PORTMICIN, A NEW ANTIBIOTIC

Sir:

In the course of our screening program of new antibiotics, a *Nocardiopsis* sp. No. 6270 isolated from a soil sample collected at Abashiri-shi, Hokkaido, Japan, was found to produce a new polyether antibiotic, portmicin[1],†. The strain No. 6270 was showed following characteristics: Color of aerial mycelium is in the white-color series; aerial mycelium forms straight or flexuous spore chain like a cobweb with ten or more spores; vegetative hyphae usually not break down to flagment; spore surface is smooth; formation melanoid pigment is negative. Analysis of whole cell hydrolysate of the strain No. 6270 showed that it contained *meso*-diaminopimelic acid and galactose. No mycolic acid is detected. The structure of portmicin was determined by NMR and X-ray studies (Fig. 1), the details of which will be reported elsewhere[2].

The strain was fermented at 30°C for 120 hours in a 200-liter tank containing 100 liters of a medium consisting of glucose 6.0%, soybean meal 2.0%, torula yeast 0.2% and $CaCO_3$ 0.3%. The fermentation broth was filtered after addition of filter aid. The acetone extract of the mycelium was concentrated *in vacuo* and the aqueous residue was combined with the filtered broth. The mixture was extracted with ethyl acetate and the extract was concentrated *in vacuo* to an oily substance. The residue was purified by chromatography on a silica gel column which was developed with *n*-hexane - ethyl acetate (1 : 1). The active fractions were combined, concentrated, and the residue was

Fig. 1. The structure of portmicin.

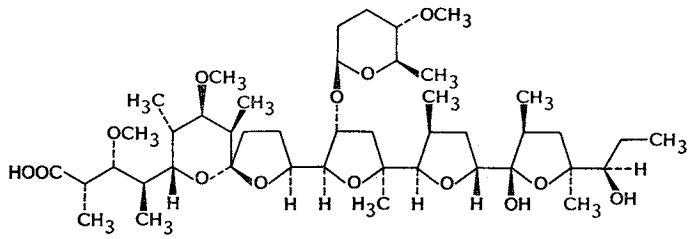
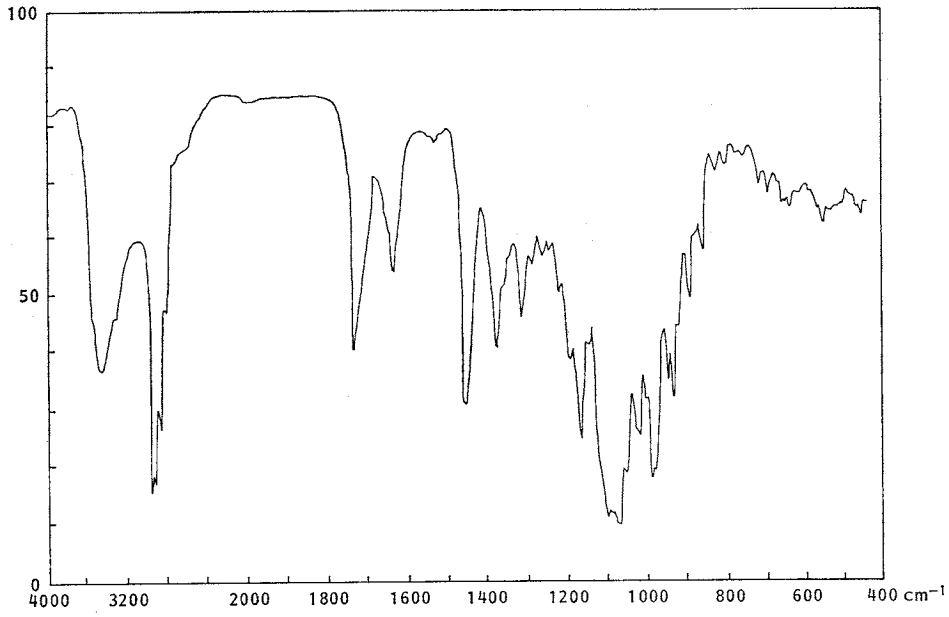


Fig. 2. IR spectrum of portmicin.



† Originally called antibiotic No. 6270.

Table 1. Antimicrobial activities of portmicin.

Test organisms	MIC (μg/ml)	Medium[a]
Bacillus cereus IAM-1729	1.56	N
B. circulans IFO 3329	1.56	N
B. subtilis PCI 219	6.25	N
Staphylococcus aureus FDA 209P JC-1	6.25	N
S. aureus (resistant[b])	6.25	N
Micrococcus flavus IFO 3242	1.56	N
Mycobacterium smegmatis ATCC 607	1.56	GN
M. avium IFO 3153	1.56	GN
Escherichia coli NIHJ JC-2	>100	N
Proteus vulgaris OX-19	>100	N
Candida albicans YU 1200	>100	P
Saccharomyces cerevisiae strain 77	>100	P
Aspergillus flavus ATCC 9643	>100	P

[a] N; Nutrient agar, GN; glycerol-nutrient agar, P; potato-sucrose agar.
[b] Resistant for penicillin, streptomycin, chloramphenicol, tetracycline, kanamycin.

recrystallized from *n*-hexane - ethyl acetate mixtures to give crystals of portmicin (51.3 g).

The free acid or sodium salt of portmicin could be obtained by shaking the ethyl acetate solution of the crystals with 0.1 N HCl or 0.1 N NaOH, respectively.

Portmicin free acid was obtained as colorless needles which melted at 115~118°C. Optical rotation showed $[\alpha]_D^{20}$ −11.5° (*c* 1.0, MeOH). Elemental analysis and field desorption (FD) mass spectrum [M^+ 828, $(M+Na)^+$ 851] indicated the molecular formula $C_{44}H_{76}O_{14}$: *Anal* Calcd for $C_{44}H_{76}O_{14}\cdot\frac{1}{2}H_2O$; C 63.06, H 9.26, O 27.68. Found: C 62.72, H 9.49, O 27.78. The sodium salt crystallized as colorless prisms with mp 232~235°C. $[\alpha]_D^{20}$ −20.0° (*c* 1.0, MeOH); *Anal* Calcd for $C_{44}H_{75}O_{14}Na$: C 62.09, H 8.88, O 26.32, Na 2.70. Found: C 62.21, H 8.29, O 26.86, Na 2.87. UV spectrum showed only end absorption. IR absorption spectrum in KBr disc is shown in Fig. 2. The antibiotic is soluble in most organic solvents but insoluble in water. The color reactions were positive to vanillin - H_2SO_4 and DRAGENDORFF's reaction, negative to ninhydrin.

Portmicin is active against Gram-positive bacteria including mycobacteria, but inactive against Gram-negative bacteria, yeast and fungi (Table 1). It showed coccidiostat activity *in vivo* when mixed in feed at the level of 6.2~25 μg/g for chickens infected with *Eimeria tenella*.

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