| REVIEW ARTICLE |

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The Role of Feline-Specific Features in Drug Safety: Risks Associated with Antibiotics, Antiparasitics, NSAIDs, and Opioids. Running head: Drug Safety in Cats

B. Söyler*
B. Dik
H. Oğuz

Abstract

Cats exhibit unique physiological, anatomical, and metabolic traits that significantly impact the pharmacokinetics of drugs, including their absorption, distribution, metabolism, and excretion. These differences, when compared to other companion animals, particularly dogs, result in a distinct sensitivity to many commonly used medications. This review aims to evaluate the pharmacological risks associated with major drug classes used in feline medicine, including antibiotics, antiparasitic agents, non-steroidal anti-inflammatory drugs, and opioids, while highlighting the role of feline-specific physiological and metabolic characteristics in drug safety. A key concern in feline pharmacology is the presence of species-specific enzyme deficiencies, most notably glucuronyl transferase and thiopurine methyltransferase. These deficiencies impair the liver's ability to conjugate and detoxify drugs, leading to a heightened risk of adverse effects and systemic toxicity. Several drug classes commonly used in feline medicine are associated with clinically relevant adverse effects; aminoglycosides may cause nephrotoxicity, whereas tetracyclines have been linked to dental discoloration and oesophageal injury. Fluoroquinolones are known to induce retinal degeneration and potential blindness in cats, and acetaminophen is highly hepatotoxic and often fatal, even at low doses. The primary objective of this review is to provide veterinarians with a comprehensive understanding of the pharmacological risks associated with drug use in cats, thereby facilitating more informed and evidence-based prescribing decisions. In light of the species-specific physiological and metabolic characteristics of cats, individualised dosing protocols and appropriate therapeutic alternatives should be considered to enhance drug safety and minimise the risk of severe or potentially life-threatening adverse drug reactions.

Keywords: *Anatomical and physiological differences; cats; toxicity; medicines.*

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Büşra SÖYLER* (corresponding author), kilinnc.busra@gmail.com, orcid.org/0009-0006-9648-7029; Burak DİK, burakdik@selcuk.edu.tr, orcid.org/0000-0003-2738-6911; Halis OĞUZ, halisoguz@selcuk.edu.tr, orcid.org/0000-0002-9236-0630.

Department of Pharmacology and Toxicology, Veterinary Faculty, Selcuk University, 42000 Konya, Turkey

Introduction

Species-specific metabolic, physiological, and anatomical characteristics play a critical role in determining the safety, efficacy, and appropriate use of drugs in domestic animals. Especially in small animal practice, drug selection, administration method, frequency and dosage are important. The use of most drugs in cats may be similar or the same as in dogs, though cats are more sensitive to drugs. Adverse and toxic effects that may occur due to drug use during treatment can only be prevented by careful and safe use of drugs (Court, 2013). This review gives a detailed overview of those drugs that are risky to use in cats and their possible toxic effects.

Physiological and anatomical differences between cats and other species

Anatomical and histological differences are decisive in the use of drugs in veterinary medicine. In cats, the distal 8% of the oesophagus and approximately 16% of the circular muscle layer consist of smooth muscle tissue. This is the main reason why cats retain some foreign bodies including drug tablets in the lower part of the oesophagus, and may cause problems in the use of drugs with high acidity (Traş and Üney, 2016).

The most important difference seen in cats is the enzyme difference. Glucuronidation, catalysed by UDP (uridine 5'-diphospho) -glucuronosyltransferase (UGT) enzymes, is an important metabolic process that promotes the conjugation of many different drugs, toxins and endogenous compounds (such as steroids and bilirubin) with glucuronic acid and their elimination into urine and/or bile. Deficient glucuronidation is one of the oldest known pharmacological idiosyncrasies of cats. It has been noted that this deficiency in cats cannot be generalised to all glucuronic acid conjugated drugs and is dependent on the drug structure. In particular, this was observed to affect compounds with a simple planar phenolic structure. It has been shown that phenolic compounds are mainly metabolised in the liver by UGT1A isoforms (UGT1A6 and UGT1A9). It has been reported that cat liver expresses only two different UGT1A isoforms, UGT1A1 and UGT1A2, and has no expression associated with UGT1A6 or UGT1A9 (Papich, 2015).

