Natural Product Ingestions by Pets

Tina Wismer, DVM, MS

Abstract
Data from the American Society for the Prevention of Cruelty to Animals Animal Poison Control Center (APCC) for 2018 were examined for trends in natural product ingestions by pets. The most dangerous ingestions included 5-hydroxytryptophan (5-HTP), xylitol, alpha-lipoic acid, hops (Humulus lupulus), and cholecalciferol. These products can cause life-threatening clinical signs if timely treatment is not sought. Fortunately, many common ingestions (multivitamins, omega fatty acids, melatonin, probiotics) cause only mild stomach upset. Pet owners should not assume that natural products are safe and should seek veterinary assistance if needed.

Introduction
Using the broadest definition, natural products are any substances produced by living organisms (1). These products may be extracted from cells, tissues, or secretions of animals, plants, fungi, or bacteria (2). The Association of American Feed Control Officials defines natural as a feed or feed ingredient derived solely from plant, animal, or mined sources; the FDA defines natural to mean nothing artificial or synthetic has been added (3, 4). For today’s consumer, the term natural product has been expanded to refer to cosmetics, dietary supplements, and foods produced from natural sources without added artificial ingredients.

The use of natural products by consumers is very common in the U.S., with estimates of overall use ranging from 34% to 76% depending on the therapies included and the population (5). The most commonly used natural products are vitamins and herbal medicines. Natural products are purchased by owners who are concerned about their own health or the health of their pets. Unfortunately, because these are over-the-counter (OTC) products, some owners may not treat them as pharmaceutically active products. Pets commonly get into bottles, dropped pills, and pill minders. Ingestion of natural products by pets mirrors trends on the human side. When a natural supplement becomes popular, there are more opportunities for pets to be exposed. Natural products are also marketed toward pets. The pet supplement industry in the U.S. was estimated at $636 million in 2018 (6). These products many times are in a chewable form, which are very palatable and increase the risk of overdose if pets have access to the container.

There may be a prevailing view that because something is natural, it is automatically beneficial and without harm. The complexity of natural products should not be underestimated and may be dangerous in overdose situations. Although some natural products are very safe, others can be deadly after ingestion (Table 1).

Clinical signs are sometimes consistent from species to species; for example, laxatives can cause diarrhea in all mammals, whereas in other cases, species differences come into play, as in the case of xylitol,
which is toxic to dogs but not to humans or cats. Because cats and ferrets are obligate carnivores, they have fewer hepatic metabolizing pathways, which can increase the risk of toxicosis. They also lack the ability to glucuronidate, which can make them more susceptible to phenolic plant extracts.

The American Society for the Prevention of Cruelty to Animals Animal Poison Control Center (APCC) is a 24-hr veterinary toxicology hotline that serves veterinarians and pet owners. Data collected during 2018 were examined to look for natural product exposures in pets. Although not every potential poisoning is reported to the APCC, incidence rates can be compared to the general population. In 2018, the APCC received phone calls concerning 210,202 exposures to 31,859 different products.

Due to the large number of natural products available, this paper will focus on nonprescription products that are available OTC. It will not cover whole food products, natural insecticides such as boric acid or abamectins (natural fermentation products of soil bacterium), or natural rodenticides such as cellulose-based products or strychnine (alkaloid derived from Strychnos nux-vomica trees). Because the focus is on health improvement products, the risks from nicotine and naturally based cleaning products will also not be mentioned. This paper will concentrate on the most common and the most dangerous natural products that our pets are exposed to (Tables 2, 3).

