The Role of Synthetic Amino Acids in Monogastric Animal Production[a] - Review -

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ABSTRACT : The present paper gives a general overview on amino acid nutrition mainly focused on the concept of ideal protein and amino acid requirements in swine and poultry. Also, the nutritional, economic and environmental roles of synthetic amino acids are presented. A special emphasis has been given to the protein sparing effect by the supplementation of synthetic amino acids into diet and to the effect of this supplementation on growth performance and reduction of environmental pollutants in swine and poultry manure. It is concluded that the supplementation of limited amounts of synthetic amino acids (0.1 to 0.3%) to diets for swine and poultry could spare 2 to 3 percentage units of dietary protein and substantially reduce nutrient excretion, especially nitrogen. Immunocompetency as affected by amino acid nutrition is also introduced and the importance of threonine for the synthesis of immunoproteins in colostrum and milk to maintain piglets' health and intestinal integrity has been emphasized. Finally, some speculation on the future of global amino acids market is presented in conclusion. (*Asian-Aus. J. Anim. Sci. 2000. Vol. 13, No. 4 : 543-560*)

Key Words : Synthetic Amino Acids, Ideal Protein Profile, Swine, Poultry

INTRODUCTION

Dietary proteins are essential for the normal growth and reproduction of animals. Production cost of meats is mainly associated with the need to supply dietary energy and protein. Proteins are one of the costly major items in animal diets. Therefore, maximizing the efficiency of protein and amino acids utilization is very important for the reduction of feed costs and maximization of lean meat production with an absolute minimum intake of amino acids. In the last two decades, many swine researchers have focused their attention on the concept of an ideal protein for better performance by efficient utilization of their feed nutrients. Synthetic amino acids made easier to fomulate diets with an ideal amino acid profile. With the discovery of threonine (McCoy et al., 1935), all of the amino acids have been known, and it has now been possible to use synthetic amino acid mixtures as a substitute for protein. Nowadays, as the mass-production of crystalline amino acids is available, the use of crystalline amino acid is widely spread in manufacturing of feed for animals.

The amount of amino acids used in animal production has been considerably increased (table 1). The annual growth rate of the amino acid market in the world is 4.5% in average during the past few years. It is remarkable that the proportion of amino acid production used for animal feeds represents more than half (56%) of the total amino acid production and that proportion is likely to be increased in the next century.

Among this mass-production of crystalline amino acids, L-lysine and DL-methionine are commonly used to replace or supplement natural protein sources in lysine and methionine. Many researches (Hansen and Lewis, 1993; Han, 1996; Tuitoek et al., 1997) have clearly shown the protein sparing effect of using synthetic amino acids to balance low crude protein diets of monogastric animals.

Supplements of synthetic amino acids to animal diets are important not only on nutritional and economic aspects, but also on environmental aspects. Recently, there has been an increasing concern of the negative impact of livestock production systems on the environment all over the world. The increased concentration of animals together with environment constraints (i.e. reduction of land and water pollution by nitrogen and phosphorus from manure spreading) have forced the nutritionists to propose new feeding strategies for animals. The most efficient technique consists in reducing the amount of nitrogen intake and keeping the amino acid supplies adequate for meeting the animals's requirements. The primary solution to this kind of problem is using a highly utilizable source for animal feeds to reduce the nitrogen excretion in animal manure. As it is well known, synthetic amino acids enhance the digestibility of amino acids (nitrogen), as well as they promote high lean growth. This is one of the important roles of synthetic amino acids in animal nutrition.

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Table 1. Predicted annual growth of amino acids market in the world (Unit : billion $)

	1995	1996	1997	1998	1999	2000		
						Value	Growth rate (%)	Proportion (%)
Animal feed	1.60	1.70	1.80	1.90	2.01	2.13	6.0	56
Food	0.94	0.97	1.00	1.03	1.06	2.09	3.0	33
Medical use	0.32	0.33	0.34	0.35	0.36	0.37	2.0	11
Total	2.86	3.00	3.14	3.28	3.43	3.59	4.5	100

Amino acids are also related to the production of antibodies in animals. Lactating sows could theoretically produce enough antibodies, if they had appropriate levels of immunoproteins in their blood or mammary gland for a continuous supply of immunoglobulins to their baby pigs. This may be possible by supplementing sow diets with crystalline threonine (Chung, 1997).

This manuscript will first briefly review the general aspects of amino acid nutrition, and then discuss the role of crystalline amino acids in animal production and in the reduction of environmental pollution by monogastric animals. The interaction between immune system and amino acid nutrition will also be discussed. Finally, a global view of amino acid market in animal feed industry will be introduced, with the aim of providing effective ways of improving continuously animal production in the 21st century.

AMINO ACID REQUIREMENTS AND IDEAL AMINO ACID PROFILES OF DIETS

Feed cost is a major factor in animal production, representing 50 to 70 percent of the total cost of animal production. Logically, improving animal productivity can be obtained from the maximum expression of genetic potential of animals by nutritional approaches. Protein is costly item in pig diets, and this implies maximizing the efficiency of protein and amino acid utilization in animal feeds. Cleary, it is required to formulate diets containing amino acids at minimal required levels for maximal lean growth with minimal excesses. As a consequence, the use of ideal protein concept in feed formulation is very helpful in achieving this goal.

The concept of supplying dietary amino acids in a pattern to match the animal's amino acid needs has been developed as the "ideal protein" concept. However, the idea of ideal protein is not a new concept. Mitchell (1964) discussed the concept of an ideal protein or perfect amino acid balance and recognized that chemical scoring (Mitchell and Block, 1946) using egg protein as the ideal standard was flawed because egg protein was too rich in some essential amino acids, such as isoleucine, for example, being present at twice the level that most animals require. Cole (1978) proposed that diet formulation for pigs could be done on the basis of ideal amino acid ratios, and ARC (1981) subsequently suggested ideal ratios of amino acids for pig diets.

Since the suggestion of an ideal amino acid profile by the ARC (1981), this pattern has received considerable attention (Wang and Fuller, 1989, 1990; Fuller et al., 1989; Chung and Baker, 1992a) and many countries (USA, UK, Australia, New Zealand, etc.) have tried to modify the ideal amino acid pattern in their own feeding recommendations on the basis of the results of research on the ideal protein requirements for pigs. The ARC ideal protein was reassessed and improved by Wang and Fuller (1989). However, the ideal amino acid pattern from Wang and Fuller (1989) neither contained arginine nor histidine (Chung and Baker, 1992b). The ideal protein concept has been reviewed extensively for the starter pigs by Baker and Chung (1992) and for growing-finishing pigs by Friesen (1994). The benefits of an ideal protein concept in diet formulation is to set all essential amino acid requirements on the basis of lysine.

Table 2 summarized the ratios proposed by Chung and Baker (1992b) and derived from NRC (1998) for amino acid requirements recommended relative to lysine. There were some discrepancies within studies and the actual recommended ratios of the amino acid in an ideal protein. For example, NRC (1998) recommendation of pig amino acid requirements is somewhat lower than that of ARC (1981), except for tryptophan, threonine and sulfur amino acids. When the estimates of ideal amino acid ratios between in 1980s and in 1990s are compared, the ratio of threonine to lysine has been increased by 5% from 60 to 65%.

Owen et al. (1995b) indicated that 27.5% methionine as a percentage of dietary lysine resulted in optimal growth performance of young pigs from 4 to 15 kg. The optimal ratio of 27.5% for methionine to lysine obtained by Owen et al. (1995b) is in close agreement with the 30% proposed by Chung and Baker (1992b). However, ratios for the other amino acids have not been confirmed. Bergstrom et al.

