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Environmental stress, sorghum cyanogenic potential, and systemic cyanide toxicity risk in ruminants: A review

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Abstract

This review aims to develop an integrated framework for understanding cyanide toxicity risk in sorghum-based ruminant production systems by linking plant cyanogenic potential with ruminal detoxification capacity under environmental stress conditions. Relevant peer-reviewed studies on dhurrin biosynthesis, environmental modulation, ruminal cyanide detoxification, pathophysiology, clinical manifestations, and mitigation strategies were critically synthesized to construct a systems-based risk perspective. Dhurrin accumulation is strongly influenced by genotype, growth stage, nitrogen fertilization, and drought stress. Environmental factors, such as temperature fluctuations, soil nutrient status, and plant physiological responses, may further modify cyanogenic potential and influence variability in hydrogen cyanide (HCN) concentration in sorghum tissues. Toxicity in ruminants depends not only on forage HCN concentration but also on the interaction between ruminal HCN release and sulfur-mediated detoxification pathways. Once absorbed, cyanide inhibits mitochondrial cytochrome c oxidase, leading to impaired oxidative phosphorylation and systemic hypoxia. Variability in clinical outcomes reflects differences in intake patterns, nutritional status, rumen microbial activity, and detoxification capacity. Cyanide risk in sorghum–ruminant systems is a product of coordinated plant, environmental, and animal factors rather than a static concentration threshold. Integrated strategies involving genetic selection, agronomic management, feed processing, nutritional balance, monitoring, and clinical preparedness are essential to ensure safe and sustainable sorghum utilization.

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Introduction

Sorghum (*Sorghum bicolor L. Moench*) is an important cereal and forage crop in ruminant production systems, particularly in dry tropical and subtropical regions (1,2). The crop exhibits high drought tolerance, uses water efficiently, and produces substantial biomass on marginal land. These characteristics make sorghum a strategic forage resource for maintaining feed availability under conditions of climate variability and limited agricultural inputs (3–6).

Despite these agronomic advantages, sorghum forage carries a recognized toxicological risk due to the presence of cyanogenic compounds, primarily the cyanogenic glycoside dhurrin (7–11). Dhurrin plays an important role in plant

defense against herbivores and environmental stress (12–14). Under certain conditions—including early vegetative growth, drought stress, nutrient imbalance, or tissue damage—dhurrin may be enzymatically hydrolyzed, releasing hydrogen cyanide (HCN). Hydrogen cyanide is a potent respiratory toxin capable of causing acute poisoning in ruminants (15–17).

Numerous cases of cyanide poisoning associated with sorghum forage have been reported across diverse livestock production systems (10,18–22). Common risk factors include young plant growth stages, environmental stress conditions, and inappropriate feeding management. Ruminants are particularly susceptible compared with monogastric animals because ruminal fermentation facilitates rapid hydrolysis of cyanogenic glycosides and accelerates HCN release (10,23). Clinical signs may develop quickly and can lead to severe outcomes or sudden death if treatment is delayed (18,19,21,22).

In practical feeding systems, cyanide toxicity risk is often assessed using a threshold concentration of hydrogen cyanide (HCN) in forage. Guidelines from Purdue University and Kansas State University classify 500–750 ppm HCN (dry matter basis) as potentially toxic, while concentrations exceeding 750 ppm are considered highly hazardous (24). However, field observations indicate that clinical poisoning does not always correspond strictly to these fixed threshold values. This inconsistency suggests that cyanide concentration alone is insufficient to fully explain toxicity risk. Instead, toxicity risk likely depends on the interaction between cyanide release from plant tissues and the detoxification capacity of ruminants under specific environmental and management conditions.

Research on sorghum has clarified many aspects of dhurrin biosynthesis, genetic regulation, and environmental modulation (25–28). At the same time, veterinary and toxicology studies have described the physiological mechanisms and clinical consequences of cyanide exposure in ruminants (18,23). However, these two research domains are often addressed independently. As a result, the mechanistic links between plant metabolism, environmental stress responses, ruminal detoxification dynamics, and systemic toxicity remain insufficiently integrated.

This review integrates these elements into a unified system-based framework. Specifically, this review examines dhurrin biosynthesis and regulation, environmental and genetic influences on cyanogenic potential, mechanisms of cyanide release and ruminal detoxification, and the clinical manifestations of cyanide toxicity in ruminants. By integrating plant and animal perspectives, this review aims to clarify how cyanide risk develops in sorghum-based feeding systems and to support safer and more sustainable forage management under environmental stress.

Materials and methods

This review was conducted using a structured narrative review approach to synthesize current knowledge regarding cyanogenic potential in sorghum and cyanide toxicity risk in ruminants. Peer-reviewed articles published between 2015 and 2026 were primarily included to ensure recent scientific relevance, although several earlier foundational studies were also incorporated when they provided important mechanistic and physiological insights.

Literature searches were performed using the Scopus, Web of Science, and PubMed databases. Search terms included combinations of keywords related to *sorghum*, *dhurrin*, *cyanogenic compounds*, *hydrogen cyanide (HCN)*, *cyanogenic glycosides*, *ruminal detoxification*, *sulfur metabolism*, *environmental stress*, *drought stress*, *plant maturity*, *genotype*, *plant parts*, and *cyanide toxicity in ruminants*. References cited in key articles were also manually screened to identify additional relevant studies.

This study was designed as a structured narrative review rather than a formal systematic review or meta-analysis. Therefore, the literature selection process remained iterative, allowing additional relevant studies to be incorporated during manuscript development based on thematic relevance and contribution to mechanistic understanding.

Studies were selected based on their relevance to one or more of the following aspects: (1) physiological regulation and biosynthesis of dhurrin in sorghum; (2) environmental and agronomic factors influencing cyanogenic potential, including drought stress, fertilization, genotype, plant maturity, and plant parts; and (3) cyanide detoxification mechanisms and toxicity responses in ruminants. Studies lacking direct relevance to cyanogenic compounds in sorghum or cyanide metabolism in animals were excluded.

The selected literature was qualitatively synthesized to evaluate how plant metabolism, environmental conditions, processing practices, and animal physiological responses interact to determine cyanide toxicity risk under practical feeding conditions. In addition, reported HCN concentrations from selected studies were compiled into a comparative summary table. Extracted data were categorized according to genetic, growth-related, agronomic, environmental, biotic stress, and processing factors to facilitate comparative interpretation of cyanogenic responses across studies. Where possible, HCN values were standardized to mg/kg dry matter to facilitate cross-study comparison across different cultivars, environmental conditions, plant parts, growth stages, and processing methods.

The synthesized evidence was subsequently interpreted to develop a more dynamic risk-based perspective on cyanide toxicity in sorghum, emphasizing the interaction between cyanogenic potential and ruminal detoxification

capacity rather than reliance solely on fixed HCN threshold values.

Results and discussions

Cyanogenic glycosides in plants

Cyanogenic glycosides are widely distributed plant secondary metabolites that store a cyanide moiety in a chemically stable glycosidic form. Upon tissue disruption, enzymatic hydrolysis can liberate hydrogen cyanide (HCN), constituting a rapid, inducible chemical defense mechanism (29).

HCN release is typically initiated when cyanogenic glycosides contact β-glucosidase following cell disruption, yielding a cyanohydrin intermediate that subsequently decomposes to HCN and a corresponding carbonyl compound (13). Released HCN inhibits aerobic cellular respiration in herbivores and pathogens, thereby limiting tissue loss and deterring further attack.

The defensive deployment of cyanogenic glycosides is tightly regulated. For example, studies on linamarin indicate that bioactivation potential can be maintained across the diurnal cycle even when biosynthesis flux varies, consistent with rapid transcriptional reprogramming of genes that enable plants to adapt abiotic and biotic stressors (6,30-33).

Beyond deterrence, cyanogenic glycosides have been implicated in broader plant metabolic functions, including roles in reactive oxygen species (ROS) buffering. They also serve as temporary reservoirs of reduced nitrogen and carbon that may be remobilized during early development or stress recovery.

Major cyanogenic glycosides include dhurrin in sorghum, linamarin and lotaustralin in cassava, taxiphyllin in young bamboo, and amygdalin in bitter almond (34). Concentrations vary among species, plant organs, and developmental stages, reflecting a trade-off between defensive capacity and resource allocation.

The role of dhurrin in sorghum growth and adaptation

Dhurrin is the predominant cyanogenic glycoside in sorghum and contributes to both inducible defense and nitrogen storage, particularly during early growth (7,8,35,36). Elevated dhurrin levels in seedlings suggest functional importance prior to fully established photosynthesis. During this stage, dhurrin can serve as a temporary nitrogen reserve, supporting early development.

Transcriptomic studies indicate that dhurrin biosynthesis increases in response to herbivore attack, including aphids, in coordination with stress signaling pathways and other secondary metabolites (14). Dhurrin, therefore, acts as an inducible defense metabolite; however, elevated dhurrin levels can increase cyanogenic risk potential when sorghum is used as forage, creating a direct trade-off between plant protection and ruminant feed safety.

