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Review Article

# The uniqueness and superiority of energy utilization in yaks compared with cattle in the highlands: A review

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ABSTRACT

Yaks living on the Qinghai-Tibetan Plateau for a long time have evolved a series of mechanisms to adapt to the unique geographical environment and climate characteristics of the plateau. Compared with other ruminants, yaks have higher energy utilization and metabolic efficiency. This paper presents possible mechanisms responsible for the efficient energy utilization, absorption and metabolism resulting from the unique evolutionary process of yaks. It is hoped that the information discussed in this review will give a better insight into the uniqueness and superiority of yaks in regards to energy metabolism and utilization compared with cattle and open new avenues for the targeted regulation of energy utilization pathways of other ruminants.

## 1. Introduction

The Qinghai-Tibetan Plateau, known as the "Roof of the world", is the highest plateau in the world. It has unique environmental conditions characterized by high ultraviolet radiation, low atmospheric pressure and low oxygen concentration (Miao et al., 2015). Grassland ecosystems are prevalent on this plateau. Yaks (*Bos grunniens*), inhabiting the plateau are major sources of dietary protein and income for local residents. They are well adapted to this unique environment which has limited forage resource availability during the cold season. Over the past decades, many researchers have studied the adaptability of yaks to the plateau environment from several facets (Qiu et al., 2012), including molecular phylogeny, morphological adaptations and physiological functions (Lalthantluanga et al., 1985; Guo et al., 1995; Shao et al., 2010; Mipam et al., 2012; Chen et al., 2015; Lan et al., 2018). In the context of energy metabolism, yaks have a higher ability to utilize energy sources, absorb nutrients and require less energy for their maintenance compared with domestic cattle (*Bos taurus*) (Brosh et al., 2004; Wei et al., 2016a; Zhang et al., 2016). In the area of nitrogen utilization, yaks have lower urinary nitrogen excretion (Long et al., 1999b). This paper discusses the characteristics of energy utilization and its possible mechanism in yaks, aiming to get a better understanding of their energy utilization characteristics and provide guidance and reference for targeted regulation of energy utilization of other ruminant species.

## 2. Higher efficiency of energy acquisition-anatomical, behavioral and molecular level adaptations

### 2.1. Anatomical and behavioral adaptations

Low temperature is one of the key environmental features on the Qinghai-Tibetan Plateau. To adapt to this condition, yaks have evolved a series of physiological characteristics to maintain body temperature. Apart from having fewer sweat glands, which are shorter in both diameter and length as mentioned in Table 1, the yak's

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**Table 1.**
Comparison of main parameters of physiological and anatomical adaptation between cattle and yaks.

| Item | Yaks | Cattle | References |
|---|---|---|---|
| Average height (2-year-old), cm | 92.5 | 98 | Han et al. (1989) |
| Chest girth (2-year-old), cm | 130 | 135 | Han et al. (1989) |
| Weight (2-year-old), kg | 115 | 170 | Han et al. (1989) |
| Number of sweat glands | 615.82 | 1,729 | Das et al. (2014) |
| Diameter and length of sweat glands | smaller | larger | Das et al. (2014) |
| Thorax | larger | smaller | Yang et al. (2017) |
| Rib number | higher | lower | Yang et al. (2017) |
| Numbers of goblet cells in the mucosal epithelium | | | |
| Anterior tracheal, $\times 10^{-3}/\mu m$ | 35.6 | 4.6 | Wei et al. (2013) |
| Middle tracheal, $\times 10^{-3}/\mu m$ | 46.7 | 7.3 | Wei et al. (2013) |
| Posterior tracheal, $\times 10^{-3}/\mu m$ | 53.8 | 21.1 | Wei et al. (2013) |
| The ratio of pulmonary arteriolar thickness to vascular diameter | 5 | 16.40 | Chen et al. (2006) |
| Mitochondria density in cardiocytes, $\mu m^3/\mu m^3$ | 0.213 | 0.118 | Shen et al. (2019) |

body surface is covered by long, dense, shaggy fur, which thickens their thermal insulation layer to reduce heat loss, especially during the cold season. Thus, yaks can graze on the highland grasslands even under −30 to −40 °C in a harsh winter. This may be attributed to the unusual eating behaviors of yaks, that is, the grass is pulled into the mouth by the labia oris and the tongue is not extended out of the mouth, which prevents frostbite of lingual tissue and the loss of heat and water. This feature is dissimilar to that of cattle as they pull grass into the mouth using the tongue (Shao et al., 2010).

