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Review

Condensed Tannins Attributes: Potential Solution to Fescue Toxicosis?

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Abstract: Tall fescue (*Schedonorus arundinaceous* (Schreb.) Dumort. nom. cons. *Lolium arundinaceum* (Schreb.) Darbysh.) toxicosis results from the consumption of alkaloids released by wild-type endophytes (*Epichloe coenophiala*) that live in symbiosis with the plant. Alkaloid consumption causes significant production and reproductive losses which cost the U.S. beef industry approximately $2 billion every year. Incorporating species that contain condensed tannins (CTs) into forage systems may be an effective strategy to reduce the effects of fescue toxicosis in livestock. It has been hypothesized that stable complexes formed between CTs and toxic alkaloids could help reduce their absorption through the gastrointestinal epithelia, thus reducing their toxic effects. However, it is not yet clear whether CTs are effective in reducing the effects of fescue toxicosis in grazing systems. A comprehensive literature search was carried out using Google Scholar to identify studies relevant to the research question, from which the cited articles were selected. This review covers the value and issues of tall fescue employed as useful forage, summarizes the impact endophyte-infected tall fescue can have on cattle, and sets out the current management strategies implemented to minimize fescue toxicosis. The review continues with a brief summary of tannin structure and the well-documented benefits that CT-containing forages can contribute to the productivity and sustainability of ruminant agriculture. Finally, a summary of the potential forage sources, mechanisms, and benefits of CTs in reducing the negative post-ingestion effects of fescue alkaloids in livestock is provided.

Keywords: tall fescue; endophytes; alkaloids; ruminants; legumes; proteins

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1. Introduction and Background

1.1. High-Valued Forage

Tall fescue (*Schedonorus arundinaceous* (Schreb.) Dumort. nom. cons. *Lolium arundinaceum* (Schreb.) Darbysh.) is the primary cool-season pasture forage species found in the north–south transition zone of the U.S.—a region commonly called the "fescue belt." It is grown on over 14 million hectares of pasture and hay land across the U.S. [1]. Introduced into North America from Europe during the late 1800s [2], tall fescue spread rapidly throughout the southeastern U.S. following the release of 'Kentucky 31' in 1942. This cultivar has become the primary cool-season forage grown in the region [3,4] because it can be easily established, is highly persistent and adaptable to diverse climatic conditions, and can tolerate insect/pest infestation and limited management [5]. In the U.S., it is predominantly adopted in the north–south transition zone between the temperate and subtropical regions of the humid eastern U.S. [6].

Tall fescue's nutritive value is similar to other cool-season forages through much of the growing season, but it is generally more nutritious in the fall due to greater leaf retention [7–9] and the increased concentrations of sugars and osmolytes [10] that protect its leaves from freezing. The plant retains leaf tissues and relatively high nutritive value into the winter season [8], which makes it valuable for stockpiling [11]. Deferred grazing on tall fescue pastures provides an opportunity for farmers to extend the grazing season in the winter months, thereby reducing the winter feed expenses which account for the majority of costs in beef cattle production systems in this region.

1.2. Issues with Tall Fescue

Despite these positive agronomic traits and forage quality characteristics, animals that graze on tall fescue display a number of symptoms associated with the reduced animal performance collectively known as fescue toxicosis [12]. This syndrome is characterized by three primary symptoms: fescue foot, fat necrosis, and summer slump [3,13].

Fescue foot, a condition that includes tissue necrosis and dry gangrene of the feet (and also the tips of ears and tails), often results in lameness in cattle [14]. This is more common in the northern U.S. but also occurs in the southern regions during exposure to cold temperatures [15]. Fat necrosis occurs when visceral adipose tissues harden in the abdominal cavity. This disrupts digestion and increases dystocia during calving [15]. In extreme cases of fescue foot and bovine fat necrosis, function is impaired to the point that the animal must be euthanized. Summer slump, the most widespread syndrome associated with fescue toxicosis, occurs throughout the fescue belt during periods of high temperatures. The most common symptoms associated with summer slump include retention of winter hair coat, elevated core body temperature (and thus significant heat stress), reduced animal weight gain, and reproductive losses along with various other physiological and behavioral changes [16]. Collectively, fescue toxicosis causes significant production and reproductive losses [17–19] that result in an annual loss of $2 billion to the U.S. beef industry [20].

Although issues related to animal performance on tall fescue were noted after the release of Kentucky 31, it was not until the late 1970s when Bacon et al. [21] associated the presence of a fungal endophyte in fescue with these disorders. Planting endophyte-free tall fescue cultivars soon became a means of eliminating toxicosis, but this strategy largely failed. The presence of endophytic fungi in tall fescue makes the plant persistent, robust, adaptive, and resistant to insects, pests, and diseases [22]. The endophytic fungus, *Epichloe coenophiala*, is present in over 90% of U.S. pastures [23,24], and fescue stands without an endophyte often do not persist under typical grazing management and environmental conditions.