**Herbals and Plant Derivatives**

Herbs and plant-derived products are complex items that have multiple phytochemicals, or biologically active compounds (7). These compounds can act synergistically, additively, or antagonistically. The active components can vary by the part of the plant (root, leaves, berries, blossoms, bark) and form of preparation (whole herb, teas, capsules, tablets, extracts, and tinctures [alcohol- and nonalcohol-based], essential oils, salves, balms, ointments, and lotions). Growing conditions and environmental stresses (insects, mycotoxins) can also affect the composition and concentration of the phytochemicals (8). Many are potent compounds to deter herbivory (feeding) (9). The lack of standardization of herbal and other natural products may be problematic. In the U.S., herbal medicines for humans are considered dietary supplements and are regulated by the FDA under the Dietary Supplement Health and Education Act of 1994. This act does not require premarket approval and relies on the marketer to ensure the safety and labeling compliance of their products. For animals, regulation is different. Herbal compounds may be classified as foods (if on the Association of American Feed Control Officials list) or as drugs, which would fall under the FDA. Historically, some herbal preparations have been contaminated by pesticides, heavy metals, or other adulterants.

The most common plant-derived compounds that are encountered by animals are essential oils, which can be single oil or combination products. Herbals can also be single plants, such as St John’s wort (Hypericum perforatum) for treating depression, or combination products to treat certain medical conditions. Some herbal products (echinacea [Echinacea purpurea], astragalus [Astragalus membranaceus], garlic [Allium sativum]) can

<table>
<thead>
<tr>
<th>Table 1. Most Dangerous Natural Products for Pets</th>
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</thead>
<tbody>
<tr>
<td>Substance</td>
</tr>
<tr>
<td>5-HTP</td>
</tr>
<tr>
<td>Xylitol (dogs)</td>
</tr>
<tr>
<td>Alpha-lipoic acid (cats)</td>
</tr>
<tr>
<td>Hops (dogs)</td>
</tr>
<tr>
<td>Cholecalciferol</td>
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</tbody>
</table>

Abbreviation: 5-HTP, 5-hydroxytryptophan.

Table 2. Most Common Natural Products Marked for Humans That Are Ingested by Pets

<table>
<thead>
<tr>
<th>Category</th>
<th>Common Ingredients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xylitol</td>
<td>Xylitol</td>
</tr>
<tr>
<td>Cholecalciferol (vitamin D)</td>
<td>Cholecalciferol</td>
</tr>
<tr>
<td>Essential oils</td>
<td>Menthol, tea tree, lavender, eucalyptus</td>
</tr>
<tr>
<td>Multivitamins</td>
<td>Vitamins A, B, C, D, E, and K plus minerals</td>
</tr>
<tr>
<td>Omega fatty acids</td>
<td>Fish oil, flaxseed oil</td>
</tr>
<tr>
<td>Melatonin</td>
<td>Melatonin</td>
</tr>
</tbody>
</table>

Table 3. Most Common Natural Products Marketed for Veterinary Use That Are Ingested by Pets

<table>
<thead>
<tr>
<th>Category</th>
<th>Common Ingredients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joint supplements</td>
<td>Glucosamine, chondroitin, MSM</td>
</tr>
<tr>
<td>Calming supplements</td>
<td>Tryptophan, theanine, valerian, CBD</td>
</tr>
<tr>
<td>Multivitamins</td>
<td>Vitamins A, B, C, D, E, and K plus minerals</td>
</tr>
<tr>
<td>Grass savers</td>
<td>Methionine</td>
</tr>
<tr>
<td>Omega fatty acids</td>
<td>Fish oil</td>
</tr>
<tr>
<td>Probiotics</td>
<td>Lactobacillus spp., Bacillus spp., Bifidobacterium spp.</td>
</tr>
</tbody>
</table>

Abbreviations: CBD, cannabidiol; MSM, methylsulfonylmethane.
stimulate the immune system and promote infection resistance (10). Sleep aids are commonly ingested by pets. These may be a combination of ingredients, including hops (Humulus lupulus), valerian (Valeriana officinalis), tryptophan, chamomile (Matricaria chamomilla), and other herbs (11).