In addition to enzyme differences, cats also have a deficiency of thiopurine methyltransferase (TPMT) in the erythrocytes. Erythrocyte TPMT activity is significantly lower in cats compared with both dogs and humans. In cat erythrocytes, TPMT appears to have low activity and a monopolar distribution (Foster et al., 2000).

In humans and most other species, N-acetylation, catalysed by the N-acetyltransferase enzymes NAT1 and NAT2, is an important metabolic pathway for a number of arylamine drugs, including isoniazid, various sulfonamide antibiotics, dapsone, hydralazine, and procainamide. However, dogs and all other carnivore species are completely devoid of this metabolic pathway as they lack both genes encoding these enzymes. Cats express NAT1 in small amounts compared to other species, but are lacking in NAT2, which contributes to acetaminophen toxicity (Papich, 2015).

Another species difference between cats and dogs that can lead to adverse reactions in cats after the administration of specific drugs is the susceptibility of feline erythrocytes (haemoglobin) to oxidation and thus to methaemoglobinaemia. Drugs reported to cause methaemoglobinemia in cats include urinary antiseptics containing methylene blue, acetaminophen and related compounds, benzocaine, and propylthiouracil. Feline haemoglobin can contain up to 20 sulfhydryl groups compared to a maximum of four in other species. These sulfhydryl groups are generally reactive and therefore prone to interact with reactive parent drugs or metabolites (Boothe, 1990).

Disadvantages of antibiotic use in cats

Aminoglycoside antibiotics

Ototoxicity, neuromuscular blockade and nephrotoxicity are the most frequently reported side effects of aminoglycosides (Mercer, 2022a). Cats are more sensitive to the nephrotoxic effects of aminoglycosides than other species (Bilgili and Doğan, 1991).

Aminoglycosides may cause ototoxicity, which may manifest as auditory or vestibular dysfunction. Binding to or damage to mitochondria plays an important role in ototoxicity. Vestibular injury leads to nystagmus, incoordination and loss of the corrective reflex. Cats are particularly susceptible to toxic vestibular effects and aminoglycosides should not be applied topically to the ear unless the tympanic membrane is intact (Mercer, 2022a).

Ototoxicity is increased by diuretics, especially furosemide, and concomitant administration of aminoglycosides with diuretics further enhances this toxicity (Mercer, 2022a). Aminoglycosides should not be used together with cephalosporins and furosemide because of the sensitivity to nephrotoxicity in cats. In addition, in case of fever, dehydration, shock, chronic renal failure, liver disorders, the use of these antibiotics is contraindicated as it will increase nephrotoxicity (Şahin and Çamkerten, 2003).

Neuromuscular blockade may be exacerbated when aminoglycosides are administered simultaneously with muscle relaxants and inhalation anaesthetics (Mercer, 2022a).

Amikacin

Amikacin administration is associated with a higher incidence of auditory adverse effects in cats. Amikacin may cause additional nephrotoxicity when

used in combination with cephalosporins, especially this interaction has been more clearly demonstrated with two cephalosporin antibiotics (cephaloridine and cephalothin). Concomitant use with general anaesthetics or neuromuscular blocking agents potentiates the neuromuscular blockade side effect (Plumb, 2011).

In a controlled experimental study (n = 5 per group), amikacin was administered at two dose levels (90 mg/kg/day and 45 mg/kg/day), corresponding to approximately 6-fold and 3-fold multiples of the reported clinical reference dose for humans (15 mg/kg/day), respectively. Cochlear ototoxicity was observed in 3 of 5 cats in the high-dose group after approximately 40.7 treatment days (Christensen et al., 1977).

Streptomisine-dihydrostreptomisine

It has been observed that streptomisine-dihydrostreptomisine is more ototoxic than other aminoglycosides in cats. Therefore, its use in cats should be used with extreme caution or avoided whenever possible (Liman, 1990). High doses of streptomycin cause restlessness, dyspnoea and loss of consciousness. Cats have a special idiosyncrasy to streptomycin and even a normal therapeutic dose can cause nausea, salivation, vomiting and ataxia. When antibiotic treatment is prolonged, vestibular dysfunction can occur with nystagmus, loss of balance and sometimes permanent deafness (Wilkinson, 1968).

