The Toxicology of Sulphur and Nitrate in Ruminants

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Sulfur, in either its inorganic or organic forms is essential in the diets of ruminants. Many studies have shown that ruminants require no more than 0.2% dry matter total sulfate sulfur in their rations to satisfy rumen microbial protein synthesis and tissue sulfur needs. In most instances ruminants receive adequate quantities of sulfur from a balanced ration, and supplementing the element is not necessary. Total sulfate intake that exceeds 0.3% dry matter has potential to decrease feed intake and cause either direct or indirect toxicities.

Sulfur Metabolism

Sulfur and its compounds are very rapidly reduced in the rumen to sulfide [sulfate (SO_4)>>sulfite (SO_3)>>sulfide (S_2)]. The optimum pH for this reduction is around 6.5. It is the sulfide that is readily absorbed across the rumen wall. Sulfates are not absorbed in the rumen but are absorbed to some extent (30-40%) in the intestine. Sulfur containing amino acids (methionine and cysteine) is also reduced to sulfide in the rumen, and therefore contributes to the total sulfides available for absorption. Rumen microorganisms incorporate sulfide in protein synthesis, but when in excess, sulfide inhibits cellulose digestion by these organisms. Adequate dietary sulfur also enhances non-protein nitrogen (urea) utilization in the rumen.

Once absorbed sulfur is incorporated in sulfur containing amino acids (cysteine, cystine, cystathionine, and methionine). Deficiency of sulfur and therefore the S-containing amino acids results in abnormal keratinization of hooves, hair and wool. The latter may contain up to 4% sulfur. Muscle and brain contain 0.25% and 0.5% sulfur respectively. Vitamins, biotin and thiamine, essential in lipid and energy metabolism also require sulfur. Sulfur is also important in the thiosulfate (S_2O_3) binding and detoxification system of cells. Insulin, glutathione, and hemaglobin incorporate sulfur in their structures, as does chondroitin sulfate, an important component of cartilage. Animals therefore, deficient in sulfur generally show signs of poor growth and wasting.

Paper presented at the American College of Veterinary Internal Medicine's Third Annual Medical Forum, June 1-5, 1985 in San Diego, CA. Published by kind permission of the Proceedings Editors.

Sulfur Toxicity

Direct toxicity of sulfur in ruminants rarely occurs naturally. The feeding of "self limiting" rations containing 2% gypsum ($CaSO_42H_2O$) has been associated with toxicity, especially if the total dietary intake of sulfate exceeds 2% of the ration. Sulfates can also be a problem where livestock are allowed to drink water from wells containing in excess of 2500 ppm of sulfate (see Table 1).

Excessive sulfide production in the rumen can result in the rapid build-up of toxic hydrogen sulfide (H_2S) gas. Sheep experimentally dosed with high levels of sulfate intraruminally collapsed and died due to the effects of H_2S on the central nervous system. Since the liver efficiently removes H_2S absorbed into the portal vasculature, toxicity of H_2S in ruminants is apparently due to the eructation and inhalation of H_2S produced in the rumen.

A more common manifestation of sulfate toxicity in cattle appears to be the development of polioencephalomalacia (PEM) when cattle are fed rations containing in excess of 2% sulfate. Rumen sulphite destroys thiamine produced by rumen microflora. However this apparent sulfate induced PEM is not simply attributable to thiamine deficiency, since treatment with thiamine is not always effective. The PEM lesions in the brain may be the cumulative effects of decreased thiamine, sulfate induced copper deficiency, and H_2S toxicity. A water deprivation/salt toxicity problem may also be a factor in sulfate toxicity since cattle frequently develop this PEM syndrome during the summer, when water requirements are maximum. The high sulfate content of many wells makes the water unpalatable and cattle develop a water deprivation syndrome that may produce malacia of the brain. Other sources of sulfate with potential for toxicity in ruminants include zinc sulfate foot baths used in treating foot rot, sulfur treatment for fungal and parasitic dermatitis and industrial pollutants.

The Effects of High Dietary Sulfate on Other Trace Minerals

High levels of sulfate (>.4%) in high protein diets of ruminants can produce copper deficiency through the formation of cupric sulfide which is poorly absorbed across the rumen. High levels of molybdenum (MO>5 ppm) in the presence of low or marginal dietary copper (<5 ppm) also result in copper deficiency owing to the antagonistic effect of

Mo on copper at the intestinal cells' brush border. In the event that the diet contains adequate copper, but high levels of both Mo and sulfur, the sulfate may overcome the effects of Mo, since they both require the same carrier for absorption across the cell membranes. This seems to be especially true at the distal renal tubules where sulfate competes with Mo for reabsorption. In general, though, high Mo and S in the diet induce a copper deficiency state. Secondary copper deficiency can also be induced by high levels of dietary zinc, iron, lead, and calcium carbonate. Conversely, the addition of selenium (Se) to the diet in copper deficient areas appear to enhance copper intake. High levels of dietary sulfate inhibits Se absorption to the pont of causing muscular dystrophy.

