



P-ISSN: 2349-8528

E-ISSN: 2321-4902

IJCS 2018; 6(5): 1559-1561

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Received: 11-07-2018

Accepted: 15-08-2018

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Understanding cyanogenic glycoside toxicity in livestock: A review

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Abstract

Ingestion of high concentrations of cyanogenic glycosides from cyanophoric plants has resulted in mortality in numerous species of animals. Death has been reported more in grazing and browsing animal species such as cattle, sheep, and goats than in those usually kept under intensive system of management like pigs and poultry. This is because it's possible to consume larger doses of the glycosides from fresh, cyanophoric plant materials than in processed products usually given to pigs and poultry. Under certain conditions, several plants can accumulate large quantities of cyanogenic glycosides which upon ingestion convert to prussic acid. The risk of prussic acid poisoning in livestock is substantially increased during periods of drought, and drought breaks, when stressed, stunted plants begin to grow. Prussic acid is a potent poison, once ingested, it enters the bloodstream of affected animals and is transported throughout the body. It then inhibits oxygen utilisation by disrupting the electron transport chain (ETC) of the mitochondria, so that the animal dies from asphyxia. The present review article is an attempt to understand the multiple facets of cyanide toxicity in livestock and the possible mitigation strategies.

Keywords: cyanogenic glycoside, prussic acid poisoning, HCN

1. Introduction

Glycosides in general are compounds that consists of a carbohydrate moiety (sugar) attached by an ester bond to a non-carbohydrate moiety (referred to as aglycone). The structure and/or properties of the aglycone moiety are used to identify the glycosides. Various examples are Saponins, Cyanogens, Glucosinolates, Vicine and Convicting. The cyanogenic glycosides may be defined chemically as glycosides of the α -hydroxynitriles and is a secondary metabolites of plants. They are amino acid-derived plant constituents. The biosynthetic precursors of the cyanogenic glycosides in plants are the different L-amino acids, which are hydroxylated to form N-hydroxylamino acids which are then converted into nitriles and are further hydroxylated and glycosylated to form cyanogenic glycosides (Vetter, 2000) [2]. All known cyanogenic glycosides are β -linked, mostly with D-glucose. In animals they are not toxic unless hydrolyzed by dilute acids, plant enzymes or rumen microorganisms to form free HCN. Cyanide toxicity is also called as Prussic Acid Poisoning. The β -glucosidases enzymes are found in plant cytoplasm, while glycosides are stored in plant vacuoles, any damage from chewing or wilting allows the contact of the enzyme with its substrate and subsequently broken down to form HCN. The conversion of cyanogens to HCN is enhanced when there is damage to plant cell (crushing, mastication, wilting or freezing stress). Leaves of cherry, cyanogenic acacia species and young sorghum leaves have frequently caused death in grazing animals.

2. Incriminating sources

There are at least 2650 species of plants that produce cyanogenic glycosides (Cheeky and Peter, 1989). These plants also possess a corresponding hydrolytic enzyme (β -glycosidase), which are brought together when the cell structure of the plant is disrupted by a predator, with subsequent breakdown to sugar and a cyanohydrin, which rapidly decomposes to hydrogen cyanide (HCN) and an aldehyde or a ketone (Hosel, 1981; Moller and Seigler, 1999) [3, 7]. The glycosides, cyanohydrins and hydrogen cyanide are collectively known as cyanogens. This combination of cyanogenic and hydrolytic enzyme is the means by which cyanogenic plants are protected against predators (Moller and Seigler, 1999) [7]. The best characterized

cyanogenic glucoside is amygdalin which is present especially in the seeds and leaves of the cherry, almond, peach, etc. Cherry kernels yield about 170mg/100 g and bitter almond pulps contain about 250mg/100 g (Ashraf *et al.*, 2010) [1]. Various sources of Cyanogenic glycosides are presented in Table 1, 2 and 3.