Table 2. Ideal amino acid patterns for various growth stages of pigs

Sources	Weight (kg)	Lys	Arg	His	Trp	Ile	Leu	Val	Phe+Tyr (Phe)	Met+Cys (Met)	Thr	Lys requirements
Cole (1978)	20~50	100	-	40	18	50	100	70	100	50	60	
Fuller et al. (1979)	35~	100	-	32	12	44	84	63	96	53	56	7.3 g/16 g N
ARC (1981)	15~50	100	-	33	15	55	100	70	96	50	60	7.0 g/16 g N
Yen et al. (1986a)	25~55	100	30	35	20	55	100	70	100	50	57	18.0 g/d (boar)
Yen et al. (1986b)	50~90	100	30	35	20	55	100	70	100	50	57	22.9 g/d (boar)
Tokach et al. (1994)	3~5	100	-	-	18	60	-	-	-	55 (27.5)	65	1.70% of diet
NRC (1998)	3~5	100	39	32	18	55	100	69	94 (60)	57 (27)	65	1.50% of diet
	5~10	100	40	32	18	54	98	68	93 (59)	56 (26)	64	1.35% of diet
	10~20	100	40	31	18	55	97	69	92 (59)	57 (26)	64	1.15% of diet
	20~50	100	39	32	18	54	95	67	92 (58)	57 (26)	64	0.95% of diet
	50~80	100	36	32	19	56	95	69	93 (59)	59 (27)	68	0.75% of diet
	80~120	100	32	32	18	55	90	67	92 (57)	58 (27)	68	0.60% of diet
Fuller et al. (1989)	30~50	100	-	-	19	61	110	75	122	59	75	5.9 g/16 g N
Wang & Fuller (1989; WFIP)	25~50	100	-	-	18	60	110	75	120	63	72	6.5 g/16 g N
Wang & Fuller (1990)	30~	100	-	-	20	61	110	75	122	61	64	*modified WFIP
Cole (1994)	25~50	100	-	33	19	50	100	70	100	50	66	
Chung & Baker (1992a; IFP)	10~	100	42	27	14	57	87	60	83	61	57	1.38% of diet, (purified)
Chung & Baker (1992b; IIP)	10~	100	42	32	18	60	100	68	95	60	65	1.20% of diet, modified IFP
Baker (1995)	5~20	100	42	32	17	60	100	68	95 (48)	60 (30)	65	
	20~50	100	36	32	18	60	100	68	95 (48)	62 (30)	67	
	50~110	100	30	32	19	60	100	68	95 (48)	65 (30)	70	
Cho et al. (1998)	4~7	100	-	-	-	-	-	-	-	57.5	51.5	1.65% of diet

(1995), in examining an appropriate threonine to lysine ratio, did not show any response to increasing threonine to lysine ratios from 50 to 75% at two different dietary lysine levels (1.15 and 1.5% digestible lysine) in segregated early weaning (SEW) pigs. Cho et al. (1998) also observed a similar ratio (51.5%) for threonine : lysine with 14-day-old piglets. With the adoption of SEW, there has been marked changes in amino acid nutrition for very young pigs. Tokach et al. (1994) suggested appropriate lysine level and optimum ratios for other amino acids to lysine for optimum growth of SEW pigs (table 3 and 4) showing marked increases in the level of lysine recommended, and variable according to age.

Theoretically, an ideal pattern of amino acids should exist for each physiological function, more clearly, but different for maintenance, protein accretion, reproduction and lactation. Because the maintenance requirements for lysine are low relative to the maintenance requirements for certain other amino acids such as threonine and sulfur amino acids, ideal ratios of certain amino acids for young pigs cannot be applied without adjustment to older market-type pigs (Baker, 1995). Of the total requirement for a given amino acid, protein accretion comprises well over 90% of the need for pigs weighing 10 kg, but as pigs approach slaughter weight, maintenance represents greater prominence in the total requirement for an amino acid (Fuller et al., 1989; Black and Davies, 1991; Chung and Baker, 1992b). With an increasing contribution for maintenance as for an animal reaching slaughter weight, the ratio of sulfur amino acids: lysine must be increased, probably in a straight-line fashion, as a growing pig advances from 10 kg to 110 kg. Recently, Lenis (1996) slightly modified the apparent ileal digestible amino acid recommendations

Table 3. Recommended lysine levels for segregated early weaned pigs (SEW)

	Body weight (kg)	Total lysine (%)	Digestible lysine (%)
SEW	<5	1.7 ~1.8	1.4 ~1.5
Transition	5~7	1.5 ~1.6	1.25~1.35
Phase 2	7~11	1.34~1.45	1.10~1.20
Phase 3	11~23	1.25~1.35	1.05~1.15

(Tokach et al. 1994)

for Dutch growing pigs, considering the increasing contribution for maintenance of the sulfur amino acids (SAA) and threonine during the growing period (table 5). For entire males and fast growing females the recommendations are 10% higher in amino acid levels expressed as g/kg diet. Also, Baker (1996, 1997) adjusted his recommendations for SAA and threonine in a similar way by considering the effect of maintenance. According to Lenis et al. (1999), the optimum ratio between essential amino acid N and total N for N utilization was between 0.45 and 0.55, depending on dietary protein level.

Table 4. Recommended ratio (%) of dietary amino acids relative to lysine for SEW and starter pigs

Amino acids	NRC (1998)[a] (3~5 kg)	Tokach et al. (1994) (3~5 kg)	Chung & Baker (1992b) (10 kg)
Lysine	100	100	100
Isoleucine	55	60	60
Methionine	27	27.5	30
Methionine+cystine	57	55	60
Threonine	65	65	65
Tryptophan	18	18	18

[a] Recommendations of NRC (1998) are based on total dietary levels. Recommendation of Chung and Baker (1992b) are based on a true digestibility basis.

The ideal amino acid pattern can be affected by various factors such as stage of growth (Black and Davies, 1991), genotype (Grandhi and Cliplef, 1997), production function of animals (Pettigrew, 1993) and efficiency of utilization of amino acids (Baker, 1993). As mentioned above, the ideal amino acid pattern has been challenged by a better understanding of amino acid nutrition and metabolism as well as research on the factors affecting the amino acid composition of an ideal protein.

With regard to poultry nutrition, it is well known that amino acid requirement of broilers is affected by age, sex, temperature, breed and amino acid balance. The protein and amino acid requirement of broilers suggested by research organizations is presented in table 6. The requirement for protein and amino acids for broilers has been splitted into three growth phases (NRC, 1994) and two growth phases (ARC, 1981 and SCA, 1987). The estimates of NRC (1994) seemed accurate because the nutrient requirements of growing animal especially, protein and amino acid varied sharply as growth advances. The arginine requirement recommended by NRC (1994) is higher and histidine requirement is a little bit lower than that of ARC (1981). Basically, there is no important difference in amino acid requirement for broilers between ARC (1981) and SCA (1987).

