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(Article begins on next page)

# 1 **Plants and zootoxins: toxico-epidemiological investigation in domestic animals**

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5

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14

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16

## 17 **Abstract**

18 An epidemiological study on animal poisoning due to plants and zootoxins has been carried  
19 out by the Poison Control Centre of Milan (CAV) in collaboration with the University of

20 Milan (Italy). During the period January 2015 - March 2019, the CAV received 932 calls on  
21 animal poisonings, 12.66% (n = 118) of which were related to plants and zootoxins. Among  
22 these, 95 enquiries (80.51%) concerned exposures to plants and 23 (19.49%) to zootoxins.

23 The dog was the species most frequently involved (67.80% of the calls, n = 80), followed by  
24 the cat (26.27%, n = 31). As for the plants, several poisoning episodes were related to  
25 glycoside-, alkaloid-, oxalate- and diterpenoid-containing species. *Cycas revoluta*, *Euphorbia*  
26 *pulcherrima* and *Hydrangea macrophylla* were the most often reported plants. The outcome  
27 has been reported for half of the episodes (51.58%, n = 49) and it was fatal for 3 animals  
28 (6.12%).

29 Regarding the zootoxins, the majority of the enquiries were related to viper (*Vipera aspis*),  
30 but exposures to pine processionary (*Thaumetopoea pityocampa*), common toad (*Bufo*  
31 *bufo*), salamander (*Salamandra salamandra*), and jellyfish (phylum Cnidaria) were also  
32 reported. The outcome was known in 65.22% of the cases with just one fatal episode.

33 This epidemiological investigation depicts an interesting overview on the issue of plant and  
34 zootoxin exposures in domestic animals, highlighting the relevance of these agents as  
35 causes of animal poisoning and providing useful information for prevention and diagnosis.

36

37 **Keywords (max 6):** domestic animals; exposure; plants; zootoxins; toxico-epidemiology

38

### 39 **1. Introduction**

40 In Europe, even if the number of toxic plants, containing phytotoxins belonging to different  
41 chemical classes (*i.e.* alkaloids, glycosides, proteins, etc.)(Welch, 2019), is not comparable to  
42 that of the American and African continent, dangerous species are not lacking (Anadón et  
43 al., 2018), and neither are zootoxins, produced by poisonous/venomous animals for food  
44 procurement and as a defense technique (Gwaltney-Brant et al., 2018).

45 Thus, domestic animal poisoning due to the exposure to plants and zootoxins is not a rare  
46 occurrence but a recognized and well-documented issue of great interest for its scientific  
47 significance and animal health impact (Anadón et al., 2018; Caloni et al., 2018; Gwaltney-  
48 Brant et al., 2018).

49 Even more than 10% of the calls on animal poisoning received by European poison centers  
50 are related to plant exposures (Barbier, 2005; Campbell, 1998; Cortinovic and Caloni, 2013;  
51 Keck et al., 2004; McFarland et al., 2017), while zootoxins are generally responsible for a  
52 lower (2-5%) but not negligible number of cases (Barbier, 2005; Caloni et al., 2012; Lassak,  
53 2005). Moreover, new toxico-epidemiological trends in plant and zootoxin poisonings are  
54 likely to surface, facilitated by the current global trade in ornamental plants and exotic pets  
55 (Elwin et al., 2020; Schaper et al., 2019) and the ongoing climate change that may influence  
56 the geographical distribution of poisonous/venomous terrestrial and aquatic animal species  
57 (Needleman et al., 2018a; Needleman et al., 2018b).

58 The aim of the paper is to depict an insight on plant and zootoxin exposures in domestic  
59 animals, providing data regarding the causative agents, incidences and emerging trends,  
60 species involved, route of exposure, clinical presentation and outcome.

61

### 62 **2. Material and methods**

63 The Poison Control Center of Milan (CAV), which has been operating since 1967, deals with  
64 and analyses cases on suspect animal poisonings and since 1990, collaborates with  
65 toxicologists of the University of Milan (Caloni et al., 2012).

66 After each toxicological consultation, the normal procedure requires to fill in a form,  
67 specifically intended for the data collection, with information on the species/breed,  
68 suspected poisoning agent, route of exposure and clinical signs. These data are stored in a  
69 database that is continuously updated, also by means of follow-up calls to determine the  
70 final outcome.

71 All the cases of suspected animal poisoning collected by CAV from January 2015 to March  
72 2019 have been reviewed in order to select the episodes related to plant and zootoxin  
73 exposures. Using these data, a toxicological analysis has been performed on the bases of  
74 animal species and plants/zootoxins implicated, site of exposure (indoor/outdoor and  
75 location), route of exposure, clinical signs and final outcome. In the case of plant poisoning  
76 episodes, all the plants were classified according to their toxic principles to verify the  
77 correspondence with the observed clinical signs.

