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西藏胡黄连的化学成分

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摘要 胡黄连(*Picrorhiza kurrooa* Royle ex Benth.)为我国传统中药，一向依赖进口。本世纪70年代以来，在西藏和云南西北部发现西藏胡黄连(*P. scrophulariiflora* Pennell)并栽培作为印度产胡黄连的代用品。本文详细研究西藏胡黄连的化学成分，分离到3个已知的环烯醚萜甙，分别为amphicoside，catalpol和aucubin，一个已知的酚甙androsin；两个葫芦素类苦味甙，其中一个已知化合物鉴定为25-乙酰氧基-2β-葡萄糖氧基-3，16，20-三羟基-19-失羊毛甾烷-5，23-二烯-22-酮。另一个新化合物经光谱分析，化学结构证明为2β-葡萄糖氧基-3，16，20，22-四羟基-9-甲基-19-失羊毛甾烷-5，24-二烯。研究结果表明，西藏胡黄连与印度产的胡黄连化学成分十分相似，联系到二者在植物形态上的相似性和地理分布上的连续性，从化学的角度进一步证明这两种植物在系统演化上的密切关系，而且为国产西藏胡黄连作为进口印度胡黄连的代用品提供了依据。

关键词 西藏胡黄连；玄参科；葫芦素甙；环烯醚萜甙

化学成分，

CHEMICAL CONSTITUENTS FROM PICRORHIZA SCROPHULARIIFLORA

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Abstract From the roots of *Picrorhiza scrophulariiflora* Royle ex Benth. a new bitter cucurbitacin glycoside was isolated together with three known iridoidal glycosides, amphicoside (picroside-Ⅱ) (3), catalpol (4), aucubin (5), a phenol glycoside, androsin (6) and a known cucurbitacin glycoside (2). By means of spectroscopic evidence (UV, IR, FAB-MS, ^{1}H, ^{13}C NMR, DEPT, COSY), the structure of the new compound was elucidated as 2β-glucopyranosyloxy-3, 16, 20, 22-tetrahydroxy-9-methyl-19-norlanosta-5, 24-diene (1). The results show that the chemical constituents of *P. scrophulariiflora* are very similar to those of *P. kurrooa*. Further considering the resemblance in plant morphology and the continual distribution in geography, it could be concluded that the two species are very close in the phylogeny, and both can be used as the same traditional drug.

Key words *Picrorhiza scrophulariiflora*; Scrophulariaceae; Cucurbitacin glycosid; Iridoidal glycosides

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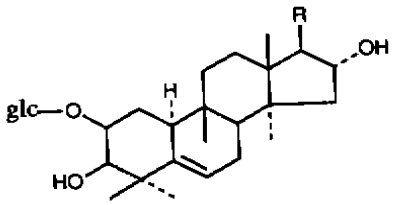
Although *Picrorhiza kurrooa* Royle ex Benth (Scrophulariaceae) has been used as a traditional drug in China for a long time, it was dependent on importation from India before the 70′ s of this century. Since 1965, another unique species of the same genus, *P. scrophulariiflora* Pennell, which was found on high altitute region (over 4400m) in the southeast of Tibet and the northwest of Yunnan, has been cultivated successfully and used to replace *P. Kurrooa*. It is known that a lot of phytochemical research has been reported on *P. kurrooa* [1-5]. (In this paper, we describe the isolation and structural elucidation of cucurbitacin, iridoidal and phenol glyosides from the roots of) *P. scrophulariiflora*, and discuss the relationship of chemical and morphological significance between this two phants.

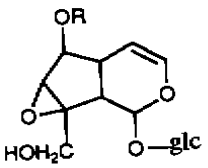
RESULTS AND DISCUSSION

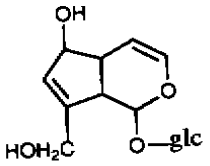
The n-BuOH soluable fraction of an ethanol extract of the roots of *P. scrophulariiflora* was chromatographed on repeated silica gel and reversed phase column chromatographies to give six glycosides (1— 6). Among which, three were identified as known iridoidal glycosides amphicoside (picroside-Ⅱ)(3), catalpol (4) and aucubin(5), one was phenol glycoside androsin (6) . In the remaining two cucurbitacin glycosides, compound 2 was identified as known 25-acetoxy-2β glucopyranosyloxy-3, 16, 20-trihydroxy-9-methyl-19-norlanosta-5, 23-diene-22-one [1, 2] and compound 1 is a new glycoside.