5-Hydroxytryptophan, Tryptophan
Tryptophan and 5-hydroxytryptophan (5-HTP) (Griffonia simplicfolia seed extract, hydroxytryptophan, L-5-hydroxytryptophan, pretonine, oxitriptan) are both supplements that are used to promote sleep. Tryptophan absorption into the CNS is rate limited and causes only mild gastrointestinal (GI) signs. However, 5-HTP is one of the most dangerous natural products for pets.

5-HTP is a precursor to serotonin, a CNS neurotransmitter that is a promoter of platelet aggregation and has stimulatory effects on smooth muscle of the respiratory and GI tracts and cardiovascular system (12). It is used as an OTC remedy for obesity, depression, anxiety, insomnia, premenstrual syndrome, stress, pain, and compulsive gambling (12).

Normally, the body produces serotonin through a series of chemical steps, starting with the amino acid L-tryptophan being converted to 5-HTP via tryptophan hydroxylase in a rate-limiting fashion. Once formed, 5-HTP is converted to serotonin by aromatic L-amino acid decarboxylase (13). Overdoses bypass the rate-limiting step and get directly into the CNS. This can lead to serotonin syndrome due to overstimulation of serotonin receptors.

Serotonin syndrome in humans is a group of symptoms, including cognitive, autonomic, and somatic effects. Even low doses (<3 mg/kg) in dogs can cause clinical signs, which can develop within 30 to 60 min of ingestion. These may include lethargy and ataxia, and higher doses cause serotonin-like syndrome (tachycardia, mydriasis, agitation, vomiting, hyperthermia, seizures, tremors, vocalizing) and potentially death. The minimum lethal dose in dogs is 128 mg/kg (14). Clinical signs may persist for 24 to 48 hr.

Early decontamination may prevent clinical signs. Because of the potential for rapid onset of signs, decontamination should be done under veterinary supervision. Emesis should be followed by activated charcoal. IV fluids should be started and the cardiovascular (heart rate, blood pressure) and neurologic status (disorientation) monitored. Symptomatic care should be given as needed. Acepromazine (0.025 mg/kg IV, titrating up as needed) works well for agitation, methocarbamol (50–150 mg/kg IV) for tremors, and propranolol (0.02 mg/kg IV, titrating up as needed) for tachycardia. Thermoregulation is essential in hyperthermic animals to prevent organ damage or disseminated intravascular coagulation. Cyproheptadine (dogs: 1.1 mg/kg PO or rectally BID–TID; cats: 2–4 mg), a nonselective serotonin antagonist, has been used to reduce the duration of signs.

Prognosis is generally good if rapid and aggressive care is instituted. Disseminated intravascular coagulation is possible in severely hyperthermic animals. Rhabdomyolysis can also be seen from prolonged muscle activity due to tremors/seizures. No long-term effects are expected in those surviving the initial episode.

Hops
Common hop is a member of the Cannabaceae family and is used in beer brewing. Herbally, it is used to soothe mood disturbances and enhance sleep, among other uses. The amount of hops will vary from product to product. Some contain a large quantity of hops and others only a small amount. In many cases, the amount is not noted on the label. Ingestion of hops by dogs can cause a malignant hyperthermia-like syndrome (15). The toxic principle is unknown, but hops contain a number of active constituents: alpha and beta acids (bitter-flavored components) from the resin glands; 3 primary essential oils, including humulene (alpha-caryophyllene), myrcene (beta-caryophyllene), and farnesene; 20 different phenolics; and sulfur-containing compounds. Hops are reported to have both estrogenic (8-prenylnaringenin, a potent phytoestrogen) and serotonin properties. The exact mechanism of action of toxicity is unknown, but theories include inhibition of electron transfer (such as an oxidative uncoupler), alteration of mitochondrial activity, and serotonin syndrome (11).