Gentamicin

Gentamicin causes cochlear toxicosis (hearing loss) and vestibular toxicosis (hearing and balance loss) in cats (Liman, 1990). Gentamicin should not be used with ampicillin sodium, furosemide, cephalothin sodium, heparin sodium, cefopirin sodium. In case of their use, the toxic effect on kidney and inner ear increases (Anonymous, 2024a).

Tetracycline antibiotics

Tetracyclines cause hypoplasia of teeth and developmental disorders in long bones. In addition, they cause necrosis in the liver, inflammation in the pancreas, destruction of kidney tissue and antianabolic effect by stopping protein synthesis. In cats, tetracyclines may cause symptoms such as high fever, vomiting, diarrhoea and depression when used at recommended doses (Akkan and Karaca, 2003).

Doxycycline

Doxycycline is more effectively absorbed from the gastrointestinal tract than other tetracyclines. This is because minocycline and doxycycline are the most lipophilic active ingredients among the tetracyclines. Doxycycline is eliminated by bile and diffusion into the large intestine. In cats, doxycycline is indicated for the treatment of *Bordetella*, *Chlamydia* and *Mycoplasma* spp. infections (Albarellos and Landoni, 2009). The most commonly described doxycycline-induced side effects in dogs and cats include gastrointestinal system disorders, tooth discolouration and hepatoxicity (Schulz et al., 2013). Oesophageal stricture formation was determined in four cats treated with oral doxycycline, while signs of oesophagitis and ulceration were also observed (German et al., 2005). In another study, 168 cats were given 2 to 24 mg/kg doxycycline daily and 12.8% of the cats showed signs of vomiting under doxycycline treatment. Cats treated with aluminium-containing antacids or antiemetics had a reduced risk of developing vomiting during treatment. In the same study, 17 of 156 cats developed diarrhoea during treatment and 10 of 138 cats developed fever. Doxycycline given by injection increased the risk of developing fever in cats, but tooth discolouration and oesophageal stricture were not observed (Schulz et al., 2013).

Studies in humans and animals have confirmed that the high acidity of the doxycycline solution is the main factor for its irritant effects. While doxycycline hyclate solution (hydrochloride monohydrate) has been reported to be highly acidic, doxycycline monohydrate solution has been found to be considerably less acidic (German et al., 2005). It has been shown that doxycycline treatment with food may reduce gastrointestinal side effects in cats, and therefore this recommendation seems appropriate for application in cats (Schulz et al., 2013).

Oxytetracycline

Gastrointestinal disorders in cats usually occur with therapeutic doses given orally and consist of diarrhoea, colicky pains, vomiting, depression and anorexia (Wilkinson, 1968). In a three-year-old, neutered, male, domestic, shorthair cat treated for *Haemobartonella felis* infection, oral doxycycline administered at 10 mg/kg twice daily was replaced after seven days with oral oxytetracycline at 10 mg/kg three times daily. Approximately 10 days after the initiation of oxytetracycline therapy, dysphagia and regurgitation of solid food and some liquids were observed. Repeated oral administration of doxycycline and oxytetracycline tablets for 17 days may lead to oesophageal retention, potentially resulting in severe esophagitis and subsequent multiple oesophageal strictures (McGrotty and Knottenbelt, 2002). Furthermore, experimental studies have demonstrated that doxycycline and oxytetracycline preparations can induce deep oesophageal ulceration, and it has been emphasised that administration of oral tetracyclines with food or water may reduce the risk of oesophageal injury (Carlborg et al., 1983). Oxytetracycline should be used with caution in patients with renal or hepatic insufficiency, and dose adjustment should be conside-

red based on clinical status, along with close monitoring of renal and hepatic functions (Plumb, 2011).

Fluoroquinolone antibiotics

The use of fluoroquinolones in young animals is known to cause arthropathy. Cartilage damage in young animals occurs due to the chelation of drug molecules with magnesium, which is necessary for the healthy development of the cartilage matrix (Ural, 2021). Fluoroquinolones may cause blindness in cats due to the weak retinal-blood barrier based on breast cancer resistance protein (BCRP) (Traş and Üney, 2016). Fluoroquinolones may also cause neurotoxic effects and convulsions may occur at high doses due to gamma-aminobutyric acid (GABA) receptor antagonism (Mercer, 2022b).