78

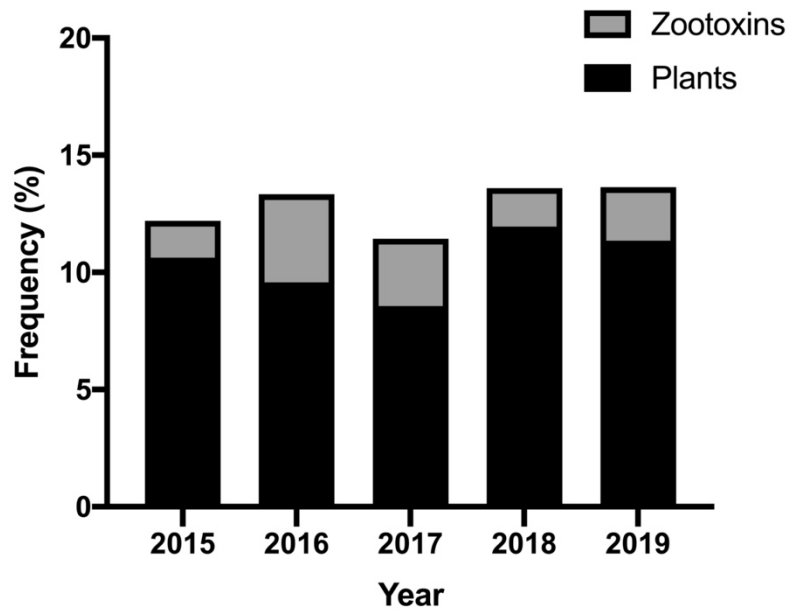
### 79 **2.1. Statistical analysis**

80 Data analysis was performed with IBM SPSS Statistics for Mac, Version 26.0 (Armonk, NY:  
81 IBM Corp.), while graphs were created using Prism for Mac, Version 9 (GraphPad Software  
82 Inc., La Jolla, CA, USA).

83

### 84 **3. Results**

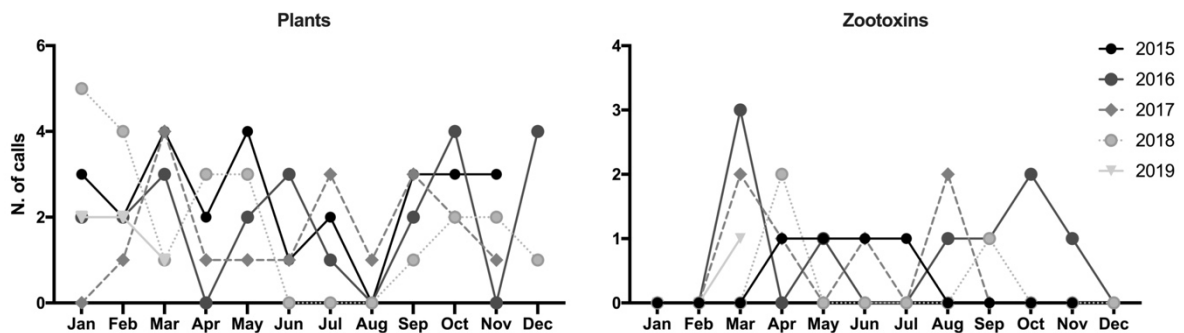
85 During the period from January 2015 to March 2019, the Poison Control Center of Milan  
86 (CAV) received 932 enquiries on animal poisonings, 12.66% (n = 118) of which were related  
87 to plants and zootoxins. Among these, 95 enquiries (80.51%) concerned exposures to plants  
88 and 23 (19.49%) to zootoxins. The frequency of calls on plant- and zootoxin-related animal  
89 poisonings over the years is depicted in Figure 1, while Figure 2 reports the monthly  
90 distribution. The majority of the requests were toxicological enquiries from veterinarians (n  
91 = 93; 78.81%), while 23 calls (19.49%) were from animal owners and in 2 cases (1.70%) the  
92 caller was unknown.



93

94 Figure 1. Frequency of domestic animal exposure (per cent) to plants and zootoxins over the  
 95 years, based on the calls received by CAV from January 2015 to March 2019.

