



Review Article

Constraints on the utilization of cereal straw in lactating dairy cows: A review from the perspective of systems biology

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ABSTRACT

Cereal straw, a human inedible crop byproduct, can be used as a roughage source in ruminants. However, the nutrition density and palatability are very low, limiting its efficient utilization in animal production. This review aims to systematically provide an overview of the limitations of cereal straws, which is crucial for developing new strategies to enhance the efficient use of cereal straws by lactating dairy cows. Evolutionary molecular biology makes it possible to comprehensively understand the limitations of using cereal straw as a roughage source in dairy cows by different techniques, e.g., multi-omics. Main constraints for utilization of cereal straw and stover in lactating dairy cows include low contents of easily fermented carbohydrates (pectin) and essential amino acids (Met, Phe, and branched-chain amino acids), high content of lignin and silica, and low nutrient digestibility. These cause insufficient supply of the precursors for milk synthesis and result in increased loss of nutrients in feces and urine. Several molecular mechanisms are revealed by multi-omics techniques, including changed amino acid and glucose metabolism, altered rumen microbial composition and function, and differential expression of miRNAs, mRNA, and protein in multi-organs that are associated with milk synthesis. These can be targets of approaches to improve the utilization of cereal straw by dairy cows. In addition, much attention should be given to the efficient countermeasures, including pretreatments by fibrolytic enzymes or steam explosion, dietary formulations such as supplement of pectin, methionine, and branched-chain amino acids, and feeding with other functional feedstuffs, which may improve the feeding and economic value of cereal straw for lactating dairy cows. The newly revealed functional genes (such as *BAG3* in the rumen, *PC* in the liver, *CSN1S2* in the mammary gland) and biomarkers (hippuric acid) as well as the integrative signaling and metabolic pathways (phenylalanine metabolism) related to the shortages of cereal straws could be used as nutritional or genetic regulatory targets to improve dairy cow production.

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1. Introduction

Cereal straw is a type of human inedible crop byproduct. Many kinds of cereal straws are produced each year worldwide. Among

them, corn stover, rice straw and wheat straw are the byproducts of corn, rice and wheat plants after grain harvesting, respectively. Some cereal straw and stover are utilized as roughage for ruminants after dehydration, ensiling, or ammonification treatments, and some are used as compost. Still, most cereal straw is used for burning, heating, or discarding (Cao et al., 2016a), resulting in a massive waste of resources and environmental pollution.

China, one of the largest producers of cereal straw globally, approximately produces 653 million tonnes of crop straw annually, with most being corn, rice, and wheat straw during 2000–2017 (Zhuang et al., 2020). In addition, feed is the most considerable expense of dairy farms. The use of dried cereal straws as feed for herbivorous livestock is common in developing countries due to the shortage of high-quality forages. Thus, the effective utilization of

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dry cereal straw is an important issue and requires researchers to develop solutions. Due to increasing global economic and environmental concerns, more attention has been given to the possibility of the efficient use of cereal straw as a source of roughage for ruminants.

Several strategies have been applied to improve the utilization efficiency of cereal straw, such as pretreatments and additional bio-activators (Bae et al., 1997; Eun et al., 2006; Zhu et al., 2017). However, efficient strategies have not been well clarified, which may be attributed to the vague understanding of the limitations of these cereal straws used to feed dairy cows. In recent years, the rapid development of advanced nutritional physiology and molecular biology techniques has provided several efficient methods to solve these problems. For example, metabolomics has been widely used as a new technology in dairy research (Ametaj et al., 2010), and multi-omics technology has been introduced into research on lactation physiology (Li et al., 2017; Xue et al., 2020a). These new technologies play a key and influential role in discovering complex biological systems for specific nutritional biomarkers (Xue et al., 2020a), providing novel insights into elucidating the biological mechanisms of metabolism and the utilization of nutrients from cereal straws in dairy cows.

In this review, we summarized the recent advances in the utilization of cereal byproducts such as corn stover, rice straw, and wheat straw in the diets of lactating dairy cows. Based on our systematic studies on lactating dairy cow with corn stover or rice straw to replace alfalfa hay plus wild ryegrass hay as main forage source, the diets, gastrointestinal tract, liver, mammary gland, digesta, feces, blood, and milk were set as research targets from the perspective of nutritional characteristics, microbiology, nutritional physiology, and molecular biology. Then, we aimed to evaluate the feasibility of using cereal straws as a roughage source for lactating dairy cows and to explore efficient regulation measures to improve its utilization efficiency.

2. Nutritional characteristics of cereal straws

2.1. Chemical composition and feed intake

Cereal straws are the air-dry residues or byproducts of the cereal crops after the grain is harvested, which is the mainly illustrated target of this review. The nutritive value of corn stover, rice straw, and wheat straw for ruminants is relatively low due to its high lignocellulosic content (lignin, 5.83% to 7.2%, DM basis) and low contents of crude protein (CP, 2.4% to 8.4%, DM basis) (Table 1), metabolizable energy, minerals, vitamins, and easily fermented carbohydrates, as well as their poor palatability and low nutrient digestibility (NRC, 2001), which restricts the ruminal synthesis of microbial protein (MCP) in dairy cows (Lascano and Heinrichs,

