

Communications to the editor

A NEW ANTIFUNGAL
ANTIBIOTIC, PRUMYCIN

Sir:

In the course of screening studies for antifungal antibiotics, a new antibiotic, prumycin was isolated from a cultured broth of a *Streptomyces* sp. strain No. F-1028, which was obtained from a soil sample collected at Kagawa Prefecture, Japan, in 1969. Prumycin is a water soluble, basic substance with a molecular formula of $C_8H_{19}N_3O_5$. The antibiotic is active against some bacteria and fungi, especially *Sclerotinia* sp. and *Botorytis* sp. The following medium was used for production of the antibiotic: glucose 2.0%, peptone 0.5%, meat extract 0.5%, sodium chloride 0.5%, dry yeast 0.3%, and calcium carbonate 0.3%. The pH of the medium was adjusted to 7.0 with sodium hydroxide before sterilization. Antimicrobial activity reached a maximum after 45 hours in a jar fermentor. The antifungal activity was determined by the paper disc plate method using *Sclerotinia cinerea* as a test organism. The culture filtrate was passed through a column of Amberlite IRC-50 (Na^+) and the column was washed with water. The antibiotic was then eluted with 1N hydrochloric acid and the active eluate concentrated under reduced pressure. After purification by column chromatography on active carbon, using distilled water as a developer, the crude sample was applied to a Sephadex G-10 column and the column developed with distilled water. The active fraction was concentrated *in vacuo* and acetone was added to yield a white powder.

The active substance was then crystallized from methanol to form colorless needles or plates of prumycin hydrochloride: m.p. ca. 195°C (dec.), $[\alpha]_D^{25} +63.2^\circ$ (c 1, H_2O). The UV spectrum showed only an end absorption; the IR spectrum measured on a KBr tablet is shown in Fig. 1. Based on elemental analysis and the potentiometric titration method (pK_{a1}' : 7.02, pK_{a2}' : 8.16 equivalent weight: 122.5), the molecular formula of prumycin was proposed as $C_8H_{19}N_3O_5$. Anal. Found for the hydrochloride $C_8H_{19}N_3O_5 \cdot 2HCl$: C 30.94, H 6.58, N 13.39, Cl 23.18, O 25.91%. Calcd.: C 30.97, H 6.82, N 13.54, Cl 22.85, O 25.82%.

Prumycin is readily soluble in water, soluble in methanol and dimethyl sulfoxide, slightly soluble in ethanol, and insoluble in most organic solvents. It gives positive color reactions with ninhydrin, ELSON-MORGAN, TOLLENS, BENEDICT and EHRLICH reagents, but negative reactions with MOLISCH, SAKAGUCHI, maltol and ferric chloride reagents. The IR spectrum and color reactions indicate that prumycin belongs to the amino-sugar group of antibiotics. Prumycin was very stable in acidic solution, but unstable in alkaline. The following R_f values were found in thin-layer chromatography with silicic acid (Kieselgel-G, Merck): 0.68 with the propanol-pyridine-acetic acid-water system (15:10:3:12) and 0.21 with the butanol-acetic acid-water system (3:1:2).

As is shown in Table 1, prumycin was principally active against phytopathogenic fungi such as *Sclerotinia sclerotiorum* and *Botorytis fabae*, but inactive against most bacteria and yeasts. The oral administration of 500 mg/kg prumycin in mice caused no

Fig. 1. Infrared spectrum of prumycin hydrochloride (KBr tablet).

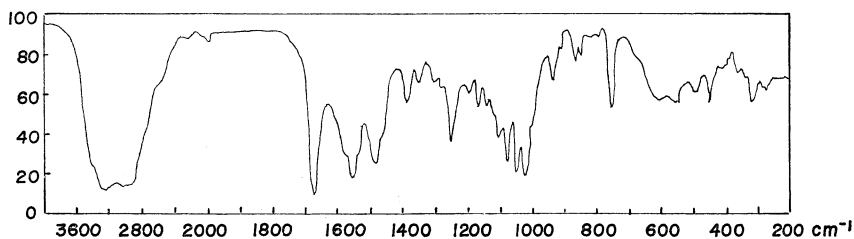


Table 1. Antimicrobial activity of prumycin hydrochloride

Test organisms	MIC (mcg/ml)	Me- dium	Test organisms	MIC (mcg/ml)	Me- dium
<i>Staphylococcus aureus</i> FDA 209P	>100	N	<i>Botrytis fabae</i>	6.25	P
<i>Bacillus subtilis</i> PCI 219	>100	N	" <i>cinerea</i>	6.25	P
<i>Sarcina lutea</i> PCI 1001	3.12	N	" <i>cryptoneriae</i>	>100	P
<i>Salmonella typhimurium</i>	>100	N	<i>Cochliobolus miyabeanus</i>	50	P
<i>Escherichia coli</i> NIHJ	100	N	<i>Collectotrichum lagenarium</i>	50	P
<i>Pseudomonas aeruginosa</i> P-3	>100	N	<i>Candida albicans</i>	>100	P
<i>Klebsiella pneumoniae</i>	>100	N	<i>Saccharomyces cerevisiae</i>	>100	P
<i>Shigella sonnei</i>	100	N	<i>Cryptococcus neoformans</i>	>100	P
<i>Vibrio comma</i> 904	12.5	N	<i>Hormodendrum pedrosoi</i>	25	P
<i>Proteus vulgaris</i> OX-19	>100	N	<i>Fusarium moniliforme</i> USDA 1004-1	>100	P
<i>Mycobacterium</i> ATCC 607	>100	N	<i>Penicillium notatum</i>	>100	P
<i>Xanthomonas oryzae</i>	50	P	<i>Trichophyton rubrum</i>	100	P
" <i>citri</i>	>100	P	" <i>mentagrophytes</i>	100	P
<i>Alternaria mali</i>	>100	P	<i>Trichosporon beigellii</i>	>100	P
" <i>kikuchiana</i>	>100	P	<i>Glasosporium laeticolorot</i>	50	P
" <i>japonica</i>	50	P	<i>Glomerella cingulata</i>	100	P
<i>Sclerotinia cinerea</i>	12.5	P	<i>Ophiobolus miyabeanus</i>	25	P
" <i>sclerotiorum</i>	1.56	P	<i>Aspergillus niger</i>	>100	P

Media N: nutrient agar at 37°C for 24 hours.

P: potato agar at 27°C for 48 hours.

toxic reaction. Nojirimycin¹⁾ and ezomycin²⁾ have antimicrobial activities similar to that found for prumycin. Prumycin differs however from these known antibiotics in elemental analyses, UV spectrum, IR spectrum and color reactions. Consequently, prumycin is proposed as a new antibiotic.

TOJU HATA
SATOSHI ŌMURA
MICHIKO KATAGIRI
KIYOO ATSUMI
JUICHI AWAYA

Kitasato Institute
Minato-ku, Tokyo, Japan

SHIZUO HIGASHIKAWA
KAZUOMI YASUI
HARUKO TERADA
SHIMPEI KUYAMA

Nihon Tokushu Noyaku Seizo K. K.
Hino-shi, Tokyo, Japan

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