SUPPLEMENTARY MATERIAL

Chemical Constituents from *Artemisia vulgaris* and Their Antiausterity Activities against the PANC-1 Human Pancreatic Cancer Cell Line

Ashraf M. Omar, Dya Fita Dibwe, Ahmed M. Tawila, Sijia Sun, Min Jo Kim and Suresh Awale*

*Division of Natural Drug Discovery, Institute of Natural Medicine, University of Toyama, 2630 Sugitani, Toyama 930-0194, Japan.*

**ABSTRACT:**

The 70% ethanolic extract of *Artemisia vulgaris* showed preferential cytotoxicity against PANC-1 human pancreatic cancer cells under a nutrient-deprived condition with PC_{50} 12.5 μg/mL. A phytochemical investigation of this extract yielded a new bicyclic [4:3:0] sesquiterpene named (+)-vulgaric acid (1), together with eight previously reported compounds. The structural elucidation of 1 was achieved by HRFABMS and NMR analysis. The absolute configuration of 1 was deduced by computational calculations of ECD data. All isolated compounds were tested for preferential cytotoxicity against PANC-1 cells, and apigenin (3) showed the strongest activity with PC_{50} 30.7 μM.

**Keywords:** *Artemisia vulgaris*; Sesquiterpene; Anti-austerity; ECD calculation
Table of contents

Table S1. Preferential Cytotoxicity (PC_{50})^a of Compounds 1–9 against the PANC-1 Human Pancreatic Cancer Cell Line in Nutrient-Deprived Medium (NDM).

Figure S1. $^1$H NMR spectrum of vulgaric acid (1)  
P3
Figure S2. $^{13}$C NMR spectrum of vulgaric acid (1)  
P4
Figure S3. $^1$H-$^1$H COSY spectrum of vulgaric acid (1)  
P5
Figure S4. HMQC spectrum of vulgaric acid (1)  
P6
Figure S5. HMBC spectrum of vulgaric acid (1)  
P7
Figure S6. $^1$H-$^1$H NOESY spectrum of vulgaric acid (1)  
P8
Figure S7. HRFABMS spectrum of vulgaric acid (1)  
P9
Figure S8. IR spectrum of vulgaric acid (1)  
P10
Figure S9. UV spectrum of vulgaric acid (1)  
P11

Figure S10. Most stable conformers of (6R)-1 calculated at the DFT/B3LYP/6-31G* level of theory. Relative populations are in parentheses.  
P12

Figure S11. Experimental and calculated ECD spectra of 1.  
P12
Figure S12. Plausible biosynthetic pathway for 1.  
P13
Figure S13. Preferential cytotoxic activities of compounds 1–9 against PANC-1 cells  
P14
Table S1. Preferential Cytotoxicity (PC$_{50}$)$^a$ of Compounds 1–9 against the PANC-1 Human Pancreatic Cancer Cell Line in Nutrient-Deprived Medium (NDM).

<table>
<thead>
<tr>
<th>compound</th>
<th>PC$_{50}$, $\mu$M$^a$</th>
<th>compound</th>
<th>PC$_{50}$, $\mu$M$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>67.7</td>
<td>7</td>
<td>41.8</td>
</tr>
<tr>
<td>2</td>
<td>87.5</td>
<td>6, 8</td>
<td>$&gt;100$</td>
</tr>
<tr>
<td>3</td>
<td>30.7</td>
<td>9</td>
<td>79.7</td>
</tr>
<tr>
<td>4</td>
<td>57.6</td>
<td>arctigenin$^b$</td>
<td>0.7</td>
</tr>
<tr>
<td>5</td>
<td>73.9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$^a$ Concentration at which 50% of cells were killed preferentially in NDM. $^b$ Positive control.
Figure S1. $^1$H NMR spectrum of vulgaric acid (1) in CDCl$_3$
Figure S2. $^{13}$C NMR spectrum of vulgaric acid (1) in CDCl$_3$
Figure S3. $^1$H-$^1$H COSY NMR spectrum of vulgaric acid (1) in CDCl$_3$
Figure S4. HMOC spectrum of vulgaric acid (1) in CDCl₃.
Figure S5. HMBC spectrum of vulgaric acid (1) in CDCl₃
Figure S6. $^1$H-$^1$H NOESY spectrum of vulgaric acid (I) in CDCl$_3$
Figure S7. HRFABMS spectrum of vulgaric acid (1)
Figure S8. IR spectrum of vulgaric acid (1)
Figure S9. UV spectrum of vulgaric acid (1)
Figure S10. Most stable conformers of (6R)-1 calculated at the DFT/B3LYP/6-31G* level of theory. Relative populations are in parentheses.

Figure S11. Experimental and calculated ECD spectra of 1.
Figure S12. Plausible biosynthetic pathway for 1.
Figure S13. Preferential cytotoxic activities of compounds 1–9 against the PANC-1 human pancreatic cancer cell line in nutrient-deprived medium (NDM, red color) and Dulbecco’s modified Eagle’s medium (DMEM, blue color).