Hypoxia is another environmental feature of the highlands. Resulting from the process of long-term natural selection, yaks have a larger thorax and a higher number of ribs and more goblet cells in the mucosal epithelium of the trachea compared with cattle (Table 1). Additionally, the absolute thickness of the air-blood barrier of yaks is close to that of rats and is about one-quarter that of pigs, dogs and sheep (Chen et al., 2006). Conversely, Weibel (1972) reported that the thickness of the air-blood barrier in mammals was positively correlated with body weight. The thin air-blood barrier reduces resistance during the process of oxygen diffusion, which is beneficial for increasing ventilation and blood flow in the lungs of yaks under hypoxia (Yang et al., 2017). Furthermore, as shown in Table 1, yaks have more erythrocytes and hemoglobin in the blood than cattle, suggesting a stronger capacity to transport oxygen. These traits may increase aerobic respiration in the mitochondria, the site of adenosine-triphosphate formation, and consequently improve metabolic efficiency in yaks (Shen et al., 2019).

### 2.2. Molecular-level adaptations

Previous studies have also found that yaks have adaptations at the molecular level which provide an evolutionary advantage in maximizing energy acquisition. Results of genome analysis reveal that functional categories and pathways related to hypoxia are enriched in yaks, comprising 2 important regulators (*Adam17* and *Arg2*) and 1 target gene (*Mmp3*) of hypoxia-inducible factor-1$\alpha$ (*HIF-1*$\alpha$) (Qiu et al., 2012). Xiong et al. (2015) found a higher mRNA expression of *HIF-1*$\alpha$ in several tissues of yaks compared with cattle. *HIF-1*$\alpha$ is a core transcription factor for sensing cell hypoxia and its gene expression is upregulated under hypoxia (Minet et al., 1999). The upregulated *HIF-1*$\alpha$ can further enhance gene transcription of erythropoietic, angiogenic and glycolytic proteins and subsequently attenuate injuries caused by hypoxic exposure (Mei et al., 2008; Rosenberg, 2009; Sousa et al., 2010). This indicates that yaks are better adapted to hypoxic conditions compared with cattle, based on the higher expression of *HIF-1*$\alpha$ and a greater number of erythrocytes.

Several differences involved in the process of energy metabolism have also been identified between yaks and cattle. For example, results of genome analysis indicated that the *CAMK2B* gene function to regulate gastric acid secretion in the rumen would be positively selected in the pathway of volatile fatty acid (VFA) production in yaks (Allen et al., 2009; Weimer et al., 2009; Qiu et al., 2012). Based on the comparative transcriptome analysis of 6 tissues collected from cattle and yaks, Ma et al. (2021) found that among differential genes related to energy metabolism, *TPI1* (triosephosphate isomerase) was up regulated and *G6PC* (the gene encoding glucose-6-phosphatase) was downregulated. These genes are crucial in the processes of glycolysis (Shimoda et al., 2012) and gluconeogenesis (Jia et al., 2012), respectively. Thus, yaks may have adapted to high altitude environments through shifting the energy metabolism pathway from gluconeogenesis to glycolysis to provide more ATP. Further, the relative abundance of 4 enzymes in the respiratory chain and phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit alpha isoform were higher in the muscle of yaks compared with cattle, based on proteomic analysis (Xin et al., 2020), suggesting a higher ability of glucose uptake and glycogen synthesis in the muscle of yaks at high altitude (Cross et al., 1995; Knight et al., 2006).

