1 GENERAL INTRODUCTION

1.1 METABOLIC, OSMOREGULATORY AND NUTRITIONAL FUNCTIONS OF BETAINE IN MONOGASTRIC ANIMALS

1.1.1 ABSTRACT

This review focuses on the metabolic and osmoregulatory functions of betaine and its impact on nutrient digestibility and performance in pigs and poultry. Betaine is the trimethyl derivative of the amino acid glycine, and is present in plant and animal tissue. It has been shown to play an important role in osmoregulation of plants, bacteria and marine organisms. Due to its chemical structure, betaine exerts a number of functions both at the gastrointestinal and metabolic level. As a methyl group donor, betaine is involved in the transmethylation reactions and donates its labile methyl group for the synthesis of several metabolically active substances such as creatine and carnitine. Therefore, the supplementation of betaine may reduce the requirement for other methyl group donors such as methionine and choline. Beneficial effects on intestinal cells and intestinal microbes have been reported following betaine supplementation to diets for pigs and poultry, which have been attributed to the osmotic properties of betaine. Furthermore, betaine potentially enhances the digestibility of specific nutrients, in particular fiber and minerals. Moreover, at the metabolic level, betaine is involved in protein and energy metabolism. Growth trials revealed positive effects of supplemental betaine on growth performance in pigs and poultry, and there is evidence that betaine acts as a carcass modifier by reducing the carcass fat content. In conclusion, due to its various metabolic and osmoregulatory functions, betaine plays an important role in the nutrition of monogastric animals.

1.1.2 INTRODUCTION

Betaine supplementation to diets for livestock has increased during the last decade (Feng et al., 2006; Fernandez-Figares et al., 2008). Betaine, the trimethyl derivative of the amino acid glycine, is a naturally occurring compound, which is widely distributed in many plants and animal tissues. It is present in large quantities in aquatic invertebrates and sugar beets, but also in wheat, wheat products and lucerne meal (Kidd et al., 1997; Chendrimada et al., 2002). Common sources of betaine are sugar beets and their by-

products such as molasses and condensed molasses solubles (Eklund et al., 2005). As a feed additive, betaine is also available in purified form and most commonly added to animal diets in the form of anhydrous betaine, betaine monohydrate and betaine hydrochloride (Kidd et al., 1997; Eklund et al., 2005). Chemically, betaine is stable and non-toxic (Yu et al., 2004).

Due to its chemical structure (Figure 1), betaine has a number of different functions both at the gastrointestinal and metabolic level (Eklund et al., 2005). Betaine donates its labile methyl group which can be used in transmethylation reactions for synthesis of substances like carnitine and creatine (e.g. Kidd et al., 1997). Therefore, the dietary supplementation of betaine may reduce the requirement for other methyl group donors such as methionine and choline (Siljander-Rasi et al., 2003). Betaine acts as an osmoprotectant in plants (e.g. Xing and Rajashekar, 2001), bacteria (e.g. Pichereau et al., 1999), and marine organisms (e.g. Clarke et al., 1994). In vertebrates, betaine is used by numerous tissues as an osmolyte (e.g. Law and Burg, 1991). Due to its osmotic properties, betaine may have the potential to improve the digestibility of specific nutrients (Eklund et al., 2006a, b). Furthermore, betaine is involved in protein and energy metabolism due to its methyl group donor function (Eklund et al., 2005). The animal's betaine need is strongly influenced by the concentration of other methyl group donors in the diet and the occurrence of osmotic stress in the intestinal tract or other organs. If the total betaine need cannot be met by endogenous metabolism, dietary betaine supplementation may be beneficial to maintain or to improve animal health and performance (Kidd et al., 1997). Studies on the dietary effect of betaine revealed variable results, both in nutrient digestibility and animal performance (Øverland et al., 1999; Attia et al., 2005; Eklund et al., 2006a, b). The objective of this paper is to review the metabolic and osmoregulatory functions of betaine and its impact on nutrient digestibility and performance criteria in pigs and poultry.
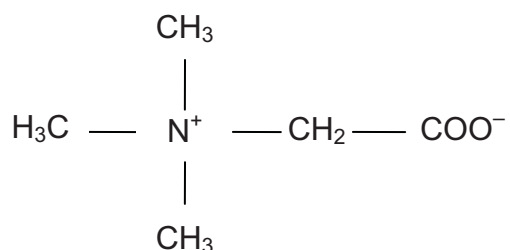
$$H_3C - \overset{\overset{\displaystyle CH_3}{|}}{\underset{\underset{\displaystyle CH_3}{|}}{N^+}} - CH_2 - COO^-$$

