Discovery:

Andre's Manuel del Rio of Mexico City was apparently the first to recognize the new metal named in 1801, erythronium after the red colour of its salts. However, principal credit for the discovery of vanadium must be given to Nils Gabriel Sefstrom, a Swede. With the aid of Berzelius in Stockholm, Sefstrom succeeded in preparing in 1831 an oxide of a new element that Berzelius named vanadium (Weeks, 1956). It was nearly hundred years later that Marden and Rich (1927) made the first pure metal
beads so that the physical properties of the metal could be determined. Vanadium (V) is a bright white ductile metal with a melting point of 1,980 ± 10°C, a boiling point of 3,380°C at 1 atm, and a specific gravity of 6.11 at 18.7°C (Weast, 1970).

**Vanadium Chemistry:**

Vanadium is a transition element of the first transition series and belongs to group Va. It has five valence electrons giving rise to a maximum oxidation state of +5. Although compounds of vanadium are known that contain vanadium in oxidation states of 0, +2, +3, +4 and +5, vanadium in the +4 and +5 valence states is the most stable. Discrete V⁴⁺ and V⁵⁺ are not known to exist and usually are found bound to oxygen as a negatively charged polymeric oxyanion that tends to complex to polarizable ligands like phosphorus and sulfur (Buckingham, 1973 and Clark, 1973). Vanadium in the +5 oxidation state is reduced to vanadium +4 by relatively mild reducing agents. Rubinson (1981) reviewed the material about the biochemical active form of vanadium and the following generalizations appear to be justified. At low normal concentrations in mammals and birds, the free vanadium will be in hydrated monomeric form. In the body fluids at pH 4-8, the predominant species will be VO₃⁻ ( +5 oxidation state), vanadate (metavanadate). VO₃⁻ may enter certain cells by an anion transport system and be reduced
by glutathione to $V_2O_2^{2+}$ (+4 oxidation state), vanadyl which is the most stable oxidation state for vanadium. Vanadium in the +3 oxidation state, as in $V_2O_3$, is completely basic hexaquo ion $[V(H_2O)_6]^{3+}$. This is the species that probably accounts for the "green tongue" that is symptomatic of acute exposure to vanadium. However, several bright green complexes of vanadium +4 are known (Cotton and Wilkinson, 1962; Durrant and Durrant, 1970) which might also account for the green tongue symptom.

**Distribution:**

Vanadium is one of the most abundant trace elements in nature. Its geochemical and biochemical behaviour is primarily a function of oxidation state (Goren, 1966). Natural sources of air-borne vanadium are believed to be marine aerosols and continental dust. Several investigators have reported the presence of this element in coal, oil, mineral ores (i.e., carnotite, colusite and roscoelite) and in basic rocks such as gabbros, lime-stones, sandstones and shales (Fairbridge 1972 and Lee & Von Lehmden 1973). Concentrations of this metal are known to increase in the close physical environments of various industrial operations using the fossil fuel sources e.g. coal, oil shale and crude oil (Parker et al 1978). The principal source of vanadium in soil is the parent rocks from which it is formed. The different soil had been reported to
contain 3 to 310 μg/g vanadium and the highest concentrations are found in shales and clays. Durfor and Becker (1963) found that 91% of drinking water samples had vanadium below 10 μg/litre. Vanadium was undetectable in many samples; the maximum concentration found was 70 μg/litre and the average was about 4.3 μg/litre. The amount of vanadium reported in plants, animals and humans, was directly related to their physical environment (Bertrand, 1950; Schroeder, 1970a; Cowhill, 1973; Byrne and Kosta, 1973; Phillips et al, 1982). Vanadium was found in both terrestrial and aquatic animals, the liver and skeletal tissue showing the highest amount (Bertrand, 1950). Fukui and Feinke (1962) reported that the concentration of vanadium in soft tissues of fish was 1,000 times that in sea weed and mollusks. The highest concentration of vanadium in marine organisms have been found in certain sea squirts (Phallusia mamillata, 1,900 μg/g) and certain sea cucumbers (Usticopus mobili, 1,200 μg/g). Trivalent vanadium is present in certain ascidians as a chromoprotein called hemovanadin with sulfuric acid in green cells called vanodocytes, in other forms, the hemovanadin is present free in plasma (Saulkner-Hudson, 1964).

Nutritional Importance:

Vanadium is known to be essential for the mold Aspergillus niger (Bertrand, 1942) and the green alga Scenedesmus obliguus (Arnon and Wessel, 1953; Arnon, 1958).
A requirement for vanadium by the yeast *Candida albopilis* is demonstrable at high temperature (Hoitman et al., 1969).

