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Acute Toxicity of Nitrofurazone to Channel Catfish, *Ictalurus punctatus*, and Goldfish, *Carassius auratus*

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Nitrofurazone (5-nitro-2-furaldehyde semicarbazone) is a nitrofuran, a group of organic compounds which have inhibitory activity against many Gram-negative and Gram-positive bacteria and against some protozoan parasites (Anonymous 1959). Nitrofurazone is used to control swine enteritis, as a topical antiseptic and to control coccidiosis in domestic animals (Jones 1977). Although not approved by the United States Food and Drug Administration for use with food fish, nitrofurazone has been found effective in fish against external and internal infections by various species of Aeromonas, Pseudomonas and myxobacteria and can be administered either as a food additive or as a bath treatment (Wellborn 1979). Attempts to control the microsporidian parasite Pleistophora ovariae in golden shiners, Notemigonus crysoleucas, with nitrofurazone met with equivocal results (Nagel and Summerfelt 1977).

The following experiment was performed to determine acute toxicity, including lesions, of nitrofurazone to channel catfish, Ictalurus punctatus, and goldfish, Carassius auratus, fingerlings. Toxicity of nitrofurazone to channel catfish was determined with low dissolved oxygen concentrations (2 mg/L) to simulate conditions frequently encountered in channel catfish culture. Information about toxic levels of drugs and the lesions occurring in exposed fish is important to determine the safety of treatment levels and the effects of toxic concentrations.

MATERIALS AND METHODS

All fish used in these experiments were obtained from the Alabama Agricultural Experiment Station. The fish were acclimated to laboratory conditions for at least 7 days prior to use by holding them in aerated 100-L tanks supplied with flowing water. They were not fed for 48 h prior to and during the study. Mortality was less than 2% during acclimation. All tests were conducted under static conditions in non-aerated 50-L glass aquaria containing dechlorinated municipal water. Water characteristics were measured by the methods described by

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Boyd (1979) and were as follows: total alkalinity, 27.0 mg/L; total hardness, 38 mg/L; pH, 7.8±0.2; and temperature, 26°C ± 2°C for the channel catfish and 22°C ± 1°C for the goldfish. Dissolved oxygen (DO) concentrations were measured every 24 h with a YSI oxygen probe; minimum DO concentrations during goldfish and channel catfish exposures were 7.0 mg/L and 2.0 mg/L, respectively.

Nitrofurazone was obtained from Eaton Veterinary Products, Norwich, New York, as a yellow crystalline powder containing 4.59% active ingredient. The nitrofurazone was dissolved in each tank immediately before starting the test. Ten fish were placed in each aquarium and checked every 2 h during the first 12 h and at intervals of 12 h or less thereafter for 100 h. Dead fish were removed upon observation.

The channel catfish were of uniform size and averaged 8.5 cm in total length and 4.2 g in weight. Two tests were performed with channel catfish. In the first experiment the concentrations of nitrofurazone were 0, 10, 18, 32, 57, 75 and 100 mg/L. In the second experiment the concentrations of active ingredients used were 0, 10, 13, 17, 23 and 30 mg/L.

The goldfish averaged 3.3 cm in total length and 1.3 g in weight. Nitrofurazone concentrations of active ingredient for the goldfish exposures were 0, 50, 63, 79, 100, 126, 159, 200, and 251 mg/L.

The concentration-response relationship for each observation period was determined using a computer program (PROBIT procedure; SAS Institute, Inc. 1982). Toxicity curves (LC50 versus time) were plotted as a graphical summary of the mortality data (Sprague 1973).

Skin, gill, and trunk kidney samples from channel catfish and whole goldfish were fixed in Bouin's fluid. Paraffin sections were stained with hematoxylin and eosin and examined with a light microscope.

RESULTS AND DISCUSSION

The LC50 values for channel catfish ranged from 84 mg/L for 4 h to 19 mg/L for 48 h (Fig. 1). The 48-h LC01 (lethal concentration to 1% of the fish) for channel catfish was 13.5 mg/L (95% confidence interval, 8.3-15.6 mg/L).

