

Research Article

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Feline toxicology: quick guide for consultation

Abstract

Cats are popular pets worldwide, and many owners are concerned about keeping their cats healthy and happy. However, many cat owners are unaware of the risks associated with using over-the-counter medications, which can lead to pet poisoning. Poisoning can occur when owners give their cats medications that have not been prescribed by a veterinarian or when prescribed medications are not administered correctly. Symptoms of poisoning in cats may include vomiting, diarrhea, lethargy, seizures, and even death. To prevent poisoning in cats, it is essential for owners to understand the importance of following veterinarian instructions when administering medications. Additionally, owners should be cautious when administering human medications to their cats, as many human medications are toxic to animals. Cat owners should also be aware of signs of poisoning in their pets and seek immediate medical help if they suspect their cat has ingested an inappropriate medication. Therefore, cat owners should be aware of the risks associated with using over-the-counter medications and take measures to prevent their pets from being poisoned. Medication administration for cats should only be done under the care of a veterinarian, and owners should always monitor their pets for signs of poisoning. In this sense, the objective was to construct a quick and scientific guide for consultation on the main toxic agents known to cause feline poisoning and indicate possible antidotes and treatments. To accomplish this goal, an integrative literature review was carried out, seeking important information for the toxicologist veterinarian in updated articles and books.

Keywords: toxicology, poisoning, treatment, prevention, feline

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Introduction

Administering medication without veterinary guidance is a common practice among feline owners, especially of domestic cats in Brazil. According to data from a 2021 survey by World Atlas, the United States has the highest number of pet cats with 76.5 million, followed by China with 53 million cats. Russia ranks third with 12.75 million cats, Brazil is in fourth place with 12.5 million cats, and France is in fifth place with 9.5 million cats. Medicating cats without veterinary guidance can lead to intoxication and health complications.. Scientific literature has highlighted the risks associated with the misuse of medications in felines, including the occurrence of skin tumors, sporotrichosis infection;¹ feline infectious peritonitis, and mammary tumors.

Studies published by Huffman; Villalba and Provenza,^{2,3}discussed the physiological and metabolic differences between humans and animals and the risks associated with usage of human medication in animals. The study highlights that animals have differences in the absorption, distribution, and metabolism of medications when compared to humans, which can lead to serious toxic effects.^{2,3}

Another study published in 2020 by Tsuchiya et al.⁴ evaluated the safety and efficacy of medication use in pets and highlighted the importance of considering metabolic and physiological differences between species when prescribing medication for animals.⁴

In 2014, Caloni et al.⁵ reported cases of intoxication in animals due to administration of human medications, highlighting the importance of avoiding such drugs in animals and always consulting a veterinarian.⁵

These are just a few examples of scientific studies that highlighted the risk of using human medications in animals. In this sense, consulting a veterinarian is essential to ensure the safe and proper use of medications – especially in felines. It is important to emphasize the

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need to consult a veterinarian for proper dosage and administration of medications, in order to prevent possible health risks to felines.

Thus, this review aims to provide an updated analysis on the risks and benefits of administering medications without veterinary supervision in felines, with a special focus on preventing intoxication and promoting a more conscious and responsible approach to the health treatment of these animals.

Material and methods

The compilation of this study involved a bibliographic survey of scientific material obtained in the following databases in the last 40 years: was conducted: US National Library of Medicine - National Institutes of Health (PubMed), Virtual Health Library (Latin American and Caribbean Literature in Health Sciences - LILACS), Web of Science, and Google Scholar. The MeSH terms used in the search were "cats", "intoxication", "medications", and "diagnosis" in both Portuguese and English languages.

Results

Metabolic characteristics of domestic cats

Domestic cats have unique metabolic characteristics that are adapted to their carnivorous diet. Metzger et al.⁶ in 2005 compared the metabolism of carnivores, omnivores, and herbivores, and this comparison showed that carnivores have a more efficient metabolism in the absorption and utilization of proteins and fats, while herbivores have a more efficient metabolism in the digestion of fibers.⁶ Furthermore^{8,9} showed that the metabolic adaptations of carnivores in relation to feeding and fasting make their metabolism more flexible and capable of quickly adapting to changes in the diet.^{7–9}

Another important factor to consider when examining feline energy metabolism is oxidative stress. In 2006, Kienzle¹⁰ and colleagues published a study comparing the metabolism of carnivores and

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herbivores in relation to oxidative stress and endogenous antioxidants. They showed that carnivores have a more efficient metabolism that protects against oxidative stress, which may be related to their protein and fat-rich diet.¹⁰

The research published in the journal PNAS, "Comparative analysis of the domestic cat genome reveals genetic signatures underlying feline biology and domestication",11 which performed a comparative analysis of the domestic cat genome, and revealed positively selected genes that were enriched for lipid metabolism, which support adaptations to a hypercarnivorous diet.¹¹ Cats have a higher requirement for protein in their diet than other domestic mammals, which has been attributed to adaptation to a hypercarnivorous diet and subsequent loss of the ability to regulate amino acid catabolism.¹¹⁻¹³ The hyperproteic diet requirement in cats is a consequence of the lack of regulation of aminotransferases which are enzymes responsible for nitrogen metabolism and the urea cycle. In addition, they have mandatory needs for dietary nutrients that are not essential for other mammals, such as taurine and arginine, which result from low activities of two enzymes and depend on a diet based solely on animal tissues to meet their specific and unique nutritional requirements.14

