JOURNAL OF CLINICAL MICROBIOLOGY, Oct. 2000, p. 3905 Vol. 38, No. 10
0095-1137/00/$04.00+0

Can Antitumor Platinum Compounds Be Effective against *Candida albicans*?—A Screening Assay Using Disk Diffusion Method

For the first time, we report that the antitumor drug cisplatin exhibits antifungal activity against *Candida albicans*, a disease-causing pathogen among cancer patients (4). The efficacy of this drug against *C. albicans* combined with the high demand for development of antifungal agents, especially in immunocompromised patients, prompted us to undertake a screening assay for different platinum compounds against *C. albicans* using a disk diffusion method (2).

A series of antitumor drugs were evaluated by the disk diffusion assay; only cisplatin exhibited antifungal activity. The inorganic compound *cis*-diamminedichloroplatinum, commonly known as cisplatin, is one of the most widely used anticancer agents with well-established effectiveness against a number of cancers, particularly metastatic testicular tumors. However, one of the major drawbacks in using cisplatin has been the severe side effects, such as cytotoxicity and nephrotoxicity, that have often accompanied the treatment of cancer.

Since its discovery in 1967 by Rosenberg, when it was known to induce filamentous growth in bacterial cells, the mode of action of cisplatin, particularly the molecular mechanism underlying its antitumor activity, has been under intensive study. Cisplatin is known to form a covalent adduct with many biological molecules, the principle target being DNA. Recent in vivo studies have shown that cisplatin inhibits rRNA synthesis in HeLa cell lines (1) as well as self-splicing reaction of the group I intron ribozyme of pre-rRNA (3), suggesting that it can be a potential target for RNA binding while exerting its biological activity. It is noteworthy to mention that *C. albicans* also possess this group I self-splicing intron.

C. albicans (ATCC 10261) was obtained from the American Type Culture Collection through Rajendra Prasad (JNU, Delhi, India.) and subsequently cultured on Sabouraud dextrose agar (SDA). Cisplatin was obtained commercially (Tamil Nadu Dadha Pharmaceuticals Company, Chennai, India) and prepared fresh each time by dissolving in sterile water. Whatman no. 4 filter paper was used for preparing diffusion disks, and the disks were saturated with platinum compounds or amphotericin B in concentrations ranging from 20 to 100 μg/ml. SDA plates were inoculated with the fungus, and the drug-impregnated disks were aseptically placed on the agar surface. The plates were incubated for 12, 24, and 48 h, zone diameters were measured (Table 1), and cisplatin results were compared with the antifungal drug amphotericin B. All of these experiments were repeated three times to confirm reproducibility of results.

TABLE 1. Comparison of zones of inhibition obtained with cisplatin and with the standard antifungal agent amphotericin B on *C. albicans*

Drug	Zone of inhibition (mm) at drug concn (μg/ml) of:				
	20	40	60	80	100
Cisplatin		10	18	25	28
Amphotericin B	8	12	20	26	30

In this disk diffusion system, cisplatin showed an inhibitory effect at concentrations as low as 40 μg/ml against *C. albicans* whereas the other platinum-containing drugs did not show any inhibitory effect even at higher concentrations. We also found that this zone of inhibition persists for up to 40 h at a 20-μg/ml concentration. This is presented as a preliminary report on the antifungal activity of cisplatin. Additional studies should be carried out with other pathogenic fungal strains in order to truly determine its therapeutic efficacy as an antifungal drug.

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