Natural Product Sciences
17(3) : 181-182 (2011)

A New Pyrrole Constituent from the Fruits of *Lycium chinense*†

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Abstract – Phytochemical investigation of *Lycium chinense* fruits led to isolation of a new pyrrole compound. The structure of this compound was confirmed as a 5-methoxymethyl-1*H*-pyrrole-2-carbaaldehyde, a new natural product, by interpretation of 1D (^{1}H, ^{13}C) and 2D (HMQC, HMBC) spectroscopic data along with HRMS and IR spectroscopic data.
Keywords – *Lycium chinense*, Solanaceae, pyrrole, 5-methoxymethyl-1*H*-pyrrole-2-carbaaldehyde

Introduction

The dried mature fruits of *Lycium chinense* Miller (Solanaceae) have been used traditionally as components of herbal medicines. Previous studies have reported the occurrence of peptides, alkaloids, cerebrosides, carotenoids and glycolipids in this herbal medicine. Further, the pharmacological investigations demonstrated antifibrotic (Kim *et al*., 2002; Kim *et al*., 2009) hypotensive, hypoglycemic, anti-aging and hepatoprotective effects (Kim *et al*., 1999; Ha *et al*., 2005) as well as prevention of stress-induced ulceration in experimental animals (Xiao *et al*., 1993; Han *et al*., 2002; Lin *et al*., 2004). As a part of our ongoing phytochemical investigations on the fruits of *L. chinense* (Chin *et al*., 2003; Jung *et al*., 2005), a new pyrrole constituent was isolated. Herein, we describe the isolation and structure elucidation of a new pyrrole derivative from these fruits.

Experimental

General – EI-MS spectra were obtained on a JEOL JMS-AX505WA. IR spectra were recorded on a JASCO FT/IR-300E. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a JEOL spectrometer at 300 MHz and at 75 MHz, respectively. Column chromatography was performed using Sephadex LH-20 (Pharmacia, NJ, USA) and Kiesegel 60 (Art. 7734; Merck, Darmstadt, Germany). HPLC was performed on a column of Alltech (Conosil, 10 μm, 250 × 7.8 mm i.d., USA). TLC was conducted on pre-coated Kiesegel 60 F_{254} plates (Art. 5715; Merck, Darmstadt, Germany). Spots on the TLC were detected under UV light.

Plant material – The dried fruits of *L. chinense* were purchased from Chungyang Agricultural Cooperatives Federation in Korea and identified by one of the authors (J.K.). A voucher specimen (SNUPH-0028) was deposited at the College of Pharmacy, Seoul National University.

Extraction and isolation – The dried fruits of *L. chinense* (120 kg) were refluxed in MeOH to obtain a crude extract (37.5 kg). This extract was dissolved in water and partitioned with $CHCl_3$-MeOH (CM; 3:1) to yield 10 kg of crude extract. A portion of the CM extract (1 kg) was applied to a Sephadex LH-20 column (CH_2Cl_2-MeOH = 2:1) and fractionated into 11 sub-fractions (CM 1-11). CM11 (30 g) was subjected to silica gel column chromatography with a gradient of $CHCl_3$-MeOH (100:1-0:100) and 11 sub-fractions (CM11-1 to CM11-11) were collected. CM11-4 (3 g) was chromatographed on a silica gel column (*n*-hexane-acetone = 5:1 to 0:100), yielding 10 sub-fractions. Of the 10 sub-fractions, sub-fraction 6 was fractionated by using a Sephadex LH-20 column (MeOH) into seven sub-fractions. The fourth sub-fraction was separated by HPLC using a Conosil column eluted with *n*-hexane-isopropyl alcohol (9:1, 2 ml/min) and compound **1** was isolated (6.7 mg, t_R 31.80 min).

Compound 1 (5-methoxymethyl-1*H*-pyrrole-2-carbaaldehyde): brown liquid, HREI-MS 139.0630 (calcd for $C_7H_9NO_2$ 139.0633) IR ν max (neat, cm^{-1}): 3250, 2820, 2860, 1650. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 10.10 (NH), 9.47 (1H, s, CHO), 6.89 (1H, t, *J* = 3.5 Hz, H-3),

†Dedicated to Prof. Young Choong Kim of the Seoul National University for her leading works on Pharmacognosy

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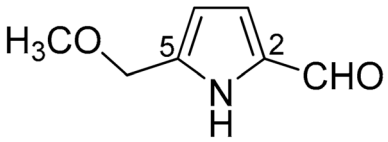

Fig. 1. The structure of compound **1**.

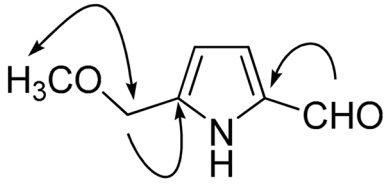

Fig. 2. Key HMBC correlations.

