Apratoxin E, A New Cytotoxic Peptolide from the Guamanian Marine Cyanobacterium *Lyngbya bouillonii*

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Introduction

Marine cyanobacteria are a potential source of novel bioactive compounds. Particularly *Lyngbya* species are prolific producers of interesting secondary metabolites. The cyanobacterium *Lyngbya bouillonii* from Apra Harbor, Guam has recently yielded one potent cytotoxin, apratoxin A,[1] which exhibits a unique cytotoxicity profile against the NCI's 60 cell lines and therefore potentially a novel mode of action.[2] Several slightly less potent analogues have been isolated in due course.[3,4] To further define the structure-activity relationships within this class of cytotoxins, we have searched for novel apratoxins in a *L. bouillonii* that inhabits deeper water at the same collection site where we found apratoxin A.[5]

Experimental

^{1}H, ^{13}C, and 2D NMR spectra for Guamanian *Lyngbya* metabolites were recorded on a Bruker Avance II 600 MHz NMR spectrometer equipped with NHMF Lab's 1 mm triple-resonance high-temperature superconducting (HTS) cryogenic probe.

Results and Discussion

The marine cyanobacterium *Lyngbya bouillonii* was collected at Apra Harbor, Guam at a depth of 12-14 m. The sample was freeze-dried, extracted with EtOAc-MeOH (1:1), fractionated by silica gel chromatography and reversed-phase HPLC to yield a novel apratoxin A analogue, which we termed apratoxin E (Fig. 1).[5] The structure was elucidated by 1D and 2D NMR analysis in $CDCl_3$ and benzene-d_6. Apratoxin E was several-fold less potent than apratoxin A with IC_{50} values of 21, 72 and 59 nM against HT29 colon adenocarcinoma, HeLa cervical carcinoma and U2OS osteosarcoma cells, respectively.

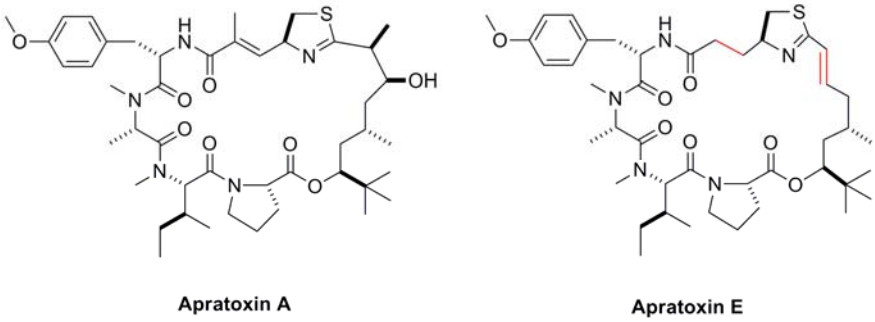

Fig. 1. Structures of apratoxins A and E.

Conclusions

A new apratoxin was isolated from *Lyngbya bouillonii*, expanding the structure-activity relationship in this series of cytotoxins. The search for apratoxins that occur naturally in minor amounts is ongoing, and the 1-mm HTS probe may prove useful for determining the structures of sub-milligram quantity samples.

Acknowledgements

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References

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