Review Articles

Recent progress on essentiality of the ultratrace element vanadium in the nutrition of animal and man

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Abstract

In 14 experiments with intraunterinely depleted goats getting < 20 μg V/kg ration DM, V-deficient goats suffered pain in the extremities, developed swollen tarsal joints of the forefeet, glandular hyperplasia of the endometrium and increased size of pancreas, thymus and thyroid compared with controls. The normative requirement of Vanadium (V) for animals amounts to > 20 μg diet DM and < 5 μg V/day for adult humans.

Keywords : vanadium, essentiality in animal, geological influences, intake of man, foodstuffs

Introduction

Although evidence that vanadium is essential for growth in higher plants is inconclusive, the essentiality of this element for algae species is unquestionable. Vanadium is essential for several species of green algae (*Scenedesmus obliquus, Chlorella pyrinoidosa*), yellow-green algae (*Bumilleriopsis filiformis*), and brown algae (*Fucus spiralis*). Vanadium at very low concentrations (0.1-1 mg V/L stimulates growth, but at higher concentrations stimulates both growth and - to a greater extent - also chlorophyll formation [1].

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 [2, 3].

Between 1971 and 1974 four research groups described possible signs of vanadium deficiency in animals which were largely refuted [4, 5, 6, 7, 8]. The most substantive evidence for vanadium essentiality was provided ten years later, from deficiency with goats which started 1980 [9] and rats [10].

Informations to material and methods are given by Anke et al., Res. Trace Elements, 16 : 2005.

The essentiality of vanadium in animal

In 14 experiments with goats, the animals with < 10 - 20 μg V/kg dry matter of the semisynthetic ration ate 20 % less feed during lactation than the control goats (Table 1). During pregnancy the deficiency animals equalized this deficit. The vanadium-deficiency did not influence intrauterine growth, neither in female nor in male kids. After intrauterine vanadium depletion, the post-natal development of both sexes was significantly reduced. Kids with normal supply during intrauterine development grew normally.

The vanadium-poor nutrition lowered the success of first mating and the conception rate of the she-goats significantly. The she-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 milk, in normal amounts and with normal milk fat content.

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Several blood parameters were estimated with the usual methods. 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.

Vanadium-deficiency goats suffered pain in the extremities, swollen forefoot tarsal joints, and skeletal deformations in the forelegs (Figure 1) [11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22].

In goats with vanadium deficiency, glandular or glandulocystic hyperplasia of the endometrium was observed. The sizes of the pancreas, thymus and thyroid of vanadium-deficient goats were insignificantly increased in comparison to the same tissues of control goats [23, 24].

Figure 1 Newborn kid of a vanadium deficiency goat

A vanadium-deficiency nutrition of rats showed increased thyroid weight 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 [25, 26, 27]. Vanadium may well be found essential for some enzyme reactions, perhaps one that is involved in thyroid metabolism.

In the brown alga Ascophyllum nodosum, the activity of the enzyme bromoperoxidase is essentially influenced by vanadium [28, 29, 30]. By means of vanadate, the inactive apoenzyme can be reconstituted to active holoenzyme. Vanadium is an essential element for alga 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

Table 1 Influence of vanadium-poor nutrition on feed intake, growth, reproduction performance mortality and tissues components of goats

Parameter (n;n)$^{3)}$		Control goats	V deficiency goats	p$^{2)}$	%$^{1)}$
Number of goats in the experiments		63	72	-	-
V-content of the ration, μg/kg DM		2400	< 20	< 0.001	0.8
Feed intake	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	17.5	15.2	< 0.05	87
	undepleted, 101-268 day	96	95	> 0.05	99
	intrauterine depletion g/day	96	80	< 0.001	83
Reproduction performance	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	
	Sex (female = 1)	1.60	0.86	< 0.001	
Mortality	Kids, 7th to 9th day, %	5	24	< 0.001	-
	Adults, 1^{st} year	11	43	< 0.001	
Serum content	Creatinine (μmol/l)	87	105	< 0.01	121-
	Triglycerides (μmol/l)	180	290	< 001	161
	γ-glutamyl transferase (U/l)	45	58	< 0.05	129
Tissues, V-content	Kidney (n 13 ;11)	1563	234	< 0.001	15
	Uterus (n 7;5)	603	97	< 0.05	16
	Lungs (n 16;10)	311	57	< 0.001	18
	Spleen (n 7;10)	910	184	< 0.001	20
	Ribs (n 17;8)	2608	525	< 0.001	20