In summary, in high-altitude environments, yaks not only maintain normal energy production under hypoxic pressure, but also optimize nutritional assimilation under limited forage resources. This is also in agreement with findings based on the differential serum metabolites between grazing yaks and cattle, that the pathways of “energy metabolism” and “metabolism of phenylalanine, arginine, proline and glutamine” were enriched in yaks (Huang et al., 2022). Research on the evolution of anatomical physiology as well as multi-omics analysis reveals that yaks have the potential to utilize energy more efficiently than cattle in the highlands. However, the actual mechanism of energy utilization in yaks is affected by environmental interaction and genes that regulate physiological function and therefore, should be further studied from multiple perspectives.

## 3. Higher energy production-potential of rumen microbes in yaks to produce more VFA and less methane during degradation of plant fibers

### 3.1. Ruminal degradation of plant fibers

The microorganisms inhabiting the rumen, including bacteria, fungi, protozoa and archaea (Kamra, 2005), secrete carbohydrate active enzymes to degrade complex carbohydrates into disaccharides or monosaccharides. These short-chain oligosaccharides are further utilized by rumen microorganisms to produce VFA, $H_2$ and methane, among others (Lourenço et al., 2010), of which VFA are the major energy source for the hosts (Shabat et al., 2016). Previous studies reported that yaks have a higher lignocellulose degradation rate than other domestic animals (Dai et al., 2012; Wei et al., 2016a), suggesting a greater efficiency of energy utilization in yaks when fed low-quality forages. This may be attributed to a number of mechanisms. Firstly, An et al. (2005) reported a greater abundance of total cellulose-degrading bacteria and a lower relative abundance of total starch-degrading bacteria in the rumen of yaks compared with cattle, suggesting that yaks could degrade plant fibers more efficiently. The ratio of Firmicutes to Bacteroidetes in the rumen is positively correlated with fiber degradation ability (Fernando et al., 2010; Hu et al., 2017). This ratio is normally higher in the rumen of yaks compared with cattle (0.81 vs. 0.30) when grazing in highlands (Xin et al., 2019), possibly indicating a

