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CHEMICAL CONSTITUENTS OF *Rhododendron primulaeflorum*

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Rhododendron primulaeflorum Bur. et Franch. from the family of Ericaceae comprises about 20 genera and about 800 species in China. *R. primulaeflorum* is a shrub distributed mainly in the southwest district of China, especially in the Tibetan Autonomous Region, Yunnan, and Sichuan provinces [1]. The leaves and flowers of *R. primulaeflorum* are important Tibetan medicines as it clears away heat, is used for detumescence, and tonifies the kidney. In Tibet and the western part of China, it is widely used to cure pulmonary disease, dropsy, indigestion, gastroptosis, and gastrectasis. The essential oils from it are used in curing chronic tracheitis [2]. The Chinese Pharmacopoeia (1977 edition) listed *R. primulaeflorum* as an official drug. However, phytochemical studies of this plant have not been reported previously. Recently we have systematically investigated the chemical constituents of this plant. This study was carried out with the purpose of validating the medicial use of this plant. In this paper, we describe the isolation and structural elucidation of 22 compounds. All of them were isolated from this plant for the first time.

Fresh samples of *R. primulaeflorum* Bur. et Franch. were collected in Xianggelila, Geza, Yunnan Province in China, in July, 2006. The plant material was identified by Prof. Zheng Hanchen, Department of Phytochemistry, Second Military Medical University. A voucher specimen (collection No. SJTUYCDJ) is deposited at the Herbarium of the School of Pharmacy, Shanghai Jiao Tong University, Shanghai, China.

The dried aerial parts of *R. primulaeflorum* (15.0 kg) were extracted with 95% ethanol three times at 60°C to afford the ethanol extract (2019.3 g). Then the extract was suspended in 4 L water and partitioned successively with petroleum ether, chloroform, ethyl acetate, and *n*-butanol, respectively. By using a series of chromatographic techniques, such as silica gel column (mesh 200–300), Sephadex LH-20, and prep-HPLC, compounds **1**–**22** were isolated.

The compounds were identified using UV, IR, MS, and NMR spectral data and determined as lyoniside (**1**) [3], nudiposide (**2**) [3], ssioriside (**3**) [4], umbelliferone (**4**) [5], scopoletin (**5**) [6], isovanillin (**6**) [7], noregenin (**7**) [8], 3,5,7-trihydroxychromone-3-*O*-α-L-arabinopyranoside (**8**) [9], *cis*-taxifolin (**9**) [10], *trans*-taxifolin (**10**) [10], (+)-catechin (**11**) [11], (–)-epicatechin (**12**) [12], proanthocyanidin A-1 (**13**) [13, 14], proanthocyanidin A-2 (**14**) [13, 14], avicularin (**15**) [15], usinc acid (**16**) [16], uvaol (**17**) [17], ursolic acid (**18**) [18], oleanolic acid (**19**) [19], lupeol (**20**) [20], β-sitosterol (**21**) [21], and daucosterol (**22**) [22].

Lyoniside (**1**). White crystal, mp 162–164°C; ESI-MS *m/z*: 551.3 $[M-H]^-$, 575.3 $[M+Na]^+$; ^{1}H NMR (500 MHz, CD_3OD, δ, ppm, J/Hz): 1.69–1.72 (1H, m, H-8′), 2.05–2.08 (1H, m, H-8), 2.64 (1H, dd, J = 15.0, 11.5, H-7′), 2.72 (1H, dd, J = 15.0, 4.5, H-7′), 3.17 (1H, dd, J = 11.5, 10.5, H-5″), 3.22 (1H, dd, J = 9.0, 7.5, H-2″), 3.32 (3H, s, 5′-OCH_3), 3.42 (1H, dd, J = 9.8, 3.7, H-9), 3.48 (1H, m, H-4″), 3.56 (1H, dd, J = 11.0, 6.5, H-9′), 3.66 (1H, dd, J = 11.0, 4.5, H-9′), 3.75 (3H × 2, s, 3-OCH_3, 5-OCH_3), 3.83 (1H, dd, J = 11.5, 6.0, H-5″), 3.84 (1H, dd, J = 9.8, 4.9, H-9), 3.85 (3H, s, 3′-OCH_3), 4.23 (1H, d, J = 7.5, H-1″), 4.38 (1H, d, J = 6.5, H-7), 6.42 (1H × 2, s, H-2, H-6), 6.57 (1H, s, H-2′); ^{13}C NMR (125 MHz, CD_3OD, δ, ppm): 33.9 (C-7′), 40.5 (C-8′), 42.9 (C-7), 46.7 (C-8), 56.6 (3′-OCH_3), 56.9 (3-OCH_3, 5-OCH_3), 60.0 (5′-OCH_3), 66.1 (C-9′), 66.9 (C-5″), 71.1 (C-9), 71.3 (C-4″), 74.9 (C-2″), 78.0 (C-3″), 105.5 (C-1″), 106.9 (C-2, 6), 107.8 (C-2′), 126.4 (C-6′), 130.1 (C-1′), 134.6 (C-4), 138.9 (C-4′), 139.4 (C-1), 147.6 (C-5′), 148.6 (C-3′), 148.9 (C-3, 5) [3].