In the 1950s, H. M. Scott at Illinois historically began developing a purified crystalline amino acid diet for chicks, culminating in the Dean and Scott (1965) publication that described an efficient chemically defined diet wherein all amino acids were present at levels close to the animal's requirement (table 7). Continued work on the Dean and Scott amino acid profile for chicks resulted in modifications, bringing both amino acids and total nitrogen levels close to the chick's minimal requirement for growth and maintenance (Baker et al., 1979). The modified reference standard (Baker et al., 1979) provides a good starting point for the development of an ideal protein for broiler chickens. In terms of using pig ideal protein amino acid ratios, there are some marked differences between poultry and swine concerning amino acid nutrition. First, arginine is very important because it is not synthesized by poultry. Second, the sulfur amino acid requirement is higher, while the tryptophan requirement is lower for poultry than for pigs. Finally, small quantities of glycine (or serine) and proline are necessary in diets for poultry (Baker et al., 1968; Akrabawi and Kratzer, 1968; Garber and Baker, 1973). Baker and Chung (1992) finalized the minimum dietary requirement for broiler chicks based on the previous stated research results (table 8). Later, Baker and Han (1994) estimated ideal rations of amino acids relative to lysine for growing broilers

Table 5. Recommended concentrations (g/kg) and amino acid ratios (in bold) of apparent ileal digestible amino acids for maximum performance in feeds for growing pigs

Feed for	Net energy (MJ/kg)	Lysine	Methionine+ cystine[1]	Threonine	Tryptophan
piglets (8 to 25 kg)	9.67	10.0 (**100**)	5.9 (**59**)	5.7 (**57**)	1.9 (**19**)
starter pigs (25 to 45 kg)	9.49	9.0 (**100**)	5.3 (**59**)	5.1 (**57**)	1.7 (**19**)
growing pigs (45 to 70 kg)	9.23	7.5 (**100**)	4.5 (**60**)	4.4 (**59**)	1.4 (**19**)
finishing pigs (70 to 110 kg)	9.23	6.2 (**100**)	3.8 (**61**)	3.7 (**60**)	1.2 (**19**)
growing/finishing pigs (45 to 110 kg)	9.23	7.0 (**100**)	4.3 (**61**)	4.2 (**60**)	1.3 (**19**)

[1] Based upon methionine representing 54% of the total content of ileal digestible sulfur containing amino acids; in the finishing feed 50% will be sufficient. (Lenis, 1996)

Table 6. Amino acid requirements of broilers

	NRC			ARC		SCA	
	0~3 wk	4~6 wk	7~8 wk	0~4 wk	5~8 wk	0~4 wk	5~8 wk
ME (kcal/kg)	3,200	3,200	3,200	3,100	3,100	3,000	3,200
CP (%)	23.0	20.0	18.0	18.8	15.6	-	-
Amino acids (%) :							
Arginine	1.44	1.20	1.00	1.03	0.76	1.02	0.94
Glycine+serine	1.50	1.00	0.70	1.40	1.02	-	-
Histidine	0.35	0.30	0.26	0.48	0.36	0.40	0.35
Isoleucine	0.80	0.70	0.60	0.85	0.64	0.57~0.8	0.51
Leucine	1.35	1.18	1.00	1.47	1.07	0.16~1.94	1.22
Lysine	1.20	1.00	0.85	1.10	0.80	1.13	0.90
Methionine+cystine	0.93	0.72	0.60	0.92	0.67	0.85	0.59
Methionine	0.50	0.38	0.32	0.48	0.36	0.45	0.35
Phenylalanine+tyrosine	1.34	1.17	1.00	1.58	1.16	1.36	1.13
Phenylalanine	0.72	0.63	0.54	0.85	0.64	0.79	0.63
Threonine	0.80	0.74	0.68	0.74	0.53	0.68	0.54
Tryptophan	0.23	0.18	0.17	0.21	0.15	0.21	0.17
Valine	0.82	0.72	0.62	0.98	0.71	0.77~1.06	0.73

(NRC, 1994; ARC, 1981; SCA, 1987)

Table 7. Composition (% of diet) of chick amino acid standards developed at the University of Illinois

	Dean Standard[1]	Reference Standard[2]	Modified Reference Standard[3]
Arginine	1.10	1.00	0.95
Histidine	0.30	0.30	0.33
Lysine	1.12	0.95	0.91
Tyrosine	0.63	0.45	0.45
Tryptophan	0.23	0.15	0.15
Phenylalanine	0.68	0.50	0.50
Methionine	0.55	0.35	0.35
Cystine	0.35	0.35	0.35
Threonine	0.65	0.65	0.65
Leucine	1.20	1.20	1.00
Isoleucine	0.80	0.60	0.60
Valine	0.82	0.82	0.69
Glycine	1.60	1.20	0.60
Proline	1.00	0.20	0.40
Glutamic acid	12.00	10.00	12.00
Total amino acid (%)	23.03	18.72	19.93
Total Nitrogen (%)	2.83	2.33	2.37

[1] Dean and Scott (1965). (Baker and Chung, 1992)

[2] Huston and Scott (1968).

[3] Sasse and Baker (1973), with histidine modified slightly in 1979 (Baker et al., 1979).

Table 8. Ideal indispensable amino acid profiles as % of lysine for broiler chicks in two age categories[1]

	Days posthatching	
	0 to 21	21 to 49
Lysine	100	100
Arginine	105	105
Histidine	37	37
Tryptophan	16	17
Isoleucine	67	67
Leucine	111	111
Valine	77	77
Phenylalanine + Tyrosine[2]	105	105
Methionine + Cystine[3]	72	75
Threonine[4]	67	73
Proline	33	20
Glycine (or Serine)	67	50

(Baker and Chung, 1992)

[1] The listed ratios apply to digestible amino acid concentrations.

[2] At least 50% of the aromatic amino acids should be provided as phenylalanine.

[3] Sulfur amino acids were increased slightly in the early growth period compared to that calculated from modified reference standard ratios - to cover sulfur amino acid need for the more rapid feathering strains. At least 50% of the sulfur amino acid should be provided as methionine.

[4] Threonine level was decreased slightly in the early growth period from that calculated from modified reference standard ratios - based upon data of Katz and Baker (1975).

beyond 3 week of age to be 37% for methionine, 38% for cystine, 70% for threonine and 17% for tryptophan. In corn-soybean mixture, the limiting order of amino acids were suggested as 1) Met, 2) Thr, 3) Lys, 4) Val, 5) Arg and 6) Trp (Fernandez et al., 1994). More recently, Emmert and Baker (1997) have obtained evidences that the ratios of sulfur amino acids to lysine does not change in broiler chicks between hatching and 8 weeks posthatching.

The physiological demand by laying hens for particular amounts of individual amino acids is to produce protein for both egg and body tissues. Usually amino acids requirements are best expressed directly in terms of daily intakes of amino acids, generally mg/day rather than as a percentage of the diet (SCA, 1987). NRC (1994) thus has calculated weekly requirements based on body weight and daily feed intake of laying hens. An important difference between NRC, ARC and SCA requirements is that only the NRC requirements are expressed for different ages. As shown in table 9, estimates of SCA (1987) are much higher than other feeding standards, and NRC and ARC show similar requirements in amino acids for layers.

PROTEIN SPARING EFFECT

It is generally admitted that there has been considerable progress over the years in the productivity of animals by continuous genetic improvement and by the advancement of animal nutrition. Improved productivity needs more and more nutrients to sustain the optimum growth of animals. However, a great deal of production costs of animal feeds depends on the prices of protein sources. Therefore, maximizing the efficiency of protein utilization through optimum amino acids balance is very critical. A simple means of improving dietary amino acid balance is to partially replace some of the standard protein sources (e.g., soybean meal) with purified synthetic amino acids. If these diets are properly formulated and produced, they should support at least the same levels of performance as compared to corn-soybean based diets (Tuitoek et al., 1997).

