CORIOLIN, A NEW BASIDIOMYCETES ANTIBIOTIC

TOMIO TAKEUCHI, HIRONOBU IINUMA, JUNKO IWANAGA,
SHUJI TAKAHASHI, TOMOHISA TAKITA and HAMAO UMEZAWA

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

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A new antibiotic, coriolin, was isolated from a Basidiomycetes, *Coriolus consors*. Coriolin is extracted with ethyl acetate from the cultured broth and crystallized as colorless needles, m. p. 175~176°C, $C_{15}H_{20}O_5$. It inhibits growth of Gram-positive bacteria and *Trichomonas vaginalis*.

A new antibiotic, coriolin, has been isolated from a cultured broth of a Basidiomycetes, *Coriolus consors*, a mushroom widely distributed in Japan (Japanese name: Nikuusuba-take). In this report, production, isolation as well as physical, chemical and biological properties of the antibiotic are presented.

1. Production and Isolation of Coriolin

Mycelium of *Coriolus consors* was grown at 27°C for 14 days in a medium containing wood dust immersed in a solution of 2.0 % glucose and 0.5 % dried beer yeast. The mycelium found on the surface of this wood dust medium was then used to inoculate a production medium for submerged culture. The medium used in the submerged fermentation contains 5.0 % glucose, 0.2 % peptone, 0.5 % dried beer yeast, 0.2 % KH_2PO_4, 0.1 % $MgSO_4 \cdot 7H_2O$ and 1.6 % $CaCO_3$. The duration was for 7 days at 27°C.

The fermented broth was filtered and the antibiotic substance in the filtrate was extracted with ethyl acetate. After evaporating the solvent, 4.57 g of the crude material was obtained from 12.9 liters of the filtrate. It was purified by silica-gel chromatography using benzene - acetone (100 : 20) as developing solvent. The active fraction was further chromatographed on silica-gel using chloroform - methanol (100 : 2) and ethyl acetate. The purified powder was crystallized from ethyl acetate-chloroform and 228 mg of colorless needles were obtained.

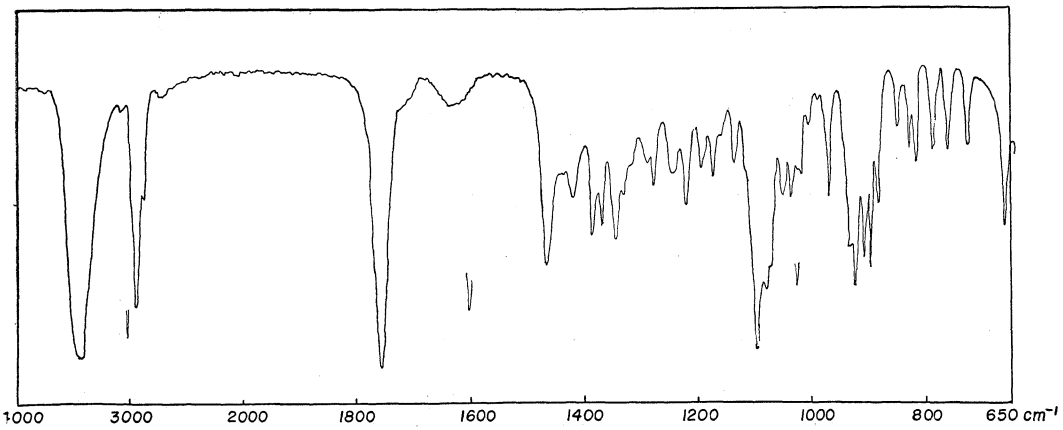
2. Physical and Chemical Properties

Coriolin crystallizes as colorless needles melting at 175~176°C (dec.). It is soluble in methanol, ethanol, ethyl acetate and acetone, and slightly soluble in chloroform, benzene, carbon tetrachloride and water. The molecular weight determined by the mass spectroscopy is 280.

Analysis Found: C 63.63, H 7.15, N 0.
Calcd. for $C_{15}H_{20}O_5$: C 64.27, H 7.19.

