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CYTOTOXICITY OF 7-DIHYDROBENFLURON ON P 388 AND EHRLICH CELLS

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The new cytostatic drug Benfluron is presently being tested in clinical trials. It is a 5-(2-N,N-dimethylaminomethoxy)-7-oxo-7H-benzo(c)fluorene(I). On incubation of (I) with homogenate fractions of mammalian livers the N-oxide (II) and 5-(2-N,N-dimethylaminoethoxy)-7 hydroxy-7H-benzo(c)fluorene(III) were identified as products. In the present study, the cytotoxic activity and mode of action of Benfluron metabolite (III) were studied.

7-Dihydrobenfluron(III) in the highest concentrations tested (300 and 150 μ M) inhibited the incorporation of 14 C-labelled precursors into the TCA-insoluble fraction of both EAC and P 388 cells. Aerobic glycolysis was stimulated. The endogenous respiration of Ehrlich cells was inhibited proportionally to the concentrations studied. Significant depression of T-SH and NP-SH in both types of cells was found after exposure to the highest concentrations. There was no loss of transplantability of EAC cells after treatment of the cells with the drug.

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IMMUNORADIODETECTION OF CIRCULATING TUMOUR ASSOCIATED ANTIGENS IN PATIENTS WITH OVARIAN CARCINOMA USING MURINE MONOCLONAL ANTIBODIES

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Two monoclonal antibodies, MOv2 and MOv8, directed against human ovarian carcinomas, were produced in our laboratories. Their reactivity by immuno-fluorescence on cryostatic sections is very similar. In fact, both are capable of recognizing 100% of mucinous ovarian tumours, 60% of serous types and 20% of undifferentiated histotypes. Biochemical characterization of the target antigens and cross-inhibition experiments indicate that the determinants recognized can be carried by two different epitopes present on the same molecules or on molecules associated under physiological conditions. In fact, both monoclonals recognize carbohydrate determinants heterogeneously expressed on mucins, on glycoproteins and in some cases, on glycolipids. An immunoradiometric assay (IRMA) was performed using polystyrene beads coated with the same monoclonal antibody also used as a tracer. With this type of assay sera from patients with immunoreactive ovarian carcinoma were found positive using both MOv2 IRMA and MOv8 IRMA, but 10-15% of sera from healthy donors were also found to be positive. A new assay using MOv2 (IgM) linked to beads and MOv8 (IgG) as a tracer is now being investigated since improvement of the specificity of the test has been observed in preliminary studies on normal sera.

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CORRELATION OF ESTROGEN AND PROGESTERONE RECEPTOR LEVELS WITH HISTOLOGY AND ELASTOSIS IN HUMAN MAMMARY CANCER

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Histologic features and presence of elastosis have been correlated with estrogen (ER) and progesterone (PR) receptor levels determined in 100 patients by a histochemical method with estradiol 17β -bovine serum albumin-fluorescein isothiocyanate conjugate and with hydroxyprogesterone- 11β -bovine serum albumin-tetramethylrhodamine isothiocyanate.

The results obtained were as follows:

1. The highest ER and PR activity levels were obtained in invasive ductal carcinoma with tubular features and lobular carcinoma;
2. Marked elastosis was found mainly in invasive ductal and lobular carcinoma;
3. A definitive association was found between elastosis and the ER and PR activity level in human breast cancer.