Signs start within 3 hr and begin with agitation, tachypnea, and abdominal discomfort. There is rapid progression to profound hyperthermia (>108°F) and death. If the dog is still asymptomatic, vomiting should be induced and a dose of activated charcoal administered. Intravenous fluids should be started to prevent myoglobin- or hemoglobin-induced renal failure. If the dog is already hyperthermic, active cooling measures should be instituted (cool baths, fans, chilled fluids). Disseminated intravascular coagulation should be monitored in cases with severe hyperthermia. The urine may be a dark-brown color, and serum creatine kinase may be markedly elevated (11). Dantrolene
(2–3 mg/kg IV or 3.5 mg/kg PO), a direct-acting skeletal muscle relaxant, works the best to reduce body temperature. Signs may persist for 24 to 48 hr after ingestion. Prognosis is poor to guarded, and many affected animals die. Rigor mortis occurs quickly, often within 10 to 15 min (11).

## Caffeine

Caffeine is a methylxanthine. It is a naturally occurring alkaloid found in more than 60 plant species, including tea (*Camellia sinensis*), chocolate (*Theobroma cacao*), coffee (*Coffea arabica*), guarana (*Paullinia cupana*), yerba mate (*Ilex paraguariensis*), and cola (*Cola acuminata*) (16). Caffeine is commonly found in OTC weight loss and “stay awake” products as 200-mg tablets. Guarana is approximately 3.6% to 5.8% caffeine by weight.

Methylxanthines stimulate the CNS and cardiovascular systems, leading to vomiting, restlessness, hyperactivity, tachycardia, and tachypnea. These initial signs can progress to muscle tremors and seizures as well as other cardiac arrhythmias. Methylxanthines are well absorbed orally, and clinical signs start within minutes to 2 hr. Elimination half-lives are variable between species; however, it is 4.5 hr in dogs (17). The minimum lethal dose in dogs is 140 mg/kg and 100 mg/kg for cats. If signs are controlled, most pets will recover in 24 to 48 hr.

If asymptomatic, emesis can be attempted. Activated charcoal should be given if the amount ingested is more than a lethal dose and the patient is not vomiting. IV fluids should be started, and respiratory rate, along with heart rate, rhythm, and blood pressure, should be monitored.

Acepromazine (0.025 mg/kg IV, titrating up as needed) or benzodiazepines (diazepam 0.5–2 mg/kg IV) can be used for agitation, methocarbamol (50–150 mg/kg IV) for tremors, and propranolol (0.02 mg/kg IV, titrating up as needed) for tachycardia.

## Essential Oils

Essential oils are plant derivatives. They are the compounds that give some plants their characteristic odor. All essential oils contain terpenes (organic compounds with very strong odors and tastes) and a variety of other compounds (esters, oxides, phenols, aldehydes, ketones, and alcohols) (18). The toxicity of essential oils is related to both the concentration and type of essential oil.

Essential oils are very popular in both human and veterinary products (Table 4). They are very safe when used under veterinary supervision. Toxicity is dose-related, and problems arise with application of 100% oils applied dermally (especially to wounds or abraded skin) or in the ear (aurally). Cats appear to be more sensitive than dogs to essential oils because they are primarily metabolized in the liver by glucuronide and glycine conjugates. Grooming behavior can also increase toxicity from dermal exposures (19).

Application of the undiluted products can cause skin and oral irritation, lethargy, vomiting, hypersalivation, ataxia, and muscle tremors (20, 21). Essential oils can penetrate the skin and cause peripheral vasodilation, leading to hypotension and hypothermia (22). Exposure to 100% pennyroyal (*Mentha pulegium*) oil or melaleuca (*Melaleuca alternifolia*) oil may also lead

