RHODIOCYANOSIDES A AND B, NEW ANTIALLERGIC CYANOGLY COSIDES FROM CHINESE NATURAL MEDICINE "SI LIE HONG JING TIAN", THE UNDERGROUND PART OF RHODIOLA QUADRIFIDA (PALL.) FISCH. ET MSE.

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Two new antiallergic cyanoglycosides named rhodiocyanosides A and B were isolated from the Chinese natural medicine "Si Lie Hong Jing Tian" (Shihtsukoukeiten in Japanese), the underground part of Rhodiola quadrifida (Pall.) Fisch. et Mey., together with two new glycosides, octyl α-L-arabinopyranosyl(1-6)-β-D-glucopyranoside and gossypetin 7-O-β-D-glucopyranosyl(1-3)-α-L-rhamnopyranoside. Their chemical structures were determined on the basis of chemical and physicochemical evidence. Rhodiocyanosides A and B exhibited inhibitory activity on the histamine release from rat peritoneal exudate cells sensitized with anti-DNP IgE. In addition, rhodiocyanoside A was found to inhibit the PCA reaction in rats.

KEY WORDS rhodiocyanoside; cyanoglycoside; Rhodiola quadrifida; antiallergic activity; histamine release inhibitor; passive cutaneous anaphylaxis reaction

The Chinese natural medicine "Si Lie Hong Jing Tian" (Shihtsukoukeiten in Japanese), which is produced from Rhodiola quadrifida (Pall.) Fisch. et Mey. (Crassulaceae), has been used as a hemostatic, an antibiotic, and an endemic liniment for burns. In the chemical study of this natural medicine, several components such as rhodioloside(salidroside) and flavonol glycosides were isolated.1) As part of continuing studies on the bioactive constituents of natural medicine,2) we have isolated new antiallergic cyanoglycosides, rhodiocyanosides A(1) and B(3) together with two new glycosides, octyl α-L-arabinopyranosyl(1-6)-β-D-glucopyranoside(4) and gossypetin 7-O-β-D-glucopyranosyl(1-3)-α-L-rhamnopyranoside(5), and four known compounds, rhodioloside,1,3) n-hexyl β-D-glucopyranoside,4) tricetin,5) and gossypetin 7-O-α-L-rhamnopyranoside,6) from the underground part of Rhodiola quadrifida (Pall.) Fisch. et Mey. This paper communicates the structure elucidation of 1, 3–5, and the antiallergic activity of 1 and 3.7)

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The MeOH extract of the underground part was subjected to XAD-2 column chromatography, and then the MeOH-eluate was purified by repeated ordinary SiO₂(CHCl₃-MeOH-H₂O) reversed phase SiO₂(chromatorex ODS DM 1020T, H₂O-MeOH) column chromatography and finally HPLC (YMC-Pack R & D, H₂O-MeOH) to furnish 1 (0.113% from the crude drug), 3 (0.009%), 4 (0.009%), 5 (0.004%), rhodioloside (0.016%), n-hexyl β-d-glucopyranoside (0.003%), tricetin (0.001%), and gossypetin 7-O-α-L-rhamnopyranoside (0.001%).

