Xylitol Toxicity in Dogs

Christopher M. Piscitelli, MS, DVM
Florida Veterinary Specialists and Cancer Treatment Center
Tampa, Florida

Eric K. Dunayer, MS, VMD, DABT, DABVT
ASPCA Animal Poison Control Center
Urbana, Illinois

Marcel Aumann, DMV, DACVIM, DACVECC
Florida Veterinary Specialists and Cancer Treatment Center
Tampa, Florida

Abstract: Xylitol, a sugar substitute used in sugar-free gum, oral care products, and baked goods, is gaining popularity in the United States. Xylitol consumption is considered harmless to people but is known to cause life-threatening toxicoses in dogs. Dogs that ingest doses of >0.1 g/kg of xylitol are at risk for developing hypoglycemia, while dogs that ingest >0.5 g/kg may develop acute liver failure. Treatment includes dextrose supplementation for hypoglycemia and aggressive monitoring, treatment, and supportive care for dogs experiencing hepatotoxicosis. The prognosis for dogs with uncomplicated hypoglycemia is good, whereas the prognosis for dogs that develop severe hepatotoxicosis is guarded to poor.

Xylitol is a five-carbon sugar alcohol that is commonly used as a sweetener in sugar-free candy and gum, baked goods, desserts, beverages, cereals, and toothpaste.1 Although xylitol is a manufactured sweetener, it is naturally found in low concentrations in such foods as berries, fruits, vegetables, and mushrooms.2 In addition, xylitol is an intermediate product in normal glucose metabolism.

Although xylitol is considered safe in people, it has significant toxic effects in dogs. Xylitol has long been known to cause hypoglycemia in dogs; more recent case reports have implicated it as a cause of acute liver failure.3,4 Hypoglycemia has been reported in dogs ingesting >0.1 g/kg of xylitol, while dogs ingesting >0.5 g/kg are at risk for developing hepatotoxicosis.5 The severity of hepatotoxicity may be idiosyncratic rather than dose dependent because not all dogs that have ingested doses well above 0.5 g/kg have developed liver failure.

According to the ASPCA Animal Poison Control Center, the number of cases of xylitol toxicosis in dogs has significantly increased since the first reports in 2002 (FIGURE 1).

Metabolism

In humans, ingested xylitol is absorbed over 3 to 4 hours.6 In dogs, peak plasma levels of xylitol are reached within 30 minutes of ingestion.7 Studies in rats have shown that most ingested xylitol is metabolized by the liver, where it is oxidized and enters the pentose phosphate pathway.8,9 Most of the xylitol is converted to glucose; a small amount is converted to lactate.8,9 The initial steps of xylitol metabolism after entering the glycolytic pathway of the liver are insulin independent.

Mechanism of Toxicosis

Experimental studies in the 1960s and 1970s demonstrated profound species differences with respect to the effect of xylitol administration on insulin levels. In humans, rats, rhesus monkeys, and horses, the increase in insulin levels after xylitol administration is negligible compared with that after glucose administration.10,11 In contrast, xylitol administration has been shown to cause significantly increased insulin levels in dogs, rabbits, baboons, cows, and goats compared with administration of an equivalent dose of glucose.10,12 No data are available for cats or ferrets.

In dogs, xylitol ingestion may lead to a dose-dependent 2.5- to 7-fold increase in the insulin level compared with ingestion of an equal volume of glucose.7,5 This increase in the insulin level after xylitol ingestion may lead to severe hypoglycemia. Hepatotoxic effects of xylitol, including liver enzyme elevations and hepatic necrosis, have also recently been reported in dogs.5,4

Two mechanisms have been proposed for xylitol-induced hepatic necrosis.7 Hepatic metabolism of xylitol via the pen-
Xylitol Toxicity in Dogs

Clinical Signs and Clinicopathologic Changes
Dogs commonly vomit after ingesting xylitol.1 Hypoglycemia usually occurs within 30 to 60 minutes after ingestion; however, it may be delayed for up to 12 to 48 hours after ingestion.3 The variable onset of hypoglycemia may be related to the type of xylitol product consumed, variations in insulin secretion among dogs, or liver failure. In a case report of xylitol toxicity in eight dogs, hypoglycemia developed 24 to 48 hours after ingestion.5 This delay in hypoglycemia was attributed to ongoing liver failure rather than xylitol’s effect on insulin secretion.1 Clinical signs of hypoglycemia may include altered mentation, dullness, weakness or recumbency, ataxia, altered vision, and seizures.15 Clinical signs of hypoglycemia may progress rapidly in dogs after xylitol ingestion.5

Hyperglycemia has also been reported following xylitol ingestion.5 This may be a result of the Somogyi phenomenon, which occurs with insulin overdose. A rapid and profound decline in blood glucose secondary to excess insulin stimulates the release of diabetogenic hormones such as glucagon, epinephrine, cortisol, and growth hormone, leading to a rebound hyperglycemia.18

