



Antinutrients in Ruminant Feeds: A review

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Abstract: The current challenges in ruminant production are the development of strategies to reduce the cost of feeding, improve the quality of products as well as mitigate the negative impact of production on the environment. Plant-based feeds are chiefly available for animals and may be used to reduce the cost of feeding. However, the presence of toxic substances known as antinutrients limits their full utilization in livestock industries. They are present in different feeds of energy and protein sources. The antinutrients such as saponins, cyanogenic glycosides, goitrogen, lectin, phytoestrogen, oxalate, protease inhibitors, trypsin inhibitors, alkaloids, mimosine, and phytates are harmful to animals when consumed in large quantities. They have unpalatable effects on the digestive system, as well as the overall production performance and welfare of the animals. The exact effects of antinutrients on ruminant gut microbiota and microbiome have not been adequately reported. However, different strategies to enhance the bioavailable nutrients such as milling, soaking, steaming, fermentation, germination, autoclaving, and the use of supplements have been established to improve the quality of plant-based feed and to ameliorate their disastrous effects on the overall quantity and quality of production characterizing of animals.

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Introduction

The importance of nutrition in livestock enterprise has been fully documented as nutrition gulps about 70% of production. The current challenges in ruminant production are the development of strategies to reduce the cost of feeding, improve the quality of products as well as mitigate the negative impact of production on the environment (Yacout, 2016). Feeds of plant origin are chiefly available in many developing countries for animal utilization (Le Houérou, 2000). Yacout (2016) reported that the use of plant-based feeds may subsidize feeding costs and eco-friendly influence. However, as good as plant-based feeds are, the presence of antinutrients impaired their full utilization by animals, and this deficiency is a great concern of many researchers as well as livestock industries globally (Yacout, 2016). Silage, hay, and green fodder contain vital nutrients, but the presence of some toxic materials or incriminating factors reduce their full utilization (Ramteke et al., 2019b). Some antinutrients also affect animal performance. Phytoestrogen or lignin components of sunflower have been reported to have negative effects on the reproductive qualities of ewes (Alharthi et al., 2021). These toxic materials (antinutrients) are also referred to as allelochemicals (Kumar, 1992). Recently, the

deleterious effects of antinutrients on the gut microbiota of *Homo sapiens* and animals have started gaining momentum.

Antinutrients are organic or synthetic substances that either by themselves or via their metabolic products block the absorption and utilization of nutrients (Akande et al., 2010; Yacout, 2016). They are found mostly in plants of energy and protein sources and have negative effects on the overall well-being as well as the productive performance of the farm animals (Epafras and reas, 2019). Many of these compounds are present virtually in every plant that is used in practical feeding (D'mello, 2000).

Several reviews have been based on general antinutrients as well as general strategies to reduce their harmful effects in ruminant feeding, to the best of our knowledge, highly perilous anti-nutrients, as well as their effects on the digestive system, reproductive system, and gut microbiota of ruminants, have not been properly documented. Therefore, the objective of this review is to elucidate some toxic dangerous antinutrients, specific economic treatment strategies, their effects on nutrient utilization, digestive and reproductive performance as well as the well-being of the gut microbiota of ruminants.

Classification of Antinutrients

The presence of antinutritional factors in feeds does not only affect their full utilization but also animals' welfare. Therefore, based on their effects on feed utilization and consequential effects on animals.

Antinutritional factors are classified into four groups as follows:

- a. Factors that affect carbohydrates digestion such as amylase inhibitors, the phenolic compound.
- b. Factors that affect mineral utilization such as phytase
- c. Factors that affect protein digestion as well as utilization such as tannins, saponins, and protease inhibitors.
- d. Factors that stimulate the immune system and may cause a damaging hypersensitivity reaction such as antigenic proteins (Huisman and Tolman, 1992).

Classification Based on Chemical Properties

Antinutrients are recently classified based on their chemical structures or properties and, their effects on nutrient utilization (Ramteke et al., 2019b);

Group A: Proteins a. Lectins (Haemagglutinins) b. Protease inhibitor;

Group B: Glycosides a. Goitrogens b. Cyanogen c. Saponins;

Group C: phenols a. Tannins b. Gossypol; and

Group D: Miscellaneous a. Anti-vitamins b. Anti-metals.

