# The best methyl donor for animal feed

Malcolm Mottram

Mal.mottram@feedworks.com.au

When thinking about methyl donors used in animal feeds we probably gravitate to the following group of **choline, betaine, methionine and folic acid.** In fact, that's pretty much spot on. But which is the best and why?

**Natural Betaine is the <u>best</u> methyl donor because it can be directly used in the transmethylation cycle without needing conversion (unlike choline & folic acid), it spares methionine and reduces homocysteine (which is toxic).**

**Here are some key facts around methylation in the body and why natural betaine is your best choice.**

1. S-adenosyl-methionine (SAM) is part of the transmethylation cycle that provides the methyl donor that is critical for creatine synthesis, phosphatidylcholine formation, DNA/RNA synthesis, immune modulation and more the 100 other functions within the body. T

2. While S-adenosyl-methionine (SAM) donates the methyl group, the methyl group must come from somewhere in order for SAM to have one to donate. That's where choline, betaine, methionine & folic acid from animal feed come into the picture as potential methyl donors. See Figure 1.

3. Beyond the essential role choline plays in the body; it has probably been traditionally added to animal feeds as a methyl donor. However, as a methyl donor it's not very effective. There are many reasons for that, but the major reason is that choline must first be converted to betaine. The conversion of choline to betaine occurs in the mitochondria of liver cells in a 2-step process that is rate limited. Because of this process, choline doesn't meet the bodies demand for methyl groups. So, choline is not the best methyl donor in animal feeds.

4. In the past methionine made up the shortfall for methyl donors in animal feeds by providing methyl groups to S-adenosyl-methionine (Figure 1.). Methionine is an essential building block for protein and that's where its principal role should be focused. Wherever possible methionine should NOT be pulled away to the transmethylation cycle. It's also important to consider total sulphur amino acids including cysteine in feed to ensure methionine is utilised effectively (more on that later).

5. Folic acid as a methyl donor has also been promoted as another option. We've heard about its role in pregnancy but as a methyl donor it must first be activated with a methyl group that comes from the body's methyl group pool. So obviously folic acid is not contributing as a methyl donor in the greater scheme and is therefore not the best methyl donor.

6. Natural betaine is the best methyl donor, recycling homocysteine to methionine in the transmethylation cycle (Figure 1.). This conserves methionine as a building block for protein synthesis. There are several reasons why I say betaine is the "best" methyl donor in animal feeds.

    a. Choline conversion is inefficient and inadequate as mentioned above.
    b. If homocysteine is not recycled to methionine it builds up and is toxic to the body. It has been found that 135 genes are affected by homocysteine toxicity.
        i. The biochemical pathways where homocysteine becomes toxic include those associated with the metabolism of glucose, insulin, lipids, lactate, calcium, chloride, the immune system (cytokines and anti-oxidant activity), the circulatory system (blood coagulation, blood pressure, vasodilation, nitric oxide and atherosclerosis), the nervous system, the cell cycle and cell death. That's why homocysteine is associated with heart disease.
    c. Given methionine's critical role as a building block of protein, the body does not want to waste a valuable amino acid. However, health comes first, and a lack of methyl donors will pull methionine to the transmethylation cycle. You could add lots of methionine to animal feed, but the penalty is homocysteine toxicity. Not ideal and very costly.

7. Methyl groups are critical to the body. Most methyl groups are used to form creatine from Guanidinoacetic acid (GAA) and to create phosphatidylcholine. They together account for 2/3 of the methyl groups required. However, a very important role of methyl donors is DNA/RNA gene expression. Gene expression and its role in foetal programming is something that is of great interest and a topic for another day.

    a. Creatine is a critical component in energy metabolism in the muscle. This constant loss of creatine is proportional to muscle mass and must be replaced by resynthesis of creatine. **Without constant replacement of creatine muscle mass is reduced. Without constant creatine synthesis through methylation we have a problem.**

    b. Phosphatidylcholine is synthesised in the liver from phosphatidyl ethanolamine and requires the transfer of three methyl groups from SAM. Phosphatidylcholine is the most abundant phospholipid in cell membranes and plays a key role in keeping membranes fluid and membrane receptors mobile. It is also an important component of bile, which assists in the digestion of lipids from the gut, and of lipoproteins, which transport lipids in the blood circulation.

In writing this article something stood out. Evolution is a wonderful thing. The transmethylation cycle is a wonderful example of something simple being complicated but when understood being simple.

While methionine is an essential part of the transmethylation cycle, the body wants to conserve its methionine for use in protein synthesis, so it creates a penalty by building up homocysteine and uses the most effective methyl donor to remethylate homocysteine to methionine. **The best methyl donor is natural betaine. Our experience is with Betafin over last 20-30 years with research across many animal species (pigs, poultry, cattle) which gives us great confidence in its attributes.**

If you wish to know why natural betaine is the best betaine source to use, well we have another article on that. Feel free to contact me if you wish.

Mal.mottram@feedworks.com.au

Ph +61 407 366 118

Figure 1. Methyl Donors in feed and the Transmethylation cycle