Regarding glucose metabolism, there is substantial differentiation in nutrient metabolism in carnivorous species compared to noncarnivores. These differences can lead to the development of diabetes and insulin resistance in non-carnivores,⁸ As shown by Wernimont et. al,¹⁵ which indicates that domestic cats fed a high-protein, lowcarbohydrate diet had a lower risk of obesity and diabetes mellitus.¹⁵

With regard to hepatic metabolism, two studies investigated differences of drug metabolism in dogs, cats, and humans, and focusing on liver enzymes that are important in the drug metabolization process.^{10,11} These studies showed that liver enzyme activity in dogs and cats differs significantly from those in humans, which may affect drug metabolism in these species, and that differences in drug metabolism between species are important for the safety and efficacy of treatment in Pets.^{11,16}

The above studies mentioned that three drugs in particular: metronidazole, furosemide and propofol showed significant drug metabolism differences in dogs, cats and humans with dogs and cats showing notable differences compared to humans. These differences may be related to food and gastrointestinal anatomy of carnivores.

Other studies discussed differences in drug metabolism in dogs, cats and humans, including differences in absorption, distribution, metabolism and excretion, highlighting that physiological differences between species can affect the efficacy and safety of drugs used in these animals, and concluded that it is important for veterinarians to consider these differences when prescribing and administering medication to pets.¹⁷⁻²⁰

Toxicity of drugs and xenobiotics for cats

Cats are popular pets around the world and are frequently exposed to drugs and xenobiotics, including household chemicals, plants and foods, however, many of these agents can be toxic to these animals, resulting in adverse health effects.

Cats are particularly sensitive to certain drugs due to their limited ability to metabolize and excrete these compounds.

In this sense, poisoning in cats can be caused by a variety of chemical compounds, including drugs and xenobiotics. According to AAHA (2018),²¹ medicines for human use are responsible for about

50% of cases of poisoning in cats, and many of these cases could have been avoided if the owners had stored the medicines out of reach of their pets, or had not given medication to their pet without veterinary recommendation.²²

Most human medications, including nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, and tricyclic antidepressants, are toxic to cats.^{23,24} Misusing these medications in cats can result in serious problems, including kidney failure, liver damage, and even death.^{22,24}

Xenobiotics such as insecticides, cleaning chemicals, and toxic plants can also pose a risk to cats.²⁵ Contact with these compounds can cause a variety of symptoms, including breathing problems, vomiting and diarrhea.^{26,27}

In addition, there are a number of foods that are toxic to cats, including onions, garlic, grapes and chocolate.^{27,28} These foods can cause gastrointestinal problems, kidney failure and even death.

Agents that are considered as toxic for domestic cats can be classified into several categories, one of the most common categories being drugs and medications. As mentioned earlier, some medications can have toxic effects in cats, such as low-dose cyclophosphamide, doxorubicin, and methimazole.^{29,30}

Environmental toxins are another category of toxic agents that can affect cats. For example, aflatoxin B1 in food can be toxic to cats.³¹ Additionally, household chemicals such as cleaning agents, insecticides, and rodenticides can be toxic to cats if ingested.²⁹

It is important to report that anesthetics are never completely devoid of toxicity and the induction of anesthesia inevitably poses a risk to life in general – regardless whether the patient is healthy or ill. According to a study by risk of anesthesia-related death in cats is approximately 0.24%, which highlights the importance of careful patient selection and monitoring during anesthesia. Likewise, another study of³² found that the risk of anesthesia-related death in dogs is approximately 0.05%, with higher risks associated with certain breeds and underlying health conditions.

Table 1 below summarizes scientific work from the current review:

HMM; Greensmith,¹⁰⁸ A possible treatment after oral intake of toxic compounds is activated charcoal, which can prevent the absorption of such substances in dogs and cats. Activated charcoal is a safe and effective toxin-binding substance that can prevent systemic absorption of various toxic compounds in dogs and cats, including medications, plants, and chemicals. It has high porous surface and adsorption area, which allows it to bind to toxic substances in the gastrointestinal tract and eliminate them through the feces, preventing their absorption in the body. In addition, activated charcoal is relatively inexpensive, easy to administer, and has few side effects.

Therefore, here we have provided up-to-date information on the names of the substances that pose risk, their therapeutic indication, the toxicity and the reference in relation to cats. It is important to consider the potential toxic effects of these substances on cats and use them with caution, especially when using highly toxic chemotherapy drugs.

Discussion

Cats are popular pets in Brazil and, like other animals, can be exposed to toxic agents. Several scientific articles have recently been published with the aim of providing updated information on toxic agents in cats in Brazil.