Figure 1. Chemical structure of betaine

1.1.3   Effects of Betaine on Animal Performance and Carcass Characteristics

Dietary betaine supplementation may affect animal performance and carcass characteristics, even though the effects are variable (Attia et al., 2005; Dunshea et al., 2007; Fernandez-Figares et al., 2008). Some of the investigated effects of betaine supplementation on performance of pigs and poultry are presented in Table 1 and 2, respectively. In some studies, the addition of betaine to the diet improved weight gain and feed conversion in pigs (e.g. Wray-Cahen et al., 2004; Yu et al., 2004; Dunshea et al., 2007), and poultry (e.g. Attia et al., 2005; Hassan et al., 2005), though the results of several other studies revealed minimal or no effect of betaine supplementation on animal performance (e.g. Esteve-Garcia and Mack, 2000; Feng et al., 2006). Dietary supplementation of betaine to a pig's diet improved weight gain and feed efficiency up to 15 and 8%, respectively (Wang and Xu, 1999; Zou et al., 2002; Yu et al., 2004; Huang et al., 2008). Moreover, betaine has been shown to improve feed efficiency of pigs housed under sub-optimal hygienic conditions (Spreeuwenberg et al., 2007). In poultry, dietary supplementation of betaine to diets with adequate methyl group donors improved weight gain and feed efficiency by approximately 3 to 15% (Hassan et al., 2005). Moreover, betaine may enhance performance of *Eimeria*-infected chicken indirectly, by support of the intestinal structure and function in the presence of coccidial infection, but also directly, by partial inhibition of coccidial invasion and development (Augustine et al., 1997; Matthews et al., 1997; Matthews and Southern, 2000). During periods of osmotic disturbance, caused by water salinity stress in broiler chickens, betaine is involved in the protection of intestinal epithelia, resulting in an improved growth and feed efficiency (Honarbakhsh et al., 2007a, b). Furthermore, under heat stress conditions, supplementation of betaine has shown to enhance egg production and egg shell quality in laying hens (Ryu et al., 2002), and to improve weight gain of broilers (Farooqi et al., 2005). In contrast, Zulkifli et al. (2004) could not show any effects of betaine on weight gain and feed conversion in broilers reared under heat stress conditions.

Chapter 1

Table 1. Effect of supplemental betaine in the diet on performance traits of pigs

