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Folic acid and vitamin B_{12} requirements of dairy cows: A concept to be revised

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Abstract

Based on a limited number of research studies conducted on steers, it seems that the supply in folic acid could be limiting based on estimated ruminal synthesis and dietary supply. Folic acid has the single, important biochemical function in mammals to accept and release one-carbon units. This role is essential for the synthesis of purine and pyrimidine and the de novo provision of methyl groups for formation of the primary methylating agent, *S*-adenosylmethionine. Given its metabolic roles, folic acid is critical for cell division and protein metabolism, and therefore is an ideal candidate to begin with while reviewing B-vitamin requirements of dairy cow for an optimal productivity. Moreover, metabolisms of folic acid and vitamin B_{12} are closely linked, utilization of folates by cells being dependent of vitamin B_{12} supply. Studies reported in the present paper demonstrate that the supply in these two B-vitamins is not always sufficient to maximize health and productivity of dairy cows. Supplementation in those vitamins, especially during early lactation, improved lactational performance, metabolic efficiency and nutritional quality of milk. However, other research needs to be conducted to overcome the problems caused by the massive destruction of dietary supplements of those vitamins in rumen.

Keywords: Dairy cow; Lactation; Folic acid; Vitamin B_{12}

1. Introduction

Approximately 80 years ago, Bechdel et al. (1928) demonstrated that bacteria present in the rumen of a cow produced high levels of B-vitamins, even if the animal was fed a diet providing very small amounts of those vitamins. Moreover, over the years since the discovery of B-vitamins, it appears that true deficiency of these vitamins is rare in animals with a functional rumen. It is generally accepted that B-vitamin requirements can be met through synthesis by ruminal bacteria and escape of dietary sources from the rumen (NRC, 2001). Consequently, very few research efforts were oriented towards definition of dairy cow requirements for B-vitamins. However, over the last 50 years, milk and milk component yields increased drastically. It is likely that vitamin

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requirements increased accordingly and that synthesis by ruminal microflora alone may not be sufficient to meet these new needs.

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*-adenosylmethionine (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). Therefore, among all B-vitamins, folic acid is an ideal candidate to begin with while reviewing B-vitamin requirements of dairy cow for an optimal productivity.

2. Mode of action of folates

In most species, ingested folic acid is rapidly reduced and methylated across the gastrointestinal wall and the liver to 5-methyl-tetrahydrofolate (5-methyl-THF) (Le Grusse and Watier, 1993). In humans, plasma folates are present as monoglutamate of 5-methyl-THF (Lucock, 2000); this is also the case in cows (unpublished data). However, retention and concentration of folates by tissues require conversion of pteroylmonoglutamates to pteroylpolyglutamates (Shane, 1989). The 5-methyl-THF is a poor substrate for the enzyme responsible for the elongation of the glutamate chain (Shane, 1989) and the methyl group can be removed only through a vitamin B_{12}-dependent reaction in which this methyl group is transferred to homocysteine for methionine regeneration (Shane et al., 1977). Demethylation of 5-methyl-THF is rate-limiting for cellular accumulation of folates (Lucock, 2000). Once in the cell, the active form of folic acid is polyglutamated THF, which acts cyclically as an acceptor/donor of one-carbon units (Bässler, 1997).

The folates are involved in two major metabolic pathways, the DNA cycle and the methylation cycle (Fig. 1). 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).

2.1. DNA cycle

The THF obtains one-carbon units from either serine to form 5,10-methylene-THF or from formate to form 10-formyl-THF. Two units of 10-formyl-THF

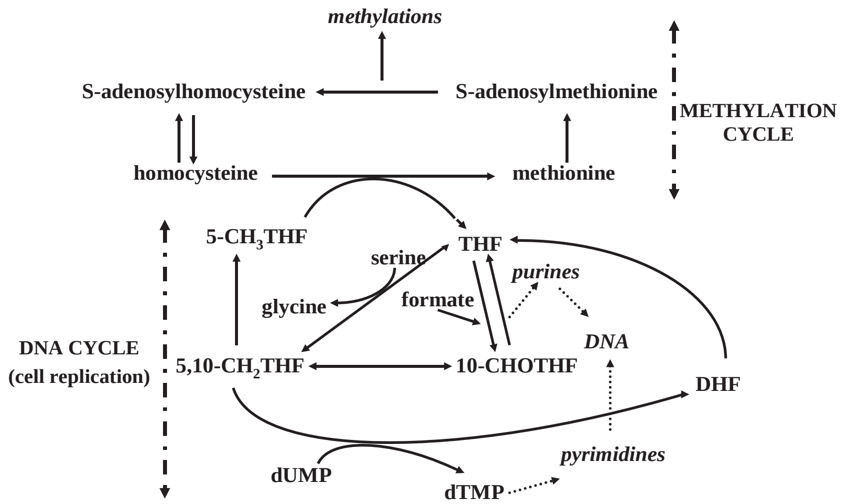

Fig. 1. The two major folate-dependent biological pathways: DNA and methylation cycles. DHF: dihydrofolate; THF: tetrahydrofolate; 5-CH_3-THF: 5-methyl-tetrahydrofolate; 5,10-CH_2-THF: 5,10-methylene-tetrahydrofolate; 10-CHO-THF: 10-formyl-tetrahydrofolate; dUMP: desoxyuridylate; dTMP: thymidylate. Dotted lines indicated incompletely described metabolic pathways.