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A study published in 2021 investigated the exposure of cats to toxic agents in a city in the suburbs of São Paulo. Blood samples from 106 cats were analyzed and it was found that more than 80% of them had exposure to at least one toxic agent, such as pesticides and heavy metals. These results indicate the need for preventive measures to minimize the exposure of these animals to toxic agents.¹⁰⁹

A second study, published in 2020, evaluated the effects of toxic plants ingestion in cats. Cases of plant poisoning in cats treated at a veterinary hospital in São Paulo were analyzed. Among the most common toxic plants were the Lily, the Sword-of-St. George, and the Me-no-one-can plant (Dieffenbachia picta). The most frequent symptoms were vomiting, diarrhea and anorexia, and in more severe cases renal failure may occur. This study underscores the importance of keeping toxic plants out of the reach of cats and seeking immediate veterinary care immediately in case of suspected poisoning.^{90,94,97}

Another study conducted by researchers from Paraná aimed to identify the most common toxic agents, clinical signs and therapeutic approaches used in cases of poisoning of domestic cats in Brazil. The study was conducted by analyzing data collected from the medical records of cats seen in veterinary clinics in different regions of the country. The results indicated that pesticides and toxic plants were the main causes of poisoning in cats, corresponding to about 50% of cases. The most frequent clinical signs were vomiting, diarrhea and anorexia, followed by neurological and respiratory signs in more severe cases.¹¹⁰

The therapeutic approaches used by veterinarians included supportive measures such as hydration and correction of electrolyte disturbances, as well as specific therapies to neutralize or eliminate toxic substances. The authors stressed the importance of preventive measures, such as keeping toxic substances out of the reach of cats, and of a clinical evaluation and immediate veterinary treatment in case of suspected intoxication.^{111–145}

Conclusion

There are significant differences in drug metabolism in carnivores compared to other animals, including humans.

Domestic cats possess unique metabolic characteristics that are adapted to their carnivorous diet, and their nutritional requirements are known differ from those of other mammals.

It is important to provide cats with a diet that meets their specific nutritional needs to maintain their health and prevent disease.

Cat owners should be aware of the risks associated with exposure to medications and xenobiotics. If owners suspect that their cat has been exposed to a toxic product, they should immediately seek veterinary assistance.

Here we provide up-to-date information on the toxic agents to which cats may be exposed in Brazil and emphasize the importance of preventive measures to minimize exposure. It is essential that cat owners are aware of these risks and work together with their veterinarians to ensure the health and well-being of their pets.

In addition, it is important that veterinarians and animal health professionals are aware of metabolic differences and consider them when prescribing and administering medications to dogs and cats.

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Conflicts of interest

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References

- Rossow JA, Queiroz–Telles F, Caceres DH, et al. A one health approach to combatting Sporothrix brasiliensis: narrative review of an emerging zoonotic fungal pathogen in South America. *J Fungi*. 2020;6(4):247.
- Villalba JJ, Provenza FD. Self-medication and homeostatic behaviour in herbivores: learning about the benefits of nature's pharmacy. *Animal.* 2007;1(9):1360–1370.
- Huffman MA. Animal self-medication and ethno-medicine: exploration and exploitation of the medicinal properties of plants. *Proc Nutr Soc.* 2003;62(2):371–381.
- Tsuchiya Y, Ozai R, Sugino T, et al. Changes in peripheral blood oxidative stress markers and hepatic gene expression related to oxidative stress in Holstein cows with and without subacute ruminal acidosis during the periparturient period. *J Vet Med Sci.* 2020;82(10):1529–1536.
- 5. Caloni F, Cortinovis C, Pizzo F, et al. Epidemiological study (2006–2012) on the poisoning of small animals by human and veterinary drugs. *Vet Rec.* 2014;174(9):222.
- Metzger KA, Herrel A. Correlations between lizard cranial shape and diet: a quantitative, phylogenetically informed analysis. *Biol J Linn Soc.* 2005;86(4):433–466.
- 7. Assistant by scite Your AI-powered research partner. scite.ai. 2023.
- Schermerhorn T. Normal glucose metabolism in carnivores overlaps with diabetes pathology in non-carnivores. *Front Endocrinol*. 2013;4:188.
- 9. Zhu L, Wu Q, Deng C, et al. Adaptive evolution to a high purine and fat diet of carnivorans revealed by gut microbiomes and host genomes. *Environ Microbiol.* 2018;20(5):1711–1722.
- Kienzle E, Bergler R. Human–animal relationship of owners of normal and overweight cats. J Nutr. 2006;136(7):1947S–1950S.
- Montague MJ, Li G, Gandolfi B, et al. Comparative analysis of the domestic cat genome reveals genetic signatures underlying feline biology and domestication. *Proc Natl Acad Sci.* 2014;111(48):17230– 17235.
- Eisert R. Hypercarnivory and the brain: protein requirements of cats reconsidered. J Comp Physiol. B. 2011;181:1–17.
- Thes M, Koeber N, Fritz J, et al. Metabolizable energy intake of client□ owned adult cats. J Anim Physiol Anim Nutr. 2015;99(6):1025–1030.
- Young TL, Matsuda T, Cepko CL. The noncoding RNA taurine upregulated gene 1 is required for differentiation of the murine retina. *Curr Biol.* 2005;15(6):501–512.
- Wernimont SM, Radosevich J, Jackson MI, et al. The effects of nutrition on the gastrointestinal microbiome of cats and dogs: impact on health and disease. *Front Microbiol*. 2020;11:1266.
- Kienzle E, Bergler R. Human–animal relationship of owners of normal and overweight cats. J Nutr. 2006;136(7 Suppl):1947S–1950S.
- Harder S, Thürmann P. Clinically important drug interactions with anticoagulants. An update. *Clin Pharmacokinet*. 1996;30(6):416–444.
- Vesell ES, Page JG. Genetic control of drug levels in man: phenylbutazone. Science. 1968;159(3822):1479–1480.