Classification Based Nutrient Utilization

Group A: Substances impairing metabolic utilization of proteins:

- a. Saponins
- b. Haemagglutinins
- c. Protease inhibitor

Group B: Substances tumbling solubility or prying with the utilization of Minerals:

- a. Phytate
- b. Oxalate
- c. Gossypol

Group C: Substances increasing demands of certain vitamins:

- a. Anti-vitamin (Fat-soluble vitamins) such as B1, B6, B12, and Nicotinic acid
- b. Anti-vitamin (water-soluble vitamins) such as A, D, E, K.

Metabolites of Antinutrients

Generally, metabolites have been classified as primary and secondary. Contemporary chemistry has defined the role of primary plant metabolites in

fundamentals of life functions such as storage, respiration, cell division, and growth. They include the components of processes such as glycolysis, the Krebs or citric acid cycle, photosynthesis, and associated pathways (Hussein and El-Anssary, 2019). Primary metabolites such as proteins, sugars, amino acids, are similar in all living cells. Secondary plant metabolites are several chemical compounds produced from primary metabolites (David, 1998). Albrecht in 1910 explained that secondary metabolites are products of nitrogen metabolism. Secondary plant metabolites are classified based on their chemical structures as follows phenolics, saponins, carbohydrates. In addition to, phenolics, the largest group of plant secondary metabolites are structurally sub-classified as tannins, flavonoids, lignans (Hussein and El-Anssary, 2019).

The above-mentioned metabolites (perfectly referred to as anti-nutrients) are toxic substances found in the diets of humans and animals. They disorder the normal physiological functions of animals and humans. The animal performance and behavioral pattern, as well as adaptation to feed are good indicators to predict the effects of antinutrients (Ehsen et al., 2016). Some major damages of antinutrients or secondary metabolites that lead to morbidity and mortality include reduced-immune competence as well as a negative impact on growth and production performance and welfare of the animal (D'mello, 2000; Panhwar, 2005). According to Penhwar (2005), these secondary metabolites can impair the digestibility of essential nutrients by harming normal metabolism, initiating various syndromes that diminish growth rate, reduce palatability and their extreme amounts could be fatal. The consequential effect of feeding animals such diets is related to a decrease in weight gain and economic loss. Therefore, antinutrients are also known as antinutritional factors, secondary substances, or plant secondary metabolites (Epafras and reas, 2019).

Effects of Major Antinutrients on Nutrition

Antinutrients are present in plants, which contain energy and protein sources for farm animals. The major antinutrients include for example but are not limited to saponins, toxic amino acids, chlorogenic acid, amylase, phytic acid, gossypol, cyanogenic glycosides, tannins, oxalates, goitrogens, lectins (phytohemagglutinins), and protease inhibitors. These antinutrients pose a major setback and threat in the use of plants in ruminant feeds without effective processing, and they have negative impacts on protein digestibility and amino acid availability in foods, as well as and plant protein sources (Gilani et al., 2005; Akande et al., 2010). In a recent study, it was indicated that antinutritional factors in cereals reduce the bioavailability of nutrients such as carbohydrates, proteins, vitamins, dietary fiber, minerals, and

phytochemicals (Saurabh et al., 2021). As well as affect the normal growth, reproduction, and health of the animal and human body. The level of concentration of these antinutritional factors varies with plant species, cultivar, and post-harvest treatment or processing methods. The presence of antinutrients in livestock feeding reduces their full utilization. (Akande et al., 2010).

The Science of Goitrogens

Goitrogen is a natural or synthetic organic compound that interferes with the efficiency of the thyroid gland by preventing follicular cells of the thyroid gland to take iodine from the blood. The

goitrogenic substances are found in some feeds such as cassava, sweet potato, and millet (Akande et al., 2010). They have been reported to cause enlargement of the thyroid gland and subsequently inhibit the synthesis and release of thyroid hormones (triiodothyronine-T3 and thyroxine-T4; (Akande et al., 2010). The deficiency of T3 and T4 has been found to reduce the production performance of animals (Olomu, 1995). The effects of goitrogens have been combated with the help of iodine supplementation rather than heat treatment (Liener, 1975). Some common goitrogenic substances, mechanisms of action, and dietary sources are provided in Table 1 (Bertinato, 2021)