Adding crystalline amino acids to feeds at levels of 0.1 to 0.2% can reduce protein levels by at least 2 percentage units (Han, 1996). This reduction allows excesses of essential amino acids to be minimized corresponding to better essential amino acid balance (Fancher and Jensen, 1989). The protein sparing effects resulting from use of synthetic amino acids have been studied by many researchers. In pigs, the protein sparing effects of synthetic amino acids reported in the literature over the last two decades are summarized in tables 10 and 11. This summary shows that 2 to 4 percentage units of dietary protein can be spared by use of synthetic amino acids with no decrease in weight gain or feed conversion. Lysine, as the first limiting amino acid in corn-soybean meal based diets plays an important role in lean growth of animals.

Bowland (1962) already reported similar performances in pigs fed 13% of crude protein (CP) diet with 0.2% added lysine compared with pigs fed 16% of CP diet. Also, Sharda et al. (1976) showed a 2 percentage units of protein sparing effect when lysine content was adjusted with supplemented synthetic lysine. Han et al. (1978) also suggested that 0.2% of synthetic lysine could spare 2 percentage units of CP without growth depression. Similar trends were observed by Easter and Baker (1980). They noted that synthetic lysine spared 1 to 2 percentage units of protein, without difference in carcass quality among treatments. Chae et al. (1988) reported that

Table 9. Amino acid requirement of layers (mg/day)

	NRC				ARC	SCA
	0~6 wk	6~12 wk	12~18 wk	18 wk~1st egg		
Arginine	486	474	431	536	513	730
Glycine+serine	340	331	302	379	-	-
Histidine	126	126	109	143	174	200
Isoleucine	291	286	257	321	550	660
Leucine	534	486	450	571	681	1,000
Lysine	413	343	289	371	750	710
Methionine+cystine	301	297	270	336	471	540
Methionine	146	143	129	157	350	340
Phenylalanine+tyrosine	340	474	431	536	696	940
Phenylalanine	262	257	231	286	394	510
Threonine	330	326	238	336	360	550
Tryptophan	83	80	71	86	170	140
Valine	301	297	264	329	552	710

(NRC, 1994; ARC, 1981; SCA, 1987)

finishing pigs fed a diet with 2% lower CP levels were not restricted in growth when the lysine level was adjusted to the level of the high CP control diet.

Our research team (Han et al., 1995b) conducted an experiment on the effect of gradual supplementation of 0.1 to 0.4% crystalline lysine in low protein (16% CP) diets on growth performance and nutrient excretion in weaning pigs. Results demonstrated similar growth performance in pigs fed a 16% CP diet supplemented 0.1% of lysine compared to pigs fed a control diet (18% CP). Moreover nutrient excretion was lower in pigs fed the low protein (16% CP) diet with 0.2% of synthetic lysine; nitrogen excretion was reduced by 17.7%.

Coma et al. (1995) conducted an experiment with gradual supplementation of synthetic lysine from 0.15 to 0.45% in corn-soybean meal based diet (14% of CP) in pigs of 25 to 30 kg body weight. They noted that increased levels of lysine improved growth performance by 14.5 to 42.3%, and it reduced nitrogen excretion from 31.8 to 38.5%. Supplements of 0.2% synthetic lysine showed protein sparing effect of 2 percentage units with a improvement of weight gain and feed efficiency in growing (14% CP)-finishing (12% CP) pigs (Williams et al., 1984).

Gatel et al. (1992) showed protein sparing effect of 1.3 percentage units in growing pigs (44 kg of body weight) and 1.1 percentage units in finishing pigs (84 kg of body weight) by supplementation. They suggested that addition of other amino acids (methionine, threonine and tryptophan) together with lysine could result in protein sparing effect of 2.6 percentage units. Jin et al. (1998) reported a protein sparing effect of 3 percentage units using lysine, methionine, threonine and tryptophan in weaning pigs, and the order of limiting amino acids in low protein diet (15% of CP) was lysine, threonine and methionine as the first, second and third, respectively.

It should be noted that there have been different results regarding performance of pigs fed even lower CP diets. Kerr (1993) reported that supplementation of 0.35% of lysine, 0.16% of threonine and 0.07% of tryptophan in diets for growing pigs made it possible to lower the protein level by 4 percentage units without restraining growth performance. They also observed reduced nitrogen and energy excretion by 29.3% and 4.4%, respectively. Canh et al. (1998) studied three diets with different crude protein levels (16.5, 14.5 and 12.5%), but with similar concentrations of net energy and ileal digestible lysine, methionine+cystine, threonine and tryptophan in growing-finishing pigs. No significant effects of reduced protein levels on daily gain, feed intake, feed conversion ratio, or carcass yield were observed. Also Tachibana (1998) found no negative effects of a 4 percentage unit dietary crude protein reduction in the diet of growing pigs. However, Cromwell et al. (1996) showed that pigs can perform optimally at 4 percentage units crude protein reduction with supplementary amino acids, but carcass leanness was reduced. Tuitoek et al. (1997) also found increased fat content in the carcass and reduced ADG and feed efficiency in pigs fed diets

Table 10. Amino acid supplementation of low-protein diets for growing pigs as percent

Weight range (kg)	Control	AA supplement of low protein diet						References
	CP	CP	Lys	Met	Thr	Try	Ile	
5~20	21	17	0.26	0.05	0.04	-	-	Hansen et al. (1993)
7~20	18	15	0.18	-	-	0.05	-	Yen et al. (1982)
8~20	18	14	0.50	-	0.13	-	-	Corley et al. (1983)
10~20	19	12	0.46	0.27	0.47	0.17	0.19	Brudevold et al. (1994)
18~33	16	13	0.17	-	-	-	-	Yen et al. (1982)
18~35	16	12	0.30	0.10	0.10	0.04	-	Rissei et al. (1983)
20~40	16	12	0.30	0.10	0.10	0.04	-	Russell et al. (1986)
23~40	16	11	0.30	-	0.10	0.04	0.07	Russell et al. (1983)
20~50	16	12	0.11	0.07	-	-	-	Hansen et al. (1993)
20~50	16	12	0.30	-	-	0.14	-	Sharda et al. (1976)
20~50	16	14	0.14	-	-	-	-	Sharda et al. (1976)
20~50	16	12	0.25	-	-	0.02	-	Corley et al. (1980)
50~90	13	10	0.34	-	-	0.02	-	Corley et al. (1980)
56~93	14	10	0.30	0.10	0.10	0.04	-	Cromwell et al. (1983)
50~99	13	10	0.11	-	-	0.11	-	Sharda et al. (1976)
50~90	13	10	0.25	-	-	0.03	-	Sharda et al. (1976)
10~25	18	16	0.25	-	-	-	-	Chae et al. (1988)
9~25	18	16	0.20	-	-	-	-	Han et al. (1995)
20~55	16	12	0.28	-	0.12	0.05	0.07	Tuitoek et al. (1997)

(Han, 1996)

with protein levles reduced by 4 percentage units even when the low protein diets with synthetic amino acids (lysine, threonine, tryptophan, isoleucine and valine) were fed to meet ideal amino acid ratios. Yu et al. (1991) observed that pigs fed diets reduced by 5 percentage units of crude protein and containing lysine, threonine, tryptophan and methionine would not perform optimally. More recently, Mavromichalis et al. (1998) shows valine to be a key limiting amino acid for 10-20 kg pigs fed a 13.5% CP diet, reduced from 19.2% CP.