Trace amounts of vanadium, corresponding to those quantities normally found in nutrients and tissue, are apparently essential for the chick and rat. Several investigators (Hopkins and Kohr, 1971; Schwarz and Hilne, 1971; Strasia, 1971; Neilsen and Ullerich, 1973; Waters, 1977; Davies, 1981; Kentz, 1974) have demonstrated vanadium deficiency in the chick and rat. Diets containing less than 10 µg/kg resulted in significant reduction in feather growth in chicks but did not affect their growth rate (Hopkins and Kohr, 1971). Rats fed a diet deficient in vanadium produced fewer offspring in the third or fourth generation compared with vanadium supplemented control (Hopkins and Kohr, 1974). Vanadium-deficient chicks showed reduced vanadium concentrations in kidney, liver and heart; reduced weight gain and feather growth; retarded skeletal development; increased plasma triglyceride concentrations and variably altered plasma concentration of cholesterol (Hopkins and Kohr, 1974).

Hoshchin et al. (1965) observed that vanadium at high concentrations reduced hemoglobin content and produced anaemia in experimental animals. However, rats fed diets containing less than 100 ppb vanadium showed an increase in hematocrit (Strasia, 1971). A similar result was reported in chicken consuming a 30-50 ppb vanadium in diet.
(Nielsen and Ollerich, 1973). Geyer (1953) noted that vanadium is able to decrease the incidence of dental caries when added to the diet of hamsters while others were unable to demonstrate a clear beneficial effect in human beings (Hein and Wisotzky, 1955; Muhler, 1957; Hadji markos, 1966, 1968; McLundie et al, 1968). A decreased urinary output of ascorbic acid was reported in persons exposed to vanadium (Watanabe et al, 1965).

**Toxicological effects of Vanadium in experimental animals:**

Priestley (1876) showed that sodium vanadate solution given to pigeon, guinea pig, rat and rabbit by various routes has the effect on central nervous system causing drowsiness with convulsions followed by gradual paralysis of respiration and motion. Some other workers also performed similar experiments and reported similar results (Larmuth, 1877; Dowdeswell, 1878). Proescher et al (1917) reported in mice, rat, guinea pigs and rabbits, the lethal effect of different vanadium preparations affecting the central nervous system as well renal necrosis and pulmonary haemorrhage. The LD50 and the toxicity of various vanadium salts through different routes have been studied in rat, mouse and rabbit by various workers (Kassmann, 1956; Browning, 1962; Schroeder et al, 1963; Paulkner-Hudson, 1964; Schroeder 1970a, Cheng-i-Wei et al, 1982; Llobet and Domingo, 1984; Domingo et al, 1985). It has been observed that the toxicity of
vanadium is low when administered by oral route, moderate by the respiratory route and high by injection. As a general rule, toxicity increases as valency increases, the pentavalent vanadium being the most toxic. An oral administration of ammonium vanadyl tartrate to human beings did not have much effect, except cramps and diarrhoea (Dimond et al., 1963).

The toxicological study of vanadium is very rare in fishes. The earlier work of Proescher et al. (1917) is not of much significance. The other study of vanadium toxicity in fishes was conducted by Tarzwell and Henderson (1960). This study was found to be of limited use in evaluating the toxicity of vanadium. A comparative study of the LC50 of various vanadium salts on two species of freshwater fishes have been reported (Knudston, 1979).

**Human Industrial Exposure:**

Dutton (1911) was believed to be the first man to describe the health effects of industrial exposure to vanadium bearing ores. He reported a dry, paroxysmal cough with hemoptysis and irritation of eyes, nose and throat. A temporary increase in haemoglobin and red-cells was followed by a reduction in both and the onset of anaemia. A generalized systemic action of vanadium showing severe conjunctivitis, rhinitis, chronic productive cough, tightness of chest, tremors of fingers, palpitation and
Green tongue was reported in industrial workers exposed to vanadium dust (Symanski 1939; Rundberg, 1939; Balestra and Koffino, 1942; Lyons, 1946, 1948). An extensive report was presented on dust content of air in metallurgical plants producing vanadium pentoxide with similar clinical findings (Sjoberg, 1950; Sjoberg and Ringer, 1956). A clinical report was presented in the workers involved in boiler cleaning operation which include primary symptoms such as sneezing, nasal discharge and sore throat followed by secondary symptoms like dry cough, wheezing, labored breathing, lassitude and depression (Williams, 1952; Frost, 1951; Hickling, 1958; Roschchin, 1962 and Troppens, 1969). Troppens (1969) described the first symptoms as swelling of face and eyes as early as 20 minutes after entering the boiler area which disappeared after removal from exposure for 2-3 weeks. It has been reported that vanadium exposed workers are more susceptible to cold and other respiratory illness than others (Roschchin, 1962, 1967; Schumann Vogt, 1969; Troppens, 1969). Recent studies by Waters et al (1974, 1975) had demonstrated that vanadium salts are quite toxic for alveolar macrophages in vitro. In view of the role of the alveolar macrophage in pulmonary defense, these studies suggest that vanadium exposure may impair the lung's resistance to respiratory infection.
Metabolic Alterations:

Lowdeswell (1878) observed well-marked fatty changes in the livers of dogs and cats poisoned by ammonium metavanadate. Lyonnet et al (1899) found an increased urea excretion in patients treated with sodium vanadate, believing that some cellular oxidations were promoted by this salt. A decreased level of cystine content of rat hair, fed with 25 to 1,000 ppm of vanadium, was recorded, however, a similar decreased level of cystine content in the finger nails of vanadium exposed workers was also noted (Mountan et al., 1953, 1955).

Hergel et al (1958) reported the increased catabolism of cysteine and cystine by exposure to vanadium. A decreased concentration of coenzyme A and thioctic acid was found in the liver of white rats receiving sodium metavanadate by diet and by intraperitoneal injection (Mascitelli-Coriandoli and Critterio, 1959a, and 1959b).

Curran (1954) was the first to report that vanadium depressed the incorporation of isotope-labelled acetate into liver cholesterol in vivo in rats and in vitro. Subsequently, it was observed that the site of inhibitory action of vanadium was at the level of squalene synthetase (Azarnoff and Curran, 1957, Azarnoff et al., 1961). Vanadium was also shown to mobilize arterial cholesterol in atherosclerotic rabbits more rapidly as compared to control (Curran and Costello, 1956). In 1959 Curran et al
conducted a clinical study in which five normal adult males were fed 150-200 mg/day soluble diammonium oxytartarovanadate (20-30 mg V/day) for 6-weeks and reported significantly reduced plasma cholesterol. However, Lewis (1959a) studied vanadium exposed workers and reported slightly lower serum cholesterol than controls. Patients given vanadium salt did not show statistically significant lowered level of cholesterol (Somerville and Davies, 1962; Dimond et al, 1963; Schroeder et al, 1963). Curran and Burch (1967) suggested that a regulatory enzyme of cholesterol biosynthesis, aceto acetyl coenzyme A deacylase is activated in young animals and inhibited by in older ones by vanadium. After exposing the group of rabbits to a grinding aerosol of vanadium trioxide (45-75 mg/m³, 2 hr/day, 12 months), there was a progressive weight loss, declined leucocyte count, declined serum ascorbate and haemoglobin, increased blood cholinesterase activity and decreased monoamine oxidase activity (Roschin 1963, 1967; Roschin et al, 1965; Johnson et al, 1974). Pazynich (1966) exposed the rats for 70 days through continuous inhalation and reported depressed whole blood cholinesterase and serum β-globulin, and decreased total serum proteins at high level exposure.

Aiyar and Sreenivasan (1961) had shown that vanadium salts inhibit succinic dehydrogenase which would reduce ATP synthesis. Wright et al (1960) suggested that
Vanadium uncouples mitochondrial oxidative phosphorylation in liver homogenates in vitro, resulting in depletion of the ATP energy source. The addition of 25 ppm vanadium as ammonium metavanadate in the diet was reported to uncouple oxidative phosphorylation at all three phosphorolyating sites in the liver mitochondria of young chicks (Hathcock et al, 1966). They suggested that vanadate replaces the phosphate ion in reactions leading to ATP synthesis similar to arsenate. Ammasara et al (1981) reported that the rate of NADH oxidation with oxygen is stimulated 10 to 20 fold in presence of vanadium.

Vanadate is a well known inhibitor of the Na⁺, K⁺ -ATPase (Rifkin, 1965; Beauge and Glynn, 1978 and Hansen, 1979). However, Heide et al (1983) found the vanadium to inhibit the oxidative demethylation of the substrates of cytochrome P-450 dependent monoxygenase system in vivo in mice. It has been observed that vanadate produced an insulin-like stimulation of adipocyte glucose oxidation (Tolman et al, 1979; Jubyak and Kleinzeller, 1980; Tamura et al, 1984). However Bosch et al (1987) reported that vanadate inactivated rat hepatocyte glycogen synthetase and activated glycogen phosphorylase in a dose- and time-dependent manner. Thus, in the hepatocyte, vanadate exerts opposite effects than in the adipocyte and skeletal muscle, where it has an insulin-like effect.