

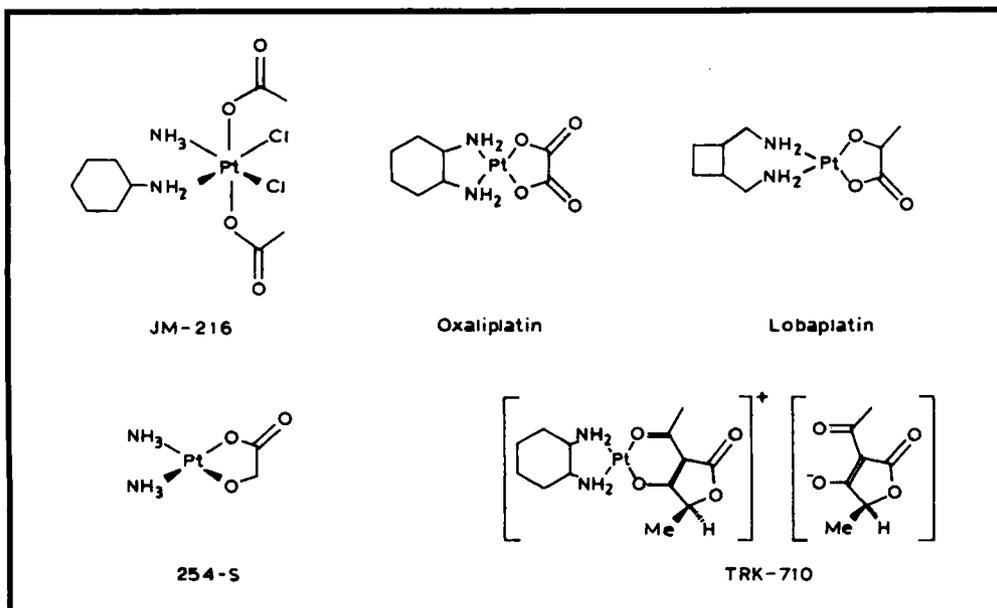
Platinum Co-ordination Compounds for Cancer Chemotherapy

A new feature of the Seventh International Symposium in the series on Metal Co-ordination Compounds in Cancer Chemotherapy, held in Amsterdam from 1st to 4th March, 1995, was the presentation of the Barnett Rosenberg award for contribution to the field of platinum-based chemotherapy. The recipient of the award, Professor Ken Harrap of the Institute of Cancer Research, London, described to the audience the history of the development of cisplatin and carboplatin and the selection of JM-216 as a candidate for an orally administered agent. He concluded by reporting ongoing work aimed at identifying compounds capable of extending the application of platinum chemotherapy by overcoming the resistance seen to cisplatin and carboplatin. In particular he highlighted the potential of *trans* compounds, an area which was raised in a number of other presentations on novel compounds.

In presentations on clinical experience with the newer platinum analogues, JM-216 was

shown to have myelosuppression as its dose limiting toxicity in a daily $\times 5$ schedule, and it has now entered Phase II trials in Europe for the treatment of lung cancer. Oxaliplatin, an analogue which has been in trials for some time now, was shown to offer benefit in colorectal cancer when combined with other drugs and using chronomodulated delivery. Lobaplatin continues to be evaluated in Phase II trials in Europe. In Japan, approval has been sought for the marketing of 254-S which has shown activity in the treatment of head and neck and gastro-intestinal tumours, and a new second generation analogue, TRK-710, has entered Phase I testing.

A debate on the relative merits of cisplatin and carboplatin in the clinic concluded it was clear that carboplatin was preferred in a palliative setting and in high dose treatments. In testicular and good-prognosis ovarian cancer patients, where cisplatin drug combinations are known to produce a high percentage of cures,



concern regarding the therapeutic equivalence of carboplatin limits its use as an alternative. The different toxicities of the two drugs give each advantages in particular combinations for specific treatments, and in this context it was noted in several presentations that the combination of carboplatin and paclitaxel (taxol) is showing promise in ovarian and lung cancers. Confirmation of these early results by more definitive studies is eagerly awaited.