<table>
<thead>
<tr>
<th>Essential Oils</th>
<th>Source</th>
<th>Some Common Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tea tree, melaleuca oil*</td>
<td><em>Melaleuca alternifolia</em></td>
<td>Antibacterial, antifungal, anti-inflammatory, insect repellent</td>
</tr>
<tr>
<td>Lavender</td>
<td><em>Lavandula spp.</em></td>
<td>Sleep, promote calm, decrease stress</td>
</tr>
<tr>
<td>D-limonene, linalool</td>
<td><em>Citrus spp.</em></td>
<td>Flea dips, cleaning products</td>
</tr>
<tr>
<td>Eucalyptus oil</td>
<td><em>Eucalyptus globulus</em></td>
<td>Insect repellent, nasal decongestant</td>
</tr>
<tr>
<td>Menthol</td>
<td><em>Mentha spp.</em></td>
<td>Cough drops, muscle rubs</td>
</tr>
<tr>
<td>Wormwood, absinthe*</td>
<td><em>Artemisia absinthium</em></td>
<td>Anthelmintic</td>
</tr>
<tr>
<td>Citronella</td>
<td><em>Cymbopogum nardus</em></td>
<td>Insect repellent</td>
</tr>
<tr>
<td>Pennyroyal oil*</td>
<td><em>Mentha pulegium</em></td>
<td>Insect repellent, abortifacient</td>
</tr>
<tr>
<td>Cinnamon oil</td>
<td><em>Cinnamomum spp.</em></td>
<td>Muscle rubs, insect repellent</td>
</tr>
<tr>
<td>Thuja*</td>
<td><em>Thuja occidentalis</em></td>
<td>Muscle rubs, abortifacient</td>
</tr>
<tr>
<td>Peppermint oil</td>
<td><em>Mentha x piperita</em></td>
<td>Digestive issues, thunderstorm phobia</td>
</tr>
<tr>
<td>Lemongrass oil</td>
<td><em>Cymbopogon citratus</em></td>
<td>Decrease stress, insect repellent</td>
</tr>
</tbody>
</table>

*Highly toxic in concentrated forms.
to hepatic necrosis, seizures, and death (22). Paralysis (transient) has occurred in small breed dogs when melaleuca oil has been applied down the spine (23).

If diluted properly in a carrier oil, essential oils have a high margin of safety. Caution should be taken to ensure the carrier oil does not increase the risk of ingestion. In veterinary medicine, essential oils are most commonly used for treating flea infestations, hot spots, and other dermatological conditions. These topical products and others, such as perfumes, soaps, shampoos, and lotions, contain low concentrations of essential oils and are not problematic. Essential oils can also be vaporized (heated) or diffused into the air to ease congestion or for aromatherapy. Inhalation is rarely an issue in dogs and cats without underlying respiratory disorders.

With dermal exposures, a bath with liquid dishwashing detergent is recommended. Water alone will just spread the essential oil. The use of vegetable oil can help remove essential oils from the ear canal or eye. Due to a risk of aspiration pneumonia, emesis is contraindicated in most cases of oral exposure (22). Intravenous fluids and antiemetics should be employed if needed. Signs occur from almost immediately up to 8 hr post exposure (22). Mild exposures generally resolve in a few hours. With large exposures, signs can be prolonged over 2 to 3 d due to enterohepatic recirculation. Most animals have a good prognosis with appropriate treatment.

**Cannabidiol**

The main toxic principle of marijuana (*Cannabis* spp.) is a resin called tetrahydrocannabinol (THC); however, the plant contains more than 85 cannabinoids. Cannabidiol (CBD) is a cannabinoid that does not have the psychoactive properties of THC. Two main cannabinoid receptors, CB1 and CB2, have been identified. CB1 receptors, primarily found in the CNS, are associated with psychoactive effects, whereas the peripheral CB2 receptors are associated with the immune system and play a part in inflammation and pain regulation (24, 25).

CB2 selective agonists have been shown to be effective in the treatment of pain, various inflammatory diseases, osteoporosis, and anticonvulsant activity in humans. Cannabinoids have also been suggested for pain control, stress reduction, and appetite stimulation in pets. Two studies have been completed in dogs, and there is some evidence that CBD may be helpful in
alleviating osteoarthritis pain and decreasing epileptic seizures (26, 27).

As with other non-premarket regulated products, there is variable quality, and the APCC as well as the Pet Poison Helpline (Minnesota) have had reports of dogs ingesting CBD-only labeled products and developing the same clinical signs as found in THC ingestion (28). It is unknown if this is a quality control issue, a dosing issue, or if dogs synthesize different metabolites than people.

