The Mediterranean sponges *Aplysina aerophoba* and *A. cavernicola* accumulate brominated isoxazoline alkaloids including aplysinamisin-1 (1), aerophobin-2 (2), isofistularin-3 (3) or aerothionin (4) at concentrations up to 10% of their respective dry weights. In laboratory feeding experiments employing the polyphagous Mediterranean fish *Blennius sphinx* crude extracts of both *Aplysina* sponges were incorporated into artificial fish food at their physiological concentrations (based on volume) and offered to *B. sphinx* in choice feeding experiments against untreated control food. In addition to the *Aplysina* sponges, extracts from nine other frequently occurring Mediterranean sponges were likewise included into the experiments. Both *Aplysina* species elicited strong feeding deterrence compared to the other sponges tested. Bioassay-guided fractionation of *A. cavernicola* yielded the isoxazoline alkaloids aerothionin (4) and aplysinamisin-1 (1) as well as the 3,4-dihydroxyquinoline-2-carboxylic acid (8) as major deterrent constituents when tested at their physiological concentrations as present in sponges. Aeroplysinin-1 (5) and dienone (6), however, which are formed in *A. aerophoba* and *A. cavernicola* from isoxazoline precursors through bioconversion reactions upon tissue injury showed no or only little deterrent activity. Fractionation of a crude extract of *A. aerophoba* yielded aerophobin-2 (2) and isofistularin-3 (3) as major deterrent constituents against *B. sphinx*. We propose that the isoxazoline alkaloids 1–4 of Mediterranean *Aplysina* sponges as well as the 3,4-dihydroxyquinoline-2-carboxylic acid (8) (in the case of *A. cavernicola*) act as defensive metabolites against *B. sphinx* and possibly also against other predators while the anti-bacterically active bioconversion products aeroplysinin-1 (5) and dienone (6) may protect sponges from invasion of bacterial pathogens.

**Key words:** Chemical Defense, Fish Feeding Assay, *Aplysina* Sponges