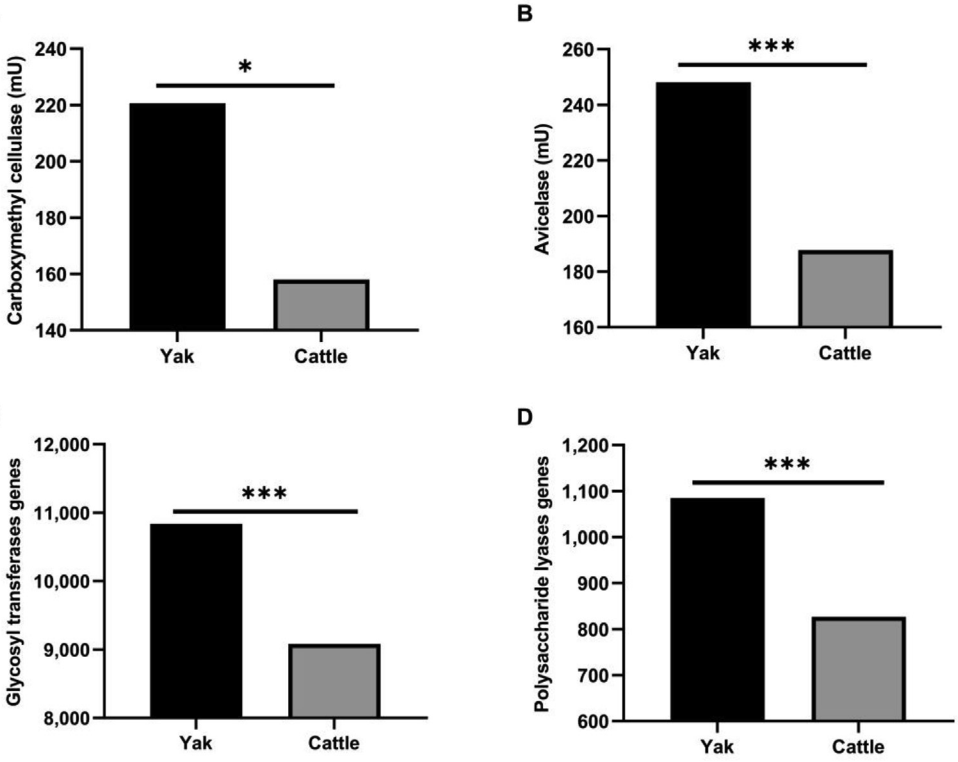

**Fig. 1.** Comparison of cellulose degradation ability between yaks and cattle (Zhao et al., 2021). (A and B) The activities of carboxymethyl cellulase and avicelase in the rumen, respectively. (C and D) The abundances of glycosyl transferases and polysaccharide lyases in the rumen metagenome of yaks and cattle. Asterisk denotes statistically significant differences, $*P < 0.05$; $***P < 0.001$.

stronger ability of the ruminal microbes to utilize fibrous materials in yaks. Additionally, Christensenellaceae were higher in yaks than cattle (10.0% vs. 2.09%) (Xin et al., 2019). The bacteria in the Christensenellaceae family secrete several glucoside hydrolases including α-arabinosidase, β-glucosidase and β-galactosidase, which possibly improve the utilization of small-molecular sugars in yaks (Myer et al., 2015; Perea et al., 2017). Secondly, a higher abundance and diversity of rumen anaerobic fungi was found in yaks compared with cattle under grazing conditions (Wang et al., 2019). The process of fiber degradation can be accelerated in the rumen of yaks by anaerobic fungi through secretion of a large amount of cellulase, which acts by physically destroying the cell wall structure of plants (Kameshwar and Qin, 2018). Thirdly, the higher activities of cellulase, hemicellulose and carboxymethylcellulase secreted by rumen microbes can help yaks degrade fibrous materials (Zhao et al., 2021; Zhou et al., 2018) as seen in the results shown in Fig. 1. However, the amylase activity in the rumen of grazing yaks is lower than in cattle, which might slow down starch degradation in the rumen (Zhao et al., 2021). Since grazing is the major feeding pattern rather than feeding with diets rich in grains, whether yaks could effectively utilize grains rich in starch is still unclear and needs further investigation.

### 3.2. High VFA production and low methane emission in the rumen of yaks

For ruminants, VFA are the main energy source for the host, while methane emission is regarded as an energy waste product during ruminal digestion and is known to aggravate global warming due to its greenhouse potential (Johnson, 1995). An in vitro rumen fermentation study, using oat hay as a substrate, reported that ruminal fluid collected from grazing yaks on the Qinghai-Tibetan Plateau produced higher total VFA and lower methane compared with ruminal fluid taken from domestic cattle (Zhang et al., 2016; Mi et al., 2017). In vivo studies also found the content of VFA produced in the rumen of yaks was significantly higher than that of cattle grazed on the same pasture (Huang et al., 2012; Shi et al., 2019) or house-farmed with mixed rations containing 50% hay and 50% concentrate (Zhou et al., 2018). In summary, the differences between yaks and cattle in the long-term evolutionary process may eventually lead to different efficiencies in energy utilization, reflected by ruminal VFA production. Furthermore, an in vitro study reported that methane production from the ruminal fluid of yaks was lower compared with cattle (4.7 vs. 6.2 mmol/d) (Mi et al., 2017). In vivo studies also found similar results, with 1.7 g of methane/kg $W^{0.75}$ produced in yaks under grazing conditions compared with 3.2 to 4.2 g of methane/kg $W^{0.75}$ in cattle (Thorpe, 2009; Ding et al., 2010). Lower hydrogen recovery and $H_2$ production in the rumen of yaks could be the reason for the smaller amount of methane emission compared with cattle (Mi et al., 2017). However, both ruminal VFA and methane production are affected by the type of diet (Shibata and Terada, 2010), therefore, the specific mechanism of ruminal energy metabolism in yaks fed with rations containing different ratios of concentrate also needs to be studied. Fig. 2 shows the differences in metabolic pathways for methane and VFA between cattle and yaks.