2011; Zhu et al., 2013a; Wang et al., 2014). In addition to its abundant content of cell walls, the ruminal degradability of rice straw is limited by its epidermal surface, in which a high concentration of silica exists and acts as a physical barrier preventing bacterial attachment (Widyastuti et al., 1987). Rice straw (5.32% to 11.7%, DM basis) and wheat straw (7.3%, DM basis) had higher silica content, which is even higher than their CP levels (Table 1), indicating that silica, in addition to lignin, is also a critical limiting factor in the cell wall degradation of rice straw. On the other hand, significant variations exist in nutritive value between different morphological fractions of wheat straw and corn stover (Tan et al., 1995; Tang et al., 2006; Li et al., 2014). For instance, the CP content differed in the following order: leaf blade > tassel > whole corn stover > leaf sheath > stem > ear husk (Tang et al., 2006; Li et al., 2014). The CP level in the leaf blade of corn stover can reach 13% (DM basis), indicating that the leaf blade of corn stover can be considered a good protein forage source for ruminants. The ruminal degradation rate and effective degradability of corn stover fractions are also quite variable (Li et al., 2014). Thus, these different characteristics of the corn stover fractions suggest that it would be efficient and cost-saving only to use the relatively high nutritional fractions, such as the leaf blade and husk, instead of the whole plant. However, the development of new technology is required to separate the different fractions of corn stover. The low CP and high fiber content in cereal straws, especially for their high proportion of lignin and silica, are the main nutritional constraints for using straw as feed source in dairy cow.

In a series of our studies, we did not find an apparent difference in diet DM intake in dairy cows when corn stover (30%, DM basis) or rice straw (30%, DM basis) is included in the diets to replace alfalfa hay and Chinese wild ryegrass (Zhu et al., 2013a; Wang et al., 2014). Litherland et al. (2013) found that feeding of wheat straw (30%, DM basis) prepartum did not affect postpartum DM intake compared to grass hay, which was inconsistent with conventional cognitive that the cows would not like to ingest rough cereal straws. This is partly because forage palatability is not associated with a nutritive value (Marten and Andersen, 1975). Furthermore, energy intake is generally associated with diet digestibility. Hence, feeding of cereal straws with lower energy density may promote the cows to ingest more for energy requirement (Hayirli et al., 2002). Thus, the feed intake might not be one of main constraints for the straws used in the cows' diet.

2.2. Digestibility

Digestibility is an essential indicator for improving the efficiency of energy utilization by dairy cows, and is affected by dietary ingredients and their compositions (Reynolds et al., 2011; Wang et al., 2014). Dairy cows fed equivalent concentrations of forage fiber (180 g/kg forage neutral detergent fiber) from corn silage, alfalfa hay, wheat straw, and corn stover as the roughage sources showed similar milk yields and total tract digestibility (Eastridge et al., 2017), indicating that digestibility might be mainly affected by the dietary fiber content. A lower milk yield is associated with the lower apparent digestibility of nutrients in corn stover- (30%) and rice straw (30%)-based diets than in the alfalfa hay diet (Wang et al., 2014). The difficult digestion of cereal straws is attributed to the lignification and cross-linkages between lignin polymers and polysaccharides in the cell walls (Jung and Deetz, 1993). In addition, the ratio of dietary phenolic acid to ferulic acid also acts as a limiting factor for the degradation of the forage cell wall in ruminant animals (Cao et al., 2016a). Thus, pretreatment of the cell wall of cereal straw should be able to increase its digestibility. Besides, when evaluating ruminants' digestibility, the rumen degradation is an important factor. In practice, the in vitro and in situ methods

Table 1

The reported chemical composition of corn stover and rice straw (% DM)¹.

Item	Corn stover	Rice straw	Wheat straw
Organic matter	92.1–93.8	85.0–87.9	90.4–94.2
Crude protein	5.30–8.40	4.80–6.88	1.88–4.60
Ether extracts	0.84–2.00	2.10	1.20–1.60
Non-fiber carbohydrate	11.6–20.2	5.20	7.30
Neutral detergent fiber	52.1–76.2	66.2–76.9	75.0–87.4
Acid detergent fiber	30.4–48.1	40.4–45.5	53.6–58.2
Lignin	5.91–7.20	5.83–18.5	8.90–19.0
Silica	0.37–2.68	5.32–11.7	7.30

¹ These data come from the previous studies (Man and Wiktorsson, 2001; Pan and Sano, 2005; Eun et al., 2006; Ko et al., 2006; Li et al., 2012; Litherland et al., 2013; Wang et al., 2014; Shi et al., 2015; Cao et al., 2016a,b; Omidi-Mirzaee et al., 2017; Hanlon et al., 2020).

were usually used to evaluate the ruminal degradation of roughage. The in vitro DM degradation in corn stover is generally higher than in rice straw (52.7% vs. 45.3%; [Chen et al., 2017](#)). The in vitro rumen DM degradation is much lower for wheat straw (25.0%) than for corn stover and rice straw ([Thareja et al., 2006](#)). However, the in vitro rumen DM degradation of alfalfa hay showed nearly 70% ([Xue et al., 2019](#)). Thus, the much low rumen degradation and apparent digestibility of cereal straw is one of main constraints for using straw as feed source in dairy cows.