1.3. The Perpetrators

The disorders associated with fescue toxicosis are understood to arise from a group of alkaloids produced by the fungal symbiont. These include ergovaline, ergotamine, ergocristine [25], and, likely, the hydrolysis product of these compounds, lysergamide. The chemical structures of these compounds are given in Figure 1. Among the different ergot alkaloids, ergovaline comprises 10–50% of the total ergot alkaloids and 85–97% of the total ergopeptide alkaloids [26–28]. Because of its greater concentration, ergovaline is considered to be the major toxic agent for grazing livestock [25,29,30].

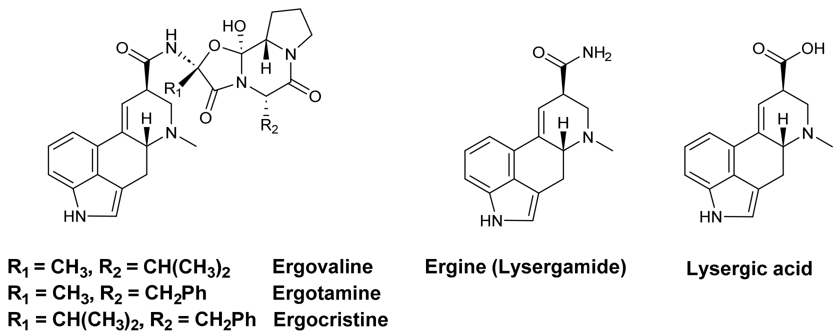

Figure 1. Chemical structures of the alkaloids associated with the wild-type endophytes (*Epichloe coenophiala*) (modified from Schiff [31]).

After being consumed, the toxic alkaloids in tall fescue are absorbed through the gastrointestinal epithelia either passively or via a facilitated/active transport mechanism [32]. The rate and extent of absorption of the ergot alkaloids are significantly influenced by their physiochemical properties. Ergot alkaloids are composed of a tetracyclic ergoline ring and share a similar structure to biogenic amine neurotransmitters such as serotonin, dopamine, norepinephrine, and epinephrine (Figure 2) [32–34]. The similarity in structure between ergot alkaloids and biogenic amine neurotransmitters allows the alkaloids to bind the biogenic amine receptors and elicit the negative effects in livestock that lead to fescue toxicosis [35–38].

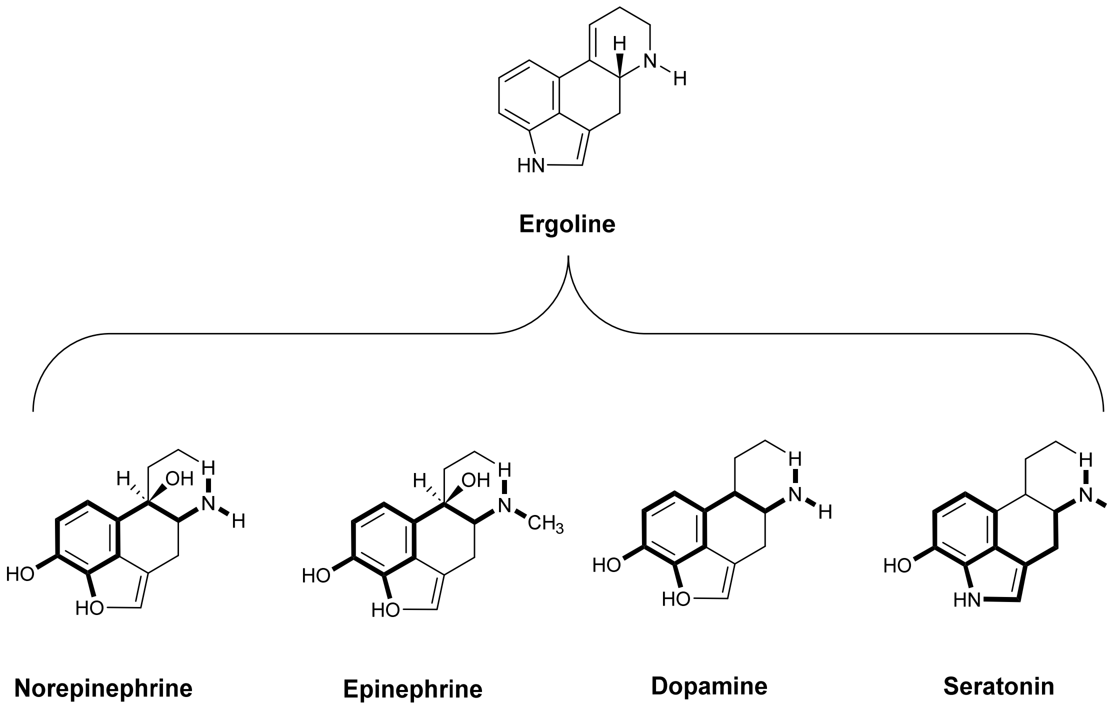

Figure 2. The tetracyclic ergoline ring system overlaid with catecholamines and serotonin (bold) to demonstrate the similarities between these structures. The ergoline ring system serves as a suitable pharmacophore for these neurotransmitters (modified from Britt [39]).

