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In vivo anti-diabetic activity and speciation studies of a non-toxic binuclear oxalate-bridged oxidovanadium(IV) complex

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In the last two decades, vanadium complexes have been extensively evaluated as anti-diabetic drugs due to their insulin-like and insulin-mimetic properties.[1] Recently, our research group reported the synthesis, characterization and *in vitro* antidiabetic activity of the centrosymmetric oxidovanadium(IV) complex $(Et_3NH)_2[\{VO(OH\}_2)(ox)_2(\mu\text{-}ox)]$ (**V_2**), where ox^{2-} = oxalate.[2] HepG2 cells treated with **V_2** in culture medium DMEM increased the uptake of the 2-NBDG (2-[N-(7-nitrobenz-2-oxa-1,3-diazol-4-yl)amino]-2-deoxy-D-glucose), a fluorescent glucose analog, with better or similar response than the insulin.[2] In view of the promising results, the antidiabetic activity of **V_2** was evaluated *in vivo*. All animal procedures were pre-approved by the institutional ethical committee (code 1381). An aqueous solution of **V_2** was administered by oral gavage to streptozotocin (STZ)-induced diabetic rats at 10 and 30 mg kg^{-1} for 12 days, without induced liver injury. **V_2** at 100 mg kg^{-1} in association with insulin caused a 3.4 times decrease in blood glucose in STZ rats (424 mg dL^{-1}), reaching concentrations similar to those in the normoglycemic animals (126 mg dL^{-1}). Compared to insulin alone, the association with **V_2** caused an additional decrease in blood glucose of 39% and 65% at 30 and 100 mg kg^{-1}, respectively.[3] Stability studies performed by electron paramagnetic resonance (EPR) in aqueous solutions contrast with the extensive speciation observed in DMEM. The EPR spectra showed a broad line (g = 1.986 and $\Delta_{p\text{-}p}$ =23 mT), suggesting that the binuclear structure of **V_2** is maintained for at least 24 h even at low concentrations. The complex **V_2** is a promising candidate as an insulin adjuvant to improve glycemic control in diabetes treatment.

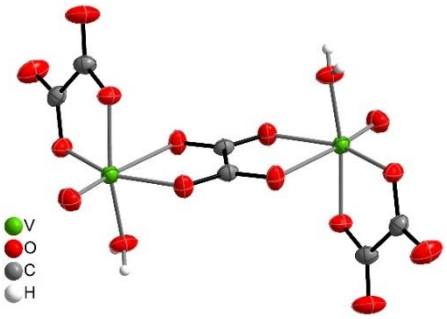

Figure 1. Ball and stick representation of the $[\{VO(OH\}_2)(ox)_2(\mu\text{–}ox)]^{2-}$ anion.

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