

Advances in Cyclotide Research and Drug Discovery

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Abstract

The prototypic cyclotide, kalata B1, was discovered during ethnobotanical observations of African indigenous healers using plant decoctions from *Oldenlandia affinis* (Rubiaceae) to hasten uterine contractions. During the past three decades, a substantial body of research has indicated that this family of exceptionally stable circular phytopeptides demonstrate a plethora of therapeutic properties which make them promising candidates for drug discovery. The current research builds on our established protocols for the extraction and identification of novel cyclotides using a combination of HPLC, LC-MS, and nanospray MS-MS sequencing. Purified cyclotides, such as cycloviolacin O2 (CyO2) from *Viola odorata* (Violaceae) were investigated, and nontoxic doses ($< 0.5 \mu\text{M}$) displayed selective inhibition against drug resistant breast cancer cells (MCF-7/ADR) and HIV-infected lymphocytes (HuT78, PM1) and monocytes (U1). Cyclotides actively disrupted membranes via pore formation and enhanced the uptake of FDA approved anti-cancer drugs (doxorubicin) and HAART medications (saquinavir, nelfinavir and enfuvirtide) during evaluations of cytotoxicity (MTT and CCK), membrane disruption (Sytox Green), p24 antigen levels (ELISA) and fluorescence uptake (microscopy and cytometry). Taken together, this research substantiates the assertion that a systematic investigation of the bioactivity of plant-derived cyclotides may yield innovative approaches to the treatment of some of the world's most devastating diseases.



Biography

Samantha L. Gerlach earned her Ph.D. and the George Henry Penn Memorial Award for Best Dissertation from the Ecology and Evolutionary Biology Department at Tulane University in 2010. She is an Assistant Professor of Botany, Conservation, and Ecology in the Biology Department (S.T.E.M. Division) of Dillard University in New Orleans, Louisiana, USA. She has over 30 publications and serves as a Research Associate in Pharmacology at the Brain Chemistry Labs with the Institute of EthnoMedicine. Dr. Gerlach is a Distinguished Teaching Scholar with the Association of College and University Educators. She has conducted field and laboratory research in over 12 countries which predominantly focuses on the discovery and medicinal activity of cyclotides and Pacific ethnobotany. She serves as a review editor for the Ethnopharmacology Division of *Frontiers in Pharmacology*.

Publications

1. The Membrane-Active Phytopeptide Cycloviolacin O2 Simultaneously Targets HIV-1-infected Cells and Infectious Viral Particles to Potentiate the Efficacy of Antiretroviral Drugs
2. Mesenchymal stem cells are attracted to latent HIV-1-infected cells and enable virus reactivation via a non-canonical PI3K-NF κ B signaling pathway
3. Nelfinavir targets multiple drug resistance mechanisms to increase the efficacy of doxorubicin in MCF-7/Dox breast cancer cells
4. Cycloviolacin O2 (CyO2) Suppresses Productive Infection and Augments the Antiviral Efficacy of Nelfinavir in HIV-1 Infected Monocytic Cells
5. A Systematic Approach to Document Cyclotide Distribution in Plant Species from Genomic, Transcriptomic, and Peptidomic Analysis

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