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Nudiposide (**2**). White amorphous powder, mp 106–108°C; ESI-MS *m/z*: 551.3 $[M–H]^–$, 575.3 $[M+Na]^+$; ^{1}H NMR (500 MHz, CD_3OD, δ, ppm, J/Hz): 1.70–1.72 (1H, m, H-8′), 2.02–2.05 (1H, m, H-8), 2.68 (2H, dd, J = 10.0, 6.5, H-7′), 3.13 (1H, dd, J = 11.5, 10.5, H-5″), 3.19 (1H, dd, J = 9.0, 7.5, H-2″), 3.30 (3H, s, 5′-OCH_3), 3.59 (1H, dd, J = 10.5, 5.0, H-9), 3.63 (2H, dd, J = 10.5, 5.0, H-9′), 3.75 (3H × 2, s, 3-OCH_3, 5-OCH_3), 3.81 (1H, dd, J = 10.5, 4.5, H-9), 3.84 (3H, s, 3′-OCH_3), 3.86 (1H, dd, J = 11.0, 5.0, H-5″), 4.09 (1H, d, J = 7.5, H-1″), 4.22 (1H, d, J = 7.0, H-7), 6.38 (1H, s, H-6), 6.41 (1H, s, H-2), 6.57 (1H, s, H-2′); ^{13}C NMR (125 MHz, CD_3OD, δ, ppm): 34.0 (C-7′), 40.7 (C-8′), 43.3 (C-7), 46.9 (C-8), 56.6 (3′-OCH_3), 56.8 (3-OCH_3, 5-OCH_3), 59.9 (5′-OCH_3), 66.1 (C-9′), 67.1 (C-5″), 71.2 (C-9), 71.3 (C-4″), 74.9 (C-2″), 77.9 (C-3″), 105.0 (C-1″), 107.1 (C-2, C-6), 107.8 (C-2′), 126.3 (C-6′), 130.1 (C-1′), 134.6 (C-4), 138.9 (C-4′), 139.6 (C-1), 147.6 (C-5′), 148.7 (C-3′), 148.9 (C-3, C-5) [3].

Ssioriside (3). White crystal, mp 140–142°C; ESI-MS *m/z*: 553.3 $[M–H]^–$, 577.3 $[M+Na]^+$; ^{1}H NMR (500 MHz, CD_3OD, δ, ppm, J/Hz): 1.94 (1H, m, H-8′), 2.07 (1H, m, H-8), 2.52–2.65 (2H, m, H-7′), 2.70 (2H, dd, J = 14.0, 7.0, H-7), 3.18 (1H, m, H-5″), 3.22 (1H, dd, J = 9.0, 8.0, H-2″), 3.48 (1H, dd, J = 9.0, 4.0, H-9′), 3.57 (1H, dd, J = 9.0, 4.0, H-9′), 3.67 (1H, dd, J = 9.0, 4.0, H-9), 3.74 (3H × 2, s, 3′-OCH_3, 5′-OCH_3), 3.75 (3H × 2, s, 3-OCH_3, 5-OCH_3), 3.85 (1H, m, H-5″), 3.98 (1H, dd, J = 9.0, 4.0, H-9), 4.19 (1H, d, J = 8.0, H-1″), 6.33 (1H × 2, s, H-2′, H-6′), 6.35 (1H × 2, s, H-2, H-6); ^{13}C NMR (125 MHz, CD_3OD, δ, ppm): 36.1 (C-7′), 36.3 (C-7), 41.4 (C-8), 43.9 (C-8′), 56.6 (3′-OCH_3, 5′-OCH_3), 56.7 (3-OCH_3, 5-OCH_3), 62.7 (C-9′), 66.9 (C-5″), 70.8 (C-9), 71.3 (C-4″), 75.1 (C-2″), 78.0 (C-3″), 105.3 (C-1″), 107.2 (C-2, C-6), 107.3 (C-2′, C-6′), 133.1 (C-1′), 133.3 (C-1), 134.3 (C-4′), 134.4 (C-4), 148.9 (C-3, C-5, C-3′, C-5′) [4].

