Chemoprotective effect of polyoxovanadates against alkylating agents *in vivo* and solution speciation studies

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In recent decades, vanadium compounds have been extensively studied due to their potential application in catalytic, magnetic and electronic systems, and in medicinal chemistry. This element has produced promising results in studies of biological systems, presenting activity in both the suppression and spread of tumors. The element also plays a role in DNA maintenance, which leads to cell protection from genomic instability.[1] Recently, our research group reported the synthesis of $(Me_4N)_6[V_{15}O_{36}(Cl)]$ (**A**) employing a new synthetic route with mild conditions and low-cost reagents.[2] This aggregate showed chemoprotective activity against the alkylation reaction of the DNA plasmid pUC19 by potentially carcinogenic agents. In this work, the mixed valence polyoxovanadates **A** and $(NH_4)_7[H_6V_{14}O_{38}(PO_4)]\cdot 9H_2O$ (**B**) were evaluated for their chemoprotective activity against the alkylating agent diethylsulphate (DES) using *Escherichia coli* DH5α cell cultures as a model system. Both products showed to be non-toxic to *E. coli* cultures in concentrations up to 10.0 and 1.0 mmol L^{-1}, respectively. The *E. coli* cultures treated with DES in the presence of product **A** presented a chemoprotective effect of 30-40% as compared to control cells only with the addition of DES. In contrast, compound **B** was unable to protect the bacteria from the alkylating agent, enhancing the deleterious effect of DES on bacterial growth. Speciation studies were carried out by ^{51}V NMR and EPR in aqueous solution and Luria (LB) broth, aiming to simulate the biological assay conditions. The ^{51}V NMR analysis showed that the structure of **A** was more stable in LB, as it does not produce significant amounts of low nuclearity vanadium(V) species observed in aqueous solution ($H_2VO_4^-$, $H_2V_2O_7^{2-}$, $V_4O_{12}^{4-}$ and $V_5O_{15}^{5-}$). In the case of **B**, the structure suffers breakage, supported by the appearance of signals at δ = -524, -506 and -425 ppm, typical of the three different coordination environments of vanadium(V) in the decavanadate anion, $[HV_{10}O_{28}]^{5-}$. Residual signals of the fully oxidized species $[H_4V_{14}O_{38}(PO_4)]^{5-}$, detected in the aqueous solution of **B**, can also be observed in LB. For **A**, decavanadate was only formed after addition of a large excess of DES to the solutions. Studies indicate that the chemoprotective effect against alkylating agents is not only highly dependent on the solution stability of the POVs, but is also limited by the formation of decomposition products such as decavanadate and mononuclear vanadyl(IV) species, which are weakly reactive.

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