VII-D Research on the Relationship between Structure of Vanadyl Complex and Insulin-Mimetic Activity

Insulin-dependent diabetes mellitus (IDDM) shows hyperglycemia owing to deficiency of insulin, causing many serious secondary complications. To prevent the complications, IDDM is controlled by daily injections of insulin. Therefore, we have developed orally active insulin-mimetic vanadyl complexes.

VII-D-1 Syntheses, Structure, and Insulin-like Activities of Oxovanadium (IV) Complexes with Tetra- and Penta-Dentate Histidine Derivatives

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$[VO(^{pm}H)(ClO_4)]$, $[VO(Me_4)]$, and $[VO(^{(pm)_2}H)](ClO_4)$ complexes were prepared and their X-ray structures were analyzed. Among them, in vitro insulin-mimetic activity of $[VO(^{pm}H)(ClO_4)]$ was found to be higher than that of vanadyl sulfate as a positive control.

VII-D-2 Insulin-Mimetic Vanadyl-Dithiocarbamate Complexes

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Five vanadyl-dithiocarbamate complexes with $VO(S_4)$ coordination mode such as VO-DMD, VO-DED, VO-PYD, VO-MGD and VO-SAD were prepared and their *in vitro* and *in vivo* insulin-like activities were examined. VO-PYD complex was concluded to be a potent agent on daily oral administration to treat insulin-dependent diabetes in experimental animals.

VII-D-3 A New Insulin-mimetic Vanadyl Complex, (*N*-Pyridylmethylaspartate) Oxovanadium (IV) with $VO(N_2O_2)$ Coordination Mode, and Evaluation of its Effect on Uptake of *D*-Glucose by Ehrlich Ascites Tumor Cells

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A new *in vitro* assay method using Ehrlich ascites tumor cells for the insulin-mimetic activity of a compound was proposed. By using this method, VO-(PASP), VO(PA) and VO(MPA) complexes have been found to have good insulin-mimetic activities.