Proceedings of the 4th International Conference on Biological Engineering and Medical Science
DOI: 10.54254/2753-8818/62/20241480

Roles and mechanisms of methionine on milk productivity of dairy cows

Ranyue Guo

College of Animal Science and Technology, Jilin Agricultural University, Jilin, China

Gry18147722228@outlook.com

Abstract. The dairy industry has been an important part of the world's food industry. There are many factors affecting the milk production performance of cows, among which the nutritional factors are very important. Methionine has been found to have a critical role. Supplementation of methionine in a lactating diet can improve the lactating performance of dairy cows. Methionine, as one of the limiting amino acids (AA), enhances the biosynthesis of proteins in breast cells. Methionine can affect AA transportation by regulating the mTOR signaling pathway and regulating gene expression, such as the SLC1A5 gene (encoding ASCT2). Furthermore, methionine can also be used to synthesize glutathione (GSH) to improve the antioxidant capacity. Supplementation of rumen methionine showed immunity-enhancing effects. This review summarizes the effects of different forms of methionine supplementation on the performance of lactating dairy cows, including rumen methionine, N-acetyl-l-methionine (NALM), and coated methionine. This review discusses the role of methionine in dairy cow nutrition and the approaches of methionine supplements to improve lactation performance, aiming to provide an explanation for nutrient regulation in dairy cow feeding, in order to improve dairy cow productivity. Future research is required to better elucidate the methionine-associated metabolic changes during lactylation, as well as practical to optimize the approaches to improve dairy production.

Keywords: dairy cow, methionine, lactation properties.

1. Introduction

With the development of animal husbandry and technological advances, nutrients are important for dairy cows to produce milk. Methionine, also known as methionine, is the only amino acid containing sulfur among essential amino acids and plays an important role in nutrient supplements [1]. The fertility of cows is the key to ensuring the economic benefit of pasture. However, in recent years, large-scale breeding and feeding management have been incomplete, leading to the serious problem of nutritional deficiency of dairy cows, affecting the fertility of dairy cows. The nutritional deficiency of dairy cows is manifested as wasting and decreased production performance, such as weight loss, subcutaneous fat reduction, milk production reduction, and milk quality reduction. It even reduces fertility. Inadequate nutrition can reduce the quality and quantity of a cow's eggs, making it difficult to conceive. Nutrient-deficient cows are prone to miscarriage and premature birth after pregnancy, which seriously reduces reproductive efficiency [2].

One nutritional element that may have an important role in reproduction in lactating dairy cattle is amino acid (AA) nutrition. One essential AA that could potentially be limiting reproduction in lactating dairy cows is methionine. Methionine is one of the limiting amino acids of lactating cows, which affects the protein nutrient supply and lactation performance of dairy cows. Studies have shown that the content of milk protein in milk is more sensitive to supplementation of methionine than milk yield, especially after cows reach peak milk production [2]. Thus, supplementation of low-protein diets with specific AA is a promising strategy to counteract the potential negative effect of overall metabolizable protein deficiency on dairy cows' productivity.

In this review, recent research progress from methionine, different methionine types and other effects of amino acids on cows, are summarized.

2. Role of methionine in normal cow dairy production

Methionine plays important roles in cow diary production, including biosynthesis of proteins, affecting AA through multiple signaling pathways, as well as anti-oxidant and immunity-enhancing effects (Table 1).

2.1. Biosynthesis of proteins and peptides

Methionine is the only sulfur-containing amino acid in animal essential amino acids, which can be divided into D type, L type and DL type according to optical activity, and L type can be absorbed and utilized by animal tissue cells [3]. In mammary cells, amino acids play a role in signaling regulation. Free amino acids (FAAs) are the main precursors of milk protein synthesis, and peptide-binding amino acids (PBAAs) in the blood supplement the supply of FAAs. In order to increase milk protein concentration and yield, providing sufficient and balanced amino acids is essential to improve milk protein concentration and yield of dairy cows [4]. It is also an important factor affecting amino acid nutrition metabolism and milk protein synthesis [2]. Therefore, L-methionine is one of the important raw materials for the synthesis of milk protein in breast cells. L-methionine is transported into the breast cells by specific transporters, which participate in the synthesis of polypeptide chains of ribosomes and form milk proteins. Research has shown that dietary supplementation of rumen methionine can increase plasma methionine concentration and significantly increase milk protein production and concentration [5].