In literatures on chickens, by supplementing a 14.4% CP diet fed to female broilers from 36 to 63 days with additional methionine and lysine, Lipstein and Bornstein (1975) observed similar growth and feed efficiency compared to that obtained with a 18.1% CP diet. Results of an additional experiment in the same publication indicated that adding the same two essential amino acids to a 15.5% CP diet demonstrated similar growth performance and feed conversion rate to chicken's receiving a 20.2% CP diet during the 35 to 62-day period. When formulating diets without a CP restriction and with methionine and lysine supplementation, Waldroup et al., (1976) demonstrated that dietary CP could be reduced by approximately 2 percentage units without compromising broiler performance during the finisher period. Hurwitz at al. (1980) reported that from 0 to 8 weeks of age similar

Table 11. Effects of synthetic amino acid supplementation on growth performance, feed conversion and nutrient excretion in pigs compared to control diets

CP level	Added (%)				Weight	ADG	G/F	Excretion (%)*			References
C-L[1] (%)	Lys	Met	Thr	Trp	(kg)	(%)	(%)	DM	N	P	
18~16	0.10	-	-	-	9~25	+2.8	+1.5	-16.7	-10.6	-14.7	Han et al. (1995)[3]
18~16	0.20	-	-	-	9~25	-1.3	+0.0	-22.5	-17.7	-20.9	Han et al. (1995)[3]
18~16	0.40	-	-	-	9~25	+1.5	+1.0	-16.3	-4.0	-15.8	Han et al. (1995)[3]
18~15	0.05	0.025	-	-	9~25	-22.4	-12.7	+1.8	+13.7	-4.5	Han et al. (1995)[3]
18~15	0.10	0.050	-	-	9~25	-19.8	-8.7	-2.9	+11.6	-9.7	Han et al. (1995)[3]
18~15	0.20	0.100	-	-	9~25	-12.0	-7.9	+3.1	+2.7	-7.4	Han et al. (1995)[3]
16~14	0.05	-	-	-	20~35	-4.2	+0.4	-	-	-	Chae et al. (1988)[3]
16~14	0.05	-	-	-	35~60	-0.3	+1.1	-	-	-	Chae et al. (1988)[3]
14~14	0.15	-	-	-	25~30	+14.5	-	-	-33.7	-	Coma et al. (1995)[3]
14~14	0.30	-	-	-	25~30	+36.0	-	-	-31.7	-	Coma et al. (1995)[3]
14~14	0.45	-	-	-	25~30	+42.3	-	-	-38.5	-	Coma et al. (1995)[3]
14~12	0.10	-	-	-	34~103	+8.5	+12.3	-	-	-	Williams et al. (1984)[3]
14~12	0.20	-	-	-	34~103	+13.3	+16.8	-	-	-	Williams et al. (1984)[3]
14~12	0.30	-	-	-	34~103	+15.0	+17.6	-	-	-	Williams et al. (1984)[3]
14~12	0.40	-	-	-	34~103	+13.1	+17.2	-	-	-	Williams et al. (1984)[3]
14.5~11.0	0.15	-	-	-	50~90	+5.9	+5.3	-	-	-	Hahn et al. (1995)[3]
14.5~11.0	0.225	-	-	-	50~90	-1.8	+5.0	-	-	-	Hahn et al. (1995)[3]
14.5~11.0	0.30	-	-	-	50~90	-1.8	+4.3	-	-	-	Hahn et al. (1995)[3]
13.5~10.0	0.15	-	-	-	90~110	+9.9	+2.9	-	-	-	Hahn et al. (1995)[3]
13.5~10.0	0.22	-	-	-	90~110	+2.9	+2.2	-	-	-	Hahn et al. (1995)[3]
13.5~10.0	0.30	-	-	-	90~110	+3.9	+1.8	-	-	-	Hahn et al. (1995)[3]
16.9~15.6	0.24	-	-	-	44.2	-	-	-	-13.9	-	Gatel et al. (1992)[4]
14.6~13.5	0.22	-	-	-	84.1	-	-	-	-19.3	-	Gatel et al. (1992)[4]
16~12	0.34	-	0.16	0.07	22.3	-3.6	-4.0	-4.4[2]	-29.3	-	Kerr et al. (1995)[4]
18~15	0.28	-	-	-	14~26	-8.7	-7.1	-0.1	-6.7	+1.6	Jin et al. (1998)[3]
18~15	0.28	0.04	-	-	14~26	-7.1	-6.2	-1.1	-7.6	-0.6	Jin et al. (1998)[3]
18~15	0.28	-	0.12	-	14~26	-3.5	-3.5	-4.7	-11.0	-1.4	Jin et al. (1998)[3]
18~15	0.28	0.04	0.12	-	14~26	+0.2	-1.0	-7.3	-17.2	-0.6	Jin et al. (1998)[3]
18~15	0.28	0.04	0.12	0.02	14~26	+0.6	-1.0	-7.9	17.7	-0.6	Jin et al. (1998)[3]

* Compared to control treatment. (Han, 1996)

1 Control high protein diet-low protein diet.

2 Energy excretion.

3 Corn-soybean meal based diets.

4 Wheat-barley-soybean meal based diets.

growth but not equal feed efficiency were achieved with diets containing approximately 3 percentage units less CP than those based on suggested requirements by the National Research Council (NRC, 1971). Also, Uzu (1983) supplemented a 16% CP diet for broilers from 28 to 49 days of age with additional methionine and lysine and observed equal growth, but not feed efficiency, compared to results obtained by feeding a 20% CP diet. A following report noted that adding methionine and lysine to a 16.5% CP diet produced from 18 to 49-day similar body weight gain and feed efficiency to that observed with a 19.5% CP diet (Uzu, 1986).

Research at Seoul National University showed a protein sparing effect by using synthetic amino acids in broiler diet (Heo et al., 1995). In this experiment a reducing of 2 percentage units of crude protein but an addition of 0.1% of extra lysine has not been followed by a reduction in performance of broilers. Cho et al. (1996) reduced crude protein in the diet by 3 percentage units but lysine and methionine, threonine and tryptophan were added to set the same level as that of control diet. There were no significant differences among treatments in growth performance, and the efficiency of lysine and methionine were improved. This was caused by the high digestibility of the supplemented synthetic amino acids. When 0.07% of lysine was added to the diets of layers, egg mass and the efficiency of egg production were not affected by a lowering in the protein level by 2 percentage units (Kim and Han, 1996). Further effects of synthetic amino acids in broilers will be stated in the later part of this review.

DEVELOPMENT OF LOW-POLLUTION DIETS

In the past, the aim of feeding program and diet formulations were maximizing production performance without special concern for nutrient oversupply. However, with the increased public concerns on environment, animal production has to minimize excessive nitrogen and phosphorus output in animal excreta. Therefore, animal nutrition has recently focused on not only improving of animal productivity, but also developing low-pollution diets.

Nitrogen and phosphorus are the most important contributors to pollution from animal manure, and consequently it is important to maximize their efficiency. Excretion of N and P in swine and poultry manure can be substantially reduced by several nutritional strategies. One of the most effective ways to reduce pollutants from animal manure is to use synthetic amino acids in feed manufacturing. Because of the cost, most amino acids except lysine and methionine have been mainly used in research experiments or medical purposes. However, recent environmental concerns have forced the introduction of other amino acids in feed manufacturing.

Basically the concept of low-pollution diet originated from the protein sparing effect. An excess of dietary protein or deficiency in calories from carbohydrates and/or fat will cause a proportion of proteins to be used for energy. In either case, protein will be broken down and carbon used for energy, thus nitrogen will be excreted as urea in mammals or as uric acid in poultry. Protein and other dietary nitrogenous materials that resist or escape digestion in the intestinal tract are excreted in faeces. A large part of the nitrogen losses are associated with inefficiencies of digestion and absorption but more generally in protein synthesis after absorption, so the excretion of nitrogen in faeces and urine may be influenced by dietary manipulation. Providing diets with highly digestible amino acids such as synthetic amino acids may improve absorption and protein synthesis. This will reduce the amount of nitrogen in the diet, which will in turn reduce nitrogen excretion.