Hypokalemia and hypophosphatemia commonly develop in dogs after xylitol ingestion. These conditions are likely due to both an intracellular shift of potassium and increased cellular permeability to phosphate ions secondary to increased insulin levels.3,19 Hyperphosphatemia has been reported in dogs after xylitol ingestion3 as well as in humans with acetaminophen-induced acute liver failure.17 Hyperphosphatemia may be associated with increased mortality in humans with acute liver failure2 and was identified in four of five dogs with liver failure after xylitol ingestion that died or were euthanized.5,4

Two recent case reports investigated a possible relationship between acute hepatic failure and xylitol ingestion in dogs.20 Todd and Powell1 described a case of an English springer spaniel that ingested 3.7 g/kg of xylitol and developed acute liver failure. This dog was discharged after 3 days of hospitalization and made a full recovery. Dunayer and Gwaltney-Brant3 described eight dogs of various breeds that ingested xylitol at doses ranging from 1.4 to 16 g/kg. Six of the eight dogs did not demonstrate any initial clinical signs of hypoglycemia and presented in acute hepatic failure 9 to 72 hours after ingestion.5

Clinicopathologic findings in all nine dogs in these case reports included moderate to severe hypoglycemia, severely prolonged clotting times, mild to moderate thrombocytopenia, markedly increased alanine aminotransferase, mild to moderate hyperbilirubinemia and hyperphosphatemia, and a mild to moderate increase in alkaline phosphatase.3 Five of the eight dogs in the case report by Dunayer and Gwaltney-Brant died or were euthanized. The ingested dose of xylitol did not correlate with survival, as the dog with the highest ingested dose (16 g/kg) lived, and the dog with the lowest ingested dose (1.4 to 2.0 g/kg) died.3

Postmortem Findings
Necropsy results of three dogs with known xylitol toxicoses have been reported.3 All three dogs were icteric, had evidence of coagulation abnormalities (e.g., petechiae, ecchymotic lesions), and had diffuse hemorrhage into multiple organs and body cavities. All three dogs had histopathologic liver changes consistent with acute hepatotoxicosis, including severe acute periportal and midzonal hepatic necrosis with periportal vacuolar degeneration, diffuse hepatic necrosis, and moderate to marked subacute centrilobular hepatocyte loss and atrophy with lobular collapse and disorganization.3 The dogs were not evaluated for bacterial or viral causes of liver disease.3

Treatment
When possible, the dose of xylitol ingested should be calculated or estimated to guide treatment recommendations.
The amount of xylitol in a stick of chewing gum varies depending on the brand and may not be indicated on the label. If the total sugar alcohol content is labeled and xylitol is the first ingredient listed, the xylitol content should be estimated as the total sugar alcohol content. For gum products that do not have xylitol listed as the first ingredient, 0.3 g/piece of gum has been recommended as an estimation of xylitol content. One cup of xylitol weighs approximately 190 g, which can be used as an estimation of xylitol content in baked goods.

Dogs ingesting >0.1 g/kg of xylitol are at risk for developing hypoglycemia, while dogs ingesting >0.5 g/kg are at risk for developing hepatotoxicosis. Dogs should be hospitalized and monitored for hypoglycemia if they have ingested >0.1 g/kg of xylitol. Emesis should be attempted only if the animal is not exhibiting clinical signs of hypoglycemia. Based on the results of an in vitro study, activated charcoal does not seem to bind xylitol significantly; however, the author of the study advocates its use if a large amount of xylitol was ingested.

Dogs ingesting between 0.1 and 0.5 g/kg of xylitol should be monitored for the development of hypoglycemia every 1 to 2 hours for at least 12 hours. If hypoglycemia develops, or if the dog presents with hypoglycemia, an intravenous dextrose bolus of 1 mL/kg of 50% dextrose solution (0.5 g/kg) diluted 1:2 with a crystalloid solution should be administered. A 2.5% or 5% dextrose constant-rate infusion should be started after the intravenous dextrose bolus to maintain a normal blood glucose level. Potassium and phosphorus levels should be checked every 4 to 6 hours and supplemented if the patient becomes hypokalemic or significantly hypophosphatemic. Liver enzymes, total bilirubin level, platelet count, erythrocyte count, and coagulation times should be evaluated on presentation and thereafter monitored every 24 hours for 72 hours.

Dogs ingesting >0.5 g/kg of xylitol should be immediately started on intravenous dextrose supplementation as described above even if their blood glucose level is normal on presentation, and the blood glucose level should be monitored every 2 to 4 hours thereafter. Supplementation of dextrose can be discontinued after 24 hours if the blood glucose level remains within normal limits. Other laboratory monitoring should be conducted as described above. Liver protectants and antioxidants, including N-acetylcysteine, S-adenosylmethionine, silymarin, and vitamin E, should be considered in patients at risk for hepatotoxicosis. These products may be beneficial, although their efficacy has not been proven to affect the outcome in patients with hepatic injury secondary to xylitol toxicosis. Coagulopathies should be treated with fresh or fresh-frozen plasma if hemorrhage is ongoing or suspected, or before an invasive procedure. Whole blood should be used in patients with significant anemia. Secondary complications associated with acute liver failure include hypoglycemia, hepatic encephalopathy, infections, acute renal failure, and acute respiratory distress syndrome.

