Exploiting Floridian Marine Cyanobacteria for Drug Discovery

S. Matthew (UF, Medicinal Chemistry); K. Taori (UF, Medicinal Chemistry); J.C. Kwan (UF, Medicinal Chemistry); V.J. Paul (Smithsonian Marine Station); H. Luesch (UF, Medicinal Chemistry)

Introduction

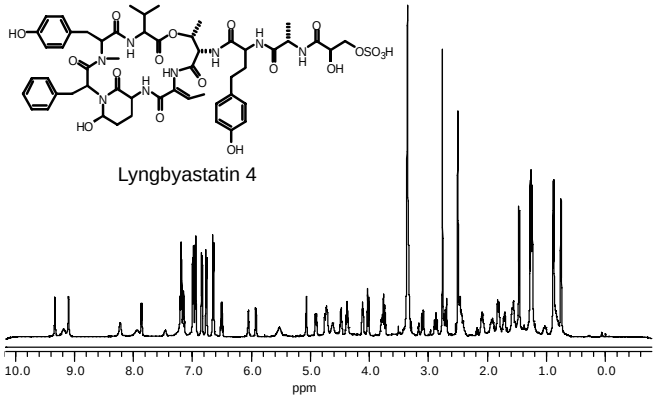
There is an urgent need to identify novel active chemotypes and pharmacophores as leads for effective drug development in many therapeutic areas. Our research is based on the hypothesis that marine cyanobacteria are a potential source of novel bioactive compounds. There is substantial evidence for the large biosynthetic capacity of cyanobacteria to produce chemically diverse secondary metabolites of biomedical utility. Florida harbors possibly the most marine biodiversity in the continental United States, and therefore there is a high probability of discovering novel and intriguing structures. One major problem is that oftentimes only submilligram quantities of active component can be isolated, hampering structure elucidation.

Experimental

^{1}H, ^{13}C, and 2D NMR spectra for cyanobacterial metabolites were recorded on Bruker Avance NMR spectrometers (500 MHz , 2.5 mm probe; 600 MHz warm bore, 5 mm probe; 750 MHz, 2.5 mm probe) or Bruker Avance II 600 MHz spectrometer equipped with NHMF Lab's 1 mm triple-resonance high-temperature superconducting (HTS) cryogenic probe.

Results and Discussion

Marine cyanobacteria of the genera *Symploca* and *Lyngbya* were collected off the coast of Florida, extracted and scrutinized for compounds with biomedical utility. Several extracts of *Lyngbya confervoides* collections from Ft. Lauderdale and the Florida Keys yielded novel protease inhibitors, lyngbyastatins 4–7 (Fig. 1),[1,2] which displayed exceptional potency in inhibiting elastase. Active extract components were isolated by bioassay-guided fractionation and analyzed by NMR (Fig. 1). Lyngbyastatins 5 and 6 were isolated in extremely low yield (0.47 and 0.17 mg, respectively), yet structure determination could be achieved thanks to the 1-mm HTS cryogenic probe.[2]



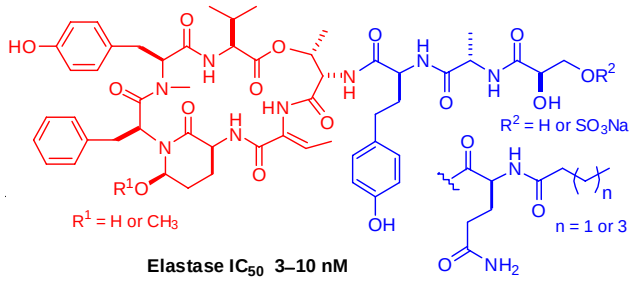


Fig.1. ^{1}H NMR and structure of lyngbyastatin 4 (left) and structures of all related metabolites, lyngbyastatins 4–7 (right).[1,2]

Conclusions

Cyanobacteria continue to yield new bioactive metabolites. The 1-mm probe was essential for the successful NMR analysis.

Acknowledgements

Florida Sea Grant College Program NA06OAR4170014, External User Program of NHMFL at AMRIS (NSF), and J. Rocca.

References

[1] Matthew, S. *et al.*, Journal of Natural Products, **70**, 124-127 (2007).
[2] Taori, K. *et al.*, Journal of Natural Products, **70**, 1593-1600 (2007).