

6. Bioinorganic Therapy



PS6.1 — MO

RUTH MARGALIT

HARRY B. GRAY

Arthur Amos Noyes Laboratory
California Institute of Technology
Pasadena, California 91125
U.S.A.

MICHAEL CLARKE

Department of Chemistry
Boston College
Chestnut Hill, Massachusetts
U.S.A.

S.C. SRIVASTAVA

Department of Chemistry
Brookhaven National Laboratory
Upton, New York
U.S.A.

BIOLOGICAL TISSUE DISTRIBUTION OF $\text{Ru}(\text{NH}_3)_5\text{-BLEOMYCIN}$

The reaction of $\text{Ru}(\text{NH}_3)_5\text{H}_2\text{O}^{2+}$ with the chemotherapeutic agent bleomycin at pH 7.2 gives a Ru-modified derivative. The modified bleomycin has been purified and characterized (by ^1H NMR and differential pulse electrochemistry) as $\text{Ru}(\text{NH}_3)_5^{3+}\text{-(pyrimidine)-BLM}$.

A model compound, $\text{Ru}(\text{NH}_3)_5\text{His}^{3+}$, was found to be effective in the scission of DNA strands, *in vitro*, when combined with a reducing agent. The activity of $\text{Ru}(\text{NH}_3)_5\text{BLM}$ in DNA strand scission will be presented and discussed. The distribution of the radioactive drug $^{106}\text{Ru}(\text{NH}_3)_5\text{BLM}$ in normal and tumor-bearing mice has been studied.



PS6.2 — TU

M.G. BASALLOTE

E.J.G. CONEJERO

R. VILAPLANA

F. GONZÁLEZ-VÍLCHEZ

Departamento de Química Inorgánica
Facultad de Ciencias
Apto. 40, Puerto Real, Cádiz
Spain

PLATINUM COMPLEXES OF EDDA AND ITS ETHYL ESTER: SYNTHESES AND ANTITUMOR PROPERTIES

Structure-activity relationship for antitumor properties of platinum complexes is still not clear, although *cis*- $[\text{PtA}_2\text{X}_2]$ compounds seem to be active when A ligands are inert and X ligands can be easily replaced in biological media. The nature of A is of great importance for the antitumor activity of the complex, with little changes in its structure leading sometimes to main changes in activity. Therefore we are testing complexes of this type with new structures in order to obtain *cis*-DDP analogs with higher therapeutic indexes.

We have shown recently activity against Ehrlich ascites tumor for some platinum complexes with aminopolycarboxylic ligands [1]. However, $[\text{Pt}(\text{EDDA-H}_2)\text{Cl}_2]$ was showed to be inactive in a previous study by SPEER *et al.* [2]. One interesting problem in structure-activity relationship is that related to the effect of the charge of the complex, active compounds being normally neutral complexes. So esterification of carboxylic groups in ligands must lead to an increase in the activity of the complexes. However, the results of previous studies with similar ligands [3,4] by other authors are contradictory and new data must be obtained for solving the problem. In this sense, we report in this paper the results of a new test of this compound and of its analog with the ethyl ester of the ligand.