Identity of Aabomycin A with Venturicidins

Hiroyuki Akita, Harutami Yamada, Takeshi Oishi and Isamu Yamaguchi*

Riken Institute (The Institute of Physical and Chemical Research), Synthetic Organic Chemistry Laboratory and *Microbial Toxicology Laboratory, 2-1, Hirosawa, Wako-shi, Saitama 351-01, Japan

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Aabomycin A has been reported to be a new antifungal antibiotic produced by Streptomyces sp. No. 325-17.1) It exhibited inhibitory activity against many fungi, especially against Pyricularia oryzae, and low toxicity for higher plants and animals.1) The structure of aabomycin A has not yet been determined, but with respect to the physico-chemical properties (mp 144-145°C, [α]D0 + 93.5° (c=1, CHCl3)), aabomycin A was reported to resemble venturicidin A (12); an antifungal 20-membered macrolide-like antibiotic, mp 142-143°C, [α]D10 +114° (c=1.0, CHCl3)). From thin-layer chromatography of a silica gel TLC plate (E. Merck, Art. 5554), both compounds showed almost the same Rf value (0.55) in a developing solvent of benzene-acetone (3:1).3)

In order to re-examine the purity of aabomycin A, a preliminary analysis by high-performance liquid chromatography (HPLC; reversed-phase column, YMC-Pack A 312 ODS (6mm x 150mm); solvent, CH3CN-H2O (7:3); flow rate, 1.5 ml/min) was carried out, and aabomycin A was found to be a ca. 3:1 mixture of two components (retention times of 8.4 min and 10.2 min). For the purpose of obtaining a substantial amount of these two components, 15 mg of aabomycin A was subjected to preparative HPLC (reversed-phase column, YMC-Pack S 343 (1-15 ODS), 20 mm x 300 mm; solvent, CH3CN-H2O (7:3); flow rate, 5 ml/min) to separate the less polar fraction A1 (11 mg; retention time, 62.4 min) from the more polar fraction A2 (4 mg; retention time, 53.2 min). Fraction A1, a white amorphous powder with mp 142-144°C and [α]D0 +98.8° (c=0.9, CHCl3) showed IR (CHCl3) absorptions due to hydroxyl groups and amide (3440 cm⁻¹) and carbonyl groups (1710 cm⁻¹). The fast atom bombardment mass spectrum (FAB-MS) of A1 did not exhibit a prominent M⁺ ion peak, but in the presence of aqueous NaCl, a prominent ion peak at m/z 788 (M⁺ + 39) clearly appeared in the FAB-MS spectrum. FAB-MS measurement of A1 was also carried out in the presence of aqueous KCl to confirm the molecular formula of A1, and showed a prominent ion peak at m/z 772 (M⁺ + 23). Consequently, the molecular ion peak was determined as m/z 749, which indicates C41H67NO11 as the molecular formula of A1. From an analysis of the fragmentation pattern in the FAB-MS, the following results became clear: 1) The mass number at m/z 599 (M⁺ -190) shows cleavage of the C14-oxygen bond and the elimination of 3-O-carbamyl-2-deoxy-D-β-rhamnoside as a sugar part. 2) The mass numbers at m/z 541 (M⁺ -190 -H2O) and m/z 523 (M⁺ -190-2 x H2O) indicate two consecutive dehydrations from the aglycone part, which means the presence of two hydroxyl groups in the aglycone part. According to the FAB-MS analysis of A1 and other physico-chemical properties (mp, [α]D and Rf value), fraction A1 was concluded to be identical to venturicidin A (1). Fraction A2, a white amorphous powder with mp 80°C and [α]D0 +90.0° (c=0.4, CHCl3) was found to possess hydroxyl groups (3460 cm⁻¹, 3590 cm⁻¹) by the IR (CHCl3) spectrum. From two FAB-MS measurements of A2, two prominent ion peaks at m/z 792 (M⁺ +23, in the presence of aqueous NaCl) and at m/z 745 (M⁺ +39, in the presence of aqueous KCl) were clearly observed. These results allowed the molecular formula of A2 to be determined as C40H66O10 (MW 706). In the FAB-MS spectrum of fraction A2, the following typical fragmentation patterns were found: 1) The mass number at m/z 559 (M⁺ -147) indicated the liberation of 2'-deoxy-D-β-rhamnoside as a sugar part. 2) The similarity of the fragmentation pattern in the region less than m/z 559 to that of fraction A1 suggested that the structure of the aglycone of fraction A2 was the same as that of fraction A1. Consequently, the FAB-MS results suggest that fraction A2 would be identical to venturicidin B (2).2)

For a direct comparison, purified samples of venturicidin A (1, [α]D10 +109.3° (c=1.08, CHCl3) and venturicidin B (2, [α]D10 +76.7° (c=0.6, CHCl3) were obtained from commercially available venturicidin A (1) from Sigma Co., Ltd. and of authentic venturicidin B (2) by using the same preparative HPLC conditions as already mentioned. The spectral data (400 MHz NMR, IR, [α]D, HPLC) of fractions A1 and A2 were found to be identical with those of venturicidin A (1) and venturicidin B (2), respectively.

Note

Agric. Biol. Chem., 54 (9), 2465-2466, 1990

2465
Thus, aabomycin A was determined to be a ca. 3:1 mixture of venturicidin A (1) and venturicidin B (2).

The biological activities of the purified venturicidins A and B are under investigation.

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References