Table 1: Different Cyanogenic glycosides and their plant sources
Adapted from Merks veterinary manual

S.No	Cyanogenic Glycoside	Common name of plant	Latin name (Plant)
1	Linamarin	Lima beans	<i>Phaseolus lunatus</i>
		Cassava	<i>Manihot</i>
2	Amygdalin	Almonds	<i>Prunus amygdalin</i>
3	Dhurin	Sorghum	<i>Sorghum album</i>
			<i>Sorghum bicolor</i>
4	Taziphyllum	Bamboo shoots	<i>Sambusa vulgaris</i>
5	Prunacin	Stone fruits	<i>Prunus spp</i>

Table 2: Cyanogenic plant families and their species

Family	Plants Species
Poacea	Sorghum (<i>Sorghum bicolor</i>)
	Johnson grass (<i>Sorghum halapense</i>)
	Sudan grass (<i>Sorghum vulgare</i>)
Fabaceae	Lima beans (<i>Phaseolus vulgaris</i>)
Caprifoliaceae	Sambucus or Elderberry (<i>Sambucus nigra</i>)
Euphorbiaceae	(<i>Manihot esculenta</i> [Cassava])
Rosaceae	Bitter almond (<i>Prunus amygdalus</i>)

Adapted from Merks veterinary manual

Table 3: Types of plants with cyanogens and their examples

Plant type	Examples
Grains, forage crops, and grasses	Corn, flax, Sorghum, Sudangrass, Arrow grass, Velvet grass, White clover, Indian grass, Birdsfoot trefoil, Johnson grass
Trees	Apricot, Peach, Cherry, Chokecherry, Elderberry, Apple, Wild black cherry
Landscape and house plants	Eucalyptus, Hydrangea

Adapted from Merks veterinary manual

They are also found in food sources for humans viz; Sorghum (*Sorghum spp.*), Corn (*Zea mays*), Clovers (*Trifolium spp.*) and Cassava (*Manihot esculenta*). Poorly prepared diets (Improperly boiled) often leads to tropical ataxic neuropathy, pancreatic lesions and hypothyroidism.

3. Mechanism of intoxication

Cytochrome C oxidase is the final electron carrier protein in the electron transport chain. Cyanide uncouples (inactivates) cytochrome C oxidase in mitochondria. As a consequence, the electron transport chain is disrupted, meaning that the cell can no longer aerobically produce ATP for energy (95% of the energy produced by the body comes from aerobic respiration). Tissues that mainly depend on aerobic respiration, such as the central nervous system and the heart, are particularly affected. Cyanide causes an increase in blood glucose and lactic acid levels and a decrease in the ATP/ADP ratio indicating a shift from aerobic to anaerobic metabolism. Cyanide activates glycogenolysis and shunts glucose to the pentose phosphate pathway decreasing the rate of glycolysis and inhibiting the tricarboxylic acid cycle. Hydrogen cyanide will reduce the energy availability in all cells, but its effect will be most immediate on the respiratory system and heart. Although the liver cytochrome oxidase is not inhibited by cyanide, the brain

cytochrome is supposed to be the site of lethal action (Oslen and Klein, 1947) [8].

4. Toxicity

The lethal dose of HCN for cattle and sheep is about 2.0 mg/kg of body weight (Kingsbury 1964) [5]. Tolerance to levels of HCN in livestock is given in Table 4.

Table 4: Livestock tolerance to levels of prussic acid in feed (dry matter basis)

Prussic acid (HCN) ppm	Effect on livestock
Less than 500	Generally considered safe
From 500 to 750	Potential for toxicity exists, thus should not be the sole source of feed
Greater than 750	Dangerous and will cause death

Adapted from Merks veterinary manual

5. Ruminants' vs non-ruminants (extent of toxicity)

Ruminants are more susceptible than non-ruminants due to high pH of rumen (around 7). High water content in rumen and due to presence of Rumen microflora. All these factors combine to promote hydrolysis of glycosides to HCN. The microbial hydrolysis of β -D-glucosides such as Miserotoxin or Prunacin occurs very slowly in the digestive tract of non-ruminants, so the intact glycoside is usually absorbed. This accounts for the lower toxicity of glycoside in non-ruminants than in ruminants

