Asian J. Exp. Sci., Vol. 19, No. 2, 2005, 127-134

Vanadium Toxicity

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Abstract : Vanadium is distributed extensively in nature. It is a trace element and is present in almost all-living organisms including man. Essentiality of this element in cellular functions is yet to be established. Biological importance of vanadium was originally recognised by its ability to inhibit membrane sodium pump. Its capacity to affect the activities of various other intracellular enzyme systems and to modify physiological processes is now documented. Vanadium is used extensively in various heavy industries. The incidence of exposure to toxic levels of vanadium to industrial workers has been an increasing concern for toxicologists. Disposition of vanadium in specific tissues may be involved in the pathogenesis of certain neurological disorders and cardiovascular diseases. An attempt is made to broadly document what is known of various biological/toxicological actions of vanadium.

Key words : Vanadium, CVS, Myocardium, Vascular smooth muscle, Respiratory system.

Introduction :

Nils Gabriel Sefstrom (Swedish Chemist) was the first person recognised vanadium compound as a new metal in 1831. The attractive beautiful multi-colours prompted him to name "Vanadis" after the legendary Norse Goddess of Beauty. John Priestly of Manchester reported on the physiological action of vanadium in animals and John Priestly described the toxicity of vanadium forms. In 1899 vanadium was widely used in France for the treatment of anaemia, tuberculosis, chronic rheumatism, diabetes and anorexia. Most food materials used for human consumption contain vanadium in a non-toxic form.

Chemistry :

Metallic vanadium does not occur in nature, but available as vanadium compound. Metallic vanadium reacts with oxygen, nitrogen, and carbon at relatively low temperature (< 300°C) and forms oxidation states of 1^-, 0, 2^+, 3^+, 4^+, and 5^+, the last four being the most common. Vanadate

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polymerises to a cage-like structure of a decamer (V_{io}) gaining a golden yellow colour (Table 1). Chemical reactions of vanadium are similar to those of phosphorus in many respects.

Table 1 : Vanadium and some compounds

Compounds	Forms	Colour	Meeting Point (oC)	Boiling Point (oC)	Water solubility (g/l)
Vanadium	metal	grey	1890	3380	insoluble
Vanadium pentoxide	crystal	yellow or red	690	1750	0.7
Vanadium trioxide	crystal	black	1970	—	slight
Sodium meta vanadate	crystal	colourless or green	630	—	211
Vanadium tetra chloride	liquid	red/brown	–28	148.5	reacts
Vanadyl sulphate	crystal	bluish green			soluble
Decavandate	crystal	yellow orange			

Biological aspects :

Vanadium is an ultratrace metal, present in mammalian tissues at concentrations below 1μM (Nechay *et al.*, 1986). Vanadium content in biological samples may be estimated by various methods such as atomic absorption spectrometry, neutron activation analysis, inductively coupled plasma, dc arc emission, dc plasma atomic emission spectroscopy, mass spectroscopy, mass spectrometry, spectrophotometry and energy dispensive x-ray fluorescence.

Vanadium toxicity :

Power- and beat-producing plants using fossil fuels (petroleum, coal, oil) cause the most widespread discharge of vanadium into the environment.

Burning of coal wastes or dumps of coal dust in mining areas are other sources of vanadium discharge into the atmosphere. In the distillation and purification of crude oil, distilled petroleum fuels contribute less vanadium to the atmosphere.

Toxicity on organisms in the environment :

The growth of an aquatic plant is stimulated by trace quantities of vanadium (1-10 μg/l), but concentrations above 100 μg/1 are toxic. Some marine invertebrates, such as the tunicates, accumulate vanadium levels up to 0.3% dry weight. Invertebrates are generally less sensitive to vanadium (9-day LC_{50} values in the range of 10-65 mg/l) than fish (4-6 day LC_{50} values in the range of 0.5-22 mg/l). The pH is an important modulator of vanadium toxicity. Vanadium in soils at concentrations of 10 mg/kg or more is toxic for terrestrial plants (Arnon, 1958).

Toxicity on experimental animals :

Vanadium compounds are acutely toxic by most routes of exposure, in most species. In general, the toxicity of vanadium compounds increases with the Oxidation State. The rabbit and guinea pig are more sensitive than the rat and mouse. Repeated administration of vanadium compounds produces changes in protein metabolism, lipid profile, enzyme activities, reproductive activities, and other metabolic actions. Due to poor absorption from the gastrointestinal tract, the metal is not very toxic for human beings when ingested.

Toxicity on human beings :

In the past, vanadium compounds were prescribed as therapeutic agents for anaemia, chlorosis, tuberculosis and diabetes. Vanadium was also used as an antiseptic, a spirochetocide and as a tonic. Clinical picture of poisoning shows a broad spectrum of toxic effects of vanadium on the respiratory, circulatory and central nervous systems, the digestive organs, kidneys, and skin (Table 2). Vanadium poisoning in humans can be diagnosed on the basis of a history of exposure, the clinical picture, a green tongue (due to the hexa-aqua ion), and measurements of vanadium levels in blood cells, plasma and urine. The value of various tests of the secondary

metabolic effects of poisoning is disputed. Dimercaprol and ascorbic acid may have value in the treatment of poisoning in human beings. There are no adequate epidemiological studies of mortality in occupationally exposed populations.