2. Effects of Fescue Toxicosis: Uptake by and Impacts on Ruminants

The toxic alkaloids in tall fescue act as vasoconstrictors that restrict the blood vessels and reduce circulation to the body's extremities [25,40]. In the summer, this results in decreased heat dissipation, thus increasing the internal core body temperature of animals and causing heat stress. Some of the classic signs of fescue toxicosis associated with heat stress in livestock include increased body temperature, high respiration rate, salivation, and excessive time spent standing in shade or water [37]. Various studies have reported an increase in the internal core body temperature of animals due to fescue toxicosis [41–48]. Fescue toxicosis is also associated with lower pregnancy and calving rates and delayed conception in livestock [49,50], thus severely impacting their reproductive success.

Animals experiencing fescue toxicosis also exhibit longer hair coats during the spring and summer months [3,51,52]. Along with the retention of winter hair coat, animals may experience continuous growth of hair even during the summer months [53]. The follicular cycle in cattle is regulated by the prolactin hormone secreted by the pituitary gland [54], and the prolactin level increases as a function of an increased day length [53]. However, toxic alkaloids such as ergovaline within tall fescue act as dopamine agonists that mimic the binding of dopamine and block dopamine D2 receptors, reducing the synthesis and secretion of prolactin from the pituitary gland [45]. As serum prolactin levels are depressed, hair growth is not inhibited [18,54,55], resulting in accelerated and continued hair growth in cattle grazing on wild-type endophyte-infected tall fescue compared with those grazing on non-toxic tall fescue. Past studies have reported consistently low prolactin levels in cattle exhibiting symptoms of fescue toxicosis [13,52]. There is also speculation that the longer and rough hair coat in animals may be the result of nutrient deficiency in animals experiencing fescue toxicosis as a result of vasoconstriction, peripheral ischemia, and/or biochemical alterations in their hair follicles [56].

Heat stress due to fescue toxicosis can severely impact the behavior and time budget of grazing livestock [13,37,41,52,56–60]. Heat stress, with the increase in core body temperature, causes affected animals to seek out water sources such as streams and ponds to cool themselves down [61]. When cattle enter streams or ponds to cool down, they may defecate and urinate in the water, which can introduce excess nutrients, bacteria, and other contaminants into the aquatic ecosystem. Over time, this can lead to a range of environmental problems, including eutrophication (excessive growth of algae and other aquatic plants), oxygen depletion, and harmful algal blooms, causing negative impacts on aquatic organisms and environmental health.

3. Current Tall Fescue Management Strategies to Mitigate Fescue Toxicosis

Several management strategies have been studied to reduce the effect of fescue toxicosis such as supplementing animals on wild-type endophyte-infected tall fescue with vitamin E, thiamine, and protein [62–64] or implementing the ammoniation of feedstuffs [65]. However, these strategies require additional handling and expenses and may not always be practically appropriate. The use of vaccines [66] or dopamine antagonists [67] to mitigate fescue toxicosis has not been feasible as such practices require multiple injections of pharmacological materials which are expensive and place additional stress on animals. Other strategies such as the use of different leguminous forages inter-seeded with tall fescue to dilute the effect of toxic alkaloids have been implemented to variable effects. Several studies have reported the inclusion of leguminous forages such as red (*Trifolium pratense* L.) and white clover (*T. repens* L.) into tall fescue stands as an effective strategy to increase animal performance [68–70], and "Dilution is the solution to pollution" has become an often-used mantra to encourage the incorporation of legumes in a pasture to dilute the concentrations of toxins in the animals' diets. However, the improvement in performance may only reflect greater intake and a higher plane of nutrition associated with clover consumption [69]. Although some clovers do contain isoflavones, such as biochanin A, that cause arterial vasodilation, thus reducing the effects of fescue toxicosis [71–73], the benefits that these treatments provide fall short of the benefits provided by switching to non-toxic forage [20].