Lower methanogenesis in the rumen of yaks could be attributed to the different ecology of rumen microbiome between yaks and cattle, since ruminal metabolic pathways are closely related to the rumen microbiome (Wallace et al., 2019). Ruminal methanogens are a major contributor of methane emission from ruminants, of which Methanobacteriales is the most abundant archaea in the rumen. Previous research has reported that the relative abundance of Methanobacteriales and Methanomicrobiales is much lower in the rumen of yaks compared with cattle (12.4% vs. 21.5%, and 0.96% vs. 9.8%), and there are some differences in diversity as shown in

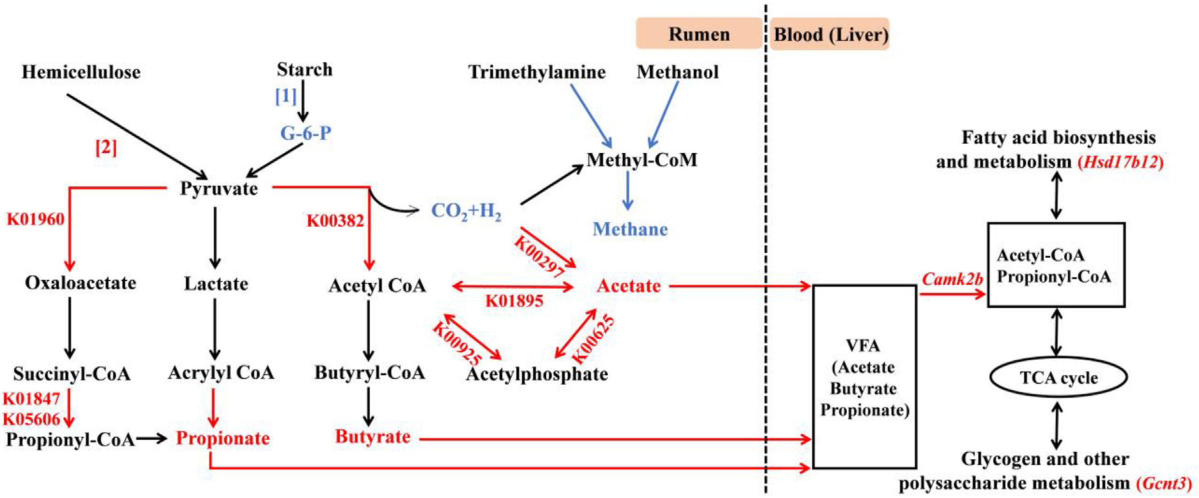

**Fig. 2.** Metabolic pathways of the formation and transport of VFA and methane. Metabolic pathways upregulated in yaks are highlighted in red. Metabolic pathways shown in blue are downregulated in yaks (Qiu et al., 2012; Zhang et al., 2016; Zhao et al., 2021). K00297 = methylenetetrahydrofolate reductase (NADPH); K01895 = acetyl-CoA synthetase; K00925 = acetate kinase; K00625 = phosphate acetyltransferase; K01960 = pyruvate carboxylase subunit B; K00382 = dihydrolipoamide dehydrogenase; K01847 = methylmalonyl-CoA mutase; K05606 = methylmalonyl-CoA/ethylmalonyl-CoA epimerase; (1): GH57, GH13-8, GH13-12, CBM48 (amylase); (2): GH48, GH5, GH45 (Cellulase), GH44, GH16, GH17, GH11 (Hemicellulase). VFA = volatile fatty acid; TCA = tricarboxylic acid.

