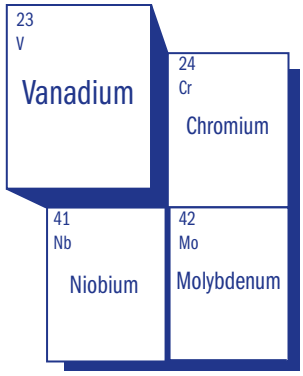
Monograph

Vanadium/ Vanadyl Sulfate



Introduction

The chemical element vanadium was first discovered by Spanish-born Mexican mineralogist, Andrés Manuel del Río, in 1801. He originally named the element "panchromium" because of the spectrum of colors associated with various oxides of the metal, but changed the name to "erythronium," because most of the mineral salts turned red upon heating. Later, del Rio was convinced by fellow scientists that he had really found impure chromium and not a new element. To his regret, that same element was "rediscovered" 30 years later by Swedish chemist, Nils Gabriel Sefstrom, who named it vanadium, after the Nordic goddess of beauty, Vanadis (Freyja).[1]

Nutritionally, vanadium is thought to be a cofactor in various enzymatic reactions. Data from animal and human studies suggest vanadium mimics the action of insulin.[2] Consequently, it may serve a beneficial role in promoting healthy glucose metabolism in individuals with diabetes or dysglycemia. Dietary sources for vanadium include mushrooms, shellfish, black pepper, parsley, dill seed, and grains.

Biochemistry

Vanadium is considered an essential nutrient in some animals.[3] For instance, vanadium is essential in the diets of chickens; a deficiency has an adverse affect on bones, feathers, and blood. In humans, classification of vanadium as an "essential nutrient" is still a topic of debate among various research groups.[3] Some consider vanadium to be an ultra-trace element, requiring dietary intake of only 20 mcg per day.[4]

Certain mushrooms species, such as *Amanita muscaria*, contain amavadine, (S,S)-2,20-(hydroxyimino) di-propionic acid (V[hida]2), a natural, vanadium-containing compound thought to act as a mediator in the oxidation of thiol compounds with carboxylic or ester groups, such as cysteine and glutathione.[3]

Various forms of vanadium are used in foods or supplements, or found in drinking water. The most common forms are provided below with the percentage of elemental vanadium:[5]

- vanadyl sulfate: 31-percent vanadium
- sodium metavanadate: 42-percent vanadium
- sodium orthovanadate: 28-percent vanadium

An average diet supplies 6-18 mcg of vanadium per day, with an estimated five percent of ingested vanadium being absorbed. Vanadium is converted *in vivo* to a vanadyl cation where it can form complexes with substances such as ferritin and transferrin. The highest concentrations of vanadium in the body are found in the liver, kidney, and bone.[5]

Pharmacokinetics

Animal studies using venous injection of radio-labeled vanadium observed the element, at least in this form, was poorly taken up by the tissues, and the primary route of excretion was in the urine.[6] Insulin appears to affect the metabolism of vanadium. The half-life of vanadium varies, with insulin-sensitive tissue such as liver and fat metabolizing vanadium more quickly.[7]

Orally ingested vanadium is approximately 1-10 percent absorbed, depending on a number of factors, including whether or not the metal is complexed to a ligand. Vanadium is eliminated from body organs and excreted relatively quickly.[6]

There is limited published data regarding the pharmacokinetics of vanadium compounds in humans. In healthy individuals, studies show blood vanadium levels of 0.4-2.8 mcg/L. The upper limit found in urine of healthy individuals is 22 mcg/L with excretion values at approximately 8 mcg/24 hours.[6]

In one pharmacokinetic study, five healthy volunteers received intravenously 90 mL of 20-percent albumin infusion solution containing 47.6 mcg vanadium. Serum vanadium concentrations were measured over the next 31 days. After 12 days, approximately 52 percent of the dose was recovered in the urine.[8]

Mechanisms of Action

Although evidence alludes to the potential health benefits of vanadium, its mechanism of action in this regard remains somewhat obscure. Animal and human experiments suggest vanadium exerts potent insulin-mimetic effects *in vitro* and *in vivo* when used in pharmacological doses.[9] It is thought that increased insulin sensitivity may be due to vanadium inhibiting protein tyrosine phosphatase.[10] Further, some research indicates vanadium compounds may reduce gluconeogenesis and increase glycogen deposition.[11]

Deficiency States and Symptoms

In animals, vanadium deficiency can result in infertility, anemia, compromised iron metabolism, and poor bone, tooth and cartilage formation.[12] Vanadium deficiency has not been described in humans.

Clinical Indications

In the early 20th century, vanadium was thought to be a panacea.[13] Consequently, it has been long believed to have some pharmacological and nutritional importance. Vanadium compounds were studied as possible treatments for syphilis, hyperlipidemia, and dental caries.[14] Today, focus is heavily weighted on vanadium's insulin-mimetic and antidiabetic properties.

