

## FOLIC ACID IN RUMINANT NUTRITION

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### Abstract

*Folic acid plays an essential role in ruminant nutrition. Microorganisms in the rumen can synthesise folates, but these amounts are not sufficient to achieve the best efficiency of dairy cows. However, the amount of folates synthesised in the rumen could possibly, to some extent, be affected by the forage: concentrate ratio. The supply of folates by the diet and the synthesis by ruminal microflora is sufficient to prevent folic acid deficiency in dairy cows and to maintain normal gestation and lactation. Degradation of orally supplemented folic acid in the rumen seems to be very high (about 97 %), as supplementation of folic acid hardly increases folate concentrations in the digesta at the duodenum. However, it must be considered that dietary supplements of folic acid higher than 0.5 mg/kg body weight increased serum folate concentrations in all available studies and milk folate concentrations in most studies. Additionally, milk production tended to be increased in some studies. Therefore, degradation of folic acid in the rumen may be overestimated as folates can be absorbed at the proximal duodenum. For future research it is necessary to consider the whole flow and the metabolic pathways of folates from the rumen to duodenum, blood, tissue, milk and transfer to calf to declare requirement values for cows.*

**Key words:** Folic acid, folate, dairy cows.

### INTRODUCTION

Folic acid is one of the vitamins in the B complex and it is necessary for the synthesis of nucleic acids. Their biologically active forms are folates. Folates are essential for the transfer of one-carbon units from donor molecules into biosynthetic pathways leading to methionine, purine and pyrimidines. In general, it is assumed that B-vitamin requirements for ruminants can be met by microbial synthesis in the rumen, even when the animals are fed a diet providing very small amounts of those vitamins.

Folic acid has the single, important biochemical function in mammals to accept and release one-carbon units (Choi and Mason, 2000). This role is essential for the synthesis of purine and pyrimidine and the de novo synthesis of methyl groups for formation of the primary methylating agent, S-adenosylmethionin (Bailey and Gregory, 1999). Given this last role, the metabolic demand for folic acid is likely to be high because exogenous supply of methyl groups is low in ruminants (Snoswell and Xue, 1987). Moreover, it seems that the

supply in folic acid could be limiting based on estimated ruminal synthesis and dietary supply (Zinn et al., 1987; NRC, 2001).

Folic acid is very important during lactation and for DNA synthesis of fetal and placental tissues during pregnancy (McNulty et al., 1993), therefore a suboptimal supply should be avoided. In agricultural practice in dairy cows, gestation and lactation are concomitant during several months per year, so the avoidance of progressive folate deficiency must be a priority. The objective of this review is to elucidate the relationship between dietary folic acid levels and milk production in dairy cows and emphasize the importance of folic acid and its duty on the metabolism.

### CHEMICAL STRUCTURE

The vitamin folic acid (chemical name pteroylglutamic acid) consists of three parts: a pteridine nucleus, para-aminobenzoic acid and glutamic acid (Girard, 1998). The name folic acid is deduced from folium, the Latin word for leaf, because native forms of folic acid were originally isolated from spinach leaves (Mitchell

et al., 1944). In chemistry the name folic acid is only used for the synthetic form. It is a stable compound and the basal structure of a wide family of vitamin coenzymes (Lucock, 2000). In nature, more than 100 compounds, with the basal structure of folic acid, feature a common vitamin activity. These pteroylglutamate forms of folic acid are generally called folates (Finglas et al., 2003; Girard, 1998; Bender, 1992).

## **ABSORPTION AND BIOCHEMICAL FUNCTIONS**

There are several excellent reviews on absorption and biochemical functions of folates (Scott, 1999; Bassler, 1997). Derived from studies with non-ruminant animals, two mechanisms of folate absorption from the intestinal tract seem to exist: an active saturable process and a non-saturable passive process. In fact, the relative importance of passive absorption changes according to folate supply, increasing with the amounts of folates available (Selhub et al., 1983; Bassler et al., 2002). However, folates are perhaps degraded, converted and synthesised in the four stomachs of ruminants (Zinn et al., 1987), and even absorbed on a small scale (Re'rat et al., 1958). Unfortunately the forms and the availability of the forms present in rumen contents and duodenal digestion are unknown

The folates are involved in two major metabolic pathways, the DNA cycle and the methylation cycle. When the supply in one-carbon units is inadequate, the utilization of folate coenzymes for biological methylation and nucleotide synthesis appears to compete (Choi and Mason, 2000).

A deficit of folates can lead to a decrease in S-adenosylmethionine levels and to an abnormal DNA precursor metabolism resulting in faulty DNA synthesis and a decrease in NAD (James et al., 1994), as a decrease in NAD levels is consistent with an increase in DNA repair activity (James et al., 1989).