The significance of dhurrin for agronomic adaptation remains context-dependent. Several dhurrin-deficient mutants exhibit reduced early vigor (15,37,38). Dhurrin reduction does not always compromise plant survival, but its effects vary with developmental stage and magnitude of stress exposure.

Dhurrin accumulation has also been associated with adaptation to dry and climatically unstable environments and may act as a remobilizable nitrogen pool during post-stress recovery (36,39,40). Overall, dhurrin represents a multifunctional metabolite at the interface of defense, growth, and environmental adaptation. Clarifying this balance is critical when developing new sorghum varieties aimed at safe and sustainable forage use.

Dhurrin biosynthesis

Dhurrin biosynthesis in sorghum initiates from L-tyrosine and proceeds through compartmentalized reactions spanning the endoplasmic reticulum, cytoplasm, and vacuole (27,35,41,42). The first and rate-limiting step is catalyzed by cytochrome P450 CYP79A1, which converts L-tyrosine into (E)-p-hydroxyphenylacetaldoxime (43,44). As this step controls pathway flux, variation in CYP79A1 expression is a major determinant of dhurrin accumulation across genotypes and environments (45,46).

The intermediate is then converted by CYP71E1 into p-hydroxymandelonitrile, an unstable cyanohydrin that can release hydrogen cyanide (41). To prevent self-toxicity, the compound is rapidly glycosylated by UGT85B1 to form stable dhurrin (44,47,48). Glycosylation, therefore, links biosynthesis with intrinsic detoxification.

Dhurrin is stored in the vacuole and kept separate from β-glucosidase (49). Cyanide is released only after tissue damage disrupts this compartmentalization (13,50). Dhurrin concentration varies with genotype, growth stage, and environmental conditions (7,27,51,52).

Although the biosynthetic pathway is well described, its quantitative contribution to field-level HCN variation remains unresolved. Most mechanistic studies were conducted under controlled conditions (27,36,51). Genetic or structural interventions have mainly focused on reducing dhurrin content. However, their long-term effects on plant performance and forage safety in commercial systems remain poorly documented.

Distribution of dhurrin in sorghum

Dhurrin distribution in sorghum varies across organs, growth stages, genotypes, and environments (7,12,51,53). The highest concentrations are found in young leaves and actively growing shoots. Levels may reach around 1000 mg HCN/kg dry matter (DM) in traditional varieties and can be higher in wild types (11,51,54). This pattern reflects the defensive role of dhurrin in tissues most exposed to herbivory (13,50).

Dhurrin declines as leaves mature. Reduced biosynthesis, compound degradation, and nitrogen remobilization contribute to this decrease (36). This developmental gradient explains why forage harvested at later stages generally carries lower cyanide risk than young forage.

In stems, dhurrin levels are lower than in leaves and unevenly distributed. Concentrations are higher in young internodes and in the cortex compared with the pith (31,55,56). These differences likely reflect variation in tissue function and protection needs (57).

Roots show a distinct pattern. Overall levels are lower than in leaves but vary among cultivars. In some genotypes, root concentrations may approach or exceed leaf levels (58–60). Dhurrin accumulates mainly in the epidermis and outer cortex, which supports a role in defense against soil pathogens and nematodes (14,61).

Mature grains contain very low or undetectable cyanide levels (7,55). Dhurrin may be present during early seed development but declines sharply toward physiological maturity. In contrast, higher concentrations are often detected in protective floral structures such as glumes and lemmas (31,56). This distribution is consistent with the protection of reproductive tissues.

Across development, dhurrin increases during early vegetative growth, peaks before or around the generative phase, and then declines in vegetative organs after flowering (55). These changes are linked to carbon–nitrogen allocation and developmental regulation of biosynthetic genes (36). At the cellular level, dhurrin is mainly stored in vacuoles of epidermal and mesophyll cells (56). Genotype–environment interactions strongly influence the stability of these patterns (27,51).

Overall, dhurrin distribution supports its dual function as a defense compound and a dynamic nitrogen reserve. However, most data are derived from limited cultivars and controlled conditions. Direct links between organ-level distribution and field toxicity events remain poorly quantified. As a result, organ-specific dhurrin profiles cannot yet be translated reliably into forage-level HCN risk without integrated field validation.

Metabolic regulation and recycling dhurrin in sorghum

Dhurrin metabolism is tightly regulated to maintain defense function while preventing self-toxicity (8,35). Biosynthesis is highly active during early growth, especially in seedlings and developing tissues (55,62). However, dhurrin does not accumulate indefinitely. It is continuously metabolized throughout plant development (7,17,63).

In maturing plants, degradation exceeds biosynthesis, reducing the dhurrin pool. This pattern supports the concept of cyanogenic glycosides as temporary nitrogen reserves (12,15,36). Thus, dhurrin functions both as a defense compound in early growth and as a remobilizable resource in later stages.

Metabolite and transcript analyses show that dhurrin turnover is active during early development. Accumulation of p-hydroxybenzaldehyde, a degradation product, correlates with expression of biosynthetic and dhurrinase genes (9,37,62). Catabolic genes such as β-glucosidase, nitrilase 4 (NIT4), and glutathione S-transferase (GST) exhibit genotype-dependent expression patterns, indicating that recycling occurs through a branched, genetically variable network (42,56).

Although β-glucosidase-mediated hydrolysis releases HCN during defense (13), plants detoxify endogenous cyanide through alternative pathways, including β-cyanoalanine synthase (β-CAS) and nitrilase 4 (NIT4), which convert cyanide-derived intermediates into amino acids and related compounds (9). Evidence from mutant studies supports the formation of downstream metabolites such as p-hydroxyphenylacetic acid from dhurrin turnover (7,15). These pathways allow degradation without excessive release of free HCN.

During seed development, expression of recycling-related genes increases while dhurrinase expression declines (7,42). This pattern indicates a developmental shift from bioactivation toward safer metabolic recycling. Overall, dhurrin regulation is spatially and temporally coordinated. It supports defense in early growth and nitrogen recovery in later stages.

Because gene expression and enzyme activity respond to environmental and internal signals, dhurrin metabolism links plant stress responses to potential cyanide risk in forage systems. This regulatory network is therefore relevant for breeding strategies and feed management.

Factors affecting dhurrin accumulation in sorghum

Dhurrin content in sorghum varies widely across genotypes, developmental stages, environmental conditions, and harvest practices (28,51,62,64). These factors regulate biosynthesis, tissue distribution, and degradation dynamics. As a result, cyanogenic potential differs substantially among varieties and production systems.c

Dhurrin accumulation is highest during early vegetative growth. Genetic background determines baseline biosynthetic capacity, while environmental stress, such as drought, temperature extremes, and nitrogen availability, modulates gene expression and metabolite levels (27,57). Harvest timing further influences risk, because young forage generally contains more dhurrin than mature plants.

Mechanical damage, grazing, cutting, and processing practices affect whether stored dhurrin is exposed to β-glucosidase. Tissue disruption accelerates hydrolysis and increases the likelihood of hydrogen cyanide release. Therefore, cyanide risk depends not only on dhurrin concentration but also on post-harvest handling and feeding management (18,23).

As summarized in Figure 1, cyanogenic potential results from the interaction between plant age, genetics, environment, and harvest management. Dhurrin accumulation alone does not determine toxicity. Risk emerges when accumulated dhurrin is rapidly hydrolyzed under conditions that exceed the animal's detoxification capacity.

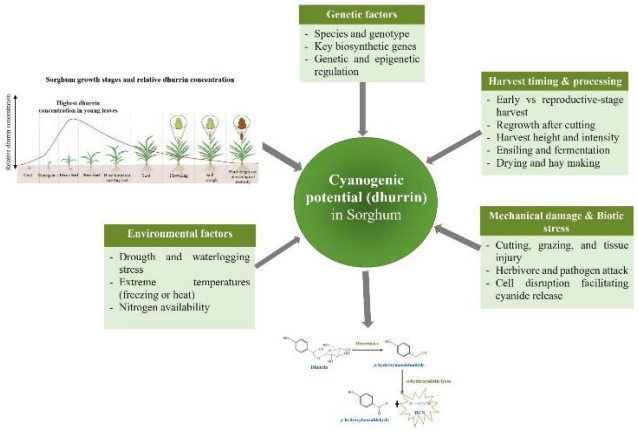

Figure 1: Interaction between plant regulation, environmental stress, and harvest practices in shaping cyanide risk in sorghum.

Genetic factors

Genetic variation strongly influences dhurrin biosynthetic capacity in sorghum (58,60,65). Differences among genotypes are primarily driven by the regulation of key enzymes in the cyanogenic pathway, including CYP79A1, CYP71E1, and UGT85B1 (9,35). Variation in expression and enzyme activity determines the potential for dhurrin accumulation in specific tissues.

