metals

Editorial

The Biological Applications of Metals and Metal Complexes

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1. Introduction and Scope

Over the course of biological evolution, approximately 25 to 30 elements have been recognized as essential for the proper functioning of biological systems since the emergence of life. Within this group, 10 are classified as metallic elements, commonly referred to as “inorganic elements” [1,2]. Metals such as sodium (Na), potassium (K), magnesium (Mg), calcium (Ca), iron (Fe), manganese (Mn), cobalt (Co), copper (Cu), zinc (Zn), and molybdenum (Mo) are elements essential for life, and our body must have adequate amounts of them, while others are considered possibly essential, such as V and Cr, even if they are present in vestigial amounts [1,2]. Contaminant metals and/or semi-metals such as arsenic (As), lead (Pb), mercury (Hg), cadmium (Cd), and aluminum (Al) are detrimental to living systems [3]. Other nonessential metals, such as gold (Au), silver (Ag), platinum (Pt), and ruthenium (Ru), have been recognized for their diverse biological applications in the treatment of human diseases and are now being explored as potential candidates for future drug development [4–15]. Recent decades have seen important advances in our knowledge of mechanistic bioinorganic chemistry and a steady change in the traditional view of the many roles that metals and their complexes play in biological systems.

This Special Issue provides insights into the applications of metals and their complexes in biology and biomedicine. A wide range of topics are addressed, including the use of vanadium (V) and gold (Au) complexes as anticancer agents against human melanoma and neuroblastoma, the interactions between vanadium–copper complexes and DNA/tRNA via H-bonds and hydrophobic interactions, and the reactivity of polyoxovanadates (POVs) with biologically relevant labile compounds such as ATP [16–19]. Besides metal complexes, silver nanoparticles are described to present potent activity against human liver and breast cancer cells, whereas ZnO nanotubes are also described to have anti-toxoplasmosis activity [20,21]. Altogether, this Special Issue on The Biological Applications of Metals and Metal Complexes has received six contributions, encompassing the exploration of vanadium (V), silver (Ag), gold (Au), and zinc (Zn) compounds in various biological contexts. So far (April 2023), these papers have garnered a total of 60 citations and 8000 views, indicating an average of 10 citations and 1340 views per publication.

2. Contributions

The first paper published in the present Special Issue (SI) is entitled “Vanadium and melanoma: a systematic review”. Since 1999, Aureliano’s research group, in collaboration with other scientists, has conducted a series of in vitro and in vivo studies focused on vanadium compounds, particularly decavanadate ($[V_{10}O_{28}]^{6-}$, V_{10}). The primary objective of these investigations has been to evaluate the potentially toxic effects of V_{10} [15], as well as its interactions with proteins [22,23]. Furthermore, the research aims to explore the anticancer properties of vanadium compounds and polyoxovanadates (POVs), both individually [15,16] and in combination with metformin, specifically in relation to human melanoma cells [24]. These studies represent only a portion of the broader range of research conducted by the group [25–27]. The review underscores the significant potential of vanadium compounds and/or vanadium materials in exhibiting anticancer activities, offering a promising avenue for the treatment of melanoma. The findings highlighted in the review strongly support the notion that leveraging these compounds and materials can serve as a valuable approach to combating melanoma and its associated challenges [16].

The second paper published in the present Special Issue is entitled "Ternary Copper Complex of L-Glutamine and Phenanthroline as Counterions of Cyclo-Tetravanadate Anion: Experimental–Theoretical Characterization and Potential Antineoplastic Activity", by the research group of Professor Enrique González-Vergara from the Benemérita Universidad Autónoma de Puebla, Puebla, Mexico. Professor Enrique González-Vergara is a highly renowned researcher, particularly recognized for his significant contributions within the field of the antidiabetic properties of metformin–decavanadate (Metf-V_{10}) [28–31]. Metf-V_{10} stands out as an intriguing hybrid compound, offering a unique combination of metformin and decavanadate. [31]. Metf-V_{10} has shown in vivo nontoxicological effects on the liver and kidney, being overall considered a better treatment than metformin in diabetes [30]. Previous research led by Enrique González-Vergara and his colleagues has suggested that Metf-V_{10} could potentially serve as a more potent treatment option for cancer compared to metformin [32]. In line with this, the present paper shifts its focus towards investigating the interactions of $[Cu(L\text{-}Gln)(phen)(H_2O)]_4$ (V_4O_{12}) with DNA and RNA. The findings described in the study indicate that molecular docking studies strongly support the hypothesis that the anticancer activity of POVs can be attributed to their interaction with DNA and tRNA through hydrogen bonds and hydrophobic interactions [17]. These results provide compelling evidence for the mechanism by which POVs exert their therapeutic effects and shed light on the underlying molecular interactions that contribute to their anticancer properties.