2.3. Lactation performance

Milk production is always decreased when dairy cows are fed low-quality cereal straw diets, with nearly 3 to 4 kg/d reduced milk yield ([Zhu et al., 2013a](#); [Wang et al., 2014](#)). Dry and old corn stover limits feed intake in ruminants due to the low moisture content and harsh physical factors (>5% lignin content), making it hard to chew. The inclusion of corn stover in a total mixed ration (TMR) has been refused by ruminants due to its poor palatability, restricting milk synthesis ([Keys and Smith, 1983](#)). However, improved lactation performance (48.3 and 48.4 vs. 45.6 kg/d) has been reported in high-producing dairy cows fed alkali-treated rice straw and wheat straw to replace one-third of their forage sources, which has been attributed to an increased dietary sodium concentration, dietary cation–anion difference, total tract digestibility, and feed intake ([Omid-Mirzaee et al., 2017](#)). In addition, it is found that milk yield tended to be higher in the cows fed wheat straw prepartum (30%) compared to those fed grass hay (30%) ([Litherland et al., 2013](#)). Therefore, cereal straw is a potential feed source for dairy cows when used reasonably.

3. Metabolism and utilization of cereal straws in lactating cows

3.1. Ruminal microbial protein synthesis

Dairy cows fed corn stover as a primary roughage source have lower rumen MCP yields than those fed an alfalfa hay diet ([Zhu et al., 2013a](#); [Wang et al., 2014](#)). The non-fiber carbohydrate (NFC) content is much higher in alfalfa hay (22.4%) than in corn stover (11.6%) or rice straw (5.2%) ([Wang et al., 2014](#)). The MCP that flowed to the duodenum increased or decreased linearly with a inclusion of concentrate at a high (80%) or low level (20%) in dairy heifers fed corn stover diet, respectively ([Lascano and Heinrichs, 2011](#)). Therefore, increased supply of readily fermentable carbohydrates is critical to improve the MCP yield when lactating cows are fed a low-quality roughage such as corn stover or rice straw. The relative abundances of ruminal genera *Prevotella* and *Selenomonas* in cows fed a corn stover (19%) diet were decreased compared with cows fed alfalfa (17%) diet, but the proportion of ruminal genera *Anaerotruncus*, *Papillibacter*, *Thermoactinomyces* *Bacillus*, and *Streptomyces* increased ([Zhang et al., 2014](#)). *Treponema saccharophilum* is a pectinolytic bacterium isolated from the bovine rumen. There exists a clear association of *T. saccharophilum* with an alfalfa hay diet, and *T. saccharophilum* plays a vital role in pectin digestion in the rumen ([Liu et al., 2014](#)). Thus, it is speculated that a shortage of pectin, the main non-fiber component in alfalfa ([Martin and Mertens, 2005](#)), may be the limiting factor for MCP synthesis when cows are fed a cereal straw diet compared to alfalfa based diet.

3.2. Amino acid metabolism

Metabolizable amino acids (AA) are the available AA supply for milk protein synthesis ([Arriola Apelo et al., 2014](#)). Lower flows of

digestive AA and total metabolizable protein were observed in cows fed corn stover and rice straw than in alfalfa-fed cows ([Wang et al., 2014, 2016a](#)). Leu in corn stover or rice straw diets is in short supply, and cows fed corn stover or rice straw have a lower absorbable Leu proportion in the duodenum, which may restrict balanced AA absorption ([Wang et al., 2018c](#)). In addition, the AA composition of rumen undegraded protein (RUP) can affect AA flow in the small intestine, leading to the limitation of one or several AA ([Boisen et al., 2000](#)). There were apparent differences in the AA profiles between corn stover or rice straw and their residues after ruminal degradation, indicating the importance of measuring the AA composition of RUP of corn stover and rice straw when included in the diets of dairy cows ([Wang et al., 2018a](#)). The key limiting AA for cows fed cereal straw as the main roughage source is important and should be clarified. The arterial concentration and mammary uptake of branched-chain AA in cows fed corn stover or rice straw diet are significantly lower than those in cows fed alfalfa diets ([Wang et al., 2016a](#)), suggesting that branched-chain AA may be the limiting AA in cereal straw diets. The ratio of uptake to output of Leu and Met is much lower in cows fed a corn stover diet than in alfalfa-fed cows ([Wang et al., 2016a](#)). Both Leu and Met should be supplemented when corn stover is used to feed lactating dairy cows.

3.3. Glucose metabolism

Rice straw-fed cows have a reduced milk lactose concentration and blood glucose compared to alfalfa-fed cows ([Wang et al., 2016b](#)). The mRNA abundance of both mitochondrial phosphoenolpyruvate carboxykinase and pyruvate carboxylase is dramatically lower in the liver of cows fed rice straw than in alfalfa-fed cows, suggesting a low gluconeogenesis rate in rice straw-fed cows, which is consistent with the mechanisms of ruminal propionate ([Wang et al., 2016b](#)). However, the low mammary uptake function in rice straw-fed cows could not be related to the mRNA expression of glucose transporters in the mammary gland, including glucose transporters 1 (GLUT1), GLUT3, and GLUT8. Other factors, such as blood flow, may play a pivotal role in the glucose supply for mammary lactose synthesis ([Zhao, 2014](#)). Lactose concentration is relatively constant during normal consecutive lactations among individual cows ([Gibson, 1984](#)), except under conditions of severe underfeeding ([Sutton, 1989](#)), because lactose accounts for approximately 50% of the total osmotic pressure of milk, and the remainders are contributed by milk ions, proteins, citrate, and other substances ([Gáspárdy et al., 2004](#)). Milk concentrations of Na⁺, K⁺, and Cl⁻ also maintain osmotic pressure ([Oshima et al., 1980](#)). Indeed, the milk K⁺ concentration in cows fed rice straws was significantly higher than in alfalfa-fed cows ([Wang et al., 2016b](#)). Milk K⁺ may compensate for the decreased lactose content in cows fed rice straw. Thus, a dietary supply of ions would be a potentially helpful choice to maintain the osmotic pressure balance and normal milk synthesis when cows are fed rice straw as their primary roughage source.

