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Synthesis of macromolecular vanadium metallocomplex and its acute oral toxicity evaluation

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Abstract

Diabetes mellitus (DM) is a severe chronic disease affecting virtually all kinds of metabolic processes in the human body. As incidence and prevalence of DM are increasing worldwide, WHO estimates the number of people living with diabetes to be as high as half a billion and still rising. Long-term health complications of DM, such as diabetic nephropathy, retinopathy, neuropathy, and cardiovascular pathology, although preventable in most cases, are known to be severe, potentially life-threatening and often irreversible, which makes the search for new effective antidiabetic drugs a research priority and one of the most pressing issues in health care today.

To date, the insulin-mimetic properties of vanadium compounds have been the subject of quite a significant number of studies. *In vivo* experiments have shown that vanadium, acting in an insulin-like fashion, takes part in the regulation of glucose and lipid metabolism. In particular, vanadium stimulates glucose uptake and metabolism in insulin target tissues, increases the intensity of glycogen and lipid biosynthesis, and inhibits that of gluconeogenesis, glycogenolysis, and lipolysis. Organic vanadium complexes are known to be less toxic than its inorganic salts, which are characterized by a number of potentially serious adverse effects, mainly but not exclusively on the central nervous system and the kidneys; in addition to lower toxicity, organic vanadium compounds have been found to have higher bioavailability when to compared to those of inorganic nature. Such observations clearly hold promise for the development of an entirely novel therapeutic class of antidiabetic drugs.

The aims of this study are to obtain new polymeric vanadyl(VO^{2+}) derivatives based on poly-*N*-vinylpyrrolidone (PVP) that would exert hypoglycemic effect *in vivo*, and to explore the possibilities of using such compounds or formulations derived thereof for type 2 DM prophylaxis and/or treatment. This work gives a method of obtaining and isolation of an oxovanadium(IV)-polymer metallocomplex, and describes the structural features of said compound, confirmed experimentally. The results of the acute oral toxicity study revealed that the newly synthesized compound is of low toxicity, having a median lethal dose (LD_{50}) that is at a level well above those typical of inorganic vanadium salts.

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