3,5,7-Trihydroxychromone-3-*O*-α-L-arabinopyranoside (**8**). White amorphous powder, mp 184–186°C; ESI-MS *m/z*: 325.1 $[M–H]^–$, 349.2 $[M+Na]^+$; ^{1}H NMR (500 MHz, C_5D_5N, δ, ppm, J/Hz): 3.90 (1H, dd, J = 13.0, 3.0, H-5′), 4.34 (1H, dd, J = 8.0, 3.0, H-3′), 4.42 (1H, dd, J = 8.0, 3.0, H-2′), 4.73 (1H, m, H-4′), 5.51 (1H, d, J = 6.0, H-1′), 6.59 (1H, d, J = 2.0, H-8), 6.68 (1H, d, J = 2.0, H-6), 8.34 (1H, s, H-2), 13.07 (1H, s, 5-OH); ^{13}C NMR (125 MHz, C_5D_5N, δ, ppm): 66.2 (C-5′), 68.2 (C-4′), 71.6 (C-2′), 73.5 (C-3′), 94.4 (C-8), 99.6 (C-6), 103.6 (C-1′), 105.6 (C-10), 139.7 (C-3), 147.2 (C-2), 157.9 (C-9), 162.8 (C-5), 165.7 (C-7), 177.7 (C-4) [9].

Proanthocyanidin A-1 (**13**). White amorphous powder, mp 280–282°C; ESI-MS *m/z*: 575.2 $[M–H]^–$, 599.1 $[M+Na]^+$; ^{1}H NMR (500 MHz, CD_3OD, δ, ppm, J/Hz): 2.59 (1H, dd, J = 16.5, 8.5, H-4′α), 2.98 (1H, dd, J = 16.5, 5.5, H-4′β), 4.09 (1H, d, J = 3.0, H-3), 4.16 (1H, d, J = 4.0, H-3′), 4.27 (1H, d, J = 3.0, H-4), 4.76 (1H, d, J = 8.0, H-2′), 5.96 (1H, d, J = 2.0, H-6), 6.09 (1H, d, J = 2.0, H-8), 6.11 (1H, d, J = 8.0, H-6′), 6.84 (1H, d, J = 8.0, H-13), 6.87 (1H, dd, J = 9.0, 2.0, H-14′), 6.89 (1H, d, J = 9.0, H-13′), 6.98 (1H, d, J = 2.0, H-10′), 7.05 (1H, dd, J = 8.0, 2.0, H-14), 7.17 (1H, d, J = 2.0, H-10); ^{13}C NMR (125 MHz, CD_3OD, δ, ppm): 28.7 (C-4′), 29.2 (C-4), 67.6 (C-3), 68.3 (C-3′), 83.8 (C-2′), 96.5 (C-6′), 96.6 (C-8), 98.2 (C-6), 100.4 (C-2), 102.8 (C-4′a), 104.0 (C-4a), 106.5 (C-8′), 115.4 (C-10), 115.6 (C-10′), 115.7 (C-13′), 116.4 (C-13), 119.8 (C-14), 120.3 (C-14′), 130.9 (C-9′), 132.1 (C-9), 145.6 (C-12), 146.3 (C-12′), 146.6 (C-11), 146.7 (C-11′), 150.8 (C-8′a), 152.1 (C-7′), 154.0 (C-8a), 156.1 (C-5′), 156.6 (C-5), 158.0 (C-7) [13, 14].

