The owner of Piper, a 4-year-old, 23.8-lb (10.8-kg) spayed miniature Australian shepherd crossbreed, reported to an animal poison control center that, one hour earlier, the dog had ingested 225 to 240 fast-dissolve 5-mg melatonin tablets (strawberry flavored).

Presentation
Piper was lethargic and had spontaneously vomited unspecified material that matched the color of the pills. Large, acute overdoses of melatonin in dogs are typically well tolerated, although transient vomiting and lethargy may be noted. However, on examination of the product label, xylitol was found at the top of the “other ingredients” list, causing greater concern.

Each fast-dissolve tablet contained 0.25 g (250 mg) of xylitol, resulting in a dose of 5.2-5.5 g/kg body weight. In dogs, doses exceeding 0.1 g/kg may result in hypoglycemia, with doses greater than 0.5 g/kg carrying the added risk for hepatic necrosis. Because of the massive dose of xylitol consumed and the dog’s clinical state, immediate referral to an emergency hospital was made.

Physical Examination Findings
Piper was presented to a 24-hour care facility 1.5 hours after ingesting the pills. On presentation, the dog had improved and appeared bright, alert, and responsive with normal vital signs. There were no abnormal findings noted on examination nor any apparent lethargy. This is an atypical presentation, as most dogs that have ingested xylitol doses of this magnitude are presented with lethargy or weakness due to hypoglycemia.
Diagnosis

Initial laboratory values revealed normal CBC, moderately elevated alanine aminotransferase (ALT; 312 U/L), mild hypokalemia (3.6 mEq/L), mild hyponatremia (134 mEq/L), and severe hypophosphatemia (0.8 mg/dL), with the remainder of the chemistry profile and coagulation parameters within normal limits (Table).

Hypokalemia and hypophosphatemia are anticipated findings in cases of xylitol toxicosis and are thought to be secondary to increased serum insulin concentrations that cause intracellular shifts. Piper's blood glucose was likely checked immediately on presentation using a glucometer, but this value was not recorded.

Serum chemistry profiles obtained 17 hours post-ingestion revealed a significant increase in ALT at 1289 U/L coupled with a mild increase in activated partial thromboplastin time (aPTT; 114.2 seconds) consistent with hepatocellular injury. Aspartate aminotransferase (AST) was not measured. At 24 hours post-ingestion, ALT became too high to read (>2000 U/L) until 60 hours after ingestion, at which point the level began a slow, progressive decrease (Table). ALT was not diluted.

Treatment & Long-Term Management

On presentation, additional vomiting was induced using apomorphine. The dog produced at least 4 bouts of vomitus that contained visible tablets, both whole and partially dissolved. Based on the condition of the tablets, it was not possible to accurately quantify the amount of product produced.

Because of the risk for severe hypoglycemia and hepatic necrosis, the following therapies were immediately instituted:

- Plasmalyte (IV) with 2.5% dextrose (15-30 mL/hr). Dextrose administration, even in states of euglycemia, may be helpful if hepatotoxic doses of xylitol were ingested.
- Acetylcysteine (140 mg/kg IV loading dose, followed by 70 mg/kg IV q6h at 7 doses) can help restore or maintain glutathione concentrations in the liver.
- Denosyl (225 mg PO q24h; denosyl.com) contains SAMe (S-Adenosylmethionine), which, along with helping to restore glutathione concentrations in the liver, provides support for transmethylation, transsulfation, and aminopropylation pathways.
- Marin Plus Chew for Dogs (1 chew PO q24h; marinplusliver.com) contains silymarin, Vitamin E, and other ingredients that aid in hepatoprotection. Silymarin is thought to act as an antioxidant and free radical scavenger by inhibiting lipid peroxidase and β-glucuronidase.

Daily glucose curves checked glucose every 2 to 4 hours, and the dextrose dose was increased to 5% PRN to maintain euglycemia. Because of the dog's significant increase in ALT and concurrent increase in aPTT on the second day of hospitalization, the following treatments were initiated:

- Vitamin K (5 mg/kg SC q24h)
- Fantoprazole (1.6 mg/kg IV q24h)
### LABORATORY FINDINGS

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Reference Range</th>
<th>Time Since Ingestion (Approximate)</th>
<th>2 h</th>
<th>17 h</th>
<th>24 h</th>
<th>36 h</th>
<th>60 h</th>
<th>72 h</th>
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<td>Albumin</td>
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<td>2.8</td>
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<td>Total protein</td>
<td>5.4-8.2 g/dL</td>
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<td>6.6</td>
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<tr>
<td>ALT</td>
<td>10-118 U/L</td>
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<td>312</td>
<td>1289</td>
<td>&gt;2000</td>
<td>&gt;2000</td>
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<td>1606</td>
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<tr>
<td>Total bilirubin</td>
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<td>Glucose*</td>
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<td>Calcium</td>
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<td>17.6**</td>
<td>16.5**</td>
<td>16.3**</td>
<td>15.5**</td>
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<td>aPTT</td>
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<td>114.2</td>
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<td>WBC</td>
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<td>10.5</td>
<td>10.55</td>
<td>10.7</td>
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</table>

*Blood glucose concentrations while receiving 2.5%-5% dextrose supplementation

**After fresh frozen plasma transfusions

N/A = not available
Two fresh frozen plasma transfusions (125 mL/kg over 3 and 4 hours, respectively)
– Plasma transfusions are typically reserved for cases in which the PT/aPTT exceeds 1.5 times normal values and/or clinical evidence of a coagulopathy is present. In the author’s opinion, they were not yet indicated in this case.

Overall, Piper tolerated hospitalization well with bright response and good appetite. Except for one episode of liquid diarrhea with frank blood (ie, hematochezia) on the third day of hospitalization, no major physical abnormalities were appreciated.

Piper was discharged 4 days' postingestion with Vitamin K1 (25 mg PO q24h for 10 days), Denosyl (225 mg PO q24h for 60 days), Marin Plus Chews (1 chew [based on body weight dosing] PO q24h for 60 days), and omeprazole (20 mg PO q24h for 14 days).

**Prognosis & Outcome**

After discharge, Piper continued to do well at home. She was presented to the same hospital 6 months later with a perforated intestinal foreign body that was successfully corrected via surgery. Pre-anesthetic blood work, including a CBC and serum chemistry profile, revealed no abnormalities. In general, the prognosis following xylitol toxicosis is good to excellent if appropriate medical care is received.

**References**

1. Product data obtained directly from the manufacturer (2015).