF, Van Den Brink N (2014b) Adverse outcome pathway and risks of anticoagulant rodenticides to predatory wildlife. Environ Sci Technol 48:8433–8445

Rattner BA, Horak KE, Lazarus RS, Schultz SL, Knowles S, Abbo BG, Volker SF (2015) Toxicity reference values for chlorophacinone and their application for assessing anticoagulant rodenticide risk to raptors. Ecotoxicology 24:720–734

Redpath SM, Thirgood SJ (1999) Numerical and functional responses in generalist predators: hen harriers and peregrines on Scottish grouse moors. J Anim Ecol 68:879–892

Riley SPD, Bromley C, Poppenga RH, Uzal FA, Whited L, Sauvajot RM (2007) Anticoagulant exposure and notoedric mange in bobcats and mountain lions in urban Southern California. J Wildl Manag 71:1874–1884

Ruder MG, Poppenga RH, Bryan JA, Bain M, Pitman J, Keel MK (2011) Intoxication of nontarget wildlife with rodenticides in northwestern Kansas. J Wildl Dis 47:212–216

Ruiz-Suárez N, Henríquez-Hernández LA, Valerón PF, Boada LD, Zumbado M, Camacho M, Almeida-González M, Luzardo OP (2014) Assessment of anticoagulant rodenticide exposure in six raptor species from the Canary Islands (Spain). Sci Total Environ 485–486:371–376

Sage M (2008) Transfert de bromadiolone (appâts/sols – campagnols de prairie – renards): Etude environnementale de la persistance et mesure indirecte de l'exposition. Universite de Franche-Comte. U.F.R. Des Sciences et Techniques. These Docteur, 227 pp

Sage M, Coeurdassier M, Defaut R, Lucot E, Barbier B, Rieffel D, Berny P, Giraudoux P (2007) How environment and vole behaviour may impact rodenticide bromadiolone persistence in wheat baits after field controls of *Arvicola terrestris*? Environ Pollut 148:372–379

Sage M, Coeurdassier M, Defaut R, Gimbert F, Berny P, Giraudoux P (2008) Kinetics of bromadiolone in rodent populations and implications for predators after field control of the water vole, *Arvicola terrestris*. Sci Total Environ 407:211–222

Sage M, Fourel I, Cœurdassier M, Barrat J, Berny P, Giraudoux P (2010) Determination of bromadiolone residues in fox faeces by LC/ESI-MS in relationship with toxicological data and clinical signs after repeated exposure. Environ Res 110:664–674

Salim H, Noor HM, Hamid NH, Omar D, Kasim A, Abidin CMRZ (2014) Secondary poisoning of captive barn owls, *Tyto alba javanica* through feeding with rats poisoned with chlorophacinone and bromadiolone. J Oil Palm Res 26:6272

Sánchez-Barbudo IS, Camarero PR, Mateo R (2012) Primary and secondary poisoning by anticoagulant rodenticides of non-target animals in Spain. Sci Total Environ 420:280–288

Sarabia J, Sánchez-Barbudo IS, Siqueira W, Mateo R, Rollán E, Pizarro M (2008) Lesions associated with the plexus venosus subcutaneus collaris of pigeons with chlorophacinone toxicosis. Avian Dis 52:540–543

Saravanan K, Kanakasabai R (2004) Evaluation of secondary poisoning of difethialone, a new second-generation anticoagulant rodenticide to barn owl, *Tyto alba* Hartert under captivity. Indian J Exp Biol 42:1013–1016

Savarie PJ, Hayes DJ, McBride RT, Roberts JD (1979) Efficacy and safety of diphacinone as a predacide. Avian Mamm Wildl Toxicol 693:69–79

Shore RF, Birks JDS, Freestone P, Kitchener AC (1996) Second-generation rodenticides and polecats (*Mustela putorius*) in Britain. Environ Pollut 91:279–282

Shore RF, Birks JDS, Freestone P (1999) Exposure of non-target vertebrates to second-generation rodenticides in Britain, with particular reference to the polecat *Mustela putorius*. N Z J Ecol 23:199–206

