FLAVONOID GLYCOSIDES FROM *Antidesma ghaesembilla*

Le Canh Viet Cuong¹, Do Thi Trang¹, Nguyen Thi Cuc¹, Nguyen Xuan Nhiem¹, Hoang Le Tuan Anh¹, Le Mai Huong², Chau Van Minh¹, Phan Van Kiem³

¹Institute of Marine Biochemistry, Vietnam Academy of Science and Technology (VAST)
²Institute of Natural Products Chemistry, VAST

Received 23 January 2015; Accepted for Publication 18 March 2015

Abstract

Four flavone glycosides were isolated from the leaves of *Antidesma ghaesembilla*. They were elucidated to be vitexin, orientin, isovitexin, and homoorientin by 1D- and 2D-NMR and in comparison with literature data. These compounds have been reported from the genus *Antidesma* for the first time.

Keywords. *Antidesma ghaesembilla*, vitexin, orientin, isovitexin, homoorientin.

1. INTRODUCTION

*Antidesma* is a genus of tropical plants belonging to Euphorbiaceae family, comprise about 100 species in the world and 29 species in Vietnam. The leaves of *A. ghaesembilla* have been used in traditional medicine for treatment of skin diseases and headache [1]. In addition, its fruits have been used to treat sore throat and lung disease [1]. However, there are few reports about chemical constituents and biological activities of this plant [2, 3]. As part of our ongoing chemical investigations on the genus *Antidesma*, we report herein the isolation and structural elucidation of C-glucose flavones from the leaves of *A. ghaesembilla*.

2. MATERIAL AND METHODS

2.1. Plant Material

The leaves of *Antidesma ghaesembilla* Gaertner were collected in Dak Lak province, Vietnam, in March 2013, and identified by Dr. Nguyen Quoc Binh, Vietnam National Museum of Nature. A voucher specimen was deposited at Institute of Marine Biochemistry, VAST.

2.2. General experimental procedures

All NMR spectra were recorded on a Bruker AM500 FT-NMR spectrometer (500 MHz for ¹H-NMR and 125 MHz for ¹³C-NMR). NMR measurements, including ¹H-NMR, ¹³C-NMR, HSQC, and HMBC experiments, were carried out using 5-mm probe tubes at temperature of 22.2 °C. Melting points were recorded in Kofler micro-hotstage. Optical rotations were determined on a Jasco DIP-1000 polarimeter. Column chromatography was performed using a silica-gel (Kieselgel 60, 70-230 mesh and 230-400 mesh, Merck) or RP-18 resins (30-50 µm, Fujisilisa Chemical Ltd.), thin layer chromatography (TLC) using a pre-coated silica-gel 60 F₂₅₄ (0.25 mm, Merck) and RP-18 F₂₅₄S plates (0.25 mm, Merck).

2.3. Extraction and isolation

The dried leaves of *A. ghaesembilla* (2.5 kg) were sonicated in MeOH three times to yield 115.0 g of a dark solid extract, which was then suspended in water and successively partitioned with dichloromethane and ethyl acetate (EtOAc) to obtain dichloromethane (AG1, 30.0 g), ethyl acetate (AG2, 20.0 g), and water layers (AG3, 65.0 g) after removal solvent in vacuo. The EtOAc layer (AG2, 20.0 g) was chromatographed on a silica-gel column eluting with CH₂Cl₂/MeOH/water (5/1/0.1, v/v/v) to give three fractions, AG2A-AG2C. The AG2B fraction was chromatographed on a RP-18 column eluting with MeOH/water (1/1.5, v/v) to yield compounds 1 (15.0 mg) and 2 (7.0 mg). The water layer (AG3, 65.0 g) was chromatographed on a Diaion HP-20 column eluting with water to remove sugar, then increase concentration of methanol in water (25, 50, 75, and 100 %) to obtain four fractions, AG3A-AG3D. The AG3D fraction was...
3. RESULTS AND DISCUSSION