The third paper published in the present Special Issue is entitled "Kinetic and Interaction Studies of Adenosine-5′-Triphosphate (ATP) Hydrolysis with Polyoxovanadates", by the research group of Professor Tatjana Parac-Vogt from Leuven, Belgium. Professor Parac-Vogt is a well-known researcher for studying polyoxometalates (POMs) as artificial enzymes by using POMs as catalysts for the hydrolysis of peptide bonds [33]. Additional computational studies have focused on the characterization of the reaction mechanism and the rationalization of the observed selectivity [34,35]. In this study, the authors have specifically investigated the reactivity of two POVs, V_{10} and $[H_xPV_{14}O_{42}]^{(9-x)-}$ (PV_{14}), towards ATP, the fundamental bioenergetic molecule that crucially serves as the primary currency for energy exchange within cellular systems [18]. It is worth noting that both V_{10} and PV_{14} have been previously identified as inhibitors of P-type ATPases [36,37]. V_{10} has been characterized as a noncompetitive inhibitor, while PV_{14} has been recognized as a mixed inhibitor in relation to the native substrate MgATP [36,37].

From the research group of Professor Ana Mata, Extremadura University, Spain, we received the publication entitled "Gold Compounds Inhibit the Ca^{2+}-ATPase Activity of Brain PMCA and Human Neuroblastoma SH-SY5Y Cells and Decrease Cell Viability" [19]. Gold compounds have shown anticancer, antiviral, and antibacterial activities [6,10,12]. Professor Ana Mata's research endeavors encompass various aspects, including investigating the association between calcium homeostasis and neurological disorders, such as Alzheimer's disease. Her work has shed light on the role of the plasma membrane calcium ATPase (PMCA) and the sarco(endo)reticulum calcium ATPases (SERCA) under these conditions [38–40]. The authors demonstrate that gold compounds exhibit notable affinity as inhibitors of the Ca^{2+}-ATPase activity within purified PMCA fractions. Furthermore, they highlight the profound cytotoxic effects of these gold compounds on human neuroblastoma cells [19].

The fifth contribution is an article entitled "Silver Nanoparticles: An Instantaneous Solution for Anticancer Activity against Human Liver (HepG2) and Breast (MCF-7) Cancer Cells" [20] from Professor Rizwan Wahab, King Saud University, Riyadh, Saudi Arabia.

Professor Rizwan Wahab's research group and collaborators possess extensive expertise in the synthesis and characterization of metal nanoparticles and nanocomposites, as well as exploring their potential anticancer activities [41,42]. In this particular study, the focus is on silver nanoparticles and their impact on human liver (HepG2) and breast (MCF-7) cancer cells. The results reveal that silver nanoparticles exhibit cytotoxic effects by inducing apoptosis through the activation of the p53 and caspase pathways [20]. This investigation contributes to our understanding of the potential therapeutic applications of silver nanoparticles in targeting liver and breast cancer cells, emphasizing their ability to trigger programmed cell death pathways.