Table 1: Goitrogenic substances, dietary sources, and their mechanism of action

Goitrogenic substances	Proposed mechanism of action	Dietary sources
Thiocyanate	Thiocyanate competes with iodide for thyroidal uptake	Sorghum, cassava, sweet potato, linseed, lima beans
Flavonoids	Weaken thyroid peroxidase activity	Millet, soy
Goitrins	Decrease production of thyroid hormone	Rapeseed, cabbage
Iodine	High iodine intake causes thyroid dysfunction	Drinking water, iodine-containing food, supplement

Goitrogen has also been reported to cause thyroidal diseases such as hypothyroidism (Liu, 2013; Petroski and Minich, 2020). Hypothyroidism is closely related to cholesterol. Hyperlipidemia and hypolipidemia are caused by hypothyroidism and hyperthyroidism respectively in adult males (Wang et al., 2017). Imbalance of lipids (dyslipidemia) especially cholesterol in the blood could affect the reproductive functions of animals because cholesterol is the precursor of steroid hormones (Bae et al., 2019).

The Science of Lectins

Lectins are also known as hemagglutinins, are glycoproteins of non-immune origin. They are

carbohydrate-binding proteins found in plants, animals, and microorganisms (Mishra et al., 2019). Mishra et al. (2019) reported that over 500 lectins are produced by plants primarily as a defense mechanism against molds, fungi, insects, and diseases. Without any modification, they can bind with carbohydrates, glycoproteins, glycolipids, and polysaccharides (Popova and Mihaylova, 2019). Lectins have also been reported to have the ability to recognize animal cell carbohydrates (Boyd and Shapleigh, 1954). Lectins play several roles as shown in Table 2. However, not all lectins are toxic to animals (Popova and Mihaylova, 2019).

Table 2. Roles of lectins

Dietary source	Roles	Reference
Wheat, beans, peas	1. Can cause a leaky gut syndrome	1. (Mishra et al., 2019)
	2. Make cells act as if stimulated by insulin	2. (Mishra et al., 2019)
	3. Can cause autoimmune diseases	3. (Karpova, 2016)
		4. (Popova and Mihaylova, 2019)

The Science of Mimosine

Many toxic non-protein amino acids are found in the foliage and seeds of plants. The common one is mimosine. Other include canavanine and djenkolic acids (Akande et al., 2010). Mimosine, a non-protein toxic amino acid has a structural similarity with tyrosine. Mimosine is present in the genus *Leucaena leucocephala* in which the level of mimosine in the leaf is about 2-6% and varies depending on the stem, leaf,

and maturity (Akande et al., 2010). Mimosine toxicity causes eye cataracts, alopecia, reproductive failure, and poor growth in monogastric (Ramteke et al., 2019b). The foremost clinical symptoms of toxicity in polygastrics include alopecia, dullness, poor body growth, poor wool development, mouth, and oesophageal lesions, swollen and raw coronets above the hooves, lameness, low serum thyroxine level, and goiter (Ramteke et al., 2019a). According to Ramteke

et al.(2019b), symptoms may be due to the metabolite of mimosine in the rumen and others to 3,4 dihydroxypyridine. Leucaena feeding has also been associated with a decrease in calving percentage (Jones et al., 1989).

The Science of Phytate

Phytates, also known as phytic acid or Myo-inositol hexaphosphate (IP6) is another antinutrient of plant origin, are mostly found in many vegetable products (Petroski and Minich, 2020; Popova and Mihaylova, 2019). Plant parts such as nuts, seeds, grains, store phosphorus as phytic acid in their husks in the form of phytate salt or phytin. Their presence may decrease the bioavailability of minerals, solubility, functionality, and digestibility of carbohydrates and proteins (Kadam et al., 1990). Phytate is highly concentrated in the bran of grains (Wcislo and Szarlej-Wcislo, 2014). Phytic acid is found in the cotyledon layer and can be removed before consumption in legumes (Nissar et al., 2017).

The digestive enzyme phytase can unlock the stored phosphorus as phytic acid. The phytic acid can hinder the absorption of other minerals such as magnesium, zinc, iron, and calcium by binding to them in the absence of phytase (Akond et al., 2011). This leads to the formation of highly insoluble salts that are not properly absorbed by the gastrointestinal tract resulting in a lower bioavailability of minerals (Akond et al., 2011). Phytates have also been reported to impede digestive enzymes like amylase, trypsin, and pepsin (Kumar et al., 2010). Similar phytate values to that of legumes are generally found in unprocessed cereals, though processed cereals contain significantly less. Processing significantly reduces the phytate contents of many legumes, grains, and seeds (Petroski and Minich, 2020).

