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Revisión

Vanadium - An element both essential and toxic to plants, animals and humans?

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ABSTRACT

Vanadium was discovered in 1802/1803 by the Spanish mineralogist A. M. del Río in Mexico. Vanadium are present in the earth's crust at an average concentration of 110 mg/kg. Vanadium is concentrated mainly in mafic rocks (basalt 200-250 mg/kg) and shales (100-130 mg/kg), lowest concentrations were found in limestones and dolomites (10-45 mg/kg). The average vanadium content of soils worldwide have been calculated to vary from 18 (peat) and 115 mg/kg (Rotliegende weathering soils). Burning of fossil fuels caused about 110000 t V/a to enter the atmosphere globally. With help of indicator plants (wheat, rye, red clover) the local plant bioavailable vanadium offer is to investigate.

All foodstuffs, rich in starch and sugar and of animals are poor in vanadium (5-40 µg V/kg dry matter, dm); mushrooms and leafy vegetable contain higher levels of vanadium (100 to > 1000 µg V/kg dm). Beer and wine (30 to 45 µg/l deliver much vanadium. In Germany and Mexico women with mixed diet take in 10 to 20 µg V/day and men 20 to > 35 µg V/day. The high intake results from the higher beer consumption of men. Vegetarians take in significantly more vanadium. The vanadium concentration of organs and milk is not homeostatically regulated. Most tissues of the fauna reflect the vanadium status.

Faecal excretion of the nutritional vanadium intake amounts to 96% in men and non lactating women and to 79 in lactating women. On an average, adults of both sexes and with either form of diet eliminate 4% of the vanadium intake renally. Lactating women secret 17% of the vanadium intake into the milk.

Vanadium is essential for several species of green algae, fungi and nitrogen-fixing microorganisms. The inactive apoenzymes of bromoperoxidase, iodoperoxidase and chloroperoxidase can be reconstituted by vanadium to active haloenzymes. The normative vanadium requirement for animals is with < 10 µg/kg feed dry matter or < 10 µg V/day of man small. Intrauterine vanadium depleted goats developed poorly, their conception rate were significant by reduced, they exhibited a higher rate of spontaneous abortion, increased ratio of female to male kids born and a higher mortality. Vanadium deficient kids suffered of skeletal deformations in the forelegs. The size of their pancreas, thymus and thyroid were insignificantly increased. Vanadium may well be found essential for some halogenperoxidases, perhaps one, that is involved in thyroid metabolism.

It is to distinguish between nutritional (µg/day), pharmacological (mg/day) and toxic (mg/kg food dry matter) of vanadium.

Vanadium phytotoxicity (chlorosis and dwarfing) under field conditions is extremely rare. Intake of feed with 10 to 300 mg V/kg feed dry matter animals induced black diarrhoea, weakness, spontaneous abortions, decreased milk production and high mortality in animals.

Vanadium inhibits the Na^+ - K^+ ATPase and open the potassium-channels of the erythrocyte membrane. In humans, the threshold level for vanadium toxicity is > 3 mg/day. Higher doses can induces diarrhea, green tongues, haematological changes and lowered cysteine content in hair and nails.

Key words: Vanadium.— Food chain.— Essentiality.— Pharmacological effects.— Toxicity.

RESUMEN

El vanadio. ¿Un elemento tanto esencial como tóxico para plantas, animales y seres humanos?

El vanadio fue descubierto por el mineralogista español A. M. del Río, en México, en los años de 1802/1803. La corteza terrestre de 16 km de espesor contiene 110 mg de vanadio por kg. A través de los combustibles fósiles se difunden anualmente en el medio ambiente 110.000 toneladas de vanadio. Con ayuda de plantas indicadoras se puede determinar la oferta local de vanadio.

El vanadio es esencial para varias especies de algas, hongos y bacterias fijadoras de nitrógeno. La apoenzima de la peroxidasa de bromo, yodo y cloro necesita el vanadio para la formación de la holoenzima.

La necesidad normativa de vanadio relativa al ser humano asciende a > 10 µg/día y el de la fauna a 10 µg/kg de la materia seca del forraje.

Hay que distinguir entre los efectos farmacológicos, nutritivos y tóxicos del vanadio. Son raras las intoxicaciones por el vanadio. El vanadio frena la ATP-asa de Na^+ - K^+ y abre los canales de potasio de la membrana de los eritrocitos. Los 10-20 mg/día se consideran como valor límite del consumo de vanadio. Mayores dosis provocan trastornos gastrointestinales e implican con frecuencia tinciones verdes de las mucosas (por ejemplo, de la lengua), alteraciones hematológicas y concentraciones reducidas de la cisteína en los pelos y en las uñas.

Palabras clave: Vanadio.— Cadena alimentaria.— Esencialidad.— Efecto farmacológico.— Toxicidad.

RESUMEN EXTENSO

El vanadio fue descubierto por el mineralogista español A. M. del Río, en México, en los años de 1802/1803. La corteza terrestre de 16 km de espesor contiene 110 mg de vanadio por kg. A través de los combustibles fósiles se difunden anualmente en el medio ambiente 110.000 toneladas de vanadio. Con ayuda de plantas indicadoras se puede determinar la oferta local de vanadio.

Todos los alimentos ricos en almidón y azúcar o de origen animal son pobres en vanadio (5-40 µg/kg de materia seca). Los hongos y las hortalizas de muchas hojas pueden contener gran cantidad de vanadio (100-1100 µg de vandio/kg de materia seca). La cerveza y el vino proporcionan mucho vanadio (30-45 µg de vanadio/litro).

Las mujeres europeas y mexicanas que se nutren de comida mixta ingieren como promedio 10-20 µg y los hombres 20->35 µg de vanadio por día. El consumo de cerveza y vino aumenta considerablemente la cantidad de vanadio ingerido. Los vegetarianos ingieren significativamente más vanadio que las personas que se nutren de comida mixta.

Las personas de uno u otro sexo excretan el 96 por 100 del vanadio por vía fecal y el 4 por 100 por vía renal. Las madres lactantes segregan el 79 por 100 por vía fecal, el 4 por 100 por vía renal y el 17 por 100 a través de la leche.

El vanadio es esencial para varias especies de algas, hongos y bacterias fijadoras de nitrógeno. La apoenzima de la peroxidasa de bromo, yodo y cloro necesita el vanadio para la formación de la holoenzima.

La necesidad normativa de vanadio relativa al ser humano asciende a > 10 µg/día y el de la fauna a 10 µg/kg de la materia seca del forraje. Las cabras pobres en vanadio intrauterino crecen significativamente menos, su tasa de concepción es más baja y su mortalidad es superior a la de las cabras que cuentan con una oferta normal de vanadio. Tenían el páncreas, la glándula tímica y la glándula tiroides aumentados de modo insignificante. Puede ser que el vanadio repercuta en el metabolismo de la glándula tiroides a través de las peroxidasas de halógeno.