Shore RF, Birks JDS, Afsar A, Wienburg CL, Kitchener AC (2003) Spatial and temporal analysis of second-generation anticoagulant rodenticide residues in polecats (*Mustela putorius*) from throughout their range in Britain, 1992-1999. Environ Pollut 122:183–193

Shore RF, Malcolm HM, Wienburg CL, Walker LA, Turk A, Horne JA (2005) Wildlife and pollution: 2001/2002 – Annual Report. Joint Nature Conservation Committee Report 352. Peterborough, UK

Shore RF, Malcolm HM, Mclennan D, Turk A, Walker LA, Wienburg CL, Burn AJ (2006) Did foot-and-mouth disease-control operations affect rodenticide exposure in raptors? J Wildl Manag 70:588–593

Singleton GR, Krebs CJ, Davis S, Chambers L, Brown P (2001) Reproductive changes in fluctuating house mouse populations in southeastern Australia. Proc R Soc London/Biol Sci 268:1741–1748

Singleton GR, Hinds LA, Krebs CJ, Spratt DM (eds) (2003) Rats, mice and people: rodent biology and management. ACIAR Monograph No. 96, Canberra – Australia, p 564

Singleton GR, Belmain S, Brown P, Hardy B (eds) (2010) Rodent outbreaks: ecology and impacts. International Rice Research Institute, Los Baños – Philippines, p 286

Spurr EB, Foote D, Perry CF, Lindsey GD (2003a) Efficacy of aerial broadcast application of baits containing 0.005% diphacinone in reducing rat populations in Hawaiian forests. Pacific Islands Ecosystems Research Center, U.S.Geological Survey, Unpublished Report QA-02. Washington, DC

Spurr EB, Lindsey GD, Forbes PC, Foote D (2003b) Effectiveness of hand broadcast application of baits containing 0.005% diphacinone in reducing rat populations in Hawaiian forests. Pacific Island Ecosystems Research Center. US Geological Survey, Unpublished Report QA-01. Washington, DC

Spurr EB, Maitland MJ, Taylor GE, Wright GRG, Radford CD, Brown LE (2005) Residues of brodifacoum and other anticoagulant pesticides in target and non-target species, Nelson Lakes National Park, New Zealand. New Zeal J Zool 32:237–249

Stansley W, Cummings M, Vudathala D, Murphy LA (2014) Anticoagulant rodenticides in red-tailed hawks, *Buteo jamaicensis*, and great horned owls, *Bubo virginianus*, from New Jersey, USA, 2008-2010. Bull Environ Contam Toxicol 92:6–9

Stenseth NC, Leirs H, Skonhoft A, Davis SA, Pech RP, Andreassen HP, Singleton GR, Lima M, Machang'u RS, Makundi RH, Zhang Z, Brown PR, Shi D, Wan X (2003) Mice, rats, and people: the bio-economics of agricultural rodent pests. Front Ecol Environ 1:367–375

Stone WB, Okoniewski JC, Stedelin JR (1999) Poisoning of wildlife with anticoagulant rodenticides in New York. J Wildl Dis 35:187–193

Stone WB, Okoniewski JC, Stedelin JR (2003) Anticoagulant rodenticides and raptors: recent findings from New York, 1998-2001. Bull Environ Contam Toxicol 70:34–40

Terraube J, Arroyo B, Madders M, Mougeot F (2011) Diet specialisation and foraging efficiency under fluctuating vole abundance: A comparison between generalist and specialist avian predators. Oikos 120:234–244

Thomas PJ, Mineau P, Shore RF, Champoux L, Martin PA, Wilson LK, Fitzgerald G, Elliott JE (2011) Second generation anticoagulant rodenticides in predatory birds: Probabilistic characterisation of toxic liver concentrations and implications for predatory bird populations in Canada. Environ Int 37:914–920

Tosh DG, McDonald RA, Bearhop S, Llewellyn NR, Fee S, Sharp EA, Barnett EA, Shore RF (2011a) Does small mammal prey guild affect the exposure of predators to anticoagulant rodenticides? Environ Pollut 159:3106–3112

