STUDY OF THE REACTIVITY OF CARBOSILANE METALLODENDRIMERS CONTAINING N-DONOR MONODENTATE OR N,N-CHELATING RUTHENIUM (II) ARENE COMPLEXES WITH DIFFERENTS BIOMOLECULES

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Since DNA replication is a key event for cell division, it is among critically important targets in cancer chemotherapy. Most cytotoxic platinum drugs form strong covalent bonds with DNA bases [1]. However, a variety of platinum compounds act as DNA intercalators upon coordination to the appropriate ancillary ligands [2]. The more thoroughly studied ruthenium antitumor agents have displayed differences with respect to their interactions with DNA depending on their structure [3]. In this context, we evaluated the effect of DNA interactions that could, to some extent, contribute to the observed cytotoxicity of the new metallodendrimers synthesized.

We followed the interaction of selected compounds by electrophoresis in agarose gel with *plasmid (pBR322)* DNA. For these compounds we also studied their interaction with *Calf Thymus* DNA (CT DNA) by circular dichroism (CD). The CD spectral technique is very sensitive to diagnose alterations on the secondary structure of DNA that result from DNA-drug interactions.

Human serum albumin (HSA) is the most abundant carrier protein in plasma and is able to bind a variety of substrates including metal cations, hormones and most therapeutic drugs. It has been demonstrated that the distribution, the free concentration and the metabolism of various drugs can be significantly altered as a result of their binding to the protein [4]. In all cases the compounds caused a concentration dependent quenching of fluorescence

without changing the emission maximum or the shape of the peak. All these data indicate an interaction of the compounds with HSA.

Cathepsin-B (Cat-B) is an abundant and ubiquitously expressed cysteine peptidase of the papain family, which has turned out to be a prognostic marker for several types of cancers [5]. Cathepsin-B seems to be involved (along with other Cathepsins) in metastasis, angiogenesis and tumor progression [6]. It has been proposed that Cat-B may be a possible therapeutic target for the control of tumor progression [7]. RAPTA-Ru compounds which inhibit Cat-B with IC_{50} in the low micromolar range can reduce the mass and number of metastases *in vivo* [8]. Therefore, we studied the inhibition of Cathepsin-B by highly cytotoxic first generation dendrimers.

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