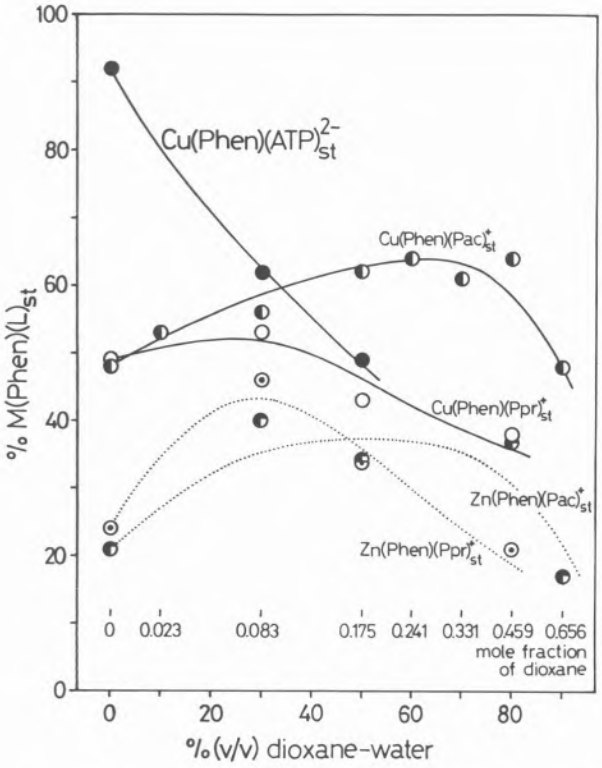

Figure

Formation degree of the intramolecular aromatic-ring stack (eq. (2)) in Cu(Phen)(ATP)$^{2-}$ and several other ternary complexes containing Cu^{2+} (full lines) or Zn^{2+} (dotted lines) in dependence on the percentage of dioxane added to the aqueous reagent mixture. The data are taken from refs. [5] and [6] (I=0.1; 25°C). Abbreviations: L, ligand; M, metal ion; Pac, 2-phenylacetate; Phen, 1,10-phenanthroline; Ppr, 3-phenylpropionate

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PS5.60 — TU

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REACTION OF [*cis*-Pt(NH$_3$)$_2$Cl$_2$] WITH RIBOSE DINUCLEOSIDE MONOPHOSPHATES. HPLC INVESTIGATION ON THE TIME DEPENDENT FORMATION OF THE REACTION PRODUCTS

The coordination of the aquated antitumor drug [*cis*-Pt(NH$_3$)$_2$Cl$_2$] to the chromosomal DNA in the cell is generally accepted to be its primary way of action. Early investigations have shown that the preferred binding site is the N7 atom or occasionally the N1 atom of the purine bases and the N3 atom of the pyrimidine bases.

Even the reaction of [*cis*-Pt(NH$_3$)$_2$Cl$_2$] (*cis*-DDP) with short DNA fragments like ApA, ApG, GpA and GpG results in a variety of products. The time dependent formation of these products has been investigated by reversed phase liquid chromatography. 1:1 mmolar ratios of the dinucleotides and *cis*-DDP have been reacted for several hours at 37°C in dark vials. Every hour a certain injection onto the column was chromatographed.

The HPLC measurements of the reaction system ApA/*cis*-DDP show that two major products are formed during a reaction time of 48 hours. In the reaction system of GpA and *cis*-DDP we observe the formation of an intermediate with highest intensity after 13 hours. It was eluted after 30 minutes, whereas the major product peak is eluted after 16 minutes. The formation of an intermediate is also observed in the ApG/*cis*-DDP system. It has its maximum absorbance after 8 hours and is eluted after the main product peak. GpG forms

with *cis*-DDP only one product [1]. During a reaction time of 16 hours no intermediate can be observed. The major products were characterized with spectroscopic and other analytical methods.

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INTERACTIONS OF WATER-SOLUBLE PORPHYRINS AND METALLOPORPHYRINS WITH NUCLEIC ACIDS AND DERIVATIVES — THE INFLUENCE OF THE METAL

Water-soluble cationic porphyrins and some of their metal derivatives are able to bind to DNA by intercalation and by external electrostatic association [1].

We have shown by thermal denaturation measurements and use of restriction enzymes that the intercalation is dependent on the geometry of the porphyrin: tetradentate metalloporphyrins bind more strongly than pentadentate ones, and specifically into G-C sequences. This is in agreement with the results obtained by PASTERNACK [2].

In order to define the nature and the strength of the binding of cationic porphyrins and metalloporphyrins to DNA, the interactions of these porphyrins with DNA fragments have been investigated by an ^1H NMR method. High values are found for the association constants. It can be concluded that complexes with purine derivatives are more stable than complexes with pyrimidine ones and metalloporphyrins give more stable complexes than porphyrins free bases. Their stability is due to hydrophobic interactions in addition to electrostatic attractions. The complexes have all approximately the same geometry.

Water-soluble cationic porphyrins and metalloporphyrins have been tested in the photodegradation of the plasmid pBR 322 DNA, using visible light. Only the diamagnetic metalloporphyrins (Zn, Sn, Pd) and the porphyrins free bases are able to cleave pBR 322 DNA. This is in agreement with their $^1O_2$ quantum yield [3].

These results strongly suggest the possibility of using such porphyrins in the phototherapy of tumors.

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