RICCARDIN C, A BISBIBENZYL COMPOUND FROM *Primula macrocalyx*

Yu. S. Kosenkova,[1] M. P. Polovinka,[1] N. I. Komarova,[1] D. V. Korchagina,[1] N. Yu. Kurochkina,[2] V. A. Cheremushkina,[2] and N. F. Salakhutdinov[1]

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The perennial herbaceous plant *Primula macrocalyx* Bge. (Primulaceae) has been used in folk medicine to treat paralysis; the powder of dry leaves, scurvy, tuberculosis, and fever. Tibetan medicine considers this plant capable of inhibiting tumor growth, accelerating wound healing, and curing blood diseases [1, 2]. The chemical composition of *P. macrocalyx* is practically unstudied.

Plant material of *P. macrocalyx* (aerial part and roots) was collected in Altai (near the village Anos, Chemalsk Region) in August 2004 and 2005. The species was defined by staff of the Laboratory of Medicinal Plants of the Central Siberian Botanical Garden (SBG) of the Siberian Division, Russian Academy of Sciences. A voucher specimen of the plant is stored in the herbarium of the SBG.

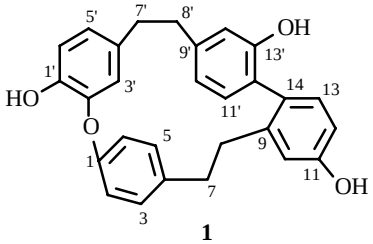
We developed the conditions for extracting compounds from the aerial part and roots of the plant in order to study the chemical composition. The best method was successive soaking of plant raw material in hexane and acetone. First, the aerial part (94.24 g) was soaked in hexane (4 × 0.5 L, 48 h until the extract was colorless) for maximum removal of lipophilic substances, chlorophyll, and pigments. Plant raw material was then soaked in acetone (4 × 0.5 L, 24 h). This produced an extract (1.5 g) containing one main compound that we isolated by successive column chromatography over silica gel (elution by $CHCl_3$ with an ethanol gradient) and reversed-phase resin (LiChrosorb RP-18, elution by 90% MeOH). The course of the chromatography was monitored by analyzing separate fractions (TLC) on Silufol or Sorbfil plates using ethanol (2%) in $CHCl_3$ to afford **1** (0.02 g, 1.3% of the extract mass, 0.02% of the dry raw material mass).

PMR and ^{13}C NMR spectra were recorded for **1** (Bruker AM-400 spectrometer, operating frequency 400.13 for ^1H and 100.61 MHz for ^{13}C).

PMR spectrum (DMSO-d_6, δ_H 2.50, J/Hz, 55°C): 9.09 (1H, br.s, OH-11), 8.78 (1H, br.s, OH-1′), 8.64 (1H, s, OH-13′), 6.85 (1H, d, J = 8.3, H-13), 6.82 (2H, br.d, J = 8, H-3, H-5), 6.80 (1H, d, J = 2.5, H-10), 6.77 (1H, d, J = 8.0, H-6′), 6.70 (1H, d, J = 7.6, H-11′), 6.68 (2H, br.d, J = 8, H-2, H-6), 6.65 (1H, dd, J = 8.0, 2.0, H-5′), 6.63 (1H, dd, J = 8.3, 2.5, H-12), 6.32 (1H, d, J = 1.7, H-14′), 6.09 (1H, dd, J = 7.6, 1.7, H-10′), 5.34 (1H, d, J = 2.0, H-3′), 2.80 (4H, br.s, 2H-7, 2H-8), 2.61 (2H, m, 2H-7′), 2.56 (2H, m, H-8′).

^{13}C NMR spectrum (DMSO-d_6, δ_C 39.50, 55°C): 156.29 (s, C-11), 153.40 (s, C-13′), 152.74 (s, C-1), 146.96 (s, C-2′), 144.05 (s, C-1′), 142.73 (s, C-9), 139.89 (s, C-9′), 139.12 (s, C-4), 131.94 (d, C-13), 131.74 (d, C-11′), 131.67 (s, C-4′), 129.18 (s, C-14), 128.97 (2d, C-3, C-5), 125.55 (s, C-12′), 121.48 (2d, C-2, C-6), 121.45 (d, C-5′), 119.49 (d, C-10′), 116.59 (d, C-3′), 116.02 (2d, C-10, C-6′), 115.61 (d, C-14′), 112.71 (d, C-12), 37.27 (t) and 34.72 (t, C-7, C-8), 36.99 (t, C-8′), 36.08 (t, C-7′).

Based on PMR and ^{13}C NMR spectra (2D, LRJMD) and comparison of them with the literature [3, 4], the structure riccardin C was proposed for **1**.



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1) Novosibirsk Institute of Organic Chemistry, Siberian Division, Russian Academy of Sciences, 630090, Novosibirsk, pr. Akad. Lavrent′eva, 9, e-mail: kosen@nioch.nsc.ru; 2) Central Siberian Botanical Garden, Siberian Division, Russian Academy of Sciences, ul. Zolotodolinskaya, 101. Translated from Khimiya Prirodnykh Soedinenii, No. 6, pp. 591-592, November-December, 2007. Original article submitted October 5, 2007.

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According to the literature, **1** and bisbibenzyl compounds related to it exhibit a broad spectrum of cytotoxic, antibacterial, and fungicidal activity and are used as inhibitors of 5-lipoxygenase [5, 6] and inducible NO-synthase [7]. Furthermore, riccardin C (**1**) increases the expression of genes ABCA1 and ABCG1, thereby activating reverse transport of cholesterol [8].

Riccardin C was isolated previously exclusively from bryophytes, Japanese moss-liverworts [3, 4]. The isolation of the valuable biologically active metabolite riccardin C from *P. macrocalyx* is the first example of the isolation of such a compound from higher flowering plants.

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