

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*¹⁾ and their structures were determined by the authors.²⁻⁵⁾ 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 1N 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 $[\alpha]_D^{25} + 9^\circ$ (c 1, water). Anal. calcd. for C₂₁H₃₉N₅O₁₈·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*-acetyl-mono-*N*-methyl-octa-*O*-methyldestomycin C* (mp 121~122°C; *m/e* 793, C₃₈H₆₃N₈O₁₆).

* The derivative was synthesized from tri-*N*-acetyldestomycin C (mp 194~210°C, dec.) by the method of HAKOMORI⁶⁾ and confirmed to be identical with tri-*N*-acetyl-di-*N*-methyl-octa-*O*-methyldestomycin A.⁵⁾

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.⁵⁾ Methyl talopyranoside was obtained by methanolysis with 3% hydrogen chloride in methanol and identified by gas chromatography of its trimethylsilylated derivative.⁷⁾

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 chemical shifts of destomycins

Carbon	Destomycin A (δ)	Destomycin B (δ)	Destomycin C (δ)
1	58.7d	58.6d	58.6d
2	32.2t	28.2t	28.6t
3	50.8d	58.6d	58.6d
4	76.6d	73.7d	73.9d
5	86.7d	87.0d	86.9d
6	75.6d	75.1d	75.4d
7	32.0q	31.8q	32.0q
8		31.8q	32.0q
1'	100.5d	100.4d	100.5d
6'	62.0t	61.5t	62.0t
1''	121.2s	121.7s	121.2s
6''	52.3d	52.5d	52.3d
7''	62.7t	62.7t	62.7t
	76.1d	81.0d	76.1d
	75.6d	76.2d	75.5d
	74.7d	75.1d	74.7d
2'-5'	73.0d	74.5d	73.0d
2''-5''	72.4d	73.0d	72.4d
	69.9d	70.0d	69.9d
	69.9d	69.0d	69.9d
	64.4d	68.8d	64.4d

δ : ppm from TMS using dioxane ($\delta=67.4$ 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*-talopyranosyl]-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 A¹⁾; 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 LD₅₀ of destomycin C in mice was 6.25~12.5 mg/kg intravenously.

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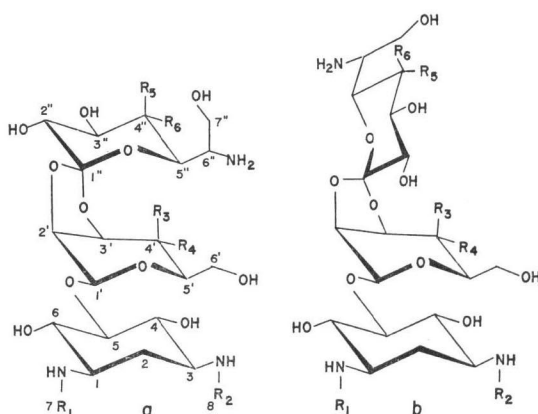
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Destomycin A: **Ia** or **Ib**; R₁=CH₃, R₃, R₅=OH, R₂, R₄, R₆=H

Destomycin B: **IIa** or **IIb**; R₁, R₂=CH₃, R₄, R₆=OH, R₃, R₅=H

Destomycin C: **IIIa** or **IIIb**; R₁, R₂=CH₃, R₃, R₅=OH, R₄, R₆=H

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