The most common clinical signs after ingesting products labeled as CBD-only, even at therapeutic doses, are ataxia and lethargy (approximately 10% of cases). With high doses of CBD, urinary incontinence, hyperesthesia, and disorientation along with bradycardia, hypothermia, mydriasis, and tremors can be seen (28). Clinical signs can develop as soon as 30 min after oral ingestion and may last up to 24 to 48 hr.

Many of these patients are showing signs consistent with THC intoxication, and therefore the treatment is the same. If the signs are more than mild, IV fluids should be started. Respiratory function, heart rate, blood pressure, and body temperature should be monitored, and the animal should be kept warm and quiet, with minimal sensory stimuli, and body position rotated q 4 hr if the animal is recumbent. IV fat emulsions (20% solution) may be helpful for severely affected (comatose) animals. If appropriate treatment is implemented, the prognosis is good, and no permanent effects should be anticipated. There have been no deaths reported in pets ingesting CBD-only products.

**Vitamins**

Multivitamins are a very common item that pets ingest. There are hundreds of different versions of multivitamins. Some are formulated for men, some for women, some for children, and others for pets. Although vitamin supplements may contain both natural and synthesized products, for the purpose of this paper, both forms will be considered under the category of “vitamins” due to their frequency of ingestion. Because ascorbic acid and B vitamins are water soluble, any excesses will just be excreted in the urine. There is no accumulation; therefore, no toxicosis develops. Toxicosis can be seen with parenteral or chronic dosing. In dogs and cats, large acute doses of vitamins A, E, and K just cause vomiting and diarrhea. Chronic overdosing is much more concerning, as is vitamin D.

**Cholecalciferol (Vitamin D)**

Vitamin D is commonly ingested by pets. Many people take vitamin D supplements for bone health because it is critical to calcium and magnesium absorption in the body. With overdoses, elevations of serum calcium and phosphorus occur, leading to soft tissue mineralization and renal failure (29).

Cholecalciferol is absorbed from the GI tract and transported in blood bound to carrier proteins. Cholecalciferol is metabolized to 25-hydroxycholecalciferol (calcifediol) and then to 1,25-dihydroxycholecalciferol (calcitriol is the active metabolite). Calcitriol increases serum calcium by increasing intestinal absorption of calcium, stimulating bone resorption, and increasing renal tubular reabsorption of calcium. Elevations in phosphorus can be seen within 12 hr and elevations of calcium, BUN, and creatinine within 24 hr. Vomiting, depression, polyuria, and polydipsia occur approximately 12 to 18 hr post ingestion. Renal failure can occur within 24 to 48 hr due to vasoconstriction and mitochondrial calcification secondary to hypercalcemia (29). Problematic doses can be as low as 0.1 mg/kg (1 IU vitamin D = 0.025 mcg cholecalciferol).

If pills/capsules have been ingested, emesis is recommended within 30 to 60 min. Decontamination should begin with 1 dose of activated charcoal, followed by cholestyramine (300 mg/kg q 8 hr for 4 d). Cholestyramine is a resin that binds bile acids and breaks the enterohepatic recirculation cycle. Baseline (<8 hr post exposure) calcium, phosphorus, BUN, and creatinine values should be obtained for future comparison. Calcium levels should be monitored daily for 4 d, and if no elevations of calcium are seen, no further treatment is needed.

If the animal becomes hypercalcemic, 0.9% NaCl should be started IV. Sodium competes with calcium for reabsorption in renal tubules. The use of a bisphosphonate should be considered to inhibit osteoclastic bone resorption. Either pamidronate (1.3–2.0 mg/kg diluted in 150 ml saline and administered over 2 hr) or zoledronic acid (0.25 mg/kg diluted in 50–100 ml 5% dextrose in water and given over 15 min) should be administered to inhibit osteoclast activity (30, 31).