Pasture renovation of wild-type endophyte-infected tall fescue with novel endophyte-infected tall fescue can be an option to deal with fescue toxicosis as these cultivars have comparable nutritional quality and productivity to wild-type endophyte-infected tall fescue but without any harmful effects on livestock. Past studies have reported higher gain and serum prolactin levels, along with lower respiration rates and rectal temperatures in animals on novel endophyte-infected tall fescue than those grazing on wild-type endophyte-infected tall fescue [19,74]. However, renovating pastures to non-toxic tall fescue or other species of grass is usually expensive, costing approximately \$600 per ha^{-1} [20], and it is likely not profitable for producers with temporary land lease agreements or in areas where land is highly erodible. Renovation usually requires three years of improved productivity for the renovation to be economically profitable [75]. There remains a need to identify the most effective ways for producers to deal with fescue toxicosis in livestock that is both economically viable and practically feasible. Supplying feed supplements that can limit the absorption of toxic alkaloids in the digestive tract can be one of the potential ways to deal with fescue toxicosis. Tannins, a group of heterogeneous polyphenolic polymers, may have some potential to alleviate the effects of fescue toxicosis due to their high affinity towards nitrogenous compounds such as alkaloids to form complexes.

4. Tannin Biochemistry

Plants produce secondary metabolites (more recently referred to as specialized metabolites) [76] with complex structures as defensive compounds that make the plants competitive in their environment [77]. Among the various secondary plant metabolites, tannins are considered one of the most important and abundant [78] and are produced to meet various physiological demands and as a response to stressors [79]. Tannins are phenolic compounds of medium to high molecular weight and, except for some of the higher molecular weight structures, most are soluble in water (20–35 °C) [80]. They can be broadly classified into two different classes based on their chemical structures and properties: hydrolyzable tannins (HTs) and condensed tannins (CTs) (Figure 3) [81]. These two groups of tannins have different molecular weights and chemical structures, and they can produce different effects on herbivores when ingested, especially on ruminants [80]. HTs contain carbohydrates, generally D-glucose, as a central core [82], with an additional phenolic acid attached, such as ellagic acid or gallic acid [83]. HTs are limited in availability in plants compared to CTs. There are some plants that contain HTs in leaves, such as chestnut trees (*Castanea* sps.) and blackberry bushes (*Rubus allegheniensis*) or the forb such as small burnet (*Sanguisorba minor*) [84], whereas sufficiently high concentrations of HTs typically occur in berries, fruits, and nuts [85]. In addition, HTs can form toxic compounds which, when ingested by ruminants, can induce several detrimental effects including damage to the liver and kidney and even death [86]. For these reasons, producers have been advised to avoid incorporating plants with HTs into their cropping systems. Thus, the remaining portion of this review will focus on CTs.

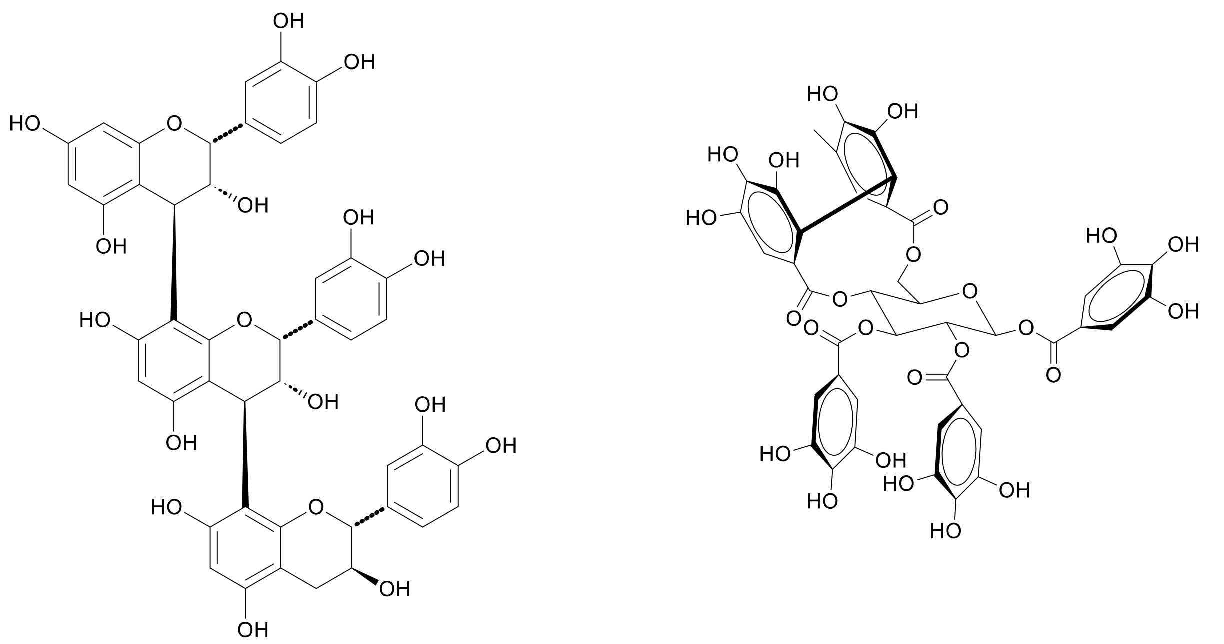

Figure 3. Representative chemical structures of condensed (**left**) and hydrolyzable (**right**) tannins.