Animal	Betaine Level (%)	Betaine Effects	Reference
Gilts; 60–103 kg	0.13	–	Cadogan et al. (1993)
Grower–finisher pigs; 34–102 kg	0.10	–	Smith et al. (1994)
Barrows, gilts; 83–16 kg	0.13	–	Cera and Schinckel (1995)
Gilts; 60–104 kg	0.10	↑ ADG	Smith et al. (1995)
Lactating sows	0.20	–	Campbell et al. (1997a)
Barrows; 30 kg	0.13	↑ ADG ↑ ADFI	Campbell et al. (1997b)
Finisher pigs	0.20	↑ ADG	Urbanczyk (1997)
Barrows, gilts; 30–112 kg	0.20	–	Urbanczyk (1997)
Gilts; 55–110 kg	0.13	–	Matthews et al. (1998)
Pigs; 56–113 kg	0.11	↑ ADG ↓ FCR	Cromwell et al. (1999)
Pigs; 24–113 kg	0.11	–	Cromwell et al. (1999)
Pigs; 30–112 kg	0.20	–	Hanczakowska et al. (1999)
Pigs; > 20 kg	1.05	–	Øverland et al. (1999)
Barrows; 20–65 kg	0.15	↑ ADG, 10%	Wang and Xu (1999)
Gilts; 20–65 kg	0.15	↑ ADG, 15%	Wang and Xu (1999)
Barrows, gilts; > 10 kg	0.08	↑ ADG, 12% ↑ ADFI, 9% ↓ FCR, 3%	Yu and Xu (2000)
Grower pigs; > 21 kg	0.10	↑ ADG, 13.3%	Feng and Yu (2001)
Finisher pigs	0.10	↑ ADG, 5.7%	Feng and Yu (2001)
Barrows; 50–110 kg	0.25	–	Matthews et al. (2001a)
Piglets; 5–12 kg	0.06	↑ ADG, ADFI	Matthews et al. (2001b)
Barrows, gilts; 66–88 kg	0.13–0.30	↓ ADFI	Matthews et al. (2001c)
Finisher pigs; 53–113 kg	0.11	↓ FCR	Pettey et al. (2001)
Barrows, gilts; 83–118 kg	0.13	–	Pettey et al. (2001)
Barrows, gilts; > 30 kg	0.25–1.00	↑ ADG ↓ FCR	Siljander-Rasi et al. (2003)
Weanling pigs	0.08	↑ ADG, 8.7%	Yu et al. (2001)
Grower pigs	0.10	↑ ADG, 13.2%	Yu et al. (2001)
Finisher pigs	0.18	↑ ADG, 13.3%	Yu et al. (2001)
Barrows; 30 kg	0.13–0.50	–	Fernandez-Figares et al. (2002)
Barrows; gilts; 83–116 kg	0.13	↓ ADFI	Lawrence et al. (2002)
Grower–finisher pigs	0.10	↑ ADG, 13% ↓ FCR, 8%	Zou et al. (2002)
Barrows; > 46 kg	0.13	–	Schrama et al. (2003)
Boar; > 64 kg	0.15	↑ ADG	Suster et al. (2004)
Gilts; 20–30 kg	0.13–0.50	↑ ADG ↓ FCR	Wray-Cahen et al. (2004)
Grower pigs; 20–64 kg	0.10–0.20	↑ ADG ↑ ADFI ↓ FCR	Yu et al. (2004)
Finishing barrows; > 62.5 kg	0.13	–	Feng et al. (2006)
Barrows, gilts; 55–90 kg	0.13	↑ ADG	Huang et al. (2006)
Boar, gilts; > 58 kg	0.13	↑ ADG, 8%	Dunshea et al. (2007)
Finishing pigs	0.13	↑ ADG, 5.5%	Huang et al. (2007)
Piglets	0.20	↓ FCR	Spreeuwenberg et al. (2007)
Gilts; 20–50 kg	0.50	–	Fernandez-Figares et al. (2008)
Barrows, gilts; 55–90 kg	0.13	↑ ADG	Huang et al. (2008)

–, No effect (P>0.05); ↑, increase (P<0.05); ↓, decrease (P<0.05)
ADFI, Average daily feed intake; ADG, Average daily gain; FCR, Feed conversion rate

Table 2. Effect of supplemental betaine in the diet on performance traits of poultry