Compound 1 was obtained as a yellow amorphous powder. The $^1$H-NMR of compound 1 (in DMSO-$d_6$) showed the signals of four aromatic protons of the AA′BB′ coupling system in B ring at $\delta_H$ 6.89 (2H, d, $J = 8.0$ Hz) and 8.02 (2H, d, $J = 8.0$ Hz); two singlet protons at $\delta_H$ 6.27 (1H, s) and 6.77 (1H, s) assigned to a flavone aglycone; one anomeric proton at $\delta_H$ 4.69 (1H, d, $J = 10.0$ Hz), assigned to a C-sugar unit. The $^{13}$C-NMR and DEPT spectra of the signals of 21 carbons, including one carbonyl at $\delta_C$ 182.04, eight non-protonated carbons at $\delta_C$ 104.59, 104.59, 121.59, 155.98, 160.38, 161.12, 162.68, and 163.91, eleven methine carbons at $\delta_C$ 70.54, 70.84, 73.36, 78.65, 81.80, 98.14, 102.41, 115.80, 2, 128.92 × 2, and one methylene carbon at $\delta_C$ 61.28. The $^1$H- and $^{13}$C-NMR data of 1 were similar to those of vitexin [4]. The HMBC cross peaks from H-3 ($\delta_H$ 6.77) to C-1′ ($\delta_C$ 121.59)/C-2 ($\delta_C$ 163.91)/C-4 ($\delta_C$ 182.04)/C-10 ($\delta_C$ 105.7); from H-6 ($\delta_H$ 6.27) to C-5 ($\delta_C$ 160.38)/C-7 ($\delta_C$ 162.68)/C-8 ($\delta_C$ 104.59)/C-10 ($\delta_C$ 104.00) confirmed that two singlet protons were at C-3 and C-6. The large coupling constant $J_H$=1H,1H,2=10.0$ Hz and $^{13}$C-NMR chemical shifts of sugar moiety ($\delta_C$ 73.36, 70.84, 78.65, 70.54, 81.80, and 61.28) were very typical of C-glucopyranosyl moiety. In addition, this sugar was attached to C-8 confirming by the HMBC correlation between glc H-1′ ($\delta_H$ 4.69) and C-8 ($\delta_C$ 104.59). The HMBC correlations between H-2′ ($\delta_H$ 8.02)/H-3′ ($\delta_H$ 6.89) and C-4′ ($\delta_C$ 161.12) suggested that the hydroxyl group was at C-4′ of flavone. Consequently, the structure of 1 was determined to be vitexin.

The $^1$H-NMR of 2 (DMSO-$d_6$) showed revealed the signals of three aromatic protons of ABX aromatic system in B ring at $\delta_H$ 6.86 (1H, d, $J = 8.0$ Hz), 7.48 (1H, br s), and 7.53 (br d, $J = 8.0$ Hz); two singlet protons at $\delta_H$ 6.26 (1H, s) and 6.63 (1H, s), assigned to a flavone aglycone; one anomeric proton at $\delta_H$ 4.69 (1H, d, $J = 10.0$ Hz), assigned to a C-sugar unit. The $^1$H- and $^{13}$C-NMR of 2 were almost similar to those of 1 except for an addition of hydroxyl group at C-3′ in B ring as orientin. In addition, its NMR data were identical to those of orientin and found to match [4].

The $^1$H-, $^{13}$C-NMR and DEPT spectra of 3 revealed the signals of the flavone glycoside, including one carbonyl, eight non-protonated, eleven methines, and one methylene. The $^1$H- and $^{13}$C-NMR data of 3 were found to be similar those of vitexin except for the position of C-sugar at C-6. The sugar was proved to be C-glucose by comparing its NMR data to those of vitexin (1). The position of this sugar at C-6 was confirmed by the HMBC correlation between glc H-1′ ($\delta_H$ 4.87) and C-6 ($\delta_C$ 109.51). The positions of the remaining functional groups were based on the HSQC and HMBC spectra. Thus, the structure of 3 was determined to be isovitexin [5].
Table 1: The \(^1\)H- and \(^13\)C-NMR data for compounds 1-4 and reference compounds