Various forms of vanadium compounds are currently being tested for enhancing insulin sensitivity more effectively. Based on previous research, bis(maltolato) oxovanadium(IV) (BMOV) and the ethylmaltol analog, bis(ethylmaltolato)oxovanadium(IV) (BEOV), are being investigated as potential insulin enhancing agents for diabetes mellitus. Seven type 2 diabetic subjects were given oral doses of BEOV (AKP-020), 20 mg daily for 28 days. Researchers observed reductions in fasting blood glucose and hemoglobin A1c (HbA1c), and improved responses to oral glucose tolerance testing, compared to exacerbated diabetic symptoms in the two placebo controls.[15]

Diabetes

In the late 19th and early 20th centuries, before the 1922 discovery of insulin, French physicians found administering sodium metavanadate ($NaVO_3$) improved the health of patients with diabetes mellitus.[16] Vanadium, as vanadyl sulfate, is believed to regulate fasting blood sugar levels and improve receptor sensitivity to insulin.[17] Based on available research, vanadyl sulfate appears to be a useful intervention for type 2 diabetic individuals with insulin resistance. Vanadyl sulfate has been reported to be 6-10 times less toxic than vanadate.[2]

In a single-blind, placebo-controlled study, the effect of vanadyl sulfate was examined on eight male and female subjects with type 2 diabetes. Treated subjects received 50 mg vanadyl sulfate twice daily for four weeks, followed by a four-week placebo phase. Modest improvements in fasting glucose and hepatic insulin resistance followed the treatment period and were sustained throughout the placebo period.[17]

Two small studies (one with six type 2 diabetic patients, one with seven type 2 diabetic patients) demonstrated a beneficial effect of vanadyl sulfate at a dose of 100 mg/day in improving insulin sensitivity.[18,19] The first study examined the effect of 100 mg vanadyl sulfate daily for three weeks. Measurement of fasting plasma glucose and insulin-mediated glucose disposal during pre- and post-treatment periods showed a beneficial effect of vanadyl sulfate on improving both hepatic and peripheral insulin sensitivity. These effects were sustained for up to two weeks after the vanadyl sulfate was discontinued.[18]

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Similarly, the second study provided 100 mg vanadyl sulfate daily for three weeks to moderately obese type 2 diabetic and non-diabetic subjects. A decrease in fasting plasma glucose and significant improvement in insulin sensitivity was observed in the type 2 diabetic subjects; no change was observed in the obese non-diabetic subjects. The authors concluded that this dose of vanadyl sulfate could improve insulin sensitivity in type 2 diabetic subjects, but not alter insulin sensitivity among obese, non-diabetics.[19]

Another study examined the effect of vanadyl sulfate at various daily dosages of 75 mg, 150 mg, or 300 mg in 16 type 2 diabetics for six weeks. Although glucose metabolism did not increase in those given 75 mg/day, 60 percent of subjects taking 150 mg/day and 50 percent of subjects taking 300 mg/day improved significantly. Furthermore, fasting glucose and HbA1c decreased in the higher-dose groups. No change was observed in blood pressure at any dose. Some participants on the higher doses experienced minor gastrointestinal discomfort. Subjects on 300 mg/day experienced a decrease in total cholesterol, associated with a decrease in high-density lipoprotein.[20]

Vanadium also appears to have a protective effect on diabetic cataracts and nephropathy in STZ-diabetic rats,[21] a protection slightly improved with the addition of vitamin E. Vanadium has insulin-like effects and is currently being considered for oral therapy. It also reduces gluconeogenesis and increases glycogen deposition.[11] Vanadium salts induced sustained falls in blood glucose in diabetic rodents.[22]

Impaired Glucose Tolerance/Prediabetes

In a recent trial, researchers studied the effect of vanadyl sulfate on individuals with impaired glucose tolerance (IGT), a risk factor for developing type 2 diabetes. A randomized, double-blind, placebo-controlled trial was conducted on 14 overweight/obese patients with IGT. Subjects were given either vanadyl sulfate (50 mg twice daily) or placebo for four weeks. A metabolic profile was performed pre- and post-intervention and insulin sensitivity was assessed using the euglycemic-hyperinsulinemic clamp technique. At the end of the trial there were no significant differences in baseline characteristics between groups.[23]

Drug-Nutrient Interactions

Anticoagulant/Antiplatelet Drugs

In vitro studies of sodium orthovanadate (vanadate) demonstrated prolonged clotting time, which was additive in the presence of heparin. This suggests the vanadate form of vanadium may potentiate anticoagulant therapy when administered concurrently.[24]

Antidiabetic Drugs

Concurrent use of vanadyl sulfate with insulin or oral hypoglycemic agents for diabetes may have an additive effect, as vanadyl sulfate can increase insulin sensitivity in individuals with type 2 diabetes.[17-19]

Side Effects and Toxicity

Mild gastrointestinal discomfort in the form of abdominal cramps and loose stools has been reported with ingestion of vanadyl sulfate at therapeutic doses.[17]

Toxicity studies on rats concluded vanadyl sulfate, in doses necessary to cause euglycemia, was not toxic after one year of administration; however, vanadium may be retained in organs for months after conclusion of administration.[25]

Acute vanadium toxicity has not been observed in humans. In rats, acute poisoning from sodium vanadate resulted in enteritis, mild liver congestion, and slight renal tubule degeneration.[26]

Dosage

There is no RDA for vanadium. A daily intake of 10-100 mcg is considered safe and adequate from food sources. The average diet supplies between 6-18 mcg of vanadium daily.

A therapeutic dosage for management of type 2 diabetes is at least 50 mg vanadyl sulfate twice daily.[17-19]

Warnings and Contraindications

Caution should be used when combining vanadium supplements with any blood-sugar lowering medication as the combination may induce hypoglycemia.

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