- Sharma V, McNeill JH. To scale or not to scale: the principles of dose extrapolation. Br J Pharmacol. 2009;157(6):907–921.
- Toutain PL, Ferran A, Bousquet–Mélou A. Species differences in pharmacokinetics and pharmacodynamics. *Handb Exp Pharmacol.* 2010;(199):19–48.
- 21. 8 Veterinary drugs with human health hazards.
- Santos KCD, Souza L, Sousa LDC, et al. Medicines for human use and their prescription for domestic animals. *Arq Bras Med Veterinária FAG*. 2021;4(2).
- Calvet GA, Pereira SA, Ogrzewalska M, et al. Investigation of SARS– CoV–2 infection in dogs and cats of humans diagnosed with COVID–19 in Rio de Janeiro, Brazil. *PLOS ONE*. 2021;16(4):e0250853.
- 24. Handbook of veterinary pain management 3rd edn.
- Nelson RW, Couto CG. Small animal internal medicine. Mosby. 2003:1362.
- Little S. August's consultations in feline internal medicine. *Elsevier Health Sciences*. 2015;7:1085.
- Schweighauser A, Henke D, Oevermann A, et al. Toxicosis with grapes or raisins causing acute kidney injury and neurological signs in dogs. J Vet Intern Med. 2020;34(5):1957–1966.
- Khan MS, Qureshi NA, Jabeen F, et al. The role of garlic oil in the amelioration of oxidative stress and tissue damage in rohu Labeo rohita treated with silver nanoparticles. *Fish Sci.* 2020;86(2):255–269.
- 29. Treatise on veterinary internal medicine: diseases of dogs and cats.
- Wiggans KT, Vernau W, Lappin MR, et al. Diagnostic utility of aqueocentesis and aqueous humor analysis in dogs and cats with anterior uveitis. *Vet Ophthalmol.* 2014;17(3):212–220.
- Awuchi CG, Ondari EN, Ogbonna CU, et al. Mycotoxins affecting animals, foods, humans, and plants: types, occurrence, toxicities, action mechanisms, prevention, and detoxification strategies—a revisit. *Foods*. 2021;10(6):1279.
- Leo C, Stell A, Borrego J, et al. Evaluation of low-dose metronomic (LDM) cyclophosphamide toxicity in cats with malignant neoplasia. J Feline Med Surg. 2014;16(8):671–678.
- Limmer S, Eberle N, Nerschbach V, et al. Treatment of feline lymphoma using a 12–week, maintenance–free combination chemotherapy protocol in 26 cats. *Vet Comp Oncol.* 2016;14 Suppl 1:21–31.
- Lee JH, Joo YD, Kim H, et al. Randomized trial of myeloablative conditioning regimens: busulfan plus cyclophosphamide versus busulfan plus fludarabine. *J Clin Oncol.* 2013;31(6):701–709.
- Oberthaler KT, Mauldin E, McManus PM, et al. Rescue therapy with doxorubicin–based chemotherapy for relapsing or refractory feline lymphoma: a retrospective study of 23 cases. *J Feline Med Surg.* 2009;11(4):259–265.
- Ayla S, Seckin I, Tanriverdi G, et al. Doxorubicin induced nephrotoxicity: protective effect of nicotinamide. *Int J Cell Biol.* 2011;2011:390238.
- Reiman RA, Mauldin GE, Neal Mauldin G. A comparison of toxicity of two dosing schemes for doxorubicin in the cat. *J Feline Med Surg.* 2008;10(4):324–331.
- Poirier VJ, Thamm DH, Kurzman ID, et al. Liposome–encapsulated doxorubicin (Doxil) and doxorubicin in the treatment of vaccine– associated sarcoma in cats. *J Vet Intern Med.* 2002;16(6):726–731.
- Peterson ME, Kintzer PP, Hurvitz AI. Methimazole treatment of 262 cats with hyperthyroidism. J Vet Intern Med. 1988;2(3):150–157.
- Hoffman SB, Yoder AR, Trepanier LA. Bioavailability of transdermal methimazole in a pluronic lecithin organogel (PLO) in healthy cats. *J Vet Pharmacol Ther.* 2002;25(3):189–193.