Fig. 3C (Huang et al., 2012). Moreover, the hydrogenotrophic pathway is the main methanogenesis pathway in the rumen and contributes to approximately 82% of methane synthesis (Kittelmann et al., 2013), because over 78% of ruminal methanogens could produce methane through this pathway (Dan et al., 2016). The relative abundance of $H_2$ producers including *Coprococcus*, *Succiniclasticum*, and *Clostridium* was lower in the rumen of yaks compared with cattle (Kittelmann et al., 2014; Mi et al., 2017), possibly causing a reduction in methanogenesis due to a lack of substrates. Ren et al. (2020) found that several bacterial species including *Roseburia* spp., *Quinella* spp., *Fretibacterium* spp., *Ruminococcus gauvreauii*, *Erysipelotrichaceae UCG 004* and *Selenomonas* were significantly enriched in the rumen fluid of yaks. Among them, *Quinella* spp. ferments glucose to produce acetate and propionate and is associated with low methane production (Krumholz et al., 1993). In addition, fungi and methanogens have a mutually beneficial symbiotic relationship (Wei et al., 2016a), and through comparative analysis of the diversity and richness of rumen fungi between yaks and cattle, it was found that there was a significant difference in Shannon and Simpson indices (2.82 vs. 1.74; 0.16 vs. 0.49) (Wang et al., 2019), with the results of genus abundance of rumen fungi in yaks and cattle shown in Fig. 3A and B. Therefore, it is further speculated that differences in rumen fungi may indirectly lead to alterations in methane production.

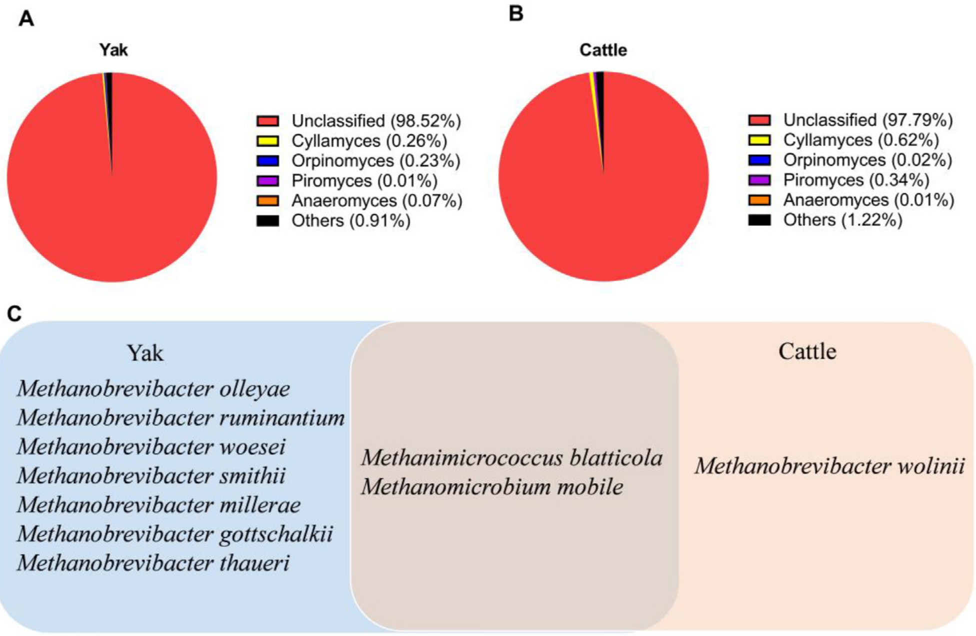

**Fig. 3.** Comparison of main fungi and methanogens in rumen of yaks and cattle (Huang et al., 2012; Wang et al., 2019a). (A and B) Genus composition of rumen fungi in yaks and cattle, respectively. The “others” represent the abundance of rumen fungi lower than 1%. (C) Comparison of main methanogens in the rumen of yaks and cattle.

In summary, it is speculated that the differences in methane production between yaks and cattle could possibly be attributed to: 1) the different structure of ruminal methanogens in yaks, and 2) the lack of substrates for methanogenesis due to a smaller number of bacterial $H_2$ producers. It is worth noting that the number of unclassified bacterial species in the rumen of yaks was double the number in cattle (An et al., 2005), which would also affect bacterial metabolic processes in yaks and needs to be further investigated.