In table 12 potential reduction of N excretion as well as cost factor associated with the use of synthetic amino acids are presented when diets that differ in protein levels but balanced for amino acids using synthetic amino acids are fed. When some of the soybean meal is replaced with lysine · HCl, both feed cost and N excretion are reduced. But there may be a limited economical feasibility of using various amino acids to reduce dietary protein levels. The potential of the use of synthetic amino acids is likely to be closely related to prices of the soybean meal and synthetic amino acids.

Nitrogen excretion can be substantially lowered by reducing the protein level by more than 2 percentage units. Feeds must be supplemented with lysine, methionine and, in most case, also with threonine and tryptophan. Lenis (1989) and Schutte et al. (1990) reported that lowering dietary crude protein level for growing-finishing pigs by 2 percentage units reduced N excretion by approximately 20%.

In a review of literature, Lenis and Jongbloed (1999) concluded that even larger reductions in dietary protein level are possible if appropriate levels of amino acids are supplemented to low protein diets. Gatel et al. (1992) reported that in nitrogen balance trial, finishing pigs (57 kg of body weight) fed diets of 2.6 percentage units lower CP with adequate supplementation by four amino acids (lysine, methionine, threonine and tryptophan) and showed a decrease of 31.5% of total nitrogen excretion. Oldenberg and Heinrichs (1996) reported that there was no negative effect on performance and carcass leanness of reducing dietary protein levels from 17 to

13.5% between 50 and 110 kg live weight, and N excretion was reduced significantly by lowering protein levels in the diet.

Table 12. The estimated reduction in N excretion and the estimated cost of diets with varying protein levels but balanced for amino acids using synthetic amino acids

	Corn-SBM-pmx.	+Lysine	+Lysine +threonine +tryptophan
Ingredient composition (%)			
Corn	75.85	79.38	83.28
Soybean meal	21.15	17.50	13.40
Premix	3.00	3.00	3.00
Lysine · HCl	-	0.12	0.25
Threonine	-	-	0.06
Tryptophan	-	-	0.02
Calculated content (%)			
Total crude protein	16.5	15.2	13.7
Digestible lysine	0.70	0.70	0.70
Digestible threonine	0.46	0.42	0.42
Digestible tryptophan	0.14	0.12	0.12
Digestible methionine	0.24	0.22	0.21
Digestible Met+Cys	0.47	0.44	0.41
Ingredient cost ($/ton)	220.6	218.7	239.1
Reduction in N excretion (%)*		-11	-24

de Lange (1997)

* % reduction as compared to feeding the corn-SBM-premix diet without any added synthetic amio acids.

Jin et al. (1998) investigated the effects of synthetic amino acids on nutrient digestibility and excretion in weaning pigs. They reported that the addition of amino acids (lysine, methionine, threonine and tryptophan) to the low protein diet (15% CP) did not impair weight gain and feed conversion ratio. Meanwhile nutrient excretion was significantly reduced.

In addition, more recently, Lenis and Jongbloed (1999) reported that reducing dietary crude protein levels with the supplementation of amino acids can reduce N excretion as well as manure volume. Because reduced dietary protein levels usually involves a reduction of the dietary level of soybean meal in the diets, and because soybean meal contains approximately 2.0 to 2.2% potassium, this will result in a significant decrease of the dietary potassium level and consequently in a lower potassium excretion. The lower dietary levels of protein and potassium may also lower water intake when available *ad libitum* to the pigs, which will reduce manure volume. Kay and Lee (1997) found an 11% decrease in slurry volume for each percent unit in reduction of dietary crude protein level.

In poultry, the effects of synthetic amino acids on growth performance and reduction of nutrient excretion was presented in table 13. The dietary essential amino acid and dietary protein levels are important to broiler performance during the growth phase (3 to 6 weeks of age) with subsequent influence on nitrogen retention. By feeding adequate and balanced levels of essential amino acids, nitrogen output expressed as grams per bird per day can be reduced (Han, 1996). Heo et al. (1995) reported that growth performance of broiler was

Table 13. Effects of synthetic amino acid supplementation on growth performance and nutrients excretion in broiler chicks and layer hens compared to control diets

CP level C-L[1] (%)	Added (%) Lys	Met	Thr	Trp	Age (week)	ADG (%)	Gain/ Feed (%)	Excretion (%) DM	N	P	References
23~21	0.20	-	-	-	0-3	+0.9	+3.0	-7.9	-10.0	-	Heo et al. (1995)[4]
21~19	0.20	-	-	-	4-6	-0.4	-1.0	-5.0	-18.5	-	Heo et al. (1995)[4]
23~20	0.10	0.100	0.1	0.1	0-3	+1.6	+2.1	-18.4	-28.4	-8.9	Cho et al. (1996)[4]
20~17	0.10	0.100	0.1	0.1	4-6	+15.6	+0.4	-18.4	-40.0	-24.7	Cho et al. (1996)[4]
22~20	0.10	-	-	-	0-6	-0.9	-2.4	-	-	-	Han et al. (1978)[4]
22~20	0.20	-	-	-	0-6	-3.3	-0.0	-	-	-	Han et al. (1978)[4]
16~14	0.07	-	-	-	37-43	-2.3[2]	-1.8[3]	-13.5	-13.6	-	Kim et al. (1996)[4]
23~20	0.05	0.29	-	-	1-3	+4.0	+2.8	-	-	-	Parr and Summers (1991)[4]
22~18	0.03	0.13	-	-	4-6	-2.3	-1.3	-	-	-	Fancher and Jensen (1989)[4]
23~21	-	0.22	-	-	0-3	-2.1	-1.5	-	-	-	Summers et al. (1992)[4]
24~20	0.28	0.30	-	-	0-4	-0.5	+2.6	-	-	-	Summers and Leeson (1992)[4]
23~19	0.27	0.12	0.16	-	1-3	0.0	-1.02	-	-	-	Han et al. (1992)[5]

(Han, 1996)

[1] Control high protein diet - Low protein diet.
[2] Eggs mass (g/hen/d).
[3] Egg mass/feed intake (g/hen/d).
[4] Corn-soybean meal based diets.
[5] 0.31% Arg, 0.22% Val was additionally supplemented.

not affected by the crude protein level when lysine and methionine were added. It was shown that 0.1% of lysine supplementation could lower a dietary protein level by 2 percentage units. Furthermore, dry matter and nitrogen excretion were decreased by 4.3 and 15.4%, respectively in starter period from 0 to 3 weeks, and 3.9 and 18.5% in finishing period from 3 to 6 weeks, respectively. Increased levels of supplementary lysine and methionine could reduce the crude protein level in the diet by 3 percentage units during the starter period. However, during the grower period, growth performances was impaired by the decreased crude protein level, resulting probably from the imbalance of other amino acids in the previous period.

According to Cho et al. (1998) there was a possibility of decreasing 3 percentage units of crude protein by the supplementation of lysine, methionine, threonine and tryptophan in the diets of broilers. The supplementation by 0.1% of each amino acids could reduce the dietary protein by 3 percentage units as well as nitrogen and dry matter excretion. By supplementing with the four amino acids mentioned earlier, weight gain and feed efficiency were improved by 1.6 and 15.6%, respectively in starter period (0 to 3 weeks), and by 2.1 and 0.4%, respectively in grower period (3 to 6 weeks). Dry matter and nitrogen excretion were reduced by 18.4 and 28.4% respectively, in starter period (0 to 3 weeks) and by 18.4 and 40.0% in grower period (3 to 6 weeks), respectively. In this study, threonine was the third limiting amino acid in a corn-soybean meal based diet, and threonine supply is required to maintain growth performance of broilers when dietary protein level was reduced by 3 percentage units compared to control diet. Fancher and Jensen (1989) observed similar growth performance of broiler chicks fed either 22% CP diet or 18% CP diet with a 0.03% lysine and 0.13% methionine supplement. Summers et al. (1992) found that methionine supplementation only might be able to spare dietary protein level by 2 percentage units in broiler diets. Summers and Leeson (1992) even indicated that with supplementation of lysine and methionine, crude protein level could be reduced by 4 percentage unit.