Hay que distinguir entre los efectos farmacológicos, nutritivos y tóxicos del vanadio. Son raras las intoxicaciones por el vanadio (clorosis, enanismo) en las plantas. Los animales manifiestan, después del consumo de 10 a 300 mg de vanadio por kg de materia seca del forraje, en función de su especie, dispepsias, trastornos del esqueleto, una fortaleza mermada y una mortalidad superior. El vanadio frena la ATP-asa de Na^+ - K^+ y abre los canales de potasio de la membrana de los eritrocitos. Los 10-20 mg/día se consideran como valor límite del consumo de vanadio. Mayores dosis provocan trastornos gastrointestinales e implican con frecuencia tinciones verdes de las mucosas (por ejemplo, de la lengua), alteraciones hematológicas y concentraciones reducidas de cisteína en pelos y en uñas.

INTRODUCTION

Vanadium (V) was discovered in 1802/1803 by the Spanish mineralogist A. M. del Río in Mexico. The element was rediscovered in 1831 by the Swedish chemist Selfström in iron ore smelting products and named vanadium in honour of Vanadia, the northern Germanic goddess of beauty, more commonly known as Freya. In the same year, the identity of the element was established by Wöhler (102).

In 1876, Priestley and Gamgee (100) reported on the toxicity of sodium vanadate in several species of animals. A classic paper for the pharmacological and toxicological actions of vanadium appeared in 1912 (69). At the same time, high vanadium concentrations were discovered in the blood of ascidian worms (58). During the following 50 years it was found that vanadate inhibits ATPase (104), and in the 1980s vanadium was identified as an insulin-mimetic agent (113). The first vanadium-containing enzyme, bromoperoxidase, was isolated some years later from marine algae (128). The most substantive evidence for vanadium essentiality in higher animals was found in goats and rats in the 1980s (11, 94).

With an annually world production of about 50000 t V_2O, vanadium is used in steel production. Small amounts of the element also occur in fossil fuels (105, 121). The possibly essential, pharmacollogial effective and toxic element is extensively used in industry and constitutes a factor of environmental pollution.

MATERIAL AND METHODS

Vanadium analyses were carried out after dry ashing the biological material by means of sequential ICP OES at the line position of 292, 402 nm (Spectroflame-D, Spectro Analytical Instruments). Accuracy of the measurement was examined with the reference materials «bush tweigs and leaves (GBWO7602)», APS1075, trace metals in drinking water and AEA H-G mixed human diet (67, 68, 110). Daily duplicates of all consumed foods and drinks were collected from seven men and seven women on seven subsequent days and their daily urine and faeces were analysed. The vanadium intake was determined and vanadium balance was calculated. Duplicates and foodstuffs were collected or bought in 1988, 1992 and 1996 in Germany and analysed (Table 1).

The effect of a vanadium poor nutrition was studied in 14-fold repetition with a semisynthetic ration and goats.

Fox Pro (Version 2.6 Microsoft) and SPSS/PC + for Windows (Version 6.0. SPSS Inc.) were used for data handling and statistics.

TABLE 1. *Number of the anaylsed samples*

Kind of samples, table	**n[1)]**
Wheat, rye, red clover, meadow red clover (Table 2)	898
Indicator plants, examination (Table 3)	25
Plant species (Table 4)	236
Seeds, fruits (Table 5)	57
Bulgs of roots, stems, tubes (Table 6)	173
Winter feed of games (Table 7)	83
Plants of different age (Table 8)	96
Insects, mollusc, mammals (Table 9)	130
Animals and man (Table 10)	235
Man (Table 11)	109
Foods (Table 12)	2.090
Duplicates (Table 13)	1.750
Tissues, goats (Table 14)	1.069
Faeces, urine (Table 15)	574
Faeces, urine, milk (Table 16)	105
SUM	**7.630**

n[1)] = number.

RESULTS AND DISCUSSION

Sources and Uses

Vanadium is present in the earth's crust at an average concentration of 110 mg/kg. It exists as a sulphide or in the oxidized form. Of the 60 known vanadium minerals, only patronite (V_2S_5), roscoelite (K (Al, V) $_2$ [AlSi$_2$ O$_{10}$] (OH, F)$_2$)), carnotite (K U O_2 VO_4 1.5 H_2O) and vanadinite [Pb$_5$ (VO_4)$_3$ Cl] are commercial sources of vanadium. In none of these ores, vanadium is present with more than 3%. Vanadium is often obtained as a by-product of mining for other valuable materials. One example is carnotite, a uranium-vanadium ore mined in Australia and the United States (63, 45, 70).

Small amounts of vanadium also occur in fossil fuels from Venezuela, Angola, California, Iran, Iraq, and Kuwait (> 0.1% up to 1% V). Indonesian, Libyan and West African oils contain but neglegible amounts of vanadium (121). Vanadium is concentrated in the ash when these fuels are burned.

A major commercial use of vanadium has been in steel production. Vanadium steel which contains from 0.1-3% vanadium is tough, strong and heat-resistant, and withstands strain, vibration and shock.

Another important use of vanadium is as a catalyst in a variety of reactions. Vanadium pent oxide put on an inert support material is the principal catalyst used in the oxidation of SO_2 to SO_3 in the production of sulphuric acid, and for the conversion of naphthalene into phthalic anhydride during the formation of plastics. In addition, vanadium oxychloride, tetrachloride and triacetylacetonate are used as polymerization catalysts in the production of soluble copolymers of ethylene and propylene. In the reaction vessels, these polymers are viscous liquids, which can trap the vanadium catalysts and result in a vanadium content of as much as 500 mg/kg in products used for the packaging of food and pharmaceuticals. Furthermore, the disposal of spent catalysts could also be a point source for a contamination of the biosphere and of food with vanadium (28, 22). Furthermore, vanadium is used for the production of yellow pigments and ceramics.

Distribution in the Environment

The general abundance pattern of vanadium in common rocks shows that this ultratrace element is concentrated mainly in mafic rocks (basalt, gabbro; 200-250 mg V/kg) and shales (100-130 mg/kg).

Lowest concentrations were found in limestones, dolomites (10-45 mg/kg), sandstones (10-60 mg/kg) and syenites, granites and gneisses (30-100 mg/kg). The geochemical characteristics of vanadium are strongly dependent on the oxidant state (+ 2, + 3, + 4 and + 5) and on the acidity of the media. Vanadium does not form its own minerals, but rather replaces other metals (Fe, Ti, Al) in crystal structures. During weathering, vanadium is adsorbed or incorporated into mineral structures of clay or iron oxides.

Highest concentrations of vanadium in soil are reported in soils of mafic rocks (150-460 mg/kg), while the lowest (5-22 mg/kg) were found in peat soils. Loamy and silty soils, as well as some ferralitic soils (Rotliegende), also contain large amounts of vanadium, which exceed those of the parent materials. The average vanadium content of soils world-wide has been calculated to vary from 18 to 115 mg/kg. The geometric mean of vanadium concentration in soils varied between 60 and 100 mg/kg.