%$^{1)}$ = Control goats = 100 %, V-deficiency goats = x %; p$^{2)}$ = Significance level, Student test; n$^{3)}$ = Number

Table 2 Influence of the geological origin of the site on the relative vanadium content of the flora in Central Europe (n=898)

Geological origin of the site	Relative index
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

Table 3 Vanadium intake of German and Mexican adults with mixed and ovo-lacto-vegetarian diets depending on time and gender (μg/day) (n=1750)

Form of diet	Country (n; n)	Women		Men		Fp1)	%
		s	x	x3)	s2)	p	
Mixed	Germany (G) 1.	8.3	9.3	19	16		204
diet	Germany 4.	5.3	25	36	54	< 0.001	144
(Md)	Germany 8.	15	11	33	35		300
	Mexico (M) 8.	11	20	20	14	> 0.05	100
Vegetarian (V)	Germany 8.	103	49	39	34	> 0.05	80
Fp1)	MD G 1.: MDG 8.	< 0.001					
p	MD G 8.: MDM 8.	> 0.05					
p	MD G 8.: VG 8.	< 0.001				-	
	MD G 1.: MDG 8.	118		174			
%	MD G 1.: MDG 8.	182		61			
	MD G 1.: MDG 8.	445		118			

Fp1) = Significance level, one or multifactoral variance analysis; s2) = Standard deviation; x3) = Arithmetic mean

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 vanadium 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, 32, 33, 34, 35].

Feeding of the vanadium-deficiency ration reduced life expectancy significantly. Within the first year, 43% of the animals of a group without vanadium 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 vanadium-deficient goats survived. Vanadium-deficient she-goats had only 50% the life-span of control goats. The normative requirement of vanadium for animals is very small, amounting to > 20 μg/kg feed dry matter (Table 1).

The influence of the geological origin of the soil on the vanadium content of the vegetation

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 soils of Rotliegende, loess and granite produce a vanadium-rich flora (Table 2).

Diluvial sands, gneiss, moor, peat and alluvial riverside soils deliver only 60% of the vanadium amount found in the vegetation of the Rotliegende [24].

The vanadium intake of humans

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 3).

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).

The vanadium intake shows no normal distribution between the two sexes (Figure 2). Nearly 50% of the men took in portions with 15 to 20 μg V/day, while the portions taken in by 8% of the men had very high vanadium contents (> 80 μg/day), due to their high consumption of beer. Women do not drink as much beer as men. Accordingly, 75% of women took in < 20 μg V/day, while only 1 % had an intake of > 80 μg V/day.

Nursing mothers (12.1 μg V/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. Ovolacto-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 of adult humans decreases with increasing age [24].

The vanadium content of feedstuffs and beverages

Generally, seeds, cereal products, bread, cake and pastries, tubers and fruits have, on average, a low vanadium content (5 to 40 μg/kg DM). Mushrooms, red radish, leafy vegetables (lettuce, spinach) as well as herbs contain much higher levels of vanadium (100-2.400 μg V/kg DM) (Table 4) [36, 37]. Animal foodstuffs deliver on average lower vanadium amounts in the food chains. Especially cow's milk (12 μg/kg DM, and cheese (3-14 μg/kg DM) provide lower vanadium amounts to humans. Breast milk (34 μg V/kg DM) contains more vanadium than cow's milk. Formulas for babies deliver 2 to 17 μg V/kg DM [38].