The ultraviolet absorption spectrum exhibits only end absorption. The infrared absorption spectrum is shown in Fig. 1. The molecular formula $C_{15}H_{20}O_5$, taking account of origin of this antibiotic, suggests that coriolin would have a sesquiterpenoid

Fig. 1. Infrared absorption spectrum of coriolin (KBr)



structure. Studies of the structural elucidation will be published in another paper.

3. Biological Properties

The antibacterial and antifungal spectra obtained by the agar dilution method are shown in Tables 1 and 2. As shown in these tables, coriolin inhibits growth of Gram-positive bacteria at 6.25~12.5 mcg/ml, some of Gram-negative bacteria at 50~100 mcg/ml. It shows no activity against most yeasts and fungi at 100 mcg/ml. Some activity was noted against *Torula utilis* and *Xanthomonas oryzae*.

It inhibits *Trichomonas vaginalis* at 6.25 mcg/ml. The daily intraperitoneal injection of 50 mcg/mouse for 10 days is not effective against EHRLICH ascites tumor, but slightly effective against Leukemia-1210. However it inhibits growth of YOSHIDA sarcoma cell (61.6 % inhibition at 5 mcg/ml).

Table 1. Antibacterial spectra of coriolin

Test organism*	Minimal inhibitory concentration mcg/ml	Test organism*	Minimal inhibitory concentration mcg/ml
Staphylococcus aureus FDA 209P	12.5	*Bacillus anthracis*	12.5
// // R1**	12.5	*Bacillus cereus* ATCC 10702	12.5
// // R2	12.5	*Bacillus subtilis* NRRL B-558	12.5
// // R3	6.25	// // PCI 219	12.5
// // R4	6.25	*Bacillus brevis* IAM 1031	6.25
// // R5	12.5	*Corynebacterium bovis* 1810	25
// 193	12.5	*Bacterium succinicum* IAM 1017	>100
// // R6	6.25	*Escherichia coli* NIHJ	50
// 52-34	12.5	*Salmonella typhi*	100
// // R7	12.5	*Shigella flexneri* 1a (Ew8)	50
// 308A-1	12.5	*Proteus vulgaris* OX 19	100
// // R8	12.5	*Pseudomonas fluorescens*	>100
// Terajima	25	*Pseudomonas aeruginosa* A 3	>100
// Smith	12.5	*Klebsiella pneumoniae* PCI 602	50
Sarcina lutea PCI 1001	12.5	*Seratia marcescens*	>100
Micrococcus flavus FDA 16	12.5		

* Nutrient agar, 37°C, 24 hours.

** R 1=Streptomycin and streptothricin resistant, R 2=Actinomycin resistant, R 3=Actinoleukin resistant, R 4=Bryamycin resistant, R 5=Novobiocin resistant, R 6=Erythromycin resistant, R 7 =Tetracycline, erythromycin and chloramphenicol resistant, R 8=Enduracidin resistant.

Table 2. Antifungal and anti-trichomonas activity of coriolin

Test organism*	Minimal inhibitory concentration mcg/ml	Test organism*	Minimal inhibitory concentration mcg/ml
Candida tropicalis NI 7495	>100	*Aspergillus niger*	>100
Candida albicans Yu-1200 Yamazaki	>100	*Penicillium chrysogenum* 49-133	>100
Candida krusei NI 7492	>100	*Gibberella fujikuroi*	>100
Saccharomyces cerevisiae	>100	*Pellicularia sasakii*	>100
Torula utilis 4001	12.5	*Pyricularia oryzae*	>100
Cryptococcus neoformans NI 7496	>100	*Helminthosporium oryzae*	>100
Trichophyton mentagrophytes 598	>100	*Xanthomonas oryzae*	3.12
Trichophyton asteroides 429	>100	*Trichomonas vaginalis* TV1099**	6.25

* One percent glucose nutrient agar, 27°C, 24 hours.
** Horse serum 10%, meat extract 1%, peptone 1%, glucose 1%, agar 0.2%, 37°C, 24 hours.

Mice survived for more than a month after administration of 31 mg/kg intravenously.

A comparison of the physical, chemical and biological properties of other basidiomycete-derived antibiotics shows illudins S[1] and M[1], illudol[2], and marasmic acid[3] significantly different from coriolin.

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