

# Behind the Scenes in Pharmacognosy

## Absorbing Enlightenment from the Sea Sponge

In July of this year, the *Journal of Natural Products* published "Hexaprenoid Hydroquinones from the Sponge *Haliclona* (aka *Adocia*) sp.", by Drs. Lyndon West and D. John Faulkner. First author, Dr. West, is a native of New Zealand and a third generation Faulkner-ite. He obtained his Ph.D. in Organic Chemistry in 2001 from Victoria University of Wellington, New Zealand with Dr. Peter Northcote, working on the isolation and structural elucidation of secondary metabolites from marine invertebrates. Dr. Northcote obtained his Ph.D. at the University of British Columbia with Dr. Raymond Andersen, who in turn obtained his Ph.D. with Professor D. John Faulkner at Scripps Institution of Oceanography in San Diego, California. Dr. West then worked for two years as a postdoctoral research chemist with Prof. Faulkner. After Prof. Faulkner's sudden death in 2002, he joined Sequoia Sciences, a high throughput drug discovery company in San Diego, where he was carrying out the isolation and structural elucidation of terrestrial natural products.



Drs. John Faulkner, Raymond Andersen, Peter Northcote, and Lyndon West (left to right).

Dr. West was appointed as an Assistant Professor in the Department of Pharmaceutical and Biomedical Sciences in the College of Pharmacy at the University of Georgia in 2005 and is an associate member of the UGA Center for Drug Discovery. Dr. West's research at UGA focuses on the isolation and structural elucidation of biologically active natural products from marine organisms. The West lab is targeting molecules that have both unique structures as well as the potential for biomedical application. Dr. West has a strong interest in the development of novel simple approaches for the separation of marine natural products to accelerate the discovery of drug leads.

### How did you become interested in marine natural products?

At the end of my B.S. in Organic Chemistry I was fortunate to work as a summer researcher in Dr. Peter Northcote's Marine Natural Products Laboratory working on the isolation and quantification of a potent cytotoxin from a very interesting marine sponge. The more research I did, the more interested I was in learning about why marine organisms contain these complex chemicals and what the biomedical potential of these compounds was. This curiosity led to me to continue and do my Ph.D. in marine natural products chemistry. During my Ph.D. and postdoctoral research, I have been privileged to have met and worked with many exceptional scientists with a love for marine science and marine natural products chemistry and have been given many opportunities that I could never have dreamed of. In particular, I was able to learn to scuba dive to collect samples, which has allowed me to travel and dive in many unique locations.

### Who in your laboratory carried out the research?

The work described in the paper was carried out by me while working as a postdoctoral researcher in Dr. Faulkner's laboratory.

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**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?**

The paper describes the isolation and structural determination of three new merotriterpenoids from a marine sponge collected in Palau. The compounds were detected using a strategy developed during my Ph.D. to increase the chances of discovering new potentially biologically active compounds from marine organisms. The approach exploits the amphiphilic nature of biologically active compounds and uses a technique called cyclic loading together with polymeric chromatographic support to separate compounds with a high probability of exhibiting *in vitro* and *in vivo* activity. We have found that by using the polymeric chromatographic support HP-20 instead of traditional silica-based supports (e.g. silica gel and C18) to pre-fractionate the crude organic extracts, bioactive compounds such as peptides, polyketides, alkaloids and terpenoids, can be efficiently separated from the major water-soluble carbohydrates, salts, and non-polar fats and steroids. With HP-20, we can create discrete fractions of intermediate polarity with an increased probability of containing the biological active components, while eliminating the unwanted compounds that represent the majority of the mass of the extract. These pre-fractionated "enriched" materials can then be examined biologically and spectroscopically for the presence of novel compounds using 1D and 2D NMR spectroscopy to prioritize specimens.

**What impact does this research have?**

The search for new drug leads is a crucial element in pharmaceutical research. Natural products provide us with molecules that would be inaccessible via other routes and also provide templates for new drug design. Despite the fact that the biodiversity in the marine environment far exceeds that of the terrestrial environment, research of marine natural products is still in its infancy. Over the past 50 years marine organisms have proven to be a rich source of structurally and functionally diverse compounds with useful and sometimes sensational pharmacological activity. The identification of these compounds has primarily relied on either bioassay-directed isolation or classic natural products research which involved isolating the most abundant compounds and then hoping to find a use for them. The rapid developments of high-throughput screening and new access to large-scale screening efforts using highly specific, mechanism-based techniques will lead to new opportunities for natural products chemists by providing small molecules that can be used as chemical probes to study function at the molecular, cellular, and *in vivo* level. Natural products are again being seen as good source of structural diversity. In providing compounds for molecular libraries it is the structural diversity and potential for biological activity that is important.



Dr. Lyndon West at the 2006 ASP Annual Meeting.

**What was it like to work with Dr. Faulkner? What would you like us to know about him?**

It was an honor and a privilege to have worked with Prof. Faulkner at Scripps Institute of Oceanography. He was a dedicated and hardworking scientist who had a genuine love of marine natural products chemistry. This scientific curiosity and rigor will be passed down to those who work in my laboratory.

Amy Keller and Dr. Lyndon West contributed to this article.