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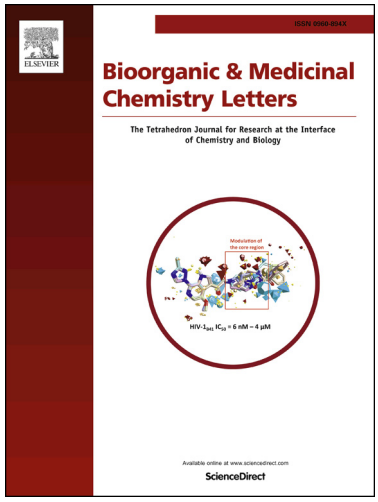

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Jennifer M. Giulietti, Patrick M. Tate, Ang Cai, Bongsup Cho, Seann P. Mulcahy

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DNA-binding studies of the natural β-carboline eudistomin U

Jennifer M. Giulietti,[a] Patrick M. Tate,[a] Ang Cai,[b] Bongsup Cho,[b] and Seann P. Mulcahy[a]*

[a]*Providence College, Department of Chemistry and Biochemistry, 1 Cunningham Square, Providence, RI 02918, USA*
[b]*University of Rhode Island, Department of Biomedical and Pharmaceutical Sciences, College of Pharmacy, 7 Greenhouse Road, Kingston, RI 02881*

*Corresponding author. Tel.: +1-401-865-1280; fax: +1-401-865-1438; e-mail: smulcahy@providence.edu

Abstract: Eudistomin U is a member of the β-carboline class of heterocyclic amine-containing molecules that are capable of binding to DNA. The structure of eudistomin U is unique since it contains an indole ring at the 1-position of the pyridine ring. While simple β-carbolines are reported to intercalate DNA, an examination of the mode of binding of eudistomin U has been lacking. We report preliminary spectroscopic (UV-Vis, thermal denaturation, CD) and calorimetric (DSC) data on the binding of eudistomin U to DNA, which suggest that eudistomin U binds weakly according to a mechanism that is more complicated than other members of its class.

Keywords: β-carboline, DNA, eudistomin U, UV-Vis, thermal denaturation, circular dichroism, differential scanning calorimetry

Targeting DNA as a macromolecular receptor is an attractive route for perturbing biological processes with small molecules.[1,2] DNA is an appealing target since its inherent chirality makes possible the rational design of molecular probes. In addition to the carbon-centered chirality of the nucleotide building blocks, DNA also possesses helicity that is necessary for molecular recognition. Of the many small molecules that bind to DNA, polyamides,[2] octahedral metal complexes,[3] *cis*-platin,[4] peptide nucleic acid,[5] polyimides,[6] and natural products like mitomycin[7] and daunorubicin,[8] are the most studied. Investigations into their binding thermodynamics, binding kinetics, and sequence specificities have enhanced our understanding of ligand–DNA interactions and provide further motivation for the search of new architectural motifs with similar potential as probes for chemical biology.

β-carbolines are naturally occurring or synthetic small molecules that also bind DNA noncovalently.[9] These molecules are indolo[3,2-*b*]pyridines, which are flat, aromatic amines capable of inserting themselves in between base pairs of duplex DNA. Simple β-carbolines such