

The Anticancer Drug Adriamycin Interacts with the Human Erythrocyte Membrane

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Z. Naturforsch. **54c**, 271–277 (1999); received October 26/November 30, 1998

Adriamycin, Anticancer Drug, Erythrocyte Membrane, Phospholipid Bilayer

Adriamycin is an aminoglycosidic anthracycline antibiotic widely used in the treatment of cancer. Increasing reports point to the involvement of cell membranes in its mechanism of action. The interaction of adriamycin with human erythrocytes was investigated in order to determine the membrane binding sites and the resultant structural perturbation. Electron microscopy revealed that red cells incubated with the therapeutical concentration of the drug in human plasma changed their discoid shape to both stomatocytes and echinocytes. According to the bilayer couple hypothesis, this means that adriamycin was incorporated into either the inner or outer leaflets of the erythrocyte membrane. To explain this unusual result, the drug was incubated with molecular models. One of them consisted of dimyristoylphosphatidylcholine (DMPC) and dimyristoylphosphatidylethanolamine (DMPE) multilayers, representative of phospholipid classes located in the outer and inner leaflets of the erythrocyte membrane, respectively. X-ray diffraction showed that adriamycin interaction perturbed the polar head and acyl chain regions of both lipids. Fluorescence spectroscopy on another model, consisting of DMPC large unilamellar vesicles (LUV), confirmed the X-ray results in that adriamycin fluidized its hydrophobic moiety. It is concluded that adriamycin incorporates into both erythrocyte leaflets affecting its membrane structure.

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