The LC50 values for goldfish ranged from 178 mg/L for 7 h to 71 mg/L for 96 h (Fig. 1). The 48-h LC01 for goldfish was 48.4 mg/L (95% confidence interval, 29.7-57.2 mg/L).

Channel catfish exposed to concentrations of 30 mg/L or more and goldfish exposed to 63 mg/L or more exhibited an immediate coughing response. Within 12 h, these concentrations of nitrofurozone caused strands of mucus to trail from the gill

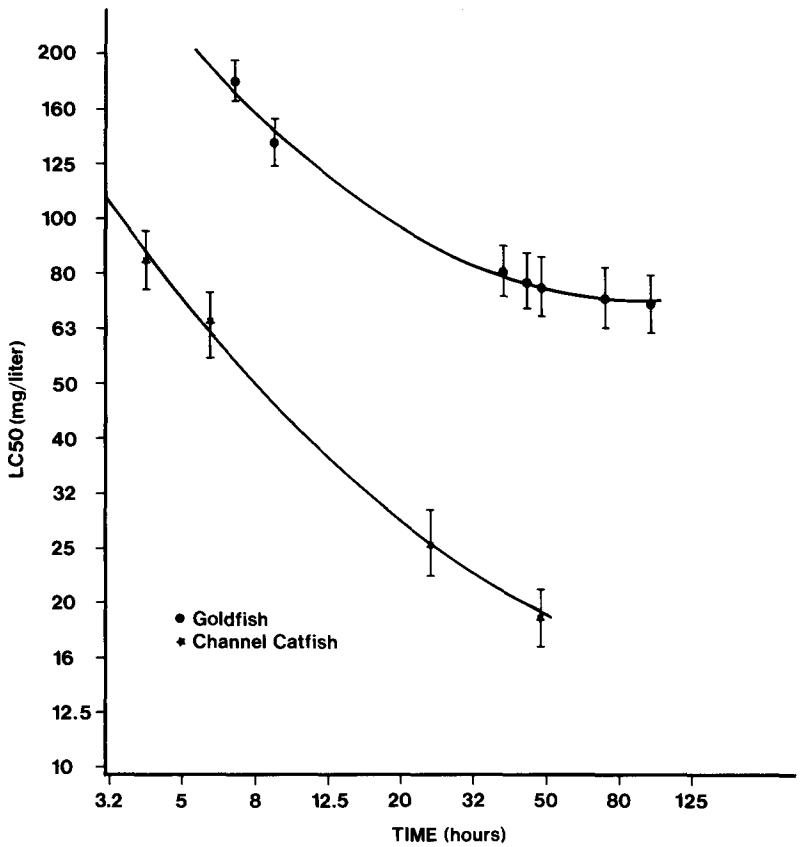

Figure 1. Nitrofurazone LC50 plotted against time of exposure for channel catfish and goldfish. Vertical lines indicate the 95% confidence intervals.

chambers and other body surfaces of both species. Moribund fish hung listlessly at the surface and exhibited exaggerated opercular movements. During the hour preceding death, fish exposed to these high concentrations swam erratically, and some of the channel catfish hung motionless, exhibiting muscle spasms.

After 48 h, inflammation, indicated by lymphocyte infiltration, was evident in the epidermis of channel catfish exposed to 17 mg/L (Fig. 2b). After 100 h, there was focal epidermal necrosis (Fig. 2c), the epidermis in eroded zones being only 1-3 cells thick and covered with a thick layer of mucus (Fig. 2d). Alarm substance cells were either atrophied or missing. The underlying musculature was edematous and the muscle cell nuclei enlarged. The trunk kidney and gills appeared normal.