4. The underlying mechanism revealed by functional omics

Most studies on cereal straw in dairy cows are focusing on the exact effects on animal and milk performance. However, the underlying mechanism had received little concern due to the limitations of traditional nutritional methods. Thus, our group conducted mechanism research using functional omics and molecular methods to relate with the apparently inhibited milk performance phenotype (such as decreased milk yield and milk protein, fat, and lactose content) in lactating dairy cows fed large ratio of corn stover or rice straw. These applications of functional omics in dairy cows

can help provide new insights into addressing complex biological questions of lactation (Zhang et al., 2013; Sun et al., 2017; Xue et al., 2020a), which make it possible to detect the nutritional limitations of cereal straws fed to dairy cows.

4.1. The single omics

4.1.1. Microbiome

The rumen microbiome plays a vital role in the degradation of forages (Matthews et al., 2019). Using metagenomics, it is found that the relative abundance of rumen *Treponema* genus, *T. saccharophilum*, and *Treponema succinificiens* species related to pyruvate production and the relative abundance of the *Succinimonas* genus, *Saccharomyces amylolytica* and succinate pathway related to succinate production decreased when cows were fed a 30% corn stover-based diet (Sun et al., 2020). Thus, corn stover could drive shifts in the rumen microbiome with altered specific propionate biosynthesis, which can interact with the host glyco-metabolism and be consistent with their decreased milk yield and milk lactose synthesis (Wang et al., 2014).

4.1.2. Transcriptome-mRNA

The rumen epithelium has essential contributions to nutrient absorption and rumen health. RNA-seq-based transcriptomics was successfully conducted to reveal the effects of cereal straws on the rumen wall (Wang et al., 2017) and other digestive and metabolic organs (Wang et al., 2021). The larger particles in rice straw with more significantly mechanical stimulation effects resulted in thicker rumen papilla, restricting the absorption of nutrients and reducing lactation performance (Wang et al., 2017). Functional classification revealed that cereal straw diets could induce dynamic changes in ion binding function, proliferation and apoptotic processes, and complement activation of rumen epithelium (Wang et al., 2017). During these affected pathways, the expression differences in *HLA-DQA1*, *HSPB8*, and *BAG3* determined the changed morphology of the rumen epithelium, indicating that macro-autophagy occurred due to the lower energy supply from the cereal straw diets (Wang et al., 2017). Cows fed cereal straws also had changes in gene expression, such as *CA1*, *BPIFA2C*, and *S100A8* in the duodenum, *S100A12* and *HMGCS2* in the jejunum, *GLYCAM1* and *CYP2B6* in the liver, and *APOE* in the mammary gland, which are associated with nitrogen (N) metabolism and milk performance (Wang et al., 2021). Low-quality cereal straw diets may change the expression patterns of functional genes in the critical digestive and metabolic organs of dairy cows.

4.1.3. Transcriptome-miRNA

The miRNA-mediated regulatory mechanisms are important post-transcriptional regulation processes in dairy cows. The biological process or physiological functions in metabolic tissues, including the rumen, duodenum, jejunum, liver, and mammary gland, make up the entire biological system in dairy cows. Feeding low-quality cereal straw diets (corn stover and rice straw) influences the expression of feed and N utilization efficiency-associated miRNAs in the rumen (miR-99b), duodenum (miR-2336), jejunum (miR-652), liver (miR-1), and mammary gland (miR-181a) (Wang et al., 2016c). The expression of miRNAs in the rumen (miR-378 and -345-3p), duodenum (miR-199b), jejunum (miR-330, -425-3p, -2285p, -197, 2419-3p and 2419-5p), liver (miR-1), and mammary gland (miR-2285t and -2443) were associated with AA uptake; ruminal miR-103, -155, -504, -21-3p, mammary -142-3p and let-7c were associated with AA transport; miR-497 in the liver and let-7b, -7c, -7a-3p, miR-106b, -1296, -188, -149-5p and -6119-3p in the mammary gland were associated with AA phosphorylation. The expression of

all these miRNAs was affected by cereal straw diets. These identified miRNAs provide a fundamental understanding of the molecular regulatory mechanism through miRNA regulation and may explain the reduced feed and N efficiency in cows fed cereal straw diets (Wang et al., 2016c).

