DESTOMYCIN C, A NEW MEMBER OF DESTOMYCIN FAMILY ANTIBIOTICS

Sir:

Two aminoglycoside antibiotics, destomycins A and B were isolated from a culture filtrate of Streptomyces rimofaciens and their structures were determined by the authors. We have found a new minor antibiotic named destomycin C in a crude powder of destomycins. In this communication, the isolation, characterization and structural study of destomycin C are presented. The structure has been elucidated by comparison of its carbon-13 spectrum with those of destomycins A and B.

The crude powder (20 g) which was obtained from a culture filtrate (6.2 liters) of Streptomyces rimofaciens by adsorption on a column of Amberlite IRC-50 (NH₄⁺) resin and elution with 1 N aqueous ammonia, was separated into destomycin A (13.4 g) and a mixture (3.78 g) of destomycins B and C by column chromatography on silica gel (Wakogel C-200), eluted with a mixture of butanol-28 % ammonia-ethanol (4:3:1 in volume). The mixture (3.2 g) of destomycins B and C was chromatographed on a column of Dowex 1×2 (OH⁻) resin by development and elution with water. In this chromatography, destomycin B (1.13 g) was eluted first and thereafter destomycin C (1.41 g). Destomycins A, B and C were distinguished by thin-layer chromatography on Silica gel G (E. Merck, Art 5714) using a solvent mixture of butanol-ethanol-chloroform-17 % ammonia (4:5:2:5 in volume) Rf 0.13, 0.17 and 0.18, respectively.

Destomycin C is a colorless, hygroscopic powder melting at 182~190°C under decomposition. It shows [α]D²⁵ +9° (c 1, water). Anal. calc'd for C_{21}H_{39}N_{3}O_{13}·H₂O: C 45.07, H 7.39, N 7.51, O 40.03. Found: C 45.46, H 7.49, N 7.81, O 39.34.

The formula was confirmed by the carbon-13 spectrum and the mass spectrum of tri-N-acetyldestomycin C (mp 121~122°C; m/z 793, C_{38}H_{58}N_{6}O_{18}).

<table>
<thead>
<tr>
<th>Carbon</th>
<th>Destomycin A (δ)</th>
<th>Destomycin B (δ)</th>
<th>Destomycin C (δ)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>58.7d</td>
<td>58.6d</td>
<td>58.6d</td>
</tr>
<tr>
<td>2</td>
<td>32.2t</td>
<td>28.2t</td>
<td>28.6t</td>
</tr>
<tr>
<td>3</td>
<td>50.8d</td>
<td>58.6d</td>
<td>58.6d</td>
</tr>
<tr>
<td>4</td>
<td>76.6d</td>
<td>73.7d</td>
<td>73.9d</td>
</tr>
<tr>
<td>5</td>
<td>86.7d</td>
<td>87.0d</td>
<td>86.9d</td>
</tr>
<tr>
<td>6</td>
<td>75.6d</td>
<td>75.1d</td>
<td>75.4d</td>
</tr>
<tr>
<td>7</td>
<td>32.0q</td>
<td>31.8q</td>
<td>32.0q</td>
</tr>
<tr>
<td>8</td>
<td></td>
<td>31.8q</td>
<td>32.0q</td>
</tr>
<tr>
<td>1'</td>
<td>100.5d</td>
<td>100.4d</td>
<td>100.5d</td>
</tr>
<tr>
<td>6'</td>
<td>62.0t</td>
<td>61.5t</td>
<td>62.0t</td>
</tr>
<tr>
<td>1''</td>
<td>121.2s</td>
<td>121.7s</td>
<td>121.2s</td>
</tr>
<tr>
<td>6''</td>
<td>52.3d</td>
<td>52.5d</td>
<td>52.3d</td>
</tr>
<tr>
<td>7''</td>
<td>62.7t</td>
<td>62.7t</td>
<td>62.7t</td>
</tr>
</tbody>
</table>

Destomycin C shows only uv end absorption and ir ν max (KBr) 3400, 2880, 1630, 1585, 1475, 1370, 1340, 1250, 1150, 1080, 1030, 885, 855, 800 and 785 cm⁻¹. The pmr spectrum of destomycin C in D₂O using tetramethylsilane as the external reference, shows the presence of two N-methyl groups (δ 2.86 ppm) and is very similar to that of destomycin A. Methyl talopyranoside was obtained by methanolysis with 3 % hydrogen chloride in methanol and identified by gas chromatography of its trimethylsilylated derivative.

On the carbon-13 Fourier-transform NMR spectrum of destomycin C (D₂O, Varian XL-100 spectrometer), the chemical shifts of the two sugar moieties are in good agreement with those of destomycin A (Ia or Ib) and the chemical shifts of the inositol moiety are in good agreement with those of destomycin B (IIa or IIb), as shown in Table 1. Thus, the structure of destomycin C was elucidated.

Table 1. Carbon-13 shifts of destomycins

* The derivative was synthesized from tri-N-acetyldestomycin C (mp 194~210°C, dec.) by the method of HAKOMORI and confirmed to be identical with tri-N-acetyl-di-N-methyl-octa-O-methyldestomycin A.

Δ: ppm from TMS using dioxane (δ=67.4 ppm) as the internal reference. s, d, t, q: multiplicity on off-resonance; singlet, doublet, triplet and quartet, respectively.
to be 5-O-[2, 3-O-(6-amino-6-deoxy-L-glycero-
D-galacto-heptopyranosylidene)-β-D-talopy-
ranosyl]-1, 3-di-(methylamino)-1, 2, 3-trideoxy-
myo-inositol (IIIa or IIIb).

The antimicrobial spectrum of destomycin C was very similar to that of destomycin A; it also showed the anthelmintic activity against round worm in domestic fowls as confirmed by the reduction of fecal egg counts after oral administration. The LD$_{50}$ of destomycin C in mice was 6.25~12.5 mg/kg intravenously.

Acknowledgements

The authors wish to express their deep gratitude to Prof. H. Umezawa, Director of Institute of Microbial Chemistry for his guidance and encouragement. They are also grateful to the members of Meiji Seika Kaisha, Ltd. for isolation of destomycins.

MASARU SHIMURA

YASUHARU SEKIZAWA

Research Laboratories, Meiji Seika Kaisha, Ltd.,
Moro-oka-cho, Kohoku-ku,
Yokohama, Japan

KATSUHARU IINUMA

HIROSHI NAGANAWA

SHINICHI KONDO

Institute of Microbial Chemistry
Kamiosaki, Shinagawa-ku, Tokyo,
Japan

(Received October 12, 1974)

References