Cyanogenic potential is not a uniform trait. It varies across organs and reflects genotype-specific responses to environmental conditions. Comparative studies show that wild and domesticated sorghum differ in tissue distribution patterns. For example, *Sorghum macrospermum* has lower dhurrin levels in aerial tissues than *Sorghum bicolor*, while root concentrations may remain similar (55,65). Selection for low aerial dhurrin does not necessarily eliminate cyanogenic capacity in other organs. Root dhurrin may function as a nitrogen reserve under nutrient-limited conditions (15,58).

Genomic studies using Quantitative Trait Loci (QTL), Single Nucleotide Polymorphism (SNP), and Genome-Wide Association Study (GWAS) approaches have identified structural and regulatory loci associated with dhurrin variation (9,45,46,49,66). Transcription factors and epigenetic mechanisms also contribute to regulation. However, dhurrin expression is strongly influenced by genotype–environment interactions. A low-dhurrin phenotype under one condition may not remain stable under stress (60). This instability complicates the development of consistently low-dhurrin cultivars.

Studies of dhurrin-deficient mutants, such as SbEMS2447 (CYP79A1), show that suppression of the pathway does not always reduce biomass under herbivory (67). However, responses vary among mutants (31,68). Reduction of dhurrin is often accompanied by shifts in other secondary metabolic pathways, including phenylpropanoid and jasmonate pathways (69). These adjustments indicate metabolic flexibility but may also alter stress tolerance and long-term performance.

Overall, genetics defines the baseline capacity for dhurrin production and distribution. Yet cyanide risk in feeding systems depends on how these genetic traits interact with plant age, environmental stress, and harvest management, as outlined in Figure 1.

Plant growth stage

Growth stage is a significant determinant of dhurrin concentration and HCN potential in sorghum (39,55). Dhurrin increases soon after germination and peaks during the early vegetative phase, about 2–4 weeks after planting (27,36,55). At this stage, concentrations may exceed 1000 mg HCN/kg dry matter (7,45,55).

As plants mature, dhurrin levels decline. This decrease is associated with reduced expression of biosynthetic genes, shifts in nitrogen allocation toward structural and reproductive growth, and the activation of metabolic recycling pathways. During the generative phase, concentrations often fall below 200 mg HCN/kg dry matter, a range generally associated with a lower acute toxicity risk in ruminants (70).

However, this ontogenetic pattern is not uniform across genotypes. Some accessions show gradual declines, while others display non-linear fluctuations during development (71). Plant age alone, therefore, cannot guarantee forage safety. Many harvest recommendations are based on a narrow range of production environments and may not apply under stress, such as regrowth after cutting or frost exposure (52,72).

Recent genomic and transcriptomic studies indicate that developmental dynamics are shaped by genotype-specific regulation of genes in the cyanogenic pathway (42,45). Growth stage should therefore be considered within a broader regulatory framework that includes genetic and environmental influences, as summarized in Figure 1.

Environmental conditions

Environmental stress strongly influences cyanogenic potential in sorghum. Among abiotic factors, drought is the most consistent trigger of increased dhurrin accumulation (51,52,73). Under drought, HCN levels may rise from about 700 mg/kg to over 1,100 mg/kg dry matter (12,51,52). This increase is associated with reduced growth, lower biomass

dilution, shifts in nitrogen allocation, and activation of stress-related pathways (17,40).

However, higher dhurrin levels under drought do not always indicate improved protection against oxidative stress. Dhurrin may function as a secondary defense strategy or as a temporary nitrogen reserve for post-stress recovery (38). The response is genotype-dependent and interacts with nitrogen supply. Combined drought and high nitrogen fertilization can markedly increase dhurrin levels while maintaining biomass production (74,75). Thus, agronomic resilience does not necessarily translate into safer forage.

High temperature and salinity also increase cyanogenic potential (71,76). Temperature effects vary across agroclimatic regions. Salinity often increases dhurrin in leaves and stems but may reduce it in roots, suggesting preferential allocation to aerial tissues during stress (77).

Nitrogen imbalance further modulates dhurrin levels. Both deficiency and excess can increase cyanogenic glycosides, depending on genotype and environment (36,78). This pattern confirms the close link between dhurrin metabolism and nitrogen dynamics.

Freezing events can also alter cyanide risk. Frost may increase apparent HCN release through cellular disruption, although rapid degradation can reduce measurable levels in damaged tissues (31,56). Outcomes depend on the balance between tissue damage, volatilization, and metabolic turnover.

Physiologically, stress increases risk not only by enhancing biosynthesis but also by disrupting cellular compartmentation. Dhurrin is stored in the vacuole, while activating enzymes are separated in intact cells (28,41). Membrane damage allows substrate–enzyme contact and accelerates HCN release. Despite different stress types, the underlying mechanism often converges on increased hydrolysis and cyanide exposure, as summarized in Figure 1.

Harvest time and processing

Harvest timing influences dhurrin concentration in sorghum. Some studies report higher levels in the morning compared with the afternoon or evening, although results vary with weather and growth stage (30,56). Therefore, the time of harvest can modify cyanogenic potential, but it does not act independently of plant condition.

Postharvest processing plays a significant role in reducing cyanide risk. Ensiling and controlled fermentation are among the most effective methods. Reductions of 60–80% have been reported under well-managed conditions (79,80). Heat treatment can also lower cyanide content, though nutrient losses may occur (29). In contrast, drying and long-term storage do not consistently decrease dhurrin or HCN potential. Sorghum hay may still release cyanide during ruminal fermentation (81).

Forage safety, therefore, depends on combined factors. Harvest stage, processing method, and cultivar selection must be considered together. Effective cyanide risk management requires integrating these elements into practical feeding systems.

Mechanical damage and biotic stress

Mechanical damage and biotic stress directly affect cyanide risk in sorghum. Dhurrin is not only a constitutive defense compound but can also be induced by herbivory signals such as methyl jasmonate (50). This indicates that cyanogenic potential may increase in response to biotic attack.

Tissue disruption has an immediate effect. In intact cells, dhurrin and its activating β-glucosidase are spatially separated. Wounding disrupts this compartmentation, allowing rapid hydrolysis and HCN release (13,50). Herbivore or pathogen attack can also stimulate systemic signaling, increasing dhurrin levels in tissues that appear undamaged. As a result, visually healthy forage may still carry elevated cyanogenic risk (13).

Although plant age, environment, genotype, and management practices determine overall dhurrin accumulation, concentration alone does not define toxicity. Actual poisoning risk depends on the extent of hydrolysis and the release of HCN. Therefore, understanding the mechanism of cyanide release is essential for explaining how sorghum's toxic potential is expressed during processing and after ingestion by ruminants.

Cyanide release from dhurrin

Cyanide is released from dhurrin when plant tissue integrity is disrupted. This may occur through mechanical damage, herbivory, feed processing, or during ruminal digestion (13,24,50). In intact cells, dhurrin is separated from its activating enzymes. Tissue disruption allows these components to interact and initiates hydrolysis.

The first step is cleavage of the β-glycosidic bond by β-glucosidase. This reaction releases glucose and p-hydroxymandelonitrile (17,48). The cyanohydrin intermediate is unstable. It can decompose spontaneously or be further cleaved by hydroxynitrile lyase, producing p-hydroxybenzaldehyde and HCN. The speed of this process depends on enzyme activity, environmental conditions, and substrate availability.

The amount of HCN released is influenced by three main factors: dhurrin concentration, β-glucosidase activity, and the extent of tissue damage (13). Plants with higher dhurrin content have greater potential to release cyanide when damaged.

In ruminants, the process becomes more complex. Ruminal microorganisms also possess β-glucosidase activity and can hydrolyze dhurrin present in feed. The reaction rate depends on dhurrin concentration, microbial population, ruminal pH, and feed retention time. Thus, cyanide release continues after ingestion and is shaped by rumen conditions.

The rumen can detoxify cyanide through rhodanese (thiosulfate sulfurtransferase), which converts cyanide into the less toxic thiocyanate (82). This mechanism requires adequate sulfur supply and functional microbial activity. Detoxification capacity is limited. When cyanide intake exceeds this capacity, HCN can accumulate rapidly and cause systemic toxicity (18,57).

Most current models of cyanide release and detoxification are based on in vitro systems or acute high-dose experiments. Their relevance to field conditions, where animals consume forage ad libitum, remains uncertain. Factors such as dietary composition, sulfur status, and microbial adaptation are often not fully considered when defining safety thresholds. Moreover, few studies link ruminal HCN dynamics with production responses over medium-term feeding periods. The potential effects of repeated sublethal exposure, therefore, remain insufficiently understood.