96



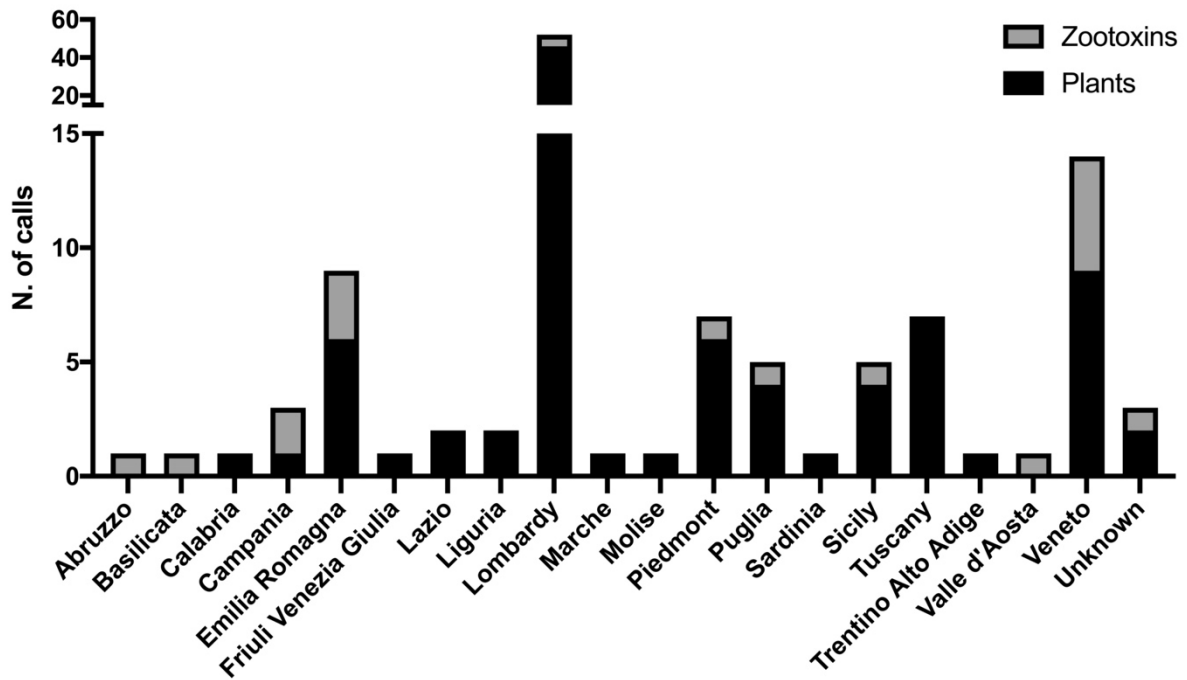
97

98 Figure 2. Monthly distribution of the calls related to plants and zootoxins, received by CAV  
 99 from January 2015 to March 2019.

100

101 As for the geographical origin, most of the enquiries were from Lombardy (n = 52; 44.07%),  
 102 followed by Veneto (n = 14; 11.86%), Emilia Romagna (n = 9; 7.63%), Piedmont (n = 7;  
 103 5.93%) and Tuscany (n = 7; 5.93%) (Figure 3).

104



105

106 Figure 3. Geographical distribution of the calls related to animal poisoning by plants and  
 107 zootoxins received by the Poison Control Centre of Milan (CAV) during the period January  
 108 2015 - March 2019

109

110 In total, 46.61% of the exposures to plants and zootoxins occurred indoor (n = 55) and  
 111 47.46% outdoor (n = 56), while for 7 episodes the site was unknown (5.93%).

112 In particular, plant poisonings occurred indoor in 50 cases (52.63%), outdoor in 38 cases  
 113 (40.00%) and for 7 episodes (7.37%) this information was not available. As for the zootoxins,  
 114 5 exposures happened indoor (21.74%) and 18 (78.26%) outdoor (Figure 4).

115



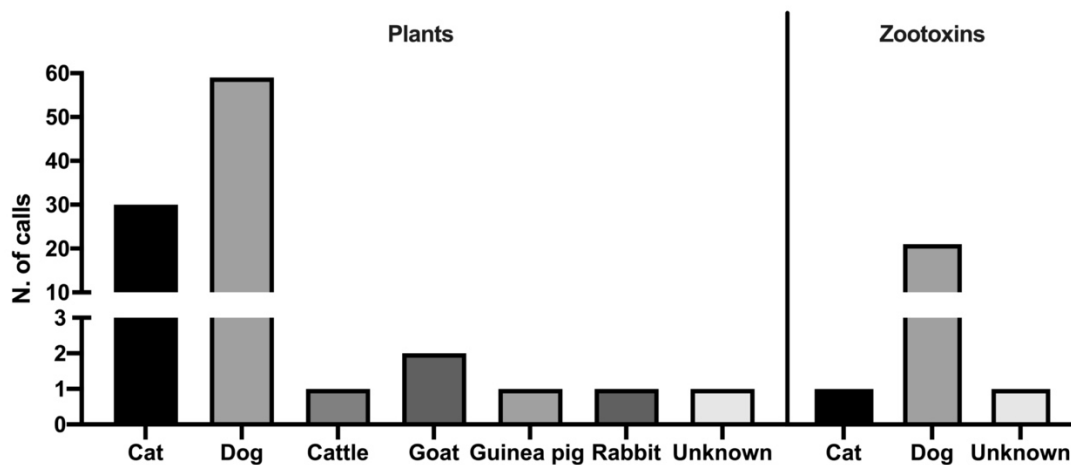
116

117 Figure 4. Site of exposure to plants and zootoxins according to the calls received by the  
 118 Poison Control Centre of Milan (CAV) during the period January 2015 - March 2019.

119

120 The species most frequently involved was the dog (67.80% of the calls, n = 80), followed by  
 121 the cat (26.27%, n = 31). Two episodes concerned goats (1.69%) and single cases were  
 122 reported to involve cattle, a guinea pig and a rabbit (0.85% each) (Figure 5).