6.22 (1H, t, J = 3.5 Hz, H-4), 4.47 (2H, s, CH_2-5), 3.30 (3H, s, OCH_3). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 179.0 (CHO), 137.9 (C-5), 132.7 (C-2), 121.8 (C-3), 110.1 (C-4), 66.9 (5-CH_2), 58.2 (OCH_3).

Results and Discussion

Compound **1** was obtained as a brownish liquid and exhibited a molecular ion peak at *m/z* 139.0630 in the HREIMS, corresponding to a molecular formula of $C_7H_9NO_2$. In the IR spectrum, the two C-H stretching bands at 2820 and 2860 cm^{-1} along with a strong carbonyl band at 1650 cm^{-1} indicated the presence of an aldehyde functionality. Also, a single N-H stretching band at 3250 cm^{-1} was suggestive of a secondary amine group. The ^{1}H-NMR data exhibited two triplet signals at δ_H 6.89 (1H, H-3) and 6.22 (1H, H-4) with coupling constants of 3.5 Hz, implying the presence of a heterocyclic ring containing nitrogen atom, particularly a 2,5-disubstituted pyrrole ring, while the coupling constants for 2,3- or 2,4-disubstituted pyrrole ring were in the range of 1.3-2.9 Hz or 2.3-3.2 Hz, respectively (Chin *et al*., 2003). The signals for an aldehyde at δ_H 9.47 (1H, s), a secondary amine at δ_H 10.10 (1H, s), an oxygenated methylene at δ_H 4.47 (2H, s, CH_2-5) and a methoxy group at δ_H 3.30 were also observed in the ^{1}H-NMR spectral data. The HMBC correlations of δ_H 4.47 to δ_C 58.2 and 110.0, as shown in Fig. 2, confirmed the methoxy group was connected to the oxygenated methylene group affixed to a pyrrole ring. The proton signal at δ_H 9.47 displayed the cross peak with δ_C 132.7, allowing the position of the aldehyde group at C-2. Therefore, the structure of this compound was determined to be 5-methoxymethyl-1*H*-pyrrole-2-carbaaldehyde. This pyrrole compound was isolated from natural sources for the first time.

References

Chin, Y.-W., Lim, S. W., Kim, S.-H., Shin, D.-Y., Suh, Y.-G., Kim, Y.-B., Kim, Y. C., and Kim, J., Hepatoprotective pyrrole derivatives of *Lycium chinense* fruits. *Bioorg Med Chem Lett* **13**, 79-81 (2003).

Ha, K.T., Yoon, S.J., Choi, D.Y., Kim, D.W., Kim, J.K., and Kim, C.H., Protective effect of *Lycium chinense* fruit on carbon tetrachloride-induced hepatotoxicity. *J Ethnopharmacol* **96**, 529-535 (2005).

Han, S.H., Lee, H.H., Lee, I.S., Moon, Y.H., and Woo, E.R., A new phenolic amide from *Lycium chinense* Miller. *Arch Pharm Res* **25**, 433-437 (2002).

Jung, K., Chin, Y.-W., Kim, Y.C., and Kim, J., Potentially hepatoprotective glycolipid constituents of *Lycium chinense* fruit. *Arch Pharm Res* **28**, 1381-1385 (2005).

Kim, H.P., Lee, E.J., Kim, Y.C., Kim, J., Kim, H.K., Park, J.-H., Kim, S. Y., and Kim, Y.C., Zeaxanthin dipalmitate from *Lycium chinense* fruit reduces experimentally induced hepatic fibrosis in rats. *Biol Pharm Bull* **25**, 390-392 (2002).

Kim, S.Y., Choi, Y.H., Huh, H., Kim, J., Kim, Y.C., and Lee, H.S., New antihepatotoxic cerebroside from *Lycium chinense* fruits. *J Nat Prod* **60**, 274-276 (1997).

Kim, S.Y., Kim, H.P., Yang, H., Lee, M., Ryu, H.J., Jang, Y.P., Sung, S. H., and Kim, Y.C., Antifibrotic activity of LCC, a cerebroside of *Lycium chinense* fruit, in bile duct-ligated rats. *Nat Prod Sci* **15**, 101-105 (2009).

Lin, F.M., Chiu, C.H., and Pan, T.M., Fermentation of a milk-soymilk and *Lycium chinense* Miller mixture using a new isolate of *Lactobacillus paracasei* subsp. *paracasei* NTU101 and *Bifidobacterium longum*. *J Ind Microbiol Biotechnol* **31**, 559-564 (2004).

Received December 13, 2010
Revised March 7, 2011
Accepted March 9, 2011