Other treatments for acute hypercalcemia include furosemide and prednisolone (with fluids adjusted accordingly). Steroids reduce bone resorption, decrease intestinal absorption, and increase renal excretion of calcium. Phosphate binders (aluminum hydroxide 30–90 mg/kg/day PO divided) should also be administered, and the animal should be maintained on a low-calcium diet.
Calcifediol has a long half-life (16–30 d), which may prolong treatment; therefore, blood values should be monitored frequently for up to 6 weeks. Prognosis worsens with prolonged elevations in calcium because lesions from soft tissue mineralization (renal, cardiac, GI) are poorly reversible and may result in long-term sequela.

Other Natural Health Products
There are many other natural products, ranging from coenzyme Q10 to pheromones, to which pets can be exposed. Although most are not a toxicologic concern, the most common and most dangerous are reviewed below.

Alpha-Lipoic Acid
Alpha-lipoic acid (lipoic acid, thiocystic acid, acetate replacing factor, biletan, lipoicin, thioctaid, thioctan) is a fat-soluble, sulfur-containing, vitamin-like antioxidant. It has been promoted as an antioxidant to treat diabetes, HIV, cancer, and “liver ailments.” It increases intracellular glutathione and regenerates ascorbic acid, vitamin E, coenzyme Q10, and NADPH/NADH (citric acid cycle) (32). The danger with pet ingestion is that alpha-lipoic acid is synergistic with insulin, causing hypoglycemia (33).

Therapeutic doses are published for both cats (1–5 mg/kg, not to exceed 25 mg/day) and dogs (up to 200 mg/day) (33). Problems arise with overdoses. Cats are considered to be 10 times more sensitive than dogs, rats, or humans. In cats, 30 mg/kg caused neurologic signs and mild hepatocellular damage (34).

Clinical signs of toxicosis include vomiting, ataxia, hypersalivation, tremors, and seizures. Hypoglycemia and increased liver and renal values have been reported. Signs occur within 30 min to 4 hr and can last up to 24 hr. Decontamination may consist of inducing emesis and administering activated charcoal within 1 hr if asymptomatic. Blood glucose, liver enzymes, BUN, and creatinine should be monitored. Hypoglycemia should be controlled and liver function supported (S-adenosyl-L-methionine, N-acetylcysteine, silymarin) (27). Coagulation parameters should be monitored and plasma transfusions given if needed. Most animals return to normal within a few days.

Omega Fatty Acids
Essential fatty acids are polyunsaturated fatty acids that are found in both marine and fish oils (eicosapentaenoic acid and docosahexaenoic acid) and alphalinolenic acid, which is found in plant oils such as hemp (Cannabis sativa) and flaxseed (Linum usitatissimum). These compounds are considered anti-inflammatory supplements that support cardiovascular health. Fish oils are commonly ingested by pets and, although acute overdoses are generally not serious, they can cause oily diarrhea and present a risk of vomiting and aspiration. Treatment is symptomatic and supportive. The decrease in platelet aggregation and increase in bleeding time seen with chronic dosing of fish oil is not seen in acute overdoses.

Melatonin
Melatonin is a hormone produced in the pineal gland and extrapineal tissues from tryptophan. It is most commonly used as a sleep aid. Melatonin is used therapeutically in dogs at doses of 1.5 to 12 mg TID for alopecia-X, 3 to 6 mg BID for Cushing’s, and 0.1 mg/kg PO TID for a sleep aid. With overdoses, vomiting, somnolence, and lethargy can be seen, but severe signs are not expected. The most serious problem seen with melatonin is that many of the quick-dissolve formulas contain xylitol (see below).

Methionine
Methionine is an essential amino acid for mammals. It is a common ingredient in multivitamins, joint care products, liver “detoxifying” agents, urinary acidification products, and grass saver tablets/chews. In small animals, methionine overdoses are usually seen secondary to ingestion of urinary acidifiers or grass saver products (36). Therapeutic doses for urine acidification are 0.2 to 1 g PO q 8 hr for dogs and 0.2 to 1 g PO q 24 hr for cats.