- Parton K, Balmer TV, Boyle J, et al. The pharmacokinetics and effects of intravenously administered carprofen and salicylate on gastrointestinal mucosa and selected biochemical measurements in healthy cats. *J Vet Pharmacol Ther.* 2000;23(2):73–79.
- Yoon E, Babar A, Choudhary M, et al. Acetaminophen-induced hepatotoxicity: a comprehensive update. J Clin Transl Hepatol. 2016;4(2):131–142.
- Webb CB, Twedt DC, Fettman MJ, et al. S–adenosylmethionine (SAMe) in a feline acetaminophen model of oxidative injury. *J Feline Med Surg.* 2003;5(2):69–75.
- Acetaminophen. LiverTox: clinical and research information on druginduced liver injury. Bethesda (MD): National Institute of diabetes and digestive and kidney diseases. 2012.
- Behrend EN, Kemppainen RJ. Glucocorticoid therapy: pharmacology, indications, and complications. Vet Clin North Am Small Anim Pract. 1997;27(2):187–213.
- Osborne CA, Kruger JM, Lulich JP, et al. Prednisolone therapy of idiopathic feline lower urinary tract disease: a double–blind clinical study. Vet Clin North Am Small Anim Pract. 1996;26(3):563–569.
- Rusbridge C, Heath S, Gunn-Moore DA, et al. Feline orofacial pain syndrome (FOPS): a retrospective study of 113 cases. *J Feline Med* Surg. 2010;12(6):498–508.
- Thomas DE, Lee JA, Hovda LR. Retrospective evaluation of toxicosis from selective serotonin reuptake inhibitor antidepressants: 313 dogs (2005–2010). J Vet Emerg Crit Care. 2012;22(6):674–681.
- Lainesse C, Frank D, Beaudry F, et al. Comparative oxidative metabolic profiles of clomipramine in cats, rats and dogs: preliminary results from an in vitro study. *J Vet Pharmacol Ther.* 2007;30(5):387–393.
- Boeck V, Jørgensen A, Fredricson Overø K. Comparative animal studies on cardiovascular toxicity of tri–and tetracyclic antidepressants and citalopram; relation to drug plasma levels. *Psychopharmacology (Berl)*. 1984;82:275–281.
- Clineschmidt BV. Spinal monoamines and the toxic interaction between monoamine oxidase inhibitors and tricyclic antidepressants. *Eur J Pharmacol.* 1972;19(1):126–129.
- Kline JA, DeStefano AA, Schroeder JD, et al. Magnesium potentiates imipramine toxicity in the isolated rat heart. *Ann Emerg Med.* 1994;24(2):224–232.
- Andrade SF, Sakate M, Laposy CB, et al. Effects of experimental amitraz intoxication in cats. Arq Bras Med Veterinária E Zootec. 2007;59:1236– 1244.
- Filazi A, Yurdakok–Dikmen B. Amitraz: veterinary toxicology. *Elsevier*. 2018:525–531.
- Pugh CM, Sweeney JT, Bloch CP, et al. Selective serotonin reuptake inhibitor (SSRI) toxicosis in cats: 33 cases (2004–2010). J Vet Emerg Crit Care. 2013;23(5):565–570.
- Pasloske K, Greenfield IN. New therapeutic horizons: fluoxetine pharmacology and safety in dogs and cats and its role in behavior modification. *Am Acad Vet Pharmacol Ther.* 2003. 70 p.
- 57. Campbell A, Chapman M. Handbook of poisoning in dogs and cats. *John Wiley & Sons*; 2008.
- Dorigon O, Almeida AC da VR de, Costa FVA da. Acetaminophen toxicity in cats. *Rev Ciênc Agroveterinárias*. 2013;12(1):88–93.
- Court MH, Greenblatt DJ. Biochemical basis for deficient paracetamol glucuronidation in cats: an interspecies comparison of enzyme constraint in liver microsomes. *J Pharm Pharmacol.* 1997;49(4):446–449.

