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Insulinomimetic activity of vanadyl complexes with halogenated picolinic acids

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Abstract:

Vanadyl ion and its complexes have been found to normalize the blood glucose levels in both type 1 and 2 diabetic animals. We have developed various types of vanadyl complexes, and found that the bis (picolinato) oxovanadium (IV) [VO(pa)₂] complex is an effective agent for treating diabetes mellitus. Then, we used VO(pa)₂ as a leading compound for developing more active agents with hypoglycemic effects. By introducing an electron-withdrawing group such as a halogen atom into the pyridine ring of picolinic acid, seven kinds of vanadyl picolinate complexes were prepared. The structures of these complexes were characterized by elemental analysis and physical methods such as visible, IR, and ESR absorption spectra, and magnetic susceptibility. Introduction of an iodine to the picolinic acid gave a stronger insulinomimetic activity than that of VO(pa)₂. The hyperglycemia of streptozotocin-induced insulin dependent diabetic mice was normalized when bis(4-chloropicolinato)oxovanadium(IV) [VO(4cpa)₂] or bis(4-iodopicolinato)oxovanadium(IV) [VO(4ipa)₂] was given by a single intraperitoneal injection. The metallokinetic features of vanadyl species in the blood were examined by using the blood circulation monitoring-electron paramagnetic resonance (BCM-EPR) method. Vanadyl concentrations in the blood of normal rats given VO(4cpa)₂ and VO(4ipa)₂ remained higher and longer than those of VO(pa)₂ because of their slower clearance rates. On the basis of the results, we conclude that introduction of a halogen atom to 4th position of picolinic acid enhances insulinomimetic activities and reduces clearance rate of the vanadyl species from the blood.

Key words: [diabetes](#), [vanadium\(IV\)](#), [complex](#), [insulinomimetic activity](#), [halogenated picolinic acid](#)

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