ZYGOSPORIN A, A NEW ANTIBIOTIC FROM *ZYGOSPORIUM MASONII*

Sir:

During the course of our studies on fungal metabolites, we found that the fungus *Zygosporium masonii* produced a new cytotoxic antibiotic zygosporin A, which was isolated as colorless needles, m. p. 268~270°C (decomp.) and $[\alpha]_D$ −7.5°. The fungus was obtained from a dead leaf of *Daphniphyllum macropodum* and identified according to HUGHES[1]. Fermentations were conducted under submerged culture conditions for 7 days at 28°C in a medium containing 3 % glucose, 2 % peptone and 0.5 % sodium chloride. The final pH of this medium was adjusted to 6.8 prior to sterilization. The metabolite was recovered from the culture filtrate by ethyl acetate extraction and purified by direct recrystallization from acetone.

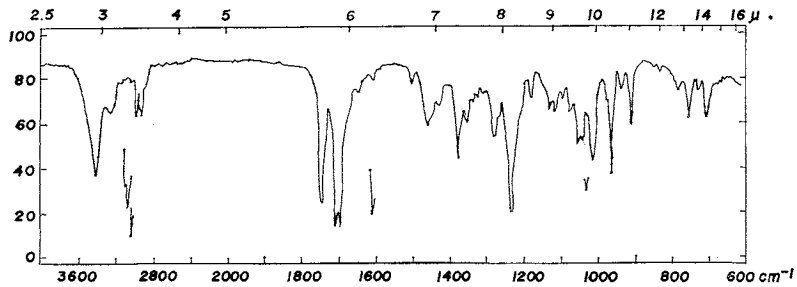
Zygosporin A has a molecular formula of $C_{30}H_{37}O_6N$* (molecular weight: 507, by mass spectrometry), showed no characteristic absorption band in the ultraviolet, and revealed absorption at frequencies of 3404, 1742, 1703, 1693, 1233, 1049, 1009, 962, 907, 751, and 706 cm^{-1} in the infrared spectrum (Fig. 1). The n.m.r. spectrum showed signals at τ 9.07 (d., J=6.8, CH_3), 8.82 (d, J=6.3, CH_3), 8.51 (s. CH_3-$\overset{OH}{\overset{|}{C}}$-), 7.76 (s. CH_3-COO-), 6.23 (d.-m. J=10.4 -$\overset{OH}{\overset{|}{C}}$H), 5.42 (s.), 4.95 (m., 1 H), 4.75 (m.), 4.43 (m.), 4.02 (d., J=3.1), 3.76 (d., J=3.1), and 2.77 (m.) in deuterochloroform (Fig. 2).

Zygosporin A showed a characteristic cytotoxicity *in vitro* producing a blocked cytoplasmic cleavage, the nuclear division continuing with the production of multinucleated cells, which were similar to that of cytochalasins[2,3]. Cytotoxicity (ED_{50}) of zygosporin A against HeLa cells (monolayer culture) and JTC-13 cells (stationary suspension culture) was 0.89 μg/ml and 0.42 μg/ml, respectively. Zygosporin A showed no inhibition of microorganisms tested, except *Trichomonas vaginalis*, which was inhibited at a concentration of 12.5 μg/ml.

The acute toxicity (LD_{50}) in mice was determined subcutaneously and orally, as 1.85 mg/kg and 36.0 mg/kg, respectively.

Confirmation of the structure of zygosporin A is now under investigation in our laboratory.

Fig. 1. Infrared spectrum of zygosporin A (KBr-disk).



* Although it was reported by I.C.I. group** that both cytochalasin C and D had the same molecular formula, $C_{30}H_{37}O_6N$, physical data of these compounds had not been described at all, and also the chemical property of zygosporin A was found to differ from those of cytochalasin C and D.

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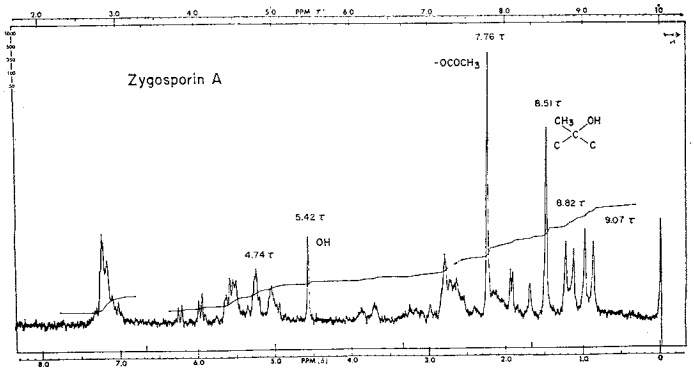
Eig. 2. N.m.r. spectrum of zygosporin A ($CDCl_3$).



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References

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