Compound 1 exhibited a quasimolecular ion peak at m / z 561 $[M(C_{36}H_{60}O_{11})H]^-$ in its negative FAB mass spectrum. The IR spectrum displayed absorptions at 3400 (OH) and 1630 (C=C) cm^{-1}. The ^1H NMR spectrum showed the characteristic signals of a 11-deoxocucurbitacin skeleton [2] , to which a β-gluco-pyranosyloxy moiety linked at C-2. This was supported by the presence of eight methyl signals at δ 0.94—1.77, a broad H-2 doublet at δ 4.28, a H-3 doublet at δ 3.60, an olefinic H-6 signal at δ 5.59 (d, J=4.9Hz) and the characteristic signals of the D-glucopyranosyl moiety (H-1, δ 4.30, d, J=7.8Hz; H-6a, δ 3.90, br d , J=11.8Hz; H-6b, δ 3.67, dd, J=11.8, 5.4Hz). The ^{13}C NMR spectrum of 1 was in good agreement with that of 2 except the signals of the side-chain. But the ^1H and ^{13}C NMR signals due to the side-chin of compound 1 were superimposable on those of a known compound whose structure was 2β-glucopyranosyloxy-16, 20, 22-trihydroxy-9-methyl-19-norlanosta-5, 24-diene-3, 11-dione [3] . Further, a 2D ^1H-^1H COSY experiment showed cross peaks between the broad triplet signal at δ 5.23 (H-24) and the signals at δ 2.30 (H-23a) and δ, 2.21(H-23b); the latter two were coorelated with a downfield signal at δ 3.37(H-22). These correlation pattern supported that the side-chain of compound 1 should possess a double bond at C-24 (25) and a hydroxyl group at C-22. Therefore, the structure of compound 1 was shown to be 2β -glucopyranosyloxy-3, 16, 20, 22-tetrahydroxy-9-methyl-19-norlanosta-5, 24-diene.

It is noted that the chemical constituents of *P. scrophulariflora* and *P. kurrooa* are very similar. Both contain aromatic acids [6] , phenol glycosides, iridoidal glycosides, cucurbitacin glycosides and D-mannitol (Tab. 1). The morphological difference of the two species only shows in the flowers (Tab. 2). Furthermore, a continuous and limited geographical distribution in the south Himalaya region indicate that the two species is a natural taxa and show very close relationship in the phylogeny. Based on the above evidence, it can be suggested that *P. scrophulariiflora* should be used as a traditional drug in place of *P. kurrooa*.







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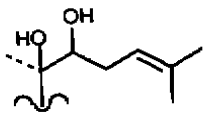
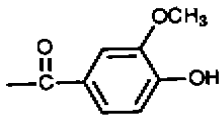
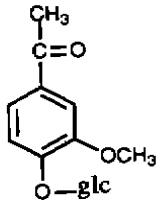
1　R=



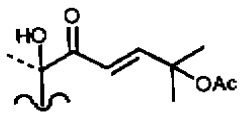
3　R=





4　R = H

2　R=



glc = - -D-glucopyranosyl　　6

Tab. 1　Comparison of chemical constituents between *P. scrophulariiflora* and *P. kurrooa*

Constituents	*P. scrophulariiflora*	*P. kurrooa*
D—mannitol	+	+
aromatic acid		
cinnamic acid	+	+
vanillic acid	+	+
ferulaic acid	+	+
phenol glycosides		
picein	−	+
androsin	+	+
iridoidal glycoside		
catapol	+	−
picroside—I	+	+
picroside—II	+	+
picroside—III	+	+
minecoside	−	+
veronicoside	−	+
6—feruloylcatapol	−	+
aucubin	+	−
cucurbitacin glycosides	+	+

Tab. 2 Comparison of plant morphology between *P. scrophulariiflora* and *P. kurrooa*

	P. scrophulariiflora	*P. kurrooa*
bracteole	ovoid	elongate ovoid of lanceolate
corrolla	9–12mm long, 4 valve indifferent length, liplike, no echinid	no more than 5mm long, 5 valve in same length, echinid
stamen	4, two longer	4,same
capsule	9–12mm	6mm

EXPERIMENTAL

Mps. uncorr. ^1H and ^{13}C NMR were recorded on Bruker AM–400 with TMS as int. standard.

Plant material: The cultivated roots of *P. scrophulariiflora* was collected in La–Mei–Rong (Alt. 3200 m) of Yunnan province, China. A specimen has been deposited in the Herbarium of the Kunming Institute of Botany.

