Isolation and Characterization of Polyoxins J, K and L, New Components of Polyoxin Complex*

Sir:

We wish to add three new polyoxins to the components of the polyoxin complex, nine of which, from A to I, were hitherto described by us.^{1~4)}

The polyoxin complex was prepared from the culture filtrate of *Streptomyces cacaoi* var. *asoensis* as described before.⁴⁾ It was passed through a column of Amberlite 4B (-Cl type) to remove polyoxins D, E and F. The effluent was further purified with the buffered Dowex 50W chromatography. The purified material was subjected to the repeated cellulose column chromatographies. The stepwise elution with the solvent system, butanol-acetic acid-water (4:1:0.5)→(4:1:2), resulted in the separation of each component. Polyoxins I, H, K, A, J, C, G, L and B were eluted in this order.

New components, polyoxins J, K and L were obtained as colorless amorphous powder and their purities were proved on thin layer chromatography and paper electrophoresis. Physico-chemical properties were summarized in Table I and Fig. 1. Alkali hydrolysis^{4,5)}

of them in the similar way to other polyoxins, revealed their molecular constituents as summarized in Table II.⁸⁾ It is striking that polyoxins K and L have uracil instead of 5-substituted uracils contrary to the case of other polyoxins.⁴⁾

Activities against some phytopathogenic

FIG. 1. Infrared Spectra of Polyoxins J, K and L (KBr).

TABLE I. PHYSICO-CHEMICAL PROPERTIES OF POLYOXINS J, K AND L.

Polyoxin	Formula (M.W.)	Theoretical			Found			pKa'	Eq. Wt.	[α] _D ²⁵ (c=1, water)	UV maxima	
		C%	H%	N%	C%	H%	N%				0.05N HCl	0.05N NaOH
J	C ₁₇ H ₂₅ N ₅ O ₁₂ (491.41)	41.55	5.13	14.25	41.71	5.25	13.90	3.0 7.1 9.9	521	+31.7°	264(3.91)	267(3.81)
K	C ₂₂ H ₃₀ N ₆ O ₁₃ (586.53)	45.05	5.16	14.33	44.25	5.07	13.92	3.0 7.2 9.3	603	-16.5°	259(3.95)	262(3.86)
L	C ₁₆ H ₂₃ N ₅ O ₁₂ (477.40)	40.26	4.86	14.67	40.45	5.09	14.37	3.0 7.1 9.4	509	+34.4°	259(3.96)	262(3.85)

* This is Part X of a series of papers entitled as "Studies on Polyoxins, Antifungal Antibiotics"

1) S. Suzuki, K. Isono, J. Nagatsu, T. Mizutani, Y. Kawashima and T. Mizuno, *J. Antibiotics*, **18A**, 131 (1965).

2) K. Isono, J. Nagatsu, Y. Kawashima and S. Suzuki, *Agr. Biol. Chem.*, **29**, 848 (1965).

3) S. Suzuki, K. Isono, J. Nagatsu, Y. Kawashima, K. Yamagata, K. Sasaki and K. Hashimoto, *ibid.*, **30**, 817 (1966).

4) K. Isono, J. Nagatsu, Y. Kawashima, K. Kobinata, K. Sasaki and S. Suzuki, *Agr. Biol. Chem.*, **31**, 190 (1967).

5) K. Isono and S. Suzuki, *ibid.*, **30**, 813 (1966).

6) K. Isono and S. Suzuki, *ibid.*, **30**, 815 (1966).

7) K. Isono and S. Suzuki, *Tetrahedron Letters*, **1968**, 1133.

8) The structures of polyoxins K and L as well as other polyoxins were presented at the Annual Meetings of the Agricultural Chemical Society of Japan, April 1968 at Nagoya. A manuscript is now in preparation.

fungi were shown in Table III being compared with that of polyoxin A. The agar dilution technique was employed and the minimal inhibitory concentrations were observed after 48 hr incubation at 28°C. Like other polyoxins, they were essentially not

TABLE II. THE MOLECULAR CONSTITUENTS OF POLYOXINS J, K AND L.

Polyoxin	Chromophore	Polyoximic acid ⁽⁶⁾	Polyoxamic acid ^(5,7)
J	thymine	—	+
K	uracil	+	+
L	uracil	—	+

TABLE III. ANTIFUNGAL ACTIVITIES OF POLYOXINS A, J, K AND L.

Test-organism	Minimal inhibitory concentration (mcg/ml)			
	A	J	K	L
<i>Piricularia oryzae</i>	<1.56	12.5	<1.56	6.25
<i>Cochliobolus miyabianus</i>	3.12	6.25	3.12	6.25
<i>Pellicularia sasakii</i>	>100	>100	100	100
<i>Alternaria kikuchiana</i>	50	25	25	12.5
<i>Sclerotinia cinerera</i>	6.25	6.25	1.56	3.12
<i>Cladosporium fulvum</i>	50	12.5	50	>100
<i>Corticium rolfsii</i>	25	>100	12.5	100
<i>Guignardia loricata</i>	1.56	1.56	1.56	<1.56

effective to yeasts and bacteria.

We are indebted to Dr. Y. Sumiki of this Institute for his interest and Mr. S. Sasaki, Toa Noyaku Co. Ltd. for the biological assay. We wish to thank Kaken Chemical Co. Ltd. for the supply of polyoxin complex.

Kiyoshi ISONO
Kimie KOBINATA
Saburo SUZUKI

*The Institute of Physical and
Chemical Research, Yamato-machi, Saitama*

Received May 1, 1968