Beer, wine and sparkling wine are with 28 to 45 μg V/L extremely rich. Vanadium enrichment of beer has been traced to filtration with filters containing diatomaceous earth. White, red and sparkling wines are also rich in vanadium. The reason for this could be the use of unwashed grape of the one hand with dust from the environment and on the other hand the filtration with diatomaceous earth. Beer and wine have been found to be the main supplies of vanadium to man in Europe, supplying 75% (man) and 41% (women) of the daily intake, respectively on average. Thus, vegetable food supplies 17% (man) and 43% (women), and food of animal origin 8 and 16% of the vanadium intake of man and women, respectively [24, 36, 37, 38, 39].

Discussion

The daily vanadium intake of women and men on average of a week differ extremely and do not follow a Gaussion distribution, especially in men (Figure 2 and 3). Women without beer consumption took in < 15 μg V/day on the average of a week. These were 73% of tested population, whereas only 25% of the men consumed < 15 μg V/day. More than two third of the tested men consumed between 15 and 160 μg V/day on the average of a week.

Vanadium deficiency has not been investigated in humans. None of the men consumed on the average of a week < 5.0 μg V/day (Figure 3). On the average of a week men took in between 5.1 and 160 μg V/day. Women consumed in the same time between 3.6 and 77 μg V/day. If vanadium is an essential element for man the normative requirement of adult humans is < 5 μg/day.

In order to disentangle nutritional from pharmacological observations, it is necessary to identify the essential biochemical function of vanadium in higher animals and man. Both effects demands quite different amounts of vanadium (μg and mg/kg food DM).

For example, vanadium (III) and (IV) (and its low

Table 4 The vanadium content of foods (μg/kg dry matter, DM) and beverages (μg/L) (147 different feeds and beverages ; n 2090)

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

molecular weight V complexes) exhibited insulin - mimetic activities. Insulin-mimetic antidiabetic vanadium and V-(N) complexes are successful used for the treatment of diabetes mellitus type 2 non-insulin dependent [40]. Type 1 diabetes mellitus can be controlled only by daily injections of insulin, type 2 diabetes mellitus is treated by several therapeutics (V (III), V (IV), Zn (II), Mn (II) exhibited insulin-mimetic activities).

Vanadium compounds have also been shown to inhibit markedly the growth of humans tumor colony formation [41]. Vanadyl complexes of 1, 10-phenanthroline and related derivates develope strong antitumor activities [42].

In humans, the threshold level for vanadium toxicity is approximately 10 to 20 mg/day [1]. The dose of vanadium intake deciates above the appearing of deficiency symptoms, normal development, benefical effects and poisoning in animals and man.

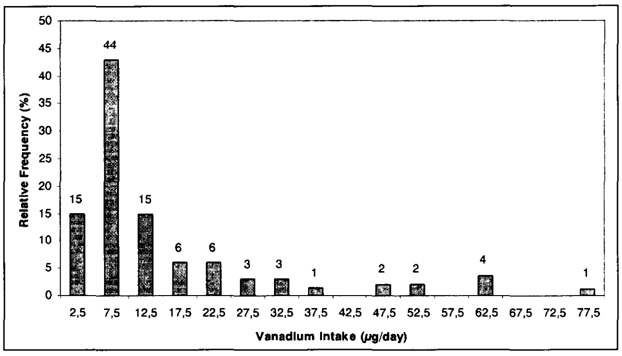

Figure 2 Frequency distribution of vanadium intake of women

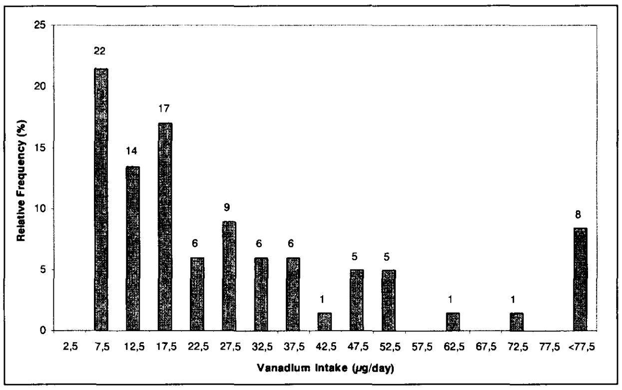

Figure 3 Frequency distribution of vanadium intake of men

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