Vomiting and ataxia within 3 to 6 hr of ingestions were the most common clinical signs associated with methionine toxicosis in dogs and cats. Ataxia has been reported in dogs with doses greater than 210 mg/kg. The toxic mechanism is undetermined, but it is likely from the homocysteine metabolites produced in the liver (37). Dogs ingesting large doses can have
HempRx

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clinical signs that mimic hepatic encephalopathy. Cats given DL-methionine (1 g/kg/day) developed severe hemolytic anemia and Heinz-body formation after 6 to 10 d (38). This is thought to be due to oxidative damage to the RBCs by metabolites of methionine. No deaths in dogs ingesting greater than 7 g/kg have been reported. Most animals recover in 24 to 48 hr.

**Probiotics and Digestive Enzymes**

Probiotics and digestive enzymes have become very popular in both human and veterinary medicine. They are commonly ingested by pets. Fortunately, only mild GI signs are expected.

**Other Concerns**

In many cases, the products themselves may be safe, but the inactive ingredients can be problematic. Gummy or soft chewable forms of vitamins and supplements have become quite popular. The concern with these types of products is the potential of electrolyte abnormalities due to fluid shifts into the GI tract. Large amounts of corn syrup or sugar alcohols will pull free water into the GI tract and cause vomiting and osmotic diarrhea. This large free water loss can lead to hypernatremia and secondary neurologic signs.

Xylitol is a sugar alcohol and natural sweetener. Found in many quick-dissolve and chewable medications, it is considered safe in humans and cats; however, in dogs, xylitol causes a rapid, dose-dependent insulin release followed by hypoglycemia. Signs can include vomiting, weakness, ataxia, depression, hypokalemia, seizures, and coma. Some dogs have developed liver necrosis following ingestion of xylitol (39). The working theory is that xylitol uses the pentose phosphate pathway instead of tricarboxylic acid (Krebs cycle) for metabolism, leading to a decrease in ATP production. Studies in both rats and guinea pigs have shown this to be true, but there have been no studies performed in dogs. Hypoglycemia can start at a dose of 100 mg/kg and liver necrosis at approximately 400 to 500 mg/kg.

Treatment of xylitol ingestion by dogs should include emesis if asymptomatic. Dogs can show signs of hypoglycemia in as few as 30 min or as long as several hours. The time frame difference arises from the different products containing the xylitol. If ingested as powdered xylitol, baked goods, mints, or gums with xylitol crystals on the outside, clinical signs are seen quickly. If clinical signs of hypoglycemia develop, dextrose should be given (bolus with or without a constant rate infusion). Dextrose decreases the need for gluconeogenesis and may be liver supportive. S-adenosyl-L-methionine (precursor for glutathione, methyl donor) and N-acetylcysteine (antioxidant, precursor of L-cysteine that increases glutathione production) may be started, but it is unknown how efficacious they are. Liver values, especially ALT, can increase within hours after ingestion. With liver necrosis, coagulation values should be monitored and plasma given if needed.

**Conclusion**

Natural products remain popular in both human and veterinary medicine. It is important to recognize that appropriate use is critical. Overdoses can be life-threatening to our pets. Because natural products have active constituents, these can act additively, antagonistically, or synergistically with other supplements or pharmaceuticals. Toxicosis can be worsened in some cases if the animal is already on another medication (natural or not). It is important to get a detailed history to help with prognosis. Pet owners need to treat natural products just like any other medication and keep them away from pets so that accidents do not occur.

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**References**


34. Hill AS, Werner JA, Rogers QR, O’Neill SL, Christopher MM. Lipoic acid is 10 times more toxic in cats than reported in humans, dogs, or rats. *J Anim Physiol Anim Nutr (Berl)*. 2004;88:150–156.