Clinical Signs of Excess Dietary Sulfur

Ruminants with acute sulfur toxicity may show signs that vary from anorexia, rumen atony and watery diarrhea, to colic, respiratory distress and death. These effects are probably due to the action of H_2S on the CNS. Deaths may also result from vascular necrosis of the rumen and abomasum. A watery black diarrhea due to the presence of sulfides and the smell of H_2S on the breath of poisoned animals is often characteristic.

In less acute cases of sulfate poisoning, signs of polioencephalomalacia and secondary copper deficiency may predominate. Cattle that chronically consume water with sulfate levels in excess of 2500 ppm show depression, blindness, diarrhea, dysphagia with food held in the mouth and sometimes sudden death. Where secondary copper deficiency exists signs of anemia, diarrhea, lameness due to osteoporosis, achromatrichia, infertility and poor growth rates may be superimposed on the signs of sulfate toxicity.

Diagnosis

A diagnosis of sulfate toxicity in ruminants can be made by showing a total daily intake of sulfate greater than 0.4% of the ration. This will require analysis of both feed and water sulfate-sulfur levels. Serum and liver copper levels should be evaluated when sulfate levels are high or clinical signs are suggestive of hypocuprosis.

TABLE 1. Dietary Mineral Levels for Ruminants

	Acceptable Dietary Levels (Dry Matter)	Potentially Toxic Feed Levels	Normals (ppm) Blood	Liver
Sulfate sulfur	0.2%	>0.4%		
Copper (Cu)	20-50 ppm	>100 ppm*	.6-1.3	Sheep 200-500 Cattle 100-1000+
Molybdenum (Mo)	2-3 ppm	>5-10 ppm*	<.05	<3-4
Zinc	20-40 ppm	>500 ppm	.8-1.2	

*The Cu:Mo ratio should be 2:1 in the diet of ruminants to prevent deficiency or toxicity of copper.

ppm = mg/kg = mg/liter = ug/ml

TABLE 2. Upper Safe Levels in Livestock Water (ppm).

Sulfate	2500 (total intake of food + water must be considered in determining toxic levels)
Copper	1 (unpalatable above this level)
Zinc	15 (joined galvanized and copper pipes)
Total dissolved solids (TDS)	< 7000 - upper limits should not be used for pregnant, lactating or young livestock
	>7000 - generally unacceptable for livestock especially in hot environments

REFERENCE
Nutrient Requirements of Beef Cattle. 6th edition, 1964.
Mineral Tolerance of Domestic Animals. NRC, 1980.

Nitrate Toxicity in Ruminants

Nitrate (NO_3) poisoning continues to be a problem for livestock because of the heavy use of nitrogen fertilizers to increase crop yields to meet animal production needs. High levels of NO_3 in plants and water sources are the primary cause of acute NO_3 poisoning in ruminants. Severe economic losses occur as a result of sudden deaths and abortions in ruminants consuming high levels of NO_3 in their diet. However, there is considerable variation in the quantity of NO_3 in the diet that will cause acute poisoning because various factors affect a ruminant's ability to tolerate and adapt to NO_3 in its diet. There is little if any evidence to substantiate a diagnosis of chronic nitrate poisoning in ruminants.

Factors Affecting Nitrate Accumulation in Plants

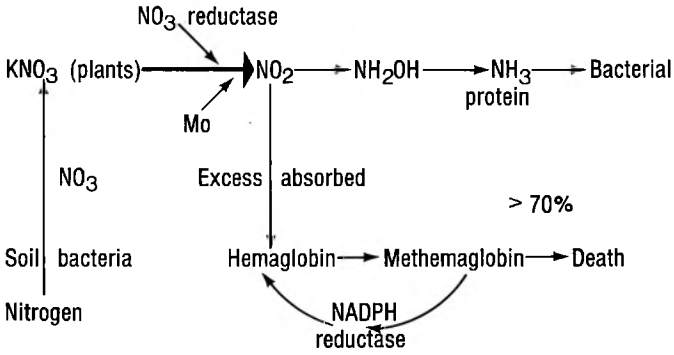
Plants primarily absorb NO_3 from the soil. The amount of NO_3 in soil is influenced by nitrogenous fertilizers and the amount of decaying organic material present in the soil. Nitrate uptake by plants is enhanced by the presence in the soil of water, an acidic pH, and low levels of molybdenum, phosphorus and sulfur. Young rapidly growing plants usually contain more NO_3 than do mature plants. Nitrate is absorbed by the plant roots and is transported to the leaves, where in the presence of sunlight it is reduced by photosynthesis to amino acids and plant protein. Plant stems contain the greatest quantities of NO_3 especially at night, under cloudy or shady conditions, and whenever there is a decreased leaf surface area as may occur following hail storms, frost, plant diseases, etc. Plants that are stressed or are treated with herbicides also accumulate more NO_3.

