Abstract

Doctoral thesis includes synthesis of ligands, as well as synthesis and structural characterisation of complexes with potential insulin-like hypoglycaemic activity, namely VO^{2+}, VO_2^+ and Zn^{2+} complexes with picolinato and *β*-diketonato type of ligands. Having in mind known insulin-like activity of $VO(pic)_2 \cdot H_2O$, complexes of $VO(pic)_2$ and 4-apy, DMAP or im (**V1**–**V3**), as well as aqua-analogues **V4**–**V7** with picCN, picFF, Hhypic and prz derivatives of pic ligand were synthesised and their crystal structures determined. Both compound types crystallize in *cis*-octahedral form as *OC*-6-23 and/or *OC*-6-24 isomers. EPR spectroscopy confirmed the existence of **V4**–**V7** *OC*-6-23 and/or *OC*-6-24 isomers in solutions, accompanied by partial isomerization into *OC*-6-42 isomer. Study of **V4** and **V5** at different pH (EPR and pH-metric titration) and interactions of **V4**–**V7** compounds with blood serum proteins apo-hTf and HSA are also presented. VO_2^+ compounds **V8**–**V12** with two pic or prz type of ligands crystalize in ionic form with *OC*-6-33 or *OC*-6-22 isomers of *cis*-octahedral complex anions, while VO_2^+ compound with pic and chlorido ligand crystallize in a shape of distorted trigonal bipyramid. Among Zn^{2+} picolinates **Z1**–**Z22** (picCN, picFF, Hhypic, 4MeOqc) *cis*–*trans* isomerism depending on the presence of neutral O- and N-donors and steric hindrance of anionic ligands occurred. In the presence of neutral O-donor ligands (**Z1**–**Z9**) or sterically hindered Hhypic and 4MeOqc ligands (**Z17**, **Z21**, **Z22**) *trans*-octahedral *OC*-6-12 isomers are formed, while with mono- or bidentate N-donor ligands *cis*-octahedral *OC*-6-13 complexes are formed. Similar isomerism is present in the case of Zn^{2+} tfpb *β*-diketonates **Z36**–**Z40**. With O-donors *trans*-octahedral *OC*-6-12 isomers, contrary with N-donors *cis*-octahedral *OC*-6-33 and *OC*-6-32 isomers are formed. Crystal structure of VO^{2+} compound with tfpb ligands (**V17**) with interesting polymeric structure is also determined. With new amido and amino type of 6-substituted (di)picolinato ligands two VO^{2+} and several Zn^{2+} complexes were prepared, while ester analogue hydrolyses in solution of metal ions and forms VO_2^+ and Zn^{2+} complexes (**V14**, **Z23**). In the presence of VO^{2+} ions the hydrolysis of amido analogues is also common, while amino ligands are stable in VO^{2+} and Zn^{2+} solutions. VO^{2+} complex **V15** with amide **7** has octahedral structure with one amido and one dipic ligand, while aqua-VO^{2+} complex **V16** with amine **11** has *trans*-octahedral structure. With Zn^{2+} ions and amides monomeric, tetranuclear and polymeric compounds **Z24**–**Z30** were formed, while with Zn^{2+} ions and amido ligands water soluble complexes **Z31**–**Z33** were formed. Inhibition of free fatty acids release from rat adipocytes of VO^{2+}, VO_2^+ and Zn^{2+} compounds with adequate solubility in water was also defined. The most promising insulin-like inhibition has been found in the case of VO^{2+}, VO_2^+ and Zn^{2+} complexes with Hhypic ligands and of Zn^{2+} compound with amide **7**.

Keywords: vanadium, zinc, coordination compounds, diabetes, hypoglycaemic activity.