

Melamine and Cyanuric Acid-Induced Crystalluria, Uroliths, and Nephrotoxicity in Dogs and Cats

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KEYWORDS

- Melamine • Cyanuric acid • Uric acid monohydrate
- Nephrotoxicity • Wheat gluten • Uroliths • Crystalluria

DEFINITIONS

What Is Gluten?

Gluten is a concentrated vegetable protein consisting of a composite of the proteins gliadin and glutenin. These exist, conjoined with starch, in the endosperms of some grass-related grains, notably wheat, rye, and barley. Gliadin and glutenin make up about 80% of the protein contained in wheat seed. Since they are insoluble in water, these proteins can be purified by washing away the associated starch. Worldwide, gluten is an important source of nutritional protein, both in foods prepared directly from sources containing it and as an additive to foods otherwise low in protein.

What Is Rice Protein Concentrate?

Rice protein is a form of concentrated vegetable protein that is made by separating and isolating the protein portion from the carbohydrate portion of rice. It is used in many pet foods as part of the formulation. Rice protein concentrate adds plant proteins that contain little, if any, gluten.

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What Is Wheat Flour?

Wheat flour is made by grinding cleaned wheat grains. Wheat gluten is the primary protein component of wheat flour. Wheat gluten is made by hydrating wheat flour and mechanically separating the wheat gluten from the starch and other components.

What Is Wheat Gluten?

Wheat gluten is the primary protein component of wheat flour. A vegetable protein, wheat gluten is used as a binding agent to thicken gravy in the manufacture of certain types of pet food.

What Is Melamine?

Melamine is an organic base. Its molecular formula is C₃H₆N₆ (**Fig. 1**). It is a small molecule containing a relatively large quantity of nonprotein nitrogen. Melamine-related compounds include cyanuric acid, ammeline, and ammelide (see **Fig. 1**). Although it can be metabolized by some bacteria, it apparently cannot be metabolized by mammals. Melamine is of no known nutrient value to dogs or cats.

Because of its high nitrogen content, melamine has been used as a fertilizer in some parts of the world. It has also been used as an industrial binding agent, a flame retardant, and as a polymer in the manufacture of cooking utensils and plastics (eg, Formica, dishes made of plastic). Addition of melamine and related compounds as ingredients in animal or human food is illegal in the United States. Melamine seems to have a wide margin of safety. If consumed, it is relatively nontoxic to man and animals. In mice and rats, chronic exposure to melamine causes urolithiasis.¹⁻⁵ Chronic irritation of the urothelium by uroliths induces urothelial hyperplasia and subsequent urinary bladder neoplasia in these rodents. Melamine has also been reported to cause diuresis in rats and dogs,^{6,7} crystalluria in mice, rats, and dogs,^{1-3,8-10} and fatal uremia characterized primarily by crystalluria in sheep.¹¹ Apparently melamine and related compounds do not accumulate in the body. Instead, they are rapidly eliminated by the kidneys.¹² Melamine is a common additive in animal feeds in China. Recently it has been determined that a combination of melamine and cyanuric acid are lethal nephrotoxins in cats and dogs.¹³⁻¹⁸ A combination of these two compounds is lithogenic in dogs. The lithogenicity of melamine and cyanuric acid has apparently not been reported in cats; however, these two compounds together have been shown to cause the rapid formation of characteristic microscopic crystals in the urine and renal tubules of dogs and cats.

What Is Cyanuric Acid?

Cyanuric acid is structurally related to melamine (see **Fig. 1**) It is possible that the cyanuric acid in pet food was a result of bacterial metabolism of melamine. It has been used as a stabilizer of chlorine in outdoor swimming pools and hot tubs to minimize the decomposition of hypochlorous acid. Hypochlorous acid tends to lose its potency in sunlight. Cyanuric acid associates with hypochlorous acid and stabilizes its structure but does not affect its antimicrobial potency. Unfortunately, a paucity of data is available about the toxicity of cyanuric acid in mammals. Sodium cyanurate fed chronically to mice and rats caused uroliths, indicating poor solubility.³

BACKGROUND

On March 16, 2007, Menu Foods Inc. located in Ontario, Canada, a manufacturer of pet food, issued a voluntary recall of canned pet food because of concerns about adverse effects of some of their products on kidney function of cats and dogs.^{19,20} The

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