Cyanide metabolism in the ruminant digestive system

Dhurrin hydrolysis and cyanide release in the rumen

In ruminants, cyanide toxicity depends on the balance among three processes: HCN release in the rumen, systemic absorption, and detoxification to thiocyanate. Risk increases when release exceeds detoxification capacity.

Dhurrin hydrolysis begins during mastication and continues in the rumen. Tissue disruption allows β-glucosidase from plant cells and ruminal microorganisms to cleave dhurrin into glucose and p-hydroxymandelonitrile (13,50). The intermediate compound is unstable and decomposes into HCN and p-hydroxybenzaldehyde, either spontaneously or through hydroxynitrile lyase activity.

The ruminal environment favors this reaction. Cattle maintain a normal core body temperature of about 38.5–39.0°C; rumen temperature is similar, providing a warm, moist, anaerobic setting that supports microbial and enzymatic activity (83). As a result, cyanogenic glycosides can be rapidly hydrolyzed after ingestion.

The rate of HCN release depends on dhurrin concentration, the degree of tissue damage, and microbial activity (81). Young sorghum typically releases more cyanide than mature plants because it contains higher dhurrin levels. This explains the frequent reports of livestock poisoning from grazing fresh young sorghum (18,20,21,23).

Once released, HCN becomes available for ruminal absorption and systemic exposure. Toxicity is therefore governed by kinetics rather than forage concentration alone. Most available data come from controlled experiments using uniform forage and stable ruminal conditions. In field situations, animals consume mixed forages with variable dhurrin levels and uneven tissue damage from cutting, wilting, or selective grazing. Average dhurrin content per kg dry matter may therefore underestimate short-term HCN release peaks, which are critical for acute poisoning risk.

Cyanide absorption and detoxification in ruminants

Free cyanide released in the rumen diffuses rapidly across the rumen epithelium into the bloodstream. This process has long been recognized in ruminant toxicology (83) and remains supported by more recent evaluations of rumen cyanogenic dynamics (10,18,20,21). Therefore, systemic exposure depends not only on the cyanogenic potential of the forage but also on the balance between cyanide release and detoxification rates.

Under normal physiological conditions, absorbed cyanide is converted to thiocyanate, which is considerably less toxic. This reaction is catalyzed by rhodanese and requires adequate sulfur availability (41,82). The liver is the primary site of detoxification, although ruminal microbes may contribute to sulfur-dependent transformations. Detoxification capacity, however, is finite and influenced by nutritional status.

Toxicity develops when cyanide absorption exceeds enzymatic conversion to thiocyanate (18,19,21). Circulating cyanide binds to cytochrome c oxidase in mitochondria and inhibits oxidative phosphorylation. As a result, cellular oxygen utilization is impaired, leading to functional hypoxia despite adequate blood oxygen levels. This mechanism remains the central explanation for acute cyanide poisoning in livestock.

Differences in clinical outcome among animals consuming similar forage can be explained by this kinetic imbalance. Sulfur intake, rumen microbial adaptation, feed intake rate, and individual metabolic capacity all influence detoxification efficiency (10,23,82). Cyanide toxicity should therefore be viewed as a dynamic metabolic interaction rather than a direct reflection of forage cyanide concentration alone.

Chronic exposure represents a distinct risk profile. Sustained elevations of thiocyanate may interfere with iodine uptake and thyroid hormone synthesis, potentially affecting growth and reproductive performance (41). Recent evaluations in ruminant feeding systems also suggest subclinical impacts under prolonged exposure. Although evidence under field conditions remains limited, these findings indicate that repeated low-level exposure may influence productivity even in the absence of acute intoxication.

Factors affecting cyanide metabolism and toxicity

Cyanide metabolism and toxicity in ruminants result from interactions among feed characteristics, animal factors, and environmental conditions. Risk cannot be explained by a single variable. Dietary characteristics strongly influence cyanide exposure. Essential factors include dhurrin concentration, forage form (fresh, wilted, or silage), and the availability of nutrients that support detoxification, especially sulfur and protein (41,84). Ensiling and controlled fermentation generally reduce dhurrin content and slow

cyanide release, thereby lowering acute toxicity risk (79,80). However, the degree of reduction depends on management quality and fermentation conditions.

Feeding rate and intake pattern are also relevant. Rapid consumption of high-dhurrin forage may produce short-term peaks of HCN release in the rumen, even when average dietary levels appear moderate. Thus, intake dynamics influence systemic exposure.

Animal-related variables modify detoxification capacity. Species differences, age, nutritional status, and rumen microbial adaptation all contribute to variability in response (10,21). Animals gradually adapted to small amounts of cyanogenic feed often tolerate higher levels than naïve animals, particularly when sulfur intake is adequate.

Rhodanese activity plays a central role in detoxification. Its efficiency depends on sulfur availability, metabolic status, and rumen conditions. Young animals and those with nutritional deficiencies are generally more susceptible. In contrast, animals with stable rumen function and balanced diets tend to show greater tolerance.

The rumen microbiota is another key component. Diverse and stable microbial populations may enhance cyanide transformation and support detoxification pathways (84). Optimal rumen pH and consistent feeding management help maintain this functional stability.

Environmental conditions influence risk indirectly by altering plant cyanogenic potential. Drought and high temperatures can increase dhurrin accumulation in sorghum (51,73). When stressed, forage is consumed rapidly without adaptation, increasing the risk of poisoning.

Field cases often involve a combination of factors: stressed plants, high intake, and limited sulfur supplementation. These combined conditions create a mismatch between cyanide release and detoxification capacity.

Most practical recommendations remain qualitative and are based largely on case reports. Few studies have quantitatively modeled the combined effects of forage cyanogenic potential, processing method, sulfur status, body weight, and microbial adaptation. As a result, defining a clear numerical safety margin for sorghum inclusion in ruminant diets remains challenging.

Conceptually, cyanide toxicity risk should be viewed as the outcome of three interacting components: cyanide release capacity of the feed, detoxification capacity of the animal, and environmental conditions that modulate both. Systemic risk emerges when release capacity exceeds detoxification capacity within a given environmental context. This integrative framework is summarized in Figure 2.

Systemic toxicity emerges from the interaction between feed cyanogenic potential (HCNp), animal detoxification capacity (sulfur supply, rumen microbiota, rhodanese activity), and environmental stressors. Toxic risk increases when cyanide release exceeds detoxification capacity, leading to systemic Cyanide ion (CN^-) accumulation and cellular hypoxia.

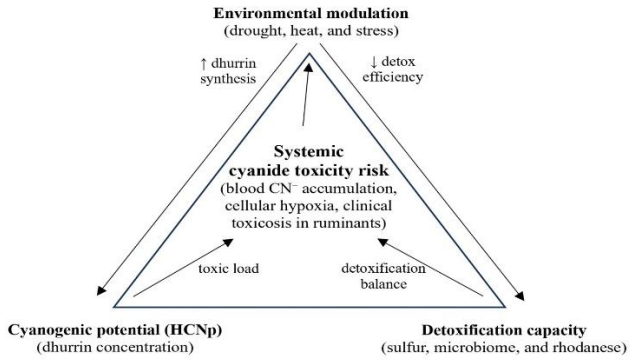

Figure 2: Integrative framework of cyanide toxicity risk in sorghum–ruminant systems.

Pathophysiology of cyanide poisoning in ruminants

Cyanide poisoning in ruminants occurs when the rate of HCN release and absorption exceeds the animal's detoxification capacity, primarily through conversion to thiocyanate via the rhodanese system (10,23). Although classical toxic thresholds are often expressed as mg HCN/kg body weight, such values do not fully account for ruminal release dynamics and absorption kinetics (10,85). Toxicity, therefore, reflects a metabolic imbalance rather than a fixed dietary concentration.

At the cellular level, cyanide binds to cytochrome c oxidase in the mitochondrial electron transport chain. This inhibits oxidative phosphorylation and blocks cellular oxygen utilization. ATP (Adenosine Triphosphate) production declines rapidly, leading to acute bioenergetic failure. Tissues with high oxygen demand, particularly the central nervous system and myocardium, are affected first (86,87).

As mitochondrial respiration becomes impaired, cells shift toward anaerobic metabolism. Lactate accumulates, metabolic acidosis develops, and systemic oxygen delivery becomes functionally ineffective despite adequate arterial oxygen tension. This mismatch between oxygen availability and utilization explains the rapid onset of neurological signs, respiratory distress, and cardiovascular instability observed in acute cases (87,88).

In ruminant production systems, the severity of this cascade depends not only on total cyanide intake but also on the speed of ruminal release and the efficiency of detoxification. Environmental stress that increases dhurrin accumulation or accelerates hydrolysis can intensify the metabolic burden placed on detoxification pathways. Thus, plant physiology, rumen kinetics, and systemic bioenergetics are mechanistically linked in the development of clinical cyanide toxicosis.

