Insulin-mimetic oxovanadium-picolinates

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Oxovanadium complexes of the type shown in the Figure have been designed so as to fulfil a couple of indispensable preconditions for a vanadium-based, anti-diabetic drug to be applied orally, viz. (i) stability in the acidic to slightly alkaline pH range; (ii) efficient absorption by the gastrointestinal tract; (iii) stability towards ligand exchange during transport in the bloodstream; (iv) balanced lipophilicity and/or constituents recognizable by membrane receptors in order to facilitate transmembrane transport; (v) low toxicity; and (vi) high insulin-mimetic potential, i.e. stimulation of cellular uptake and degradation of glucose, and inhibition of lipolysis [1].

Vanadium complexes containing 1,5-dipicolinato ligands modified in the 5-position, i.e. in the periphery of the complex, are an excellent basis for the design of the respective properties. The most efficient cellular uptake combined with low cytotoxicity and high insulin-mimetic potential has been noted for R = CH₃ and D-galactose-orthoformiate, in in vivo tests with Simian virus modified mice fibroblasts (glucose metabolism) and rat adipocytes (inhibition of lipolysis) [2].

Results of these tests, syntheses and structure information on several of the vanadium complexes is provided, as well as speciation studies in pH 2-9 range in the presence of low and high molecular mass blood constituents.
