IL-4

Discovery and Development of Natural Products for Controlling Noxious Bacteria in Freshwater Aquaculture

N. P. Dhammika Nanayakkara

National Center for Natural Products Research, Research Institute of Pharmaceutical Sciences, School of Pharmacy, University of Mississippi, University, MS 38677, USA
E-mail: dhammika@olemiss.edu

The uptake of certain natural compounds released by cyanobacteria (blue-green algae) imparts off-flavors in the flesh of freshwater fish raised in production ponds and reservoirs in the tropics and during the warm months in temperate zones. These off-flavors can render fish unpalatable and unmarketable. Although several natural compounds can cause off-flavor problems the monoterpenes, geosmin and 2-methylisoborneol (MIB) have been identified as the metabolites responsible for the majority of episodes. MIB imparts a "musty" or "lagoon" off-flavor whereas geosmin causes "earthy" or "woody" off-flavors. While these compounds are not harmful to fish or humans at levels encountered in aquatic systems they can be detected by humans in fish at concentrations below 0.1 parts per billion.

The MIB producing cyanobacterium, *Planktothrix perornata* [Skuja] [previously designated as *Oscillatoria* perornata (Skuja)], causes a majority of off-flavor problems in channel catfish (*Ictalurus punctatus*) production ponds in the southern United States. Depending on the frequency, off-flavor problems can cost producers as much as $25-65 million annually. One management approach for the mitigation of musty off-flavor in farm-raised channel catfish is the application of chemicals to production ponds to kill or prevent the growth of undesirable cyanobacteria. Currently, only copper-based compounds, such as copper sulfate and chelated copper compounds, and the herbicide diuron are approved by United States Environmental Protection Agency (USEPA) for use in fish production ponds for managing musty off-flavor episodes. Copper-based products and diuron are limited in their usefulness in controlling cyanobacteria due to their accumulation in the environment, lack of selectivity towards noxious cyanobacteria, and the small margin of safety between phytotoxic concentrations and ichthyotoxic concentrations.

As part of a research program to discover natural product-based algicides for the selective control of cyanobacteria, a large number of natural products and their analogs have been evaluated. Among the compounds tested, optimum activity and selectivity were shown by 9,10-anthraquinone and 2-methyl-9,10-anthraquinone. However, due to their extremely low solubility in water these two compounds were found to be ineffective as selective algaecides to control the abundance of *P. perornata* in catfish production ponds. In an effort to increase the utility of anthraquinones as potential selective algicides, several structural modifications to the anthraquinone nucleus were carried out to retain the activity and increase the solubility in water. Development work was performed on the most promising compound to evaluate its viability as a safe alternative for controlling *P. perornata* in catfish production ponds.