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 IC₅₀ 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 IC₅₀ for chemically modified
adriamycin is significantly lower than the IC₅₀ values for the free drug, both for
promyelocytic cell line HL-60 and for tumour cells resistant to adriamycin (HL-
60ADR).