As folates influence DNA synthesis and the methionine cycle, they are involved in the metabolic pathways of reproduction and milk protein synthesis; therefore they are very important especially in gestating and lactating cows. An additional special situation for cows is that they have a very high demand for methyl groups in early lactation. Concurrently some

precursors for methylated compounds (for example, serine and glycine) are also needed for gluconeogenesis, as the amounts of glucose reaching the small intestine through the digestive system are generally low. So, coincident demand for precursors of methylated compounds leads to competition between different metabolic pathways, for example, gluconeogenesis, lecithin synthesis, DNA synthesis and remethylation of methionine (Girard and Matte, 2006; Bruesemeister and Suedekum, 2006).

## **SOURCES AND STABILITY OF FOLATES**

Folic acid is widely distributed in nature; green leafy materials, cereals and extracted oilseed meals are good sources of the vitamin. Folic acid is reasonably stable in foods stored under dry conditions but it is readily degraded by moisture, particularly at high temperatures. It is also destroyed by the ultraviolet light (Mcdonald et al., 2002).

## **INDICATIONS OF A FOLIC ACID REQUIREMENT FOR DAIRY COW**

Obviously, in high-producing dairy cows that are in gestation and lactation, frequently both at the same time, for the greatest part of their life, demand for methylneogenesis as well as DNA biosynthesis and cell division are highly solicited pathways, which are likely to rely heavily on folate metabolism. Although recovery of nucleic acids from microbial digestion could decrease the pressure on the DNA cycle competition between gluconeogenesis and methylneogenesis for substrates are likely to be high in lactating high-producing dairy cow, especially in early lactation. During those periods when there is a shortage in precursors for de novo synthesis of methylated compounds, an adequate supply in folates should improve efficiency of transfer of one-carbon units. Thus, an adequate supply of both methyl group precursors and the appropriate co-factors (folates, B12) is likely to be crucial for an optimal metabolic efficiency and milk production (Girard and Matte, 2005). A few observations on cattle suggest that, in spite of an adequate ruminal function, folate supply could vary in time. In growing steers, folate supply, evaluated from the amounts

reaching the duodenum, was marginal as compared to requirement evaluated from recommendations for a 35 kg growing pig and adapted for steers on a body weight basis (Zinn et al., 1987). Some other observations seem to substantiate folate supply variations in cows. Non-gestating cows have serum concentrations of folates superior to those of gestating cows (Arbeiter and Winding, 1973; Tremblay et al., 1991). Total serum folates of dairy cows decrease by 40% from 2 months after calving to next calving (Girard et al., 1989). Changes in serum concentrations are likely to give an indication that the relationship between folate supply and its tissue utilization differs among the different physiological stages studied substantiating this choice of vitamin for further studies in dairy cows.

### **MICROBIAL SYNTHESIS, DEGRADATION AND ABSORPTION OF FOLATES IN THE GASTROINTESTINAL TRACT OF RUMINANTS**

It is well known that the microbial activity and the ruminal population are influenced by the level of concentrates in the diet and the type of feed (Hungate, 1966). As some bacterial species are able to synthesise folates, and some others need them (Wolin and Miller, 1988), different amounts of folates can be synthesised and used in the rumen depending on the feed composition. For steers, Hayes et al. (1966) and Girard et al. (1994) described a relationship between the proportion of concentrates in the diet and the amount of folates in the rumen. High-concentrate diets resulted in an increase of folates.

### **EFFECTS OF SUPPLEMENTED FOLIC ACID ON RUMINANTS**

M. Duplessis et al. (2014) reported that milk fat concentration was decreased during the first 60 DIM (days in milk) for both primiparous and multiparous cows receiving the vitamin supplement. Also they found that supplementation of folic acid and vitamin B-12 given 21 day before the expected calving date until 60 DIM did not increase milk yield of dairy cows in early lactation and during the 305 day lactation period in commercial dairy herds.

Supplementation of folic acid does not influence feed intake (Graulet et al., 2007). For gestating primiparous and multiparous cows, Girard et al. (1995) found a non-significant increase in milk production of 14% in the last part of lactation due to an i.m. injection of 160 mg folic acid once per week.

Girard et al. (1989) observed that total serum folates of dairy cows decreased by 40% from 2 months postpartum (around mating) to parturition. According to that study of dairy cows, which are generally considered to be independent of an exogenous supply of folic acid (Agricultural Research Council, 1980; National Research Council, 1989) the synthesis of folates by ruminal microorganisms was not sufficient to prevent a decline in serum folates during gestation and lactation.

### **CONCLUSIONS**

It is concluded from this review that folic acid plays an important role in the synthesis of milk protein from dietary protein. However; the levels at which folic acid should be supplemented in dairy cattle diets are not determined clearly in many studies. Future research on ruminant diets should be headed towards on determining the folic acid digestion mechanism at rumen and intestinal level and their role in milk protein synthesis. Research efforts should also be focused on finding the balance between supply and demand of folic acid in ruminant diets.

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