All plants can accumulate nitrate to varying degrees, but some common species of weed (Kochia weed, Amaranthus, Chenopodium, Helianthus, Salsola, Cirsium, Rumex, etc.) and certain crop plants (oats, corn, alfalfa, sweet clover, sorghums, soybeans) will accumulate potentially toxic levels of NO_3, especially if fertilized.

Other than NO_3 of plant origin, livestock may be poisoned by water that is contaminated with NO_3,. Shallow wells, collection ponds for run-off water, sewage water, etc., can have toxic amounts of nitrate and nitrite.

Nitrate Toxicity

Ruminants are more susceptible to NO_3 poisoning than monogastric animals because rumen microflora readily convert nitrate to toxic nitrate (NO_2) in the reduction process of forming bacterial protein (Fig 1).



Nitrate poisoning is the product of NO_3 and NO_2 consumed in the feed and water. The quantity of NO_3 that will cause poisoning in ruminants is variable and depends on: a) the rate of NO_3 consumption, b) the type of feed, c) the amount of carbohydrate in the ration, and d) the stage of adaptation to NO_3 in the diet. The LD 50 for a single oral dose of NO_3 in cattle and sheep has been found to be 0.5 gm KNO_3/kg body weight. In reviewing the literature the quantity of NO_3 causing toxicity ranges from 15 gm to 45 gm of KNO_3/CWT orally. In general, daily NO_3 consumption in ruminants should be <2% dry matter of the total ration. Ruminants that are receiving grain or other available carbohydrates can tolerate much higher quantities of NO_3 than those animals on poor quality forages. Tolerance also develops if ruminants are gradually fed increasing amounts of NO_3 on a daily basis. The addition of recommended doses of monensin to rations high in NO_3 may precipitate poisoning because it increases NO_2 producing rumen bacteria.

Nitrite, often present in water, is about 2.5 more toxic than NO_3 in ruminants, and about 10 times as toxic as NO_3 in monogastric animals.

Effects of Nitrate on Animals

Toxic levels of NO_3 (>2% dry matter) leads to a rapid build-up of NO_2 in the rumen, which is absorbed into the blood oxidizing ferrous iron to ferric iron (Fe+++) to form methemaglobin. Signs of hypoxia develop when 20-30% of the hemaglobin is converted to methemaglobin. Death results when there is 70-80% methemaglobin. Fetal death and abortion occurs only when near fatal levels of methemaglobin develop in the dam. High levels of NO_3 in the ration do not induce vitamin A deficiency, when the ration is correctly balanced. Similarly claims that NO_3 will cause hypothyroidism are not substantiable when the ration contains adequate iodine. Nitrate up to 3% of the total ration has been shown to have no effect on feed consumption, weight gain or milk production so long as the cattle were on a balanced high energy and protein ration. Reduced reproductive performance in cattle on high NO_3 feeds (>2% intake) is also unfounded when a balanced ration is fed.

Chronic NO_3 or NO_2 poisoning is unlikely since ruminants efficiently utilize NO_3 in the rumen for bacterial protein production.

Diagnosis of NO_3 and NO_2 Poisoning

A diagnosis of NO_3 poisoning should be confirmed by demonstrating significant levels of NO_3/NO_2 in the forage consumed, rumen contents, water and serum. Aqueous humor is also useful for NO_3 analysis if the carcass is too autolyzed. It is important to calculate the total nitrate-nitrite intake in both the food and water in order to establish poisoning.

NITRATE CONVERSION FACTORS

NO = nitrate-nitrogen (NO -N) × 4.45
NO = nitrate-nitrogen (NO -N) × 3.29
NO = KNO × 0.6
PPM = % NO × 10,000
% NO = PPM × 0.0001
PPM = mg/kg = mg/L

RECOMMENDATIONS FOR FEEDING FORAGES CONTAINING NO_3*

% NO Dry Matter Basis	NO mg/kg Dry Matter	Comment
Below .44	4400	Safe to feed
.44-.66	4400-6000	Safe to feed nonpregnant animals. Limit its use for pregnant animals to 50% of the total ration.
.66-.88	6600-8800	Safe if limited to 50% of the total dry matter in the ration.
.88-1.54	8800-15,400	Limit forage to 35% total dry matter of the ration.
1.54-1.76	15,400-17,600	Limit forage to 25% total dry matter of the ration. Not for pregnant animals.
Over 1.76	17,600	Potentially toxic to ruminants.

ACCEPTABLE NO LEVELS IN WATER*

	NO mg/L (ppm)	NO -N mg/L
Cattle/sheep	445	100
Pigs	934	207
Man	45	10

*Toxicity may occur at lower levels if animals are not fed a balanced energy-protein ration.

REFERENCE

1. Nutrients and toxic substances in water for livestock and poultry. National Academy of Science, Washington, DC, 1974.
2. Accumulation of Nitrate. National Academy of Sciences, 1972.