DETECTION OF DNA CROSS LINKING AGENTS WITH A VISCOSIMETRIC TECHNIQUE

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We have used a new oscillating crucible viscometer. In this system compounds inducing single strand breaks in alkali reduce the time needed for reaching maximum viscosity and decrease plateau viscosity (Parodi et al., J.Mol.Biol. 147, 501-521, 1981). This method is capable of detecting DNA damage induced in vivo in different tissues (liver, kidney, lung) at dosages well below acute LD_{50}, and it is by far more sensitive than alkaline elution or alkaline sucrose gradients (Carlo et al., Carcinogenesis 4, 137-140, 1983). Here, we have investigated the action of a cross linking agent, Mitomycin C, on liver DNA after treatment in vivo. Mitomycin C, when given alone, had no effect on the disentanglement time, however it increased plateau viscosity. When Mitomycin C was given in association with dimethylsulphate, the decrease of the time needed for reaching maximum viscosity, induced by dimethylsulphate alone, was unaffected. However, at different dosages of dimethylsulphate, there was always a significant increase in the plateau viscosity, dose dependent with the dosage of Mitomycin C.

ACUTE NON-LYMPHOCYTIC LEUKAEMIA SECONDARY TO TREATMENT OF OTHER MALIGNANT DISEASES - THE BEST CHARACTERIZED CHEMICALLY-INDUCED MALIGNANCY IN MAN.

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Secondary acute non-lymphocytic leukaemia (S-ANLL) has during recent years appeared as the most serious long term complication to therapy of a number of malignant diseases including the lymphomas, multiple myeloma, polycythaemia and solid tumours (primarily ovarian carcinoma). Increasing age predisposes to S-ANLL, and in most cases the leukaemia is closely related to treatment with alkylating agents. The risk of leukaemia seems dose-related. S-ANLL is often preceded by a preleukaemic phase with clonal cytogenetic abnormalities of the bone marrow. Development of overt leukaemia is at least in some cases followed by additional cytogenetic abnormalities possibly reflecting a further evolution from a premalignant to a completely leukaemic cell. The characteristic cytogenetic abnormalities of S-ANLL are defects of chromosomes 5 and 7 observed in 80-90% of the patients. In addition chromosomes 3 and 17 are non-randomly involved. In the preleukaemic phase some cytogenetically abnormal cells may differentiate to apparently normal granulocytes, which related to cytogenetic characteristics, may show decreased neutrophil chemotaxis.

REPARATIVE SYNTHESIS OF DNA IN HUMAN LYMPHOCYTES CAUSED BY SIX ANTINEOPLASTIC ANTIBIOTICS.

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The DNA damaging activity of doxorubicin (a), daunorubicin (b), 4'-epidoxorubicin (c), 4-demethoxydaunorubicin (d), 4-demethoxydoxorubicin (e) and 4'-desoxydoxorubicin (f) was studied in a short-term in vitro system which utilized human lymphocytes. The parameter studied was the amount of unscheduled DNA synthesis (reparative synthesis) determined as tritiated thymidine (^{3}H-TdR) uptake by the cells cultured in presence of 10^{-3} - 10^{-5}M doses of the chemicals, 10 mM hydroxyurea, to block the DNA replicative synthesis and with or without a microsomal metabolizing mixture. Data showed an increase in ^{3}H-TdR uptake in treated cultures compared with controls of 250% for f, 50% for a, 40% for c, 20% for d and no increase for b and e. These results were obtained after 4 hr of culture with 10^{-3}M doses and only without the metabolic activation of the drugs.

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