(II) complexes with thiocarbamate derivatives as ligands, in order to prepare new antitumor platinum metal complexes with a better therapeutic index than *cis*-platin [6, 7].

The present note reports a new series of platinum-(II) and palladium(II) complexes containing as ligands dithiocarbamic esters of the type $L = R_1R_2N{\cdot}CSSR$ ($R_1 = R_2 = R = Me$, L = TMDT; $R_1 = R_2 = Me$, R = Et, L = DMDTE; $R_1 = R_2 = R = Et$, L = TEDT; $R_1 = R_2 = Et$, R = Me, L = DEDTM). Whereas by reacting PtX_2 and PdX_2 (X = Cl, Br) with TMDT and DMDTE, complexes of 1:1 molar ratio, MLX_2, and 1:2, ML_2X_2 have been isolated, with DEDTM and TEDT only 1:1 adducts have been obtained. On the basis of the IR data the ligands act as monodentate through the thiocarbonyl group in the 1:2 complexes; for the 1:1 a tetracoordination by one bidentate (S,S) dithiocarbamic ester molecule and two halides is suggested.

The cytostatic activity was evaluated on KB cells according to protocols suggested by the National Cancer Institute (Bethesda) [8].

Results of an *in vitro* assay are expressed as concentration of the compound in culture medium (μg/ml) required to inhibit growth by 50% (ID_{50}).

Some of the compounds showed significant cytostatic activity in the preliminary test. Particularly $Pd(DMDTE)X_2$ (X = Cl, Br), $Pt(DMDTE)Br_2$ and $Pd(DMDTE)_2Br_2$ have ID_{50} values in the 0.5–1 μg/ml interval. The ligands alone did not show any activity.

From the preliminary results the palladium complexes seem to possess a higher cytostatic activity than platinum analogues.

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Peroxides of Vanadium and Related Metals in Biological and Medicinal Chemistry

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Ions of vanadium and other transition metals of d^0 or low d^n electron configuration are present in substantial amount in selected human tissues and blood. Vanadium is one of the elements recently recognised as essential for mammals [1]. In a very low concentration [2] it is thought to be widely distributed in tissues, but its biological function remains unknown. Complexes of vanadium and related metals with peroxo group, stabilized in specific ligand fields [3], exist in solid state and aqueous solutions. Such compounds of biologically important metals can help us understand the metal interactions with dioxygen moiety in living matter [4]. We have prepared and characterized a number of peroxo complexes of vanadium, niobium, tantalum and lanthanides, some containing various heteroligands (*e.g.*, oxalates, amino-carboxylates). Antitumor activity (ILS 25–32%), using L1210 murine leukemia test systems, has been found for some of these vanadium complexes [5]. They represent a new type of antitumor metal agents, quite different from a previously reported vanadocene dichloride [6]. A change in toxicity has been observed among analogous peroxo and nonperoxo niobate complexes. The relationship between the chemical properties of these compounds and their biological effects is studied by observing properties of complex peroxo species in aqueous solutions. Proton and ^{13}C NMR spectra of heteroligands offer an indirect evidence for peroxo group presence in the metal ligand sphere. Individual resonance patterns and specific chemical shifts are observed in saturated deuterium oxide solutions for particular complex polyhedra present in the solid state. Peroxo → metal charge transfer band is pH dependent and distinct for different ligand spheres. Redox potentials measured upon oxidation by various oxidants depend upon the type of the complex, showing significant differences ($\geqslant$300 mV). Vanadium complexes are particularly interesting in this respect because of a conceivable intramolecular redox process [7]. Under proper tuning by heteroligands the reactivity of coordinated peroxo group is expected to be modified, and eventually undergo one electron oxidation. Antitumor activity and toxicity of vanadium complexes can accordingly be associated with free radical processes [8], in addition to previously observed perturbation of enzymes involving phosphate metabolism, and perhaps sodium pump. For such speculations more reliable analyses of vanadium in tissues are of primary importance [9].

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Physico-Chemical Aspects in Silicosis

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Silicosis is a pulmonary disease which afflicts persons who inhale over long periods of time freshly-ground silica-containing dust. Its mechanism of action at the molecular level is not yet understood.

The majority of crystalline SiO_2 forms are pathogenic whereas the amorphous silicas are largely inactive. The primary cause of silicosis has thus to be sought in the structural and surface characteristics of the SiO_2 particles.

Recent biological work envisages in the engulfment of the SiO_2 particles into a macrophage the first step ending up with the formation of the silicotic nodule in the lung [1–3]. Intermediate stages of the process are illustrated in Fig. 1. Any silica particle exhibits a membranolytic action on the phagolysosome, probably related to the surface hydroxyls configuration, with consequent release of lytic enzymes into the cytoplasm, death of the macrophage and release of the free SiO_2 particle in the lung tissue where it can be phagocytosed by another macrophage. This does not imply any fibrotic action *per se*. If the process takes place with *freshly ground, crystalline* SiO_2, namely quartz, tridymite and cristobalite, within the phagolysosome a fibrogenic factor is also formed, which, when released in the lung tissue, stimulates fibroblasts to an abnormal production of collagen, and hence the formation of the silicotic nodule. Membranolysis can be reduced or blocked by chemical modification of the surface, however the intimate cause of silicosis relies on the catalytic role of crystalline SiO_2 in the production of the 'factor'.

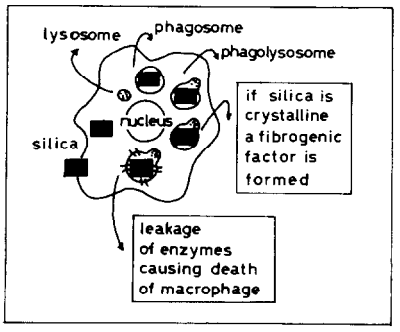

Fig. 1. Membranolytic effect of silica on macrophages.

Virtually any difference in surface properties between amorphous and crystalline silicas may account for their different biological activities.

We have investigated, so far, the formation of free radicals at the crushed surface (E.S.R.), the heat of interaction with water molecules (adsorption microcalorimetry) and the kinetics and energy of interaction with some aminoacids (immersion calorimetry) on amorphous and crystalline silicas of comparable size [4].

Free radicals are produced by mechanical grinding of quartz, and readily react with various atmospheric components yielding paramagnetic species such as $SiO_2^{\bullet}$ and $SiCO_2^{\bullet}$, possible intermediates in the formation of the fibrogenic factor.

Water vapour reacts with silicas in various ways depending on the dehydration degree of the surface. The heat of adsorption on micronized quartz (~5 m^2 g^{-1}), low and high surface area amorphous silicas (porasil ~ 16 m^2 g^{-1}), (aerosil ~ 380 m^2 g^{-1}) all outgassed *in vacuo* below 423 K (in order to prevent elimination of silanols), are reported in Fig. 2 as a function of water uptake. Micronized quartz exhibits at low coverages an interaction energy (~210 kJ mol^{-1}) which is much higher than the corresponding one on the two amorphous silicas (~125 kJ mol^{-1}).

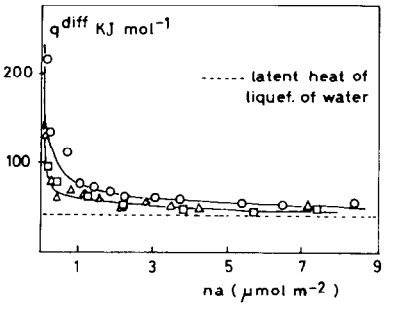

Fig. 2. Heat of adsorption *vs* water vapour uptake: ○ Quartz, □ Porasil, △ Aerosil.