Toxic effects of the fish drug acriflavine on ampullary electroreceptors of catfish

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Abstract—The fish anti-ectoparasite drug acriflavine proved to damage ampullary electroreceptor organs in the transparent catfish, *Kryptopterus*. We tested concentrations of 0.5–10 mg/l, and recorded both morphological changes and electrosensitivity in two types of experiments: short-term (2 h) with continuous monitoring and long-term (weeks) with occasional testing of receptor functioning. At the recommended therapeutical concentration (10 mg/l) and lower, the electrosensitivity is abolished within minutes to 0.5 h. The spontaneous spike rate is affected less. Recovery takes place at the lower concentrations only and even then is only partial (less organs, lower electrosensitivity). Most organs degenerated visibly in 1–3 days. Many receptors degenerated beyond recovery, leaving gaps in the original pattern. Some surviving organs have, after 15 weeks, a far too low electrosensitivity. The acriflavine is thought to damage the receptor cells rather than the nerve fibres.

Keywords: *Ictalurus nebulosus*; *Kryptopterus bicirrhis*; sensory transduction; ampullary electroreceptor; siluridae; skin; trypaflavine.

1. INTRODUCTION

The drug acriflavine, also called trypaflavine, is used frequently to combat protozoan ectoparasites like *Ichthyophthirius*, *Chilodonella* and *Costia* in aquarium fishes. In particular, newly imported batches of fish are treated on a routine basis, often with a cocktail of drugs, either to treat or to prevent an outbreak of ectoparasites.

Acriflavine consists of a mixture of two related substances: 3,6-diamino-10-methylacridinium and 3,6-diaminoacridinium. It is sold in two forms: the neutral form, also called ‘neutral trypaflavine’ or ‘Euflavine’, and the acid form, acriflavine–HCl, also called ‘acid trypaflavine’ or ‘Panflavin’ (Budavari *et al.*, 1989). Acriflavine was introduced by Schäperclaus in the 1930s as a synthetic and hence cheap alternative to quinine. As a drug against ectoparasites, it even proved to be superior to quinine. Since then, acriflavine (HCl) is mentioned as a cure against
ectoparasites in most books on fish pathology, usually for application as a long-term bath.

Recommended concentrations, however, vary over a wide range. Schäperclaus (1954) studied the action of concentrations of 100 µg/l, and 1, 10 and 100 mg/l on guppies (*Poecilia reticulata*), and found that the animals withstood the treatments up to 10 mg/l for at least 2 days. Following Schäperclaus, most authors recommend these values for both the therapeutic concentration and the duration of treatment (e.g. Pinter, 1968; Mawdesley-Thomas, 1972; Schäperclaus, 1979, 1990; Amlacher, 1981). Herwig (1979) mentioned 10 p.p.m. for 2 h of the acid form and states that it is not as safe as the neutral form. Van Duijn (1973) recommends that the neutral form should be used, in concentrations of 0.02–0.04 mg/l, i.e. much lower than the other authors.

The present study was prompted by the occurrence of empty electroreceptor ampullae in a batch of transparent catfish, *Kryptopterus bicirrhis*, treated with acriflavine. Ampullary electroreceptors occur in freshwater silurids and in several families of electric fish, and are part of the octavolateralis sensory system (for a review, see Bretschneider and Peters, 1992). The superficial position of these sense organs in the integument makes them sensitive indicators of toxic substances, such as cadmium and pesticides (Peters *et al.*, 1989, 1995). Observation of the effects of intentional poisoning might further yield clues as to the normal functioning of skin sense organs as well as the mode of operation of the toxic substances.

2. MATERIALS AND METHODS

We tested the long-term influence of acriflavine (days to months) on the transparent catfish because (i) we found deleterious effects in this fish species and (ii) because these fish are so transparent that the skin can be viewed by transmitted-light, bright-field microscopy. Most suited for observation of the electroreceptors is the long, thin and transparent anal fin. Functioning of the receptors was measured at intervals of 1 day or more. At the same time, photographs and video recordings were made.

In addition, we tested acriflavine on the electroreceptors of the catfish species *Ictalurus nebulosus*. This fish is so large as to allow chemicals to be added in a rubber ring fitting tightly to the skin (Peters *et al.*, 1988, 1989). In this experiment, the neural activity (spontaneous firing rate and electrosensitivity) of the electroreceptor organs was monitored continuously.

Measurements, photographs and video recordings of the experimental animals made just before the addition of acriflavine served as controls; in addition, we recorded from two non-treated *Kryptopterus* from the stock tanks during the first days of the experiment.

2.1. Long-term experiments

To test the long-term influence of acriflavine on electroreceptors, we applied several concentrations of acriflavine on small batches of young, adult transparent catfish,