

Discovery and structure determination of new bioactive compounds from bacteria inhabiting marine and symbiotic environments

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Natural products have been playing a key role in drug discovery. However, bioactive small molecules with new carbon backbones are still urgently required because drug-resistant diseases have become more widespread and the side effects of clinically-used drugs are problematic. Today, the most impressive remaining frontiers are largely microbial, and exploring unique or uninvestigated environments with suitably improved microbiological and chemical techniques. We have been focusing on bacteria inhabiting marine and symbiotic environments because secondary metabolites of bacteria in these habitats are not thoroughly studied.

LC/MS-based chemical analysis of symbiotic bacteria in insects led to the discovery of the structurally new bioactive secondary metabolites. New cyclic peptides, marcepins A-E, were isolated from a *Serratia marcescens* strain from the gut of the dung beetle, *Copris tripartitus*. These cyclic peptides displayed inhibitory activities against MRSA. Structurally novel naphthoquinone oxindole alkaloids, coprisidins A and B, were isolated from a dung beetle-gut associated *Streptomyces* sp. Marine bacteria are also prolific sources of new bioactive compounds. New cyclic peptides, ohmyungsamycins A and B, were discovered from a sand beach strain of *Streptomyces*. The ohmyungsamycins strongly inhibited *Mycobacterium tuberculosis*. Mohangamides A and B, new dilactone-tethered pseudo-dimeric peptides inhibiting *Candida albicans* isocitrate lyase, were discovered from an actinomycete strain collected in an intertidal mudflat. The discovery of structurally, biologically, and biosynthetically interesting secondary metabolites from bacteria inhabiting marine and symbiotic environments demonstrates that studying relatively-uninvestigated bacteria in search for new bioactive compounds could be a promising strategy for drug discovery.