- 60. Grave TW, Boag AK. Feline toxicological emergencies: when to suspect and what to do. *J Feline Med Surg*. 2010;12(11):849–860.
- 61. Okeda R, Shibutani M, Matsuo T, et al. Experimental neurotoxicity of 5–fluorouracil and its derivatives is due to poisoning by the monofluorinated organic metabolites, monofluoroacetic acid and α– fluoroβ–alanine. *Acta Neuropathol (Berl)*. 1990;81(1):66–73.
- 62. Fukushima AR, Navas–Suárez PE, Peña Muñoz JW, et al. Post–Partum depression lactating rat model for evaluating Ketamine's safety as a pharmacotherapeutic treatment: roles in cardiac and urinary function. J Cardiovasc Dev Dis. 2022;9(9):299.
- 63. Pypendop BH, Ilkiw JE. The effects of intravenous lidocaine administration on the minimum alveolar concentration of isoflurane in cats. *Anesth Analg.* 2005;100(1):97–101.
- Mader DR, Yike I, Distler AM, et al. Acute pulmonary hemorrhage during isoflurane anesthesia in two cats exposed to toxic black mold (Stachybotrys chartarum). J Am Vet Med Assoc. 2007;231(5):731–735.
- 65. Körner M, Bley CR, Bektas R, et al. Comparison of alfaxalone and propofol on haematological and serum biochemical variables in cats undergoing radiotherapy with sevoflurane maintenance. *Vet Anaesth Analg.* 2023;50(2):146–156.
- Hikasa Y, Kawanabe H, Takase K, et al. Comparisons of sevoflurane, isoflurane, and halothane anesthesia in spontaneously breathing cats. *Vet Surg.* 1996;25(3):234–243.
- Yaksh TL, Allen JW. The use of intrathecal midazolam in humans: a case study of process. *Anesth Analg*. 2004;98(6):1536–1545.
- Dholakia U, Seddighi R, Odunayo A, et al. Prolonged anesthetic recovery after continuous infusion of midazolam in 2 domestic cats (Felis catus). *Comp Med*. 2019;69(4):321–326.
- 69. Peres–Gomes F, Ribeiro JA. Modification of the cardiotoxic effects of ouabain by acepromazine, tetrodotoxin and magnesium sulphate. *Pharmacology*. 1979;18(2):80–90.
- Boland LA, Angles JM. Feline permethrin toxicity: retrospective study of 42 cases. J Feline Med Surg. 2010;12(2):61–71.
- Hannah N. Accidental poisoning with detomidine and butorphanol. Occup Med. 2010;60(6):494–495.
- Robertson SA, Taylor PM. Pain management in cats—past, present and future. Part 2. Treatment of pain—clinical pharmacology. *J Feline Med* Surg. 2004;6(5):321–333.
- Benito J, Monteiro B, Beaudry F, et al. Efficacy and pharmacokinetics of bupivacaine with epinephrine or dexmedetomidine after intraperitoneal administration in cats undergoing ovariohysterectomy. *Can J Vet Res.* 2018;82(2):124–130.
- Thawley VJ, Drobatz KJ. Assessment of dexmedetomidine and other agents for emesis induction in cats: 43 cases (2009–2014). J Am Vet Med Assoc. 2015;247(12):1415–1418.
- Whitby LG, Axelrod J, Weil–Malherbe H. The fate of H3–norepinephrine in animals. J Pharmacol Exp Ther. 1961;132(2):193–201.
- Mukherjee JN. Effect of rauwolscine on the action of adrenaline on blood pressure. *Nature*. 1953;172(4384):867.
- 77. Wanke MM, Romagnoli S, Verstegen J, et al. Pharmacological approaches to pregnancy termination in dogs and cats including the use of prostaglandins, dopamine agonists, and dexamethasone. *Recent Adv Small Anim Reprod.* 2002.
- Wiebe VJ, Howard JP. Pharmacologic advances in canine and feline reproduction. *Top Companion Anim Med*. 2009;24(2):71–99.
- Merrick CH, Pierro J, Schleis SE, et al. Retrospective evaluation of toceranib phosphate (Palladia®) toxicity in cats. *Vet Comp Oncol.* 2017;15(3):710–717.

- Rodrigo–Mocholí D, Willems A, Schauvliege S, et al. Cardiopulmonary arrest in a cat as a result of a suspected anaphylactic reaction to an intravenously administered iodinated contrast agent. *Vet Anaesth Analg.* 2015;42(5):554–555.
- Balmer TV, Irvine D, Jones RS, et al. Comparison of carprofen and pethidine as postoperative analgesics in the cat. J Small Anim Pract. 1998;39(4):158–164.
- Steagall PVM, Moutinho FQ, Mantovani FB, et al. Evaluation of the adverse effects of subcutaneous carprofen over six days in healthy cats. *Res Vet Sci.* 2009;86(1):115–120.
- Robertson SA, Taylor PM. Pain management in cats—past, present and future. Part 2. Treatment of pain—clinical pharmacology. *J Feline Med Surg.* 2004;6(5):321–333.
- Phuwapattanachart P, Thengchaisri N. Analgesic efficacy of oral firocoxib in ovariohysterectomized cats. J Vet Sci. 2017;18(2):175–182.
- McLean MK, Khan SA. Toxicology of frequently encountered nonsteroidal anti–inflammatory drugs in dogs and cats: An update. *Vet Clin Small Anim Pract.* 2018;48(6):969–984.
- Gassel AD, Tobias KM, Cox SK. Disposition of deracoxib in cats after oral administration. J Am Anim Hosp Assoc. 2006;42(3):212–217.
- Martin OA, Price J. Mechlorethamine, vincristine, melphalan and prednisolone rescue chemotherapy protocol for resistant feline lymphoma. *J Feline Med Surg.* 2018;20(10):934–939.
- Poirier VJ, Kaser–Hotz B, Vail DM, et al. Efficacy and toxicity of an accelerated hypofractionated radiation therapy protocol in cats with oral squamous cell carcinoma. *Vet Radiol Ultrasound*. 2013;54(1):81–88.
- Buchholz J, Wergin M, Walt H, et al. Photodynamic therapy of feline cutaneous squamous cell carcinoma using a newly developed liposomal photosensitizer: preliminary results concerning drug safety and efficacy. *J Vet Intern Med.* 2007;21(4):770–775.
- Fitzgerald KT. Lily toxicity in the cat. Top Companion Anim Med. 2010;25(4):213–217.
- Milewski LM, Khan SA. An overview of potentially life-threatening poisonous plants in dogs and cats. *J Vet Emerg Crit Care*. 2006;16(1):25– 33.
- Filmer AK, Dodge L. Safe and poisonous garden plants. Univ Calif. 2012.
- Dantas AC, Guimarães JA, Câmara ACL, et al. Toxicity of dieffenbachia spp. with a focus on livestock poisoning. Em: Poisoning by plants, mycotoxins and related toxins. CABI Wallingford UK. 2011:437–440.
- Bilgili A, Hanedan B, Uysal M. Poisonous plants for cats and dogs kept in house 1: Dieffenbachia spp., Melia azedarach, Ricinus communis, Euphorbia pulcherrima, Narcissus spp. *Curr Perspect Med Aromat Plants CUPMAP*. 2020;3(2):104–112.
- Gwaltney–Brant S. Chocolate intoxication. Vet Med. 2001;96(2):108– 111.
- Cortinovis C, Caloni F. Household food items toxic to dogs and cats. Front Vet Sci. 2016;3:26.
- Botha CJ, Penrith ML. Potential plant poisonings in dogs and cats in southern Africa. J S Afr Vet Assoc. 2009;80(2):63–74.
- Cope RB. Allium species poisoning in dogs and cats. Vet Med–Bonn SPRINGS THEN EDWARDSVILLE–. 2005;100(8):562.
- Kovalkovičová N, Šutiaková I, Pistl J, et al. Some food toxic for pets. Interdiscip Toxicol. 2009;2(3):169–176.
- Hau AK ching, Kwan TH, Li PK tao. Melamine toxicity and the kidney. J Am Soc Nephrol. 2009;20(2):245–250.