Industrial processing of certain mineral ores (ore smelters, cement, and phosphate rock plants) and the burning of coal and oil will increase the deposition of vanadium residues in soils. Combustion of vanadium-rich fuel oils is an especially serious source of vanadium in soils (71).

Small amounts of vanadium compounds are found in air where there is no known anthropogenic contamination (0.02-0.08 ng/m^3). About 65000 t of vanadium per year naturally enter the earth's atmosphere (dust, erosion of soil and rocks, marine aerosols). The vanadium concentration over populated areas is often greater than over unpopulated regions (130). During cold periods the concentrations of vanadium are usually higher than in warm weather. The increases in vanadium have been assumed to be due primarily to fly ash formed during the burning of fossil fuels. Burning these fuels in the past caused about 110000 t of V/a to enter the atmosphere globally (96).

The concentration of vanadium in sea water is in the order of 2 µg/L, but it is about 5 times higher in the deep sea compared to the surface (27). The vanadium concentration in drinking water in Germany varies with the geological origin of the site, with levels between 0.18 µ/L (Keuper, slate, phyllite, Bunter) and 1.10 µg/L (Rotliegende, Muschelkalk), with an average of 0.43 µg/L and a median of 0.28 µg/L. The differences are insignificant (63). In the USA and Japan, the concentration of vanadium in drinking water varies in the same range.

Vanadium in plants, animals and humans

Plants

The geological origin of the material for soil formation and, thus, the natural anthro-pogenic vanadium offer influence the vanadium content of the flora, depending on species and parts of plants. The effect of the origin of the soil on the vanadium content was investigated by way of indicator plants (wheat, rye, red clover). The geological origin with the highest vanadium content in plants was equated with 100, and the other regions were related to it. The soils of Rotliegende, loess and granite produce a vanadium-rich flora (Table 2).

Table 2. *Influence of the geological origin of the site on the relative vanadium content of the flora (n wheat 352, rye 235, acre red clover 180, meadow red clover 131)*

Geological origin of the site	Relative number
Rotliegende weathering soils	100
Loess	96
Granite, syenite weathering soils	88
Boulder clay	79
Muschelkalk weathering soils	79
Keuper weathering soils	75
Bunter weathering soils	73
Phyllite weathering soils	70
Slate weathering soils	67
Diluvial sands	66
Gneiss weathering soils	63
Moor, peat	61
Alluvial riverside soils	60

Diluvial sands, gneiss, peat and alluvial riverside soils deliver only 60% of the vanadium amount found in the vegetation of the Rotliegende.

The vanadium content of wheat, rye and red clover as a field crop originating from 25 plots of 1m² each correlated with r values between 0.75 and 0.90. This shows the suitability of the three species as indicator plants of the bioavailability of vanadium in the soil (Table 3).

TABLE 3. *Correlations of the vanadium concentration in three plant species growing in the same place*

Species (n)[3]	**p**[2]	**r**[1]
Rye: wheat (14)	< 0.01	0.75
Rye: red clover (field) (7)	< 0.05	0.76
Wheat: red clover (field) (4)	> 0.05	0.90

[1] r = correlation coefficient.
[2] p = significance level of the t-test according to Student.
[3] n = number.

Anthropogenic vanadium emissions are indicated even years after the closure of the vanadium source, as it was demonstrated in the vicinity of cement and phosphate factories (table 3) (4).

TABLE 4. *Vanadium contents of several plant species and plant parts from a normal and a vanadium-polluted area (μg/kg dry matter)*

Species resp. part of plants (n; n)	**Control area**		**V-polluted area**		**p**	**%**[1]
	s[2]	**x**[3]	**x**	**s**		
Tomato (11;4)	6.0	8.6	24	29	> 0.05	279
Onion (11;13)	22	22	58	89	> 0.05	264
Asparagus (2;5)	12	52	128	60	> 0.05	246
Kohlrabi (12;3)	13	15	35	15	< 0.05	233
Sweet cherry (6;3)	3.0	7.9	14	4.0	< 0.05	177
Cucumber (15;8)	26	35	49	31	> 0.05	140

TABLE 4. *Vanadium contents of several plant species and plant parts from a normal and a vanadium-polluted area (µg/kg dry matter)* (cont.)

Species resp. part of plants (n; n)	**Control area**		**V-polluted area**		**p**	**%[1]**
	s[2]	**x[3]**	**x**	**s**		
Meadow red clover (15;6)	23	55	75	20	> 0.05	136
Potato peel (18;5)	343	458	606	295	> 0.05	132
Leek (6;7)	28	85	112	91	> 0.05	132
Lettuce (16;9)	250	287	338	172	> 0.05	118
Green wheat (13;18)	16	29	34	16	> 0.05	117
Chive (17;13)	43	94	98	77	> 0.05	104

[1] Control area = 100%, V-polluted area = x%. [2] s = standard deviation. [3] x = arithmetic mean.

Vanadium concentrations in several plant species vary with their leaf-stalk ratio. Leaves store high vanadium amounts. Seeds and fruits prove to be particularly poor in vanadium (Table 5).

TABLE 5. *Vanadium contents of several seeds and fruits (µg/kg dry matter)*

Species (n)	**x**	**s**	**Species (n)**	**x**	**s**
Wheat (23)	6.2	4.2	Apple (39)	19	15
Rape (8)	8.7	10	Pear (10)	23	17
Morello cherry (8)	9.0	7.8	Rye (21)	23	19
Sweet cherry (9)	9.7	4.0	Dwarf bean (17)	25	17
Tomato (15)	13	16	Strawberry (7)	38	36

Bulges of roots (carrots), stems (kohlrabi) and tubes (potatoes) are poor in vanadium, with the exception of potato peel (Table 6).

Table 6. *Vanadium contents of several bulges of roots, stems and tubes (μg/kg dry matter)*

Species (n)	**x**	**s**	**Species (n)**	**x**	**s**
Kohlrabi (25)	29	18	Carrot (34)	71	43
Onion (25)	41	66	Asparagus (7)	99	70
Potato without peel (38)	43	107	Leek (14)	118	65
White radish (6)	65	55	Potato peel (24)	471	240

The leaves of all plant species and especially the perennial plants on which game feeds in winter prove to be extremely rich in vanadium (Table 7) (4).

Table 7. *Vanadium content of several winter grazing of game (μg/kg dry matter)*

Species (n)	**x**	**s**	**Species (n)**	**x**	**s**
Pine bork (29)	690	500	Raspberry (10)	1399	913
Spruce bork (17)	854	407	Pine twigs (5)	1626	552
Spruce twigs (8)	1002	523	Heather (8)	3111	973
Bilberry herb (3)	1020	327	Oak twigs (3)	3136	350

The vanadium porphyrin abundant in oil has formed *post mortem* from chlorophyll. By measurements of the vanadium content in tree rings, the yearly increase in atmospheric vanadium from vanadium-rich gasoline can be mapped (80).