Extraction and Isolation: The powdered roots (2800g) were extracted with 90% EtOH under reflux. After removal of the solvent by evapn, the combined extracts (400 g) were suspended in H_2O and then extracted with EtOAc and n–BuOH. The H_2O layer was concd in vacuo and the residue was crystalized with MeOH to afford D–mannitol (11.5 g). The EtOAc extract was proved to contain aromatic acids. The n–BuOH extract was chromatographed on a macroporous resin D–101 column with aq. EtOH: fr. A (195. 4 g) and B(2. 9 g)were obtained from 50% and 70% EtOH, respectively. Fr. A(20 g) was subjected to column chromatography on silica gel ($CHCl_3$–MeOH, 20: 1 to 4: 1), affording compounds 1 (1.5 g), 2(5.5 g) and 6(200 mg). 1 was further purified by a column on Lobar RP–8 with 40% MeOH. Fr. B was subjected to column chromatography on silica gel ($CHCl_3$–MeOH, 8 : 1), then to a column on Lobar Rp–8 (70% MeOH) to yield compounds 3 (200 mg), 4 and 5(both minor).

Compound 1. Amorphous white powder from MeOH, mp 175— 179℃, $[\alpha]_D^{20}$–4. 90 (c 0. 98, MeOH); FAB–MS (Neg.)m / z: 651 〔M–H〕$^-$, 633 〔M–H_2O–H〕$^-$, 490 〔M–162〕$^-$; UVλ_{max}(nm): 202; IRν_{max}(cm^{-1}): 3400, 2930, 2860, 1630. ^1H NMR (CD_3OD) δ: 0.94(3H, s), 1.03(3H, s), 1.08(3H, s), 1.11 (3H, s), 1.18(3H, s), 1.24(3H, s), 1.62(3H, s), 1.77(3H, s)(8× CH_3); 1.88(1H, dd, H–7b), 2.21(1H, dd, J=6.6, 14.OHz, H–23b), 2.30(1H, br dd, J=6.2, 13.6Hz, H–23a), 2.39(1H, d, H–17), 2.42(1H, br d, H–7a), 3.37(1H, tr, H–22), 3.60(1H, br, H–3), 3.67(1H, dd, J=5.4, 11.8Hz, glc H–6b), 3.90 (1H, br d, J=11.8Hz, glc H–6a), 4.28(1H, br d, J=11.3Hz, H–2), 4.30(1H, d, J=7.8Hz, glc H–1), 4.56(1H, tr, J=7.4Hz, H–16), 5.23(1H, tr, J=6.9Hz, H–24), 5.59(1H, br d, J=4.9Hz, H–6). ^{13}C NMR see Table 3.

Compound 2. Amorphous powder from MeOH, mp 125—128℃, FAB–MS (Neg.)m / z: 707 〔M–H〕$^-$, 689 〔M–H_2O–H〕$^-$, ^1H NMR (CD_3OD) δ: 0.94(3H, s), 1.02 (3H, s), 1.03(3H, s), 1.10(3H, s), 1.18(3H, s), 1.39(3H, s), 1.54(3H, s), 1.56(3H, s)(8× CH_3); 2.00(3H, s, OAc), 2.34(1H, d, J=7.2Hz, H–17), 2.43(2H, br d, J=15.3Hz, H–7), 3.68(1H, dd, J=10.7, 5.2Hz, glc H–6b), 3.89(1H, d, J=10.7Hz, glc H–6a), 4.29(1H, br d, J=10.6Hz, H–2), 4.43(1H, d,

J=7.7Hz, glc H-1), 4.47(1H, br t, J=7.8Hz, H-16), 5.58(1H, d, J=5.2Hz, H-6), 6.77(1H, d, J=15.8Hz, H-23), 6.95(1H, d, J=15.8Hz, H-24). ^{13}C NMR see Table 3 [1, 2].

Tab.3 ^{13}C NMR chemical shifts of compounds 1 and 2 in pyridine-d_5 (δ value: ppm)