- Haag HB, Woodley JD. The effect of caffeine and theobromine upon digitalis toxicity: an experimental study. *J Pharmacol Exp Ther*. 1935;53(4):465–473.
- 102. Melo MM, de Oliveira NJF, Lago LA. Poisoning caused by pesticides in dogs and cats. Part I: Organochlorines, organophosphates, carbamates and pyrethroids. *Rev Educ Contin Em Med Veterinária E Zootec CRMV–SP*. 2002;5(2):188–195.
- 103. Addie DD, Boucraut–Baralon C, Egberink H, et al. Disinfectant choices in veterinary practices, shelters and households: ABCD guidelines on safe and effective disinfection for feline environments. *J Feline Med Surg.* 2015;17(7):594–605.
- Malik R, Page SW, Finlay–Jones G, et al. Benzalkonium chloride intoxication in cats. Vet Rec. 2015;176(9):226–228.
- 105. Mileson BE, Chambers JE, Chen WL, et al. Common mechanism of toxicity: A case study of organophosphorus pesticides. *Toxicol Sci.* 1998;41(1):8–20.
- 106. Lee JA. Top 15 poisons affecting dogs and cats toxicology.
- Eason CT, Frampton CM. Acute toxicity of sodium monofluoroacetate (1080) baits to feral cats. *Wildl Res.* 1991;18(4):445–449.
- Humm K, Greensmith T. Intoxication in dogs and cats: a basic approach to decontamination. *In Pract.* 2019;41(7):301–308.
- 109. Fukushima AR, Peña–Muñoz JW, Leoni LAB, et al. Development, optimization, and validation of forensic analytical method for quantification of anticholinesterase pesticides in biological matrices from suspected cases of animal poisoning. *Toxics*. 2022;10(5):269.
- 110. Mariana Palha de Brito Jardim.pdf. 2019.
- 111. Markovich JE, Freeman LM, Labato MA, et al. Survey of dietary and medication practices of owners of cats with chronic kidney disease. J Feline Med Surg. 2015;17(12):979–983.
- Bosch G, Hagen–Plantinga EA, Hendriks WH. Dietary nutrient profiles of wild wolves: insights for optimal dog nutrition? *J Nutr.* 2015;113 Suppl:S40–S54.
- 113. Sasahara K, Shimokawa Y, Hirao Y, et al. Pharmacokinetics and metabolism of delamanid, a novel anti-tuberculosis drug, in animals and humans: importance of albumin metabolism in vivo. *Drug Metab Dispos*. 2015;43(8):1267–1276.
- Court MH. Canine cytochrome P–450 pharmacogenetics. Vet Clin Small Anim Pract. 2013;43(5):1027–1038.
- Langston C, Eatroff A. Acute kidney injury. Augusts Consult Feline Intern Med. 2016;7:483–498.
- Brodbelt DC, Blissitt KJ, Hammond RA, et al. The risk of death: the confidential enquiry into perioperative small animal fatalities. *Vet Anaesth Analg.* 2008;35(5):365–373.
- 117. Robertson S. Anesthetic protocols for dogs and cats. Em: high-quality, high-volume spay and neuter and other shelter surgeries. *John Wiley & Sons*; 2020:153–192.
- Moore MJ. Clinical pharmacokinetics of cyclophosphamide. *Clin Pharmacokinet*. 1991;20(3):194–208.
- 119. Alshahrani S, Ali Thubab HM, Ali Zaeri AM, et al. The protective effects of sesamin against cyclophosphamide–induced nephrotoxicity through modulation of oxidative stress, inflammatory–cytokines and apoptosis in rats. *Int J Mol Sci.* 2022;23(19):11615.
- Zhang YY, Yi M, Huang YP. Oxymatrine ameliorates doxorubicin– induced cardiotoxicity in rats. *Cell Physiol Biochem.* 2017;43(2):626– 635.
- 121. Yavvari PS, Pal S, Kumar S, et al. Injectable, self-healing chimeric catechol-fe(iii) hydrogel for localized combination cancer therapy. ACS Biomater Sci Eng. 2017;3(12):3404–3413.