High concentrations of vanadium are also found in a few species of the mushroom genus Amanita. The vanadium-containing compound found in mushrooms was named amavadine. The physiological function of amavadine is unknown. Wever and Krenn (1990) (132) suggested that amavadine acts as a cofactor with an oxidase or peroxidase function. Up to now it remains a mystery as to why just Amanita species have designed such an efficient chemistry for vanadium enrichment (81, 23).

Vanadium in plants decreases significantly with increasing age. From the beginning of May to the middle of June, vanadium contents were found to abate to a third of the initial level (Table 8).

TABLE 8. *Variation of the vanadium contents of several plant species with the stage (age) of vegetation (µg/kg dry matter)*

Species (n)		4.5	17.5	31.5	14.6	LSD[2]	%[1]
Wheat	x	87	41	42	33	31	38
(6; 6; 6; 6)	s	16	13	14	30		
Rape	x	119	107	83	34	66	29
(6; 6; 6; 6)	s	31	39	62	19		
Field red clover	x	105	52	42	34	20	32
(6; 6; 6; 6)	s	15	11	5.8	15		
Lucerne	x	145	79	49	58	42	40
(6; 6; 6; 6)	s	46	15	9.4	16		

[1] 4.5 = 100%, 14.6 = x%. [2] LSD = least significant difference.

Animals and Humans

The vanadium concentration in organs and in milk is not homeostatically regulated. This is the case for all species investigated (Table 9): grasshopper (160 µg/kg dry matter), carrion beetle (212 µg/kg), spider (429 µg/kg), wood louse (1,674 µg/kg), slug (449 µg/kg), edible snail (488 µg/kg), earth worm (5,450 µg/kg), mice, voles and shrews (Sorex araneus, x = 254 µg/V, s = 127). The vanadium concentrations of their bodies are fixed by the intake of vanadium and vary extremely.

Table 9. *Vanadium contents of several species of insects, molluscs and mammals (µg/kg dry matter)*

Insects (n 18)		Molluscs (n 27)		Mammals (n 85)	
Tettigonia	x 160	Arion	449	Apodemus	56
viridissima	s 131	rufa	231	flavicollis	21
Silpha	x 212	Helix	488	Clethrionomys	133
obscura	s 157	pomatia	432	glareolus	85
Carabus	x 349	Lumbricus	5450	Apodemus	137
hortensis	s 351	terrestris	3251	sylvaticus	54
Armadillidium	x 1674			Microtus	211
vulgare	s 118			arvalis	184

The very high vanadium amounts in wood-lice and earth worms are caused by the intake of earth. Mice and voles provide the cat with 50 to 200 µg V/kg dry matter (16). Commercial cat food supplies European cats with 40 to 200 µg V/kg dry matter. The daily vanadium intake of the cat through commercial food varies between 3 and 12 µg (17). The vanadium concentrations in the organs of mammals varies depending on the local vanadium offer and is not species-specific in most cases (Table 9). The variation of vanadium concentration in the organs of the local populations of wild ruminants is similar. Wild boars with a stomach vanadium content of 350 to 1600 µg/kg dry matter store significantly more vanadium in the analyzed tissues than wild ruminants (Table 10). Similarly to wild ruminants, hares accumulate vanadium in ribs and livers.

Table 10. *Vanadium contents of several tissues of animals and man (age 11 to 89 years) (µg/kg dry matter)*

TISSUE	n	KIDNEY	LIVER	RIBS
ROE DEER	(n 18)	60	24	47
RED DEER	(n 18)	53	25	52
MOUFLON	(n 18)	49	26	58
FALLOW DEER	(n 83)	111	57	76
WILD BOAR	(n 11)	209	119	104
WOMEN	(n 44)	28	61	40
MEN	(n 43)	25	67	26

In adult humans (Table 11), the vanadium content of the organs analyzed was not affected by gender and corresponded to that of the animal species investigated. However, from babies and toddlers to people of age 89, the vanadium content in kidneys, prostate glands and ribs decreases significantly to between 10 and 30% of the amount registered in babies (Table 11). Both sexes show vanadium depletion by the time of the onset of puberty. The vanadium content in the liver has been found the only one not affected by age (from birth till 89 years) (12, 14).

Table 11. *Influence of age and sex on the vanadium concentration in human ribs (µg/kg dry matter)*

Age in years (n; n)	**Women**		**Men**		**Fp**	**%**[1]
	s		x		x	s
< 1 (4;3)	78	104	416	564	> 0.05	400
1 – 3 (3;8)	23	24	51	34		212
4 – 10 (2;6)	6.7	27	32	18		119
11 – 20 (2;5)	20	29	22	7.1		76
21 – 30 (4;2)	44	37	12	15		32
31 – 40 (5;2)	14	18	32	26		178
41 – 50 (5;6)	15	21	23	18		110
51 – 60 (5;7)	14	28	16	13		57
61 – 70 (4;6)	33	42	27	13		64
71 – 80 (8;6)	23	24	29	22		121
> 80 (9;7)	18	26	37	23		142
Fp	< 0.05		< 0.01			
%[2]	25		8.9			

Fp = significance level in one factorial or multiple variance analysis. [1] women = 100%, men = x %. [2] < 1 year = 100%, > 80 years = x %.

Vanadium Content of Foods and Beverages

Seeds, cereal products, bread, cake and pastries, tubers and fruits generally have a low vanadium content (5 to 40 µg/kg dry matter). Mushrooms, red radish, leafy vegetables (lettuce, spinach) as well as herbs contain much higher levels of vanadium (100-2,400 µg V/kg dry matter (Table 12).

TABLE 12. *Vanadium contents of foods and beverages (µg/kg dry matter, µg/L beverage) (147 different foods and beverages; n 2090)*

Plant foods (range)		Animal foods (range)		Beverages	
Bread, cake (6-23)	13	Formula milk (3-17)	9.1	Drinking water	0.43
Flours, pulses (1-77)	14	Dairy products (2-31)	9.3	Whisky, brandy	0.48
Sugar-rich foods (8-31)	17	Meat, sausage (10-95)	31	Coke, lemonade	0.83
Fruits (9-55)	23	Breast milk	34	Advocaat, juice	6.2
Vegetables (7-625)	41	Fish, tinned fish (16-92)	36	Beer	28
Spices (16-2356)	218	Eggs	75	Wine, sparkling wine	45

The investigation of European vegetable foodstuffs based on conventional and organic farming showed that, as a rule, organically produced wheat flour, bread, fruits and vegetables delivered less vanadium than conventionally produced ones. The missing of phosphate fertilization which delivers vanadium to the plants becomes noticeable in organic farming production. In contrast to this fact, brown sugar produced ecologically from sugar cane contained more vanadium than conventionally refined beet sugar. The use of this sugar delivers much vanadium to the food chain. Therefore, ecologically produced chocolate and sweets are richer in vanadium than conventionally produced brands (15).