**Conclusion**

Cases of xylitol toxicity in dogs will likely increase as human use of xylitol-containing products becomes more common. Client education by veterinarians is important because the labels of most xylitol-containing products do not warn users of the potential dangers to dogs of ingesting xylitol.

Xylitol toxicosis should be considered as a diagnostic differential for dogs presenting with hypoglycemia, acute liver enzyme elevations, or acute liver failure. The prognosis for dogs that develop uncomplicated hypoglycemia is good, whereas the prognosis for dogs that develop hepatotoxicosis and liver failure is guarded to poor.

### Key Facts

- Dogs that ingest >0.1 g/kg of xylitol are at risk for developing hypoglycemia.
- Dogs that ingest >0.5 g/kg are at risk for developing hepatotoxicosis and acute liver failure.
- Hypoglycemia usually occurs within 30 to 60 minutes after ingestion.
- Dogs may present with acute liver failure without initial clinical signs of hypoglycemia.
- For dogs that develop acute liver failure, the ingested dose does not appear to correlate with survival.
- For dogs that ingest 0.1 to 0.5 g/kg of xylitol, treatment consists mainly of hospitalization, monitoring and treating for hypoglycemia, and monitoring and treating for liver toxicity.
- For dogs that ingest >0.5 g/kg of xylitol, treatment consists of hospitalization, dextrose supplementation, monitoring, and treating for acute liver failure.
- The prognosis for dogs that develop uncomplicated hypoglycemia is good, whereas the prognosis for dogs that develop hepatotoxicosis and liver failure is guarded to poor.

### References

Xylitol Toxicity in Dogs


CE TEST This article qualifies for 3 contact hours of continuing education credit from the Auburn University College of Veterinary Medicine. To take individual CE tests online and get real-time scores, visit Vetlearn.com. Those who wish to apply this credit to fulfill state relicensure requirements should consult their respective state authorities regarding the applicability of this program.

1. Which product does not commonly contain xylitol?
   a. baked goods
   b. sugar-free gum
   c. potato chips
   d. cereal
   e. toothpaste

2. In dogs, peak plasma levels of xylitol are reached within _______ minutes after ingestion.
   a. 15
   b. 30
   c. 60
   d. 90
   e. 120

3. Dogs that ingest _______ of xylitol are at risk for developing _______.
   a. 0.01 g/kg; hypoglycemia
   b. 0.1 g/kg; hypoglycemia
   c. 0.1 g/kg; liver failure
   d. 0.3 g/kg; liver failure
   e. 0.4 g/kg; liver failure

4. Which statement(s) regarding xylitol ingestion in dogs is correct?
   a. Hypoglycemia commonly develops 30 to 60 minutes after ingestion.
   b. Hypoglycemia can develop up to 48 hours after ingestion.
   c. In a recent case report, hypoglycemia that developed in dogs 24 to 48 hours after xylitol ingestion was thought to be due to liver failure.
   d. Dogs commonly vomit after xylitol ingestion.
   e. all of the above

5. _______ is/are not a common clinical sign of xylitol toxicosis.
   a. Vomiting
   b. Seizures
   c. Ataxia
   d. Cardiac arrhythmias
   e. Altered vision

6. _______ is not a known clinicopathologic finding after xylitol ingestion in dogs
   a. Hypoglycemia
   b. Hyperglycemia
   c. Coagulopathy
   d. Hyperkalemia
   e. Hyperphosphatemia

7. If xylitol is not the first ingredient listed, a stick of gum should be estimated to contain _______ of xylitol.
   a. 0.1 g
   b. 0.2 g
   c. 0.3 g
   d. 0.4 g
   e. 0.5 g

8. How many grams does one cup of xylitol weigh?
   a. 110
   b. 130
   c. 150
   d. 170
   e. 190

9. Which statement(s) regarding the treatment of xylitol intoxication is correct?
   a. Dogs ingesting >0.1 g/kg of xylitol should be hospitalized and monitored for hypoglycemia.
   b. Emesis should only be attempted if the patient is not displaying clinical signs of hypoglycemia.
   c. Dogs ingesting >0.5 g/kg of xylitol should be hospitalized and started on fluids with dextrose supplementation even if the blood glucose is normal.
   d. Liver protectants should be considered in dogs ingesting >0.5 g/kg of xylitol.
   e. all of the above

10. Which statement(s) regarding the prognosis of xylitol toxicosis in dogs is correct?
    a. It is good for dogs that develop uncomplicated hypoglycemia.
    b. It is guarded for dogs that develop uncomplicated hypoglycemia.
    c. It is good for dogs that develop hepatotoxicosis and liver failure.
    d. It is guarded to poor for dogs that develop hepatotoxicosis and liver failure.
    e. a and d