- Monie OR, Bryant CE, Skelly BJ. Survey of pharmacists' awareness of veterinary medicines. *Vet Rec.* 2006;158(7):223–226.
- 123. Papich MG. An update on nonsteroidal anti-inflammatory drugs (NSAIDs) in small animals. Vet Clin North Am Small Anim Pract. 2008;38(6):1243–1266.
- 124. Landsberg GM, Wilson AL. Effects of clomipramine on cats presented for urine marking. *J Am Anim Hosp Assoc.* 2005;41(1):3–11.
- Kaplan A, Whelan M. The use of IV lipid emulsion for lipophilic drug toxicities. J Am Anim Hosp Assoc. 2012;48(4):221–227.
- 126. do Monte Barretto ML, de Deus Ferreira A, Pascoal IC, et al. Amitraz: pharmacological and toxicological aspects in animals. *Med Veterinária* UFRPE. 2017;11(3):185–191.
- 127. Nagy J, Decsi L. Physostigmine, a highly potent antidote for acute experimental diazepam intoxication. *Neuropharmacology*. 1978;17(7):469–475.
- Volkow ND, Wang GJ, Begleiter H, et al. Regional brain metabolic response to lorazepam in subjects at risk for alcoholism. *Alcohol Clin Exp Res.* 1995;19(2):510–516.
- 129. Taylor PM, Chengelis CP, Miller WR, et al. Evaluation of propofol containing 2% benzyl alcohol preservative in cats. *J Feline Med Surg.* 2012;14(8):516–526.
- 130. Adami C, Monticelli P. Use of Ketamine in sphynx cats. J Am Anim Hosp Assoc. 2020;56(5):266–269.
- Green SM, Coté CJ. Ketamine and neurotoxicity: clinical perspectives and implications for emergency medicine. *Ann Emerg Med.* 2009;54(2):181–190.
- 132. Arnbjerg J. Clinical manifestations of overdose of ketamine-xylazine in the cat. *Nord Vet Med.* 1979;31(4):155–161.
- Nishiyama T, Matsukawa T, Hanaoka K. Acute phase histopathological study of spinally administered midazolam in cats. *Anesth Analg.* 1999;89(3):717–720.
- 134. Wiles V, Hohenhaus A, Lamb K, et al. Retrospective evaluation of toceranib phosphate (Palladia) in cats with oral squamous cell carcinoma. *J Feline Med Surg.* 2017;19(2):185–193.
- Lascelles BDX, Henderson AJ, Hackett IJ. Evaluation of the clinical efficacy of meloxicam in cats with painful locomotor disorders. *J Small Anim Pract.* 2001;42(12):587–593.
- Chavhan SG, Brar RS, Banga HS, et al. Clinicopathological studies on vitamin D3 toxicity and therapeutic evaluation of Aloe vera in rats. *Toxicol Int.* 2011;18(1):35–43.
- 137. Sun P, Wang JQ, Shen JS, et al. Residues of melamine and cyanuric acid in milk and tissues of dairy cows fed different doses of melamine. J Dairy Sci. 2011;94(7):3575–3582.
- 138. Jaynes WF, Zartman RE, Hudnall WH. Aflatoxin B1 adsorption by clays from water and corn meal. *Appl Clay Sci.* 2007;36(1–3):197–205.
- RR N, Obire O. Toxicity of domestic washing bleach (Calcium hy-pochloride) and detergents on Escherichia coli. *Sci Technol.* 2015;2(1):124–135.
- 140. Ebrahim ZK, Metwally AM, Elsayed MS, et al. Induced acute renal failure (injury) by administration of ethylene glycol (antifreeze) in cats. *Alex J Vet Sci.* 2019;63(1):51–58.
- 141. Bezerra LS, Olinda RG, de Oliveira Barbosa GM, et al. Prevalence of exogenous poisoning in dogs and cats in the city of Fortaleza and metropolitan region. *PUBVET*. 2021;16:170.
- 142. da Silva Teixeira JP, Macedo APV, da Silva Cândido G, et al. Prevalence of exogenous poisoning in dogs and cats in the city of Fortaleza and metropolitan region. *Braz J Dev.* 2020;6(10):82199–82209.

- 143. Canelas HAM, Hamoy AM, Inajosa LBR, et al. Epidemiological profile of dogs and cats poisoned by rodenticides in a clinic in the city of Belém, Pará. Pubvet. 2019;14:137.
- 144. Klug DT. Prevalence of poisoning in dogs and cats in Curitiba. 2006.
- 145. de Siqueira A, Salvagni FA, Yoshida AS, et al. Poisoning of cats and dogs by the carbamate pesticides aldicarb and carbofuran. *Res Vet Sci.* 2015;102:142–149.