New findings in the study on the intercalation of bisdaunorubicin and its monomeric analogues with naked and nucleus DNA.

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Streszczenie

DNA is a target molecule for anthracycline anticancer drugs. We have used new anthracycline derivatives, bisdaunorubicin (WP631) and its monomeric analogues (WP700 serie), and look if there was a relation between the drug binding affinity to naked DNA and to cell nucleus in the cell with its cytotoxicity. Circular dichroism (CD) and fluorescence were used to follow the interaction of anthracycline derivatives with naked DNA and cell nuclei. WP631 interacts with DNA at two distinct stoichiometries, 6:1 and 3:1 base pair (bp)/WP631 molecule (3:1 and 1.5:1 per anthracycline rings). Monomeric daunorubicin (DNR) with its amino sugar N-bound to amino- and nitro-substituted benzyl moiety, representing *p*-xylenyl linker present in WP631 bisintercalator, is much more binding to DNA than DNR or WP631. These findings are supported by the study of drug binding by nuclei of K562 cells. Around 70% of WP700 intercalate to nucleus DNA in the steady-state, while only 45% of DNR intercalate DNA in the cell. The binding of WP631 by K562 cells is even less effective (~20%). WP 700 compounds, which are very similar to each other in their binding to DNA, self-association and cell accumulation, differ very distinctly in their cytotoxicity power. The most effective compounds are amino-benzyl derivatives of WP 700 series. The nitro-benzyl compounds have very low toxicity, even if they bind to DNA with similar power with that of the amino derivatives. The comparison of the all data clearly indicates no relation between cytotoxicity of the drug and its ability to intercalate DNA.

Adres publiczny

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