Treated goldfish dying during the first 48 h of exposure had more mucus on their gills than the control goldfish. Hydropic

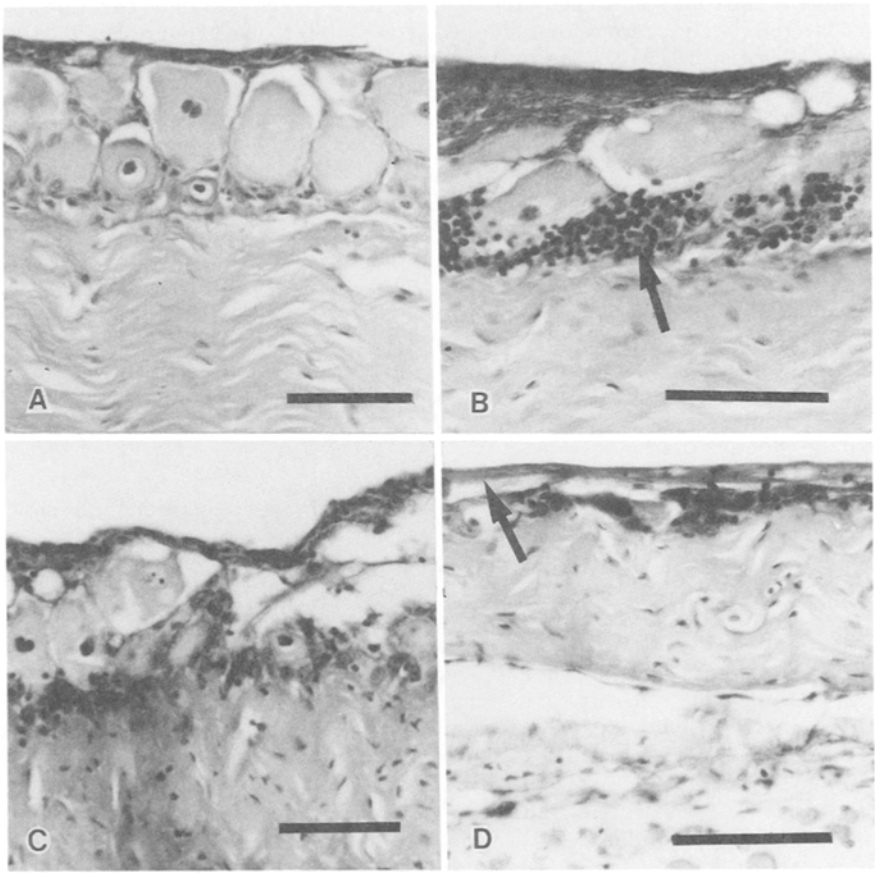

Figure 2. Sections of skin from control channel catfish and channel catfish exposed to 17 mg/L Nitrofurazone (scale line = 50 um). a) Control with normal alarm substance cells (arrows). b) Epidermis is infiltrated with lymphocytes (arrow) after 48 h. c) Epidermis is necrotic and exfoliated after 100 h. d) Another area of eroded epidermis is covered with a thick layer of mucus (arrow) after 100 h.

degeneration and partial detachment of the pharyngeal epithelium and edema of the gill lamellae occurred in some specimens. Skin lesions were not apparent in goldfish.

Under the conditions of this study, nitrofurazone was approximately four times more toxic to channel catfish than to goldfish. Goldfish are also more resistant to nitrofurazone than adult Cuban topminnows, Poecilia vittata, and Mexican molly, Poecilia mexicana, which were all killed in 30 mg/L in 4.0 and 3.3 h, respectively (Baldwin 1980). Because of the variation in toxicity between species, a safe level must be established before using this drug on a different species.

The concentrations of nitrofurazone usually recommended for use in prolonged bath treatments range from 5 mg/L (Wellborn 1979) to 10 mg/L (Herwig 1979). These levels would be safe for use with channel catfish even under the low DO conditions used in our tests. Goldfish can tolerate much higher concentrations of nitrofurazone than the recommended treatments, but whether increased concentrations would significantly improve efficacy of the treatments is not known.

Skin and muscle lesions observed in channel catfish in this study were similar to the early stages of those described by Mitchell et al. (1978) in channel catfish exposed to nifurpirinol, a related compound. Comparable lesions were not reported in other studies with nitrofurans and did not occur on goldfish during our toxicity tests. The reason for the sensitivity of channel catfish to the skin-lesion-producing effects of nitrofurans should be determined.

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