Much research is now being devoted to the understanding of cellular control mechanisms

involved in cell proliferation and cell death. While it was initially proposed that chemotherapeutic agents capable of influencing these mechanisms might replace the use of cytotoxic therapy, presentations at this symposium suggested that it is more likely that they will be used in combination with cytotoxic compounds, such as the platinum drugs, to increase their effectiveness. It seems likely therefore that the platinum drugs will remain a vital part of cancer chemotherapy and a topic of international interest for some time to come.

C.F.J.B.

Platinum Interlayers Improve Capacitor Performance

The small non-volatile ferroelectric capacitors used in commercial memory devices need to have low leakage currents, to prevent charge loss and early breakdown of the device, and to have acceptable dielectric breakdown properties. Capacitors used in such devices must also be able to withstand, without breaking down, the repeated in use switching that is typical for such devices.

Thin film lead zirconate titanate (PZT) capacitors, when grown on oxide electrodes, such as those of ruthenium or lanthanum strontium cobalt, have excellent resistance to the loss of polarisation that occurs upon repeated switching; indeed PZT films grown on ruthenium oxide specifically by the sol-gel process are free of polarisation fatigue for up to 10^{11} cycles.

However, capacitors produced in this way have high leakage currents and inconsistent properties. Nevertheless, it is suggested that if these problems were overcome, these capacitors could be used successfully in non-volatile ferroelectric memory devices.

Researchers from North Carolina State University and MCNC Electronics Technology Division, North Carolina, have now produced capacitors with reduced leakage and smaller property variations by introducing a thin interlayer of platinum on the ruthenium oxide electrode (H. N. Al-Shareef, K. R. Bellur, A. I. Kingon and O. Auciello, "Influence of Platinum Interlayers on the Electrical Properties of $\text{RuO}_2/\text{Pb}(\text{Zr}_{0.53}\text{Ti}_{0.47})\text{O}_3/\text{RuO}_2$ Capacitor Heterostructures", *Appl. Phys. Lett.*, 1995, **66**, (2), 239–241).

Capacitors were fabricated by first depositing the lower ruthenium oxide electrode onto single crystal magnesium oxide by ion beam sputtering, followed by the deposition of a platinum layer, about 100 Å thick, on top of the electrode

either by ion beam- or magnetron sputter deposition. The PZT thin film of thickness 2400 Å was then deposited using a spin-on sol-gel process, followed by annealing. The upper ruthenium oxide electrode was deposited by ion beam sputtering and patterned using positive photolithography, followed by ion beam etching by argon ions.

The variations in the properties are caused because the films that are grown on ruthenium oxide are non-uniform and inhomogeneous, due to the presence of second phases. The high current leakage may be the result of a conductive pyrochlore-type second phase. In contrast, films that are grown on platinum are single phase, uniform and homogeneous, due to the easier nucleation of perovskite PZT on platinum than on ruthenium oxide electrodes.

The leakage current in capacitors with a platinum interlayer was reduced by two to four orders of magnitude, which made them more reliable, while still retaining the excellent resistance to fatigue typical of the unmodified capacitors. The difference between switched and non-switched polarisation for capacitors with the platinum interlayer was of the order of $50 \mu\text{C}/\text{cm}^2$, which remained constant for up to 10^{11} cycles. The effective resistivities of capacitors with magnetron- and ion beam sputter-deposited platinum films were about 5×10^9 and $5 \times 10^{10} \Omega \text{ cm}$, respectively, compared to values for capacitors without the platinum film of 10^6 to $10^7 \Omega \text{ cm}$. The remanent polarisation values deviated by only 3 to 4 per cent for capacitors containing the platinum interlayer compared to about 20 per cent for capacitors without the platinum interlayer.

The best results were obtained when the platinum interlayer was deposited at an elevated temperature, rather than at room temperature.