123



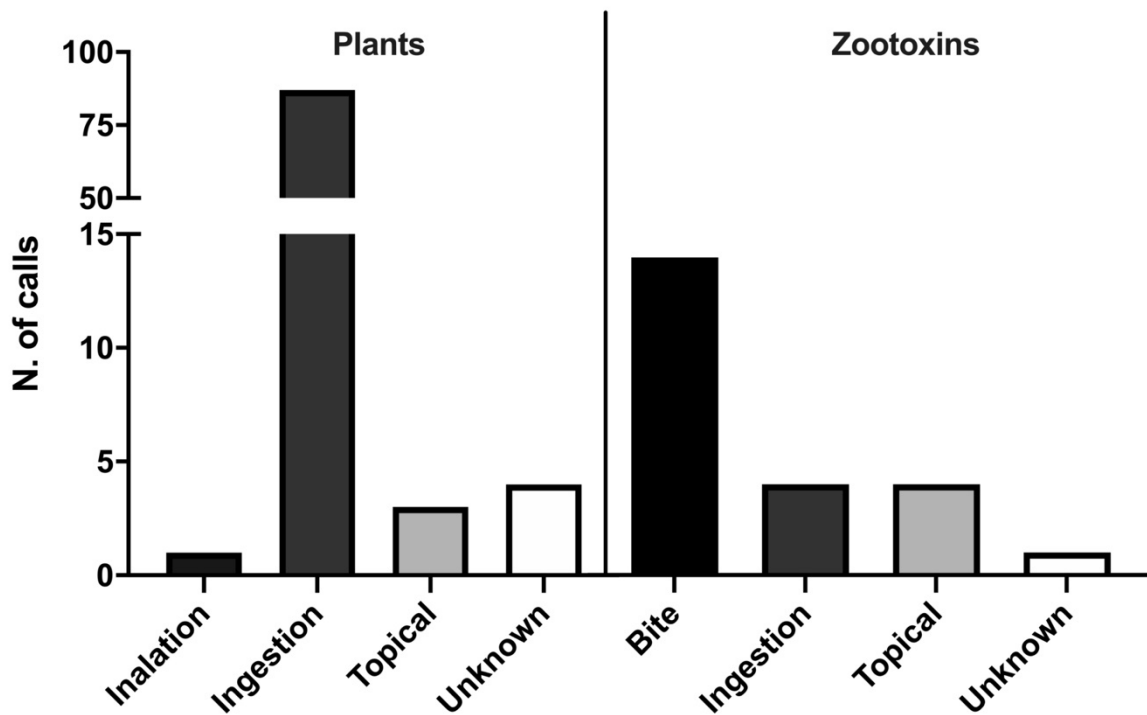
124

125 Figure 5. Species involved in suspected poisonings by plants and zootoxins based on the  
 126 calls received by the Poison Control Centre of Milan (CAV) during the period January 2015 -  
 127 March 2019.

128

129 Ingestion was the most common route of exposure (77.12% of the poisoning episodes, n =  
 130 91), followed by injection (snake bites; 11.86%, n = 14) but also inhalation (0.85%, n = 1) and  
 131 topical (5.93%, n = 7) exposures were reported (Figure 6).

132



133

134 Figure 6. Routes of exposure to plants and zootoxins reported to the Poison Control Centre  
 135 of Milan (CAV) during the period January 2015 - March 2019.

136

137 One-hundred and ten poisoning episodes resulted from single exposures (93.22%), 4 cases  
 138 were due to repeated exposures (3.39%, all plant-related poisonings) and for 4 cases the  
 139 frequency was unknown (3.39%, all involving plants).

140

### 141 3.1 Involved plants

142 The involved plants are listed in Table 1. Among them, know toxic species can be found,  
 143 together with plants which are not reported in literature as related to poisoning episodes in  
 144 animals (*Arbutus unedo*, *Camellia japonica*, *Chlorophytum comosum*, *Jasminum officinale*,  
 145 *Juglans regia*, *Maclura pomifera*, Fam. Orchidaceae, *Saintpaulia spp.*).

146

Scientific name	Common name	Toxins	Poisoned animals
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<i>Acacia dealbata</i>	Mimosa	Cyanogenic glycosides	3 cats
<i>Aesculus hippocastanum</i>	Horse chestnut (conkers)	Aesculin (glycosidic saponin) and other saponins.	2 dogs
<i>Aloe vera</i>	Aloe vera	Saponins, anthraquinones	1 cat
<i>Anemone spp.</i>	Anemone	Protoanemonin	1 dog
<i>Anthurium spp.</i>	Flamingo flower	Insoluble calcium oxalates	3 cats, 1 dog
<i>Arbutus unedo</i>	Strawberry tree	Non-toxic	2 dogs
<i>Arum spp.</i>	Arum	Calcium oxalate, proteolytic enzyme	2 dogs
<i>Atropa belladonna</i>	Deadly nightshade	Tropane alkaloids (atropine, scopolamine, and hyoscyamine)	1 dog
<i>Aucuba japonica</i>	Japanese laurel	Iridoid glycoside aucubin	1 cat
<i>Buxus sempervirens</i>	Common box	Alkaloids	1 dog
<i>Camellia japonica</i>	Camellia	Non-toxic	1 dog
<i>Capsicum annuum</i>	Chili pepper	Capsaicin, capsaicinoids	1 dog
<i>Chlorophytum comosum</i>	Spider plant	Non-toxic	1 dog
<i>Cinnamomum camphora</i>	Camphor tree	Camphor	1 dog
<i>Clivia spp.</i>	Clivia	Lycorine and other alkaloids	1 cat
<i>Cycas revoluta</i>	Sago palm	Azoglycosides (cycasin, macrozamin, and neocycasin); $\beta$ -N-methylamino-L-alanine; unidentified high-molecular-weight compound	9 dogs
<i>Dianthus spp.</i>	Carnation	Triterpenoid saponins	1 dog
<i>Dracaena marginata</i>	Red-margined dracaena	Steroidal saponins and glycosides	1 cat
<i>Euphorbia pulcherrima</i>	Poinsettia	Diterpenoid euphorbol esters and steroids	1 cat, 5 dogs, 1 Guinea pig, 1 rabbit
<i>Ficus benjamina</i>	Weeping fig	Proteases (ficin, and ficusin)	1 cat
<i>Hedera helix</i>	English ivy	Triterpenoid saponins (hederagenin)	1 dog
<i>Hedera helix hibernica</i>	Irish ivy	Triterpenoid saponins (hederagenin)	1 dog
<i>Helleborus niger</i>	Christmas rose	Cardiac glycosides, saponins, protoanemonin	1 cat
<i>Hyacinthus orientalis</i>	Hyacinth	Alkaloids ( <i>i.e.</i> , lycorine) and insoluble calcium oxalates	1 dog
<i>Hydrangea macrophylla</i>	Bigleaf hydrangea	Cyanogenic glycoside (hydrangin)	7 dogs
<i>Jasminum officinale</i>	Jasmine	Non-toxic	1 cat, 1 dog

