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A New Cyclic Peptide from *Schnabelia tetradonta*

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Abstract: A new cyclic octapeptide (schnabepeptide B) was isolated from the aerial part of *Schnabelia tetradonta* (Sun) C. Y. Wu et C. Chen (Lamiaceae). Its structure was elucidated as cyclo-(NH-Trp-Gly[1]-Leu[1]-Gly[2]-Pro[1]-Pro[2]-Leu[2]-Pro[3]-CO) on the basis of extensive 2D NMR and MS spectra.

Keywords: *Schnabelia tetradonta,* cyclopeptide, schnabepeptide B.

Schnabelia tetradonta (Sun) C. Y. Wu et C. Chen (Lamiaceae), commonly called "Jin Gu Cao", is an endemic herbaceous plant distributed in the southwest region. It is used as a febrifuge to relieve internal fevers and as a remedy for rheumatism treatment in traditional Chinese medicine[1]. A cyclic octapeptide, schnabepeptide, has been isolated and found to show immunosuppression activity on T/B lymphocytes from a closely related species, *S. oligophylla*[2]. As a continuation of our investigation on the new bioactive cyclopeptide from plants of the endemic genus, a new cyclopeptide, named schnabepeptide B, was isolated from the aerial parts of *S. tetradonta*. This paper deals with the isolation and structural elucidation of schnabepeptide B.

Dried and powered aerial parts of *S. tetradonta* (10 kg) were extracted with ethanol. The extract was suspended in H_2O and extracted with petroleum ether and then ethyl acetate. The ethyl acetate extract (51 g) was subjected to chromatography repeatedly on silica gel column to give **1** (20 mg).

Schnabepeptide B was negative to ninhydrin reaction. A molecular formula of $C_{42}H_{59}N_9O_8$ for **1** was established from HRESIMS at *m/z* 818.4555 $[M + H]^+$ (calcd 818.4559), indicating 18 degrees of unsaturation. The IR absorptions at 3330 and 1650 cm^{-1} were attributed to amino and amide carbonyl groups, respectively. Its peptide nature was suggested by five amide NH proton signals (δ 9.53, 10.18, 8.91, 8.43, 9.20) and eight amide carbonyl carbon resonances (δ 173.9, 171.0, 172.7, 167.0, 170.7, 172.3, 174.1, 170.6) observed in the ^1H and ^{13}C NMR spectra. Detailed analysis of NMR spectra (^1H- ^1H COSY, HMQC and HMBC) of **1**, suggested that glycine (2 eq), leucine (2 eq), proline (3 eq) and tryptophan (1 eq) units were present in the molecule. The sequence of these amino acid residues was determined by NOESY and HMBC experiments as shown in **Figure 1**. The presence of two peptide fragments (-Pro[3]-Trp-

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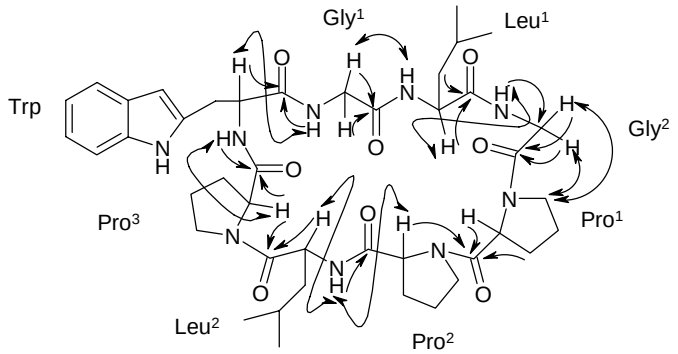
Gly[1]-Leu[1]-Gly[2]-Pro[1]- and -Pro[2]-Leu[2]-) was established by NOESY correlations observed for Pro[3] α-H (δ 4.68)/Trp NH (δ 9.53), Trp α-H (δ 4.94)/Gly[1] NH (δ 10.18), Gly[1] α-H (δ 4.65, 3.80)/Leu[1] NH (δ 8.91), Leu[1] α-H (δ 5.15)/Gly[2] NH (δ 8.43), Gly[2] α-H (δ 4.40, 4.18)/Pro[1] δ-H (δ 3.34) and Pro[2] α-H (δ 4.29)/Leu[2] NH (δ 9.20). The HMBC correlations observed for Pro[1] α-H (δ 4.15)/Pro[1] C=O (δ 170.7), Pro[2] α-H (δ 4.29)/Pro[1] C=O (δ 170.7), and Pro[3] α-H (δ 4.68)/ Leu[2] C=O (δ 174.1), Leu[2] α-H (δ 9.20)/Leu[2] C=O (δ 174.1) suggested the connectivity across the amide bonds of Pro[1]-Pro[2] and Leu[2]-Pro[3]. Thus, the sequence assignment can be accompleshed. Furthermore, the following MS fragments that supported the amino acid sequence of **1** were detected in the FABMS spectrum: *m/z* 818 $[M + H]^+$, 688 $[M + H - C_9H_8N]^+$, 632 $[M + H - Trp]^+$, 422 $[M + H - Trp - Pro^3 - Leu^2]^+$, 325 $[M + H - Trp - Pro^3 - Leu^2 - Pro^2]^+$, 228 $[M + H - Trp - Pro^3 - Leu^2 - Pro^2 - Pro^1]^+$, 721 $[M + H - Pro^2]^+$, 511 $[M + H - Pro^2 - Leu^2 - Pro^3]^+$, 268 $[M + H - Pro^2 - Leu^2 - Pro^3 - Trp - Gly^1]^+$, and 195 $[M + H - Leu^2 - Pro^3 - Trp - Gly^1 - Leu^1 - Gly^2]^+$. Therefore, the structure of schnabepeptide B (**1**) was elucidated as cyclo-(NH-Trp-Gly[1]-Leu[1]-Gly[2]-Pro[1]-Pro[2]-Leu[2]-Pro[3]-CO).

Figure 1 Key HMBC and NOESY correlations for compound **1**



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