HONGCONIN, A NEW NAPHTHALENE DERIVATIVE FROM THE RHIZOME OF ELEUTHERINE AMERICANA (HONG-CONG)

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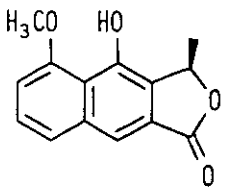
Abstract —— A new naphthalene derivative, hongconin was isolated from the rhizome of Eleutherine americana Merr. et Heyne (Iridaceae) (Chinese name; Hong-Cong) along with three known naphthalene derivatives (1-3). The structure of hongconin was determined to be (4) by spectral and X-ray analyses.

Eleutherine americana Merr. et Heyne (Iridaceae) is a herbal plant cultivated in Hainan Island of South China. The rhizome of this plant was used as a folk medicine for the treatment of coronary disorders[1]. The biological activity of Hong-Cong was confirmed by pharmacological test using isolated guinea pig heart and Hong-Cong was also shown to be effective to angina pectoris in a preliminary clinical trial[2].
In a previous paper[3], we reported the isolation of three known naphthalene derivatives, eleutherol (1), eleutherin (2) and isoeleutherin (3)[4], and a new naphthalene derivative named hongconin. These four naphthalene derivatives showed the effect of increasing coronary flow on isolated guinea pig heart[5].
This communication describes the structural elucidation of hongconin (4). Repeated chromatographic seperation of ethanolic extracts of the plant gave hongconin (4),

which was recrystallized from n-hexane-ether, mp 135°C, $C_{16}H_{16}O_5$, $[\alpha]_D^{20}$-26° (C=1.94, $CHCl_3$). When crystals stood for long time in the air, they turn brownish yellow gradually. The ^{1}H-nmr spectrum (δ ppm in $CDCl_3$) showed following signals: chelated OH (1H, S) at δ 12.72; phenolic OH (1H, S) at δ 8.87 ; three aromatic H at δ 8.00 (1H, d, J=7Hz), δ 7.28 (1H, t, J=7Hz) and δ 6.95 (1H, d, J=7Hz) ; OCH_3 (3H, S) at δ 4.02 and two O-CH-CH_3 groups at δ 5.41 (1H, q, J=7Hz), δ 4.63 (1H, q, J=7Hz), δ 1.58 (3H, d, J=7Hz) and δ 1.48 (3H, d, J=7Hz). Irradiation at the signal of δ 7.28 collapsed doublets at δ 8.00 and 6.95 to two singlets. When the signal at δ 8.00 was irradiated, a triplet and a doublet at δ 7.28 and 6.95 changed to AB-type quartet. The three aromatic protons are assignable to the aromatic protons (C-6, C-7 and C-8) of the substitution pattern same as those of (1-3). The irradiation of the quartet at δ 5.41 collapsed a doublet methyl signal at δ 1.58 to a singlet. A doublet methyl signal at δ 1.48 also changed into a singlet by the irradiation of a quartet methine signal at δ 4.63. The two hydroxyl signals observed at δ 12.72 and 8.87 are assignable to phenolic hydroxyl groups chelating to a carbonyl and a methoxyl group. Acetylation of hongconin (4) with acetic anhydride and sulphuric acid yielded a diacetate, $C_{20}H_{20}O_7$. The ir spectrum ($CHCl_3$) of the diacetate shows absorptions of acetoxyl groups at 1775 and 1770 cm^{-1}, and the carbonyl group adjacent to aromatic ring at unusually high wave number, 1702 cm^{-1}. This indicated the presence of acetoxyl group at peri-position to the carbonyl group. Hongconin (4) was readily formulated as (4) from spectral data and biosynthetic relation among the naphthalenic compounds obtained from the same plant. Due to the possible presence of tautomeric isomers, the structure of hongconin (4) was finally determined by the X-ray analysis. Crystals obtained from n-hexane-ether were found suitable for the single crystal X-ray analysis. The crystal is orthorhombic with space group $P2_12_12_1$ and it contains four molecules in a cell of dimension: a=16.037(8), b=20.092(10), c=4.315(2) Å; D_X=1.32 g. cm^{-3}; V=1390.4 Å^3. A total of 1194 reflections were recorded using a Philips PW 1100 diffractometer with monochromated CuKα radiation. The structure was solved by the direct method (MULTAN) and refined by the block-diagonal least-squares method (HBLS). A final R value reduced was 0.094 with anisotropic temperature factor for all 21 atoms. The formula of hongconin is (4) or its enantiomer. The structures of naphthalene congeners produced by Eleuterine plants clearly indicate that they are biogenetically related to antibiotics such as kalafungin (5)[6], nanaomycins D (6)[7], A (7), C (8) and B (9)[8]. The parent carbon skeleton of those derived from the higher plants has apparently undergone a decarboxylation. Recently it was reported that a mixture of naphthalene derivatives prepared for clinical use to angina pectoris was as effective as dipyridamol in clinical trials[9].



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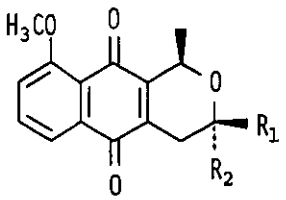
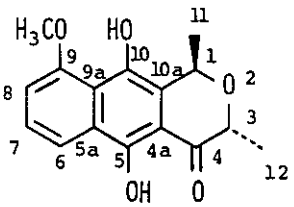


2 : R_1= CH_3 , R_2= H

3 : R_1= H , R_2= CH_3



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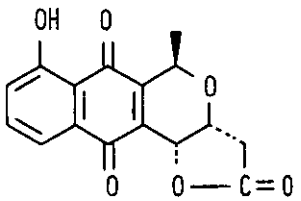

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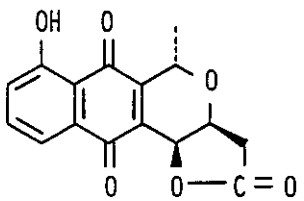

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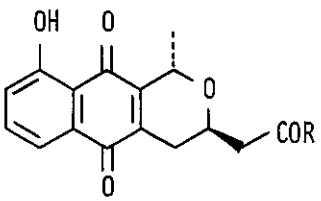
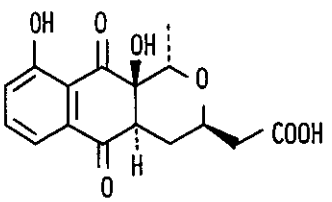


7 : R = OH

8 : R = NH_2



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