Mechanisms of toxicity at the cellular level

The primary molecular target of cyanide is cytochrome c oxidase (Complex IV) in the mitochondrial electron transport chain (86,88,89). Cyanide (CN^-) binds to ferric iron (Fe^{3+}) at the heme a_3–CuB catalytic center, inhibiting electron transfer from cytochrome c to oxygen. As a result, the reduction of O_2 to H_2O is blocked, and terminal electron flow is halted (90,91).

Inhibition of Complex IV disrupts the proton gradient across the inner mitochondrial membrane and suppresses ATP synthesis through oxidative phosphorylation. Cellular ATP levels decline rapidly, the NADH/NAD^+ ratio increases, and mitochondrial membrane potential ($\Delta\Psi m$) collapses (86,92). Cells shift toward anaerobic glycolysis, but this compensation is insufficient to sustain high-energy tissues.

This state produces histotoxic hypoxia, in which oxygen delivery may remain adequate but cellular utilization fails (88). Electron accumulation in upstream complexes, particularly Complexes I and III, promotes electron leakage to molecular oxygen and enhances superoxide formation. Increased reactive oxygen species (ROS) further amplify mitochondrial dysfunction and oxidative stress (93,94).

Excess ROS induces lipid peroxidation, protein oxidation, and damage to mitochondrial and nuclear DNA (95). The combined effects of ATP depletion and oxidative injury lead to loss of cellular integrity. Depending on exposure intensity and duration, cells undergo necrosis due to energy failure or activate mitochondrial apoptotic pathways (89,90).

Most kinetic parameters describing cyanide–mitochondrial interactions are derived from non-ruminant experimental models (96,97). Direct validation under dietary exposure conditions in ruminants remains limited. Therefore, extrapolation of toxic thresholds should consider species-specific factors, including rumen detoxification dynamics and systemic metabolic adaptation.

Impact on tissues and organs

Organs with high aerobic energy demand are the primary targets of cyanide toxicity, especially the central nervous system and myocardium (10,23). Neurons depend heavily on oxidative phosphorylation to maintain ion gradients and synaptic transmission. Inhibition of mitochondrial ATP production, therefore, rapidly disrupts neuronal function, leading to ataxia, tremors, seizures, depression of consciousness, and, in severe cases, coma.

The myocardium is similarly vulnerable due to its high mitochondrial density and continuous energy requirement. Impaired oxidative phosphorylation reduces contractility and may trigger arrhythmias (10). Combined neurological and cardiovascular dysfunction explains the rapid progression and sudden death observed in acute cyanide poisoning (18).

Systemic effects extend beyond these primary targets. Cyanide-induced bioenergetic failure can promote peripheral vasodilation, partly mediated by altered nitric oxide signaling, which exacerbates hypotension and functional hypoxia (88). Secondary perfusion impairment may affect the liver, kidneys, and lungs, contributing to multi-organ dysfunction in severe cases (23).

Acute and chronic poisoning

Acute cyanide poisoning develops when rapid HCN release overwhelms short-term detoxification capacity. Lethal doses are generally reported at 2–4 mg HCN/kg body weight in adult cattle and 1.5–2.0 mg/kg in sheep (10,19). Following ingestion of highly cyanogenic forage, blood cyanide concentrations may rise within 15–30 minutes and exceed 1.0 mg HCN/L in fatal cases.

Clinical signs progress quickly and reflect systemic bioenergetic failure. Early manifestations include tachypnea, dyspnea, tachycardia, muscle tremors, and anxiety. As mitochondrial inhibition intensifies, animals may collapse and die from respiratory and cardiovascular failure (18–20). The rapid onset underscores the importance of release kinetics rather than total dietary concentration alone.

Chronic exposure represents a different scenario. Repeated intake of sublethal doses allows partial detoxification but may lead to sustained elevations of thiocyanate. Thiocyanate competes with iodide in the thyroid gland and can interfere with thyroid hormone synthesis, potentially reducing circulating T_4 and T_3 concentrations (98). Over time, altered thyroid function may impair growth, feed efficiency, and reproductive performance. Immune competence may also be affected. These effects are often subclinical and therefore underreported in field conditions.

Overall, cyanide toxicosis progresses from ruminal HCN release and absorption to mitochondrial inhibition, systemic energy failure, and organ dysfunction (Figure 3). Outcome severity reflects the balance between exposure and detoxification capacity rather than forage concentration alone.

In field settings, acute severity often reflects a temporal mismatch: short peaks in ruminal HCN release can exceed detoxification capacity even when average dietary cyanide appears moderate. Onset and outcome vary with forage cyanogenic potential, rumen kinetics, sulfur status, and individual metabolic capacity. Acute cases involve rapid systemic accumulation and mitochondrial inhibition, whereas chronic exposure is associated with sustained thiocyanate formation and potential thyroid dysfunction (98).

Current risk assessment approaches often rely on static dose thresholds. While practical, such models do not fully capture dynamic interactions among plant metabolism, rumen hydrolysis, and systemic bioenergetics. Integrating these components provides a more realistic framework for

evaluating cyanide risk in sorghum-based production systems.

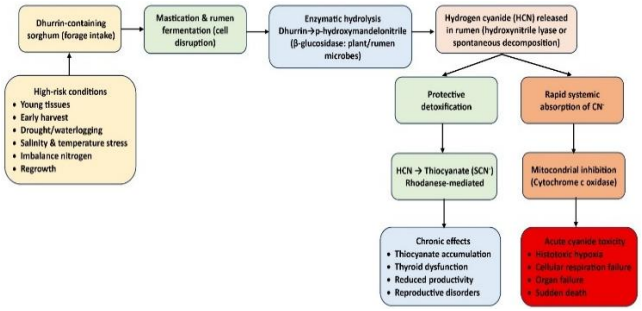

Figure 3: Multilevel cascade linking plant cyanogenic potential to systemic toxicity in ruminants. Following ingestion of dhurrin-containing forage, ruminal hydrolysis releases HCN. The resulting cyanide may be detoxified to thiocyanate or absorbed into systemic circulation. The relative balance between these two pathways determines clinical outcome.

Clinical symptoms and diagnosis of cyanide poisoning in ruminants

Clinical manifestations of cyanide poisoning in ruminants depend on the dose absorbed, the rate of ruminal HCN release, and detoxification capacity. Acute intoxication is defined by rapid onset (often minutes to 1 h) and severe cardiorespiratory and neurological signs. Chronic exposure produces gradual, often nonspecific effects on productivity and thyroid function. Detailed signs and dose–response relationships are summarized in the subsections below; early recognition of the acute syndrome is critical to reduce mortality. Chronic exposure may reduce growth, feed efficiency, and reproductive performance, with signs consistent with thyroid dysfunction; these manifestations are frequently subtle and underreported in the field (98).

Diagnosis relies on an integrated approach. A history of recent access to young, stressed, or regrowth sorghum is a critical clue. Rapid progression after consumption supports acute cyanide toxicosis. Laboratory confirmation may include blood cyanide or thiocyanate, rumen content analysis, and thyroid evaluation in suspected chronic cases. Because HCN volatilizes rapidly, timely sampling is essential (19,23).

Overall, clinical presentation reflects the dynamic imbalance between ruminal cyanide release and systemic detoxification. Recognition of this process supports timely feed withdrawal and treatment (see Diagnosis subsection).

Acute clinical symptoms

Acute cyanide poisoning occurs when ruminants ingest large quantities of cyanogenic forage within a short period, typically at doses of 2–4 mg HCN/kg body weight in cattle and 1.5-2.0 mg/kg in sheep (10,19). Clinical signs usually develop within 10–60 minutes, depending on ruminal HCN concentration and absorption rate (23).

Early manifestations primarily involve the respiratory and cardiovascular systems. Respiratory rate may increase from normal values (15–25 breaths/min) to 40–60 breaths/min, accompanied by deep, gasping respiration and dyspnea. Tachycardia is common (100–140 beats/min; normal 60–80 beats/min), sometimes with arrhythmia and progressive hypotension (23). Behavioral signs include anxiety, agitation, and restlessness.

A characteristic finding is bright red or pink mucous membranes, reflecting histotoxic hypoxia: oxygen delivery is adequate, but mitochondrial utilization is impaired (18,87). As toxicity progresses, neurological signs include ataxia, muscle tremors, hypersalivation, and convulsions; collapse and death may follow from respiratory or cardiovascular failure (10,23). Fatal cases may occur within 15 minutes to 2 hours when blood cyanide exceeds approximately 1.0 mg HCN/L (18,19). Survivors may show transient weakness, inappetence, and incoordination for several days. Pathophysiologically, acute poisoning reflects ruminal HCN release that exceeds ruminal detoxification capacity, with rapid inhibition of respiration in high-demand tissues (10,23)

Chronic clinical symptoms

Chronic cyanide poisoning results from repeated ingestion of low to moderate cyanide doses over weeks to months, typically at sublethal levels that allow partial detoxification. Clinical manifestations develop gradually and are often nonspecific, making field diagnosis challenging.