The various formulae for the nutrition of babies offer between 4 and 17 µg V/kg dry matter. Like cow's milk, most formulae in Germany deliver < 10 µg V/kg dry matter. Mother's milk contains 34 µg V/kg dry matter, i.e., more than cow's milk. The vanadium content in human milk should be subjected to further investigation so that baby food can be prepared according to physiological principles.

Varying with species, meat and fish contain little vanadium (20 to 40 µg/kg dry matter). The vanadium content in hen's eggs varies extremely. The cause of vanadium accumulation in hen's eggs may be a high vanadium content in the calcium carbonate fed to hens, or the vanadium emission from the burning of fuel oil for heating. A high vanadium amount accumulated in eggs has no adverse effect on human health. Organic farming animal foodstuffs may contain significantly less vanadium than conventionally produced ones.

The main vanadium supplier of man is beer, which contains between 18 and 36 µg V/L. Vanadium enrichment of beer has been traced back to filtration with filters containing diatomaceous earth. White, red and sparkling wines are also very rich in vanadium. The reason for this could be the use of the unwashed grape, with deposits of dust from the environment and vanadium emissions (vanadium steel, silica gel, bentonite) during the different stages of production (65, 64, 15, 13, 74) and/or filtration with diatomaceans earth.

Beer and wine have been found to be the main suppliers of vanadium to men and women in Europe, supplying 75% and 41% of the daily intake, respectively. Thus, vegetable food supplies 17 and 43%, and food of animal origin 8 and 16 % of the intake of men and women, respectively (13).

Vanadium Intake

The vanadium intake of women and men was systematically investigated by the duplicate portion technique in Germany and Mexico. 19 test populations at the age of 20 to 69 years collected duplicates of all consumed foodstuffs, sweets and beverages on 7 consecutive days (Table 13).

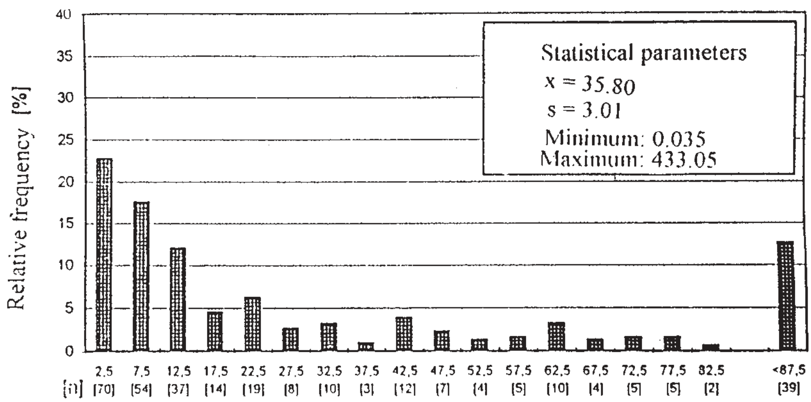
In Germany, men with mixed diets take in double the vanadium amount ingested by women. The high intake results from the higher beer consumption of men (1 L beer ~ 28 µg V).

TABLE 13. *Vanadium intake of adult Germans and Mexicans with mixed and ovo-lacto-vegetarian diets depending on time and sex (µg/day)*

Form of diet	Country (n; n)[8)]	Women s	Women x	Men $x^{4)}$	Men $s^{3)}$	$p^{2)}$	%[1)]
	G[5] 1988 (196;196)	8.3	9.3	19	16	< 0.001	204
Mixed	G 1992 (294;294)	3.3	25	36	3.0	< 0.001	144
(Md)	G 1996 (217;217)	15	11	33	35	< 0.001	300
	M[6] 1996 (98;98)	11	20	20	14	> 0.05	100
Veg.[7]	1996 (70;70)	103	49	39	34	> 0.05	78
	G 1988;1996	118		174			
%	G:M 1996	182		61		–	
	Md:Veg. 1996	445		118			

[1] Women = 100%, men x %; [2] p = significance level of the t-test according to Student; [3] s = standard deviation; [4] x = arithmetic mean; [5] G = Germany; [6] M = Mexico; [7] Veg. = ovo-lacto-vegetarian diet; [8] n = number.

The vanadium intake shows no normal distribution between the two sexes (Figure 1). Nearly 40% of the men took in portions with low amounts of vanadium (< 10 µg/day), while the portions taken in by 13% of the men had very high vanadium contents (> 88 µg/day), due to their high consumption of beer (> 2 L/day).



Vanadium intake [µg/d]

FIGURE 1. *Frequency distribution of vanadium intake of men.*

Women do not drink as much beer as men. Accordingly, more than 55% of women took in < 10 µg V/day, while only 3% had an intake of > 88 µg V/day (3).

Nursing mothers (12.1 µg/day) consumed the same amount of vanadium in comparison to non-lactating women (12.2 µg/day). Mexican women and men with mixed diets took in the same amount of vanadium as Europeans. Ovo-lacto-vegetarians do not drink much beer and wine, which are rich in vanadium. They prefer vegetables, cacao products and nuts, which are rich in vanadium, too. The vanadium intake decreases with increasing age (3).

Estimates for the American intake of vanadium (based on a food intake of 500 g dry weight) are 10 to 60 µg/day (57). This calculation with a dry matter intake of 500 g is too high. European women take in 300 g/day and men 380 g/day (mixed diet). Generally, the calculation of the trace element intake with the help of the market basket overestimates the intake (3).

Vanadium deficiency has not been investigated in humans. Most diets, on a weekly average, supply > 10 µg V/day, which suggests that a dietary intake of 10 µg V/day probably meets any postulated vanadium requirement.

Absorption and Distribution of Vanadium

A significant amount of vanadium absorption occurs in the upper gastrointestinal tract. Most ingested vanadium probably is transformed to VO^{2+} in the stomach and passes into the duodenum in this form (97, 133, 54).

In serum, absorbed vanadium is transported mainly bound to transferrin (77, 76). Vanadium in rats' milk was found mainly in the protein fraction and perhaps in lactoferrin. In this form, vanadium is transferred from the mother to the pups. In older rats, vanadium is apparently converted into vanadyl-transferrin and ferritin complexes in plasma and body fluids (42, 107).

The vanadium status of tissues and organs is not homeostatically regulated. In goats with high (2000 µg V/kg) and low (< 20 µg V/kg) vanadium concentrations in the feed dry matter, all parts of the body reflect the different vanadium intakes significantly (table 14). The vanadium content of kidneys, uterus, lungs, spleen and ribs of goats with low vanadium intake is reduced to between 15 and 60 % of the amount found in the same tissues of goats with high vanadium intake. The vanadium contents of hair, serum and milk, which are easily available, are good indicators of the vanadium offer to animals and humans (63).

