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[Short Communication]

Isolation of Arteannuic Acid from *Artemisia annua*

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개똥쑥(*Artemisia annua*)에서 Arteannuic acid의 분리

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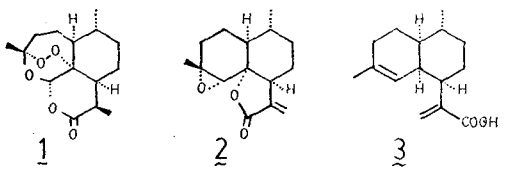
Artemisia annua, known as a traditional herb medicine against *Plasmodium* infection(malaria) in Korea and China, yields a potent active principle, arteannuin, also known as qinghaosu or artemisinin(1)[1]. Its lactone endoperoxide sesquiterpene structure draws considerable attention from synthetic organic chemists[2,3]. Clinical development of arteannuin or its derivatives into commercial drugs is progressing[1]. Other known constituents of *A. annua* related to arteannuin, arteannuin B(2) and arteannuic acid(3), have been suggested as biosynthetic precursors of arteannuin[4,5]. Specifically, arteannuic acid was believed to suffer $^1O_2$-mediated peroxidation to produce arteannuin B, which in turn would give arteannuin[6]. Interestingly, arteannuic acid was also a precursor for the chemical synthesis of arteannuin[3].

Isolation of arteannuic acid has already been described[5,7]. However, the Chinese report[5] is not readily accesible in Korea due to political reasons, and Roth's group[7] did not publish spectroscopic data. Here, we report the isolation of arteannuic acid through column chromatography and its spectroscopic data.

Two hundred grams of the ground leaves of *A. annua* was extracted with petroleum ether for two days. Dark syrup resulting from rotary evaporation was dissolved in 20ml of $CHCl_3$ and then 180ml of MeCN was added. Insoluble residue was filtered off, and the filtrate was left standing at room temperature for 2~3 weeks to yield crystals of arteannuic acid. Because the separation of the crystal from the tarry residue was difficult, the residue was subjected to silica gel chromatography. Fractions containing material with R_f-value of 0.6~0.7 under the conditions stated below were collected and concentrated to syrup. Crystallization was effected in EtOH-H_2O and recrystallized in the same solvent system. The collected acid was washed with cold MeCN and dried over P_2O_5 under reduced pressure to give 300mg of off-white crystal of arteannuic acid.



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The following physical data was consistent with the structure of arteannuic acid: R_f 0.65 (silica, 7.5% EtOAc in $CHCl_3$); mp 123~126°C, Literature, 123~126°C[7] and 131°C[5]; IR(KBr) ν_{max} 3400~2500(carbonyl OH), 1690(C=O), 1620 (C=C); ms(EI, 70eV), m/e(relative intensity) 236[M+2]$^+$ (0.8), 235[M+1]$^+$ (7.6), 234[M]$^+$ (45), 189(16), 136(38), 121(100), 105(21), 93

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(43), 79(22); pmr(200MHz, $CDCl_3$, TMS) δ 6.33(s,1H), 5.55(s,1H), 4.98(s,1H), 2.72~2.61 (m,2H), 1.59(s,3H), 0.95(d, J=6Hz, 3H), 0.95~0.91(m,11H); cmr(50MHz, $CDCl_3$, TMS) δ172.9(s, carboxylic), 142.6(s), 135.0(s), 126.6 (s), 120.2(d, 151Hz), 43.0(d, 25Hz), 40.5(d, 30Hz), 37.9(d, 128Hz), 35.3(t, 126Hz), 27.6(d, 123Hz), 26.4(t?), 26.0(t?), 25.6(t, 124Hz), 23.7 (q, 132Hz), 19.7(q, 124Hz); uv(EtOH) $\lambda_{max}(\epsilon)$ 343(33). Analysis, calculated for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found; C, 77.09; H, 9.44.

To confirm the intermediacy of the acid in arteannuin biosynthesis, labelling of the acid with ^3H and the use of the labelled acid for feeding to tissue culture are the on-going efforts in this lab.

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References

1. Klayman, D.L.: Science, 228 : 1049(1985)
2. Schmid, G. and Hofheinz, W.: J. Am. Chem. Soc., 105 : 624(1983)
3. Xu, X.-X., Zhu, J., Huang, D.-Z. and Xhou, W.-S.: Tetrahedron, 42 : 819(1986)
4. Jeremić, D., Jokić, A., Behbud, A. and Stefanović, M.: Tetrahedron Lett., 3039(1973)
5. Tu, Y.-Y., Ni, M.-Y., Chung, Y.-Y. and Li, L.-N.: Chung Yao T'ung Pao, 6 : 31(1981), Chem. Abstr., 95 : 175616u(1981)
6. El-Feraly, F.S., Al-Meshal, I.A., Al-Yahya, M.A. and Hifnawy, M.S'.: Phytochemistry, 25 : 2777(1986)
7. Roth, R.J. and Acton, N.: Planta Medica, 501(1987)