## 4. Higher efficiency of nutrient absorption

### 4.1. Physiological advantages of nutrient absorption

Yaks have evolved notably different gut function to other ruminants, possessing a greater density of ruminal papillae in the rumen epithelium and more pleats in the mucosa surface of their abomasum compared with cattle (Beiranvand et al., 2014; Wang et al., 2015), which increases the surface area of the gastrointestinal tract and improves absorptive capacity. Unlike cattle, the orifices between the reticulum and omasum in yaks can shrink to decrease the passage rate of less nutritious forages during the cold season, leading to prolonged and sufficient digestion of this feed under poor forage conditions (Ghoshal and Bal, 1989). This change is regarded as one of the ways that yaks have adapted to the highland environment.

### 4.2. Absorption of VFA

The VFA produced in the rumen are mainly absorbed through the ruminal epithelium. Comparative transcriptome analysis of the ruminal epithelium showed significant upregulation of 36 genes participating in the process of VFA transport in yaks compared with cattle (Zhang et al., 2016), which could increase the transport capacity of the ruminal epithelium in yaks and further improve energy utilization. However, the actual uptake rate of VFA is still unknown and needs to be further investigated by rumen perfusion experiments.

### 4.3. Absorption of ammonia and small peptides

Ammonia is an important nitrogenous substance for the growth of rumen microbes during protein degradation, with an optimal level of 60 to 300 mg/L (Preston and Leng, 1988). An extremely low concentration of ruminal ammonia (below 50 mg/L) caused by the lack of dietary protein in the highlands would limit microbial production and productivity (Satter and Slyter, 1974), especially during the cold season. For example, Shi et al. (2019) reported that ruminal ammonia concentration in 4-year-old yaks was higher than in cattle (2.52 to 7.54 mg/100 mL vs. 0.87 to 2.16 mg/100 mL) under grazing conditions during the cold season. The greater level of ruminal ammonia could be attributed to a higher urea reuse capacity in yaks compared with cattle. Part of the blood urea could return to the rumen largely through the epithelium (about 90%) (Russell and Rychlik, 2001) and then be reused by rumen microbes. This urea reuse would provide more nitrogen for rumen microbes despite a lower supply of dietary protein. Previous studies have reported that the amount of nitrogen reabsorbed from the blood to the rumen is significantly higher in yaks than cattle, which possibly results in more efficient rumen microbial protein synthesis when on low protein diets, suggesting a better ability in yaks to save dietary nitrogen (Shi et al., 2019; Zhou et al., 2017). The reason could be that the higher concentration of ruminal VFA in yaks promotes urea reuse through upregulation of the urea transporter *UT-B* gene. This gene is able to transport blood urea into the rumen and its expression is positively correlated with ruminal VFA concentration (Abdoun et al., 2010). In addition, a higher expression of small peptide transporter in the jejunum of yaks compared with local cattle when fed rations containing 10.3 or 37.6 g N/kg dry matter has also been observed (Wang et al., 2016). The above transporters would help yaks to utilize nitrogen sources more efficiently. However, to our knowledge, there is no study that has focused on determination of actual transport rate and therefore more research is required in this area.

## 5. Lower energy and nitrogen requirements for maintenance of the hosts

### 5.1. Lower energy requirements

It is reported that the energy requirements for maintenance of 2- to 3-year-old castrated yaks are significantly lower than that of the cattle (460 kJ/kg $BW^{0.75}$ vs. 545 kJ/kg $BW^{0.75}$) (Hu, 1992; Brosh et al., 2004). Another study reported that the metabolic weight of yaks was $BW^{0.52}$, while that of cattle was $BW^{0.75}$, indicating more efficient utilization of nutrients in yaks (Zhou et al., 2017). The fasting heat production of growing yaks was significantly lower than that of cattle at the same altitude (3,000 to 4,000 m) in summer. Whereas the fasting heat production of cattle increased significantly with altitude, that of growing yaks showed no differences at varying altitudes (Han et al., 2002). This may be related to evolution of adaptive mechanisms in yaks living on the plateau, such as the formation of fewer sweat glands and longer hair to reduce heat loss and conserve energy. Thus, having low maintenance energy requirements is advantageous for yaks to adapt to the limited of forage and shortage of dietary energy during winter on the Qinghai-Tibetan Plateau.