<i>Juglans regia</i>	English walnut (husks)	Non-toxic	3 dogs
<i>Lantana camara</i>	Lantana	Pentacyclic triterpenoids	1 dog
<i>Lilium spp.</i>	Lily	Steroidal glycoalkaloids and steroidal saponins	2 cats, 1 dog
<i>Maclura pomifera</i>	Osage orange	Non-toxic	1 dog
<i>Mespilus germanica</i>	Medlar (fruits)	Cyanogenic glycosides, hydrocyanic acid	1 dog
<i>Nandina domestica</i>	Heavenly bamboo	Cyanogenic glycosides; protoberberine and berberine alkaloids	1 cat, 1 dog
<i>Narcissus spp.</i>	Daffodil	Lycorine and other alkaloids; insoluble calcium oxalates	2 cats, 1 dog
<i>Nerium oleander</i>	Oleander	Cardiac glycosides: oleandrin, oleandrogenin; neroside and oleandroside	1 cat, 1 cow, 2 dogs
Orchidaceae (Fam.)	Orchid	Non-toxic	1 dog
<i>Pelargonium spp.</i>	Geranium	Monoterpene alcohols: geraniol, linalool	1 cat
<i>Persea americana</i>	Avocado	Persin (long-chain fatty alcohol)	1 cat
<i>Phytolacca americana</i>	Pokeweed	Saponins (phytolaccosides), alkaloids, insoluble calcium oxalates, other compounds (histamine, potassium salts)	1 dog
<i>Primula spp.</i>	Primrose	triterpene saponins; quinones (primin and related hydro-quinones); phenolic derivatives (resorcinol, saligenin); alcoholic glycosides; (salicin, salicilin derivatives); lactones	1 cat, 1 unknown
<i>Prunus domestica</i>	Plum (fruits)	Cyanogenic glycosides	1 dog
<i>Prunus laurocerasus</i>	Cherry laurel	Cyanogenic glycosides amygdalin and prunasin	1 dog, 2 goats
<i>Pteridium aquilinum</i>	Eagle fern	Norsesquiterpene glycoside ptaquiloside; thiaminase	1 cat
<i>Ranunculus spp.</i>	Buttercup	Protoanemonin	2 cats
<i>Ricinus communis</i>	Castor bean	Phytotoxalbumin ricin; piperidine alkaloid ricinine	1 dog
<i>Saintpaulia spp.</i>	African violet	Non-toxic	1 cat
<i>Senecio vulgaris</i>	Groundsel	Pyrrolizidine alkaloids	1 cat
<i>Solanum pseudocapsicum</i>	Winter cherry	Solanine, solanocapsine and other alkaloids	1 dog
<i>Spathiphyllum spp.</i>	Peace lily	Insoluble calcium oxalates	1 dog
<i>Taxus baccata</i>	European yew (flowers and berries)	Taxine alkaloids, cyanogenic glycosides and irritant oils	1 cat

<i>Viscum album</i>	Mistletoe	Viscotoxins, toxic alkaloids and lectins	1 dog
<i>Zantedeschia aethiopica</i>	Calla lily	Insoluble calcium oxalates and proteolytic enzymes	1 cat

147

148 Table 1. Plants involved in animal poisoning episodes, based on the calls received by CAV  
 149 during the period January 2015 - March 2019.

150

### 151 3.1.2 Clinical signs and outcome

152 In the majority of the cases, symptoms started within few hours of ingestion, but in some  
 153 animals the symptom onset occurred after days from the exposure. The most frequently  
 154 reported clinical signs due to plant exposures were gastrointestinal (mainly vomiting and  
 155 sialorrhoea but also diarrhea/melena), neurological (in particular asthenia and ataxia but also  
 156 mydriasis, agitation, hallucinations, convulsions and hypertonia) and cardiorespiratory  
 157 (arrhythmias, bradycardia, hypotension and dyspnea).

158 The outcome has been reported only for half of the episodes (51.58%, n = 49) and it was  
 159 positive for 46 animals (93.88%) and fatal for 3 animals (6.12%). The fatal episodes were  
 160 related to the ingestion of *Capsicum annuum* (a dog), *Nerium oleander* (a dog) and *Prunus*  
 161 *laurocerasus* (a goat).

162

### 163 3.2 Involved zootoxins

164 The zootoxins involved in episodes of animal poisoning reported to CAV are indicated in  
 165 Table 2.

166

Scientific name	Common name	Poisoned animals
<i>Bufo bufo</i>	Common toad	3 dogs
Cnidaria (phylum)	Jellyfish	2 dogs
<i>Thaumetopoea pityocampa</i>	Pine processionary	1 dog, 1 unknown
<i>Salamandra salamandra</i>	Salamander	2 dogs
<i>Vipera aspis</i>	Viper	1 cat, 13 dogs

167 Table 2. Zootoxins involved in animal poisoning episodes, based on the calls received by CAV  
 168 during the period January 2015 - March 2019.

