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Synthesis, kinetics, mechanisms, and bioactivity evaluations of a novel Zn(II) complex

Anwesha Dey,†[a] Ramesh Kumar, †[b] Bhramar Dutta, [c] Rajib Bandopadhyay,[c] Sankha Chakrabortty, [d] Moonis Ali Khan, [e] Rijuta Ganesh Saratale,[f] Ganesh Dattatraya Saratale,[g] Byong Hun Jeon *[b] and Alak K. Ghosh *[a]

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Zn(II)-based anticancer drugs can be suitable alternatives to conventional Pt(II)-based drugs because of the unique chemical properties of Zn(II) and low toxicity. In this study, a new hexadentate and heteroleptic Zn(II) complex ($[Zn(bpy)_2(OAc)_2]$, **1**) was prepared with a conventional *N*,*N*-donor ligand (2,2′-bipyridine) and a leaving group (OAc) and characterized *via* ESI-MS, UV-Vis, and FT-IR spectroscopy. Kinetic and mechanistic investigations of **1** were performed using two biologically relevant ligands (DL-penicillamine and L-cysteine) to understand its selectivity and reactivity. Substitution reactions were determined to be two-step processes in the associative activation mode. Bioactivity studies of **1** revealed moderate to strong DNA-binding, cleaving ability, and antimicrobial properties.

Introduction

Transition metal complexes are being explored as alternative antitumor agents to Pt(II) complexes, owing to their lower toxicity and higher efficacy compared to that of the latter.[1] In particular, Ru(III), Ga, and As complexes have emerged as promising anticancer drugs.[2] Some Zn(II) coordination complexes also showed promising DNA binding ability and antitumor activity.[3,4] This is attributed to their unique chemical properties, diverse biological functionality, and lower toxicity at even higher doses compared to other metals,[5,6] negligible side effects compared to the available anticancer drugs,[7] and affordability.

Zn has three unique chemical properties: (i) it has a $3d^{10}$ electronic configuration in the +2 state; thus, the Zn(II) coordination complexes have no ligand-field stabilization energy.[8] Hence, they do not have preferential geometry and can form readily exchangeable, flexible, but strong complexes with organic ligands;[9] (ii) Zn(II) has a filled 3d orbital and is thus redox inactive. Hence, they are highly stable in biological reactions and can easily enter biological systems without causing oxidative stress-mediated damage; and (iii) Zn(II) is classified as a borderline metal ion by Pearson in 1963.[10] Therefore, it does not have preference among N, O, or S for coordination. In addition, Zn is an essential trace element and the second-most abundant element in the body.[11] It is crucial for all forms of life on the planet. Zn is present in all body fluids and tissues, with maximum fractions in the muscle tissue, skeleton, and liver.[12] It has diverse biological functions owing to its redox-inactive nature. Zn(II) complexes strengthen the immune system;[13] regulate RNA transcription and DNA synthesis;[14] heal wounds;[15,16] maintain cell growth, cell division, differentiation, proliferation,[17] and prostaglandin function;[14] regulate body fluid pH; enhance collagen formation in hair, nails, and skin;[18] and improve memory and mental health.

The physicochemical properties of Zn(II), such as its diamagnetism, strong Lewis acidity, and d^{10} configuration, enable the formation of different coordination geometries with chelating ligands of diverse donor atoms and hapticity.[3] Moreover, Zn(II) complexes have exhibited antiproliferative activity, fast ligand exchange, Lewis acid activation, and catalytic activities in hydrolysis and DNA cleavage.[19,20] In addition, they are non-toxic, even at high dosages. They have a preventative effect on infectious diseases and are less harmful anticancer drugs.[21] In particular, zinc phthalocyanines serve as photosensitizers or light-sensitive compounds during the photodynamic treatment of tumor cells by producing reactive oxygen species (ROS).[22] Moreover, Zn(II) forms dimeric and polymeric complexes with various donor atoms, such as N, O, and S, in ligands of different

[a]*Department of Chemistry, The University of Burdwan, Burdwan (E) 713104, West Bengal, India. E-mail: akghosh@chem.buruniv.ac.in*

[b]*Department of Earth Resources & Environmental, Engineering, Hanyang University, 222-Wangsimni-ro, Seongdong-gu, Seoul 04763, Republic of Korea. E-mail: bhjeon@hanyang.ac.kr*

[c]*Department of Botany, The University of Burdwan, Burdwan (E) 713104, West Bengal, India*

[d]*School of Chemical Engineering, Kalinga Institute of Industrial Technology, Bhubaneswar 751024, Odisha, India*

[e]*Chemistry Department, College of Science, King Saud University, Riyadh 11451, Saudi Arabia*

[f]*Research Institute of Integrative Life Sciences, Dongguk University-Seoul, Ilsandong-gu, Goyang-si, Gyeonggido 10326, Republic of Korea*

[g]*Department of Food Science and Biotechnology, Dongguk University-Seoul, 32 Dongguk-ro, Ilsandong-gu, Goyang-si, 10326, Gyeonggi-do, Republic of Korea*

† These authors contributed equally.