6. Clinical signs

Livestock show symptoms within minutes of ingesting feed containing prussic acid which include:

1. Excitement, tachypnoea, dyspnoea, salivation, staggering, and collapse.
2. Sudden death and cherry-red discoloration of venous blood
3. Death resulting from asphyxiation, usually occurs within 30 to 45 minutes after onset of symptoms.

7. Diagnosis

To ensure a successful treatment, the livestock owners should obtain a swift and accurate diagnosis in consultation with a veterinarian. Cyanide analysis should be performed on the questionable feeds or the contents of animal's rumen or stomach. Differential diagnosis is important because many of the clinical signs of prussic acid poisoning are similar to those of nitrate poisoning.

Some of the distinguishing characteristics which to help differentiate between prussic acid and nitrate poisoning are; Nitrate poisoning causes the animal's tongue and eyes to turn blue (cyanotic mucus membranes) and its blood to turn dark chocolate brown, whereas in Cyanide toxicity, HCN causes the animal's blood to turn a bright cherry red (Krantz 2011) [6]. Providing sodium nitrite to animals suffering from nitrate poisoning could make the condition worse. To perform an accurate chemical analysis that leads to a correct diagnosis, quality testing of samples is therefore very important.

Prussic acid levels are reported to increase in plants during the morning hours and the highest content is present in leaves (Whittier 2011) [14]. In order, to obtain a good sample, it is best to sample leaves. The sample must remain fresh. Drying of sample causes loss of prussic acid (Volatile). Airtight containers, such as a plastic bag, freeze the sample, can be used for shipment to the testing lab in a cooler with an ice pack via overnight express (Sulc, 2012) [10].

8. Treatment

The antidote of cyanogenic glycoside toxicity is the sodium nitrite (NaNO₃) injection. It converts a portion of the haemoglobin's iron from ferrous iron to ferric iron, thus converting the haemoglobin into Methemoglobin. As such cyanide is more strongly drawn to methemoglobin than to the Cytochrome C Oxidase of the cells, thus it is effectively pulled off the cells and onto the methemoglobin. Once bound with the cyanide, the Methemoglobin becomes Cyanmethaemoglobin.

The next part of the cyanide antidote kit is sodium thiosulfate, which is administered intravenous. The sodium thiosulfate reacts with cyanmethaemoglobin in presence of Rhodinase enzyme (or thiosulfate sulfotransferase is an enzyme widely distributed in animal tissues). It converts Cyanide of cyan meth HB into thiocyanate, releasing the haemoglobin, and then thiocyanate is finally excreted by the kidneys via urine. Method of treatment is as follows

1. IV administration of 2.2 ml of 20% solution of sodium nitrite plus 6.6 ml of 20% solution of sodium thiosulfate
2. Give this mixture intravenous per 100kg BW
3. Repeat in a few minutes if animal doesn't respond

9. Management points

Due to the severity of HCN poisoning and the potential economic loss, prevention is the best approach. The following list provides some preventive measures.

