

## Pennyroyal oil toxicosis in a dog

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A 7-year-old 30-kg female mixed-breed dog was treated topically for fleas by its owner, using 60 ml of pennyroyal oil (100%) obtained from a local health food store. Less than 1 hour after application, the dog became listless, and the concerned owner attempted to remove the oil by shampooing the dog. The dog began vomiting 2 hours after application. Within 30 hours, the dog had diarrhea, hemoptysis, and epistaxis, and was lethargic. The dog was admitted to a veterinary hospital where, despite supportive therapy, it developed seizures and died. The dog was submitted to the diagnostic laboratory for postmortem examination.

At necropsy, the nutritional and hydration status of the dog was fair. The carcass had a strong aromatic odor. The haircoat was damp and matted, consistent with the application of an oily preparation. Oral mucous membranes and conjunctivae were congested. There was a small amount of blood and saliva in the mouth, and black tarry feces were evident around the anus and on the tail. Several erythematous areas were found on the medial aspect of both thighs and the abdomen.

The trachea contained blood-tinged, frothy exudate. Approximately 200 ml of blood was found free in the thoracic cavity. The lungs were uniformly congested and edematous, and had patchy areas of subpleural hemorrhages. Hemorrhage and congestion also were found in the mediastinum, pericardium, and the walls of the left ventricle. The esophagus, stomach, and small intestine contained blood. The liver was congested with blood and had an accentuated lobular pattern. The caudal liver lobe had a laceration 5 cm long  $\times$  1 cm deep. Patchy subdural hemorrhage was observed in the brain.

The major histopathologic abnormality was in the liver, in which there was extensive areas of hepatocellular necrosis, resulting in almost total

obliteration of the lobular architecture. Vacuolar changes consistent with fatty infiltration were seen in the intact hepatocytes in the portal triad. In addition to the liver lesions, there was congestion, hemorrhage, and edema in the lungs; hemorrhagic foci in the epicardium; and congestion of the mesenteric lymph nodes, spleen, and kidneys.

Because the gross and histopathologic alterations in the liver were suggestive of exposure to a hepatotoxin, a toxicologic examination was performed on liver specimens. The compound identified by gas chromatography-mass spectrometry<sup>a</sup> was pulegone, the main ingredient of pennyroyal oil (Fig 1). A sample of the essential oil of pennyroyal was used to confirm the identification of pulegone. Because evidence of coagulopathy was observed, an anticoagulant screen was performed; however, none of the anticoagulants included in the screen was detected. The final diagnosis was pennyroyal oil toxicosis.

Pennyroyal oil is a volatile oil derived from the leaves and flowering tops of plants of the Labiatae family, commonly known as pennyroyal, squaw mint, or mosquito plant.<sup>1,2</sup> The scientific names of these plants, *Mentha pulegium* and *Hedeoma pulegoides*, derived from the Latin "pulex," meaning flea, acknowledge the long history of pennyroyal oil as a flea repellent.<sup>3</sup> Additionally, pennyroyal oil has been used in folklore medicine to induce menstruation and abort pregnancy in human beings.<sup>1,4,5</sup> It also is used as a fragrance component and flavoring agent.<sup>6</sup>

Pulegone is a ketone, 5-methyl-2-(1-methylethylidene) cyclohexanone, which constitutes 85% of pennyroyal oil, and is primarily responsible for the toxic effects.<sup>1,3,6-8</sup> Studies have shown that (R)-(+)-pulegone is bioactivated in the liver to the putative toxin, menthofuran.<sup>3,6</sup> Evidence of menthofuran was not obtained in this case, using gas chromatography-mass spectrometry and reconstructed ion chromatograms.

The effects of pennyroyal oil appear to be dose related, and histologic changes have been seen in human beings after ingestion of 500 mg of penny-

<sup>a</sup>5890 gas chromatograph and 5970 mass selective detector, Hewlett Packard, Palo Alto, Calif.

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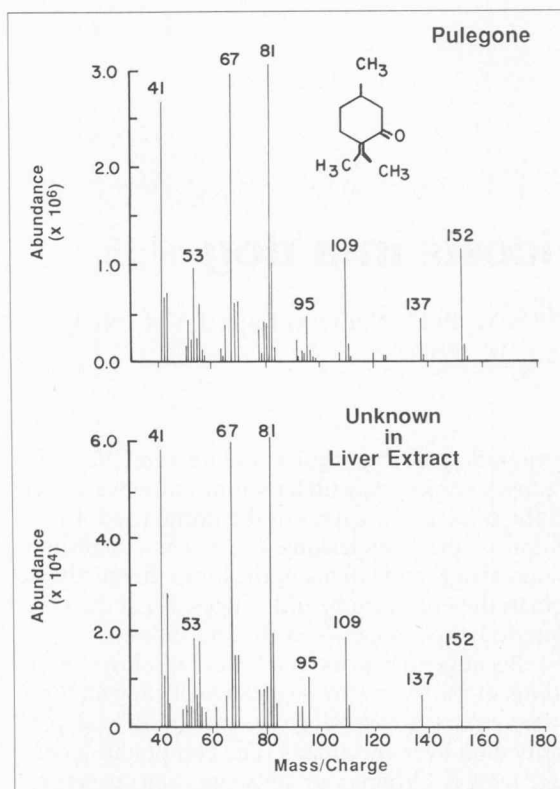


Figure 1—Electron-impact mass spectrum (70eV) of reference pulegone (top) and a compound extracted from liver of the affected dog. The compounds were analyzed on a 15 m × 0.239 mm (ID) DB5 bonded phase capillary column in a gas chromatograph-mass spectrometer. The injector was at 210 C with a 20:1 split. The column temperature was held at 80 C for 0.5 minutes and ramped from 80 to 180 C at 17 C/min. The reference compound and unknown eluted at 2.9 and 2.8 minutes, respectively. The molecular weight of pulegone is 152.

royal oil/kg of body weight (425 mg of pulegone/kg).<sup>8,9</sup> The dog of this report was dermally exposed to an estimated 2,000 mg of pennyroyal oil/kg (1,600 mg of pulegone/kg). To our knowledge, studies designed to determine the dermal toxicity of pennyroyal oil have not been done.

Clinical signs in human beings and other animals have included nausea, emesis, dyspnea, gastrointestinal bleeding, seizures, and coma, followed by coagulation abnormalities, disseminated intravascular coagulation, massive hepatic necrosis, and death.<sup>1,4,10</sup> Histopathologic changes commonly seen are centrilobular hepatic necrosis, diffuse pulmonary damage, and cyst-like spaces in the

white matter of the cerebellum.<sup>3,7-9</sup> An antidote is not available to treat suspected pennyroyal oil toxicosis. Immediate treatment should include induction of emesis followed by administration of activated charcoal and a cathartic. In case of suspected topical overdose, an animal should be washed thoroughly with a mild detergent to emulsify the oil. Shampooing must be repeated until residue is no longer detected. Additional therapy is supportive and based on clinical signs. Because hepatic necrosis is likely to develop within 24 hours, a CBC, determination of electrolytes and creatinine values, liver function tests, urinalysis, and coagulation profiles are suggested. Animals should be observed for development of hemorrhage secondary to coagulation abnormalities and treated with plasma or blood transfusions as needed. Seizures may be controlled by diazepam.<sup>1</sup>

Health food stores and pet shops sell many products containing pennyroyal oil, including flea shampoos, flea powders, and the pure oil itself. Veterinarians should be aware of these products and educate their clients of the possible toxic hazards that exist when such products are used.

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