4.1.4. Metabolome

In recent years, studies based on metabolomics profiling of rumen fluid, milk, blood, and urine from lactating dairy cows have been conducted to investigate the metabolic changes and capture specific biomarkers and pathways related to the nutritional limitations of cereal straws (Zhao et al., 2014; Sun et al., 2015; Wang et al., 2018b, 2020). In detail, most metabolites decreased in the rumen fluid and increased in the urine in the cows fed corn stover diets (Sun et al., 2015), which explained the apparent data showing a higher N loss and lower N utilization efficiency in two cereal straws diets (Wang et al., 2014). The cows fed corn stover had lower levels of acetate, valerate, hydrocinnamate, and methylamine but higher levels of glucose, Gly, propionate, and isovalerate than those fed a higher-quality diet (Zhao et al., 2014). The increased hippuric acid and decreased N-methyl-L-glutamic acid in the urine of cows fed a corn stover diet compared to alfalfa diet-fed cows showed a significant correlation with milk yield (Sun et al., 2016). Hippuric acid was also the best predictive metabolite of low milk production and for discriminating the effects of corn stover and alfalfa diets across the liver, serum, and urine using biomarker signature analysis (Sun et al., 2020). In addition, increased arterial phenyl propanoate and 4-hydroxyproline and reduced phenylalanine are crucial limiting factors when cows are fed low-quality cereal straws (Wang et al., 2020). In considering the different results of studies based on the different metabolic organs or body fluids, the metabolic pathways of the tricarboxylic acid cycle, Gly, Ser, and Thr metabolism; Phe metabolism; Tyr metabolism; and Phe, Tyr and Try biosynthesis showed the most variation when two low-quality cereal straw diets were fed to cows (Sun et al., 2015, 2020; Wang et al., 2018b, 2020).

On the other hand, the tricarboxylic acid cycle, Glu metabolism, and Gly biosynthesis and degradation pathways, as well as the potential biomarkers of lactobionic acid, citric acid, orotic acid, and oxamide revealed the probable critical metabolic mechanism in discriminating lactating from nonlactating procedures (Sun et al., 2017). Thus, we propose that cows fed cereal straw would consume food with lower nutrient densities and affect the internal lactating biological process. The arterial plasma metabolome is more pronounced than the vein in reflecting the effects of the different dietary treatments (Wang et al., 2018b, 2020).

4.2. The integrative omics

Multi-omics techniques have been used in animal nutrition studies, which could help to reveal the biological mechanism of milk production under different feed regimes or nutritional statuses (Sun et al., 2018, 2020; Xue et al., 2020a, 2020b). Through integrated transcriptomic and proteomic analyses based on the RNA-seq method with the iTRAQ proteomic technique, several crucial biological processes in the mammary gland that restrict the rice straw used as a roughage source in lactating dairy cows were proposed. These biological processes included reduced ribosomal activity and enhanced protein degradation, increased protein processing in the endoplasmic reticulum and endoplasmic reticulum-associated protein degradation, and a decreased abundance of transcripts/proteins related to cell growth/development, with a total of 554 differentially changed transcripts and 517 differentially changed proteins (Dai et al., 2017). These mechanisms in the mammary gland that change in cows fed rice straw diets can direct

future work to better understand how the mammary gland is affected by feeding strategies. We also used integrated metabolomics, metagenomics, and transcriptomics for the rumen fluid, liver, and mammary gland to identify the key mutual metabolic nodes (propionate, glucose, and amino acids) in these organs that led to lowered milk yield and quality when cows consumed corn stover (Sun et al., 2020).

4.3. The impact on animal health

Most studies focus on animal production performance, with less understanding of the potential health risk under long-term feeding of crop byproducts to dairy cows. The blood concentrations of nonesterified fatty acids, β -hydroxybutyrate, triacylglycerol, and glucose indicate a negative energy balance and a liver metabolic disorder (Akgül et al., 2017). When cows are fed rice straw-based diets, their changed blood biochemical parameters and liver histomorphology indicate a liver disorder. Based on the metabolites and mRNA/miRNA targeted genes, a hepatic disorder risk existed with enriched hepatic ketogenesis through the linoleic acid pathway in cows fed a rice straw-based diet (Sun et al., 2018). Thus, attention should be given to animal welfare when cows are fed cereal straw, especially rice straw.

4.4. The impact on the environment

Inefficient utilization of cereal straw by animals may negatively affect the environment, including increased N excretion in urine and feces (Wang et al., 2014). Urinary N is mainly derived from excess rumen degradable protein because the absorbed ammonia from the rumen can be converted to urea in the liver and excreted in the urine and milk in dairy cows (Jongebreur and Monteny, 2001). Shifting urine N to fecal N excretion reduces its harmful effect on environmental N pollution in a dairy farm (Castillo et al., 2000). Thus, nutritional measures can be used to increase the N utilization efficiency and reduce excess and rapid N degradation. Cows fed a cereal straw-based diet have a much higher content and yield of urine urea N, which is attributed to the changed urine urea N yield-associated functional gene networks that drive the increased urine urea N yield in cows fed cereal straw (Wang et al., 2021). These functionally related genes might be possible targets to modulate N excretion waste for the environmentally friendly development of the dairy industry.

5. Potential efficient measures to optimize the usage of cereal straw in ruminants

Considerable effort has been made to improve the utilization efficiency and feeding value of cereal straw using pretreatments to enhance its digestibility, including biological, chemical, and physical pretreatments (Bae et al., 1997; Eun et al., 2006), as well as providing nutritional supplements based on the lack of nutrients in cereal straw (Zhu et al., 2013b; Wei et al., 2019) (Table 2). However, the commercial application of these strategies is limited due to cost, potential environmental problems, and animal health issues. From the view of animal nutritionists, there are many potential strategies to improve the utilization efficiency of cereal straw by ruminants through a comprehensive understanding of the biologically limiting factors of cereal straw.