CTs (proanthocyanidins), which are more common than HTs in plants and are found in higher concentrations, consist of polymerized flavan-3-ol monomers and vary in location and number of hydroxyl groups and stereochemistry [87,88]. They are widely distributed in different leguminous types of forage such as birdsfoot trefoil (*Lotus corniculatus* L.), sainfoin (*Onobrychis viciifolia* Scop.), and sericea lespedeza (*Lespedeza cuneate* (Dum. Cours.) G. Don) [89]. Less-utilized. types of leguminous forage containing CTs include Illinois bundleflower (*Desmanthus illinoensis*), big trefoil (*Lotus pedunctulatus*), panicled leaf ticktrefoil (*Desmodium paniculatum*), sunshine mimosa (*Mimosa stringillosa*), purple prairie clover (*Dalea purpurea*), and rabbit's foot clover (*Trifolium arvense*). Generally, plants contain CTs in their leaves and stems, although they may be present in flower petals only in some legumes such as white and red clover [90]. Procyanidin and prodelphinidin are the primary CTs present in these species [91].

5. Beneficial Effects of Condensed Tannins in Ruminant Production Systems

5.1. Increase in Nitrogen-Use Efficiency

A high percentage of the proteins in temperate forages are rapidly rumen-degradable [92]. The degradation of these proteins by rumen microbes and the consequent loss of N (through conversion to NH_3) present significant production and environmental costs for ruminant livestock systems [93]. In addition to the lower N-use efficiency, there are higher metabolic energy costs for N excretion. The increased excretion of urinary N can, in turn, cause negative environmental impacts through gaseous and leaching losses [94,95].

CTs have a high binding affinity towards various nitrogenous compounds and form complexes with these materials. At moderate concentrations (typically 2–4% of DM), CTs bind with protein at near-neutral pH levels (6.5–7.5) of the rumen, forming condensed tannin–protein complexes and largely protecting the complexed protein from degradation. When the digesta reaches the abomasum, the lower pH (<3.5) allows the condensed tannin–protein complexes to dissociate and release the proteins [96,97]. This process increases the supply of escape protein to the hindgut and can result in improved animal performance with increased body weight gain, milk production, and reproductive performance and reduced infestation of gastrointestinal parasites [98]. It can also shift N loss pathways from readily leached or volatilized urea N in urine to more stable N complexes in feces, slowing the loss of fecal N to the environment [99–101]. For example, Perez-Maldonado and Norton [102] reported that supplementing sheep and goats with tanniferous legumes (*Desmodium intortum* and *Calliandra calothyrsus* with CT levels of 9.5 g kg^{-1} DM and 22.5 g kg^{-1} DM, respectively) resulted in a 14% increase in fecal N. Reducing urinary N can help decrease the environmental losses resulting from nitrate leaching, NH_3 volatilization, and nitrous oxide emissions [103].

5.2. Mitigation of Methane Production

Several studies also have demonstrated that dietary CT inclusion can reduce rumen methanogenesis [104–106]. Methane alone accounts for 39% of the total greenhouse gas emissions from the livestock industry [107]. It is produced in the rumen as a byproduct of microbial fermentation and represents a significant loss of energy from the diet, ranging from 2–12% [108]. During the microbial fermentation of hydrolyzed dietary carbohydrates, such as cellulose, hemicellulose, pectin, and starch, an excessive amount of H_2 is produced in the rumen, along with CO_2. Methanogenic archaea in the rumen transform CO_2 to CH_4, reducing excessive H_2 and minimizing the negative effects of H_2 accumulation on the enzymatic activity and digestion of microbes [109]. However, this results in a loss of CH_4 from the animal to the environment [110], with corresponding negative effects on the environment in terms of increased greenhouse gas emissions. Various studies have reported that CTs can reduce CH_4 production by ruminants [111] both in vitro [112,113] and in vivo [114,115]. The mechanism behind this is not fully understood, but there is a hypothesis that CTs may directly impede the growth of methanogen microorganisms in the rumen [98,116]. The indirect suppression of methanogens in the rumen may occur by reducing the hydrogen available to microorganisms [117]. This reduced activity of methanogens in the rumen may also result in a reduced acetate-to-propionate ratio, as more hydrogen is transferred to propionate [118]. In addition, CTs have been shown to serve as hydrogen acceptors, and the presence of CTs in the diet of ruminants may reduce the availability of hydrogen in the rumen to form CH_4 [119,120].