169

### 170 3.2.2 Clinical signs and outcome

171 In all the reported cases, symptoms started within 24h of exposure. Neurological (tremors,  
172 convulsions, asthenia and ataxia) and cardiorespiratory (arrhythmias, bradycardia,  
173 hypotension and dyspnea) signs were the most frequently described, together with local  
174 manifestations depending on the affected part (sialorrhea, edema, hyperemia and pain).  
175 The outcome was positive for 14 animals (60.87%), fatal for 1 animal (4.35%) and unknown  
176 in 8 cases (34.78%). In particular, the only fatal poisoning was related to the ingestion of  
177 larval forms of *Thaumetopoea pityocampa* by a dog.

178

#### 179 **4. Discussion**

180 The data collected in this study emphasizes the not negligible impact of plants and zootoxins  
181 on animal poisoning, categories that are often wrongly regarded as minor agents of  
182 intoxication.

183 During this period, 12.66% (n = 118) of the total calls received by the Poison Control Center  
184 of Milan (CAV) were related to plants (95 enquiries, 10.19% of the total enquiries of the  
185 period) and zootoxins (n = 23, 2.47%).

186 As for the monthly distribution of the enquiries, peaks have been observed at the beginning  
187 of the year and in spring (Figure 2), trends that are similar to those reported in the  
188 European literature (Anadón et al., 2018).

189 Regarding the plants, around half of the exposures occurred indoor (52.63%) and were  
190 related to houseplants (*i.e.*, *Dracaena marginata*, *Euphorbia pulcherrima*, *Spathiphyllum*  
191 *spp.*, *Zantedeschia aethiopica*, etc.). Glycoside-containing species were responsible for a  
192 considerable number of poisoning episodes in dogs. Among them, several cases have been  
193 associated to the exposure to sago palm (*Cycas revoluta*), a popular ornamental palm-like  
194 plant with well-known toxic effects on animals (Cortinovic and Caloni, 2013; Cortinovic and  
195 Caloni, 2017; Fatourechi et al., 2013; Forrester et al., 2019). All parts of the plant, and in  
196 particular the seeds, contain phytotoxins: the azoglycosides cycasin (hepatotoxic and  
197 carcinogenic), macrozamin and neocycasin, the neurotoxic amino-acid  $\beta$ -N-methylamino-L-  
198 alanine and an unidentified high molecular weight compound (Botha and Penrith, 2009;  
199 Clarke and Burney, 2017; Forrester et al., 2019). Many poisoning cases involving dogs are  
200 described in literature, and in Europe episodes have been previously reported in Italy by  
201 CAV (Caloni et al., 2013; Caloni et al., 2017; Cortinovic and Caloni, 2013) and in Sweden by  
202 the Swedish Poisons Information Centre (Holmgren and Hultén, 2009). Dogs are also

203 frequently exposed to cyanogenic glycoside-containing plants: for instance, many poisoning  
204 cases were related to bigleaf hydrangea (*Hydrangea macrophylla*), characterized by the  
205 presence of the cyanogenic glycoside hydrangin. Heavenly bamboo (*Nandina domestica*)  
206 (which contains protoberberine and berberine alkaloids besides the cyanogenic ones),  
207 cherry laurel (*Prunus laurocerasus*), plum (*Prunus domestica*) and medlar (*Mespilus*  
208 *germanica*) were also reported as causes of intoxication by cyanogenic glycoside-containing  
209 plants in dogs, and the exposure to oleander (*Nerium oleander*), a species containing potent  
210 cardiac glycosides, resulted in a fatal outcome.

211 Glycoside-containing plants were also responsible of intoxications in cats. Heavenly bamboo  
212 (*Nandina domestica*) and oleander (*Nerium oleander*) were found responsible of poisoning  
213 episodes in this species as well as in dogs, and other cases were related to mimosa (*Acacia*  
214 *dealbata*), buttercup (*Ranunculus spp.*) and Japanese laurel (*Aucuba japonica*).

215 Several poisoning episodes involving glycoside-containing plants have been described in  
216 literature. In particular, cases due to bigleaf hydrangea (*Hydrangea macrophylla*) exposures  
217 are frequently reported (Caloni et al., 2013; Caloni et al., 2012; Le Mura, 2018), and a fatal  
218 intoxication in a cat has been observed by CAV in a ten-year survey (Caloni et al., 2013).

219 Also a fatal case of oleander (*Nerium oleander*) exposure, a plant frequently implicated in  
220 companion animal poisoning in Europe (Barbier, 2005; Caloni et al., 2013; Giuliano Albo and  
221 Nebbia, 2004; Mygdal et al., 2015; Sapin, 2004), has been described before in pets by CAV  
222 (Caloni et al., 2013). Moreover, many European investigations have reported pet poisoning  
223 incidents due to glycoside-containing species (Barbier, 2005; Lassak, 2005; McFarland et al.,  
224 2017; Sapin, 2004) and, in Germany, *Prunus spp.* represents the first category listed in the  
225 top five plant species responsible for enquiries to the poison centers for animal exposures  
226 (McFarland et al., 2017).