5.1. Chemical and physical pretreatments

It is inferred that chemical and physical pretreatments enhance the nutritive value of rice straw by improving rumen fermentation and fibrolytic enzyme activities that mainly result from the

increased available substrate and have significant influences on the rumen microbial distribution and populations (Chen et al., 2008). It is found that shortly chopped wheat straw with a 2.54-cm screen improved feed intake in dry cow and improved metabolic health in early lactation (Havekes et al., 2020). The increased nutrient intake and digestibility of rice straw by pretreatment with urea and calcium hydroxide are associated with increased milk protein and fat concentrations and improved DM intake and digestibility (Wanapat et al., 2009). However, alkali treatment of cereal straw has potentially harmful effects on animal health and high treatment costs (Jackson, 1977). Feeding CaO-treated corn stover (5% CaO) as a part of roughage can improve profitability (an additional \$0.70 to 0.81 income over feed cost per cow per day) without negatively affecting the lactation performance of mid- to late-lactation cows (Shi et al., 2015). The addition of urea (50 g/kg of rice straw, DM basis) to fresh rice straw can help preserve and improve the ensiling nutritional value (Man and Wiktorsson, 2001). The cows fed a diet containing 20% wheat straw treated with 3% NaOH plus 3% Ca(OH)₂ and 40% alfalfa haylage had similar milk performance with those fed a diet containing 60% alfalfa haylage (Haddad et al., 1998). The inclusion of NaOH-treated wheat straw (7.6%, DM basis) improved the milk yield and milk protein yield due to the higher DM intake and N intake (Hanlon et al., 2020). However, chemically treated cereal straw should be used carefully to avoid adverse effects.

5.2. Biological pretreatment

Using exogenous enzymes is a potential way of improving rice straw cell wall degradation and in vitro digestibility (Eun et al., 2006). Many enzymes have been investigated for their pretreatment effect on cereal straw, including β -glucosidase, cellulase, xylanase, and ligninolytic enzymes. The use of exogenous fiber-degrading enzymes may be a potential means to upgrade rice straw as roughage in ruminants (Beauchemin et al., 2004). The application of fibrolytic enzyme preparations and yeast cultures (2.5 to 7.5 g/kg of straw DM) could improve in vitro gas production and enhance the in vitro digestibility of rice straw, wheat straw, and corn stover (Tang et al., 2008). The addition of cellulase or xylanase increased the fermentation kinetics of corn stover, with an optimum dose of both cellulase and xylanase (40 μ g/g DM), but cellulase was more active and efficient than xylanase (Vallejo et al., 2016). Adding *Lactobacillus acidophilus* (0.75×10^7 cfu/mL) to corn stover and rice straw as a substrate increased in vitro gas production and the ruminal ammonia-N concentration (Chen et al., 2017). A diet containing 30% *Pleurotus ostreatus* treated wheat straw increased DM intake (12.2 vs. 10.6 kg), DM digestibility (58.8% vs. 52.3%), and milk yield (9.0 vs. 7.5 kg/d) (Fazaeli et al., 2004). Supplementation with essential oils (a mixture of thymol, eugenol, vanillin, guaiacol, and limonene) improved milk production (31.8 vs. 23.5 L/d) and reduced the milk urea concentration and somatic cell count in high-yielding dairy Chios ewes when they are fed a mixture of corn silage, lucerne hay, and wheat straw (Giannenas et al., 2011).

5.3. Optimizing the diet formula

The optimization of the dietary formula is an efficient strategy to improve the utilization of cereal straws. There is an optimal ratio between whole plant corn silage and corn stover for higher milk production and lower methane emissions when fed to dairy cows with different levels of milk production (0, 10, 20, and 30 kg/d) (He et al., 2021). The maximal profit could be obtained when the ratio of whole plant corn silage to corn stover was 16:84, 22:78, 44:56, and 88:12. Non-fiber carbohydrate is a critical limiting factor for the utilization of cereal straw by lactating dairy cows (Zhu et al., 2013a;

Table 2
Efficient countermeasures for improvement of the nutritional value, in vitro rumen fermentation, or animal performance when cereal straws are used as feed substrates.