### 5.2. Lower nitrogen requirements and lower urinary nitrogen output

Previous studies have reported that yaks possess a higher capacity to utilize nitrogen, especially under the conditions of low protein ration (Long et al., 2005; Zhang et al., 2012). This is mainly reflected in yaks having lower nitrogen requirements than cattle. The recommended daily nitrogen requirement for maintenance of cattle is 0.88 g N/kg $BW^{0.75}$ (Ministry of Agriculture of the People's Republic of China, 2006), while that of yaks is only 0.40 to 0.53 g N/kg $BW^{0.75}$ (Long et al., 2004), suggesting a much lower nitrogen requirement for yaks. In addition, apparent digestibility and retention of dietary nitrogen are also higher in yaks with a lower urinary nitrogen output compared with local cattle under conditions of limited dietary nitrogen (Long et al., 1999). This may be attributed to the glomerular filtration rate and excretion of some plasma purine derivatives through renal tubules being lower in yaks than in local cattle (Wang et al., 2009a), which further proved that yaks have lower nitrogen excretion and higher nitrogen deposition. Low energy and nitrogen requirements for maintenance in yaks is beneficial for maximizing the use of limited forage resources to survive on the plateau and adapt well to high altitudes (Wang et al., 2009b).

## 6. Outlook

In summary, the adaption of yaks to high altitude is attributed to the combined effects of multiple tissues, organs and genes under the extreme conditions of the Qinghai-Tibet Plateau. In this paper, we have discussed studies on the adaptability of yaks to the plateau environment, focusing on different facets including anatomy, behavior and nutrient utilization. However, there is still a big research gap. Firstly, a larger number of rumen microorganisms are still unrecognized or unidentified in yaks compared with cattle, which makes the understanding of microbial functions and metabolism in the rumen of yaks difficult. Secondly, the actual expression of VFA related transporters and the absorption rate of ruminal nutrients, including VFA and ammonia, still need to be investigated; albeit few studies have compared the expression of these genes between yaks and cattle. Thirdly, the existing research on yaks has concentrated on issues of energy metabolism in isolation rather than on the systematic study of energy utilization, which would provide a better understanding of adaptive mechanisms. All of these studies could provide a holistic view of the adaptability of yaks to the environment of the Qinghai-Tibetan Plateau and open new avenues for the protection of unique germplasm resources of yaks.

The rumen microbes of yaks have the potential to efficiently utilize lignocellulose in low-quality forages. The potential of such microbes is still untapped due to lack of studies on their identification and characterization. Isolation and culture of the unique strains of rumen microbes in yaks would also be beneficial for the production of industrialized enzymes. For example, feruloyl and acetyl esterase secreted by anaerobic rumen fungi isolated from yaks displays unique enzymatic characteristics (Cao et al., 2013). Rumen fungi in yaks have also been shown to possess high fibrolytic activity (Wei et al., 2016b). Characterization of rumen fungi and other unique microbes and study of their role in fiber and other macromolecule degradation in yaks could help to achieve targeted regulation of fiber and other macromolecule degradation capacity and efficient energy utilization in other ruminants on the plateau and plain areas.

Lastly, although yaks display good adaptability and efficient energy utilization on the plateau, it is unclear whether these advantages are maintained at lower altitudes. Some unanswered questions in this regard are as the following. 1) Can the lungs of yaks adapt to the low-altitude environmental conditions, where air density, humidity and ambient temperature are relatively high? The plateau and plain conditions also differ in many other aspects. 2) Yaks typically inhabit highlands with low temperatures, whether the lower number of sweat glands and long fur exert a heat stress for yaks on the plains? Further studies are required to gain better understanding of the adaptive mechanisms of yaks to extreme conditions.

## 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, and 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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