Enrofloxacin

In a study conducted in cats, it was reported that enrofloxacin may cause acute and diffuse retinal degeneration, the visual loss that develops is usually permanent. The retinal toxicity of enrofloxacin in cats appears to be influenced not only by the administered dose but also by the duration of exposure and cumulative retinal drug accumulation. Gelatt et al. (2001) recommended that the commonly used dose of 5 mg/kg once daily should not be exceeded in cats because enrofloxacin may induce acute and diffuse retinal degeneration leading to permanent visual impairment. Subsequently, the other authors have suggested an even more conservative approach, recommending that the total daily dose should not exceed 2.5 mg/kg and that treatment duration should be kept as short as possible, emphasising the role of cumulative exposure in the development of retinal lesions (Saroglu and Erdikmen, 2008). Consistent with this concept, the product information indicates that ocular toxicity has been observed in cats receiving doses greater than 15 mg/kg/day for 21 consecutive days (EMA, 2026). Taken together, these findings suggest that enrofloxacin-associated retinotoxicity cannot be explained solely by a single dose threshold. Rather, both dose magnitude and treatment duration contribute to retinal drug accumulation and toxicity risk, indicating that lower doses may also become hazardous when administered for prolonged periods.

Moreover, it was observed that enrofloxacin treatment may cause age-related retinal degeneration. In general, older cats (>12 years) developed blindness at significantly lower doses than younger cats (<9 years). Altered drug distribution in geriatric cats due to age-related renal or hepatic impairment may result in drug accumulation, high peak concentrations of the drug, or altered metabolism of the drug, which may contribute to retinal degeneration (Wiebe and Hamilton, 2002).

Known risk factors for cats are:

1. High doses of enrofloxacin in plasma concentrations,
2. Rapid IV (Intravenous) administration,
3. Long-term treatment,
4. Advanced age.
5. Other factors may include prolonged exposure to UVA (Ultraviolet A) light during treatment, drug interactions, and altered metabolism or reduced elimination of enrofloxacin leading to drug accumulation (Giguère and Dowling, 2013).

Sulfonamides

Excessive or prolonged administration of sulphonamide may cause poisoning in cats. Acute poisoning may result from oral overdose or rapid IV injection of a sulfonamide Wilkinson (1968). When sulfonamides are administered, they cause the formation of crystals, tubular obstruction and tubular ulceration, haematuria, oliguria and renal colic as a result of precipitation in the renal tubules, collecting ducts, pelvis renalis and lower parts (Şahin and Çamkerten, 2003).

Sulfasalazine

Sulfasalazine is used to treat inflammatory bowel disease in cats. Although the exact mechanism of action for its therapeutic effects in the treatment of colitis in small animals has not been established, it is believed that sulfasalazine alters the course of antibacterial activity after conversion to sulfapapyridine and 5-aminosalicylic acid (5-ASA, meselamine) by bacteria in the gut (Plumb, 2011). Sulfasalazine should not be used in cats because it is converted to aminosalicylic acid in the gastrointestinal tract (Yazar, 2023).

Other Antibiotics

Chloramphenicol

The main toxic effects of chloramphenicol in humans are dose-dependent bone marrow suppression resulting from nonspecific dose-dependent aplastic anaemia or protein suppression. Chloramphenicol toxicity in animals is related to both the dose and duration of treatment, and cats are more likely to develop toxicity than dogs (Prescott and Baggot, 2000). When cats are given daily doses of 50 mg/kg for three weeks, bone marrow suppression can be observed (Mercer, 2022b). Therefore, the duration of treatment should not exceed 10 days, especially in cats. Because chloramphenicol cannot be cleared from the bloodstream as quickly in cats as in other species (Prescott and Baggot, 2000; Anonymous, 2024b).

Metronidazol

Central nervous system (CNS) side effects due to metronidazole use have been reported in humans, rats, dogs and cats. In dogs and cats, central

vestibular and cerebellar dysfunctions resulting in ataxia, nystagmus, head tilt, tremors, and seizures have been commonly reported in cases of metronidazole toxicosis (Olson et al., 2005).