Tosh DG, Shore RF, Jess S, Withers A, Bearhop S, Montgomery IW, McDonald RA (2011b) User behaviour, best practice and the risks of non-target exposure associated with anticoagulant rodenticide use. J Environ Manag 92:1503–1508

Tosh DG, McDonald RA, Bearhop S, Llewellyn NR, Montgomery WI, Shore RF (2012) Rodenticide exposure in wood mouse and house mouse populations on farms and potential secondary risk to predators. Ecotoxicology 21:1325–1332

Valchev I, Binev R, Yordanova V, Nikolov Y (2008) Anticoagulant rodenticide intoxication in animals – a review. Turkish J Vet Anim Sci 32:237–243

Vandenbroucke V, Bousquet-Melou A, De Backer P, Croubels S (2008) Pharmacokinetics of eight anticoagulant rodenticides in mice after single oral administration. J Vet Pharmacol Ther 31:437–445

Vidal D, Alzaga V, Luque-Larena JJ, Mateo R, Arroyo L, Viñuela J (2009) Possible interaction between a rodenticide treatment and a pathogen in common vole (*Microtus arvalis*) during a population peak. Sci Total Environ 408:267–271

Viñuela J, Villafuerte R, Blanco JC (1999) Incremento de la persecución de depredadores en España: sus causas y su efecto sobre el milano real. In: Viñuela J, Martí R, Ruiz A (eds) El milano Real en España. SEO/BirdLife, Madrid, Spain, pp 199–211

Walker LA, Shore RF, Turk A, Pereira MG, Best J (2008a) The predatory bird monitoring scheme: identifying chemical risks to top predators in Britain. J Hum Environ 37:466–471

Walker LA, Turk A, Long SM, Wienburg CL, Best J, Shore RF (2008b) Second generation anticoagulant rodenticides in tawny owls (*Strix aluco*) from Great Britain. Sci Total Environ 392:93–98

Walker LA, Chaplow JS, Moeckel C, Pereira MG, Potter ED, Shore RF (2014) Anticoagulant rodenticides in predatory birds 2012: a Predatory Bird Monitoring Scheme (PBMS) report. Centre for Ecology & Hydrology, Lancaster. 18 pp. http://pbms.ceh.ac.uk/sites/pbms.ceh.ac.uk/files/PBMS%20Report%20Rodentocide%202012.pdf

Watt BE, Proudfoot AT, Bradberry SM, Vale JA (2005) Anticoagulant rodenticides. Toxicol Rev 24:259–269

Weber P (2001) Vitamin K and bone health. Nutrition 17:880–887

Welling PG, Lee KP, Khanna U, Wagner JG (1970) Comparison of plasma concentrations of warfarin measured by both simple extraction and TLC methods. J Pharm Sci 59:1621–1625

Willis P, Macris J, Denis E, Hodgson P, Coon W, Gamble J, Duff I (1953) Clinical evaluation of dipaxin, an oral anticoagulant. J Lab Clin Med 52:968–968

Wilson DE, Reeder DM (eds) (2005) Mammal species of the world: a taxonomic and geographic reference, vol Vol. 12. JHU Press, Baltimore

Winters AM, Rumbeiha WK, Winterstein SR et al (2010) Residues in Brandt's voles (*Microtus brandti*) exposed to bromadiolone-impregnated baits in Mongolia. Ecotoxicol Environ Saf 73:1071–1077

Witmer GW (2007) The ecology of vertebrate pests and integrated pest management (IPM). In: Kogan M, Jepson P (eds) Perspectives in ecological theory and integrated pest management. Cambridge University Press, Cambridge, UK, pp 393–410

Zamorano E, Palomo L, Vargas J (1988) La rata negra (*Rattus rattus* Linneo, 1758) como plaga de los cultivos ibéricos de caña de azúcar. Detección, estima y control de los daños ocasionados. Boletín Sanid Veg Plagas 14:227–240