# ANTITUMOR ACTIVITY OF CYTOCHALASIN D

Sir:

We have recently isolated zygosporin A[1], an antibiotic having a characteristic cytotoxicity *in vitro*. This antibiotic has been identified as cytochalasin D[2].

The strong growth inhibitory activity of this antibiotic against cultured cells and its interesting cytotoxic character, cytoplasmic cleavage inhibition with the production of multinucleated cells, prompted us to test its antitumor activity. Animal experiments were performed as described previously.[3]

The intraperitoneal administration of cytochalasin D caused inhibition of the growth of ascites hepatoma AH-130 in rats (Table 1). The antitumor activity was proportional to the dose given. Antitumor activity was not, however, observed with EHRLICH ascites tumor in mice (Table 2). Furthermore, this antibiotic did not inhibit the growth of leukemia L-1210 or NF sarcoma in mice.

We have previously reported[4] the selective antitumor activity of quinoxaline antibiotics, where quinomycin A is mainly active against ascites hepatoma AH-130 in rats and quinomycin C is mainly active against EHRLICH ascites tumor in mice, even though these two antibiotics have similar chemical structures. This selectivity was confirmed by their tumor spectra[5].

To evaluate the selective activity of cytochalasin D, its effectiveness on a number of experimental animal tumor systems was tested. The results are shown in Tables 3 and 4. Cytochalasin D had essentially no inhibitory effect against mouse tumors, but showed a marked inhibitory effect on MURPHY-STURM lymphosarcoma, and a slight effect on WALKER carcinosarcoma 256 in rats.

The characteristic multinucleated tumor cells were clearly observed in smears taken during ascites tumor treatments in both

Table 1. Effect of cytochalasin D on rat ascites hepatoma AH-130

| Dose mg/kg/day | No. of deaths | Carcass wt. change (g) | Ascites volume (ml) | TPCV* (ml) | Tumor index** | Effect |
|---|---|---|---|---|---|---|
| 5 | 5/5 | — | — | — | — | Toxic |
| 2.5 | 0/5 | −15.3 | 38.9 | 1.97 | 0.42 | + |
| 1.25 | 1/5 | −28.8 | 48.3 | 2.67 | 0.56 | ± |
| 0.63 | 0/5 | −26.6 | 48.3 | 3.34 | 0.71 | ± |
| 0.32 | 0/5 | −22.2 | 39.0 | 4.79 | 1.01 | − |
| Control | 0/5 | −20.0 | 36.0 | 4.73 | 1.00 | |

* TPCV: Total packed cell volume. ** Tumor index=$\frac{\text{Treated}}{\text{Control}}$

Table 2. Effect of intraperitoneal injection of cytochalasin D on EHRLICH ascites carcinoma

| Dose mg/kg/day | No. of deaths | Tumor index | Effect |
|---|---|---|---|
| 10 | 5/5 | — | Toxic |
| 5 | 3/5 | — | Toxic |
| 2.5 | 0/5 | 1.02 | — |
| 1.25 | 0/5 | 0.96 | — |
| Control | 0/5 | 1.00 | |

Table 3. Effect of cytochalasin D on mouse tumors

| Tumor | Dose* mg/kg/day | Results at end of second week average weight change (g) | | Tumor index | Evaluation |
|---|---|---|---|---|---|
| | | treated/control | No. of death | | |
| Sarcoma 180 (solid) | 2.5 | −3.0/− 3.0 | 2/5 | 0.92 | − |
| Sarcoma 180 (ascites) | 1.25 | +3.0/+ 4.0 | 0/5 | 1.29 | − |
| EHRLICH carcinoma (ascites) | 1.25 | +3.5/+ 4.0 | 2/5 | 0 91 | − |
| KREBS II carcinoma ( 〃 ) | 1.25 | +4.5/+ 7.0 | 0/5 | 0.79 | − |
| BASCHFORD carcinoma ( 〃 ) | 2.5 | +1.0/+ 2.0 | 0/5 | 1.04 | − |
| MIYONO adenocarcinoma | 2.5 | +4.5/+ 8.0 | 1/5 | 1.10 | − |
| WAGNER osteogenic sarcoma | 2.5 | +1.0/+ 5.0 | 0/5 | 0.88 | − |
| RIDGWAY osteogenic sarcoma | 2.5 | +5.0/+ 6.0 | 0/5 | 0.92 | − |
| HARDING-PASSEY melanoma | 2.5 | +6.5/+11.0 | 0/5 | 0.95 | − |
| FRIEND virus leukemia | 2.5 | +8.5/+12.0 | 0/5 | 0.92 | − |

* Treatment (i.p.) was started 24 hours after tumor inoculation and continued for 7 days.

Table 4. Effect of cytochalasin D on rat tumors

| Tumor | Dose mg/kg/day | Results at end of second week average weight change (g) | | Tumor index | Evaluation |
|---|---|---|---|---|---|
| | | treated/control | No. of deaths | | |
| WALKER carcinosarcoma 256 | 2.5 | +30/+51 | 0/5 | 0.57 | ± |
| Fibrosarcoma No. 1 | 2.5 | +28/+28 | 0/5 | 0.80 | − |
| MURPHY-STURM lymphosarcoma | 5.0 | − 2/+35 | 2/10 | 0.23 | ++ |
| | 2.5 | +20/+43 | 0/ 5 | 0.35 | + |
| BABCOCK kidney tumors | 2.5 | +22/+40 | 0/ 5 | 0.91 | − |

mice and rats. Further experiments are necessary to elucidate the selectivity of this antitumor activity.

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