In a study involving two cats, one cat was given a metronidazole dose of 111 mg/kg/day for about 8 weeks, followed by 222 mg/kg/day for 4 days, and the other cat was given 58 mg/kg/day for 6 months. Neurological abnormalities included ataxia, blindness, disorientation, hyperactivity, vertical nystagmus, altered mentation and seizures (Caylor and Cassimatis, 2001). Another study demonstrated that standard oral administration of metronidazole (20 mg/kg metronidazole benzoate, corresponding to 12.4 mg/kg metronidazole base) in cats for 7 days induces DNA damage (genotoxicity) in peripheral blood mononuclear cells (PBMC). Additionally, metronidazole exposure within the therapeutic concentration range (0.4–8 mg/ml) resulted in genotoxic effects in both PBMC and feline T-cell lymphoma cells incubated in vitro (Sekis et al., 2009).

Clindamycin

In cases reported in cats receiving clindamycin, oesophageal injury was observed after oral administration and oesophageal damage was reported to occur when clindamycin capsules (75 mg twice daily) were administered without food and water (Beatty et al., 2006). In a study, it was determined that clindamycin alone produced neuromuscular blockade in vitro and prolonged the effects of non-depolarising agents (Best et al., 1999). When administered together with anaesthetic agents and skeletal muscle relaxants, neuromuscular effects increase. Therefore, concurrent use with these drugs should be avoided (Mercer, 2022c).

Use of anthelmintic drugs and contraindications

Ivermectin

In cats, ivermectin is authorised for heartworm treatment and prevention, ear mite treatment and hookworm treatment. Although ivermectin is generally considered safe for cats, toxicity has been reported in some cats (Avcı and Yıldız, 2023).

Acute poisoning symptoms in cats are observed approximately 10 hours after the overdose occurs. These symptoms include anorexia, mydriasis, tremor, ataxia and paralysis of the hind legs (Avcı and Yıldız, 2023). In one study, clinical signs including mydriasis, blindness, weakness, depressed mentation, tremor, abnormal gait, dysorexia and anorexia were observed in 6 of 20 cats following administration of ivermectin at a dose of 4 mg/kg subcutaneously, which corresponds to approximately a 20-fold overdose compared with the recommended extra-label dose of 0.2–0.3 mg/kg in veterinary practice (Jourdan et al., 2015). In a case report, a Persian kitten exposed to 5 times the treatment dose of ivermectin by its owner developed clinical signs including ataxia, loss of vision, deep respiration, dilated pupils, decreased pupillary reflexes, and lateral recumbency 6 hours later (Sidhu et al., 2019).

Ivermectin has also been observed to cause toxicity due to mutation in the MDR1 (Multi-Drug Resistance 1) gene in some dog breeds (Avcı and Yıldız, 2023). Although the presence of mutation in the MDR1 gene has been investigated in cats showing side effects to drugs carried by P-gp (P-glycoprotein), similar to those in dogs, no clear data have been obtained (Mealey and Burke, 2015).

Use of Antiprotozoan Drugs and Contraindications

Albendazole

Albendazole is a benzimidazole group anthelmintic and antigiardial drug (Plumb, 2011). Albendazole has been associated with bone marrow suppression in dogs and cats, so other drugs should be preferred for giardia treatment in small animals. Adverse effects of albendazole include anorexia, lethargy and bone marrow toxicity. Leukopenia and thrombocytopenia are possible in dogs and cats. Albendazole has an affinity for rapidly dividing cells and can cause toxicity to bone marrow and intestinal epithelium (Papich, 2015).

Use of ectoparasitic drugs and contraindications

Pyrethroids

Pyrethrins cause hyperexcitability with cytotoxicity. The molecular targets of pyrethrins and pyrethroids are similar in mammals and insects. These targets include voltage-gated sodium chloride channels and calcium channels, GABA-gated chloride channels, nicotinic receptors, membrane depolarisation and intercellular gap junctions. Mammals are less susceptible to pyrethrin and pyrethroid toxicosis than insects. This is because mammals have a faster metabolic clearance, higher body temperatures and a lower affinity for pyrethrins/pyrethroids (Ensley, 2018). In some countries, pyrethroid-induced poisoning has been reported to be one of the most common types of poisoning in cats (Berny et al., 2010). Since feline liver is deficient in glucuronide conjugation, cats are more likely to develop pyrethroid toxicosis than dogs (Anadón et al., 2009).