Item	Animal	Measures	Response	Source
Corn stover	Dairy cows	5% CaO-treated	Increased digestibility and profit without negatively affecting the lactation performance	Shi et al. (2015)
Corn stover	Dairy cows	Lys, Met, and starch together	Increased the efficiency of nitrogen utilization and improved milk performance	Zhu et al. (2013b)
Corn stover	Dairy cows	0, 60, 120, or 180 g/d of <i>Saccharomyces cerevisiae</i> fermentation product	Enhanced milk persistency under hot environment; dose-dependent and greater effects being observed with higher levels	Zhu et al. (2017)
Corn stover	Dairy cows	Increasing dietary content of non-fiber carbohydrate (NFC)	Improved milk performance compared to lower NFC corn stover diet and a similar milk performance with the alfalfa hay diet	Wei et al. (2018)
Corn stover	Dairy cows	5.12% Molasses	No negative effects on feed efficiency, ruminal fermentation, or blood biochemical variables compared with alfalfa diet, but with higher economic merit	Wei et al. (2019)
Corn stover	Dairy cows	Optimal ratio of whole plant corn silage to con stover silage (WPCS:CSS) for different production levels	At production levels of 0, 10, 20, and 30 kg milk/cow/d, the WPCS:CSS to maximize the profit of dairy farmers was 16:84, 22:78, 44:56, and 88:12, respectively	He et al. (2021)
Corn stover	In vitro	Steam explosion	Enhanced digestibility and in vitro rumen volatile fatty acids production	Zhao et al. (2018)
Corn stover	In vitro	Cellulase or xylanase at 40 µg/g DM	Increased in vitro gas production	Vallejo et al. (2016)
Corn stover	In vitro	Pectin	Increased rumen volatile fatty acids production	Liu et al. (2014)
Fresh rice straw	In vitro	5% Urea-treated	Improved the ensiling nutritional value	Man and Wiktorsson (2001)
Rice straw	Dairy cows	2.2% urea +2.2% calcium hydroxide-treated	Increased DM intake and digestibility Improved milk protein and fat concentrations	Wanapat et al. (2009)
Rice straw	Dairy goats	Orange leaves	Reduced CH ₄ emissions and improved the milk quality (greater milk fat content, and concentrations of monounsaturated and polyunsaturated fatty acids)	Fernández et al. (2021)
Rice straw	Dairy goats	Lemon leaves	Reduced CH ₄ emissions and affected milk performance such as improving the milk fat production and the milk thrombogenic index	Romero et al. (2020)
Rice straw	In vitro	Combining ammonia treatment (30 g/kg DM) and exogenous enzymes (1.25 mg/g DM substrate)	Improved the cell wall degradation and in vitro digestibility	Eun et al. (2006)
Rice straw	In vitro	Fiber-degrading enzymes	Increased the nutritive value of rice straw	Beauchemin et al. (2004)
Wheat straw	Dairy ewes	Essential oil including thymol, eugenol, vanillin, guaiacol, and limonene (100 and 150 mg/ewe per day)	Improved feed utilization and reduced the milk urea concentration and somatic cell count	Giannenas et al. (2011)
Wheat straw	Dairy cow	NaOH-treated	Improved DM intake and result in higher milk yield	Hanlon et al. (2020)
Wheat straw	Dairy cow	3% NaOH plus 3% Ca(OH) ₂	Diet with 20% treated wheat straw had similar milk performance with 20% alfalfa haylage	Haddad et al. (1998)
Wheat straw	Dairy cow	Chopped with a 2.54-cm screen	Shorter chopped wheat straw improved dry cow intake and resulted in greater metabolic health and rumen stability in early lactation	Havekes et al. (2020)
Wheat straw	Dairy cow	30% <i>Pleurotus ostreatus</i>	A diet containing 30% <i>Pleurotus ostreatus</i> treated wheat straw increased DM intake, DM digestibility, and milk yield	Fazaeli et al. (2004)
Corn stover and rice straw	In vitro	0.75 × 10 ⁷ cfu/mL <i>Lactobacillus acidophilus</i>	Increased in vitro gas production and ruminal NH ₃ -N concentration	Chen et al. (2017)
Corn stover and rice straw	In vitro	3 g/L <i>Saccharomyces cerevisiae</i> fermentation product	Increased in vitro total volatile fatty acids in corn stover and microbial protein in rice straw linearly	Mao et al. (2013)
Rice straw, wheat straw, maize stover, and maize stover silage	In vitro	Fibolytic enzyme preparation and yeast culture (2.5, 5.0, and 7.5 g/kg of straw)	Enhanced in vitro DM digestibility and in vitro OM digestibility	Tang et al. (2008)