Rhodiocyanoside A (1), a white powder, [α]D -16.1°(MeOH), C₁₁H₁₇NO₆, UV(log ε, MeOH) : 208(4.03)nm, IR(KBr) : 3410, 2222, 1655, 1076cm⁻¹, positive mode FAB-MS : m/z 260(M+H)⁺, negative mode FAB-MS : m/z 258(M-H)⁻, furnished the tetraacetate (1a), 8 colorless oil, [α]D -10.4°(MeOH), C₁₉H₂₅NO₁₀, IR(KBr) : 2235, 1757, 1231, 1042cm⁻¹, negative mode FAB-MS : m/z 426(M-H)⁻ by acetylation with Ac₂O and pyridine. Enzymatic hydrolysis of 1 with β-glucosidase or naringinase gave the aglycone, rhodiocyanogenin(2), colorless oil, C₅H₃NO, IR(film) : 3300, 2222, 1655cm⁻¹, El-MS : m/z 97(M⁺), while methyl d-glucoside was identified by methanalysis of 1 with 9% HCl-dry MeOH. The 1H NMR(CD₃OD) and 13C NMR(Table 1) spectra of 1 and 2 which were assigned by DEPT, COSY(1H-1H, 1H-13C), HMBC, COLOC, and HOHAHA(1H-1H, 1H-13C), indicated the presence of trisubstituted olefin [1 : δ 6.46(qdd, J=1.7, 6.3, 6.9); 2 : δ 6.36(tq, J=1.3, 6.6)(3-H)] which was bonded with methyl [1 : δ 1.93(ddd, J=1.3, 1.3, 1.7); 2 : δ 1.96(tq, J=1.0, 1.3)(5-H)], nitrile group, and oxymethylene [1 : δ 4.43(qdd, J=1.3, 6.9, 13.5), 4.54(qqq, J=1.3, 6.3, 13.5); 2 : δ 4.26(dd, J=1.0, 6.6)(4-H₂)₄ bearing a β-D-glucopyranoside moiety in the case of 1[δ 4.30(d, J=7.9, 1-H)]. The geometric structure of the trisubstituted olefin in 1 was characterized by the NOESY experiment of 1 and 2 ; namely, the NOE correlations were observed between 5-H₃ and 3-H and between 3-H and 4-H₂. Based on the above given evidence, the structure of rhodiocyanoside A(1) was determined.

Rhodiocyanoside B(3), a white powder, [α]D -12.2°(MeOH), C₁₈H₂₁NO₁₁, UV(log ε, MeOH) : 279(3.99), 217(4.48)nm, IR(KBr) : 3410, 2230, 1714, 1620, 1529, 1075cm⁻¹, positive mode FAB-MS : m/z 449(M+Na)⁺, showed the signals due to butenenitrite moiety (δ 6.86(dd, J=5.9, 6.2, 3-H), 4.53(dd, J=6.2, 14.5), 4.69(dd, J=5.9, 14.5)(4-H₂), 4.88(s, 5-H₂)), β-D-glucopyranosyl moiety (δ 4.43(d, J=7.6, 1-H)), and galloyl group (δ 7.09(s, 2",6"-H)) in the 1H NMR(CD₃OD) spectrum of 3. In the NOESY data of 3, the NOE correlations were observed in the following pairs of protons [5-H₂ & 3-H ; 3-H & 4-H₂]. Detailed comparison of the 1H NMR and 13C NMR data(Table 1) for 3 with those for 1 led us to formulate the structure of rhodiocyanoside B(3).

Octyl α-L-arabinosyl(1-6)-β-D-glucopyranoside(4), a white powder, [α]D -29.2°(MeOH), C₁₉H₃₆O₁₀, IR(KBr) : 3410, 1074cm⁻¹, 1H NMR(CD₃OD) : δ 4.26(d, J=7.6, 1'-H), 4.32(d, J=6.6, 1"-H), 0.90(t, J=6.4, 1'H₂), negative mode FAB-MS : m/z 423(M-H)⁻, liberated 1-octanol, methyl L-arabinoside, and methyl d-glucoside by the methanalysis. Ordinary acetylation of 4 furnished the hexaacetate(4a). Finally, examination of the 13C NMR of 4(10) and 4a led us to characterize the structure of 4. Gossypetin 7-O-β-D-glucopyranosyl(1-3)-α-L-rhamnopyranoside(5), a yellow powder, [α]D -50.8°(MeOH), C₂₇H₃₆O₁₇,
Table 3. Effect of Rhodiocyanoside A(1) and DSCG on the Passive Cutaneous Anaphylaxis Reaction in Rats

<table>
<thead>
<tr>
<th></th>
<th>Dose (mg/kg)</th>
<th>Time (min)</th>
<th>Area of bluing spots (cm²)</th>
<th>Inhibition (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>100</td>
<td>20</td>
<td>1.74±0.08</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>100</td>
<td>60</td>
<td>1.28±0.14**</td>
<td>26.9</td>
</tr>
<tr>
<td>DSCG</td>
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<td>20</td>
<td>0.94±0.13**</td>
<td>46.2</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>50</td>
<td>0.84±0.25**</td>
<td>51.8</td>
</tr>
</tbody>
</table>

Test samples were injected intravenously at each time prior to the challenge. Each value represents the mean±S.E. of 5-8 experiments. Asterisks denote the significant differences from the control at *p<0.01, **p<0.05, respectively.