The lethal dermal dose of permethrin in cats is approximately 100 mg/kg and the mortality rate due to pyrethroid poisoning in cats has been reported to be between 2.5–17% (Bahçivan and Oğuz, 2019).

Poisoning can be observed with accidental exposure of cats to permethrin-containing products sold in the form of drops or baths for dogs (Canbar and Yazar, 2020). Most permethrin spot-on products are labelled for use in dogs only and can be obtained without a prescription. Permethrin toxicity usually occurs when a permethrin spot-on product licensed for dogs is accidentally applied, but cats actively grooming or in close physical contact with recently treated dogs may be at risk of toxic exposure (Anadón et al., 2009). In one study, the most common clinical findings in 20 cats exposed to permethrin were muscle fasciculations, tremors and ataxia. Pityalysis, hyperthermia, vomiting and dyspnoea were also observed (Dymond and Swift, 2008). The onset of clinical signs usually occurs within a few minutes to a few hours after exposure but can last up to 24 hours (as a result of dermal absorption and prolonged exposure from grooming) and in some cases up to three or more days (Anadón et al., 2009). It has generally been observed that almost two-thirds of affected cats are one year of age or younger, which may indicate individual or age-related sensitisation to permethrin (Linnett, 2008).

Non-steroidal Anti-inflammatory Drugs (NSAIDs) and Contraindications

Paracetamol

Acute accidental or intentional administration of NSAIDs in dogs and cats is quite common due to their widespread availability and use (Sidhu et al., 2021). Acetaminophen (paracetamol) is a synthetic non-opiate derivative of p-aminophenol, an NSAID widely used for its antipyretic and anaesthetic effects (Court and Greenblatt, 1997). Paracetamol provides pharmacological effect by inhibiting cyclooxygenase (Cox) pathways. In mammals, acetaminophen is converted to non-toxic products in the liver by conjugation with glucuronic acid and, to a lesser extent, sulphate and excreted by the kidneys. A small fraction is metabolised to N-acetyl-para-benzoquinonimine, a highly toxic metabolite, via the cytochrome P-450 enzyme pathway producing acetaminophen (NAPQI) (Allen, 2003). In most mammals, acetaminophen exposure becomes toxic when the glucuronidation and sulphation pathways are saturated and cellular glutathione stores are reduced to less than 70% of normal values. In such cases, NAPQI binds to cellular proteins and membranes, causing disruption of protein function and damage to cell membranes, typically leading to cell damage and death in hepatocytes (Allen, 2003).

Paracetamol poisoning occurs with clinical signs of anorexia, dullness, facial and paw oedema, respiratory problems, haematuria (Pothiappan et al., 2014). There is no safe dose of acetaminophen for cats. The toxic dose has been reported as 50 to 100 mg/kg body weight (BW), but signs of toxicity and death have been observed even at a dose of 10 mg/kg (Aronson and Drobatz, 1996). There are several reasons why cats are more susceptible to acetaminophen toxicosis than other species. Firstly, cats lack a specific form of the enzyme glucronyl transferase, which is required to conjugate acetaminophen to glucuronic acid. For a given dose of acetaminophen, less than 3% acetaminophen glucronide is excreted by cats, whereas humans and dogs eliminate 50-60% as glucronide conjugate. Glutathione stores are rapidly depleted in the liver as well as in the erythrocyte. This glutathione depletion leaves hepatocytes and erythrocytes unprotected from the oxidising effects of the reactive acetaminophen metabolite. Feline haemoglobin (Hb) is prone to oxidation. Methaemoglobinaemia resulting from acetaminophen administration can lead to haemoglobin denaturation and haemolytic anaemia (Aronson and Drobatz, 1996). In case of acetaminophen poisoning in cats, respiratory distress and depression and weakness and signs such as dark brown or pale mucous membranes, icterus and pigmenturia have been reported by owners (Allen, 2003).