One syndrome associated with prolonged consumption of cyanogenic forage is cystitis–ataxia syndrome, which has been reported primarily in horses; descriptions in cattle and goats exist, but the syndrome is less consistently established in ruminants (99,100). Where reported, it is characterized by progressive hind-limb ataxia, tail paresis, urinary incontinence, and eventual recumbency, with degenerative central nervous system changes and secondary urinary tract lesions secondary to neurogenic dysfunction. The precise toxic mediator remains debated, and repeated exposure to cyanogenic compounds has been implicated in its pathogenesis (99,100).

In ruminants, chronic sorghum-associated cyanide exposure more commonly presents as reduced productivity rather than overt neurological disease. Animals may exhibit decreased feed intake, reduced weight gain, lower milk yield, and impaired reproductive performance (23). Subclinical thyroid dysfunction represents a key mechanism, as thiocyanate competes with iodide uptake and may disrupt thyroid hormone synthesis (98). In advanced cases, goiter and altered T_3/T_4 concentrations may be observed.

When neurological signs occur in chronic intoxication, they are typically mild and may include subtle incoordination, weakness, and lethargy. Because these manifestations overlap with nutritional deficiencies and parasitic or metabolic disorders, chronic cyanide exposure is often underdiagnosed.

Unlike the acute form, chronic poisoning reflects sustained exposure in which detoxification to thiocyanate continues but leads to cumulative endocrine and physiological consequences. At the herd level, such subclinical effects may contribute to progressive reductions in productivity and reproductive efficiency.

Diagnosis of cyanide poisoning

Diagnosis of cyanide poisoning in ruminants requires integration of exposure history, clinical findings, and laboratory confirmation when available.

A detailed history is critical. Recent access to young, regrowth, drought-stressed, or heavily fertilized sorghum strongly increases suspicion (38,55,73). Rapid onset of signs following forage consumption further supports the diagnosis. Because hydrogen cyanide is highly volatile and rapidly lost postmortem, timely sampling of rumen contents or blood is essential.

Clinical examination in acute cases typically reveals bright red mucous membranes, marked tachypnea (often 40–60 breaths/min), tachycardia (100–140 beats/min), dyspnea, and neurological signs (ataxia, seizures) as detailed above. Body temperature is usually normal or slightly decreased and is not a reliable discriminator.

Laboratory confirmation may include measurement of blood cyanide concentrations. Values above 0.5 mg HCN/L support exposure, while concentrations exceeding approximately 1.0 mg HCN/L are frequently associated with fatal outcomes (19). Because the blood half-life of cyanide is short (approximately 30–60 minutes), samples must be collected as early as possible. In suspected chronic exposure, elevated thiocyanate concentrations in blood or urine may provide supportive evidence.

Feed analysis is equally important. Forages containing more than 500 mg HCN/kg dry matter are generally considered high risk, with levels above 750 mg/kg classified as very hazardous (24). Rapid field screening methods, such as picrate paper tests, can help identify high-cyanide forage (23).

Differential diagnoses include nitrate/nitrite poisoning, organophosphate or carbamate toxicosis, severe hypoxia due to respiratory disease, hypoglycemia, and other toxic encephalopathies. A key distinguishing feature is mucous membrane color: nitrate poisoning typically produces brownish or cyanotic mucosa due to methemoglobinemia, whereas cyanide poisoning maintains a bright red coloration.

Early recognition and immediate withdrawal of suspect feed are essential. When confirmed or strongly suspected, prompt therapeutic intervention should not be delayed while awaiting laboratory results.

Cyanide poisoning risk mitigation and management strategies within the crop–ruminant system

Mitigation of cyanide poisoning in sorghum-based production systems requires coordinated interventions across the crop–ruminant chain (Figure 4). Because toxicity reflects the balance between ruminal HCN release and detoxification capacity rather than forage concentration alone (10,23), no single preventive measure is sufficient; the integrated framework below summarizes genetic, agronomic, processing, feeding, monitoring, and emergency measures in sequence.

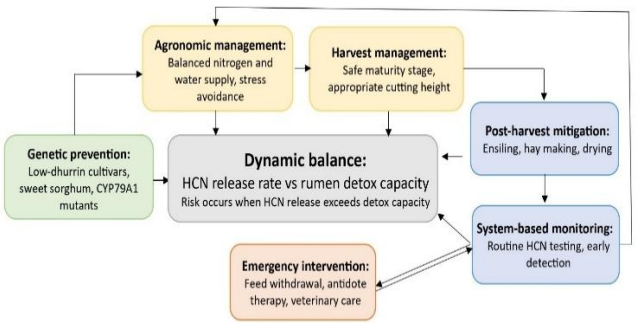

Figure 4: Integrated risk mitigation strategies for cyanide toxicity in sorghum-based ruminant systems. This framework illustrates that cyanide risk is influenced by the interaction between plant HCN release and ruminant detoxification capacity. Upstream interventions include genetic selection and agronomic management to limit cyanogenic potential, whereas downstream measures involve harvest practices, post-harvest processing, monitoring, and emergency response. Effective risk control requires coordination across all management levels rather than reliance on a single control point.

Genetic selection

Genetic selection represents the most upstream and sustainable strategy for mitigating cyanide risk in sorghum-based systems. Substantial variability in dhurrin content exists among genotypes. For example, *Sorghum macrospermum* has been reported to contain up to 1,000-fold lower dhurrin concentrations than S. bicolor, with relatively stable expression under drought conditions (42,58,65). However, cyanogenic potential does not consistently align with wild or cultivated status, as some wild sorghums exhibit higher dhurrin levels than commercial sudangrass hybrids (26,55,81).

At the varietal level, forage sorghums and sweet sorghums commonly range between 50–200 mg HCN/kg dry matter under normal conditions, although concentrations

may exceed 400 mg/kg during early vegetative stages in specific cultivars (55,62). These developmental fluctuations highlight a key breeding challenge: ensuring expression stability across growth phases and environmental conditions.

Importantly, reduced dhurrin content does not necessarily correlate with decreased biomass yield, suggesting that low-cyanogenic lines can be developed without significant productivity penalties. Advances in molecular breeding, including characterization of CYP79A1 variants and transcriptomic profiling, provide tools for more precise selection of cyanogenic traits (42,46,101).

Nevertheless, dhurrin serves physiological functions in nitrogen storage and herbivore defense (36,50). Excessive reduction may therefore introduce agronomic trade-offs, including altered nitrogen allocation or increased pest susceptibility. Breeding objectives should focus on maintaining dhurrin within a safe, agronomically functional range rather than on complete elimination.

Because environmental stress can elevate dhurrin even in low-cyanogenic cultivars, genetic selection should be complemented by field monitoring under high-risk conditions. Stability of dhurrin expression across seasons and stress scenarios remains a critical criterion for the development of forage varieties suited to ruminant production systems.

Cultivation management

Crop management strongly influences dhurrin accumulation by regulating nitrogen availability, water status, and growth conditions. Nitrogen supply is a significant determinant of cyanogenic potential. Several studies report increased HCN concentrations under moderate to high nitrogen fertilization rates, particularly when nitrogen is not balanced with other nutrients such as sulfur (31,54,78). Excessive nitrogen inputs may therefore elevate cyanogenic risk, especially under environmental stress. Fertilization should be matched to crop demand and avoided under drought or other stress that promotes dhurrin precursors through altered amino acid metabolism (31,54,78).

Water availability also modulates dhurrin expression. Adequate irrigation generally reduces HCN concentrations, whereas drought or water deficit conditions increase cyanogenic levels (38,40,67). Improvements in soil physical properties, including biochar application, have been associated with modest reductions in HCN concentration, suggesting that soil management can contribute to metabolic stabilization (102).

Plant growth stage represents the most practical management variable. Dhurrin concentrations are highest during early vegetative stages (approximately 15–30 days after planting) and decline toward reproductive maturity (7,55). Harvesting during early growth or immediately after rapid regrowth following stress significantly increases risk. Temperature extremes can further elevate cyanogenic levels, indicating that forage feeding should be delayed after severe heat or cold events.

Collectively, nitrogen management, water status, growth stage, and temperature interact to shape a dynamic cyanogenic profile in sorghum. Effective cultivation management requires adapting agronomic practices to environmental conditions and integrating routine pre-harvest risk assessment to minimize cyanide exposure in ruminant systems.

Feed processing

Post-harvest processing is a critical control point for reducing cyanogenic risk before forage is offered to ruminants. Unlike genetic and agronomic strategies that influence dhurrin accumulation in the plant, processing primarily limits HCN availability before ingestion. Reduction mechanisms include HCN volatilization, microbial or enzymatic degradation, and partial enzyme inactivation via physical treatment.

