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The ability of glass fibers and different types of asbestos to induce morphological transformation of Syrian hamster embryo cells has been compared. An increased transformation frequency was obtained with glass fiber (GF) 100 as well as chrysolite, crocidolite, amosite and anthophyllite, while no significant increase was observed for GF 100 and TiO_2. GF 100 was less potent than chrysolite, but more potent than crocidolite, amosite and anthophyllite. By comparing the transformation frequency and toxicity, it could be concluded that induction of transformation could not be caused by unspecific cytotoxic effects. In contrast to earlier studies, no synergistic effect was observed between benzo(a)pyrene and asbestos fibers. Electron microscopical studies show that the fibers were rapidly phagocytosed, and blebs appeared on the cell surface. The formation of blebs depended on the fibers used. The localization of the blebs seemed not to be specifically associated with area of physical interaction with the fibers.

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CYTOTOXICITY OF BENFLURON METABOLITES ON P388 AND EHRLICH CELLS

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The new cytostatic drug Benfluron is currently being tested in clinical trials. In the present study the cytotoxicities and mode of action of 2 metabolites of Benfluron(A), namely 7-dihydrobenfluron(B) and N-oxide(C), have been investigated. Both metabolites are cytotoxic against the two tumour types tested (P388 and Ehrlich tumour cells) but they are less active than the parent compound (A). In order to elucidate the mode of action, the effects of both B and C on aerobic glycolysis, different kinds of respiration, level of ATP and thiol groups, integrity of cell membranes and loss of transplantability have been compared. Both B and C have shown at least two modes of action according to the concentration tested. In low concentration both metabolites interfere probably with DNA synthesis and subsequently with RNA and protein biosynthesis. At the highest concentrations there is damage to cell membranes.

DNA DAMAGE AND IN VITRO EVALUATION OF ANTICANCER DRUG SCHEDULE DEPENDENCY OF N,N-BIS(CHLORETHYL)-3-CHLORPROPIOAMIDINE OXALATE

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It has been recently shown that N,N-bis(chlorethyl)-3-chlorpropioamidine oxalate possesses antitumour activity in vivo and is worthy of further evaluation. This study was aimed at characterization of its cytotoxicity in vitro and elucidating the possible mechanism of action in terms of effects on cellular DNA. As a result it was found (by clonogenic cell survival assay) that the drug produced exponential reduction in cell survival and similarly shaped dose-response curves when given by short or continuous exposure. That data, as well as the low ID50 ratio, characterize the cytotoxicity of the drug as schedule independent and suggest cell cycle non-specificity. It was found also (by using DNA unwinding assay and a nucleoid sedimentation technique) that the drug in pharmacologically relevant concentrations caused single DNA strand breaks, which increased with drug concentration. Considering all the data, it is probable that drug-induced DNA breaks are the major cause for the drug cytotoxicity.

PROGRESSION OF ENDOMETRIAL ADENOCARCINOMAS AS REFLECTED BY NUCLEAR DNA CONTENT AND CELLULAR ESTROGEN RECEPTORS

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The results from a combined retro- and prospective study of variations of nuclear DNA and cellular estrogen receptors of normal and hyperblastic endometrium and of endometrial adenocarcinomas in relation to the clinical stage, the histological grade and the growth pattern of the tumours, to the incidence of metastases and to the survival rates of the patients has been evaluated. The errors and the validity of DNA measurements on smear preparations and histological sections by direct microspectrophotometry and of flow cytometric determination of tumour cell