Acetylsalicylic acid

Acetylsalicylic acid is the most widely used over-the-counter drug and the most commonly used anti-inflammatory drug in animals (Kore, 1990). Acetylsalicylic acid acts by irreversibly suppressing the Cox enzyme that enables the formation of endoperoxides from arachidonic acid and inhibiting prostaglandin synthesis. It has been reported that the drug permanently reduces both prostaglandin and thromboxane A2 formation but does not affect leukotrienes. The drug is metabolised primarily by the enzyme UDP (uridine 5'-diphospho)-glucronyl transferase in the liver. Since this enzyme is deficient in cats, these animals are predisposed to salicylate toxicity, especially with repeated administration (Karademir and Boyacıoğlu, 2014). Following both oral and intravenous administration, acetylsalicylic acid pharmacokinetics in cats have a relatively slow salicylic acid clearance (4–5 mL/kg/h) and prolonged elimination half-life (22–45 hours) compared to other species. As a result, the recommended acetylsalicylic acid dose is smaller in cats than in other species, and the dose interval should be longer (Lascelles et al., 2007).

For relief of pain and fever, the recommended doses in cats are approximately 10 to 20 mg/kg every 48 hours. Salicylates should be administered with caution to very old and very young cats and those with kidney or liver disease (Kore, 1990). Gastric ulceration occurs readily when acetylsalicylic acid is administered in cats (25–100 mg daily) and the incidence appears to have little relationship to the dose administered (Bugat et al., 1976). Clinical signs of acute overdose may include depression, vomiting, hyperthermia, electrolyte disturbances, metabolic acidosis, bleeding disorders, convulsions, coma and death (Lascelles et al., 2007).

Ibuprofen

Ibuprofen [2-(4-isobutylphenyl) propionic acid] is an NSAID with anti-inflammatory, antipyretic and analgesic properties in humans and animals. Ibuprofen has pharmacological effects similar to other NSAIDs such as acetylsalicylic acid, phenylbutazone and indomethacin. Ibuprofen is commonly used to treat acute and chronic rheumatoid arthritis and osteoarthritis, as well as headache, fever and various joint, musculoskeletal and gynaecological disorders (Khan and McLean, 2012). Toxicity is manifested by gastrointestinal and kidney damage (Kore, 1990). Central nervous system depression, hypotension, ataxia, cardiac effects and seizures may also occur (Khan and McLean, 2012). Intakes greater than 300 mg/kg in dogs or cats have resulted in clinical signs of acute renal failure. Deaths have been reported to the International Animal Poison Information Center after intakes greater than 600 mg/kg in dogs and cats (Kore, 1990). Cats are susceptible to ibuprofen toxicity at about half the dose that cause toxicity in dogs. Cats are particularly susceptible to NSAID toxicity because they have a limited glucronyl conjugation capacity.

Opioid analgesic drug use and contraindications

Morphine

Substances such as morphine suppress the CNS in humans, monkeys and dogs, but cause stimulation in other animal species. Vomiting and clonic muscle spasms in dogs; constipation in cats with CNS stimulation up to the level of insanity; dilation of pupils in cats, sheep and horses; narrowing of pupils to the size of pinheads in humans, rats and dogs are the main symptoms. Since morphine also causes the release of histamine, narrowing of the respiratory tract, redness of the face and neck, and itching are noteworthy (Kaya, 2002). Opioid-related hyperthermia can also occur in cats. Morphine over 1.0 mg/kg may cause hyperthermia in cats (Robertson, 2008). Cattle, goats, horses and cats may show signs of hyperthermia, while rabbits and dogs may develop hypothermia (Plumb, 2011). Species differences in opioid-induced behaviour may be due to differences in the distribution of opioid receptors in the CNS, though the distribution of these receptors in cats is unclear, and more detailed research is required (Kamata et al., 2012). It is a misconception that cats are at risk of experiencing high levels of excitability or 'morphine frenzy' following opioid administration. Recent studies suggest that the behavioural effects of appropriate dosing usually include euphoria, purring, rolling and kneading with the front paws (Robertson, 2005).