In one layer study, Kim et al. (1997) stated that 0.07% of lysine supplement could lower the crude protein level by 2 percentage units without any depression in egg production. Furthermore dry matter and nitrogen excretion were decreased by 13.5 and 13.6%, respectively.

THE INTERACTION BETWEEN IMMUNE SYSTEM AND AMINO ACID NUTRITION

With the fact that the detrimental effect of disease and immunological stress on growth rate and efficiency of gain in food animals is of considerable economic importance, recent nutritional experiments have been focused on improving productivity and health status at the same time. However, data showing an interaction between immune system and amino acid nutrition in pigs and chickens are very scarce, although recently some interesting results were presented (Williams et al., 1997a, b; Stahly, 1996).

It is well known that immunoglobulins are proteins that function to inactivate or destroy antigens in the body. These immunoproteins mainly consist of threonine, leucine and valine (Beacom and Bowland, 1951). Table 14 illustrates the composition of selected amino acids in colostrum and milk immunoproteins (Bowland, 1966). Threonine represents the largest proportion of immunogloblins from colostrum and milk and is essential for the synthesis of immunoproteins. Because immunoproteins are extracted from the blood stream by the mammary gland during late gestation, pregnant sows fed threonine-deficient diets may be unable to produce adequate levels of immunoproteins in blood. This inadequacy may be restored by supplementing diets with crystalline threonine (Cuaron et al., 1984). It seems logical that maintaining adequate levels of immunoproteins in the blood circulation and in the mammary gland before farrowing, during parturition and the subsequent lactation will ensure piglets to receive adequate levels of immunoproteins from colostrum and milk in order to maintain their health and intestinal integrity. Likewise, it is critically important for lactating sows to consume adequate levels of threonine and other amino acids in order to maximize milk production to support maximal growth of piglets before weaning (Chung, 1997). As a part of the structure of mucus glycoproteins, thereonine also contributes to one of the most extensive and important innate defense barriers against bacterial and viral invasion (Reeds and Hutchens, 1994). As these proteins are continually secreted from the external surfaces of the intestine and lung, their continual synthesis persistently drains an individual's threonine supplies.

Besides theonine, it is also established that there are important interactions between some specific amino acids (arginine and glutamine) and immune function. Recent study indicates a specific role of arginine in the regulation of imflammation (and perhaps immune function) because nitric oxide production from arginine plays an important role in macrophage cytotoxic functions and in the interactions between macrophagses and lymphocyte adhesion and activation (Kirk and Barbul, 1990).

Glutamine is an abundant free amino acid in the plasma of animals (Wu et al., 1994) and in sow's milk (Wu and Knabe, 1994). Glutamine is also a major fuel for rapidly dividing cells, including activated lymphocytes, for maintenance of gut associated lymphatic tissues and production of secretory immunoglobulin A and intestinal integrity (Alverdy, 1990). Recently, Wu et al. (1996) reported that glutamine supplementation (1.0%) increased prevented jejunal atrophy as indicated by villus height during the first week postweaning and increased the gain:feed ratio by 25% during the second week postweaning.

Table 14. Amino acid composition of immunoproteins from colostrum and milk

Amino acid	Immunoprotein (%)	
	Colostrum	Milk
Threonine	10.3	10.6
Lysine	6.2	6.3
Arginine	5.1	4.8
Cystine	3.1	3.2
Isoleucine	3.1	3.0
Histidine	1.8	1.9
Methionine	1.1	0.9

(Bowland, 1966)

Nutrient requirements of pigs are dependent on the type and rate of metabolic processes that occur in the body. These processes are regulated by the genetic contribution of the pig and environmental factors to which the animal is exposed. Factors that stimulate the immune system result in metabolic processes which reduce feed intake and tissue growth, particularly protein-rich tissues. Exposure of animals to pathogenic (i.e., endotoxin) antigens results in cytokine release (Klasing, 1988). Cytokines such as interleukin-1 (IL-1) and tumor necrosis factor (TNF) activate the immune system (Dinarello, 1984) and interfere with N metabolism and alter metabolic process in animals (Klasing, 1988). Metabolically, cytokine (IL-1, TNF) administration induces anorexia (Mrosovsky et al., 1989), depresses protein synthesis (Jepson et al., 1986), and stimulates protein degradation (Klasing et al., 1987) in skeletal muscle. Similarly, acute activation of the immune system via administration of nonpathogenic antigens results in lower voluntary feed intake, body growth rate, and efficiency of feed utilization in chicks (Klasing et al., 1987; Klasing and Barnes 1988) and pigs (van Heugten et al., 1994; Webel et al., 1997). The immunogen administration triggered the release of TNF, IL-6 and cortisol which have been shown to induce protein and lipid degradation in many species (Webel et al., 1997). Webel et al. (1997) also suggested that cytokines might have a direct role in inducing muscle protein catabolism.

Because immune system activation changes metabolic processes within the body, nutrients are deviated from the growth process and toward support of immune system function (Beisel, 1977). Amino acids liberated from muscle breakdown (Klasing and Austic, 1984a,b) can be utilized for the synthesis of acute phase proteins in the liver and used as an energy source (Wannemacher, 1977). These changes in metabolism suggest altered nutritional requirements during immunologic challenge. Webel et al. (1998) studied the lysine requirement of chicks challenged by immunogen administration and found that the dietary lysine concentration required to maximize protein accretion was not affected by immune challenge due to the reduced feed intake, but the absolute lysine intake required to maximize growth performance was lower in an immune challenged chicks. However, little information are available on the interaction between immune system activation and nutrient requirements. Therefore, nutrient requirement recommendations have been determined without consideration to level of immune system activation.

In chickens, the influence of the metabolic changes on particular amino acid requirements, e.g., SAA and lysine, under stressful conditions has been partially characterized. SAA might be required in increased amounts for the synthesis of acute phase proteins which are concerned with defence mechanisms against tissue damage and infections (Grimble, 1992).

Klasing and Barnes (1988) observed a lower requirement for lysine and methionine in immunologically stressed chick, probably due to a much lower growth rate in the challenged chicks. However, van Heugten et al. (1994) reported that there was no differences in protein requirements for growth and efficiency of feed utilization between immunologically challenged and control pigs either during or after immunologic challenge.

Stahly (1996), in his review of the impact of immune system activation on nutrients needs suggested that because the amino acids make up of proteins in tissues differ from those associated with maintenance function, dietary amino acid needs are not equally altered when the animal's immune status is shifted. For example, lysine represents a major component of body tissue proteins (65 to 70 g/kg) but a relatively small component of the proteins (24 g/kg) associated with maintenance functions (Fuller et al., 1989; Wang and Fuller, 1989). In contrast, sulfur amino acids represent a small portion of tissue proteins (16 g/kg) and a large proportion of proteins (49 g/kg) associated with maintenance functions. Thus, factors that increase tissue growth relative to maintenance needs in pigs would raise the animal's dietary lysine and methionine needs, but the magnitude of the change would be greater for lysine (table 15). The observation that the optimum ratio of digestible SAA to digestible lysine in pigs is less in animals experiencing a low versus high level of immune system activation supports the previous hypothesis.

