Studies of Fish Responses to the Antifoulant Medetomidine

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ABSTRACT

Growth of marine organisms, fouling, on man-made constructions submerged in the water is regarded as a major problem. For vessels, fouling increases drag and thereby fuel consumption, wherefore antifouling paints are used. Traditionally, they contain toxic compounds, and several of these have unwanted effects in the environment. Today the search for environmentally acceptable and efficient alternatives is intense.

Medetomidine, originally used as a veterinary sedative, inhibits barnacle settling at nanomolar concentrations. It is presently under evaluation for use as an antifouling agent. The studies within this thesis were performed to investigate medetomidine responses in fish. The focus was to identify early effects, occurring from low concentrations. Studies have been performed in the species rainbow trout, Atlantic cod, turbot, Atlantic salmon and three spined stickleback. Exposure time vary from 1 up to 54 days, and a set of parameters have been investigated including biochemical biomarkers, growth and related parameters, behaviour and large scale gene expression.

Paleness is the most obvious effect of medetomidine in fish and appears from 0.5 to 50 nM, depending on species. Colour was observed and quantified, and the function of melanophores (pigment cells) after long term exposure to medetomidine was investigated. It is suggested that melanophores are functional after treatment, and thus the colour change may be reversible. Although not lethal per-see, paleness may have consequences for fish predator-prey interactions (camouflage), social signalling and UV protection.

Medetomidine also showed to affect the activity of the hepatic enzyme Cytochrome P4501A (CYP1A), measured as EROD activity. A minor increase in activity was observed *in vivo* in several of the investigated species. *In vitro*, medetomidine showed instead to be a potent inhibitor of EROD activity with median inhibition values (IC50) in the nanomolar range. An inhibited CYP1A activity may interfere with fish detoxification of toxicants abundant in the aquatic environment.

No significant effects were found on growth rate, but the results indicate lowered blood glucose levels and decreased liver size after medetomidine treatment and thus a shift in carbohydrate metabolism. The large scale gene expression study revealed no significant differences among treatments. We found no effects on glutathione or glutathione dependent enzymes in any of the studies. In the behavioural studies, fish were less active and had less appetite in medetomidine treatments compared to control. Medetomidine had no effects on investigated antioxidant enzymes and showed no cytotoxicity.

Among the responses studied within this thesis, paleness and inhibition of EROD activity are perhaps the most important. These effects appear early and are clear and consistent among several species.

Keywords: Fish, Medetomidine, Antifouling, Ecotoxicology, Biomarker

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