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ORIGINAL ARTICLE

Oxovanadium(IV) complexes of medicinal relevance: Synthesis, characterization, and 3D-molecular modeling and analysis of some oxovanadium(IV) complexes in O,N-donor coordination matrix of sulfa drug Schiff bases derived from a 2-pyrazolin-5-one derivative

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Abstract The present paper reports the synthesis and characterization of some new oxovanadium(IV) complexes of composition $[VO(L)_2(H_2O)]\cdot H_2O$, where LH = *N*-(4′-butyrylidene-3′-methyl-1′-phenyl-2′-pyrazolin-5′-one)sulfadiazine (bumphp-sdzH), *N*-(4′-butyrylidene-3′-methyl-1′-phenyl-2′-pyrazolin-5′-one)sulfaguanidine (bumphp-sgnH), *N*-(4′-butyrylidene-3′-methyl-1′-phenyl-2′-pyrazolin-5′-one)sulfani-lamide (bumphp-snmH), and *N*-(4′-butyrylidene-3′-methyl-1′-phenyl-2′-pyrazolin-5′-one)sulfamerazine (bumphp-smrH). These complexes were prepared by the reaction of vanadyl sulfate pentahydrate with the ligands in 1:2 metal–ligand ratios, in ethanol. The compounds so obtained were characterized by different physicochemical studies, such as, elemental analyses, molar conductance, and magnetic measurements, thermogravimetry, cyclic voltammetry, infrared, electron spin resonance, and electronic spectral studies. The overall IR studies conclude that the ligands in the present investigation behave as monobasic bidentate O,N-donors. The 3D molecular

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modeling and analysis for bond lengths and bond angles have also been carried out for one of the representative compounds, $[VO(bumphp\text{-}sdz)_2(H_2O)]\cdot H_2O$ (**1**) to substantiate the proposed structure. Based on these studies suitable octahedral structures have been proposed for these complexes.

1. Introduction

Acylpyrazolones, originally investigated by Jensen (1959a,b), have been employed for several applications (Marchetti et al., 2000a,b), *viz*., as pigments for dyes, as metal extractants from acidic solutions and also as sequestering agents toward polluting metal ions, such as cadmium and lead. These ligands have played and continue to play an important role in the development of coordination compounds that have found wide application in several fields, from new materials to catalysts, as precursors for CVD in the microelectronic industry and as potential antitumourals (Marchetti et al., 2005).

The pyrazolone derivatives have been reported to possess strong antibacterial, antihistaminic and antifungal, analgesic, antipyretic, anti-inflammatory, and anti-rheumatic activities (Merck Index, 1983). They also show antidiabetic (Goodman and Gilman, 1970), anticancer (Garg and Singh, 1970), and antineoplastic (Wilson and Bottigleri, 1962) properties.

The derivatives of Sulfonamide exhibit a range of bioactivities, including anti-angiogenic (Funahashi et al., 2002; Semba et al., 2004), anti-tumor (Semba et al., 2004; Sawiński et al., 2005), anti-inflammatory and anti-analgesic (Chen et al.,2005), anti-tubercular (Gadad et al., 2004), anti-glaucoma (Agrawal et al., 2004), anti-HIV (Yeung et al., 2005), cytotoxic (Encío et al., 2005), anti-microbial (Nieta et al., 2005), and anti-malarial (Domínguez, et al., 2005) agents. The sulfonamide derivatives are also known to exhibit a wide variety of pharmacological activities (Yoshino et al., 1992; Toth et al., 1997; Medina et al., 1999) through exchanges of different functional groups without the modification of the structural $–S(O)_2N(H)–$ feature. The synthesis of metal sulfonamide compounds had received much attention due to the fact that sulfanilamides were the first effective chemotherapeutic agents to be employed for the prevention and cure of bacterial infections in humans (Mohamed and Gad-Elkareem, 2007). The pharmacological activity of these types of molecules is often enhanced by complexation with metal ions (Bult and Sigel, 1983; Casanova et al., 1983). Moreover, some metal complexes of these ligands have been found to promote rapid healing of burns in human and animals (De Oliveira et al., 2008; Baenziger et al., 1983).