Table 15. Impact of level of chronic immune system (IS) activation on dietary digestible lysine (L) and sulphur amino acid (SAA) needs of pigs[a]

Pig weight (kg)	IS Activation	Amino acid need, g/kg diet[b]		Ideal SAA:L[c]
		L	SAA	
9	Low	13.4	6.4	0.48
	High	10.7	5.9	0.55
14	Low	12.2	6.2	0.51
	High	9.9	5.9	0.58

[a] Adapted from Williams and Stahly (1995).
[b] Digestible amino acid needs determined from break point analysis of gain:feed data.
[c] Ideal ratio of amino acids based on the dietary concentrations of digestible L and SAA required to optimize gain:feed ratio.

Table 16. Amino acid composition (expressed as % of lysine) of acute-phase and skeletal muscle protein

Amino acids	C-reactive	fibrinogen	α 1-acid glycoprotein	skeletal muscle
Lysine	100	100	100	100
Threonine	82	78	99	48
Tryptophan	59	46	40	13
Methionine	23	42	15	26
Cysteine	18	19	24	13
Isoleucine	76	42	64	49
Valine	108	62	61	55
Leucine	128	81	135	83
Phenylalanine	148	60	85	41
Tyrosine	70	73	99	37
Histidine	23	35	23	52
Arginine	51	109	69	70

(Reeds et al., 1994)

The amino acid composition of muscle protein and acute phase protein is shown in table 16. Recently, Williams et al. (1997a, b) reported that low immune activated pigs with greater body nitrogen accretion capacity required higher dietary lysine concentrations and daily lysine intakes than high immune activated pigs in order to express this elevated capacity for protein tissue growth. Williams et al. (1997c) also reported that alterations in the distribution of accrued protein in body tissues were observed between low and high immune activation pigs. This may suggest that the ideal ratio of amino acids to lysine may be affected as there are differences in patterns of amino acid among body tissue as well as those associated with maintenance functions like the synthesis of acute phase protein (Reeds at al., 1994).

TRENDS IN AMINO ACID MARKET

Nowadays, synthetic amino acids are commonly added to swine and chicken diets to reduce feed costs and improve amino acid ratios and potentially reduce environmental pollutants, especially nitrogen. L-lysine · HCl is the most commonly used, and DL-methionine is used in SAA deficient diets. Recently, synthetic L-threonine and L-tryptophan have become commercially available due to the advanced technology, which reduced the production cost. The use of these synthetic amino acids leads to additional benefits such as follow:

① Reduce production cost by reducing basic protein source in animal feed
② Improve digestibility
③ Reduce nitrogen excretion
④ Meet animal requirements accurately

The production of methionine and its increase to the year of 2,000 was presented in table 17. World market for methionine grew at a rate of 6% during the late 1990s. It is expected that the production of methionine will be 580,000 MT. In 1998 the price has been largely reduced to 2,300 $/MT due to temporary economic crisis all around world, compared with 3,300 $/MT in the previous years. However, it is thought that the price will be stable at 2,700 $/MT in the year 2,000.

The production of lysine and its increase to the year of 2,000 was presented in table 18. The production of lysine has been increasing by 11% of annual growth on average. If 146,000 MT were produced in 1990 it is expected to be 415,000 MT in the year 2,000. The increasing feed grain price and particularly that of soybean meals may stimulate the

Table 17. Methionine production and its annual growth in the world (Unit : 1,000 MT*, million $)

		1996	1997	1998	2000	Annual growth (%)
Production	Quantity[a]	478	478	523	580	6
	Amount of money	1,577	1,581	1,202	1,566	-0.2
Price ($/MT)		3,300	3,300	2,300	2,700	-

* MT : is metric tons; [a] Methionine hydroxy analogue (MHA) production is included.

Table 18. Lysine production and its annual growth in the world (Unit : 1,000 MT*, million $)

		1990	1992	1995	1997	2000	Annual growth (%)
Production	Quantity	146	218	276	326	415	11
	Amount of money	336	480	635	815	1,080	12
Price ($/MT)		2,300	2,200	2,300	2,500	2,600	-

* MT : is metric tons.

Table 19. Threonine production and its annual growth in the world (Unit : MT*, million $)

		1990	1992	1995	1997	2000	Annual growth (%)
Production	Quantity	1,500	3,000	5,000	7,200	12,000	23
	Amount of money	17	30	33	36	60	13
Price ($/kg)		11.5	10	6.5	5	5	-

* MT : is metric tons.

use of synthetic amino acids in animal feed. Furthermore, World Trade Organization (WTO) system may hasten this trend a large extent in the near future.

Most of amount was produced by Ajinomoto Co. and ADM Co. Some of these companies have planned to increase their production capability in the near future to face an increasing demand. Also these companies are producing other amino acids (threonine, tryptophan) in cooperation with other companies.

Recently the attention has been focused on threonine by the researcher of swine industry, because it is regarded as a second limiting amino acid in corn-soybean based diet but more clearly in corn-leguminous feeds diets. As the importance of immune system is highlighted with some new technologies in swine industry such as SEW, more attention will be paid to threonine, a key component of immunoprotein. As shown in table 18, threonine production is increasing at 23% of annual rate because of a low price. In 1995 the price has been reduced to 6,500 $/MT, and it is thought to go down to 5,000 $/MT in the year 2,000, boosting again its use in monogastric feeds formulas.

CONCLUSION

Advances made in fermentation technology in manufacturing of synthetic amino acids provides commercial availability of crystalline amino acids at reasonable prices for use in swine and poultry diets. These synthetic amino acids have brought about many changes in animal nutrition as well as the animal feed industry. Researchers began the use of synthetic amino acids to investigate the requirement of animals with purified diet and developed ideal amino acid profiles which fit more accurately requirements of individual amino acids and their optimum ratios in protein supplying to animals. Also, extensive research conducted with synthetic amino acids have shown the beneficial effects of synthetic amino acid supplementation on animal production and on the reduction of environmental pollutants.

Concerning the nutritional and environmental aspects, small amounts of synthetic amino acids (0.1 to 0.3%) could spare dietary protein by 2 to 3 percentage units as well as increase their digestibility and absorption in animals. Thus, improving the dietary amino acid profile in the diet via use of crystalline amino acids may result in an additional reduction of the nutrient excretion, especially nitrogen. The value of synthetic amino acids is largely determined by their costs relative to the cost of conventional protein sources, especially soybean meal. The use of synthetic amino acid in monogastric animal diets will be necessary to meet the strong demand for environmental protection endangered by animal production.

With the detrimental effect of immunological stress on animal productivity, research pertaining to the interaction between immune system and amino acid nutrition have been recently activated, but little information is still currently available. Threonine is one of the essential amino acids required for the synthesis of immunoproteins. Therefore, it is critically important particularly for lactating sows to consume adequate levels of threonine and other amino acids in their diets in order to ensure that piglets receive adequate levels of immunoproteins from colostrum and milk. Changes in metabolism resulted from immunological stress may affect nutrient requirements during immunologic challenge. Therefore, additional research on nutrient requirement recommendations based on immune system activation are required.

With the current cost of synthetic amino acids, it is still difficult to commonly use other crystalline amino acids such as L-threonine and L-tryprophan in practical diet for animals. However, this will change as the availability and price of these amino acids improves followed continuously growing global amino acids market. Also, synthetic amino acids will play an important role in animal nutrition in the future, saving proteins and limiting the risks of nitrogen pollution associated with the spreading of animal manures.

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