TABLE 14. *Vanadium contents of organs and tissues in goats with high and low vanadium offer (µg/kg dry matter)*

Organ, tissue (n)	**Control goats**		**V-deficiency goats**		**p**	**[%]**[1]
	s	**µg/kg dm**	**µg/kg dm**	**s**		
Kidney (13;11)	876	1563	234	102	< 0.001	15
Uterus (7;5)	358	603	97	28	< 0.05	16
Lungs (16;10)	146	311	57	17	< 0.001	18
Spleen (7;10)	521	910	184	82	< 0.001	20
Ribs (17;8)	1598	2608	525	231	< 0.001	20
Carpal bones (20;7)	1264	2385	605	489	< 0.001	25
Heart (12;12)	110	277	77	34	< 0.001	28
Liver (7;9)	174	347	105	58	< 0.01	30
Skeletal muscle (12;10)	44	135	48	14	< 0.001	36
Hair (10;14)	91	144	58	40	< 0.01	40
Aorta (13;13)	61	159	70	31	< 0.001	44
Pancreas (5;8)	150	247	115	65	< 0.05	47
Cerebrum (3;9)	20	100	47	12	< 0.001	47
Ovary (8;8)	307	832	402	177	< 0.01	48
Blood serum (µg/l) (17;17)	45	50	26	14	< 0.05	52
Milk (444;307)	19	15	8.8	15	< 0.001	59

[1] Control goats = 100%, deficiency goats = x %.

The vanadium concentration in children's hair indicated the vanadium pollution very well and better than that in nails (75). For the identification of the vanadium status, all organs are suitable, and especially the blood (59, 106). The highest levels of vanadium are stored in bones, kidneys, spleen and ovary, the lowest in the aorta, hair, muscle and, especially, in milk (Table 14).

Excretion and Balance of Vanadium

Animals and humans excrete most of the consumed, unabsorbed vanadium with the faeces (25). The absorbed vanadium is removed from the body mainly with urine and milk (3) and partly with bile (29). The biological half-life of vanadium excreted in urine is 20-40 hours. Animal studies indicate that the elimination of vanadium from the body following inhalation of vanadium oxides is biphasic, with an initial rapid elimination (10-20 hours) and a longer terminal phase (40-50 days) (103, 78). Rats excrete 8 and 10% of injected vanadium with the faeces and bile, respectively (133, 62). The elimination half-lives of vanadium in rats were found to range between 11 and 132 hours for soft tissues and 376 hours for the bone. During the first day, 49% of the dosage was eliminated with the urine and 8% with the faeces (1). The half-life for the elimination of vanadium from the bodies of vanadium-fed diabetic rats was found to be about 12 d (101).

Faecal excretion of the nutritional vanadium intake amounts to 96% in men and non-lactating women, and to 79% in lactating women (Table 15). Most of this vanadium is not absorbed. The form of diet (mixed or ovo-lacto-vegetarian) (Table 15) has no influence on the faecal excretion rate. On average, adults of both sexes and with either form of diet eliminate 4% of the nutritional vanadium intake renally (range: 2-6%).

The mean apparent rate of vanadium absorption by adults of both diet forms amounts to 10%, and the mean vanadium balance is + 6%, with a variation between + 23 and – 15%.

TABLE 15. *Vanadium balance of adult people with mixed and ovo-lacto-vegetarian diets (n 287;287)*

Parameter		Women		Men	
		Mixed diet	Vegetarian diet	Mixed diet	Vegetarian diet
Intake, µg/day		11.3	48.7	32.6	38.6
Excretion	Faeces, µg/d	11.5	36.7	36.4	34.7
	Urine, µg/d	0.7	0.6	0.9	1.7
	Faeces, %	94	98	98	95
	Urine, %	6	2	2	5
Apparent absorption rate, %		–	33	–	11
Balance	µg/day	– 0.9	+ 11.4	– 5.0	+ 2.2
µg/d	%	– 8.0	+ 23	–15	+ 5.7

On average, a nursing mother transfers 17% of her vanadium intake to her baby through the milk (Table 16) and excretes only 5% through her kidneys, whereas renal excretion in a young, non-nursing woman amounts to 9%. The apparent rate of vanadium absorption in non-nursing young women is 8.9%, which corresponds to the 10% registered for adults in general.

The vanadium balance of nursing women is negative. The negative balance of lactating mothers demonstrates that the stores of vanadium in the bones are reduced after birth (3, 14). In animals, the balance of macro-, trace and ultratrace elements during lactation is mostly negative (49).

TABLE 16. *Vanadium balance of non-nursing and nursing women with mixed diet*

Parameter (n)		Non-nursing		Nursing		p	%
		s	x	x	s		
Intake, µg/day (49;49)		13	7.9	12.1	14.0	> 0.05	153
Excretion	Faeces, µg/d (49;49)	6.8	7.2	15.6	19.1	> 0.05	217
	Urine, µg/d (49;49)	1.4	0.7	0.8	1.0	> 0.05	114
	Milk, µg/d (0;7)	–		3.4	2.9		
	Faeces, %	91		79			
	Urine, %	9		4			
	Milk, %	–		17			
Apparent absorption rate, %		8.9		–			
Balance	µg/day	± 0.0		– 7.7			
	%	± 0.0		– 64			

The Essentiality of Vanadium

Essentiality to Plants

The evidence that vanadium is essential for the growth of higher plants is not yet conclusive, while the essentiality of this element for algal species is unquestionable. Vanadium is essential for several species of green algae (Scenedesmus obliquus, Chlorella pyrenoidasa), yellow-green algae (Bumileriquisis filiformia) and brown algae (Fucus spiralis). A very low concentration (0.1-1 µg V/L) of vanadium induces growth. At higher concentrations, growth is still stimulated, but chlorophyll formation even more.

In the brown alga Ascophyllum nodosum, the activity of the enzyme bromoperoxidase is essentially influenced by vanadium (21, 128, 35). By means of vanadate, the inactive apoenzyme can be reconstituted to active holoenzyme. Vanadium is an essential element for algae and probably for other organisms. The reactivation of apoperoxidase by vanadium is inhibited by phosphate. Since vanadium-dependent bromoperoxidases have been found in a number of marine red algae and terrestrial lichens, vanadium-dependent iodoperoxidases have also been detected in brown seaweed, and a chloroperoxidase has been identified in the fungus Curvularia inaequalis. The mechanisms of action of vanadium in the haloperoxidases has not been firmly established. In the bromoperoxidases, H_2O_2 reacts with vanadium as V^{5+} to form a dioxygenium species which reacts with bromide to yield an oxidized bromine species, the intermediate that forms the carbon-halogen bond (31, 129, 132, 127, 115).