Proanthocyanidin A-2 (**14**). White amorphous powder, mp 273–275°C; ESI-MS *m/z*: 575.2 $[M–H]^–$, 599.1 $[M+Na]^+$; ^{1}H NMR (500 MHz, CD_3OD, δ, ppm, J/Hz): 2.77 (1H, dd, J = 17.0, 3.0, H-4′α), 2.95 (1H, dd, J = 17.0, 5.0, H-4′β), 4.08 (1H, d, J = 3.0, H-3), 4.24 (1H, m, H-3′), 4.43 (1H, d, J = 3.0, H-4), 4.92 (1H, d, J = 2.0, H-2′), 6.03 (1H, d, J = 2.0, H-6), 6.10 (1H, d, J = 2.0, H-8), 6.12 (1H, s, H-6′), 6.82 (1H, d, J = 8.0, H-13), 6.83 (1H, d, J = 8.0, H-13′), 6.86 (1H, dd, J = 9.0, 3.0, H-14′), 6.98 (1H, d, J = 2.0, H-10′), 7.04 (1H, dd, J = 8.0, 3.0, H-14), 7.17 (1H, d, J = 3.0, H-10); ^{13}C NMR (125 MHz, CD_3OD, δ, ppm): 29.2 (C-4), 29.8 (C-4′), 66.9 (C-3′), 67.9 (C-3), 81.7 (C-2′), 96.5 (C-6′), 96.6 (C-8), 98.3 (C-6), 100.1 (C-2), 102.4 (C-4′a), 104.3 (C-4a), 107.2 (C-8′), 115.6 (C-10), 115.7 (C-10′), 115.9 (C-13′), 116.1 (C-13), 119.8 (C-14′), 120.4 (C-14), 131.1 (C-9′), 132.4 (C-9), 145.6 (C-12), 145.9 (C-12′), 146.2 (C-11), 146.7 (C-11′), 152.1 (C-8′a), 152.2 (C-7′), 154.2 (C-8a), 156.5 (C-5′), 156.9 (C-5), 158.0 (C-7) [13, 14].

REFERENCES

1. Reipublicae Popularis Sinicae, Flora, Beijing, Science Press, Tomus **57** (1), 1999.
2. Z. Q. Li, W. J. Zhang, X. J. Hu, J. M. Diqing, L. R. Cicheng, and B. M. Danzeng, *J. Chin. Med. Mater.*, **20**, 332 (1997).
3. S. K. Sadhu, A. Khatum, P. Phattanawasin, T. Ohtsuki, and M. Ishibashi, *J. Nat. Med.*, **61**, 480 (2007).
4. K. Yoshinari, Y. Sashida, and H. Shimomura, *Chem. Pharm. Bull.*, **37**, 3301 (1989).
5. L. Y. Kong, Y. Li, Z. D. Min, X. Li, and T. R. Zhu, *Phytochemistry*, **41**, 1423 (1996).

6. Y. M. Liu, G. Y. Liang, J. X. Zhang, K. Y. Wu, B. X. Xu, and B. Luo, *Chin. Pharm. J.*, **37**, 577 (2002).
7. Q. Z. Wang, J. Y. Liang, and J. Chen, *J. China Pharm. Univ.*, **36**, 520 (2005).
8. W. Zhu, Z. B. Tu, L. Y. Huang, and B. N. Zhou, *Nat. Prod. Res. Dev.*, **7**, 39 (1995).
9. Z. M. Feng, Y. H. Wang, and P. C. Zhang, *Acta Pharm. Sinica*, **40**, 150 (2005).
10. K. Eberhard and Edmond P. M. Li, *J. Nat. Prod.*, **58**, 450 (1995).
11. L. L. Ding, S. C. Wang, and Z. T. Wang, *China J. Chin. Mater. Med.*, **32**, 1893 (2007).
12. J. Lu and L. Y. Kong, *SNO-TCM*, **9**, 12 (2007).
13. H. X. Lou, Y. Yamazaki, T. Sasaki, M. Uchida, H. Tanaka, and S. Oka, *Phytochemistry*, **51**, 297 (1999).
14. K. Kamiya, C. Watanabe, H. Endang, M. Umar, and T. Satake, *Chem. Pharm. Bull.*, **49**, 551 (2001).
15. C. Zhang and Y. X. Fang, *China J. Chin. Mater. Med.*, **28**, 429 (2003).
16. X. L. Wang and B. L. Yang, *Chinese Traditional and Herbal Drugs*, **35**, 1090 (2004).
17. X. Z. Xu and X. Tian, *China J. Chin. Mater. Med.*, **25**, 225 (2000).
18. D. J. Yang, R. J. Ma, L. Wang, K. Sun, L. Ding, and H. Wang, *J. Northwest Normal Univ.*, **41**, 59 (2005).
19. W. D. Xu, H. W. Lin, F. Qiu, and W. S. Chen, *J. Shenyang Pharm. Univ.*, **24**, 402 (2007).
20. W. L. Mei, H. F. Dai, and D. G. Wu, *Chin. J. Med. Chem.*, **16**, 240 (2006).
21. Z. H. Liu and Z. X. Yang, *China Pharmacist*, **10**, 978 (2007).
22. T. Y. Chen and S. J. Long, *W C J. P S*, **21**, 129 (2006).