Table 2 : Clinical features of workers exposed to vanadium (V_2O_5)

Symptoms	Physical findings
Cough	Tremors of hands
Sputum	Hypertension
Exertional dyspnoea	Wheezes, rales or rhonchi
Ear, nose, throat irritation	Hepatomegaly
Headache	Eye irritation
Palpitation	Injected pharnynx
Epistaxis wheezing	Green tongue

Absorption :

The absorption and distribution of vanadium compounds depends on the route of entry and the solubility of the compounds in the fluids. The solubility of vanadium in biological media varies. The following compounds are listed in decreasing order of solubility :

(a) in gastric juice : vanadyl sulphate: sodium vanadate, ammonium vanadate and vanadium pentoxide;

(b) in blood serum and in 0.22% sodium carbonate solution: sodium vanadate, ammonium vanadate, vanadium pentoxide, and vanadyl sulphate.

The compounds, which show higher the solubility in water and biological media, exhibit the more toxicity due to better absorption (Roshchin *et al.*, 1980). Soluble vanadium compounds, inhaled and deposited in the lung, are readily absorbed. It has been estimated, that about

25% of soluble vanadium compounds may be absorbed via the respiratory tract (ICRP, 1960). Absorption from the respiratory tract was demonstrated in workers exposed to vanadium dust, who showed increased concentrations of vanadium in the urine (Maroni *et al*., 1983). In general, vanadium salts are poorly absorbed from the human gastrointestinal tract. The International Commission on Radiological Protection (ICRP, 1960) estimates for the gastrointestinal absorption of soluble vanadium compounds is 2%. Roshchin *et al.* (1980) found a low degree of absorption. Though dermal absorption has been reported in animal studies, according to USDHEW (1977), the skin appears to be a minor route of vanadium uptake for human beings. In an *in vitro* study using V_{48} radiotracer, there was no penetration of human skin samples (Roshchin *et al.*, 1980).

Distribution and biotransformation :

Absorbed vanadium is transported mainly in the plasma (Roshchin *et al*., 1980). Highest concentrations tend to occur in the liver, kidney, and lung. It is mainly stored in fat and serum lipids (Schroeder *et al*., 1963). Owing to low gastrointestinal absorption, ingested vanadium is predominantly eliminated unabsorbed in the faeces. The main route of excretion is through the kidneys. The ratio of amounts eliminated in the urine and faeces is 5 : 1 (Talvitie and Wagner, 1954). In animal studies Mitchell and Floyd (1954) showed that ascorbic acid increases the elimination of vanadium in both urine and faeces. Vanadium in tissues, such as bone is released slowly.

Highlights of mechanism with special reference to cardiovascular toxicity :

Vanadium is known for its spasmogenic property in various smooth, cardiac and skeletal muscles. Highlights are given below :

1. Intravenous infusions of cumulative doses of vanadate produced significant increase in arterial blood pressure. Potent vasoconstrictor effects *in vitro* as well as in animals were demonstrated in several laboratories. Vasoconstrictor effects of

vanadate are due to inhibition of Ca-ATPase and reduction in calcium efflux (O'neal *et al.*, 1979).

2. Some of its effects are definitely not due to alteration in Na, K-ATPase activity (Ozaki *et al.*, 1980, Hudgins and Bond 1979). The responses of vascular smooth muscles to vanadate compounds remained unaffected in sodium free medium.

3. Deprivation of vital ions in the extracellular medium does not drastically affect the responses of vanadium. Vanadate acts at an intracellular site (Nayler and Sparrow, 1983).

4. Vanadate has to enter the cell through the ionic pore and produce its effects on the contractile protein. Phosphorylation of myosin light chain by protein kinase is involved (Murphy, 1994). Inorganic phosphate competes for the anionic site of the cell for the entry.

5. Vascular effects of vanadate are independent of extracellular calcium levels. Calcium channel blockers do not effectively block the responses ofvanadate.

6. Vanadate has a distinct effect on mobilisation of intracellular calcium in a variety of smooth muscles.

7. Its vasoconstrictor effects are not blocked by alpha blocking agents, while effects of alpha agonist such as norepinephrine, phenylephrine, etc. are blocked.

Conclusion :

There is lack of data on several aspects of the health effects of vanadium compounds. Confirmative mutagenicity and carcinogenicity studies are not consistent and they should be given high priority with long-term exposure studies. It is important to develop specific indicators for the detection of early adverse effects of vanadium on man.

Epidemiological studies on occupational hazards should be

encouraged. This is an important aspect with regards to worker protection. There are considerable geographical variations in vanadium concentrations in air and water. Epidemiological studies on populations living in areas with high vanadium exposure should be carried out focusing on possible interactions with other pollutants.

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