

**A TRANSFERRIN CONJUGATE OF ADRIAMYCIN  
-SYNTHESIS AND POTENTIAL CHEMOTHERAPEUTIC EFFICACY**

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The anthracycline antibiotic adriamycin-ADR (doxorubicin) is a commonly used chemotherapeutic agent in the treatment of a wide variety of human leukemias. The resistance of leukemic cells to chemotherapeutic agents is a serious problem that severely limits the success of treatment. Acquired resistance to antileukemic drugs has been associated with the reduction of intracellular drug concentration through the overexpression of P-glycoprotein (Pgp) or multidrug resistance protein (MRP).

A number of studies have indicated that chemically modified drugs, e. g. conjugate adriamycin with the serum protein transferrin, significantly increased the therapeutic index of these drugs and overcame resistance to conventional therapy.

Transferrin exhibits a significant uptake in tumor cells due to high amounts of specific transferrin receptors (150,000-1,000,000 per cell) on the surface of tumor cells. The binding of adriamycin to transferrin alters drug distribution and protects the normal cells against oxidative damage.

In this report the effect of adriamycin-transferrin conjugate on the survival of two human promyelocytic cell lines: HL-60 and HL-60ADR (resistant to adriamycin) was studied. Cells were treated with different concentrations of a conjugate for 72h. Adriamycin-transferrin cytotoxicity was estimated by the colorimetric MTT assay, and the  $IC_{50}$  was calculated.

We also determined the membrane fluidity of the studied cells. Membrane fluidity was monitored by fluorescence spectroscopy.

Our results show that the cell membrane of line HL-60ADR, resistant to adriamycin, was significantly less fluid than that of normal HL-60.

Moreover, these studies have indicated that the  $IC_{50}$  for chemically modified adriamycin is significantly lower than the  $IC_{50}$  values for the free drug, both for promyelocytic cell line HL-60 and for tumour cells resistant to adriamycin (HL-60ADR).