Ensilage is the most practical and widely applicable method. Under optimal fermentation conditions (pH 4.0–4.5 for approximately 30–45 days), HCN concentrations may decrease by 60–75% (80). In contrast, poorly controlled fermentation (pH > 5) achieves substantially lower reductions. Effective ensiling, therefore, depends on adequate compaction, appropriate moisture content, and sufficient fermentable substrate to support rapid acidification.

The use of β-glucosidase-producing lactic acid bacteria, particularly Lactobacillus spp., has been reported to enhance dhurrin degradation compared with spontaneous fermentation (103). Supplementation with fibrolytic enzymes, such as cellulase or xylanase, may further strengthen substrate accessibility and microbial breakdown (80).

Hay drying reduces HCN primarily through volatilization and partial inactivation of plant enzymes, although complete elimination is not guaranteed (81,104). Under certain conditions, cyanide release may recur after rehydration of dried forage (81). Intensive heat treatment can achieve greater reductions, but its practical use is often limited by cost and scale constraints.

In high-risk situations—such as early vegetative harvest, regrowth after drought, or excessive nitrogen fertilization—fresh forage feeding should be avoided. Ensiling with adequate fermentation time and pH control represents the most reliable mitigation strategy. Verification of HCN levels before feeding further enhances safety.

Feed management

Feed management represents the final mitigation layer before plant cyanogenic potential translates into biological exposure in ruminants. At this stage, risk depends not only

on dhurrin concentration but also on feeding practices and ruminal dynamics. Sorghum should not be used as a sole feed when HCN concentrations are elevated. Mixing with other forages (e.g., grasses, legumes, or cereal grains) or concentrates serves as a dilution strategy and helps stabilize ruminal fermentation, thereby reducing peak cyanide release following rapid intake (83).

Mode of utilization substantially influences risk. Direct grazing of young or stressed sorghum poses the greatest danger due to rapid consumption and limited pre-ingestive HCN loss (24). In contrast, silage is generally safer because fermentation partially reduces HCN content (80,103). Under high-risk conditions—such as early vegetative growth or post-drought regrowth—fresh feeding should be avoided, and gradual dietary introduction is recommended to allow ruminal adaptation. Releasing hungry animals onto high-risk pastures should be strictly avoided.

Detoxification efficiency depends on the availability of sulfur for thiocyanate formation. Supplementation with sulfur sources (e.g., sulfate or thiosulfate) has been reported to enhance cyanide detoxification capacity (82,84,105). Maintaining adequate mineral balance is therefore essential in sorghum-based feeding systems.

Practical feeding decisions should combine forage HCN analysis with intake pattern and sulfur status rather than a single concentration cut-off. Institutional guidelines often classify 500–750 mg HCN/kg dry matter (DM) as potentially toxic and >750 mg/kg DM as highly hazardous (24); under field conditions, dilution, adaptation, and slower intake may reduce—but not eliminate—risk at intermediate concentrations (55,83). When analysis is unavailable, young vegetative sorghum, post-drought regrowth, and stressed stands should be treated as high-risk regardless of published "safe" ranges (38,52,73).

Overall, the feeding strategy determines whether cyanide exposure remains within physiological tolerance or progresses to toxicity. Integrating HCN concentration data with practical feeding management provides a more reliable safeguard than relying solely on fixed numerical limits.

Management of acute poisoning

Acute cyanide poisoning in ruminants is a rapidly progressive emergency caused by cytochrome c oxidase inhibition and cellular respiratory failure; clinical signs and diagnostic criteria are described in the Clinical Symptoms and Diagnosis section. Treatment must not be delayed pending laboratory confirmation when exposure to high-risk sorghum is likely (18,19,23).

Standard antidotal therapy consists of intravenous sodium nitrite followed by sodium thiosulfate. Sodium nitrite induces methemoglobinemia, which sequesters circulating cyanide; sodium thiosulfate provides sulfur for rhodanese-mediated conversion of cyanide to thiocyanate (82). Commonly reported field dosages for cattle are approximately 3 g sodium nitrite and 15 g sodium thiosulfate in water, with proportionally lower doses for small ruminants (84). In some settings, sodium thiosulfate alone or hydroxocobalamin has been used as an adjunct or alternative (82,84).

Supportive care—including oxygen, fluid therapy, and cardiorespiratory monitoring—is essential. Prognosis is strongly time-dependent; survival decreases when treatment is initiated after advanced signs, and high exposures (>3 mg HCN/kg body weight) may be fatal within ~2 h if untreated (10,19).

Emergency treatment is the final layer in the mitigation hierarchy (Figure 4). Given rapid progression and limited field access to antidotes in many production systems, prevention, feed withdrawal, and early recognition remain the primary means of reducing mortality (23,24).

Integrated risk management strategy

Effective cyanide risk management in sorghum-based systems depends on cumulative effects across the production chain (Figure 4). Risk is governed by the relationship between plant-derived HCN release and ruminal detoxification, not by dhurrin concentration alone (10,23).

Upstream (crop level): Genetic selection for stable, agronomically acceptable cyanogenic potential; balanced nitrogen and water management; harvest at safer growth stages; and caution after drought, frost, or rapid regrowth (7,38,55,58).

Midstream (post-harvest): Ensiling, drying, or other processing to reduce bioavailable HCN before feeding, with verification of fermentation quality and residual concentrations (80,81,103).

Downstream (animal level): Dilution with non-cyanogenic forages, gradual introduction, avoidance of hungry animals on high-risk pasture, and sulfur adequacy to support thiocyanate formation (82,83,84,105).

Monitoring and contingency: Pre-feeding HCN testing in high-risk scenarios; clinical preparedness and antidote availability for acute cases (see Management of acute poisoning); emergency management remains a last resort (18,23,24).

No single layer is sufficient in isolation. System safety requires consistent application of genetic, agronomic, nutritional, and clinical measures aligned with local environmental variability. Compiled literature data demonstrated substantial variability in sorghum HCN concentrations depending on genotype, developmental stage, environmental stress, agronomic management, and post-harvest processing (Supplementary Table S1). Across studies, elevated HCN concentrations were commonly associated with early vegetative growth, drought and salinity stress, and nitrogen fertilization, whereas plant maturity, ensiling, and post-harvest intervals generally reduced HCN concentrations.

Conclusion

Cyanide risk in sorghum–ruminant systems is a dynamic systems outcome, not a fixed forage concentration. Firm evidence supports four conclusions: dhurrin and releasable HCN are strongly shaped by genotype, growth stage, and environmental stress (including drought and nitrogen status); tissue and ruminal hydrolysis can generate short HCN peaks that exceed detoxification capacity; absorbed cyanide inhibits cytochrome c oxidase, causing histotoxic hypoxia with rapid clinical deterioration in acute cases; and coordinated mitigation across breeding, agronomy, processing, feeding, monitoring, and emergency response is more reliable than any single intervention.

The added value of this review is an integrated framework that links plant cyanogenic regulation, rumen kinetics, systemic toxicology, and field management—explaining why stress-tolerant or productive sorghum is not automatically safe and why static thresholds often fail under grazing, rapid intake, or post-stress regrowth.

Critical gaps remain in quantifying stress–genotype–stage effects on bioavailable HCN, peak ruminal release relative to sulfur supply, commercial validation of processing, and sublethal chronic effects on productivity. Future work should build multivariable, field-tested risk tools and longitudinal studies linking pre-feed cyanogenic profiles, animal exposure markers, and health or production outcomes. Until then, safe use requires stable low-to-moderate cyanogenic cultivars under local stress, cautious harvest and ensiling, diet dilution and sulfur adequacy, pre-feed testing after high-risk events, and prevention-first management with emergency therapy as a last tier—preserving sorghum's role as a climate-resilient forage within physiological tolerance.

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Ethical approval

This manuscript is a review article that synthesizes data from previously published studies. It does not involve any experimental procedures on animals or humans conducted by the authors.

Conflict of Interest

The authors declare that there are no conflicts of interest regarding the publication and/or funding of this manuscript.