The conversion of atmospheric nitrogen to ammonia by nitrogen-fixing microorganisms is catalyzed by the enzyme nitrogenase. Vanadium-dependent nitrogenase has been characterized for Azotobacter vinelandii and A. chroococcum (40). This effect of vanadium was discovered in 1986, when a vanadium-containing nitrogenase was isolated from mutants of two species of Azotobacter unable to synthesize molybdenum-nitrogenase (41).

Essentiality to Animals

Some ascidians accumulate vanadium (vanadocytes in blood cells) in amounts that exceed that present in sea water by 4 million times. Suggested functions for vanadocytes include production of the cellulose of the tunic, reversible trapping of oxygen under conditions of low oxygen tension, and acting as an antimicrobial agent (82, 114).

Between 1971 and 1974 four research groups described possible signs of vanadium deficiency. In 1984 it was realized that these findings had some shortcomings (87, 88, 95). Many of the findings may have been the consequence of a high vanadium supply that induced pharmacological changes in animals fed with unbalanced diets (91, 86). The most substantive evidence for vanadium essentiality was provided in the nineteen-eighties, from deficiency experiments with goats (11, 94).

In 14 experiments with goats, the animals with < 10 µg V/kg dry matter of the semisynthetic ration ate 20% less feed during lactation than the control goats (Table 17) (14).

TABLE 17. *Influence of vanadium-poor nutrition on feed intake, growth, reproduction performance and mortality of goats*

Parameter		Control goats	V-deficiency goats	p	%
Feed consumption	Non pregnant, g/day	685	598	< 0.001	87
	Pregnant, g/day	595	666	< 0.001	112
	Lactating, g/day	646	518	< 0.001	80
Growth	Birth, kg	2.6	2.6	> 0.05	100
	91st day of life, kg	17.5	15.2	< 0.05	87
	Undepleted, 101st-268th day, g/day	96	95	> 0.05	99
	Intrauterine depletion g/day	96	80	< 0.001	83
Reproduction	Success of first mating, %	70	48	< 0.001	
	Conception rate, %	86	73	< 0.01	
	Matings per gravidity	1.5	2.2	< 0.001	–
	Abortion rate, %	1	19	< 0.001	
	Ratio & : %, & = 1	1.60	0.86	< 0.001	
Mortality	Kids from 7th to 91st day, %	5	24	< 0.001	–

During pregnancy the deficiency animals equalized this deficit (63). The vanadium deficiency did not influence intrauterine growth, neither in female nor in male kids (52).

After intrauterine vanadium depletion, the post-natal development of both sexes was significantly reduced. Kids with normal supply during intrauterine development grew normally (66).

The vanadium-poor nutrition lowered the success of first mating and the conception rate of the she-goats significantly. The nanny-goats with poor vanadium intake needed significantly more matings for pregnancy, exhibited a higher rate of spontaneous abortion and an increased ratio of female to male kids born. A quarter of kids from vanadium-deprived goats died between days 7 and 91 of life with some of the deaths preceded by convulsions; only 5% of kids from vanadium-supplemented goats died during the same time.

The vanadium-deficiency goats produced normal milk, in normal amounts and with normal milk fat contents (8, 7, 20).

Several blood parameters were estimated with the usual methods (Table 18). Of these, only the concentrations of creatinine and triglycerides and the activity of γ-glutamyl transferase were significantly higher in vanadium-deficient compared to control animals (52).

TABLE 18. *Influence of vanadium deficiency on the blood parameters of goats*

Parameter	**Control goats**		**Vanadium-deficiency goats**		**p**	**(%)**
	s	**x**	**x**	**s**		
Creatinine (μmol/L)	15	87	105	17	< 0.01	121
Triglycerides (μmol/L)	80	180	290	130	< 0.01	161
γ-glutamyl transferase (U/L)	18	45	58	17	< 0.05	129

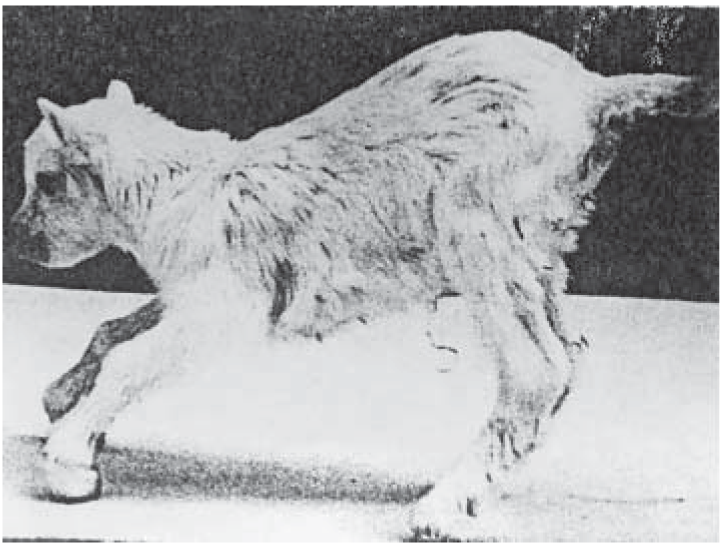


FIGURE 2. *Newborn kid of a vanadium-deficient goat with skeleton injuries.*

Deficiency goats suffered pain in the extremities, swollen forefoot tarsal joints, and skeletal deformations in the forelegs (5). In goats with vanadium deficiency, glandular or glandulocystic hyperplasia of the endometrium was observed (83). The sizes of the pancreas, thymus and thyroid of vanadium-deficient goats were insignificantly increased in comparison to the same tissues of control goats (21).

Already Uthus and Nielsen (125) and Nielsen (90) reported that a vanadium-deficiency nutrition of rats showed increased thyroid weights and thyroid-to-body weight ratios, and decreased growth. This study also showed that stress factors, which change the thyroid status or iodine metabolism, enhance the response to vanadium deprivation.

Vanadium may well be found essential for some enzyme reactions, perhaps one that is involved in thyroid metabolism.

Feeding of the V-deficiency ration reduced life expectancy significantly. Within the first year, 43% of the animals of a group without V supplementation died, compared to only 11% in the control group. At the end of the experiment, 16% of the control goats were still alive, whereas only 3% of the V-deficient goats survived (Table 19).

Table 19. *Influence of vanadium deficiency on the mortality of goats*

Period and number of goats which died (n; n)	**Control goats** %	**Vanadium-deficient goats** %	**p**
1^{st} year (7;31)	11	43	< 0.001
2^{nd} year (17;22)	27	31	> 0.05
3^{rd} year (14;10)	21	13	> 0.05
4^{th} year (13;4)	20	6	< 0.05
5^{th} year (2;2)	3	3	> 0.05
> 5 years (1;1)	2	1	> 0.05
Goats surviving (10;2)	16	3	< 0.001

Vanadium-deficient nanny-goats had only 50% the life-span of control goats. The normative requirement of vanadium for animals is very small, amounting to < 10 µg/kg dry feed matter (12, 6, 7, 14, 2, 9, 10).