The Science of Protease Inhibitors

Proteinases are enzymes with numerous roles in improving the nutritional qualities of various protein

molecules (Salas et al., 2018). Several proteolytic actions such as transmission and cellular apoptosis, signal initiation, blood coagulation, inflammatory response, and many hormone processing pathways are carried out by proteases inhibitors (TR Gomes et al., 2011).

Protease inhibitors are mostly found in raw cereals and legumes, particularly soybean (Popova and Mihaylova, 2019). Antinutrient activities associated with protease inhibitors include poor food utilization (Kadam et al., 1990), and growth inhibition (Adeyemo and Onilude, 2013). Endopeptidases can cleave peptides within the molecule pancreatic hypertrophy, whereas Exopeptidases eliminate amino acids from the C- or N-terminus (Sakamoto et al., 2014). High levels of protease inhibitors have been reported to lead to a raised secretion of digestive enzymes by the pancreas (Logsdon and Ji, 2013). Plant serpins, one of the largest protease inhibitors, are predominant in cereals are usually referred to as suicide inhibitors (Santiya et al., 2020). protease inhibitors in diets can hinder proteolytic enzyme activity within the gastrointestinal tract (GIT) of animals (Nørgaard et al., 2019).

The Science of Oxalates

Oxalate is an antinutrient that can form insoluble salts with minerals, such as iron, calcium, potassium, magnesium, and sodium. These compounds are found in slight amounts in both mammals and plants (Petroski and Minich, 2020). It has been suggested that plants produce oxalic acid for a plethora of functions ranging from detoxification of heavy metals, calcium regulation to plant protection (Franceschi and Nakata, 2005). Oxalate is an anti-nutritional content, when oxalate is digested; it binds with the nutrients in the gastrointestinal tract preventing them from being accessible to the body (Ramteke et al., 2019b). Table 3 summarizes the role of oxalic acid.

Table 3. Roles of oxalates

Dietary source	Roles	Reference
Raw legumes, whole grains, sweet potatoes amaranth,	1. Nutritional deficiencies	(Ramteke et al., 2019b)
	2. Rapid and labored respiration, depression, weakness, coma, and death	(Petroski and Minich, 2020)
	3. Kidney stone formation	

The Science of Phytoestrogens

Phytoestrogens are plant-based compounds with structural similarities to the primary sex hormone (estradiol (E2)) in females (Rietjens et al., 2017). Due to their similarity to the normal estradiol in the animal body, they bind to estrogen receptors and subsequently

modulate estrogenic activity. They are classified into phenolic compounds stilbenes, isoflavones, lignans, coumestrol, and isoflavones (Desmawati and Sulastri, 2019). Lignans and Isoflavones have received much attention because of their relevance to human nutrition (Petroski and Minich, 2020). Flavonoids and

Isoflavones are primarily found in soybeans and contain biochanin A, glycitein, daidzein, and genistein. Flaxseeds and other cereals contain lignan phytoestrogens (Rietjens et al., 2017). Isoflavone

glycosides are hydrolyzed to their physiologically active aglycone metabolites by the microbiome (Petroski and Minich, 2020). The summary of the roles of phytoestrogens is presented in Table 4.

Table 4. Role of phytoestrogens

Dietary source	Role	Reference
Beans (soy, lupines), grain, linseed	1. Endocrine disruptors	(Patisaul, 2017)
	2. Stimulate the growth of estrogen-sensitive Cancers	(Sirotkin and Harrath, 2014)
	3. Interfere with reproduction, bone remodeling, skin, cardiovascular, nervous, immune system, and metabolism	

Toxicity of Antinutrients

The toxic effects of antinutrients in ruminant nutrition have not been well established, unlike in human nutrition. The detrimental effects among others include reduced feed intake, poor feed conversion rate, and death (Epafras and reas, 2019). The consequential effects of many antinutrients affect animal performance. Phytoestrogens or lignin components of sunflower hulls have been reported to have negative effects on the reproductive qualities of ewes if overconsumed (Alharthi et al., 2021). Meaning that concentration-dependent of antinutrients need to be established. Similarly, lignans and phytoestrogens have been reported to induce infertility in *Homo sapiens* (Popova and Mihaylova, 2019).