1. Animals should not be allowed to graze on Sorghum and Sudangrass when they are in an immature state. (Forages should have to attain a height of 15 to 18 inches before grazing).
2. New varieties of Sudan grass and sorghum x Sudan grass with lower cyanogenic content should be considered when selecting seed.
3. Ensure that animals have been provided sufficient feed, such as hay, and are not hungry when they enter fresh pastures. This will reduce the amount of prussic acid consumed and allow more time for the animal to detoxify low levels of HCN.
4. Take care to ensure that animals have no access to affected fruit and shade tree leaves when they are allowed to inhabit areas adjacent to orchards and landscape plants. (Risk increases when only limited feed is available, resulting in animals being more attracted to nearby leaves).
5. Depending on the initial level of prussic acid, processing, such as chopping, haying, or ensiling, allows the prussic acid to volatilize, thus reducing it to acceptable levels in the feed. Though, only laboratory testing can confirm these levels.
6. Drying of young leaves that are usually highest in HCN reduces toxicity.
7. Ensiling Reduces toxicity as HCN is liberated during curing
8. Feeding of plant parts during drought or stressful conditions should be avoided.
9. Don't graze animals on plants with HCN in early growth stages, after cutting, or after frost or after wilting
10. Test forages for HCN before grazing if uncertain
11. Cure hay before feeding

10. Conclusions

Cyanogenic glycosides poses a potential health hazard to animals. Proper feeding management can avert the susceptibility of animals to prussic acid poisoning thereby

reducing mortality and economic losses. Timely accurate diagnosis and treatment in the event of poisoning can help to save animal life and the livestock owners from suffering losses.

11. References

1. Ashraf M, Ahmad MSA, Ozturk M. eds. Plant adaptation and phytoremediation. New York, NY: Springer, 2010.
2. Cheeke, Peeter R, Toxicants of Plant Origin, 2010, 2. Glycosides. Florida. Library of Congress Cataloguing-in-Publication Data, (ISBN 0-8493-6691-6), 1989, 43-58.
3. Hosel W. The enzymatic hydrolysis of cyanogenic glucosides. In B. Vennesl and, E. E. Conn, C. J. Knowles, J. Westley, and F. Wissing (Eds.), Cyanide in biology. London: Academic Press, 1981, 217-232.
4. Kerr SR. Selected Poisonous Plants of the Pacific Northwest. Washington State University Extension Publication 1007-2005. <http://www.animalag.wsu.edu/forages/Kerr-PoisonousPlants1007-2005.pdf>, 2005.
5. Kingsbury JM. Poisonous Plants of the United States and Canada," Prentice-Hall, Englewood Cliffs, New Jersey, 1964.
6. Krantz J. Nitrate Poisoning: Symptoms Resemble Those of Prussic Acid. South Dakota State University Extension Publication, 2011. <http://igrow.org/livestock/beef/nitrate-poisoning-symptoms-resemble-those-of-prussicacid/>.
7. Moller BL, Seigler DS. Biosynthesis of cyanogenic glycosides, cyanolipids and related compounds. In B.K. Singh (Ed.), Plant amino acids biochemistry and biotechnology, 1999, 563-609.
8. Olsen NS, Klein JR. Effect of cyanide on the concentration of lactate and phosphates in brain. Journal of Biological Chemistry. 1947; 167(3):739-746.
9. Rawat Kanchan, Nirmala C, Bisht MS. Processing Techniques for Reduction of Cyanogenic Glycosides from Bamboo Shoots. 10th World Bamboo Congress, Korea, 2015.
10. Sulc M. Testing for Prussic Acid Content in Forages. CORN. Newsletter-32. Crop Observation and Recommendation Network. Ohio State University Extension, 2012. <http://corn.osu.edu/newsletters/2012/2012-32>.
11. Tewe OO, Maner IH. Performance and pathophysiological changes in pregnant pigs fed cassava diets containing different levels of cyanide. Research in Veterinary Science. 1981a; 30:147-151. Marcel Dekker.
12. The Merck Veterinary Manual. Cyanide Poisoning in Livestock. Available Online at http://www.merckmanuals.com/vet/toxicology/cyanide_poisoning/overview_of_cyanide_poisoning.html?qt=cyanide_poisoning_in_livestock&dalt=sh.
13. Vetter J. Plant cyanogenic glycosides. Toxicon. 2000; 38(1):11-36.
14. Whittier JC. Prussic Acid Poisoning. Colorado State University Extension Publication No. 1.612. <http://www.ext.colostate.edu/pubs/livestk/01612.html>, 2011.