UV (log ε, MeOH) : 260(4.17), 280(4.06), 340(3.90)nm, IR(KBr) : 3389, 1655cm⁻¹, negative mode FAB-MS : m/z 625(M-H)+, liberated gosseptin¹¹ by the enzymatic hydrolysis with naringinase. Based on comparison of the ¹³C NMR data for 5¹² with those for gosseptin 7-O-α-L-rhamnopyranoside and observation of the HMBC correlations between 1'-H and 3'-C and between 1'-H and 7-C, the structure of 5 was determined.

Inhibitory effect of rhodiocyanosides A(1) and B(3) on the histamine release from rat peritoneal exudate cells sensitized with anti-dinitrophenylated IgE(anti-DNP IgE) by the antigen-challenge with dinitrophenylated bovine serum albumin(DNP-BSA)¹³ is summarized in Table 2. Rhodiocyanoside A(1), which is a major component of the Chinese natural medicine “Shiretsukoukeiten”, has been found to exhibit activity inhibiting the histamine release; rhodiocyanoside B(3) shows a little activity. Furthermore, 1 also exhibits inhibitory effect on rat 48h passive cutaneous anaphylaxis(PCA) reaction¹³ as shown in Table 3. Those activities of the major component may be preliminary evidence to substantiate the traditional effect of this natural medicine.

REFERENCES AND NOTES

8) ¹H NMR data of 1a : δ 2.01, 2.03, 2.06, 2.10(3H each, all s), 2.01(6H, br s)(Acx4, 5-H3), 4.17(dd, J=2.4, 12.3), 4.27(dd, J=4.8, 12.3)(6'2H2), 4.42(qdd, J=1.4, 6.7, 12.2), 4.52(qdd, J=1.4, 6.7, 12.2)(4-H2), 4.55(d, J=7.6, 1'2-H), 6.24(qdd, J=1.4, 6.7, 6.7, 3-H3).
9) 4a, a white powder, IR(KBr) : 1760, 1055cm⁻¹, ¹H NMR(CD3OD) : δ 0.90(t, J=6.6, 1-H3), 1.96, 2.00, 2.01, 2.05, 2.08, 2.12(Acx6).
10) The ¹³C NMR(CD3OD) data of 4 : δC 14.4(1-C), 23.7(2-C), 30.8, 30.4, 30.5, 27.1(3-C, 4, 5, 6-C), 33.0(7-C), 71.0(8-C), 104.3(1'2-C), 75.0(2'-C), 77.9(3'2-C), 71.5(4'-C), 76.7(5'-C), 69.4(6'-C), 105.1(1''-C), 72.3(2''-C), 74.1(3''-C), 69.4(4''-C), 66.7(5''-C); 4a : δC 14.4(1-C), 23.7(2-C), 30.6, 30.4, 30.4, 27.0(3-C, 4, 5, 6-C), 33.0(7-C), 70.9(8-C), 101.7(1'-C), 72.9(2'-C), 74.6(3'-C), 70.3(4'-C)* 73.9(5'-C), 69.3(6'-C), 101.9(1''-C), 70.5(2''-C)* 71.7(3''-C), 68.3(4''-C), 64.1(5''-C), 20.6, 20.6, 20.6, 20.8, 20.8, 20.9, 171.1, 171.2, 171.4, 171.6, 171.7, 171.9(Acx6). *Assignments may be interchangeable.
12) The ¹³C NMR(DMSO-d6) data of 5 : δC 147.3(2-C), 135.8(3-C), 176.2(4-C), 104.4(10-C), 151.4(5-C), 98.2(6-C), 149.4(7-C), 127.2(8-C), 144.3(9-C), 122.1(1'2-C), 115.8(2'-C), 145.0(3'-C), 147.8(4'-C), 115.5(5'-C), 120.2(6'-C).

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