A New Benzylisoquinoline of Annona Cherimola

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ABSTRACT

(-)-Zishenine (1), a new benzylisoquinoline, has been isolated from the roots of Annona cherimola Mill. (Annonaceae). The structure was characterized and identified by spectral analysis.

Keywords

Annona cherimola, Annonaceae, (-)-zishenine, Benzylisoquinoline.

Introduction

Annona cherimola Mill. (Annonaceae) is a subtropic fruit tree cultivated in the southern part of Taiwan. It grows indigenously in Ecuador and Peru and has been used for the treatment of skin disease, especially for boil in folk medicine [1]. Although Annonaceous acetogenins constitute the majority of natural products from Annonaceae of Taiwan, a large but significant number of alkaloids have been described [2]. These include oxaaporphines, aporphines, benzylisoquinolines, proaporphines, isoquinolones, and some amides. As part of our continuing investigation on the alkaloids of Formosan Annonaceous plants, we have isolated several alkaloids from the methanol stem extract of A. purpurea [3]. The chemical and the biological activity of the roots of A. cherimola have not yet been reported. In the course of screening for biologically and chemically novel agents from Formosan Annonaceous plants [3-26], A. cherimola was chosen for further phytochemical investigation. These observations provide useful information for potential chemopreventive drug design. The MeOH extract of its roots was subjected to solvent partitioning and chromatographic separation to afford a new benzylisoquinoline alkaloid. In this paper, we report the isolation and structural elucidation of this new alkaloid.

(-)-Zishenine (1) was obtained as a brown oil from CHCl₃, positive to Dragendorff’s test. Its molecular formula was deduced as C₂₁H₂₇NO₄ by HR-ESI-MS (m/z 380.1837 ([M + Na]+; calc. 380.1838)). The UV spectrum of (-)-zishenine (1) contained absorption bands typical of the benzylisoquinoline derivatives [27]. The ¹H NMR spectrum of (-)-zishenine (1) contained an AA’XX’ pattern at δ 7.01 (2H, d, J = 8.0) and 6.80 (2H, d, J = 8.0) for H-10 & 12 and H-9 & 13, a singlet at δ 2.53 for N-CH₃, and a singlet at δ 5.80 for H-1 in the aromatic region, in addition to four singlet methoxyl groups at δ 3.52, 3.78, 3.83 and 3.85 and seven aliphatic protons at δ 2.78 (4H, m), 3.21 (2H, m) and 3.73 (1H, t, J = 6.0), accounting for 27 protons. H-1 unusual high field position indicating that this proton lies below the plane of the benzene ring. The significant downfield signal at δ 3.73 (1H, t, J = 6.0) for H-7a indicated an electron-withdrawing group bonded to the nitrogen atom. The structure (-)-zishenine (1) was also confirmed by 2D NMR experiments. A COSY correlation was observed between the H-5 and H-6, between OMe-2, OMe-3 and OMe-4 as...
well as H-7a, H-8, H-9/H-13, H-10/H-12 and OMe-11, were observed in the NOESY spectrum. These observations confirmed the structure of 1 as the new benzylisoquinoline alkaloid, which we name (-)-zishenine.

(-)-Zishenine (1). Brown oil (CH$_2$Cl$_2$); [α]$^D_{25}$ -24.5° (c 0.15, CH$_2$Cl$_2$). UV (MeCN, $\lambda_{max}$, nm) (log ε): 280 (3.52). IR (neat, $\nu_{max}$, cm$^{-1}$): 2900, 1210, 920. $^1$H NMR (400 MHz, CDCl$_3$), 6, ppm, J/Hz: 2.53 (3H, s, N-CH$_3$), 2.78 (4H, m, H-5, 6), 3.21 (2H, m, H-8), 3.52 (3H, s, C2-OCH$_3$), 3.73 (1H, t, J = 6.0, H-7a), 3.78 (3H, s, C11-OC$_3$), 3.83 (3H, s, C3-OCH$_3$), 3.85 (3H, s, C4-OCH$_3$), 5.80 (1H, s, H-1), 6.80 (2H, d, J = 8.0, H-9,13), 7.01 (2H, d, J = 8.0, H-10,12). HR-ESI-MS m/z 380.1837 [M + Na]$^+$ (calcd for C$_{21}$H$_{27}$NO$_3$Na, 380.1838).

Acknowledgment
This investigation was supported by a grant from the Fooyin University awarded to C. Y. Chen.

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Chem Pharm Res, 2023
Volume 5 | Issue 1 | 2 of 3