Antinutrient and Gut Microbiota

All microorganisms of the ruminant host and their genomes are called microbiota and microbiome respectively (Alexander and Plaizier, 2016). Microbiota and their genomes have been reported to play indispensable roles in animal immunity, health, and digestion (Bäckhed et al., 2005). Gut microbiota has been defined as a microbial organ that offers metabolic abilities to digest plant material that is lost or missing in the host ruminant animal (Yoon et al., 2015). The microbiota has been reported to be a source of animal and human pathogens. Proper manipulation of the microbiota has been reported to help improve ruminant performance (Alexander and Plaizier, 2016).

The microorganisms within the gastrointestinal tract (GIT) are called gut microbiota and they have been widely reported to play several functions in the GITs of *Homo sapiens* (Krajmalnik-Brown et al., 2012) and farm animals as well as other vertebrates (Gebreselassie, 2017). Several pieces of evidence suggest that the gut microbiota also plays a critical role in the harvest, storage, and outflow of energy gained from the feed (Gebreselassie, 2017). Krajmalnik-Brown et al. (2012) explained that the composition of gut microbiota is different from one species of animal to other. The exact effect of antinutrients on gut microbiota remains unclear.

However, it has been hypothesized that under normal conditions, the gut microbiota of vertebrates may prevent pathogen colonization and play a vital role in their health (Ringø et al., 2016).

Approaches to Control Antinutrient Effects

Several methods have been used to reduce or get rid of the harmful effects of different antinutritional factors in animal feeds. The methods include making hay, silage with inoculants, using polyethylene glycol (PEG), urea, or biological treatment with fungi. It has been well established that PEG can effectively remove many antinutrients, but its adoption is not economical in most cases (Ramteke et al., 2019b). For example, the deleterious effect of tannins can be economically removed by feeding animals 1% urea. Grinding and pelleting have also been suggested to be good strategies to improve the nutritive qualities of animal feeds (Alharthi et al., 2021).

The bulk of strategies for reducing or ameliorating the disastrous effects of antinutritional factors is available in human nutrition. The methods could help improve the quality of ruminant feeds. Common strategies include milling, soaking, fermentation, sprouting, germination, gamma radiation, and genomic technology (Popova and Mihaylova, 2019; Samtiya et al., 2020). Milling is the most traditional technique to separate the grains from the bran layer. In this method, grains are ground into powder/flour, and it has been reported to be useful in removing phytic acid, tannin, and lectins present in the bran of grains (Samtiya et al., 2020). However, the limitation of this technique is that several minerals are lost during milling (Gupta et al., 2015). Soaking is a physical treatment method to remove water-soluble antinutrients. Soaking usually involves the use of distilled water, 1% NaHCO₃, and mixed salt solutions. It has been reported that soaking using those combinations reduced phytates and phenols by 21% and 33% respectively (Devi et al., 2018). Soaking reduced soluble sugars, tannins, and the total proteins in soybean flour. Soaking has been reported as one of

the excellent ways of removing or deactivating enzyme inhibitors, though lectin is not affected by this method

(Shi et al., 2017). Table 5 summarizes methods to remove some antinutrients.

Table 5. Methods to remove some antinutrients

Antinutrients	Treatments methods	References
Goitrogens	Boiling, steaming	(López-Moreno et al., 2022)
Lectins	Boiling, soaking, autoclaving, fermentation, and germination	
Oxalate	Steaming, boiling, Soaking, pairing with high calcium foods	(Liu, 2004)
Phytates	germination, fermentation, Soaking, boiling	(López-Moreno et al., 2022)

Conclusion

This review provides vital information on some highly toxic antinutritional components of feeds, their effects on the productivity and welfare of farm animals as well as human health. The antinutrients presented were goitrogens, lectins, phytoestrogens, oxalates, protease inhibitors, mimosine, and phytate. These antinutrients interfere with reproductive and digestive systems when present in high or inadequate concentrations. They also interfere with the absorption of nutrients. The bulk of available information on the effects of antinutrients on gut microbiota is on *Homo sapiens*. A paucity of information still exists on the exact roles antinutrients play on the gut microbiota of ruminants as well as other vertebrates.

Nowadays, many overcoming strategies are used to combat the effects of these feed antinutrients, which include milling, soaking, autoclaving, hay and silage making, and supplement. Therefore, the deleterious effects of the above antinutrients on overall animal performance can be reduced with the help of suitable processing/treatment techniques. However, the suitability and cost-effectiveness of different processing techniques have not been fully established in ruminant nutrition.

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