ANTITUMOR EFFECTS OF SILVER ELECTRODES IN VITRO.

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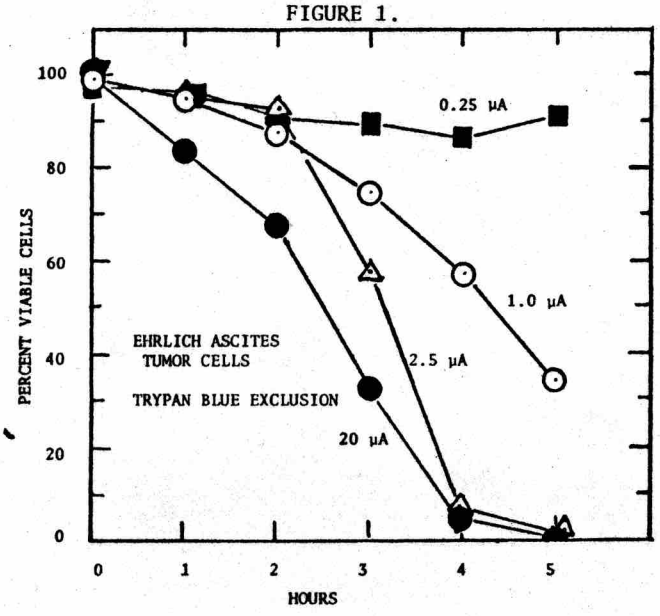
Silver anodes have been shown to be bacteriostatic and antifungal at currents as low as 10 nA/mm^2 (1). This is true even for antibiotic resistant strains. Tumor cells are also capable of rapid multiplication and have surface properties different from normal tissue. Thus, the possibility that electrochemical products from silver electrodes could also be effective against tumor cells was investigated. The results show that free-floating tumor cells can be significantly inhibited by a silver anode carrying a few microamperes of direct current.

Ehrlich's ascites fluid tumor cells were aspirated from the peritoneum of female Swiss mice 7-10 days after innoculation. The fluid was diluted 1:300 in culture medium (Dulbecco's-Eagle's medium, Flow #1-088D) and placed in Plexiglas chambers outfitted with electrodes, and agar bridges separating anode and cathode sides(1). Constant direct currents from 0.2 to 20 μA were applied to the 2 cm silver wire electrodes during incubation at 37°C. Viability was measured by the Trypan blue dye exclusion method as well as by bioassay. Light and electron microscopy were used to study the nature of the effects on the cells.

Results of the Trypan blue viability tests on the ascites tumor exposed to the silver anode are shown in Figure 1. The rate of cell death (dye uptake) increased with current level and time, but significant killing never occurred before 2 hours of exposure. Even when cells were treated for two hours or less and then incubated without current for 3 hours, no significant killing was observed. Cathode chamber cells for 2.5 and 20 μA showed some dye uptake (10-20%) only after 5 hours of current. Controls, without electrodes, remained 95-100% viable throughout.

Mixed cultures of tumor cells and mouse bone marrow cells were diluted with media previously treated with a silver anode and tested for viability. After 4.5 hours of incubation, 24% of the bone marrow cells and 83% of the ascites tumor cells took up the dye, suggesting a greater sensitivity of the latter.

FIGURE 1.



Tumor cells, after exposure to the silver anode were bioassayed by innoculating them into Swiss mice and measuring tumor growth and survival. After 4 weeks, all control mice, which received untreated tumor, had died. Half of the mice receiving tumor from the 0.2 μA silver anode chamber survived. All animals in both the 2.0 and 20 μA anode groups survived and showed no sign of tumor growth. Thus, the bioassay confirmed the Trypan blue findings. Irreversible loss of tumorigenicity occurs at the silver anode.

Light microscopic findings thus far indicate many enlarged and fragmented cells in the anode chambers. Seen by electron microscopy the treated tumor cells showed clumping in the endoplasmic reticulum, vacuole formation and ultimate destruction of the cell. These observations show that direct cellular effects occurring in response to the silver electrode in vitro. are sufficient to produce subsequent loss of tumor viability in vivo. The role of the Ag ion, complexed Ag ion, or other oxidation product in this phenomenon is not clear at this time. The usefulness of the silver electrode in the treatment of free-floating tumors, including certain leukemias, should be explored.

1. J.A. Spadaro, et al, Antimicrob. Ag. and Chemother. 6, 637 (1974).

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