Vanadium plays an important role in life and one of its most relevant properties identified thus for is its capacity to act as an insulin-enhancing agent, either in the form of its inorganic salts or complexes with organic ligands (Rangel et al., 2006). It has been observed that simple inorganic vanadium compounds are more toxic than vanadium compounds with organic ligands and the efficacy of metal based therapeutic agents' changes drastically by making changes in the organic ligands that are attached to the metal center (Mahroof-Tahir et al., 2005). For any complex considered for therapeutic use, it is important to consider the intrinsic toxicity of the ligand, especially if the treatment is predicted for long periods (Pressoa et al., 2003). Great efforts have, therefore, been made to synthesize oxovanadium(IV) complexes of high biological activity and low toxicity which are readily absorbed. Many oxovanadium(IV) complexes with various coordination modes (Thompson and Orvig, 2001; Sakurai et al., 2002; Thompson et al., 1999; Maurya and Rajput, 2006; Ghosh et al., 2005) have been prepared, *viz*., $VO(O_4)$, $VO(S_2N_2)$, $VO(S_4)$, $VO(N_3O)$, and $VO(N_2O_2)$, and the relationship between their structures and insulin-mimetic activities has been examined by evaluating both *in vivo* and *in vitro* results. The bis(ethylmaltolato)oxovanadium(IV) (BEOV) has completed phase I clinical trial in humans in the treatment of type-1 and type-2 diabetes mellitus (Thompson and Orvig, 2006).

Besides the antidiabetic action, vanadium complexes are known to possess potent anticancer activity (Kieler et al., 1965; Dessoize, 2004), which deserves increasing attention for the application to biomedical sciences (Etcheverry et al., 2008). Recent studies indicate the chemopreventive efficacy of vanadium in the inhibition of chemically induced carcinomas of the liver, colon, and mammary gland and has substantially documented the role of vanadium in the prevention of DNA–protein crosslinks, DNA chain break, chromosomal aberrations (Molinuevo et al., 2008; Chakraborty et al., 2006; Chattopadhyay et al., 2005; Kanna et al., 2004, 2005; Ray et al.,2004, 2005), reduction of tumor incidence and average number of tumors (33, Bishayee et al., 2000; Kanna et al., 2003), suppression of tumor marker genes like GST, GST-P, GGT, and MT (Ray et al., 2004). On the other hand, when using *in vitro* models it has been shown that some vanadium complexes displayed antitumoural actions (Barrio et al., 2003; D'Cruz and Uckun, 2002; Ding et al., 1999; Etcheverry et al., 2002; Evangelou et al., 2002; Molinuevo et al., 2004). Knowledge gained from *in vitro* studies has advanced vanadium research into the preclinical *in vivo* phase (Bishayee et al., 2010).

It has also been recognized that vanadium as a micronutrient prevents the minor wear and tear of the essential critical molecules of the cell like DNA, proteins, etc. in humans (Fenech and Ferguson, 2001) Thus, it has a role in DNA maintenance reactions and may protect the genomic instability that may be leading to cancer (Ray et al., 2006).

Recent studies (D'Cruz et al., 2003; Shigeta et al., 2003) showed that oxovanadium complexes of thiourea and vanadium substituted polyoxotungstates exhibit potent anti-HIV properties toward infected immortalized T-cells. However, the instability of vanadium(IV) complexes under physiological conditions has been frequently encountered (Raymond et al., 2007). Some oxovanadium(IV) complexes of porphyrin derivatives {$[VO(N_4)]$ type} were evaluated for their inhibitory effects on HIV-1(BaL) (Human Immunodeficiency Virus) replication in Hut/CCR5 cells (Raymond et al., 2007).

Earlier reports from our laboratory described the synthesis and characterization of metal chelates of ruthenium(II) (Maurya et al., 1994), dioxomolybdenum(VI) (Maurya et al.,