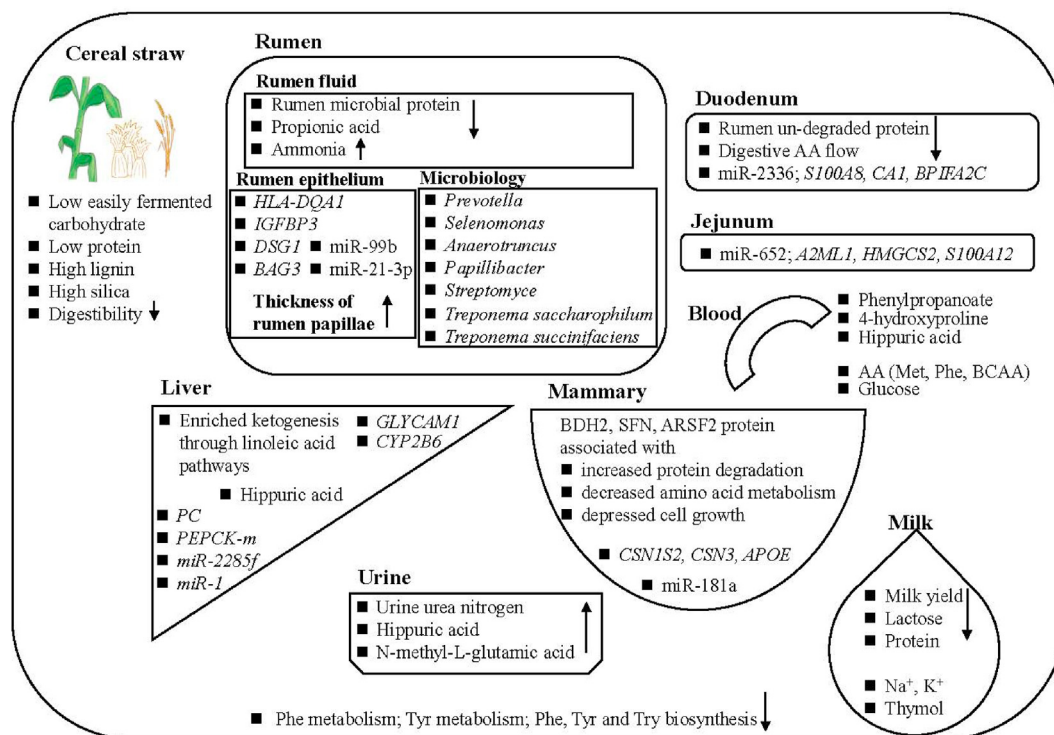


Fig. 1. The overall network of the limiting factors of cows fed low-quality cereal straw (corn stover, rice straw) on phenotypes (including lactating performance and general characteristics) and underlying molecular mechanisms. The upwards arrows indicate the increase and the downwards arrows represent the decrease of the expressions of genes compared with the cows fed a high-quality forage diet (alfalfa). AA = amino acid; BCAA = branched chain amino acids.

Cantalapiedra-Hijar et al., 2014; Wang et al., 2014). Supplementation of starch to a corn stover diet achieved similar MCP synthesis and metabolizable protein compared with the alfalfa diet, and supplementation of AA and starch together improved the AA balance and increased the efficiency of N utilization to a similar level as that of alfalfa hay (Zhu et al., 2013b). Feed efficiency and N conversion can be improved by increasing the NFC content in a corn stover-based diet, reaching a milk performance similar to an alfalfa hay-based diet (Wei et al., 2018). A recent study found that a corn stover-based diet supplemented with molasses not only had no adverse effects on feed efficiency, ruminal fermentation, and blood biochemical variables compared with an alfalfa-based diet but also had a higher income relative to the feed cost (Wei et al., 2019), indicating the efficient role of molasses in mid-lactation. It has been reported that total volatile fatty acids in corn stover and MCP in rice straw increased linearly with an increasing level of a *Saccharomyces cerevisiae* fermentation product (Mao et al., 2013). When the dairy cows receiving diets containing corn stover as low-quality roughage were supplemented with *S. cerevisiae* fermentation product, the milk persistence of mid-lactation cows were maintained (Zhu et al., 2017).

Thus, based on the molecular determinants of the nutritional shortage of cereal straws for lactating dairy cows, supplementation with functional feed sources and specific nutrients such as pectin, glucose, Met, Phe, and branched AA or treatment with targeted biologically active small molecules may activate key targeted genes and metabolic pathways. They may be an alternative and efficient way to improve the feeding and economic value of low-quality cereal straws for lactating dairy cows.

Although we conducted a series of studies to reveal the mechanism that resulted in the inhibited milk performance under corn stover and rice straw-based diet (30%), we have yet not clarified

what the targeted elements or nutrients of straws that modulated these key genes, proteins, metabolites, and pathways are. Further studies are warranted to clarify these limiting factors.

6. Conclusions

The effective use of cereal straw is of great practical significance. It is necessary to reveal the limiting factors, including critical nutrients, precursors, genes, proteins, metabolites, and pathways (Fig. 1). The shortage of easily fermented carbohydrates, such as pectin, and essential AA (Met, Phe, and branched-chain AA), high content lignin and silica, and low digestibility in cereal straw, will cause insufficient supply of precursors for milk synthesis and result in increased urea N output through several molecular mechanisms, as revealed by multi-omics techniques. Feeding corn stover or rice straw alters signaling and metabolic pathways such as Phe metabolism, Tyr metabolism, and Phe, Tyr and Try biosynthesis, thus resulting in lower nutrient absorption, anabolism, and precursor supply for milk production. Much attention should be paid to these functional molecular targets efficiently utilizing cereal straw as a roughage source in lactating dairy cows. Future strategies in combination with nutritional manipulation (supplement of pectin, AA and feed with other functional feedstuffs) and pretreatments of cereal straw to increase its digestibility (fibrolytic enzymes or steam explosion) should be developed to support the full use of cereal straw as a roughage source in dairy cows, which, in turn, will improve the economic value of low-quality cereal straws in dairy feeding systems. Based on the above, we recommend that the use of cereal straw should be dependent on the exact nutrient composition and physical pattern. Generally, the suitable levels of straws included in the lactating dairy cows should not exceed 15% on a DM basis.

Author contribution

Bing Wang and **Huizeng Sun**: Writing – original draft, Writing – original draft preparation; **Diming Wang** and **Hongyun Liu**: Writing – review & editing, Reviewing and editing; **Jian-Xin Liu**: Writing – review & editing, Reviewing, editing and final version.

Declaration of competing interest

We declare that we have no financial and personal relationships with other people or organizations that can inappropriately influence our work, there is no professional or other personal interest of any nature or kind in any product, service and/or company that could be construed as influencing the content of this paper.

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