

Vanadium Salts versus Diabetes: An Overview

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ABSTRACT

Vanadium is an ultra trace element, widely distributed in the nature and its compounds would closely mimic the physiological action of insulin by initial entry into the portal system. This mini review summarized the latest advancements in this field, considering the vanadium compounds effective in organic or inorganic forms. The major concern related to the use of vanadium salts is the safety profile. Vanadate has insulin-like effects on the metabolism of glucose both *in vivo* and *in vitro* in various tissues. Vanadium salts such as Na_3VO_4 , NaVO_3 , VOSO_4 , $\text{VO}(\text{acac})_2$, and $\text{VO}(\text{Et-acac})_2$ mimic several of the metabolic and growth-promoting effects of insulin. Some traditional medicines from a number of plants and plant products with antidiabetic activity also show great promise. Some studies have suggested that vanadium compounds help to normalize blood glucose levels in people with both type I and type II diabetes.


Introduction

Vanadium is a trace mineral that is present in many foods and may be essential, in small amounts, in the body. It may be involved in normal bone growth. However, scientists are not sure about exactly what effects vanadium may have, or what amount might be beneficial for any condition. They do know that vanadium may be unsafe at high doses. Most of the studies examining vanadium have been animal studies; only a few clinical trials involving humans have been done. Because of that, vanadium is not recommended for any disease or condition. However, it may have an effect on blood sugar in people with diabetes. Vanadium, atomic number 23, atomic weight 50.94, is a first-row transition metal that shows a wide range of oxidation states in monomeric, oligomeric, and polymeric species in solution.^[1] It exists in oxidation states of $-I$, 0 , $+II$, $+III$, $+IV$, and $+V$; the latter two are stable solution

structures at physiological pH: vanadyl ($+IV$) and vanadate ($+V$). The oral administration of inorganic vanadium (IV , V) salts have shown antidiabetic activity.^[2-4] Vanadium compounds show insulin-like effects *in vivo* and *in vitro*. Several clinical studies have shown the efficacy of vanadium compounds in type 2 diabetic subjects. Orally administered sodium vanadate has been reported to improve DM in human diabetes before the discovery of insulin and its clinical use to treat DM has been previously demonstrated. Vanadium compounds have been shown to be effective in animal models such as spontaneously diabetic (BB) rats and insulin-resistant Zucker fa/fa rats and recently in human trials.^[5,6]

An overview

Vanadium salts being used as a metallotherapeutic appeared in 1899.^[7] Early interest in vanadium as a metallotherapeutic waned, even as the exploration of vanadium's biological effects in plants and animals continued. For example, during the first half of the 20th century, Bertrand, *père et fils*, published 18 articles on perceived biological activities of vanadium (as reported in^[8]) particularly in plants and fungi. The discovery that vanadium (V), as vanadate, was an extremely potent enzymatic inhibitor was completely unanticipated. A number of laboratories world-wide had noticed that a particular commercial preparation of ATP (from Sigma Chemical Co.) gave anomalously low catalytic rates in a standard ATPase assay.^[9] But safety, tolerability, pharmacokinetics, and bioavailability of escalating doses of a vanadium complex for therapeutic use in diabetic mellitus were assessed in 2003.^[10] But, later vanadium-based hypoglycemic agents appeared in the market as vitamin and mineral supplements.^[11] Since 1922, after the discovery of insulin,^[12]

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various observations have been made on vanadium's ubiquitous nature and pharmacological effect that led to a series of clinical trials in humans which proved its role as a potential cholesterol-lowering pharmaceutical agent.^[13-16] Vanadium is an essential trace element of unknown function in cellular regulation and an indigenous constituent of most mammalian tissues. Vanadate has insulin-like effects on the metabolism of glucose both *in vivo* and *in vitro* in various tissues. Vanadium salts such as Na_3VO_4 , NaVO_3 , VOSO_4 , $\text{VO}(\text{acac})_2$, and $\text{VO}(\text{Et-acac})_2$ mimic several of the metabolic and growth-promoting effects of insulin. Today the scientific strategies to overcome the barriers to oral insulin administration are also underway with the use of permeation enhancers, protease inhibitors, enteric coatings, polymer microsphere formulations, and drug delivery techniques. With the help of this brief authors effort for identifying and developing specific vanadium compounds for insulin mimic in present scenario.

Vanadium salts like sodium orthovanadate, sodium metavanadate, and vandyl sulfate have action like insulin and they lower blood glucose levels in various animal models and have potential as hypoglycemic agents.^[17,18] Recently, vanadium salts like $\text{VO}(\text{acac})_2$ and $\text{VO}(\text{Et-acac})_2$ have been reported to have *in vivo* insulin-like effects in diabetic Wistar rats.^[19] Further, the organic form of vanadium is recognized as safer and more absorbable, and able to deliver a therapeutic effect; as a result, numerous organic complexes of vanadium have been developed.^[20-29]

Vanadium activates the glycogen synthase and tyrosine kinase activity of the insulin receptor in adipocytes. It increases the concentration of fructose 2,6-biphosphate and activates glycolysis in hepatocytes. Vanadium also stimulates glycogen synthesis in muscle. The oral administration of vanadate by streptozotocin-induced diabetic (STZ-D) rats causes normalization of hypoglycemia and tissue responsiveness to insulin.^[30] Tolman *et al.*^[31] observed an increased incorporation of glucose into glycogen in the presence of vanadate. STZ-D results decreased the activities of glycogen-metabolising enzymes in liver, and insulin therapy restores these enzyme activities.^[32] Other researches also highlight the physiological and pharmacological effects of vanadium.^[33,34] Vanadium salts, at doses ranging from 0.1 to 0.7 mM/kg/day,^[35-39] normalized blood glucose and lipid levels, improved insulin sensitivity, and impaired antioxidant status and fluid intake.^[40,41] Further, the improved potency and the efficacy of ligand binding of vandyl ions have been achieved by various other investigators.^[42-44] Absorption, distribution, metabolism, and excretion (ADME) of vanadium compounds are reported as a chronic treatment alternative for diabetics.^[45-47] Some traditional medicines from a number of plants and plant products with an antidiabetic activity also show promising effect.^[48-51] *Ipomoea aquatica*, a leafy vegetable, and *Agaricus campestris* possess insulin-like activities.^[52-54] Curcumin and *Allium sativum* also show an antioxidant and antidiabetic activity.^[55,56]

Discussion

Summary of key findings

Primary outcomes

Vanadium compounds for treatment of diabetes are now on the threshold of becoming a practical alternative to other oral hypoglycemic agents. The therapeutic potential has been repeatedly demonstrated, the mechanism is now accepted as being multifactorial, and the serum protein, transferrin, has

been identified as the most likely circulatory transport protein for absorbed vanadium ions. Some studies have suggested that vanadium compounds help to normalize blood glucose levels in people with both type I and type II diabetes.

Secondary outcomes

Many organovanadium compounds have been reported to exert potent insulinomimetic effects both *in vitro* and *in vivo*. Vanadium obviously has the potential to affect many areas in the body for better or worse.

Results as they relate to a prior hypothesis

Many organovanadium compounds have been reported to exert potent insulinomimetic effects both *in vitro* and *in vivo*.

Strengths and limitations: Vanadium obviously has the potential to affect many areas in the body for better or worse. The most significant research on vanadium to date involves its insulin-like properties and its possible role in treating diabetes.

Future research directions: Further, research is required for the development of oral formulations in human beings. There is also a need to work on the natural resources containing vanadium elements which can be utilized as a dietary supplement helpful in managing diabetic patients.

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