Animal	Betaine Level (%)	Betaine Effects	Reference
Broilers	0.05–0.15	↑ ADG ↓ FCR	Virtanen and Rosi (1995)
Broilers	0.08	↑ ADG ↓ FCR	Virtanen and Rosi (1995)
Broilers, unsexed	0.15	↑ ADG ↓ FCR	Augustine et al. (1997)
Broilers	0.10–0.50	↑ ADG ↓ FCR	Matthews et al. (1997)
Broilers	0.10	↓ FCR	Matthews et al. (1997)
Broilers	0.15	↓ FCR 0–14 d	Teeter et al. (1999)
Broilers	0.10	↑ ADG 21–35 d	Teeter et al. (1999)
Broiler; female	0.10	↑ ADG ↓ FCR	Waldenstedt et al. (1999)
Broilers	0.08	↑ ADG ↑ Total plasma protein	Matthews and Southern (2000)
Broilers; female	0.05	–	Esteve-Garcia and Mack (2000)
Broilers; male	5–10	–	Zulkifli et al. (2004)
Broilers; male	0.05–0.10	–	Pirompud et al. (2005)
Broilers; male			Waldroup and Fritts (2005)
0–14 d	0.10	–	
0–35 d	0.10	↓ FCR	
0–42 d	0.10	↓ FCR	
0–49 d	0.10	–	
Broilers; unsexed	0.10	↑ ADG (under heat stress)	Farooqi et al. (2005)
Broilers; unsexed	0.04–0.07	↑ ADG ↓ FCR ↑ Feather weight	Attia et al. (2005)
Broilers; unsexed	0.07–0.14	↑ ADG ↓ FCR	Hassan et al. (2005)
Broilers; unsexed	0.28	–	Pillai et al. (2006)
Broilers; male			Waldroup et al. (2006)
0–14 d	0.10	–	
0–35 d	0.10	↓ FCR	
0–42 d	0.10	↓ FCR	
0–56 d	0.10	–	
Broilers; male	0.05	↑ ADG ↓ FCR	Zhan et al. (2006)
Broilers; unsexed	0.05–0.10	↑ ADG ↓ FCR	El-Husseiny et al. (2007)
Broilers; male	0.08–0.23	↑ ADG ↓ FCR	Honarbakhsh et al. (2007a, b)
Turkeys	0.10	–	Remus (2001)
Turkeys	0.09	↑ ADG (8 and 11 weeks)	Noll et al. (2002)
Turkeys	0.09	–	Noll et al. (2002)
Meat ducks; female	0.50	↑ ADG ↓ FCR	Wang et al. (2004)
Layer; ISA	0.04–0.08	↑ Egg production ↑ Concentration of VLDL ↑ Vitellogenin	Lu and Zou (2006)
Layer; ISA Brown	0.03–0.12	↑ Egg weight ↑ Serum estradiol ↑ Melatonin	Park et al. (2006)

–, No effect (P>0.05); ↑, increase (P<0.05); ↓, decrease (P<0.05)
ADG, Average daily gain; FCR, Feed conversion rate

Different studies revealed considerable changes in carcass composition in pigs (Table 3) and poultry (Table 4). Dietary betaine has been shown to exert positive effects on carcass characteristics of pigs by increasing carcass lean content, longissimus muscle area and loin depth, associated with a reduction in carcass fat content and back fat thickness, although without influencing performance (Cadogan et al., 1993; Smith et al., 1995; Yu et al., 2004; Huang et al., 2008). Studies in pigs revealed that dietary betaine reduced carcass fat content up to 18%, and raised the lean content of the carcass up to 8% (e.g. Wang and Xu, 1999; Feng et al., 2006). In growing pigs kept under a restricted feeding regime, betaine induced lower fat concentrations in the carcass, associated with a higher protein deposition (Fernandez-Figares et al., 2002). Following betaine supplementation to diets for poultry, several authors reported a reduction in abdominal fat weight, whereas breast meat yield was increased in broiler chicken (Zhan et al., 2006), turkeys (Noll et al., 2002) and meat ducks (Wang et al., 2004). In contrast, other studies did not show any effects of betaine supplementation on carcass characteristics in pigs (e.g. Fernandez-Figares et al., 2008) and poultry as well (Waldroup and Fritts, 2005).

The involvement of betaine in lipid metabolism offers an interesting perspective in meat production to satisfy consumer's needs for lean meat. Due to the reduction of carcass fat content and increase in carcass lean, betaine is often referred to as 'carcass modifier'. The mode of action of betaine as 'carcass modifier' may be related to its methyl group donor properties (Eklund et al., 2005). The improvement in carcass lean percentage may be attributed to a higher availability of methionine and cystine for protein deposition (McDevitt et al., 2000). An enhanced utilization of dietary amino acids for protein synthesis may result in fewer amino acids available for deamination and eventual synthesis of adipose tissue (Wallis, 1999). Accordingly, changes in hormone levels and growth factors involved in the regulation of fat synthesis and degradation, as well as lower activities of lipogenic enzymes have been observed following dietary betaine supplementation (Huang et al., 2006). Moreover, it is well known that betaine as a methyl group donor provides its methyl group for synthesis of lecithin, which facilitates the transport of fat through the body (Saunderson and MacKinlay, 1990). In addition, betaine may improve choline availability, thus providing more choline for the synthesis of very low density lipoprotein. The production of very low density lipoprotein prevents the deposition of fat in the liver and accelerates the removal of fat from the liver (Yao and Vance, 1990).