2.2. The role of methionine in AA transporter system

Amino acid transporters related to methionine were found in the detection of dairy cow mammary epithelial cells: ASCT2 transporter encoded by SLC1A5 gene, LAT1 amino acid transporter encoded by SLC7A5 gene and SNAT2 transporter encoded by SLC38A2 gene [6-8]. When methionine concentration was 0.6 mmol /L, mammary epithelial cell viability and milk protein synthesis, β-casein (CSN2) gene, SLC1A5 gene (with the strongest effect) and SLC7A5 gene expression were significantly increased.

mTOR signal, Ribosomal protein S6 kinase beta 1, Ribosomal kinase beta 1, at this dose, the phosphorylation of S6K1 is most effective with the expression of eukaryotic translation initiation factor 4E egg binding white (4EBP1) gene [6-8]. There are two mTOR complexes in the mTOR signaling pathway, among which mTORC1 is the most important target in the methionine-regulated milk Protein signaling pathway, S6K1 and 4EBP1 are downstream regulatory molecules of mTORC1, and mTORC2 is related to Protein kinase B and Akt. Methionine is more capable of regulating the activity of mTORC1 [9]. Methionine enters breast cells through these amino acid transporters, and then regulates the expression of JAK2 /STAT5, mTOR, P13K and other signaling pathways [10].

The uptake of PBAAs in breast cells can promote milk protein synthesis and secretion. This stimulating effect may be achieved in breast epithelial cells by enhancing the availability of intracellular substrates, cell proliferation, and signaling pathways. Specifically, PBAAs can be used as a nutrient substrate for milk protein synthesis. PBAAs are transported into cells by PepT2 and hydrolyzed into free amino acids (FAAs) in mammary epithelial cells for milk protein synthesis. In addition, PBAAs ingestion in its complete form can reduce competition for FAAs through amino acid transporters, thus promoting milk protein synthesis. Studies have shown that PBAAs can enhance milk protein synthesis compared to the same amount of FAAs. PBAAs can reduce competition during amino acid absorption by promoting the expression of amino acid transporters and the total intake of certain FAAs. In addition, PBAAs can also be used as signaling molecules to regulate milk protein synthesis. Met-Met can promote casein synthesis through JAK2STAT5 and mTOR signaling pathways [4]. Supplementation with EAAs increases MP synthesis by enhancing mTOR and JAK2-STAT5 pathways, but inhibits GCN2 pathways in MAC-T cells and the positive regulation of MP synthesis by EAAs mediated by seryl-tRNA synthase (SARS) [11]. Met-Met can enhance the activities of STAT5, JAK2, mTOR, 4EBP1, and S6k1, thereby improving the proliferation, survival, and β-casein synthesis of mammary epithelial cells [4].

2.3. Anti-oxidant and immunity-enhancing effects

Methionine can be directly involved in the biosynthesis of animal proteins and peptides. Methionine can be converted into cysteine, used to synthesize glutathione (GSH), which improves the antioxidant capacity of the animal body [12]. Therefore, supplementation of rumen methionine during the peripartum of dairy cows can reduce the incidence of oxidative stress. Supplementation of rumen methionine in the late perinatal period can significantly increase the contents of β-carotene and vitamin E in the plasma of dairy cows because vitamin E can significantly reduce the incidence of postpartum mastitis and postpartum endometritis in dairy cows [13].

Methionine can also be metabolized into S-adenosylmethionine to affect the chemical levels of methyl-mediated cell inflammation in animals [14]. Supplementation of rumen methionine in the late perinatal period can reduce the inflammatory response of dairy cows and improve the immune capacity of the body. Methionine by itself does not have any effect on immune function, but metabolites of methionine such as homocysteine and glutathione can improve animal immune function [15].

