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Platinum Compounds in Cancer Chemotherapy

A seminar on "Organometallic Compounds in Cancer Chemotherapy" took place at the Physikzentrum, Bad Honnef, West Germany, on March 4th and 5th 1985. It was sponsored by the Heraeus Foundation set up for the furtherance of scientific research by Wilhelm Heinrich Heraeus, grandson of the founder of the German precious metal and speciality chemical company W. C. Heraeus G.m.b.H. Inevitably platinum complexes dominated the proceedings.

The clinical importance to date of cisplatin was summarised by Professor S. Seeber (University of Essen). After reiterating the significance of the drug in the treatment of genito-urinary tumours, he went on to indicate its potential use in combination with other drugs in the treatment of certain types of lung cancer, including small cell, adeno- and epidermoid carcinomas. Promising results are also being obtained on rarer oesophageal tumours.

Dr. M. J. Cleare (Johnson Matthey) summarised the current status of analogue studies. Second generation drugs have clearly emerged on the basis of comparable therapeutic activity to cisplatin associated with considerably reduced toxicity. Of these carboplatin (JM8) was the most advanced. Data from numerous clinical trials suggest that JM8 will be registered for use in ovarian cancer in the near future. There is evidence to suggest that some of the cisplatin analogues, particularly iproplatin (JM9), may have a slightly different spectrum of tumour activity compared to the parent drug. However, Dr. Cleare felt that improved activity should be the subject of research aimed at a third generation platinum drug. A likely approach was to design targeted platinum complexes with some biological selectivity towards tumour cells. In this regard, Professor J. Karl of Regensburg University described some elegant studies aimed at developing platinum complexes with specific activity towards hormone dependent breast cancers. Platinum complexes have been synthesised using ligands which have proven ability to bind covalently to estrogen receptor sites. This work could be of significance in extending platinum drug activity but caution must be expressed; a genuine advantage of complex over free ligand has yet to be established.

Active platinum complexes with bidentate organic diamine ligands were described by Dr. H. Brunner of Regensburg University and Dr. H. A. Meinema (TNO-Utrecht).

The reaction of platinum compounds with DNA seems to hold the key to their anti-cancer activity. Dr. N. P. Johnson of CNRS, Toulouse and Dr. B. Lippert of the Technical University at Munich, discussed studies on model Pt-DNA adducts. It appears clear that the primary site of DNA attack is the N7 position on guanine. Ninety per cent of the mono-functional platinum lesions rapidly chelate with another adjacent purine base (primarily but not exclusively guanine). M.J.C.