DRUG TARGETING BY PEPTIDE CONJUGATES

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Antitumour effect of chemotherapy is frequently restricted by dose-limiting toxicities, including side effects (e.g. cardiotoxicity, multidrug resistance (MDR)). One of the novel approaches to destroy tumor cells is to deliver drug directly to the cancer cells by its covalent peptide conjugate [1,2]. We have developed two groups of conjugates in which drugs (e.g. acid labile *cis*-aconytil daunomycin (cAD), methotrexate, ferrocenecarboxylic acid) are coupled either to branched chain polymeric polypeptides, (poly[Lys-(DL-Ala$_m$-X$_i$)] (X = Glu, EAK, or X = Ser, SAK) with different charge characteristics [3] or to Arg-based oligopeptides. The synthesis, purification and structure determination as well as their biological properties (e.g. toxicity, fluorescence properties, *in vitro* cytotoxic effect) of these constructs will be outlined. We found that these peptide conjugates – depending on the structure of the peptide moiety - have enhanced antitumour effect *in vitro* even in MDR resistant cells. To understand the mechanism of action we have analysed the uptake of daunomycin and daunomycin-polypeptide conjugates by flow-cytometer on sensitive and multidrug resistant HL 60 cells and the localization of these compounds were compared by confocal laser microscopy. We observed that peptides studied have intracellular transporting ability to translocate attached entities across the cell membrane.

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