Table 1. Effects of methionine

Targets	Effects	Ref(s)
Synthesis of proteins	As raw materials for the synthesis of milk protein	[2,3]
mTORC1	Increase LAT1, regulating amino acids transportation	[2,9]
Synthesis of homocysteine	Immunity enhancing effect	[14,15]
Synthesis of glutathione	Anti-oxidant effects	[12]

2.4. Feedback loop of methionine

In order to maintain the balance of methionine nutrition in the mammary gland, the body of dairy cows can make corresponding adjustments to the change of methionine concentration. When the plasma methionine concentration decreases, the body will maintain the circulation of methionine in the mammary gland by increasing the blood flow and the mammary gland affinity for methionine [16].

3. Methionine derivatives and forms as additives

Research has tempted to use methionine derivatives and forms as additives in cow diet, including Rumen-protected methionine (RPM), Methionine dipeptide (Met-Met), N-acetyl-l-methionine (NALM), coated methionine, etc. (Table 2).

3.1. RPM

By coating technology, Met is added to feed in the form of RPM to improve its utilization in dairy cows. Studies have shown that RPM supplementation can significantly improve the health status, feed utilization efficiency and production performance of lactating cattle. Although RPM has a positive effect on lactating cattle, its effect is influenced by a number of factors. Feed formula, feeding management level, environmental conditions and individual differences may affect the effect of RPM [17].

3.2. Met-Met

BMECs was cultured in the penetrating chamber. After BMECs formed cell layer, 0.5 mmol/L Met-Met was added to the culture medium in the upper chamber and the lower chamber of the penetrating chamber, respectively, and no Met-Met was added as the control. After 24 hours of culture, BMECs were collected and detected by Western blot. The results showed that after BMECs was cultured in penetrating chamber for 6 days, the cell layer was compact. Met-Met supplementation significantly increased the phosphorylation levels of mTOR, S6K1 and AKT in the culture medium of upper and lower ventricle ($P<0.05$). The results showed that Met-Met in the culture medium of the upper and lower ventricles could be taken up by BMECs for milk protein synthesis, and Met-Met in the basement membrane promoted milk protein synthesis by activating mTOR and AKT signaling pathways [18].

3.3. NALM

The method of supplementing NALM as metabolic protein (MP) to protect rumen methionine source in 8 lactating dairy cows was studied. Within each square, cows were randomly assigned to four diets for four 21-day periods (14 days for treatment adaptation and 7 days for data collection and sampling). NALM products were added to MPD+NALM and MPA+NALM at a content of 30 g/day, arranged by a 2 × 2 factorial method. Regardless of MP concentration, the addition of NALM did not affect dry matter intake (DMI) or milk production. In addition, the NALM mechanism makes the concentration of true protein in milk similar to the yield. The addition of NALM increases the milk fat concentration and milk yield, and tends to increase the energy corrected milk yield. In addition, both fat-corrected milk yield /DMI and energy-corrected milk yield /DMI tended to increase by 3.5%, and the positive effect of MPA diet was greater than that of MPD diet, indicating a tendency of interaction between MP and NALM. The effects of diet treatment were similar. Plasma methionine concentrations increased in the MPD group but not in the MPA group, resulting in MP and NALM interactions. The overall results of this study show that NALM has little effect on rumen metabolism, but can increase milk fat concentration, thereby improving milk fat yield and feed efficiency [19].

3.4. Coated methionine

Twenty Holstein cows with the body weight of (634±38) kg and milk yield of 40 kg were randomly divided into 2 groups with 5 replicates per group and 2 cows per replicate. Cows in the control group were fed a low protein basal total mixed diet, and cows in the treatment group were fed a low protein basal total mixed diet +0.4 g/kg coated with methionine. Results showed that there were no significant differences in feed intake, milk yield, 4% fat corrected milk and fat, protein and lactose yield between control group and treatment group ($P > 0.05$). Thus, low protein diet supplemented with 0.4 g/kg coated methionine has no negative effect on milk yield of dairy cows [20].

