SETAMYCIN, A 16-MEMBERED MACROLIDE ANTIBIOTIC IDENTIFICATION AND NEMATOCIDAL ACTIVITY

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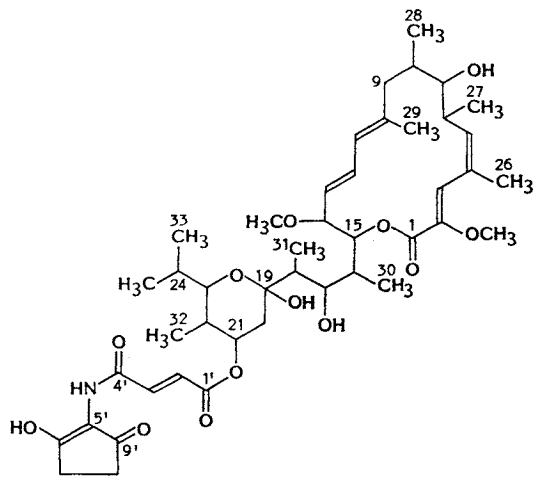
Setamycin which has been isolated by ŌMURA *et al.*,[1,2] is a macrolide antibiotic possessing activities against trichomonads, some fungi and Gram-positive bacteria. The morphological and physiological properties of its producing organism led to a new genus designated as *Kitasatosporia setae* of the order *Actinomycetales*.[3] Recently, many unusual 16-membered macrolides[4] such as hygrolidins,[5,6] L-681,110 antibiotics,[7] bafilomycins,[8,9] leucanicidin[10] and L-155,175 antibiotic,[11] have been reported. Setamycin also has been estimated as a macrolide belonging to this family from its spectral data and biological properties. In this paper we wish to describe the identification and biological properties of setamycin.

The molecular formula, $C_{42}H_{61}NO_{12}$ for setamycin was tentatively proposed by the elementary analysis and ^{13}C NMR spectral data, in our previous paper.[1] However, the molecular formula was revised to be $C_{44}H_{65}NO_{13}$ from the subsequent electron impact mass spectrum (EI-MS) and 400 MHz ^1H and ^{13}C NMR spectral analysis of setamycin. As a result, setamycin was identified with bafilomycin B_1. Comparison of the mass spectra for both antibiotics showed the same fragmentation peaks (*m/z* 568, 525, 399, 368, 338, 211, 169, 137, 113, 109). The appearance of characteristic fragment peak at *m/z* 211 is assignable to flavensomycinoic acid which has been involved in the molecules of bafilomycin B_1,[9] virustomycin A[12] and L-155,175 antibiotic.[11] The ^{13}C NMR spectrum (Fig. 1) of setamycin exhibited the presence of total 44 carbons. Complete ^{13}C chemical shift assignments (Table 1) of setamycin were made by comparison of ^{13}C NMR spectra of L-681,110 A_1, L-155,175 and bafilomycin A_1, because of no ^{13}C NMR data of bafilomycin B_1. Setamycin was finally identified with bafilomycin B_1 by HPTLC (RP-18, Rf 0.28 (90% MeOH)) and Silica gel TLC (Merck 60 F_{254}, Rf 0.65 (EtOAc)).

It is well known that some of these unusual



Setamycin

Fig. 1. The ^{13}C NMR spectrum of setamycin (100 MHz, $CDCl_3$).

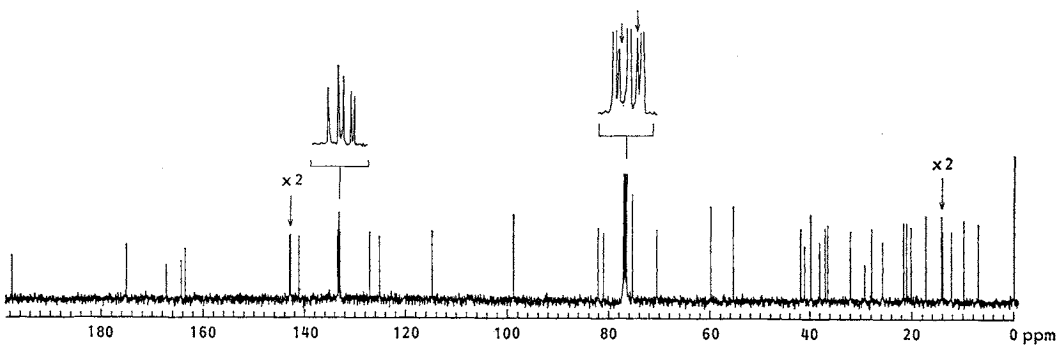


Table 1. ^{13}C Chemical shift assignments of setamycin (100 MHz, $CDCl_3$).

Carbon No.	δ_C (ppm)	Carbon No.	δ_C (ppm)
C-1	167.3	C-23	75.5
C-2	141.2	C-24	27.9
C-3	133.4	C-25	12.3
C-4	133.3	C-26	7.1
C-5	143.0	C-27	14.0
C-6	36.7	C-28	17.3
C-7	81.2	C-29	9.8
C-8	37.1	C-30	20.2
C-9	41.2	C-31	21.6
C-10	142.8	C-32	14.3
C-11	133.0	C-33	21.0
C-12	125.2	2-OCH_3	59.9
C-13	127.1	14-OCH_3	55.5
C-14	70.6	C-1′	164.3
C-15	77.2	C-2′	133.6
C-16	38.2	C-3′	133.0
C-17	82.2	C-4′	163.6
C-18	42.0	C-5′	114.9
C-19	98.8	C-6′	175.2
C-20	40.0	C-7′	25.8
C-21	76.8	C-8′	32.2
C-22	40.0	C-9′	197.7

Chemical shifts are in ppm downfield of internal $(CH_3)_4Si$.

macrolides show inhibitory activities against the growth of eukaryotes such as cestodes, insects and fungi.[13] Setamycin (bafilomycin B_1) possesses antinematodal activity in addition to antiprotozoal activity. The nematocidal activity against the pine wood nematode *Bursaphelenchus lignicolus* was assayed by the method reported in new nematocidal antibiotics, jietacins.[14] The IC_{50} (50% mortality) of setamycin was 10 μg/ml. On the other hand, the activity of avermectin B_{1a} which has been used as a nematocidal drug in veterinary field,[15] was IC_{50} 0.1 μg/ml. Leucanicidin showing an anti-*Leucania separata* activity, was found to possess a nematocidal activity (IC_{50} 10 μg/ml). Furthermore, the finding of the nematocidal activity of L-681,110 antibiotics[16] indicates that various antiparasitic activities seem to be general for these unusual macrolides.

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