Diving into the chemistry of sponge exo-metabolomes: contribution of brominated specialized metabolites

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SESAM project

Context

- Sponges produce **structurally diverse specialized metabolites** known for their biological/pharmacological potentials.[1,2] In particular, the Mediterranean sponges ***Aplysina cavernicola*** and ***Agelas oroides*** produce **brominated** alkaloids with antimicrobial/anti-biofilm properties.[3,4]
- A few targeted studies, performed on Caribbean species from the same genus, reported that the most abundant brominated alkaloid (e.g. aerothionin, oroidin) were detected in the seawater surrounding the sponges (●●●).[5,6]
- Hence, such exo-metabolites (**EM**) could be collected from the seawater without destroying the sponge biomass.

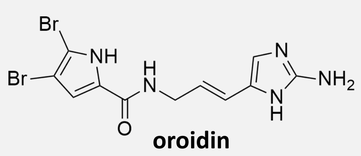
What is the proportion (diversity & quant.) of specialized metabolites released by *A. cavernicola* & *A. oroides* in their surroundings?

Aplysina cavernicola (Vacelet, 1959)

aerothionin

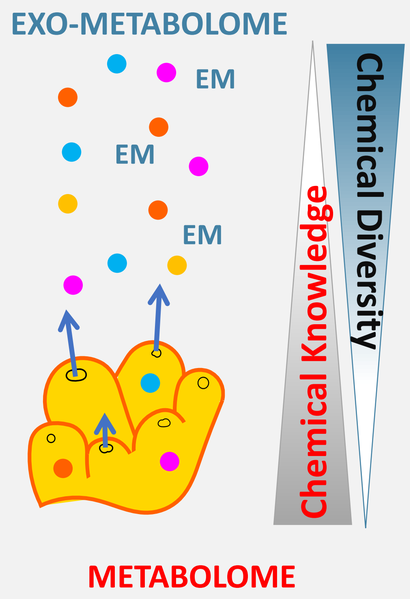
Bromotyrosine spiroisoxazoline alkaloids

Agelas oroides (Schmidt, 1864)

