SUPPLEMENTARY MATERIAL

Cytotoxic Oplopane Sesquiterpenoids from *Arnoglossum atriplicifolium*

Jason A. Clement^{a,b,*}, Rachel M. Bleich^a, Hailey E. Campbell^a, Kristin Naylor^a, Matthew J. Flood^a, Ryan M. Kelly^c, Shi-Biao Wu^d, Edward J. Kennelly^d and Jeffrey D. Schmitt^c

^a Department of Chemistry and Physics, Natural Sciences Building 231, Western Carolina University, Cullowhee NC, 28723, USA; ^b Natural Products Discovery Institute, Baruch S. Blumberg Institute, Doylestown, PA, 18902; ^c Bent Creek Institute, Asheville NC, 28806, USA; ^d Department of Biological Sciences, Lehman College, City University of New York, Bronx, NY 10468

*Corresponding author. Email: jason.clement@npdi-us.org

Pale Indian plantain (*Arnoglossum atriplicifolium* (L.) H. Rob.) is a plant with traditional medicinal usage among the Cherokee Native American tribe for treating cancer. Two oplopane sesquiterpenoids were isolated from an extract of *Arnoglossum atriplicifolium* from western North Carolina. The compounds were isolated by bioassay-guided fractionation using an MCF-7 breast tumor cell line assay. The known compound (1*S*,6*R*,7*R*,8*R*)-1-acetoxy-6,7-diangeloxy-8,10-epoxy-2-oxo-oplopa-3,14*Z*,11,12-dien-13-al (**1**) had an EC₅₀ value of 9.0 μM against MCF-7 cells, while the new compound (1*S*,3*R*,6*R*,7*R*,8*R*,11*S*)-1-acetoxy-6, 7-diangeloxy-8, 10, 11, 13-bisepoxyoplopan-2-one (**2**) had an EC₅₀ value of 96 μM. The compounds were characterized by 1D and 2D NMR spectroscopy and by comparison with literature values in the case for **1**. Based on NOESY analysis, a correction of the relative configuration for **1** is presented. The presence of these compounds may help to explain the folk remedy usage of this plant as an anticancer agent.

Keywords: Oplopane; sesquiterpenoid; *Arnoglossum atriplicifolium*

Figure S1: ^1H NMR spectrum of compound **1** (in C_6D_6 , 300 MHz)

Figure S2: ^{13}C NMR spectrum of compound **1** (in C_6D_6 , 75.6 MHz)

Figure S3: COSY spectrum of compound **1** (in C₆D₆, 300 MHz)

Figure S4: NOESY spectrum of compound **1** (in C₆D₆, 300 MHz)

Figure S5: HSQC spectrum of **1** (C₆D₆)

Figure S6: HMBC spectrum of **1** (C_6D_6)

Figure S7: ^1H NMR spectrum of compound **2** (in CDCl_3 , 300 MHz)

Figure S8: ^{13}C NMR spectrum of compound **2** (in CDCl_3 , 75.6 MHz)

Figure S9: COSY spectrum of compound **2** (in CDCl₃, 300 MHz)

Figure S10: NOESY spectrum of compound **2** (in CDCl₃, 300 MHz)

Figure S11: HSQC spectrum of **2** (CDCl₃)

Figure S12: HMBC spectrum of **2** (CDCl₃)