C	2	1	C	2	1
1	28.0 t	28.5(28.8)* t	20	80.2 s	76.6(77.0) s
2	76.7 d	76.6(77.5) d	21	25.4 q	24.5(24.1) q
3	75.7 d	75.7(77.8) d	22	204.6 s	81.1(82.4) d
4	41.6 s	41.6(42.2) s	23	122.8 d	31.5(32.2) t
5	141.6 s	141.6(141.6) s	24	149.6 d	124.3(123.5) d
6	120.0 d	120.0(121.5) d	25	79.9 s	131.8(133.4) s
7	24.7 t	24.7(25.3) t	26	26.3 q	25.9(26.1) q
8	42.7 d	42.9(44.0) d	27	26.7 q	18.0(18.1) q
9	34.9 s	34.5(35.2) s	28	27.2 q	27.2(27.2) q
10	37.0 d	36.9(37.9) d	29	26.2 q	26.2(26.2) q
11	30.9 t	31.3(31.2) t	30	18.7 q	18.1(19.0) q
12	32.0 t	32.1(32.8) t	glc-1	101.7 d	101.3(101.9) d
13	49.0 s	48.8(49.4) s	2	75.5 d	75.7(75.2) d
14	49.0 s	49.4(49.6) s	3	78.8 d	78.6(78.0) d
15	46.8 t	46.1(46.1) t	4	71.3 d	71.7(71.6) d
16	71.7 d	71.7(72.6) d	5	78.6 d	78.7(78.0) d
17	60.2 d	56.9(57.1) d	6	62.7 t	62.7(62.7) t
18	18.6 q	18.5(18.6) q	OAc	21.8 q	
19	20.0 q	28.0(28.4) q		169.8 s	

* measured in CD_3OD

Amphicoside (picroside-Ⅱ) (3). Amorphous powder from MeOH, FAB-MS(Neg.) m/z: 511 [M($C_{23}H_{28}O_{13}$)-H]$^-$, 349 [M-162-H]$^-$, 183 [M-167-162]$^-$; ^{1}H NMR (DMSO) δ: 3.88(3H, s, OMe), 3.92(2H, dd, J=6.0, 13.7Hz, H-10), 3.61(1H, d, J=8.0Hz, glcH-1), 4.96(1H, tr, J=5.4Hz, H-4), 5.06(1H, dd, J=8.0, 1.2Hz, H-6), 5.11(1H, d, J=10.0Hz, H-1), 6.44 (1H, dd, J=6.0, 1.5Hz, H-3), 6.89(1H, d, J=9.0Hz, Ar H-5), 7.43(1H, d, J=1.8Hz, Ar H-2), 7.55(1H, dd, J=9.0, 1.8Hz, Ar H-6). ^{13}C NMR (DMSO) δ: 93.3(1), 141.4(3), 102.1(4), 35.4(5), 80.0(6), 58.5(7), 66.1(8), 42.1(9), 58.8(10), 98.2(glc-1), 73.7(glc-2), 77.7(glc-3), 70.6(glc-4), 76.7(glc-5), 61.7(glc-6), 120.3(Ar-1), 113.0(Ar-2), 152.2(Ar-3), 147.7(Ar-4), 115.5(Ar-5), 124.1(Ar-6), 56.0(OCH_3), 165.9(C=O) [7].

Catapol (4). Amorphus, FAB-MS(Neg.) m/z: 361 [M($C_{15}H_{22}O_{10}$)-H]$^-$, 199 [M-162-H]$^-$. ^{13}C NMR (DMSO) δ: 93.5(1), 140.2(3), 103.4(4), 37.6(5), 76.6(6), 59.7(7), 65.0(8), 42.4(9), 59.2(10), 98.1(glc-1), 73.6(glc-2), 77.4(glc-3), 70.3(glc-4), 76.9(glc-5), 61.3(glc-6) [3].

Aucubin (5). Amorphous powder from MeOH, FAB-MS(Neg.) m/z: 345 [M($C_{15}H_{22}O_9$)-H]$^-$, 183 [M-162-H]$^-$. ^{13}C NMR (DMSO): δ 98.3(1), 140.5(3), 105.2(4), 44.8(5), 80.7(6), 129.4(7), 146.3(8), 46.6(9), 60.9(10), 95.6(glc-1), 73.6(glc-2), 77.4(glc-3), 70.5(glc-4),

76.6(glc-5), 61.5(glc-6) [3].

Androsin (6). White crystals from MeOH, mp 220-221℃, FAB-MS (Neg.) m/z: 327 [M($C_{15}H_{20}O_3$)-H]$^-$, 165 [aglycone-H]$^-$. ^{1}H NMR (DMSO) δ: 2.54(3H, s, $COCH_3$), 3.83(3H, s, MeO), 4.37(1H, d, J=7.2Hz, glu H-1), 7.17(1H, d, J=8.6Hz, H-5), 7.46(1H, d, J=2.0 Hz, H-2), 7.58(1H, dd, J=8.6, 2.0 Hz, H-6). ^{13}C NMR (DMSO) δ: 131.1(1), 111.4(2), 150.9(3), 149.0(4), 114.5(5), 122.9(6), 196.7(7), 26.7(8), 55.9(MeO), 99.5(glc-1), 73.3(glc-2), 77.4(glc-3), 69.8(glc-4), 77.1(glc-5), 60.8(glc-6) [5].

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