Conclusion

The assumption that drugs commonly used in small animal practice are equally safe and effective in cats is fundamentally flawed. Cats possess unique anatomical, physiological, and metabolic characteristics, including limited activity of UGT, TPMT, and NAT1 enzymes, as well as a relatively high proportion of smooth muscle in the distal oesophagus. These species-specific features can markedly influence drug disposition and increase susceptibility to adverse drug reactions. Despite increasing awareness of feline-specific drug sensitivities, the precise mechanisms underlying adverse drug reactions and drug hypersensitivity in cats remain poorly understood. The existing body of literature is limited, highlighting a significant knowledge gap in veterinary pharmacology and toxicology. Addressing this gap will require further research focusing on feline-specific drug metabolism, toxicity mechanisms, pharmacogenetic factors, and individual variability in therapeutic responses. A deeper understanding of these processes is essential for optimising drug safety, improving therapeutic efficacy, and minimising the risk of adverse drug reactions in feline patients. Ultimately, such advances will contribute to improved animal welfare and support the continued development of evidence-based veterinary medicine.

Cats evolved as obligate carnivores with minimal exposure to plant-derived phenolic compounds, resulting in reduced activity of several UGT enzyme families involved in xenobiotic metabolism. Consequently, their capacity to metabolize many drugs, including NSAIDs, differs from that of other species and requires particular clinical attention.

Conflict of interest

There is no conflict of interest.

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> Uloga specifičnih osobina mačaka u sigurnosti lijekova: Rizici povezani s antibioticima, antiparaziticima, NSAID-ima i opioidima. Uvod: Sigurnost lijekova kod mačaka

Büşra SÖYLER* (dopisni autor), kilinnc.busra@gmail.com, orcid.org/0009-0006-9648-7029; Burak DİK, burakdik@selcuk.edu.tr, orcid.org/0000-0003-2738-6911; Halis OĞUZ, halisoguz@selcuk.edu.tr, orcid.org/0000-0002-9236-0630.

Department of Pharmacology and Toxicology, Veterinary Faculty, Selcuk University, 42000 Konya, Turkey

Mačke posjeduju jedinstvene fiziološke, anatomske i metaboličke osobine koje značajno utječu na farmakokinetiku lijekova, uključujući njihovu apsorpciju, distribuciju, metabolizam i izlučivanje. Ove razlike, u usporedbi s drugim kućnim ljubimcima, posebice psima, rezultiraju izrazitom osjetljivošću na mnoge uobičajeno korištene lijekove. Cilj ovog preglednog rada je procijeniti farmakološke rizike povezane s značajnim skupinama lijekova koji se koriste u liječenju mačaka, uključujući antibiotike, antiparazitike, nesteroidne protuupalne lijekove i opioide, uz istovremeno naglašavanje specifičnih fizioloških i metaboličkih karakteristika mačaka koje utječu na sigurnu uporabu pojedinih lijekova. Ključna briga u farmakologiji mačaka je mogućnost nedostataka enzima specifičnih za vrstu, od kojih su najznačajniji glukuronil transferaza i tiopurin metiltransferaza. Ovi nedostaci narušavaju sposobnost jetre da konjugira i detoksicira lijekove, što dovodi do povećanog rizika od nuspojava i sistemske toksičnosti. Nekoliko skupina lijekova koje se obično koriste u liječenju mačaka povezano je s klinički značajnim nuspojavama; aminoglikozidi mogu uzrokovati nefrotoksičnost, dok su tetraciklini povezani s promjenom boje zuba i ozljedom jednjaka. Poznato je da fluorokinoloni izazivaju degeneraciju mrežnice i potencijalnu sljepoću kod mačaka, a acetaminofen je vrlo hepatotoksičan i često fatalan, čak i pri niskim dozama. Primarni cilj ovog preglednog rada je pružiti veterinarima sveobuhvatno razumijevanje farmakoloških rizika povezanih s primjenom lijekova kod mačaka, čime se na temelju informacija olakšava donošenje odluka o propisivanju lijekova temeljenih na činjenicama. S obzirom na specifične fiziološke i metaboličke karakteristike mačaka, treba razmotriti individualizirane protokole doziranja i odgovarajuće terapijske alternative kako bi se povećala sigurnost liječenja i smanjio rizik od teških ili potencijalno po život opasnih nuspojava lijekova.

Ključne riječi: *anatomske i fiziološke razlike; mačke; toksičnost; lijekovi.*