<table>
<thead>
<tr>
<th>Pos</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(\delta_c^a)</td>
<td>(\delta_c^b)</td>
<td>(\delta_c^b)</td>
<td>(\delta_c^b)</td>
</tr>
<tr>
<td></td>
<td>(\delta_c^a) (mult., (J), Hz)</td>
<td>(\delta_c^a) (mult., (J), Hz)</td>
<td>(\delta_c^a) (mult., (J), Hz)</td>
<td>(\delta_c^a) (mult., (J), Hz)</td>
</tr>
<tr>
<td>Aglycone</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>165.0 163.91 -</td>
<td>164.2 164.05 -</td>
<td>164.3 165.95 -</td>
<td>163.6 163.28 -</td>
</tr>
<tr>
<td>3</td>
<td>102.5 102.41 6.77 (s)</td>
<td>102.4 102.34 6.63 (s)</td>
<td>103.9 103.60 6.52 (s)</td>
<td>102.6 102.80 6.67 (s)</td>
</tr>
<tr>
<td>4</td>
<td>182.7 182.04 -</td>
<td>182.0 181.95 -</td>
<td>182.9 183.78 -</td>
<td>181.7 181.86 -</td>
</tr>
<tr>
<td>5</td>
<td>160.3 160.38 -</td>
<td>160.5 160.35 -</td>
<td>157.5 -</td>
<td>160.6 160.68 -</td>
</tr>
<tr>
<td>6</td>
<td>98.5 98.14 6.27 (s)</td>
<td>98.3 98.11 6.26 (s)</td>
<td>110.1 109.51 -</td>
<td>108.9 108.87 -</td>
</tr>
<tr>
<td>7</td>
<td>162.3 162.68 -</td>
<td>162.8 162.69 -</td>
<td>165.0 163.02 -</td>
<td>163.1 163.66 -</td>
</tr>
<tr>
<td>8</td>
<td>104.6 104.59 -</td>
<td>104.6 104.52 -</td>
<td>94.7 95.71 6.42 (s)</td>
<td>93.2 93.52 6.48 (s)</td>
</tr>
<tr>
<td>9</td>
<td>155.6 155.98 -</td>
<td>156.0 155.97 -</td>
<td>162.1 158.82 -</td>
<td>156.1 156.21 -</td>
</tr>
<tr>
<td>10</td>
<td>104.1 104.00 -</td>
<td>104.0 103.94 -</td>
<td>104.8 104.55 -</td>
<td>103.4 103.40 -</td>
</tr>
<tr>
<td>1'</td>
<td>122.1 121.59 -</td>
<td>122.0 121.93 -</td>
<td>122.2 123.02 -</td>
<td>121.4 121.43 -</td>
</tr>
<tr>
<td>2'</td>
<td>129.0 128.92 8.02 (d, 8.0)</td>
<td>114.1 113.99 7.48 (br s)</td>
<td>128.9 129.37 7.79 (d, 8.0)</td>
<td>113.1 113.30 7.40 (d, 2.0)</td>
</tr>
<tr>
<td>3'</td>
<td>115.0 115.80 6.89 (d, 8.0)</td>
<td>146.0 145.79 -</td>
<td>116.8 117.10 6.88 (d, 8.0)</td>
<td>145.8 145.75 -</td>
</tr>
<tr>
<td>4'</td>
<td>161.3 161.12 -</td>
<td>149.9 149.66 -</td>
<td>162.7 162.02 -</td>
<td>149.7 149.72 -</td>
</tr>
<tr>
<td>5'</td>
<td>115.0 115.80 6.89 (d, 8.0)</td>
<td>115.8 115.62 6.86 (d, 8.0)</td>
<td>116.8 117.10 6.88 (d, 8.0)</td>
<td>115.7 116.06 6.89 (d, 8.0)</td>
</tr>
<tr>
<td>6'</td>
<td>129.0 128.92 8.02 (d, 8.0)</td>
<td>119.4 119.33 7.53 (br d, 8.0)</td>
<td>128.9 129.37 7.79 (d, 8.0)</td>
<td>118.7 118.97 7.42 (d, 2.0, 8.0)</td>
</tr>
<tr>
<td>6 or 8-C-Glc</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1&quot;</td>
<td>73.9 73.36 4.69 (d, 10.0)</td>
<td>73.5 73.37 4.69 (d, 10.0)</td>
<td>75.6 75.35 4.87 (d, 10.0)</td>
<td>72.8 73.06 4.59 (d, 10.0)</td>
</tr>
<tr>
<td>2&quot;</td>
<td>71.0 70.84 3.84 (dd, 9.0,10.0)</td>
<td>70.9 70.76 3.84 (dd, 9.0,10.0)</td>
<td>72.9 72.47 4.19 (dd, 9.0, 10.0)</td>
<td>69.9 70.62 4.04 (dd, 9.0,10.0)</td>
</tr>
<tr>
<td>3&quot;</td>
<td>79.0 78.65 3.29</td>
<td>78.9 78.74 3.30</td>
<td>80.6 80.25 3.46</td>
<td>78.7 78.95 3.16</td>
</tr>
<tr>
<td>4&quot;</td>
<td>70.2 70.54 3.34</td>
<td>70.8 70.68 3.37</td>
<td>71.9 71.73 3.46</td>
<td>70.4 70.22 3.22</td>
</tr>
<tr>
<td>5&quot;</td>
<td>81.3 81.80 3.26</td>
<td>82.0 81.95 3.27</td>
<td>83.0 82.56 3.90</td>
<td>81.4 81.55 3.14</td>
</tr>
<tr>
<td>6&quot;</td>
<td>61.4 61.28 3.52 (dd, 5.5,11.0)</td>
<td>61.8 61.62 3.53 (dd, 5.5,11.0)</td>
<td>62.7 62.82 3.72 (dd, 5.5,11.0)</td>
<td>61.2 61.49 3.43 (dd, 5.5,11.0)</td>
</tr>
<tr>
<td></td>
<td>3.76 (br d, 11.0)</td>
<td>3.79 (br d, 11.0)</td>
<td>3.86 (br d, 11.0)</td>
<td>3.69 (br d, 11.0)</td>
</tr>
</tbody>
</table>

\(^a\)Recorded in DMSO-d\(_6\), \(^b\)recorded in CD\(_3\)OD, \(^*\)\(\delta_c\) of vitexin [4], \(^5\)\(\delta_c\) of orientin [4], \(^6\)\(\delta_c\) of isovitexin [5], \(^7\)\(\delta_c\) of homoorientin [4].

Figure 2: The important HMBC correlations of compounds 1 and 3.
By similar way, compound 4 was defined as homoorientin [4]. This is the first report of compounds 1-4 from genus Antidesma.

REFERENCES


Corresponding author: Phan Van Kiem
Institute of Marine Biochemistry, Vietnam Academy of Science and Technology
18, Hoang Quoc Viet, Cau Giay, Hanoi, Vietnam
E-mail: phankiem@yahoo.com.