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ACCESSING PLANT-ASSOCIATED MICROBIAL DIVERSITY FOR DISCOVERY OF SMALL MOLECULE BIOACTIVE AGENTS

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The growing body of evidence suggests that plant-associated microorganisms, especially rhizosphere and endophytic microorganisms, represent a huge and largely untapped resource of natural products with chemical structures that have been optimized by evolution for biological relevance. The possibility that plant-associated microbial diversity is influenced by the diversity of plant species and environmental factors suggests a greater potential for harvesting unique secondary metabolites from rhizosphere and endophytic microorganisms found in association with hitherto unexploited floristically diverse plant communities such as those in the U.S. Southwestern desert. In our search for novel small molecule bioactive agents, we have constructed a microbial library consisting of over 27,000 rhizosphere bacteria, 3,500 rhizosphere fungi, and 500 endophytic fungi. Extracts derived from cultures of some selected strains have been screened in assays for inhibition of cancer cell proliferation and migration, and heat shock modulation. Organisms producing metabolites active in these assays were identified, cultured on large-scale and the derived extracts have been subjected to bioactivity-guided fractionation to obtain a variety of natural products with diverse structures (e.g. **1 – 14**), and potential applications in agriculture and cancer chemotherapeutics. Isolation, characterization, chemistry, and biology of some selected small molecule metabolites and the significance of their natural occurrence will be presented.

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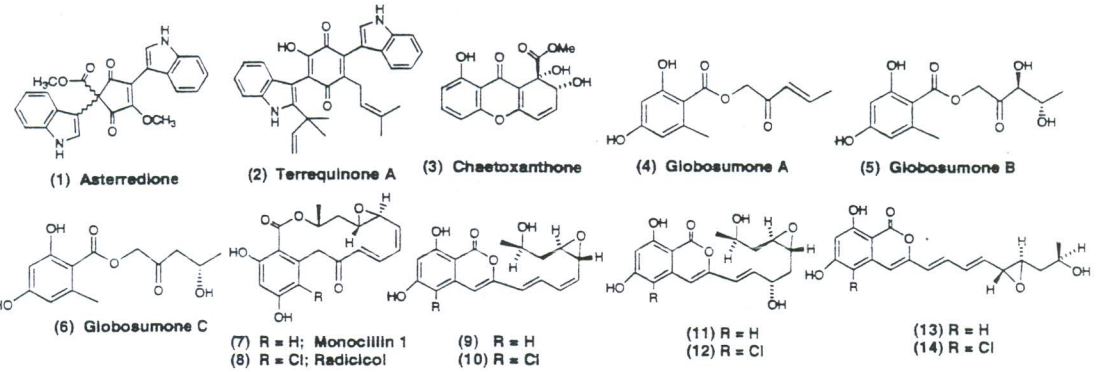

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