In a study by Animut et al. [114], goats were fed Kobe lespedeza (*Lespedeza striata*), a combination of Kobe lespedeza and quebracho tannin (*Schinopsis quebracho-colorado*), sericea lespedeza, or a combination of Kobe lespedeza and sericea lespedeza (CT levels were 151, 198, 140, and 146 g kg^{-1} DM, respectively) to assess the levels of methane emissions. Subsequently, polyethylene glycol (PEG) was mixed with these treatments and fed to the goats in the second phase. Across all experimental diets, DM intake and N digestibility were lower in the goats whose diets did not include PEG compared to those that were fed PEG. Methane emissions were higher in the goats whose diets included PEG (19.1 L day^{-1}) than those whose diets did not include PEG (9.01 L day^{-1}), suggesting that CT consumption may have reduced CH_4 production. Similar findings have been reported with diverse tannin sources. Pellikaan et al. [113] added 100 g kg^{-1} CT to rumen liquid obtained from lactating dairy cows and measured the in vitro CH_4 production. The amount of CH_4 produced was lower with CTs from *Schinopsis* (quebracho) and *Vitis* (grape) spp. Kongvongxay et al. [115] reported reduced CH_4 emissions in goats fed *Mimosa pigra* (40 to 80 g kg^{-1} DM of CT) at 25, 50, and 75% of the diet, with the greatest reduction observed at 50% of the diet.

5.3. Natural Anti-Parasitic Agents

It bears mentioning that directly feeding CTs or forage containing CTs are increasingly viewed as a potential means of controlling gastrointestinal parasites [82,121]. The search for alternatives to synthetic parasite control is particularly important given the increase in resistance to commercial anthelmintics [122–124]. Much of this work has focused on small ruminants such as sheep and goats [125–130], but the inclusion of dietary CTs has also reduced parasite burdens in cattle [131–134] and horses [135–138]. Along with reducing worm burden, consuming tannin-containing forage may also increase the immune response [139].

6. Condensed Tannins: A Potential Solution for Fescue Toxicosis?

Along with protein, CTs possess a strong binding affinity for the steroidal and protein-like alkaloids that are produced by the endophytic fungus within tall fescue [96,140,141]. This affinity of tannins for alkaloids can potentially benefit livestock by reducing the post-ingestion effects of fescue toxicosis. Various studies in the past have demonstrated that the inclusion of CT-based forage in the diets of animals that consume wild-type endophyte-infected tall fescue can potentially reduce the effects of toxic alkaloids. Lisonbee et al. [121] reported a greater consumption of tall fescue with a high alkaloid concentration in lambs with an intraruminal infusion of CTs compared to that of lambs with no infusion. Lambs, when offered choices among three types of forage with high plant secondary metabolite levels after infusion, consumed more of the high-alkaloid varieties of tall fescue than the control lambs. The authors concluded that tannin infusion increased the lambs' preference for forage varieties with high alkaloid concentrations, likely due to the formation of insoluble complexes. In another study by Catanese et al. [142], lambs were housed individually and fed wild-type endophyte-infected tall fescue. The lambs' diets were supplemented with either beet pulp (control), fresh-cut sainfoin and beet pulp (SAIN), or fresh-cut sainfoin plus PEG mixed in the beet pulp (SAIN + PEG). After initial exposure, the lambs were given a choice between endophyte-free tall fescue or orchard grass, and their preference was evaluated. Subsequently, the lambs were allowed to graze on either wild-type endophyte-infected tall fescue and sainfoin or a monoculture of wild-type endophyte-infected tall fescue. The lambs in the SAIN group consumed more wild-type endophyte-infected tall fescue than the lambs in the control group. Compared to the lambs on the control treatment, the lambs in the SAIN group had lower rectal temperatures, higher leukocyte and lymphocyte counts, and higher globulin and prolactin concentrations in their plasma. The authors concluded that sainfoin supplementation reduced the effects of fescue toxicosis in the lambs, resulting in an increase in the intake of tall fescue infected with the wild-type endophyte.

In another study, Villalba et al. [143] fed two legume species, sainfoin (2.9% CT) or cicer milkvetch (CIC, 0% CT), and a mixed ration containing tall fescue seed (50:30:20 seed: beet pulp: alfalfa (*Medicago sativa* L.)) with two levels of endophyte infection (endophyte-infected tall fescue seed (3150 ug L^{-1} ergovaline) or endophyte-free tall fescue seed) to 4-month-old lambs in individual pens. The lambs that were offered sainfoin ate more wild-type endophyte-infected tall fescue than the lambs that were offered CIC. The lambs, when supplemented with sainfoin as opposed to CIC, had lower rectal temperatures. The authors concluded that the CTs in sainfoin mediated the effects of the toxic alkaloids in tall fescue seed by binding with these alkaloids and inactivating them. Lyman et al. [144] studied how the utilization of wild-type endophyte-infected tall fescue was affected when heifers first grazed on birdsfoot trefoil or alfalfa. The heifers spent more time grazing on the wild-type endophyte-infected tall fescue following a 30-min period of grazing on the birdsfoot trefoil compared to the animals that grazed on wild-type endophyte-infected tall fescue first and then on birdsfoot trefoil. The authors concluded that the intake of wild-type endophyte-infected tall fescue increased when the cattle ate legumes with an increased amount of CTs. Lyman et al. [145] also found that intake by sheep fed either gramine or ergotamine, along with tannin- or saponin-containing foods, was greater than the intake of sheep fed gramine or ergotamine only. The authors concluded that CTs and saponins can help neutralize the negative effects of alkaloids on animals.