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الإجهاد البيئي، وإمكانات الذرة الرفيعة السيانوجينية، وخطر سمية السيانيد الجهازية في المجترات: مراجعة بحثية

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الخلاصة

تهدف هذه المراجعة إلى تطوير إطار متكامل لفهم مخاطر سمية السيانيد في أنظمة إنتاج المجترات القائمة على الذرة الرفيعة من خلال ربط إمكانات السيانيد النباتية بقدرة إزالة السموم من الكرش في ظل ظروف الإجهاد البيئي. تم تجميع الدراسات ذات الصلة التي استعرضها الأقران حول التخليق الحيوي للدورين، والتشكيل البيئي، وإزالة السموم من السيانيد الكرشي، والفيزيولوجيا المرضية، والمظاهر السريرية، واستراتيجيات التخفيف بشكل حاسم لبناء منظور المخاطر القائم على الأنظمة. يتأثر تراكم الدورين بشدة بالنمط الجيني ومرحلة النمو والتسميد بالنيتروجين وإجهاد الجفاف. العوامل البيئية، مثل تقلبات درجات الحرارة، وحالة مغذيات التربة، والاستجابات الفسيولوجية النباتية، قد تزيد من تعديل إمكانات السيانوجين وتؤثر على التباين في تركيز سيانيد الهيدروجين في أنسجة الذرة الرفيعة. السمية في المجترات لا تعتمد فقط على تركيز هن العلف ولكن أيضا على التفاعل بين إطلاق هن الكرش ومسارات إزالة السموم بوساطة الكبريت. بمجرد امتصاصه، يمنع السيانيد أوكسيديز السيتوكروم سي الميتوكوندريا، مما يؤدي إلى ضعف الفسفرة التأكسدية ونقص الأكسجة الجهازي. يعكس التباين في النتائج السريرية الاختلافات في أنماط المدخول، والحالة التغذوية، والنشاط الميكروبي للكرش، والقدرة على إزالة السموم. خطر السيانيد في أنظمة الذرة الرفيعة المجترة هو نتاج عوامل نباتية وبيئية وحيوانية منسقة بدلا من عتبة تركيز ثابتة. الاستراتيجيات المتكاملة التي تشمل الانتقاء الجيني، والإدارة الزراعية، ومعالجة الأعلاف، والتوازن الغذائي، والرصد، والاستعداد السريري ضرورية لضمان الاستخدام الآمن والمستدام للذرة الرفيعة.

Supplementary Table: Compiled HCN concentrations reported in sorghum under different genotypes, developmental stages, environmental conditions, and post-harvest treatments

Category	Factor/ Treatment	HCN concentration	Effect	Main Observation	Reference	Basis
Genetic	Low-cyanide genotype	0.18–55 mg/kg	↓	*tcd1* genotypes showed lower HCN than *Sorghum bicolor*	(106)	DW
Genetic	Low-cyanide genotype	0.0–3120 mg/kg	↓	*acdc1* and *tcd1* mutants showed lower HCN than *Sorghum bicolor*	(54)	DW
Genetic	Plant part	120–3120 mg/kg	↑	Leaves contained higher HCN than stems and roots	(54)	DW
Genetic	Variety	15.6–55.4 mg/kg	↓	Cultivar JS-2002 showed lower HCN than cultivar Chakwal	(107)	NA
Genetic	Variety	56–723 mg/kg	↓	Cultivar JS-2002 showed lower HCN than Chakwal and local sorghum	(108)	FW
Genetic	Variety	21.1–98.1 mg/kg	↓	Cultivar JS-2002 showed lower HCN than Chakwal and local sorghum	(109)	FW
Genetic	Variety	28.5–70.5 mg/kg	↓	Genotype IS18551 showed lower HCN than ICSV705, ICSV700, SL-44, PSC-4, and SWARNA	(70)	DW
Genetic	T0 generation	46.8–102.08 mg/kg	↓	Accessions showed lower HCN than controls	(47)	DW
Genetic	T1 generation	57.4–292.5 mg/kg	Variable	HCN concentrations varied among accessions	(47)	DW
Genetic	T2 generation	38.4–189.1 mg/kg	↓	Accessions showed lower HCN than controls	(47)	DW

Category	Factor/ Treatment	HCN concentration	Effect	Main Observation	Reference	Basis
Genetic	T3 transgenic progenies	187.0–240.8 mg/kg	Variable	HCN concentrations varied among transgenic progenies	(47)	DW
Genetic	Sorghum hybrids	7.1–65.5 mg/kg	↑	Aphid low-sensitive hybrids showed higher HCN than medium- and high-sensitive hybrids	(110)	DW
Genetic	Variety	192.8–244.9 mg/kg	↑	Sudan grass, Jumbo grass, and *Sorghum halepense* showed higher HCN than *Sorghum bicolor*	(111)	DW
Growth-related	Growth stage	143.8–3068.8 mg/kg	↓	HCN at 15 DAS was higher than at 30, 45, and 60 DAS and at 25% flowering	(112)	DW
Growth-related	Growth stage	70–1120 mg/kg	↓	Younger plants showed higher HCN than mature plants	(54)	DW
Growth-related	Growth stage	56–723 mg/kg	↓	3-leaf stage showed higher HCN than pre-booting and 50% heading stages	(108)	FW
Growth-related	Growth stage	57–227 mg/kg	↓	Dough stage showed lower HCN than booting stage	(113)	DW
Agronomic	Row spacing	110.3–119.6 mg/kg	NS	Higher HCN at 30 cm spacing than at 45 or 60 cm spacing	(114)	FW
Agronomic	Cutting interval	64.8–159.2 mg/kg	↓	Higher HCN at 45 CDI than at 60, 75, and 90 CDI	(114)	FW
Agronomic	Ratoon cropping	45.88–84.97 mg/kg	↓	Ratoon sorghum showed lower HCN than seed-grown sorghum	(115)	FW
Agronomic	Biofertilizer application	60.0–86.6 mg/kg	↓	Liquid biofertilizer reduced HCN compared with untreated plants	(116)	FW
Agronomic	Planting space	145.78–234.67 mg/kg	Variable	Planting space showed inconsistent effects on HCN concentration	(78)	DW
Agronomic	Fertilization	145.78–234.67 mg/kg	Variable	Fertilization showed inconsistent effects on HCN concentration	(78)	DW
Agronomic	Nitrogen fertilization	40–1120 mg/kg	Variable	Nitrogen fertilization altered HCN concentrations, but responses were inconsistent	(54)	DW
Agronomic	Zn and B application	13.29–102.2 mg/kg	↓	Zn and B application reduced HCN compared with untreated plants	(107)	NA
Agronomic	Cutting interval	13.29–102.2 mg/kg	↓	Harvesting at 75 DAS resulted in lower HCN than harvesting at 60 DAS	(107)	NA
Agronomic	Cutting interval	48.31–175.51 mg/kg	↓	HCN at 20 DAS was higher than at 40 DAS	(117)	NA
Agronomic	Farmyard manure (FYM)	56.07–168.19 mg/kg	↓	10 t/ha FYM tended to reduce HCN compared with lower rates	(117)	NA
Agronomic	NPK fertilization	48.31–175.51 mg/kg	↑	HCN increased with increasing NPK rates	(117)	NA
Agronomic	Biofertilizer application	55.65–169.45 mg/kg	NS	Biofertilizers did not significantly affect HCN concentration	(117)	NA
Agronomic	Seeding rate	18.4–113.2 mg/kg	↑	Seeding rate of 100 kg/ha produced higher HCN than 75 or 125 kg/ha	(109)	FW

Category	Factor/ Treatment	HCN concentration	Effect	Main Observation	Reference	Basis
Agronomic	Nitrogen fertilization	21.2–102.0 mg/kg	↑	Nitrogen fertilization increased HCN compared with unfertilized plants	(109)	FW
Agronomic	Ratoon cropping	3499.6–5458.9 mg/kg	↓	Ratoon sorghum showed lower HCN than seed-grown sorghum	(80)	DW
Agronomic	Irrigation×planting arrangement	236.88–520.79 mg/kg	↑	Combined irrigation and planting arrangement increased HCN compared with controls	(102)	DW
Agronomic	Irrigation × biochar	236.88–457.12 mg/kg	↑	Combined irrigation and biochar treatments increased HCN compared with controls	(102)	DW
Agronomic	Planting arrangement×biochar	205.89–236.88 mg/kg	↓	Twin-row planting with 6 t/ha biochar reduced HCN compared with conventional planting	(102)	DW
Environmental	Salinity stress	121.0–144.96 mg/kg	↑	HCN increased with increasing salinity stress	(118)	DW
Environmental	Drought stress	58.66–77.85 mg/kg	↑	Drought stress increased HCN synthesis compared with non-stressed plants	(115)	FW
Environmental	Location (cool vs. warm region)	57–227 mg/kg	↑	Warmer regions showed higher HCN than cooler regions	(113)	DW
Biotic stress	Aphid infestation	28.5–70.5 mg/kg	↑	Aphid-infested sorghum showed higher HCN than non-infested plants	(70)	DW
Biotic stress	Aphid infestation	7.1–65.5 mg/kg	↓	Aphid infestation reduced HCN compared with non-infested plants	(110)	DW
Processing	Post-cutting interval	33–723 mg/kg	↓	Longer post-cutting intervals reduced HCN concentration	(108)	FW
Processing	Ensiling	0.36–1.71 mg/kg	↓	Longer ensiling periods reduced HCN concentration	(103)	DW
Processing	Additive application	0.36–1.71 mg/kg	↓	Additives reduced HCN compared with untreated silage	(103)	DW

Note: HCN= hydrogen cyanide; DAS= days after showing; CDI= cutting days interval; DW= dry weight basis; FW= fresh weight basis; NA= basis not available in the original study; NS= not significant. Arrows indicate relative increases, decreases, or differences in HCN concentration reported within individual studies.