227 Oleander (*Nerium oleander*) and cherry laurel (*Prunus laurocerasus*) were also responsible  
228 for poisoning cases in cattle and goats, respectively, the latter with a fatal outcome. Indeed,  
229 many episodes of glycoside-containing plant intoxications have been described in  
230 ruminants: sheep and goat poisonings due to exposure to cherry laurel (*Prunus*  
231 *laurocerasus*) have been reported in literature (Schediwiy et al., 2015) also with a fatal  
232 outcome (Schmidt et al., 2013), while oleander (*Nerium oleander*) is a very frequent cause  
233 of plant poisoning in ruminants (Caloni et al., 2013; Caloni et al., 2012; Cortinovis and  
234 Caloni, 2013; Garcia-Arroyo et al., 2017; Guitart et al., 2010; Rubini et al., 2019) in Europe.

235 Alkaloid-containing plants were also often involved in companion animal intoxications. As  
236 for the dog, episodes due to deadly nightshade (*Atropa belladonna*), common box (*Buxus*  
237 *sempervirens*), chili pepper (*Capsicum annuum*), mistletoe (*Viscum album*) and winter cherry  
238 (*Solanum pseudocapsicum*) were recorded. Chili pepper (*Capsicum annuum*), a plant  
239 containing capsaicin and capsaicinoid alkaloids and known to induce acute toxicity in several  
240 animal species (Glinsukon et al., 1980; Surh and Sup Lee, 1995), was responsible for a fatal  
241 episode involving a dog.

242 Other poisoning cases in dogs were due to exposures to daffodil (*Narcissus spp.*) and  
243 hyacinth (*Hyacinthus orientalis*), two species containing alkaloids (*i.e.*, lycorine) as well as  
244 insoluble calcium oxalates. Daffodil (*Narcissus spp.*) was also related to intoxications in cats,  
245 together with clivia (*Clivia spp.*), groundsel (*Senecio vulgaris*) and European yew (*Taxus*  
246 *baccata*). Cases of companion animal poisoning by alkaloid-containing plants are well  
247 documented in the European literature (Berny et al., 2010; Caloni et al., 2013; Caloni et al.,  
248 2012; Caloni et al., 2017; Campbell, 1998; Campbell and Chapman, 2000a, b; McFarland et  
249 al., 2017) and in particular, various episodes of intoxication due to exposures to European  
250 yew (*Taxus baccata*)(Caloni et al., 2013; McFarland et al., 2017) and mistletoe (*Viscum*  
251 *album*)(Caloni et al., 2013; Campbell, 1998; Campbell and Chapman, 2000b) have been  
252 reported.

253 Oxalate-containing plants are another class often implicated in pet poisoning.  
254 Arum (*Arum spp.*) and peace lily (*Spathiphyllum spp.*) were responsible for intoxications in  
255 dogs whereas flamingo flower (*Anthurium spp.*) caused intoxications both in the dog and the  
256 cat and calla lily (*Zantedeschia aethiopica*) in one cat. These plants, and in particular peace  
257 lily (*Spathiphyllum spp.*) and calla lily (*Zantedeschia aethiopica*), which are widespread and  
258 popular ornamental species, are frequently mentioned in reports on domestic animal  
259 poisoning episodes by European authors (Caloni et al., 2013; Caloni et al., 2012; Lassak,  
260 2005; Le Mura, 2018; Sapin, 2004), confirming the toxicological risk related to exposure to  
261 this plant class.

262 Weeping fig (*Ficus benjamina*), a protease-containing plant, and aloe vera (*Aloe vera*),  
263 together with red-margined dracaena (*Dracaena marginata*), two saponin-containing  
264 species, were found responsible of cat poisoning episodes (one case each).

265 Weeping fig, whose leaves and cortex contain ficin, a proteolytic enzyme, and other toxic  
266 substances such as furocoumarins and ficusin (ASPCA, 2020; CABI, 2014), has been reported

267 by the CNITV (Centre National d'Informations Toxicologiques Vétérinaires) as the major  
268 responsible of plant poisoning episodes in animals in France (Barbier, 2005). Similarly,  
269 another author stated, on the bases of the data collected by CNITV, that weeping fig was  
270 one the most frequently ingested plants by small animals (Keck et al., 2004). In accordance  
271 with that, two Italian papers pointed out that *Ficus spp.* was among the most frequently  
272 implicated plants in cat poisoning episodes (Giuliano Albo et al., 2003; Giuliano Albo and  
273 Nebbia, 2004), while two investigations by CAV reported *Ficus benjamina* has a culprit of  
274 intoxication also in the dog (Caloni et al., 2013; Caloni et al., 2012). Red-margined dracaena  
275 (*Dracaena marginata*) is another plant frequently mentioned in the European literature as a  
276 cause of poisoning both in cats and dogs (Barbier, 2005; Caloni et al., 2013; Lassak, 2005;  
277 Sapin, 2004; Schediwy et al., 2015).

278 Another saponin-containing plant, horse chestnut (*Aesculus hippocastanum*), which  
279 contains aesculin, a glycosidic saponin (Campbell, 1998), has been implicated in dog  
280 intoxications, as it has been formerly observed by CAV in a 2000–2011 survey (Caloni et al.,  
281 2013) and in other European countries (Campbell, 1998; Lassak, 2005; Sapin, 2004;  
282 Schediwy et al., 2015). Cases of dog poisoning by two species of ivy, namely English ivy  
283 (*Hedera helix*) and Irish ivy (*Hedera helix Hibernica*), which contain triterpenoid saponins  
284 (*i.e.*, hederagenin) were also registered (one each). In Germany, *Hedera spp.* is included in  
285 the top five plant species responsible for calls to the poison centers for animal exposures  
286 (McFarland et al., 2017) and cases involving English ivy (*Hedera helix*) have been reported in  
287 England (Campbell, 1998) and France (Lassak, 2005).

