Coordination Chemistry Reviews 253 (2009) 1597–1598

Contents lists available at ScienceDirect

Coordination Chemistry Reviews

journal homepage: www.elsevier.com/locate/ccr

Preface

The use of metal complexes in medical therapy can be traced back to 3500 B.C. Due to its intriguing physico-chemical properties, gold is one of many metals used in medicine (termed Chrysotherapy) despite its potential toxic properties. Au is used as an additive in food (E 175 in the *Codex Alimentarius* established in 1963 by the FAO and WHO) consumed by various people, which advocate particular diets, for example vegetarians and vegans, and some religious groups. In addition, Au is utilized in food decoration in the form of gold leaf, and as a component of some alcoholic drinks such as Goldschläger, Gold Strike, and Goldwasser. Pure gold indeed is non-toxic *per se* and acts as non-irritating agent when ingested.

Au(I) compounds have several roles in biochemistry due to their structural properties (Abdou et al.). Au(I) is a soft d^{10} thiophilic metal ion which has a tendency towards thiol groups with low pKa affinity and phosphine donor ligands in a linear two-coordinate geometry [1]. Au(III) has been also utilized to prepare pharmacological compounds, however their instability, with the reduction to Au(I), is one of the major causes of several applicative problems including metal cytotoxicity (Wai-Yin and Chi-Ming).

Pharmacologically, Au compounds have been largely used as therapy for rheumatoid arthritis (*e.g.*, the pioneeristics and as well as myochrysin and solganol which are still in use) and in some rare skin diseases as well as in the autoimmune blistering disease treatments [4]. Navarro herein also reports novel potential applications of gold compounds as antiparasitics mainly for tropical endemic diseases such as leishmaniasis, trypanosomiasis, schistosomiasis, etc.

However it is as an anticancer metal, tentatively put forward as a possible substitute of Pt, that gold has been recently used as stated by Otto Ingo. Gold–phosphine complexes for instance (Kang) have shown a great potential for their anticancer activity and have luminescent properties that make such compounds suitable for several biophysical and biomedical applications. However the relatively high toxicity of gold–phosphine as well as other Au compounds, and lack of selectivity also poses some limitation [5]. From this perspective, like most heavy metals, Au complexes deserve some caution for their toxicity proved in humans causing several collateral effects. Forms of a sort of dermatitis and stomatis have been well described in the literature, and Au organic compounds might also derange the clinical scenario affecting proteinuria, consequent to kidney damage, with the risk of causing nephritic syndrome and immunological complications. Again, Au may act as a hapten with an overexpression of antibodies mainly in the glomerular subepithelium. Other toxicological aspects of Au have been recently reported as secondary effects of some pharmacological compounds (*e.g.*, auranofin) such as a fall in the hemoglobin level, leukopenia, lowering of granulocytes, decrease in platelets content, hematuria, pruritus, rash and persistent diarrhea.

At the subcellular level mitochondria appear to be a particular target of Au action (Otto Ingo) inducing a severe modification of their membrane permeability [2], in addition to an overaccumulation of the metal in the phagolysosomes forming cellular organelles termed *aurosomes* and also inducing an inhibition of a lysosomal strategic enzyme like cathepsin [1,3]. At the level of transcription, gold appears to be an important inhibitor of NF-κB, a key transcription factor for the production of TNF[a] (Tumor necrosis factor). Furthermore, Bindoli et al. herein describe the strong effect of gold compounds on thioredoxin reductase confirming an anticarcinogenic property through their anti-mitochondrial activity. Finally, Suwalsky et al. try to explain some aspects of gold toxicity studying the interaction between some gold compounds and cell membrane models demonstrating the powerful ability of $HAuCl_4$ to perturb the cell lipid bilayer.

In the last few years there has been an increase in studies of Au chemistry for novel therapeutical approaches mainly in the field of some forms of cancer treatment [6,8]. For instance, the structure and properties of gold nanoparticles [7] (see Zhenxin Wang) make such compounds useful for a wide array of biological applications. Toxicity, however, is always lurking behind the corner, because at high concentrations these systems, using MTT, hemolysis, and bacterial viability as biomarker assays, showed that 2 nm core particles might express differential toxicity among various cell types. Several studies showed that in Gold-complexes while cationic particles are toxic, the anionic particles are, apparently, less toxic.

Potential applications of gold nanoparticles, as a potential instrument in phototherapy, imaging, gene delivery for the treatment of various forms of cancer, have also been recently considered. Since the absorption energy appears to be concentrated on the surface clusters of nanoparticles, heat transfer mechanisms from metal-nanoparticles, i.e. a hyperthermia technique, could also be an interesting property of Au-nanoparticle applications in cancer treatment.

Recently, a class of nanostructures called Gold nanocages was prepared based on the galvanic replacement reaction between Ag nanocubes and $HAuCl_4$. The Au nanocages, having a tunable surface resonance peak that extends into the near-infrared, were shown to destroy breast cancer cells *in vitro* by using immuno-targeted Au nanocages as an effective photo-thermal transducer.

These few recent "newsflashs" of the highly promising implications of Au compounds in biomedicine could be a reasonable premise of this special issue devoted to relevant studies on gold chemistry and biochemistry. It is from this perspective of a hopefully near future application in clinical treatments which

0010-8545/$ – see front matter
doi:10.1016/j.ccr.2009.01.022

constitutes one of the major commitments of our research work, bearing in mind our practical aims from *bench to bed*

References

[1] C.G. Shaw, Chem. Rev. 99 (1999) 2589.
[2] M.P. Rigobello, G. Scutari, R. Boscolo, A. Bindoli, Br. J. Pharmacol. 136 (2002) 1162.
[3] S.S. Gunatilleke, A.M. Barrios, J. Med. Chem. 49 (2006) 3933.
[4] P. Iranzo, M.M. Alsina, I. Martinez-De Pablo, S. Segura, J.M. Mascarò, C. Herrero, J. Eur. Acad. Dermatol. Venerol. 21 (2007) 902.
[5] O. Rackham, S.J. Nichols, P.J. Leedman, S.J. Berners-Price, A. Filipovska, Biochem. Pharmacol. 74 (2007) 992.
[6] V. Milacic, C. Di, L. Ronconi, K.R. Landis-Pirowar, D. Fregona, Q. Ping Dou, Cancer Res. 10 (2007) 10478.
[7] D.O. Lapotko, E.Y. Lukianova-Hleb, A.A. Oraevsky, Nanomed 2 (2007) 241.
[8] E.R. Tienkink, Crit. Rev. Oncol. Haematol. 42 (2002) 225.

Guest Editor
Paolo Zatta*
University of Padova, CNR-Institute for Biomedical Technologies, viale g colombo, 35121 Padova, PD, Italy

*Tel.: +39 0498276331.
E-mail address: zatta@mail.bio.unipd.it

20 January 2009

Available online 29 January 2009