The sixth contribution in this collection is titled "Decorative Multi-Walled Carbon Nanotubes by ZnO: Synthesis, Characterization, and Potent Anti-Toxoplasmosis Activity." It is the result of a collaborative effort between Princess Nourah Bint Abdulrahman University in Riyadh, Saudi Arabia, and two Egyptian universities, Alexandria University and Pharos University. These research teams have extensive experience in the characterization of metal nanoparticles and their applications in various fields, including environmental studies [43–46]. In this groundbreaking study, the authors present, for the first time, the remarkable antiparasitic effect of well-dispersed multiwalled carbon nanotubes lined with ZnO (ZnO-MWCNT) against *Toxoplasma gondii* infection in mice [21]. This research highlights the potential application of ZnO-MWCNT as a novel and effective therapeutic approach for combating *Toxoplasma gondii*, opening up new possibilities for treating this parasitic infection. All in all, the Special Issue contains six papers dealing with the biological applications of vanadium, silver, gold, and zinc (Figure 1).

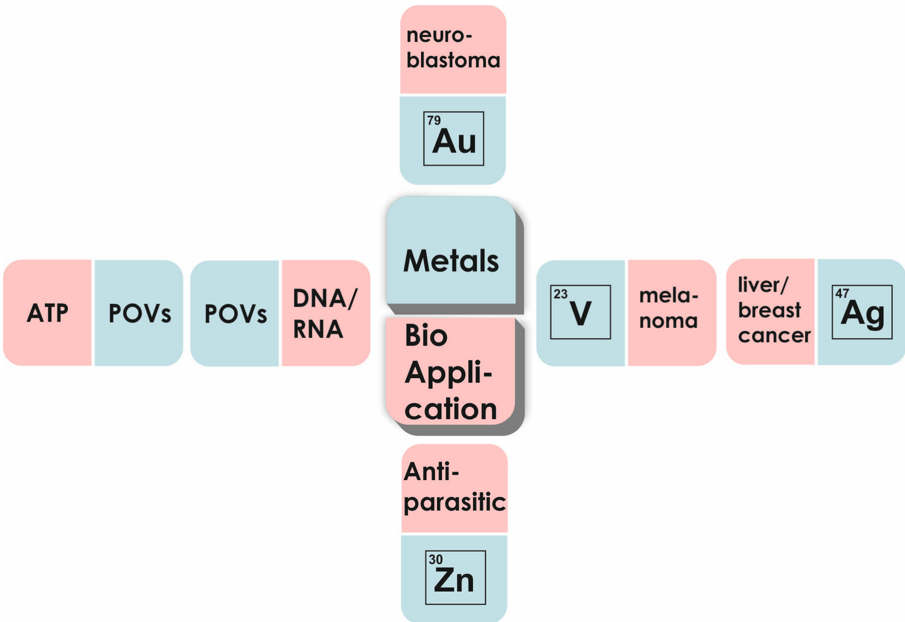

Figure 1. Emerging biological applications of vanadium, gold, silver, and zinc in the 21st century, demonstrating anticancer and antiparasitic activities, as well as POVs interacting with DNA and ATP biomolecules. Each domino represents a paper in the Special Issue.

3. Conclusions and Outlook

In recent years, there has been an increasing interest in the potential applications of metals in biology, including vanadium, silver, gold, and zinc. Polyoxometalates (POMs), which are a diverse family of metal–oxo anions of early transitional metal ions (Mo, W, V), are also gaining increasing interest in biomedicine due to their anticancer activities, among others. The present Special Issue reflects distinct and emergent 21st century biological applications of metal compounds and metal nanoparticles which exhibit anticancer, antiparasitic, and antidiabetic activities besides the use of POMs as artificial enzymes and the contribution of computational studies for understanding POVs' interactions with biomolecules such as DNA (Figure 1). Within this Special Issue, a total of 28 authors from 6 countries were involved, including many young researchers, thus pointing out a new generation of scientists in the field. In fact, the future is bright for metal applications in biology!

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Abbreviations

ATPase	Adenosine triphosphatase
PMCA	Plasmatic membrane calcium ATPase
POMs	Polyoxometalates
POVs	Polyoxovanadates
PV_{14}	Phosphotetradecavanadate
SERCA	Sarco(endo) plasmatic membrane calcium ATPase
V_{10}	Decavanadate
ZnO-MWCNT	Well-dispersed multiwalled carbon nanotubes lined with ZnO

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