

# Chemical Defense of Mediterranean Sponges *Aplysina cavernicola* and *Aplysina aerophoba*

Carsten Thoms<sup>a</sup>, Matthias Wolff<sup>fb</sup>, K. Padmakumar<sup>c</sup>, Rainer Ebel<sup>a</sup>,  
and Peter Proksch<sup>a,\*</sup>

<sup>a</sup> Institut für Pharmazeutische Biologie, Universität Düsseldorf, Universitätsstraße 1,  
Geb. 26.23, D-40225 Düsseldorf, Germany. Fax: +49-211-81-11923.  
E-mail: proksch@uni-duesseldorf.de

<sup>b</sup> Zentrum für Marine Tropenökologie, Fahrenheitstr. 6, D-28359 Bremen, Germany

<sup>c</sup> Department of Aquatic Biology and Fisheries, Kerala University Campus, Kariavattom,  
Trivandrum-695581, India

\* Author for correspondence and reprint requests

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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 antibiotically 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