A study by Owens et al. [146] investigated if the consumption of alfalfa or birdsfoot trefoil prior to wild-type endophyte-infected tall fescue or reed canary grass (*Phalaris arundinacea* L.) by lambs would provide benefits not possible when wild-type endophyte-infected tall fescue or reed canary grass was eaten alone. The total dry matter, nitrogen, and energy intakes were greater in lambs fed alfalfa or birdsfoot trefoil prior to consuming wild-type endophyte-infected tall fescue or reed canary grass than those of lambs fed wild-type endophyte-infected tall fescue or reed canary grass only. The lambs fed birdsfoot trefoil ate slightly less reed canary grass, but they ate much more wild-type endophyte-infected tall fescue than the control group. The lambs ate less birdsfoot trefoil compared to alfalfa, but they were stimulated to consume wild-type endophyte-infected tall fescue to a greater degree by the birdsfoot trefoil than they were by the alfalfa. The authors concluded that the enhanced intake of wild-type endophyte-infected tall fescue by the lambs fed birdsfoot trefoil was likely due to the high affinity of trefoil tannins for fescue alkaloids. Maughan et al. [147] reported a greater intake of forage per kg of grain in cattle fed tall fescue mixed with condensed tannin-containing sainfoin compared to cattle fed tall fescue with saponin-containing alfalfa. Compared with the alfalfa-fed cattle, the sainfoin-fed cattle had improved carcass characteristics and comparatively redder colored steaks. The fatty acid composition of the steaks from the cattle fed alfalfa had lower levels of 16:0 and 16:1 n7 and higher levels of 16:1 n7t, 22:0, 20:5 n3, 22:5 n3, and 22:6 n3 compared to the sainfoin-fed cattle. However, Grote et al. [148] reported no differences in the prolactin levels typically associated with fescue toxicosis in ewes fed wild-type endophyte-infected tall fescue silage and supplemented with quebracho tannin at 0, 10, and 30 g kg^{-1} of silage dry matter (DM). In addition, CT supplementation at 30 g kg^{-1} DM reduced DM and organic matter digestibility. The authors concluded that the supplementation of CT did not prevent decrease in prolactin associated with tall fescue toxicosis.

CTs have a strong affinity for nitrogenous compounds, such as alkaloids. These compounds bind with CTs within the rumen, making them more likely to pass unabsorbed through the gastrointestinal tract of an animal and reducing the negative effects of alkaloids on the animals [82]. The chemical interaction between CTs and alkaloids is proposed to involve two steps. In the first step, the alkaloids are complexed by the CTs, leading to aggregation and subsequently resulting in the precipitation of the complex [149,150]. Stable complexes are formed between alkaloids and CTs at near-neutral pH levels (6.5–7.5) of the rumen [141]. The formation of these complexes depends on many factors, including the structure of the individual compounds and the chemistry of the solution [151–153]. Since the association between CTs and alkaloids is highly dependent on pH, a stable complex may be disrupted at a lower pH in the abomasum. As most of the ergot alkaloids are weak bases and are amphipathic, pH can play a significant role in water/lipid partitioning and their absorption [32]. Since ergopeptide alkaloids become charged at low pH levels, it is less likely that they are absorbed in the abomasum at lower pH levels [154]. Thus, absorption of these toxic alkaloids is limited in the abomasum and intestine in ruminants [155,156]. Since the ruminal pH of forage-fed animals is close to neutral, the rumen does not require a mucosal layer to protect tissues from digesta [157]. Alkaloids that escape rumen absorption due to the formation of complexes with CTs are metabolized and excreted in feces [140]. Reducing alkaloid absorption (and the corresponding negative effects on animal physiology) can thus support the increased intake of forage with toxic alkaloids [141].

Although CTs have the potential to reduce the post-ingestion effects of toxic alkaloids, the extent of this benefit may vary depending on their concentration in ruminants' diets. Excessive dietary CT causes various detrimental effects such as the decreased palatability, DM intake, and digestibility of essential nutrients such as protein, carbohydrates, and fats, thereby lowering feed efficiency and animal productivity [158–160]. This presents uncertainties about how to achieve the positive benefits of CTs while avoiding the negative effects that may arise from excessive dietary concentrations or their inappropriate chemical properties. Thus, further study is needed for a comprehensive understanding of the chemistry of and mechanisms controlling alkaloid–tannin interactions to optimize their benefits for fescue-based livestock systems.