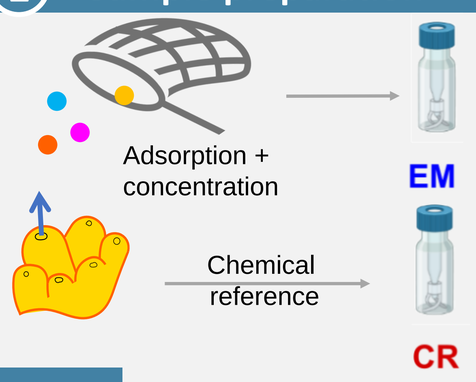


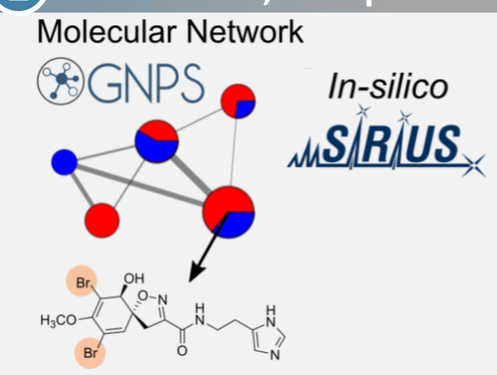
oroidin

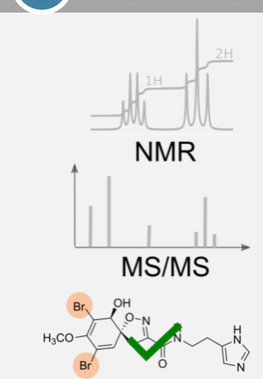
Bromopyrrole alkaloids

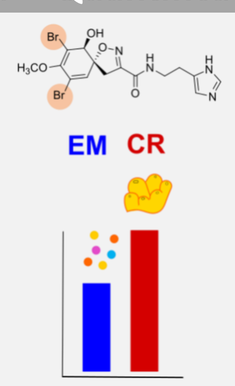


1 Sample preparation — MS² acquisition & processing — 2 Annotation, Dereplication — 3 Identification & Quantification



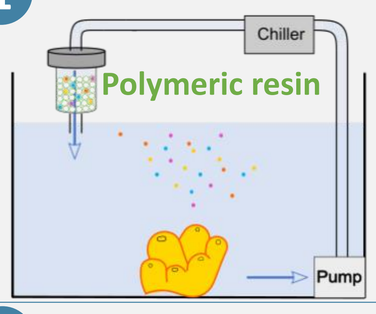






Results

1 Exo-metabolites (EM) concentration

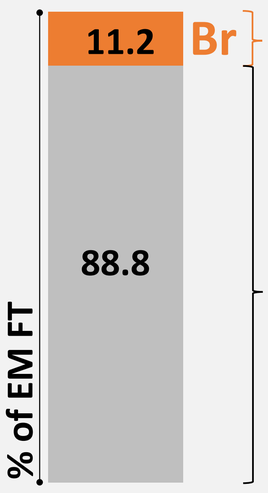


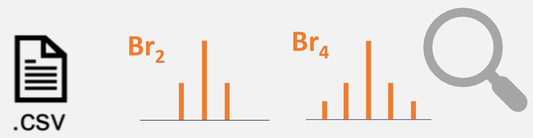
- Comparison of different polymeric resins

→ Solid phase selection according sponge chemistry

- Variation of the experiment duration
- Metabolite adsorption with/without stress

