Behind The Scenes in Pharmacognosy

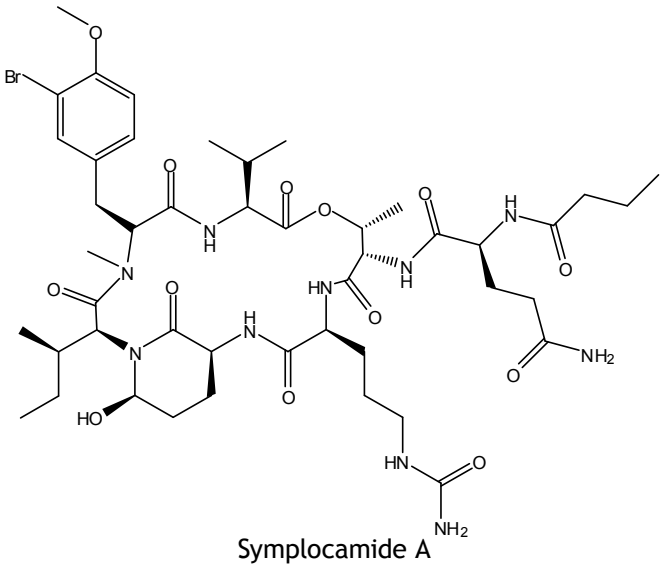
Chymotrypsin Inhibitors and Mini Golf

By Amy Keller

In January of this year, the article entitled, "Symplocamide A, a Potent Cytotoxin and Chymotrypsin Inhibitor from the Marine Cyanobacterium *Symploca* sp." by Roger G. Linington, Daniel J. Edwards, Cynthia F. Shuman, Kerry L. McPhail, Teatulohi Matainaho, and William H. Gerwick, appeared in the *Journal of Natural Products* 71st volume. The *Newsletter* interviewed first author and ASP member Dr. Roger Linington, who took time out his busy schedule to give us insight into an interesting study.

How did you become interested in the natural products of marine organisms?

I was originally trained as a synthetic medicinal chemist, looking at natural products from the perspective of total synthesis. While in graduate school at University of British Columbia, I took a course on 2D NMR from ASP member Dr. Raymond Andersen and later applied to join his research program. My first project was looking for antimitotic agents from marine invertebrates, and from the moment I acquired my first crude NMR I was hooked.



Symplocamide A

Who in your laboratory carried out the research?

This was a project completed while I was still a postdoc in ASP member Dr. Bill Gerwick's lab before I moved to University of California, Santa Cruz (UCSC) to start my own research program in July 2007. It was a combined effort between Dan Edwards, Cynthia Schuman and myself, with help from ASP member Dr. Kerry McPhail and Dr. Lohi Matainaho, and guidance from Dr. Gerwick.

Could you provide a brief explanation of the work and results in your own words? In what way are the data in your paper new?

This work was part of an ongoing investigation into cancer cell cytotoxins from marine cyanobacteria. Symplocamide A is a new member of a large class of cyanobacterial metabolites, many of which have been shown to inhibit serine proteases. Symplocamide A is one of the most potent inhibitors of chymotrypsin in this class, and shows over 200-fold selectivity for chymotrypsin over trypsin in vitro. Because symplocamide A possesses a number of unique structural features never previously observed for this class of compounds, its discovery represents an important extension of the existing pharmacophore for peptidic protease inhibitors.

In addition to the chemical and biological evaluation of this new metabolite we also conducted an exhaustive review of the structural features and biological profiles for all other natural products in this series. This provided us with a number of new insights into the SAR features that these compounds display, and highlighted the dramatic variations in biological activity that can be observed with only small variations in chemical structure.

LINDSEY PALENTINO


The Linington group (left to right): Roger Linington, Chad Renzelman, Chris Rundell, Navid Adnani, Laura Sanchez, Cecile Mioni, and Kelly Peach

What is a favorite nonscientific activity of your lab?
Mini golf.

What is your lab's motto?
Walk your own line.

What is your greatest extravagance in the lab?
House nitrogen.