

Effect of *cis*, *trans*-diamminedichloroplatinum(II) and DBP on human serum albumin.

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Streszczenie

Both isomers of diamminedichloroplatinum(II) bind to albumin and induce the formation of the albumin dimer (MW approximately 140 kDa). The *trans* isomer exhibits a much greater tendency to induce a protein dimerization than the *cis* isomer. Under similar experimental conditions, the phosphonic derivative of diammineplatinum(II) (DBP) does not induce any dimer formation. The amount of bound complex per mol of human serum albumin (HSA, for an incubation time of 7 days) was found to be 6, 10.5 and 1 mol for *cis*-, *trans*-DDP and DBP, respectively. The relative fluorescence intensity of platinum-bound HSA decreases to about 55% for *cis*-DDP, 45% for *trans*-DDP and to 85% for DBP when compared to the complex-free protein, suggesting that the binding occurs in the proximity of the Trp214 residue. The structural studies (CD) have shown that only DDP-isomers cause the distinct modification of HSA native structure (alpha-helical content). Pt(II) complexes binding to HSA affect the affinity of HSA towards heme and bilirubin. High excess of DDP prevents the heme and bilirubin binding, while DBP affects this binding much less effectively due to the low amount of the protein-bound complex. Reactions of platinum complexes with albumin are believed to play an important role in the metabolism of this anticancer drug. The minor effect of DBP on HSA may indicate that the toxicity of the phosphonate analog is much lower than toxicities of DDP isomers, most likely due to kinetic reasons.

Adres publiczny

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