Pyrrolocin A, a 3-Decalinoyltetramic Acid with Selective Biological Activity, Isolated from Amazonian Cultures of the Novel Endophyte Diaporthales sp. E6927E.

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Abstract

Natural products remain an important source of new therapeutics for emerging drug-resistant pathogens like Candida albicans, which particularly affects immunocompromised patients. A bioactive 3-decalinoyltetramic acid, pyrrolocin A, was isolated from extracts of a novel Amazonian fungal endophyte, E6927E, of the Diaporthales family. The structure of the natural product was solved using NMR and CD spectroscopy and it is structurally related to the fungal setins, equisetin and phomasetin, which are well-characterized tetramic acid antibiotics specific for Gram-positive organisms. We show that the compound inhibits growth of Staphylococcus aureus and Enterococcus faecalis. It shows selective and potent bioactivity against fungal strains, with an MIC of 4 μg/mL for C. albicans, 100 μg/mL for Aspergillus sp. and greater than 100 μg/mL for Saccharomyces cerevisiae. Further, the compound is less toxic to mammalian cells (IC50 = 150 μg/mL), with an inhibitory concentration greater than forty times that for C. albicans. Pyrrolocin A retained potent activity against eight out of seventeen strains of clinical Candida sp. isolates tested.

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