THE FAECAL RATIO OF LITHOCHOLIC ACID TO DEOXYCHOLIC ACID MAY BE AN IMPORTANT AETIOLOGICAL FACTOR IN COLO-RECTAL CANCER. R.W.Owen, M.Dodo, M.H.Thompson and M.J.Hill. PHLS Centre for Applied Microbiology and Research, BMRL, Porton Down, Salisbury, Wilts. SP4 OJG, U.K.

Bile acids especially lithocholic acid (LA) and deoxycholic acid (DCA) have been shown to be co-carcinogeneic or co-mutagenic by several assay systems. The purpose of this study was to quantitate individual faecal bile acids in colo-rectal cancer (CRC) patients, adenoma subjects and healthy control persons. Faecal samples were continually extracted in a Soxhlet apparatus with organic solvents and the resulting extracts were fractionated by DEAP-LH-20 column chromatography into neutral steroids, free bile acids, glycine conjugated bile acids, taurine conjugated bile acids and sulphated steroids. Individual steroids were quantitated by GLC. The results showed that total major faecal bile acid concentrations were not significantly different between the study groups. However the LA:DCA ratio was much higher in the CRC group (1.43, $p < 0.05$) compared to the control group (0.72). Subjects with small adenomas (0 - 0.4 cm diameter) had a LA:DCA ratio (0.55) similar to controls whilst large adenomas subjects (>0.9cm diameter) exhibited a ratio (1.24) similar to the CRC group. It is concluded that the ratio of LA:DCA may be an important aetiological factor in colo-rectal cancer. Furthermore the ratio may be a useful discriminant for detecting high CRC risk within a population.

IN VITRO MODEL FOR THE CHEMOTHERAPY OF LEUKAEMIA USING A BIOLOGICAL FUNCTION OF THE TARGET CELL.
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The drugs used in cancer chemotherapy have some side effects due to their poor specificity for tumour cells. It is possible to increase the therapeutic index with the development of new drugs or by targetting the drug to the cell. We present the use of a biological function of the target cell to increase the specifity of the drug. Daunorubicin was first conjugated to a high molecular weight protein polymer by means of glutaraldehyde cross-linking through the free amine groups. Polymerisation was obtained by incubation at different periods at 37°C.

The sensitivity of the cell line was tested with daunorubicin, an anthracycline, for different periods and concentrations. The effect of daunorubicin-albumin polymers was compared at equimolar concentrations. A ten fold increase in the activity of the drug was measured. This effect was obtained with phagocytic $P388D_1$ cells. Phagocytosis was found necessary for the increase in activity since minimal effect of drug-protein polymer was obtained when phagocytosis was blocked or when drug-protein polymer conjugates competed with a drug free polymer. This approach has some clinical application for the treatment of leukaemia patients with phagocytic cancer cells.

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CHEMOTHERAPY OF LEUKAEMIC CDF_1 MICE USING A BIOLOGICAL FUNCTION OF THE TARGET CELL.
M.Pagé and J.Lagueux. Départmente Biochimie, Faculté de Médecine, Université Laval, Québec, Canada.

We have described an in vitro model for the chemotherapy of leukaemia using a biological function of the target cell. The model is based on the phagocytic properties of mouse leukaemia $P388D_1$ cells.

One million macrophage-like $P388D_1$ cells were implanted intraperitoneally on day 0. Animals were treated every day from day 1 to 5 with free and polymerised albumin bound daunorubicin at 240, 1200 and 2400 µg/kg.

The optimal concentration of free daunorubicin gave 125% the survival time of control while the optimal concentration of the polymer bound drug almost doubled the survival time. At equimolar concentrations, the drug-protein polymer was found less toxic than the free drug and there was an increase of up to 340% in survival time when compared to the highest dose of daunorubicin used.

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