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Editors

Encyclopedia of Metalloproteins

With 1109 Figures and 256 Tables

Springer Reference

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Preface

Metal ions play an essential role in the functioning of all biological systems. All biological processes occur in a milieu of high concentrations of metal ions, and many of these processes depend on direct participation of metal ions. Metal ions interact with charged and polar groups of all biopolymers; those interactions with proteins play an especially important role.

The study of structural and functional properties of metal binding proteins is an important and ongoing activity area of modern physical and chemical biology. Thirteen metal ions – sodium, potassium, magnesium, calcium, manganese, iron, cobalt, zinc, copper, nickel, vanadium, tungsten, and molybdenum – are known to be essential for at least some organisms. Metallo-proteomics deals with all aspects of the intracellular and extracellular interactions of metals and proteins. Metal cations and metal binding proteins are involved in all crucial cellular activities. Many pathological conditions are correlated with abnormal metal metabolism. Research in metallo-proteomics is rapidly growing and is progressively entering curricula at universities, research institutions, and technical high schools.

Encyclopedia of Metalloproteins is a key resource that provides basic, accessible, and comprehensible information about this expanding field. It covers exhaustively all thirteen essential metal ions, discusses other metals that might compete or interfere with them, and also presents information on proteins interacting with other metal ions. *Encyclopedia of Metalloproteins* is an ideal reference for students, teachers, and researchers, as well as the informed public.

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Gold(III) Complexes, Cytotoxic Effects

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Synonyms

Anticancer characteristics of gold(III) complexes; Antiproliferative characteristics of gold(III) compounds; Antitumor effects of metal-based drugs; Cytotoxic potential of gold(III) complexes; Gold(III) complexes as anticancer agents; Mechanisms of action of gold(III) compounds; Toxicity of gold(III) complexes

The Definition and Importance of the Subject

Gold(III) is isoelectronic with platinum(II), and tetracoordinate gold(III) complexes have the same square-planar geometries as cisplatin, the drug that is currently used for the treatment of several solid tumors. However, effectiveness of cisplatin is limited by toxic side effects and tumor resistance that often leads to the occurrence of secondary malignancies. Several recently published studies that tested anticancer characteristics of gold(III) complexes showed promising results: high cytotoxic effect in vitro and in vivo was noticed against representative tumor cell lines with reduced, or even no, systemic and renal toxicity, suggesting some of the newly synthesized gold(III) compounds as novel, effective anticancer agents. The results achieved so far are summarized here, focusing on the latest in-depth mechanistic studies that have recently provided insights into gold(III) compound mechanism of action and their antitumor, cytotoxic potential, thus opening up new prospects for further pharmacological testing and, hopefully, to enter clinical trials.

Introduction

Gold compounds have a long tradition in applications in medicine as drugs. One of the major goals of modern bioinorganic and bio-organometallic medicinal chemistry research is the development of novel metallo-drugs with a pharmacological activity different from platinum drugs (Casini and Messori 2011). Among the new non-platinum antitumour drugs, gold complexes have recently gained considerable attention as a class of compounds with different pharmacodynamic and pharmacokinetic properties than cisplatin, but with strong cell growth–inhibiting effects. In many cases, the cell growth–inhibiting effects could be related to antimitochondrial effects that make the gold complexes interesting drugs (Nobili et al. 2010). Some gold complexes described as antiproliferative comprise a broad variety of different species including phosphine complexes, as well as gold complexes in different oxidation states (Nobili et al. 2010). Also, some gold(I) compounds used for the treatment of rheumatoid arthritis, such as gold thiolates, were considered for possible antitumor activity. It has been shown that gold(I) compounds inhibit tumor cell proliferation in vitro, but unfortunately their in vivo effectiveness as well as significant nephrotoxicity and poor chemical stability limited their use (Casini and Messori 2011). However, the unique chemistry of the gold center, a great propensity to form strong gold–gold bonds (the so-called aurophilic interactions), and rich redox chemistry were further exploited and a variety of gold-based pharmacologically active compounds were synthesized so far (Djeković et al. 2012).

Gold(III) complexes have been synthesized and characterized and show greater chemical stability and a far better toxicological profile than gold(I) complexes. During the early 1990s, there was a revival of interest toward gold(III)-based antitumor compounds in an attempt to obtain pharmaceutically useful substances with an even better stability profile. As a result, several square planar gold(III) complexes, isoelectronic and isostructural with Pt(II), were prepared and tested as potentially new anti-tumor drugs (Che and Sun 2011).