Table 2. Effects of different methionine on milk production of dairy cows

Methionine format	Design	Results	Ref(s)
Rumen-protected methionine (RPM)	Multiple studies	Significantly improve production performance	[17]
Methionine dipeptide (Met-Met)	Controlled experiment	Synthesis of milk protein	[18]
N -acetyl- l -methionine (NALM)	4 × 4 Latin square design	Increase milk fat concentration and milk fat yield	[19]
Coated methionine	Controlled experiment	No negative effect	[20]

4. Conclusion

Methionine, as an essential amino acid in dairy cow nutrition, plays an important role in the growth, health and lactation performance of dairy cows. Feed supplemented with methionine increased milk yield and milk component content of dairy cows. Methionine participates in the protein synthesis and metabolism process in dairy cows, improves the nutritional level of dairy cows, and thus promotes the milk performance of dairy cows. Methionine can also regulate AA transportation through multiple signaling pathways, such as mTOR signaling pathway. Met-Met can increase the activities of STAT5, JAK2, mTOR, 4EBP1, and S6k1. Supplement of methionine can regulate AA transportation-related gene expression, such as the SLC1A5 gene (encoding ASCT2). Moreover, by synthesizing GSH, methionine can improve the antioxidant capacity. Supplementation of rumen methionine showed immunity-enhancing effects. RPM, Met-Met, N-acetyl-l-methionine (NALM), and coated methionine added to the cow diet did not show significant adverse effects. Further research can be conducted on the direction of methionine's effect on dairy cow health. However, methionine may also cause some adverse consequences. Thus, further research is required to decide an appropriate amount of methionine.

References

[1] Song XY 2024. China Dairy 0 14-17.
[2] Pszczolkowski VL and Arriola Apelo SI 2020 J. Anim. Sci. Biotechnol. 11 108
[3] Wang H, Elsaadawy SA, Wu Z and Bu DP 2021 Front. Vet. Sci. 8 780731
[4] Zhou M, Xu L, Zhao F and Liu H 2021 Biology 10 104414
[5] Toledo MZ, *et al*. 2021 JDS 104 7583-603
[6] Dai W, Zhao F, Liu J and Liu H 2019 J. Agric. Food Chem. 68 13038-45
[7] Duan X, Lin Y, Lv H, Yang Y, Jiao H and Hou X 2017 DNA and Cell Biology 36 1126-33
[8] Qi H, Meng C, Jin X, Li X, Li P and Gao X 2018 J. Agric. Food Chem. 66 11027-33
[9] Zhang Y, *et al*. 2018 Amino acids 50 105-15
[10] Toledo MZ, Baez GM, Garcia-Guerra A, Lobos NE, Guenther JN, Trevisol E, Luchini D, Shaver RD and Wiltbank MC 2017 PLoS One 12 e0189117
[11] Dai WT, White RR, Liu JX and Liu HY 2018 J. Dairy Sci. 101 10456-10468
[12] Martinov MV, Vitvitsky VM, Banerjee R and Ataullakhanov FI 2010 BBA Advances 1804 89-96
[13] Mou XY and Guo YQ 2023 Dairy Industry of China 36-43.
[14] Pfalzer AC, Choi SW, Tammen SA, Park LK, Bottiglieri T, Parnell LD and Lamon-Fava S 2014 Physiol. Genomics. 46 617-23
[15] Li Xikang 2024 Dairy Industry of China 28-31
[16] Liu W, Xia F, Hanigan MD, Lin XY, Yan ZG, White RR, Hu ZY, Hou QL and Wang ZH 2019 JDS 102 4094-104
[17] Wang XY, Wei Y and Li N. 2019 Journal of Feed Research 44 126-129
[18] Qi YH, Huang F, Du XY, Liu GQ, Wang CF and Zhou MM. 2023 Chinese Journal of Animal Nutrition 35 6026-6032.
[19] Fagundes MA, Yang SY, Eun JS, Hall JO, Moon JO and Park JS. 2018 JDS 101 7082-94
[20] Qin X, Liu WQ, Zhu MX, Wang GY and Li ZZ 2021 China Feed 59-62