7. Common Condensed Tannin-Containing Forage Legumes in U.S. Pasture Systems

Several forage legumes that contain CTs are commonly found in pasture systems across the U.S. Sainfoin is a non-native perennial legume primarily used as hay or grazed in pastures alone or in grass–legume mixtures. It has been used as a forage legume for centuries in Europe and Asia, and it was introduced to North America in approximately 1900. It is largely adapted to the Intermountain and Rocky Mountain regions of the U.S. [161]. It contains a higher concentration of CTs, ranging from 30–80 g kg^{-1} DM [162], and it is primarily concentrated in the aerial parts of the plants within the cell vacuoles [163]. Sainfoin can provide similar benefits to both sheep [164] and cattle [165] compared to alfalfa [166] in terms of yield and nutritive value.

Birdsfoot trefoil is a perennial forage legume distributed throughout a majority of the U.S. It is a non-bloating pasture legume that can improve animal productivity and can be a good grazing alternative to alfalfa in the northcentral U.S. [167]. It contains 10–40 g kg^{-1} DM of CT [168].

Purple prairie clover is a native perennial legume that is well-suited to the prairies of North America. It has high palatability and digestibility compared to other native legumes [169]. It contains a high concentration (58–94 g kg^{-1} DM) of CT and possesses strong anti-microbial, anti-parasite, and antioxidant properties [170–172].

Sericea lespedeza is a perennial legume indigenous to eastern and central Asia, and it is adapted to the warm climatic conditions, along with the acidic and infertile soils, of the southeastern U.S. [173,174]. However, it is considered low-quality forage as it contains high levels of CTs and indigestible fiber that reduce the palatability of the forage, especially when it is mature. Sericea lespedeza contains CTs at a concentration of approximately 120 g kg^{-1} DM [175–177] that can cause detrimental effects on grazing livestock. However, low tannin-containing forage cultivars of sericea lespedeza, such as 'AU Grazer', have been introduced through selection efforts that do not cause detrimental effects to livestock [178]. This cultivar of sericea lespedeza is an effective alternative to anthelmintic drugs in controlling gastrointestinal parasites [179–181], especially barber's pole worm (*Haemonchus contortus*) [182], and it reduces CH_4 emissions [183,184] in small ruminants. A meta-analysis conducted on feeding studies using 'AU Grazer' demonstrated that the inclusion of moderate amounts (<60%) of this cultivar in diets effectively mitigated fecal egg counts of *H. contortus* and reduced methane production, but it negatively impacted total tract digestibility and average daily weight gain [185].

These are the most commonly found tanniferous forage legumes used in U.S. pasture systems. Other less-utilized tanniferous forage legumes include Illinois bundleflower, big trefoil, panicled leaf ticktrefoil, sunshine mimosa, and rabbit's foot clover. Along with their high protein content, these forage legumes also contain CTs that can induce both positive and detrimental effects on ruminants. It is important to point out that all of these forage legumes accumulate CTs with unique structures and compositions [91], and these features vary depending on harvest time (maturity), the specific cultivar, the weather of the growing season, and the location. The CTs from these temperate legumes can improve the efficiency of energy and protein utilization in ruminants [186]. Their strong binding affinity for nitrogenous compounds protects proteins from degradation by rumen microbes, thus improving the protein supply to the hindgut [100], reducing gastrointestinal parasites and bloating [88], and inhibiting methane and ammonia production in the rumen [106,187].

8. Conclusions

Pasture systems throughout the U.S. contain several forage legumes that are rich in CTs. The type and concentration of CTs in these forage legumes depend on the location and season of growth, the cultivar, and the level of maturity. The pasture inclusion of tanniferous forage or supplementing ruminant diets with CT-containing legumes can help increase the supply of rumen-undegradable protein and decrease gastrointestinal parasite infestation, thus improving ruminant overall productivity. CTs can also help shift the site of N metabolism and absorption, re-partitioning urinary ammonia (NH_3-N) to fecal N in ruminants, which, along with reducing the production of methane gas in the rumen, can reduce specific negative impacts of livestock production systems on the environment. Along with these benefits, CTs may also help reduce the post-ingestion effects of fescue toxicosis in livestock. CTs have a high affinity towards various nitrogenous compounds such as alkaloids, thus forming complexes and limiting their absorption through the gastrointestinal epithelium. The pasture inclusion of CT-based forage with wild-type endophyte-infected tall fescue can help producers deal with the effects of fescue toxicosis, a malady that substantially reduces the productivity and profitability of grazing production systems located in the fescue belt. This practice offers the potential for further exploration to understand the interaction of CTs with a different class of alkaloids in the rumen environment and the capacity of these tannins to improve the reproduction and growth of ruminants. However, CTs in livestock diets also have adverse effects on ruminants, such as reduced voluntary feed intake and digestibility. Therefore, it is necessary to determine the optimum dose of CTs for animals that may reduce the toxic effects of the alkaloids found in tall fescue while minimizing any detrimental effects from the CTs themselves.

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