Supporting Information

Hapalindoles from the Cyanobacterium *Hapalosiphon* sp. Inhibit T Cell Proliferation
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Fig. 1Sa-c. Inhibition of T cell proliferation by *Hapalosiphon* sp. extract fractions.

Fig. 2S. Base peak chromatogram and extracted ion chromatograms.

Fig. 3S. $^1$H NMR spectrum (400 MHz) of 1 in CDCl$_3$.

Fig. 4S. NOESY NMR spectrum (600 MHz) of 1 in CDCl$_3$.

Fig. 5S. $^1$H NMR spectrum (400 MHz) of 2 in CDCl$_3$.

Fig. 6S. NOESY NMR spectrum (400 MHz) of 2 in CDCl$_3$.

Fig. 7S. $^1$H NMR spectrum (400 MHz) of 3 in DMSO-$d_6$.

Fig. 8S. NOESY NMR spectrum (400 MHz) of 3 in DMSO-$d_6$.

Fig. 9S. $^1$H NMR spectrum (600 MHz) of 4 in DMSO-$d_6$.

Fig. 10S. $^{13}$C NMR spectrum (150 MHz) of 4 in DMSO-$d_6$.

Fig. 11S. HSQC-DEPT NMR spectrum (600 MHz) of 4 in DMSO-$d_6$.

Fig. 12S. HMBC NMR spectrum (600 MHz) of 4 in DMSO-$d_6$.

Fig. 13S. NOESY NMR spectrum (600 MHz) of 4 in DMSO-$d_6$.

Fig. 14S. COSY NMR spectrum (600 MHz) of 4 in DMSO-$d_6$.

Fig. 15S. $^1$H NMR spectrum (600 MHz) of 5 in DMSO-$d_6$.

Fig. 16S. HSQC-DEPT NMR spectrum (400 MHz) of 5 in DMSO-$d_6$.

Fig. 17S. HMBC NMR spectrum (600 MHz) of 5 in DMSO-$d_6$.

Fig. 18S. NOESY NMR spectrum (600 MHz) of 5 in DMSO-$d_6$.

Fig. 19S. COSY NMR spectrum (600 MHz) of 5 in DMSO-$d_6$. 
Fig. 1Sa. HPLC-UV chromatogram (260 nm) of the *Hapalosiphon* sp. CBT1235 extract microfractionation as described in the methods section of the manuscript.

Fig. 1Sb. Inhibition of T cell proliferation by *Hapalosiphon* sp. extract fractions. Primary human lymphocytes were cultured in the presence of medium (NC) or were stimulated with anti-human CD3 and anti-human CD28 mAb (PC; 100 ng/mL). Activated T cells were further incubated with cyclosporine A (CsA; 5 µg/mL) or dilutions of 24 *Hapalosiphon* sp. extract fractions. Cell division analysis was carried out using CFSE staining and flow cytometry. Data of two independent experiments are presented as mean ± SD in relation to stimulated T cells (PC = 100%). The most active fraction 18 was dereplicated and shown to contain hapalindol derivatives.
Fig. 1Sc. Impact of *Hapalosiphon* sp. CBT1235 fraction 18 on T cell proliferation and apoptosis induction. Primary human lymphocytes were cultured in the presence of medium (NC) or were stimulated with anti-human CD3 and anti-human CD28 mAb (PC; 100 ng/mL). Activated T cells were further incubated with cyclosporine A (CsA; 5 µg/mL), camptothecin (CPT; 30 µg/mL), or different dilutions of the *Hapalosiphon* sp. CBT1235 fraction 18, which has been identified as the most active out of 24 fractions (Fig. 1S). Cell division analysis was carried out using CFSE staining and flow cytometry. Levels of apoptosis were determined using flow-cytometric analysis of annexin V-stained cells. (A) Effects of *Hapalosiphon* sp. CBT1235 fraction 18 on lymphocyte proliferation. (B) Induction of apoptosis by *Hapalosiphon* sp. CBT1235 fraction 18. Data of four (A) or three (B) independent experiments are presented as mean ± SD in relation to stimulated T cells (PC = 100%). Asterisks indicate significant differences from PC controls (**p < 0.01, ***p < 0.001).
**Fig. 2S.** Base peak chromatogram (pos. mode) of *Hapalosiphon sp.* extract (top) and extracted ion chromatograms of hapalindole A-formamide 4 (m/z 357.1723 [M+H]⁺, middle, tᵣ 9.99 min) and hapalindole J-formamide 5 (m/z 323.2114 [M+H]⁺, bottom, tᵣ 10.03 min), showing the presence of the formamides in freshly prepared untreated biomass extracts.
Fig. 3S. $^1$H NMR spectrum (400 MHz) of 1 in CDCl$_3$. 
Fig. 4S. NOESY NMR spectrum (400 MHz) of 1 in CDCl₃.
Fig. 5S. $^1$H NMR spectrum (400 MHz) of 2 in CDCl$_3$. 
Fig. 6S. NOESY NMR spectrum (400 MHz) of 2 in CDCl$_3$. 
Fig. 7S. $^1$H NMR spectrum (400 MHz) of 3 in DMSO-$d_6$. 

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Fig. 8S. NOESY NMR spectrum (400 MHz) of 3 in DMSO-$d_6$. 
Fig. 9S $^1$H NMR spectrum (600 MHz) of 4 in DMSO-$d_6$. 
Fig. 10S $^{13}$C NMR spectrum (150 MHz) of 4 in DMSO-$d_6$. 

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Fig. 11S HSQC-DEPT NMR spectrum (600 MHz) of 4 in DMSO-$d_6$. 
Fig. 12S. HMBC NMR spectrum (600 MHz) of 4 in DMSO-d$_6$. 
Fig. 13S. NOESY NMR spectrum (600 MHz) of 4 in DMSO-$d_6$. 
Fig. 14S. COSY NMR spectrum (600 MHz) of 4 in DMSO-$d_6$. 
**Fig. 15S.** $^1$H NMR spectrum (600 MHz) of 5 in DMSO-$d_6$. 

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