F. Tumor Diagnosis

Effect of Membrane Active Agents on the Uptake of Tumor Scanning Reagents into Tumor Cells

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Polyenes, like amphotericin B, and vitamin A are reported to cause an increase in the uptake of antitumor agents into animal cells by acting on cellular membranes. We are studying on the effect of these membrane active agents on the uptake of Ga-67 citrate and Co-57 bleomycin into Ehrlich ascites tumor cells in vitro. The cells were harvested 6 to 8 days after intraperitoneal transplantation in ddk mice, washed 3 times by centrifugation with 0.9% NaCl solution and resuspended in 2 m*l* of the washing solution (5×10^7 cells in each tube). 0.05 μCi of Ga-67 citrate or Co-57 bleomycin was added to each tube. As membrane active agents, amphotericin B (E R Squibb and Sons Inc.), vitamin A (Chocola A of Eisai KK) or lysozym (Neuzym of Eisai KK) was tested. The final concentration adopted was 2.5–50 μg/m*l* for amphotericin B, 2.5–50 IU/m*l* for vitamin A, and 100–1,000 μg/m*l* for lysozym respectively. After incubation at 37° C for 1 hour, the suspensions were centrufuged and the cells were washed 3 times with 0.9% NaCl solution. The radioactivity retained in the cell pellet was then measured in a well scintillation counter. The radioactivity in the cell pellet thus prepared was about 10% and 45% of the added dose of Ga-67 citrate and Co-57 bleomycin respectively. Amphotericin B increased the uptake of Ga-67 citrate into the cells upto about 2.5 times as much as the control. But a part of the increase may be due to cell swelling observed on phasecontrast microscopy. Lysozym at the concentration of more than 600 μg/m*l* also increased Ga-67 uptake without any cell swelling. No other combination of isotope and membrane active agents increased the uptake.

An-aproach to the Chelating Structure of Co-bleomycin

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With the intention of studying the imaging efficiency of the components in Co-BLM complexes, the stability and the structure of each complex has been planed to examine.

Commercial Bleomycin (BLM) consists of A! (67%), B_2 (25%), Demethyl A_2 (8%), and some minor components. BLM-A_2, -B_2 and DMA_2 were separated on CM-Sephadex C-25 column. To this was added 1, 2 equivalent (mole), $CoCl_2$: $6H_2O$ respectively. Obtained each complex gave two spots in Silicagel TLC and also showed two peaks in C-25 column chromatography and high speed liquid chromatography. These phenomena were considered that each BLM component formed two complexes. These two were separated preparatively with high speed liquid chromatography (column : μ-Bondapack C-18 4 mm i,d, $\times$ 90 cm), to determine the molar ratio of cobalt to BLM. Quantitative analysis of cobalt and BLM were carried out with the atomic absorption spectropholometry and ultra violet absorption. Consequently about 1 equivalent of cobalt to BLM was included in A_2 and B_2 complexes, DMA_2 was contained 0.6 equivalent cobalt and no difference was found in two types of complexes.

The ratio of two type complexes were invariable with reference to both BLM and cobalt concentrations. This, however, changed with the lapse