288 The diterpenoid-containing species poinsettia (*Euphorbia pulcherrima*), a plant frequently  
289 associated with poisoning episodes in domestic animals (Barbier, 2005; Bertero et al., 2020;  
290 Caloni et al., 2013; Caloni et al., 2012; Caloni et al., 2017; Campbell and Chapman, 2000c;  
291 Cortinovis and Caloni, 2013; Curti et al., 2009; Le Mura, 2018; McFarland et al., 2017), has  
292 been found responsible for intoxications mainly in dogs, but also in a cat, a guinea pig and a  
293 rabbit. Lilies (*Lilium spp.*), plants known for their nephrotoxic effects in cats, which may lead  
294 to acute renal failure (Panziera et al., 2019), had been related to 2 episodes involving cats  
295 and one involving a dog. Indeed, while the cat is the only species known to develop renal  
296 failure after the ingestion of *Lilium spp.*, dogs may show gastrointestinal signs (Bates et al.,  
297 2015b; Botha and Penrith, 2009). Poisoning cases by lilies, particularly in cats, are numerous  
298 and reported all over Europe (Balka et al., 2011; Barbier, 2005; Berny et al., 2010; Caloni et

299 al., 2013; Caloni et al., 2012; Caloni et al., 2017; Fourez, 2014; Schediwy et al., 2015;  
300 Sturgeon and Campbell, 2006).

301 Finally, it is worthwhile to mention that even if English walnut (*Juglans regia*) is not reported  
302 in literature as responsible for animal poisoning episodes, the onset of tremorgenic  
303 syndromes with tremors, ataxia, hyperesthesia have been described in dogs after the  
304 ingestion of moldy walnuts due to mycotoxin contamination (Munday et al., 2008; Richard  
305 et al., 1981), generally by penitrem A and roquefortine (Walter, 2002). In our cases,  
306 however, the 3 dogs that ingested English walnut husks developed just mild gastrointestinal  
307 symptoms with no neurological signs.

308 As for the zootoxins, the dog was the species most commonly concerned, with just one case  
309 related to a cat. Episodes involving venomous viper (*Vipera aspis*), common toad (*Bufo*  
310 *bufo*), salamander (*Salamandra salamandra*) and pine processionary (*Thaumetopoea*  
311 *pityocampa*) were reported, similarly to what has been described in literature (Berny et al.,  
312 2010; Caloni et al., 2017; Lervik et al., 2010; Niza et al., 2012; Pelander et al., 2010; Pouzot-  
313 Nevoret et al., 2017; Pouzot-Nevoret et al., 2018). In particular, dog poisonings due to pine  
314 processionary (*Thaumetopoea pityocampa*) are very common in Europe (Caloni et al., 2018;  
315 Caloni et al., 2012; Guitart et al., 1999; Kaszak et al., 2015; Lassak, 2005; Perez-Lopez et al.,  
316 2004; Pouzot-Nevoret et al., 2017), as well as cases due to venomous viper bites (Barbier,  
317 2005; Caloni et al., 2018; Caloni et al., 2012; Caloni et al., 2017; Lassak, 2005; Lervik et al.,  
318 2010; Schediwy et al., 2015). Episodes involving salamander, whose skin glands produce  
319 neurotoxic alkaloids (*i.e.* samandarin and samandaron) (Erjavec et al., 2017) and common  
320 toad, whose parotid glands secrete biogenic amines and steroid derivatives (*i.e.*,  
321 bufodienolide and bufotoxin, with digitalis-like effects) which can cause from local irritation  
322 to systemic signs (gastrointestinal, cardiac and neurological alterations)(Barbosa et al.,  
323 2009), have also been reported in the European literature (Barbier, 2005; Curti et al., 2009;  
324 Erjavec et al., 2017; Lassak, 2005; Schediwy et al., 2015; Scheer et al., 2005).

325 Moreover, 2 cases related to exposures to jellyfish (phylum Cnidaria) have been registered:  
326 the dogs involved developed oral irritation, sialorrhoea and minor gastrointestinal signs with  
327 a positive outcome. Canine exposures to jellyfish have also been reported in England by the  
328 Veterinary Poisons Information Service (VPIS), with similar symptoms (Bates et al., 2015a).  
329 Indeed, cnidarians are very common in the European seas and several species possess  
330 remarkable stinging properties (Killi et al., 2020).



331

## 332 **5. Conclusion**

333 This survey presents an interesting insight on the issue of plant and zootoxin poisoning in  
334 domestic animals, topic that is often disregarded and scarcely investigated. Actually, the  
335 information showed by our research proves the relevance of plants and zootoxins as  
336 poisoning agents and point out the need to carry out a continuous and widespread  
337 investigation on domestic animal exposures, to promptly identify and appropriately respond  
338 to emerging toxicological risks. In this regard, the importance of a proper classification of  
339 the plants on the basis of their taxonomic features need to be stressed, being a crucial step  
340 for the identification of the toxins involved and in light of the species-specific toxicity that  
341 characterizes many compounds.

342

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346

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