Essentiality to Humans

The same is true for the normative vanadium requirement of man. A daily dietary intake of 10 µg or less probably would meet any postulated normative requirement (7, 3, 92, 93). The individual daily intake of vanadium in Germany and Mexico in every case reached > 8 µg/day on a week's average. World-wide, typical diets generally supply 15 to 30 µg V/day (85, 30, 29, 44, 98).

Pharmacological Effects

To disentangle pharmacological from nutritional observations it is necessary to identify the essential biochemical function of vanadium in higher animals. Both effects demand quite different amounts of vanadium (µg or mg/kg food). On the other hand it is difficult to distinguish pharmacological from toxic doses of vanadium. The differences are species-specific and dependent on time, mode of administration, and the chemical form of vanadium. In the past, the amounts of vanadium used in *in vitro* and *in vivo* experiments were mostly pharmacological or toxic doses, and much higher (thousand-fold) in comparison to the nutritional intake of animals and man.

Vanadium and its compounds mimics the actions of insulin in isolated cell systems, and these compounds produce dramatic decreases in blood glucose levels in animal models of both types of diabetes mellitus (50, 108, 119). *In vitro* and *in vivo* studies with animals indicated that vanadium increases the glucose transport activity and improves glucose metabolism (24). The action of vanadium is related to the translocation of glucose through the plasma membrane. Inhibition of phosphotyrosine, phosphatase and protein tyrosine kinase activation is probably involved in the action of vanadium on glucose homeostasis (111). The enhancement of glucose uptake, glycolysis and glycogen synthesis by vanadate is less than by insulin, but vanadate produces greater simulation of lactate and glucose oxidation than insulin (26).

In addition to the insulin-mimetic effect of vanadium compounds, vanadium affects signal transduction mechanisms and proto-oncogene expression *in vitro* (118). At concentrations > 5 mM, orthovanadate is cytotoxic to proliferating cells, including primary culture and tumor cell lines (32, 38).

Vanadyl sulphate with doses up to 60 mg/day is a common supplement used by weight lifters, shot-putters and weight trainers to improve their performance. A 12 week, double-blind, placebo-controlled clinical trial did not detect any haematological abnormalities at doses of 0.5 mg vanadyl sulphate/kg day (46).

The Toxicity of Vanadium

Toxicity to Plants

Vanadium phytotoxicity under field conditions is extremely rare (51). However, under man-induced conditions, vanadium concentrations as high as 0.5 mg/L in the nutrient solution and 140 mg/kg in the soil solution may be toxic to plants. The phytotoxicity of vanadium (chlorosis and dwarfing) may appear at about 2 mg V/kg dry matter (34).

A vanadium amount of 30 mg/kg soil induced a vanadium concentration of 170 µg V/kg dry matter in green oats, of 250 µg/kg in green mustard and of 700 µg V/kg dry matter in spinach without signs of intoxication (84).

Toxicity to Animals

For animals, vanadium is a relatively toxic element (89) (Table 20). In young cattle, 10 mg V/kg live mass induced diarrhoea and weakness (99); heifers and cows with high vanadium intake developed inappetence, black diarrhoea, lethargy, dehydration, spontaneous abortions and decreased milk production (47).

Table 20. *Vanadium concentrations in the fodder, or vanadium doses, that inhibit health and/or performance*

Animal species	**Vanadium concentration in the fodder with 88 % dry mass (mg/kg) or vanadium dose (mg/kg live mass)**	**Effects**	**Literature**
Cattle	Starting at 10 mg/kg live mass	Diarrhoea, Weakness	99, 47
Sheep	Starting at 200 mg/kg fodder	Reduced fodder intake and reduction of the development of live mass	(53, 54, 55, 56)
	Above 200 mg/kg fodder	Diarrhoea, histopathologic changes of the organs	
	Above 300 mg/kg fodder	Increased mortality	
	40 mg/kg live mass	Acute intoxication, lethal effect	
Fowl, laying hen	above 20 mg/kg fodder	Damage of the skeletal system, fewer eggs, fewer hatchlings, increased mortality	(18, 112, 120, 124)
Broiler	above 5 mg/kg fodder	Reduction in the development of live-mass	

The no-observed-effect level of the reproductive toxicity of vanadium in male mice was 40 mg/kg/day (79). 5, 10 and 20 mg V/kg/day given to adults rats do not influence their reproduction performance, but produced toxic effects in the offspring (39). A high vanadium intake decreases the water and food intake of rats and lowers their body weight. Changes in erythrocyte indices probably result from direct action of vanadium (134). Vanadium-induced morphological changes in the kidney were more pronounced with age (36).

The addition of 200 mg Cu/kg feed or 0.5 to 2.0% sodium chloride lessened the growth-retarding effect of vanadium in chicken (60, 61).

Toxicity to Humans

In humans, the threshold level for vanadium toxicity is near 10 (to 20) mg/day. Schroeder et al. (109) administered 4.5 and 9 mg V/day for 6 to 16 months without apparent detrimental effects; Curran et al. (33) supplemented 13.5 mg V/day for 6 weeks, with no sign of intolerance toxicity being found. On the other hand, Somerville and Davies (116) gave 13.5 mg V/day for 5 months. 40% of the patients exhibited gastrointestinal disturbances and 40% exhibited green tongues. After intakes of 4.5 to 18 mg V/day over 6 to 10 weeks, the patients developed green tongues, cramps and diarrhoea (37, 19).

In animals and humans, vanadium generally causes pulmonary effects of acute vanadium pentoxide inhalation (73, 126), haematological changes following vanadium exposure (72), and a lowered cysteine content in hair and nails (122). The coenzyme A content of the organs is decreased after feeding high doses of vanadium. One of the compounds involved in the synthesis of coenzyme A is thioethanolamine, which is derived from cysteine by decarboxylation. Therefore, a decrease in cystine caused by vanadium was presumably the reason for reduced amounts of coenzyme A. Coenzyme A is involved in the synthesis of cholesterol, and therefore may affect the occurrence of atherosclerosis.

In mammals it was shown that vanadium is a strong inhibitor of Na^+ - K^+ ATPases (31). This inhibitation is caused by the substitution of vanadate for phosphate in the ATP-driven reactions (43, 117). Vanadium pentoxide also seems to open the K-channels of the erythrocyte membrane (48, 131). Hemodialysis patients may exhibit extremely high levels of serum vanadium (123).

Table 21. *Normative requirement and maximial tolerable intake of vanadium in man (70 µg/body weight; 350 g/day matter intake/day)*

Parameters	**Normative requirement**	**Maximal tolerable intake**
Vanadium intake, µg/day	~ 10	~ 3000
Vanadium intake, µg/day body ...., day	~ 0,15	~ 40
Vanadium, by consumed day matter	~ 30	~ 1000

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