2 Chemical diversity of *A. cavernicola* EM

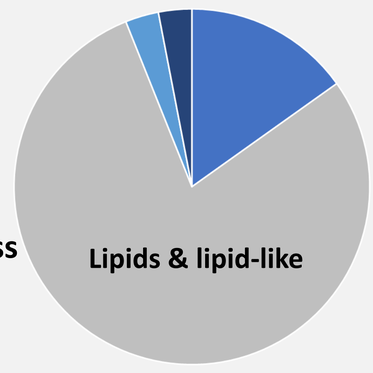




Analysis of Mzmine extracted features
MS isotopic pattern

Reproducibly detected → SIRIUS

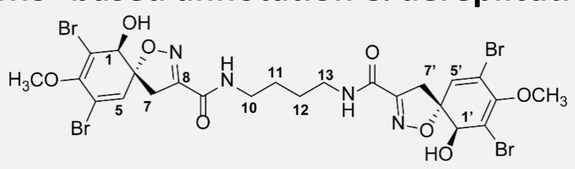
Chemical superclass
Sirius score > 100

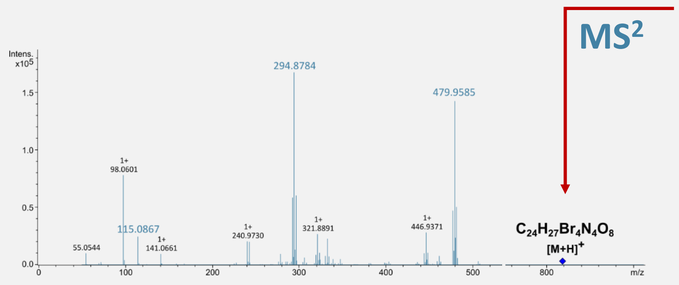


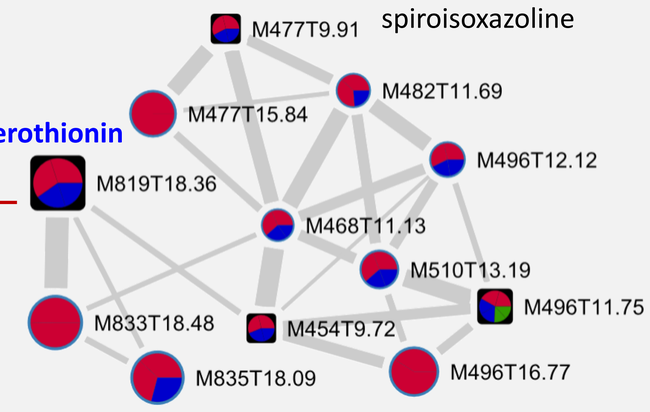
- **11%** of the total detected EM features were found to be **brominated** (structures with 2 /4 Br) & could correspond to ***A. cavernicola*** **specialized metabolites.**
- **79%** of the reproducibly detected EM features belong to the class of **lipids and lipid like molecules.**

3 Identification of brominated exo-metabolites

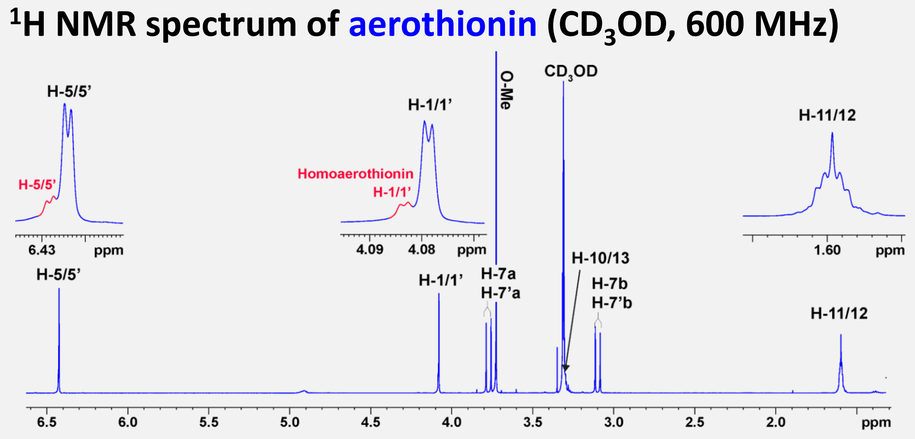
MS² based annotation & dereplication

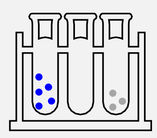






^{1}H NMR spectrum of aerothionin (CD_3OD, 600 MHz)





Isolation

Raw data

1D/2D NMR + MS² Public DB (GNPS- ZENODO)

- A total of **6 characteristic brominated alkaloids** identified by MS and NMR analyses after purification were detected in the seawater, including aerothionin.
- All their MS and NMR data will be shared in open access database.

Conclusions & Perspectives

- **The present experimental and analytical workflow enable us to determine the proportion & identity of brominated exo-metabolites (EM) recovered from the seawater surrounding *A. cavernicola***. The same workflow was implemented with ***A. oroides***. Quantitative analysis are in progress. Collectively, those EM are possibly released through the sponge metabolic activities & cellular turnover.[7]
- Such results will serve as a stepping stone to:
  - guide ***in situ*** **field work** to study the release of specialized metabolites by both sponge species
  - propose a **valorisation of sponge chemical diversity without collecting their biomass**

References:
1. Carroll, A. R., *et al. Nat. Prod. Rep.* (**2022**) 2. Pawlik, J., *et al. Mar. Ecol. Prog. Ser.* 127, 183–194 (**1995**) 3. Peng, J., *et al. AlkaloidsChemBiol.* 61: 59–262 (**2005**) 4. Richards, J., *et al. Bioorg Med Chem Lett.* 18(15):4325-7 (**2008**) 5. Walker, R. P. *et al. Mar Biol* 88, 27-32 (**1985**), 6. Richelle-Maurer, E, *et al. Biochemical Systematics and Ecology* 31, 1073–1091, (**2003**) 7. de Goeij, J. M., *et al. Science* 342, 108–110 (**2013**)

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